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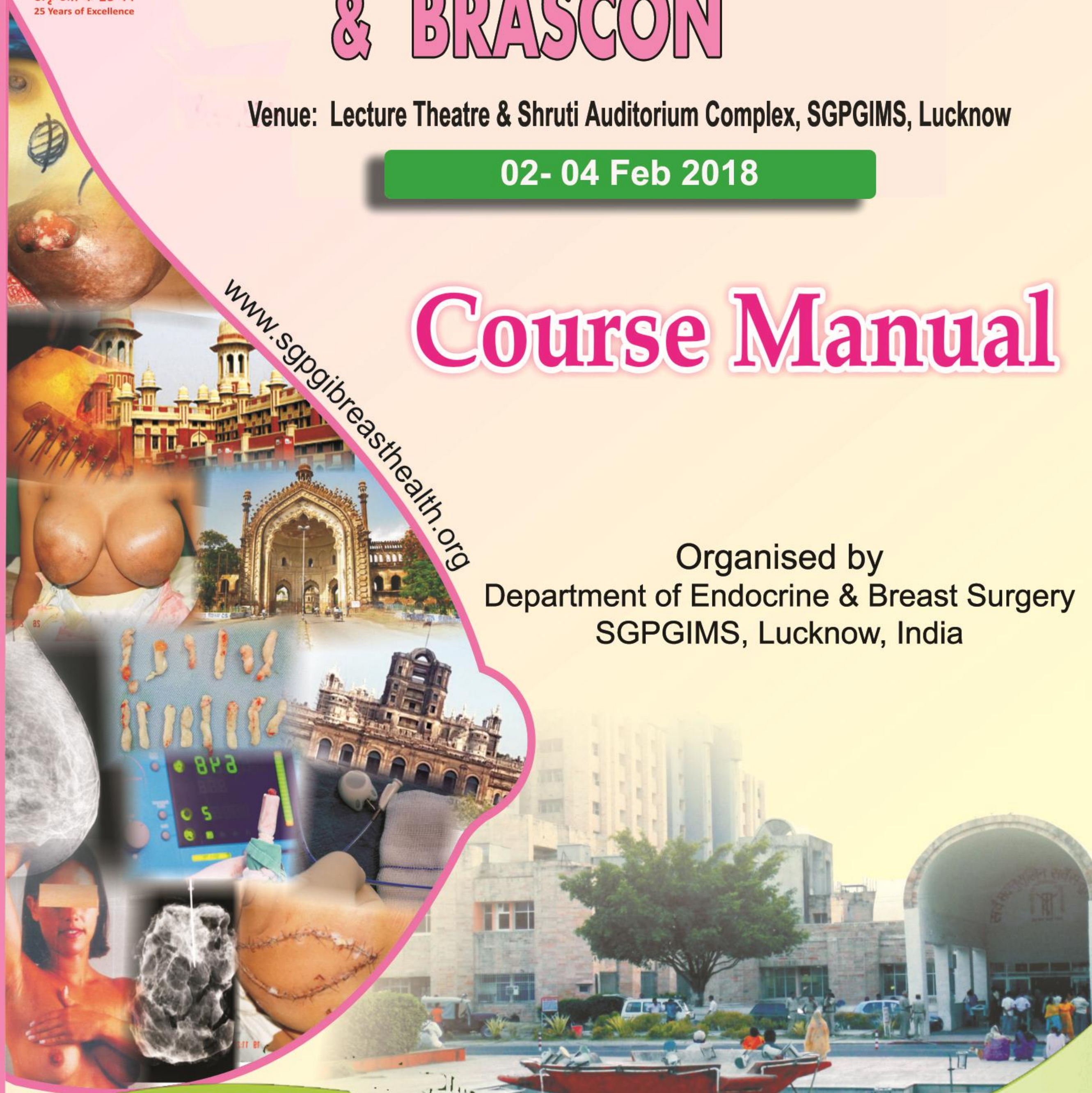
आत्मना सर्गो जितः
उत्कृष्टता के 25 वर्ष
25 Years of Excellence

SGPGI Breast Course 2018 & BRASCON

SGPGI BREAST HEALTH PROGRAM
Saving Lives & Breasts

Venue: Lecture Theatre & Shruti Auditorium Complex, SGPGIMS, Lucknow

02- 04 Feb 2018



Course Manual

Organised by
Department of Endocrine & Breast Surgery
SGPGIMS, Lucknow, India

SGPGIMS, Lucknow	SGPGI Breast Health Program	Breast Surgery International	BRASCON	UP Chapter of ASI
www.sgpgi.ac.in	www.sgpgibreasthealth.org	www.bsisurgery.org		www.upchapterasi.com

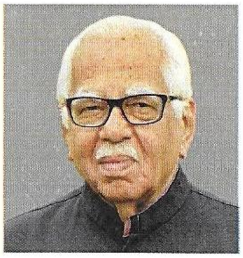
www.sgpgibreasthealth.org

SGPGI Breast Course 2018 & BRASCON 2018

Department of Endocrine Surgery & Breast Surgery
Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow
2nd – 4th Feb 2018

Course Manual Contents

Ram Naik
Governor, Uttar Pradesh



सत्यमेव जयते

Raj Bhavan
Lucknow - 226 027

17 January, 2018

Message

I am indeed happy to learn that the Department of Endocrine and Breast Surgery, Sanjay Gandhi Post Graduate Institute of Medical Science, Lucknow is organizing 'SGPGI Breast Course 2018' from 2nd to 4th February, 2018.

Majority of breast cancer in India is managed at relatively advanced stage. Social and cultural inhibitions prevalent in the Indian society prevent women from seeking appropriate and timely advice and treatment to compound this problem. I am sure that the efforts towards creating awareness about early detection and appropriate treatment of breast cancer will benefit women.

I extend my best wishes on the occasion.

(Ram Naik)

Telephone : 0522-2236497 Fax : 0522-2239488 Email : hgovup@nic.in Website : www.upgovernor.gov.in

No – O – /CM–1/2018

Yogi Adityanath

CHIEF MINISTER
UTTAR PRADESH

Dated :

Message

I am happy to know that the Department of Endocrine and Breast Surgery, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow is organizing 'SGPGI Breast Course 2018' from 2nd to 4th February, 2018.

Cancer is considered as one of the most dreaded diseases. Early stage cancers are a lot easier to treat. Raising awareness for prevention as well as early treatment of the disease plays a crucial role in mankind's fight against cancer.

It is commendable that this course is targeted largely to young and practicing surgeons, surgical and radiation oncologists, general surgical trainees and breast surgeons. I understand that the course faculty would include eminent experts and medical specialists. I hope that during the event participants would discuss and share the latest trends in providing effective health care.

My best wishes for the entire endeavour.

(Yogi Adityanath)

Rajive Kumar
I.A.S.

Lal Bahadur Shastri Bhawan
Lucknow- 226001
Uttar Pradesh
E-mail : csup@nic.in
Ph.: (0522) 2238212, 2236296 (O)
(0522) 2239461, 2237299 (R)
(0522) 2239283 (FAX)

Dated : January 02, 2018

MESSAGE

It gives me immense pleasure to know that the Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, which is the first Institute to offer M.Ch. in Endocrine Surgery, is organizing "SGPGI Breast Surgery Course" from 02nd-04th February, 2018. This will open up the vistas for World class care, besides offering a very comprehensive breast cancer care program and perhaps the most inclusive endocrine and breast surgical training postgraduate program. The alumni of the department of Endocrine and Breast Surgery have established themselves as leaders in establishing various new departments of Endocrine and Breast surgery at the national level.

I wish the participants and the organizers all the best and hope that the participants shall add a lot to their experience and able to face the challenges of chronic diseases successfully.

(Rajive Kumar)
Chief Secretary, Govt. of U.P. &
President, SGPGIMS

आत्मना संगों जितः

Sanjay Gandhi Postgraduate Institute of Medical Sciences
Raebareli Road, Lucknow-226 014 (U.P.) INDIA

Prof. Rakesh Kapoor
M.S., M.Ch. (Urology), F.A.M.S., F.N.A.Sc.
Director

Message

Its gives me great pleasure to know that the department of endocrine surgery is organizing "SGPGI Breast Course 2018 and BRASCON" on 02-04 Feb 2018. The department of Endocrine Surgery has been regularly organizing the Breast Course as an endeavor to update the knowledge and skill in the field of Breast Surgery. In the capacity of Director of the institute, I feel privilege to write a few words about the department.

Endocrine Surgery is one of the few super specialty department started at SGPGIMS by our great visionary founders. Despite initial spectacles, today this department has developed into full functioning department with six full time faculty members. Breast cancer is the most common cancer amongst Indian women and the leading cause of cancer related deaths. Majority of breast cancers in India are managed at relatively advanced stages and the single most significant reason for this is lack of awareness amongst rural women. The conditions ever since its inception. Breast Health Program, as an area of future development was identified in 1999 and has progressed in both research and patient care.

I am convinced that the department is geared to meet the future demands and challenges of the ever evolving world of knowledge and education apart from skill development. I wish all the success for upcoming "SGPGI Breast Course 2018" and future development of the department.

(Prof. Rakesh Kapoor)
Director

Phone Office : 91-0522-2668112, 2668216; PBX: 2668004-08, 2668716-719; Extn. : 4001, 4129 (Reception)
Fax : 91-0522-2668129, 2668017 & 2668078; Mobile : 8004904798; E-mail : director@sgpgi.ac.in, rkapoor@sgpgi.ac.in

Sanjay Gandhi Post Graduate Institute of Medical Sciences
Raebareli Road, Lucknow-226014 (U.P.) India

Prof. Rajan Saxena
MS, FAMS, FACS
Head, Surgical Gastroenterology & Liver Transplant Unit

Message

Breast Cancer continues to be one of the most important public health challenges in the society. The burden is more in low and middle income countries like India due to lack of awareness among the public and primary care givers. In India the patient usually comes at a late stage of tumor then the western world. In the absence of dedicated trained endocrine and breast surgeons and clinics in our country the only portion left is to educate the post graduates and young practicing surgeons through workshops, seminars and post graduate course. That is what SGPGI Endocrine Surgery department envisages to do.

A high index of suspicion is required to diagnose early Breast cancer. Early diagnosis and treatment is the key to the success in management of these tumours. The management of these tumors requires multi-disciplinary approach. Keeping this in mind, the department of Endocrine Surgery at Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow launched a structures program in this course to cover all aspects of multidisciplinary management.

On behalf of Department, I welcome the entire panel of eminent International and national experts to Lucknow and thank them for joining our endeavor to spread knowledge and educate our postgraduate and delegates from different part of countries.

We sincerely hope, the postgraduate and delegates participating in this event will find it useful to enrich their knowledge about contemporary diagnosis and management of Breast diseases in day to clinical practice and shall pass on the benefit to their patients.

Prof. Rajan Saxena, MS, FAMS, FACS
'Padma Shri' Awardee
Head, Department of Surgical Gastrenterology and Liver Transplant Unit
Sanjay Gandhi Post Graduate Institute of Medical Sciences, Raebareli Road, Lucknow-226014, INDIA

Sanjay Gandhi Postgraduate Institute of Medical Sciences
Raebareli Road, Lucknow-226014 (UP), INDIA

Dr. S.K. Mishra
Professor & Head
Department of Endocrine Surgery &
Nodal Officer, Telemedicine

Phone : +91-0522-2668004-8, Extn. (0) 2376 (R) 2377
Fax : +91-0522-2668777 (0), 2668017, 2668078
E-mail : skmishra@sgpgi.a.c.in, skmishra_1956@yahoo.com

Message

The department of Endocrine & Breast Surgery was established on 7th September 1989 and we have celebrated silver jubilee in 2014. Our department regularly organizes educational event like Course, Seminar and Workshop to update knowledge and skill of young professionals. The relationship of endocrine and breast diseases in known since the ancient medical history. World over endocrine surgeons also take care of breast disease so the department of endocrine surgery at SGPGI also included care of breast disease early in its development and identified it as a thrust area for future development in the year 1999 when we completed first decade of the department. The department is fortunate to get the support from ancillary departments to deliver state-of-the-art clinical care for breast diseases in particular Breast Cancer.

We hope, the participants will find the course beneficial to update their knowledge and skills in the specialty of breast surgery.

(Prof. S.K. Mishra)
HOD, Endocrine Surgery

Department of Endocrine & Breast Surgery
Sanjay Gandhi Post Graduate Institute of Medical Sciences
Raebareli Road, Lucknow-226 014, INDIA
www.sgpgi.ac.in

Dr. Gaurav Agarwal
MS, DNB (Surgery), Post-Doctoral Certificate (Endocrine Surgery), FACS
Certificate of Royal Australasian College of Surgeons (Endocr Surg)
Professor

Convener
SGPGI Breast Health Program
www.sgpgibreasthealth.org

Message

Breast cancers and variety of benign breast diseases affect a huge number of Indian women. Breast cancer is the commonest cancer occurring in Indian women, and is a major health issue currently. Majority of breast cancer patients are treated by surgeons, and oncologists who practice outside of comprehensive cancer centers or institutions. It is vital to have appropriate and cost-effective treatment infrastructure and expertise at even the remote places so that basic safe and effective treatment can be made available to all breast cancer patients. The department of Endocrine & Breast Surgery, SGPGIMS; and the SGPGI Breast Health Program conceived "SGPGI Breast Courses" to be held periodically with the aim of imparting knowledge and training to surgeons and oncologists.

The SGPGI Breast Course 2018 and BRASCON is being organized by the SGPGI Breast Health Program in collaboration with the Breast Surgery International; Society for Breast Reconstructive and Aesthetic Surgery; and the UP Chapter of Association of surgeons of India. It has been our endeavor to make the scientific program of this course comprehensive, addressing most of the contemporary and contentious issues relating breast cancer management. A galaxy of eminent breast surgeons and oncologists- including the overseas faculty from BSI will be serving as the faculty for this course. Besides, faculty from various collaborating departments at SGPGI, notably Radiation oncology, Pathology and Radiology, besides the host departments- Endocrine & Breast surgery, and Plastic & Reconstructive surgery have contributed immensely to this organization and I are thankful to them all from bottom of my heart.

As the course director and organizing chairman, I wish to put on my record my deepest appreciation and gratitude towards the SGPGIMS authorities, the leadership of the BSI, and UPChapter of ASI, my department colleagues and residents, sponsors, and all individuals and organizations who have helped and supported us.

This course manual compiled by Dr Sabaretnam M , along with colleagues in department of Endocrine & Breast Surgery gives the course participants a ready reckoner of the Breast Oncoplasty articles. I hope the readers would find it useful, especially those who have difficulty in accessing medical literature in remote places.

I thank all faculty and participants of the SGPGI Breast course 2018 and BRASCON. Please do send us your valuable feed-back of this course- so that we can further improve our future breast courses. With warm wishes for a productive, pleasant and comfortable stay at SGPGI during the "SGPGI Breast Course-2018" and BRASCON.

Dr. Gaurav Agarwal
Course Director & Organizing Chairman

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E-mail : gaurav@sgpgi.ac.in, gauravbsi@gmail.com, Web Profile : www.sgpgibreasthealth.org/ProfileDrGaurav

Sanjay Gandhi Postgraduate Institute of Medical Sciences,
Raebareli Road, Lucknow, India-226014.

Dr. Mayilvaganan Sabaretnam
M.B.B.S, M.S, M.Ch, FAES, FICS, FAIS
Assistant Professor

Department of Endocrine Surgery
Endocrine & Breast OPD:
Monday & Saturday

Message

On behalf of the organizing committee of the SGPGI Breast Course 2018, I welcome you all. Breast Cancer has emerged as a major health problem over last few years. With increasing incidence of breast cancer and also because of the lack of world class facilities in developing country like India, these kind of courses can be a bridge to practicing surgeons, oncologists, radiation oncologist and pathologists to learn the newest in their field from pioneers. It was with this motto the present course was designed.

This course manual, with help from Mrs.Prabha Gola and Mr. Repu Daman provides some latest guidelines and original articles regarding treatment of breast cancer. As the organizing secretary of this course, I wish to put on record my deepest appreciation and gratitude towards the SGPGIMS authorities, the leadership of BSI, UP Chapter of ASI, my department Faculties, residents, sponsors and persons and organizations, who have helped us and supported us in this task. My sincere thanks to all International faculty, National faculty and Alumni faculty for their time and valuable contributions to this course.

My heartfelt thanks to Prof.Gaurav Agarwal, Organizing Chairman and Nodal Officer, SGPGI Breast Health Program for the trust showed in me to organize this endeavor and for his constant support. There may have been many short comings in the organization of this course and in our hospitality, responsibility for which are entirely mine. Your frank and constructive feedback would help us improve our courses towards creating a better learning experience for all of us.

M. Sabaretnam.

Dr. Sabaretnam M.

About the Department of Endocrine & Breast Surgery, SGPGIMS, Lucknow

About the Department of Endocrine & Breast Surgery, SGPGIMS, Lko

The Department of Endocrine & Breast Surgery at SGPGIMS, Lucknow is a pioneer in the field of clinical practice, training and teaching as well as research in the areas of endocrine and breast surgery in India. It was established in September 1989, and was the first academic department of Endocrine & Breast Surgery in India which offered opportunity for dedicated training in this specialty. The department is credited with starting the first post-doctoral certificate course (PDCC) in Endocrine Surgery in India in 1997, and later was the first one to start a three year MCh Endocrine Surgery course in the year 2004 after due permission from the Medical Council of India. Besides the six faculty members, the department has a sanctioned strength of 4 MCh students per year, and has hospital service senior residents and short term trainees from time to time, besides research staff, technicians, and office staff. Alumni of the department are currently involved in academic or institutional practice of Endocrine & Breast surgery at various parts of the country, and abroad. Most of them are professors, heads, faculty members or senior consultants in various reputed teaching institutions or corporate hospitals in major cities of India.

The department attracts large numbers of referrals from various parts of India, and neighboring countries for complex endocrine and breast surgical problems, and is acknowledged as one of few high-quality centers for complex re-operative thyroid surgery, surgery for primary hyperparathyroidism, pheochromocytoma and other adrenal tumors, multiple endocrine neoplasia syndromes; and sentinel lymph node biopsy, breast conservation and oncoplastic surgical procedures as part of comprehensive multi-modal treatment for early and advanced breast cancers. The department has pioneered minimally invasive endocrine surgical procedures, notably laparoscopic adrenal surgery, minimally invasive parathyroidectomy and video-assisted thoracoscopic (VATS) thymectomy; and sentinel lymph node biopsy and conservation/ oncoplastic breast surgery in the country.

The department faculty members have carried out, and are currently involved with clinical and basic research in fields of endocrine oncology- notably thyroid oncogenesis, parathyroid tumorogenesis, pheochromocytoma etc; breast surgery and oncology- including genetic basis of breast oncogenesis, diabetic foot care and utilization of tele-medicine technology in endocrine surgical teaching, training and research. The department faculty and residents have to their credit large number of scientific publications in reputed indexed international journals. These scientific papers have addressed various contentious issues of endocrine and breast surgery, and some are widely cited in medical literature.

List of PDCC (Endocrine Surgery) recipients

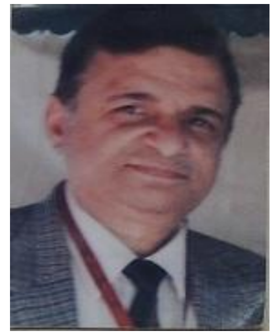
Dr. Gaurav Agarwal	1997
Dr. Anjali Mishra	1997
Dr. Mukta Baxi	1998
Dr. Anand K Mishra	1998
Dr. Dilip K Kar	1999
Dr. Rajiv K Agarwal	1999
Dr. Nikhil Singh	2000
Dr. Sanjay Domnik Fartado	2001
Dr. Manish Kaushal	2001
Dr. Robbie K George	2002
Dr. Raj Sekher Perumalla	2002
Dr. S.G. Mahesh	2003
Dr. K.R. Vasudevan	2004
Dr. Satyajeet Verma	2005

List of MCh (Endocrine Surgery) recipients

Dr Anand Mishra	2006
Dr Nil Kamal Kumar	2007
Dr PV Pradeep	2007
Dr Vivek Aggarwal	2007
Dr PRK Bhargav	2009
Dr Ranjith Sukumar	2009
Dr. Pooja Ramakant	2010
Dr Prateek K Mehrotra	2010
Dr Dhalapathy Sadacharan	2011
Dr Sudhi Agarwal	2011
Dr M Sabaretnum	2012
Dr Deependra N Singh	2012
Dr Ritesh Agrawal	2013
Dr Kulranjan Singh	2013
Dr Geetika Nanda	2013
Dr Sunil MB Barua	2014
Dr Naval Bansal	2015
Dr Chitresh Kumar	2015
Dr. Om Prakash Prajapati	2015
Dr. Roma Pradhan	2015
Dr. Ashwini C	2016
Dr. Navneet Tripathi	2016
Dr. Sendhil Rajan	2016
Dr. Chandan Kumar Jha	2017

Faculty Members

Prof S K Mishra



Prof A K Verma

Prof Amit Agarwal

Prof Gaurav Agarwal

Dr Anjali Mishra

Dr Gyan Chand

Dr Sabaretnam M.

Resident Doctors


Dr. Chaitra


Dr. Kushagra Gaurav


Dr. Aromal Chekavar


Dr. Raouef Ahmad


Dr. Goonj Johri

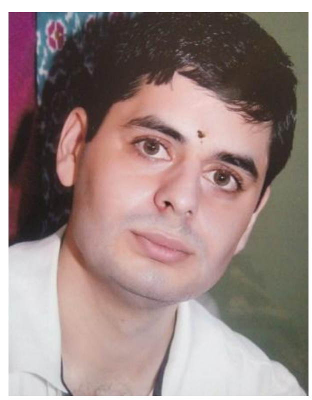

Dr. Sapna Bothre

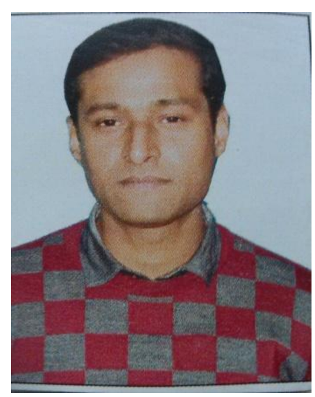

Dr. Mohd. Rashid


Dr. Sanjay


Dr Ramya V C


Dr. Mahalaxmi


Dr. Suneel Mattoo


Dr Nitish Gupta

Office/ Secretarial Support

Mr R A Pal

Mr Siddiqui

Mr Dhan Singh

Mr Mewa Lal

Lab Support

Mr Satish Babu

Mrs Meera Srivastava

OT Staff


Mrs. Scott


Mr Phanish Mani Tripathi


Mrs Ranjana Masse


Mrs Hemlata


Mrs Mohini James


Mrs Liji Joseph


Mr. RijoyJohny


Ms. Sujata Pal


Ms. Madhu Lata


Ms. Deepti Verma


Ms. Amrita Maurya


Mr Ram Avadh


Mr Ram Kumar


Mr. Jitendra

Ward Staff


Mrs Badni R Mehta


Mrs Mamta Khan


Mrs Suchinta Daniel


Mrs Sheela


Mrs Kanti


Mrs Sushila


Mrs Doris Kumar


Mrs Anita Kumari


Mrs Kimberly M Mathai


Mohd Yusuf Khan


Mrs Rina Anand


Mrs Prema Devi

Mrs Hemlata Jayant

Ms. Nancy Arora

Ms. Kavita Anand

Ms. Rinku Yadav

Ms. Anuparna Pal

Mr. Janved Gautam

Mr. Hari Ram

Mohd Irfan

Mr. Puranmashi

Ms. Meera Devi

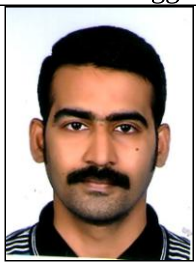
Mr. Vishal

List of Alumni

Sl No.	Name of Alumnus	Year of joining & completion of course and degree/residency	Present affiliation/address	Email/Mobile No.
1.	Dr. Taranpareet Singh	1990 - 1991 / SR		
2.	Dr. Vivek Khandelwal	1991 - 1991 /SR	Gaziabad	
3.	 Dr. Ajay K Sharma	1991 - 1994 / SR	Sub-Dean, Consultant Surgeon in Transplantation and Surgery; Director of Critical Care Course (CCRISP) in Liverpool;	Ajay.Sharma@rlbuht.nhs.uk
4.	Dr. Ravindra Surange	1991 - 1993 / SR		
5.	 Dr. Sangeeta Thakur	1991 - 1994 / SR	Consultant Endocrine Surgeon Mediwin Hospitals, Raghava Ratan Towers, Chirag Ali Lane, Hyderabad-500 001	09848027414
6.	 Dr. Amit Agarwal	1993 – 1997 / SR	Professor Dept. of Endocrine Surgery Sanjay Gandhi PGIMS, Lucknow	amit@sgpgi.ac.in
7.	 Dr. Gaurav Agarwal	1994–1997/SR, 1977/PDCC	Professor Dept. of Endocrine Surgery Sanjay Gandhi PGIMS, Lucknow	gaurav@sgpgi.ac.in
8.	 Dr. Anjali Mishra	1996-1999/SR, 1997/PDCC June1999-Sep 2001/ RA	Additional Professor Dept. of Endocrine Surgery Sanjay Gandhi PGIMS, Lucknow	anjali @sgpgi.ac.in
9.	 Dr. Mukta Baxi	1997 – 1999 /SR, 1998/PDCC	Consultant Endocrine, Breast and Onco surgery, Fortis Hospital, NOIDA	muktabaxi@hotmail.com muktabaxi@yahoo.com

10.	 Dr. Dilip K Kar	1997 – 2000 / SR, 1999/PDCC	Consultant Endocrine and Onco Surgeon, Kalinga Hospital Bhubneswar, Odhisha	dilipkars@yahoo.com, dilipkars@rediffmail.com Ph: 09425030400
11.	 Dr. Anand K Mishra	1997-1999/SR 1998/PDCC Jan 2004- Dec 2006/ SR MCh	Associate Professor, Dept. of Surgery, CSMMU Lucknow	mishra101@gmail.com
12.	 Dr. Rajeev Agarwal	1997- 2000/ SR 1999/PDCC	Associate Professor, Dept. of Surgery, Hind Medical College, Lucknow	9839255110
13.	Dr. Ravindra Verma	1998- 1999/ SR	Ghaziabad	
14.	Dr. Durga D Samat	1999 – 2000/ SR	House No. Type IV/2 Central Excise & Customs Colony Mahaveer Nagar-III, Kota-5	
15.	Dr. Parvinder S. Lubana SR	Jan 2000- June 2000/SR	C/o Dr. Suresh Gupta, B-16, IInd Floor, Kailash Golony, New Delhi.	
16.	Dr. Suren Kumar Das SR	2001 SR	Neelakantha Nagar Gosanenuagaon, Berhampur Dist. Orissa-760 003	
17.	Dr. Nityanand Pathak	11.12.2001	S/o Sri Ram Bhageshwar Pathak Vill.-Dharampura, PO-Bereja Dist. Chapra (Saran) Bihar	
18.	Dr. Rajshekher Perumalla	2000 – 2002 / SR 2001/PDCC	Senior Consultant & Transplant Surgeon, Global Hospital Chennai	rajasekharperu@yahoo.com
19.	Dr. Sanjay Dominic Fartado	2000 – 2001/ SR 2001/PDCC	No. 4, John Cox Hall Torbay Hospital, Lawes Bridge, Torquary TQ2 7AA UK. Sanjay_f@yahoo.com	Sanjay_f@yahoo.com

20.	 Dr. Manish Kaushal	2000 –2002 / SR 2002/ PDCC	Associate Professor, Department of Surgery, MGM Medical College and associated MY Hospital and Govt. Cancer Hospital Indore, MP	drmanishkaushal@gmail.com 919425067722
21.	 Dr. Nikhil Singh	2000 – 2003 /SR 2002/ PDCC	Associate Professor, Dept. of Surgery, SN Medical College, Lucknow	nikhilsingh73@yahoo.com
22.	Dr Shelly Gill	Jan 2001- June 2001		
23.	Dr. S.G. Mahesh	Dec 2001 – Aug 2003 / SR 2003/PDCC	House No. 180, 2nd Cross 2nd Stage, AGB Layout, Bangalore-560 086 Ph: 050-3598051	Maheshsg2001@yahoo.com
24.	Dr. Robbie K George	2002-2004 SR 2003/PDCC	Specialty Registrar University Hospital Belfast U.K.,	robbiegeorge@rediffmail.com
22.	 Dr. Gyan Chand	2002 -2003 SR	Additional Professor, Dept. of Endocrine Surgery, Lucknow	gyan133@sgpgi.ac.in
25.	Dr.KR Vasudevan	2003 – 2004/ SR 2004/PDCC	House No. 227A, D Type MPT Colony, Sada PO, Goa-403804 Sir Ganga Ram Hospital , New Delhi	
26.	Dr. Jaideep Trivedi	2003 – 2004/ SR		
27.	 Dr. Satyajeet Verma	2004 – 2005/ SR 2005/ PDCC	Professor Department of Surgery, Mahamaya Rajkiya Allopathic Medical College, Ambedkar Nagar, UP	vsatyajeet@rediffmail.com

28.	 Dr. Farah Aarshad	2003- 2006/ SR	Dr Farah Arshad Consultant Endocrine and Breast Surgery Sahara Hospital, Lucknow	
29.	Dr. Nil Kamal Kumar	July 2004- July 2007/ SR MCh	Assistant Professor, Dept. of Surgery, Guru Ram Rai Medical College, Dehradun	nkmch2007@gmail.com
30.	 Dr. Pradeep PV	Jan 2005 – Dec 2007/ SR MCh	Consultant Endocrine Surgeon Baby Memorial Hospital Calicut, Kerala 673010	pradeepputhenveeti@yahoo.com 04952377158, 08281021234, 09490492876
31.	 Dr. Vivek Aggarwal	Jan 2005 – Dec 2007/ SR MCh	Consultant Surgeon, Sir Ganga Ram Hospital, Delhi	drvivekaggarwal@yahoo.com
32.	 Dr. PRK. Bhargav	Jan 2005- June 2006/ SR July2006- June 2009/ SR MCh	Associate Professor of Endocrine Surgery Consultant Endocrine and Metabolic Surgeon Endocare Superspeciality Hospital, 29-19-59, Dornakal Road, Suryaraopeta, Vijayawada	kingbhargav@gmail.com 9490130798; 0866-6617633
33.	 Dr. Ranjith Sukumar	July 2006-June 2009/ SR MCh	Associate Professor and Head, Dept. of Endocrine surgery, MES Medical College, Palachode Malaparamba, Kolathur, Perinthalmanna, Malappuram	ranjithsukumar@yahoo.co.in
34.	 Dr Prateek K Mehrotra	Mar 2006- June 2007/ SR July 2007- June 2010/ SR MCh	Consultant Endocrine and Breast Surgeon, Shahara Hospital, Lucknow	drprateekmehrotra@yahoo.com

35.	 Dr Pooja Ramakant	July 2006-June 2007 / SR July 2007- June 2010/ SR MCh	Associate Professor, Dept. of Surgery, Unit 6, CMC, Vellore	poojaramakant@rediffmail.com
36.	 Dr. Dhalapathy Sadacharan	Aug 2007- June 2008/ SR July 2008- June 2011/ SR MCh	Assistant Professor Department of Endocrine Surgery Madras Medical College, Chennai India Consultant: Apollo Hospital, Vijaya Hospital, Sooriya Hospital	drsdhalapathy@gmail.com
37.	 Dr Sudhi Aggarwal	July 2008- Dec 2011/ SR MCh	Consultant Breast and Endocrine Surgeon Meerut Superspeciality Clinic, Chhippi Tank, Meerut UP Assistant Professor Subharti Medical College Meerut UP	sud_soni@rediffmail.com
38.	 Dr Saba Retnam	Aug 2008- June 2009/ SR July 2009- June 2012/ SR MCh	Asst professor, Dept. of Endocrine Surgery Sanjay Gandhi PGIMS, Lucknow	drretnam@gmail.com
39.	 Dr Dipender N Singh	July 2009- June 2012/ SR MCh	Dr Deependra Narayan Singh Consultant Endocrine & Breast Surgeon Fortis Escort Hospital Jaipur	
40.	 Dr. Ritesh Agarwal	July 2009- June 2010/ SR Julyl 2010- June 2013/ SR MCh	Consultant Endocrine & Breast Surgeon Bombay Hospital Mumbai	drriteshagrawal@rediffmail.com; rag476@gmail.com

41.	 Dr. Kulranjan Singh	July 2010- June 2013/ SR MCh	Assistant Professor Department of General Surgery KGMC, Lucknow	
42.	 Dr. Gitika Nanda	July 2010 - Jan 2014/ SR MCh	Consultant Endocrine & Breast Surgeon Ajanta Hospital, Lucknow	
43.	 Dr. Sunil M.B. Barua	Aug 2011 – Aug 2014/ SR MCh	Consultant Endocrine & Breast Surgeon Gawahati Assam	
44.	 Dr Naval Bansal	July 2012 – June 2015/ SR MCh	Consultant Fortis hospital, Mohali	bansal_naval@yahoo.com
45.	 Dr Chitresh Kumar	July 2012 – June 2015/ SR MCh	Senior Research Associate, Deptt of Surgical disciplines, AIIMS, New Delhi	Drk.chitresh@gmail.com
46.	 Dr Om Prakash Prajapati	July 2012 – June 2015/ SR MCh	Consultant at Galaxy hospital, Varansi	dropmrcool@gmail.com

47.	 Dr Roma Pradhan	July 2012 – Dec 2015/ SR MCh	Assistant Prof., Endocrine and Breast Surgeon, Sikkim Manipal Institute of Medical Sciences, Sikkim Manipal University	
48.	 Dr Ashwini C	July 2013 – June 2016/ SR MCh	Consultant Endocrine and Breast Surgery, Hyderabad	
49.	 Dr Navneet Tripathi	July 2013 – June 2016/ SR MCh	Consultant, Deptt of Endocrine and Breast surgery, Vivekanand Polyclinic and Institute of Medical Sciences (VPIMS), Lucknow Consultant Endocrine and Breast Surgery HealthCity Multispecialty Hospital Lucknow	drnavneet.online@gmail.com endonavneet@gmail.com
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51.	 Dr Chandan K Jha	July 2014 – July 2017/ SR MCh	Consultant Endocrine and Breast Surgery, Patna	cjhadmch@gmail.com

Department Publication 2015-2017

Index Journal

Book Chapters:

1. Agarwal G, Singh KR, Chand G. Update on surgical management of primary hyperparathyroidism.Puneet (ed). "**Recent advances in Surgery**" (Jaypee Bros). In press (2017)
2. Agarwal G, Nanda G. Endemic Iodine Deficiency and Goiters: Epidemiology, Patho-physiology and Management. In Clark OH, Duh QY, Kebebew E, Gosnell J, Shen WT (Eds) "**Textbook of Endocrine Surgery"** 3rd ed. Pittsburgh, Jaypee Bros. Medical publishers. 2016:pp 23-42. ISBN 9798351528067.
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3. Yadav SK, Bothra S, Chekavar AS, Mayilvaganan S, Verma AK. A Rare Complication of Left Open Adrenalectomy. Chirurgia (Bucharest, Romania: 1990). 2016;111(5):432-4.
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31. Bansal N, Mishra SK, Sabaretnam M. Papillary Thyroid Carcinoma with Exclusive Involvement of a Functioning Recurrent Laryngeal Nerve may be Treated with Shaving Technique. World J Surg. 2015 Jul;39(7):1852.

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Non Indexed
Original Articles

1. Mayilvaganan S, Bothra S, Rashid M, Chekavar A, Verma AK, Agarwal A. Transection of Sternocleidomastoid for Selective Neck Dissection in Recurrent Papillary Thyroid Cancers. World J EndocSurg 2017;9 (1):32-34.
2. Sarathi V, Sabaretnam M, Shah N. Genotype–phenotype Correlation in Children with Pheochromocytoma and Paraganglioma. World J EndocSurg 2016;8 (3):208-211.

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1. Kumar A, Tripathi SK, Kumar V, Johri G, Singh SK, Chand G. Rare Sebaceous Cyst Carcinoma: A case report with review of literature. American Journal of Cancer Case Reports. 2017; 5(1)6-12.

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1. Mishra P, Mayilvaganan S, Agarwal A. Statistical Methods in Endocrine Surgery Journal Club. World J EndocSurg 2015;7(1):21-23.
2. Mayilvaganan S, Agarwal A. Safety and Cost Efficiency in Thyroid Surgery. World J EndocSurg 2015;7(1):26-27.

Scientific Committee

(SGPGI Breast Course 2018 & BRASCON 2018)

SGPGI Breast Course 2018 & BRASCON2018

Department of Endocrine Surgery

Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow

2nd – 4th Feb 2018

Organizing Committee

Patrons	Prof. Rakesh Kapoor Director, SGPGI Prof. M. L. Bhatt Vice Chancellor, KGMU Prof. RajanSaxena Dean, SGPGI
Mentors & Senior Advisors	Prof. S. K. Mishra HoD, Dept. of Endocrine Surgery Prof. A. K. Singh
Course Director & Organizing Chairman	Prof. Gaurav Agarwal
Organising Secretary **SGPGI Breast Course 2018**	Dr Saba Retnam M.
Organising Secretary **BRASCON2018**	Dr. Ankur Bhatnagar
Chairman Reception	Dr. Rajiv Agarwal
Joint Secretary	Dr. Amit Agarwal Dr. Vijay Datta Upadhyaya
Chairman Scientific	Dr. Vijay Kumar Dr. Vijay Datta Upadhyaya
Co-Chairman Scientific	Dr. Brajesh Mishra Dr. Divya Narayan Updahyaya
Coordinator Operative Workshop	Dr Richa Srivastava

Scientific Program

SGPGI Breast Health2018 & BRASCON2018

SGPGI Breast Course 2018 and BRASCON --- 02-04 February 2018 --- SCIENTIFIC PROGRAM OUTLINE

details on http://www.sgpgibreasthealth.org

Date:--->	DAY-1 Friday 02nd Feb 2018		DAY-2 Saturday 03rd Feb 2018				DAY- 3 Sunday 04th Feb 2018		
Venue: ----> Time: I	Vivekanand Institute of Medical sciences, Nirala Nagar LKO	Lecture Theatre-2, Shruti Auditorium complex, SGPGIMS	Lecture theatre- 1, **PLENARY HALL** Shruti Auditorium complex, SGPGIMS	Lecture theater-2, **BREAST COURSE HALL** Shruti Auditorium complex, SGPGIMS	Lecture theatre- 3, **BRASCON HALL** Shruti Auditorium complex, SGPGIMS	Dept of Radiothearpy, **A Block**, SGPGIMS	Lecture theater-2, Shruti Auditorium complex, SGPGIMS	Lecture theatre- 3, Shruti Auditorium complex, SGPGIMS	Lecture theatre- 4, Shruti Auditorium complex, SGPGIMS
7:30							Breakfast with the Chiefs of Breast Fellowship Programs	BRASCON: Meet the Professor	
8:00	Workshop-1 Live Operative Workshop Operative 1								
8:30			Workshop-3: UG master-class with breast cases		BRASCON: Session 1	Workshop-4: Breast cancer RT planning practicum	Award Posters/ Papers session	BRASCON: Breast reconstruction session	
9:00									Workshop-6: Venous access in breast cancer patients & Chemoport usage
9:15				Session-I: Diagnosis, Staging and Treatment Planning of Breast Cancer	BRASCON: Sessions 1 and 2				
9:30							Session- IV: Oncoplastic Surgery	Oncoplastic session in LT-2	
11:00	Workshop-1 Live Operative Workshop Operative 2						Tea/ Coffee Break	Tea/ Coffee Break	Tea/ Coffee Break
11:30							Session- V: Locally Avanced Breast Cancer	BRASCON: Mastopexy/Others	
11:45			**INAUGURATION**	INAUGURATION in LT-1	INAUGURATION in LT-1	INAUGURATION in LT-1			
12:30			**Plenary Lecture**	Plenary Lecture in LT-1	Plenary Lecture in LT-1	Plenary Lecture in LT-1			
13:00			Lunch	Lunch	Lunch	Lunch	Lunch	Lunch	
14:00	Workshop-1 Live Operative Workshop Operative 3		Workshop-5: Mastology for Gynecologists	Session-II: Early Breast Cancer	BRASCON: Sessions 3, 4 and 5		Session- VI: Metastatic Breast Cancer	BRASCON: Best paper session	
14:30		Workshop 2: Breast Imaging and Interventions Workshop							
16:00				Tea Coffee Break			Session- VII: Operative Videos		Workshop-7: Lymphedema workshop
16:30				Session-III: Pot purri-contentious issues in breast cancer management					
17:00							**Valedictory & Prize Distribution**		LTLT-2
17:30	Tea/ coffee. Disperse	Tea/ coffee. Disperse	Tea/ coffee. Disperse		Meet the professor		High tea. Disperse		
18:30			Breast Quiz in LT-2	**Breast Quiz**	Breast Quiz in LT-2	Breast Quiz in LT-2			
20:00		Faculty Dinner Guest House SGPGI	**Shaam-e-Awadh & Dinner at Guest House**						

SGPGI Breast Course 2018 & BRASCON	1	Scientific Program	2nd-4th February 2018
Day-1. Friday 2nd February, 2018			
Vivekanand Institute of Medical sciences, Nirala Nagar Lucknow- Seminar Hall and Operation Theatre complex			
08:00 AM- 05:00 PM	**Workshop 1: Live Operative Workshop**	Three parallel Operating Rooms to be run	
	Proposed Cases	Operating Surgeons	Moderators:
	Mastectomy with Axillary Clearance with Immediate Reconstruction DIEP Flap	**Breast/ Onco Surgeons:** Pooja Ramakant, Gaurav Agarwal, Navneet Tripathy, Anurag Srivastava, Gitika N Singh. **Plastic Surgeons:** Vinay Kant, Brijesh Mishra, Bhagwat Mathur, GDS Kalra, Rajiv Agarwal, Rajan Arora, Rahul Kapoor, RK Mishra	**Breast/ Onco Surgeons:** Vijay Kumar, Uttam Soni, Vibhor Mahendru, KK Agarwal, Anand Mishra, AA Sonkar, Arun Chaturvedi, Kulranjan . **Plastic Surgeons:** Bhagwat Mathur, Divya Narayan Upadhyaya, Rajat Srivastava, Jayanto Tapadar, Pradeep Goil, Prem Shankar, Reetesh Purwar, Andreas Gravanis, Devjay Sharma, Arun Mathur
	Nipple & Skin sparing Mastectomy for Phylloides with immediate Reconstruction with pedicle LD Flap and implant		
	Mastectomy with Axillary Clearance with Immediate Reconstruction with Pedicled supercharged TRAM Flap		
	Breast Conserving Surgery (BCS)with Breast reshaping		
	Inverted Nipple Correction		
	Nipple reconstruction		
	Gynaecomastia Correction- Liposuction with Trans-Nipple resection		
	Breast Reduction		
	Breast Augmentation		
Day-1. Friday 2nd February, 2018			
Mini-auditorium, A Block, first floor (entrance through department of Anesthesiology) SGPGIMS			
02:00-05:30 PM	**Workshop-2: Breast Imaging and Interventions Workshop**	Conveners: Selvi Radhakrishna, Namita Mohindra, Gitika N Singh	
	Faculty/ Resource persons	Selvi Radakrishna, Subhash Ramani, Gitika Nanda Singh, Namita Mohindra, Neeraj Jain	
	Title	Speaker	Duration
	Welcome & Introduction to Breast Imaging & Interventions Workshop	Namita Mohindra	10 min
	Breast Ultrasonography and interventions: Talk and Demonstration, Hands-on Experience	Selvi Radhakrishna, Namita Mohindra, Gitika N Singh,	50 min
	Vacuum assisted biopsy	All faculty	60 min
	Mammographic wire localization	Subhash Ramani	30 min
	How to pick up early lesions on mammography	Subhash Ramani	30 min
	Tips and tricks of Breast Imaging & Interventions	All faculty	30 min
5:30 PM	Tea and Disperse		
Day-2. Saturday 3rd February, 2018			
08:00 am onwards	**Registration**		
PLENARY HALL (Lecture theatre- 1), Shruti Auditorium complex, SGPGIMS			
08:30- 11:30AM	**Workshop-4: Breast master-class for Undergraduates**	Chairpersons: VK Kapoor, Gurpreet Singh, Navneet	Faculty in-charge: Pooja
08:30AM	Registration for Master class for Ugs		
	Title	Gitika Nanda Singh, Kulranjan Singh	Duration
9:00AM	Welcome, Introduction	Pooja Ramakant	5 min
	symptoms	Kulranjan Singh	20 min
	Case-1 : young woman with benign breast mass	Gitika Nanda Singh	30 min
	Case-2 : postmenopausal lady with breast lump and axillary lymphadenopathy	Sendhil Rajan	30 min
	How to score well in clinical case presentation:Long case of breast pathology	Pooja Ramakant	20 min
	How to score well in clinical case presentation:short case of breast condition	Pooja Ramakant	20 min
	open mike: Q& A; clearing any doubts of the students	All faculty and Panelists: MJ Paul, Diptendra Sarkar,	30 min
11:45AM	**Inauguration**		
12:35	**SGPGI Breast Orations- 2018: "Current paradigms of breast cancer management"**	Cheng-Har Yip	20 minutes
01:00-02:00 PM	Lunch + Poster Viewing		
02:00 - 05:00 PM	**Workshop 5- Mastology Refresher for Gynecologists**	Chairpersons: Amrit Gupta, Indu Tandon, Beena Tandon	Faculty in-charge: Anjali Mishra, Rapporteur: Sanjay Yadav
	Title	Speakers	Duration
	Introduction to breast diseases	Anjali Mishra	15+5 min
	Abberrations of Normal Development & involution: management	Sudhi Agrawal	15+5 min
	Pregnancy & Lactation	Amita Panday	15+5 min
	Mastalgia	Pooja ramakant	15+5 min
	Inflammatory conditions	Navneet Kaur	15+5 min
	Common neoplastic conditions in women	DG Vijay	15+5 min
	Breast cancer screening as applicable to Indian scenario	Vani parimar	15+5 min
	Public awareness of breast cancer: lecture and skit	Deepa Kapoor, Nema Pant and team	40 min
Day-2. Saturday 3rd February, 2018			
BREAST COURSE Hall (Lecture theatre- 2), Shruti Auditorium complex, SGPGIMS			
08:30-09:15 AM	Combined session with BRASCON in BRASCON HALL (LT-3)		
9:15 AM	Welcome, Introduction to SGPGI Breast Course- 2018	Gaurav Agarwal	
09:30-11:30 AM	**Session I Diagnosis and Evaluation of a suspected breast cancer patient**	Chairpersons: Amit Agarwal, Narendra Krishnani, Om Prakash Prajapati	Faculty in-charge: Amit Agarwal; Rapporteur: Chaitra S
	Title	Speaker	Duration
9:30AM	Breast cancer Screening & early diagnosis of breast cancer: India centric approach	Anand Mishra	12+3 min
	Approach to a patient with breast lump: Triple assessment	Sanjeev Gupta	12+3 min
	Surgical treatment of Breast cancer: How it has evolved over the decades	Arun Chaturvedi	12+3 min
		Chairpersons: Kamal Kataria, Naval Bansal, Neeraj Kumari	*ZYDUS/CADILA SESSION*
	strategies	Nuzhat Hussain	14+3 min
	Diagnostic breast imaging	Subhash Ramani	14+3 min
	Breast cancer staging and treatment planning overview	Chintamani	12+3 min
	Discussion: Breast cancer diagnosis and staging	Gaurav Agarwal, and all faculty of the session	
11:45AM- 12:35 PM	**Inaugration in Plenary Hall (LT-1)**		
12:35-01:00 PM	**SGPGI Breast Oration-2018: "Current paradigms of breast cancer management"**	Cheng Har Yip	20 min
01:00- 02:00 PM	LUNCH + Poster viewing		

02:00- 04:00 PM	**Session II: Conservatism in management of Early Breast cancer**	Chairpersons: Gyan Chand, Sanjay Gambhir, Chandan K Jha	Faculty in-charge: Gyan Chand; Rapporteur: Raouef Ahmed Bichoo
02:00-03:20 PM	Title	Speaker	*ROCHE SESSION*
	Breast Conservation is the norm in management of EBC	Neeraj Garg	12+3 min
	Conservatism in management of axilla in EBC: various scenario	Ashutosh Kothari	14+3 min
	Patient friendly Adjuvant RT for EBC(APBI, Hypofractionation)	Ashwini Budrukkar	12+3 min
	Minimising Adjuvant systemic treatment in EBC: when and how to omit cytotoxic therapy	Manish Kumar	14+3 min
	Ductal & Lobular carcinoma in situ: mangement strategies	Gurpreet Singh	12+3 min
03:20 - 04:00 PM	**Panel Discussion I: Case based discussion on EBC**	Chairpersons: Beena Ravi, Dr Peeyush Ranjan, Dr Chitresh	40 min
		Panelists:	Moderator:
	Case- based discussion: 3 cases of Early breast cancer	Nita Nair, Sumohan Chatterjee, Ravi Kant, Punita Lal (rad	Kanchan Kaur
04:00 - 04:15 PM	Tea / coffee break		
04:15 - 05:35 PM	**Session III: Pot- pourri: Contentious issues in breast cancer management**	Chairpersons: Anand Aiyer, Vivek Aggarwal, Anshul Gupta	Faculty in-charge: Kulranjan Singh; Rapporteur: Ramya VC
	Title	Speaker	*INTAS SESSION*
	Fertility issues in young breast cancer patient survivor	Rajeev Agrawal	12+3 min
	Management of familial and genetic breast cancer	Mikael Hartmann	12+3 min
	Current indications and practice of Adjuvant Hormonal and Targeted therapy in breast	Peush Bajpai	14+3 min
	Breast Cancer risk assessment	Uttam Soni	12+3 min
	Systemic treatment strategies for Triple negative and BRCA mutated breast cancers	Manish Kumar	14+3 min
05:35- 06:15 PM	**Panel Discussion II: Issue based discussion**	Chairpersons: Sushma Agrawal, Manish Ora, Ritesh	40 min
	Issues to be dicussed	Panelists:	Moderator:
	Breast cancer screening: Is it needed in a developing countries; Essential breast cancer	Cheng-Har Yip, Vani Parmar, Vinod Jain, B Paul (Rad	Mikael Hartmann
6:15PM	**PG Breast Quiz**		
Day-2. Saturday 3rd February, 2018			
BRASCON HALL (Lecture theatre- 3), Shruti Auditorium complex, SGPGIMS			
8:30 - 09:15 AM	**Session I: Breast Reconstruction: Basics (Combined with Breast Course)**	Chairpersons: Neeraj Garg, Neeraj kant Agarwal ,Vishal Mago ,Anurag Pandey	
	Title	Speaker	Duration
	Current Status of Breast Reconstruction: Overview	Pradeep Goil	8+2 min
	Which Oncoplastic Procedure for which tumour site : Quadrant wise approach	Ashutosh Kothari	12+3 min
	Types of Mastectomies- Latest Concept—Preserving the skin flap	Vibhor Mahendru	8+2 min
	Radiation Therapy- How it influences Breast Reconstruction-TMH Perspective	Vinay Kant Shankdhar	8+2 min
9:15 -11:30 AM	**Session II: Autologous Breast Reconstruction**	Chairpersons: Vijay Kumar, Rajan Arora , Pradeep Tiwari, Reetesh Purwar	
	Title	Speaker	Duration
	Oncoplastic breast recon for central quadrant lesions(grisotti)	Ashutosh kothari	8+2 min
	LD Flap ± Implant for Breast Reconstruction (Video)	Prateek Arora	13+2 min
	Extended LD Flap for Breast Reconstruction	Bhagwat Mathur	8+2 min
	DIEP Flap Planning, Choice of perforator and flap raising(Video)	Andreas Gravanis	13+2 min
	TUG Flap	Andrea Figus	13+2 min
	PAP Flap	Andrea Figus	13+2 min
	Breast reconstruction with ALT flap: An Alternative Approach	Krishna Prasad Prusthi	8+2 min
	Discuusion		10 min
10:55 - 11:05	Tea/ Coffee break		
		Chairperson: Vaibhav Khanna, Ashutosh Kothari, Mohit Jain, Saurabh Rai	
	Optimizing Esthetic Outcome in Micro-surgically Reconstructed Breast	Andrea Figus	13+2 min
	Management of complications in Micro-surgically Reconstructed Breast	Vinay Kant Shankdhar	10 +2 min
	Radiation Therapy in Micro-surgically Reconstructed Breast	Andreas Gravanis	10+2 min
11:45– 12:35 PM	**INAUGRATION in PLENARY HALL (LT-1)**		
12:35– 01:00 PM	**SGPGI Breast Oration-2018 in PLENARY HALL (LT-1)**		
01:00– 02:00	LUNCH		
02:00 -03:00 PM	**Session III: IMPLANT BASED BREAST RECONSTRUCTION**	Chairpersons: SD Pandey, Adarsh, Saumya Mathews, Tarun Jain, Vikas Kakkar	
	Title	Speaker	Duration
	Two Stage Breast Reconstruction- Concept and Technical Approach	P. Cordeiro	13+2 min
	Radiation and Implant Reconstruction –Timing for prosthesis exchange and Outcome	P. Cordeiro	13+2 min
	Prepectoral Breast Reconstruction with Implant and ADM (BRAXON)	Neeraj Garg	10+2 min
	Management of Complications- Implant Based Reconstruction	P. Cordeiro	13+2 min
3:00– 4:15 PM	**Session IV: BREAST AUGMENTATION**	Chairpersons: Bhagwat Mathur, Peter Cordeiro, Rahul Kapoor, KP Prusthy	
	Title	Speaker	Duration
	Clinical Evaluation of Patient for Breast Augmentation	Divya Narayan Upadhyaya	6+2 min
	Pre Op Counseling, Marking and Legal Considerations	Srinivas	6+2 min
	Selection of Breast Implant	Sandip Basu	6+2 min
	How I do it (Video Presentation)	Andreas Gravanis	10+2 min
	How I do it - Subfascial	R.K Mishra	8+2 min
	How I do it - Endoscopic	Rajiv Agarwal	8+2 min
	Complications and its Management	R.K Mishra	8+2 min
	Discussion : 10 min		
04:15 - 05:30 PM	**Session V: BREAST REDUCTION**	Chairpersons: Saumya, Debarati Chattopadhyaya, Mahendra Mohan Gupta, Raj Kumar Mish	
	Title	Speaker	Duration
	Clinical Evaluation of Patient for Breast Reduction	Vijay Kumar	8+2 min
	Pre-op Counseling and Legal Considerations	Brijesh Mishra	6+2 min
	Various Techniques and Indications	Neeraj Kant Agarwal	10+2 min
	How I do it (a) Wise Pattern Video Presentation	Bhagwat Mathur	18+2 min
	(b) Vertical Scar video presentation		
	Breast Reduction in Unmarried Females-Special Considerations	Debariti Chattopadhyay	6+2 min

	Complications of Breast Reduction and Its Management	Prateek Arora	6+2 min
	Discussion(10 min)		
05:30- 06:10 PM	**MEET THE PROFESSOR / OPEN HOUSE DISCUSSION**		
	Breast Augmentation	Adreas Gravinis	RK Mishra
	Breast Reduction	Bhagwat Mathur	Pradeep Goil
	Implant based Breast Reconstruction	Peter Cordeiro	Neeraj Garg
	Microvascular Breast Reconstruction	Andrea figus	Vinay Kant
	BCS and Oncoplasty for Plastic Surgeons	Ashutosh Kothari	
06:15 PM onwards	**BREAST QUIZ in Breast Course Hall (LT-2)**		
Day-2. Saturday 3rd February, 2018			
Seminar Room, Department of Radiotherapy , A-Block, SGPGIMS			
Workshop- 3	**Breast Radiotherapy Planning Workshop**	Convener: Punita Lal	
8:30 AM	Registration	Faculty: Santam Chakraborty, Ashwini Budrukkar , Kirti Srivastav, Shantanu Sapru, Rohini Khurana, Maria Das	
08:45-11:30 AM	Breast Radioiotherapy planning Practicum		
07:30 PM onwards	**Dinner and Live Music at Dr BC Joshi Guest House, SGPGIMS (Opp Director's Bungalow)**		
Day-3. Sunday 4th February, 2018			
7.30 AM	Breakfast with Chiefs of Breast Fellowship Programs	Opportunity for students to interact with program	60 min
		SK Mishra, MJ Paul, Anurag Srivastava, SVS Deo, Gurpreet Singh, Vani Parmar, Sumohan Chatterjee, Mikael Hartmann	
BREAST COURSE Hall (Lecture theatre- 2), Shruti Auditorium complex, SGPGIMS			
8:30 A M	**Award Posters/ Papers Session**	Chair persons: Chintamani, Diptendra Sarkar, Navneet Kaur	50 min
	Best 6 posters adjudged previous day		
9:30 A M	**Session IV: Oncoplastic Surgery Symposium**	Chairpersons: Bhagwat Mathur, Manish Kaushal, Satyajeet Verma	
	Title	Speaker	Duration
	Introduction to Oncoplastic Breast Surgery for surgeons and radiation oncologists	Sumohan Chatterjee	12+3 min
	Which oncoplastic procedure for which tumor site: Quadrant-wise approach	Ashutosh Kothari	12+3 min
	Extreme Oncoplasty- an alternative to total mastectomy	Chaityanand Koppiker	12+3 min
		Chairpersons: Peter Cordiero, Rahul Khanna, Vijay Kumar	
	Radiation therapy considerations in patients undergoing oncoplastic breast surgery	Santnam Chakraborty	12+3 min
	Breast imaging and surveillance following BCS and oncoplastic surgery	Neeraj Jain	12+3 min
	Management of post BCS ipsilateral breast tumour recurrence	SVS Deo	12+3 min
11.00 A M	**TEA/Coffee Break**		
11.15 AM	**Session V: LABC**	Chair Persons: Sanjeev K Gupta, Kirti Srivastava, Nikhil Sing	*MYLAN SESSION*
	Management of LABC: Overview	Dipten Sarkar	12+3 min
	NACT in LABC: how to choose the right regimen, assess response and when to switch to	Bhavesh Parekh	14+3 min
	Neo-adjuvant anti-HER2 and neoadjuvant hormone treatment in LABC (14+3min)	Peush Bajpai	14+3 min
		Chairpersons: Aakash Agarwal, Sharad Singh, Vivek Aggarwal	
	Breast conservation surgery in LABC	Vani Parmar	12+3 min
	Post-NACT management of axilla in breast cancer	MJ Paul	12+3 min
	Inflammatory breast cancer	Rahul Khanna	12+3 min
12:50 PM	**PANEL DISCUSSION III: Issue based discussion on LABC Management**	Moderator: Gaurav Agarwal	40 min
		Panelists: Cheng-Har Yip, Manish Kumar, SVS Deo, Nita	
		Rajeev Gupta, RK Srivastava, Manoj Prashar	
1:30PM	**Lunch**		
2:15PM	**Session VI: Metastatic Breast Cancer**	Chairpersons: Gurpreet Singh, Shaleen Kumar, CS Sarangi	*PFIZER SESSION*
	Title	Speaker	Duration
	Management strategies in pts with MBC: Current philosophy (12+3min)	Gaurav Gupta	12+3 min
	Role of surgery for breast primary in MBC (12+3min)	Nita Nair	12+3 min
	Management of skeletal metastases in breast cancer patients (12+3min)	Gaurav Prakash	12+3 min
	Emerging therapies for MBC: Beyond cytoxics, hormones and trastuzumab- CDK4/6	Poonam Patil	14+3 min
3:30 PM	**PANEL DISCUSSION IV: Advanced Breast Cancer: Issue based discussion**	Chairpersons: Mikael Hartmann, AK Verma, Kintu Lugawa, AK Mohanty	*ROCHE SESSION*
	a. Palliative care- what every surgeon/oncologist must know	Panelists: Bhavesh Parekh (med onc), Manoj Prashar (med onc), Vani Parmar, Punita Lal, Sanjay Dhiraaj (Anesth), MLB Bhatt (Rad Onc), Cheng-Har Yip, Kirti Srivastav (Rad Onc)	Moderator: Gaurav Gupta
	b. When to choose dignity of death over prolongation of life		
	c. End of life issues		
4:00 PM	**Session VII Breast Surgery at the Movies**		
	Post mastectomy reconstruction: Implant based using ADM (6min)	Sumohan Chatterjee	6 min
	Post mastectomy reconstruction: dermal sling (6min)	Chaityanand Koppiker	6 min
	Oncoplastic surgery: Grisotti (6min)	Ashutosh Kothari	6 min
	Superior or inferior pedicle mammoplasty (6min)	Navneet Kaur	6 min
	SLNB and ALND (6min)	V Seenu	6 min
	MRM (6min)	DG Vijay	6 min
	Round block oncoplasty (6min)	Vedant Kabra	6 min
	Skin sparing mastectomy with implant using BRAXON (6min)	Neeraj Garg	6 min
05:00PM	**Valedictory, Prize distribution**		
05:15PM	Tea/Coffee and Disperse		
Day-3. Sunday 4th February, 2018			
BRASCON HALL (Lecture theatre- 3), Shruti Auditorium complex, SGPGIMS			
8:30- 9:30 AM	**BREAST RECONSTRUCTION**	Chairperson: KS Jaiswal , Vibhor Mahendru, Farah Arshad Vinay Kant	

	Title	Speaker	Duration
	DIEP Flap- Expanding the Horizon	Saumya Mathews	10+2 min
	Nipple Reconstruction	Saumya	10+2 min
	Post Burn Breast Reconstruction	Arun Bhatnagar	13+2 min
	Phylloids tumor	UttamSoni	10+2 min
9:30-11:00 AM	**ONCOPLASTIC SURGERY (combined session in BREAST COURSE HALL (LT-2)**		
11:00 - 11:15 AM	Tea / Coffee Break		15 min
11:15-11:45 AM	**MASTOPEXY**	Chairpersons: Andreas Gravvanis, Anubhav Gupta, Divya Narayan, Shobhit Sharma	
	Title	Speaker	Duration
	Indications and technique	Anurag Pandey	8+2 min
	How I do it- • Augmentation Mastopexy	Bhagwat Mathur	18+2 min
	• Doughnut Mastopexy		
	Discussion		10 min
11:45 – 01:00 PM	**OTHER CONDITIONS**	Chairpersons: Nikhil Singh, Richa Srivastava, Anjali Mishra, Brijesh Mishra, Andreas Gravvanis	
	Title	Speaker	Duration
	Gynaecomastia Clinical Evaluation and patient selection	Anubhav Gupta	8+2 min
	Gynaecomastia- How I do it- Video presentation	RK Mishra	10+2 min
	Breast Management in Gender Re assignment Surgery	Ashwani Dash	13+2 min
	Inverted Nipple Correction (Video)	Bhagwat Mathur	10+2 min
	Tubular Breast Management	Bhagwat Mathur	
	Breast Asymmetry Management	Bhagwat Mathur	13+2 min
	Discussion		10 min
01:00- 02:00 PM	**Lunch**		
02:00-4:00 PM	**BEST PAPER SESSION**	Chairperson: Neeraj Garg, Anupama Singh, SD Pandey, Anrdreas Gravvanis	
	Title	Speaker	Duration
	Latissimus dorsi flap: A robust and cost-effective option for breast reconstruction	Pankaj Sharma	8+2 min
	Indian experience with lateral chest wall perforator flaps in partial breast reconstruction	Shashank Nigam	8+2 min
	Gigantomastia due to retromammary lipoma: An aesthetic management	Debarati Chattopadhyay	8+2 min
	Utility of External Oblique Myocutaneous Flaps in massive skin defects post Mastectomy	Utsab Man Shrestha	8+2 min
	Breast Augmentation With Silicone Implant: A Single Institutional Experience	Gautam Prakash	8+2 min
	A prospective study on functional impairment following latissimus dorsi flap following modified radical mastectomy.	Guru Prasad Reddy	8+2 min
	Immediate Breast Reconstruction With Diep Flap After Modified Radical Mastectomy: Our Initial Experience	Manojit Midya	8+2 min
	Unusual Mammoplasty In Post-Burn Breast Deformity	Nikhilesh Gaur	8+2 min
	Nipple Reconstruction With CV Flap: Our Experience	Pawan K Dixit	8+2 min
	Quality of Life Assessment in Patients Undergoing Oncoplastic Breast Surgery	Ravi K Singh	8+2 min
	Aesthetics in breast reconstruction for Poland's syndrome: what we can achieve?	Shivangi Saha	8+2 min
	Breast Reduction Using Supero-Medial Pedicle Technique-Our Centre Experience	Shobhit Sharma	8+2 min
4:00 -5:00 PM	**OPERATIVE VIDEO SESSION- COMBINED SESSION In BREAST COURSE HALL (LT-2)**		
05:00- 05:15 PM	Valedictory Function		
Day-3. Sunday 4th February, 2018			
WORKSHOP HALL (Lecture theatre- 4), First Floor, Shruti Auditorium complex, SGPGIMS			
08:30 to 11:00 AM	**Workshop-6: Venous Access in Cancer Patients, Chemoport Workshop**	Conveners: Puneet Goyal, Kulranjan Singh, Sudhir Kumar	
	Introduction, welcome	Puneet Goyal	5 min
	Venous access in cancer patients- an overview	Vedant Kabra	15+5 min
	TIVADs: introduction, merits and demerits	Kul Ranjan Singh	15+5 min
	TIVAD implantation (15+5 mins)	Puneet Goyal	15+5 min
	Maintenance of TIVADS: tips 7 tricks; trouble shooting; explantation (15+5 mins)	Ruchi Verma	15+5 min
	Hands on experience with usage of TIVAD (3 work stations)	Uttam Soni, DG Vijay, Puneet Goyal, Ruchi Verma,	50 min
04:00-05:00 PM	**Workshop-7: Lymphedema workshop**	Chairpersons: Neeraj Rastogi, Roma Pradhan, Sister Chhaya	
	Prevention of lymphedema in breast cancer patients (12+3min)	Rohini Khurana	
	device, bandages and bandaging techniques	Anurekha Gogia/ team	
05:00PM	**Valedictory, Prize distribution**		
05:15PM	Tea/Coffee and Disperse		

List of Faculty

List of Faculty SGPGI Breast Course 2018

(As on 16Jan2018. list likely to change- this is only a provisional list)

Overseas

Name	***Place***
Ashutosh Kothari	London UK
Cheng Har Yip	Kualalumpur, Malaysia
Mikael Hartmann	NUS, Singapore
Neeraj Garg	London UK
Sumohan Chatterjee	Manchester, UK
Bhagwat Mathur	Chelmsford, UK
Andreas Gravvanis	Athens, Greece
Peter G. Cordeiro	MSKCC, New York, USA

National

Aakash Gaind	Max, Dehradun
Anu Tiwari	Kanpur
Anurag Srivastava	AIIMS, New Delhi
Ashwini Budrukkar	TMH, Mumbai
B Paul	KNRCC, Allahabad
Bina Ravi	AIIMS, Rishikesh
ChaityanandKoppikkar	Pune
Chintamani	VMMC, New Delhi
DG Vijay	HCG, Ahmedabad
Diptendra Sarkar	IPGMER, Kolkata
Gaurav Prakash	PGIMER, Chandigarh
Gurpreet Singh	PGIMER, Chandigarh
Kamal Kataria	AIIMS, New Delhi
Kanchan Kaur	Medanta, Gurugram
Manish Kaushal	Indore
Manish Kumar (Col)	R&R, Delhi
MJ Paul	CMC, Vellore
Navneet Kaur	UCMS, Delhi
Nita Nair	TMH, Mumbai
Peeyush Ranjan	AIIMS, New Delhi
Peush Bajpai	Max, Delhi
Poonam Patil	Manipal, Bengaluru
Rahul Khanna	IMS BHU, Varanasi
Rajeev Agrawal	Medanta, Gurugram

Ravi Kant	AIIMS,Rishikesh
Sanjay Kala	GSVM MC, Kanpur
Sanjeev K Gupta	IMS BHU, Varanasi
Santam Chakraborty	TMC, Kolkata
SarvajeetVerma	MC, AmbedkarNagar
Satyajeet Pradhan	IMS BHU, Varanasi
SelviRadhakrishna	Chennai
SubhashRamani	TMH, Mumbai
SVS Deo	AIIMS-IRCH, New Delhi
UttamSoni	Jaipur
V Seenu	AIIMS, New Delhi
Vani Parmar	TMH, Mumbai
VedantKabra	Fortis Memorial, Gurgaon
PradeepGoil	SMS, Jaipur
GDS Kalra	SMS, Jaipur
Srinivas JS SandipBasuI	PGMER,Kolkatta
Krishna Prasad Prusthi	Vishakapatnam
Neeraj Kant Agarwal	BHU, Varanasi
Debariti Chattopadhyay	AIIMS,Rishikesh
Saumya Mathews	TMH, Mumbai
Saumya Max	Delhi
Arun Bhatnagar	AIIMS, Bhopal
Vivek Singh	Ganga Ram, Delhi
Vinay Kant Shankdhar	TMH, Mumbai
Anubhav Gupta	Ganga Ram, Delhi
Ashwani Dash	Apollo, Indore
Rajan Arora	Rajiv Gandhi, Delhi
Prateek Arora	Max, Delhi
Dr Shobhit Sharma	SRMS, Bareilly
Rahul Kapoor	Rajiv Gandhi, Delhi
Jayanto K Tapadar	Varanasi

Lucknow Faculty

Aakash Agarwal	RMLIMS, Lucknow
Abhinav A Sonkar	KGMU, Lucknow
AK Verma	Lucknow
Col AnandAiyar	CH CC, Lucknow
Anand K Mishra	KGMU, Lucknow
ArunChaturvedi	KGMU, Lucknow
Ashish Singhal	RMLIMS, Lucknow

Farha Arshad	Sahara, Lucknow
Ajeet K Gandhi	RMLIMS, Lucknow
Gaurav Gupta	RMLIMS, Lucknow
Gitika Nanda Singh	KGMU, Lucknow
Kirti Srivastava	KGMU, Lucknow
Kulranjan Singh	KGMU, Lucknow
Madhup Rastogi	RMLIMS, Lucknow
Manoj Prasher (Col)	CH CC, Lucknow
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Navneet Tripathi	Vivekanand, Lucknow
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Vivek Garg	LCI, Lucknow
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Divya Narayan Upadhyaya	KGMU, Lucknow
R.K Mishra	SIPS, Lucknow
Rajiv Agarwal	Plastic Surg SGPGI, Lko
Ankur Bhatnagar	Plastic Surg SGPGI, Lko
Anupama Singh	Plastic Surg SGPGI, Lko
Vijay Kumar	KGMU, Lucknow
Brijesh Mishra	KGMU, Lucknow
Anurag Pandey	Sahara Hospital, Lucknow
SD Pandey	Vivekanand, Lucknow
Amit Agarwal	Vivekanand, Lucknow
Richa Srivastava	Vivekanand, Lucknow

SGPGI Alumni Faculty

Arun K Mohanty	SCB MC, Cuttack
Ashwini Reddy	Hyderabad
Chandan K Jha	AIIMS, Patna

Chitresh Kumar	AIIMS, New Delhi
CS Sarangi	SCB MC, Cuttack
Deependra N Singh	Jaipur
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Naval Bansal	Chandigarh
Om Prakash Prajapati	Varanasi
Ritesh Agrawal	Mumbai
SendhilRajan	St John's, Bengaluru
Sudhi Agrawal	Meerut
Sunil MB Barua	Guwahati
Vivek Aggarwal	Delhi

SGPGIMS Lucknow Faculty

Anshul Gupta	Hematol SGPGI, Lko
Manish Ora	Nuclear Med SGPGI, Lko
Maria Das	Radiother SGPGI, Lko
N Krishnani	Pathol SGPGI, Lko
Namita Mohindra	Radiol SGPGI, Lko
Neeraj Jain	Radiol SGPGI, Lko
Neeraj Kumari	Pathol SGPGI, Lko
Neeraj Rastogi	Radiother SGPGI, Lko
Puneet Goyal	Anesthesia SGPGI, Lko
Punita Lal	Radiother SGPGI, Lko
Ruchi Verma	Anesthesia SGPGI, Lko
Sanjay Dhiraaj	Anesthesia SGPGI, Lko
Sanjay Gambhir	Nuclear Med SGPGI, Lko
Shagun Misra	Radiother SGPGI, Lko
Shaleen Kr	Radiother SGPGI, Lko
Shubha Phadke	Medical Genetics, Lko
Soniya Nityanand	Hematol SGPGI, Lko
Sushma Agrawal	Radiother SGPGI, Lko
Vineeta Agrawal	Pathol SGPGI, Lko
SK Mishra	Endocr Surg SGPGI, Lko
Amit Agarwal	Endocr Surg SGPGI, Lko
Anjali Mishra	Endocr Surg SGPGI, Lko
Gyan Chand	Endocr Surg SGPGI, Lko
Sabaretnam M	Endocr & Breast Surg SGPGI, Lko
Gaurav Agarwal	Endocr & Breast Surg SGPGI, Lko

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Abstracts

SGPGI Breast Course 2018

Title: Correlation of chemokine CXCL12 expression in breast cancer with other prognostic markers

Authors: Ankur Agrawal, Vivek Srivastava, MA Ansari, Dept of General Surgery, IMS, BHU, Varanasi
Presenting Author: Ankur Agrawal, Ph- 9808567850, mail- ankuragr07@gmail.com

Objectives:
To assess expression of CXCL-12 in breast cancer patients and correlation of dysregulated expression of CXCL-12 with lymphatic vascular invasion (LVI) and other established clinico-pathological prognostic parameters.

Materials and methods:
25 breast cancer cases from a single unit of general surgery were included. After clinical and color Doppler evaluation, MRM was done. Representative sections from formalin fixed mastectomy specimens were taken. Detailed histopathological examination with regard to pathological tumor size, grading, vascular invasion, nodal involvement and receptor status was done. LVI and CXCL12 assessment was done by IHC in tissue blocks using mouse anti-human D2-40 antibody (Dako antibody solutions, USA) and mouse anti-human MAb clone79018 CXCL12 antibody (R&D systems, USA), respectively. Correlation of CXCL-12 expression with various clinico-pathological parameters was done.

Results:
CXCL12 staining was positively seen in 76% (n=19) of patients. Positive staining was determined by final immuoreactive score of patient, calculated by multiplying intensity of CXCl12 staining on slide section with percentage of slide section showing CXCL12 staining. LVI positivity was observed in 74% CXCL12 positive patients on H&E staining (p=0.013) and in 63% CXCL12 positive patients on D2-40 staining (p=0.047). 15 out of 19 CXCL12 positive patients showed high grade tumor on histopatholgical examination (p=0.001). 75% patients who were CXCL12 positive had palpable ipsilateral axillary lymph nodes (p=0.002). We also calculated association of CXCL12 expression with number of histologically positive lymph nodes (p<0.001).

Conclusions:
CXCL12 expression correlates with lymphatic invasion and also with other prognostic parameters like nodal status, grading and clinical stage. This highlights CXCL12/CXCR4 axis as a potential new target for diagnostic and therapeutic strategies. Development of new drugs which block expression of CXCL12 may open new gates in cancer treatment.

Title: Comparative study of Doppler, MAGS, and CD31 assay as vascularity index in advanced breast carcinoma

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Introduction: Assessment of angiogenesis in solid tumors has always been a subject of high priority research. Angiogenesis index calculated in breast cancer as a part of pre treatment workup can prove to be of therapeutic and prognostic significance.

Materials and Methods: a prospective study undertaken in 25 advanced breast cancer patients over period of 2 years. The angiogenesis was assessed by means of immunocytochemistry, Microscopic angiogenesis grading and color Doppler study. Results compared with presence of metastasis, occurrence of recurrence and the response following chemotherapy.

Results: Assessment of MVD done with MAGS and CD31 assay correlated with Doppler assessment (pO.OOl). High MVD associated with higher percentage of metastasis (pO.OOl), and higher chances of local recurrence ($p<0.02$). The MVD assessed using CD31 assay showed statistical significance for presence of metastasis (d.f=2, pO.Ol). While results obtained with MAGS also showed similar finding (2 d.f, $p<0.02$). Both the results are statistically significant. Recurrences were more in cases high pre chemotherapy vascularity. However this did not show a significant result when the assessment was done with MAGS (d.f =2, $p<0.1$). When comparing the local recurrence with MVD assessed using CD31 assay the results were statistically significant (d.f=2, $p<0.05$).

Response assessed by RI change correlated fairly with response assessed with use of MAGS. However the CD31 assay showed only slight correlation with response assessed with RI.

Conclusions: The study has validated the role of angiogenesis assessment in breast cancer, in which pre chemotherapy MVD was associated with poorer patient prognosis. This also suggests role of high vascularity as important step in tumor dissemination. Poorer response to chemotherapy predicted higher possibility of local recurrence.

Assessment of MVD also correlated with non invasive assessment done by color Doppler ultrasound which suggests that modality can be an adjunctive tool for the angiogenesis assessment.

Predictive factors of local recurrence-free interval in patients with Phyllodes tumor of the breast

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Background: Phyllodes tumor(PT) is a rare entity accounting for 1% of breast neoplasms with a high propensity of recurrence. Our study aims to identify factors that are predictive of local recurrence-free interval(LRFI) in patients with PT.

Materials and Methods: Clinical data of all patients diagnosed with a PT(n=57) treated at our tertiary care referral centre in South India between February 2010 and December 2017 were reviewed. The Pearson χ^2 test was used to investigate the relationship between clinical features of patients and histotypes of the tumours. Survival curves were obtained using the Kaplan-Meier method based on the log-rank test. Multivariate Cox regression analyses were performed to identify factors that are predictive of LRFI.

Results: Mean age was 38.3 years (SD=13.6) and the mean follow-up was 18 months (SD=13.5). The median tumor size was 5cm (IQR 3 and range 3-22cm). 64.9%(n=37) of the tumours were benign, 21.1%(n=12) of the tumours were borderline and 14%(n=8) of the tumours were malignant. Out of the 57 patients, 42.1%(n=24) patients underwent wide local excision, 26.3%(n=15) of patients (who had benign findings on FNAC) underwent excision. 31.6%(n=18) underwent mastectomy. Of the 57 patients, 17(29.8%) patients developed local recurrence, and one patient developed distant metastasis. Out of the 17 patients, 3 patients were not willing for completion surgery. For the patients who developed local recurrence, the median age at the diagnosis of primary tumor was 42(IQR 21) years, median duration prior to presentation was 134 days(IQR 309), and the median size of primary tumor was 7cm(range 3-22 cm). 41%(n=7) of the recurrent tumours were benign, 29.4 %(n=5) were borderline and 29.4 %(n=5) were malignant. The median LRFI was 20 months(range 7-60). Multivariate cox regression analyses showed that mitotic rate>10/hpf(p=0.04), stromal overgrowth(p=0.05), margin status(p<0.001) and pre-operative neutrophil-to-lymphocyte ratio(NLR, p=0.04) were significant predictors of LRFI.

Conclusion: In this study, patients with a high mitotic rate, positive margins, stromal overgrowth and NLR>3.5 were associated with lower rates of LRFI.

Title: Round Block Technique Of Breast Oncoplasty: An initial experience

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Background: Round block technique or doughnut mastopexy was first described by Benelli in 1990 and has since been widely used as a volume displacement technique in breast oncoplasty[1][2].It is particulary useful in small to medium breasts without ptosis and for tumors located near the nipple areola complex while confining the incision to the areolar margins [2].Even so its use has been extended to tumors in any quadrant of breast and multicentric tumors[3][4].Here we report our experience with the round block technique in two cases.

Methods: Round block was performed by first de-epithelializing a rim of skin around the areola. The tumor was then accessed via an incision through the de-epithelialized skin, leaving the nipple areolar complex vascularized on the dermal pedicle. The breast tissue was then dissected as much as possible to allow complete resection of the tumor and remodeling to cover the tumor defect. A purse-string was then done to approximate the incision opening to match the size of the contralateral areola. The neo-areola was recentralized and fixed circumferentially with non absorbable sutures. The aesthetic result was evaluated by comparing the pre and post operative photographs with regard to breast shape, nipple position and volume symmetry of bilateral breasts.

Results: Preoperative marking, Periareolar doughnut of skin de-epithelialized., Intraoperative tumor dissection, Post tumor excision, Photograph showing Circalage completed, Final result , Post operative photograph showing comparison with the contralateral breast, will be presented.

Conclusion: The aesthetic result was good in both patients using round block technique of breast oncoplasty .The technique is easily reproducible but patient selection is important.

Title –prognostic factors in carcinoma breast

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Background: Breast carcinoma is one of the most common malignancy in women. In recent years mortality from breast cancer has declined in the India , likely as a result of more widespread screening resulting in earlier detection as well as advances in standard practice to administer systemic therapy to all patients with lymph node-positive disease. Prognostic factors may select patients most likely to recur without adjuvant therapy and therefore potentially benefit from therapy. In addition, predictive factors may identify the appropriate therapy for an individual patient. Prognostic factors, i.e, those that predict the risk of recurrence or death from breast cancer, include number of positive axillary nodes, tumor size, tumor grade (histologic or nuclear), lymphatic and vascular invasion, and the estrogen-receptor (ER) and progesterone-receptor (PR) positivity.

Methods: The patients in “Neoadjuvant/Hormonal therapy group” will under core cut biopsy with assessment of Estrogen Receptor, Progesterone Receptor and Her-2-neu status before starting therapy. Patients tumour type and grade will be noted methods. Patients will be followed by histopathology for type and grading of tumour as well as margin status and hormonal receptor status

Results A total of 58 cases with proven breast carcinoma were observed. The ER, PR status, HER2NEU status, tumour size & stage of carcinoma were taken into consideration. A total of 21 out of 58 patients had ER,PR status positive out of these patients, there was 1 (4.76%) recurrence. While amongst 37 patients with negative ER, PR status, 5 patients (13.5%) had recurrences. 28 out of 58 patients had positive HER2NEU status. 5 (17.86%) out of these 28 patients showed recurrence. Amongst 30 patients who had a negative HER2NEU status, there was 1 (3.33%) case with recurrence. Using the TNM Staging, maximum cases were found to be in stage II (n=28) followed by stage I (n=15), stage III (n=11) & stage IV (n=4)

Conclusion: It was observed that patients with ER, PR positive status & patients with HER2NEU negative status had better prognosis. Prognosis of patients in stage I & II is found to be better than patients in stage iii and iv.

Title: Post Traumatic Necrotizing Soft Tissue Infection Of Breast- A Case Report

Authors: Saumya Agrawal, Bina Ravi, Amit Gupta, Ashish Gupta, Deepshikha, Mukund Mundra, Harindra Sandhu, Dept of Surgery, AIIMS, Rishikesh

Background: Necrotizing fasciitis is a rare infection of skin and underlying soft tissue. It primarily involves the extremities and rarely the breast. Primary NF of the breast in a non lactating otherwise normal female is still rarer. The authors are presenting a patient of necrotizing fasciitis of the breast after sustaining a penetrating injury. She was managed successfully with debridements and negative pressure wound therapies. To our knowledge only 19 such cases have been reported in indexed literature so far. This is also the eighth case of primary NF of the breast in a non lactating female without any associated immunosuppression which makes the basis of reporting this case.

Case: A 80 years old female patient presented to the surgical outpatient with history of a penetrating injury to her right breast. She was hit by a bull with its horns causing this injury over her right breast. For these complaints she was treated at private hospital where the wound was irrigated and sutured. She was given a course of antibiotics and NSAIDs. Three days following this she developed pain, foul smelling discharge, black discoloration of her breast along with gradual increase in size of the wound. She was not relieved of her symptoms even after aggressive non surgical treatment. She was referred to our centre three weeks following the incident. There was no history of illnesses like diabetes mellitus, hypertension and any other systemic illness.

She was not on any regular medications like steroids. There was no history of any substance abuse. On presentation, patient was conscious, oriented and afebrile. She had a pulse rate of 80/min, blood pressure 100/50 mmHg and respiratory rate of 18/min on room air. Examination of her right breast revealed a 10 x 8 cm ulcerated wound involving whole of the breast including nipple areola complex and extending to axilla (Figure 1). There was foul smelling discharge from the wound and the base of the ulcer was necrotic and there was presence of extensive slough on the edges of the wound. local temperature was raised and breast was tender on palpation. Laboratory investigations revealed haemoglobin of 11.8g/dl, total leucocyte count of 28000 cells/dl with neutrophilia. Blood glucose was 74 mg/dl at presentation. serum sodium was 125mEq/L and serum creatinine was 2.01. C-reactive protein was 179.5 at presentation with the calculated LRINEC score of 11, a high suspicion for necrotising fasciitis was raised and she was started on aggressive management. After proper resuscitation and optimization of the patient she was taken up for extensive debridement (Figure 2). Broad spectrum antibiotics were started. Serial debridements were done over next 4 days.

The general condition of the patient started improving with aggressive therapy. Negative pressure wound therapy was instituted to promote the healing for next 10 days (Figure 3). This was effective and the wound granulated well with no evidence of active infection. The patient was discharged in a satisfactory condition. At 2 months follow up, the patient is doing fine and the wound has healed well.

Conclusion: Primary NF of the breast is a rare infection. In general, it is associated with increased mortality and morbidity. Surgical debridement along with suitable antibiotic cover offers the only chance of survival. Hyperbaric oxygen and negative pressure wound therapy offers the chance of early wound healing and breast conservation.

Title: Excision of Benign Breast Lumps: Lessons Learnt

Authors: **Drs Asit Kumar[1]**, Chandan Kumar Jha[1], Prashant Kumar Singh[4], Shashikant Kumar[2], Ruchi Sinha[3], Manoj Kumar[5]
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Background
There are no universally accepted guidelines for excision/observation of benign breast lumps (BBL). Once a diagnosis of benign breast lump is achieved after triple assessment, further mangement is guided by the preferences of the surgeon and the patient. The aim of this study was to analyze our experience of excision of BBL and to develop a model to guide the management of such lumps.

Methods
We retrospectively analyzed the clinical, radiological, and pathological records of patients who underwent excision for a BBL at our institute between Jan.2015- Nov.2017. Patients who underwent core biopsy during evaluation were excluded. We categorized the histological diagnoses in two groups, Group I- fibroadenoma/fibrocystic disease; Group II- lesions at risk of recurrence (carcinoma, phylloides, granulomatous mastitis, microglandular hyperplasia).

Results
135 lumps were excised in 95 female patients whose mean age was 25.9$\pm$ 10.8 years. 94 lumps were BIRADS category II while 41 were BIRADS category III. FNAC ruled out malignancy in all (fibroadenoma-75, fibrocystic disease-41, benign epithelial cells-19). Median clinical tumor size was (3.4$\pm$3.2 cm)(range:1-20cm) and median pathological tumor size was 3.5$\pm$3.01 (1-19 cm). Histology showed the lumps to be fibroadenoma in 103(76.3%), fibrocystic disease in 13(9.6%), phylloides in 7(5.2%), carcinoma in 4(3.0%), granulomatous inflammation in 3(2.2%), microglandular hyperplasia in 4(3.0%) and lipoma in 1(0.7%). Group II diagnoses were equally prevalent in BIRADS II and BIRADS III category but there was a insignificant trend towards higher incidence of malignancy in lumps more than 5 cm (p=0.078). Incidence of Group II histological diagnosis was significantly high in lumps more than 3 cm.

Conclusion
Benign lumps more than 3 cm need to be excised, but after thorough evaluation, with a high degree of suscpicion for a non fibroadenoma/ fibrocystic disease pathology. Excision with a clear margin may help.

Title:- Correlation between clinico-radiological assessment and histopathological evaluation of response to neoadjuvant chemotherapy in breast cancer patients.

Authors:- Anupama Kumari, Pranjal Bhardwaj, Sanjeev kr. Gupta
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Background:- Neoadjuvant chemotherapy(NACT) is the standard of care in patients with locally advanced breast cancer (LABC) . Along with downstaging of tumor it also provides opportunity for aasesment of tumor response to chemotherapeutic agents. Response evaluation is usually done by clinical and radiological assessment during the course of chemotherapy but pathological response is considered to be the gold standard for which detailed histopathological examination of surgical specimen is required. Aim of the present study was to compare and correlate the clinical and radiological assessment of tumor response with the pathological response.

Methods:- Thirty patients with LABC were included in this study. Triple assessment was done to establish the diagnosis before starting NACT. After completion of NACT these patients were reassessed clinically and radiologically (mammography) and then were subjected to Modified Radical Mastectomy(MRM). Both response evaluation was done using Response Evaluation Criteria in solid tumors(RECIST). Pathological response was done by comparing true-cut and MRM specimen for reduction in cellularity of tumor cells using Miller-Payne criteria.

Result:- In this study 30% patients showed complete clinical response, 13.3% patients showed Complete Radiological Response and 26.7% patients showed complete pathological response.

Conclusion:- Results show that both methods of assessment of response (clinical and radiological) suffer from poor sensitivity rates(62.5% vs 37.5%). On comparison clinical response correlated better and was a better predictor of pathological response. Therefore, evaluation of clinical response is better and obviously cheaper than subjecting the patient to repeated imaging studies.

Title: Androgen receptor expression in breast cancer and its correlation with clinico-pathological parameters

Authors: Era Parasar, Sanjeev Kr.Gupta. Dept. Of General Surgery, IMS, BHU, Varanasi

Background: Breast cancer is the commonest cancer amongst women. It is a heterogeneous disease with varying molecular and clinical characteristics. Hormones play an important role in breast carcinogenesis and the prognostic and predictive role of estrogen (ER) and progesterone receptor (PR) is well established. The role of androgen receptors (AR) is still unclear. The aim of this study was to evaluate androgen receptor expression in breast cancer and correlate it with ER, PR, HER 2-neu status and clinico-pathological parameters.

Methods: 80 cases of histologically proven breast cancer were included in the study after clearance from the Institute Ethics Committee and informed consent. The following clinical and pathologic parameters were assessed; age, menopausal status, parity, family history, tumour size, lymph node status, histological type and grade of the tumour. Immunohistochemical evaluation was done for ER, PR, AR and HER 2 neu status and cases were labeled as positive if > 10% tumour cells showed nuclear staining.

Results: Clinical attributes of the study population showed that 50% of the patients were > 45 years of age and postmenopausal. Majority of the cases had tumors > 5 cm (70%) and lymph node involvement (65%). 72 cases (90%) were infiltrating ductal cancer. 60% had Grade 3 tumors and the remaining had Grade 2 tumors. Expression of the steroid receptors ER, PR and AR was observed in 32 (40%), 34 (42.5%) and 36 (45%) cases respectively. HER 2-neu positivity (3+) was seen in 28 cases (35%). 22 cases (27.5%) were triple negative of which 10 cases (45.4%) were AR positive. There was no significant correlation between age, parity, family history, tumor size and lymph node involvement with AR expression. AR expression was significantly higher in postmenopausal women (P<0.01). While the AR expression was higher in Grade 2 tumors as compared to Grade 3 tumors, the difference was not significant.

Conclusion: High AR positivity in the study group indicates that it has some role in breast carcinogenesis particularly in postmenopausal women. Larger data sets will help in defining better the interplay between the various receptors and the potential role of AR as a target of endocrine therapy .

Title:- The accuracy of core biopsy in determining histological grade and receptor status in invasive breast cancer.

Authors: Tanya Singh, Sanjeev Kr.Gupta. Dept. Of General Surgery, IMS, BHU, Varanasi

Background: core needle biopsy is one of the key components of “triple assessment” of breast lumps. The histological type,grade and receptor status as determined by the core biopsy help in therapeutic decision making in breast cancer patients particularly in selection of preoperative systemic therapy.The aim of this study was to determine the accuracy of preoperative core biopsy for assessing histological type , grade and receptor status in comparison to the histopathology of definitive surgical specimen.

Methods: After obtaining approval from the institute Ethical Committee and informed consent, 60 patients with a palpable breast lump which was diagnosed as invasive breast cancer were included in this study. Patients who were to receive neoadjuvant chemotherapy or who had biopsy done elsewhere were excluded.The tissue sections of core biopsy and definitive surgical specimen were assessed by two pathologists independently for histological type , grade and estrogen (ER) and progesterone (PR) and human epidermal growth factor receptor 2 (HER-2).

Results: There was perfect agreement between the core biopsy and histopathology of postoperative surgical specimen regarding the histological type.The concordance for tumour grade was only 63% being better for poorly differentiated cancers. Concordance between core biopsy and surgical specimen biopsy for ER, PR and HER – 2 status was 68.9% , 71.3% and 75.8% respectively.

Conclusions: The disparity between the assessment of grade and receptor status between core biopsy and definitive surgical specimen necessitates caution in using these results for determining therapeutic interventions. It is possible that the discordance may be due to intra-tumoral heterogeneity.

Title- Study of incidence and pattern of rare tumors of breast

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Background: Lesions in the breast vary from simple fibroadenoma to various commoner carcinomas like infiltrating ductal carcinomas, to rarer entities, such as angiosarcoma, hemangiopericytoma, nodular hidradenoma, pleomorphic variant of lobular carcinoma, medullary carcinomas and carcinoid tumors;

Methods: All the breast specimens submitted for histopathological evaluation over a period of 6 months were considered. All the breast cases, irrespective of the sex and age of the patient, were included. There were no exclusion criteria. Specimens were received and preserved in 10% formalin and were subjected to routine histopathological processing. Hematoxylin and eosin sections were studied and a morphological diagnosis was arrived at, based on the findings of the hematoxylin and eosin sections.

Results: A total of 25 specimen were received in the surgical pathology section of the department of pathology. Out of 25 specimen 9 excision biopsies and 16 mastectomy specimens were received, out of which12 mastectomy specimens were accompanied by axillary lymph node dissection.1(15.18%) inflammatory lesions, 1 (15.18%) fibrocystic changes and 20 (80.9%) tumors were encountered. Among the tumors, 10 (52.32%) were benign, one (0.42%) was borderline and rest were malignant. Out of the 10 benign tumors, 6 were fibroadenomas and 4 were phyllodes tumor., invasive duct carcinoma was the commonest malignancy . Four cases of infiltrating ductal carcinoma with neuroendocrine differentiation were seen. Six (9.23%) cases of invasive lobular carcinoma (ILC) were seen, out of which four cases were of the pleomorphic variant and two cases each were medullary and mucinous/colloid carcinoma. One case each of undetermined/unclassified carcinoma, apocrine carcinoma, cribriform carcinoma and tubular carcinoma found

Conclusion: It was observed that Breast cancer is strongly related to age with only 5% of all breast cancers occurring in women under40 years old.

Title: Clinico-radiologisc, Histopathological and Immunohistochemical study in Phylloides tumor.

Authors: Santna Hansda, Seema Khanna, Ashish Verma, Neeraj Dhameja. Institute of Medical Sciences, Banaras Hindu University, Varanasi

Introduction: Phyllodes tumors are very rare fibroepihelial components representing less than 1% of all breast neoplasm. They make 0.3 to 0.5% of female breast tumors.

Methods: The study includes 15 prospective cases and 15 retrospective cases, carried out in the Department of General Surgery,Pathology and Radiology between June 2015 to May 2017 including HPE specimens of last 4 years cases of phyllodes tumor (2011 to 2014).Clinical assessment of all cases was carried out and the details were recorded in the proforma. Core needle biopsy and Doppler USG for pulsatility index, resistivity index, Vmax was performed preoperatively. Histopathological examination and VEGF expression (IHC) was studied on the excised specimen postoperatively. IHC analysis for VEGF was also carried out on retrospectively retrieved archival specimen.

Results: The age of the patients of phyllodes tumor ranged from 30-60years with mean age being 45.36+_8.55 years. Majority of patients presented with tumor size >5cm.On Doppler ultrasound 73.33% patients had low pulsatility index, 80% had low resistivity index and 53.33% showed low Vmax. Benign phyllodes was most common histopathological finding (86.66%).High stromal cellularity was found in 3 patients only.73.33% of tumor have VEGF expression and 26.67% did not show any expression for VEGF.It showed statistical significant correlation between VEGF expression and tumor size ($p = 0.001$) and with stromal cellularity ($p= 0.001$).100% patients with low pulsatility index and 91.7% with low resistivity index showed VEGF expression. No significant correlation with Vmax.

Conclusion: No single histopathological feature could reliably predict the behaviour and combination of tumor size, margin, atypia, stromal overgrowth and mitotic activity is helpful. Histopathological examination is the golden standard for the diagnosis of phyllodes tumor. Doppler ultrasound may guide in differentiating a malignant phyllodes from benign and in deciding the margin of excision.

Case series of Carcinoma Breast with Thyroid pathology (Ca thyroid)

Authors: Akanksha Chikhlikar Aich, Piyush Tripathi, Sanjit Agarwal, SoumendraNath Ray, Rosina Ahmed.

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Introduction-
The introduction of PET-CT based staging for locally advanced breast cancer is predicted to increase the pickup of pathology that would otherwise remain unknown. Our institutional staging protocol was changed from CT thorax and abdomen with bone scan, to PET-CT, on Jan 1st 2017. We report a series of patients with thyroid pathology identified on PET-CT in a 1 year time period. Only a few cases of synchronous thyroid and breast cancer have been published. The first report on this dual malignancy was written by Billroth in 1889. According to the data, the incidence of a second primary tumor in cancer patients is approximately 10%.

Materials and methods-
This is a retrospective analysis of the patients treated in TMC, Kolkata in 2017 and the data were collected from the institutional Redcap database. Of the 600 patient operated in the TMC last year approx 40% were LABC and for which staging was done by PET-CT.

Results-
PET-CT identified 7 patients with thyroid pathology. Out of these, 2 had papillary ca of thyroid and underwent total thyroidectomy, 1 had follicular neoplasm but refused thyroid surgery, 1 had benign follicular nodules, 1 had benign adenomatous nodule, 1 had atypia and 1 had benign diffuse enlargement of thyroid. All had ca breast.
One patient of Papillary ca thyroid, MRM with Total thyroidectmy was done in the same setting and in other Axillary clearance with total thyroidectmy was done in the same setting as she was operated outside in Bangladesh. Rest of the patient are in follow up.

Conclusion-
Previous studies have mainly focused on possible increases in the incidence of contralateral breast carcinoma. However, the risk of concurrent thyroid carcinoma among women with breast cancer has not been explored in recent years they remain a possibility; therefore, more attention should be paid to these cases.

Keywords- breast cancer, PET CT, Papillary Ca.thyroid.

Understanding and practices of gynaecologists related to Breast cancer screening, detection, treatment and common breast diseases: a study from North India

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Background: Knowledge of breast cancer risk factors and screening practices in a community is largely influenced by practicing gynaecologist in that area, as they are the first contact point for women with breast diseases. We assessed the understanding and knowledge of gynaecologists about breast cancer: screening, risk factors, clinical signs, management and common benign breast diseases.

Methodology: This cross-sectional study was carried out in Uttar Pradesh from April to August 2017. 152 gynaecologists were assessed using a self designed questionnaire to assess knowledge of risk factors, clinical signs, screening practices and management of breast cancer and common benign breast diseases. Further the results were compared based on their education: undergraduates UG doctors {no-residency in obstetrics & gynaecology} Vs Post graduates PG doctors {residency in obstetrics & gynaecology}.

Results:69.1% and 87.5% of gynaecologists possess excellent-very good knowledge of risk factors and clinical signs of breast cancer respectively. The knowledge of PG Doctors seems to be better in this aspect than UG doctors (p=0.05). 85% participants were aware that breast cancer screening decreases breast cancer related mortality and 61% considered CBE as most relevant screening investigation(66.1% PG participants and 41.9% UG participants; p=0.04). 30.3% regularly offer breast cancer screening at their centre. 58.5% did not consider screening mammography as cost effective for their patients (57.9% PGs and 61.3% UGs; p=0.72) and 41.4% considered it to be a time consuming process (39.7% PGs and 48.4% UGs; p=0.38). 99.3% like to follow a patient with familial breast cancer by themselves and 0.7% like to refer them to specialist. 52% gynaecologists were convinced of BCS as a surgical option but 50% feared leaving diseased breast behind in BCS.

Conclusion: Despitethat the knowledge regarding risk factors, clinical signs and treatment of breast cancer and benign breast diseases was found adequate amongst the gynaecologists, this did not apply totheir clinical practice. Structured and continuous training of gynaecologists may improve outcome of patients with breast diseases.

Title: To assess the feasibility and oncological safety of axillary reverse mapping in early breast cancer, using premixed autologous serum and indocyanine green dye flourescence technique and an in-house near-infrared fluorescence imaging system and methylene blue dye.

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Background: Lymphedema remains as the most troublesome sequel following axillary dissection in breast cancer patients. Incidence of lymphedema ranges from 11-30% of patients undergoing axillary lymph node dissection (ALND). Axillary reverse mapping (ARM) is a technique described to map and preserve arm lymphatics, to reduce the incidence of lymphedema after ALND. Preserving the arm nodes with metastatic tumour is a major concern.

Aim : To determine the metastatic rate and compare the detection rates of arm lymphatics and arm nodes, between premixed autologous serum and indocyanine green (ICG) dye, using an in-house near infrared (NIR) fluorescent imaging system and methylene blue dye, in patients with early breast cancer.

Methods: This IRB approved study included 52 patients with early breast cancer, undergoing ALND, equally allocated into two groups. In one group standardized solution of patient's serum and ICG was injected intradermally posterior to the proximal part of the arm inter-muscular groove and in-house NIR imaging system was used and 2ml of methylene blue was injected at the same site in the other group. The identified ARM node is sent for histo-pathological examination to detect metastasis.

Results and conclusion: After identifying the accurate site of injection, the identification rate of arm lymphatics and arm lymph node using patient's serum and ICG and methylene blue were comparable. Metastatic rate in the arm node was low (5.8%). Thus ARM technique is feasible and safe in patients with early breast cancer.

Title: Comparison Of Psychological Outcomes In Breast Cancer Patients After Breast Conservation Surgery Versus Mastectomy

Authors: Ankit Gangwar, Gitika Nanda Singh, Vinod Jain
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Introduction: Quality of life (QOL) is an important indicator of treatment efficacy in breast cancer patients. For Early breast cancer (EBC), mastectomy is usually chosen option both by patients and doctors. Post mastectomy body image changes are often associated with decreased quality of life (QOL). The aim of this study is to compare the QOL in patients undergoing BCS versus MRM for early breast cancer.

Materials & Methods: 64 patients with EBC were enrolled in either group (BCS or MRM) based on informed choice by patients and followed up post-op (FU1), after completion of chemotherapy i.e. 6 month after surgery (FU2) and after completion of treatment i.e.12 months after surgery (FU3). Translated copies of European Organization for Research and treatment (EORTC) QLQ-C30 to measure general QOL and QLQ-BR23 for breast cancer specific symptoms were filled by patients.

Results: After completion of treatment i.e. in follow-up 3 patients in BCS group had better global health status score (BCS80.17±9.21 Vs MRM 67.65±13.90, P<.001), physical functioning(BCS 80.97±7.58 Vs MRM 71.23 ± 10.95,P=.003) , role functioning (BCS 83.90± 10.78 MRM 72.99± 16.90,P=.003), emotional functioning(BCS 79.70±9.02 Vs MRM 69.98±10.31,P<.001), social functioning(BCS 80.18±9.46 Vs MRM 69.09±20.76,P=.014) except cognitive score(BCS 68.06±5.71 Vs MRM 73.89±16.34,P=0.542) with better body image(BCS 74.32±9.41 Vs MRM 64.42±17.48,P=0.018) and future prospective score (BCS 76.32±9.57 Vs MRM 58.25±17.22 ,P<.001). Symptom score such as fatigue in FU1(BCS 37.68±133.89 Vs MRM 45.82±19.55,P=.027) and FU3(BCS 15.97±15.56 Vs MRM 24.81±8.77,P<.001), appetite loss score in FU2 (BCS 16.56±20.83 Vs MRM 27.02±19.02,P=.022), arm symptoms in FU1(BCS 10.77±11.00 Vs MRM 20.32±15.40,P=.046) and FU3(BCS 7.92±11.38 Vs MRM 14.66±14.61,p=.023) was found to be better in BCS than MRM group.

Conclusion: BCS for early breast cancer has a better impact on Quality of Life in late postoperative periods. Also, Quality of Life improves progressively with time.

Title: Dosimetric comparision and clinical feasibility of Deep Inspiration Breath Hold (DIBH) technique in left sided Breast cancer patients.

Authors: Resham Srivastava, Shagun Misra, SA Yoganathan, S.K.Senthil Kumar, KJ Maria Das, Mranilini Verma, Punita Lal

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Background: A slice of heart, especially the region of left anterior descending coronary vessel (LAD), comes into the beam trajectory when irradiating left sided breast cancers. This may have long term cardiac implications. To keep the heart away from the bi-tangential beams while the radiation beam is on - (DIBH) technique is practiced. We plan to compare this technique with the standard practice of free breathing .

Material and Methods: Left sided breast cancer patients after BCS or post mastectomy were enrolled as per our institutional DIBH protocol. We have analysed the dosimetric comparision of cardiac and LAD doses and efficiency of the process.

Results: We have trained left sided breast cancer patients of age< 65years of age . Seven patients were trained for the procedure and out of these 3 patients underwent treatment according to DIBH technique. Among remaining 4 patients 2 were unable to hold their breath inspite of 3 training sessions, in one on planning scan heart was already out of tangential trajectory in free breathing and in one no dosimetric benefit was observed on plan. Therefore DIBH technique was abandoned in these 4 cases.

Training time as an OPD exercise was 15 minutes, to capture free breathing and breath hold scan was 45 minutes. Time taken to plan by the physicist was 30 minutes. First day treatment setup and treatment time was45 minute and rest of days it was 25 minutes.

Average of mean dose received by heart in free breathing versus breath hold was 5.5Gy versus 2.5Gy and mean LAD dose received was 33Gy versus 22Gy.

Conclusion: Radiotherapy of the left breast in DIBH can be incorporated into daily routine. Although time taken by DIBH technique is more than usual routine patients but is associated with significant dose reduction to the heart and LAD.

Title: Unusual Breast Pathologies Masquerading As Breast Carcinoma

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Background: Unusual pathologies of breast mimicking breast cancer pose a great diagnostic & often therapeutic challenge. It is optimal to make correct pre-operative diagnosis and differentiate them from breast carcinoma for appropriate management. We aim to discuss our experience in last one year based on a series of such cases.

Methods: This is a descriptive analysis of seven patients with unusual breast pathology, managed in Department of Endocrine Surgery, King George Medical University from June 2016-October 2017.

Results: We had seven rare cases of which Primary Osteosarcoma of breast (n=1), Metaplastic carcinoma (n=2), Non-Hodgkins Lymphoma(NHL) (n=1), Fibromatosis(n=1), Plasma cell Mastitis (n=1), Arterio-Venous Malformation of Breast {AVM} (n=1)

SNo	Age/ Sex	Core Biopsy	Treatment/ Surgery	Final HPE	Adjuvant Treatment	Follow-up
1	60/F	Mesenchymal Tumour	Modified Radical Mastectomy (MRM)	Osteosarcoma	Chemotherapy & Radiation	6 months recurrence Then lost to follow up
2	30/F	Mesenchymal Tumour	Oncoplastic surgery	Fibromatosis	NIL	1.5 years follow up no recurrence
3	35/F	Not Done	Simple Mastectomy	Arterio-Venous Malformation	NIL	1.5 years follow up no recurrence
4	35/F	Infiltrating ductal Carcinoma (IDC)	Left MRM	Metaplastic Carcinoma	Chemotherapy	1 year follow up recurrence free
5	37/F	Metaplastic carcinoma	-	-	-	Lost to follow up
6	50/F	NHL	Chemo – therapy	-	-	Lost to follow up
7	45/F	Plasma cell Mastitis	Lumpectomy	Plasma cell Mastitis	Nil	1year follow up no recurrence

Conclusion: Cautious interpretation of clinical, radiological & pathological parameters is necessary for more accurate diagnosis & management of these rare breast pathologies.

Title: Apparently Inoperable Breast Cancers! Feasibility Of Aggressive Resections

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Background: Aggressive breast malignancies extensively involving adjacent vital structures are often inoperable, even after neoadjuvant therapies. This series of 3 cases aims to assess feasibility of aggressive surgery in patients with large tumors with a multidisciplinary approach.

Methods: Three patients with malignant breast tumors of different histology, involving chest wall(n=2) & axilla(n=1) were operated between September 2017-December 2017.

Discussion:

Patient-1: 40 year old lady presented with huge lump over left upper chest. She had undergone lumpectomy in 2004 & second surgery{Modified Radical Mastectomy(MRM), subsequent LD cover} 18 months back for recurrence. She noticed lump 12 months back over same area, diagnosed as recurrent malignant phyllodes tumor of left breast. On imaging, tumor invaded left 2nd-4th ribs and costal pleura, bulky fixed axillary nodes indenting axillary vessels. She underwent composite resection of lump & chest wall with partial-pleurectomy followed by prosthetic reconstruction. Adjuvant radiation is planned.

Patient-2: 30 year old lady who underwent MRM in 2016, presented with fungating mass since 2 months, diagnosed as recurrent leiomyosarcoma of right breast. On imaging, tumor was indistinctly involving right 2nd-5th ribs. She underwent wide excision of tumor. Ribs were successfully preserved. Defect wasn't reconstructed primarily in view of infection/edema. After raw area is apt, reconstruction with LD is planned.

Patient-3: 32 year old lady diagnosed with right breast carcinoma in 2014, underwent MRM elsewhere. HPE revealed triple negative IDC(pT2N0M0). She defaulted on adjuvant therapy and developed large fungating right axillary mass fixed to chest wall in July 2017. She underwent 2 lines of NACT followed by WLE of axilla with LD reconstruction of axillary wall.

Conclusion: Well-planned, aggressive surgery involving multidisciplinary teams give a good outcome in tumors which are seemingly inoperable. Selection of appropriate cases who benefit from such resections is the key to successful and meaningful outcomes in such scenarios.

Title: Primary angio-sarcoma of breast a rare case report

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Primary angiosarcoma (AS) of the breast is an extremely rare tumor. Radiological findings are non-specific. Fine needle aspiration (FNA) yields a high false negative result so a tissue biopsy is mandated for a confirmed diagnosis. Surgical removal is the mainstay of the treatment. Role of adjuvant chemo radio therapy is debatable. Prognosis is usually poor. We report a case of a seventy years old lady presenting with a huge left breast mass. Sono-mammography revealed a thick walled cystic mass filled with turbid fluid in left breast. FNA from elsewhere was reported as ductal carcinoma. As the patient presented to us, we confirmed the mass as AS on trucut biopsy. The patient was treated with WLE following which she was referred for adjuvant radiotherapy. Follow up on second postoperative month was uneventful.

Title: Indian Surgeon's Perspective Regarding Breast Conservation Surgery

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Introduction: Most women with early breast cancer have a choice between Mastectomy and Breast conservation surgery (BCS), and the decision making is a complex process both for the patient and the surgeon. BCS has two aspects oncological clearance and aesthetic preservation. .Surgeons play an important role in the decision making.We aimed to study Indian surgeon's perspective regarding breast conservation surgery

Materials & Methods: We developed closed end questionnaire with 20 questions regarding various aspects of BCS. The Questionnaire was developed by two endocrine and Breast surgeons trained in Questionnaire development. The link to the questionnaire was sent by emails to various general surgeons, oncosurgeons and breast surgeons around India and they filled the questionnaire at www.sgpgibreast.in Website. The authors had access to the responses once the questionnaire was submitted.

Results: 81 surgeons from all over India participated. Demographic details are provided in Table1.

Table 1 : Frequency Distribution of Demographic Variables

Variable's	Frequency	Percentage
Age		
20-30	27	33.3
31-40	33	40.7
41-50	11	13.6
>50	10	12.3
Sex		
Male	66	81.5
Female	15	18.5
Education		
Specialty	49	60.5
Super Specialty	31	38.3
Other	1	1.2
Clinical practice in years		
0-5	40	49.4
5-10	14	17.3
>10	27	33.3

Chi square test and Fischer test was used for analysis. When Female and Male surgeons were compared there was no signifant (<0.05) response difference in 14 questions.

Conclusion: There are considerable differences among surgeons depending on the level of training and facilities available in their institution. It is an ongoing study and final results are awaited.

Ipsilateral breast tumor recurrence following breast conservation surgery: Are the outcomes same for primary surgery and surgery following neoadjuvant chemotherapy?

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Introduction: Breast conservation surgery (BCS) is the standard procedure for majority of breast cancer patients. However, BCS rates are lower in our country compared to the western world due to socio-economic reasons and advanced disease at presentation. Many such patients are treated with neoadjuvant chemotherapy (NACT), following which the safety of BCS is not very well established. This retrospective study compared the pathological and outcome parameters of primary and post-NACT BCS.

Methods: All non-metastatic breast cancer patients undergoing BCS from 2011-2015 with a minimum 1 year follow-up were included. Outcome parameters in terms of margin infiltration, ipsilateral breast tumor recurrence (IBTR) and local recurrence free survival were compared between patients undergoing primary and post-NACT BCS.

Results: Inclusion criteria were met by 129 patients of whom 95 underwent primary and 34 post-NACT BCS. Patients in both groups underwent similar multi-modality treatment as per institutional protocols. Sixty nine percent patients had cT2/cT3 disease with significantly higher disease stage seen in post-NACT group. Post-NACT patients more frequently required oncoplastic volume displacement or replacement surgery(p=.002). Re-excision of infiltrated margins was needed more frequently in primary BCS c.w. post-NACT BCS group(14.4% vs 9.6%; p=0.40). In mean follow up of 30.6 months, IBTR was seen in 9.6% post-NACT patients, c.w. 2.1% primary BCS patients(p=.114). Recurrence rates didn't vary significantly with menopausal status, hormone receptor & HER2neu status or re-excision of margins in either group; or with downstaging in post-NACT patients. The stage-wise local recurrence-free survival didn't differ significantly between the groups.

Conclusion: Outcomes are similar in suitable patients undergoing primary or post-NACT BCS. Post-NACT BCS is safe even in large and T4 tumors, though many require oncoplastic procedures for satisfactory cosmesis. In select patients with advance stage disease, the benefits of BCS can be offered with the help of NACT, without compromising the chances of cure.

A Comparison of Digital Mammography and Digital Breast Tomosynthesis findings with Histomorphological characteristics of Breast Cancer

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Background: Digital mammography (DM) and digital breast tomosynthesis (DBT) features of breast cancer are important tell-tales of tumor characteristics and behaviour. Some series have shown that DBT helps delineate features of breast lumps, often better than DM. In this prospective study, we correlated the DBT features with histomorphological characteristics of breast cancer specimens.

Methods: From January 2016, 150 consecutive patients undergoing breast imaging had their DM and DBT reviewed separately by two radiologists independently, who were blinded of the cytology/histology of the lumps and the original DM/DBT reporting. Out of these, patients with final histopathology of breast cancer 93 were recruited for this study, and their DM and DBT findings were compared, and were correlated with histomorphological features.

Results: Ninety three patients were included in this study. Significant inter-observer variability was seen in interpreting both DM and DBT. The reporting of mammographic findings also varied significantly between DM and DBT reporting of each individual observer. DBT significantly increased the forced BIRADS scoring ($p<.001$) compared with DM. Lesion morphology was better defined in DBT compared to DM. Margins of masses were more often spiculated in hormone positive tumors. Higher intensity of HER2neu scoring were associated with calcifications more frequently. Margins of mass didn’t vary significantly with HER2 scores, though frequency of spiculated margins increased with increasing intensity of HER2. Forced BIRADS scores varied significantly ($p<.001$), with more intense HER2 immunostaining being more frequently associated with BIRADS 5 score. Presence of calcifications did not vary significantly with presence of DCIS or LVI. Triple negative breast cancers had lower BIRADS score and more frequently were seen to have decreased BIRADS score on DBT than DM compared to other molecular subtypes.

Conclusion: The DM and DBT features vary with the intensity of HER2 immunostaining, hormone receptor positivity and molecular subtype of breast cancer. DBT upstages BIRADS score and lesion morphology without any significant correlation with histomorphological features

Frozen section histology aids in single step oncologically safe and cost-effective breast conservation surgery

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Background:
Obtaining uninfiltrated margins is vital in achieving low ipsilateral breast tumor recurrence(IBTR) rates following breast conservation surgery(BCS). Utility of intra-operative frozen section histology(FS) is still debatable due to added costs of the process and increased operating time. In this retrospective analysis, we studied the ability of FS to avoid re-operations in those with infiltrated margins and its cost-efficacy.

Methods:
Patients undergoing BCS during 2011-2015 with a minimum follow-up of 1year were included. Based on FS and/or paraffin histopathology(PS), patients with infiltrated margins, extensive DCIS necessitating mastectomy, re-operations avoided by FS section and its cost-efficacy etc. were evaluated.

Results:
Of 144 patients, based on FS, 17(11.8%) required margin(s) re-excision; 9(6.25%) needed mastectomy (extensive-DCIS/infiltrated margins after re-excision). Twenty-six(18.05%) patients were thus spared of re-operations by using frozen section. Two(1.4%) patients with un-infiltrated margins on FS needed re-operation for infiltrated margins on PS. Considering the costs (144FS+2 reoperations) and savings (26avoided reoperations), FS usage was 5.5 times more cost-efficacious than PS for achieving un-infiltrated margins. Cost incurred per saved re-operation by FS was Rs5438. Probability of IBTR in patients who underwent margin(s) re-excision was lesser than those who didn't need re-excision (00 vs 04, p=0.056) and didn't vary with size of tumor.

Conclusions:
Frozen section usage can thus facilitate single-step safe BCS by avoiding re-operation in those with infiltrated margins, hence improving the acceptability of BCS in Indian patients, even in those with relatively larger tumors, for whom, the possible need and costs of reoperation are major deterrents against BCS.

Title: Histomorphological Correlation Of Her2/Neu Status Of Breast Cancer With Digital Mammography And Digital Breast Tomosynthesis In Self-Detected Tumours

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Background: Digital breast tomosynthesis (DBT) helps delineate features of breast lumps, often better than digital mammography (DM). Patient detected lumps are the most common presentation of breast cancer in India and other developing countries, rather than screen detected tumors, which form the basis of majority literature published from the western world. Immunohistochemistry (IHC) plays a major role in deciding treatment regimens for breast cancer patients and are often expensive and, sometimes, not readily available in developing countries. DM and DBT can play a major role in the initial phases of planning of management of breast cancer patients, even before the histopathology and IHC reports are available, as certain mammographic features correlate to some IHC characteristics. HER2Neu is one such important marker.

In this prospective pilot study, we correlated the DM and DBT features with HER2Neu status of these palpable tumors, to see if HER2Neu status of 0, 1+, 2+ and 3+ have any distinguishing features on mammography, and to see if either DM or DBT can delineate tumors based on HER2Neu status.

Methods: Between January to May 2016, 100 consecutive patients with self-detected lumps undergoing breast imaging for suspicion of malignancy had their DM and DBT reviewed separately by two radiologists independently, who were blinded of the cytology/histology of the lumps and the original DM/DBT reporting. Patients who had prior intervention core, incisional or excisional biopsy were excluded because this which would cause errors in reporting due to distortion in imaging. Patients whose immunohistochemistry reports were unavailable or inadequate were excluded. Patients whose final histopathology was benign were excluded. Sixty three patients remained with histology proven breast cancer and were recruited for this study, and their DM and DBT findings were compared, and were correlated with HER2neu status (scores 0 to 3+).

Results: DBT significantly changed forced BIRADS scoring ($p<.001$), lesion morphology ($p<.001$) and margin status ($p<.001$) compared to DM. Lesion morphology varied significantly on DBT with HER2neu score ($p=.032$). HER2-0 tumors mostly presented as a mass without microcalcifications (93.8%) whereas HER2-3+ tumours were equally likely to present as mass with (46.2%) or without (46.2%) microcalcifications. Margins of mass didn't vary significantly with HER2 scores, though frequency of spiculated margins increased with increasing intensity of HER2. When present, the morphology of calcification varied with HER2 status ($p=.008$). No significant difference in the number of lesions detected, lesion visibility, associated architectural distortion, skin or trabecular thickening.

Forced BIRADS scores varied significantly on DBT ($p<.001$), with more intense HER2 immunostaining being more frequently associated with BIRADS 5 score, but not on DM ($p=.449$). HER2 status did not vary significantly with cT, cN stages, histology type, grade, presence of DCIS or LVI. HER2 0 and 1+ tumours were more frequently associated with estrogen receptor negativity (68.8% and 67.7% respectively) than 2+ and 3+ tumours (25% and 34.6% respectively, $p=.042$).

On sub-group analysis, there were 11 triple negative breast cancers (TNBC) with HER2-0 score. All of these presented as masses without microcalcifications (lesion morphology- $p=.014$) and more commonly had well defined (27.3%) margins (margin variability $p=.001$) more commonly having well defined (27.3%), obscured (9.1%) or microlobulated (36.4%) margins and less commonly spiculated margins (9.1% vs 57.7%) compared to other subtypes. They had lesser BIRADS 5 presentation than other subtypes ($p<.001$). Skin thickening and associated architectural distortion were significantly infrequent ($p=.016$ and .005 respectively). When TNBCs with HER2-0 and 1+ or TNBC with HER2-0, 1+ and 2+ scores were clubbed together, lesion morphology was no longer significantly different from other molecular subtypes ($p=.347$ and $p=.748$, respectively).

Conclusions: The DM and DBT features vary with the intensity of HER2 immunostaining and though HER2-0 and 1+ are clubbed together as HER2neu negative cancers, they can differ in the tumor morphology.

Title: Breast Cancer In Uganda (Africa) And Barriers To Care: Synospsis Of Literature And Situational Survey.

Author: Dr. Kintu Luwaga Ronald. Mulago National Referral Hospital / Makerere University - College of Health Sciences - Kampala, Uganda.

Background: Uganda has about 40million people. Breast cancer is the second commonest cancer among women and its incidence has risen to 45/100,000 (2016). About 1500 new cases emerge annually, but the majority don't reach hospital. Of those who get to hospital, about 80% present with late-stage disease. There is also a high dropout rate from therapy. The 5yr cumulative breast cancer survival is 51.8% (2015).

Methods: Literature was reviewed for key statistics of breast cancer in Uganda and Africa, and a situational survey conducted in Uganda by direct assessment and interviews of selected breast cancer care stakeholders, as well as review of relevant registers and websites.

Results: Many still hold beliefs that prevent them from seeking proper care, including a fatalistic attitude. Alternative medicine still has a profound influence but is unregulated. Patients opt for it out of desperation and pressure. Inadequate awareness and lack of consistent and resource-appropriate screening limits early detection. Inadequate diagnostic facilities, where by only 13 Laboratories offer histopathology examination and only 3 centres do Immunohistochemistry (IHC). Genetic screening remains unavailable. The country has few (32) pathologists and the Uganda Cancer Institute has none.
Treatment costs are hardly affordable. Health insurance is very limited, and costs are escalated by long and repeated travels for treatment. Only 2 specialised breast cancer treatment centres exist in the country, the newer one operates at minimal capacity. There is a severe deficiency of personnel, with only 5 qualified medical oncologists to treat all cancers and 5 surgeons in the specialised breast care centres. Radiotherapy services have been erratic, until recently. The public health sector is weak and lacks an aggressive National cancer control program. There is inadequate research and information regarding breast cancer across Africa as a whole, associated with absence of a clear scientific policy to standardise therapy.

Conclusion: The Incidence of breast cancer is increasing rapidly while survival rates remain low. There multiple barriers to care which include negative and fatalistic beliefs, lack of access to diagnostic and treatment facilities, and qualified personnel. These findings lay a basis for a detailed study into the factors associated with barriers to breast cancer care and the possible solutions.

Fungating Breast Cancer: Clinicopathological Profile and Outcome in a Developing Country

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Introduction: Fungating breast cancer (FBC) is a rare entity in developed nations. But such phenomenon is not uncommon in our country. The aim of this study is to review clinico-pathological profile and outcome of FBC in a developing country.

Materials & Methods: This is retrospective review of prospective data of Breast cancer (BC) patients managed at our institute (Jan 2005 - Dec 2015). Clinico-pathologic profile management details and outcome were analyzed. Kaplan Meier method was used to determine overall survival (OS). Log rank test was performed to compare survival in various subgroups.

Results: Seventy nine patients were detected to have FBC constituting 3.3% of BC and 24.8% of T4b lesions. Mean age of patients was 55 $\pm$ 11 years. 96% were women and 67 % belonged to rural areas. 75 % women were postmenopausal. Mean duration of lump was 16$\pm$11 months. The mean tumor size was 8+ 2 cm. 87 and 40 % of patients had axillary lymph node and distant metastases respectively. TNM stage distribution was- IIIB: 55.7, IIIC:2.5, and IV:41.8%. Histology was infiltrating duct carcinoma in all, Grade I- 3%, II- 45%, and III- 52 %. Hormone receptor (HR) positivity was noted in 44% and HER2/neu over-expression in 39 % tumors, whereas 32% were triple negative. Overall 95% patients received combination chemotherapy (anthracyclins and taxanes). 86 % received upfront chemotherapy, (stage III- 45 and Stage IV- 41%) whereas 9% received after breast surgery. 48 and 11% patients receiving neoadjuvant chemotherapy had partial and complete response respectively. Five patients (6.3%) died during chemotherapy remaining all completed the prescribed chemotherapy cycles. Almost all had reduction in ulcer size following chemotherapy. Overall 91% patients underwent breast surgery, 9% had upfront surgery and remaining after chemotherapy. 76% received loco-regional radiotherapy 5% before and 71% after surgery. 97% HR positive cases received adjuvant hormonal therapy (letrozole-66, tamoxifen- 31%). Median follow-up was 16 (2-93) months. Median survival was 36 months and 5 year OS was 40%. Survival in Stage III (53%) was significantly better (p=0.005) than IV (22%). Age (p=0.90), menopausal status (p=0.91), grade of tumor (p=0.18), HR positivity (p=0.1), and HER2neu over expression (p=0.43) were not found to be significant for OS.

Conclusion: Multimodality therapy in FBS results in good symptom palliation and comparable survival to those Stage III and IV patients not having fungating tumors.

Title: Neuroendocrine tumour of the Breast

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Abstract:

Primary neuroendocrine carcinoma of the breast (NECB) are rare with incidence under 0.1% of all breast carcinomas and under 1% of all neuroendocrine carcinomas.
We present here a case of lady aged 67 yrs , presented with bloody discharge from left nipple since 10 months with a small retroareolar lump of size of less than 1 cm. Mammography revealed 5.1x5.9 mm high density mass about 2-4cm deep to nipple (BIRADS- 4a) .
USG guided biopsy (vacuum assisted) revealed carcinoma breast (NST) with neuroendocrine differentiation.
Immunohistochemically, tumour cells were positive for chromgranin A , ER, PR and focally positive for synaptophysin.
Patient underwent central core excision with sentinel lymph node biopsy with HPE negative for malignancy.

Title: Infected Epidermoid Cyst Masquerading As Breast Abscess In A Male.

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Male breast abscess is a rare occurrence. Few cases have been reported earlier in association with human immunodeficiency virus infection, salmonella infection, and breast cancer. Epidermoid cyst also known as Epidermal inclusion cyst of the male breast is also an infrequent entity. Remarkably, male breast abscess resulting as a complication of epidermoid cyst has not been reported yet.

The diagnosis of male breast abscess is clinical. The typical inflammatory skin changes can be noteworthy clue to the diagnosis. Ultrasonography and fine needle aspiration cytology are useful adjuncts in making diagnosis and finding the probable etiology of the abscess. The treatment of simple male breast abscess is incision and drainage along with daily dressings. In the presence of infected epidermoid cyst as the underlying pathology, the cyst wall should be completely excised to prevent recurrence. We describe an interesting case of male breast abscess occurring due to infected epidemoid cyst which was treated adequately with incision and drainage along with cyst wall excision and post-operative regular wound dressings.

Title: Patterns of failure observed in central/Inner Vs. outer quadrant tumors in a retrospective audit of an unselected breast cancer patient population

Authors: Deepak Kumar, Mohd. Suhaib, Rajan Yadav, Punita Lal, Sushma Agarwal, Shagun Misra, S. K. Misra, Amit Agarwal, Gaurav Agarwal, A.K. Verma, Anjali Misra, Gyan Chand and Shaleen Kumar

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Background: An audit comparing the overall patterns of failure with mapping of regional nodal failure patterns in breast cancer patients presenting with central/inner (C/I) vs. outer quadrant, with/without axillary node positivity and no internal mammary chain (IMC) radiotherapy given.

Methodology: Records of 307 breast cancer patients treated between Jan'10 and July'13 with either conventional fractionation (CFRT) (50Gy/ 25fr) or Hypofractionation (HFRT) (40Gy/15) to chest wall/ whole breast ± SCF ± Axillary region were retrospectively accessed. SCF RT was given in any node positivity and axilla in N3 disease/ inadequate dissection/ physician preference. IMCRT was not used in any patient. Analysis was done in Sept'17.

Results: At a median follow-up of 49 months (1-91mos), 307 patients, 147 (48%) received CFRT and 160(52%) received HFRT. Median age was 48yrs. 151 patients (49%) underwent BCS and 156 patients (51%) MRM. 110/307 (36%) patients presented with C/I quadrant tumors and 197/307 (64%) presented with outer quadrant tumors and 157/307 (51%) were axillary node positive. During follow up a total 54/307 (18%) presented with distant failure, as the most common site, 20/110 (18%) in C/I and 34/197 (17%) outer quadrant tumors (p=0.35). Also, 13/307 (4.3%) presented with loco-regional recurrences (LRR) out of which, 1/110 (0.9%) in C/I and 12/197 (6%) in outer quadrant tumors and among all LRR, 46% in ipsilateral chest wall, 20% ipsilateral breast, 8% axillary and 16% in SCF. There were no clinically obvious recurrences observed in the IMC.

At 5 yrs OS, was 66% for C/I and 64% in patients with outer quadrant tumors. Also, lost to follow up with or without disease were 32% (35/110) and 25% (49/197) in patients with C/I and outer quadrant tumor respectively.

Conclusion: In this audit, patterns of failure were no different between C/I and outer quadrant lesions, most common regional failure was ipsilateral chest wall and there were no overt IMC relapses. .

Keywords: Internal mammary chain (IMC), Regional nodal irradiation (RNI), carcinoma breast

Abstracts

BRASCON 2018

Title: Latissimus Dorsi Flap: A Robust And Cost Effective Option For Breast Reconstruction.

Authors: Pradeep Goil Pankaj Sharma (presenting author).

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BACKGROUND: The role of breast reconstruction in a woman's physical, emotional and psychological recovery from breast cancer cannot be overemphasized. Breast reconstruction with the latissimus dorsi flap offers a straightforward solution without exposing the patient to the complications of microsurgical techniques or implant related procedures. The cost effectiveness of autologous tissue, minimal donor site morbidity, and the ability to withstand radiotherapy offers a single stage solution to the financially restricted patient coming to public hospitals; who almost always cannot afford a second attempt.

METHODS: For the period from 2010-2017, under the Department of Burns & Plastic surgery, a total of 34 patients have been operated in the past four years with pedicled autologous latissimus dorsi musculocutaneous flap for immediate breast reconstruction. All patients had operable breast cancer.

RESULTS: Majority of operated patients had either satisfactory or excellent cosmetic results as comprehended by surgeons and patients themselves. Donor site complications were seroma formation (n=7), wound dehiscence (n=4). No complication after post-operative radiotherapy was reported by any patient.

CONCLUSIONS: Today, in the era of microsurgery and breast implants, the lattisimus dorsi flap still holds its ground as a robust and cost effective option for the patient.

Indian experience with lateral chest wall perforator flaps in partial breast reconstruction

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Background
Oncoplastic breast surgery has added newer dimensions to breast conservation surgeries (BCS) by reducing the rates of mastectomy and the re-excision rates. This has been further boosted by the use of lateral chest wall perforator based flaps (LCPF), by decreased morbidity at the donor site. Pedicled perforator flaps from lateral chest wall commonly employ either solely or in combination the Lateral intercostal artery perforator flap (LICAP), Lateral thoracic artery perforator flap (LTAP) and the Thoracodorsal artery perforator flap (TDAP). Partial breast reconstruction (PBR) using these flaps is a good option in small to moderate sized non-ptotic breasts, especially for laterally placed tumors.

Methodology
We reviewed the surgical anatomy of LCPF. Thereafter, prospectively maintained database was searched to obtain patients who had these surgeries at our institute, over the past 6 months.

Results
Out of 15 patients studied, 14 were primary presentations, while 1 was in a recurrent setting. Mean age at presentation was 41.4 years. 4 patients had surgery after neoadjuvant chemotherapy (NACT), while 10 of the remaining 11 patients received adjuvant chemotherapy (ACT). Mean tumor size on preoperative assessment was 3.5 cm. Of the 15 patients, resection margin of one patient was positive for ductal carcinoma in-situ component (DCIS); she eventually needed completion mastectomy. 11 patients had LICAP based flap, 1 had LTAP based flap, while 4 had a hybrid flap based on perforators of both these vessels. Mean specimen weight of breast tissue was 170 gm. Two patients had wound complications in the form of delayed wound healing and partial flap necrosis. One of these was salvaged by prompt debridement and re-suturing, resulting in no delay in receiving adjuvant treatment.

Conclusion
LCPF in PBR are a feasible option in carefully chosen patients. Oncologically safe BCS can be performed for larger sizes of tumor, with good cosmetic outcome.

Title: Gigantomastia due to retromammary lipoma: An aesthetic management

Author: Dr Debarati Chattopadhyay

Department of Burns and Plastic Surgery, AIIMS Rishikesh

Background:: A “giant” lipoma is defined as a tumor having dimensions greater than 10 cm. Giant lipomas are rare and giant breast lipomas are exceptionally uncommon. Only six cases have been described in world literature till date. Herein we describe a case of giant breast lipoma and discuss its surgical management.

Case report: A 43-year-old lady presented with left sided unilateral gigantomastia. Clinical examination, radiology and histopathology diagnosed lipoma. Excision of the tumor was planned, together with correction of the breast deformity by reduction mammoplasty using McKissok technique. A tumor measuring 19 cm × 16 cm × 10 cm and weighing 1647 grams was removed. The nipple areola complex was set by infolding of the vertical pedicles and the lateral and medial flaps were approximated to create the final breast contour. The patient is doing well on follow up.

Discussion: Giant lipomas are rare and of them, giant breast lipomas are extremely uncommon. They can grow to immense proportions and cause significant aesthetic and functional problems. The treatment is excision. But reconstruction of the breast is almost always necessary to achieve a symmetric breast in terms of volume, shape, projection and nipple areola complex symmetry compared to the normal opposite breast. Few authors have used various mammoplasty techniques for reconstruction of the breast after giant lipoma excision. Our case has the following unique features: (i) It is the third largest breast lipoma described in the literature till date, weighing 1647 grams; (ii) The Mckissock technique has been used for parenchymal reshaping which has not been previously described for giant breast lipoma.

Conclusion: This case demonstrates that reduction mammoplasty after giant lipoma removal is highly rewarding, resulting in a smaller-sized breast that is aesthetically more pleasing, has better symmetry with the contralateral breast, and provides relief from functional mass deficit.

Title: Utility of External Oblique Myocutaneous Flaps in massive skin defects post Mastectomy

Authors: Utsab Man Shrestha, Binayak Dhungel, Punyaram Kharbuja, Kapendra S. Amatya, Prakash Raj Neupane, Janith Singh

Department of Surgical Oncology, Bhaktapur Cancer Hospital, NAMS, NEPAL

Introduction: Reconstruction of large skin defects following Mastectomy remains a technical challenge for Oncosurgeon and Plastic Surgeon alike, while skin grafts are non-aesthetic , other local fascio-cutaneous and pedicled flaps are often inadequate for full coverage. While free flaps are increasingly used for aesthetic breast reconstruction they often require expertise, equipment and time that are not frequently available in a setting like ours. Since a large cohort of Breast cancer patients often present in late stage with skin involvement; operability and outcome are often determined by whether negative margins could be achieved with satisfactory soft tissue reconstruction. As of late, we have used External Oblique Myocutaneous (EOM). Flap as means of closing such large defects with encouraging results.

Material and Methods: Between April 2015 to August 2016, 3 patients who had mastectomy with skin defect larger than 15cms underwent EOM flap procedure at Bhaktapur Cancer Hospital. All surgeries were conducted by the same team surgeons.

Result: Total of 3 patients were taken up for the surgery. The diagnoses were Ca. Breast, Glant Cystosarooma Phyllolides, Fungating Ca Breast. The defect sizes were 19 x 25 cm, 20 x 22cm and 22x24cm. There were only minor complication in the post operative period.

Conclusion: Although infrequently used, external oblique Muscle flap is a useful adjuct in patient undergoing mastectomy with massive skin void.

Keyword: External oblique, carcinoma breast, massive defects

Title: Breast Augmentation With Silicone Implant: A Single Institutional Experience

Pradeep Goil, Gautam Prakash, Manojit Midya

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INTRODUCTION:A lot of heed is given to the aesthetics of the female breast as it is considered reciprocal to feminity. There is no fixed definition to the ideal size and shape of the female breast. It varies according to the build of the individual. Unfortunately, breast development does not take place adequately in some females. This causes a sense of inferiority and low self esteem in the society. This makes such women to seek corrective surgery. It is very pertinent on the part of the reconstructive breast surgeon to plan augmentation according to the wishes of the individual patient. This can go a long way in creating a sense of positive body image.

MATERIALS AND METHODS: In the department of Plastic and reconstructive surgery, SMS Medical College Jaipur, between 2010 and 2017, 28 female patients underwent breast augmentation by a single surgeon (Dr P Goil). All patients were operated via infra-mammary incision. For augmentation, silicone implants were used in the supine position under general anesthesia. Postoperative dressing was changed after 3-5 days and breast innerware was used for next 3-4 weeks. The patients were followed up for a period of one year.

RESULTS: The majority of patients (82.1%) were less than 30 years (mean age: 27.51 years). All underwent surgery by infra-mammary incision. Silicone implants were used in all patients. Three patients had post operative infection. Two patient responded to conservative treatment and in the third patient, implant was removed. No case of capsular contracture was seen. Wound scar was normal in all patients at one year follow up period. Two patients noted mild transient decrease in inframammary sensation which recovered after six months.

CONCLUSION: Suitably performed breast augmentation using silicone breast implants results in restoration of aesthetic physical and self reliant psychological well-being of the patient with acceptable complication rates.

Title: A prospective study on functional impairment following latissimus dorsi flap following modified radical mastectomy.

Author: Dr Guru Prasad Reddy. Dept of Plastic Surgery, KGMU, Lucknow

Introduction: Breast cancer is the most common cancer in the female population worldwide. The incidence of breast cancer and its associated morbidity and mortality are on a rise in the Indian scenario. There are various reconstructive options following modified radical mastectomy for breast reconstruction. Majority of studies state the functional morbidity to be minimal, but this needs to be quantified to assess the functional impact in their day to day activities.

Methods: Patients who underwent pedicled latissimus dorsi flap for breast reconstruction following modified radical mastectomy from December 2015 to November 2016 have been included in the study. Assessment of the functional morbidity involving arm on the operated side was done at intervals.

Results: A total of 17 patients were included in the study. Three patients had severe limitation in arm movement and five patients reported moderate functional deficit in carrying out daily activities in the initial assessment. Rest of the patients had minimal (7/17) or no functional disability. All the patients reported improvement at 6 month and 12 month assessments.

Conclusion: Our results in Indian scenario are similar to studies assessing functional morbidity following breast reconstruction using latissimus dorsi flap. Although the disability following latissimus dorsi reconstruction improves over time, the patients should be explained of the same and other options for reconstruction can be suggested.

Title: Immediate Breast Reconstruction With DIEP Flap After Modified Radical Mastectomy: Our Initial Experience

Authors: Pradeep Goil, Manojit Midya, Gautam Prakash

Department of Burns, Plastic and reconstructive Surgery, SMS Medical College, Jaipur (India)

INTRODUCTION: Worldwide there has been a paradigm shift in the methods of immediate reconstruction after modified radical mastectomy. Psychological and aesthetic considerations are fundamental tenets in the post mastectomy breast reconstruction. In our department we have been providing breast reconstructive services for the last seven years. Herein we present our initial experience with the microsurgical procedure of immediate breast reconstruction using with the DIEP FLAP.

MATERIALS AND METHODS: From 2013 TO 2017, fourteen patients with breast cancer had undergone modified radical mastectomy (MRM) and immediate breast reconstruction with deep inferior epigastric artery perforator flap (DIEP) in the department of Plastic and reconstructive surgery, SMS Medical College Jaipur. Out of fourteen twelve patients underwent unilateral DIEP flap reconstruction. The remaining two patients were operated for bilateral prophylactic MRM and DIEP flap reconstruction. All twelve patients who underwent unilateral DIEP flap reconstruction had stage three disease.

RESULTS: The flaps in all the cases survived. Two patients with unilateral DIEP flap reconstruction had partial venous congestion, which resolved with conservative measures. One of the patient who underwent bilateral DIEP flap had marginal skin necrosis along the suture line. After Follow up period of one year, there was no evidence of tumour recurrence and abdominal wall hernia. The reconstructed breasts achieved satisfactory results in shape, colour and symmetry.

CONCLUSION: In our initial experience, the DIEP flap procedure can be considered as a suitable method for immediate breast reconstruction after MRM with its simultaneous advantage of abdominoplasty in obese patients.

Title: Unusual Mammoplasty In Post-Burn Breast Deformity

Authors: Nikhlesh Gaur, Debarati Chattopadhyay

Dept of Plastic reconstructive and burns surgery, All India Institute of Medical Sciences Rishikesh

Background: There are several techniques of mammoplasty. Every case has to be individualized. No definite procedure can be followed in all cases.

Methods: In the following cases of deformed breasts due to burn, combined and modified techniques of mammoplasty have been followed

Results: We used wise pattern breast reduction technique in one case and pedicled TRAM flap in other to provide symmetrical breast reconstruction in cases of post burn breast deformity

Conclusion: Aesthetic surgery procedures can be used in major breast reconstructive surgery cases with suitable modifications to provide optimal outcome with good patient satisfaction.

Title: Nipple Reconstruction With CV Flap: Our Experience

Author: Pawan Kumar Dixit, Dept of Plastic surgery, KGMU, Lucknow

There are many procedures described in literature for nipple reconstruction. Nipple reconstruction is the final step after mastectomy. Procedure chosen for nipple reconstruction needs to be reliable and convenient with acceptable projection. CV flap method for nipple reconstruction is aimed to be an effective method and reliable. In this study we report our experience with CV flap nipple reconstruction. 5 patients underwent nipple reconstruction by CV flap during in plastic surgery department. Post operative nipple projection were noted and compared with opposite nipple. Patient's satisfaction was high in overall parameters. We concluded that CV flap technique is a quick and reliable method of nipple reconstruction in post mastectomy patients

Title: Quality of Life Assessment in Patients Undergoing Oncoplastic Breast Surgery

Author: Dr Ravi Kumar Singh, Dept of Plastic Surgery , KGMU, Lucknow

Abstract:

Introduction: In developing nations the breast diseases are surgically dealt often with the primary aim of complete removal of disease with little or no concern to the cosmesis of the breast.The new concept of Oncoplastic Breast Surgery (OBS) has thus provided a hope to the patients suffering from breast diseases. It provided an intelligent removal of complete disease along with acceptable reconstruction by using basic oncologic and plastic surgery principles.

Aim: To assesses the quality of life (QOL) in patients undergoing OBS for either benign or malignant breast disease.

Material & Methods: Total 68 patients (28- Operable benign breast lumps (OBBL); 18- Carcinoma breast with OBS; 23- Carcinoma breast without OBS) at King George Medical University, Lucknow, from September 2015 to August 2017. EORTC-QOQ C-30 and 5-points Likert scale was used to assess the four basic aspects of quality of life (Physical, Social, Emotional and Functional).

Observation & Results: This prospective case series evaluation of two years of 68 patients has precluded any valid statistical analysis. Perception of body deformity, shape and symmetry of the breasts, sexual life, self-confidence, feminity and functional QOL were rated significantly lower by the patients without OBS than the patients who underwent OBS.

Conclusion: Although; further large scale studies are however required to achieve higher level of evidence and expertise in oncoplastic breast surgery, but it can be said from this preliminary study that concept of oncoplastic breast surgery is very appealing one.

Title: EORTC BR 23 Questionnaire: Acceptability in measuring quality of life in breast surgery patients in India.

Authors: Shivangi Saha, Anurag Srivastava.

Departments of Plastic & Reconstructive Surgery, and Breast endocrine and general surgery, All India Institute of Medical Sciences, New Delhi

Background: Suffering from breast cancer produces changes that can affect multiple "domains," related to the quality of life, EORTC has developed BR23 which incorporates five multi-item scales to assess side effects of systemic therapy, arm symptoms, breast symptoms, body image and sexual functioning. Single items assess sexual enjoyment, hair loss and future perspective.

In Asian society, among young girls, the thought of sex is a taboo prior to marriage. We noticed that young unmarried patients were hesitant to answer some items related to the domain assessing Sexuality.

We conducted a survey to obtain a feedback from these girls about their "point of view" on the "domain "assessing and acceptability of the Hindi version of BR23.

Methods: The study was undertaken at AIIMS Delhi between April to June 2016. The questionnaire was administered to and breast cancer patients (23) and controls (54) (relatives of patients and women with benign breast diseases). Single ladies <35 years(y) were studied (n=57).

Participants were asked to respond to BR23.Their opinion on various items of BR23 was sought on a 4 point scale as follows:

1. I am happy to answer without hesitation.

2. I feel shy because it's a matter of personal life and does not want to disclose

3. I am unhappy being asked these personal questions.

4. No response

The acceptability of the EORTC QLQ – BR23 was assessed with the response rate to various items. Opinion regarding various items of the questionnaires was also calculated.

Results: Mean age of participants were 27.8y (range 17-35 y). Mean response was 63.1% (36) for sexual function and 10.5 % for sexual enjoyment. The most common response to sexual functioning items were 3 (83.3%).

Conclusion: The items in a questionnaire seeking personal behaviour should be sensitive to the prevailing social and cultural norms, thus slight modifications in the Hindi version may be needed.

Title: Aesthetics in breast reconstruction for Poland's syndrome: what we can achieve?

Authors: Shivangi Saha, ManeeshSinghal, Shashank Chauhan, Raja Tiwari, Aniket Dave

Dept of Plastic reconstructive and burns surgery, All India Institute of Medical Sciences New Delhi

Background: Poland's syndrome is a rare congenital anomaly characterized by unilateral chest wall hypoplasia and ipsilateral hand abnormalities. Several studies have reported that patients affected by chest wall deformities often experience body image disorders and decreased "Quality of Life".We present our experience with breast reconstruction in female patients with this disorder and its impact on their quality of life by measuring the Breast Q score.

Methods: Three female patients operated for unilateral hypoplastic breast (simple type) due to Poland's syndrome underwent expander-implant based breast reconstruction in the year 2017. Their pre and postoperative Breast Q scores related to satisfaction with breasts, psychosocial well-being, physical well-being: chest and satisfaction with information were recorded at 9 months after surgery.

Results: Poland syndrome is a rare disease, and thus the number of patients to include in our study was limited thus statistically significant difference could not be achieved. However, the pre and post-surgery Breast Q scores showed a remarkable difference in these young female patients after surgery in the domain of satisfaction with breasts and psychosocial well-being.

Conclusion: Reconstruction of the thoraco-mammary deformities in Poland's syndrome presents a surgical challenge. Implant-based reconstruction is one of the simplest and commonest methods used. Although achieving results identical to the normal side is difficult but still imparts a better quality of life to the affected individual.

Title: Breast Reduction Using Supero-Medial Pedicle Technique-Our Centre Experience

Author: Shobhit Sharma. Shri Ram Murti Smarak Institute of Medical Sciences , Bareilly

Hall-Findlay EJ reported a modified vertical mammaplasty technique using medical pedicle with inferior resection of the gland in 1999.The superomedial pedicle technique has gained increasing popularity for its versatility and ability to achieve significant reduction of breast parenchyma and skin envelope with improved contour and lasting results. The superomedial pedicle brings with it the ability to have improved upper pole fullness and improved breast shape.We report our experince with this technique of breast reduction at our centre in Bareilly , a tier II city of Uttar Pradesh.

Selected Breast Publications from SGPGIMS, Lucknow

World J Surg
https://doi.org/10.1007/s00268-018-4466-4

ORIGINAL SCIENTIFIC REPORT

Surgical Outcomes of Primary Versus Post-Neoadjuvant Chemotherapy Breast Conservation Surgery: A Comparative Study from a Developing Country

Gaurav Agarwal[1] · Chaitra Sonthineni[1] · Sabaretnam Mayilvaganan[1] · Anjali Mishra[1] · Punita Lal[2] · Vinita Agrawal[3]

Abstract

Introduction In India and other developing countries, breast conservation surgery (BCS) rates in breast cancer patients are low due to advanced disease at presentation and misconceptions about BCS outcomes. Many patients presenting with large or locally advanced breast cancers (LABC) can be offered post-neoadjuvant chemotherapy (NACT) BCS, safety of which is not as well established as that of primary BCS. This retrospective study compared pathological and surgical outcome parameters in patients undergoing primary and post-NACT BCS.

Methods All non-metastatic breast cancer patients undergoing BCS during 2011–2015 with 1-year follow-up were included. Outcome parameters in form of margin infiltration, ipsilateral breast tumor recurrence (IBTR) rates and IBTR-free survival were compared between primary and post-NACT BCS patients groups.

Results One hundred and twenty-nine patients underwent BCS; 95 underwent primary and 34 post-NACT BCS. Patients in both groups underwent similar multimodality treatment as per institutional protocols. Post-NACT patients more frequently required oncoplastic volume displacement or replacement surgery ($p = 0.002$). Re-excision of infiltrated margins was needed more frequently in primary BCS compared with post-NACT BCS group (14.4 vs. 8.8%; $p = 0.40$). IBTR (Mean follow-up = 30.7 months) was seen in 8.8% post-NACT patients compared with 2.1% primary BCS ($p = 0.114$). IBTR-free survival did not differ significantly between the groups in stage-wise comparison.

Conclusion Post-NACT BCS is safe even in large tumors and LABC, though many require oncoplastic procedures for satisfactory cosmesis. In a developing country where many patients present with large breast cancers or LABC, the benefits of BCS can be offered to a majority with the help of NACT, without compromising the chances of cure.

Introduction

Breast conservation surgery (BCS) is the standard of care surgical procedure for early breast cancer (EBC) patients. Large operable (LOBC) and locally advanced breast cancer (LABC) patients are usually not considered good candidates for BCS. However, down-staging the tumors with

Presented as an oral free paper in BSI section at World Congress of Surgery-2017, Basel Switzerland.

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Published online: 18 January 2018

neoadjuvant chemotherapy (NACT) in such patients makes it possible to perform BCS in selected LOBC and LABC patients. NACT is being frequently employed in EBC as well, due to many potential advantages over adjuvant chemotherapy, which include down-staging of tumor thus reducing the breast tissue volume needed to be excised, assessing in-situ tumor response to chemotherapy and to potentially avoid micro-metastases. The validity of primary BCS in EBC has been well established by numerous large and high-quality prospective randomized controlled trials (RCTs) with long follow-up [1–3]. The safety of post-NACT BCS, however, has not been as well established as primary BCS, and to our knowledge, no randomized trials have compared outcomes of post-NACT and primary BCS. Yet, the outcomes of post-NACT BCS are usually considered similar to primary BCS, followed by adjuvant chemotherapy. This belief, especially for LOBC and LABC is based mostly on relatively low-quality retrospective data [4]. There are many studies including a few RCTs comparing outcomes of post-NACT BCS with post-NACT mastectomy which report somewhat higher loco-regional recurrence with BCS, but no detriment in the overall survival [5]. In countries with population-based breast cancer-screening programs, a large proportion of cases are screen-detected EBC [6, 7]. In developing countries, such as India, a large proportion of breast cancer patients present with LOBC and LABC [8], and so NACT is a commonly employed strategy, whenever a patient is keen to conserve her breast [9].

In this retrospective analysis of data from a prospectively maintained database, we compared the clinico-pathological features, surgical procedures, and outcome parameters of primary and post-NACT BCS, with the aim of comparing the outcomes in terms of ipsilateral breast tumor recurrence rates (IBTR) and IBTR-free survival in the two groups.

Methods

Patients undergoing curative surgery for non-metastatic breast cancer during the study period (2011–2015) were identified from the department database. Patients who underwent BCS and had a minimum follow-up of 1 year post-surgery were selected, and their data were retrieved from hospital and department electronic medical records. Clinical features and staging recorded at diagnosis, operative notes, and histopathology and cytopathology reports were retrieved. Patients were staged using TNM-AJCC staging system, 7th edition (2010). All patients received standardized multidisciplinary treatment according to institute protocols, which included preoperative evaluation with mammogram and core-needle biopsy or fine-needle aspiration cytology. Nine patients included in the study had undergone an incisional/excisional biopsy elsewhere before being referred to our institute. All patients planned to receive NACT had a core-needle biopsy for histology and biomarkers (ER, PR and HER2neu) evaluation. Most patients undergoing NACT with the intention of having BCS subsequently had tumor mapping with percutaneous sterile silver wire markers/surgical clips inserted at tumor margins, as described earlier [10]. A post-NACT mammogram was used to determine the response to NACT and the original site of tumor by visualizing the radio-opaque markers in complete responders. All patients underwent BCS in form of wide-local excision (WLE) or segmental/partial mastectomy, with or without oncoplastic reconstruction, and intra-operative margin assessment with frozen section histology of margins, followed by standard paraffin section histopathology of the whole surgical specimen. Any infiltrated margins (invasive or in-situ) were re-excised. Seven patients needed conversion to mastectomy due to multiple infiltrated margins/extensive DCIS, and so were not part of this study cohort. Type of BCS for each patient was planned to give best cosmetic outcome for volume of tissue removed; however, no formal anthropometry had been documented in the electronic records. All patients received whole-breast radiotherapy and tumor bed boost to the area marked with radio-opaque metallic clips intraoperatively as per protocols. Patients with hormone receptor positivity and/or HER2Neu positivity received appropriate hormone therapy and/or targeted therapy.

Outcome parameters in terms of margin infiltration, IBTR, and IBTR-free survival were compared between groups of patients undergoing primary and post-NACT BCS. Any margin(s) reported infiltrated at either frozen section histology or paraffin section histology was recorded as margin infiltration. Patients were deemed to have IBTR if they had recurrent breast tumor in ipsilateral breast on clinical and/or mammographic evaluation in follow-up and were confirmed as a recurrent malignant lesion on cytopathology or histopathology. Local (IBTR) recurrence-free interval was calculated from month of surgery to month of last follow-up or recurrence if it occurred earlier than last follow-up.

Statistical analysis was done using SPSS version 22.0 software (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY; IBM Corp.). IBTR-free survival was calculated by using log-rank test and Kaplan–Meier graphs.

Results

In the 5-year study period, 712 non-metastatic breast cancer patients underwent definitive surgery for tumor in the breast, out of whom 169 (23.7%) underwent BCS; 131

underwent primary BCS and 38 post-NACT BCS. Patients undergoing primary surgery were significantly ($p = 0.031$) more likely to have BCS (131 of 451, 29%) compared with patients undergoing post-NACT surgery (38 of 261, 14.5%). Ninety-five (72.5%) and 34 (89.5%) patients undergoing primary and post-NACT BCS, respectively, had the necessary minimum 1-year follow-up (Fig. 1), and were included in the final analysis. The mean follow-up was 30.7 ± 15.2 months.

Post-NACT BCS patients had significantly higher TNM stage ($p = 0.000$) and significantly higher cT and cN stage ($p = 0.000$) at presentation (Table 1). There was no significant difference in menopausal status, hormone receptor status, or HER2neu status between the groups, but the histology grade was significantly higher ($p = 0.000$) in post-NACT group. DCIS was more commonly seen in the WLE specimens in primary BCS group ($p = 0.014$). Need for re-excision of positive margins detected on frozen section histology was more frequent in primary BCS (12, 12.6%) than in post-NACT BCS (3, 8.8%) group, but this difference was not statistically significant ($p = 0.403$). Post-NACT patients required oncoplastic reconstruction with volume displacement or replacement procedures ($p = 0.002$) more frequently. Chemotherapy regimen used were similar in the two groups; 22 patients in primary BCS group were not treated with adjuvant chemotherapy based on either low-risk, stage I disease or had poor performance status or because they refused to be treated with it.

Five (3.9%) patients have had IBTR in follow-up; two (2.1%) were in the primary BCS group and three (8.8%) in post-NACT BCS group. Thus, IBTR occurred more frequently in post-NACT compared to primary BCS group, but this difference was not statistically significant ($p = 0.114$). Recurrence rates between primary BCS versus post-NACT BCS patients did not differ significantly in cT2 patients (1.5 vs. 0%, $p = 0.930$) as well as in cT3 patients, (0 vs. 10%, $p = 0.751$). Likewise, there was no statistically significant difference in recurrence rates between primary BCS versus post-NACT BCS in TNM stage II patients (0 vs. 11.1%, $p = 0.164$) as well as in TNM stage III patients (5.9 vs. 8.3%, $p = 0.630$).

Nine out of the 129 patients who underwent BCS were referred to us for definitive breast cancer surgery, following an incisional biopsy/excisional biopsy which had been performed at other centers. All of them underwent re-excision of margins to obtain negative margins, irrespective of presence of palpable tumor remnant. One of these patients had an IBTR, but a post-lumpectomy/biopsy status was not associated with a significantly higher risk of IBTR ($p = 0.308$).

In the post-NACT group patients with IBTR, one had an in-breast pathological complete response (pCR), while none of the seven with total (Breast and axilla) pCR had IBTR. Index TNM stage, cT at presentation, cN at presentation, hormone receptor status, HER2Neu status, margin resection based on frozen section histology, ypT status, ypN status, and remnant size on histopathology did not have a bearing on recurrence rates in primary or post-NACT BCS groups (Tables 2 and 3). When all patients irrespective of stage at presentation were included in the survival analysis, there was a significantly higher IBTR-free survival in the primary BCS group, compared to the post-NACT BCS group (Fig. 2 and Table 4). This can be attributed to the more advanced stage at presentation, including 8 (23.5%) with skin involvement in the post-NACT group, compared with only 1 (1%) in primary BCS group. When stage-specific subgroups were compared for outcomes, there was no statistically significant difference in IBTR-free survival in TNM stage II patients undergoing primary or post-NACT BCS ($p = 0.066$, Fig. 3 and Table 5) or in TNM stage III patients ($p = 0.833$, Fig. 4 and Table 6).

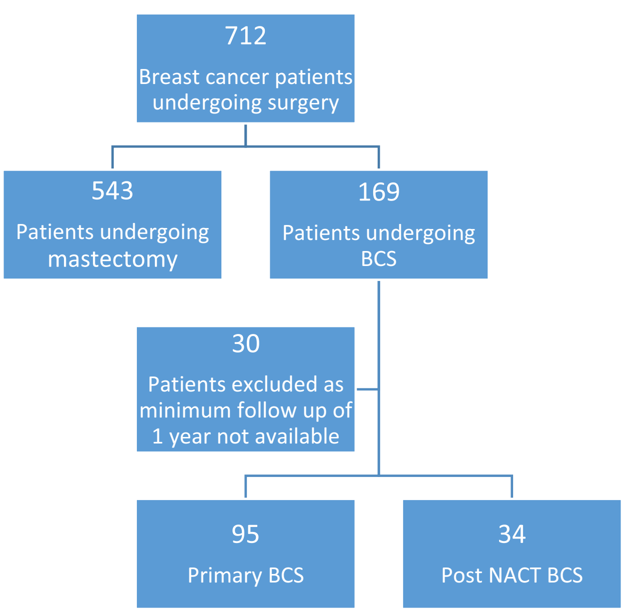

Fig. 1 Study schema: patients undergoing curative surgery for non-metastatic breast cancer (2011–2015)

Discussion

Use of NACT has improved the rates of BCS eligibility in willing patients, which has been amply proven by numerous trials, including the NSABP B-18 [11, 12]. The disease spectrum in India and other developing countries are different from developed nations [13]. When compared to western population [14, 15] BCS rates in India are lower in general. About 20% of Indian breast cancer patients

Table 1 Comparison of primary and post-NACT BCS patient groups

	Primary BCS $n = 95$	Post-NACT BCS $n = 34$	p value
Age (in years) mean ± SD	52.4 ± 12.0	50.3 ± 13.0	0.397
Menopausal status			
Postmenopausal	64 (67.3%)	20 (58.8%)	0.244
Premenopausal[a]	31 (32.6%)	14 (41.2%)	
TNM stage group			
I	29 (30.5%)	–	0.000
II	48 (50.5%)	9 (26.5%)	
III	17 (17.8%)	24 (70.6%)	
x	1 (1%)	1 (2.9%)	
cT			
1	22 (23.1%)	–	0.000
2	66 (69.4%)	5 (14.7%)	
3	3 (3.2%)	20 (58.8%)	
4	1 (1%)	8 (23.5%)	
x[b]	3 (3.2%)	1 (2.9%)	
cN			
0	67 (70.5%)	11 (32.4%)	0.000
1	27 (28.4%)	19 (55.9%)	
2	1 (1%)	2 (5.9%)	
3	–	2 (5.9%)	
Tumor grade and histology			
IDC grade-I	8 (8.4%)	1 (2.9%)	0.000
IDC grade-II	53 (55.7%)	10 (29.4%)	
IDC grade-III	29 (30.5%)	11 (32.4%)	
Others/N.A.[c]	5 (5.3%)	12 (35.3%)	
DCIS in surgical specimen	27 (28.4%)	3 (8.8%)	0.014
Hormone receptor status			
ER and PR negative	37 (38.9%)	16 (47%)	0.185
ER and/or PR positive	55 (57.9%)	15 (44.1%)	
N.A.	3 (3.2%)	3 (8.8%)	
HER2Neu receptor status			
Negative/1+	42 (44.2%)	13 (38.2%)	0.363
2+	15 (15.8%)	3 (8.8%)	
3+	35 (36.8%)	15 (44.1%)	
N.A.	3 (3.2%)	3 (8.8%)	
BCS type			
WLE only	69 (72.6%)	16 (47%)	0.002
VD oncoplasty	22 (23.2%)	10 (29.4%)	
VR oncoplasty	4 (4.2%)	8 (23.5%)	
Axillary Surgery			
SLNB alone	25 (26.3%)	1 (2.9%)	0.000
SLNB followed by ALND	4 (4.2%)	1 (2.9%)	
ALND	64 (67.4%)	32 (94.1%)	
Margin(s) re-excision based on FSB	12 (12.6%)	3 (8.8%)	0.403
Chemotherapy regimen used			
Anthracycline based	21 (22.1%)	8 (23.5%)	0.794
Anthracycline + taxane	45 (47.4%)	25 (73.5%)	
Others	3 (3.2%)	1 (2.9%)	

Table 1 continued

	Primary BCS $n = 95$	Post-NACT BCS $n = 34$	p value
Recurrence (IBTR)	2 (2.1%)	3 (8.8%)	0.114

[a]Includes perimenopausal patients

[b]Post-incisional/excisional biopsy

[c]Includes IDC that were not graded

NACT neoadjuvant chemotherapy, *BCS* breast conservation surgery, *SD* standard deviation, *cT* clinical tumor status, *cN* clinical nodal status, *IDC* infiltrating ductal carcinoma, *N.A.* not available, *DCIS* ductal carcinoma in-situ, *ER* estrogen receptor, *PR* progesterone receptor, *HER2Neu* human epidermal growth factor receptor 2, *WLE* wide-local excision, *VD* volume displacement, *VR* volume replacement, *SLNB* sentinel lymph node biopsy, *ALND* axillary lymph node dissection, *FSB* frozen section biopsy, *IBTR* ipsilateral breast tumor recurrence

Table 2 Differences between primary BCS patients with and without IBTR

Factors in primary BCS	No recurrence $n = 93$	Recurrence $n = 2$	p value
TNM stage group			
I	28 (29.4%)	1 (50%)	0.253
II	48 (51.6%)	–	
III	16 (17.2%)	1 (50%)	
x	1 (1%)	–	
cT			
1	22 (23.2%)	–	0.143
2	65 (69.9%)	1 (50%)	
3	3 (3.2%)	–	
4	1 (1%)	–	
x	2 (2.2%)	1 (50%)	
cN			
0	66 (71%)	1 (50%)	0.505
1	26 (28%)	1 (50%)	
2	1 (1%)	–	
3	–	–	
Hormone receptor status			
ER and PR negative	36 (37.9%)	1 (50%)	1.000
ER and/or PR positive	54 (56.8%)	1 (50%)	
N.A.	3 (3.2%)	–	
HER2Neu receptor status			
Negative/1+	40 (43%)	2 (100%)	0.671
2+	35 (37.6%)	–	
3+	15 (16.1%)	–	
N.A.	3 (3.2%)	–	
Margin re-excision done based on FSB	11 (11.8%)	1 (50%)	0.238
Chemotherapy	72 (77.4%)	1 (50%)	0.411

BCS breast conservation surgery, *IBTR* ipsilateral breast tumor recurrence, *cT* clinical tumor status, *cN* clinical nodal status, *N.A.* not available, *ER* estrogen receptor, *PR* progesterone receptor, *HER2Neu* human epidermal growth factor receptor 2, *FSB* frozen section biopsy

included in published literature have had BCS, with the reported BCS rates ranging between 11 and 52% [16–20]. The reasons for low BCS rates in India are many and include misconceptions about BCS such as fear of recurrence, higher costs, poorer survival, and also lack of expertise and infrastructure for surgery and radiotherapy [8, 21] outside of relatively few cancer centers for a huge population of nearly 1.3 billion people. Illiteracy and financial dependence of women in developing countries and lack of wide coverage of health insurance are key factors in determining surgical preference of the patient and may even overshadow any desire for undergoing breast

Table 3 Differences between post-NACT BCS patients with and without IBTR

	No recurrence $n = 31$	Recurrence $n = 3$	p value
Index TNM stage group			
II	8 (25.8%)	1 (33.3%)	1.000
III	22 (71%)	2 (66.7%)	
x	1 (3.2%)	–	
cT			
2	5 (16.1%)	–	1.000
3	18 (58.1%)	2 (66.7%)	
4	7 (22.6%)	1 (33.3%)	
x	1 (3.2%)	–	
cN			
0	10 (32.2%)	1 (33.3%)	0.349
1	18 (58.1%)	1 (33.3%)	
2	1 (3.2%)	1 (33.3%)	
3	2 (6.4%)	–	
Hormone receptor status			
ER and PR negative	3 (9.7)	2 (66.7%)	1.000
ER and/or PR positive	14 (45.2)	1 (33.3%)	
N.A.	14 (45.2)	–	
HER2Neu receptor status			
Negative/1+	10 (32.2%)	3 (100%)	0.200
2+	3 (9.7%)	–	
3+	15 (48.4%)	–	
N.A.	3 (9.7%)	–	
Margin re-excision done based on FSB	2 (6.4%)	1 (33.3%)	0.249
ycT			
0	16 (51.6%)	1 (33.3%)	0.705
1	4 (12.9%)	–	
2	6 (19.4%)	1 (33.3%)	
N.A.	5 (16.1%)	1 (33.3%)	
ycN			
0	21 (67.7%)	1 (33.3%)	0.279
1	5 (16.1%)	1 (33.3%)	
N.A.	5 (16.1%)	1 (33.3%)	
ypT ($n = 32$)			
0	10 (34.5%)	1 (33.3%)	0.669
1	14 (48.3%)	1 (33.3%)	
2	2 (6.9%)	1 (33.3%)	
3	2 (6.9%)	–	
4b	1 (3.4%)	–	
ypN ($n = 32$)			
0	18 (62.1%)	–	0.087
1	7 (24.1%)	1 (33.3%)	
2	2 (6.9%)	1 (33.3%)	
3	2 (6.9%)	1 (33.3%)	
Remnant size on histopathology (in cm) mean ± SD	2.57 ± 2.08	2.33 ± 1.44	0.853
pCR (breast and axilla)	7 (22.5%)	–	0.464

Table 3 continued

	No recurrence $n = 31$	Recurrence $n = 3$	p value
Anthracycline based chemotherapy	8 (25.8%)	–	0.599
Anthracycline + taxane chemotherapy	22 (71%)	3 (100%)	
Other chemotherapy	1 (3.2%)	–	

NACT neoadjuvant chemotherapy, *BCS* breast conservation surgery, *IBTR* ipsilateral breast tumor recurrence, *cT* clinical tumor status, *cN* clinical nodal status, *N.A.* not available, *ER* estrogen receptor, *PR* progesterone receptor, *HER2Neu* human epidermal growth factor receptor 2, *FSB* frozen section biopsy, *ycT* post-neoadjuvant chemotherapy clinical tumor status, *ycN* post-neoadjuvant chemotherapy clinical nodal status, *ypT* post-neoadjuvant chemotherapy pathological tumor status, *ypN* post-neoadjuvant chemotherapy pathological nodal status, *SD* standard deviation, *pCR* pathological complete response

Fig. 2 IBTR-free survival of primary BCS and post-NACT BCS patients

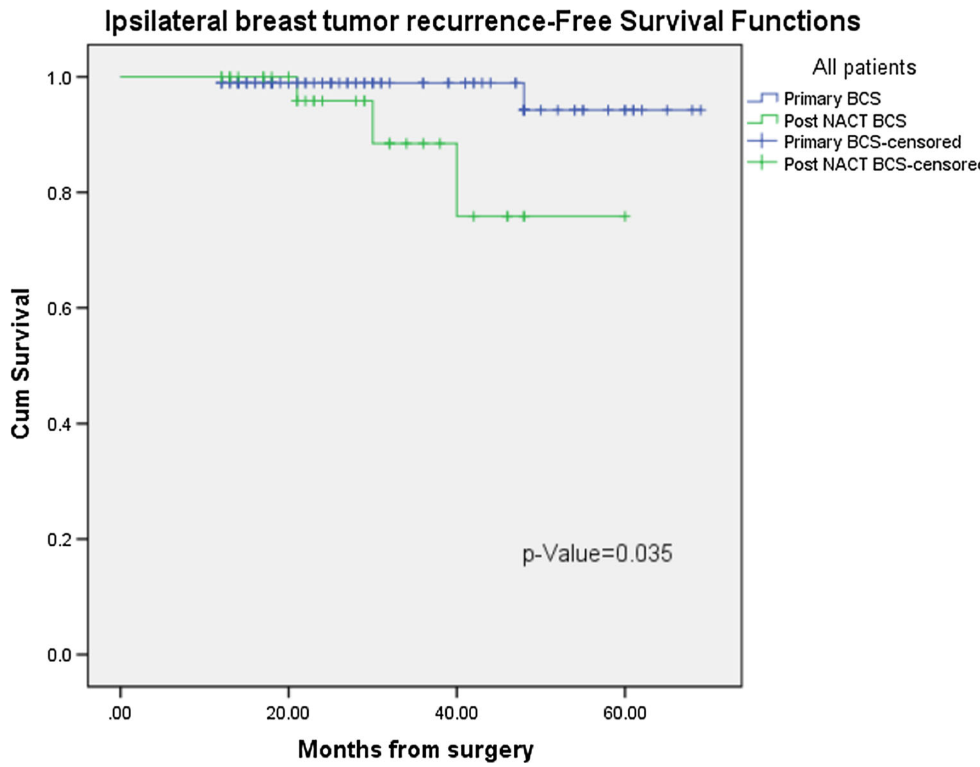

Table 4 IBTR-free survival of primary BCS and post-NACT BCS patients

BCS	Total (n)	Recurrence	Censored		Mean value (months)	95% CI	P value
			Number	Percentage			
Primary	95	2	93	97.9	67.41	65.20–69.62	0.035
Post-NACT	34	3	31	91.2	53.63	47.11–60.17	
Overall	129	5	124	96.1	65.77	63.00–68.55	

Log-rank test used to compute p value

IBTR ipsilateral breast tumor recurrence, *BCS* breast conservation surgery, *NACT* neoadjuvant chemotherapy, *CI* confidence interval

conservation. Most families have to bear the cost of cancer treatment on their own, and majority is not willing to bear the additional costs incurred on account of radiotherapy as part of BCS.

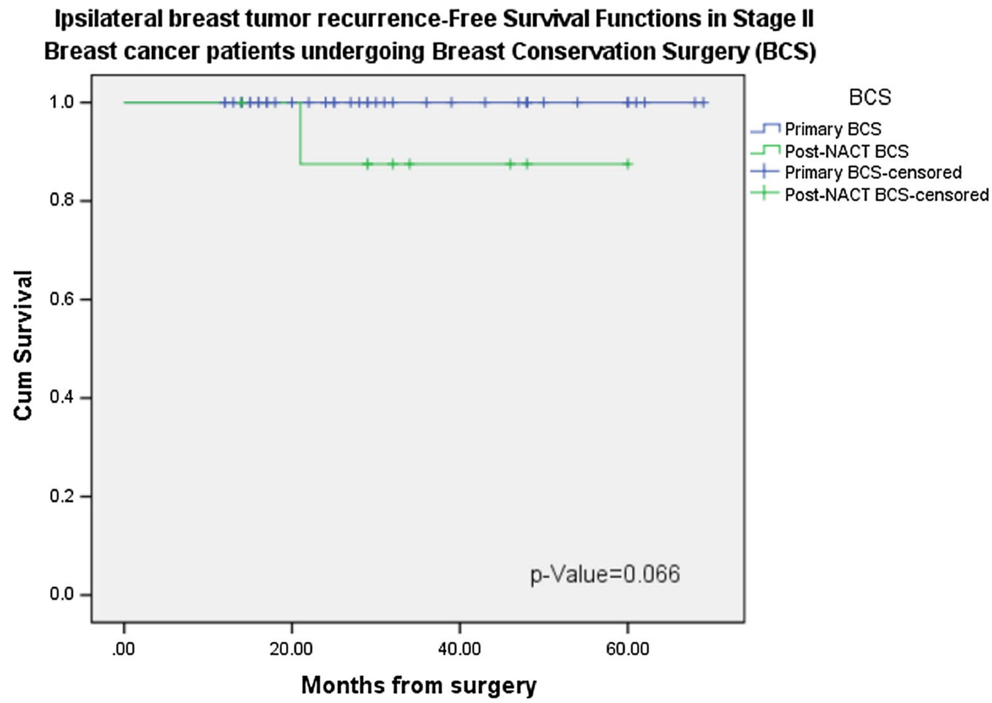

Fig. 3 IBTR-free survival of stage II primary BCS patients compared with stage II post-NACT BCS patients

Table 5 IBTR-free survival of stage II primary BCS patients compared with stage II post-NACT BCS patients

BCS	Total (*n*)	Recurrence	Censored		Mean value	95% CI	*P* Value
			Number	Percentage			
Primary	41	0	41	100	–	–	0.066
Post-NACT	9	1	8	88.0	–	–	
Overall	50	1	49	98.0	–	–	

Log-rank test used to compute *p* value

Patients completing treatment as advised by multidisciplinary team

IBTR ipsilateral breast tumor recurrence, *BCS* breast conservation surgery, *NACT* neoadjuvant chemotherapy, *CI* confidence interval

It is expected that loco-regional recurrence rates are higher in advanced stage disease [22]. As the proportion of breast cancer patients presenting with LOBC and LABC is high in India (LABC constitutes 40% of breast cancer cases at our institute), many patients are not offered BCS, except in the specialized tertiary care breast units. Although BCS can be performed with acceptable IBTR rates after NACT even in patients who present with initial skin involvement [23], it is prudent that such patients complete whole of adjuvant radiotherapy and other treatment and are followed up intensively for early detection of any recurrences. Even though the difference was insignificant in our study, patients who had undergone BCS post-NACT had a longer follow-up compared to primary BCS group patients. This is possibly due to a greater commitment and acceptance for multiple follow-up visits by these patients, who are used to frequently visiting the hospital prior to surgery for the NACT. In contrast, this would not be the case for primary BCS patients, especially those not receiving/willing for chemotherapy. Often, many patients travel long distances, for treatment in specialized cancer centers such as ours, which are far and few in India. Many patients therefore choose a local doctor for follow-up, who may or may not have the required oncological expertise.

The reported rates of IBTR in post-NACT patients are in general lower than that reported in our study (8.8%). In a retrospective study on patients undergoing post-NACT BCS carried out at the MD Anderson Cancer Center, 16 out

Fig. 4 IBTR-free survival of stage III primary BCS patients compared with stage III post-NACT BCS patients

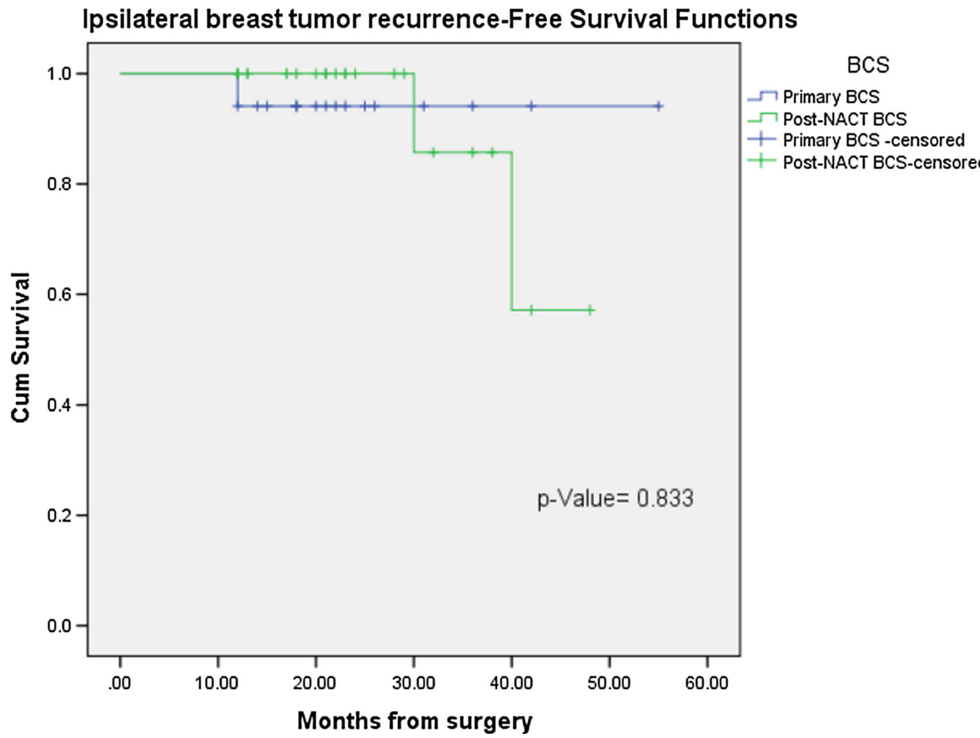

Table 6 IBTR-free survival of stage III primary BCS patients compared with stage III post-NACT BCS patients

BCS	Total (*n*)	Recurrence	Censored		Mean value (months)	95% CI	*P* value
			Number	Percentage			
Primary	17	1	16	94.1	52.47	47.66–57.28	0.833
Post-NACT	24	2	22	91.7	43.14	37.74–48.54	
Overall	41	3	38	92.7	49.07	42.89–55.26	

Log-rank test used to compute *p* value

IBTR ipsilateral breast tumor recurrence, *BCS* breast conservation surgery, *NACT* neoadjuvant chemotherapy, *CI* confidence interval

of 340 (4.7%) patients developed IBTR after a median follow-up of 60 months [24]. The factors reported in that study to be associated with IBTR and loco-regional recurrence were N2 and N3 disease, multifocal residual disease, residual tumor >2 cm, and presence of lympho-vascular invasion. Patients in our study were younger and had relatively more advanced (T2/3/4 and N2/3) disease compared with that study, and some had prior incisional/excisional biopsy elsewhere, unlike the patients in the MD Anderson study. The recurrence rates were higher in our post-NACT patients, pointing toward more aggressive disease patterns in our patient population as suggested by previous studies [13]. Similar to what was reported by Ishitobi et al. [25] for Japanese patients, the MD Anderson Prognostic Index [26] may not be applicable to Indian breast cancer patients.

Van der Hage et al. [27] studied primary versus post-NACT surgery (mastectomy or BCS) patients and reported that patients who were planned for mastectomy before NACT, but underwent BCS because of down-staging of the tumor had worse overall survival (HR, 2.53; 95% CI, 1.02–6.25) compared with patients who were initially planned to receive BCS and indeed had conservation. The authors suggested a correlation between the outcome of loco-regional treatment and tumor response to NACT, which was not possible in our study, as the number of patients who were initially planned for mastectomy, but later underwent BCS due to down-staging were few. Boughey et al. reported that in patients treated with BCS for large breast tumors (>2 cm), NACT resulted in need for less extensive resection, with no change in rates of re-excision, as compared to patients who underwent primary BCS and adjuvant chemotherapy [28]. In our study, the rate of margin re-excision was lower in post-NACT BCS, though not significantly so.

In a study by Rouzier et al. [29], the IBTR rates were 16% (±2.4%) at 5 years and 21.5% (±3.2%) at 10 years. Multivariate analysis showed that the probability of local control was decreased by the following independent factors: age $\leq$ 40 years, excision margin $\leq$ 2 mm, S-phase fraction more than 4%, and clinical tumor size more than 2 cm at the time of surgery. In our study, in the post-NACT BCS patients, the mean size of tumor at the time of surgery did not vary significantly between those with IBTR and those without. In fact, the mean tumor size was smaller in the group that recurred. Beriwal et al. [22] reported a post-NACT IBTR of 3.3%. Pre-treatment and pathologic parameters that positively correlated with IBTR were advanced stage ($p = 0.03$) and margin positivity ($p = 0.04$). No other clinical factors were predictive of higher recurrence.

In our study, we have not excluded the occurrence of a second primary in the ipsilateral breast, and hence true recurrence in scar was not distinguished from a new malignancy in the same breast. IBTR in BCS is not merely due to surgical/treatment failure but is also reflective of the innate predisposition to malignancy in breast cancer patients. IBTR has been associated with distant metastases [29] and can have a bearing on the overall survival of such patients.

Being a retrospective study in a relatively small number of patients, there are numerous limitations. Yet, the lack of literature providing comparative data on breast cancer patients undergoing primary and post-NACT BCS for large/locally advanced disease make this study worthwhile. In summation, our study which includes a cohort with LOBC and LABC patients reports an acceptably low local recurrence rate following BCS in patients who have received NACT, comparable to that in patients undergoing primary BCS. In a post-NACT patient cohort, 70% of which had stage III cancer, many with cT4 disease, BCS was safe following down-staging with NACT, though many required an oncoplastic procedure for satisfactory cosmetic outcomes. Appropriate patient selection and multidisciplinary treatment are the key factors to achieving low local recurrence rates even in patients with relatively advanced but non-metastatic breast cancers.

Acknowledgements The authors wish to acknowledge the patients, nurses and paramedics who cared for them, and the resident and consultant doctors and in the departments of Endocrine and Breast surgery, Radiation Oncology, and Pathology at the SGPGIMS Lucknow for their role in treatment and follow-up the patients and maintaining various components of the database and electronic medical records.

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Indian J Surg
DOI 10.1007/s12262-017-1666-3

EDITORIAL

Indian Solutions for Indian Problems—Association of Breast Surgeons of India (ABSI) Practical Consensus Statement, Recommendations, and Guidelines for the Treatment of Breast Cancer in India

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Received: 13 June 2017 / Accepted: 13 June 2017

Introduction

Breast cancer is considered as the most common type of female cancer accountable for nearly 23% of all cancers in women globally [1, 2]. It is believed that global prevalence of breast cancer will cross two million by the year 2030 which will have the major contributors from developing countries [3]. As far as India is concerned, the incidence rates vary across the country with northeast and metropolitan cities (Mumbai, New Delhi) showing the highest rates [4]. The factors which contribute to this variation include demographic differences (education), lifestyle factors (use of tobacco and alcohol), anthropometric factors (adiposity), and reproductive factors (age at first child and number of children) [4]. One of the most common contributors to the high mortality rate is due to the diagnosis at advance stages of the disease which can be due to low awareness, incomplete treatment regimens, and limited access to effective treatment at regional cancer centers [5–10]. As per National Breast Cancer Foundation, currently available treatments for breast cancer are based on a number of factors including size of tumor in relation to size of breast, result of specific pathology tests (hormone receptors, HER2 receptors), menopause, age, general health conditions, family history, or other risk factors [11]. The treatments include surgery, chemotherapy, radiation therapy, hormone therapy, and targeted therapy along with the involvement of nutrition and physical activity and follow-up care.

According to a report published in Breast Cancer Deadline 2020, the death rate is gradually declining after 1990 which attributes to early detection, awareness, and continuous improvement in treatment, which is a good sign [12]. Although the advancement of new technology provides hope to cure of breast cancer, still there are barriers to provide an optimal treatment to the patients globally, especially in the developing countries. So it's very important to have a universal approach and guidelines at place, especially in India where the lack of awareness among the patients is quite high. The present manuscript is developed with the help of key opinion leaders (KOLs)/experts in domain, published evidences, and practical experiences in real-life management of breast cancer to draft the consensus guidelines towards finding Indian solutions for Indian problems.

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Background and Methods

St. Gallen Consensus Conference on early breast cancer is conducted which provided mostly evidence-based, globally valid treatment recommendations for breast cancer care, with a broad spectrum of acceptable clinical practice [13]. In the year 2015, Vienna, Austria conducted St. Gallen Consensus Conference on early breast cancer, and some recommendations on the current and newer practices were added to the official St. Gallen Consensus publication [14]. These are the

Published online: 22 June 2017

globally accepted recommendations for the management of breast cancer.

In developing countries like India, there is a need to develop the guidelines to streamline the management of breast cancer. To address this issue, the expert panel of KOLs met to discuss and arrive at a consensus statement to provide community oncologists practical guidelines on the management of breast cancer in Indian patients. The discussions were based on the current practices and scenario which exist in India. The mandate was to develop practical consensus recommendations applicable globally with emphasis on countries with limited resources. The core expert group discussed over several sessions and arrived at a consensus on the methodology to be used as well as develop the survey questionnaire.

The questionnaire was developed by a panel of experts from academia and ABSI, and these were in sync with the St. Gallen Consensus panel questions which suited to Indian needs and included limitations to evaluation, surgical treatment, surgical pathology, and adjuvant/neo-adjuvant treatment. The questions were provided with three to five options—numbered 1 to 5; one of which is most appropriate answer and also had abstain option. The series of multiple choice questions included key practical issues and management challenges. Each question was projected to panel of experts and audiences and voting was comprised by experts and audiences simultaneously during the fourth ABSICON held at Bangalore from 1 to 3 July 2016. Thus, at the end of every question, audiences' views and KOLs' views were collected. The survey answers were used as the basis for formulating the consensus statement, so that community oncologists have a ready-to-use practical consensus recommendation for breast cancer management. The ABSI 2016 will therefore serve to optimize management of breast cancer in conjunction with evolving literature, good clinical judgment, and individual patient characteristics and preferences.

A total of 16 broad question categories containing 47 unique questions were part of the expert group discussions (Table 1).

Highlights of the ABSI Consensus Statement on Breast Cancer

Breast Cancer Evaluation

There were three questions related to the evaluation of breast cancer and the answers were as follows:

A. Core biopsy is mandatory/preferred modality for diagnosis of breast cancer: 90.9% of audiences had affirmative opinion in comparison to 95.2% of experts.
B. Metastatic work-up: Should be done for stage I and II breast cancers (4.7% (audience) vs 0% (expert)), recommended for stage III breast cancer (55.7% (audience) vs 75% (expert)), and should be done in all breast cancer patients (39.6% (audience) vs 25% (expert)).
C. Positron emission tomography (PET) scan is preferred modality in clinically isolated recurrences or ambiguous lesion on conventional imaging and NOT for routinely staging all breast cancer patients: 87.6% of audiences had affirmative opinion in comparison to 76.2% of experts.

Expert Group Consensus Early breast cancer may be asymptomatic and there may be absence of pain and discomfort. So, it is very important to have a proper evaluation of the breast cancer. For the evaluation, the experts recommended mandatory core biopsy (Fig. 1), metastatic work-up for stage III breast cancer, and an early diagnosis which may enable an oncologist to provide an ideal treatment for management of breast cancer. This triple assessment is mandatory for breast cancer evaluation.

Breast Cancer Screening in India

The panel drafted one question related to breast cancer screening in India; question and the result were as follows:

The most applicable/ pragmatic screening modality for breast cancer in Indian scenario: mammography (20.2% (audience) vs 05% (expert)), clinical breast examination (55.0% (audience) vs 60% (expert)), and breast self-examination (28.8% (audience) vs 20% (expert)).

Expert Group Consensus Low cancer awareness, presence of stigma, fear, gender inequity, and decreased involvement in screening behavior (e.g., breast cancer self-examination) attribute to high mortality rates among women in India [8]. The audiences and experts have comparable responses, and the experts recommended clinical breast examination (Fig. 2) to screen the cancer which can be possible through proper awareness among women in India.

Surgery of the Primary (Early Breast Cancer (EBC))

This was one of the most important categories, and there were six questions drafted by the panel for the audiences and experts. The questions and the opinions were as follows:

A. For the women undergoing breast conserving surgery for invasive EBC and proceeding to standard radiation and adjuvant systemic therapy the minimum acceptable surgical margin: no ink on invasive tumor (37.5% (audience) vs 72.7% (expert)), 1–2-mm clearance (26.9% (audience) vs 9.1% (expert)), >2–5-mm clearance (12.5% (audience) vs 9.1% (expert)), and >5-mm clearance (22.1% (audience) vs 4.5% (expert)).

Table 1 Question categories addressed by the breast cancer expert group

S. no.	Broad question category: breast cancer	Number of questions
1	Breast cancer evaluation	03
2	Breast cancer screening in India	01
3	Surgery of primary EBC	06
4	Management of locally advanced breast cancer	04
5	Surgical management of LABC	03
6	Management of Axilla in EBC	07
7	Management of Axilla in LABC/post-NACT patients	01
8	Oncoplastic surgical principles	02
9	Post-mastectomy reconstruction	01
10	Risk reducing surgery	01
11	Adjuvant radiotherapy	07
12	Surgical pathology	01
13	Biomarkers	01
14	Molecular profiling of breast cancer	02
15	Adjuvant hormonal therapy	05
16	Breast cancer in young patients	02
Total		47

EBC early breast cancer, *LABC* locally advanced breast cancer, *NACT* neo-adjuvant chemotherapy

B. Unilateral multifocal and multicentric tumors can be treated with en-bloc excision, provided margins are clear, good cosmesis is ensured, and whole breast RT is planned: Yes (42.5% (audience) vs 85.7% (expert)) and never (52.8% (audience) vs 9.5% (expert)).

C. Should the width of margin that needs to be excised dependent on tumor biology (grade, hormone receptor, HER2neu)?: Yes (17.6% (audience) vs 05.0% (expert)) and no (77.8% (audience) vs 95% (expert)).

D. Should the width of margin that needs to be excised be greater after neo-adjuvant therapy?:Yes (18.8% (audience) vs 14.3% (expert)) and no (80.2% (audience) vs 81% (expert)).

E. Frozen section for margin assessment during breast conservation surgery should be: done in all classes (29.7% (audience) vs 10.0% (expert)), in select patients where indicated, it is preferable if expertise and infrastructure exists (62.4% (audience) vs 60.0% (expert)), and not recommended (7.9% (audience) vs 30% (expert)).

F. In case margin(s) are found positive after breast conservation surgery, which statement is most appropriate: Re-excision is not mandatory if up to two margins are found infiltrated (14.2% (audience) vs 9.5% (expert)), and re-excision is mandatory in all patients, except if skin/deep fascial margin only is positive (76.4% (audience) vs 85.7% (expert)).

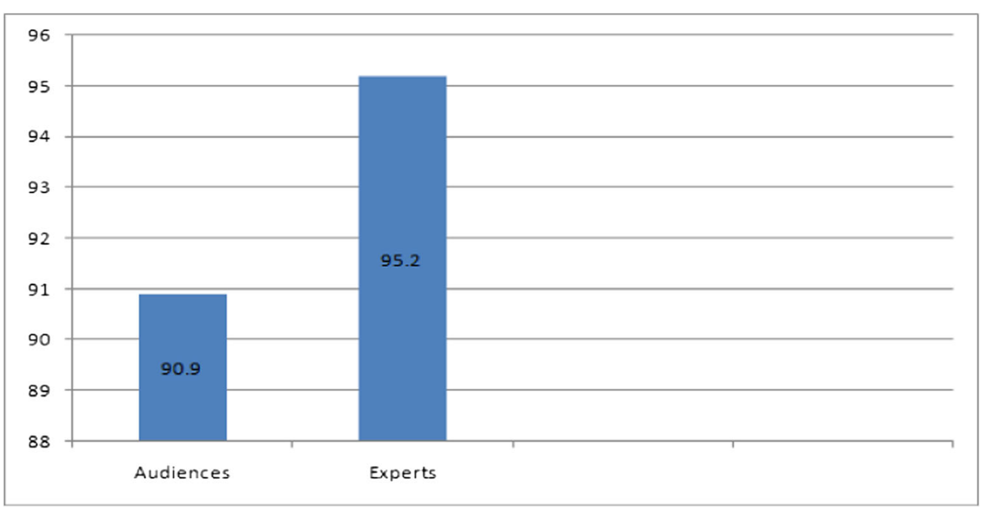


Fig. 1 Opinion on core biopsy (audiences vs experts)

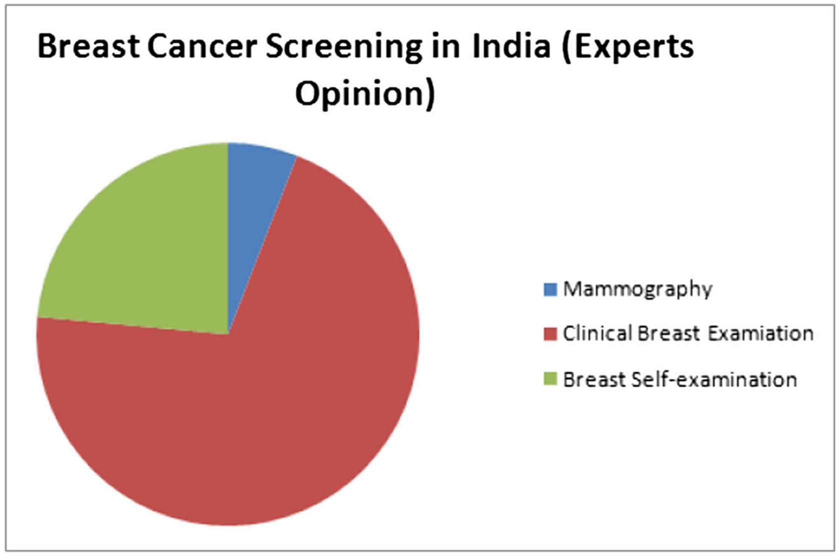


Fig. 2 Breast cancer screening in India

Expert Group Consensus For the surgical treatment of EBC, the experts recommended no ink on invasive tumor as the minimum acceptable surgical margin, en-block excision for treatment of unilateral multifocal and multicentric tumors. The experts also strongly recommended that width of margin that needs to be excised is independent of tumor biology, and it should not be greater after neo-adjuvant therapy. During surgery, frozen section for margin assessment should be preferred if expertise and infrastructure exist; and for the situations where case margin(s) are found positive after breast conservation surgery, the experts recommended mandatory re-excision in all patients, except if skin/deep fascial margin only is positive. The researches indicated that oncoplastic surgery results in excision of larger volume of breast tissue and correspondingly obtains wider surgical margins as compared to conventional breast conservation surgery [15].

Management of Locally Advanced Breast Cancer (LABC)

The panel drafted four questions for this category. The questions and the response of audiences and experts are provided below:

A. Neo-adjuvant chemotherapy is the standard of care in majority of locally advanced breast cancer patients: Yes (92% (audience) vs 90.5% (expert0) and no (6.6% (audience) vs 9.5% (expert)).
B. Most effective and practical regime for neo-adjuvant chemotherapy (NACT) includes anthracycline alone (11.7% (audience) vs 5.9% (expert)), taxanes alone (9.7% (audience) vs 0% (expert)), anthracycline followed by taxanes (69.7% (audience) vs 82.4% (expert)).
C. Best sequence/schedule of treatment for LABC patient is complete whole of NACT followed by surgery and RT (31.3% (audience) vs 66.7% (expert)), complete part of NACT followed by surgery, rest of chemo, and RT (66% (audience) vs 33.3% (expert)).
D. Best time to assess histology and hormone receptors in patients treated with NACT: Before initiation of NACT (94.5% (audience) vs 94.4% (expert)), after 2 cycles of NACT (1.4% (audience) vs 0% (expert)), after completion of NACT at surgery (2.7% (audience) vs 0% (expert)).

Expert Group Consensus For the management of LABC, the experts strongly batted for the neo-adjuvant chemotherapy as the standard of care for most of the LABC patients and anthracycline followed by taxanes as preferred and most effective practical regime for NACT. As per the experts, the sequence or schedule of treatment for LABC patients should be NACT followed by surgery and RT, and histology and hormone receptors in patients treated with NACT should be evaluated before initiation of NACT. These are the recommendations based on practical scenarios in India and can be differed as per actual/specific situations. Advances in systemic therapy, including radiation treatment, surgical management, and the development of new targeted agents, have significantly improved clinical outcomes for patients with LABC which can be used to provide optimum solutions for Indian patients [16].

Surgical Management of LABC

The panel drafted three questions for this category. The questions and the response of audiences and experts are provided below:

A. In LABC patients undergoing post-neo-adjuvant chemotherapy breast conservation surgery, which statement is most appropriate: All LABC patients are potential candidates for post-NACT-breast cancer surgery (BCS) (16.2% (audience) vs 26.3% (expert)), only a subset of LABC can be offered NACT BCS (74.3% (audience) vs 73.7% (expert)), BCS should not be offered to LABC patients (8.1% (audience) vs 0% (expert)).

B. Patients planned for NACT followed by BCS should have periphery of tumor marked before initiation or after first cycle of NACT (40.7% (audience) vs 35.3% (expert)), core of the tumor marked before initiation or after first cycle of NACT (48.3% (audience) vs 58.8% (expert)), and marking the tumor site not needed (9.7% (audience) vs 0% (expert)).

C. In patient whose tumor has responded to NACT, at surgery the extent of tissue to be excised at BCS: wide of original (pre-NACT) margins (36.6% (audience) vs 12.5% (expert)), wide of current (post-NACT) margins (60.0% (audience) vs 87.5% (expert)), and whole quadrant of breast (3.4% (audience) vs 0% (expert)).

Expert Group Consensus For the surgical management of LABC, the experts had the opinion that only a subset of LABC can be offered NACT BCS depending on the specifications, and the patients planned for NACT followed by BCS should have core of the tumor marked before initiation or after first cycle of NACT; although the patients could also have periphery of tumor marked before initiation or after first cycle of NACT for specific situations, if applicable. For the patients who have a positive tumor response to NACT, during surgery the extent to tissue to be excised at BCS should be wide of current (post-NACT) margins.

Management of Axilla in EBC

This category was very important and the panel drafted seven questions for this category. The questions and the response of audiences and experts are provided below:

A. USG-guided FNAC is preferable for preoperative staging of axilla before SLNB/ALND: Yes (45.2% (audience) vs 72.2% (expert)) and no (53.4% (audience) vs 22.2% (expert)).

B. Sentinel lymph node biopsy should be considered in clinically: Node negative axilla (93.8% (audience) vs 93.3% (expert)) and node positive axilla (6.2% (audience) vs 6.7% (expert)).

C. For sentinel lymph node biopsy (SLNB) technique which is the most appropriate statement: SLNB using blue dye alone can be performed in resource constrained setup (86.3% (audience) vs 63.2% (expert)) and combination of radioisotope and blue dye is mandatory for SLNB (12.3% (audience) vs 21.1% (expert)).

D. What is the acceptable false negative rate for SLNB: Up to 5% (43.8% (audience) vs 47.1% (expert)), up to 10% (46.6% (audience) vs 47.1% (expert)), and up to 20% (2.7% (audience) vs 0% (expert)).

E. Molecular analysis should be routinely performed for SLN assessment: Yes (13.1% (audience) vs 10.0% (expert)) and no (83.4% (audience) vs 90.0% (expert)).

F. Is completion ALND mandatory after micro-metastasis is identified in SLN: Yes (40.7% (audience) vs 5.6% (expert)) and no (55.9% (audience) vs 88.9% (expert)).

G. Should completion ALND be considered mandatory if macro-metastasis is identified in SLN: Yes (92.4% (audience) vs 61.1% (expert)) and no (6.9% (audience) vs 33.3% (expert)).

Expert Group Consensus For the management of axilla in EBC, the experts strongly recommended USG-guided FNAC for preoperative staging of axilla before SLNB/ALND and SLNB should be considered in clinically node negative axilla which can be performed in resource constrained setup using blue dye in countries like India; the acceptable false negative rate for SLNB can vary from 5 to 10%. For SLN assessment, routine molecular analysis was not recommended, and completion ALND is not mandatory after identification of micro-metastasis in SLN but it should be mandatory if macro-metastasis is identified in SLN. In current Indian scenario, the SLNB is now increasingly being considered the favored method to treat low-volume axilla, and various studies have proved its significance [17].

Management of Axilla in LABC/ Post-NACT Patients

This category had one question given below:

Which is the most appropriate statement for managing axilla in a patient planned to be treated with neo-adjuvant chemotherapy: SLNB should be performed before NACT (26.1% (audience) vs 26.7% (expert)), SLNB should be performed after NACT (34.5% (audience) vs 66.7% (expert)), SLNB is not recommended in post-NACT patients (26.1% (audience) vs 0% (expert)), and ALND can be avoided if one SLN is metastatic (7% (audience) vs 0% (expert)).

Expert Group Consensus For the management of axilla in LABC/post-NACT patients, experts recommended that SLNB should be performed after NACT for the patients planned to be treated with NACT.

Oncoplastic Surgical Principles that Every Breast Surgeon Should Know

The panel drafted two questions for this category. The questions and the response of audiences and experts are provided below:

A. After how much volume loss oncoplastic procedure should be considered after BCS: 10% (3.5% (audience) vs 14.3% (expert)), 20% (77.1% (audience) vs 71.4% (expert)), and 30% (16.0% (audience) vs 7.1% (expert)).
B. Central tumors are contraindications to breast conservation surgery: Yes (18.6% (audience) vs 6.7% (expert)) and no (81.4% (audience) vs 86.7% (expert)).

Expert Group Consensus The experts recommended that after BCS, if the volume loss is 20% then oncoplastic procedure should be considered and central tumors are not contraindications to breast conservation surgery. These are two oncoplastic surgical principles that every breast surgeon should know.

Post-mastectomy Reconstruction

This category had one question given below:

Preferred timing of post-mastectomy breast reconstruction: Immediate (76.2% (audience) vs 77.8% (expert)) and delayed (20.3% (audience) vs 22.2% (expert)).

Expert Group Consensus The experts strongly recommended that post-mastectomy breast reconstruction should be immediately performed (Fig. 3). As per the researches, breast reconstruction after resection of breast cancers is helpful in increasing the psychosocial functioning and quality of life among the treated patients [18].

Risk-reducing Surgery

This category had one question given below:

Which of the following procedures can be recommended for risk reduction in BRCA-positive women: Prophylactic bilateral mastectomy (29.3% (audience) vs 5.9% (expert)), prophylactic bilateral salpingo-oophorectomy (10.0% (audience) vs 5.9% (expert)), and both (54.3% (audience) vs 88.2% (expert)).

Expert Group Consensus The experts recommended that prophylactic bilateral mastectomy and prophylactic bilateral salpingo-oophorectomy can be performed for risk reduction in BRCA-positive women (Fig. 4). However, studies have suggested that total mastectomy provides the greatest breast cancer risk reduction due to removal of more breast tissue [19]. These surgeries are highly effective as bilateral prophylactic mastectomy has been shown to reduce the risk of breast cancer by at least 95% in women who have a deleterious mutation in the BRCA1 gene or the BRCA2 gene [20–23], while bilateral prophylactic salpingo-oophorectomy has been shown to reduce the risk of breast cancer by approximately 50% in women who have high risk of developing the disease [19].

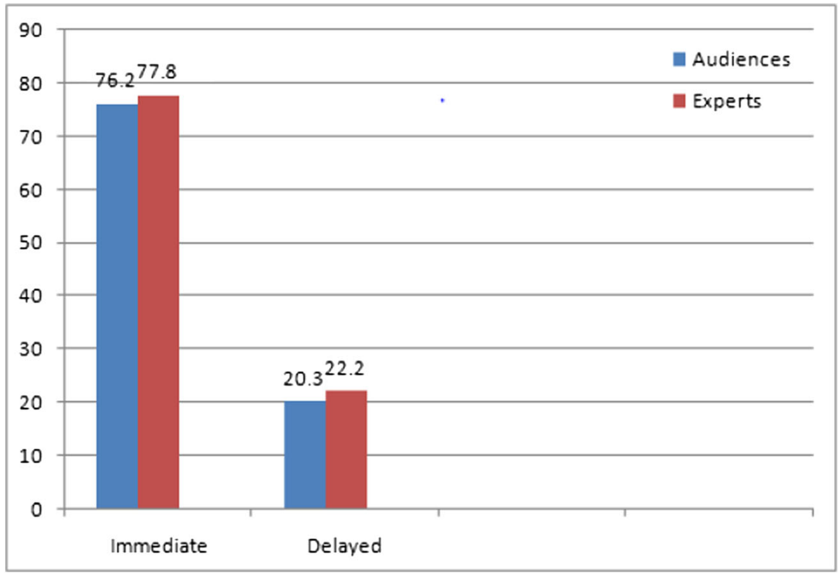
Adjuvant RT

The panel drafted seven questions for this category. The questions and the response of audiences and experts are provided below:

A. Is post-mastectomy radiotherapy recommended in T1/T2 with 1–3 node positive patients: Yes, without exception (25.9% (audience) vs 6.2% (expert)), yes, but can be omitted in selected patients (52.5% (audience) vs 62.5% (expert)), and no (20.9% (audience) vs 31.2% (expert)).
B. Does axillary radiation has any therapeutic role after complete ALND: Yes (33.3% (audience) vs 31.2% (expert)) and no (63.8% (audience) vs 68.8% (expert)).
C. Tumor bed radiation boost is mandatory following BCS for invasive ductal cancer: Yes (90.8% (audience) vs 64.7% (expert)) and no (7% (audience) vs 35.3% (expert)).
D. Most appropriate statement regarding accelerated partial breast radiation (APBI): APBI should be offered to a select group of early breast cancer patients (68.6% (audience) vs 93.3% (expert)) and APBI should be offered to all patients undergoing BCS (23.6% (audience) vs 0% (expert)).
E. In patients with T1 tumor and 1–2 metastatic SLNs, radiotherapy to axilla is a valid option instead of surgery in select cases?: Yes (59.2% (audience) vs 88.9% (expert)) and no (38.7% (audience) vs 5.6% (expert)).
F. Can radiotherapy be omitted in elderly and low-risk patients undergoing BCS: Yes (66.2% (audience) vs 87.5% (expert)) and no (29.7% (audience) vs 12.5% (expert)).
G. Approach to RT after neo-adjuvant therapy is based on: the stage before neo-adjuvant therapy (64.3% (audience) vs 76.5% (expert)), stage after neo-adjuvant therapy (32.9% (audience) vs 23.5% (expert)).

Expert Group Consensus The experts recommended that radiotherapy is recommended in T1/T2 with 1–3 node positive patients but can be omitted in selected patients and axillary radiation has no therapeutic role after complete

Fig. 3 Preferred timing of post-mastectomy breast reconstruction



ALND. Experts batted for tumor bed radiation boost following BCS for invasive ductal cancer based on selected patients. Experts strongly recommended that APBI should be offered to a select group of early breast cancer patients and for patients with T1 tumor and 1–2 metastatic SLNs, radiotherapy to axilla is a valid option instead of surgery in select cases. The experts advised to omit the radiotherapy for elderly and low-risk patients undergoing BCS and suggested that cancer stage before the neo-adjuvant therapy forms the base for radiotherapy.

After mastectomy, adjuvant treatment may include local irradiation, systemic therapy with cytotoxic chemotherapy, or endocrine therapy. The adjuvant treatment was considered useful, and a decrease was recorded in breast cancer mortality in the US and UK [24].

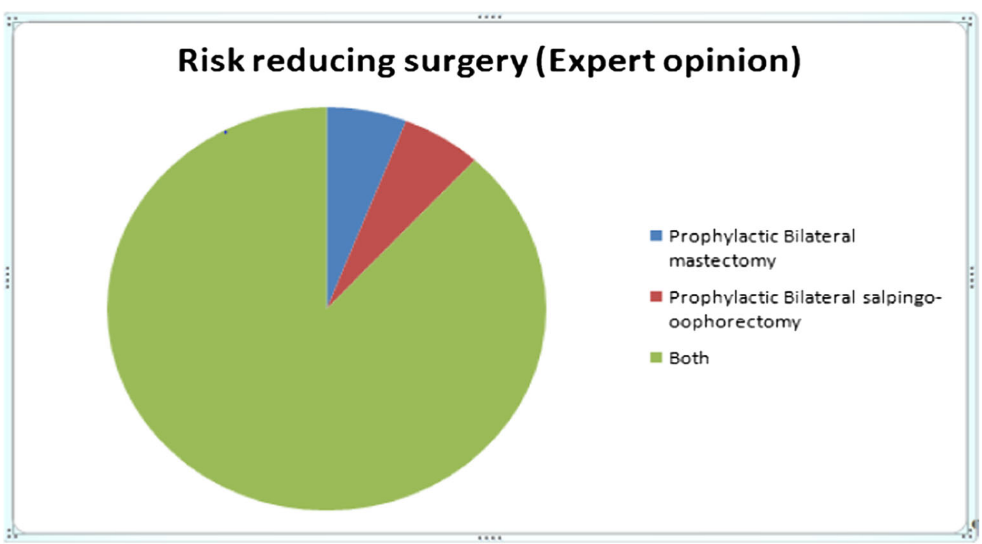
Surgical Pathology

This category had one question given below:

> Standardized reporting of breast histology including HP type, grade, margins, tumor numbers and size, lymph nodes, numbers, sizes, and number of metastatic nodes is desirable in most cases (11.6% (audience) vs 0% (expert)) and mandatory in ALL patients (87.7% (audience) vs 100% (expert)).

Expert Group Consensus The experts strongly recommended that reporting of breast histology must be mandatory in practice which should include HP type, grade, margins, tumor

Fig. 4 Expert opinion for risk-reducing surgery



numbers and size, lymph nodes, numbers, sizes, and number of metastatic nodes.

Biomarkers

This category had one question given below:

> Minimum biomarkers that should be tested in breast pathology: IHC for ER and PR (7.5% (audience) vs 0% (expert)), IHC for ER, PR and HER2neu (65.8% (audience) vs 64.7% (expert)), IHC for ER, PR, and FISH for HER2neu (8.9% (audience) vs 0% (expert)), and ER, PR, HER2neu, and Ki67 (17.1% (audience) vs 35.3% (expert)).

Expert Group Consensus The experts recommended that IHC for ER, PR, and HER2neu should be tested in breast pathology as a minimum biomarker. For selected patients, IHC for ER, PR, HER2neu, and Ki67 may also be tested.

Molecular Profiling of Breast Cancer

This category had two questions given below:

A. Multigene signature testing is routinely recommended to decide ideal adjuvant treatment: Yes (13.9% (audience) vs 15.4% (expert)) and no (80.6% (audience) vs 84.6% (expert)).
B. OncotypeDx testing is recommended for which subset of patients: Node positive, ER/PR positive, HER2neu negative (12.1% (audience) vs 6.2% (expert)), node negative, ER/PR positive, HER2neu negative (46.4% (audience) vs 87.5% (expert)), node positive, ER/PR negative, HER2neu positive (25.7% (audience) vs 6.2% (expert)).

Expert Group Consensus The experts recommended that for molecular profiling of breast cancer, multigene signature testing (Fig. 5) is not the right approach to decide the ideal adjuvant treatment and oncotypeDx testing is strongly recommended for node negative, ER/PR positive, and HER2neu negative patients.

Adjuvant Hormonal Therapy

The panel drafted five questions for this category. The questions and the response of audiences and experts are provided below:

A. What is the ideal duration for adjuvant hormonal therapy in premenopausal ER/PR+ patients: 5 years (38.6% (audience) vs 23.1% (expert)) and 10 years (60% (audience) vs 76.9% (expert)).
B. In premenopausal hormone receptor positive breast cancer patients, ovarian suppression as adjuvant therapy should be considered in addition to tamoxifen or chemotherapy: In all patients (28.7% (audience) vs 18.8% (expert)), only in high-risk patients (51% (audience) vs 68.8% (expert)), not recommended in majority (18.2% (audience) vs 12.5% (expert)).
C. Can some post-menopausal breast cancer patients be adequately treated with tamoxifen alone?: Yes (69.4% (audience) vs 57.1% (expert)) and no (27.8% (audience) vs 35.7% (expert)).
D. In a post-menopausal breast cancer patient, if an AI is used, should it be started up-front: No (7.2% (audience) vs 16.7% (expert)), yes—in all patients (53.6% (audience) vs 75% (expert)), and yes—in patients at higher risk (31.9% (audience) vs 8.3% (expert)).
E. In post-menopausal breast cancer patients treated with up-front AI, it should be used for 5 years (62.2% (audience) vs 75% (expert)), 10 years (31.9% (audience) vs 12.5% (expert)).

Expert Group Consensus For the use of adjuvant hormone therapy, the experts recommended that ideal duration for adjuvant hormonal therapy in premenopausal ER/PR+ patients is 10 years (Fig. 6) and in high-risk patients, ovarian suppression as adjuvant therapy should be considered in addition to tamoxifen or chemotherapy. Some post-menopausal breast cancer patients may or may not be adequately treated with tamoxifen alone. AI in post-menopausal breast cancer patients should be started up-front in all patients and should be used for 5 years. Tamoxifen is found effective in premenopausal and post-menopausal women with hormone-sensitive (ER-positive) breast cancer [25]. Although tamoxifen's use is associated with post-menopausal symptoms such as hot flashes and vaginal discharge [26], its overall risk-benefit ratio is considered favorable for patients, and it should be offered as adjuvant treatment to women with hormone-sensitive breast cancer [27].

Breast Cancer in Young Patients

The panel drafted two questions for this category. The questions and the response of audiences and experts are provided below:

A. Testing for BRCA1 and -2 mutations is indicated in women <40 years: Yes (65.2% (audience) vs 75% (expert)) and no (31.9% (audience) vs 25% (expert)).
B. Fertility preservation (e.g., by ovarian tissue or oocyte conservation) should be offered to women <40 years:

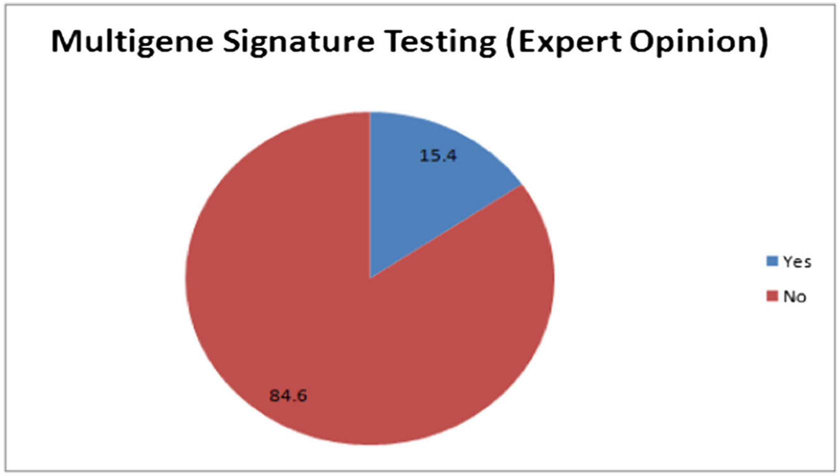


Fig. 5 Multigene signature testing

Yes (91.6% (audience) vs 84.6% (expert)) and no (4.9% (audience) vs 7.7% (expert)).

Expert Group Consensus For breast cancer in young patients, it is recommended to test the BRCA1 and -2 mutations in women <40 years of age, and it is highly recommended to offer the fertility preservation to women <40 years of age. The patients under 40 years of age comprise about 5% of the overall breast cancer population, so it's very important to diagnose the disease at early stage [28] and an improved survival with early detection is a valid argument for careful screening among young patients [29].

Conclusion

The breast cancer expert group had the specific mandate to develop practical consensus recommendations for easy application by the community oncologist. The expert panel considered the existing evidences, current practices in India, and international data and recommended the consensus guidelines which are the perfect blend of the evidences, clinical expertise, and real-life preferences. The consensus guidelines emphasize the need of mandatory core biopsy, metastatic work-up for stage III breast cancer, triple assessment, and clinical breast examination for diagnosis and screening of breast cancer in India.

The guidelines highlighted the recommendations for surgical treatment of EBC, LABC, management of LABC, use of NACT, and management of axilla in EBC and LABC. Oncoplastic surgical principles were recommended for every breast cancer surgeon. Other key highlights of the recommendations include immediate post-mastectomy breast reconstruction, prophylactic bilateral mastectomy, and prophylactic bilateral salpingo-oophorectomy for risk reduction in BRCA-positive women as one of the option, ideal scenarios for use of adjuvant radiotherapy and adjuvant hormone therapy,

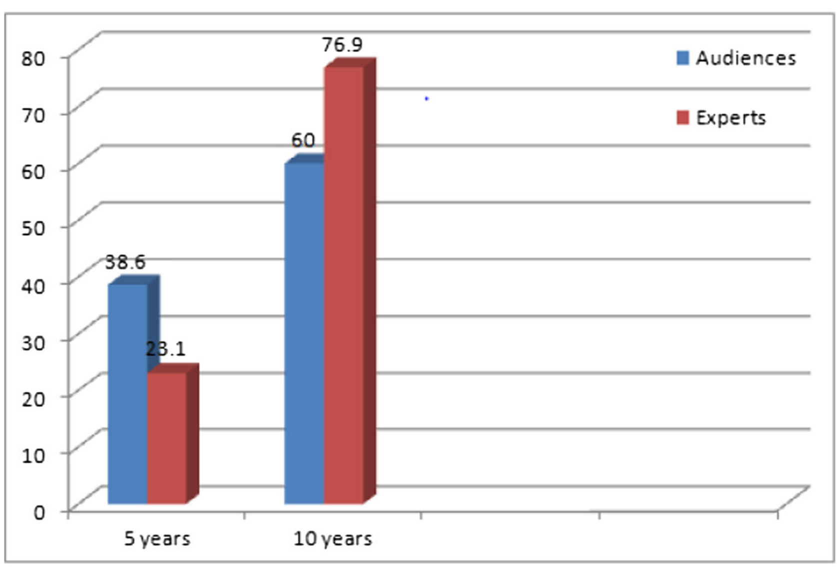


Fig. 6 Duration for adjuvant hormonal therapy

importance of reporting breast histology, molecular profiling of breast cancer, and testing of breast cancer in young patients.

Unresolved issues of importance will be addressed in the updated version of this document as more data becomes available, and the group makes insightful revisions. Therefore, the group encourages gathering real world evidences and optimum treatment options suitable for Indian patients. Although the guidelines must be very useful to the oncology surgeons to utilize these as the best practices, the main challenge will be to focus on its effective implementation and spreading the awareness among the Indian patients. The aim of these consensus guidelines is to find and define the Indian solutions for Indian problems. All those interested in contributing are requested to contact us via email. The aim is to find Indian solutions for Indian problems.

Recommendation Summary

- For the screening of breast cancer, mandatory core biopsies, metastatic work-up for stage III breast cancer, and triple assessment are recommended.
- The panel emphasizes the need of breast cancer examination to screen the cancer.
- For surgical treatment, the panel recommended no ink on invasive tumor as the minimum acceptable surgical margin and width of margin that needs to be excised is independent of tumor biology; it should not be greater after neo-adjuvant therapy.
- The panel batted for neo-adjuvant chemotherapy as the standard of care for most of the LABC patients.
- The panel recommended that only a subset of LABC can be offered NACT BCS depending on the specifications.
- For the management of axilla in EBC, the experts strongly recommended USG-guided FNAC for preoperative staging of axilla before SLNB/ALND and SLNB should be performed after NACT for the patients planned to be treated with NACT.
- The oncoplastic procedure should be considered if the volume loss is 20% after BCS and post-mastectomy breast reconstruction should be immediately performed.
- Prophylactic bilateral mastectomy and prophylactic bilateral salpingo-oophorectomy can be performed for risk reduction in BRCA-positive women.
- The experts panel batted for tumor bed radiation boost following BCS for invasive ductal cancer based on selected patients and strongly recommended that APBI should be offered to a select group of early breast cancer patients and for patients with T1 tumor and 1–2 metastatic SLNs.
- The experts advised to omit the radiotherapy for elderly and low-risk patients undergoing BCS.
- The experts strongly recommended that reporting of breast histology must be mandatory in practice.
- For the use of adjuvant hormone therapy in high-risk patients, ovarian suppression as adjuvant therapy should be considered in addition to tamoxifen or chemotherapy.
- The panel strongly recommended testing the BRCA1 and -2 mutations in women <40 years of age.

Acknowledgements We would like to thank all expert members involved in the consensus meeting of ABSI and who participated effectively to express their views and depth of practical excellence which enabled us to generate these consensus guidelines and panel of expert scientific team Gaurav Agarval, SVS Deo, and Vani Parmar coordinated with ABSI in identifying relevant questions to be voted and discussed.

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World J Surg
https://doi.org/10.1007/s00268-018-4504-2

ORIGINAL SCIENTIFIC REPORT

Prospective Randomized Trial of Use of In-House Prepared Low-Cost Radiopharmaceutical Versus Commercial Radiopharmaceutical for Sentinel Lymph Node Biopsy in Patients with Early Stage Invasive Breast Cancer

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Abstract

Background The current standard-of-care for surgical staging of the axilla in clinically node-negative (N0) early breast cancers is sentinel lymph node biopsy (SLNB), which requires expensive radiopharmaceuticals for efficacious results. In-house produced low-cost radiopharmaceuticals may be the solution and have shown efficacy in earlier observational/pilot studies. We compared SLNB using in-house prepared radiopharmaceutical (^{99m}Tc-Antimony-colloid) versus commercially marketed radiopharmaceutical (^{99m}Tc-Sulphur-colloid) in this prospective randomized study.

Study Design 78 clinically N0 early breast cancer patients (T1/2, N0 stages), undergoing primary surgery were prospectively randomized 1:1 into two groups; to receive SLNB using methylene blue, and either ^{99m}Tc-Antimony colloid (Group-1) or ^{99m}Tc-Sulphur colloid (Group-2). Completion axillary dissection was done in all (validation SLNB). SLNB indices were compared between the groups.

Results The groups were comparable with regard to age, stage, tumour size, hormone receptors and HER2neu status. Cost of the in-house prepared ^{99m}Tc-antimony colloid was 16-times lesser compared to ^{99m}Tc-sulphur colloid. SLN identification rates (IR) in Groups 1 and 2 were 100 and 97.4% respectively, ($p > 0.05$). False negative rates (FNR) in Group 1 and 2 were 6.3% (1/16 patients) and 7.7% (1/13 patients), respectively, ($p > 0.05$). There were no major allergic reactions in either group.

Conclusion In this prospective randomized trial on early breast cancer patients, accuracy of SLNB was comparable using in-house prepared, ^{99m}Tc-antimony colloid and commercially marketed ^{99m}Tc-sulphur colloid as radiopharmaceutical, while ^{99m}Tc-antimony colloid was much cheaper than ^{99m}Tc-sulphur colloid.

Introduction

Sentinel lymph node biopsy (SLNB) is the current standard of care for axillary staging in clinically node negative (N0)

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Awarded the BSI Best paper (podium) award at the World Congress of Surgery, Basel, Switzerland in August 2017.

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Published online: 30 January 2018

early breast cancers (EBC) patients. SLNB offers advantages of lesser morbidity including reduced arm oedema, and better quality of life, when compared to axillary lymph node dissection (ALND) [1]. Numerous prospective trials have confirmed the safety and oncological efficacy of the SLNB procedure in predicting the axillary staging, with SLN identification rates (SLN-IR) greater than 95% and false-negative rates (SLN-FNR) lower than 10% in EBC patients [2]. The SLNB procedure can be performed using a colour (blue) dye, radio-pharmaceutical (^{99m}Tc-sulphur/antimony/gold colloid) or a combination of blue dye and radio-pharmaceutical, which is the preferred method. Most studies of SLNB published in Western literature have used commercially available kits for blue dyes as well as radiopharmaceuticals. However, there is a relative paucity of data comparing use of various radio-pharmaceuticals in SLNB, with no prospective trials addressing low-cost methods.

In this prospective pilot validation study conducted on stage I and II (cT1/T2, N0, M0) EBC patients, we compared the relative safety and efficacy of a commercially available radiopharmaceutical (^{99m}Tc-Sulphur-colloid) with an in-house prepared low-cost radiopharmaceutical (^{99m}Tc-Antimony-colloid) for SLNB, while also comparing the costs of the low-cost method versus the commercially available kits.

Methods

This was a time-bound, prospective randomized pilot trial performed on 78 clinically N0, uni-focal, EBC patients treated at a tertiary care referral hospital from 2013 to 2015, after due approval from the Institute Ethics Committee. Patients who were pregnant, and those who did not consent for a validation SLNB, had received neo-adjuvant chemotherapy (NACT), were diagnosed to have ductal carcinoma in situ (DCIS) or multicentric tumours were excluded from this study. All patients had a pre-operative diagnosis of breast cancer made by either fine needle aspiration cytology (FNAC) or core needle biopsy, and was confirmed by final histopathology of the resected specimen. All patients underwent primary surgical management, either in the form of breast conserving surgery (BCS) or simple mastectomy (SM), along with validation SLNB (and therefore routine completion ALND in all, irrespective of SLNB histology), followed by adjuvant treatment with chemotherapy/ external beam radiotherapy (EBRT)/ anti-hormonal treatment/ trastuzumab, as indicated, as per institutional protocols.

In both groups, SLNB was performed using identical techniques. A combination of low-cost blue dye—methylene-blue (2 ml of 1% w/v aqueous solution) and 37 MBq (1 mCi) of radiopharmaceutical was used. Patients were randomized by block randomization, using online software *“GraphPad QuickCalcs®*) into two groups, to undergo SLNB using one of the two radiopharmaceuticals: either in-house prepared low-cost ^{99m}Tc-Antimony-colloid (Group I, 39 patients) or commercially available ^{99m}Tc-Sulphur-colloid (Group II, 39 patients). ^{99m}Tc-Antimony-colloid was prepared in-house by the Department of Nuclear Medicine using standard techniques [3, 4]; while Sulphur Colloid was obtained from commercially supplied kit by the Department of Atomic Energy (Mumbai, India), from a distance of 1400 km (870 miles) away from the study site. The operating surgeons were blinded to the type of radiopharmaceutical used; which was known only to the Nuclear Medicine physician (SG).The cost per patient for ^{99m}Tc-Antimony-colloid was INR 55 (USD 0.8), versus INR 850 (USD 12.4) for ^{99m}Tc-Sulphur-colloid. Most patients in both groups (Group I: 71.8%, Group II: 69.2%) had injection of the radiopharmaceutical on the evening prior to surgery; with the remainder having the dye injected on the morning of surgery. The radiopharmaceutical was injected by the Nuclear Medicine physician by a combined sub-areolar (50% of injection volume, 1 ml) and peri-tumoural (50% of injection volume, 1 ml) technique; the blue dye was injected after induction of anaesthesia in the operation room by the surgeon using the same technique. Radio-guided SLNB was done using a hand-held probe attached to the Neoprobe 2000 Gamma Detection System (Ethicon Endo-Surgery Inc, Johnson & Johnson, Cincinnati, OH, USA). Any hot and/or blue SLNs; and any suspicious enlarged non-hot & non-blue SLNs seen during surgery were removed. As part of Validation SLNB, a completion Level I and II axillary lymph node dissection was performed in all patients; Level III dissection was done only when nodes medial to the Pectoralis Minor muscle were detected to be enlarged/palpable intra-operatively.

SLN sectioning and processing for histopathological examination was performed using standard protocols [5, 6]. The SLNs of 34 patients in Group I (87.1%) and 32 patients in Group II (84.2%) were subjected to frozen section histology. All SLNs and all the axillary nodes removed at the time of ALND were fixed in 10% formaldehyde, embedded in paraffin, sectioned, and stained with haematoxyline & eosin (H&E). Evidence of lymph nodal metastases was defined as any metastatic foci greater than 2 mm in size discernable on frozen section histology and/or on H&E stained sections.

Values of true & false positive, and true & false negative SLN histology were recorded by comparison of SLN histology with the gold standard, i.e. histology of the ALND specimen. SLN identification rates (IR), false negative rates (FNR), sensitivity, and negative predictive value (NPV) of SLNB in predicting the histology of the axillary nodes were calculated and compared between the two groups. The results were also compared and with a meta-analysis of SLNB studies reporting on the SLN FNR [7], and with an EBC validation study previously published by our group [8].

Fischer's exact test was used for comparison of categorical variables, and Student's t test was used to compare continuous variables. Statistical analysis was performed using the SPSS 17 software package (SPSS Statistics for Windows, Version 17.0, SPSS Inc., Chicago, USA). Any p values ≤ 0.05 were considered statistically significant.

Results

Seventy-eight patients in total were inducted, equally distributed in Group I and Group II (39 patients each). Clinical details of patients are summarized in Table 1; patients of both groups were comparable in terms of mean age, mean tumour size, index tumour stage at time of initial diagnosis, tumour histology, tumour grade, immunohistochemical (IHC) subtype and type of breast surgery performed.

In Group I, using the combination of blue dye and low-cost radiopharmaceutical, the SLN IR was 100% (Table 2), comparable to that of Group II (97.4%, $p = 1.000$) (Table 2). Using radiopharmaceuticals alone, the IR was 97.4% in Group-I, comparable with 92.3% in Group-II ($p = 0.872$). In both groups, the median number of SLNs removed was 2 (range 0–5) (Table 3). The mean number of SLNs was comparable in the two groups (2.7 ± 1.4 nodes in Group I vs 2.6 ± 1.5 nodes in Group II, $p = 0.816$). SLN FNR (Table 2) was comparable between the two groups (6.3% in Group I vs 7.7% in Group II, $p = 1.000$).

There were no significant differences observed in the IR and FNR according to patient and tumour characteristics, and IHC. Six patients (15.4%) in Group-I and 5 (13.2%) in Group-II patients had the SLN(s) as the only lymph node(s) that was/were metastatic. Additional lymph node(s) with metastasis other than the SLN(s) was/were present in 9 (23.1%) patients in Group I and 7 (18.4%) patients in Group II. The sensitivity of the SLNB procedure in Group I was 93.8% with a negative predictive value (NPV) of 95.7%, comparable to Group II, which had sensitivity of 92.3% and NPV of 96% ($p = 1.000$). Frozen section accuracy (Concordance with final histopathology) was 97.1% (33/34 patients) in Group I and 100% (32/32 patients) in Group II. No major allergic reactions were observed in either group.

Table 1 Clinical and pathological attributes, and treatment details of patients

Attribute	Group I: antimony colloid + MB ($n = 39$)	Group II: sulphur colloid + MB ($n = 39$)	p
Mean age (years) Mean ± SD	52.5 ± 12.0	53.8 ± 13.8	0.639
Mean tumour size (cm) Mean ± SD, clinical (Range)	3.1 ± 1.0 (1.0–5.0)	3.4 ± 0.9 (1.5–5.0)	0.121
Mean tumour size (cm) Mean ± SD, pathological (Range)	2.9 ± 1.2 (1.5–6.0)	3.1 ± 1.3 (1.5–6.0)	0.348
IHC sub-type			
ER/PR positive, HER2-negative	19 (48.7%)	18 (46.1%)	1.000
Triple positive	4 (10.2%)	2 (5.1%)	0.675
ER/PR negative, HER2-positive	7 (17.9%)	8 (20.5%)	1.000
Triple negative	9 (23.1%)	11 (28.2%)	0.796
Tumour histology			
IDC	34 (87.2%)	33 (84.6%)	1.000
IDC with DCIS	5 (12.8%)	6 (15.4%)	
Tumour grade			1.000
I	1 (2.6%)	2 (5.1%)	
II	20 (51.3%)	20 (51.3%)	
III	18 (46.1%)	17 (43.6%)	
Breast surgery			0.497
Breast conserving surgery	21 (53.8%)	17 (43.6%)	
Mastectomy	18 (46.2%)	22 (56.4%)	

cm centimetres, *MB* methylene blue, *SD* standard deviation, *IHC* immunohistochemistry, *ER* oestrogen receptor, *PR* progesterone receptor; *HER2* human epidermal growth factor receptor 2, *IDC* infiltrating ductal carcinoma; *DCIS* ductal carcinoma in-situ

Table 2 Comparison of SLN results between low-cost and commercial radiopharmaceutical groups

Attribute	Group I: antimony colloid + MB ($n = 39$)	Group II: sulphur colloid + MB ($n = 39$)	p
Blue dye alone (Blue SLNs only)	1/39 (2.7%)	2/39 (5.1%)	1.000
Radiopharmaceutical alone (Hot SLNs only)	5/39 (12.8%)	4/39 (7.7%)	1.000
Both methods (hot + blue SLNs)	33/39 (84.6%)	32/39 (82.0%)	1.000
SLN identification rate (Using radiopharmaceutical alone)	38/39 (97.4%)	36/39 (92.3%)	0.872
SLN identification rate (combined method)	39/39 (100%)	38/39 (97.4%)	1.000
True positive SLN	15	12	1.000
Sensitivity	15/16 (93.7%)	12/13 (92.3%)	
False negative SLN	1	1	
False negative rate {FN/(TP + FN)}	1/16 (6.3%)	1/13 (7.7%)	
Negative predictive value	95.7%	96.0%	1.000

SLNs sentinel lymph nodes, *MB* methylene blue, *FN* false negative, *TP* true positive

Table 3 Sentinel lymph nodes removed

Number of SLNs identified	Group I: antimony colloid + MB ($n = 39$)	Group II: sulphur colloid + MB ($n = 39$)	p
0	0 (0%)	1 (2.6%)	
1	11 (28.2%)	8 (20.5%)	
2	9 (23.1%)	15 (38.5%)	
3	7 (17.9%)	4 (10.3%)	
4	6 (15.4%)	4 (10.3%)	
5	6 (15.4%)	7 (17.9%)	
Median no. of SLNs	2	2	
Mean no. of SLNs (Mean ± SD)	2.7 ± 1.4	2.6 ± 1.5	0.816

SLNs sentinel lymph nodes, *MB* methylene blue, *SD* standard deviation

Discussion

In low-and-middle income countries (LMICs), cost and availability of radio-pharmaceuticals prohibit their regular use in SLNB, even in centres which have nuclear medicine facilities, and have access to gamma probe which is often shared by various surgical teams for a variety of radio-guided procedures. Despite overwhelming evidence that SLNB is the gold standard procedure available today for surgical staging of the axilla—echoed in guidelines issued by virtually all surgical and oncological societies [6, 9], various authors have suggested other procedures, such as axillary sampling, in lieu of SLNB [10, 11], often citing cost of the procedure and material used including gamma probe, radiopharmaceutical and blue dye as being the cause of non-acceptance. Over the past two decades, an increase in the overall incidence of breast cancer in LMICs has been observed and a subsequent increase in the presentation of EBC/node-negative disease [12, 13].

The results of this prospective, randomized pilot trial imply that the accuracy of SLNB in EBC patients undergoing primary surgery using either low-cost in-house prepared radiopharmaceutical (^{99m}Tc-Antimony-colloid) or commercially available ^{99m}Tc-Sulphur-colloid is comparable, with equally efficacious results. These results were comparable to results of a previous study on EBC patients by our group, reported earlier ($n = 70$, SLN-IR 95.7% and FNR 8.7%) [8], and with the FNR of 7.5%, published in a meta-analysis of 183 studies reporting on 9220 patients [7]. These results may be less relevant in most developed countries, where, today, SLNB is the undisputed standard-of-care in managing the node-negative axilla that is available to the vast majority, if not the entire population. However, in resource-limited countries, even today, the most commonly performed procedure in N0 patients is a formal axillary dissection. The primary reason for this incongruity in treatment protocol is non-availability of suitable resources and materials for the SLNB procedure.

Commercially marketed radiopharmaceuticals such as ^{99m}Tc-Sulphur-colloid add substantial costs to breast surgery for node-negative disease. Also, these materials are not available easily in LMICs, and their procurement on a regular basis is a challenge, as these are not marketed by the manufacturers in LMICs. Also, there exists a geographic bias towards radio-pharmaceutical use: while ^{99m}Tc-Sulphur colloid is the preferred product in the United States, Canadian and Australian users prefer ^{99m}Tc-Antimony Trisulfide, while in Europe, ^{99m}Tc-human serum albumin (HSA) nanocolloids are widely used [14].

Technetium-labelled Antimony Sulphide (^{99m}TcSb^{2}S^3) has been extensively evaluated in lymphatic mapping and lymphoscintigraphy, more so during 1975–1985, perhaps more than any other ^{99m}Tc compound [14]. Early studies demonstrated the efficacy of this radiolabelled colloid providing optimal mobilization and dispersion from the interstitial injection site, with a uniform particle size of 0.003–0.03 μm [14–16].

By using in-house prepared ^{99m}Tc-Antimony colloid for SLNB, we were able to achieve a 15-fold cost reduction (INR 55 vs INR 850). This is the first study comparing in-house prepared ^{99m}Tc-Antimony colloid with a commercially available radiopharmaceutical. A literature search revealed only one other prospective trial on a total of 50 patients, which compared ^{99m}Tc-Antimony colloid with ^{99m}Tc-MIBI (methoxyisobutylisonitrile), revealing comparable efficacy between the two radiopharmaceuticals [17].

A limitation of our study is that it had a small sample size, which was due to time and grant constraints. A larger, multi-centre study of this nature would certainly be beneficial. The benefits of this study would especially appeal to breast surgeons and hospitals in LMICs, where despite an increase in the overall incidence of breast cancer including EBC and node negative disease, access to facilities offering SLNB is limited due to cost and availability of dyes.

Acknowledgements This prospective study was made possible with the aid of a SGPGIMS Intramural Grant. The authors would also like to acknowledge the Resident Surgeons of the Department of Endocrine and Breast Surgery, SGPGIMS, Lucknow; and Mr. Subhash Kheruka of the Department of Nuclear Medicine, SGPGIMS, Lucknow for their help.

Compliance with ethical standards

Conflict of interest None.

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Morbidity of Chemotherapy Administration and Satisfaction in Breast Cancer Patients: A Comparative Study of Totally Implantable Venous Access Device (TIVAD) Versus Peripheral Venous Access Usage

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World Journal of Surgery
Official Journal of the International Society of Surgery/Société Internationale de Chirurgie

ISSN 0364-2313

World J Surg
DOI 10.1007/s00268-013-2378-x

Springer

World J Surg
DOI 10.1007/s00268-013-2378-x

World Journal of Surgery

Morbidity of Chemotherapy Administration and Satisfaction in Breast Cancer Patients: A Comparative Study of Totally Implantable Venous Access Device (TIVAD) Versus Peripheral Venous Access Usage

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Abstract

Background This prospective, non-randomized, comparative study evaluated morbidity of chemotherapy administration via a totally implantable venous access device (TIVAD) versus peripheral intravenous access (PIVA), and satisfaction in breast cancer patients in a limited-resource setting.

Methods Consecutive patients receiving chemotherapy via TIVAD ($n = 114$) or PIVA ($n = 159$) were studied. Venous access-related events were recorded. Morbidity and satisfaction with TIVAD or PIVA as perceived by the patients were assessed using a specifically designed questionnaire, which patients filled after 1st cycle of, and after completion of all chemotherapy.

Results Patients in the two groups were of comparable age, body mass index, and disease stage. Acceptance of TIVAD was higher in literate patients. TIVAD did not interfere with sleep or activities in 90 % of patients. The majority (81.2 %) were satisfied with the cosmetic outcome, 91.5 % would have TIVAD re-inserted if the need arose, and 89.6 % would recommend it to others. Non-fatal complications occurred in 16 patients, and TIVAD had to be removed prematurely in five patients. In the PIVA group, 40 % needed multiple needle pricks and 55.8 % developed thrombophlebitis or staining of arms. Drug extravasation and ulceration were suffered by 8.3 and 4.2 %, respectively. However, 78.3 % of patients reported no interference with daily activities and only 26 % would prefer a TIVAD. Those receiving more than six chemotherapy cycles were dissatisfied to a greater extent with PIVA ($p < 0.05$).

Conclusions Breast cancer chemotherapy via TIVAD is safe and convenient and results in high satisfaction levels, although it involves additional expenditure. Chemotherapy via PIVA is acceptable, albeit with lower satisfaction, more so in those receiving more than six chemotherapy cycles.

Kul Ranjan Singh and Gaurav Agarwal have contributed equally and should be considered joint first authors.

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Introduction

Totally implantable venous access devices (TIVADs) were introduced in oncology practice in the 1980s, and are considered a standard of care for administration of intravenous (IV) chemotherapeutic drugs in certain centers, more so for patients needing long-term chemotherapy (CTx) and other supportive treatment [1, 2]. TIVAD use aims to achieve easy, painless, and secure venous access. Furthermore, it can reduce the apprehension and anxiety associated with IV access that increases with each subsequent cycle of CTx. Numerous studies have established TIVAD as a safe and efficacious way of administering CTx in various malignancies, including breast [3, 4]. Few studies have studied patient satisfaction with TIVAD and the impact of TIVAD on quality of life (QOL) [5–9]. No large series has looked into the safety of CTx administration via TIVAD, or patient acceptance and satisfaction with TIVAD in developing countries specifically in breast cancer patients. Unlike most other malignancies, patients with

Published online: 04 December 2013

breast cancer are almost exclusively middle age to elderly females, and in whom administration of CTx is avoided in the arm on the side of pathology.

The aim of this prospective comparative study conducted on breast cancer patients managed in a developing country was to assess the morbidity of, and patient satisfaction with, CTx administration via a TIVAD compared with a cohort of patients receiving CTx via peripheral IV access (PIVA).

Patients and methods

This was a prospective, non-randomized, comparative study of 273 breast cancer patients receiving CTx in a specialist breast cancer centre in India, with due approval from the Institute's research ethics committee. Consecutive consenting breast cancer patients who were initiated on CTx on or after 1st July 2010, and completed such treatment by 31st December 2012, were included. All patients underwent appropriate evaluation and had a comprehensive treatment plan decided by the institutional multi-disciplinary breast tumor board. Patients who were planned to receive CTx and other IV systemic treatment such as trastuzumab and zoledronic acid were counseled regarding the possible routes of IV administration, namely TIVAD and PIVA. Patients were provided detailed information in their own language about the implantation procedure of TIVAD, the processes of IV access using TIVAD and PIVA, their advantages and limitations, including potential complications, and the financial implications of both routes of CTx administration. Having understood these, the patients were asked to choose one of the two routes of CTx administration, and informed consent was obtained prior to start of treatment. A total of 114 patients consented to have TIVAD implantation for CTx, while 159 patients opted to receive CTx via PIVA.

After obtaining informed consent for TIVAD implantation, the procedure was carried out in the operating room under local anesthesia with IV prophylactic beta-lactam antibiotic. A hard-base single-chamber silastic port with 8.0 F single lumen Groshong valve tipped venous catheter (BardPort® or X-Port®, Bard access systems Inc., Salt Lake city, UT, USA) was used. The internal jugular vein (IJV) on the side opposite to the diseased side was punctured low in the neck with ultrasonography guidance using an introducer needle, through which a guide wire was introduced. C-arm fluoroscopy was used to ascertain the position of the guide wire, and the dilator and peel-away sheath were threaded over the guide wire. A venous catheter was introduced through the peel-away sheath, and tip of the catheter was positioned in the superior vena cava just short of the right atrium, as ascertained on fluoroscopy. The peel-away sheath was then removed. Using fluoroscopy, the site for the port reservoir was marked in the ipsilateral delto-pectoral groove superficial to the second rib. A subcutaneous pocket was fashioned via a 3-cm transverse skin incision. The venous catheter was threaded through a subcutaneous tunnel from the venous puncture site to the port site using the tunneler, and cut at an appropriate length. The catheter was attached to the port and the port secured to the underlying fascia. Unhindered blood withdrawal and fluid injection was ensured, and the port flushed with heparized saline. The wound at the reservoir site was closed in two layers with polyglactin 3-0 suture. The first dose of CTx was administered the morning following the procedure, or later as necessary. The TIVAD was accessed using a 23G winged scalp vein set, which was inserted to start the IV line by a doctor or nurse trained in handling the TIVAD. The TIVAD was removed under local anesthesia in the operating room a few weeks after the administration of the last dose of CTx and other IV systemic therapy, or was maintained for long-term IV access in appropriate patients. PIVA was obtained by cannulation of a forearm vein with a 20/22 G IV cannula by the same team of doctors and nurses in those receiving CTx via PIVA.

A comprehensive custom-made questionnaire was devised in English and Hindi languages with questions relating to (i) awareness and acceptance of TIVAD, (ii) insertion of TIVAD and venous access, (iii) morbidity of the IV access process and CTx administration via TIVAD or PIVA as perceived by the patient, and (iv) satisfaction. A few questions exclusive to either the TIVAD or PIVA were included. The responses were scored on a scale of 1 (agree completely/in all cycles) to 5 (don't agree at all/never). A score of 1 corresponded to the 'worst possible result' and 5 to the 'best possible result' as perceived by the patient. For satisfaction, a score of 1 corresponded to maximum satisfaction and a score of 5 to least satisfaction. All patients were asked to complete this questionnaire, either on their own or with the help of a healthcare professional, twice: once after the first CTx cycle, and the second time after completion of all intended CTx and removal of the TIVAD. The first questionnaire was used for analysis of awareness and overall acceptance of TIVAD; the second questionnaire was used for analysis of access-related symptoms, morbidity of IV access and CTx administration via TIVAD or PIVA, and overall satisfaction with the mode of CTx administration. Only those patients for whom both sets of questionnaires were available were included in the study. A total of 47 patients were excluded from the final analysis: eight patients with advanced disease died with TIVAD in situ, and 39 in the PIVA group were excluded (30 did not complete the initial or follow-up questionnaire and nine were lost to follow-up).

The perceived morbidity and satisfaction data were interpreted by an independent statistician. In view of a wide variation in perception of individual patients, the scores assigned by the patients were used only for plotting error bars to depict the mean value and one standard deviation (SD) of 95 % confidence interval (CI) to represent the overall variability/distribution of a particular measurement/parameter. The occurrence of access-related symptoms/problems and their frequency was assessed. Statistical analyses were performed using SPSS version 17.0 (SPSS, Inc., Chicago, IL, USA). Data are expressed as mean ± SD. The Chi squared test was used for categorical variables, while the *t* test was used for comparison of normally distributed parametric data, and the Mann–Whitney *U* test for non-parametric skewed data. Error bars showed the overall distribution of the measurement.

Results

Characteristics of the patients in the TIVAD group (mean age 51.5 years ± 11.3, range 28–81) were comparable to those in the PIVA group (mean age 49.1 ± 11.8, range 19–76). Patients in the TIVAD group had a mean body mass index (BMI) of 26.2 ± 3 kg/m^2 (range 20–36), which was comparable to the BMI of PIVA group patients (mean 24.5 ± 2.3 kg/m^2, range 20–29). The two groups were also comparable in terms of disease stage and chemotherapy setting, i.e. neoadjuvant CTx (NACT) or adjuvant CTx. In the TIVAD group, 57.9 % of patients received CTx in the adjuvant setting, while this proportion was 55.8 % in the PIVA group.

Acceptance of the TIVAD was higher in literate patients than in illiterate patients, and amongst those belonging to high and high–medium socioeconomic strata. The number of patients with at least 14 years of formal education, i.e. those with graduate or doctoral college education, was twice as high in the TIVAD group as in the PIVA group. The educational background and socioeconomic status were independently associated with acceptance of TIVAD. Of those who accepted TIVAD, 85.1 % were told about the TIVAD for the first time by the treating surgeon or oncologist, and the remainder heard about it from other patients. The decision to receive CTx via TIVAD was that of the patient herself in 26.3 % and that of her family members in 24.6 %. In the remainder, the decision was jointly taken by the treating surgeon and patient. Amongst the patients with PIVA-administered CTx, 56 % declined TIVAD primarily because they were not convinced about the need for TIVAD, 21.6 % declined TIVAD because of the fear of an additional surgical procedure, 20 % due to financial constraints, and 2.4 % because of fear of complications. In the TIVAD group, 77.2 % patients felt that they received adequate information about the functioning of TIVAD and its advantages and potential complications. The TIVAD implantation procedure was perceived as pain free by 54.4 % of the patients; 7.9 % thought it was painful and the remainder experienced minor pain during the procedure. A total of 97 % of patients felt that the potential utility of TIVAD was not fully exploited, as the phlebotomy technicians and nurses in community facilities were reluctant to withdraw blood samples for investigations via the TIVAD.

Of the 114 patients administered CTx via TIVAD, right IJV cannulation was used in 50 %, left IJV in 43 %, and right and left sub-clavian veins in 3.5 % each. The TIVAD was explanted a few weeks after completion of the treatment in 101, while the TIVAD was removed prematurely in five patients owing to a complication (vide infra). Eight (7 %) patients with terminal/advanced disease died with the TIVAD in situ for 45–365 days. The TIVAD was used for a mean duration of 197.5 ± 83.9 days (range 19–498). Patients in the TIVAD group received a mean of 9.83 CTx sessions (range 6–16); compared with a mean of 6.72 CTx cycles (64.2 % received six cycles and 35.8 % received eight cycles) in the PIVA group. A bias towards opting for TIVAD over PIVA in patients planned for longer-term IV therapy and more numerous CTx cycles was apparent. Financial constraints might also have resulted in a bias towards opting for PIVA in some, as TIVAD is an additional expense to the patient in our healthcare system.

None of the patients in the TIVAD group suffered life-threatening complications (e.g. pneumothorax, extravasation of drug, necrosis, hematoma formation, or bleeding). A total of 16 (14 %) patients had some complications, of which the TIVAD was salvageable in 11 patients. Four patients had infection of the TIVAD pocket, of which one one was salvageable with antibiotics and open drainage, while in the remaining three (one diabetic, two neutropenic) patients, the TIVAD had to be removed. Ports could be salvaged with debridement and secondary suturing in two patients with aseptic pressure necrosis of the skin at the TIVAD site. One patient experienced flipping of the port at the second cycle; it was repositioned and re-sutured. Two patients experienced dislodgement of the catheter, which was retrieved from the right atrium using a snare via transfemoral cardiac catheterization. One patient had IJV thrombosis after the first cycle, necessitating discontinuation of CTx and chemoport removal. The thrombus resolved with thrombolytic and anti-coagulant therapy. Six patients (5.2 %) had blockage of the catheter, the earliest of these being after the fourth cycle (84 days), needing thrombolysis, which was successful in five. In one, the remaining cycles of CTx had to be administered via PIVA. Table 1 details the perceived morbidity in the TIVAD group as assessed by nine questions pertaining to possible

Table 1 Patients' perception of morbidity due to chemotherapy administration via TIVAD ($n = 106$)

Question	Agree completely, score 1	Agree very much, score 2	Agree somewhat, score 3	Agree a little bit, score 4	Don't agree at all, score 5
1. Gives an unpleasant/foreign body sensation	2.8	3.8	10.4	4.7	78.3
2. Pain around the TIVAD site	2.8	0.9	14	8.6	73.7
3. Itching around the TIVAD site	1.9	0.9	23.6	8.5	65.1
4. Fear of infection	2.8	1.9	4.7	3.8	86.8
5. Fear of blockage	1.9	2.8	4.7	3.8	86.8
6. Fear of dislodgement	0.9	2.8	3.8	0	92.5
7. Interferes with quality of sleep	2.8	1.8	3.8	2.8	88.7
8. Interferes with arm/neck mobility	1.8	0.9	1.8	3.8	91.5
9. Interferes with day-to-day activities	3.8	0	2.8	1.8	91.5

Data are presented as %

TIVAD totally implantable venous access device

Table 2 Patients' perception of morbidity due to chemotherapy administration via PIVA ($n = 120$)

Question	In all cycles, score 1	In >50 % of cycles, score 2	In 50 % of cycles, score 3	In <50 % of cycles, score 4	Never, score 5
1. Difficulty in initiation of intravenous line	0	0	1.7	39.2	59.1
2. Need for multiple pricks	0	0	1.7	38.3	60
3. Need for second IV line for completion of chemotherapy session	0	0	0	1.7	98.3
4. Required IV line in neck or foot	0	0	0	1.7	98.3
5. Pain/redness/discomfort at site of IV access/arm	5.8	0	0.8	49.2	44.2
6. Interfered with day-to-day activities	1.7	2.5	1.7	15.8	78.3

Data are presented as %

IV intravenous, *PIVA* peripheral intra venous access

symptoms related to the presence of TIVAD in situ, apprehension about potential complications and interference with daily activities. The majority did not experience any pain or sensation of a foreign body at the TIVAD site.

Table 2 provides a summary of the perceived morbidity of CTx administration via PIVA. Thrombophlebitis and venous occlusion was seen in virtually all patients, because of which veins at various sites in the arms were used. Major causes for perception of morbidity emerged as the need for multiple pricks and pain, redness and swelling at the CTx administration site. Ten (8.3 %) patients had an episode of drug extravasation, which resulted in ulceration in five (4.2 %, Fig. 1). Tables 3 and 4 provide an account of satisfaction with CTx administration via TIVAD and PIVA, respectively. Patients administered CTx via TIVAD were quite satisfied with the venous access, including the cosmetic outcomes, and the majority felt they would have a TIVAD implanted again if the need arose. Patients in the

Fig. 1 Healed ulcer at drug extravasation site in a patient with peripheral vein-administered chemotherapy

Table 3 Assessment of satisfaction with TIVAD in patients administered chemotherapy via TIVAD ($n = 106$)

Question	Agree completely, score 1	Agree very much, score 2	Agree somewhat, score 3	Agree a little bit, score 4	Don't agree at all, score 5
1. Allowed complete and secure CTx administration	93.4	0	0	1.9	4.7
2. Satisfaction with cosmesis	81.2	5.6	10.4	0.9	1.9
3. Speeded up CTx sessions	42.5	0.9	10.4	0	46.2
4. Would get TIVAD re-inserted if the need arises	89.6	1.9	2.8	0	5.7
5. Would recommend it to others	84.9	4.7	3.8	0.9	5.7
6. Would prefer a PIVA for administration of CTx	1.9	1.9	2.8	1.9	91.5

Data are presented as %

CTx chemotherapy, *PIVA* peripheral intravenous access, *TIVAD* totally implantable venous access device

Table 4 Assessment of satisfaction in patients administered chemotherapy via PIVA ($n = 120$)

Question	Agree completely, score 1	Agree very much, score 2	Agree somewhat, score 3	Agree a little bit, score 4	Don't agree at all, score 5
1. Allowed complete and secure CTx administration	70	5.8	6.7	6.7	10.8
2. Satisfaction with cosmesis	60	10	0	7.5	22.5
3. Would receive it via PIVA if the need arises	72.5	2.5	10	2.5	12.5
4. Would recommend PIVA to others	12.5	2.5	5	7.5	72.5
5. Would prefer a TIVAD for administration of CTx	12.5	3.3	10	1.7	72.5

Data are presented as %

CTx chemotherapy, *PIVA* peripheral intravenous access, *TIVAD* totally implantable venous access device

PIVA group were not satisfied to a similar extent, and almost one-quarter of them thought they would rather have CTx via TIVAD if the need arose in the future. Patients receiving more than six cycles of CTx via PIVA were less satisfied with their venous access, and thought TIVAD would be a better choice. The difference in satisfaction levels between PIVA group patients receiving six cycles versus more than six cycles was statistically significant ($p < 0.05$). Figure 2 shows the error bars with average scores (mean and 95 % CI) of responses provided by patients in the TIVAD group to various questions relating to perceived morbidity and satisfaction. Error bars with average scores (mean and 95 % CI) of responses to questions relating perceived morbidity and satisfaction with use of PIVA are provided in Fig. 3.

Discussion

The importance of safe and secure venous access for CTx administration cannot be over emphasized, especially in view of chemotherapeutic and supportive treatment regimens that involve IV drug administration over long time periods. TIVAD usage is highly desirable, and has a proven role in CTx administration in various malignancies, with acceptable complication rates and high patient satisfaction [3–5]. CTx administration in breast cancer patients needs special consideration as veins of the ipsilateral arm are not available, owing to chances of lymph edema. Thus far, no studies have assessed patient satisfaction and perception of morbidity due to CTx administration via the TIVAD, and its impact on the QOL of breast cancer patients exclusively, nor have any been carried out in countries with limited resources. Breast cancer patients in India are mostly diagnosed at stages II and III, and face numerous challenges owing to limited resources [10]. Innovative strategies need to be devised to provide the benefit of contemporary high-quality treatment to patients in low- and middle-income countries [11]. In a prospective comparative study, we used a custom-designed questionnaire assessing acceptability, perceived morbidity of CTx administration, and overall satisfaction in breast cancer patients administered CTx via TIVAD versus those receiving CTx via PIVA.

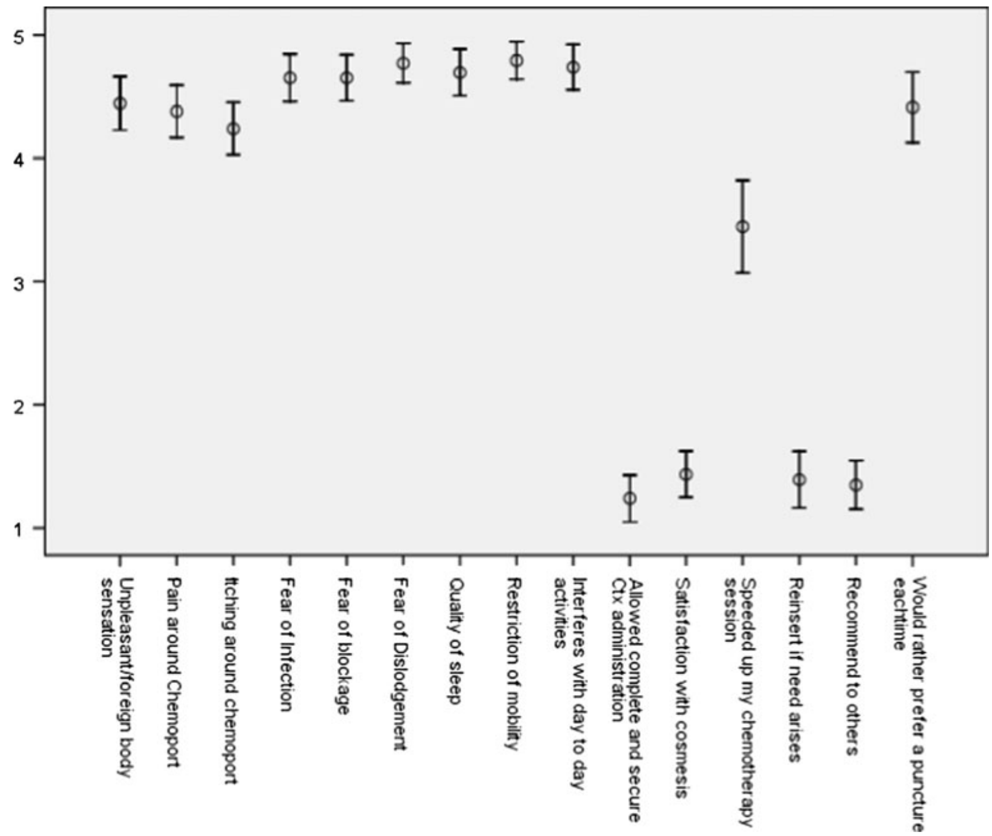

Fig. 2 *Error bars* for responses to questions relating to perceived morbidity and satisfaction with the totally implantable venous access device (corresponding to data in Tables 1, 3). Scores: *1* agree completely, *2* agree very much, *3* agree somewhat, *4* agree very little, *5* don't agree at all

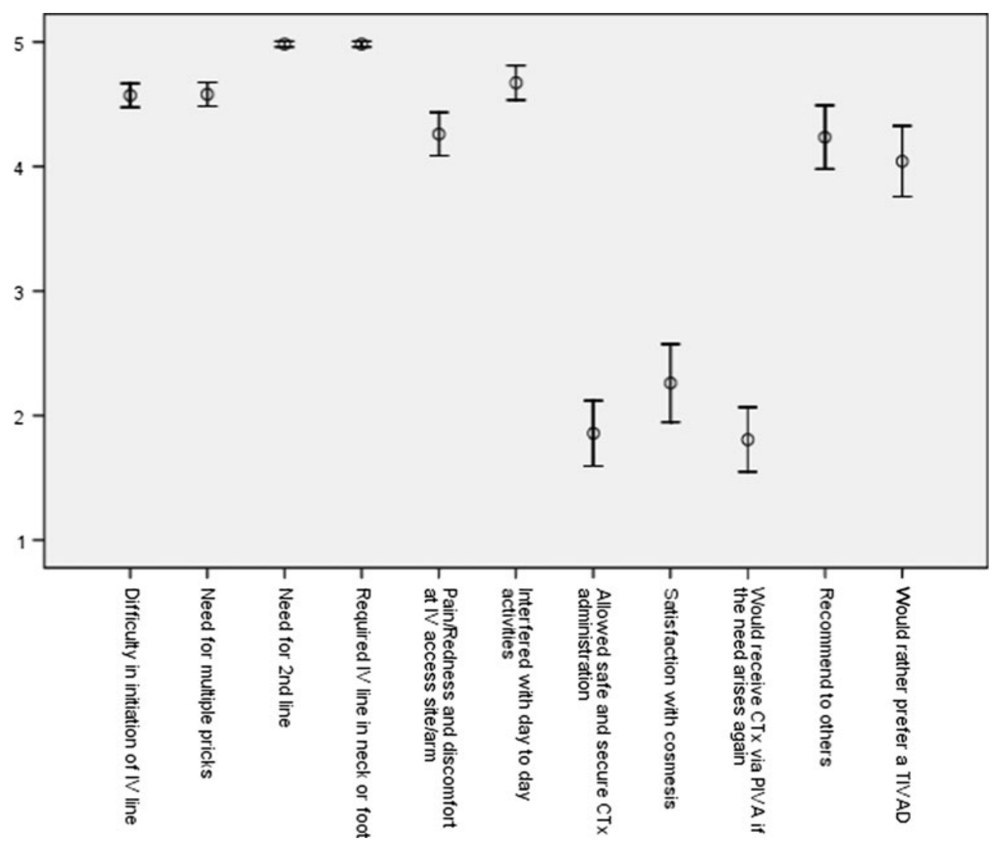

Fig. 3 *Error bars* for responses to questions relating to perceived morbidity and satisfaction with peripheral intravenous access (corresponding to data in Tables 2, 4). Scores: *1* agree completely, *2* agree very much, *3* agree somewhat, *4* agree very little, *5* don't agree at all

This was a non-randomized study, and the choice of TIVAD versus PIVA was decided by the patient herself based on her own perceptions of expected outcomes with the route of administration and the financial implications. The non-randomized design resulted in a definite bias towards choosing TIVAD over PIVA by patients planning for long-term IV therapy and a larger number of CTx cycles. Such patients indeed reported a high degree of satisfaction with use of TIVAD. Further, 20 % of patients opting for PIVA might have been biased due to financial constraints, owing to the higher cost of treatment using the TIVAD, as the cost of the TIVAD device is an additional expense to the patient in our healthcare setting. Nevertheless, even in the patient group receiving CTx via PIVA, the increase in the number of CTx sessions from six to eight led to lesser satisfaction with PIVA.

Awareness of TIVAD in our study cohort was rather low. Even after counseling about the possible routes of administration of CTx, i.e. TIVAD versus PIVA, <50 % of the patients opted for TIVAD. Level of education and socioeconomic status were independent determinants of a patient choosing TIVAD. The patients in the TIVAD group received a higher number of CTx cycles than those in the PIVA group, implying that the CTx regime and number of cycles was a determinant in favor of TIVAD. The factors determining acceptance of TIVAD have not been commented upon in other studies, including the few that have addressed impact of TIVAD usage on QOL. However, the acceptance of TIVAD is high in developed countries, while our study brings out concerns relating to additional costs and possible complications as major deterrents against TIVAD in patients in a resource-constrained environment. From the healthcare economics point of view, a study from Canada has commented that the use of TIVAD seems prudent only in patients with failed peripheral venous access, though this seems a rather impractical approach [6].

The TIVAD implantation procedure in our study was carried out in the operating room by a breast surgeon or anesthesiologist under local anesthesia using a standardized percutaneous method. TIVAD implantation in the operating room by a surgeon has been reported to be safer and more cost effective than when performed by an interventional radiologist [12]. The relatively low rate of complications in our experience confirms this view. The TIVAD implantation was perceived as painful by 7.9 %, and uncomfortable by another 37.7 % in our study, while others have reported this problem in 18–60 % of patients [7, 8, 13]. About one-quarter of the patients in the TIVAD group complained of having varying severity of pain and discomfort at the chemoport site until the time it was not removed. Pain experienced during medical procedures has a propensity to convert to chronic pain [14]. It seems logical that IV sedation with local anesthesia, or implanting the TIVAD during primary breast surgery under general anesthesia, for those planning for adjuvant CTx may prove useful, something that we have not attempted in the current study.

Venous access was easier and hassle free in the TIVAD group, and no patients needed multiple needle pricks for venous access. Close to 40 % of patients had difficulty with initiation of the IV line in the PIVA group, requiring multiple needle pricks; however, only two patients required an IV line in the neck/legs for completion of the planned CTx. No patients in the PIVA group required a cross-over to the TIVAD group in our study, in contrast to the 27 % cross-over rate from PIVA to TIVAD reported in a head-to-head comparison of ease of venous access between the two [6]. Para-medical personnel in the community are generally averse to using TIVAD and, in our study, the TIVAD was not used for venous sampling in 97 %, and only 40 % of patients felt that TIVAD had accelerated their CTx sessions. This is in contrast to corresponding figures of 30–61 and 83 %, respectively reported in high-income countries [7].

TIVAD usage for CTx is expected to impact on patient QOL and overall satisfaction with the CTx administration process. Earlier studies addressing these issues have been conducted on patients with a wide variety of malignancies, and have used generic systems to measure QOL, including the Functional Living Index-Cancer (FLIC) and the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) [6, 15]. No QOL measurement tools specific to the process of CTx administration via TIVAD or PIVA are available. In the only study providing a head-to-head comparison of TIVAD and PIVA group patients, Bow et al. [6] prospectively studied safety, efficacy, cost, and impact on QOL. However, this randomized study used the FLIC questionnaire, which is a generic and not specifically venous access-related QOL assessment in cancer patients. This study had two unevenly distributed groups despite stratification and randomization procedures, and reported that, although safe, effective, and associated with less access-related anxiety and morbidity, TIVAD usage did not result in any measurable improved QOL [6]. Two previous studies have used specific questionnaires pertaining to outcomes with TIVAD, but these studies do not provide a head-to-head comparison of morbidity and satisfaction between TIVAD and PIVA [7, 9].

High satisfaction levels observed in our study, and reported consistently in previous studies, signify high acceptability and satisfaction levels of receiving CTx via TIVAD [6, 7, 9, 13, 16]. The satisfaction rates in our study did not vary significantly between patients with some TIVAD-related complications and those without complications. Of those with complications, 75 % stated that they would get it reinserted or recommend it to others if necessary. Contrary to our findings, Ignatov et al. [9] reported a significant correlation between dissatisfaction and occurrence of complications rather than cosmesis or impaired daily activities. Our patients perceived discomfort, foreign body sensation, and itching around the TIVAD site, as has been reported in other studies, albeit to a lesser degree [7, 9]. Some 20 % of our patients were not completely satisfied with the cosmetic outcomes, similar to 8–18 % of patients in two other studies [7, 9]. We found measures like fashioning the pocket below the neckline of clothing, small incision, and skin closure with fine subcuticular sutures useful in improving cosmesis.

It seems logical that the TIVAD should be removed as soon as its intended use is fulfilled. Kreis et al. [7] found that prompt removal of the TIVAD after treatment would increase acceptance as it avoids troublesome flushing of the port. Contrary to this, Ignatov et al. [9] reported that 74 % of patients with TIVAD wanted to keep the TIVAD in situ for further use, even though 46 % of them were bothered by the need to periodically flushing the device once the treatment was over. The satisfaction levels in PIVA group patients was somewhat lower, and close to 80 % of them did not feel that CTx administration via PIVA interfered with their daily life. This was despite that more than half of the patients developed variable degrees of pain, redness, or arm edema at some stage of CTx. Administration of CTx via PIVA indeed seems a valid option, as only 12.5 % of our patients in the PIVA group felt that they would rather receive the chemotherapy via a TIVAD if the need arose in the future. However, on subgroup analysis based on number of CTx cycles to be administered, 6.5 % of those treated with six cycles felt that they would prefer a TIVAD, compared with 23.3 % of patients treated with more than six CTx cycles, which was statistically significant ($p < 0.05$). This is not surprising, as the difficulty in finding suitable peripheral veins for cannulation is proportionate to the number of CTx cycles.

The non-randomized study design was the major limitation of the current study. However, with concerns relating to cost and a subset of patients in whom TIVAD would be indicated at the outset due to poor peripheral veins or need for long-term IV therapy, a truly randomized prospective study seems difficult to perform. Hence, a comparative study between two cohorts of patients in the same timeframe would fill the void to a significant extent and substantial inferences could be drawn. The questionnaire used to assess the impact of CTx administration route on morbidity and overall satisfaction with the CTx administration process was comprehensive, designed by the investigators with help from an expert in QOL measurements with interventions.

Results of this non-randomized prospective comparative study on breast cancer patients undergoing CTx suggest that acceptance of TIVAD in patients in a resource-constrained setting is limited due to poor awareness of its virtues, concerns relating to its cost, and the need for an additional surgical procedure. CTx administration via TIVAD is safe and can be achieved without major complications that can have an impact on treatment outcomes. CTx administration via TIVAD is convenient for patients, especially when large numbers of CTx cycles need to be administered over a long time period, and results in high degrees of patient satisfaction. In comparison, CTx administration via PIVA is associated with a need for multiple needle pricks, arm pain, and morbidity, and results in dissatisfaction. In conclusion, venous access-related morbidity is lower and satisfaction higher in patients with TIVAD-administered CTx than in those with PIVA-administered CTx, more so in patients needing more than six cycles of CTx.

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World J Surg
DOI 10.1007/s00268-015-3263-6

ORIGINAL SCIENTIFIC REPORT

Generalized Multifactor Dimensionality Reduction (GMDR) Analysis of Drug-Metabolizing Enzyme-Encoding Gene Polymorphisms may Predict Treatment Outcomes in Indian Breast Cancer Patients

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Abstract

Background Prediction of response and toxicity of chemotherapy can help personalize the treatment and choose effective yet non-toxic treatment regimen for a breast cancer patient. Interplay of variations in various drug-metabolizing enzyme (DME)-encoding genes results in variable response and toxicity of chemotherapeutic drugs. Generalized multi-analytical (GMDR) approach was used to determine the influence of the combination of variants of genes encoding phase 0 (*SLC22A16*); phase I (*CYP450*, *NQO1*); phase II (*GSTs*, *MTHFR*, *UGT2B15*); and phase III (*ABCB1*) DMEs along with confounding factors on the response and toxicity of chemotherapeutic drugs in breast cancer patients.

Methods In an Indian breast cancer patient cohort ($n = 234$), response to neo-adjuvant chemotherapy ($n = 111$) and grade 2–4 toxicity to chemotherapy were recorded. Patients were genotyped for 19 polymorphisms selected in four phases of DMEs by PCR or PCR–RFLP or Taqman allelic discrimination assay. Binary logistic regression and GMDR analysis was performed. Bonferroni test for multiple comparisons was applied, and p value was considered to be significant at <0.025.

Results For ABCB1 1236C>T polymorphism, CT genotype was found to be significantly associated with response to NACT in uni-variate and multi-variate analysis ($p = 0.018$; $p = 0.013$). The TT genotype of NQO1 609C>T had a significant association with (absence of) grade 2–4 toxicity in uni-variate analysis ($p = 0.021$), but a non-significant correlation in multi-variate analysis. In GMDR analysis, interaction of CYP3A5*3, NQO1 609C>T, and ABCB1 1236C>T polymorphisms yielded the highest testing accuracy for response to NACT (CVT = 0.62). However, for grade 2–4 toxicity, CYP2C19*2 and ABCB1 3435C>T polymorphisms yielded the best interaction model (CVT = 0.57).

Conclusion This pharmacogenetic study suggests a role of higher order gene–gene interaction of DME-encoding genes, along with confounding factors, in determination of treatment outcomes and toxicity in breast cancer patients. This can be used as a potential objective tool for individualizing breast cancer chemotherapy with high efficacy and low toxicity.

Presented at the BSI program as free paper at World Congress of Surgery, Bangkok, Thailand, in Aug 2015.

Gaurav Agarwal and Sonam Tulsyan have contributed equally and are joint first authors.

Electronic supplementary material The online version of this article (doi:10.1007/s00268-015-3263-6) contains supplementary material, which is available to authorized users.

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Published online: 27 October 2015

Introduction

Breast cancer is the most common cancer amongst women [1], and the combination chemotherapeutic regimen containing anthracyclines (epirubicin, doxorubicin), alkylating agent [cyclophosphamide (CP)], and taxanes (paclitaxel, docetaxel) is a vital component of its multi-modality treatment. Locally advanced breast cancer or large operable breast cancer patients treated with neo-adjuvant chemotherapy (NACT) provide an excellent model for monitoring response to chemotherapy on the measurable breast and axillary disease. There is a large inter-individual variation in the tumor response to the chemotherapy and its toxicity. These variations may be attributed to genetic differences in various drug-metabolizing (DMEs) and transporter enzymes responsible for the metabolism and excretion of metabolized chemotherapeutic drugs. Prediction of response and toxicity to individual chemotherapy agent or combination regimen can help individualize the treatment and choose an effective and non/less-toxic treatment regimen for an individual patient.

The enzymes involved in drug metabolism, or DMEs, are classified as phase 0 (influx transporters), phase I (oxidative), and phase II (conjugative) metabolizing enzymes, and phase III transporters involved in efflux mechanisms. CP, anthracyclines and 5-Fluorouracil (5-FU) are commonly used as chemotherapeutic drugs for treatment of breast cancer patients. CP is catalyzed into its active form by various phase I hepatic cytochrome P450 (CYP) enzymes—CYP3A4, CYP3A5 [2], CYP2B6 [3], CYP2C8 [4], CYP2C9, and CYP2C19 [5]. The active metabolite diffuses into cancer cells [6] and is responsible for cell death due to its alkylating ability [7, 8]. The metabolism of anthracycline drugs involves phase 0 solute transporters (SLC22A16) [9] and phase III p-glycoproteins (ABCB1) [10]. Along with these transporters, genetic variants of phase I NADH-Quinone oxido-reductase (*NQO1*) [11] and phase II glucuronosyl transferase (*UGT2B15*) [10] have been implicated in anthracycline-based treatment outcomes in breast cancer patients. Glutathione-S-transferase (GST) enzymes are responsible for the clearance of both the drugs by phase II detoxification [12, 13]. The 5-FU is an anti-metabolite which restricts the growth of cancerous cells by interfering with the DNA and RNA synthesis. Methylene tetrahydrofolate reductase (*MTHFR)* catalyzes irreversible conversion of 5, 10 methylene tetrahydrofolate (5, 10 methylene THF) to 5 methylene tetrahydrofolate (5 methylene THF) and is the key enzyme of folate pathway. *MTHFR* genetic variants have been reported to modulate cytotoxic effects of 5-FU and methotrexate in colon and breast cancer cells [14].

Pharmacogenetic variations in DMEs are one of the possible mechanisms that may influence drug treatment outcomes. In our earlier studies, we have documented the influence of genetic variants of various drug-metabolizing pathways on CP [15]-, anthracycline [16, 17]-, and taxane [18]-based treatment outcomes. Individual polymorphism in single DME-encoding gene has limited impact on the drug response or toxicity. The role of combination of genetic variants of all the DMEs in combination chemotherapy in predicting the breast cancer treatment outcomes seems more logical and has not been evaluated so far. Thus, in this study we tried to evaluate the role of higher order gene–gene interaction in DMEs along with confounding factors in predicting response and toxicity to chemotherapy in breast cancer patients. In addition to univariate and multi-variate logistic regression, generalized multifactor dimensionality reduction (GMDR) analysis—an objective analytical tool for evaluating multifactorial impact on an association, allowing adjustment for confounding factors—was applied to explore the best prediction model of higher order gene–gene interactions with response to NACT and toxicity of chemotherapy.

Methods

The study, including the consent process was approved by the Institutional ethics committee of Sanjay Gandhi Post Graduate Institute of Medical Sciences (SGPGIMS), Lucknow, India, and the authors followed the norms of World's Association Declaration of Helsinki. Histology-proven invasive breast carcinoma patients treated between April 2010 and October 2012 at the Departments of Endocrine & Breast Surgery; and Radiotherapy, SGPGIMS were recruited. These patients were also the subjects of previously published studies, which have addressed entirely different pharmacogenomic investigations than the current study [15–17]. Informed consent was obtained from each patient. The patients were staged according to the TNM-AJCC staging system and were treated as per standard institutional protocols, which involved surgery, radiation therapy, chemotherapy, and hormonal therapy.

In 234 patients treated with NACT or adjuvant anthracycline-based combination chemotherapy, grade 2–4 toxicity was recorded according to National Cancer Institute-Common Toxicity Criteria for Adverse Events, version 3.0. Grade 2–4 anemia, leucopenia, thrombocytopenia, and dose delay/reduction due to febrile neutropenia were recorded. In 111 stage III breast cancer patients treated with NACT, the tumor response was documented, according to response evaluation criteria in solid tumors criteria [19]. Patients with complete and partial response were categorized as responders, while those with static and progressive disease with NACT were categorized as non-responders.

Selection of SNPs

On the basis of FEC/FAC metabolizing enzyme polymorphisms, 19 known single-nucleotide polymorphisms (SNPs) in 11 genes from phase 0—Solute transporter (SLC22A16); phase I—Cytochrome P450 (CYP450) and NAD(P)H dehydrogenase quinine (NQO1); phase II—glutathione-S-transferase (GST), UDP glucuronosyl transferase (UGT2B15), and methylenetetrahydrofolate reductase (MTHFR) drug-metabolizing enzymes; and phase III—p-glycoprotein (ABCB1) were selected.

Genotyping

Blood samples were collected in ethylene-diamine-tetra-acetic acid (EDTA) vials, and genomic DNA was extracted from peripheral blood leukocyte pellet using a modified salting-out method [20]. Custom-designed Taqman allelic discrimination assay was done to genotype SLC22A16 146A>G and SLC22A16 1226T>C polymorphisms, whereas CYP3A4*1B [21], CYP3A5*3 [22], CYP2B6*9 [23], CYP2C9*2 [24], CYP2C9*3 [24], CYP2C19*2 [25], GSTP1 Ile105Val [26], MTHFR 677C>T [27], NQO1 609C>T [28], ABCBI 1236C>T [29], 2677G>T/A [29], and 3435C>T [30] polymorphisms were genotyped through polymerase chain reaction (PCR)-restriction fragment length polymorphism (RFLP). Pre-designed Taqman allelic discrimination assay was also done to genotype CYP2B6*5 and UGT2B15 253A>C polymorphisms. Multiplex polymerase chain reaction (PCR) was used to determine the absent alleles of GSTM1 and GSTT1 polymorphism [31].

Statistical analysis

Descriptive statistics of patients were presented as mean and standard deviations for continuous measures, whereas frequencies and percentages were used for categorical measures. Uni-variate and multi-variate binary logistic regression was performed. In multi-variate analysis, adjustments for confounding factors like age, clinical TNM stage, pathological lymph nodal status, histologic grade, and hormone receptor and Her-2neu expression were done. Association was expressed as odds ratio (OR) with 95 % confidence intervals (95 % CIs). All statistical analyses were performed using the SPSS software version 17.0 (SPSS, Chicago, IL, USA). Bonferroni test for multiple comparisons was applied, and p value was considered to be significant at <0.025.

Furthermore, GMDR analysis (http://www.ssg.uab.edu/gmdr) was done for the detection and characterization of gene–gene interactions along with confounding factors [32]. It is a generalized MDR framework based on the score of a generalized linear model. It is applicable to both dichotomous and quantitative phenotypes that allow adjustment for covariates and is more precise and accurate than MDR. The best interaction model was selected on the basis of maximum testing accuracy (CVT) and cross-validation consistency (CVC). Permutation (p) results were considered to be statistically significant at the 0.05 level.

Results

Patient characteristics

The demographic, histopathological, and clinical characteristics of breast cancer patients are listed in Table 1. The

Table 1 Demographic, histopathological, and clinical characteristics of breast cancer patients

Characteristics	Frequency (%)
Age (years)	
Mean ± SD	48.92 ± 10.669
Stage (clinical)	
0	1 (0.4)
1	14 (6.0)
2	93 (39.7)
3	106 (45.3)
4	14 (6.0)
Missing	6 (2.6)
Lymph node (pathological)	
Positive	136 (58.1)
Negative	98 (41.9)
Grade	
1	10 (4.3)
2	135 (57.7)
3	88 (37.6)
Missing	1 (0.4)
Estrogen receptor	
Positive	112 (47.9)
negative	121 (51.7)
Missing	1 (0.4)
Progesterone receptor	
Positive	99 (42.3)
negative	132 (56.4)
Missing	3 (1.3)
Her-2neu Status	
Positive	88 (37.6)
Negative	134 (57.3)
Missing	12 (5.1)
Chemotherapy type	
Neo-adjuvant	111 (47.4)
Adjuvant	123 (52.6)

mean age of breast cancer patients was 48.9 ± 10.7 years. Of the 234 patients included in the study, NACT was administered to 111 (47.4 %) patients while adjuvant chemotherapy to 123 (52.6 %).

Logistic regression: uni-variate analysis

In uni-variate logistic regression, genotypes and alleles of a particular polymorphism were correlated with dependent variable (treatment outcomes). CT genotype of ABCB1 1236C>T polymorphism was found to be significantly associated with response to NACT ($p = 0.018$). However, none of the other polymorphisms reached statistical significance with response to NACT (Table 2). On further analysis of the data, TT genotype of NQO1 609C>T reached significant association with the absence of grade 2–4 toxicity ($p = 0.021$) (Table 3). No significant association was seen with grade 2–4 anemia, grade 2–4 leucopenia, and dose delay/reduction (Supplementary data- in Tables S1, S2, and S3).

Logistic regression: multi-variate analysis

In multi-variate logistic regression, adjustment for all the confounding factors was done along with correlation of genetic variants with treatment outcomes. Similar to the uni-variate analysis, we found CT genotype of ABCB1 1236C>T polymorphism to be significantly associated with response to NACT ($p = 0.013$) (Table 2). But no association was seen with any other polymorphisms in grade 2–4 toxicity (Table 3).

Interaction models by GMDR analysis

Finally, the GMDR analysis was performed to study the higher order gene–gene interactions or best interaction model along with the adjustment for confounding factors. The GMDR analysis yielded best models for one, two, and three factors. Three-factor model—CYP3A5*3, NQO1 609C>T, and ABCB1 1236C>T—was found to be the best gene–gene interaction model with response to NACT (CVT = 0.62) (Table 4). For grade 2–4 toxicity, two-factor model—CYP2C19*2 and ABCB1 3435C>T—polymorphisms yielded the highest accuracy (CVT = 0.57) (Table 4). However, CYP2C19*2, ABCB1 3435 C>T, and ABCB1 2677G>T/A combination of polymorphisms yielded the highest testing accuracy for grade 2–4 anemia (CVT = 0.63) and CYP2B6*9, UGT2B15 253A>C, and ABCB1 2677G>T/A for grade 2–4 leucopenia (CVT = 0.45) (Table 4). For dose delay/reduction, gene–gene interaction of NQO1 609C>T and ABCB1 1236C>T polymorphisms was found to be the best model (CVT = 0.64) (Table 4).

Discussion

Treatment protocol for breast cancer involves the combination of various chemotherapeutic drugs. Variations in genes encoding DMEs may have an effect on their respective activities and expression, thereby causing inter-patient variation in treatment outcomes [33, 34]. The current study was carried out to evaluate the association of 19 variations in 14 genes of DMEs of anthracycline-based combination (FEC/FAC) chemotherapy with treatment outcomes in terms of response to NACT and chemo-toxicity in breast cancer patients. This was carried out with logistic regression and multi-analytical strategy along with the adjustments for confounding factors, using the precise GMDR analytic methodology.

On applying uni-variate logistic regression, the only significant association we found was of heterozygous (CT) genotype of ABCB1 1236C>T polymorphism with breast cancer response to NACT ($p = 0.018$). Although in a previous study we reported a significant association of this polymorphism with response to NACT, as well as grade 2–4 anemia [35], in the current study no such association was seen with chemo-toxicity, which is perhaps a loss of statistical significance due to a larger, and so more representative, sample size. Thus, ABCB1 1236C>T polymorphism along with the known prognostic factors seems to play a significant role in predicting response to NACT in breast cancer patients. The biological relevance of this association may be due to the fact that the presence of variant allele in the ABCB1 gene may lead to a lower expression of P-gp, which further results in accumulation of drugs inside the cell, thus altering the distribution profile of the chemotherapeutic drugs inside cells. Other recent studies have reported no association of 1236C>T with response to chemotherapy in Chinese breast cancer patients [36, 37].

On uni-variate analysis, significant association of TT genotype of NQO1 609C>T was seen with the absence of grade 2–4 toxicity ($p = 0.021$). A recent study has also indicated the association of *NQO1* 609C>T with lower doxorubicin efficacy in breast cancer [38]. The authors have also reported reduced cytotoxicity of epirubicin in breast cancer individuals with variant *NQO1* 609C>T genotype. The presence of variant genotype of *NQO1* 609C>T diminishes the protein activity due to accelerated degradation by ubiquitin proteasomal system [39]. A possible explanation for such observations is that, due to diminished protein activity resulting from variant genotype, bioactivation of the chemotherapeutic drugs does not occur, as in the case of E09 and mitomycin C. As a result, the individuals with variant genotype are less likely to have chemotherapy-induced toxicity.

Next, we performed multi-variate analysis to determine the role of confounding factors like age, clinical stage,

Table 2 Association with response to NACT

Polymorphism		Genotype/ Allele	Non-responders N(%) = 45(40.5)	Responders N(%) = 66(59.5)	Uni-variate analysis		Multi-variate analysis[a]	
					OR (95 %CI)	*p* value	OR (95 %CI)	*p* value
Phase 0	SLC22A16 146A>G	AA	21 (46.7)	26 (39.4)	Reference	–	Reference	–
		AG	19 (42.2)	35 (53.0)	0.67 (0.30–1.49)	0.331	0.79 (0.31–2.00)	0.632
		GG	5 (11.1)	5 (7.6)	1.23 (0.31–4.85)	0.759	0.68 (0.14–3.24)	0.633
		A	61 (67.8)	87 (65.9)	Reference	–	Reference	–
		G	29 (32.2)	45 (34.1)	0.91 (0.52–1.62)	0.772	0.83 (0.44–1.57)	0.577
	SLC22A16 1226T>C	TT	36 (80.0)	50 (75.8)	Reference	–	Reference	–
		TC	9 (20.0)	15 (22.7)	0.83 (0.32–2.11)	0.701	1.31 (0.43–3.97)	0.628
		CC	0 (0)	1 (1.5)	0	0	0.00	1.000
		T	81 (90.0)	115 (87.1)	Reference	–	Reference	–
		C	9 (10.0)	17 (12.9)	0.75 (0.31–1.77)	0.51	0.85 (0.32–2.28)	0.761/
Phase 1	CYP3A4*1B	*1A/*1A	42 (93.3)	65 (98.5)	Reference	–	Reference	–
		*1A/*1B	3 (6.7)	1 (1.5)	4.64 (0.46–46.13)	0.190	8.55 (0.65–112.67)	0.103
		*1A	87 (96.7)	131 (99.2)	Reference	–	Reference	–
		*1B	3 (3.3)	1 (0.8)	4.51 (0.46–44.13)	0.195	4.74 (0.41–54.20)	0.210
	CYP3A5*3	*3/*3	27 (60.0)	37 (56.1)	Reference	–	Reference	–
		*1/*3	15 (33.3)	27 (40.9)	0.76 (0.34–1.69)	0.506	0.58 (0.19–1.71)	0.328
		*1/*1	3 (6.7)	2 (3.0)	2.05 (0.32–13.16)	0.447	1.65 (0.22–12.28)	0.623
		*3	69 (76.7)	101 (76.5)	Reference	–	Reference	–
		*1	21 (23.3)	31 (23.5)	0.99 (0.52–1.86)	0.979	1.03 (0.48–2.19)	0.928
	CYP2B6*5	*1/*1	38 (84.4)	58 (87.9)	Reference	–	Reference	–
		*1/*5	7 (15.6)	8 (12.1)	1.33 (0.44–3.98)	0.604	2.37 (0.50–11.08)	0.271
		*1	83 (92.2)	124 (93.9)	Reference	–	Reference	–
		*5	7 (7.8)	8 (6.1)	1.30 (0.45–3.74)	0.618	1.60 (0.46–5.54)	0.459
	CYP2B6*9	*1/*1	15 (33.3)	21 (31.8)	Reference	–	Reference	–
		*1/*9	26 (57.8)	38 (57.6)	0.95 (0.41–2.19)	0.919	1.33 (0.42–4.20)	0.617
		*9/*9	4 (8.9)	7 (10.6)	0.80 (0.19–3.23)	0.754	2.17 (0.34–13.89)	0.411
		*1	56 (62.2)	80 (60.6)	Reference	–	Reference	–
		*9	34 (37.8)	52 (39.4)	0.93 (0.53–1.62)	0.808	1.13 (0.57–2.24)	0.723
	CYP2C8*3	GG	37 (82.2)	58 (87.9)	Reference	–	Reference	–
		GA	8 (17.8)	7 (10.6)	1.79 (0.59–5.35)	0.297	1.90 (0.41–8.65)	0.406
		AA	0 (0)	1 (1.5)	0.00	1.000	0.00	1.000
		G	82 (91.11)	123 (93.18)	Reference	–	Reference	–
		A	8 (8.89)	9 (6.82)	0.588 (0.20–1.73)	0.335	0.56 (0.17–1.80)	0.334
	CYP2C9*2	*1/*1	38 (84.4)	58 (87.9)	Reference	–	Reference	–
		*1/*2	7 (15.6)	7 (10.6)	1.52 (0.49–4.70)	0.461	1.41 (0.32–6.20)	0.645
		*2/*2	0 (0.0)	1 (1.5)	0.00	0.999	0.00	0.999
		*1	83 (92.2)	123 (93.2)	Reference	–	Reference	–
		*2	7 (7.8)	9 (6.8)	1.15 (0.41–3.21)	0.786	1.03 (0.30–3.50)	0.960
	CYP2C9*3	*1/*1	37 (82.2)	54 (81.8)	Reference	–	Reference	–
		*1/*3	8 (17.8)	12 (18.2)	0.97 (0.36–2.61)	0.957	0.59 (0.16–2.19)	0.438
		*1	82 (91.1)	120 (90.9)	Reference	–	Reference	–
		*3	8 (8.9)	12 (9.1)	0.97 (0.38–2.49)	0.959	0.48 (0.15–1.55)	0.224
	CYP2C19*2	GG	14 (31.1)	23 (34.8)	Reference	–	Reference	–
		GA	25 (55.6)	35 (53.0)	1.17 (0.50–2.71)	0.709	2.04 (0.66–6.27)	0.212
		AA	6 (13.3)	8 (12.1)	1.23 (0.35–4.29)	0.743	1.87 (0.36–9.57)	0.450
		G	53 (58.9)	81 (61.4)	Reference	–	Reference	–
		A	37 (41.1)	51 (38.6)	1.10 (0.64–1.91)	0.711	1.18 (0.60–2.32)	0.618

Table 2 continued

Polymorphism		Genotype/ Allele	Non-responders N(%) = 45(40.5)	Responders N(%) = 66(59.5)	Uni-variate analysis		Multi-variate analysis[a]	
					OR (95 %CI)	*p* value	OR (95 %CI)	*p* value
	NQO1 609C>T	CC	23 (51.1)	27 (40.9)	Reference	–	Reference	–
		CT	21 (46.7)	31 (47.0)	0.79 (0.36–1.74)	0.567	0.84 (0.33–2.17)	0.729
		TT	1 (2.2)	8 (12.1)	0.14 (0.01–1.26)	0.080	0.19 (0.02–1.77)	0.145
		C	67 (74.4)	85 (64.4)	Reference	–	Reference	–
		T	23 (25.6)	47 (35.6)	0.62 (0.34–1.12)	0.115	0.69 (0.35–1.34)	0.280
Phase 2	GSTM1	Present	25 (55.6)	40 (60.6)	Reference	–	Reference	–
		Null	20 (44.4)	26 (39.4)	0.81 (0.37–1.75)	0.596	0.61 (0.25–1.48)	0.278
	GSTT1	Present	35 (77.8)	55 (83.3)	Reference	–	Reference	–
		Null	10 (22.2)	11 (16.7)	0.70 (0.26–1.82)	0.464	1.30 (0.40–4.23)	0.659
	GSTP1 313A > G	AA	24 (53.3)	33 (50.0)	Reference	–	Reference	–
		AG	18 (40.0)	25 (37.9)	0.99 (0.44–2.20)	0.980	1.21 (0.47–3.10)	0.681
		GG	3 (6.7)	8 (12.1)	0.51 (0.12–2.14)	0.363	0.36 (0.05–2.25)	0.276
		A	66 (73.3)	91 (68.9)	Reference	–	Reference	–
		G	24 (26.7)	41 (31.1)	0.80 (0.44–1.46)	0.480	0.82 (0.41–1.62)	0.579
	MTHFR 677C>T	CC	29 (64.4)	44 (66.7)	Reference	–	Reference	–
		CT	15 (33.3)	22 (33.3)	1.03 (0.46–2.31)	0.934	1.35 (0.54–3.38)	0.516
		TT	1 (2.2)	0 (0.)	0.00	1.000	0.000	1.000
		C	73 (81.1)	110 (83.3)	Reference	–	Reference	–
		T	17 (18.9)	22 (16.7)	1.16 (0.57–2.34)	0.669	1.51 (0.69–3.29)	0.299
	UGT2B15 253A > C	AA	18 (40.0)	19 (28.8)	Reference	–	Reference	–
		AC	15 (33.3)	28 (42.4)	0.56 (0.23–1.39)	0.214	0.60 (0.20–1.80)	0.370
		CC	12 (26.7)	19 (28.8)	0.66 (0.25–1.75)	0.412	0.61 (0.20–1.85)	0.386
		A	51 (56.7)	66 (50.0)	Reference	–	Reference	–
		C	39 (43.3)	66 (50.0)	0.76 (0.44–1.31)	0.329	0.75 (0.41–1.37)	0.350
Phase 3	ABCB1 1236C>T	CC	4 (8.9)	19 (28.8)	Reference	–	Reference	–
		CT	23 (51.1)	25 (37.9)	4.37 (1.29–14.77)	**0.018**	6.07 (1.47–25.02)	**0.013**
		TT	18 (40.0)	22 (33.3)	3.88 (1.11–13.50)	S	5.04 (1.10–22.99)	0.037
		C	31 (34.4)	63 (47.7)	Reference	–	Reference	–
		T	59 (65.6)	69 (52.3)	1.73 (1.00–3.02)	0.050	1.80 (0.94–3.42)	0.073
	ABCB1 2677G>T/A	GG	0 (0.0)	3 (4.5)	Reference	–	Reference	–
		GT	21 (46.7)	31 (47.0)	–	–	–	–
		TT	19(42.2)	26(39.4)	–	–	–	–
		GA	1 (2.2)	1 (1.5)	–	–	–	–
		AT	4 (8.9)	5 (7.6)	–	–	–	–
		G	22 (24.4)	38 (28.8)	Reference	–	Reference	–
		T	63 (70.0)	88 (66.7)	0.69 (0.19–2.54)	0.582	0.77 (0.17–3.44)	0.738
		A	5 (5.6)	6 (4.5)	0.85 (0.25–2.93)	0.809	1.01 (0.24–4.16)	0.988
	ABCB1 3435C>T	CC	4(8.9)	11(16.7)	Reference	–	Reference	–
		CT	20(44.4)	30(45.5)	1.83(0.51–6.57)	0.352	2.24 (0.55–9.05)	0.255
		TT	21 (46.7)	25 (37.9)	2.31(0.64–8.33)	0.201	2.42 (0.58–10.08)	0.224
		C	28 (31.1)	52 (39.4)	Reference	–	Reference	–
		T	62 (68.9)	80 (60.6)	1.43 (0.81–2.53)	0.208	1.39 (0.74–2.63)	0.299

Significant *p* values are given in bold

OR Odds Ratio, *CI* Confidence Interval

[a] Potential confounding factors are included in the multi-variate analysis

pathological lymph nodal status, histologic grade, and hormone receptor and Her-2neu expression along with genetic variations in predicting response to and toxicity of chemotherapy in breast cancer patients. Similar to uni-variate analysis, heterozygous (CT) genotype of ABCB1 1236C>T polymorphism was found to be associated with

Table 3 Association with grade 2–4 toxicity

Polymorphism		Genotype/ Allele	Grade 2–4 Toxicity N(%) = 127(54.3)	No grade 2–4 toxicity N(%) = 107(45.7)	Uni-variate analysis		Multi-variate analysis[a]	
					OR (95 %CI)	p value	OR (95 %CI)	p value
Phase 0	SLC22A16 146A>G	AA	61 (48.0)	54 (50.5)	Reference	–	Reference	–
		AG	54 (42.5)	44 (41.6)	1.08 (0.63–1.86)	0.764	0.95 (0.52–1.73)	0.884
		GG	12 (9.4)	9 (8.4)	1.18 (0.46–3.02)	0.729	1.05 (0.37–2.92)	0.925
		A	178 (69.5)	154 (71.3)	Reference	–	Reference	–
		G	78 (30.5)	62 (28.7)	1.08 (0.73–1.61)	0.67	0.99 (0.65–1.53)	0.991
	SLC22A16 1226T>C	TT	98 (77.2)	83 (77.6)	Reference	–	Reference	–
		TC	26 (20.5)	23 (21.5)	0.95 (0.50–1.80)	0.89	0.81 (0.39–1.66)	0.576
		CC	3 (2.4)	1 (0.9)	2.54 (0.25–24.89)	0.42	2.81 (0.19–40.24)	0.445
		T	224 (87.5)	190 (88.0)	Reference	–	Reference	–
		C	32 (12.5)	26 (12.0)	1.04 (0.60–1.81)	0.87	1.03 (0.56–1.92)	0.908
Phase 1	CYP3A4*1B	*1A/*1A	120 (93.5)	100 (93.5)	Reference	–	Reference	–
		*1A/*1B	7 (5.5)	7 (6.5)	0.83 (0.28–2.45)	0.741	0.89 (0.26–2.97)	0.852
		*1A	247 (97.2)	207 (96.7)	Reference	–	Reference	–
		*1B	7 (2.8)	7 (3.3)	0.83 (0.28–2.42)	0.745	0.82 (0.26–2.55)	0.744
	CYP3A5*3	*3/*3	73 (57.5)	61 (57.0)	Reference	–	Reference	–
		*1/*3	48 (37.8)	39 (36.4)	1.02 (0.59–1.76)	0.919	0.91 (0.48–1.72)	0.783
		*1/*1	6 (4.7)	7 (6.5)	0.71 (0.22–2.24)	0.567	0.86 (0.23–3.13)	0.825
		*3	194 (76.4)	161 (75.2)	Reference	–	Reference	–
		*1	60 (23.6)	53 (24.8)	0.94 (0.61–1.43)	0.773	0.94 (0.58–1.51)	0.800
	CYP2B6*5	*1/*1	112 (88.2)	92 (86.0)	Reference	–	Reference	–
		*1/*5	14 (11.0)	15 (14.0)	0.76 (0.35–1.67)	0.504	0.74 (0.29–1.89)	0.535
		*1	238 (93.7)	199 (93.0)	Reference	–	Reference	–
		*5	16 (6.3)	15 (7.0)	0.89 (0.43–1.84)	0.758	0.92 (0.41–2.08)	0.852
	CYP2B6*9	*1/*1	43 (33.9)	35 (32.7)	Reference	–	Reference	–
		*1/*9	73 (57.5)	62 (57.9)	0.95 (0.54–1.67)	0.882	0.89 (0.47–1.71)	0.748
		*9/*9	11 (8.7)	10 (9.3)	0.89 (0.34–2.35)	0.822	0.63 (0.20–1.95)	0.429
		*1	159 (62.6)	132 (61.7)	Reference	–	Reference	–
		*9	95 (37.4)	82 (38.3)	0.96 (0.66–1.33)	0.839	0.81 (0.52–1.25)	0.353
	CYP2C8*3	GG	110 (86.6)	93 (86.9)	Reference	–	Reference	–
		GA	16 (12.6)	13 (12.1)	1.04 (0.47–2.27)	0.921	0.75 (0.28–2.04)	0.586
		AA	1 (0.8)	1 (0.9)	0.84 (0.05–13.70)	0.906	0.000	1.000
		G	236 (92.9)	199 (93.0)	Reference	–	Reference	–
		A	18 (7.1)	15 (7.0)	1.25 (0.63–2.49)	0.510	0.67 (0.29–1.55)	0.354
	CYP2C9*2	*1/*1	106 (83.5)	92 (86.0)	Reference	–	Reference	–
		*1/*2	20 (15.7)	15 (14.0)	1.15 (0.56–2.39)	0.693	1.14 (0.48–2.70)	0.761
		*2/*2	1 (0.8)	0 (0.0)	0.000	1.000	0.000	1.000
		*1	232 (91.3)	199 (93.0)	Reference	–	Reference	–
		*2	22 (8.7)	15 (7.0)	1.83 (0.90–3.75)	0.095	1.43 (0.64–3.20)	0.377
	CYP2C9*3	*1/*1	102 (80.3)	96 (89.7)	Reference	–	Reference	–
		*1/*3	25 (19.7)	10 (9.3)	2.35 (1.07–5.15)	0.033	2.29 (0.97–5.41)	0.058
		*1	229 (90.2)	202 (94.4)	Reference	–	Reference	–
		*3	25 (9.8)	12 (5.6)	1.83 (0.90–3.75)	0.095	1.71 (0.79–3.69)	0.167
	CYP2C19*2	GG	42 (33.1)	42 (39.3)	Reference	–	Reference	–
		GA	70 (55.1)	49 (45.8)	1.42 (0.81–2.50)	0.214	1.70 (0.88–3.26)	0.109
		AA	15 (11.8)	16 (15.0)	0.93 (0.41–2.13)	0.878	1.12(0.42–2.97)	0.809
		G	154(60.6)	133(62.1)	Reference	–	Reference	–
		A	100(39.4)	81(37.9)	1.06 (0.41–2.13)	0.737	1.12 (0.73–1.73)	0.585

Table 3 continued

Polymorphism		Genotype/ Allele	Grade 2–4 Toxicity $N(\%) = 127(54.3)$	No grade 2–4 toxicity $N(\%) = 107(45.7)$	Uni-variate analysis		Multi-variate analysis[a]	
					OR (95 %CI)	*p* value	OR (95 %CI)	*p* value
	NQO1 609C>T	CC	62 (48.8)	43 (40.2)	Reference	–	Reference	–
		CT	59 (46.5)	50 (46.7)	0.81 (0.47–1.40)	0.468	0.94 (0.52–1.69)	0.856
		TT	6 (4.7)	14 (13.1)	0.29 (0.10–0.83)	**0.021**	0.35 (0.12–1.04)	0.061
		C	183 (72.0)	136 (63.6)	Reference	–	Reference	–
		T	71 (28.0)	78 (36.4)	0.67 (0.45–1.00)	0.050	0.65 (0.43–0.98)	0.044
Phase 2	GSTM1	Present	81 (63.8)	61 (57.0)	Reference	–	Reference	–
		Null	46 (36.2)	46 (43.0)	1.32 (0.78–2.24)	0.291	1.29 (0.73–2.30)	0.372
	GSTT1	Present	101 (79.5)	88 (82.2)	Reference	–	Reference	–
		Null	26 (20.5)	19 (17.8)	0.83 (0.43–1.61)	0.600	0.84 (0.41–1.72)	0.651
	GSTP1 313A>G	AA	56 (44.1)	54 (50.5)	Reference	–	Reference	–
		AG	60 (47.2)	46 (43.0)	1.25 (0.73–2.15)	0.402	1.49 (0.83–2.67)	0.178
		GG	11 (8.7)	7 (6.5)	1.51 (0.54–4.19)	0.424	1.37 (0.46–4.12)	0.565
		A	172 (67.7)	151 (72.0)	Reference	–	Reference	–
		G	82 (32.3)	60 (28.0)	1.22 (0.82–1.82)	0.320	1.28 (0.83–1.96)	0.254
	MTHFR 677C>T	CC	87 (68.5)	70 (65.4)	Reference	–	Reference	–
		CT	37 (29.1)	34 (31.8)	0.87 (0.49–1.53)	0.643	0.90 (0.49–1.66)	0.754
		TT	3 (2.4)	3 (2.8)	0.80 (0.15–4.11)	0.794	0.86 (0.16–4.60)	0.867
		C	211 (83.1)	174 (81.3)	Reference	–	Reference	–
		T	43 (16.9)	40 (18.7)	0.88 (0.55–1.42)	0.619	0.91 (0.55–1.52)	0.744
	UGT2B15 253A>C	AA	40 (31.5)	25 (23.4)	Reference	–	Reference	–
		AC	62 (48.8)	53 (49.5)	0.73 (0.39–1.35)	0.322	0.85 (0.42–1.720	0.662
		CC	25 (19.7)	29 (27.1)	0.53 (0.25–1.12)	0.098	0.49 (0.22–1.10)	0.087
		A	142 (55.9)	103 (48.1)	Reference	–	Reference	–
		C	112 (44.1)	111 (51.9)	0.73 (0.50–1.05)	0.094	0.71 (0.48–1.05)	0.092
Phase 3	ABCB1 1236C>T	CC	20 (15.7)	19 (17.8)	Reference	–	Reference	–
		CT	56 (44.1)	**55 (51.4)**	0.96 (0.46–2.00)	0.929	1.25 (0.56–2.76)	0.573
		TT	51 (40.2)	**33 (30.8)**	1.46 (0.68–3.15)	0.325	1.70 (0.74–3.90)	0.204
		C	96 (37.8)	**93 (43.5)**	Reference	–	Reference	–
		T	158 (62.2)	**121 (56.5)**	1.26 (0.87–1.83)	0.214	1.31 (0.88–1.95)	0.172
	ABCB1 2677G>T/A	GG	10 (7.9)	7 (6.5)	Reference	–	Reference	–
		GT	66 (52.0)	48 (44.9)	0.96 (0.34–2.70)	0.942	1.23 (0.41–3.67)	0.702
		TT	39 (30.7)	41 (38.3)	0.66 (0.23–1.92)	0.452	0.85 (0.27–2.64)	0.790
		GA	3 (2.4)	1 (0.9)	2.10 (0.17–24.59)	0.555	4.40 (0.18–106)	0.361
		AT	9 (7.1)	10 (9.3)	0.63 (0.16–2.36)	0.493	0.76 (0.18–3.15)	0.706
		G	89 (35.0)	63 (29.4)	Reference	–	Reference	–
		T	153 (60.3)	140 (65.4)	1.29 (0.53–3.12)	0.565	1.25 (0.47–3.33)	0.647
		A	12 (4.7)	11 (5.1)	1.00 (0.42–2.34)	0.997	1.03 (0.39–2.66)	0.951
	ABCB1 3435C>T	CC	18 (14.2)	18 (16.8)	Reference	–	Reference	–
		CT	66 (52.0)	46 (43.0)	1.43 (0.67–3.05)	0.348	1.63 (0.73–3.66)	0.230
		TT	43 (33.9)	43 (40.2)	1.00 (0.45–2.17)	1.000	0.94 (0.41–2.15)	0.891
		C	102 (40.2)	82 (38.3)	Reference	–	Reference	–
		T	152 (59.8)	132 (61.7)	0.92 (0.63–1.34)	0.685	0.87 (0.59–1.30)	0.523

Significant p values are given in bold

OR Odds Ratio, *CI* Confidence Interval

[a] Potential confounding factors are included in the multi-variate analysis

response to NACT ($p = 0.013$). However, association of TT genotype of NQO1 609C>T with the absence of grade 2–4 toxicity was lost on applying multi-variate analysis. This observation underscores the significance of confounding factors along with these genetic variations in predicting breast cancer treatment outcomes.

Table 4 Interaction models by GMDR analysis

Treatment outcomes	Best interaction model	CV testing accuracy#	CV consistency	*p* value	#OR (95 % CI)
Treatment response	CYP3A5*3, NQO1 609C>T, ABCB1 1236C>T	0.62	9/10	0.0001	12.15 (3.09–47.79)
Grade 2–4 toxicity	CYP2C19*2, ABCB1 3435 C>T	0.57	8/10	0.0049	3.00 (1.38–6.53)
Grade 2–4 anemia	CYP2C19*2, ABCB1 3435 C>T, ABCB1 2677G>T/A	0.63	10/10	<0.0001	5.43 (2.42–12.16)
Grade 2–4 leucopenia	CYP2B6*9, UGT2B15 253A>C, ABCB1 2677G>T/A	0.45	6/10	0.0004	5.14 (2.01–13.10)
Dose delay/ reduction	NQO1 609C>T, ABCB1 1236C>T	0.64	8/10	0.0063	4.58 (1.49–14.06)

CV cross validation

Values rounded up to 2 decimal places

Finally, GMDR analysis was performed to evaluate the higher order gene–gene interactions of DMEs along with prognostic factors in predicting breast cancer response to NACT and chemo-toxicity. In our earlier papers, we had carried out gene–gene interaction through MDR [15, 17, 18], which has several limitations. Firstly, it does not allow for adjustment of covariates such as sex, age, etc. Secondly, it is applicable only to dichotomous phenotypes, not to continuous phenotypes. In our present study, all these limitations were overcome by the use of GMDR. As was clear from our results of logistic regression, those prognostic factors like age, clinical stage, and hormone receptor along with genetic variants have a profound effect on drug treatment outcomes like response and toxicity. So, GMDR was performed to study the extensive gene–gene interactions of DMEs that takes place to determine the overall treatment outcomes along with the adjustment of prognostic factors.

In our study, the best gene–gene interaction model was selected across all multi-locus models that maximized testing accuracy and CVC for prediction of breast cancer treatment outcomes. For response to NACT, three-factor model—CYP3A5*3, NQO1 609C>T, and ABCB1 1236C>T—was considered as the best gene–gene interaction model due to higher testing accuracy (CVT = 0.62). The role of these polymorphisms exists biologically. Genetic variant of CYP3A5*3 polymorphism results in null enzyme expression and activity [40–42]. We have already discussed that variant alleles of both NQO1 609C>T and ABCB1 1236C>T polymorphisms lead to decreased enzyme activity. Thus, the combination of variant alleles may augment the effect, which is necessary to predict the drug treatment response in breast cancer patients.

For grade 2–4 toxicity, two-factor model—CYP2C19*2 and ABCB1 3435C>T—polymorphisms yielded the highest accuracy (CVT = 0.57). However, CYP2C19*2, ABCB1 3435 C>T, and ABCB1 2677G>T/A combination of polymorphisms yielded the highest testing accuracy for grade 2–4 anemia (CVT = 0.63) and CYP2B6*9, UGT2B15 253A>C, and ABCB1 2677G>T/A for grade 2–4 leucopenia (CVT = 0.45). For dose delay/reduction, gene–gene interaction of NQO1 609C>T and ABCB1 1236C>T polymorphisms was selected as the best model (CVT = 0.64) (Table 4). Thus, higher order gene–gene interactions along with covariate adjustments in complex metabolism pathway might be the candidate markers for predicting treatment outcomes in terms of both response to NACT and chemo-toxicity. Therefore, GMDR approaches seem more sensitive and accurate when predicting the treatment outcomes subject to the influence of covariate(s).

In most of our gene–gene interaction models for toxicity, ABCB1 3435C>T and ABCB1 2677 G>T/A polymorphisms were present. Polymorphism 3435C>T (Ile1144Ile) is synonymous, while 2677G>T/A results in an amino-acid change from alanine to serine/threonine at codon 893. However, another study has reported the absence of any association of 3435C>T polymorphism with chemo-toxicities [43]. Yet another recent study has also shown that patients with ABCB1 2677G/G genotype suffered more from febrile neutropenia than other genotypes [44]. CYP2C19*2 is also present in our best interaction models both for toxicity and anemia. This polymorphism results in an aberrant splice variant, caused due to an alternative reading frame and a premature stop codon [45]. CYP2C19*2 allele has been associated with a lower elimination rate constant for CP compared to the wild-type allele [46]. CYP2B6 is one of the major enzymes involved in the activation of CP [3].

Application of genomic information is now an accepted part of oncology practice, and efforts to understand the fundamental patho-biological processes triggered by cytotoxic drugs are necessary. Further, identification of the genetic factors that predispose patients to treatment toxicities are the focus of current laboratory and clinical research. The ultimate goal is to develop effective interventions to counter those toxicities and overcome the drug resistance based on identification of differences in gene expression which can predict tumor response to treatment. Pharmacogenetics is likely to play a pivotal role in guiding treatment preferences by identifying a patient's risk for treatment toxicities [47]. Association between DMEs polymorphisms and breast cancer treatment outcomes is biologically valid. Treatment outcomes like response to NACT, myelo-suppression, and other side effects of chemotherapeutic drugs are complex phenotypes. They are dependent on absorption, distribution, metabolism, and excretion (ADME) profile of the drugs. Several other factors like dosage of the drugs and various prognostic factors play an important role in treatment outcomes. Drug metabolism is again a complicated process involving four phases. All the genes of the four phases involved in metabolism of a particular drug work in a synchronized fashion. If there is any genetic variation, these genes would produce enzymes with null or decreased activity. Further, the combination of these variants may hamper drug metabolism, due to indirect effect of interacting enzymes, thus leading to poor pathological response and higher chemo-toxicity. Therefore, higher order gene–gene interaction of DMEs plays an important role in prediction of breast cancer response to NACT and chemo-toxicity.

In summary, prediction of response and toxicity to individual chemotherapy agent or combination regiment can help individualize the treatment and choose an effective and non/less-toxic treatment regimen for an individual patient. Individual gene mutation or SNPs involving one DME-encoding gene have limited impact on the drug response or toxicity. GMDR analysis—an objective analytical tool for evaluating multifactorial impact on an association, allowing adjustment for confounding factors—was applied to explore the best prediction model of high-order gene–gene interactions with response to NACT and toxicity of chemotherapy. The present study provides insights into four phases of DMEs pathways in predicting breast cancer treatment outcomes. To the best of our knowledge, this is the first report to study higher order gene–gene interactions involving DMEs along with prognostic factors with breast cancer treatment outcomes in North Indian population. Our results suggest a role of higher order gene–gene interaction of DME-encoding genes, along with other confounding factors in determination of treatment outcomes and toxicity in breast cancer patients. Ours is only a prefatory study in providing a base for future research for predicting breast cancer treatment outcomes. The relatively small sample size is one of the major limitations of this study, and our results need to be replicated in a larger cohort and in other ethnic populations.

Acknowledgments We are thankful to the Indian Council of Medical Research (Grant No. ICMRBMS/NTF/1/2010-2-11) and Department of Science and Technology (DST), Govt of India (Grant No. DST-SSD/SS/005/2009) for providing financial support to carry out this study.

Compliance with ethical standards

Conflicts of Interest The authors declare that there are no conflicts of interest.

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World J Surg (2016) 40:1583–1589
DOI 10.1007/s00268-015-3222-2

ORIGINAL SCIENTIFIC REPORT

A Comparative Validation of Primary Surgical Versus Post-neo-adjuvant Chemotherapy Sentinel Lymph Node Biopsy for Stage III Breast Cancers

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Published online: 1 September 2015

Abstract

Introduction Sentinel lymph node biopsy (SLNB) is the standard of care for staging N0 primary early breast cancers (EBC). Patients in developing countries mostly present with large (LOBC) or locally advanced cancers (LABC) and are treated with neo-adjuvant chemotherapy (NACT). Accuracy of SLNB in staging stage III N0 and post-NACT N0 patients is uncertain. This prospective validation study on LOBC/LABC patients compared the accuracy of SLNB between primary versus post-NACT surgery.

Materials and methods Fifty T3/T4, N0 patients undergoing primary surgery (Group I) and 70 LOBC/LABC (index stage) treated with NACT and N0 at the time of surgery (Group II) were inducted. Validation SLNB was performed using low-cost methylene-blue and ^{99m}Tc-Antimony colloid. SLN identification (IR) and false-negative (FNR) rates were compared between the groups. Sub-group analysis was done in Group II per index tumor and nodal stage to identify factors predicting SLN IR and FNR in post-NACT patients. SLN IR and FNR in both groups were compared with those in previously published SLN validation study and meta-analysis in EBC.

Results Using combination of blue-dye and radio-colloid, post-NACT SLN IR and FNR (82.9, 13.5 %) were far inferior to T3/T4 primary surgery group (94, 7.7 %; p values 0.034, 0.041) and in EBC. SLN IR using blue-dye alone was dismally low in post-NACT LABCs. Factors predicting unidentified post-NACT SLN and false-negative SLNB included young age, LVI, skin infiltration, extra-nodal spread or N2a stage, and UOQ tumors.

Conclusions Accuracy of SLNB in T3, N0 tumors undergoing primary surgery is comparable to that of SLNB for N0 EBC. In post-NACT patients, SLNB IR are lower and FNR are higher. Factors predictive of non-identification and false-negative SLNB include pre-NACT skin involvement (T4b), N2a stage or extra-nodal invasion and LVI, and to a lesser extent, young age and UOQ location of the tumor.

Presented at the BSI program as free paper (BSI Prize Session) at World Congress of Surgery, Bangkok, Thailand in Aug 2015.

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Introduction

Sentinel lymph node biopsy (SLNB) is the standard of care for staging the axilla in clinically node negative (N0) early breast cancer (EBC) patients undergoing primary surgical therapy. Large randomized trials in the past two decades have proven SLNB to be a safe and effective procedure for EBC patients with T1 and T2 tumors with SLN identification rates (IR) greater than 97 % and false-negative rates (FNR) lower than 10 % [1]. The benefits of lesser probability of arm edema and morbidity, and overall better quality of life, when compared with the earlier gold standard, i.e., axillary lymph node dissection (ALND) have also been established [2]. There is, however, a relative paucity of literature of SLNB in the management of N0 large operable breast cancers (LOBC, T3N0). Existing data does show that despite having a higher incidence of axillary metastatic disease in this subset of patients, results of SLNB in patients with larger tumors are comparable to those of smaller (<3/5 cm) tumors [3, 4], with FNR approaching 5 % [5, 6]. More recent trials have focused on the role that SLNB could play in the management of patients in a post-neo-adjuvant chemotherapy (NACT) setting, and a small proportion of patients included in such trials is those with LOBC or locally advanced breast cancers (LABC) [7].

The vast majority of patients in low-and-middle income countries (LMCs) present with LOBC and LABC, for whom the appropriate initial treatment is with NACT [8, 9]. Axillary lymph node pathological complete response rates have been shown to be as high as 38 %, with higher response rates attainable using taxane and anthracycline combination regimen [10]. This would theoretically imply that about one-third of LOBC/LABC patients who have N0 axilla at the time of surgery following NACT could be spared of an unnecessary ALND, if the SLNB can reliably predict the absence of metastatic axillary nodes. However, the accuracy and validity of SLNB in staging axillae of stage III but N0 patients, and post-NACT LOBC/LABC N0 patients is uncertain. In this prospective validation study conducted on stage III patients, we compared the accuracy of SLNB between patient groups undergoing primary surgery versus those undergoing post-NACT surgery. The SLN outcome indices for stage III patients in both primary and post-NACT settings were also compared with published data for EBC patients undergoing primary surgery.

Materials and methods

This was a prospective non-randomized trial performed on 120 clinically N0 (at the time of surgery), uni-focal, non-inflammatory LOBC and LABC patients treated at a tertiary care referral hospital between 2004 and 2011 with due approval from the Institute Ethics Committee. Patients who did not consent for a validation SLNB; those who had multi-centric, multifocal, ulcerated, or fungating tumors; those who had clinical/radiological evidence of enlarged axillary lymph nodes at the time of surgery; and pregnant patients were excluded from this study.

The study cohort was divided into two groups: Group I consisted of T3/T4, N0 patients undergoing primary surgery. Patients with T3/T4 (index stage) tumors treated with NACT and who were N0 at the time of surgery comprised Group II. All Group I patients underwent primary surgery in the form of either breast-conserving surgery (BCS) or simple mastectomy (SM) along with validation SLNB (and so routine completion ALND irrespective of SLNB histology), followed by adjuvant chemotherapy and external beam radiotherapy (EBRT), and hormone treatment and/or trastuzumab, as indicated. All Group II patients received NACT, followed by surgery (BCS/SM) along with validation SLNB, followed by adjuvant EBRT and hormone and/or trastuzumab treatment, as appropriate. NACT was in the form of either four 3 weekly cycles of 5-fluorouracil, epirubicin or doxorubicin, and cyclophosphamide (FEC/FAC) followed by 12 cycles of weekly paclitaxel (48/70 patients), or four 3 weekly cycles of FEC/FAC followed by four 3 weekly cycles of docetaxel (9/70 patients), or six 3 weekly cycles of FEC (9/70 patients), or six 3 weekly cycles of docetaxel, epirubicin or doxorubicin, and cyclophosphamide (TAC: 4/70 patients).

In both groups, SLNB was performed by a single surgeon (GA) using identical techniques. A combination of low-cost blue-dye—methylene-blue (2 ml of 1 % w/v aqueous solution) and radiopharmaceutical-^{99m}Tc-Antimony colloid (40 MBq), both of which were made in-house using standard reagents were used. A combined sub-areolar (50 % of injection volume) and peri-tumoral (50 % of injection volume) injection of the dyes was done. In the majority of patients (67.5 %), the radiopharmaceutical was injected on the evening prior to surgery; the remainder had injection done on the morning of surgery. A Neoprobe 2000 Gamma Detection System and hand held probe (Ethicon Endo-Surgery Inc, Johnson & Johnson, Cincinnati, OH, USA) were used for the radio-guided excision of SLNs. During surgery, any blue and/or hot SLNs (Fig. 1), and any enlarged suspicious lymph nodes were removed. Irrespective of the SLN histology, completion ALND (as part of validation SLNB) was performed in all patients at the time of the definitive surgical procedure. All patients had a Level I and II axillary clearance done, and a Level III dissection was done only when palpable nodes were discovered intra-operatively medial to the pectoralis minor muscle.

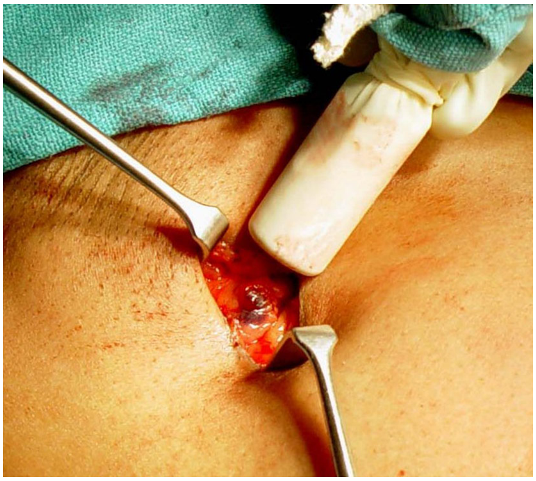

Fig. 1 Gamma probe on a hot and blue sentinel lymph node

The SLNs were sectioned and processed for histology using standard protocols [11, 12] and subjected to frozen section histology. SLNs and all the axillary lymph nodes removed at ALND were fixed in 10 % formaldehyde, embedded in paraffin, sectioned, and stained with hematoxyline & eosin (H&E). Any metastatic foci of any size discernable on frozen section histology and/or on H&E stained paraffin sections were considered as evidence of lymph nodal metastases.

Comparing the SLN histology with the gold standard, i.e., histology of the ALND specimen, the number of cases with true and false positive and true- and false-negative SLN histology was recorded. The key outcome indices of SLN IR, FNR, sensitivity, and negative predictive value (NPV) of SLNB in predicting the histology of the axillary nodes were calculated and compared between the groups I and II. In Group II, sub-group analysis was done according for the index tumor & axillary nodal stage before NACT. Factors predicting SLN IR & FNR in post-NACT patients were analyzed. The SLN IR and FNR of Group I & II study patients were further compared with those of validation SLNB results for EBC using same dyes and identical surgical and pathology techniques reported earlier by our group [13] and with a published meta-analysis of SLNB studies reporting on the SLN FNR [14]. Student's t test was used for comparing the continuous variables, and Z test for two population proportions was used for comparison of categorical variables. All statistical analyses were performed using the SPSS 17 software package (SPSS Statistics for Windows, Version 17.0, SPSS Inc., Chicago, USA). Any p values ≤ 0.05 were considered statistically significant.

Table 1 Clinical, pathological attributes, and treatment details of patients

	Group I (n = 50) T3/T4 N0 primary surgery	Group II (n = 70) T3/T4 post-NACT N0
Mean age (years) mean ± SD	51.3 ± 6.4	48.8 ± 7.5
Mean index tumor size (cm) mean ± SD	6.04 ± 0.65	6.31 ± 1.75
Index tumor stage (at time of initial diagnosis)		
T1	0	1 (1.4 %)
T2	0	3 (4.3 %)
T3	43 (86 %)	26 (37.1 %)
T4	7 (14 %)	40 (57.1 %))
IHC sub-type		
ER/PR positive/HER2-negative	22 (44 %)	29 (41.4 %)
HER2-positive	16 (32 %)	22 (31.4 %)
Triple negative	12 (24 %)	19 (27.1 %)
Tumor histology		
IDC	46 (92 %)	64 (91.4 %)
ILC	0	1 (1.4 %)
IDC with DCIS	4 (8 %)	5 (7.1 %)
Tumor grade		
I	2 (4 %)	3 (4.3 %)
II	11 (22 %)	13 (18.6 %)
III	37 (74 %)	54 (77.1 %)
NACT regimen		
Anthracyline followed by taxane	NA	57 (81.4 %)
Anthracyline only	NA	9 (12.8 %)
Anthracyline concurrent with taxane	NA	4 (5.7 %)
All chemotherapy administered pre-operatively[a]	NA	65 (92.8 %)
Breast surgery		
BCS	6 (12 %)	9 (12.8 %)
Mastectomy	44 (88 %)	61 (87.1 %)

SD standard deviation, *cm* centimeters, *IHC* immunohistochemistry, *ER* estrogen receptor, *PR* progesterone receptor, *HER2* human epidermal growth factor receptor 2, *IDC* infiltrating ductal carcinoma, *ILC* infiltrating lobular carcinoma, *DCIS* ductal carcinoma in situ *NACT* neo-adjuvant chemotherapy; *BCS* breast-conserving surgery

[a] Rest of the patients had some cycles of chemotherapy administered post-operatively

Results

One hundred and twenty patients were inducted, out of which Group I comprised 50 patients, while Group II had 70. Group I was subdivided as T3, N0 (n = 43) and T4b,

Table 2 Comparison of SLN results between primary and post-NACT surgery groups

	Group I ($n = 50$) T3/T4 N0 primary surgery	Group II ($n = 70$) T3/T4 post-NACT N0	p value
SLN identification rate	47 (94 %)	58 (82.9 %)	0.034
	T3 ($n = 43$): 95.3 %	T3, N0-1 ($n = 14$): 92.9 %[a]	NS
	T4b ($n = 7$): 85.7 %	T4b, N0-1 ($n = 28$): 89.3 %[a]	NS
		T1-3, N2a ($n = 16$): 75 %[a]	
		T4b, N2a ($n = 12$): 66.7 %[a]	
Number of nodes removed at completion ALND {mean ± SD, (range)}	15.65 ± 4.8 (9–27)	13.92 ± 5.6 (10–32)	NS
False-negative rate (%)	7.7 %	13.5 %	0.041
	T3: 4.8 %	T3, N0/N1: 0 %[a]	NS
	T4b: 20 %	T4b, N0-1: 11.8 %[a]	NS
		T1-3, N2a: 22.2 %[a]	
		T4b, N2a: 16.7 %[a]	
Sensitivity	92.3 %	86.5 %	NS
Negative predictive value	91.3 %	80.8 %	NS

SLNs sentinel lymph nodes, *NACT* neo-adjuvant chemotherapy, *NS* not significant

[a] Index stage (pre-NACT)

Table 3 Sentinel lymph nodes removed

Number of SLNs identified	Group I ($n = 50$) T3/T4 N0 primary surgery	Group II ($n = 70$) T3/T4 post-NACT N0
0	3 (6 %)	12 (17.1 %)
1	9 (18 %)	11 (15.7 %)
2	17 (34 %)	22 (31.4 %)
3	11 (22 %)	14 (20 %)
4	6 (12 %)	7 (10 %)
5	4 (8 %)	4 (5.7 %)

SLNs sentinel lymph nodes

N0 tumors ($n = 7$). Group II was also subdivided as T3, N0-1 ($n = 14$); T4b, N0-1 ($n = 28$); T1-3, N2a ($n = 16$); and T4b, N2a ($n = 12$) patients. Clinical details of patients are summarized in Table 1. In Group I, using the combination of blue-dye and radiopharmaceutical, the SLN IR was 94 % (Table 2). IR using radiopharmaceutical alone (88 %) and blue-dye alone (80 %) were both lower than the combined method. IR was higher in the T3, N0 sub-group (95.3 %) when compared with the T4b, N0 sub-group (85.7 %, $p = 0.032$). In Group II, the overall SLN IR was 82.9 % using combination dyes method, which was significantly higher compared to the IR achieved with radiopharmaceutical alone (74.1 %) or blue-dye alone (58.6 %). In the sub-group of T3, N0/N1 tumors, IR was better, at 92.9 %; with lower IR in the T4b, N0-1 sub-group (89.3 %), T1-3, N2a sub-group (75 %) and the T4b, N2a sub-group (66.7 %). In both groups, the median number of SLNs removed was 2 (range 0–5) (Table 3).

SLN IR and FNR (Table 2) in post-NACT patients (group II) were significantly inferior to those in the T3/T4 primary surgery patients (group I). SLNB results in T3/T4, N0 patients undergoing primary surgery were comparable

Table 4 Factors affecting SLN identification and false-negative rates in post-NACT stage III patients

Factors	SLN identification rate (p value)	SLN false-negative rate (p value)
Age (younger than 35 years)	0.067 (NS)	0.038
Tumor stage T4b (skin involvement)	0.015	0.041
Nodal stage N2a (matted nodes)	0.020	<0.001
Lympho-vascular invasion	0.008	0.037
Extra-nodal spread	<0.001	<0.001
Upper-outer quadrant location	0.041	0.127 (NS)

SLN sentinel lymph node, *NACT* neo-adjuvant chemotherapy, *NS* not significant

Fig. 2 Sub-areolar injection of methylene-blue in a patient with skin edema

to our validation SLNB results in EBC patients ($n = 70$, SLN IR 95.7 % and FNR 8.7 %) reported earlier [13], and with the pooled FNR of 7.5 % reported in a meta-analysis of 183 studies reporting data on 9220 patients [14].

No significant differences were noted in SLN IR and FNR according to patient and tumor characteristics, immuno-histochemical subtypes, type of chemotherapy, and response to chemotherapy. The mean number of axillary lymph nodes removed at completion ALND in group I was 15.65 (range 9–27) which were comparable to the number of lymph nodes removed at completion ALND in group II (13.92, range 10–32, $p = 0.086$). In 9 (19.1 %) in group I and 10 (17.2 %) in group II patients, SLN(s) was/were the only involved lymph node(s). Additional metastatic lymph node(s) other than the SLN(s) was/were noted in 24 (31.9 %) patients in Group I and 32 (37.9 %) patients in Group II. In group I, SLNB had a sensitivity of 92.3 % with a NPV of 91.3 %. In comparison, the sensitivity (86.5 %) and NPV (80.8 %) of SLNB in Group II were somewhat inferior, not reaching statistical significance ($p = 0.235$, $p = 0.147$, respectively). In sub-group analysis in the group II (Post-NACT patients), factors predictive of unidentified SLN and/or false-negative SLNB included the presence of skin involvement (T4b), matted lymph nodes (N2a), young age, lympho-vascular invasion (LVI), extra-nodal spread, and upper-outer quadrant location of tumor (Table 4).

Blue discoloration of urine was noted in 32 (64 %) patients in group I and 41 (58.6 %) patients in group II. Minor allergic reactions were seen in 3 (6 %) patients in group I and 5 (7.1 %) patients in group II. None of the patients in either group suffered any major anaphylactoid reaction needing additional treatment or prolonged hospitalization. None of the patients suffered skin necrosis at the injection site in either group.

Discussion

In a prospective non-randomized study performed exclusively on LOBC and LABC patients, we have compared the utility of SLNB in primary surgical setting versus post-NACT setting. While SLNB is widely recognized as the standard of care for staging axilla in N0 EBC [1, 2], its role in patients with LOBC and LABC patients, and in post-NACT N0 cases is debatable. Majority of published studies relating the accuracy of SLNB have been on EBC patients. There are just a few studies evaluating accuracy of post-NACT SLNB, and even in those, majority of patients are those of EBC, undergoing post-NACT SLNB. Validation SLNB studies, which correlate the histology of the SLN with that of the ALND specimen, are vital in establishing the applicability of SLNB in a defined subset of breast cancer patients. Key indices of quality or accuracy of SLNB in the validation studies are SLN IR, which signifies the ability of the SLNB technique to accurately identify the SLN intra-operatively; and the FNR, which provides a measure of concordance between the SLN histology and the histological status of the entire axilla [14]. The minimum desired SLN IR is 90 % and the maximum acceptable FNR when compared to the gold standard ALND is 10 % [1, 2].

Applying these yard-sticks to our study, results of our study on LOBC/LABC patients suggest that primary surgical SLNB can be safely advocated for LOBC and LABC, as the SLN IR in such scenario is >90 % and FNR was <10 %. However, post-NACT SLNB cannot provide a robust prediction of whole of axillary nodal status, as in that setting, we found the IR to be much lesser than 90 % and FNR well over 10 %. Our study further provides evidence to support use of SLNB in T3N0 patients undergoing primary surgery or post-NACT surgery. The SLN IR and the FNR of SLNB in T3, N0 breast cancer patients undergoing primary surgery or post-NACT surgery were found comparable to that of SLNB in EBC patients [13, 14]. SLN IR and FNR for T3N0 patients were not statistically different whether performed at primary surgery or as a post-NACT procedure. These observations suggest that SLNB accurately predicts the presence of axillary nodal metastases irrespective whether it is performed before (primary surgery) or after NACT in patients with T3N0 breast cancers. Previous studies have not provided a conclusive evidence of the accuracy and safety of primary SLNB in T3, N0 tumors, though a number of such studies indicate similar results [3–5, 13, 15, 16].

The role of SLNB in the post-NACT setting has been/is being investigated, which include the American College of Surgeons Oncology Group (ACOSOG) Z1071 trial [7, 17], and certain other trials [18, 19]. A recent meta-analysis has shown that post-NACT SLNB is associated with an acceptable pooled IR (89 %), but a poor FNR (14 %) [20]. This meta-analysis suggested that further studies be undertaken, especially in LABC patients, to identify factors associated with SLNB failure, with the intention of creating a well-defined ‘selection criteria’ for patients receiving NACT—aiming to achieve IR and FNR equivalent to that of SLNB in EBC patients. In our study, the SLN IR were much lower, and the FNR were much higher in post-NACT SLNB group, when compared to the SLNB results in EBC patients [13, 14] as well as those in primary surgical T3N0 group. In patients receiving NACT, factors that were found correlated with non-identified and false-negative SLN were skin involvement (T4b), matted lymph nodes (N2a), young age, LVI, extra-nodal spread, and upper-outer quadrant tumors. The SLNB accuracy was much poorer in patients with one or more of these factors, when compared to T3, N0 patients.

Our results suggest that the SLN IR is low (<90 %), and the FNR unacceptably high (>10 %) in patients with skin involvement (T4b tumors) undergoing either primary or post-NACT surgery. This observation suggests that the obliterated cutaneous and efferent lymphatic channels that result in cutaneous edema in LABC do not open up after the NACT in majority. This makes SLNB unreliable in LABC patients with post-NACT N0 axilla. A manifestation of obliterated lymphatics observed by us in such patients was the methylene-blue dye getting spread in subcutaneous lymphatics, rather than tracking up towards the axilla (Fig. 2). Similarly, patients with index stage of N2a (matted axillary nodes), and who are clinically N0 at time of post-NACT surgery are not good candidates for axillary staging with SLNB, as the IR are low and FNR are high. In other words, our results suggest that SLNB for patients with skin involvement (T4b tumors) and those with matted lymph nodes (N2a) is not adequately representative of the histology of the entire axillary nodal basin, neither when performed primarily, i.e., before administration of any chemotherapy, nor when performed following down staging with NACT. The IR with blue-dye alone in group II was particularly low, more so in the sub-group of patients with T4b and N2a disease. It may be reasonable to conclude that in post-NACT patients who had T4b or N2a stage to start with blue-dye alone method should not be used. This is of specific relevance in view of certain recommendations that SLNB using blue-dye alone is an appropriate low-cost technique for use in centers with limited resources [21].

The commonly used commercially marketed blue-dyes such as Lymphazurin™ or patent blue violet; and the branded radiopharmaceuticals such as ^{99m}Tc Sulfur colloid add a substantial cost to breast cancer surgery. We have been using generic, in-house prepared methylene-blue and ^{99m}Tc-Antimony colloid for SLNB with due approval from the institutional bodies since our initial validation study on EBC and LOBC patients [6, 13]. The choice of dyes both blue-dye and the radiopharmaceutical may be considered as a factor affecting the SLN IR as well as accuracy of the SLNB in predicting axillary nodal status by some. However, our earlier studies, as well as other studies have not found the choice of dyes to impact these key outcome indices of SLNB.

A relatively small sample size and a heterogeneous patient population are the major limitations of this study. Also, we used in-house produced low-cost blue-dye and radiopharmaceutical for the SLNB, rather than the commercially marketed dye and radiopharmaceutical, which are many fold more expensive and difficult to procure in India, and in most LMCs. Even with these limitations, we believe our study may be helpful in devising judicious management protocols incorporating SLNB in LMCs, where a substantial proportion of breast cancers is still diagnosed as LOBC and LABC [8, 9]. There are no other studies focusing on evaluating utility of SLNB specifically in LABC and LOBC patients exclusively. Such patients are invariably treated with NACT, and up to one-third of patients receiving NACT may become N0 following NACT. Such post-NACT N0 patients can potentially benefit from SLNB, and about half of them can be spared an unnecessary ALND. Our results need to be replicated or refuted in a larger, preferably multi-center study of similar nature, including patients of different ethnicities, yet uniformly of LOBC and LABC.

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World J Surg (2016) 40:1362–1372
DOI 10.1007/s00268-016-3422-4

ORIGINAL SCIENTIFIC REPORT

Outcomes of Triple-Negative Breast Cancers (TNBC) Compared with Non-TNBC: Does the Survival Vary for All Stages?

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Published online: 2 February 2016

Abstract

Background Triple-negative breast cancer (TNBC) is associated with aggressive tumor behavior and worse outcomes. In a study at a tertiary care breast unit in a developing country, clinico-pathological attributes and outcomes of patients with TNBC were compared with (c.w.) ER, PR, and/or HER2 expressing tumors (non-TNBC).

Patients and methods Medical records of 1213 consecutive breast cancer patients managed during 2004–2010 were reviewed. An evaluable cohort of 705 patients with complete treatment and follow-up (median 36 months) information was thus identified. Patients were categorized per ER, PR & HER2 status into TNBC, and ER/PR+ and/or HER2+ groups. Clinico-pathological parameters, response to NACT, and OS & DFS were compared between TNBC and non-TNBC groups.

Results TNBC patients ($n = 249$) comprised 35.3 % of the study cohort ($n = 705$), and were significantly younger than non-TNBC patients (mean age 49.1 ± 11.2y c.w. 51.8 ± 11.3, $p = 0.02$). The TNM stage at presentation was similar in the two groups (Stage I and II—37 % c.w. 44.3 %, Stage III—47.5 % c.w. 39.5 %, Stage IV—15.5 % c.w. 16.2 % in TNBC c.w. Non-TNBC; $p = 0.09$). Tumor size (5.7 ± 2.9 cm TNBC c.w. 5.4 ± 2.8 cm non-TNBC, $p = 0.22$) was similar but lymph nodal (cN) metastases were more frequent in TNBC (77.3 % c.w. 69.8 %; $p = 0.03$). TNBC had higher histologic grade (97.1 % gr II/III in TNBC c.w. 91.2 % non-TNBC, $p = 0.01$) and higher incidence of LVI (20.4 % in TNBC c.w. 13.5 %, $p = 0.03$). Patient groups received similar multi-disciplinary surgical, radiation, and systemic treatment. Comparable proportion of patients in 2 groups were treated with NACT (42 % c.w. 38 %), which resulted in pathological complete response (pCR) in 27.5 % TNBC patients c.w. 17.1 % non-TNBC patients ($p = 0.04$). Both OS (81.8 ± 4.52 c.w. 97.90 ± 3.87 months, $p < 0.001$) and DFS (89.2 ± 5.1 c.w. 113.8 ± 4.3 months, $p < 0.001$) were shorter in TNBC than non-TNBC group. On stage-wise comparison, OS differed significantly only in stage III (47.4 ± 5.3 months in TNBC c.w. 74.5 ± 4.4 in non-TNBC; $p < 0.001$). Univariate and multivariate analyses revealed tumor stage and IHC subtyping into TNBC c.w. non-TNBC as most important factors predictive of survival.

Conclusions TNBC occurred at younger age and exhibited aggressive pathology as compared to non-TNBC patients. Although patients with TNBC exhibited better chemo-sensitivity, they had worse DFS and OS compared to the non-TNBC patients. The survival of Stage III TNBC patients was significantly worse compared to non-TNBC group; while in stages I, II, and IV, survival were not significantly different.

Presented at the International Surgical Week, Helsinki Finland in Sept 2013.

Electronic supplementary material The online version of this article (doi:10.1007/s00268-016-3422-4) contains supplementary material, which is available to authorized users.

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Introduction

Background

Triple-negative breast cancers (TNBC) lack expression of estrogen receptor (ER-negative), progesterone receptor (PR-negative), and human epidermal growth factor receptor 2 (HER2-negative) [1, 2]. These tumors do not respond to hormone treatment or anti-HER2 treatment, and so chemotherapy (CTx) is the main-stay systemic treatment for such patients. TNBC accounts for about 9–21 % of all breast cancers including patients for all the stages of breast cancer [3, 4]. TNBC are known to respond better to CTx, and result in higher rates of pathological complete response (pCR) after neo-adjuvant chemotherapy (NACT) than hormone responsive or HER2 expressing breast cancer subtypes [5]. Yet, they have poorer survival outcomes compared with (c.w.) ER/PR and/or HER2 expressing subtypes [4, 6, 7].

Most of the studies reporting outcomes of TNBC in comparison to non-TNBC patients are from developed countries, in which, the majority of patients are early-stage breast cancers (EBC). Breast cancer patients in India and other developing countries are mostly diagnosed at large operable or locally advanced stages (LABC), and thus NACT is the primary treatment modality employed [8, 9]. There is lack of data from India and other developing countries, comparing the outcomes of TNBC and non-TNBC patients. This retrospective study was conducted at a specialty breast center in north India with the aim of comparing the outcomes of TNBC and non-TNBC patients, and investigating the causes for any differences in their outcomes.

Patients and methods

This retrospective study was carried out at SGPGIMS, Lucknow a tertiary health care center in India, with due clearance from the institute ethics committee. Female breast cancer patients ($n = 1213$) of all stages treated between January 2004 and December 2010 were reviewed. The data were obtained from hospital and follow-up medical records by accessing their electronic medical records, case files in the department of Endocrine and Breast Surgery as well as Department of Radiation Oncology, and the electronic records of Department of Pathology. In addition, all patients were contacted via letters, telephone, and email to derive current follow-up status. Patients for whom one or more clinical, pathological, ER/PR/HER2 information were lacking ($n = 268$) were excluded. Only such surviving patients with minimum 42 months follow-up were included. Those patients for whom current follow-up and outcome information was not available ($n = 240$) were also excluded from the study, thus leaving the study cohort of 705 qualifying patients, who were included in the final analysis.

The demographic and clinical features including age, menopausal status, family history of breast or ovarian cancers and other relevant family history, tumor stage at presentation, and treatment details including surgical, radiation, and systemic treatment were recorded. Histopathological characteristics of the tumor including pathological tumor size and lymph nodal status, tumor grade, lymphovascular invasion (LVI), margins (involved/not involved), and peri-nodal involvement (yes/no) were captured. Based on immuno-histochemical (IHC) analysis of tumor ER, PR, HER2 results, patients were divided broadly into TNBC and non-TNBC groups. ER, PR immunostaining was done on formalin fixed, paraffin embedded tissues using well-standardized techniques. Any immunostaining for ER and/or PR was taken as positive. The clone used for HER2 detection was a polyclonal (HER2 Hercep Test Kit) and the detection system was a polymer. The CAP/ASCO guideline criteria were used for the interpretation of results: HER2 score 0 (No staining observed, or membrane staining in <10 % of the tumor cells) or 1+ (faint/barely perceptible membrane staining detected in >10 % of the tumor cells; cells only stained in part of the membrane) was interpreted as negative. Score 2+ (weak to moderate complete membrane staining observed in >10 % of tumor cells) was interpreted as weak positive, and further evaluated for HER2 by fluorescent in situ hybridization (FISH) in about half of such patients. All patients with HER2 IHC score 3+ (strong and complete membrane staining observed in >30 % cells) and those with HER2/CEP17 ratio (FISH) of >2.2 were interpreted as HER2 positive tumors.

Patients with inoperable locally advanced (T4 and/or N2/3) and large operable (T3) cancers were treated with NACT. In patients treated with NACT, response was recorded as per RECIST criteria. In patients undergoing breast conservation surgery, any infiltrated margins detected either on intra-operative frozen section or post-operative paraffin section histology were re-excised. Outcomes recorded were Overall survival (OS)—defined as time period from the date of diagnosis to the date of death from any cause; and Disease-free survival (DFS)—defined as time period for which a patient survived without evidence of disease, i.e., the time duration from the first definitive treatment to the date of first event in the form of loco-regional or distant recurrence in surviving patients; or

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death from any cause in patients with no documented recurrence or metastases. Patients alive (for OS analysis)/or free of loco-regional or distant recurrence (for DFS analysis) at the end of study period (or those for whom there was no evidence to show that either has occurred) were considered to have "censored" survival times.

Statistical analysis

Differences in patient and tumor characteristics were analyzed using variance for continuous variables and Chi-square for categorical variables. The Kaplan–Meier product limit method was used for OS and DFS analysis. Log-rank test was used to compare the OS and DFS of subtypes. Univariate and multivariate analyses were done using Cox proportional hazard model to identify factors influencing OS and DFS in TNBC patients. Statistical analyses were performed using a SPSS-16 software package (SPSS, Inc., Chicago, IL). p values were considered significant if <0.05.

Results

TNBC patients constituted 35.3 % (249 of 705) of the entire study cohort. A comparison of TNBC and non-TNBC patients revealed that TNBC patients were younger (mean age of 49 ± 11.2 years, c.w.51.8 ± 11.3 years in non-TNBC group, $p = 0.002$), and more often pre-menopausal (47 % in TNBC c.w. 38.4 % in non-TNBC group, $p = 0.03$). Mean tumor size was similar in the two groups (5.7 ± 2.9 cm in TNBC c.w. 5.4 ± 2.8 in non-TNBC, $p = 0.15$). However, a higher proportion of TNBC patients had lymph node metastases (cN status) at presentation (77.3 % in TNBC c.w. 69.8 % in non-TNBC group, $p = 0.03$). 110 (15.6 %) patients had undergone some prior surgical procedure in the form of incisional or excisional biopsy or mastectomy elsewhere before presenting to our hospital, and they were equally distributed between TNBC and non-TNBC groups. Higher proportion (47.5 %) of TNBC patients presented as LABC compared to 39.5 % in non-TNBC group ($p = 0.06$). The proportion of TNBC and non-TNBC patients in early (stages I and II, 37 % TNBC c.w. 44 % non-TNBC, $p = 0.09$) and metastatic (stage IV, 15.5 % TNBC c.w. 16.2 % non-TNBC, $p = 0.82$) disease at presentation were comparable.

Infiltrating ductal carcinoma (IDC) was the commonest histo-pathological subtype in both the groups (94.2 % in TNBC, 93 % in non-TNBC group; $p = 0.33$). The histological grade III tumor proportion was higher in TNBC (56.4 %) compared to non-TNBC group (31.4 %, $p = 0.002$). The two groups were treated in comparable manner: 42.1 % of TNBC and 37.6 % of non-TNBC patients underwent NACT, with anthracyclines containing combination chemotherapeutic regimen being the commonest one—used in 66.2 % of TNBC and 61.8 % of non-TNBC patients ($p = 0.29$). Combination of

Table 1 Univariate and multivariate analysis of factors affecting overall survival

	Univariate analysis			Multivariate analysis		
	Odd's ratio	*p* value	CI	Odd's ratio	*p* value	CI
Age ≤50/>50 years	0.898	0.416	0.692–1.16			
TNM stage (I/II/III/IV)	2.475	<0.001	2.12–2.18	3.15	0.001	1.5–6.3
pT	1.35	<0.001	1.14–1.59	1.472	0.025	1.0–2.1
pN	1.47	<0.001	1.28–1.7			
Histological grade	1.51	0.007	1.12–2.05	2.907	<0.001	1.6–5.2
Group (TNBC vs non-TNBC)	1.59	0.001	1.25–2.1	1.992	0.017	1.1–3.5

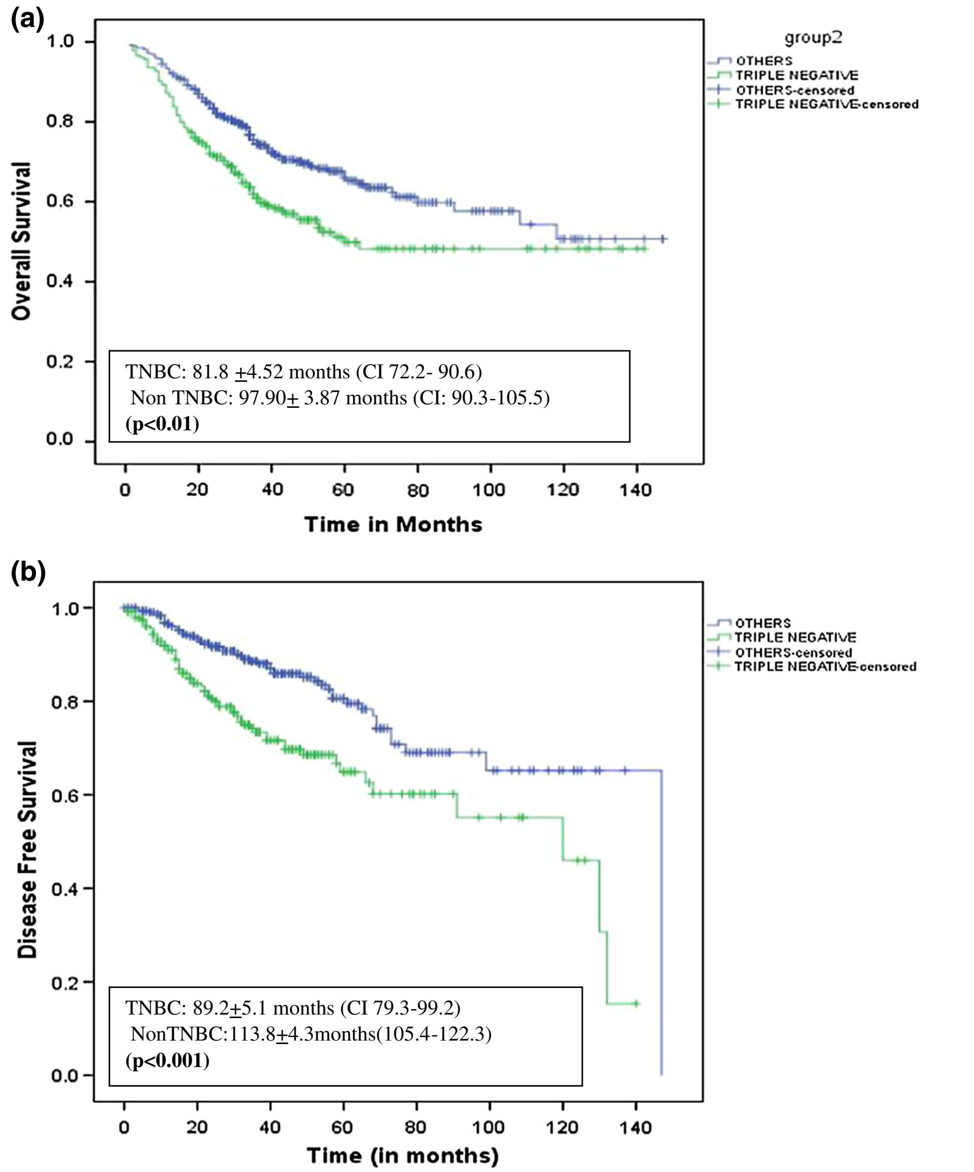
CI confidence interval, *pT* pathological tumor stage, *pN* pathological nodal stage, *TNBC* triple-negative breast cancer

Table 2 Univariate and multivariate analysis of factors affecting disease-free survival

	Univariate analysis			Multivariate analysis		
	Odd's ratio	*p*	CI	Odd's Ratio	*p*	CI
Age ≤50/>50 years	0.686	0.036	0.48–0.97	0.480	0.004	0.29–0.78
TNM stage (I/II/III/IV)	1.864	<0.001	1.4–2.3			
pT	1.275	0.020	1.0–1.5			
pN	1.648	<0.001	1.3–1.9	1.558	<0.001	1.2–1.9
Histological grade	1.549	0.030	1.0–2.2			
Group (TNBC vs non-TNBC)	2.162	<0.001	1.5–3.1	1.991	0.005	1.2–3.2

CI confidence interval, *pT* pathological tumor stage, *pN* pathological nodal stage, *TNBC* triple-negative breast cancer

Fig. 1 Comparison between TNBC and non-TNBC patients: **a** overall survival, **b** disease-free survival

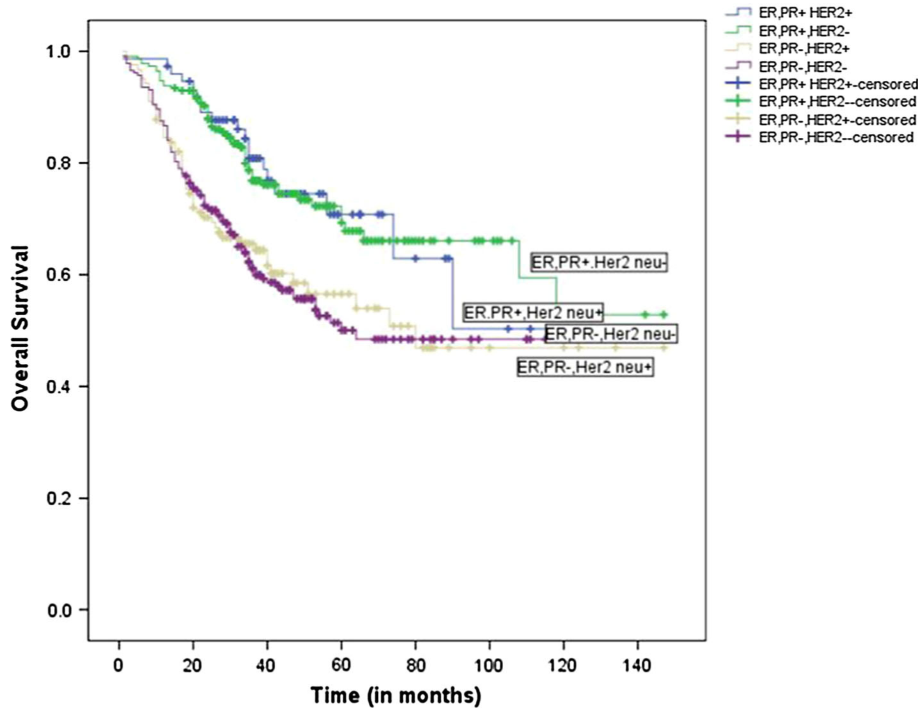


anthracyclines and taxanes were used in 28.4 % of TNBC and 33.1 % of non-TNBC patients ($p = 0.24$). In the 238 patients treated with NACT, clinical complete response (cCR) was seen in 35.9 % TNBC and 24.5 % non-TNBC patients ($p = 0.03$). Pathological complete response (pCR) was seen in 27.5 % TNBC patients and 17.1 % of non-TNBC patients ($p = 0.04$). Further details of clinical, pathology, and treatment-related variables, and their comparisons between TNBC and non-TNBC groups are provided in supplementary Table 1. Comparison of clinical, pathologic, and treatment characteristics between patient groups who were treated with adjuvant and neo-adjuvant chemotherapy is provided in supplementary Table 2.

Survival data

Over a median follow-up of 36 months (range: 1–147 months; minimum follow-up in surviving patients 42 months), the mean OS {Fig. 1(A)} with 95 % CI in TNBC patients was 81.8 ± 4.5 months (CI 72.3–90.7) which was significantly ($p < 0.001$) shorter compared to the OS in non-TNBC group (97.9 ± 3.9 months, CI 90.3–105.5). The estimated mean DFS {Fig. 1(B)} with 95 % CI in TNBC patients (89.2 ± 5.1, CI 79.3–99.2) was shorter ($p < 0.001$) c.w. that in non-TNBC patients (113.8 ± 4.3, CI 105.4–122.3). The OS (Fig. 2) varied significantly between subgroups based on ER, PR, and HER2 status ($p < 0.001$). The estimated OS was longest in subgroup with ER/PR expressing but HER2

Fig. 2 Comparison of Overall survival in patient groups based on hormone receptors and HER2 status



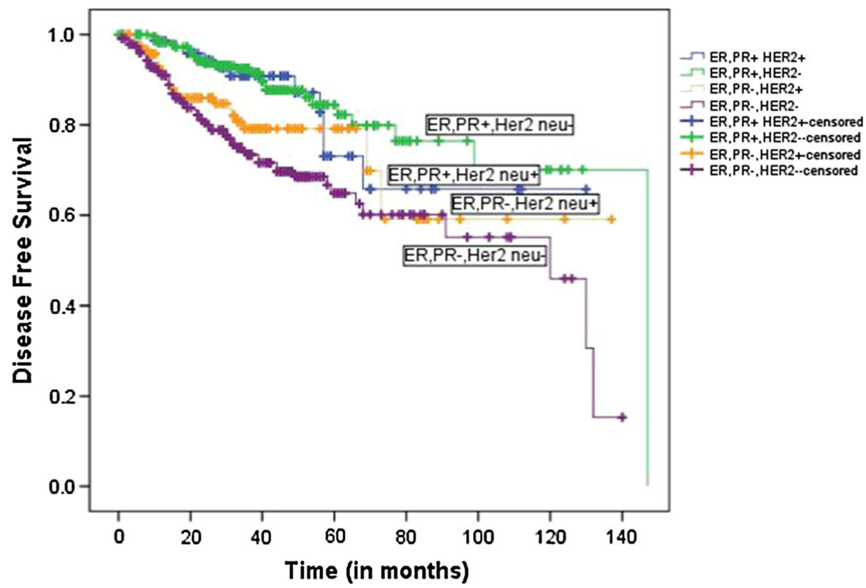
	ER,PR+,Her2-	ER,PR+,Her2+	ER,PR-,Her2+	ER,PR-,Her2-
Mean overall survival with CI	113.8±4.3months CI:(105.4-122.3)	91.6±7.8months (CI 71.7- 98.4)	85.6±6.8 months (CI: 71.3-97.8)	81.8±4.52 months (CI: 72.260- 90.68)

deficient (ER/PR+, HER2-) tumors {103.8 ± 5.2 months (CI 93.7–114.0)}, and the worst in TNBC patients {81.8 ± 4.52 months (CI 72.3–90.7)}. The estimated DFS (Fig. 3) too varied significantly between the groups ($p < 0.001$) and was longest for ER, PR+ HER2− patients {119.9 ± 5.6 (CI 108.8–131.0) months} and shortest {89.3 ± 5.1 (CI 79.3–99.2)} for TNBC patients. Supplementary Table 3 provides a comparative list of the site of distant metastasis in TNBC and non-TNBC patient groups.

Figures 4 (A), (B), and (C) provide a comparison of OS according to stage groups, namely EBC (TNM stages I and II), LABC (TNM stage III), and MBC (TNM stage IV). There was no significant difference in OS in EBC (non-TNBC 99.1 ± 6.1 months, CI 87.1–111.1 c.w. TNBC 102.6 ± 7.2 months, CI 88.5–116.6; $p = 0.308$) and MBC (TNBC 21.1 ± 3.8, CI 13.6–28.5 c.w. non-TNBC 28.4 ± 3.0, CI 22.4–34.4; $p = 0.116$). However, the OS was significantly different in stage III patients, with the mean OS in TNBC patients being 47.4 ± 5.3 months (CI 37.0–57.8) and 74.5 ± 4.4 (CI 65.924–83.092) in non-TNBC; $p < 0.001$. Figure 5 (A) and (B) shows the difference in OS and DFS, respectively, in patients who achieved pCR following NACT. The OS ($p = 0.158$) and DFS ($p = 0.40$) were similar in such TNBC and non-TNBC patients. However, comparing the OS {Fig. 6 (A)} and DFS {Fig. 6 (B)} in patients who achieved partial response to NACT, the mean OS in TNBC group was 57.4 ± 7.8 (CI 42.0–72.9) months, c.w. 79.4 ± 9.2 (CI 61.27–97.64) months in non-TNBC patients; $p < 0.001$. The DFS in partial responders TNBC patients was 67.6 ± 9.64 (CI 48.75–86.57) months, as compared to 81.45 ± 6.9 months in non-TNBC partial responders (CI 67.92–94.98; $p = 0.007$).

On univariate analysis of factors affecting OS (Table 1), TNM stage at presentation, ($p < 0.001$), pathological tumor (pT) stage ($p < 0.001$), pathological lymph nodal (pN) stage ($p < 0.001$), histo-pathological grade of the tumor ($p = 0.007$), and subtyping based on ER, PR, HER2 status, i.e., TNBC c.w. non-TNBC ($p = 0.001$) were the factors affecting OS, while the response to CTx ($p = 0.31$) and age ($p = 0.41$) had no significant impact on OS. However, on multivariate analysis, only TNM stage at presentation ($p < 0.001$), pT stage ($p = 0.025$), histo-pathological grade ($p < 0.001$), and ER, PR, HER2 sub-typing (TNBC c.w. non-TNBC, $p = 0.017$) remained significant predictors of OS. On univariate analysis, the DFS

Fig. 3 Comparison of Disease-free survival in patient groups based on hormone receptors and HER2 status



	ER,PR+,Her2-	ER,PR+,Her2+	ER,PR-,Her2+	ER,PR-,Her2-
Mean disease free survival with CI	119.9±5.6months CI:(108.9-131.0)	102.2±7.6months (CI: 87.2-117.3)	98.9±7.1months (CI: 84.8-113.0)	89.3±5.1months (CI: 79.3-99.2)

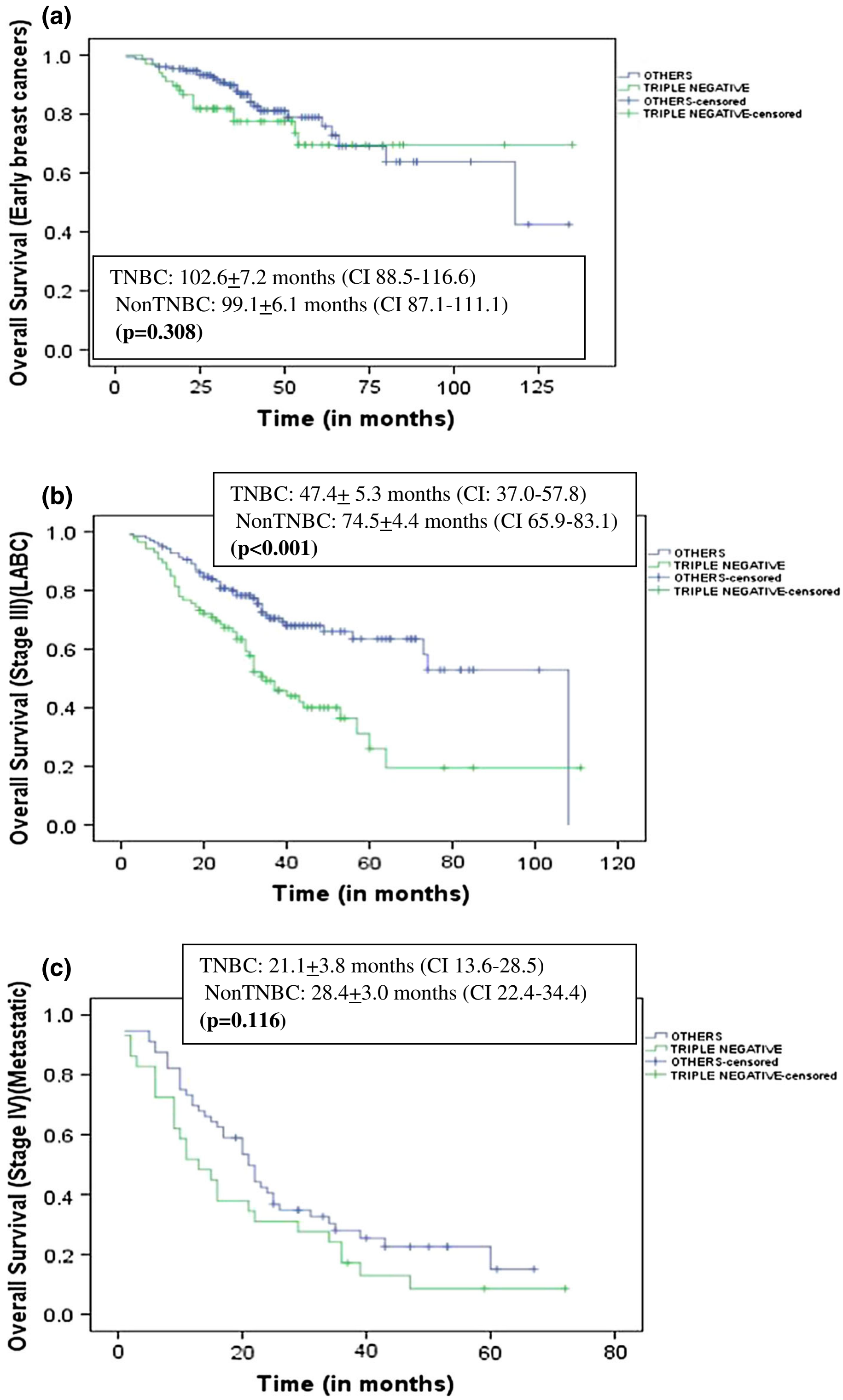
(Table 2) was predicted by age (< 50 c.w. >50 years age groups, $p = 0.036$), TNM stage at presentation ($p < 0.001$), pT stage ($p = 0.020$), pN stage ($p < 0.001$), histo-pathological grade ($p = 0.030$), and ER, PR, HER2 subtype (TNBC c.w. non-TNBC, $p < 0.001$). On multivariate analysis; age ($p = 0.036$), pN stage ($p < 0.001$), and ER, PR, HER2 subtyping, i.e., TNBC c.w. non-TNBC ($p = 0.005$) turned out to be important determinants of DFS. Thus, subtyping patients into TNBC and non-TNBC groups was an important determining factor for both OS and DFS.

Discussion

Breast cancer is a disease of biologically variable heterogeneous forms, with marked variation in the outcomes. Molecular classification of breast cancer by multi-gene expression studies using DNA microarrays provides robust prediction of outcomes and response to therapy. The commercially available assays for molecular classification are expensive, and beyond reach of most breast cancer patients, more so in countries with limited resources. Based on the IHC evaluation of ER, PR, and HER2 expression, breast cancer patients can be classified, which is relatively easy, and useful in clinical practice. The IHC classification of patients has been shown to correlate well with intrinsic classification using gene expression microarrays: ER/PR+, HER2+ with Luminal B; ER/PR+, HER2− with Luminal A; ER/PR−, HER2+ (ER−/HER2+); and ER/PR−, HER2− with triple-negative/basal-like tumors [5, 14]. TNBC has emerged as a group of breast cancer patients with unique therapeutic challenges and worst outcomes, and forms an important area of research interest.

In this retrospective study, perhaps the largest one on Indian TNBC patients treated and followed-up for intermediate to long term at a tertiary care breast center in north India, TNBC constituted 35.3 % of the whole study cohort of breast cancer patients. Previous Indian studies have documented that rates of ER negativity is higher among Indian breast cancer women [10–13]. It has been suggested that besides technical faults in detection of ER, factors contributing to high ER negativity could be younger age of patients, advanced stage at presentation, and higher grade tumors [11]. In an Indian study that compared Indian patients with those from SEER database, the ER negativity rates of Indian patients was found to be higher across all age groups, perhaps due to advanced stage of breast cancer presentation [12]. Our study found higher incidence of TNBC in younger, pre-menopausal women, which corroborates findings in other studies [14, 15]. Unlike other studies which suggest TNBC to present in more advanced stages [16], we found comparable stages at presentation in the TNBC and non-TNBC groups, which can be attributed to the late presentation of breast cancer in general in India [8, 9]. Overall, around

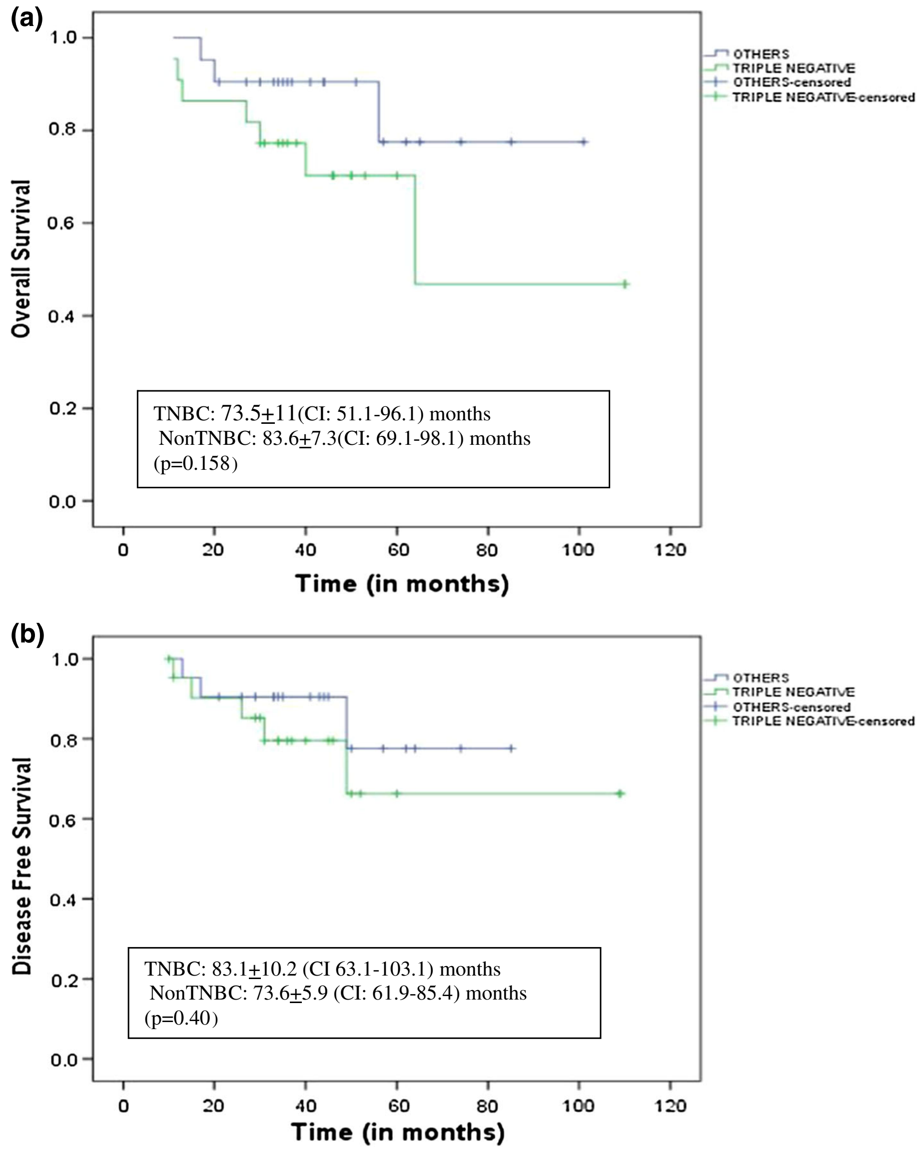
Fig. 4 Comparison of Overall survival in TNBC and non-TNBC patients: **a** Stage I and II patients, **b** stage III patients, **c** Stage IV patients



50–55 % of our patients present as LABC or metastatic breast cancers.

The mean clinical tumor size of TNBC patients (5.7 cm) in our study was similar to that in non-TNBC patients (5.4 cm). However, higher proportion of TNBC patients had clinically enlarged lymph nodes, perhaps due to large tumor size and late stage at presentation, similar to what has been reported by others [9], though some others, wherein the mean tumor size varied from 1.8 to 2.2 cm, have reported lesser incidence of nodal involvement in

Fig. 5 Comparison between TNBC and non-TNBC patients with pathological complete response to neo-adjuvant chemotherapy: **a** overall survival, **b** disease-free survival



TNBC [7]. The predominant histopathology seen in both subtypes was IDC in our study. We found large number of TNBC patients (96 %) presenting with higher tumor grades, i.e., grade II, III similar to other studies [17] which have reported more aggressive histological features such as higher grades, pushing margins, and marked apoptosis in TNBC. The incidence of LVI was also higher in TNBC in our experience, but there was no difference in margin positivity status or peri-nodal spread between subtypes.

Patients in TNBC and non-TNBC groups were offered similar surgical treatment, and around 20 % of the patients underwent BCS. Majority of the patients were treated with anthracycline-based combination adjuvant or neo-adjuvant CTx. Starting 2005, taxanes in combination with anthracyclines—either sequentially or concomitantly are being uniformly administered to TNBC patients. In the patient cohort treated with NACT, 37 % of TNBC patients had cCR and 27 % had pCR, which is comparable to other studies [5]. The OS and DFS of TNBC patients were found to be poorer, as compared to non-TNBC subtypes. On subgroup analysis, we found the highest OS and DFS in luminal subtypes followed by TNBC and HER2 enriched types, which corresponds with findings of most of other studies [14, 15].

On a subgroup analysis to evaluate the stage-wise OS and DFS, the survival rates between TNBC and non-TNBC groups were not found significantly different for stages I, II, and IV. In the stage III patients, the OS and DFS were significantly poorer in the TNBC group as compared to non-TNBC group. These findings suggest that the tumor

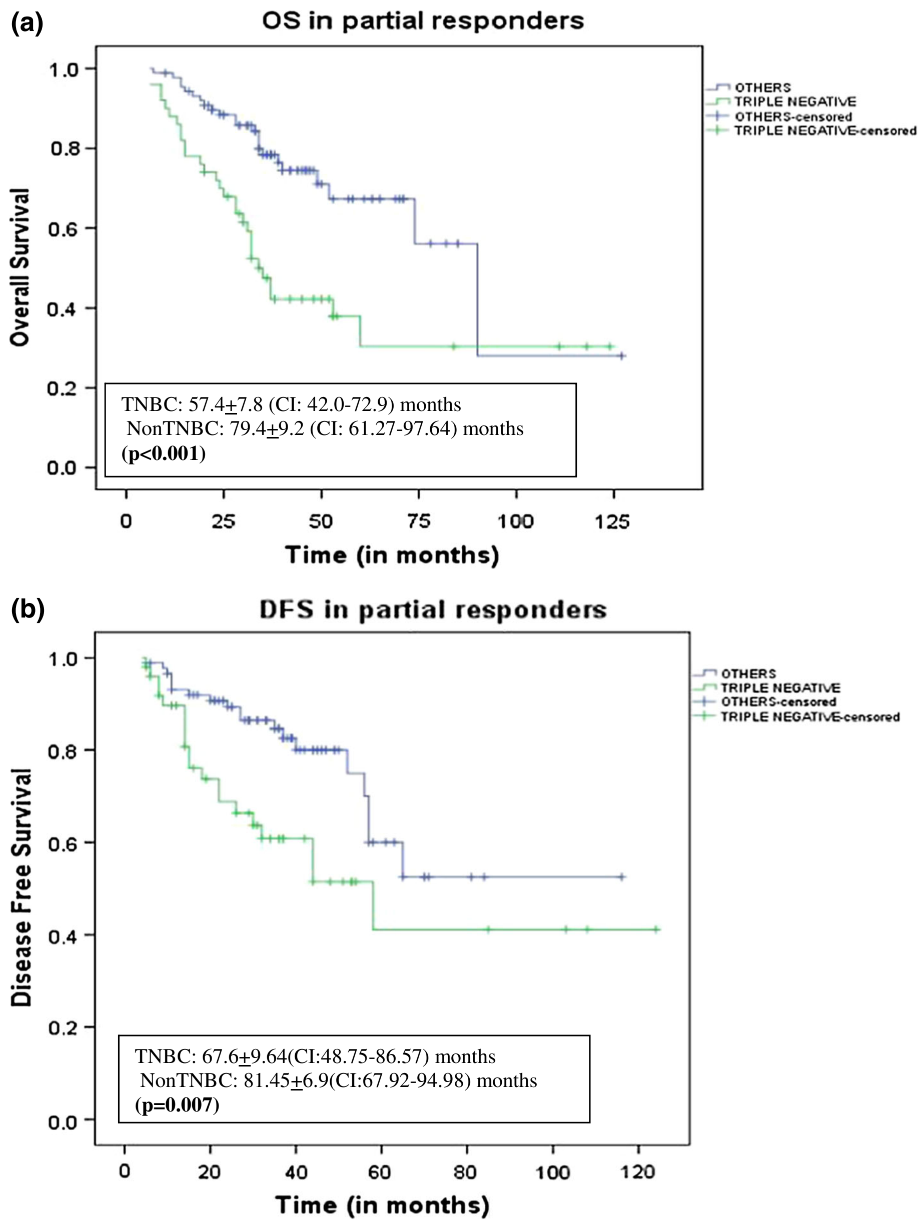


Fig. 6 Comparison between TNBC and non-TNBC patients with partial response to neo-adjuvant chemotherapy: **a** overall survival, **b** disease-free survival

biology plays a major role in patients with substantial disease burden as is the case in stage III. In patients with limited/early disease (stage I and II) or those with systemic metastases, the outcomes are impacted to lesser extent by the hormone receptor and HER2 status of the tumors. It must also be pointed out that the relatively small patient numbers in the EBC (stage I and II) and MBC (stage IV) groups might have had some bearing on the lack of significant difference in outcomes of TNBC c.w. non-TNBC patients in these subgroups. A few other studies have compared the stage-wise outcomes between various subtypes. One such study reported comparable survival rates between tumor subtypes when compared stage wise [7]. Another study reported that the survival is worse for stage II and III TNBC [18], while yet another commented that tumor biology is more important determinant of survival than tumor stage [19]. Most other studies reporting the relative outcomes of TNBC and non-TNBC have mostly included stage I and II patients, with stage III patients constituting 10–22 % of all cases. In contrast, in our study 39–48 % patients in various subtypes were stage III. Our results bring into focus the problems of breast cancer management faced in majority of low- and middle-income countries. Majority of reports in literature comparing TNBC with non-TNBC come from centers in developed nations, which focus on the early-stage disease—which make the bulk of their patients. The high proportion of LABC in our study, compared to other studies in any set-up and documentation of a significant survival difference between TNBC and non-TNBC groups in stage III patients alone are somewhat unique findings of our study.

Response to CTx plays a major role in determining the survival in breast cancer patients, more so in TNBC patients as these patients lack any targets (ER, PR, HER2) that can be treated. Patients presenting with stage III disease are candidates for NACT, and patients who achieve pCR following NACT are believed to have better OS [20], though this belief is contested by certain other studies which report no significant OS benefit in such patients. It is also widely acknowledged that higher proportion of TNBC patients can achieve pCR with NACT, as compared to non-TNBC patients, as was observed in our study too. Yet, pCR to NACT is achieved only in a small proportion of the patients, and hence the difference in OS between the TNBC and non-TNBC groups could be attributed to a large fraction of partial and poor responders where the survival varies despite NACT. TNBC/basal-like breast cancers respond better to taxane-based CTx compared to other subtypes [21]. In our study conducted on patients treated between 2004 and 2010, about 30 % patients only received taxanes containing combination CTx, though currently, taxanes administered sequentially after anthracyclines is the standard practice in our center. We found that TNBC patients who attained pCR following NACT had comparable DFS and OS to non-TNBC patients, while TNBC patients with partial response to NACT had worse survival compared to non-TNBC partial responders. These observations are consistent with other studies [5, 22].

The basal-like breast cancers or TNBC are characterized by the high expression of the proliferation cluster of genes [23] and other conventional indices of proliferation, which is also reflected in our study with higher grade tumors in TNBC group. A prognostic index that is highly influenced by proliferation genes was shown to predict pCR to doxorubicin/taxane-based CTx [24]. The paradox of higher sensitivity to NACT with anthracyclines in subtypes known to have a poor prognosis is explained by the high relapse among those with residual disease. Our study confirms the well-known TNBC paradox of higher response to CTx, resulting in higher pCR rates to NACT, yet poorer outcomes and survival compared to the ER/PR and/or HER2 expressing breast cancers. The worse outcomes in the TNBC patients may be driven by the higher relapse rates among the partial or poor responder TNBC patients, when compared to non-TNBC patients.

On univariate analysis, our results suggested the tumor stage, tumor size, nodal status, histological grade of the tumor, and the TNBC c.w. non-TNBC classification are factors that predict the OS. However, on a multivariate analysis, only the tumor stage at presentation, size, and histological grade were found to important determinants affecting OS; while the age, nodal status, and TNBC c.w. non-TNBC classification were found to be important factors affecting DFS. Other studies have reported varying determinants of the DFS and OS [25, 26], but a distinction between TNBC and non-TNBC subtypes has remained a strong determining factor for both OS and DFS, similar to our finding.

The limitations of a hospital-based retrospective study from a developing country are reflected in our study. Firstly, almost one-third of breast patients treated during the study period had to be excluded because of the lack of complete clinical, pathologic, and follow-up information. Further, this was a study spanning almost a 11-year period wherein patients treated over a 7-year period, with a rather modest duration of follow-up (median 36 months) were included. During this time period, the practices and protocols of breast cancer have evolved. Such changes include a change from anthracyclines containing combination regimen to combination of taxanes with anthracyclines as standard of care CTx for most breast cancer patients in the last few years of our study. As a result, only about a third of our patients received taxanes. Yet, as the CTx regimen used were the same for the TNBC and non-TNBC patient groups, this should not confound our primary findings. Another limitation is that HER2 evaluation by FISH was done only in selected patients with borderline HER2+ results on IHC due to the financial constraints. This might mean that we may have overestimated the TNBC and HER2 negative cases to a small extent.

In conclusion, this retrospective study comparing the TNBC and non-TNBC patients showed the triple-negative subtype (ER−/PR−, HER2−) patients are younger, have similar clinical presentations, poorer histo-pathological features, and worse overall and disease-free survival compared to the ER/PR and/or HER2 expressing subtypes. The survival varies by the stage at presentation, with significant difference in survival between stage III TNBC c.w. non-TNBC patients. The stage III TNBC patients who achieve pCR with NACT have similar survival rates as non-TNBC patients with pCR to NACT, while survival in partial or non-responder stage III TNBC patients is worse compared to partial or non-responder stage III non-TNBC patients. Stage I/II as well as stage IV TNBC patients did not have significantly worse survival compared to same stage non-TNBC patients.

Acknowledgments The authors are grateful to faculty and resident doctors of the Departments of Endocrine and Breast surgery; Radiation oncology; and Pathology at SGPGIMS Lucknow for their help with data retrieval and analysis, and with review of clinical and pathology data and material.

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Selected International Articles

Leading article

Coming of age of oncoplastic breast surgery

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Published online 5 July 2017 in Wiley Online Library (www.bjs.co.uk). **DOI:** 10.1002/bjs.10579

Breast surgery has emerged as a defined specialty across European and other countries over the past 25 years. Specialization has been driven by a rising incidence of breast cancer, the development of oncoplastic breast surgery techniques, and enhanced patient expectations in terms of treatment and outcomes. The modern specialized breast surgeon must acquire a spectrum of expertise covering oncology, radiology, breast surgery and an understanding of relevant principles and practice of plastic surgery. In addition, they must also possess excellent team working, communication and clinical decision-making skills.

Increasing use of neoadjuvant therapy to downstage locally advanced disease has permitted more successful rates of breast-conserving surgery (BCS). A progressive decrease in the proportion of patients requiring mastectomy in favour of BCS has coincided with increased demand for either immediate or delayed breast reconstruction together with the evolution of oncoplastic procedures. The latter involve utilization of surgical techniques developed by plastic surgeons for cosmetic reshaping of the breast, subsequently applied by breast surgeons in an oncological context for more extensive resections in BCS.

Surgical treatment must, on the one hand, maximize the chance of negative resection margins, thereby reducing the risk of local recurrence, but on the other hand achieve good cosmetic results. There is an innate conflict between the basic aims of oncological and plastic surgery: eradication of locoregional disease while preserving residual breast tissue for optimal cosmesis. The challenge of oncoplastic breast surgery is to reconcile oncological and aesthetic aims to optimize patient outcomes.

Oncoplastic breast surgery aims to retain or enhance the natural appearance of the breast following excision of a cancer. Techniques such as fat transfer can be employed to correct minor defects consequent to surgery and/or radiotherapy, but prevention of breast deformity is preferable to its treatment. Early concerns were raised that oncological outcomes might be compromised in attempts to minimize the volume of tissue resected for cosmetic purposes. There is no evidence, however, that oncoplastic breast conservation techniques are less likely to achieve negative resection margins, or to be associated with increased rates of re-excision[1,2]. On the contrary, owing to the greater volume of tissue removed with oncoplastic procedures, tumours can be excised with a high chance of clear resection margins at initial surgery[3]. A negative margin does not always indicate the absence of residual disease within remaining breast tissue, but implies a residual burden of tumour sufficiently low to be controlled with adjuvant treatments such as radiotherapy and chemotherapy/hormone regimens. Local recurrence is thus determined by a combination of surgery, tumour biology, radiation and systemic therapies[4]. An overall reduction in breast volume from 'displacement' techniques may also facilitate delivery of radiotherapy by optimizing breast positioning and reducing dose inhomogeneity.

Nonetheless, unresolved controversies remain for oncoplastic breast conservation, including identification of a positive resection margin following glandular mobilization, accurate targeting of the tumour bed for a radiotherapy boost[5], the upper size limit for safe breast conservation[6], and sequencing of radiotherapy with two-stage flap-based partial breast reconstruction.

Skin-sparing techniques have been widely adopted to improve cosmetic outcomes following reconstruction and are now acknowledged to be safe in terms of disease recurrence, provided tumours are non-inflammatory and there is no direct skin infiltration[7]. A further development of the skin-sparing approach is nipple-sparing mastectomy, which can further enhance aesthetic outcomes. However, preservation of the nipple–areola complex (NAC) is of unproven safety, and should be practised selectively only for small unifocal tumours located some distance from the NAC or as a prophylactic procedure[8]. The areola can readily be dissected off the underlying parenchyma without leaving remnant breast tissue, although a thin layer of breast tissue must be retained to ensure viability of the nipple.

Breast surgery is a rapidly evolving specialty with frequent exposure to novel devices and techniques. In particular, some of the newer implantable devices for breast reconstruction are released on to the market with limited clinical and scientific evaluation. The introduction of acellular dermal matrices and synthetic meshes for implant-based reconstruction have significantly broadened indications for breast reconstruction and promoted uptake. However, despite persistence of surgical enthusiasm, some devices have been officially withdrawn from clinical use owing to the emergence of safety issues. Thus, a judicious approach to the adoption of newer technologies outside the setting of clinical trials should be exercised. When trialling new devices, it is imperative to maintain a comprehensive database to permit subsequent analysis of selection criteria, complications and outcome measures. Local registries can be interlinked and form part of a national, or even global, registry.

Guidelines published by the Association of Breast Surgery in the UK for best oncoplastic practice detail key quality criteria recommendations that cover all aspects of oncoplastic breast surgery[9]. These include preoperative planning, postoperative care, complication rates, training and education, and patient satisfaction outcomes. All specialist breast surgeons should maintain personal records of procedures undertaken, including complication rates, oncological outcome data and patient satisfaction using validated tools. In addition to quality assurance, these surgeon-specific outcome data inform the consent process and aid patients in making decisions when more than one surgical option is available.

Breast surgery continues to evolve apace, and surgeons must ensure their knowledge and skills base is updated regularly. Several well established oncoplastic meetings and workshops exist that provide information on the latest and best practices[10,11]. Surgeons can further refine their practical repertoire by attending master classes in oncoplastic breast surgery, such as those under the aegis of the European Society of Surgical Oncology[12], or by visiting other institutions to gain valuable hands-on experience in new techniques. Current development of models for surgical simulation will facilitate training in more complex oncoplastic techniques. Levels of professional attainment in terms of knowledge and skills can be assessed with dedicated breast surgery examinations such as the European Board of Surgery Qualification examination[13] and the master's degree course in oncoplastic breast surgery[14], which provide a specialty-specific qualification and accreditation.

Patients are increasingly well informed about treatment options; widespread use of social media and the existence of online patient blogs and communities have led to heightened patient expectations regarding outcomes. The surgeon should be aware of unrealistic expectations and direct patients to authorized websites to gain accurate and balanced information. In addition, several tools are now available to aid patient decision-making, including three-dimensional breast simulation tools to provide a visual approximation of postoperative aesthetic outcomes.

Patients are now surviving longer owing to advances in breast cancer treatment, and expectations have increased accordingly. Improved survivorship has implications for health-related quality of life, and healthcare workers must strive collectively to ensure optimal oncological, cosmetic, functional and psychosocial outcomes. Surgeons must balance the needs of patients in each of these domains and be prepared constantly to face new challenges. The number of elderly patients with breast cancer is increasing, and oncoplastic surgery should be available to those who are otherwise fit despite their chronological age[15]. Women who have undergone oncoplastic breast conservation or whole breast reconstruction may require further surgical intervention for late complications or to enhance breast aesthetics. Budgetary restraint can be aided by sensible planning of initial breast cancer treatment that maximizes oncological and cosmetic outcomes and minimizes the need for corrective surgery at a future date.

Disclosure

The authors declare no conflict of interest.

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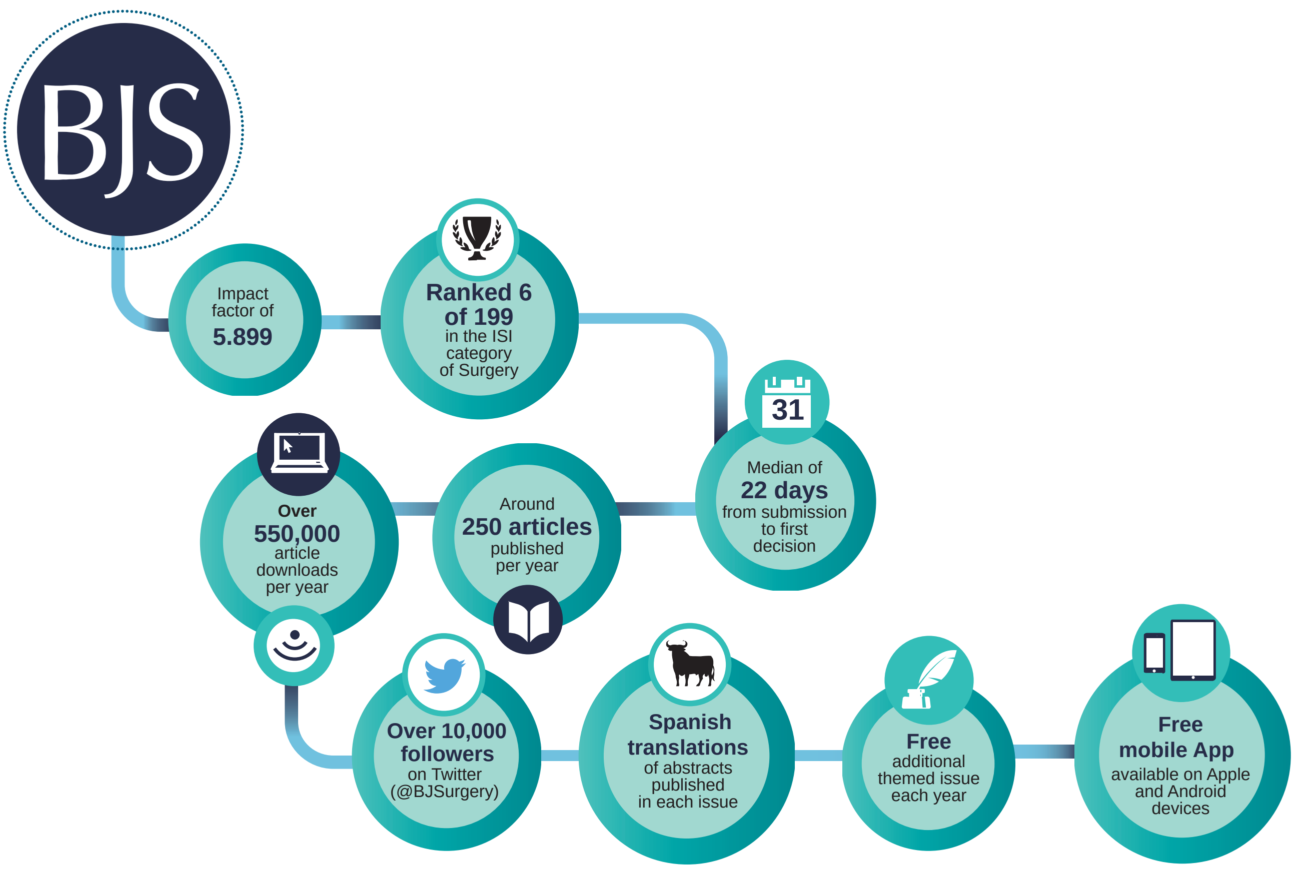

LEADING ARTICLE

Ann R Coll Surg Engl 2013; **95**: 161–162
doi 10.1308/003588413X13511609957696

Guidelines for oncoplastic breast reconstruction

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KEYWORDS
Breast cancer – Breast reconstruction – Oncoplastic surgery

Accepted 21 September 2012

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Breast reconstruction and oncoplastic techniques have been widely adopted in the surgical management of patients with breast cancer. The National Mastectomy and Breast Reconstruction Audit (NMBRA)[1] is the largest prospective audit of breast reconstruction ever carried out. It was designed and implemented by the Clinical Effectiveness Unit at The Royal College of Surgeons of England with input from the Association of Breast Surgery (ABS), the British Association of Plastic, Reconstructive and Aesthetic Surgeons (BAPRAS), and the Royal College of Nursing. The NMBRA examined a broad range of clinical and patient reported outcomes in more than 18,000 women. Factors examined included patient information and access to reconstructive services as well as the level of pain, complications, quality of life and wellbeing after surgery.

The patient reported outcomes in the NMBRA highlight the positive effects of breast reconstruction on quality of life and the very high levels of satisfaction with the clinical care provided. The audit did, however, find complication rates, levels of postoperative pain and readmission rates that were much higher than expected. There were also variations in preoperative provision of information, access to services and some clinical outcomes.

The original ABS guidelines[2] predated the NMBRA. One of the key recommendations of the audit was that new guidance should be written that describes 'best practice' and sets current standards of care. Following this, a multidisciplinary writing group of specialists with expertise in the management of patients undergoing oncoplastic procedures was set up by the ABS and BAPRAS to develop comprehensive new guidelines: *Oncoplastic Breast Reconstruction: Guidelines for Best Practice*.[3] A patient representative was involved throughout as a core member of the group. Feedback from a wide range of stakeholders has been incorporated into the document, which enjoys the support of Professor Sir Mike Richards, the National Cancer Director. The guidelines are available on the ABS and BAPRAS websites.

The NMBRA identified more than 80 unique metrics, reflecting previously undisclosed standards of care. These provided a benchmark for the selection and development of 25 new quality criteria, which form the backbone of the new guidelines (Table 1). The quality criteria were selected to be outcome based, measurable and clinically relevant. They set standards that can be used for future audits, within individual units or nationally.

Since oncoplastic breast surgery is a developing area of clinical practice with a limited evidence base, the guidance reflects a combination of peer opinion and the best available evidence informed by peer reviewed publications. External advice was commissioned on pain management from

Table 1 Example quality criteria

Quality criterion:	Local recurrence rates following oncoplastic breast surgery should be no higher than for breast cancer surgery as a whole
Target:	Local recurrence rates are less than 3% at 5 years
Quality criterion:	Implant loss at 3 months following breast reconstruction is assessed and audited
NMBRA outcome:	Of women having an implant, 9% of immediate breast reconstruction patients and 7% of delayed breast reconstruction patients reported implant loss
Target:	Complications leading to implant loss occur in less than 5% of cases at 3 months

the Royal College of Anaesthetists, and on infection control from the Healthcare Infection Society and the British Society for Antimicrobial Chemotherapy. A wide range of stakeholders with an interest in this area of clinical practice provided comments on the draft document. The guidelines are not designed to be prescriptive or legally binding but should be used to inform decision making when developing a patient management plan. They are designed to complement existing guidelines, including the ABS' *Surgical Guidelines for the Management of Breast Cancer*.[4] Ultimately, members of the multidisciplinary team remain responsible for the treatment of patients under their care.

There are four key sections in the new guidelines: the outpatient phase, the inpatient phase, clinical requirements and training requirements. The outpatient phase includes referral, assessment, information and decision making. The inpatient phase includes preoperative, intraoperative, postoperative and peridischarge periods. The clinical requirements section defines the essential components of an oncoplastic multidisciplinary team, and the caseload, casemix and staffing levels required to support an oncoplastic unit or an oncoplastic centre. The final section considers training requirements for those with a background in general surgery or plastic surgery and additional oportunities that should be available for professional development.

The guidelines contain comprehensive guidance regarding the variety and type of information that must be provided for patients to inform and support decision making about breast reconstruction. There is also important new guidance on infection control to tackle the worryingly high rates of infection and implant loss reported in the audit. Advice includes screening for methithicillin sensitive *Staphylococcus aureus* as well as for methicillin resistant *S aureus* in high risk patients (which includes patients undergoing implant-based procedures). Furthermore, there is new guidance on the use of laminar flow facilities, alcoholic skin preparation, and double glove and minimal touch techniques. For postoperative management, monitoring charts have been recommended which include a visual analogue scale for pain, a nausea scale, flap and patient monitoring, venous thromboembolism management and physiotherapy input. There is also new advice on preventing pain with multimodal analgesia including paravertebral, intrapleural, infusional and non-steroidal analgesia.

A patient version of the guidelines has been developed in collaboration with Breast Cancer Care and with the input of patient representatives. This aims to inform patients, in an accessible format and lay language, about the care and support they can expect to receive when considering or undergoing breast reconstruction.

Oncoplastic Breast Reconstruction: Guidelines for Best Practice aims to provide all members of the breast multidisciplinary team with guidance on best oncological and oncoplastic practice at each stage of a patient's journey, based on best current evidence. These guidelines reflect the findings of the NMBRA and are designed to provide quality and target standards against which care can be measured and audited, leading to improvements in clinical outcomes and patient experience. It is hoped these guidelines will also benefit professionals and service commissioners in this increasingly sophisticated area of clinical practice.

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Breast Cancer - Targets and Therapy

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ORIGINAL RESEARCH

Improved immediate breast reconstruction as a result of oncoplastic multidisciplinary meeting

This article was published in the following Dove Press journal:
Breast Cancer - Targets and Therapy
28 April 2017

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Introduction: The National Institute for Health and Clinical Excellence guidelines recommend that breast reconstruction should be available to all women undergoing mastectomy and discussed at the initial surgical consultation (2002, and updated 2009). The National Mastectomy and Breast Reconstruction Audit (2009) showed that 21% of mastectomy patients underwent immediate breast reconstruction (IBR) and 11% had delayed breast reconstruction (DBR). Breast reconstruction has been shown to have a positive effect on quality of life postmastectomy. This retrospective study investigated the impact of the introduction of a dedicated oncoplastic multidisciplinary meeting (OP MDM) on our unit's breast reconstruction rate.

Patients and methods: A retrospective analysis of 229 women who underwent mastectomy, of whom 81 (35%) underwent breast reconstruction between April 2014 and March 2016. Data were analyzed before and after introduction of OP MDM in April 2015. Data on patient age, type of surgery (mastectomy only, mastectomy and reconstruction), timing of reconstruction (IBR, DBR), and type of reconstruction (implant, autologous) were collected.

Results: Between April 2015 and March 2016, following establishment of OP multidisciplinary team in April 2015, of the 120 patients who had mastectomy, 50 (42%) underwent breast reconstruction with 78% (39/50) choosing IBR (56% implant reconstruction and 22% autologous). Compared to the period between April 2014 and March 2015 preceding the OP MDM, of 109 patients who underwent mastectomy, only 31 (28%) had breast reconstruction with 64% (20/31) choosing IBR (45% implant reconstruction and 19% autologous). The rate of DBR was lower, 22% (11/50), following OP MDM compared to 35% (11/31) before OP MDM.

Conclusion: There has been an increased uptake of breast reconstruction surgery from 28% to 42%. The biggest impact was on those opting for the immediate type reconstruction option (78%). The OP MDM has significantly contributed to this increased rate of reconstruction.

Keywords: breast cancer, delayed reconstruction, uptake rate, mastectomy

Introduction

The National Institute for Health and Clinical Excellence guidelines recommend that reconstruction should be available to all women undergoing mastectomy and should be discussed at the initial surgical consultation.[1] In the UK, the National Mastectomy and Breast Reconstruction Audit (NMBRA) showed that in 2009, 21% of mastectomy patients underwent immediate reconstruction with an additional 11% having delayed reconstruction.[2] Breast reconstruction has been shown to have a positive effect on quality of life postmastectomy.[3] Breast reconstruction rates vary widely across the UK, but overall remain low with only 16.9% of women undergoing

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immediate or delayed reconstruction (range 4.9%–81.2%, median 23.3%).[4] Rates of reconstruction could be increased with early discussion of the options when mastectomy is chosen or required.[4] Multidisciplinary team (MDT) working is considered as the "gold standard" in terms of cancer patient management. MDTs have also been shown to deliver a number of improvements in the quality of care and patient outcomes.[5–7] The oncoplastic multidisciplinary meeting (OP MDM) should be the central component of the oncoplastic services for National Health Service (NHS) and private patients. It should provide balanced information and advice about reconstruction, as well as the timing and types of appropriate procedures.[8] All cases for reconstruction should be discussed by the members of the OP MDM team during a weekly meeting. This is not currently practiced by some centers offering reconstruction although their symptomatic and screen-detected cancers are discussed at the standard breast MDT.

The aim of this study is to assess the impact of the introduction of a dedicated OP MDT on the breast reconstruction rate in a single unit.

Patients and methods

A retrospective analysis of 819 patients diagnosed with breast cancer between April 2014 and March 2016 in our Unit. Two hundred twenty-nine women had mastectomy (27.9%), of whom 81 (35%) underwent reconstruction. Data analysis was made before and after introduction of OP MDM in April 2015. Electronic data were collected including surgical operating notes, clinical letters, and breast care nurses (BCNs) records. Data from Somerset Cancer Registry (SCR) of MDT and OP MDM decisions including data records of patient age, type of surgery (mastectomy only, mastectomy with reconstruction), timing of reconstruction (immediate breast reconstruction [IBR] or delayed breast reconstruction [DBR]), and type of reconstruction (implant, autologous) were collected. Fisher's exact test was used to compare the groups. Approval of Wexham and Heatherwood Hospitals Clinical Audit Lead and committee was granted before conducting this study. The Audits Committee waived the need for individual patient informed consent as this study is registered as a Clincal Audit project (register number CA720) and retrospective in nature. Patient confidentiality and data handling are in accordance with the Data Protection Act 1998 and General Medical Council guidelines.

Results

Between April 2015 and March 2016 (following establishment of OP MDT in April 2015), 120 patients had mastectomy, of whom 50 (42%) underwent breast reconstruction with 78% (39/50) choosing IBR (56% implant reconstruction and 22% autologous) (Tables 1 and 2). This is in contrast to the period between April 2014 and March 2015 preceding the OP MDM, when of 109 patients only 31 (28%) had breast reconstruction with 64% (20/31) choosing IBR (45% implant reconstruction and 19% autologous). The rate of DBR was lower, 22% (11/50), following introduction of the OP MDT versus 35% (11/31) before OP MDM (Tables 1 and 2). Bilateral mastectomy was performed in 27 patients (11 implant reconstruction, four autologous, and 12 mastectomy alone). The increased rate of reconstruction was statistically significant at the $P<0.05$ level ($P=0.0144$).

The mean time spent on discussion for patients in the OP MDM was 10 minutes compared to 2.5 minutes in the standard breast MDT.

Table 1 Mastectomy and reconstruction type

Operation type	April 2014–March 2015		April 2015–March 2016	
	Pre onco-plastic MDM		Post onco-plastic MDM	
	Number of patients (% of total mastectomy)	Mean age (range) in years	Number of patients (% of total mastectomy)	Mean age (range) in years
Total mastectomy	109	57 (34–87)	120	59 (31–95)
Mastectomy only	78 (71.5)	63 (34–87)	70 (58.3)	67 (37–95)
Mastectomy/REC	31 (28.4)	51.5 (35–75)	50 (41.6)	51.5 (31–71)
Implant IBR	14 (12.8)	56 (40–75)	28 (23.3)	53 (35–71)
Autologous IBR	6 (5.5)	48 (39–54)	11 (9.2)	48 (31–57)
Total IBR	20 (18.3)	52 (39–75)	39 (32.5)	50.5 (31–71)
Implant DBR	2 (1.8)	49 (47–51)	1 (0.8)	52*
Autologous DBR	9 (8.2)	53 (35–70)	10 (8.3)	53 (43–65)
Total DBR	11 (10.1)	51 (35–70)	11 (9.1)	52.5 (43–65)

Notes: $X^2=5.9825$, $P=0.0144$ (significant at $P<0.05$ level). *Only one patient in this group, mean age not used.
Abbreviations: DBR, delayed breast reconstruction; IBR, immediate breast reconstruction; MDM, multidisciplinary meeting; REC, reconstruction.

Table 2 Reconstruction types and reconstruction rates

Operation type	Pre oncoplastic MDM	Post oncoplastic MDM
	Reconstruction rate % total reconstruction =31 (number of patients)	Reconstruction rate % total reconstruction =50 (number of patients)
Total reconstruction rate	28 (31/109)	41.6 (50/120)
Implant IBR	45.1 (14)	56 (28)
Autologous IBR	19.3 (6)	22 (11)
Total IBR	64.5 (20)	78 (39)
Implant DBR	6.2 (2)	2 (1)
Autologous DBR	29 (9)	20 (10)
Total DBR	35 (11)	22 (11)

Abbreviations: DBR, delayed breast reconstruction; IBR, immediate breast reconstruction; MDM, multidisciplinary meeting.

Discussion

Our breast reconstruction rate (42%) was twice the national average rate reported by NMBRA in 2009. Following the introduction of OP MDT our IBR has risen to 32.5% from 18%. Implant-based reconstructions constituted 56% of all our IBRs with an autologous IBR of 22%. These results are in line with recent analysis of National Trends in Immediate and Delayed Post-Mastectomy Reconstruction procedures in England.[9] These showed that the annual number of reconstructions increased from 2182 in 2007 (14.9% immediate reconstruction rate) to 3753 in 2013 (24.7% immediate reconstruction rate). The dominant trend in procedure type was related to implant/expander-based reconstructions, which rose from 30% of all immediate reconstruction in 2007 to 54% in 2013, and the use of free flap procedures increased marginally, the proportion rising from 17% to 21%.[9] There is still substantial regional variation in IBR rate across the English regions ranging from 13.1% to 36.7%.[10]

In our study, there was no significant difference in the cohort of mastectomy patients between 2015 and 2016 apart from the introduction of a dedicated OP MDM. We recognize that several complex factors are associated with uptake of breast reconstruction following mastectomy (age, ethnicity, income, education, tumor characteristics, health-related issues, surgeon/hospital factors, and psychological or other factors).[4,11–16] We are also aware that other factors may have contributed to this increased rate of uptake, including an increased trend in breast reconstruction nationally[9] and possible local logistical aspects (improved process in booking surgery, theater availability, and streamlined referral to plastic team); however, we believe that the introduction of the OP MDT was the key factor in this process and the comparative data in this study (Table 1) supports this assumption.

Due to the complexity of breast reconstruction surgery and the wide variety of options available, more specialist time is needed to deliver a tailored reconstruction service that meets patients' expectations. Recently, Cancer Research Campaign UK[17] concluded that there is no enough time to discuss the more complex patient during MDTs. They found that over half of the MDT discussions were less than 2 minutes long, and because of the numbers discussed, meetings could last up to 5 hours.[17] We analyzed the timing of our MDTs. Our OP MDM discussion was an average of 10 minutes per patient discussed compared to 2.5 minutes to standard MDT. To make the best use of scarce specialist time, MDT discussions should focus more on difficult cases, and processes should be put in place to enable swifter decisions on patients going through standard treatment pathways.[18]

The current standard stipulates a maximum of 31 days from decision to treat to first treatment offered to breast cancer patients.[19] We suggest that at the first week of their breast cancer diagnosis, patients who need mastectomy and are suitable for reconstruction are identified and triaged to the dedicated weekly OP MDM. Patients are seen by their breast surgeon with the BCNs for their initial results following the standard breast MDT where they are offered breast reconstruction information, options, and their initial preference explored. Preoperative photos are taken and shown in the OP MDM held the following week. In addition to oncoplastic surgeons and BCNs, plastic surgeons (with an expertise in microvascular breast reconstruction) constitute the core membership of this smaller, more specialized OP MDM. We run our weekly OP MDM immediately prior to our standard breast MDT and we allocate 10–15-minute discussion per patient compared to the standard breast MDT when patients are discussed in 2–3 minutes. OP MDM decisions are recorded electronically on SCR[20] and a hard copy is filed into the patients' file so that these decisions can be shared between the wider standard MDT members. Following the OP MDM, patients are seen again with clear recommendations and offered the best options for their reconstruction according to their tumor biology and their own expectation. Prebooked appointments are available for patients to be seen by the plastic surgeon in the same week if they are considering autologous-type reconstruction. Dedicated combined operating theater lists are available for their immediate reconstructive surgery, thus avoiding any breach of the NHS 31-day target. OP MDM allows transparent decision making, standardization of care, and prospective recording of results.[21]

Our study is unique in providing an evidence-based improvement in breast reconstruction rate following the implementation of OP MDM intervention. This has led to offering more reconstructive options to our patients and streamlining their pathway with allocated current resources achieving their tailored reconstructive surgery within strict deadline targets. We recognize that the increased uptake of reconstruction seen in our study might be coincidental, and that causality, although inferred, is unproven.

Conclusion

Our study has shown the positive impact of OP MDM in achieving a breast reconstruction rate of 42% (twice as the national average rate). Seventy-eight percent of women chose to have immediate-type reconstruction following their mastectomy, with 56% being implant-based reconstruction and 22% autologous-type reconstruction. We recommend that all units providing breast reconstruction should establish a standalone OP MDM to facilitate best patient care.

Acknowledgments

This study has been accepted as a poster presentation at the Association of Breast Surgery ABS Annual Conference, 15–16th May, 2017, Belfast, UK.

We wish to thank our Audit and IT department for their help in data collection with special thanks to our OP MDM Co-ordinator Julie Booth for her assistance in retrieval of reconstruction data from SCR.

Disclosure

The authors report no conflicts of interest in this work.

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Long-term Results After Oncoplastic Surgery for Breast Cancer

A 10-year Follow-up

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Objective: The aim of this study was to evaluate the long-term oncologic outcome after oncoplastic surgery (OPS).

Background: OPS combines wide tumor excision with reduction mammoplasty techniques thus extending breast conserving surgery to large tumors that might else be proposed a mastectomy. Little data are available about the oncologic results for breast conserving surgery of these larger tumors.

Methods: From January 2004 until March 2016, a total of 350 oncoplastic breast reductions were prospectively entered into a database. Patients were included if their breast reshaping included a reduction mammoplasty with skin excision (Level 2 oncoplastic techniques).

Results: Histologic subtypes were: invasive ductal carcinoma in 219 cases (62.6%), ductal carcinoma in situ (DCIS) in 88 cases (25.1%), and invasive lobular carcinoma in 43 (12.3%) cases. Seventy-three of the invasive cancers (27.9%) received neoadjuvant chemotherapy. The mean resection weight was 177 grams. The mean pathological tumor size was 26 mm (range 0–180 mm) and varied from 23 mm (4–180 mm) for invasive cancers to 32 mm (0–100 mm) for DCIS. Specimen margins were involved in 12.6% of the cases; 10.5% of invasive ductal, 14.7% of DCIS, and 20.9% of invasive lobular. The overall breast conservation rate was 92% and varied from 87.4% for DCIS to 93.5% for the invasive cancers. Thirty-one patients (8.9%) developed one or more postoperative complications, inducing a delay in postoperative treatments in 4.6% of patients. The median follow up was 55 months. The cumulative 5-year incidences for local, regional, and distant recurrences were 2.2%, 1.1%, and 12.4%, respectively.

Conclusions: Oncoplastic breast reductions allow wide resections with free margins and can be used for large cancers as an alternative to mastectomy.

Keywords: breast cancer, breast conserving surgery, complications, local recurrence, oncoplastic surgery, survival, therapeutic mammoplasty, treatment delay

(*Ann Surg* 2017;xx:xxx–xxx)

Breast-conserving surgery (BCS) followed by radiotherapy has become the standard of care in the treatment of early-stage breast cancer as the disease-free and overall survival were shown to be equivalent to mastectomy in multiple prospective randomized trials.[1–6] In 3 landmark randomized studies, the 5-year local recurrence rate after BCS varied from 0.5% to 12%.[2,4,5] Recent prospective randomized trials have reported ipsilateral breast tumor recurrence (IBTR) rates as low as 1.5% at 5 years after BCS and radiotherapy.[7,8] Bosma et al[9] showed in their large retrospective analysis of more than 8000 patients that the cumulative 5-year IBTR incidence was 2%. These low local recurrence rates with equivalent survival of mastectomy support the use of breast conservation as the routine approach for small breast cancers. However, for larger tumors, breast-conserving surgery can become technically more challenging for surgeons and a mastectomy is often proposed. Another option is induction medical treatment to downsize the tumor followed by a mastectomy if tumor response is not satisfactory.

Oncoplastic surgery (OPS) has recently gained a lot of interest in the breast surgical literature, as it allows extensive resections with immediate breast reshaping by mammoplasty. OPS thus extends breast conservation possibilities to larger tumors that would otherwise be destined for mastectomy.

Several OPS techniques and classifications can be found in the literature. In 2010, we published a 'quadrant per quadrant atlas' based on a 2-level classification of oncoplastic techniques.[10] Among the level I OPS techniques are the simple advancement or rotation glandular flaps that allow correction of small volumetric defects (less than 15%–20% of the breast volume) to reshape the breast. Level II OPS is based on mammoplasty techniques and involves larger resections (more than 15% of the breast volume) and skin excision. This atlas advocates a specific mammoplasty technique per tumor location, thereby offering a simple and reproducible surgical solution for all clinical scenarios.

Level 2 reduction mammoplasties enable large volume resections with a good cosmetic outcome and the possibility to preserve the patient's breast despite large tumor size. However, little data are available about oncologic results for breast conserving surgery of these large tumors. Short- and intermediate-term (up to 4.5 years) follow-up results are good with reported local recurrence rates between 0% and 4%,[11–16] although some higher local recurrence rates (6.8%–14.6%) have also been reported,[17–20] especially in patients with larger tumors.[17,19] The goal of this study was therefore to evaluate oncological long-term outcome after level 2 oncoplastic mammoplasties for large cancers.

MATERIALS AND METHODS

From January 2004 until March 2016, 350 consecutive oncoplastic level 2 mammoplasties were performed at the Paris Breast Center and prospectively entered into a database. Patients were included if they presented with a carcinoma of the breast (invasive or intraductal), if the resection weight was at least 50 grams and if the breast reshaping included a reduction mammoplasty, uni-, or bilateral.

Patient and Tumor Characteristics

The following patient and tumor characteristics were recorded: patient age, breast size (bra cup size), clinical and radiological tumor size, neoadjuvant systemic therapy, date of surgery, indication for an oncoplastic reduction, the type of mammoplasty technique, the resection weight- and volume, contralateral reduction (immediate or delayed) and technique, pathological tumor size and

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Disclosure: This work was supported by the Dutch Cancer Society Clinical KWF Fellowship (Raquel F.D. van la Parra).

The authors declare no conflicts of interest.

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ISSN: 0003-4932/16/XXXX-0001

DOI: 10.1097/SLA.0000000000002255

grade, receptor status (ER, PR, Her2), Ki67, margin status, nodal treatment and involvement, adjuvant systemic treatment and postoperative radiotherapy.

Patients were followed up every 4 months for 3 years, then every 6 months until 10 years postoperatively, then yearly. The last date of follow up was registered.

Indications

Indications for OPS included tumor size, multifocality, poor tumor location, skin retraction, previously involved margins, and major risk of deformity post standard BCS, among others. A small subgroup of patients had a small tumor, but desired a simultaneous reduction mammoplasty given their large breast size and/or ptosis. Their indication was thus registered as 'oncocosmetic.' Some patients had more than one indication.

Surgical Technique

Nonpalpable lesions were localized, either with a radiologically-guided hooked wire, or by peritumoral isotope injection under ultrasound guidance.

Preoperative markings were done in the standing position. Based on the tumor location, the appropriate mammoplasty technique was applied according to our previously published atlas.[10,21] Tumors located in the upper outer quadrant (OUQ) were treated by a lateral mammoplasty. Tumors located in the lower outer quadrant (LOQ) were treated by a J-mammoplasty, whereas tumors in the lower inner quadrant were treated by a V-mammoplasty. A superior pedicle mammoplasty was applied for tumors located at the junction of the lower quadrants and an inferior pedicle mammoplasty for tumors at the junction of the upper quadrants.

When the resection volume resulted in a noticeable asymmetry in size between the 2 breasts, a contralateral breast reduction was performed, either as an immediate or delayed procedure.

Tumor resection was a full-thickness glandular excision, from the skin to the pectoralis fascia. Clips were systematically placed into the defect for radiotherapy planning. Axillary surgery was performed through a separate incision, or an extension of an upper outer quadrant incision.

Histopathological Examination

All the specimens were weighed and oriented in the operating room. Intraoperative radiography of the specimen was performed for infraclinical tumors and correlated with preoperative radiography.

For palpable tumors intraoperative gross-examination of the margins was done by the pathologist evaluating the tumor dimensions and its distance to the closest specimen margin. In case of an involved or close margin, cavity margins were re-excised and the second specimen was sent for permanent sections.

After paraffin embedment and pathological analysis, a negative margin was defined as the absence of tumor cells at the cut edge of the specimen (no ink on the tumor). Positive margins were defined as the presence of tumor cells directly at the cut edge of the specimen (ink on the tumor). The volume of each specimen was calculated from the pathology reports by multiplying the measurements of length, width, and height.

Complications and Treatment Delay

All postoperative complications were prospectively recorded. Possible complications included fat necrosis, infections (with a proven bacteria and requiring antibiotic treatment), seroma, wound dehiscence, hematoma, and skin necrosis.

Adjuvant treatment was considered as delayed if the period between oncoplastic surgery and chemo- and radiotherapy was more than 6 weeks and 8 weeks, respectively.[22]

Systemic Treatment

Patients were submitted to neoadjuvant or adjuvant chemotherapy/hormone therapy according to our institutional protocol. All patients had postoperative radiotherapy to the breast with a boost of the tumor bed and, in selected cases, supraclavicular, and internal mammary nodes.

Statistics

Data are presented as means with the associated median and range, or as relative and absolute frequencies. Fisher exact test was used for comparison of categorical variables. A P-value equal to or less than 0.05 was considered statistically significant. Estimates of local recurrence, regional recurrence, distant metastases, and overall survival (OS) were performed. Patients were censored when they were last seen, or, for the purposes of local recurrence and distant recurrence cumulative incidence, at the time of death. OS was defined as the time from the date of surgery to the date of death due to any cause. Disease-free survival (DFS) was defined as the time from the date of surgery to the date of the first relapse or the date of death due to any cause. DFS events were defined as any ipsilateral or contralateral breast recurrence (invasive or noninvasive), regional or distant metastases. R (version 3.0.2 for Linux) and SPSS (version 23.0) were used for data compilation, validation, and analysis. Kaplan-Meier graphs were displayed and a log-rank test was used to compare the difference between survival function and to obtain P values (significance level set at $P < 0.05$ for local recurrence and survival).

RESULTS

A total of 350 consecutive patients operated with level 2 OPS techniques were included in the study. Patients and tumor characteristics are mentioned in Table 1. The mean patient age was 57 years (median 58, range 20–86 years). Seventy-three patients (27.9% of the invasive cancers) received neoadjuvant chemotherapy to downsize the tumor before BCS.

The indications for OPS were tumor size (37%), poor tumor location (22%), oncocosmetic (12%), multifocality (10%), skin retraction (9%), positive margins after previous surgery (5%), and other reasons (5%).

The most common level II technique used was a lateral mammoplasty for upper outer quadrant tumors (144/350 cases, 41.1%), followed by a superior pedicle technique (64/350 cases, 18.3%) and a J-mammoplasty (44/350 cases, 12.6%) (Table 2).[10]

Tumor histology included invasive ductal carcinoma in 239 cases (68.3%), ductal carcinoma in situ (DCIS) in 68 (19.4%), and invasive lobular carcinoma in 43 (12.3%) cases. The mean resection weight was 177 grams (median 127, range 40–1540) and the mean resection volume 331 cm^3 (median 237, range 30–4031). The mean pathological tumor size was 26 mm (median 20 mm, range 0–180 mm) and varied from 20 mm (median 15, range 0–140 mm) in the neoadjuvant treated patients, to 23 mm (median 20, range 4–180 mm) in the invasive cancers that did not receive neoadjuvant therapy, to 32 mm (median 25, range 0–100 mm) in the DCIS patients.

Margin Status

Margins were clear in 306 cases (87.4%) and involved in 44 cases (12.6%) (Table 3). The margins were involved in 25 of the 239 invasive ductal cases (10.5%), 10 of the 68 DCIS cases (14.7%), and 9 of the 34 invasive lobular cases (20.9%). Nine of the 72 patients (12.5%) who received neoadjuvant systemic therapy had involved margins. Pathological complete response was achieved in 23 patients (31.9%). Of the 44 patients with an involved margin, 12 underwent

TABLE 1. Patient and Tumor Characteristics

Characteristic	N	%
Mean Age, yrs	57 (median 58, range 20–86)	
Mean radiological tumor size, mm	28.7 (median 25, range 4–150)	
Mean histological tumor size, mm	26 (median 20, range 0–180)	
Focality		
Unifocal	292	83.4
Multifocal	58	16.6
Neoadjuvant therapy		
Yes	73	27.9*
No	189	72.1
Pathological T stage		
pTis	68	19.4
pT1	155	44.3
pT2	109	31.1
pT3	18	5.1
Histology		
Pure DCIS	68	19.4
Invasive ductal carcinoma	239	68.3
Invasive lobular carcinoma	43	12.3
Histologic subtype (invasive)		
Luminal A	166	63.4
Luminal B (Her2 negative)	3	1.1
Luminal B (Her2 positive)	17	6.5
Her2 non luminal	12	4.6
TNBC	62	23.7
missing	2	0.8
SBR grade		
I	41	14.5
II	157	55.7
III	84	29.8
Mean specimen weight, g	177 (median 127, range 40–1540)	
Mean specimen volume, cm^3	331 (median 237, range 30–4031)	
Margins		
Clear	306	87.4
Involved	44	12.6
Nodal status		
N0	248	70.9
N1	76	21.7
N2	26	7.4
Adjuvant chemotherapy		
Yes	111	31.7
No	239	68.3
Adjuvant hormonotherapy		
Yes	240	68.6
No	110	31.4

*Calculated over 262 invasive cancers.

conservative re-excision, 28 underwent mastectomy, and 4 were treated with radiotherapy alone because they had minimal margin involvement and refused further surgery. The overall breast conservation rate was 92%.

Postoperative Complications

Thirty-one patients (8.9%) developed one or more postoperative complications. There were 24 cases of fat necrosis, with secondary infection requiring antibiotic treatment in 21 cases, 5 hematomas and 3 seromas. A reoperation was required in 5 cases (2 wound infections, 2 hematomas, and 1 seroma). Neoadjuvant systemic treatment did not influence the occurrence of a complication.

The onset of a complication delayed further postoperative treatment in 16 cases (4.6%). There were no complications observed after radiotherapy.

TABLE 2. Level II OPS Techniques Applied to 350 Cases According to the 'Quadrant Per Quadrant Atlas'—Orientation For Left Breast[10]

Tumor Location	Level II OPS Mammoplasty Techniques 2	N (%)
Upper Outer Quadrant	Lateral mammoplasty	144 (41.1)
Lower pole	Superior pedicle	64 (18.3)
Lower outer quadrant	J mammoplasty	44 (12.6)
Lower inner quadrant	LIQ-V mammoplasty	27 (7.7)
Upper pole	Inferior pedicle	28 (8.0)
Upper inner quadrant	Round block	17 (4.9)
Central subareolar	Inverted T or vertical scar mammoplasty with NAC resection	14 (4.0)
Not defined	Other	12 (3.5)
Total		**350 (100)**

Recurrences and Survival

With a median follow-up of 55 months (mean 57, range 0–138) there were 6 local recurrences, 6 regional recurrences, 35 distant recurrences, and 15 deaths. The 5-year cumulative incidence for a local recurrence was 2.2% (0.2%– 4.2%), 1.1% (0%–3.6%) for a regional recurrence and 12.4% (8.2%–16.4%) for a distant recurrence (Fig. 1A–C).

Of the 6 local recurrences, 2 developed in patients with pure DCIS, and 4 developed in the invasive ductal group. The 5-years cumulative incidence for local recurrence was 4.5% for DCIS, 2.1% for invasive ductal carcinoma, and 0% for invasive lobular carcinoma. Thirty-five patients developed a distant recurrence. The 5-year cumulative incidence for distant recurrence was 2.3% for DCIS, 15.2% for invasive ductal carcinoma, and 11.5% for invasive lobular carcinoma. The only patient in the DCIS group who developed a metastasis also presented with a previous invasive local recurrence.

DISCUSSION

Oncoplastic mammoplasties are increasingly used, because they enable large volume resections with a good cosmetic outcome. They allow extending breast conserving possibilities to large tumors that would else be considered for mastectomy. However, a few studies report long-term oncologic results after oncoplastic surgery. This long-term follow-up study shows that despite a mean histologic tumor size of 26 mm (32 mm for the DCIS group), the breast conservation rate was 92% with a 2.2% 5-year local recurrence rate.

The 2.2% 5-year local recurrence rate in this study is at the lower end of other studies reporting on local recurrence after OPS (Table 4)[11,12,18,20,22–27] and comparable with results of BCS for smaller tumors.[28,29] In the study of De Lorenzi et al[27] who reported on 454 OPS cases, the 5-year local recurrence rate was 3.2%. Fitoussi et al[20] reported on a series of 540 OPS cases and found a local recurrence rate of 6.8% with a median follow up of 49 months. Grupnik et al[26] found a local recurrence rate of 2.2% in their series of

TABLE 3. Margin Status and Histology

Margin status	Overall	IDC	DCIS	ILC
Clear	306	214	58	34
Involved	44 (12.6%)	25 (10.5%)	10 (14.7%)	9 (20.9%)
Total	350	239	68	43

DCIS indicates ductal carcinoma in situ; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma.

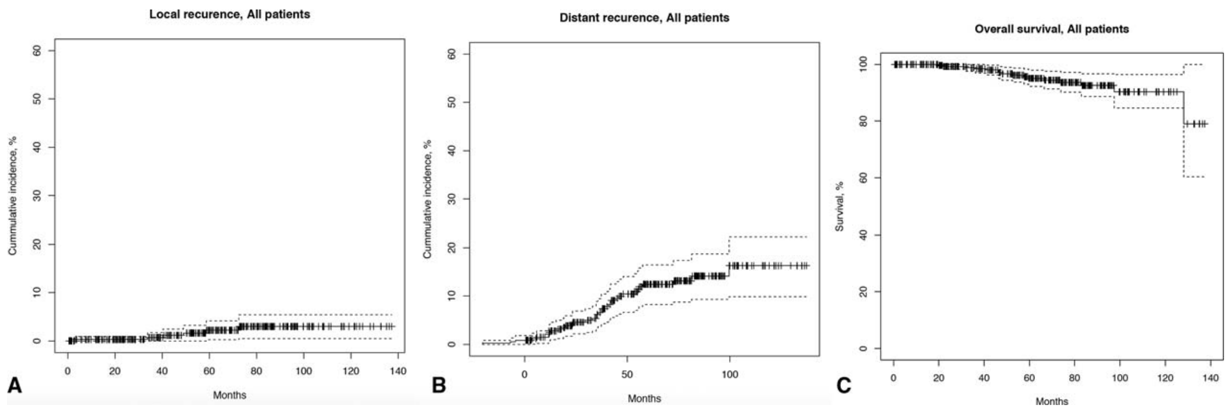

FIGURE 1. Cumulative incidence of local recurrence in the conserved breast, regional recurrence (axillary and supraclavicular), and Kaplan Meier estimates of overall survival with 95% confidence interval (dashed lines) after oncoplastic mammoplasties. A, Cumulative incidence curve for local recurrence. B, Cumulative incidence curve for distant recurrence. C, Overall survival curve.

251 OPS patients with a mean follow up of 50 months. These results compare favorably with local recurrences for small cancers, which have been reported to be between 1.8% and 12% in historical trials.[2,4,5]

Margins

Oncoplastic surgery allows for much wider excisions than traditional lumpectomy resulting in larger resections weights (177 g median in the current study, 249 grams in the meta-analysis of Losken[30]) compared with 50 grams of a standard lumpectomy.[29] This results in a lower margin involvement rate when compared to lumpectomy. In our series, margins were involved in 12.6% of cases, with a mean pathological tumor size of 26 mm, resulting in a reoperation rate of 11.5%, a rate that could not be achieved with standard lumpectomy for such large tumors.

The average reoperation rate after standard breast conserving surgery in four national databases, which included predominantly small cancers (less than 3 cms), ranges from 20 to 24%.[31–34] The analysis of the US national database showed a significant linear trend between increasing tumor size and reoperation rates.[34] For tumors smaller than 1.5 cm, the repeat surgery rate was 20.8% compared with a repeat surgery rate of 48.2% for tumors larger than 5 cm.

In the same study, the reoperation rates differed significantly with histologic subtypes, with the lowest rate of 22.2% in the invasive ductal carcinoma group and the highest rate of 30.8% in the invasive lobular carcinoma group.[34] The literature confirms that for ill-defined tumors such as DCIS and lobular invasive carcinoma, the reoperation and mastectomy rates are much higher than for well-defined invasive ductal carcinomas.[35,36] Our current study confirms that this is still the case with OPS, with 14.7% and 20.9% positive margin rates for DCIS and invasive lobular carcinoma, compared with 10.5% for invasive ductal. However, considering the mean tumor size in our population, these rates are still much lower than what would be achieved with standard lumpectomy.

In the meta-analysis of Losken et al,[30] the positive margin rate was 12.3% for the OPS cases and 20.6% after standard BCS. Margin rates in other OPS articles are equally low despite large cancers. For tumors with a median tumor size of between 2 and 3 cm, it varied from 3.3% to 23%.[11,16,19,20,24,25,37,38] For a median tumor size larger than 3 cm, the reported involved margin rate varied from 5% to 31%.[12,15,17,18,39] In the large retrospective study of Fitoussi et al[20] of 540 patients with a mean tumor size of 2.9 cm, close and/or involved margins were found in 18.9%.

Positive Margins After OPS

In the current study, 36% (16/44) of the patients reoperated for involved margins underwent a conservative re-excision and 64% a mastectomy, which is within the range of the reported mastectomy rates after oncoplastic surgery (12.5%–100%).[11,12,18,20,24–26,37]

In a previous study, we demonstrated that a positive margin after oncoplastic surgery can be accurately treated with a re-excision, providing the tumor location has been previously marked with clips.[39] However, conservative re-excision after OPS can be challenging as the initial surgery already resulted in a noticeable volume reduction of the breast. Every effort should be made to perform a re-excision, even after these larger volume oncoplastic resections.

Oncocosmetic Indications

Although we first introduced OPS for large tumors, some of the tumors in this series are small with a tumor size less than 15 mm. These patients could be treated with standard BCS. However, for patients who present with massive breast hypertrophy impairing their quality of life, a simultaneous reduction mammoplasty can be performed at the time of the cancer excision. We define this indication as oncocosmetic. These patients will have the oncological benefits of large margins and better radiotherapy because of the reduced breast volume, plus achieving a better esthetic appearance and increasing their comfort.[40] Furthermore, a reduction mammoplasty at a later stage, after completion of radiotherapy, leads to more complications, and worse cosmetic results than when performed before radiotherapy.[41] Most OPS studies also included small breast cancers in their oncoplastic reduction mammoplasty population.[11,13,16,20,24,25,42,43] Twelve % of the patients in our series were oncocosmetic indications.

Complications

OPS is associated with displacement of a larger volume of glandular tissue and long scars. The larger volume displacement leads to a higher risk of fat necrosis and complications than standard lumpectomies and surgeons should be aware of this.[12] The overall complication rate observed in this study was 8.9%, which is comparable with our previous publication[18] and to the rates reported in the studies of Rietjens et al[25] (10.8%) and Fitoussi et al[20] (8.5%) who reported on large OPS populations.

However, most OPS studies reported higher complication rates, between 16% and 30%.[13,14,18,19,22,24,27,37,38,42–45] In the study of Nizet et al,[13] the resection size was found to be the sole factor

TABLE 4. Studies Reporting Oncoplastic Reduction Mammoplasty Outcomes

Author	N	Median Tumor Size (mm)	Close/ Involved Margins	Mean Resection Weight (g)	Median FU (months)	LR	DR	OS	DFS
Cothier-Savey 1996[23]	70	–	–	350 (max 1200)	61*	8.5%‡	–	86%‡	80%‡
Clough 2003[18]	101 PS	32* (10–70)	11 (10.9%)	222 (20–1450)	46	7/101 (9.4%‡)	13/101 (12.9%)	95.7%‡	82.8%‡
McCulley 2005[24]	50	24* (6–80) US 27* (8–60) MG	4 (8%) DCIS	432 (60–930)	13*	0	0	–	–
Rietjens* 2007[25]	148	22* (3–100)	8/148 (5.4%)	198 (20–2100)	74	5 (3%)	19 (13%)	–	–
Fitoussi 2010[20]	540	29.1* (4–100)	102 (18.9%)	188 (8–1700)	49	6.8%	–	92.9%	87.9%
Chakravorty 2012[11]									
OPS	150	21 (1–98)	10/150 (6.6%)	67† (11–1050)	28	4 (2.7%) 4.3% at 6 yrs‡	2 (1.3%)	95%	–
Stand	440	18 (2–98)	64/440 (14.5%)			10 (2.2%)	33 (7.5%)		
Grubnik 2013[26]	251	15.4*	5/251 (2%)	237 (17–1316)	50*	5 (2.2%)	3	96.1%‡	92.1%‡
Mazouni 2013[12]									
OPS	45 RS	40 (10–80)	14 (31%)	NR	46	2 (4%) 5% at 46 mo‡	6 (14%)	96.2%	92.7%
Stand	240	40 (10–110)	58 (27%)			11 (5%)	22 (10%)	94.2%	92.1%
Eaton 2014[22]	86 RS	–	DCIS 14/60 (23%) IDC 1/26 (4%)	NR	54	6 (6.9%)	5 yr IBTC: inv 93%, DCIS 91% 5 yr DMFS 91% 5-yr BCSS 94%		
De Lorenzi 2016[27]									
OPS	454 RS MCA	–	53 (11.7%)	NR	86	CI 3.2% (5 yr) CI 6.7% (10 yr)	CI 7% (5 yr) CI 12.7% (10 yr)	95.9% (5 yr) 91.4% (10 yr)	83.7% (5 yr) 69% (10 yr)
Stand			91 (10%)			CI 1.8% (5 yr) CI 4.7% (10 yr)	CI 6.6% (5 yr) CI 11.6% (10 yr)	95.4% (5 yr) 91.3% (10 yr)	88.1% (5 yr) 73.1% (10 yr)
Current study	350	26 (0–180)	44 (12.6%)	177 (40- 1540)	55	2.2% 5 yr‡	12.4% 5 yr‡	95.1% 5 yr	84.8%

BCSS indicates breast cancer specific survival; CI, cumulative incidence; DFS, disease free survival; DMFS, distant metastasis free survival; DR, distant recurrence; IBTC, ipsilateral breast tumor recurrence; LR, local recurrence; MCA, matched-cohort analysis; MG, mammogram; mo, months; NR, not reported; OPS, oncoplastic surgery; OS, overall survival; PS, prospective; RS, retrospective; stand, standard breast conserving surgery.
*Mean, †Median, ‡Actuarial.

influencing the complication rate (263 cm^3 in patients with a complication vs 130 cm^3 in the others, $P = 0.024$), confirming that more complex reshapings lead to higher complication rates. The increase of complications related to mammoplasties is a major concern, as complications could delay postoperative treatment. In our series, the onset of a complication delayed further postoperative treatment in 16 cases (4.6%). Neoadjuvant treatment did not influence the complication rate. Training breast surgeons for level 2 OPS is mandatory to avoid a delay in adjuvant treatment because of technical flaws or an inappropriate choice of the optimal mammoplasty technique.[10]

OPS Indications and Multidisciplinary Setting

OPS is a surgical tool that allows much wider resections than standard lumpectomy.

In expert centers in Europe, it is a standard option, commonly proposed to patients when the tumor size or location makes a simple wide local excision either impossible or at high risk of major breast deformity. A 2010 French national survey on 25 referral centers for breast cancer showed that of the 13,762 patients evaluated, 71% underwent breast conserving surgery. Of these 13.9% received level 2 OPS, either upfront or after NAC.[46]

OPS is indicated for large tumors that do not require neoadjuvant treatment, for example, DCIS (19.4% in our series), invasive carcinomas with extensive DCIS, some lobular carcinomas, and multifocal tumors. Another indication is those tumors that did not respond well to preoperative chemotherapy. In our practice, we would not propose upfront OPS to large invasive cancers that are candidates for induction chemotherapy, but only to those patients with a poor response to induction treatment.

OPS does not interfere with postoperative radiotherapy. By placing clips at the time of the resection the tumor bed can be accurately boosted. In our series, like in all previous studies,[18,21,46–48] we did not observe any complications after radiotherapy, confirming that mammoplasties can be safely inserted into the usual multidisciplinary sequence of BCS.

Study Strengths and Limitations

The measurable outcomes of OPS are margin involvement and breast conservation rate, complication rate, survival and local recurrence rates, cosmesis, and patient satisfaction.[29,49] In this study, we focused on the oncological results, as the cosmetic outcomes have been reported in our previous publication.[21]

With a median resection weight of 177 grams, only 32% of the patients in this series had a contralateral breast reduction (74 immediate, 39 delayed), which is less than in other series. Our current policy is to propose contralateral breast reduction systematically when large resections (> 200 grams) are performed. For smaller resections, it is a case per case discussion with the patient.

CONCLUSIONS

Oncoplastic breast reductions allow wide resections with free margins and can be proposed for large cancers as an alternative to mastectomy. Despite a median tumor size of 23 mm for invasive cancers and 32 mm for DCIS, the breast conservation rate was 92% with a 2.2% 5-year local recurrence rate. Breast surgeons should include oncoplastic surgery in the surgical armamentarium for breast cancer treatment, allowing patients a higher breast conservation rate with better cosmetic and functional results.

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J Breast Health 2017; 13: 46-49
DOI: 10.5152/tjbh.2016.3165

The Main Topics at the Oncoplastic Breast Surgery Course and Expert Panel

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ABSTRACT

The Oncoplastic and Reconstructive Breast Surgery course was held in Izmir by the Izmir Breast Diseases Federation in collaboration with the Breast Diseases Federation of Turkey. The techniques of oncoplasty, the application details and experience in this subject were shared. In this text, the main topics and outcomes are briefly summarised. These evaluations can be considered highly valuable on both local and regional scales.

Keywords: Oncoplastic breast surgery, quadrantectomy (surgery for breast cancer based on tumour location), breast surgery

Introduction

The 3rd Oncoplastic and Reconstructive Breast Surgery Course was organized by the Izmir Breast Diseases Association on May 21, 2016 in co-operation with the Association of Breast Diseases Federation of Turkey. Eighty seven speakers and the participants from 17 different cities deliberated on the issue during a full-day course between 8:30 and 18:30. Experienced specialists demonstrated their own approaches with a plethora of visual material (photos, videos etc.). Participants included Mustafa Emiroglu, M. Kemal Atahan (İzmir), Bekir Kuru (Samsun), M. Ali Gülçelik (Ankara), Atakan Sezer (Edirne) as the board directors of the course and Bahadır Güllüoğlu (İstanbul) as the course consultant. Oncoplastic techniques, methods and experience in breast cancer surgery were described in detail. The main topics and messages are summarized briefly in this paper, and the assessment made on this subject Turkey is considered to be an important local and regional scale.

The status and development of oncoplastic and reconstructive breast surgery in the world and Turkey in relation to surgeons who have been working on this issue were explained briefly. Practices carried out in Turkey are almost parallel to the developments in the world. In this regard, the experience and practices about this issue must be shared with a wider community via literature. It was stressed that multi-centre studies on oncoplastic breast surgery were needed. A consensus was achieved on the requirement for general certification programs in this area to be formed by a commission planned to be constituted by oncoplastic and reconstructive surgeons among general surgeons and plastic surgeons. The importance of all aspects of the oncoplastic and reconstructive breast surgery (ORBS) was highlighted. Please see the Table 1 for details of the evaluation of oncoplastic breast surgery.

Oncoplastic breast surgery

Breast cancer surgery made progress within the last century from radical mastectomy to oncoplastic breast surgery. In 1980s, MCS revolutionized the field. In 2000s, oncoplastic breast surgery (OBS) was announced as an innovation in breast surgery. In fact, breast cancer surgery treatment is available in most of the cases in the form of standard breast aesthetics incisions without the need for oncoplastic techniques. However, one out of 4-5 patients had to undergo an aesthetical oncoplastic procedure after MCS. Therefore, surgical planning in addition to an overall assessment has gained a great deal of importance. Advanced planning before surgery is considered to be skipped by surgeons most of the time. Loss of breast tissue by more than 20% (loss of inner quadrants 10%) can lead to aesthetic problems. The importance of oncoplastic techniques are emphasised for future use. The application of these techniques simultaneously applied with lumpectomy ensures higher patient satisfaction and increases the quality of life. The simultaneous procedures were specifically discussed with high emphasis during the course.

Oncoplastic incisions are intended to prevent any defects after breast surgery. Up until recent years, it has been believed that incisions placed in parallel on both sides of maximum remaining skin tension lines (Kraissl's lines) and in the same orientation as collagen fibres (Langer's lines) are the most suitable incisions.

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Received: 04.06.2016
Accepted: 05.07.2016

Table 1. Checking the elements required for the ORBS

	Before surgery	Pre-operative	After surgery
Patient	Age, height, weight, DM, DVT , smoking history, HT, BMI, donor site (chest – abdominal wall and back), approach to the other breast	-	Expectations, compliance, complications
Tumor	stage, biology, DCIS (±), size, distance to skin and nipple	Pathological examination (limit the frozen slices)	Oncological results
Breast	Density, size, shape, ptosis, areola status, skin quality, assessment of the other breast, possible breast defect analysis	To be drained, symmetry	Aesthetic results
Surgeon	Multidisciplinary assessment, photo, experience level	Photo, experience	Photo, documentation, follow

HT: hypertension; DM: diabetes mellitus; BMI; body mass index; DCIS: ductal carcinoma; ORBS: oncoplastic and reconstructive breast surgery

Table 2. The proposed oncoplastic techniques according to breast quadrants

Location of the tumor	Small breast and medium sized breast - droopy (-)	Small breast and medium sized breast - droopy (+)	Big breast
Upper-outer quadrant	Elliptical radial incision Half bat incision (side) Round block incision Racket incision Glandular flap Lateral thoracodorsal Flap LD TRAM	Circumference incision of nipple Elliptical radial incision Half bat incision (side) Round block incision Racket incision Glandular flap Benelli mastopexy Lateral thoracic flap LD	OBR (lower, double pedicle) Elliptical radial incision Batwing incision Racket incision Lateral thoracodorsal flap Glandular flap
Upper-middle and upper-inner quadrant	Breast head circumference incision Crescent incision Batwing incision Half-batwing incision (inside) Round block incision Glandular flap Parallelogram incision Rotation flap LD	Breast head circumference incision Crescent incision Batwing incision Half-batwing incision (inside) Round block incision Glandular flap Benelli mastopexy Rotation flap	OBR (lower, double pedicle) Crescent incision Batwing incision Glandular flap Rotation flap
Central area	Round block Grisotti flap Central triangular incision Total excision-primary closure Glandular, dermoglandular flaps	Round block Benelli Grisotti flap	OBR Grisotti reduction
Lower-outer quadrant	Lateral thoracodorsal flap Glandular, dermoglandular flaps Thoraco- epigastric flap TRAM	Round block Glandular, dermoglandular flaps Mastopexy techniques Volume filling techniques from chest wall	OBR (upper, upper-inner, upper-outer pedicle) Lateral thoracodorsal flap
Lower-inner quadrant	Inframammary incisions Triangular incision Dermoglandular incision Volume filling techniques (from thoracodorsal space)	Inframammary incisions Triangular incision Dermoglandular incision Volume filling techniques (from thoracodorsal space)	OBR (upper, upper-inner, upper-outer pedicle) Dermoglandular flaps Rotation flap
Lower-middle quadrant	Rotation flap Vertical OBS incisions Triangular incision Reverse- T incision	Rotation flap Vertical OBS incisions Triangular incision Reverse- T incision	OBR (upper, upper-middle, upper-outer pedicle) Vertical OBS incisions

OBS: oncoplastic breast surgery; OMR: oncoplastic breast reduction; LD: Latissimus dorsi flap;

TRAM: transverse rectus abdominis myocutaneous flap

Table 3. Participants as speakers, panelists and chairpersons in the ORBS meeting

Mustafa Emiroğlu (İzmir)	Bekir Kuru (Samsun)	Kemal Atahan (İzmir)
Bahadır Güllüoğlu (İstanbul)	Atakan Sezer (Edirne)	M. Ali Gülçelik (Ankara)
Zafer Cantürk (Kocaeli)	Serdar Özbaş (Ankara)	Serdar Saydam (İzmir)
Cihangir Özaslan (Ankara)	M. Ali Koçdor (İzmir)	Lutfi Doğan (Ankara)
Cem Karaali (İzmir)	Hedef Ozun (Aydın)	Teoman Coşkun (Manisa)
Serhan Tuncer (Ankara)	Gürsel R. Soybir (İstanbul)	Belma Koçer (Sakarya)
Hasan Karanlık (İstanbul)	Güldeniz Karadeniz (Zonguldak)	Levent Yeniay (İzmir)
Ercüment Tarcan (İzmir)	Cem Yılmaz (İstanbul)	Aykut Soyder (Aydın)
Neslihan Cabioğlu (İstanbul)	Senem Alanyalı (İzmir)	Murat Tüzüner (İzmir)

However, Aronowittz curvilinear horizontal incisions cause tension on the breasts, prevent the enlargement of the breast skin, and cause the breast tissue to collapse in certain areas while polarising upper quadrant, and so is considered as an outdated method in recent years. The radial incisions following the growth lines of the breast are thought to be more beneficial than the former method. In addition, it was noted that the Batwing and Benelli incisions were suitable for Langer and Kraissl lines; tennis racket in upper-out quadrant, vertical and reverse T in low-in quadrant; and radial rotation flap incision in inner quadrants are also suitable for the tension lines of the breast as defined by Aronowitz.

Speakers said that the glandular and dermoglandular flap techniques should be used widely and the area of lumpectomy should be filled in a way that prevents the development of seroma. The traditional way of waiting until the lumpectomy area filling with seroma is found outdated and abandoned. These techniques should be applicable in all the quadrants of the breast especially in the upper breast.

Oncoplastic breast surgery is not a standard approach; it can be modified for each patient in various ways. Sometimes, an open surgical area is found to be an interesting and creative technique. Thoracodorsal and/or epigastric tissue volume filling techniques are recommended for any possible defects in the external quadrants.

It was emphasized that vertical mastopexy had become very popular in breast reduction surgery in recent years. Lumpectomy and oncoplastic surgery could be done in various quadrants of the breast with this technique. It is recommended for the cases in which the volume of the breast is less than 1200 cc.

Application of the Grisotti flaps is recommended in the central tumors where it is necessary to remove the areola and head of the breast for security. And the benefits of Grisotti flap were underlined. The importance and facilitations of implementing of Benelli mastopexy were assessed in medium-volume and droopy breasts.

Breast volume and the tumor-to-breast-volume ratio are mostly debated in breast surgery. Therefore, it is highlighted in this course that the volume of breast should be measured. Oncoplastic breast reduction is defined as the oncoplastic breast surgery technique that is frequently applied in the world and in Turkey. Issues of dose distribution in radiotherapy, aesthetic issues after treatments and macromastia could be resolved surgically with a single operation by this technique. It is a major surgical operation with a significant learning curve. It should not be attempted without full knowledge of at least 5 to 6 techniques. It is highlighted that this technique brings extremely high patient-satisfaction when applied as a two-sided technique.

The endoscopic breast surgery was described in detail by its sole representative in Turkey. This operation is applied in breasts that are droopy and not very big. This technique inspires hope for surgery in the medium and long terms, although it was underlined that there was a significant learning curve during the course.

Breast reconstruction techniques

Although latissimus dorsi (LD) muscle flap lost its popularity due to the high morbidity rates, it is still in use for the patients with small breasts in Turkey as an operation of out-quadrant tumours either on its own or in combination with silicone implants. It is highlighted that we should recommend a new breast construction after mastectomy. The transverse rectus abdominus myocutaneous flap (TRAM) technique can be applied in patients that have adequate abdominal tissue. It is stressed that this technique is a major surgical operation with a significant learning curve. The patients found this technique to be more comfortable in the medium and long terms.

The participating breast surgeons discussed the silicone implant applications performed simultaneously with mastectomy. In recent years, mastectomy rates have increased in breast cancer treatment and reconstruction applications are also performed simultaneously. Silicone implant usage is increased rapidly due to the surgeons' and patients' comfort and ease-of-use of these implants. The protection of the lower breast fold affects the implant application positively and brings about aesthetic results.

A careful marking of the tumor bed is recommended for radiotherapy in oncoplastic breast surgery. In this regard, it is important to co-operate with the radiation oncologist. In recent years, reconstruction techniques applied simultaneously with mastectomy have become more and more popular. There is now a stronger opinion about the application of silicone before radiotherapy. It is specified that the complications of oncoplastic and reconstructive breast surgery do not create serious oncologic problems. They do not delay the adjuvant therapy. In the event of a positive assessment of the pathological border, re-excision can be done.

The highlights in the oncoplastic approach panel according to the breast quadrants

Multi-disciplinary assessment including the plastic surgeon is recommended in the treatment of breast cancer. The importance of the patient, breast, tumor features and the experience of the surgeon were discussed in relation to the implementation of these techniques. The importance of assessment before surgery was underlined by all the panelists. Who should perform these techniques? The importance of and the need for certification training s were emphasized especially in the discussion section. In this context, the situation in Turkey was discussed in detail and the efforts made towards new developments were distinguished, as well. Breast surgeons that attended and completed the courses can perform these operations.

Some of the speakers on the panel suggested that mastectomy and OBS should be differentiated from each other. Breast surgery technique selection constituted an important section of the panel discussions. OBS recommendations of the experts participating in the panel are summarized in Table 2. Table 3 shows the panelists, speakers and presidents of the sessions.

Discussion and Conclusion

ORBS techniques demonstrate a significant growth in Turkey. Also, training and certification are very important in ORBS. We should offer patients breasts without defects, not excellent breasts. If the patients do not have very high expectations, it will increase their compliance after surgery. OBS is an approach that treats the patient, not the disease. OBS increases the role of surgeons. There are important efforts concentrated on learning and the implementation of these techniques among surgeons.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - M.E.; Design - B.K., M.E.; Supervision - B.G.; Funding - C.K.; Analysis and/or Interpretation - M.A.G., K.A., A.S.; Literature Review - M.E.; Writing - M.E.; Critical Review - B.G.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

Neoadjuvant Therapy Combined With Oncoplastic Reduction for High-Stage Breast Cancer Patients

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Objective: Oncoplastic surgery has been shown to be a good alternative to breast conservation surgery (BCS) alone for patients with breast cancer. Its role in patients with advanced disease is unclear. In this study, we evaluate the safety of oncoplastic BCS (OBCS) in patients who received neoadjuvant therapy (NT) for high stage breast cancer.

Methods: The oncologic outcomes of consecutive patients classified as high stage (>T2 or at least N1) who received NT followed by BCS at EUH by a single breast surgeon (T.M.S.) from September 2004 until June 2015 were compared with those who received BCS combined with an oncoplastic reduction. Patients were surveyed using the BREAST-Q to determine their satisfaction after surgery.

Results: A total of 87 patients were included in this series. The mean initial tumor size (4.37 vs 2.56 cm), the weight of the surgical specimen, and the post-NT tumor size were all larger in the OBCS group as compared with BCS alone (1.54 vs 1.29 cm). The mean follow-up was 44 months. The average percent reduction in tumor size in response to NT was slightly greater in the OBCS group (61 vs 52%). Oncologic outcomes were similar for OBCS reduction and BCS groups, respectively: positive margin rate, reexcision rate, completion mastectomy rate, local recurrence rate, and 5-year DSS. Patient satisfaction was similar between the 2 groups.

Conclusions: The oncoplastic approach in high stage patients treated with neoadjuvant systemic Powered by Editorial Manager and ProduXion Manager from Aries Systems Corporation therapy appears to be as safe and effective when compared to BCS alone. Oncoplastic BCS paired with NT broadens the indication for BCS for patients with larger tumor size.

Key Words: oncoplastic surgery, oncoplastic reduction, breast surgery

(*Ann Plast Surg* 2017;78: S258–S262)

Oncoplastic surgery merges oncology and plastic surgery to simultaneously treat patients with breast cancer and address tissue defects, and has gained popularity as an alternative technique to breast conservation therapy (BCT) alone.[1,2] Oncoplastic breast conservation surgery (OBCS) can be further subdivided into volume displacement and volume replacement forms of reconstruction. Oncoplastic reduction is defined as volume displacement form of reconstruction at the time of lumpectomy.[3] Oncoplastic techniques have evolved to broaden the indications for breast conservation therapy and to improve aesthetic results after BCT.[4–7] Additional oncologic benefits of oncoplastic techniques compared with BCT alone have also been well established.[8,9] Oncoplastic techniques may broaden indications of BCT to include larger tumor breast cancer (>4 cm) and locally advanced breast cancer by offering larger resection potential with wider free surgical margins, lower incidence of positive margins, and potentially fewer reexcisions and completion mastectomies.[8,9]

The ability of the OBCS technique to preferentially treat larger tumors also makes it amenable to neoadjuvant chemotherapy, and the oncologic safety of neoadjuvant therapy (NT) combined with oncoplastic reduction has also been well established.[10,11]

There has been limited evaluation of the oncologic safety of NT followed by oncoplastic reduction for higher stage breast cancer patients.[12,13] The purpose of this report is to determine whether it is safe to perform NT followed by oncoplastic reduction in higher stage breast cancer patients.

METHODS

This is a retrospective review of all patients with a diagnosis of high stage breast cancer (>T1 or at least N1) who received NT before breast conservation therapy between September 2004 and June 2015. Patients were excluded from this study if they had metastasis (M1) at the time of diagnosis or did not adhere to the recommended standard treatment for their disease. Study approval was obtained from the institutional review board.

Patients were stratified into 2 groups based on surgical procedures received: those who underwent BCT followed by immediate oncoplastic reduction (group 1) and those who underwent BCT alone without any immediate reconstruction (group 2). All BCTs were performed by a single oncologic surgeon (T.M.S.) and all additional reconstruction was performed by a single plastic surgeon (AL). Clinical and pathologic variables evaluated included patient demographics, preoperative histology and clinical stage, NT received, details of BCT as well as oncoplastic reduction if received, postoperative histology, receptor status, adjuvant therapy and clinical course after surgery. Patients were defined as high stage based on clinical stage before initiating NT (>T1 or at least N1). Intraoperative data evaluated included tumor size, specimen weights, nodal status, and specimen radiography when appropriate. In all cases, the tumor was excised by the surgical oncologist before reduction and submitted for routine pathologic analysis. All patients having preoperative imaging guidance confirmed specimen adequacy with intraoperative specimen radiography. Both pre-NT and post-NT tumor size were determined by imaging (either ultrasound or magnetic resonance imaging) and percent change in tumor size in response to NT was then calculated between the 2 tumor sizes.

Outcomes of interest included positive surgical margins, surgical reexcision, progression to completion mastectomy, local recurrence, metastasis, and death. Before the 2013 SSO/ASTRO guidelines some patients received re-excision for margins 1 mm or less.[14]

Patients from both groups were surveyed using the Breast-Q to determine patient satisfaction with their breast surgery. Surveys were mailed to patients or conducted over the telephone.

Statistical Analysis

General frequencies, chi-square and Kaplan-Meier statistical analysis were calculated using SPSS 23.0 (Armonk, NY: IBM Corp). Chi square analysis was performed to compare BCS and OBCS cohorts. Fischer's exact test was used to calculate *P* values. Survival analysis was performed using Kaplan-Meier.

RESULTS

Demographic and Clinicopathologic Results

We included a total of 87 patients in our review who received NT followed by breast-conserving therapy (BCT) as shown in Table 1.

Received December 20, 2016, and accepted for publication, after revision December 31, 2016.

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Conflicts of interest and sources of funding: none declared.

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ISSN: 0148-7043/17/7806–S258
DOI: 10.1097/SAP.0000000000001062

TABLE 1. Demographic, Clinicopathologic, and Oncologic Results

	All Patients, 87	OBCS, 47 (53)	BCS, 40 (47)	*P*
Age: mean (range), y	57 (22–86)	53 (22–73)	61 (35–86)	0.002
Race				0.41
White	43 (51)	21 (45)	22 (60)	
African-American	38 (45)	24 (51)	14 (38)	
Asian	2 (2)	1 (2)	1 (3)	
Hispanic	1 (1)	1 (2)	0	
BMI, mean (range)	30.5 (18.5–53.7)	30.8 (22.0–44.7)	28.9 (19.5–43.1)	0.43
IDC	73 (84)	36 (90)	37 (79)	0.25
ILC	12 (14)	4 (10)	8 (17)	
ER+/PR+	48 (55)	26 (55)	22 (55)	1.00
Luminal A	34 (39)	19 (30)	15 (38)	0.95
Luminal B	14 (16)	7 (15)	7 (18)	0.97
HER-2+	29 (33)	17 (36)	12 (30)	0.70
Triple-negative	22 (25)	9 (19)	13 (33)	0.24
Pre-NT AJC stage:				0.94
2	66 (74)	35 (75)	31 (78)	
3	21 (24)	12 (26)	9 (23)	
Preoperative T stage:				0.05
T1	19 (21)	6 (13)	13 (33)	
T2	49 (55)	28 (60)	21 (53)	
T3	11 (12)	9 (19)	2 (5)	
T4	8 (9)	4 (9)	4 (10)	
Preoperative N stage:				0.31
N0	39 (44)	20 (43)	19 (48)	
N1	38 (43)	23 (49)	15 (38)	
N2	9 (10)	3 (6)	6 (15)	
N3	1 (1)	1 (2)	0	
Pre-NT tumor size: mean (range), cm	3.58 (0.40–11.00)	4.37 (0.70–11.00)	2.65 (0.40–6.50)	0.001
Postoperative tumor size: mean (range), cm	1.43 (0–5.2)	1.54 (0 = 4.4)	1.29 (0–5.2)	0.28
% Reduction in tumor size, mean (range)	57 (−80 to 100)	61 (−80 to 100)	52 (−40 to 100)	0.28
Response to NT:				0.26
Complete	32 (27)	17 (36)	15 (38)	
Partial	44 (51)	26 (55)	18 (45)	
Zero	3 (4)	0	3 (8)	
Progression	8 (9)	4 (9)	4 (10)	
Positive margin	6 (7)	3 (6)	3 (8)	1.00
Reexcision	5 (6)	2 (4)	3 (8)	0.66
Reexcision positive margins	0	0	0	n/a
Completion mastectomy	5 (6)	3 (6)	2 (5)	1.00
NT				
Chemo (Adria)	41 (47)	19 (40)	22 (55)	0.19
Chemo (Tax)	21 (24)	12 (24)	9 (23)	0.83
Herc/Per chem	19 (21)	12 (24)	7 (18)	0.42
Hormonal	6 (7)	4 (9)	2 (5)	0.36
Local recurrence	5 (6)	2 (5)	3 (6)	1.00
Metastasis	12 (14)	5 (11)	7 (18)	0.37
Time to local recurrence: mean (range), mo	23 (10–48)	19 (17–22)	29 (10–48)	0.69
Time to metastasis: mean (range), mo	34 (11–71)	29 (11–71)	38 (19–59)	0.43
Death	10 (11)	4 (9)	6 (15)	0.49
NED	69 (78)	40 (85)	29 (73)	0.50
Length of follow-up: mean (range), mo	44 (2–125)	44 (2–125)	43.4 (10–101)	0.94

n/a indicates not applicable; NED, no evidence of disease.

Forty-seven patients underwent an oncoplastic reduction at the same time as BCT (group 1) and 40 patients received BCT alone (group 2). Patients in group 1 were younger (mean age, 53 vs 61; $P = .002$).

Patients in group 1 had significantly larger initial tumor sizes before NT (4.37 cm vs 2.65 cm; $P < .001$) and had a more advanced T stage (28% vs 15% T3/T4; $P = 0.05$). The majority of patients in both groups were hormone receptor positive (either ER or PR positive or both) (55% vs 55%; $P = 1.00$). There were similar rates of Her-2–positive breast cancer (36% vs 25%, $P = 0.37$) but there was a slightly higher rate of triple negatives in the group 2 (23% vs 33%, $P = 0.48$). Most patients received neoadjuvant chemotherapy in both groups. Most triple negative breast cancer patients received Adriamycin-based chemotherapy (60%) followed by taxol-based chemotherapy (40%). All eligible patients (by date) with HER-2neu amplification received herceptin or pertuzumab based induction, and a smaller percentage (7%) received hormonal NT. Response to NT was greater in group 1 compared with group 2 (average % reduction in tumor size, 61% vs 52%; $P = 0.28$) (Figs. 1–4).

The mean weight of excised tumor was larger in group 1 (152.3 vs 70.2 g; $P = 0.012$). The tumor size determined by imaging after NT and surgical excision was also larger in group 1 (1.29 cm vs 1.04 cm, $P = 0.45$).

The majority of patients received adjuvant hormonal therapy (51% vs 60%) as well as radiation (96% vs 93%) after surgery (exceptions included completion mastectomy or patient and/or Medical Doctor choice).

Oncologic Outcomes

Positive margin rate (6% vs 8%, $P = 1.00$), re-excision rate (4% vs 8%, $P = 0.66$), completion mastectomy rate (6% vs 5%, $P = 1.00$), local recurrence rate (5% vs 6%, $P = 1.00$), metastasis rate (11% vs 18%, $P = 0.37$), and death rate (9% vs 15%, $P = 0.49$) were similar between the 2 groups. The mean time to local recurrence was 23 months, and similar between the 2 groups (19 vs 29 months; $P = 0.69$). Mean time to metastasis (29 months vs 38 months; $P = 0.43$) was longer in the BCS group. Average length of follow up was 44 months for both groups combined (2–125 months) with similar rate of follow-up between the 2 groups. Five-year disease-specific survival (95% vs 100%, $P = 0.64$) were similar between groups 1 and 2, respectively. At most recent follow-up, 85% of patients in group 1 and 73% of patients in group 2 were disease-free (no evidence of disease, ($P = 0.05$).

Patient Satisfaction Results

A total of 30 patients completed a subset of questions from the postoperative BREAST-Q survey regarding satisfaction with their breast surgery. More patients from the OBCS reported to be very satisfied with the appearance ($P = 0.03$). Also, patients in the OBCS group were more often satisfied with the size of their breast postoperatively (66% vs 50%, $P = 0.63$) and how their breasts lined up with each other (53% vs 31%, $P = 0.42$). Please refer to Figure 5 for results from the patient survey regarding their satisfaction with breast surgery. We also surveyed patients subjectively, and a common theme mentioned among several patients was that radiation changed the cosmetic result of their breast after surgery.

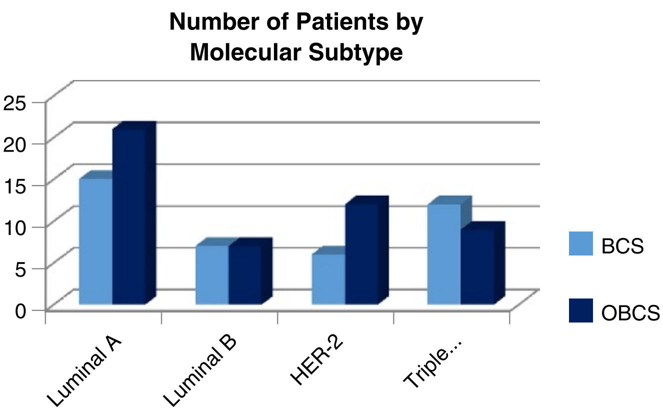

FIGURE 2. Molecular subtypes.

DISCUSSION

Currently, there is a 12.4% lifetime risk of invasive breast cancer for women in the United States. Screening and management of breast cancer has evolved over the past few decades, resulting in an increased survival rate.[15] Therefore, the surgical management of breast cancer has also shifted focus to reflect these changes in survival to enhance patient quality of life after breast cancer. Breast-conserving surgery was introduced in 1981[16] and has continued to demonstrate comparable oncological outcomes to radical mastectomy with superior quality of life for the treatment of some breast cancers.[17–19] However, breast conservation surgery has limitations to the size of tumor that can be adequately removed without significant breast deformity. Oncoplastic breast conserving surgery (OBCS) was introduced into the literature in the mid-1990s[20] as a means to expand the benefit of breast conserving to include wider excisions while maintaining cosmesis.[1] There are a variety of OBCS techniques available depending on various tumor and patient characteristics[1] that are broadly divided into volume displacement, volume replacement and reduction.[21] Oncoplastic reduction combines lumpectomy with traditional breast reduction. Although OBCS including oncoplastic reduction has been developed with oncologic safety in mind and has often shown similar oncologic outcomes to breast conserving surgery alone, little is known about the indications for and oncologic safety of oncoplastic reduction for higher-stage patients who have a higher risk of mortality from breast cancer.

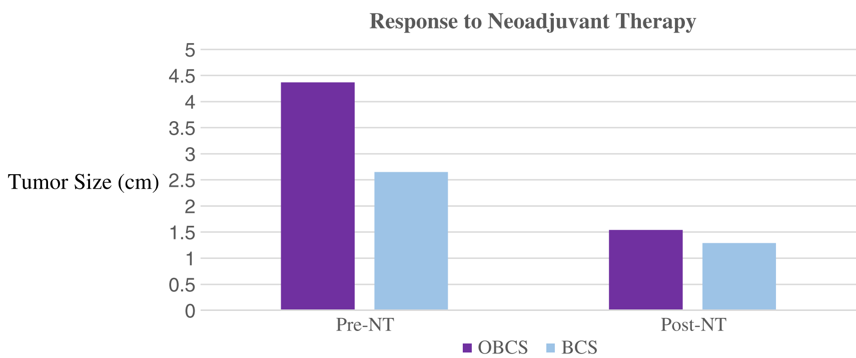

FIGURE 1. Change in tumor size in response to NT.

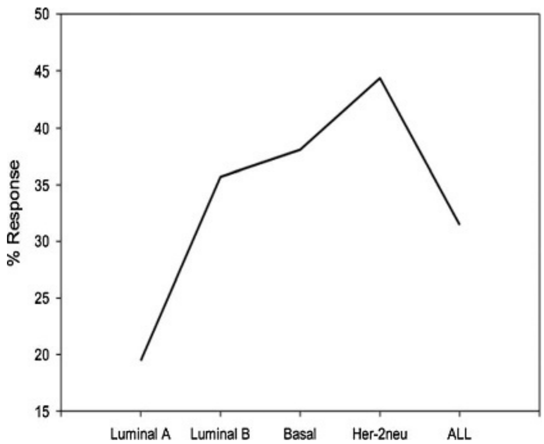

FIGURE 3. Complete pathologic response by molecular subtype.

We reviewed 87 high-stage breast cancer patients who underwent breast conserving surgery after NT. Forty patients received breast conservation therapy alone and 47 received immediate oncoplastic reduction after their breast-conserving surgery. Our patient population reflects similar demographics and clinical characteristics to high-stage breast cancer patients diagnosed and treated in the United States and were relatively similar between the 2 groups. The mean age at time of surgery of our combined groups was 57 years, slightly younger than the median age of breast cancer diagnosis in the United States (61 years)[22]; and, the patients who had oncoplastic reduction were significantly younger than those who underwent breast conserving surgery alone (53 vs 61, $P = 0.002$). This reflects a trend nationally in that younger women are more likely to pursue breast reconstruction compared to older women.[8]

The average tumor size preoperatively was significantly larger for the OBCS group compared with the BCT group (4.36 cm vs 2.54 cm, $P < 0.001$), and OBCS patients had a significantly more advanced T stage (28% vs 15%, $P = 0.05$). The ability of oncoplastic surgery and immediate reconstruction to enable greater resections with breast conserving therapy as opposed to mastectomy has been well

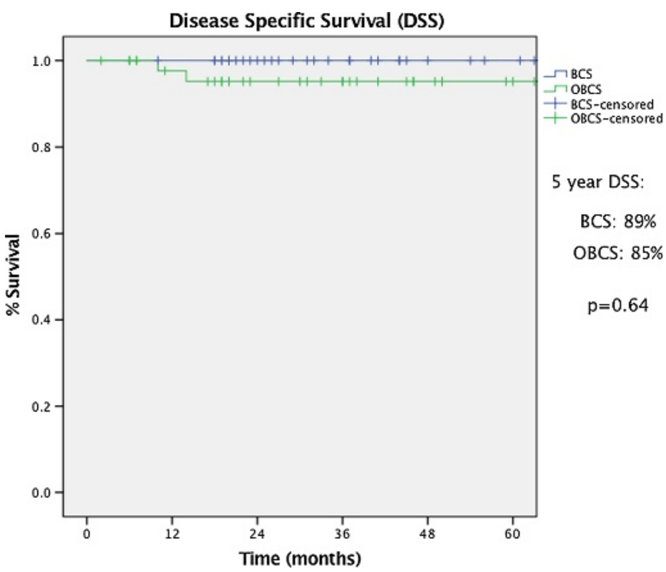

FIGURE 4. Disease-specific survival OBCS versus BCS (Kaplan-Meier) ($P = 0.64$; OBCS median OS, 123.6; BCS median OS, 101.1).

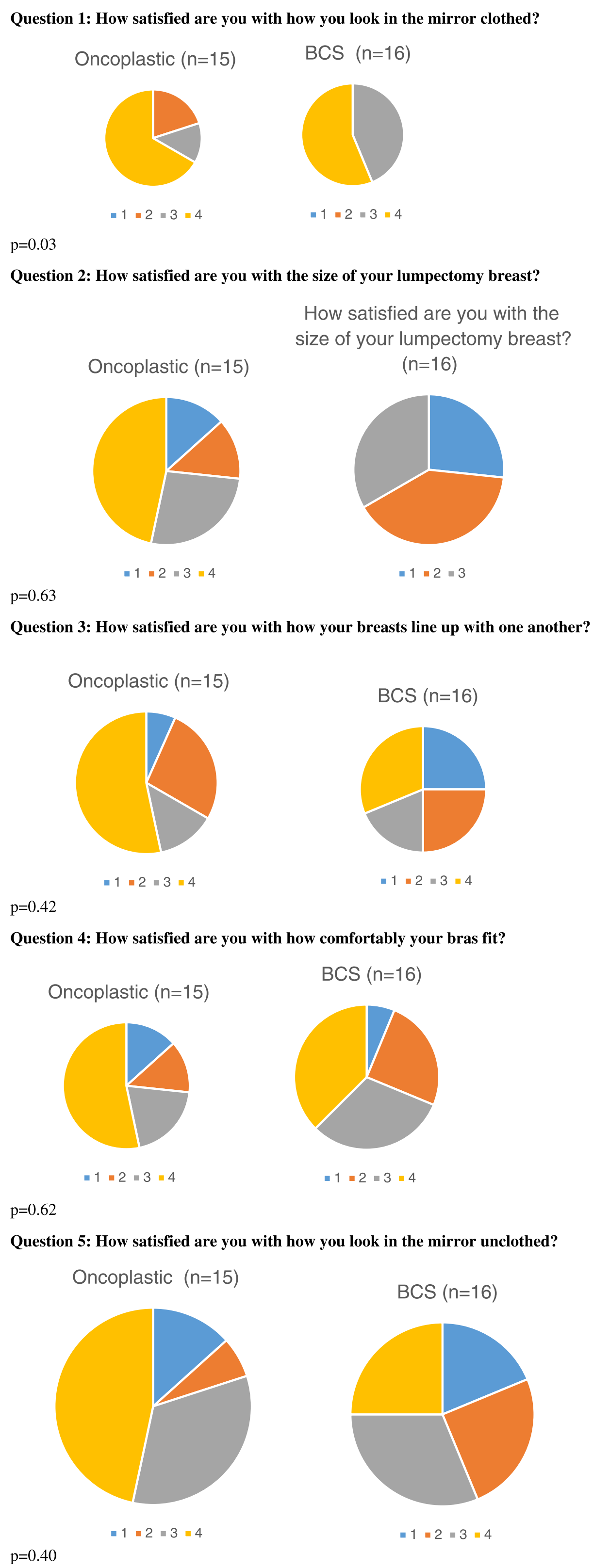

FIGURE 5. Patient satisfaction results. 1, very dissatisfied; 2, somewhat dissatisfied; 3, somewhat satisfied; 4, very satisfied.

established.[8] The OBCS patients tended to have a greater response to NT with a slightly greater average percent reduction in tumor size (69.5% vs 48.5%, $P = 0.26$), although, oncoplastic patients had larger resections (152.3 g vs 70.8g, $P = 0.012$). It is unclear why these patients may have responded to a greater degree despite similar molecular subtypes and treatment. As a result, tumor sizes were relatively similar between the 2 groups at the time of surgery (1.54 cm vs 1.29 cm, $P = 0.28$).

Our results demonstrate similar oncologic outcomes for high-stage breast cancer patients treated with oncoplastic breast-conserving surgery as compared to breast conserving surgery alone. Positive margin rate, reexcision rate, completion mastectomy rate, local recurrence, metastasis and death rate were similar between the 2 groups. In addition, 5-year disease-specific survival was similar between the 2 groups. The oncologic safety of oncoplastic techniques has been well established for lower-stage breast cancers,[23] but its safety among higher-stage breast cancer patients, particularly after NT, has been less well studied.[12,13] Although we have a small study size, our results along with others suggest that oncoplastic reduction is a safe alternative after NT for high-stage breast cancer patients and should be further studied with larger sample sizes and longer follow-up.

One of the primary benefits of oncoplastic surgery is its demonstrated ability to improve patient cosmesis and satisfaction after surgical resection for breast cancer.[8,23] Oncoplastic reduction in particular has the added benefit of reducing macromastia and because it is often performed bilaterally can retain breast symmetry after lumpectomy. Unfortunately, as has been well documented, radiation after BCT can significantly alter cosmetic results of breast reconstruction,[24] and many of our patients noted that radiation similarly negatively impacted the cosmesis of their breast after either surgery through the development of skin fibrosis, arm lymphedema, and change in the size of the radiated breast. However, in general, based on the answers to the BREAST-Q, patients who underwent oncoplastic reduction appeared more likely to be satisfied with the comfort, appearance and size of their breast compared with the patients who underwent breast conservation therapy alone.

Our study is limited to a small, retrospective review of patients whose surgery was chosen based on Medical Doctor/patient preference rather than randomization. To further evaluate the impact of oncoplastic surgery oncologic outcomes, larger prospective randomized studies with longer follow-up are needed.

CONCLUSIONS

Our results suggest that oncoplastic reduction is an oncologically safe alternative to breast-conserving surgery alone with the potential for superior patient cosmesis and satisfaction for high stage breast cancer patients after NT. Furthermore, oncoplastic reduction paired with NT appears to be able to broaden the indication for breast-conserving surgery for higher-stage patients with larger tumor sizes who would otherwise require mastectomy.

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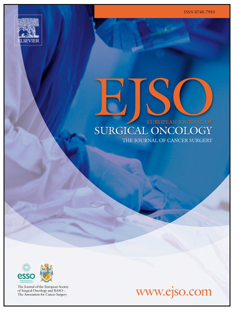
Accepted Manuscript



Objective decision making between conventional and oncoplastic breast-conserving surgery or mastectomy: an aesthetic and functional prospective cohort study

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PII: S0748-7983(16)31004-6

DOI: 10.1016/j.ejso.2016.11.010

Reference: YEJSO 4532

To appear in: *European Journal of Surgical Oncology*

Received Date: 10 July 2016

Revised Date: 12 October 2016

Accepted Date: 1 November 2016

Objective decision making between conventional and oncoplastic breast-conserving surgery or mastectomy: an aesthetic and functional prospective cohort study.

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Abstract

Background: Breast-conserving surgery (BCS) is considered the standard treatment for early-stage breast cancer. However, fair to poor cosmetic outcomes following conventional BCS have been observed in as many as one-third of cases. The aim of this study was to determine the critical tumor-to-breast volume ratio for each quadrant of the breast beyond which conventional BCS would no longer offer acceptable cosmetic and functional results or satisfactory quality of life for the patient.

Methods: A prospective cohort study was performed between December 2011 and December 2013 involving 350 patients younger than 70 years with early-stage unifocal (T≤30 mm) breast cancer who underwent wide excision and axillary sentinel lymph node biopsy followed by whole-breast irradiation. Using validated panels and software (the Breast Cancer Treatment Outcome Scale [BCTOS], EORTC Cancer Quality of Life Questionnaire number C30-BR23, and Breast Cancer Conservative Treatment - cosmetic results [BCCT.core] software), quality of life and aesthetic and functional parameters and their changes in correlation to the percentage of breast volume excised were statistically analyzed.

Results: The maximum percentages of breast volume that were resectable by conventional BCS without resulting in unacceptable aesthetic and functional outcomes or decreased quality of life were 18-19% in the upper-outer quadrant ($p<0.0001$), 14-15% in the lower-outer quadrant ($p<0.0001$), 8-9% in the upper-inner quadrant ($p<0.0001$), and 9-10% in the lower-inner quadrant ($p<0.0001$).

Conclusion: Aided by the calculated cut-off values for each breast quadrant, breast surgeons might render more objective decisions regarding performing conventional BCS, using oncoplastic techniques or choosing mastectomy with immediate reconstruction.

Keywords: breast-conserving surgery, oncoplastic surgery, mastectomy

Introduction

Breast-conserving surgery (BCS) and adjuvant whole-breast radiotherapy (WBRT) constitute the gold standard for the vast majority of patients with early-stage breast cancer.[1, 2] The main goal of BCS is the resection of the tumor with adequate surgical margins while achieving a satisfactory cosmetic result and preserving glandular function. Good aesthetics have been associated with better psychological recovery and improved quality of life.[3-8] The use of BCS began approximately three decades ago; since then, extensive experience has shown that fair to poor cosmetic outcomes following conservative BCS and WBRT are observed in as many as one-third of treated cases.[9-13]

The main reason for significant breast deformities following conventional BCS is the large volume of the resected specimen relative to the total breast volume; moreover, the location of the excision in the different breast quadrants further increases the correlation between the resected volume and a poor cosmetic outcome.

The inner quadrants are well known for being more sensitive than the outer upper quadrants to the same excised volume.[9-13] Oncoplastic breast-conserving surgery (OPS) or certain types of mastectomy with immediate reconstruction are potential solutions for these challenges; however, determining the optimal surgical method in these cases is subjective and based on experience, with few objective indicators to support this decision-making process.

This study aimed to determine the maximal tumor (specimen with wide excision)-to-breast volume ratio in each breast quadrant beyond which conventional BCS may no longer offer acceptable aesthetic/functional results or a satisfying quality of life for the patient.

Patients and methods

This prospective cohort study (ClinicalTrials.gov, Identifier: NCT01496001) was performed between December 2011 and December 2013 and involved 350 female patients with early-stage, solitary, unilateral (T≤30 mm) breast cancer. The exclusion criteria were as follows: pregnancy, age older than 70 years, a history of breast or axillary surgery, centrally localized tumors, indications for mastectomy due to clinical status, subjective or objective breast asymmetry prior to surgery, more than 5% body weight loss or gain in the 12 months after the surgery, histological results requiring completion of the surgery or histological results not indicating radiotherapy (RT). This study has been approved by the institutional research ethics committee and have been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Surgical technique and adjuvant RT

Each patient underwent a wide local excision and axillary sentinel lymph node biopsy.
All of the analyzed cases underwent WBRT, with an overall dose of 50 Gy and external beam, 6-MV photon irradiation, and, in 63 cases, the administration of an additional 16 Gy of tumor bed boost irradiation.

Assessment methods

Subjective aesthetic and functional factors were recorded using the internationally validated Breast Cancer Treatment Outcome Scale (BCTOS), which includes 22 items. Patients were instructed to rate each item on the BCTOS questionnaire on a four-point scale to evaluate the differences between the treated and untreated breasts.[14] The value of the score on each scale is the mean of the ratings for all of the items belonging to that scale.[15] A higher score reflects a poorer status (i.e., a greater difference between the treated and untreated breasts). If the subjective aesthetic and functional results rated by the patients had average scores of 2 or more, the results were considered unacceptable.

The EORTC Quality of Life Questionnaire was validated in Hungarian and used to measure the quality of life of breast cancer patients. Selected scales were used in the QLQ-C30 questionnaire, including social functioning, which consisted of 2 items, and emotional functioning, which consisted of 4 items. The scale for body image from the QLQ-BR23 questionnaire also consisted of 4 items. Potential scores range from 0 to 100, with a higher score indicating a higher prevalence. For example, a higher score for emotional functioning predicts a better quality of life, whereas a higher score for a symptom-related scale represents a higher level of symptomatology.[16] The functional factors with scores of 50 or less and the symptomatic scales with scores of 50 or more were considered to indicate an unacceptable quality of life.

To exclude subjectivity, the aesthetic results were classified objectively based on photo documentation using the Breast Cancer Conservative Treatment-cosmetic results (BCCT.core) software (version 20).[17] BCCT.core software provides an extensive set of automated measurements using digital marks to establish a 4-point classification scale (excellent, good, fair and poor) and the overall assessment of cosmetic outcomes **(Figure 1)**.[18, 19] Digital frontal photographs of the breasts were obtained from all of the patients in a standardized manner by a single photographer using a Nikon D3200, 24.2 megapixel digital camera. Objective aesthetic results classified as fair or poor by the BCCT.core software were considered unacceptable.

MRI (magnetic resonance imaging) of the breast was performed to document the oncological status and to calculate the contralateral breast volume. The breast MRI-volume calculations were performed at the GE AW 4.6 workstation, using the T1 FS or STIR sequences of the images. The non-representative parts of the measured breast were manually excised and, following the setting of the threshold limit, the parts not forming the breast were removed from the remaining pixels. At the end of the process, the real volume of the breast was automatically calculated using the previously cited workstation's volume option. Then, the contralateral, non-tumorous breast volume was determined, to which the removed specimen volume from the tumorous breast was compared, thereby calculating the percentage of breast volume excised for each quadrant.

A limitation of this study was that only a single MRI scan was obtained at the time of the oncological staging, which was performed at the 12th postoperative month. The volume of the contralateral, non-malignant breast was assessed at that time. Therefore, the exclusion criteria were a preoperative objective aesthetic classification not scaled as excellent (i.e., >10% asymmetry between the breasts) based on the preoperative photos by BCCT.core, any asymmetry subjectively observed as evaluated by a committee of 3 breast surgeons, and a >5% weight loss or gain occurring between the preoperative and postoperative 12-month time period prior to the MRI volume assessment.

The excised specimen weights and 3-dimensional diameters were measured.

Assessment time points

Following BCS, the excised specimen weights and 3-dimensional diameters were measured.

The subjective aesthetic and functional factors, quality of life and objective aesthetic factors were recorded at three different times: preoperatively, at the 4th postoperative week following the BCS and at the 12th postoperative month following the adjuvant RT.

MRI was performed at the 12th postoperative month.

Statistical methods

A descriptive statistical analysis was performed to determine the mean and median values of the patients' ages, breast volumes, and percentages of breast volume excised.

The current literature indicates that breast density ranges from 0.8-1.2 g/cm^3. [20, 21] According to the study of Parmar et al., no significant difference exists between the volume and the weight of the excised specimens. They observed the breast density to be 1.07 and 1.06 g/cm^3.[22] For the specimen weight measurements in the present study, the mean breast density value of 1 g/cm^3 was used. To evaluate the excised percentage of the breast volume in each case, the specimen weight was used for comparison to the non-malignant breast volume measured by MRI at the 12th postoperative month; thusly, the percentage of breast volume excised for each quadrant was calculated. According to the NSABP-06 trial, the specimen shape after a wide excision is considered a sphere.[23, 24] Utilizing the same formula ($V = \frac{4}{3}\pi r^3$) used by Cochrane et al. in 2003,[25] the specimen volumes (cm^3) were calculated. The correlation between the weight of the specimens and the volume of the specimens was analyzed using Spearman's rank order correlation test using the mean breast density value (1 g/cm^3).

According to the results from the 4th postoperative week regarding the effects of conventional BCS, the correlations between the percentage of breast volume removed and quality of life, subjective aesthetic and functional factors and objective aesthetic factors were examined using a Spearman's Rho statistical analysis.

The correlations between the percentage of breast volume excised and the specimen weight, as well as the clinical tumor size, were verified using a Kruskal-Wallis statistical analysis. Using receiver operating characteristic (ROC) curves, the maximal percentage of removable volume of each breast subregion was determined to obtain the maximal sensitivities and specificities regarding quality of life, subjective and functional results, and objective aesthetic results.

From the 4th postoperative week until the 12th month after BCS, the impact of the adjuvant RT on quality of life, subjective aesthetic and functional results, and objective aesthetic results were assessed using Friedman's ANOVA. Patient homogeneity was analyzed using a Mann-Whitney test by dividing the patients into two subgroups: the boost (n=63) and no boost (n=137) groups. To determine the median (min-max) values of the subjective aesthetic/functional factors, objective aesthetic factors, and quality of life (emotional functioning, social functioning, body image) in the 200 patients, the Wilcoxon signed-rank test was used.

Results

In total, 350 patients were enrolled in this study. One hundred fifty patients were excluded due to histological requirements for re-excision, mastectomy and/or axillary lymph node dissection (n=61), histological results not indicating RT (n=15), more than 5% body weight loss or gain (n=67), or voluntarily patient withdrawal (n=7). After the homogenization of the investigated population, the remaining 200 patients were statistically analyzed. The average age was 56 years (range: 32-70, median=58, r=8.068), and the mean breast volume was 625.22 cm^3 (range: 180-1950, median=550, r=305.656). The average percentage of breast volume excised was 14.73% (range: 2.72-40.81, median=13.20, r=7.27), and the average weight of the excised specimens was 85.58 g (range: 20-290, median=75.000, r=52.320). Regarding the breast cancer staging characteristics of the patients, 15 women were pTispN0(sn), 132 were pT1a-cpN0(sn), 44 were pT2pN0(sn), 3 were pT0-1pN1mi(sn), 5 were pT3pN0(sn), and 1 was pT2pN3c. The mean pathological tumor size was 15 mm (range: 2-50 mm).

Following BCS, all patients underwent WBRT, and 63 received additional boost irradiation. In total, 174 patients received adjuvant endocrine therapy, 33 patients underwent adjuvant chemotherapy (6 cycles of FAC or FEC), and 34 patients underwent adjuvant biological therapy. The effects of these therapies on quality of life and on aesthetic and functional factors were not further investigated.

According to the results from the 4th postoperative week on the effects of conventional BCS, an increase in the percentage of breast volume excised resulted in quality of life changes, such as significant deteriorations in social functioning ($r=0.649$, $p<0.0001$), emotional functioning ($r=0.623$, $p<0.0001$), body image ($r=0.771$, $p<0.0001$), and effects on subjective aesthetic and functional factors ($r=0.623$, $p<0.0001$) and objective aesthetic factors ($r=0.684$, $p=0.0001$) **(Figure 2)**. A significant correlation was found between the weight and the volume of the excised specimens ($r=0.54$, $p=0.023$).

A significant correlation was found between the increase in specimen weight and the percentage of breast volume excised ($r=0.568$, $p<0.0001$). The same correlation was found between clinical tumor size and the percentage of breast volume excised ($r=0.400$, $p=0.0015$). With the clinical tumors divided into 5 subgroups according to their sizes, the average weight of the excised specimen was determined for each subgroup, as shown by the following data: 5-9.5 mm: 66.12 g, 10-14.5 mm: 73.60 g, 15-19.5 mm: 89.54 g, 20-24.5 mm: 95.00 g, and 25-30 mm: 137.65 g.

From the removal of the clinical tumors (sizes: 5-9.5 mm, 10-14.5 mm, 15-19.5 mm, and 20-24.5 mm), a trend was found between the clinical tumor size and the excised specimen weight. Tumors between 25 and 30 mm in diameter resulted in significantly greater specimen weight loss (137.65 g on average) than did smaller tumors (p=0.0013). Based on ROC curves, the maximal percentage of removable volume of each breast subregion was determined **(Table 1)**.

Table 2 shows the median values of patient satisfaction regarding the quality of life, the subjective aesthetic/functional results and the objective aesthetic outcome at the 4th postoperative week and at the 12th postoperative month following adjuvant RT.

Regarding the boost (n=63) and no boost (n=137) groups, no significant difference was observed in the subjective aesthetic/functional results (p=0.11), objective results (p=0.19) or quality of life (emotional functioning [p=0.33], social functioning [p=0.42], body image [p=0.54]). This finding underscores the rationale for considering these two groups as one group (patients underwent adjuvant RT irrespective of receiving boost irradiation).

Assessing the impact of adjuvant RT from the 4th to the 12th postoperative month after BCS, a significant deterioration was found in the subjective aesthetic and functional factors (p=0.00013) and in the objective aesthetic parameters (p=0.00013), whereas a statistical correlation between quality of life and RT was not verified.

Discussion

A major drawback of BCT is the occurrence of unfavorable cosmetic results, which has been found in up to 33% of patients.[9-12] The volume of tissue excised is the most important factor relating to cosmetic outcome.[26, 27] Other factors influencing the final aesthetic results are the patient's age,[28, 29] BMI,[30] breast size,[31] tumor location,[32, 33] tumor size,[33] incision placement,[30, 31, 34, 35], type of conservation surgery (quadrantectomy or wide excision),[36] number of re-excisions,[26] chemotherapy[30, 33] and irradiation.[14, 33]

Recent studies have suggested a high risk of significant defects when 20% of the breast volume is excised,[37] whereas Stevenson et al. found that high risk correlated to the removal of >12% of the volume.[38] Cochrane et al. concluded that cosmesis and patient satisfaction were adversely affected when the estimated percentage of breast volume excised was >5% for medial tumors and >15% for lateral tumors.[25]

Studies on the point at which the aesthetic and functional results and the quality of life following conventional BCS are so poor that a woman might have been better served by OPS or mastectomy and reconstruction are relatively few and highly variable.

The aim of the present study was to determine the upper limit of the percentage of breast volume that could be excised before conventional BCS could no longer offer adequate cosmetic and functional results and a satisfactory quality of life.

This study shows that the percentage of breast volume excised was significantly correlated with cosmetic and functional outcomes and quality of life.

Our results show that conventional BCS did not result in unacceptable aesthetic or functional results or in a decreased quality of life when the percentage of the volume removed reached but did not exceed 18-19% in the upper-outer quadrant, 14-15% in the lower-outer quadrant, 8-9% in the upper-inner quadrant, and 9-10% in the lower-inner quadrant.

In cases involving a predictably larger volume loss than discussed above and in patients with medium or large breasts, oncoplastic BCS might be a better treatment choice than conventional BCS, whereas patients with small breasts might benefit from mastectomy and reconstruction **(Figure 3)**.

Breast-conserving surgeries were performed approximately equally among 8 general surgery specialists, which resulted in variability. Therefore, the expected specimen weight loss for a given sized tumor was determined, clarifying that the clinical tumor size may be a predictive factor of the aesthetic outcome for a given sized breast.

In general, physicians have considered cosmesis as either excellent or good in 55% to 94% of patients following RT (with a median follow-up of ≥3 years).[31, 34, 39, 40] In an older study by Harris et al.,[18] physicians rated the cosmetic results as good or excellent in 66% of patients following primary RT.

The current study also shows a significant deterioration in subjective and objective aesthetic results following RT. With conventional BCS, a relatively large residual open cavity may remain and may be filled with a hematoma or seroma, which notably worsen wound healing and may serve as a basis for adjuvant RT-enhanced fibrotic reactions.[41]

With oncoplastic techniques, no residual open cavity remains in the breast due to the mobilization of local dermoglandular flaps using different mastopexy techniques, thereby avoiding the aforementioned complications.

The limitation of the study was that at the 12th postoperative month, for financial reasons, only a single MRI scan was performed at the time of the oncological staging, the point at which the non-malignant breast volume was assessed as the comparator for the excised specimen weight. From the 4th postoperative week to the 12th month after BCS, the impact of adjuvant chemotherapy and endocrine and biological therapies on the subjective aesthetic/functional factors and the quality of life were not further investigated.

A strength of the study was the 12-month prospective evaluation based on objective (photo documentation, internationally validated computer program) and subjective (internationally validated questionnaires) measurements. The calculated cut-off values for each breast quadrant contribute more objective information to the literature, which may aid the preoperative decision-making process.

Conclusion

For a given breast, knowledge of the predictable volume loss due to tumor size and the ideal removable volume percentage of each breast quadrant may aid the surgeon in choosing an appropriate surgical technique to achieve acceptable aesthetic and functional results, thereby maintaining a sufficient quality of life. Our results reveal that when the resected volume is more than 10% of the entire breast volume in the inner quadrants and more than 15-19% of the volume of the outer quadrants, conventional BCS may not obtain acceptable or good aesthetic and satisfactory quality of life results after adjuvant RT.

Acknowledgments

The authors thank the Department of Surgical and Molecular Pathology, Radiological Diagnostics and Radiotherapy for providing data for the study.

Conflict of interest: The authors have no conflicts of interest to declare.

Financial Support: The study was performed at the National Institute of Oncology in Budapest, without special financial support.

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Figure captions

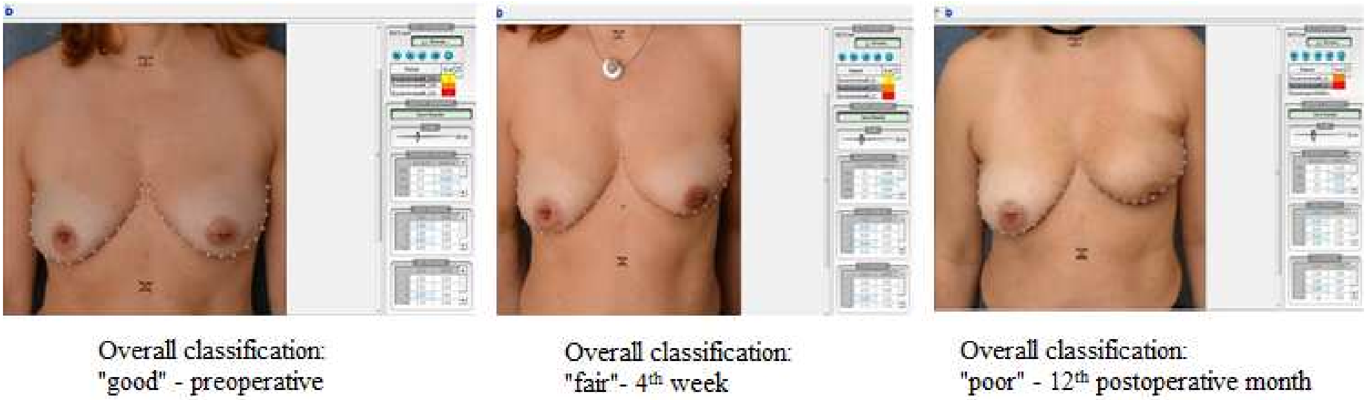

Figure 1. Examples of the classification of photographic images at 3 different times using BCCT.core software

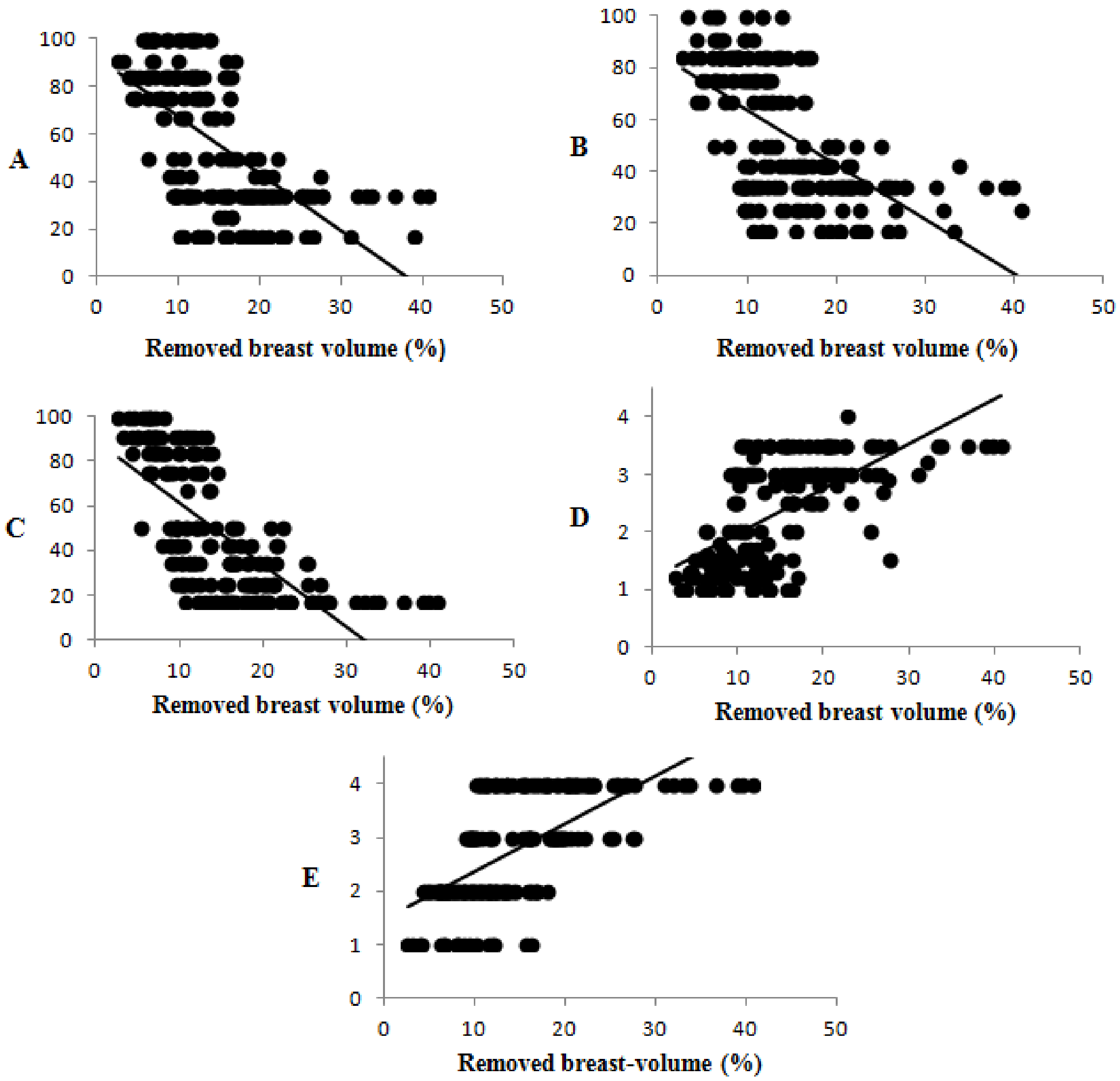

Figure 2. Significant deterioration was observed with an increase in the percentage of breast volume removed in relation to social functioning **(A)**, emotional functioning **(B)**, body image **(C)**, subjective aesthetic and functional results **(D)**, and objective aesthetic results **(E)**

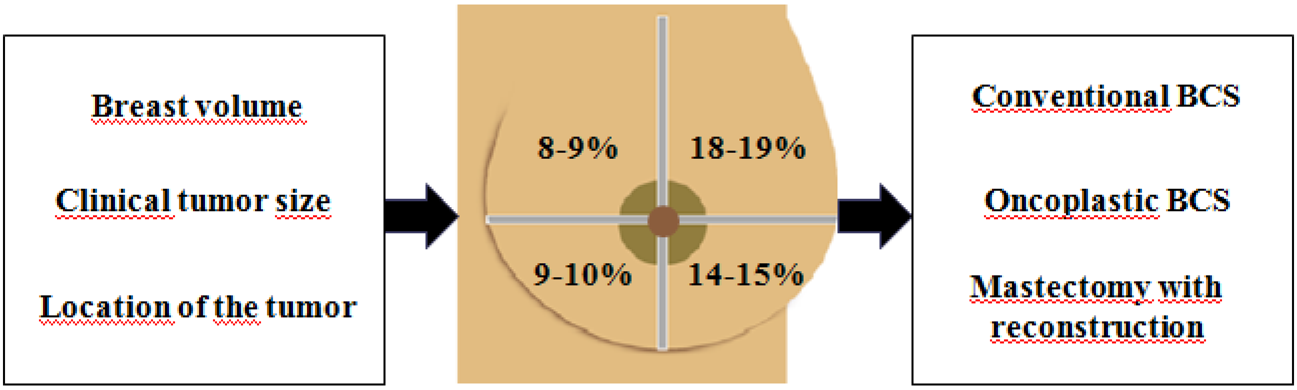

Figure 3. The algorithm used to determine the appropriate surgical strategy, considering the maximal volume of breast volume loss.

Tables

	Upper-outer quadrant (n=79)					Upper-inner quadrant (n=40)				
	Maximal cut-off value (%)	p	AUC	Sensitivity (%)	Specificity (%)	Maximal cut-off value (%)	p	AUC	Sensitivity (%)	Specificity (%)
Quality of life										
• ***Emotional functioning***	**18.26**	<0.0001	0.992	97.37	97.56	**9.48**	<0.0001	0.983	88.24	95.65
• ***Social functioning***	**17.56**	<0.0001	0.947	87.8	97.37	**9.48**	<0.0001	0.947	75	95
• ***Body image***	**18.85**	<0.0001	0.959	80	97.73	**8.88**	<0.0001	0.973	87.5	95.83
Subjective aesthetic and functional results	**18.76**	<0.0001	0.955	97.40	97.20	**8.88**	<0.0001	0.983	100	88.24
Objective aesthetic results	**18.26**	<0.0001	0.955	97.56	97.37	**8.88**	<0.0001	1	100	88.24

	Lower-outer quadrant (n=40)					Lower-inner quadrant (n=41)				
	Maximal cut-off value (%)	p	AUC	Sensitivity (%)	Specificity (%)	Maximal cut-off value (%)	p	AUC	Sensitivity (%)	Specificity (%)
Quality of life										
• ***Emotional functioning***	**15.5**	<0.0001	1	100	95.45	**9.23**	<0.0001	0.949	83.33	95.65
• ***Social functioning***	**16.07**	<0.0001	0.998	100	95	**9.53**	<0.0001	0.943	80.95	95
• ***Body image***	**15.5**	<0.0001	1	100	95.45	**8.90**	<0.0001	0.973	75	96
Subjective aesthetic and functional results	**14.51**	<0.0001	1	98	94.60	**9.65**	<0.0001	0.976	91.67	94.58
Objective aesthetic results	**14.11**	<0.0001	1	100	94.44	**9.53**	<0.0001	0.976	91.67	94.12

Table 1. The maximal percentage of volume that may be excised for each breast subregion.

	Postoperative 4th week (n=200)			Postoperative 12th month (n=200)			
	Median	Min.	Max.	Median	Min.	Max.	p
Quality of life							
• *Emotional functioning*	50.00	17.00	100.00	50.00	17.00	100.00	0.29
• *Social functioning*	67.00	17.00	100.00	67.00	17.00	100.00	0.56
• *Body image*	50.00	17.00	100.00	50.00	17.00	100.00	0.6
Subjective aesthetic and functional results	2.5	1	4	2.8	1	4	0.00013
Objective aesthetic results	2.4	1	4	2.7	1	4	0.00013

Table 2.

The median values of patient satisfaction regarding the quality of life, subjective aesthetic/functional results and objective aesthetic outcome at the 4th postoperative week and at the 12th postoperative month following adjuvant RT.

Higher scores for quality of life (range: 0-100) predict better quality of life.

Higher scores for subjective aesthetic/functional results and the objective aesthetic outcome (range: 1-4) reflect poorer status.

Original Article

Oncoplastic breast conserving surgery with tailored needle-guided excision

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Contributions: (I) Conception and design: F Hernanz; (II) Administrative support: None; (III) Provision of study materials or patients: F Hernanz, M González-Noriega, S Sánchez; (IV) Collection and assembly of data: M González-Noriega, L Paz, S Hermana; (V) Data analysis and interpretation: F Hernanz, P Muñoz; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Background: Breast conserving surgery (BCS) administered with oncoplastic approach (OBCS), when it is required, is currently the gold standard for the treatment of early breast cancer. Wire-guided localization (WL) is the most popular technique used to help surgeon in breast cancer excision. Currently, a universal and undeniable goal is to minimize the rate of positive margins and re-excision operation after BCS improving cosmetic outcome and decreasing health care costs. This study is aimed to report our experience combining OBCS and tailored WL as surgical approach for early breast cancers.

Methods: We performed a retrospective study on 148 breast cancer patients who were treated with OBCS and tailored WL, which consists in individualization of the number and location of wires depending on patient particularities, in our Breast Unit from March 2013 to December 2015. A multivariate analysis was used to determine the association between clinic-pathologic variables, which can be known preoperatively, and margin status.

Results: The rate of affected margins was 13.5% and 10.8% patients underwent re-interventions for oncologic reasons. Multifocality was strongly associated with involved margins [odds ratio (OR) 4.67].

Conclusions: OBCS together with tailored WL obtains an acceptable rate of positive margins and high rate of final BCS.

Keywords: Bracketing; oncoplastic breast surgery; surgical margins

Submitted Jun 04, 2017. Accepted for publication Jun 09, 2017.
doi: 10.21037/gs.2017.06.10
View this article at: http://dx.doi.org/10.21037/gs.2017.06.10

Introduction

Oncoplastic breast conserving surgery (OBCS) is the best option for early breast cancer aiming to achieve complete tumor excision with no involved surgical margins, which currently means "no ink on tumor" (1), and good objective cosmetic outcome. Many techniques are used to help surgeons to carry out a complete tumor excision, but needle-wired localization (WL), which is named "bracketing" when multiple wires are inserted, is one of the most commonly employed (2). We described our WL technique, which helps surgeons by marking the limits of the resection, inserting some wires 1 cm distance to radiological lesion limits, and by warning them of conflictive points which could compromise surgical technique (3).

There is a lack of publications about "bracketing" in the context of oncoplastic approach and some authors (4,5) have reported that the use of multiple needles (bracketing) to localize neoplasms was associated with higher positive margins than when a single needle was required.

We report our experience in the surgical treatment of early breast cancer combining OCBS and tailored WL and

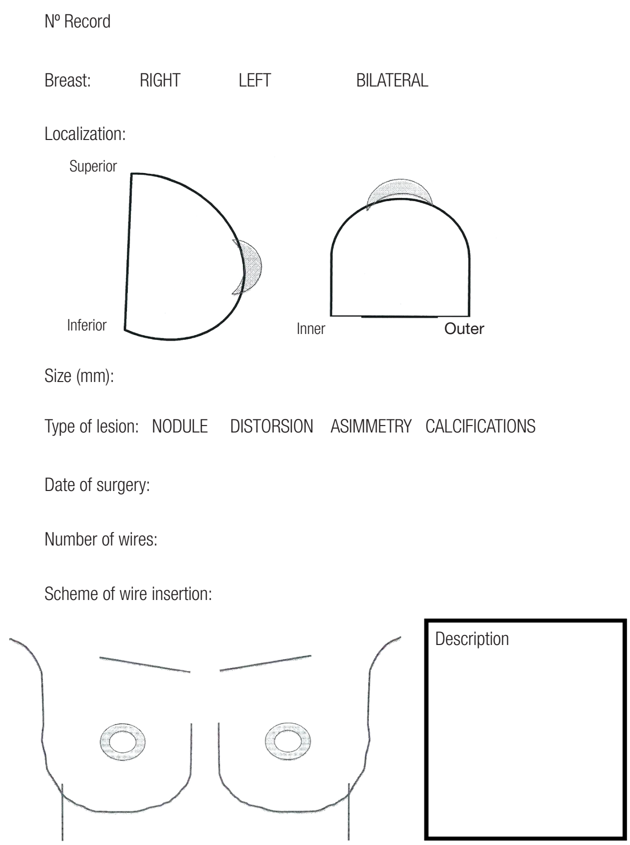

Figure 1 Drawing for planning tailored needle-guided localization.

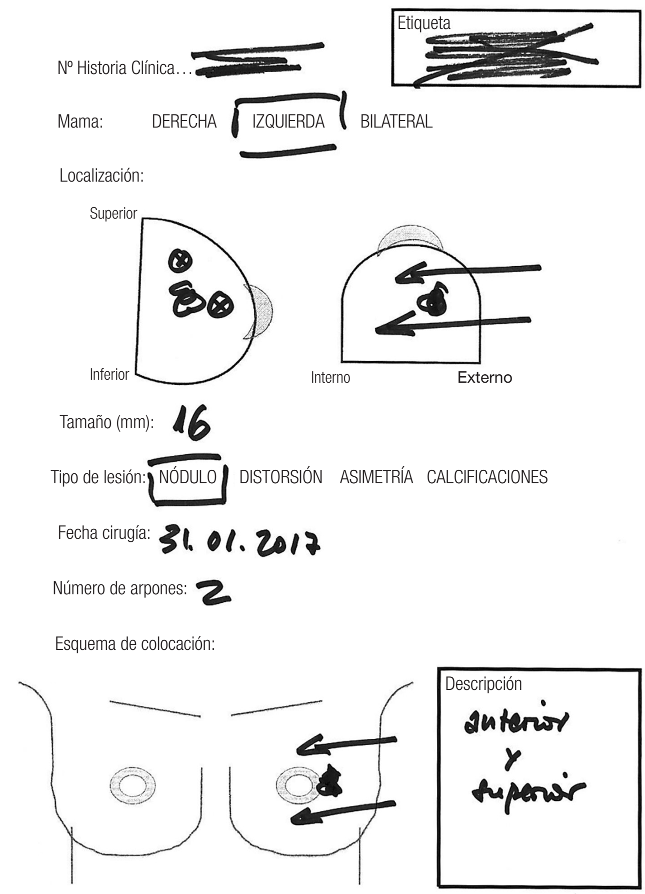

Figure 2 Planning wire localization. In a patient suffering from left breast carcinoma, a 16-mm nodule localized at the intersection of the outer quadrants, two wires were planning to be inserted laterally (anterior and superior).

the analysis of factors which are related to positive margins.

Methods

We reviewed the records of 148 patients with breast cancer who were treated with OBCS and WL in the Breast Unit of Hospital Valdecilla (Santander, Spain) from March 2013 to December 2015. At the Radiological Department, where all image data are available, the surgeon and radiologist decide and fill out the diagram (*Figures 1,2*) showing how many wires and where should be inserted. The diagram shows data concerning the affected breast, in which quadrant the lesion is located, the type of radiological lesion (nodule, distortion, microcalcifications and asymmetry), the maximum diameter of the tumor or the distance comprising the entire lesion to be removed, the day of the surgery, the number of wires and two drawings of lateral and craniocaudal mammograms where the location of the lesion and the situation of the wires can be drawn. The day of the surgery the diagram is used by the radiologist to insert the wires in the place and in the way agreed on. Wires can be inserted into the breast laterally or perpendicularly to the chest wall. This choice is mainly determined by the oncoplastic incision pattern to be used and the location of the lesion. For example, if we are going to perform a "diamond", "round block" or "batwing mammaplasty" incisions we prefer perpendicular insertions, whereas if we are going to carry out a therapeutic mammaplasty with an inverted T-incision pattern or "tennis racket" incision, a lateral insertion is preferred (*Figure 3*). However, the localization and the way in which the wires should be inserted are decided depending on the particularities of each case. In the diagram each path is drawn in a different way, lateral or perpendicular (←(x) respectively.

The number of wires used for localization was: 1 in 52 patients, 2 in 88, 3 in 7 and 4 in a patient with a bilateral cancer.

Figure 3 Wires inserted preoperatively. Appearance of the three breasts with inserted wires before surgery. Although each patient is tailored to their particularities, a lateral way is commonly used for "raquet" and reduction mammoplasty, and a vertical one for "round block" or "diamond" patter incisions.

All patients were operated on by two surgeons (Fernando Hernanz and Mónica González-Noriega) who planned and performed surgical procedures working together on the same patient most of the time. The resection was performed outside the wires and sticking to them, often two, which were located at two different points crossing orthogonally at the center of the lesion, so the surgeon had to calculate the limits of the resection by comparing the location of the two wires and thinking that they were 1 cm away from the radiological limits of the lesion (*Figure 4*). In patients with macromastia treated with therapeutic mammoplasty, as a large amount of breast tissue was removed, a wire was used to locate the lesion to avoid its being left in the breast.

After the resection was carried out, the surgical specimen was marked at superior and medial sides with some stitches (2 long and 1 short, respectively) in order to guide the pathologist, and then sent to the Radiological Department where two orthogonal digital mammograms were taken. The radiologist informed the surgeon whether the entire radiological lesion was included in the surgical specimen and if it was closed to any side. In this case, the surgeon shaved the close margin with a scalpel. Digital images of the surgical specimen could be visualized by the surgeon in the operating theatre to check the radiological margins status and to decide, with the radiologist's report, how to do margin extension. Before remodeling the breast, all four sides of the breast cavity were marked with titanium clips to facilitate radiation therapy.

Pathologic slides of the patients whose reports were informed as not having free margins in the breast tissue removed, were revised by a pathologist (MH) applying the "no ink on tumor" consensus guideline on margins for breast-conserving surgery published on March 2014 (1) because some cases had been evaluated before this criteria was released.

Statistical analysis

Firstly, we described the distribution of clinical and pathological variables in the series of patients. Secondly, we compared the distribution of categorical variables between two groups, with or without affected margins, with chi-square or Fisher tests and numerical variables with Mann-Whitney test. Lastly, Univariate and multivariate logistic regression analyses with the method enter were performed to test for association between clinic-pathologic variables and positive resection margins in 133 patients with invasive non bilateral breast cancer. Four variables were transformed: age (<50 or ≥50 years), radiologic tumor size (<20 or ≥20 mm) histologic subtype (lobular and no-lobular), and intrinsic subtype luminal B_Her2 and Her2 became one. In categorical variables the category with lower risk was considered to be the variable of reference. Analysis was performed with MedCalc Statistical Software version 17.4 (MedCalc Software BVBA, Ostend, Belgium;

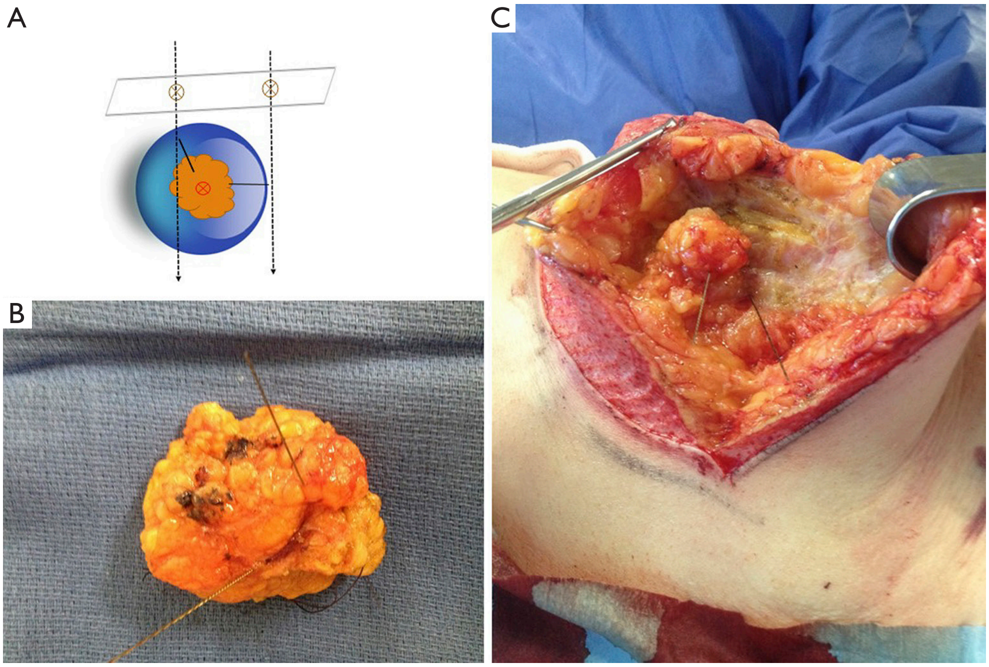

Figure 4 Wire-guided excision. (A) Sphere represents the ideal theoretical resection including the tumor or lesion with 1 cm ring of healthy breast tissue limited by wires; (B) the surgeon should estimate the limits of breast tissue resection according to the wires taking into account that they are localized 1 cm away from the lesion borders and their orthogonal lines crossing in the center of it. Surgical specimen with two inserted wires and two points in ink marked to perform the resection; (C) oncoplastic breast conserving technique a therapeutic mammaplasty with bipedicle flap to move nipple areola complex (close to forceps) showing the two inserted wires.

http://www.medcalc.org; 2017). A P value of >0.05 was considered statistically significant.

Results

Demographic characteristics of the patients are described in *Table 1*. Twenty patients had involved surgical margins (13.5%), 7 with invasive cancer, 11 with ductal carcinoma in situ (DCIS) component, and 2 both. Seventeen patients were re-operated on, 16 for oncologic reason (10.8%), 12 with affected margins having also 2 of them positive sentinel lymph node, and another 4 for positive sentinel lymph node. We performed 3 re-excisions, 9 mastectomies and 6 lymphadenectomies. The final rate of BCS was 94%. Five (41.6%) patients had residual cancer in the breast tissue and only two had more positive lymph nodes. A woman was operated on due to a surgical complication (hemorrhage). *Table 2* shows results of logistic regression analysis.

Discussion

The majority of our patients were referred from a breast cancer screening program so their ages were over 50 (average of 60); they were menopausal (91%) having non-palpable cancer with 8.8% of DCIS. Invasive cancer was most frequently luminal A and B (78%). Despite early diagnose, the radiological size average was 15 mm (9.9 SD), which had a very high correspondence with the pathological one, 15.8 mm (12.1 SD), and 20.3% had positive axillary lymph nodes. Therapeutic mammoplasty was the oncoplastic technique most frequently used with 37% of patients; in our opinion, this technique is very versatile and can be used in all quadrants on condition that the breast is medium or large-sized, or has enough degree of ptosis (6).

Bracketing comprises using two or more needles for localization of boundaries of an impalpable breast lesion. The tissue limited by them is excised and sent for histopathology. We introduce a slight modification which consists of using needles not only to localize the lesion, but also to mark the limits of the resection by inserting them at 1 cm distance to the radiological limits with the purpose of performing an accurate resection with free radiological margins. Like Tardioli *et al.* (7), who coined the term "optimized wire-guided localization" and also treated their

Table 1 Patient and tumor characteristics of 148 patients undergoing OBCS with tailored WL

Variable	Number or mean	Percentage or SD
Age (years, mean and SD)	60	6.2
Menopausal	135	91.2
Affected breast		
Right	73	49.3
Left	73	49.3
Bilateral	2	1.4
Location of the lesion through the breast		
Upper outer quadrant	53	35.8
Inferior outer quadrant	3	2
Inner inferior quadrant	9	6.1
Inner upper quadrant	8	5.4
Central	9	6.1
Intersection of upper quadrants	27	18.2
Intersection of inferior quadrant	5	3.4
Intersection of outer quadrants	32	21.6
Intersection of inner quadrants	2	1.4
Multifocal	19	12.8
Radiological size of the lesion (mm, mean and SD)	15	10
DCIS	13	8.8
Histologic subtype		
Ductal	107	72.3
Lobular	13	8.8
Mixed	10	6.8
Papillar	6	4.1
Tubular	5	3.4
Others	7	4.7
Intrinsic subtype (only invasive)		
Luminal A	68	49.6
Luminal B	39	28.5
Luminal_Her2	12	8.8
Triple negative	11	8
HerB2	7	5.1
Incision pattern		
Wise or inverted	55	37.2
Raquel or lateral	26	17.6
Omega or batwing	4	2.7
Round block	17	11.5
Parallelogram or diamond	21	14.2
Others	25	16.8
Pathological size of the lesion (mm, mean and SD)	15.7	12.14
Positive lymph nodes (axillary)	30	20.3

SD, standard deviation; DCIS, ductal carcinoma in situ.

Table 2 Univariate and multivariate analysis of 133 patients with no bilateral invasive cancer

Variable	Total (%)	Free margins (%)	Positive margins* (%)	P, OR, 95% CI	
				Univariate	Multivariate
Age (years)				0.930, 0.91, 0.11–7.84	0.831, 0.76, 0.06–9.58
<50	8 (6.0)	7 (8.1)	1 (5.6)		
≥50 (reference)	125 (94.0)	108 (89.6)	17 (94.4)		
Multifocality				0.003, 5.46, 1.78–16.75	0.019, 4.67, 1.29–16.85
Yes	19 (14.3)	12 (10.4)	7 (38.9)		
No (reference)	114 (85.7)	103 (89.6)	11 (61.1)		
Lobular histologic subtype				0.213, 2.07, 0.66–6.53	0.54, 1.54, 0.38–6.19
Yes	23 (17.3)	18 (15.7)	5 (27.8)		
No (reference)	110 (82.7)	97 (84.3)	13 (72.2)		
Radiological tumor size (mm)				0.170, 2.07, 0.73–5.88	0.637, 1.38, 0358–5.35
<20 (reference)	99 (74.4)	88 (76.5)	11 (61.1)		
≥20	34 (25.6)	27 (23.5)	7 (38.9)		
Intrinsic subtype					
Luminal A (reference)	68 (51.1)	61 (53.0)	7 (39.9)		
Luminal B	39 (29.3)	31 (27.0)	8 (44.4)	0.150, 2.25, 0.75–6.77	0.105, 2.82, 0.80–9.89
Luminal_Her2 + HerB2	16 (12.0)	13 (11.3)	3 (16.7)	0.355, 2.01, 0.46–8.83	0.645, 1.50, 0.27–8.28
Triple negative**	10 (7.5)	10 (8.7)	0 (0.0)		
Number of wires				0.037, 2.80, 1.06–7.35	0.216, 2.03, 0.66–6.26
1	48 (36.1)	44 (38.3)	4 (22.2)		
2	79 (59.4)	68 (59.1)	11 (61.1)		
3	6 (4.5)	3 (2.6)	3 (16.7)		
Positive axillary lymph nodes				0.51, 1.46, 0.47–4.49	0.95, 0.96, 0.26–3.55
Yes	29 (21.8)	24 (20.9)	5 (27.8)		
No (reference)	104 (78.2)	91 (79.1)	13 (72.2)		

P<0.05 statistic significant. *, positive margins definition as no ink on tumor; **, triple negative intrinsic subtype was exclude of univariate or multivariate analysis because there is not case with affected margins. OR, odds ratio; CI, confidence interval.

patients with oncoplastic techniques, we consider essential discussing with the radiologist the number of wires, the point and the way they should be inserted, taking into account the particularities of each case (type of radiological lesion, localization through the breast, incision patterns and OCBS technique, histological type of the tumor) tailoring the surgical approach for each patient.

Another modification is used when the oncoplastic technique requires NAP mobilization by a flap and the tumor is localized in retroareolar region. In this case, we use wires to warn the surgeon of conflictive points, such as retroareolar space, with the aim to preserve an appropriate width of the flap and get a complete tumor excision. WL is very common and it is available in almost every center. However, it has some disadvantages. It is time-consuming and disturbs and hurts patients.

We obtained a 13.5% rate of involved surgical margins by combining our tailored WL and an oncoplastic approach. This approach allows the resection of a large amount of breast tissue without compromising cosmetic outcome and which avoids dislocation of wires or their accidental section because tunneling is easier than conventional techniques. This rate is lower than others recently published, which analyzed large series of patients from population registers and similar to others OBCS series.

van Deurzen CHM (8) reported a 16.8% rate of affected margins in a population-based cohort study with data from The Dutch Pathology Register between 2009 and 2015, which consisted of a huge number of patients suffering from an invasive breast cancer [25, 315] who were treated by BCS. The multivariate logistic regression analysis found that multifocal location, lobular subtype, large tumor size and the presence of DCIS were strongly associated with involved margins [odds ratio (OR) >2].

Langhans (9) reported a positive margins rate and reoperation (17.6%) using wire-guided BCS in invasive and *in situ* ductal carcinomas in a large series of patients (4,118 women) analyzing data from Danish National Patient Registry during a period of 4 years (2010 to 2013); they found that DCIS increases the risk of affected margins 3 times over invasive cancer.

Haloua *et al.* (10) reported a 16.4% rate of involved surgical margins after BCS in a study which collected data from a Netherland network from 2012 (9,276 pathology excerpts). Laws *et al.* (11) communicated an overall positive margin rate of 20.8% in 1,165 patients from a database which captures 95% breast surgeries in Alberta (Canada).

Since the end of 1900s, when oncoplastic approach began, it has been spreading over breast units, and it has increased notably in the last decade; as an example of this, Carter *et al.* (12) state that the use of oncoplastic breast surgery experimented a nearly fourfold increase in the percentage of all breast cancer surgeries during the study period (2007 to 2014) in a single center study comprising 10,607 operations; 75% of the patients had an early cancer (T1 or T2 tumor) and the rate of positive or close margins was lower for oncoplastic techniques than conventional ones (5.8% *vs.* 8.3%).

Although it is really certain that OBCS allows carrying out a wide resection with a small alteration of breast cosmetic outcome, and consequently the rate of affected margins is lower than conventional BCS (13-15), there are many different techniques and their application is not uniform with a heterogeneous patient selection. Therefore, articles about OBCS are assorted and show a great variation of involved surgical margins rate (0 to 36%) (16,17).

Fitoussi *et al.* (18) in a large series of 540 patients who were treated with oncoplastic techniques using both volume replacement and displacement ones, obtained 18.9% of close or affected surgical margins with a 9.4% mastectomies. Clough (19), one of the pioneers of oncoplastic approach, in a total of 277 level II oncoplastic techniques performed on 272 patients, reported a rate of 11.9 % positive margins with invasive lobular carcinoma as a variable with higher risk of positive margins.

De la Cruz *et al.* (20) reviewed eleven articles on OBCS comprising 1,455 patients and found a very low rate of 7.8% with "no ink on tumor criteria", thus confirming the oncological safety of these procedures in patients with early invasive breast cancer.

Some clinical-pathological variables which can be assessed before surgery by imaging and needle biopsy, such as invasive lobular histologic subtype, large tumor size, presence of DCIS or microcalcifications on mammography, number of wires, etc. have been related to the increase of involved margins in many different studies. In our work, only multifocality, which may be the most common, increased heavily the risk of positive surgical margins. However, conservative surgery was possible in 63% of the cases with multifocal tumors.

Conclusions

In our experience, tailored WL, which requires collaborative working with the radiologist, helps the surgeon to carry out a theoretic breast tissue resection at 1 cm distance to the radiological limits of the lesion increasing the chance of obtaining pathologic free margins. Combining both approaches we obtained an acceptable rate of involved surgical margins, which is in the lower band of the range of data published, and high final rate of BCS. According to our finding, surgeons should be aware of the great risk of affected surgical margins in multifocal breast cancer.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: Access to patient data was according to permission rules from the Admission Department and Archive of our hospital (Hospital "Marqués de Valdecilla", Santander) and patient confidentiality was rigorously preserved. Written informed consent was obtained from patients for publication accompanying images.

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Cite this article as: Hernanz F, González-Noriega M, Sánchez S, Paz L, Muñoz P, Hermana S. Oncoplastic breast conserving surgery with tailored needle-guided excision. Gland Surg 2017;6(6):698-705. doi: 10.21037/gs.2017.06.10

Oncoplastic Breast Reduction Technique and Outcomes: An Evolution over 20 Years

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Background: Reduction mammaplasty at the time of lumpectomy is a good option in women with breast cancer and macromastia. We critically evaluated refinements and outcomes of this technique.

Methods: A prospectively maintained database was reviewed of all women with breast cancer who received lumpectomy and reduction mammaplasty at our institution from 1994 to 2015. Patients' demographics were reviewed. Preoperative and postoperative patient satisfaction (BREAST-Q) was determined. Comparisons were made between early and recent cases.

Results: There were 353 patients included. Average age was 54 (range, 21 to 80 years), with the largest number having stage I disease [$n = 107$ of 246 (43.5 percent)]. Average lumpectomy specimen was 207 g (range, 11.6 to 1954 g) and total reduction weight averaged 545 g (range, 21 to 4102 g). Tumor size averaged 2.02 cm (range, 0.00 to 15.60 cm). The positive margin rate was 6.2 percent ($n = 22$). Completion mastectomy rate was 9.9 percent ($n = 35$). Overall complication rate was 16 percent. The recurrence rate was 5.2 percent ($n = 10$ of 192) at a mean follow-up of 2 years (range, 2 months to 15 years). Resection weights greater than 1000 g were associated with having a positive margin (16.7 percent versus 5.0 percent; $p = 0.016$), and tended to be associated with having a completion mastectomy ($p = 0.069$). Positive margin and completion mastectomy rates have been lower in the past 10 years. Over 1 year postoperatively, women reported increased self-confidence ($p = 0.020$), feelings of attractiveness ($p = 0.085$), emotional health ($p = 0.037$), and satisfaction with sex life ($p = 0.092$).

Conclusions: The oncoplastic reduction technique is effective and results in improved patient-reported outcomes. Resections over 1000 g are associated with a higher incidence of positive margins and may increase the risk for completion mastectomy. Outcomes have improved with experience and refinement in technique. (*Plast. Reconstr. Surg.* 139: 824e, 2017.)

The concept of performing partial breast reconstruction at the time of tumor resection for women with breast cancer who wish to undergo breast conservation therapy continues to gain acceptance and popularity. This is particularly true for the oncoplastic reduction approach because of its many documented benefits for women with breast cancer and macromastia.[1–3]

The oncoplastic reduction approach is not a new concept and has continued to broaden acceptance from breast surgeons and plastic surgeons alike. The initiation of this approach was met with some early resistance by breast cancer surgeons who were concerned about the oncologic safety of manipulating the breast architecture and the potential to impact radiation therapy, recurrence, or surveillance. As our collective experience has grown, we have continued to demonstrate safety equivalence in areas of surgical margins, patient selection, outcomes, and surveillance compared with breast conservation therapy alone. We are only now starting to report larger series in the literature with longer follow-up so that we can draw valid conclusions on variables such as recurrence and refinements in technique. The number of

From the Emory Division of Surgical Oncology.
Received for publication July 27, 2016; accepted September 16, 2016.
Presented at the 2016 Meeting of the Southeastern Society of Plastic and Reconstructive Surgeons, in Orlando, Florida, June 11 through 15, 2016.

DOI: 10.1097/PRS.0000000000003226

Disclosure: *Dr. Losken is a speaker for RTI. There are no other potential conflicts to report.*

publications on the topic continues to rise, and we are now discussing different related topics such as patient-reported outcomes, intraoperative radiation therapy, extreme oncoplastic techniques, autoaugmentation reduction techniques, longer term oncologic safety, margins, and surveillance.[4–8]

The purpose of this review was to evaluate indications and outcomes in our large series of oncoplastic reduction mammaplasties in women with breast cancer. The use of patient-reported outcomes measures will help us draw conclusions from the patient's perspective. Having followed patients over a 20-year period will also allow us to compare outcomes over time and discuss refinements in technique and approach to possibly improve outcomes.

PATIENTS AND METHODS

All patients from 1994 to 2015 who underwent partial mastectomy and immediate partial breast reconstruction using reduction mammaplasty at Emory University hospitals were included in this series. Approval from the Institutional Review Board of Emory University Hospital was obtained. Data were collected from a prospectively maintained database and electronic medical records and recorded in a Microsoft Excel database (Microsoft Corp., Redmond, Wash.). Patients were typically treated by a team approach with an extirpative surgeon and a reconstructive surgeon. The indications were determined by tumor size and location, tumor size–to–breast size ratio, breast size, potential for deformity, and the need for a generous resection. All patients underwent glandular manipulation with either a mastopexy or reduction technique. The type of reduction pattern and pedicle technique was dependent on the breast size and location of the tumor. Local or distant flap reconstructions of the lumpectomy defect were not included in this series. Patients were submitted for neoadjuvant or adjuvant chemotherapy, hormone therapy, and radiation therapy according to our institutional protocol.

Surgical, oncologic, radiologic, and pathologic records were analyzed for follow-up to determine outcomes. Patients were followed up every 6 months for screening mammography for the first 2 years, and then annually. Recurrences were determined by clinical examination, radiologic tests, and/or pathologic assessment. Major complications were those that required readmission or unplanned reoperation.

Demographics and Outcomes

Patient demographics queried included diagnosis, stage, risk factors, and procedural data points (e.g., type of procedure, reduction technique, weight of specimen). Outcome variables included complications, margin status, the need for revision surgery or completion mastectomy, and tumor recurrence. More recently, data regarding patient-reported outcomes and satisfaction were collected using a validated survey (BREAST-Q), which was given preoperatively and then at least 1 year postoperatively. A total scale score was then calculated through the QScore scoring software. This ranged from 0 to 100, with a higher score correlating with greater satisfaction.[9]

Comparisons

1. Outcomes: Outcomes including positive margin, completion mastectomy, local recurrence, complications, and patient satisfaction were evaluated to determine what risk factors were associated with these outcomes.
2. Period: A comparison was made between two time points to determine whether the outcomes improved over the course of the series. An arbitrary time point of 2010 was used as the cutoff and comparisons were made between 101 patients before 2015 and 192 patients after 2010.

Pearson chi-square and Fisher's exact tests were used for all categorical data comparisons as appropriate. The *t* test and analysis of variance were used for continuous data comparisons. Continuous variables were described as mean ± SD. Multivariate logistic regression adapted adjusted for clinical characteristics (i.e., body mass index, smoking, indication for reconstruction) and postoperative complications (i.e., infection, seroma, inframammary fold problems, capsular contracture, mechanical shift, bottoming-out, rippling, and wound problems) using a logistic regression model. A value of $p < 0.05$ was considered statistically significant for all comparisons. Adjusted odds ratios and 95 percent confidence intervals were reported for the multivariate results. Statistical analyses were performed using IBM SPSS Version 23.0 (IBM Corp., Armonk, N.Y.).

RESULTS

Demographics

A total of 353 patients who underwent an oncoplastic reduction had sufficient data to be included in the series. The average age was 54 years (range, 21 to 80 years), with the majority having a body mass index greater than 30.0 kg/m^2 [$n = 219$ (62.3 percent)]. The average body mass index was 33.7 kg/m^2 (range, 19.6 to 60 kg/m^2). The majority of patients on final pathologic evaluation had infiltrating ductal or lobular carcinoma [$n = 215$ (60.9 percent)]. Stage I disease was the most common [$n = 107$ (43.5 percent)] (Table 1) and wire localization was required in 260 (73.4 percent) (Fig. 1). Ninety-three percent of patients with breast cancer had postoperative irradiation.

Intraoperative Details

The majority of patients had an axillary procedure [sentinel node biopsy, $n = 222$ (62.9 percent); axillary node dissection, $n = 30$ (8.5 percent)] at the time of tumor removal (Table 1). The average lumpectomy specimen weighed 207 g (range, 11.6 to 1954 g) and total reduction weight averaged 545 g (range, 21 to 4102 g). The average contralateral specimen weighed 586 g (range, 0 to 3217 g). The ipsilateral and contralateral pedicle types are shown in Table 2. Tumor size averaged 2.02 cm (range, 0.00 to 15.60 cm). The positive margin rate was 6.2 percent ($n = 22$) and the average distance to the closest margin was 0.51 cm (range, 0.00 to 5.0 cm).

Univariate Analysis

Total resection weight greater than 1000 g was associated with having a positive margin (27.3 percent versus 9.1 percent; $p = 0.016$) and with having a completion mastectomy ($p < 0.0001$). Patients with larger biopsy size, larger tumor size (>2.00 cm), and estrogen receptor positivity were more likely to have positive margins (Table 3). Patients with in situ disease on final pathologic evaluation had a 10.3 percent positive margin rate (eight of 78) compared with 6.0 percent for those with invasive disease (13 of 215). There was no difference in the incidence of complications between the patients with positive or negative margins.

Multivariate Analysis

Multivariate logistic regression analysis revealed that tumor size greater than 2.00 cm (OR, 4.896; 95 percent CI, 1.286 to 18.648) and total ipsilateral specimen weight of greater than 1000 g (OR, 4.638; 95 percent CI, 1.260 to 17.079) were associated with positive margins (Table 4).

Table 1. Clinical and Demographic Characteristics for the Entire Cohort

Characteristic	Value (%)
No. of patients	353
Age, yr	
Mean	54.0
Range	21.0–80.0
Age > 50 yr	231 (65.4)
BMI, kg/m^2	
Average	33.7
Range	19.6–60.2
BMI >30 kg/m^2	219 (62.3)
Final pathologic assessment	
IDC/ILC	215 (60.9)
DCIS/LCIS	78 (22.1)
Benign	60 (17.0)
Margin status	
Positive	22 (6.2)
Negative	331 (93.8)
Axillary procedure	
None	101 (28.6)
SLNB	222 (62.9)
ALND	30 (8.5)
Type of excision	
Wire localization	260 (73.4)
Excisional biopsy	86 (24.3)
Stage	
0	70 (28.5)
I	107 (43.5)
II	50 (20.3)
III	17 (6.9)
IV	2 (0.8)
Ipsilateral biopsy weight, g	
Mean	207
Range	11.6–1954
Ipsilateral total specimen weight, g	
Mean	545.4
Range	21.0–4102.0
Ipsilateral specimen >1000 g	36 (10.2)
Preoperative chemotherapy	74 (21.0)
Hormone therapy	217 (61.5)
Radiotherapy	270 (76.5)
Average margin distance, cm	0.51
Completion mastectomy	35 (9.9)
Follow-up time, days	
Mean	578.5
Range	29–5509

BMI, body mass index; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection.

Completion Mastectomy

Completion mastectomy occurred in 35 patients (9.9 percent). The diagnosis in those 35 patients who required completion mastectomy was ductal carcinoma in situ (40 percent), invasive ductal carcinoma (40 percent), and other (20 percent). On univariate analysis, as

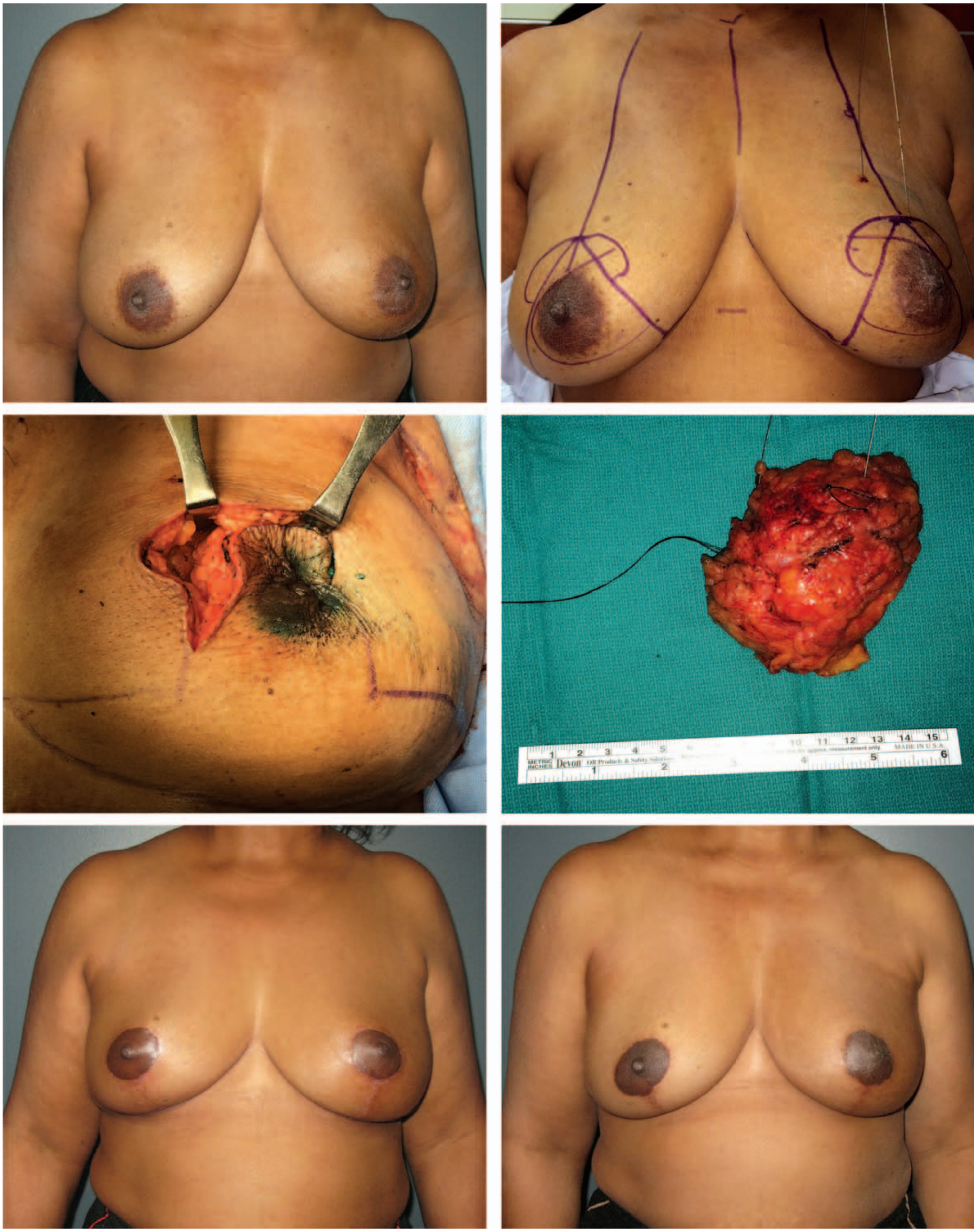

Fig. 1. (*Above*, *left*) A 34-year-old woman with macromastia and left breast cancer. (*Above*, *right*) She had the tumor bracketed in the upper central quadrant and a superomedial Wise pattern drawn out. (*Center*) The 75-g specimen and defect is shown above the nipple-areola complex. (*Below*, *left*) She is shown 1 month postoperatively after a bilateral inferior pedicle with 450 g removed from the right side and a total of 400 g removed from the left side (including the tumor specimen). The inferior pedicle technique was chosen after evaluating the tumor defect. (*Below*, *right*) Her result is shown 1 year after completion of radiation therapy.

expected, having a positive margin was associated with having a completion mastectomy ($p < 0.0001$). In the multivariate model, completion mastectomy was associated with a lower body mass index (OR, 0.864; 95 percent CI, 0.753 to 0.992) and ipsilateral specimen weight greater

Table 2. Reduction Mammaplasty Pedicle Type

	No. (%)
Ipsilateral pedicle	
Superomedial	160 (47.3)
Inferior	91 (26.9)
Superior	23 (6.8)
Superolateral	17 (5.0)
Central	21 (6.2)
Amputation	22 (6.5)
Lateral	4 (1.2)
Contralateral pedicle	
Superomedial	174 (51.6)
Inferior	89 (26.4)
Superior	23 (6.8)
Superolateral	5 (1.5)
Central	34 (10.1)
Amputation	12 (3.6)
Lateral	0 (0.0)

Table 3. Comparison of Clinical and Demographic Variables by Margin Status

	Positive	Negative	*p*
Mean age, yr	54.1	54.0	0.968
Age >50 yr	13 (59.1)	218 (65.9)	0.498
Mean BMI, kg/m^2	34.8	33.6	0.500
BMI >30 kg/m^2	12 (54.5)	207 (62.5)	0.500
Mean biopsy weight, g	320	200	0.026*
Mean specimen weight, g	637	539	0.359
Specimen >1000 g	6 (27.3)	30 (9.1)	0.016*
Tumor size			0.030*
<1 cm	3 (14.3)	108 (37.9)	
1.01–1.99 cm	6 (28.6)	88 (30.9)	
>2.00 cm	12 (57.1)	89 (31.2)	
ER-positive	18 (81.8)	199 (60.1)	0.044*
Preoperative chemotherapy	4 (19.0)	70 (22.2)	1.000
Axillary procedure			0.929
None	7 (31.8)	94 (28.4)	
SLNB	13 (59.1)	209 (63.1)	
ALND	2 (9.1)	28 (8.5)	
Reexcision	8 (36.4)	58 (17.5)	0.044*
Completion mastectomy	11 (50.0)	24 (7.3)	<0.0001*
Final mastectomy pathologic assessment			0.116
Benign	1 (4.5)	59 (17.8)	
DCIS	8 (36.4)	70 (21.1)	
IDC/ILC	13 (59.1)	202 (61.0)	

BMI, body mass index; ER, estrogen receptor; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection; DCIS, ductal carcinoma in situ; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma.
*Statistically significant.

than 1000 g (OR, 3.518; 95 percent CI, 1.149 to 10.771) (Table 5). The type of reconstructive procedure performed at the time of completion mastectomy was noted in the 28 patients: transverse rectus abdominis musculocutaneous/deep inferior epigastric perforator flap in 15 (53 percent), latissimus flap with implant in 10 (36 percent), and tissue expander/implant in three (11 percent).

Table 4. Multivariate Logistic Regression Model for Positive Margins

	OR	95% CI	*p*
Age	1.019	0.974–1.065	0.419
BMI	1.002	0.939–1.070	0.948
Final partial mastectomy pathologic assessment			
DCIS	2.313	0.208–25.715	0.495
IDC	1.375	0.136–13.862	0.787
Total ipsilateral specimen weight >1000 g	4.638	1.260–17.079	0.021
Tumor size			
<1.00 cm	Reference	—	0.05
1.01–1.99 cm	2.282	0.502–10.371	0.286
>2.00	4.896	1.286–18.648	0.020
ER-positive	1.958	0.482–7.947	0.347
Preoperative chemotherapy	1.152	0.292–4.542	0.840

BMI, body mass index; DCIS, ductal carcinoma in situ; IDC, invasive ductal carcinoma ER, estrogen receptor.
*Model $p = 0.042$.

Table 5. Multivariate Logistic Regression Model for Completion Mastectomy*

	OR	95% CI	*p*
ER	0.015	0.000–1.234	0.062
BMI	0.864†	0.753–0.992	0.037
Total ipsilateral specimen weight >1000 g	3.518†	1.149–10.771	0.028

ER, estrogen receptor; BMI, body mass index.
*Controlling for the interaction between BMI and ER-positive tumors status.
†Model $p = 0.019$.

Complications

The overall complication rate was 16.4 percent, with the majority of those being minor and on the ipsilateral breast (Table 6). There was no significant difference in overall complications on univariate analysis; however, patients with a body mass index greater than 30 kg/m^2 had a significantly higher incidence of delayed wound healing [28 of 219 (12.5 percent) versus six of 134 (4.5 percent); $p = 0.009$). On multivariate analysis, having a complication was not associated with any other comorbidities, having positive margins, or completion mastectomy. The unplanned reoperation rate for complications was 4.2 percent ($n = 15$ patients). Long-term revision surgery for symmetry in those patients who did not have a completion mastectomy occurred in 4 percent (12 of 318).

Recurrence

The recurrence rate was 5.2 percent ($n = 10$ of 192) at a mean follow-up of 2 years (range, 2 months to 15 years). On logistic regression

Table 6. Complications for the Entire Cohort

Entire Cohort	No. (%)
Any complication	58 (16.4)
Ipsilateral	52 (14.7)
Contralateral	16 (4.5)
Major	15 (4.2)
Minor	47 (13.3)
Delayed wound healing	34 (9.6)
Infection	19 (5.4)
Mastectomy skin necrosis	3 (0.8)
Hematoma	3 (0.8)
Seroma	4 (1.1)
Symptomatic fat necrosis	5 (1.4)
Nipple necrosis	5 (1.4)

Table 7. BREAST-Q Questionnaire Raw Scores

	Preoperative Score	Postoperative Score	*p*
Mirror clothed	2.51	3.46	0.099
More fitted clothes	2.12	3.73	0.320
Mirror unclothed	1.76	3.44	0.237
Confident socially	3.49	4.61	0.492
Emotionally able to do things	3.71	4.56	0.048*
Emotionally healthy	3.73	4.18	0.019*
Equal worth other women	3.99	4.36	0.573
Self-confident	3.97	4.64	0.174
Feminine in clothes	3.85	4.54	0.103
Accepting of body	3.41	4.50	0.050*
Normal	3.82	4.46	0.882
Like other women	3.64	4.50	0.876
Attractive	3.67	4.32	0.064
Sexually attractive in clothes	3.07	3.88	0.201
At ease during sex	3.11	3.43	0.306
Confident sexually	3.39	3.43	0.539
Satisfied with sex life	3.16	3.48	0.068
Breasts unclothed	2.53	3.38	0.075
Sexually attractive unclothed	2.36	3.50	0.551

*Statistically significant.

analysis, preoperative chemotherapy was associated with a risk for recurrence (OR, 4.350; 95 percent CI, 1.230 to 15.383).

Time Comparison

When the outcomes were compared in 101 patients (1994 to 2010) with 192 patients after 2011 to 2015, the positive margin rate (8 percent versus 5 percent; $p = 0.256$) and completion mastectomy rate were lower in the recent cohort (8.2 percent versus 13.2 percent; $p = 0.138$) but not significantly so. Lumpectomy weight, tumor size, and stage were similar between the two groups.

Patient Satisfaction

Over 1 year postoperatively, women reported increased emotional health (from 3.73 to 4.18; $p = 0.019$), body acceptance (from 3.41 to 4.50; $p = 0.050$), feelings of attractiveness (from 3.07 to 3.88; $p = 0.064$), satisfaction with how their breasts looked unclothed (from 2.53 to 3.38; $p = 0.075$), and satisfaction with sex life (from 3.16 to 3.48; $p = 0.068$). Raw data are listed in Table 7. There were no decreases in their overall satisfaction.

DISCUSSION

The landscape for oncoplastic reduction mammaplasty continues to evolve as we improve techniques, broaden patient indications, and continue to strive for improved outcomes.[10] Oncoplastic surgery in how it pertains to breast conservation therapy is a topic that generally stimulates interest, but has been slow to be fully adopted by many breast and plastic surgeons alike. A recent article from Canada cited lack of training, access to plastic surgeons, and poor reimbursement as barriers to the adoption of these techniques in that country.[11] We recently also demonstrated that although oncoplastic surgery was of interest to breast surgeons and plastic surgeons and that there was general agreement as to the benefits, there was disparity in terms of delivery likely because of the system-based inadequacies in the United States.[12] Both groups agreed that the aesthetic benefits were the driving force, that margin involvement was a major concern, and that resection and complex partial reconstructions were best performed using the team approach. It was also concluded that future adoption of these techniques should rely on increased training and increased awareness of these procedures. Larger oncoplastic series with longer follow-up like this one will help determine and demonstrate safety and efficacy. Our series is one of the largest, focusing on oncoplastic reduction techniques, which have gained popularity faster in the United States compared with flap reconstruction of partial mastectomy defects. Provided that the patient is a candidate for breast conservation therapy and there is sufficient breast parenchyma left following tumor resection, the breast can be shaped using the oncoplastic technique (Fig. 2).

There has been increased interest in this topic, with the number of articles in the literature rising. A recent systematic review on oncoplastic surgery demonstrated that local recurrence was found to be approximately 7 percent; positive margins, 14 percent; and good cosmesis, 86 percent.[13] They did also conclude, however, that current evidence supporting these techniques is based on poorly

Fig. 2. (*Above*) A 59-year-old woman with right invasive ductal carcinoma. (*Center*) Her tumor located in the medial quadrant is identified with wires and a Wise pattern is drawn out preoperatively. (*Below*) Her result is shown following an 83-g resection and inferior pedicle reduction on the right with a total of 435 g removed. She had a symmetry procedure on the smaller breast with 300 g removed.

designed and underpowered studies. Another systematic review looked at 6011 patients who had oncoplastic breast conserving surgery. Of the patients reviewed, 81 percent had T1 and T2 disease, with invasive ductal carcinoma being the most common histopathologic condition. Positive margins were reported at 10.8 percent; completion mastectomy, 6.2 percent; overall survival, 95 percent; and local recurrence, 3.2 percent.[14] Our larger single-center series demonstrated similar results.

The majority of patients in our series had ductal carcinoma in situ or stage I disease. We have previously shown that young patients with ductal carcinoma in situ had a 25 percent risk of having a completion mastectomy after oncoplastic reduction because of margin involvement.[15] In this series, almost 50 percent of patients with high-grade comedo ductal carcinoma in situ required completion mastectomy, and many of these were younger patients. Stricter patient selection needs to be in place for these patients when selecting oncoplastic breast-conserving surgery to minimize positive margins. We have also shown that performing an oncoplastic reduction following neoadjuvant chemotherapy in high-risk patients is as safe and effective as breast-conserving surgery alone in these patients, which is consistent with other reports in the literature.[16] We continue to see reports of series where oncoplastic reductions have been used in higher risk patients, and sometimes referred to as extreme oncoplasty, which allows breast conservation therapy in patients with large (>5 cm multifocal) tumors who otherwise would have needed a mastectomy.[7,17] These techniques have also now been described with intraoperative radiation therapy with good results from a cosmetic and oncologic perspective.[18,19] The patients in this series underwent immediate reconstructions because this is the preferred approach at our institution. We have shown in prior studies that the complication rates are significantly lower when reduction techniques are performed before radiation therapy (21 percent) compared with after radiation therapy in a delayed fashion (57 percent),[20] which has also been demonstrated by other authors.[21]

The concern for positive margins has always been one of the cited drawbacks to this approach. This is true despite many studies demonstrating positive margins being significantly lower with the oncoplastic approach compared with breast-conserving surgery alone. Our overall positive margin rate was 6.2 percent and associated with larger tumors, larger resections, ductal carcinoma in situ disease, and estrogen receptor positivity. When significant resections (>1000 g) are required even with the oncoplastic approach, perhaps these patients are better served with a mastectomy. Clough et al. found that, despite the ability to generously resect using oncoplastic reduction, large tumors were more likely to have positive margins.[22] It is incredibly important to consider tumor size when planning these procedures. We recently evaluated margin control following oncoplastic reduction and breast conservation therapy alone and found a benefit to the oncoplastic approach with a lower positive margin rate (12 percent versus 20 percent).[23] In this series, patients in the oncoplastic group had wider free surgical margins, required fewer reexcisions, and went on to completion mastectomy less often. This is likely related to the generous resection that often accompanies oncoplastic resections. Another report demonstrated a 30 percent reexcision rate following oncoplastic breast-conserving surgery and found this to be more common in overweight patients that had tumor multifocality and the presence of microcalcifications.[24] Other reports have similarly shown a significant reduction in mastectomy rate and reexcision when oncoplastic techniques are added to breast-conserving surgery.[25] Although we have shown that positive margins are easily managed with either reexcision or completion mastectomy, if patients are at high risk or there is a concern about margin status, the oncoplastic reduction can be delayed until confirmation of clear margins. The vast majority of positive margins in our series are managed by completion mastectomy because if margins are positive following the generous, often greater than 200-g tumor resection, tumor biology might suggest that these patients are better managed with completion mastectomy. All reconstructive options are still available following oncoplastic reduction and likely easier now that the breasts have been reduced.

Despite the margin advantage of this approach, there is still no demonstrable oncologic advantage over breast conservation therapy alone. Longer follow-up is now available, with one series of 82 patients at an average of 10-year follow-up having a local recurrence rate of 8.7 percent.[26] Their overall survival rate was 82 percent and similar to the previously reported 10-year survival rate of 75 percent for the National Cancer Institute study[27] and 65 percent for the European Organization for Research and Treatment of Cancer study.[28] Another study with an average follow-up of 7.2 years demonstrated a local recurrence rate of 6.7 percent.[29] The overall survival with the oncoplastic patients was equivalent to the breast conservation therapy–only patients. Our follow-up in the full series is less than 5 years, making any conclusions on recurrence limited. We have previously shown that breast recurrence tends to occur at the primary tumor site, stressing the importance of directed radiation therapy to that area.[30] Given concerns of tissue rearrangement with the reduction technique, it is important to clip the cavity or tumor bed for directed postoperative irradiation and postoperative surveillance. In addition, it is also important to mark the pathologic specimens if additional tissue is removed from around the tumor cavity. True comparisons are difficult when it comes to recurrence and survival. To draw true conclusions, studies performed with standardized patient cohorts and follow-up will need to be performed. Furthermore, there is disagreement in what to compare these oncoplastic procedures to: breast conservation therapy alone or mastectomy. Mansell et al. suggested that because of similar histopathologic results, the oncoplastic cohorts need to be compared to mastectomy patients when it comes to oncologic outcomes.[31]

The complication rate of oncoplastic reduction remains low. Although complications do exist, they are often managed with conservative treatment and do not delay initiation of adjuvant treatment. Studies have shown fewer complications in obese women and women with macromastia following oncoplastic reduction compared with mastectomy and immediate reconstruction.[32,33] Tong et al. demonstrated fewer complications requiring additional surgery (3.8 percent versus 28 percent) and fewer complications delaying adjuvant therapy (0.8 percent versus 14 percent) in the oncoplastic group for obese patients.[33] In a previous report, we have similarly shown in patients with macromastia a lower breast complication rate (22 percent versus 47 percent), shorter hospital stay (0.8 days versus 3.5 days), and fewer trips to the operating room (1.2 versus 2.7) in the oncoplastic group.[32] The complication benefits compared to mastectomy are significant, and those compared to breast conservation therapy alone are acceptable. The usual patient selections, technique adjustments, and anticipation for radiation fibrosis will minimize complications and the need for additional operations. The ipsilateral side is often left approximately 10 percent larger in anticipation for radiation fibrosis, and this will reduce the need for revisions in the long term. Revision for symmetry is often possible on the contralateral side and was performed in 4 percent in our series.

In terms of patient-reported outcomes and satisfaction, the oncoplastic reduction technique has been shown to fare favorably compared with breast conservation therapy alone and compared with mastectomy and reconstruction for women with macromastia.[34] Although we often at best wish to preserve satisfaction and quality of life when performing breast reconstruction, this approach does often show improvement. Likely because of the benefit to reduction mammaplasty, these patients in our series reported improvement in body acceptance, feelings of attractiveness, satisfaction with how their breasts appeared unclothed, and satisfaction with sex life. Their improvement in emotional health is likely attributable to the breast cancer being managed and behind them. Veiga et al. showed a positive impact on quality of life and self-esteem when comparing patients who had oncoplastic surgery compared with breast conservation therapy alone.[35] Hart et al. have similarly shown that oncoplastic reduction patients reported an unexpected increase in their ability to wear sexually provocative clothing and in their partners' perception of them as womanly.[34] Although not typically a driving force behind the selection of the oncoplastic reduction for women with macromastia and breast cancer, the quality-of-life improvements are definite benefits to this technique.

Our technique and patient selection have changed slightly over the years. Despite now having this technique as an option in women with higher stage breast cancer and in women with smaller breasts, we have shown a small reduction in positive margin rate and completion mastectomy weight over time. In women with smaller breasts, and in larger tumors in upper outer or medial locations, we have been using autoaugmentation flaps to fill the defect after a generous resection. These autoaugmentation flaps are either as extended primary pedicles or the addition of a secondary pedicle. These refinements in technique will further broaden the indications for this approach in patients and minimize the potential for secondary deformities following radiation therapy. Another concern occasionally raised is the potential impact reduction mammaplasty might have on cancer surveillance. We previously reported that mammographic stabilization in oncoplastic reduction patients was slightly longer than breast conservation therapy alone, but that the sensitivity and overall mammographic findings were similar.[36] Dolan et al. found an increased need for ultrasound and subsequent biopsies likely related to fat necrosis.[37] Others found no increased incidence of mammographic abnormalities or unnecessary biopsies despite substantial tissue rearrangement in oncoplastic patients.[38] It is important that all members of the multidisciplinary team communicate well to understand what was done and minimize unnecessary biopsies. It is also important to ensure that all glandular and skin flaps are as vascularized as possible, not only to better tolerate radiation therapy but also to minimize potential for fat necrosis.

As our collective experience with these techniques grows,[39,40] we continue to find additional benefits to oncoplastic reduction techniques and refine our procedures to minimize complications and improve cosmetic and oncologic results. It will likely be an approach that, through exposure to and education of breast surgeons and plastic surgeons, will continue to gain popularity and acceptance for the management of women with breast cancer.

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Oncoplastic breast surgery: comprehensive review

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Abstract. – Breast cancer is the most common female cancer in Western populations, affecting 12.5% of women, with 1.38 million patients per year. Breast-conserving surgery followed by postoperative radiotherapy replaced the radical and modified-radical procedures of Halsted and Patey as the standard of care for early-stage breast cancer once the overall and disease-free survival rates of breast-conserving surgery were demonstrated to be equivalent to those of mastectomy. However, excision of >20% of breast tissue, low or centrally located cancer, and large-sized breasts with various grades of breast ptosis, result a in unacceptable cosmetic outcomes.

Oncoplastic breast surgery evolved from the breast-conserving surgery by broadening its general indication to achieve wider excision margins without compromising on the cosmetic outcomes. Thus, oncoplastic breast surgery can be defined as a tumor-specific immediate breast reconstruction method that applies aesthetically derived breast reduction techniques to the field of breast cancer surgery and allows for higher volume excision with no aesthetic compromise. However, contralateral breast symmetrization should be regarded as an intrinsic component of the oncoplastic surgery. The main procedures involved are volume-displacement or volume-replacement techniques, which depend on breast size and cancer size/location. Volume-displacement or reshaping procedures apply the plastic surgery principles to transpose a dermo-glandular flap of breast tissue into the defect site, while volume-replacement techniques use autologous tissues to replace the volume loss that follows tumor resection. Furthermore, these procedures are more complex and time-consuming than those involved in breast-conserving surgery.

Based on current literature, the authors analyze the different techniques and indications of the oncoplastic breast surgery, determining its complication rate, in order to help both surgeons and their patients in the decision-making stage of breast reconstruction.

Key Words:
Reconstructive surgery, Breast cancer, Breast conservative therapy, Oncoplastic breast surgery.

Introduction

The term “oncoplasty” is derived from the Greek words “onco” (tumor) and “plastic” (to mold)[1]. It essentially merges tumor resection, which ensures oncological safety, with plastic surgery, which ensures the best cosmetic outcome. According to its original definition, oncoplastic breast surgery (OBS) focuses on favorable scar orientation/placement, significant soft tissue rearrangement, and reconstruction of the contralateral breast to achieve symmetry[1]. As stated in the Milanese Consensus Conference on Breast Conservation of 2006, the aim of OBS is to achieve wide excision and clear margins without compromising on the cosmetic outcomes; moreover, the procedure should be performed simultaneously with oncological excision[2].

The principles of oncoplastic procedures evolved in Europe in the 1990s, but it was only in 1993 that Dr. Audretsch, a German surgeon, introduced the term “oncoplastic surgery”[3]. It quickly spread through France, Italy, and the UK, where it quickly gained popularity: the rate of procedures performed increased from 40% in 1991 to 60% in 2002. OBS has more recently become popular in the USA and other countries worldwide[4,5].

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Background

Breast cancer (BC) is the most common female cancer in Western populations, affecting 12.5% of women, with 1.38 million patients per year[6,7]. The peak prevalence of BC is 61 years, and more than 65% of women affected are < 65 years old. Therefore, the affected population comprises many young women who expect the treatment to result in long-term survival and also to have good aesthetic and psychological outcomes[8].

Breast-conserving surgery (BCS) followed by postoperative radiotherapy replaced the radical and modified-radical procedures of Halsted[9] and Patey and Dyson[10] as the standard of care for early-stage BC once the overall and disease-free survival rates of BCS were demonstrated to be equivalent to those of mastectomy[11-13]. Indeed, BCS allows for removal of cancer along with a tumor-free margin. The optimal extent of this margin is still being determined, and it varies from a 2-mm negative microscopic margin to 1- to 2-cm macroscopic uninvolved tissue[14]. BCS, therefore, offers the advantages of preservation of body image, better quality of life, and reduction of psychological morbidities[11].

The standard BCS strategies are lumpectomy or quadrantectomy with or without axillary dissection and radiotherapy. The main indications for BCS are early-stage BC, ductal carcinoma *in-situ* (DCIS) and large BC preceded by neoadjuvant chemotherapy[15]. Up to 30% of patients who undergo BCS complain of residual deformities, mainly including a deficiency of glandular tissue, overlying skin retractions, delayed side effects of radiotherapy, retraction/displacement of the nipple-areola complex (NAC), reduction of mammary ptosis, and asymmetry of the breasts[16-18]. Tumor size and location, the tumor-to-breast ratio, breast shape, postoperative radiation, and liposubstitution are commonly accepted risk factors for poor cosmetic outcome[18,19].

Previous studies have demonstrated that resection of parenchymal tissue greater than 70-100 cm^2 or a tumor-to-breast weight ratio exceeding 10:1 will probably result in unfavorable outcomes[20-22]. Indeed, excision of > 20% of breast tissue has unacceptable cosmetic outcomes as the tumor-to-breast ratio is more than the absolute tumor size, which is the strongest predictive factor for poor outcomes[1,23]. Tumor location has also been proven to affect the outcome. BC located within the lower and central quadrants has the worst cosmetic results after BCS, and only a 5% reduction in breast volume is allowed when the tumor is medially located, given the paucity of tissue[1,22]. Large breasts with various grades of breast ptosis are also not suitable for BCS, because of the higher incidence of complications and radiation-induced fibrosis, given the higher dosage of radiation required for patients with macromastia[24-26]. The other risk factors can be classified as patient-related (diabetes mellitus, tobacco use, and collagen diseases), and treatment-related (re-excision lumpectomy, postoperative seroma, and radiotherapy)[27].

General Principles

OBS broadened the general indication for BCT in order to reduce the risk of late deformities and asymmetry[28]. Tumors that are up to 3 cm in diameter can be safely removed if the resection procedure is followed by postoperative radiotherapy; however, mastectomy is still the gold standard of care for larger BCs[29-30]. Recently introduced neoadjuvant chemotherapies allow for a more conservative approach, even for advanced cancers[30].

OBS can be defined as a tumor-specific immediate breast reconstruction method that applies aesthetically derived breast reduction techniques to the field of breast cancer surgery and allows for higher volume excision with no aesthetic compromise[31]. The procedures involved are more complex and time-consuming than those involved in BCT[18]. The aim of OBS is to ensure better cosmetic outcomes and eliminate the need for surgical correction of defects resulting from BCT[33,34]. The average specimen for BCT weighs 20-40 g, compared to 200 g for OBS on average (though the specimen can weigh up to 1000 g or more)[15]. Studies have reported that breast resections of 20% to 40% breast volume (normally treated by mastectomy) ensure the removal of cancer with adequate tumor-free margins and retain enough tissue for good cosmetic outcomes[35,36]. Indeed, the oncological safety of breast surgery is determined by the status of the surgical margins. Residual carcinoma at the resection margins is regarded as one of the most important risk factors for local tumor recurrence with a relative risk that is almost 15-times higher than that in patients with tumor-free margins[37-39]. Focally positive margins may also be responsible for systemic spread and, eventually, disease-specific mortality[40]. Extensive DCIS, high-grade BC, infiltrating lobular carcinoma, previous neoadjuvant chemotherapy, Her2/neu-positivity, and lower age are all associated with a higher rate of tumor-positive margins[41-43]. The accepted definition of tumor-free margins is at least a 1-mm distance between the cut edge of the specimen and the outer limit of the tumor[44]. However, a 1- to 2-mm distance between the resected edge of the specimen and the outer limit of the tumor is internationally defined as a close margin.

OBS provides the best results if the reconstruction is performed at the time of the resection (immediate reconstruction)[45,46]. The tissues surrounding the cancer should be healthy, non-irradiated and without scarring, which will result in lower complication rates and better cosmetic outcomes[47]. Moreover, the scars resulting from OBS improve after radiotherapy. Delayed reconstruction is performed at least 6 months to one year after the last radiotherapy session[48]. The techniques employed are similar to those of the immediate setting; however, the complication rate is almost double and the cosmetic outcome is usually poor. Delayed-immediate breast reconstruction has the same advantages as immediate reconstruction (the aesthetic outcomes and lower complication rates) as well as the delayed approach (oncologic safety). Delayed-immediate breast reconstruction is indicated in cases where final confirmation of a tumor-free resection margin is required prior to reconstruction; this procedure usually takes place 1-2 weeks after BC resection, prior to radiotherapy[49].

Various authors[50-53] regard contralateral symmetrization as an intrinsic component of OBS that should be performed at the same time of the reconstruction. Indeed, simultaneous surgery on both breasts can eliminate the need for a second surgery. However, radiotherapy can have unpredictable effects on the treated breast, and hormonal and chemotherapy can significantly change the overall body weight of the patient. If the excision margins are positive and re-excision or mastectomy is required, the contralateral breast may require another reconstruction procedure to correct any asymmetry that arises[36]. Therefore, symmetrization surgery may be postponed until the third or sixth month after the last adjuvant therapy session[53]. The risks and benefits of both approaches should be extensively discussed with the patient before any procedures are performed[54].

Indications

High-volume breasts with severe ptosis may be particularly suited for OBS as the margins can be wider and the results are usually more satisfactory[18]. Furthermore, resection of over 20% of the breast volume with the need for large skin resections inside the mammoplasty area is also an indication for OBS[55]. When the tumor is located in the central, medial or inferior quadrant, the cosmetic outcomes are usually better, particularly if the BC is located within the resection area of the mammoplasty[56]. Conversely, cancers located close to the skin and outside this area may need to be treated with a combination of techniques, which may not always provide the desired results. In such cases, as well as in cases of previous plastic surgery of the breast, nipple- or skin-sparing mastectomy may be the best choice[57]. Small breasts without mammary ptosis and conical breasts can be regarded as absolute contradictions for OBS, and skin-sparing or nipple-sparing mastectomy may be a better option in such cases too[58,59]. Exaggerated patient's expectations of aesthetic results, youth and previously irradiated breast are relative contraindications to OBS. Associated clinical conditions, such as uncontrolled diabetes, tobacco use, collagen diseases, and older age are associated with higher complication rates, which may affect the aesthetic outcomes[18].

Preoperative Planning

Preoperative planning is important for optimizing the surgical resection technique without compromising the final breast shape. Indeed, performing tissue removal without proper planning can result in postoperative deformities that can prevent surgeons from achieving the ideal breast shape[60]. Computer-based software or imaging techniques, such as the recently introduced 3D surface imaging devices, which evaluate breast contour, shape, position, volume, and symmetry, are useful in this regard[61-64]. Such imaging information, when combined with the surgeon's experience, is useful in this decision-making stage.

However, the primary aim of OBS is oncological safety; therefore, a clear understanding of the location and spread of the cancer is required for optimal breast resection. The invasiveness and extent of BC can be reliably predicted by mammography complemented by ultrasound examination[36]. Conversely, non-invasive BC cannot be reliably predicted by these imaging techniques. DCIS usually presents with radiologically detectable microcalcifications. However, these calcifications are only centrally located and are absent in low-grade DCIS, so they may not be reliable for predicting the entire extent of the lesion[12,65,66]. Furthermore, DCIS is usually not associated with mass-like changes that are detectable by ultrasonography, which is of little or no help in examining cancer distribution[36]. Contrast-enhanced magnetic resonance imaging (MRI) is the most feasible technique for determining the presence and size of BC as well as identifying additional invasive lesions[36]. MRI is particularly suitable for assessing invasive lobular carcinoma diffusion, as it has the lowest false-negative rate and highest accuracy[67]. However, the rate of false-positive results is high, and it is not always possible to determine the extent of non-invasive cancers. Therefore, MRI cannot be considered as the standard of care, and its use should be limited to restricted centers where MRI-guided biopsy is performed[68,69].

Technique

The OBS approach is based on two general principles: volume displacement and volume replacement, which depend on breast size, BC size, and location. Volume-displacement or reshaping procedures apply plastic surgery principles to transpose a dermo-glandular flap of breast tissue into the defect site, while volume-replacement techniques use autologous tissues to replace the volume loss that follows tumor resection[44].

There are no standardized protocols for these procedures, but there are a few basic rules[70]. Women with moderate-/large breasts, with or without ptosis, benefit from immediate breast reconstruction using of volume-replacement techniques. This is particularly true if the tumor is located within the breast resection pattern of the partial mastectomy[70]. Conversely, small breasts without ptosis usually need volume-replacement procedures, as the skin and tissue that are removed need to be replaced to ensure that the resected breast is similar in structure to the contralateral breast. BC of the upper or outer quadrant also usually requires volume-replacement techniques[49]. Before the closure of defects, metal clips must be placed on the pectoralis muscle and lateral edges of the resection bed for future radiotherapy[71].

Volume-Displacement Techniques

Small- to medium-sized breasts are best suited for OBS when the defect does not lead to significant volume alteration and asymmetry. Dermo-glandular advancement and rotation or transposition flap placement are the main procedures used for filling the dead space with the surrounding remaining breast tissue. The mammary gland is usually dissected from the underlying pectoralis muscle, and a full-thickness fibro-glandular breast flap is advanced into the defect. Reconstruction of the contralateral breast to achieve symmetry of both breasts is usually not required[36]. However, the extensive dual-plane undermining of the breast gland may harness blood supply and should be performed cautiously, especially in low-density breasts with a high fatty composition[71]. In an optimal procedure, the location of the NAC is anticipated and it is relocated accordingly, as its position progresses in the infero-lateral direction with age, particularly in young patients[53].

The ideal technique for medium to large breasts with ptosis is probably mastopexy or reduction. The tumor is included within the breast resection pattern, while the remaining breast parenchyma is used for mound reshaping. The oncoplastic approach has been described by Masetti et al[52] as a four-step procedure where skin incisions and parenchymal excisions are first planned according to reduction/mastopexy templates; this is followed by parenchymal reshaping, repositioning of the NAC, and, finally, correction of the contralateral breast to achieve symmetry.

When the BC lies beyond the resection region of the mammoplasty, breast reshaping can be combined with complete tumor removal. The key step is the preoperative decision-making process: designing the pedicle, creating the skin/parenchymal resection pattern so as to preserve the viability of the NAC, reshaping the breast mound, and closing the dead space. If the expected volume of the breast to be removed is < 20%, the remaining breast mound can be satisfactorily reshaped with simple skin and glandular undermining. Skin undermining follows the mastectomy plane, and the target can be increased from 20% to 60% of overlying skin[71]. NAC can also be undermined by complete transection of the terminal ducts with a 0.5- to 1-cm glandular tissue left attached. NAC sensitivity may be reduced, but arterial supply and venous drainage are usually maintained[72,73]. Furthermore, NAC displacement can be prevented by de-epithelization of the periareolar skin in the shape of a crescent opposed to the defect site. Immediate recentralization guarantees a better cosmetic outcome than repositioning of the NAC after radiation therapy[74]. If the volume of the breast to be removed exceeds 20-50%, more complex OBS procedures are required, which ensure a wider resection margin while preserving the final breast shape from contour deformities and asymmetry. In addition, corrective surgery for the contralateral breast to achieve symmetry should be discussed with the patient in the preoperative setting, as after OBS the breast usually appears smaller, higher, and rounder[71].

OBS is suitable for lower pole BC, since the use of BCT in these areas usually results in the "bird's beak" deformity with a downward deviation of the NAC, which can also worsen as a consequence of post-irradiation fibrosis[53,75]. Superior or superomedial pedicle inverted T or vertical scar mammoplasty allows for BC removal within the Wise pattern. The resulting cosmetic outcome is excellent in women with small-to-large breasts[76]. V-mammoplasty improves the aesthetic outcome of superior pedicle mammoplasty when the BC is located in the lower-inner quadrant. The tumor is excised *en bloc* with a pyramidal section of the gland, with its apex at the border of the areola and its base in the submammary fold. The incision is made laterally to the anterior axillary line in order to medially rotate a skin-glandular flap to fill the defect and reshape the breast. The resulting scar has a V-shape and is mainly hidden in the inframammary fold (IMF)[35] (Figure 1).

BC located in the upper inner quadrant needs to be treated with extra caution in the preoperative setting. It is an aesthetically relevant region as it is the most visible one, and, therefore, the scars are particularly difficult to hide and may distort the décolleté. Inferior medial pedicle mammoplasty provides satisfactory results and allows for safe tumor excision in the upper half of the breast while preserving the viability of the NAC[1]. Donut or round block mastopexy also allows for removal of segmentally distributed BC of the upper inner quadrant through a periareolar access point[77]. Furthermore, Clough et al[78] recently described the use of a rotation glandular flap for upper inner quadrant tumors, which can be also applied to all quadrants. However, their technique requires extensive undermining of the gland, and, therefore, should be reserved for glandular and not fatty breasts. According to Clough et al's technique, the NAC and the gland are extensively undermined through a semi-circular peri-areolar incision. Once the BC is completely resected, a wide V-shaped glandular flap is rotated medially towards the defect site via a full-thickness glandular incision created laterally from the lumpectomy cavity. Such remodeling techniques are not feasible if the skin in the upper half of the breast needs to be resected. In such cases, Silverstein's batwing mastopexy technique may be a solution[36]. According to this method, two similar half-circle incisions with angled wings are marked on either side of the NAC; the BC is located within this resection pattern and is excised at full thickness. The remaining fibroglandular tissue is advanced to close the defect; this results in the upward lift of the breast and nipple. This is a simple procedure that does not need extensive dual-plane undermining and also corrects breast ptosis[53]. A similar procedure is occasionally performed on the contralateral breast to achieve symmetry. When performing the batwing mastopexy, surgeons should not excessively reduce the sternal notch to nipple (SN-N) distance, as this could result in pseudoptosis. Indeed, undue up-

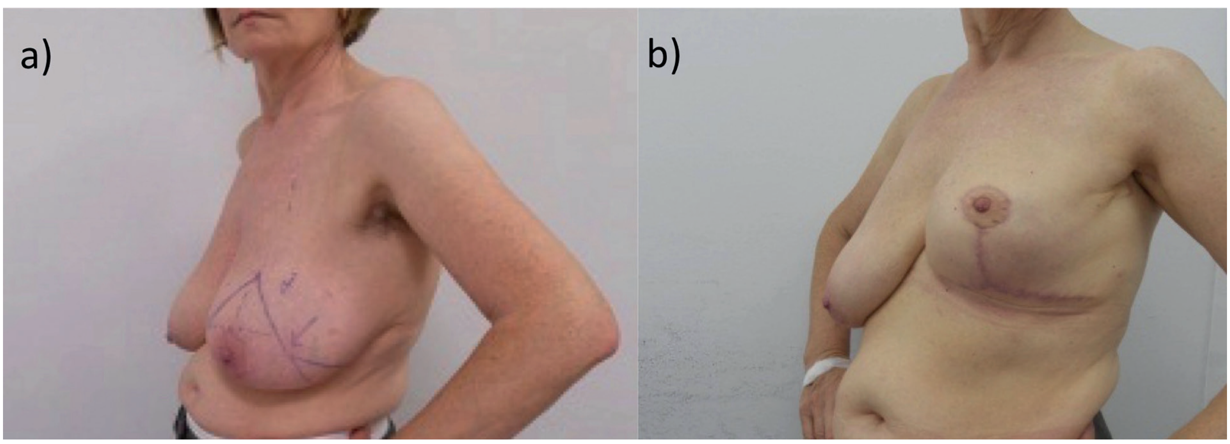

Figure 1. Picture ***a)*** shows the preoperative marking for an inverted-T wise pattern mastoplasty as the patient had a centrally located cancer of the left breast, which determined the excision of the nipple-areola complex too. Picture ***b)*** shows the patient in the ninth postoperative month after having undergone reconstruction of the nipple and areola tattooing.

ward displacement of the NAC would make the breast appear highly unnatural, and, therefore, the SN-N distance should never be less than 16 cm[79]. Both batwing and donut mastopexy also provide outstanding results for BC located in the upper and lateral quadrants. Round-block mastopexy can easily be performed on tumors in any location; however, it is most suitable for upper-pole tumors that are close to the areola and mildly ptotic breasts that can be aesthetically improved after a mastopexy[48]. Indeed, once the two concentric periareolar incisions are made and the intervening skin is de-epithelized, the skin envelope can be undermined starting from the outer incision line in any direction, in the same fashion as a subcutaneous mastectomy. The tumor and the surrounding tissue are excised from the subcutaneous plane to the pectoralis fascia, while the glandular flap from both sides is mobilized and advanced into the defect. The viability of the NAC is ensured as it is derived from the posterior glandular base. Moreover, the resulting periareolar scar stretching is lessened by a dual-layer closure with absorbable sutures, thus eliminating the need for a purse-string closure[66].

BC of the upper outer quadrant is associated with the best cosmetic outcome, since this is the most forgiving location; luckily, up to 60% of tumors occur in this region[71,80]. Racquet mammoplasty can be used to resect large sections of BC with a quadrantectomy-type incision made over the tumor from the NAC toward the axilla[81,82]. The periareolar skin is de-epithelized and the NAC is extensively undermined to relocate it to the center of the breast mound.

BC of the lower outer pole can be resected using a J-type mammoplasty that avoids lateral retraction of the breast and deviation of the NAC, which are usually associated with an inverted-T mammoplasty[83]. Similar to the V-mammoplasty, the J-type method uses a lateral and central glandular flap that is rotated towards the defect to redistribute the remaining tissue. The NAC is repositioned with a de-epithelialized superior pedicle. The final scar is in the shape of the letter J from the periareolar down to the inframammary crease.

Central and subareolar BC can be contraindications for BCT, since the NAC is involved in 50% of the cases[84]. Retro-areolar tumors or those closer than 2 cm to the nipple do not allow for preservation of the NAC that are usually removed *en bloc* with the tumor[85]. However, an inverted T, a modified Lejour or a J-closure pattern, similar to breast amputation reduction techniques, can all provide good aesthetic outcomes[85-87]. The NAC is eventually reconstructed using a local flap of choice and subsequently tattooed[88]. When the cancer is located superiorly or laterally, an elliptical skin excision centered on the NAC can also be performed, and similar surgery may be required for the contralateral breast. However, the inverted-T Wise pattern mastectomy tends to have better cosmetic outcomes as some amount of breast projection is retained; in contrast, the purse-string and transverse-scar techniques tend to flatten the breast mound[85,87] (Figure 2).

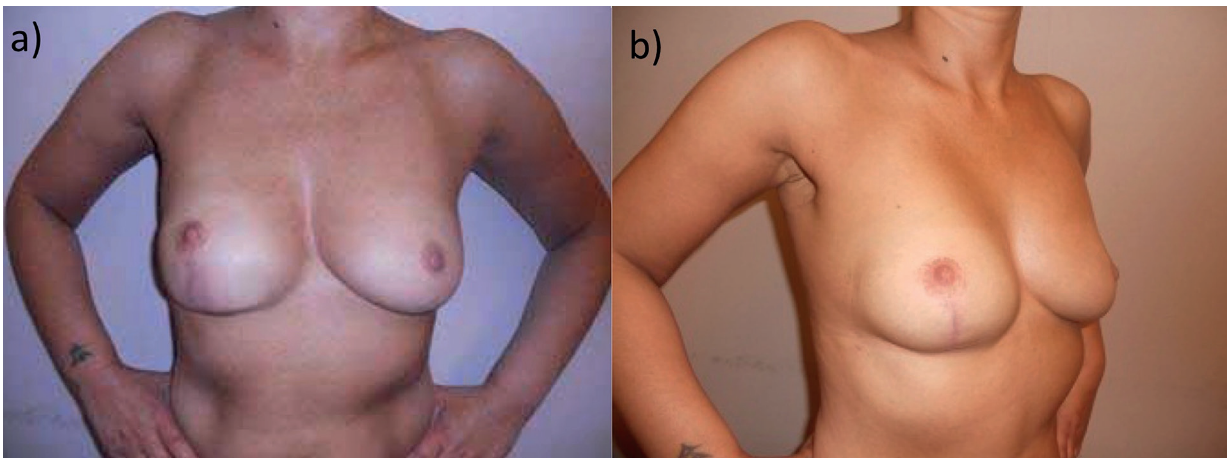

Figure 2. Postoperative picture after 6 months of a patient that has undergone inverted-T wise pattern mastoplasty for a lower pole cancer of the right breast.

Volume-Replacement Technique

Large tumors, high tumor/breast volume ratio and small breasts are often associated with defects that are difficult to reconstruct with volume-displacement techniques[89]. Indeed, in such cases the residual breast tissue is usually insufficient for proper rearrangement after a partial mastectomy, and the patient may require reconstruction using autologous local or distant flaps. Thus, volume-replacement techniques are used for the reconstruction of relatively small breasts with a large resection volume[44]. Furthermore, with the volume-replacement technique, remodeling of the contralateral breast is usually not required to achieve symmetry. The use of fascio-cutaneous flaps, myo-cutaneous local flaps, pedicled perforator flaps and even free flaps has been described for partial breast reconstruction[48].

Local fascio-cutaneous flaps can be employed in the case of small lateral defects (<10% of the breast size). The use of transposition flaps from the subaxillary area was first reported by Clough et al[16]. Munhoz et al[90] have described the placement of the lateral thoracodorsal flap (LTDF), which is ideal for lateral defects, especially in obese patients. These are essentially fascio-cutaneous flaps that rotate or transfer the skin and the subcutaneous fat of the subaxillary area to fill the breast parenchyma into the defect. Lower quadrant resection near the IMF in small-/moderate-sized breasts can be filled with a fascio-cutaneous flap harvested from below the IMF and then rotated to fill the defect created by the segmental excision[91].

Flap survival and aesthetic outcome are ensured by a careful flap design. When the defect ranges from 10% to 30% of the breast volume, a pedicled musculocutaneous flap can be harvested. The latissimus dorsi (LD) musculocutaneous flap represents a common local option[92,93]. This flap uses the LD muscle and overlying skin to fill lateral, central, inferior and even medial defects. The LD is separated from its insertions and pivoted under the axilla while preserving excellent blood supply via its vascular pedicle[94]. An LD myo-subcutaneous flap can be harvested with the help of an endoscope when the skin overlying the tumor needs to be preserved in order to avoid a scar on the back[95]. An LD musculocutaneous flap should have larger dimensions than the defect it is used to fill. Indeed, the LD muscle usually undergoes postoperative atrophy as a consequence of the surgical de-innervation and radiotherapy. Therefore, a much larger flap than needed must be harvested in order to avoid unsatisfactory results caused by the expected loss of muscle volume (Figure 3).

The pedicled perforator flap technique has an advantage over other methods of autologous breast reconstruction, as it uses well-vascularized tissues and spares the underlying muscles, which results in lower donor site morbidity in terms of muscle function and seroma formation[96]. According to the pedicle length, perforator flaps can be used to manage defects in almost every quadrant. Intercostal, thoracodorsal and superior epigastric arteries are the main pedicles that the perforator flaps can be based on[97]. The fascio-cutaneous skin paddle of the classical LD musculocutaneous flap can be raised as a pedicled perforator flap from either the thoracodorsal or intercostal vessels and used to cover lateral, central, inferior defects[98].

The thoraco-dorsal artery perforator (TDAP) flap is based on the vertical branch of the thoracodorsal artery; it can be easily used for filling in lateral, superolateral and central defects of the breast. If no suitable perforators are found, the flap can be easily converted to a muscle-sparing TDAP or muscle-sparing LD flap[99]. Either the anterior or the lateral branches of the intercostal arteries are suitable for harvesting local perforator flaps. Lateral and inferior defects of the breast can be reconstructed with the lateral intercostal artery perforator (LICAP) flap, while inferior or medial defects can be reconstructed with the anterior intercostal artery perforator (AICAP) flap[1]. Perforators of the LICAP flap are usually found 2.7-3.5 cm from the anterior border of the

Figure 3. Latissimus dorsi musculocutaneous flap elevated on its main supplying pedicle: thoracodorsal nerve, thoracodorsal artery (branch of the subscapular artery) and vein.

LD muscle, while those of the AICAP flap pierce through the rectus abdominis or the external oblique muscles[100]. The superior epigastric artery perforator (SEAP) flap can be harvested as an alternative to the AICAP flap since both share the same indications[101]. However, the SEAP flap can cover more remote defects in the breast as it has a longer pedicle provided by perforators arising from the superior epigastric artery or its superficial branch.

If the defect is large and medially located or the residual breast tissue after a partial mastectomy is minimal, mastectomy and subsequent autologous free-flap breast reconstruction may have the best cosmetic and oncological outcomes[102,103]. Other less common volume-replacement techniques are adipofascial flap placement, omental flap placement, and autologous fat graft (AFG)[104-107]. Autologous fat grafting (AFG) is also a secondary procedure that can ameliorate any residual contour deformities and asymmetry with the contralateral breast[108]. Owing to the presence of the so-called adipose-derived stem cells (ASCs), AFG displays regenerative and therapeutic properties[109,110]. ASCs can differentiate into multiple cell lineages and secrete paracrine factors[111-115]. Thus, angiogenesis and wound healing are strongly enhanced, leading to higher fat graft survival as well as dermal and subcutaneous tissue regeneration[116,117]. Moreover, AFG has positive effects in radio-induced damage of the soft tissues in reconstructed breasts[118,119]. Indeed, ASCs can thicken the subcutaneous tissue, and improve the texture of the irradiated skin by enhancing its vascular supply through the ASCs regenerative potential[104].

Outcome

The aesthetic outcome of BCT is unsatisfactory in 30% of patients, while the cosmetic failure rate of OBS is 0-18%[120]. Moreover, when BCT is implemented with the OBS technique, the failure rate drops to < 7% at 2 years[121]. Losken et al reported that the aesthetic results were good at 1 year (97.7%) and at 5 years (90.3%) in a series of 540 consecutive cases of patients with high tumor/breast volume ratios[122]. Age, BMI, size and location of the tumor, breast size, and the adjuvant treatment applied can affect the final cosmetic outcome[28]. The aesthetic results in a reported study were analyzed by means of patients' self-evaluated questionnaires or subjective scales completed by specialists[123,124]. It emerged that young patients at high social and economic levels have lower satisfaction rates[125,126]. Moreover, it appears that patients' evaluations are usually better than those of the specialists, and the interobserver agreement rate of specialists is often very low[28,127].

Studies have reported that the average complication rates (16%) associated with OBS are acceptable[28]. The common complications following volume-displacement techniques are delayed wound healing (3-15%), fat necrosis (3-10%), and infection (1-5%), which are similar to the complications associated with volume-replacement techniques, although the overall rate is slightly higher (range, 2-77%)[41,47,90]. This is probably due to additional donor site complications and potential flap loss issues[92,128]. Nevertheless, both volume-displacement and volume-replacement approaches share the same delayed complications: breast fibrosis and asymmetry.

Safety

Given the wider excision margin with OBS, the local control and oncological safety of OBS should be better than that of BCT. Based on reports in the literature, in OBS, the tumor size is usually larger (2.7 *vs*. 1.2 cm) and the specimen weight is four times higher than that with BCT[129]. Accordingly, the tumor-positive margin rate is significantly lower after OBS (12% *vs*. 21%) and the re-excision is more common when only BCT is performed (14.6% *vs*. 4%). Despite this, completion mastectomy is more common after OBS than after BCT (6.5% *vs*. 3.79%). The local recurrence rate after OBS and BCT is 4% and 7%, respectively, while the average follow-up period is reported to be longer in BCT (64 *vs*. 37 months). Losken et al[122] reported that the overall survival rate and 5-year recurrence rate after OBS are 92.9% and 6.8%, respectively.

One of the main concerns with OBS is that parenchymal manipulation, scar tissue and fat necrosis, which are a consequence of surgery, may impair the ability to adequately screen for tumor recurrence[122]. However, physical examination, radiologic imaging, and tissue sampling can overcome this issue. Indeed, mammographic sensitivity does not seem to be affected, and the qualitative changes observed are similar to those observed after BCT. However, the time required to achieve mammographic stability after OBS tends to be longer (25.6 months *vs*. 21.2 months)[130,131]. Changes and mammograms should be compared carefully over time, while ultrasound and MRI can be used to complete the diagnostic process. Fine-needle aspiration, core-needle biopsy, or surgical biopsy can be performed to rule out malignancy. Of the patients who have undergone OBS, 53% require tissue sampling procedures, while only 13% of patients who have undergone BCT require these investigations[122].

Conclusions

The primary aim of OBS is oncological safety, which is always more important than the aesthetic outcome, although the main purpose of OBS stems from a desire to improve the cosmetic outcome of BCT. Besides ameliorating the aesthetic outcomes, OBS allows for wider resections (even involving 50% of the breast volume without causing deformity), which should ensure better local control of the disease. Furthermore, the breast size is usually smaller after OBS; thus, it has a positive impact on radiotherapy planning by reducing the dosage required[54]. OBS has been defined as an oncologic-aesthetic-functional individualized surgical approach because it can improve the general indications for BCT without compromising on the aesthetics or the oncological outcomes[18].

Patients are more worried about deformities than a mismatch in the size of their breasts or scar length[132]. Therefore, the aim of OBS is to reshape the remaining breast gland while maintaining an aesthetically pleasant shape and contours. Indeed, contralateral surgeries are often performed to achieve symmetry. OBS can also prevent NAC displacement by anticipating possible NAC deviation and repositioning it at the center of the breast mound. Future studies need to further validate the oncological safety of OBS and provide surgeons with adequate preoperative tools to better plan the resection and reconstructive steps. Although OBS is more complicated and time-consuming than the conventional BCT approach and has better oncological outcomes and satisfaction rates, breast surgeons should be also trained in plastic surgery or should at least collaborate with plastic surgeons when performing OBS.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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Oncoplastic breast surgery: a regional Australian 2012 fellowship experience

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Key words
Australia, breast surgery, education, oncoplastic, surgical training.

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Accepted for publication 22 March 2013.

doi: 10.1111/ans.12318

Abstract

Introduction: Oncoplastic breast surgery (OBS) is a developing subspecialty, although many countries are struggling with how to incorporate training in OBS as part of the established breast surgery subspecialization pathways. UK and Brazil have surged ahead with established formal training programmes, whereas countries such as Australia still rely on ad hoc training by interested surgeons. Our aim was to review the possibility of including regional training centres with appropriate OBS expertise into a future formal training programme in OBS.
Methods: An 11-month self-audit was performed by the Fellow based in Port Macquarie, in a Breast Surgeons Society of Australia and New Zealand Incorporated accredited Fellowship. The audit template and reconstructive database, which were utilized in this study were supplied by Breast Surgeons Society of Australia and New Zealand Incorporated.
Results: OBS procedures made up 41% of total breast procedures performed, with 46% of these being performed by the Fellow. These oncoplastic procedures included 22 reconstructive breast procedures, with 15 (68%) being performed by the Fellow. These procedures involved mainly pedicle transverse rectus abdominis myocutaneous flap reconstruction after mastectomy and breast implant reconstruction techniques. Minor and major complications accounted for a small percentage of operated cases and are discussed.
Discussion: Current British Association of Surgical Oncology (BASO) guidelines specify recommendations regarding BASO Level I and II OBS training, experience and exposure. Based on the experience during the fellowship presented in this audit, we discuss the merits of using regional Australian hospitals like Port Macquarie Base Hospital to make up the cohort of BASO Level I units to provide the core foundation experience in OBS to the next generation of Australian oncoplastic breast fellows.

Introduction

The education and training of surgeons has long been an area of heated discussion and debate. This debate has recently focused on a developing surgical subspecialty, oncoplastic breast surgery (OBS).

Dr Werner Audrescht first coined Oncoplastic surgery as a term in 1998.[1] This approach involves appropriate oncological surgery, reconstruction of wide excision defects, immediate or delayed reconstruction and correction of asymmetry.[2]

Although many of the techniques used in OBS have been around for a long time, their application to oncological setting is relatively recent.[3] Despite this, the uptake has been rapid and welcome by the breast surgical fraternity. The development of OBS has been preceded by a number of improvements in the management of malignant breast disease, including the evolution of breast conserving therapy as well as improved adjuvant treatment.[4] New frontiers have opened up in improving reconstructive outcomes for patients undergoing oncological treatment, leading to significant benefits to patients.

The growing demand from the surgical fraternity[5,6] and patients themselves has led to the establishment of formalized training programmes in the UK and Brazil.[7] Following in their footsteps, Breast Surgeons Society of Australia and New Zealand Incorporated (BreastSurgANZ) may be well positioned to work towards the creation of a similar post-Fellowship training scheme in Breast Surgery, of which OBS training may become an important part.[8]

Table 1 British Association of Surgical Oncology recommendation for establishment of oncoplastic breast surgery (OBS) training units (adapted from[5])

Requirement	Level I	Level II
Number of annual reconstructive breast procedures	25	50
Exposure to range of core OBS procedures	Moderate	Comprehensive
Number of supervising surgeons	1 oncoplastic breast surgeon	2 specialist surgeons (including one oncoplastic breast and at least one plastic and reconstructive surgeon)
Multidisciplinary team support	Extensive	Complete (including high dependency beds, vascular imaging facilities, access to microvascular surgery)

OBS was introduced in Australia in Adelaide in the early 1990s. Since then, there has been a slow but demonstrable increase in interest from trainees in subspecialization into this area. This is supported by the increase in the number of applicants for positions with exposure to OBS. In 2012, there were 16 breast Fellows throughout Australia and New Zealand enrolled in post-Fellowship accredited posts by BreastSurgANZ. It is unclear, which of these are truly OBS training positions and which offer classical breast surgery experience only. BreastSurgANZ will be looking to establish the depth of experience provided by various positions in order to stratify and to guide future training experience.

In 2007, the British Association of Surgical Oncology (BASO) and the British Association of Plastic Surgeons (BAPS) via the Training Interface Group of Surgery put together the ‘Guide to Good Practice’ for OBS. This solid document established the definitions for levels of expertise and case mix experience in units offering OBS services.[5] BASO level I and II units are defined in this document depending on the case mix and caseload of the unit (Table 1). These guidelines suggest that the trainees should spend a 12-month post in these units as well as drawing experience from interactive demonstrations to the trainees, external resources such as conferences, master classes, workshops, literature or foreign training posts.

Also in 2007, the European Society of Breast Cancer Specialists (EUSOMA), published guidelines for standards and training of health professionals dealing with breast cancer.[6] With respect to breast surgeons, it made recommendations that they should be trained in units, which offer immediate and delayed reconstruction and oncoplastic surgery techniques to breast cancer patients. They have set a minimum requirement in exposure to reconstructive surgery and oncoplastic surgery as an assistant and principal operator, expected to be performed by the trainees. BASO and EUSOMA guidelines are comprehensive and may eventually form a foundation for future Australian guidelines.

Aims

To present, the 1-year experience of oncoplastic training in breast surgery based in a regional centre in NSW, Australia, as an indicator of current trends and future possibilities.

Further, to demonstrate that training in a regional BASO level I oncoplastic breast unit is feasible, beneficial, and perhaps even advantageous.

Methods

This is a single centre prospective review looking at the logbook of a single general surgical Fellow with an interest in OBS based in a regional centre (Port Macquarie) in northern NSW. Around 50 000 people now live in Port Macquarie, and Port Macquarie Base Hospital (PMBH) is a medium-sized 161-bed facility nearly 400 kilometres north of Sydney servicing this regional community. The North Coast Cancer Institute based at PMBH offers evidence-based management of oncology patients with regular weekly multidisciplinary meetings, providing modern chemotherapy and radiotherapy onsite with two linear accelerators, collocated in the same building as BreastScreen.

The experience included entries in the formal BreastSurgANZ logbook, as well as the Pilot BreastSurgANZ OBS Reconstructive Audit, with the template supplied by BreastSurgANZ oncoplastic subcommittee. The study looked at the entries made between February and December of 2012. The Fellow involved was a first year Fellow after completion of the Royal Australasian College of Surgeons general surgical fellowship.

For the OBS component of this 1 year general surgical fellowship, the Fellow worked under the supervision of a single general surgeon with an interest in oncoplastic breast surgery. The supervising surgeon has gained a large experience in pedicle transverse rectus abdominis myocutaneous (TRAM) flap breast reconstruction and inferior pedicle breast reduction surgery and other OBS procedures having been in independent practice for more than 15 years. He gained his initial OBS experience as a Fellow at Auckland’s St Mark’s Breast Centre and subsequently as the Lister Fellow at the Glasgow Royal Infirmary.

Results

Review of logbook data for the period from February to December 2012 demonstrated that a total of 164 breast related procedures were performed by the Fellow, under the guidance of a single mentoring oncoplastic breast surgeon (see summary of procedures in Table 2). Not presented in this discussion are other general surgical procedures performed by the Fellow during the same period, which numbered 259 in total as well as an additional 113 endoscopic procedures. Therefore, OBS cases represented 31% of the total procedures performed by the Fellow during this general surgical Fellowship year.

The Fellow’s regular operative experience was supplemented by attending weekly multidisciplinary breast cancer meetings, fortnightly BreastScreen assessment clinics as well as the Fellow’s own weekly clinic which included a mixture of follow-up and new general surgical and OBS patients. Monthly morbidity and mortality meetings for the PMBH Department of Surgery were also organized and attended by the Fellow.

Table 2 Summary of oncoplastic breast surgery Fellow's experience between February and December 2012

Operation	Primary surgeon	Assistant
Wide local excision for cancer/ductal carcinoma in situ	18	9
Re-excisions for margins	6	1
Level 1 oncoplastic wide local excision	1	1
Level 2 oncoplastic wide local excision	6	1
Simple mastectomy	5	7
Skin sparing mastectomy	6	2
Nipple sparing mastectomy	0	0
Reconstruction implant/expander	6	2
Reconstruction tissue based TRAM or LD ± implant	8	1
Symmetry procedure	3	1
Exchange of implant	1	4
Nipple reconstruction	0	0
Reduction, augmentation or mastopexy	0	25
Sentinel node biopsy	16	9
Axillary clearance	4	6
Benign or diagnostic biopsy	11	4
Laparoscopic oophorectomy	0	0

LD, latissimus dorsi; TRAM, transverse rectus abdominus myocutaneous.

With respect to breast cases, 91 of 164 (55%) were performed by the Fellow as the operating surgeon under supervision. Eighty-seven patients were public patients (four being private) admitted at PMBH.

OBS procedures made up 68 of 164 procedures (41%) overall, with 31 of these 68 (46%) being performed by the Fellow. Under close supervision of his mentor, these oncoplastic procedures included 22 reconstructive breast procedures, with 15 of these (68%) being performed by the Fellow. These procedures involved autologous tissue breast reconstruction after mastectomy (either delayed or immediate) or either immediate or delayed breast implant reconstruction techniques.

A summary of patient statistics and outcomes including complications after procedures for breast reconstructions performed by the Fellow is provided in Table 3. All autologous breast reconstructions performed were pedicle TRAM flaps. Immediate and delayed implant reconstructions utilized Allergan Natrelle implants (150, 133 and 410 implant types).

Examples of results achieved are presented in Figure 1. Minor problems were seen in three patients (see Table 3) and two patients suffered major complications. One patient developed a pulmonary embolus despite post-operative anticoagulation and negative lower legs Doppler ultrasound. She subsequently was therapeutically anticoagulated but soon thereafter developed a bleed into her abdominal wall in the operative surgical wound. This eventually required a return to theatre for evacuation of haematoma; however, the patient was subsequently stabilized on anticoagulation and was discharged home well.

Another patient developed complications relating to lateral flap necrosis. This was a very high-risk procedure from the start and the patient was counselled appropriately. However, due to patient's choice and persistence, an operation was offered. She had received a radical Halsted mastectomy 30 years prior with post-operative chest wall radiotherapy, and the quality of the chest wall and overlying skin was very poor. She also had a previous midline laparotomy for open cholecystectomy many years ago, which increased the risk of ischaemic complications. She had a previous failed implant reconstruction and was declined a free flap reconstruction by a plastic colleague. However, the patient was very keen to have the reconstruction and was accepting of high risks associated with it. Intraoperatively, a contralateral pedicle was chosen due to extensive radiotherapy damage to the mastectomy site. Not surprisingly, she developed a full-thickness flap necrosis to 20% of the flap at the lateral side, requiring debridement and vac dressings, with eventual closure by a combination of primary and secondary intention. Despite this, the patient was very happy with the results and grateful for having had the procedure. This case also provided the Fellow with valuable insight into the prevention and management of these complications, as well as the importance of case selection and the need for adequate surgical training for oncoplastic breast surgeons.

Discussion

The results presented show a broad exposure to a range of conventional and oncoplastic operative types of breast surgery (Table 2). Importantly, they also show a significant exposure to reconstructive breast surgery, skewed towards autologous reconstruction in this case, which was the preference of the oncoplastic breast surgical mentor, particularly in the setting of delayed reconstruction. This approach in itself may reflect and demonstrate the fact that patient selection, in the absence of a supporting plastic and reconstructive surgical colleague, is very important. The best available technique on the background of expertise and experience needs to be and is chosen in this setting.

A few patients undergoing delayed pedicle TRAM flap reconstruction did show some minor complications and in two cases major complications. This reflected patient characteristics and the limitations of the surgical technique used.

Development of oncoplastic skills follows a steep learning curve; therefore, the length of time it takes to get proficient with OBS is variable. The UK Oncoplastic training programme is only 1 year long,[5] while the Brazilians have spread it over 21 months, with one weekend a month dedicated to teaching a particular module in oncoplastic training.[7] A different classification of oncoplastic procedures is utilized in Brazil as compared to the UK system, Urban's classification (see Table 4[9]). At the end of training, the Brazilian cohort was able to progress their skills from Urban's level I to level II or III.[9]

The EUSOMA guidelines stipulate exactly what is considered minimum experience during one's training to successfully complete the oncoplastic Fellowship. They suggest that the fellows should have assisted 10 and personally performed five skins sparing mastectomies, observed or assisted at 10 and personally performed five remodelling procedures and observed or assisted at 10 immediate and delayed total breast reconstructions using both implants and autologous tissue.[6] These sorts of guides to training can be achieved in 1 or 2 years of post-Fellowship training, but will also significantly depend on the individual's previous experience, confidence, type of teaching provided by their mentor and support in moving forward.

Currently, acquiring experience and competence in OBS procedures is highly variable around Australia and New Zealand. This

Table 3 Summary of demographics and outcomes for reconstructions performed by the Fellow between February and December 2012

Patient	Age	Procedure	Immediate/Delayed/ = Unilateral/Bilateral	Background	LOS	Complications
M.M	52	Expander implant insertion	Immediate Bilateral	Strong FHx No genetic defect identified	1 day	
S.F	32	Expander implant insertion	Immediate Bilateral	Known BRCA1 family history	2 days	
S.M	77	Expander implant insertion	Immediate Bilateral	Strong FHx	1 day	
V.F	41	Expander implant insertion	Immediate Bilateral	Known BRCA1 family history	2 days	
T.M	53	Pedicle TRAM flap reconstruction	Delayed Bilateral	Obese 5 years post bilateral mastectomy	7 days	Seroma behind the flap with small abdominal wall hernia requiring repair.
S.C.	44	Pedicle TRAM flap reconstruction	Delayed Unilateral	2 years post mastectomy	7 days	Minor wound breakdown and fat necrosis laterally requiring minor debridement
M.M.	52	Pedicle TRAM flap reconstruction	Delayed Bilateral	3 years post bilateral mastectomy	29 days	Post-operative PE and abdominal haematoma secondary to anticoagulation requiring evacuation
M.E.	64	Pedicle TRAM flap reconstruction	Delayed Unilateral	30 years post right mastectomy	8 days	20% Flap necrosis laterally requiring debridement
K.R	54	Pedicle TRAM flap reconstruction	Delayed Unilateral (plus symmetry procedure)	2 years post left mastectomy and AC	5 days	
K.Ru.	61	Pedicle TRAM flap reconstruction	Delayed Bilateral	2 years post B/L mastectomy	11 days	Minor umbilical cellulitis

depends on the kind of exposure available, the breadth and the volume. It does matter whether the Fellow's experience is built on mostly assisting at these kinds of procedures or whether they have had ample opportunity to perform these themselves, with adequate supervision. This regional experience was unique with hands on operative experience encouraged right from the very beginning of the Fellowship. This has compensated for lower volumes that would have been achieved in a large tertiary unit.

There is a growing interest in OBS throughout the world, particularly over the last 10 years. This is indicated by an increasing literature on the subject and an increasing number of OBS courses and conferences, which are happening regularly now in most regions.[10]

The UK and Brazilian oncoplastic training programmes have become extremely popular among surgical trainees and Fellows.[7,11] The drivers for these developments have come from ever expanding interest in this field, community education, awareness and demand for this kind of surgery as well as interest from trainees and problems with recruitment in classical breast surgery.[12,13] In the UK since 2002, nine nationally appointed oncoplastic breast surgical training positions have been established, which has now produced over 80 oncoplastic Fellows, from a mix of general, breast and plastic surgical backgrounds.[14] One of the reasons for this initiative was a low rate of post-mastectomy reconstruction across UK, with low rates of discussion of this procedure and access to it for patients undergoing mastectomy for breast cancer. The National Reconstruction Audit in UK 2011 showed that these rates have significantly increased. Most women-undergoing mastectomy had the reconstructive options discussed with them and high satisfaction rates at early and medium term for patients having immediate and delayed reconstructive procedures have been achieved.[15]

Australia lacks similar infrastructure and perhaps this is one of the reasons for low reconstruction rates in Australia. The national patterns of care for breast cancer study found that only 6% of women who had a mastectomy had a breast reconstruction (or had one planned).[16]

The vast geography and public/private structure of healthcare peculiar to Australia have been some of the other reasons thought to impact on these low numbers, as well as the low numbers of OBS and plastic surgeons offering this type of surgery.

To improve these results, we need to improve patient access to well trained oncoplastic breast surgeons throughout metropolitan and regional Australia, in both public and private arenas. Currently, BreastSurgANZ is undertaking the early steps in the development of OBS. This body accredits breast surgical training positions in Australia and promotes and coordinates training exposure.

One way to help meet the growing demand in oncoplastic training is establishment of multiple accredited BASO level I and level II units. The BASO level II units are likely to be established around existing large breast units in tertiary hospitals with onsite support from plastic surgeons. These can become comprehensive oncoplastic breast units, where cross specialty training for interested oncoplastic surgeons can flourish under a standardized programme.

However, these alone will not be enough to meet the supply and demand of neither the patients spread over a large geographically diverse continent, nor the interested trainees which can miss out on an important aspect of training depending on the way their unit is set up. Therefore, it makes sense to promote a number of BASO level I

Fig. 1. (a) Seven months after bilateral breast implant reconstruction after final expansion to desired volume by patient. (b) 9 months following left breast pedicle tram flap breast reconstruction. (c) 5 months after bilateral pedicle tram flap breast reconstruction. (d) 3 months following unilateral pedicle TRAM flap reconstruction with simultaneous contralateral symmetrizing mammaplasty.

Table 4 Urban's classification for oncoplastic breast surgery procedures (adapted from Urban[9])

Level I	Level II	Level III
Monolateral breast reconstruction techniques such as aesthetic skin incisions, de-epithelization of the areaolar margins, glandular mobilization and reshaping techniques, purse string reconstruction with temporary expanders	Bilateral procedures such as lipofilling, breast augmentation, breast reduction, mastopexy, Grisotti flap, and nipple and areola reconstruction	More complex monolateral or bilateral procedures involving autologous flaps (pedicle or free flaps), immediate and delayed breast reconstruction with implants or a combination of techniques
Specific competence in plastic surgery is not required at this point	Specific competence in plastic surgery techniques of the breast is required to achieve better symmetry	A higher standard in plastic surgery techniques is required

OBS units across already existing medium-sized units in peripheral metropolitan and regional locations across Australia.

These types of units may provide core foundation training in oncoplastic surgery to the Fellows, which should be expanded on subsequently in a larger volume institution. Whether this is feasible or not, has been the purpose of this study over a period of 1 year in PMBH, which is defined as a BASO level I unit according to the UK BASO guidelines. We would argue that broad, hands on experience have been achieved in both classical and oncoplastic breast surgical techniques, including various reconstructive approaches, which will expand the armamentarium for management of patients with breast disease.

For core OBS training to happen, a number of hurdles need to be overcome.

At least one of the breast surgeons in the unit needs to be performing around 25 reconstructive procedures per annum as well other OBS procedures and only then establishment of an oncoplastic breast Fellow may be considered.

Establishing an OBS Fellow training position at the hospital may not be financially feasible in every regional situation where OBS is practiced. The Fellow's position at PMBH was funded by employing the Fellow as a junior staff specialist general surgeon, including a specific acute general surgery service commitment (which was seen as a trade off for the opportunity to receive appropriate OBS training).

BASO Level I oncoplastic training units do not incorporate direct plastic surgical input, whereas BASO Level II oncoplastic training units do. Therefore, OBS trainees are encouraged to gain exposure in a BASO Level II oncoplastic training unit following completion of a BASO Level I Fellowship if at all possible. Clearly, no one surgeon can have all of the possible skills and knowledge and hence co-operation and support is the key to the development of a well-positioned and supported oncoplastic breast surgical unit.

Despite the significant learning curve associated with OBS training, this presented Fellowship experience clearly demonstrates that this type of regional medium-sized unit approaches the criteria established for BASO Level I oncoplastic units. It can be utilized in a broader training programme to train future fellows. These types of units may also be able to provide niche skills such as pedicle TRAM flap training, which is not widely available in Australia.

Regional units such as this one suffer to some extent from lower volume than their larger counterparts in major metropolitan cities. However, this is also to the benefit of these units, as lower volume generally means more hands on training for oncoplastic breast surgeons during their OBS Fellowship years.

Importantly, it can benefit the regional centres by the development of local infrastructure to support women with breast cancer, offering them the same level of care and options available to their counterparts in larger metropolitan hospitals.

The OBS training unit environment also promotes interaction with like-minded colleagues, for more isolated practitioners in regional centres, enhancing the local surgeon's practice and helping maintain their currency. It may bring cross-fertilization of ideas as Fellows move from various locations and take their experiences with them.

Finally, it should be noted that BreastSurgANZ did not review or contribute to this manuscript and the suggestions/recommendations for OBS training are the authors own.

Conclusion

In conclusion, the results of this single-centre review suggest that regional training in BASO level I oncoplastic breast surgical units is feasible, beneficial and perhaps even advantageous. In this regional setting, oncoplastic breast surgery provides the service to the community, which is in demand. Thus, regional BASO level I oncoplastic breast surgical units should be further supported, by recognizing the valuable service they provide to breast cancer patients as well as to the training oncoplastic breast surgical fraternity.

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The Breast 34 (2017) 58–64

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Original article

Oncoplastic techniques: Attitudes and changing practice amongst breast and plastic surgeons in Great Britain

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ARTICLE INFO

Article history:
Received 12 December 2016
Received in revised form
4 April 2017
Accepted 20 April 2017

Keywords:
Oncoplastic techniques
Oncoplastic breast surgery
Plastic surgery
Questionnaire

ABSTRACT

Purpose: The availability, acceptability and practice of oncoplastic surgery has increased over the last 5 years. This study aims to describe how the breast and plastic surgical workforce has adapted to provide oncoplastic breast surgery.
Methods: A questionnaire was distributed to members of the Association of Breast Surgery and BAPRAS, and results compared to a survey completed in 2010.
Results: In 2010, 228 respondents completed the survey compared to 237 in 2015, of whom 204 were consultants (105 General or Breast Surgeons and 99 Plastic Surgeons). The range of procedures performed by Plastic Surgeons has remained static, the General and Breast Surgeons are performing proportionally more therapeutic mammaplasty ($p < 0.001$), breast reduction/mastopexy, and latissimus dorsi reconstructions. In 2015, surgeons are less concerned about the risks of lipomodelling than in 2010, with an increase the proportion of breast (55% vs. 26%) and plastic (91% vs. 58%) surgeons performing the technique.
Discussion: Specific concerns about oncoplastic surgery have decreased over the last five years, with a greater proportion of surgeons performing oncoplastic surgery including lipomodelling. The majority of breast surgeons in 2015 remain interested in further training in oncoplastic techniques (75%) but over the last 5 years, plastic surgeons interest in further training in oncoplastic surgery has dropped from 62% to 27%. About half of all breast and plastic surgeons felt that oncoplastic surgery should be available for all women and oncological and wound healing concerns had significantly reduced between 2010 and 2015 ($p < 0.05$).

1. Introduction

Oncoplastic breast surgery includes techniques, which combine mastectomy or wide local excision of breast disease with reconstruction to optimise oncological and aesthetic outcome. It encompasses a huge spectrum of techniques [1] from sympathetic scar placement, partial breast reconstruction, therapeutic mammaplasty, total breast reconstruction, procedures for symmetry and nipple reconstruction, tattooing and lipomodelling [2]. With all new developments in surgical practice, early adopters tend to seek out training from innovators, and then disseminate the new techniques to colleagues and trainees. As techniques become established, more formal training opportunities and accreditation arise such as fellowships, additional training and dissection courses, new curricula and higher degrees.

In parallel with the refinement of oncoplastic surgery techniques, other developments have accelerated the demand for reconstruction. In the UK, the National Institute for Health and Care Excellence (NICE) guidelines recommend that all women should have access to reconstruction [3]. The National Mastectomy and

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http://dx.doi.org/10.1016/j.breast.2017.04.010
0960-9776/

Breast Reconstruction Audit (NMBRA) demonstrated variation in the practice of immediate breast reconstruction across the UK, with rates ranging from 10 to 43% [4]. Increasing patient awareness and demand also provided impetus to try to reduce regional variation.

Although traditionally within the remit of Plastic Surgeons, the relatively small number of Plastic Surgery trained surgeons and increasing demand for oncoplastic surgery, impelled breast surgeons to develop their own skills in some areas of oncoplastic surgery. Patient demand for reconstruction and continually increasing breast disease workload has resulted in oncoplastic breast surgeons shifting their practice towards subspecialisation, and reducing their provision of emergency General Surgery. However it is unknown whether those practicing oncoplastic surgery come primarily from a General and Breast Surgery or Plastic Surgery background and how provision is changing over time. This study aims to describe the current practice of oncoplastic surgery in the UK and how it has changed since 2010.

2. Materials and methods

A closed ended format study specific questionnaire was created and distributed amongst surgeons in the UK with an interest in breast reconstruction surgery (Appendix 1). This was done either via email to all members of British Association of Plastic, Reconstructive and Aesthetic Surgeons (BAPRAS) and Association of Breast Surgery (ABS) members as listed in the members directory, or at the Oncoplastic and Reconstructive Breast Surgery (ORBS) meeting during September 2009 and 2014; and at the National meetings of ABS and BAPRAS in November and December 2009 and 2014 respectively. Data entry was permitted until February 2010 and 2015, respectively, and therefore are referred to as 2010 and 2015 cohorts.

Information requested by the questionnaire included the background (whether initial training was undertaken in General and Breast Surgery or Plastic Surgery), grade and seniority of the surgeon. Respondents were asked how familiar they were with various oncoplastic techniques and whether they performed surgery themselves, or with a colleague. Concerns about oncoplastic surgery were clarified. Finally, each respondent was asked if they would like more oncoplastic training.

Data were automatically transferred into a password-protected database from the electronic questionnaire. Printed questionnaire responses were manually entered into the same database. Statistical analyses were undertaken using Stats Direct (StatsDirect Ltd, Cheshire, UK). Contingency tables were examined using Fisher's exact test. Statistical significance was considered at a probability of $p < 0.05$.

3. Results

In 2010, 228 respondents completed the survey compared to 237 in 2015. These two datasets included surgeons at all levels of experience and training. From the 2010 cohort, 151 surgeons (66%) were consultants and in 2015, 204 surgeons were consultants (86%). The trainee and non-training grade surgeons were excluded from further statistical investigation as they may have had restricted independent practice, leaving only consultant grade surgeons to be taken forward into the detailed analysis. In 2010 this included 109 surgeons from a General and Breast Surgery training background and 42 from a Plastic Surgery training background; by 2015 this had changed to include 105 General and Breast Surgeons (a decrease of 3.7%) and 99 Plastic Surgeons (an increase of 136%; $p < 0.001$). The seniority amongst the General and Breast Surgeons has remained relatively static, whilst the majority of Plastic Surgeons who responded in 2010 were within five years of appointment, whereas by 2015 the cohort is similar to the General and Breast Surgeons (Fig. 1). The percentage of time spent dedicated to breast surgery was not included in the survey for either specialty, neither was time spent or procedures performed specifically in the NHS compared to privately.

There was a general acceptance that oncoplastic surgery should be available to all women, with 48% of General and Breast Surgeons and 52% of Plastic Surgeons agreeing with this. Initial concerns in

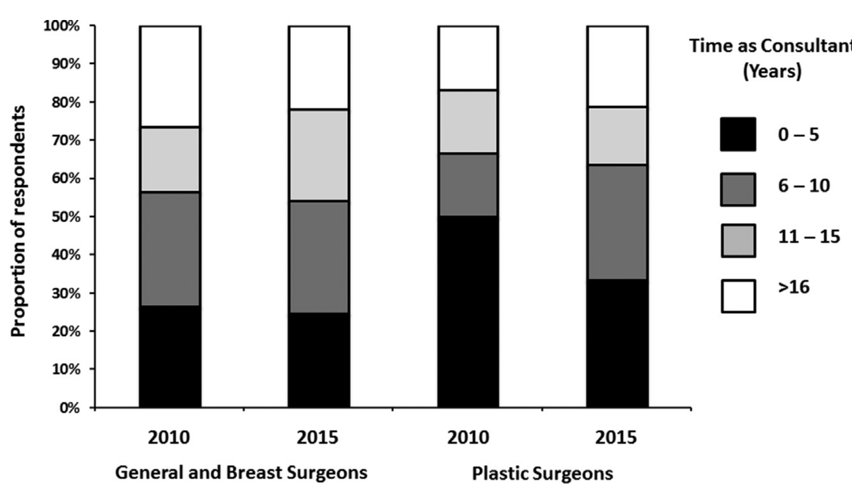

Fig. 1. The seniority of consultant responders.

2010 amongst General and Breast Surgeons about the oncological safety of the resection (expressed by 10% respondents), and Plastic Surgeons about the delays due to healing problems (expressed by 20% of respondents) were most markedly reduced in 2015 (oncological safety concerns expressed by 2% of Breast and General Surgeons; wound healing concerns expressed by 8% of Plastic Surgeons; $p < 0.02$).

The proportion of General and Breast Surgeons that are performing therapeutic mammaplasty has increased significantly since 2010 from 55% to 82% of the total cohort in 2015 ($p < 0.001$). The number of therapeutic mammaplasties performed as joint cases between General and Breast Surgeons and Plastic Surgeons has reduced threefold, and the proportion of Plastic Surgeons performing therapeutic mammaplasty alone has reduced by 27%.

The proportion of Plastic Surgeons performing mastopexy and breast reduction has remained nearly static from 2010 to 2015, with 94% of the most recent cohort performing these procedures, only a rise of 10% on the 2010 figures. The proportion of General and Breast Surgeons performing breast reduction or mastopexy has risen from 56% in 2010 to 82% in 2015. These figures relate to both cancer and non-cancer related cases. The proportion of these procedures performed as joint cases between the specialties has more than halved over this time.

The proportion of surgeons performing latissimus dorsi myocutaneous pedicled flap breast reconstruction alone is similar in the 2015 cohort with 82% of Plastic Surgeons and 81% of General and Breast Surgeons performing this technique. In 2010, 78% of Plastic Surgeons were performing this procedure, whereas only 67% of Breast and General Surgeons were carrying out this operation alone. The use of autologous fat grafting has also increased over the study period. In 2015, 91% of Plastic Surgeons and 55% of General and Breast Surgeons were performing fat grafting. Concerns about the procedure were globally reduced in 2015, compared to 2010. There was a proportional increase of 44% by Plastic Surgeons performing this procedure, but more notably an increase of 112% by General and Breast Surgeons on the 2010 figures (Fig. 2).

When questioned about who performs contralateral surgery (breast reduction or mastopexy) after mastectomy, in 2010, 41% of General and Breast Surgeons performed the operation; by 2015, this had risen to 79%. Plastic Surgeons are performing more ipsilateral surgery in 2015 than in 2010 (12% versus 1%), but this is a modest increase, considering the majority of General Surgeons with oncoplastic training perform oncoplastic surgery without the input of a Plastic Surgeon. New data acquired from the 2015 survey showed a similar proportion of surgeons from both training backgrounds using tissue expanders and implants, dermal sling techniques and acellular dermal matrices. Free flap breast reconstruction is performed by 74% of Plastic Surgeons, but only 1% of General and Breast Surgeons, although 14% of General and Breast Surgeons will perform free flap breast reconstruction on their patients as a combined case with Plastic Surgery.

When the question of further oncoplastic training opportunities was asked, General and Breast Surgeons expressed interest in 75% of cases in 2010, dropping to 71% in 2015. Plastic Surgeons expressed an interest in further training in 62% of cases in 2010, but this was only 27% by 2015. As Breast surgeons are becoming more competent in all oncoplastic procedures except free flap reconstruction it can be suggested this is the area in which further training opportunities would be sought. Conversely resectional work is infrequently performed by the Plastic surgeon, possibly due to their lack of involvement with the MDT, and therefore the acquisition of further oncoplastic techniques are not pursued. Of the 2015 cohort who commented, 47 (23%) had completed a specific oncoplastic fellowship and had already received training, and 9 (4%) cited being too old or close to retirement as reasons for lack of

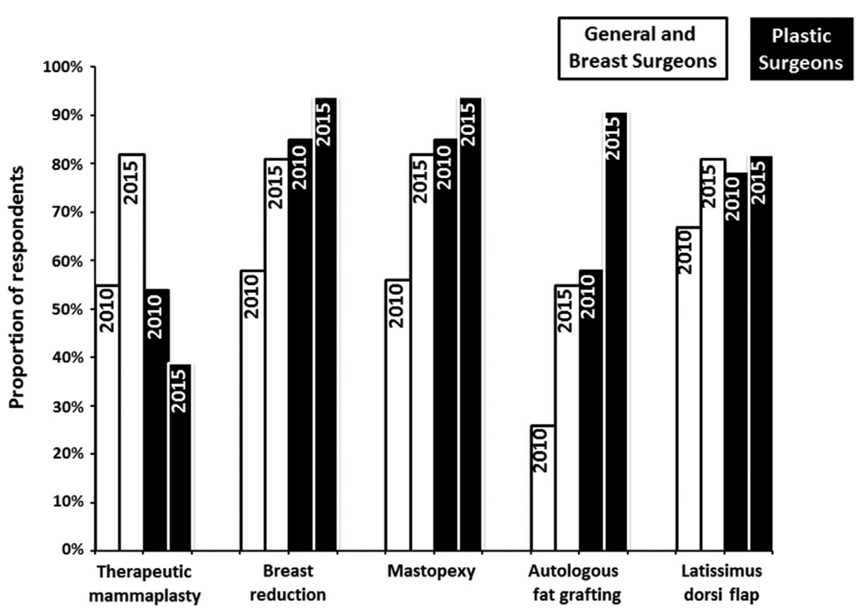

Fig. 2. Comparison of procedures performed between 2010 and 2015 surveys.

interest in further training.

4. Discussion

Total breast reconstruction, traditionally the remit of plastic surgeons, is still performed predominantly by Plastic Surgeons. Since 2010, General and Breast surgeons are performing a greater variation of techniques and increasing the procedures they offer independently with fewer joint procedures. The trend of detecting smaller cancers by screening and increasing use of neoadjuvant chemotherapy leading to partial or complete pathological response is likely to lead to a lower mastectomy rate [11] and greater prevalence of aesthetic breast conservation techniques. In addition, the ‘aesthetic’ elements of reconstruction are shifting to become integral to the initial assessment and thus undertaken by surgeons trained in both cancer resection and aesthetic reconstruction.

There are a number of factors that reduce Plastic Surgeons' capacity to perform oncoplastic techniques. There are fewer surgeons nationwide, with huge cross speciality demands from skin oncology, lower limb reconstruction, hand surgery, burns, cardiothoracics, neurosurgery, and gynaecology. Plastic Surgeons also may not generally be available in the assessment clinics or breast Multi-Disciplinary Team (MDT) meeting and may only be included in a patients' care if referred by the primary breast cancer surgeon, breast care nurse, or requested by the patient. This involvement may be limited by emergency or trauma commitments, and locoregional outpatient clinics, whereas a proportion of the general breast surgeons are dropping emergency general surgery commitments to focus on elective breast work.

There is also a short-term financial bias against microsurgical autologous reconstruction, due to insufficient tariff and longer operative time and hospital stay, despite cost effectiveness and better long-term outcomes [12–14]. This may lead hospital funding bodies to try to manage resources by encouraging and supporting implant based reconstruction (shorter hospital stay, reduced operating theatre utilization) and oncoplastic techniques.

General and Breast surgeons have enthusiastically adopted new techniques and training and the breast surgery curriculum has greater focus on oncoplastic techniques. There are more breast surgeons applying and succeeding in appointment to oncoplastic breast fellowships, since their inception 15 years ago. Since 2011, the proportion of General Surgery trainees applying for the Training Interface Group (TIG) Oncoplastic Breast Surgery Fellowship vastly outweighs Plastic surgery applicants. Of those completing the fellowship 80% (53/66) were Breast Surgery trainees, whilst only 20% 13/66 were Plastics trainees.

This discrepancy may be due to the General surgery curriculum not preparing trainees for a career in Oncoplastic surgery. Many general trainees now sit the European Board of Surgery Qualification in Breast Surgery as the FRCS lacks the depth of knowledge required as a Consultant Oncoplastic Surgeon. Breast surgery constitutes a much smaller proportion of the General surgery curriculum and training time than the Plastics equivalent.

There are also a greater number of General and Breast Surgery trained candidates at both the oncoplastic skills courses run by the Royal College of Surgeons and reading for a Masters degree in Oncoplastic surgery. In contrast, Plastic Surgeons are less well represented and, according to this survey, have less interest in training in oncoplastic techniques.

The optimization of oncological and cosmetic outcomes for patients requires all clinicians treating them to use their complimentary skills to best effect. The practice of collaborative working varies across the UK, with some units having weekly combined MDT meetings in which both General and Breast Surgeons and Plastic Surgeons plan treatment, to units in which only autologous or revision cases are referred by letter to Plastic Surgeons. By involving surgeons with skills in resectional, autologous and aesthetic skills in the initial treatment planning, it is more likely that the team will achieve the best oncological and aesthetic outcomes for the patient.

This survey did not encompass patient outcomes, and whilst the NMBRA, and ongoing iBRA national audits assessed outcomes and patient satisfaction, outcomes comparing patients operated on by either Breast or Plastic surgeons were not specifically reported. The results of this questionnaire clearly show that free tissue transfer is almost universally performed by Plastic surgeons (71/72 total combined Breast and Plastics who perform independently), whereas Breast surgeons are performing most other oncoplastic procedures independently.

It is possible that those with other general surgery or trauma commitments may be less keen to learn new techniques compared to those with full time commitment to breast surgery. Similarly those with a larger private workload may be less inclined to train further as they do not have time to perform the additional procedures.

5. Conclusions

In the last five years, a greater proportion of General and Breast surgeons are performing a wider variety of oncoplastic and aesthetic surgery. However, Plastic Surgeons have not extended their repertoire to the same extent, remaining fairly static in the variety of procedures offered. Concerns about oncological safety and wound healing of oncoplastic surgical techniques have significantly reduced overall between 2010 and 2015. There are challenges to collaborative working with the greater burden of free flap reconstruction reducing availability of Plastic Surgeons to contribute to the multidisciplinary management of patients in some regions. An increase in number of Plastic Surgeons, encouraging involvement in MDT and engagement of all specialities is important to improve and develop breast treatment for all patients.

Conflict of interest

The authors state no conflict of interest.

Funding

None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.

Appendix 1. Questionnaire

Time in consultancy:

0 - 5 years ☐
6 - 10 years ☐
11 - 15 years ☐
> 16 years ☐

Please describe your experience of the following techniques

	I perform	I perform with colleague	I am familiar with but do not perform	I am not familiar with
Therapeutic mammplasty				
Grisotti flap				
Breast reduction				
Mastopexy (breast lift)				
Fat transfer				
Latissimus dorsi flap				
Tissue expander/implant				
Dermal sling				
ADM				
Free flap				

Approximately what percentage of cases in your unit are suitable for therapeutic mammaplasty, and how many therapeutic mammaplasties are performed?

	0%	**<10%**	**11-25%**	**26-50%**	**51-75%**	**>76%**	Don't know
Suitable							
Performed							

Do you have any reservations about oncoplastic breast surgery in general?

Yes, delay in cancer surgery due the need to coordinate with plastic surgeons ☐

Yes, oncoplastic surgery requires too much theatre time ☐

Yes, adjuvant therapy may be delayed due to healing problems ☐

Yes, about the oncological safety of resection ☐

Yes, about how to proceed if margins are involved ☐

Yes, about the viability of breast parenchyma after transposition ☐

Yes, data does not yet support the use of this technique ☐

Yes, about operating on the contralateral 'normal' breast ☐

Yes, other reservations Please expand ....

No, I think oncoplastic surgery should be available to all women ☐

If you have inadequate margins for DCIS after therapeutic mammaplasty, how do you proceed?

I do not do therapeutic mammaplasty ☐
Offer radiotherapy ☐
Take down therapeutic mammaplasty and resect involved margins ☐
Offer mastectomy ☐
Other ☐ Please expand ....
This situation has not arisen in my practice ☐
Don't know ☐

If you offer oncoplastic surgery in your unit, who does the majority of ipsilateral surgery (therapeutic mammaplasty) and contralateral surgery (eg breast reduction/ mastopexy)?

	Ipsilateral surgery	**Contralateral surgery**
Plastic surgeon alone		
Plastic and general surgeon (combined)		
Plastic and general surgeon (independent)		
General surgeon with oncoplastic training		
General surgeon alone		
We do not offer oncoplastic surgery		

(***continued***).

The Association of Breast surgery at BASO, recently published a guide to good practice in oncoplastic surgery. Do you agree with their indications for therapeutic mammaplasty? 2010 data only

	Agree	Disagree
>20% breast resection		
Inferior resection		
Central resection		
Medial resection		
If axillary dissection required through WLE incision		
Large breasted women		

Fat transfer, the process of liposuction followed by injection of the processed fat, is being used to correct small defects following breast surgery. Do you think this is a good idea? (more than one answer can be given)

Yes, the benefits outweigh the risks in a fully informed patient ☐
No, multiple procedures are required ☐
No, it doesn't work ☐
No, the stem cells in fat may promote cancer recurrence ☐
No, the microcalcification that may follow can make screening more difficult ☐
No, subsequent fat necrosis may require repeated biopsies ☐
Other ☐ Please expand ....

If there were more training opportunities for oncoplastic surgery, would you be interested?

Yes ☐
No ☐

(***continued***).

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Reduction and Mastopexy Techniques for Optimal Results in Oncoplastic Breast Reconstruction

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Semin Plast Surg 2015;29:102–109.

Abstract

Breast conservation therapy has emerged as an important option for select cancer patients as survival rates are similar to those after mastectomy. Large tumor size and the effect of radiation create cosmetic deformities in the shape of the breast after lumpectomy alone. Volume loss, nipple displacement, and asymmetry of the contralateral breast are just a few concerns. Reconstruction of lumpectomy defects with local tissue rearrangement in concert with reduction and mastopexy techniques have allowed for outstanding aesthetic results. In patients who have a reasonable tumor-to breast-size ratio, this oncoplastic surgery can successfully treat the patient's cancer while often improving upon preoperative breast shape. Specific surgical guidelines in reduction and mastopexy help achieve predictable aesthetic results, despite the effects of radiation, and can allow for a single surgical procedure for cancer removal, reconstruction, and contralateral symmetry in one stage.

Keywords
- oncoplastic surgery
- breast reconstruction
- breast cancer
- breast conservation therapy

Historical Data

Breast cancer is the most common malignancy affecting women in the United States, and the second leading cause of cancer mortality in women, with a current rate of more than 230,000 new cases annually. One in eight women will develop breast cancer during her lifetime.[1] Considering these statistics, plastic surgeons must be well versed in current reconstructive options.

Although mastectomy rates are on the rise, many newly diagnosed breast cancers are still treated with breast conservation techniques. Improvements in mammography and neoadjuvant therapies have helped with early identification and downstaging of breast cancers, increasing the number of patients who are candidates for breast conservation therapy.[2–4] Early identification and adjuvant treatments have helped revolutionize the surgical approach to breast cancer from the radical operations once championed by Halsted.[5,6] In 1985, the Early Breast Cancer Trialists' Collaborative Group were among the first to establish the equivalency of mastectomy and breast conserving therapy (BCT).[2] These observations were supported by trials performed by the National Surgical Adjuvant Breast and Bowel Project (NSABP), securing the equivalency in survivorship between mastectomy and BCT.

In addition to oncologic success and decreased patient morbidity, utilization of breast conservation techniques has many other advantages. Women who have undergone breast conservation are more likely to have a better body image, feel more comfortable naked and with physical intimacy, and have fewer complications of scarring, numbness, and asymmetry.[7] A quality of life survey by Curran et al demonstrated significant benefits in cosmesis, body image, and treatment satisfaction in patients treated with breast conservation techniques.[8]

To achieve an aesthetic shape and symmetric result in the setting of breast conservation, oncoplastic breast

Issue Theme Techniques in Breast Reduction and Mastopexy; Guest Editor, Rodger H. Brown, MD

DOI http://dx.doi.org/10.1055/s-0035-1549051.
ISSN 1535-2188.

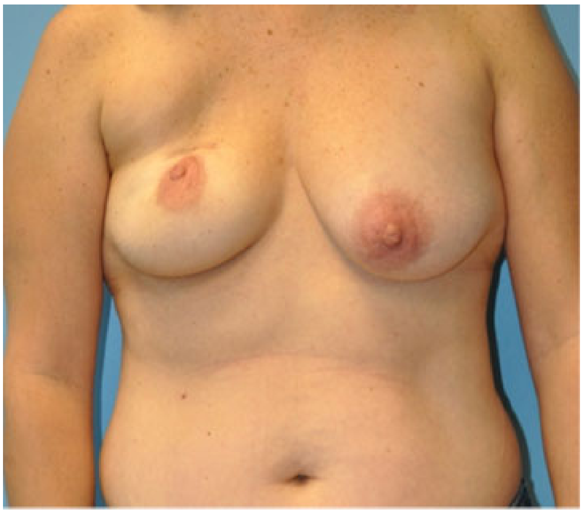


Fig. 1 Patient who underwent lumpectomy without oncoplastic surgery and a cosmetically unfavorable result.

reconstruction techniques are being utilized more frequently. An oncoplastic approach allows for resection of larger tumors without jeopardizing breast aesthetics, nipple position, and sensitivity.[9] For larger tumors or those located in a less ideal location, poor cosmetic results often occur after lumpectomy and radiation therapy alone (►**Fig. 1**). Techniques to avoid such deformities include reshaping breast tissue (volume displacement), volume replacement, and often shaping the contralateral breast for symmetry, to obtain the best cosmetic outcome.[7,10,11] Local tissue rearrangement, mastopexy, and reduction techniques can allow for volume correction and for the nipple to be relocated to a more aesthetic position, at the same time as tumor removal.[12]

Patient Selection and Surgical Planning

Patients who are candidates for breast conservation surgery should be considered for oncoplastic breast reconstruction when the expected defect will have a displeasing aesthetic result. It is our opinion that in most cases tumor excision and breast reconstruction should be performed in a team approach. At our institution, the breast surgeon/surgical oncologist perform the tumor extirpation, and the plastic surgeon performs the reconstruction concomitantly. We have found that communication and preoperative planning by the team allows for predictable, aesthetic outcomes, with margin positivity occurring less than the national average.

Criteria for breast conservation are relative and should be judged based on tumor- to breast-size ratio.[13] Traditionally, BCT was only offered for patients with lesions below 4 to 5 cm, although now it is increasingly being used for larger lesions as long as it is possible to remove the tumor and keep enough breast volume for a cosmetically acceptable result.[14] Also, the effect of neoadjuvant therapy on tumor size, decreasing the tumor- to breast-size ratio, allows more patients who were not initially candidates to undergo BCT.[13] In our opinion, most tumors more than 1 cm in size can benefit from some degree of reconstruction, whether it is simple local tissue rearrangement to prevent dimpling or full mastopexy with local tissue rearrangement. The procedure choice lies in the goals of the patient and will be discussed at length in the following sections.

The preference of the senior author is to offer oncoplastic procedures to patients who have a relatively small tumor to breast size, those who are especially motivated to save their breast, and for patients who would have a suboptimal result with either an implant or autologous-based total breast reconstruction. In patients with particularly large breasts, a concomitant reduction mammoplasty or mastopexy allows improvement on preoperative shape and asymmetry. For these patients, oncoplastic procedures can be the "silver lining" to their cancer diagnosis, often improving on their preoperative shape and size.

Patients who are not candidates for oncoplastic procedures are those unable to have BCT, such as pregnant patients unable to have radiation or those who cannot have radiation because they were previously irradiated. Multifocal tumors requiring mastectomy, those with a large tumor to breast ratio, and although our team occasionally employs a central lumpectomy, tumors behind the nipple remain a relative contraindication.

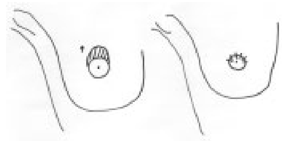
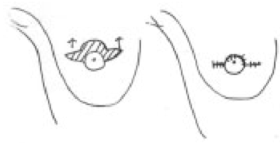
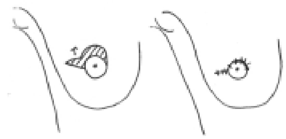
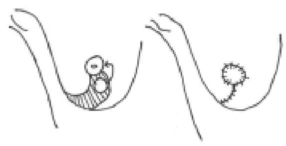
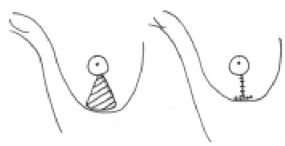
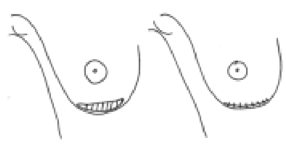
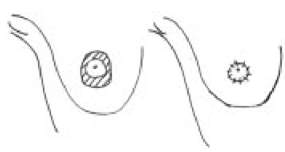
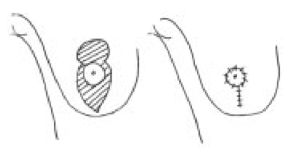
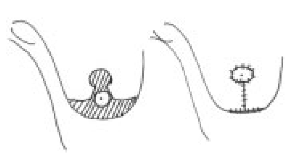
Surgical Approaches

As stated previously, oncoplastic techniques can be subcategorized into volume displacement or volume replacement procedures. Volume displacement is best for patients with medium- or large-sized breasts regardless of ptosis, but may be considered for small-breasted women who do not want mastectomy and total breast reconstruction.[11] Contralateral procedures, to match the operated breast may include reduction mammoplasty, mastopexy, or augmentation. Contralateral procedures can either be done in the immediate setting or in a delayed fashion after allowing the operated breast to have reached its final shape, usually after radiation therapy.[13] In our experience, however, certain reconstructive guidelines that will be discussed in the sections to follow allow for successful shaping of the contralateral breast at the time of ipsilateral tumor removal and reconstruction, thereby avoiding a second surgery and a period of significant asymmetry.

Incision Planning

The incision itself depends on the size and location of the tumor and what type of oncoplastic reconstruction is planned. Of great importance is diagnostic imaging, to fully understand the extent of resection required. For those patients who are candidates for lumpectomy, incisions should be placed in a cosmetic fashion. In our experience, this is commonly within the often-utilized Wise or circumvertical lift incisions. Occasionally, tumors located far from the nipple–areolar complex (NAC) will require separate incisions from standard plastic surgical approaches, even when lifting or reduction is planned.[2,7] In these cases, care and communication must be utilized to maintain skin perfusion and optimum contour. Please see ►**Table 1** for commonly used incision patterns.

Table 1 Mastopexy incision patterns

Incision pattern	Image	Clinical indications
Crescent mastopexy		Tumors above but not involving the NAC[2]
Batwing mastopexy		Lesions near or deep to the NAC, can be used for lesions larger or more medial and lateral than can be removed with crescent mastopexy[12]
Hemi-batwing		Similar to batwing, but for either a medial or lateral tumor[12]
Grisotti advancement/B-flap		Central quadrant tumors[2,13]
Triangle resection		Inferior breast lesions[2]
Inframammary resection		Posterior lesions located near the chest wall in breast with glandular ptosis[2]
Periareolar mastopexy		Periareolar lesions in patients with mild to moderate ptosis[2,12]
Vertical mastopexy		For lesions in large breasts that would benefit from reduction, skin excision patterns can be altered to accommodate the tumor.[2,12]
Wise pattern		

Abbreviations: NAC, nipple–areolar complex.

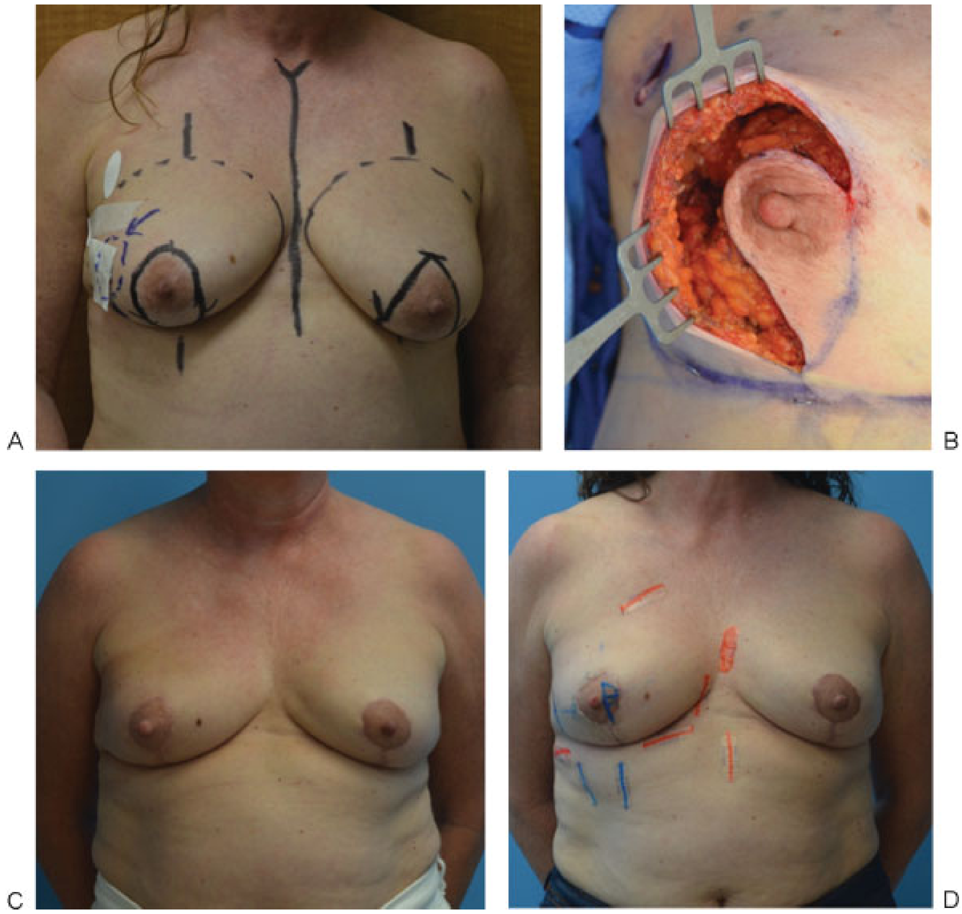


Fig. 2 Patient who had a vertical skin pattern excision. (**A**) Preoperative markings. (**B**) Intraoperative exposure. (**C**) Preradiation. (**D**) Final result at 9 months after radiation therapy.

Fig. 3 Traditional Wise-pattern markings and tumor identified with wire localization.

Breast Reduction and Mastopexy Techniques with Local Tissue Rearrangement

In our practice, the most frequently used techniques for oncoplastic surgery are reduction mammoplasty and mastopexy in concert with local tissue reconstruction of the lumpectomy defect. As mentioned previously, contralateral operations can be done concomitantly or in a delayed fashion, although we advocate for performing contralateral procedures during the initial operation. Others prefer to delay symmetry procedures for 6 months, allowing for stabilization of the effects of radiation.

Other than the ability to decrease the morbidity of macromastia and reduce asymmetry in patients with breast hypertrophy,[10] reduction mammoplasty has been shown to reduce risk of cancer in proportion to the amount of tissue removed,[15] and those with smaller breasts are at decreased risk for radiation toxicity.[16] Breast reductions can allow for a large volume of tissue removal, enhancing the chance of having negative margins. The ability to remove more tissue can allow large tumors to be removed using breast conservation techniques.[11] For women with large breasts, other advantages include those of traditional reduction mammoplasty such as reduction of upper body pain, improvement in clothing fit, and reduction of shoulder grooving from bra straps.[11]

Traditional Wise pattern or vertical breast reduction techniques are chosen depending on the degree of reduction/lifting required.[2,12] Location of the tumor must be considered when the skin excision pattern is delineated. The nipple can either be preserved on a pedicle or excised with the specimen if central lumpectomy is required for tumor removal. If the nipple is to be preserved, lesion location also dictates the choice in vascular pedicle for the NAC.[2,12] For superior lesions, an inferior pedicle is an ideal choice and is also a good choice for lower lateral or medial lesions.[2,12,13] For inferior lesions, a superior or superomedial pedicle can be chosen.[12] The skin around the nipple is de-epithelialized to allow transposition of the nipple to its new location and the breast reduction is continued in the usual fashion depending on the skin excision pattern and pedicle choice (►**Figs. 2–4**).[2]

Criticisms of utilizing the local tissue rearrangement with reduction at time of lumpectomy remain around the ability to achieve cancer-free margins. Positive margins after a concomitant breast reduction can offer a challenge; however, the team approach allows for immediate access to oncologic tumor bed for accurate and complete re-excision when needed. Clips left in the tumor bed mark the area of initial excision, and working together during the re-excision, the plastic surgeon can lead the oncologic team to the location of the tumor.

Planning for the Effect of Radiation on Reduction/Mastopexy

Radiation is essential after BCT, as it decreases the local recurrence rate significantly. Although timing of oncoplastic lumpectomy reconstruction in relation to radiation has been a topic of discussion in the literature, most centers currently agree that lumpectomy and concomitant reconstruction prior to radiation is safe and in the patients' best interest. Some argue that rearranging tissue prior to radiation alters anatomy and clouds the area in need of radiation boost. Our team, however, routinely clips the area of resection so that after rearrangement the appropriate region can undergo radiation boost therapy. Radiation oncologists and surgical oncologists have found this method acceptable for both margin identification and localization on X-ray for boost radiation. Further, combining the procedure into

Fig. 4 Patient with left upper-outer quadrant breast cancer. (**A**) Preoperative anterior view. (**B**) Preoperative lateral view. (**C**) One year after radiation, anterior view. (**D**) One year after radiation, lateral view, showing reasonable symmetry in a single surgical intervention.

one avoids a second anesthetic, avoids the ruddy/stiff nature of the tissue after the healing process begins, and allows the patient one period of recovery prior to radiation.

Although performing oncoplastic reconstruction in the immediate setting clearly has some benefit, challenges remain regarding accounting for the effects of radiation over time. The effects of radiation are progressive and irreversible. Over time, the radiated breast will tighten, become more "perky," and shrink in size. Although it is impossible to predict with precision to what degree a breast will shrink and tighten, we have several guidelines that have helped our center achieve consistent and predictable results.

When performing an oncoplastic reconstruction with reduction or lifting procedure and concomitant contralateral breast lift or reduction, it is imperative that the reconstructive surgeon remembers the effects of the planned radiation therapy and the cosmetic implications on both the affected breast and the nonaffected breast. Without consideration, symmetry in the long term will be impossible. We routinely leave the vertical limb (the distance from the inframammary fold [IMF] to the nipple) 1 cm longer on the breast that is to be radiated. This breast will not go through the natural process of ptosis and if left at the same height as the contralateral breast, long-term symmetry is lost. Along the same vein, we leave the contralateral breast that will not undergo radiation, with a vertical limb that is approximately 1 cm shorter than the affected breast. This side will "relax" with time and not suffer the tightening consequences of radiation. Following this guideline during the initial oncoplastic breast reconstruction allows for prediction (to the best of our ability) of the tightening effects of radiation, thereby allowing for appropriate postoperative nipple position over the long term.

As described, radiation therapy will indeed "shrink" the breast over the course of radiation treatment and the ensuing months after completion. Historically, plastic surgeons would completely delay reduction or lifting of the contralateral breast for 6 or more months after treatment of the ipsilateral affected breast. This can leave patients with a significant deformity and severe asymmetry, which can be challenging both emotionally and physically in clothes. To avoid such a situation and to avoid a second surgery, we simply plan preoperatively to leave the breast that will undergo radiation one-half to one-cup size larger than the nonaffected breast. Although cup size is indeed a nonspecific term, we have found that ~150 to 200 cc larger on the side to undergo radiation allows for a very predictable and reliable symmetry in the long term for most patients. Though no two breasts are ever "perfectly symmetric," the patients have been quite satisfied and none has asked for revision. One important point, however, is that in the patient undergoing mastopexy alone, contralateral reduction is often required on the nonaffected breast. Because the patient's goal may not be consistent with a reduction in size, the effects of radiation limit us and this must be disclosed preoperatively.

Although reconstruction at the time of lumpectomy is always our goal, we routinely see patients who have undergone lumpectomy and radiation without reconstruction and who now have a significant deformity. These patients complain of divot at the location of lumpectomy, nipple deviation, breast size asymmetry, and so on. In treatment of these deformities, we employ a very similar concept of surgical intervention. It has been our experience that the radiated breast will not undergo the traditional "settling" process. This breast almost behaves as though "what you see on the operative table is indeed what you get." For this reason when lifting a previously radiated breast and performing contralateral symmetry procedures, one must be mindful of the differences in tissue.

When reducing or lifting a breast that has previously undergone radiation, we prefer to leave the pedicle to the nipple as large as possible—certainly larger than the normal 7-cm reduction pedicle. This improves vascular supply and decreases the risk of insult to the nipple. Further, the mastopexy flaps on the radiated breast must be thicker than normally created, usually at least 1.5 cm in thickness, again to avoid wound-healing complications. Finally, we inset the NAC in the exact position we ultimately would prefer it to lie. Instead of planning on the breast settling, we have found that the previously radiated breast does not settle and should be placed at the level at which you prefer it, long term. The contralateral reduced or lifted breast should have a shorter IMF to nipple distance than the radiated side, usually by 1 cm, as this side will indeed settle. ►**Fig. 5** shows an example of a previously radiated breast undergoing a reduction with an example of the intraoperative measurements.

A

B,C

Fig. 5 Patient status post right lumpectomy and radiation. (A) Preoncoplastic surgery at time of referral. (B) Intraoperative view showing measurements. Note distance of inframammary fold to the nipple–areolar complex on radiated side is purposefully placed 1 cm longer to account for settling of the contralateral nonradiated breast. (C) Final postoperative result.

In our practice, following these specific guidelines have allowed for predicable results in the complex setting of radiation. The differences in tissue must be considered, as should the effects of the upcoming or previously performed radiation, as traditional breast dynamics are indeed altered.

Local Tissue Rearrangement without Reduction/ Mastopexy

Local tissue rearrangement without reduction or mastopexy is most commonly utilized for patients with minimal to no nipple ptosis and those who are pleased with their current breast size. Several techniques exist, however, in our hands, the most commonly utilized intervention in these patients is local breast advancement flaps. Once the tumor is removed, the breast parenchyma is elevated off of the pectoralis major muscle and advanced to fill the defect. The tissue from both sides of the defect is then rearranged to eliminate the cavity.[2] In our experience, local rotational breast flap closure in these smaller breasted patients without nipple ptosis utilizing 2–0 polydioxanone (PDS) plication of the breast pillars allows for bolstering of shape, filling of dead space, and avoidance of NAC displacement after radiation therapy.

Central Lumpectomy

This technique is used to resect lesions involving or just posterior to the NAC. The NAC and a cone of tissue are removed down to the level of the pectoralis fascia, or as deep as required by the oncologic scenario. Then, an inferior skin-glandular flap is rotated to fill the defect, making a smaller, but naturally shaped breast amenable to nipple reconstruction months after completion of radiation.[2] Often the scars of such a resection are similar to vertical or traditional Wise-pattern reduction, depending on the postoperative size goals.

Other Techniques

Rarely performed in our practice and beyond the scope of this article, local and regional flaps can be utilized to fill the defect caused by lumpectomy. For patients with small breasts or those requiring a large volume of replacement, local fasciocutaneous flaps, myocutaneous flaps, and free flap techniques can be utilized.[9,17] However, we prefer to save these larger options for total breast reconstruction, as utilization of these techniques “burns a bridge” in the case of cancer recurrence.

Fat grafting has emerged as an important adjunct in oncoplastic surgery.[18] For women with smaller breasts, contour defects after partial mastectomy can be managed using fat grafting techniques.[19] Questions remain, however, as to whether fat grafting into a tumor bed can affect the recurrence rate as well as the ability of breast radiologists to interpret changes after fat grafting on screening mammography.[18] In our practice, we prefer to utilize fat grafting for small defects in the setting of autologous or implant based total breast reconstruction, as these issues no longer are relevant.

Outcomes and Complications

Breast conservation has known emotional and psychological benefits over mastectomy. Patients who undergo oncoplastic procedures maintain the feel, color, and texture of their native breast. Rowland et al compared patients who underwent lumpectomy versus those who underwent mastectomy and those who underwent mastectomy and reconstruction. The lumpectomy patients had less postoperative symptoms, but also had less negative effects on body image and felt more attractive than women in the other two groups.[20] Studies consistently show high patient satisfaction with cosmetic appearance after oncoplastic reconstruction. Those who were not pleased, however, thought their breasts were too small for their body habitus.[14] We find that preoperative education regarding the effects of radiation therapy on breast size and appearance greatly improves patient satisfaction, as expectations are set appropriately.

Common complications after breast conservation therapy and oncoplastic reconstruction include hematoma, wound-healing difficulty, fat necrosis, and seroma formation. Wound-healing problems, especially at the “T” junction in the reduction and mastopexy cohort, can delay starting postlumpectomy radiation therapy. In general, radiation therapy should be started within 9 weeks of lumpectomy. Therefore, plastic surgeons should be aggressive in treating these patients with re-excision of wound and closure in a timely fashion to avoid delay in treatment.

The complication of positive margins after lumpectomy remains a challenge for the surgical team. In a prospective series of 90 oncoplastic patients out of Helsinki, 16.2% required completion mastectomy.[10] In our practice, however, the complication of positive margin after lumpectomy and oncoplastic reconstruction is less than the national average and only one patient required completion mastectomy due to inability to obtain negative margins. When margin positivity does arise, working as a team allows ease of access to tumor bed, accurate re-excision, and maintenance of aesthetic result.

Conclusion

Long-term survival rates of patients undergoing breast conservation therapy and oncoplastic reconstruction are comparable to those who undergo traditional mastectomy.[10] In patients who have a reasonable tumor- to breast-size ratio, lumpectomy and reconstruction with local breast tissue and lifting and/or reduction can successfully surgically treat the patient’s cancer while often improving upon preoperative breast deformity or asymmetry. Further, following predictable surgical guidelines in reducing or lifting breasts prior to unilateral radiation therapy allows for successful reconstruction of both breasts in a single stage.

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Plastic and Reconstructive Surgery Advance Online Article

DOI: 10.1097/PRS.0000000000004009

The Expanded Use of Auto-augmentation Techniques in Oncoplastic Breast Surgery

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Financial Disclosure Statement: None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.

Presented at the annual Plastic Surgery the Meeting, Los Angeles CA, September, 2016

Short Running Title: Auto-augmentation in Oncoplastic Surgery

This study is approved by the university's Institutional Review Board

AL: Contributed to patient enrollment, data collection, statistical analysis, and manuscript preparation.

AH: Contributed to patient enrollment, data collection, statistical analysis, and manuscript preparation.

JD: Contributed to patient enrollment, data collection, statistical analysis, and manuscript preparation.

JB: Contributed to patient enrollment, data collection, statistical analysis, and manuscript preparation.

TS: Contributed to patient enrollment, data collection, and manuscript preparation.

GC: Contributed to patient enrollment, data collection, and manuscript preparation.

Abstract

Background: Auto-augmentation techniques have been applied to oncoplastic reductions to assist with filling larger, more remote defects and women with smaller breasts. The purpose of this report is to describe the use of auto-augmentation techniques in OR and compare the results with traditional OR.

Methods: We queried a prospectively maintained database of all women who underwent partial mastectomy and OR between 1994 and October 2015. The auto-augmentation techniques were defined as 1) extended primary nipple auto-augmentation pedicle, and 2) primary nipple pedicle and secondary auto-augmentation pedicle. Comparisons were made to a control oncoplastic group.

Results: There were a total of 333 patients, 222 patients (67.7%) without auto-augmentation and 111 patients (33%) with auto-augmentation. Fifty-one patients had extended auto-augmentation pedicle, and 60 patients with a secondary auto-augmentation pedicle. Biopsy weight was smallest in the extended pedicle group (136 grams) and largest in the regular oncoplastic group (235 grams, p=0.017). Superomedial was the most common extended pedicle and lateral being the most common location. Inferorolateral was the most common secondary pedicle for lateral and upper outer defects. There were no significant differences in the overall complication rate: 15.5% in the regular oncoplastic group, 19.6% in the extended pedicle group, and 20% in the secondary pedicle group.

Conclusions: Auto-augmentation techniques have evolved to manage complex defects not amenable to standard oncoplastic reduction methods. They are often required for lateral defects especially in smaller breasts. Auto-augmentation can be done safely without increase risk of complications, broadening the indications for breast conservation therapy.

Introduction:

The oncoplastic reduction (OCR) technique has become an accepted approach for reconstructing partial mastectomy defects in women with macromastia (1-3). As it grows in popularity, the procedure continues to be refined and indications for its use continue to broaden. There are now larger series with longer follow up demonstrating oncological safety, improved patient satisfaction, and quality of life (4-6). This approach is now being used for larger tumors, higher cancer stage, and in conjunction with intraoperative radiation therapy (7-10). In addition to broadening the indications of breast conservation, these techniques have been used for larger defects and in smaller breasts. Certain sized defects and remote locations are often difficult to reconstruct using the traditional OCR techniques. One solution to this problem has been to use autoaugmentation flaps where surrounding tissue can be moved to fill difficult defects. These parenchymal flaps have been employed in the massive weight loss patients to provide additional shape and volume to deflated breasts (11). Various authors have used central, inferior, or superomedial pedicle techniques with vascularized attachments to provide suspension of the breast mound particularly in the upper pole where volume is often desired (11-14). Similar autoaugmentation flaps during OCR procedures will fill the defect and reshape the breast mound when traditional techniques would not suffice. Autoaugmentation flaps can either be used as a dermatoglandular extension of the primary pedicle beyond the nipple areolar complex (NAC) or as a secondary dermatoglandular pedicle independent of the primary nipple pedicle. Concerns have been raised as to whether these autoaugmentation flaps might result in additional fat necrosis or scar tissue and potentially impact initiation of radiation therapy or outcomes. The purpose of this review is to evaluate the indications for autoaugmentation flaps in OCR patients and assess outcomes to determine whether this approach results in higher incidence of complications.

Patients and Methods:

All patients who underwent partial mastectomy and OCR between November 1997 -October 2015 at Emory Hospital were included. Data was collected from a prospectively maintained database and electronic medical records then recorded in a Microsoft Excel database (Microsoft Corp., Redmond, Wash.). Patient demographics, risk factors, diagnosis, tumor location, tumor size, operative technique, and outcomes were reviewed. The incidence of completion mastectomy, re-excision, and re-biopsy was analyzed. The re-biopsy rate was calculated from the sum of all biopsy types: sterotactic, mammographic directed, and excisional. We used the contralateral breast reduction specimen weight as a marker for ipsilateral breast size. Since the majority of patients had a bilateral breast reduction following removal of the lumpectomy specimen from the ipsilateral cancer side, we found it easiest to estimate the ipsilateral overall breast size by using the breast reduction specimen weight from the contralateral side. For the purposes of this analysis, this method provided us with a single accurate specimen weight.

The documented surgical complications were as follows: 1) urgent or emergent return to the operating room; 2)unanticipated patient readmission; 3) breast seroma, defined by a clinically evident fluid collection requiring aspiration, drainage, or operating room washout; 4) hematoma, defined as clinically evident postoperative swelling, significant bruising requiring operating room evacuation; 5) wound infection, defined as a surgical incision with increasing erythema, tenderness, or purulent fluid on physical examination treated with oral or intravenous antibiotics or operating room wash-out; 6) partial nipple necrosis, defined as clinical evidence of full thickness necrosis requiring serial dressing changes and/or operating room or office debridement; 7) delayed wound healing, defined as superficial dehiscence at the surgical site requiring serial dressing changes and/or operating room oroffice debridement; 8) fat necrosis, defined as a clinically palpable mass or area causing pain, deformity, or skin changes or any area that required debridement for the above reasons. Additionally a wound that was intraoperatively determined to be fat necrosis was included and documented as fat necrosis. Complications resulting in unanticipated readmission or return to the operating room were documented as major complications. All others were documented as minor. For the purpose of analyzing the surgical technique in this patient population, patients with bilateral breast cancer were treated as two patients, but the complications were only counted once. For all other patients, the complications were reported per patient for both breasts.

Tumor removal and partial reconstruction was performed by a two-team approach. Additionally, positive margins requiring re-excision were also performed with both the breast and plastic surgeon. The nipple pedicle, tumor location, and specimen size was documented. Operative reports were reviewed and patients were divided into three groups based on the technique used for reconstruction.

- <u>Group 1</u>: Patients who had tumor resection and reconstruction using the regular OCR technique (Control). The defect was filled with the nipple pedicle and or the residual breast tissue (Figure 1).
- <u>Group 2</u>: Patients who had the defect filled with an extended nipple pedicle (extended autoaugmentation pedicle). The defect was filled by extending the primary nipple areolar pedicle and rotating this into the defect (Figure 2).
- <u>Group 3</u>: Patients who had the partial mastectomy defect filled with a secondary dermatoglandular pedicle (secondary autoaugmentation pedicle). The nipple

pedicle was used to reposition the nipple and a secondary independent dermatoglandular pedicle was used to fill the defect (Figure 3).

Comparisons were made between the groups to determine 1) which breast size and tumor location required what reconstructive technique, and 2) whether the autoaugmentation techniques were associated with an increased risk of complications.

Statistics:

Descriptive statistics were calculated for patients in all groups. As appropriate, the independent-samples t-test, Mann-Whitney U Test, Fischer's exact, and Chi-squared were used to determine the association between groups and the clinical variable of interest. A p-value of 0.05 was used to determine significance. Logistic regression analysis was performed to predict the development of postoperative complicatons when controlling for oncoplastic surgical technique. Additional clinical and demographic variables were included in the model from variables that were found to be significantly different among the three study groups on univariate analysis. A model for predicting the development of complications collectively was performed in addition to models for fat necrosis and delayed wound healing individually. Within the model, traditional oncoplastic breast surgery was used as the reference variable for comparision of extended and secondary pedicle groups as the purpose of the analysis was to determine if autoaugmentation resulted in differing incidence of complications. All statistical analysis was conducted using the IBM® SPSS® Statistics 24.0 (IBM Corp., Armonk, N.Y).

Results:

Demographics

There were 333 patients included. The mean age was 54 years (Range: 21-80), with an avareage body mass index (BMI) for all patients of 33.7 kg/m^2 (Range: 19.6-60.2 kg/m^2). There were 222 patients in the traditional OCR group, 51 patients who had an extended pedicle, and 60 in the secondary pedicle group. Demographics and characteristics for the three groups are found in Table 1. Patients in the secondary pedicle group were significantly older (mean age of 59.2 years, $p<0.001$). The extended pedicle group had a significantly lower BMI (mean BMI 30.2, $p=0.002$) compared to the other two groups. More patients in the extended pedicle group underwent pre-operative chemotherapy (36.7%, $p=0.028$). There were no significant differences in the other demographic variables.

Operative Variables

The majority of patients in all groups had a contralateral procedure. The superomedial nipple pedicle technique was the most common for all three groups (Table 2). The lumpectomy excision weight was smallest in the extended pedicle group (136 grams) and largest in the regular oncoplastic group (235 grams, $p=0.017$). The weight of tissue removed from the contralateral side was significantly less in the extended pedicle group (350 grams, $p<0.001$) compared to the other two groups. Tumor characteristics, positive margin rate and axillary procedures were similar among all groups.

Autoaugmentation Technique

An autoaugmentation technique was used in 33% of patients (n=111). When an extended pedicle was used, the most common extended pedicle was superomedial (68.6%), which was most commonly used for lateral (51%, n=26/51) and superior 20%, n=10/51) ($p=0.053$) defects (Table 3,4). When a secondary pedicle was used, the most common combination was inferior or inferolateral secondary pedicle (90%, n=54/60) with a superior or superomedial primary nipple pedicle. The most common defect location to use a secondary pedicle was lateral (70%,n=42/60; $p=0.05$), and this was filled with an inferiorly based secondary pedicle 95% of the time.

Location of Defect

Overall, the most common locations to require autoaugmentation techniques were lateral and medial (Table 4). Forty percent of all lateral defects were reconstructed using autoaugmentation flaps. When utilized, the most common autoaugmentation technique for lateral defects was the secondary pedicle which was used in 63% (n=42/67) of cases. Seventy two percent of all the secondary pedicles performed were used for lateral defects (p=0.050). For these lateral defects, the secondary pedicle of choice was inferior (n=13/28, 46.4%) and inferolateral (n=13/28, 46.4%). Of those receiving an inferior/inferolateral secondary pedicle, the majority were in combination with a superomedial primary nipple pedicle (70%).

Thirty nine percent of medial defects were reconstructed using the autoaugmentation flaps. The most common autoaugmentation technique for medial defects was the extended pedicle (59%, n=13/22). The most common extended pedicle used for all defect locations was a superomedial (p<0.0001). Of the superolateral defects requiring an extended pedicle, 100% were filled using a superomedial extended pedicle and 85.7% of inferolateral/lateral defects filled using the superomedial pedicle.

Breast Size

To provide a consistent estimate of breast size, the contralateral breast specimen reduction specimen weight was used as a measurement of the ipsilateral breast size. The average breast size in women that required autoaugmentation techniques was smaller than those that did not (451g vs. 654g, p<0.0001). Additionally, when an extended pedicle was used, these women were more likely to have smaller breasts when compared to no autoaugmentation technique (341g vs. 633g, p<0.0001) (Table 5). When the contralateral specimen weight was broken down into two groups based on weight, there were 85 patients with smaller breasts (< 300 grams) and

218 patients with large breasts (> 300grams). When an extended pedicle was used, 56% of the time it was in patients with small breasts. When a secondary pedicle was used, 79% of the time that was in women with large breasts.

Complications

The overall complication rate was 16.9 percent (Table 6). The were no significant differences in the incidence of complications among groups: 15.5% incidence in the regular oncoplastic group, 19.6% in the extended pedicle group, and 20% in the secondary pedicle group. Delayed wound healing was the most common complication for both the auto-augmentation group (10.5% of complications) or those not receiving auto-augmentation (9.3%). The incidence of nipple necrosis was 1.4% for the entire cohort which was similar among groups (p=0.679). Additionally, the incidence of fat necrosis was similar among all three groups (p=0.378). There were no significant differences in the other complications such as delayed wound healing, infection, skin necrosis, hematoma, and seroma.

While there was not a significant difference among the techniques of oncoplastic surgery and any of the documented complications on univariate analysis, we performed multivariate analysis to elucidate the potential influence of confounding variables. Despite having a low incidence, fat necrosis and delayed healing were specifically chosen for further analysis as these complications are of particular interest in this patient population. On binomial logistic regression analysis, the technique of oncoplastic breast surgery (traditional oncoplastic vs. extended vs. secondary pedicle) was not predictive of developing a postoperative complication collectively. An additional model for variables potentially predictive of delayed wound healing, showed that when controlling for oncoplastic surgical technique, age, BMI, and resection weight of over 300g, only increasing BMI was predictive of developing delayed healing (Odds Ratio: 1.07; 95%

CI [1.02-1.12]. When controlling for these same variables, there was not a relationship between oncoplastic technique and development of fat necrosis (Table7).

Outcomes

The mean follow up was 609 days (range: 36-5509 days). Although all groups had sufficient follow up, the oncoplastic group had a significantly longer follow up time (688 days) compared to the secondary (405 days) and extended (505 days) pedicle group (p=0.040). The recurrence rate was 5.1% (n=13/242) for the entire cohort and the re-biopsy rate was 18.9% (n=63/333) which was similar among groups (p=0.627). The rate of completion mastectomy was 10.2% (n=34/333) which was also similar among all three groups (p=0.121)

Discussion

Oncoplastic techniques have gained popularity. Along with this trend, we have seen newer techniques that braoden the indications further for this approach (15). We have shown that autoaugmentation technique is safe and effective in its ability to fill larger and more difficult defects without increased risks of complications. Whenever possible, it is often easiest to fill the lumpectomy defect with reduction or mastopexy techniques using either the planned nipple pedicle or tissue that is left behind following the mammoplasty. For example, reconstructing a lower pole defect using a Wise pattern superomedial pedicle reduction does not require additional glandular manipulation. The augmentation techniques described here are useful when the defect is too large, too remote, or there is not enough nearby parenchyma available to fill the tumor cavity. We found that the extended autoaugmentation technique is useful for medial, lateral, or upper defects, especially in women with smaller breasts. The secondary pedicle is often used for lateral or medial defects.

It is important that these glandular flaps and extension flaps are well vascularized since any fat necrosis in this patient population is always reason for concern. Poorly vascularized tissue does not tolerate radiation therapy well and may result in a more fibrotic, painful or firm breast. Careful attention to flap length and width, minimizing the amount of pedicle undermining, and de-epithelializing more when concerned will improve flap perfusion. The pedicle is often kept wide and attached to the chest wall. Back cuts are performed only as much as required to fill the defect or reshape the mound. The two pedicle approach was employed also as another option when it seemed as though the extended pedicle was getting long and less reliable. In an upper lateral defect, the secondary pedicle is preferred. The superomedial pedicle could be used for the nipple and a shorter inferioly based lateral pedicle used to fill the defect. This not only minimizes pedicle length but allows independent movement since the extended nipple pedicle rotation is limited to where the nipple needs to go ,and the attached extension will often not fill the proposed defect. It is always helpful to think about filling the defect and possibly needing autoaugmentation prior to resecting tissue. Excess tissue can be easily resected from the secondary pedicle if less volume is required.

The main variables used to determine when and what type of autoaugmentation was used during oncoplastic surgery were the size of the breast, defect size, and tumor location (Figure 4). Women with smaller breasts who have small or medium size defects in the medial or lateral locations that are not adequately filled with surrounding breast tissue are best treated with the extended pedicle (Figure 5). The tissue that is typically removed when creating the medial and lateral pillars in a vertical breast reduction or mastopexy is preserved as an extension to the superioly based pedicle. It is rotated with the nipple to the proposed location and used to fill the defect. The medial and lateral glandular pillars are then plicated in the usual manner. This tissue can also be used to fill superior defects if necessary. Larger, lateral or upper outer quadrant defects in women with larger breast however often require two pedicles (Figure 6). Once the defect is examined a superomedial pedicle is created and the nipple is rotated into the desired position. An inferiorly based lateral dermatoglandular pedicle is de-epithelialized and created based on how much is anticipated to fill the defect. The residual dermatoglandular tissue is then resected and the breast mound shaped in the usual fashion. The secondary pedicle can then independently be cut to size and placed into the defect.

The safety of the oncoplastic technique has remained under scrutiny. Overall complication rates remain relatively low and are often managed with conservative treatment. Therefore their use should not delay initiation of adjuvant treatment. Studies have shown fewer complications in obese women and women with macromastia following oncoplastic reduction compared to mastectomy and immediate reconstruction (1,16). Tong et al demonstrated fewer complications requiring additional surgery (3.8% vs 28%) and delaying adjuvant therapy (0.8% vs 14%) in the oncoplastic group for obese patients (16). In a previous report, we have similarly shown in patients with macromastia following oncoplastic reconstruction had a lower breast complication rate (22% vs 47%), shorter hospital stay (0.8 vs 3.5 days), and fewer trips to the OR (1.2 vs 2.7) (1). The complication benefits compared to mastectomy are significant, and those compared to BCT alone are acceptable. Furthermore, we have shown that complications in patients requiring autoaugmentation flaps are similar to traditional oncoplastic reduction techniques(20% versus 15%). Screening for breast cancer is always important. Studies have shown similar sensitivites for screening following oncoplastic reductions (17-19) with traditional BCT. While fat necrosis is not higher in the autoaugmentation group, it will be important to demonstrate radiographically that no differences exist. The possible change in mammographic findings was not an objective of this study, but in the authors experience as long as these flaps remain well vascularized and appropriately designed screening should not be a problem. Future studies would be necessary to evaluate if there is a diference in mammographic changes between tradiational oncoplastic surgery and those with autoagumentation flaps.

Conclusion:

The majority of patients do not require an autoaugmentation technique. It is used more often in smaller breasts, or in larger defects, especially in cosmetically sensitive areas such as medial quadrant, and upper lateral quadrant. The incidence of fat necrosis and wound healing complications is not greater with flaps and the need for additional surgery or biopsy is similar. With careful attention to flap design and blood supply, the use of autoaugmentation techniques will broaden the indications for the oncoplastic approach and likely improve results since defects are being filled with vascularized glandular tissue, without increasing complications.

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Legends

Figure 1) This is a 49 year old with a 1cm right invasive breast cancer in the lower pole (left). She underwent partial mastectomy removing 95 grams of tissue (middle). The defect was reconstructed using a superomedial pedicle reduction with an additional 400 grams removed from that side. A contralateral reduction was performed removing 540 grams. She is shown 14 months following radiation therapy to the right side (Right).

Figure 2) Illustration demonstrating an extended superomedial dermatoglandular pedicle used to provide autoaugmentation and fill the upper outer quadrant defect. ©Thieme Publishing 2017, Partial Breast Reconstruction: Techniques in Oncoplastic Surgery, Losken/Hamdi eds.

Figure 3) Illustration demonstrating a secondary inferiorly based dermatoglandular pedicle used to autoaugment the later defect and a superomedial pedicle for nipple viability. ©Thieme Publishing 2017, Partial Breast Reconstruction: Techniques in Oncoplastic Surgery, Losken/Hamdi eds.

Figure 4) An algorithm demonstrating oncoplastic technique based on breast size, defect size and location.

Figure 5) This is a 41 year old female with left upper out quadrant IDC (5a). She underwent wire localization (5b) and partial mastectomy removing 100 gram specimen (5c). An extended dermatoglandular superomedial pedicle was created to rotate tissue into the defect (5d). No additional tissue was removed. The medial and lateral pillars were plicated (5e). A contralateral reduction 105 grams was performed. She has decent shape and symmetry 1.5 years following completion of radiation therapy

Figure 6) This is a 48 year old with infiltrating ductal carcinoma (6a) with wire localization (6b) who underwent a 55 gram partial mastectomy (6c). The defect was lateral to the nipple and all the way down to the chest wall (6d). Given her breast and defect size a secondary inferiorly based pedicle was created to fill the defect. The nipple was rotated on a superomedial pedicle and a total of 175 grams was removed from that side (6e,f). A contralateral reduction was performed removing 190 grams. She is shown 1 year following completion of right radiation therapy (6g)

Table 1: Demographic Characteristics for the Entire Cohort

	Oncoplastic (n=222)	Extended Pedicle (n=51)	Secondary Pedicle (n=60)	p-value
Age, mean	53.1	52.5	59.2	<0.001*
BMI, mean	34.6	30.4	33.2	0.002*
Final Partial Mastectomy Pathology				0.935
DCIS/LCIS	48 (21.6)	12 (23.5)	12 (20.0)	
IDC	136 (61.3)	31 (60.8)	40 (66.7)	
Benign	38 (17.1)	8 (15.7)	8 (13.3)	
Preoperative Chemotherapy	40 (19.0)	18 (36.7)	13 (22.0)	0.028*
Radiation	163 (87.9)	41 (91.1)	51 (91.1)	0.674
Completion Mastectomy	28 (12.6)	3 (5.9)	3 (5.0)	0.121

Table 2: Procedure Characteristics for All Groups

	Oncoplastic (n=222)	Extended Pedicle (n=51)	Secondary Pedicle (n=60)	p-value
Reduction Pedicle Type				0.001*
Superiomedial	95 (45.7)	27 (54.0)	46 (78.0)	
Inferior	63 (30.3)	8 (16.0)	7 (11.9)	
Superior	11 (5.3)	8 (16.0)	3 (5.1)	
Superiolateral	3 (1.4)	1 (2.0)	1 (1.7)	
Central	26 (12.5)	5 (10.0)	2 (3.4)	
Amputation	10 (4.8)	1 (2.0)	0 (0.0)	
Biopsy Weight, g	235	136	183	0.017*
Total Ipsilateral, g	623	317	462	<0.0001*
Contralateral Specimen, g	656	350	544	<0.0001*
Tumor Size, cm	1.98	1.88	2.44	0.349
Positive	17 (7.7)	2 (3.9)	3 (5.0)	0.537
Negative	205 (92.3)	49 (96.1)	57 (95.0)	
Axillary Procedure				0.588
None	68 (30.6)	11 (21.6)	14 (23.3)	
SLNB	137 (61.7)	35 (68.6)	42 (70.0)	
ALND	17 (7.7)	5 (9.8)	4 (6.7)	
Nodal Status				0.122

Negative	131 (79.4)	39 (88.6)	35 (71.4)	
Positive	34 (20.6)	5 (11.4)	14 (28.6)	

Table 3: Auto-augmentation and Extended Pedicle for Entire Cohort

	n (% Total Cohort)
Any Auto-augmentation	111 (33.3)
Extended Pedicles	51 (15.3)
Superomedial	35 (68.6)
Inferolateral	1 (2.0)
Inferior	7 (13.7)
Superior	4 (7.8)
Superorlateral	4 (7.8)
Secondary Pedicles	60 (18.0)
Inferior	33 (55.0)
Inferolateral	21 (35.0)
Inferomedial	4 (6.7)
Superior	1 (1.7)
Medial	1 (1.7)

Table 4: Defect Location for each group

	Upper	Lower	Central	Medial	Lateral	Other
n	43	34	11	57	168	
Oncoplastic	32 (74%)	29 (85%)	8 (73%)	35 (61%)	101 (60%)	17
Extended	10 (23%)	0 (0%)	2 (18%)	13 (23%)	25 (15%)	1
Secondary	1 (2%)	5 (15%)	1 (9%)	9 (16%)	42 (25%)	

P value = 0.003

Table 5: Autoaugmentation techniques based on contralateral specimen weight (breast size)

	Oncoplastic (n=198)	Extended (n=48)	Secondary (n=57)
<300	46 (23.2)	27 (56.3)	12 (21.1)
>300	152 (76.8)	21 (43.8)	45 (78.9)

p-value= 0.0001

Table 6: Complications for the Entire Cohort

	Total	Oncoplastic	Extended Pedicle	Secondary Pedicle	p-value
Any Complication	56 (16.9)	34 (15.5)	10 (19.6)	12 (20.0)	0.606
Ipsilateral Complication	50 (15.1)	28 (12.7)	10 (19.6)	12 (20.0)	0.235
Contralateral Complication	16 (4.8)	13 (5.9)	1 (2.0)	2 (3.3)	0.414
Major	15 (4.5)	10 (4.5)	3 (5.9)	2 (3.3)	0.813
Minor	45 (13.6)	27 (12.3)	7 (13.7)	11 (18.3)	0.478
Delayed Wound Healing	33 (10.0)	20 (9.1)	5 (9.8)	8 (13.3)	0.623
Infection	18 (5.4)	8 (3.6)	5 (9.8)	5 (8.3)	0.119
Partial Mastectomy Skin Necrosis	3 (0.9)	3 (1.4)	0 (0.0)	0 (0.0)	0.466
Hematoma	3 (0.9)	2 (0.9)	1 (2.0)	0 (0.0)	0.554
Seroma	4 (1.2)	3 (1.4)	0 (0.0)	1 (1.7)	0.679
Symptomatic Fat Necrosis	5 (1.5)	2 (0.9)	1 (2.0)	2 (3.3)	0.378
Nipple Necrosis	4 (1.2)`	3 (1.4)	0 (0.0)	1 (1.7)	0.679

Table 7. Binomial Logistic Regression Models for Predicting Incidence of Postoperative Complications

Variable		Sig	Odds Ratio	95% Confidence Interval	
Complications, Any	Extended	0.253	1.64	0.96	1.01
	Secondary	0.336	1.64	0.70	3.84
Delayed Wound Healing	Extended	0.275	1.88	0.61	5.86
	Secondary	0.202	1.91	0.71	5.12
Fat Necrosis	Extended	0.274	4.04	0.33	49.45
	Secondary	0.208	3.84	0.47	31.14

* All models controlled for age, BMI, size of resection (<300 g resection, >300g resection), and oncoplastic technique

Figure 2

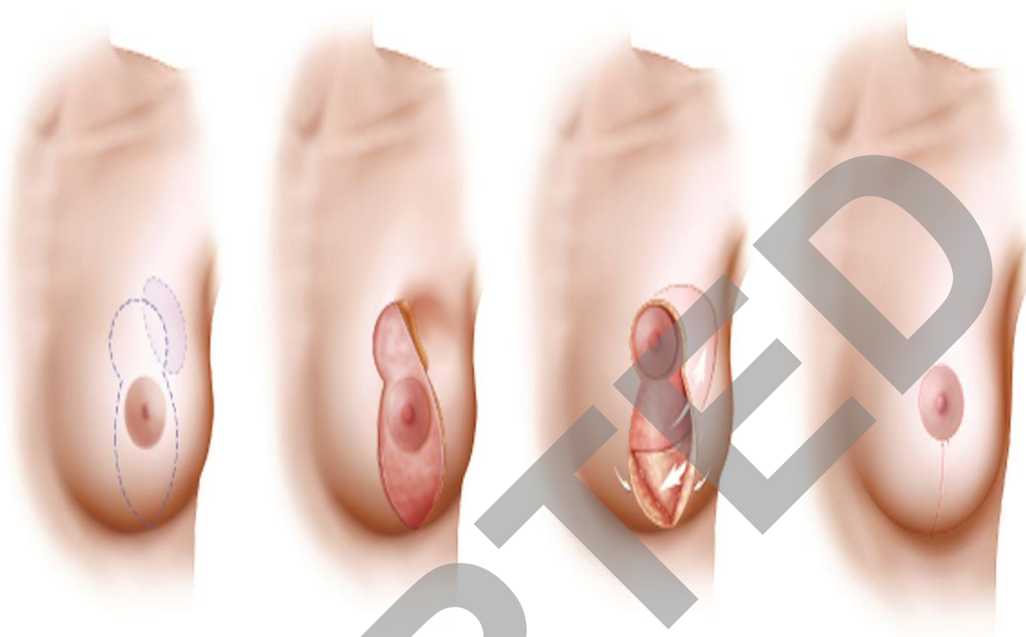


Figure 3

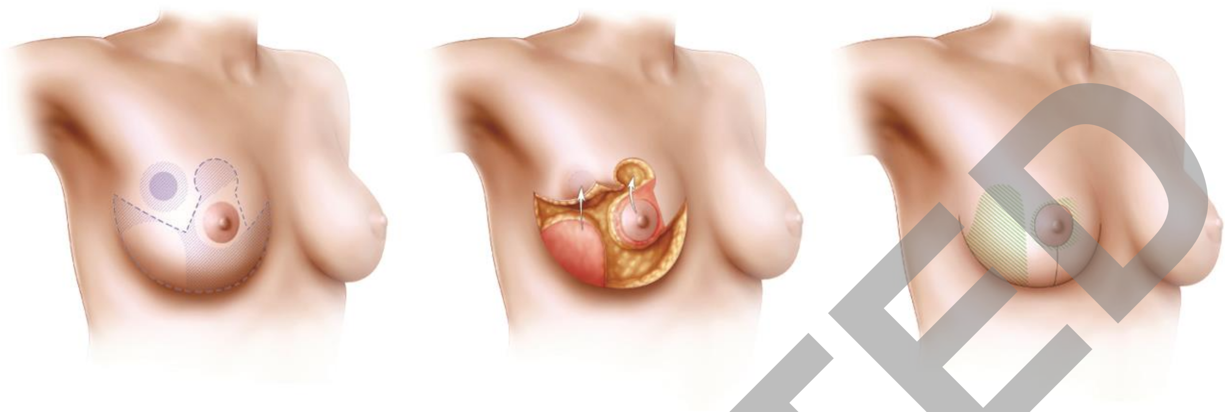
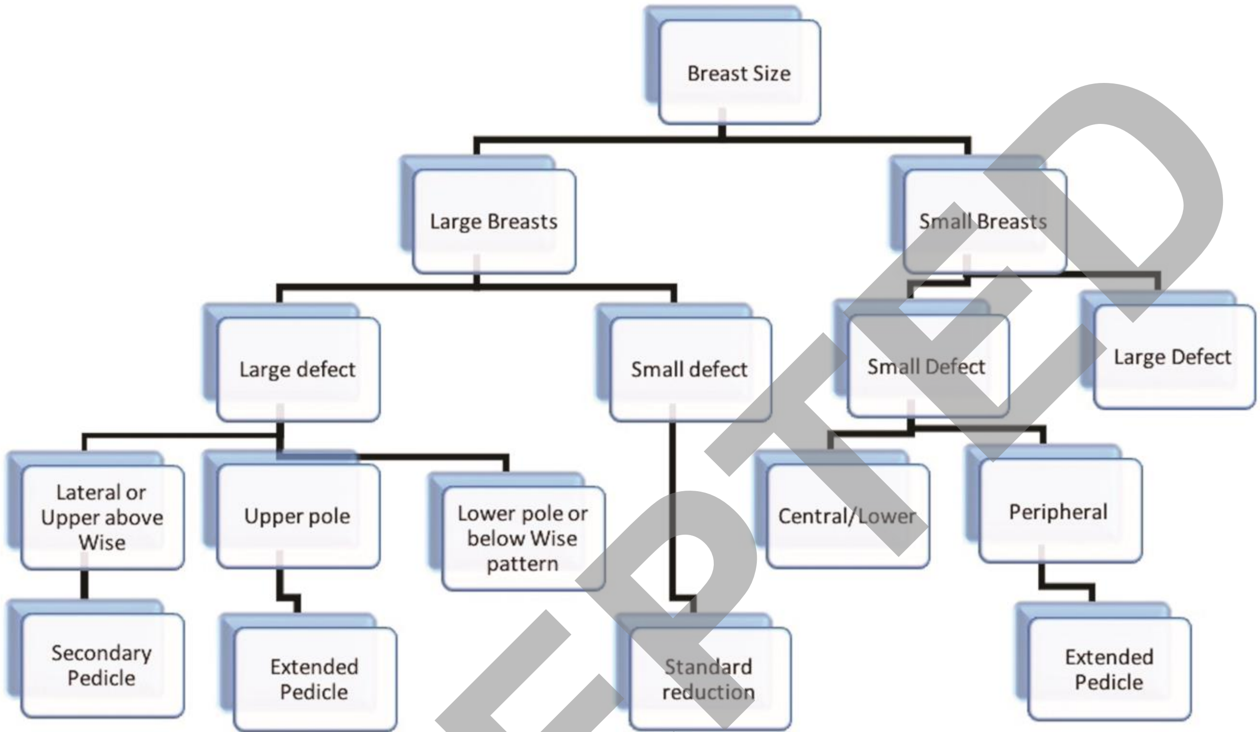


Figure 4



Breast Size
Large Breasts
Small Breasts
Large defect
Small defect
Small Defect
Large Defect
Lateral or Upper above Wise
Upper pole
Lower pole or below Wise pattern
Central/Lower
Peripheral
Secondary Pedicle
Extended Pedicle
Standard reduction
Extended Pedicle

Figure 5

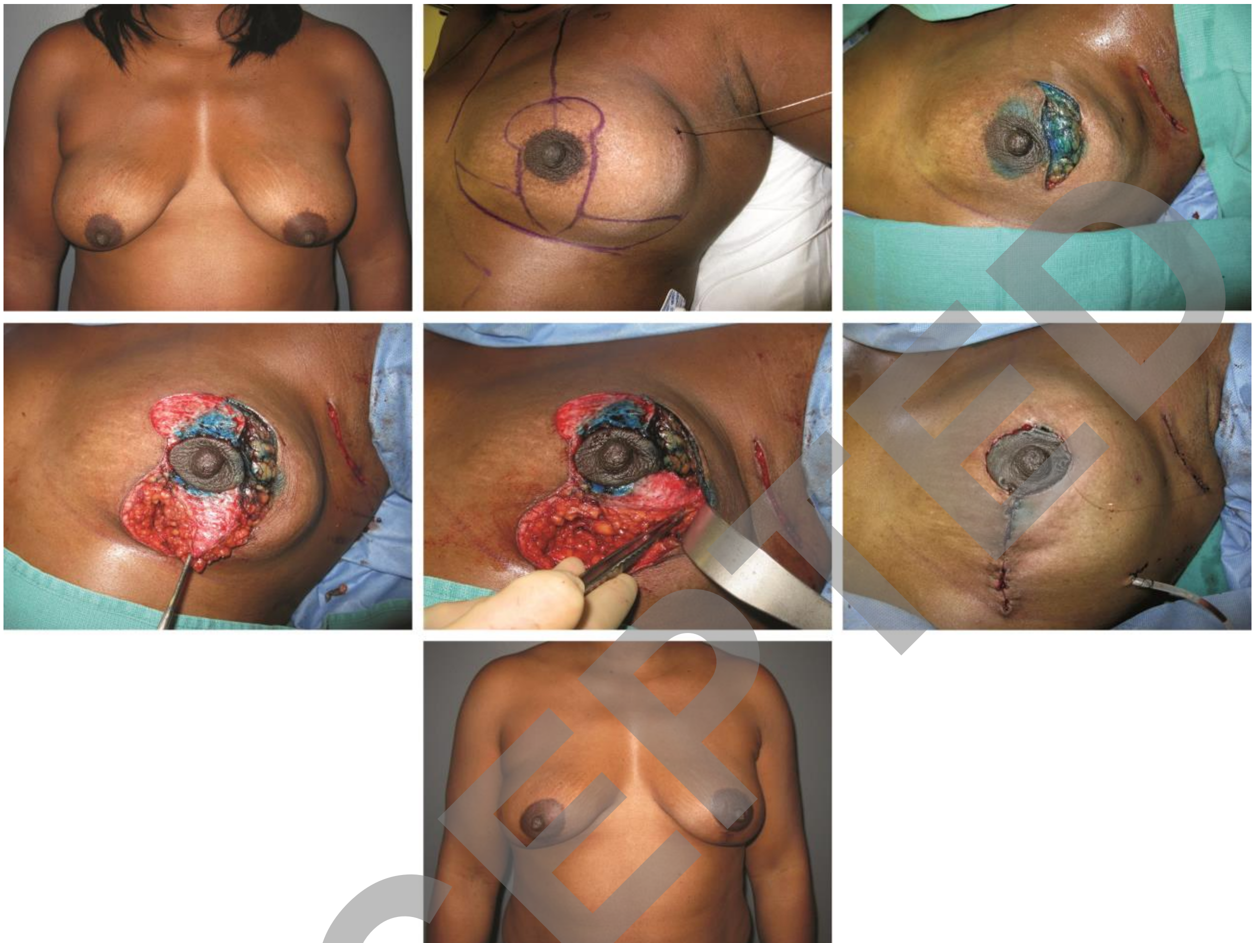


Figure 6

Technical Article

J Breast Health 2017; 13: 46-49
DOI: 10.5152/tjbh.2016.3165

The Main Topics at the Oncoplastic Breast Surgery Course and Expert Panel

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ABSTRACT

The Oncoplastic and Reconstructive Breast Surgery course was held in Izmir by the Izmir Breast Diseases Federation in collaboration with the Breast Diseases Federation of Turkey. The techniques of oncoplasty, the application details and experience in this subject were shared. In this text, the main topics and outcomes are briefly summarised. These evaluations can be considered highly valuable on both local and regional scales.

Keywords: Oncoplastic breast surgery, quadrantectomy (surgery for breast cancer based on tumour location), breast surgery

Introduction

The 3rd Oncoplastic and Reconstructive Breast Surgery Course was organized by the Izmir Breast Diseases Association on May 21, 2016 in co-operation with the Association of Breast Diseases Federation of Turkey. Eighty seven speakers and the participants from 17 different cities deliberated on the issue during a full-day course between 8:30 and 18:30. Experienced specialists demonstrated their own approaches with a plethora of visual material (photos, videos etc.). Participants included Mustafa Emiroglu, M. Kemal Atahan (İzmir), Bekir Kuru (Samsun), M. Ali Gülçelik (Ankara), Atakan Sezer (Edirne) as the board directors of the course and Bahadır Güllüoğlu (İstanbul) as the course consultant. Oncoplastic techniques, methods and experience in breast cancer surgery were described in detail. The main topics and messages are summarized briefly in this paper, and the assessment made on this subject Turkey is considered to be an important local and regional scale.

The status and development of oncoplastic and reconstructive breast surgery in the world and Turkey in relation to surgeons who have been working on this issue were explained briefly. Practices carried out in Turkey are almost parallel to the developments in the world. In this regard, the experience and practices about this issue must be shared with a wider community via literature. It was stressed that multi-centre studies on oncoplastic breast surgery were needed. A consensus was achieved on the requirement for general certification programs in this area to be formed by a commission planned to be constituted by oncoplastic and reconstructive surgeons among general surgeons and plastic surgeons. The importance of all aspects of the oncoplastic and reconstructive breast surgery (ORBS) was highlighted. Please see the Table 1 for details of the evaluation of oncoplastic breast surgery.

Oncoplastic breast surgery

Breast cancer surgery made progress within the last century from radical mastectomy to oncoplastic breast surgery. In 1980s, MCS revolutionized the field. In 2000s, oncoplastic breast surgery (OBS) was announced as an innovation in breast surgery. In fact, breast cancer surgery treatment is available in most of the cases in the form of standard breast aesthetics incisions without the need for oncoplastic techniques. However, one out of 4-5 patients had to undergo an aesthetical oncoplastic procedure after MCS. Therefore, surgical planning in addition to an overall assessment has gained a great deal of importance. Advanced planning before surgery is considered to be skipped by surgeons most of the time. Loss of breast tissue by more than 20% (loss of inner quadrants 10%) can lead to aesthetic problems. The importance of oncoplastic techniques are emphasised for future use. The application of these techniques simultaneously applied with lumpectomy ensures higher patient satisfaction and increases the quality of life. The simultaneous procedures were specifically discussed with high emphasis during the course.

Oncoplastic incisions are intended to prevent any defects after breast surgery. Up until recent years, it has been believed that incisions placed in parallel on both sides of maximum remaining skin tension lines (Kraissl's lines) and in the same orientation as collagen fibres (Langer's lines) are the most suitable incisions.

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Received: 04.06.2016
Accepted: 05.07.2016

Table 1. Checking the elements required for the ORBS

	Before surgery	Pre-operative	After surgery
Patient	Age, height, weight, DM, DVT , smoking history, HT, BMI, donor site (chest – abdominal wall and back), approach to the other breast	-	Expectations, compliance, complications
Tumor	stage, biology, DCIS (±), size, distance to skin and nipple	Pathological examination (limit the frozen slices)	Oncological results
Breast	Density, size, shape, ptosis, areola status, skin quality, assessment of the other breast, possible breast defect analysis	To be drained, symmetry	Aesthetic results
Surgeon	Multidisciplinary assessment, photo, experience level	Photo, experience	Photo, documentation, follow

HT: hypertension; DM: diabetes mellitus; BMI; body mass index; DCIS: ductal carcinoma; ORBS: oncoplastic and reconstructive breast surgery

Table 2. The proposed oncoplastic techniques according to breast quadrants

Location of the tumor	Small breast and medium sized breast - droopy (-)	Small breast and medium sized breast - droopy (+)	Big breast
Upper-outer quadrant	Elliptical radial incision Half bat incision (side) Round block incision Racket incision Glandular flap Lateral thoracodorsal Flap LD TRAM	Circumference incision of nipple Elliptical radial incision Half bat incision (side) Round block incision Racket incision Glandular flap Benelli mastopexy Lateral thoracic flap LD	OBR (lower, double pedicle) Elliptical radial incision Batwing incision Racket incision Lateral thoracodorsal flap Glandular flap
Upper-middle and upper-inner quadrant	Breast head circumference incision Crescent incision Batwing incision Half-batwing incision (inside) Round block incision Glandular flap Parallelogram incision Rotation flap LD	Breast head circumference incision Crescent incision Batwing incision Half-batwing incision (inside) Round block incision Glandular flap Benelli mastopexy Rotation flap	OBR (lower, double pedicle) Crescent incision Batwing incision Glandular flap Rotation flap
Central area	Round block Grisotti flap Central triangular incision Total excision-primary closure Glandular, dermoglandular flaps	Round block Benelli Grisotti flap	OBR Grisotti reduction
Lower-outer quadrant	Lateral thoracodorsal flap Glandular, dermoglandular flaps Thoraco- epigastric flap TRAM	Round block Glandular, dermoglandular flaps Mastopexy techniques Volume filling techniques from chest wall	OBR (upper, upper-inner, upper-outer pedicle) Lateral thoracodorsal flap
Lower-inner quadrant	Inframammary incisions Triangular incision Dermoglandular incision Volume filling techniques (from thoracodorsal space)	Inframammary incisions Triangular incision Dermoglandular incision Volume filling techniques (from thoracodorsal space)	OBR (upper, upper-inner, upper-outer pedicle) Dermoglandular flaps Rotation flap
Lower-middle quadrant	Rotation flap Vertical OBS incisions Triangular incision Reverse- T incision	Rotation flap Vertical OBS incisions Triangular incision Reverse- T incision	OBR (upper, upper-middle, upper-outer pedicle) Vertical OBS incisions

OBS: oncoplastic breast surgery; OMR: oncoplastic breast reduction; LD: Latissimus dorsi flap;

TRAM: transverse rectus abdominis myocutaneous flap

Table 3. Participants as speakers, panelists and chairpersons in the ORBS meeting

Mustafa Emiroğlu (İzmir)	Bekir Kuru (Samsun)	Kemal Atahan (İzmir)
Bahadır Güllüoğlu (İstanbul)	Atakan Sezer (Edirne)	M. Ali Gülçelik (Ankara)
Zafer Cantürk (Kocaeli)	Serdar Özbaş (Ankara)	Serdar Saydam (İzmir)
Cihangir Özaslan (Ankara)	M. Ali Koçdor (İzmir)	Lutfi Doğan (Ankara)
Cem Karaali (İzmir)	Hedef Ozun (Aydın)	Teoman Coşkun (Manisa)
Serhan Tuncer (Ankara)	Gürsel R. Soybir (İstanbul)	Belma Koçer (Sakarya)
Hasan Karanlık (İstanbul)	Güldeniz Karadeniz (Zonguldak)	Levent Yeniay (İzmir)
Ercüment Tarcan (İzmir)	Cem Yılmaz (İstanbul)	Aykut Soyder (Aydın)
Neslihan Cabioğlu (İstanbul)	Senem Alanyalı (İzmir)	Murat Tüzüner (İzmir)

However, Aronowittz curvilinear horizontal incisions cause tension on the breasts, prevent the enlargement of the breast skin, and cause the breast tissue to collapse in certain areas while polarising upper quadrant, and so is considered as an outdated method in recent years. The radial incisions following the growth lines of the breast are thought to be more beneficial than the former method. In addition, it was noted that the Batwing and Benelli incisions were suitable for Langer and Kraissl lines; tennis racket in upper-out quadrant, vertical and reverse T in low-in quadrant; and radial rotation flap incision in inner quadrants are also suitable for the tension lines of the breast as defined by Aronowitz.

Speakers said that the glandular and dermoglandular flap techniques should be used widely and the area of lumpectomy should be filled in a way that prevents the development of seroma. The traditional way of waiting until the lumpectomy area filling with seroma is found outdated and abandoned. These techniques should be applicable in all the quadrants of the breast especially in the upper breast.

Oncoplastic breast surgery is not a standard approach; it can be modified for each patient in various ways. Sometimes, an open surgical area is found to be an interesting and creative technique. Thoracodorsal and/or epigastric tissue volume filling techniques are recommended for any possible defects in the external quadrants.

It was emphasized that vertical mastopexy had become very popular in breast reduction surgery in recent years. Lumpectomy and oncoplastic surgery could be done in various quadrants of the breast with this technique. It is recommended for the cases in which the volume of the breast is less than 1200 cc.

Application of the Grisotti flaps is recommended in the central tumors where it is necessary to remove the areola and head of the breast for security. And the benefits of Grisotti flap were underlined. The importance and facilitations of implementing of Benelli mastopexy were assessed in medium-volume and droopy breasts.

Breast volume and the tumor-to-breast-volume ratio are mostly debated in breast surgery. Therefore, it is highlighted in this course that the volume of breast should be measured. Oncoplastic breast reduction is defined as the oncoplastic breast surgery technique that is frequently applied in the world and in Turkey. Issues of dose distribution in radiotherapy, aesthetic issues after treatments and macromastia could be resolved surgically with a single operation by this technique. It is a major surgical operation with a significant learning curve. It should not be attempted without full knowledge of at least 5 to 6 techniques. It is highlighted that this technique brings extremely high patient-satisfaction when applied as a two-sided technique.

The endoscopic breast surgery was described in detail by its sole representative in Turkey. This operation is applied in breasts that are droopy and not very big. This technique inspires hope for surgery in the medium and long terms, although it was underlined that there was a significant learning curve during the course.

Breast reconstruction techniques

Although latissimus dorsi (LD) muscle flap lost its popularity due to the high morbidity rates, it is still in use for the patients with small breasts in Turkey as an operation of out-quadrant tumours either on its own or in combination with silicone implants. It is highlighted that we should recommend a new breast construction after mastectomy. The transverse rectus abdominus myocutaneous flap (TRAM) technique can be applied in patients that have adequate abdominal tissue. It is stressed that this technique is a major surgical operation with a significant learning curve. The patients found this technique to be more comfortable in the medium and long terms.

The participating breast surgeons discussed the silicone implant applications performed simultaneously with mastectomy. In recent years, mastectomy rates have increased in breast cancer treatment and reconstruction applications are also performed simultaneously. Silicone implant usage is increased rapidly due to the surgeons' and patients' comfort and ease-of-use of these implants. The protection of the lower breast fold affects the implant application positively and brings about aesthetic results.

A careful marking of the tumor bed is recommended for radiotherapy in oncoplastic breast surgery. In this regard, it is important to co-operate with the radiation oncologist. In recent years, reconstruction techniques applied simultaneously with mastectomy have become more and more popular. There is now a stronger opinion about the application of silicone before radiotherapy. It is specified that the complications of oncoplastic and reconstructive breast surgery do not create serious oncologic problems. They do not delay the adjuvant therapy. In the event of a positive assessment of the pathological border, re-excision can be done.

The highlights in the oncoplastic approach panel according to the breast quadrants

Multi-disciplinary assessment including the plastic surgeon is recommended in the treatment of breast cancer. The importance of the patient, breast, tumor features and the experience of the surgeon were discussed in relation to the implementation of these techniques. The importance of assessment before surgery was underlined by all the panelists. Who should perform these techniques? The importance of and the need for certification training s were emphasized especially in the discussion section. In this context, the situation in Turkey was discussed in detail and the efforts made towards new developments were distinguished, as well. Breast surgeons that attended and completed the courses can perform these operations.

Some of the speakers on the panel suggested that mastectomy and OBS should be differentiated from each other. Breast surgery technique selection constituted an important section of the panel discussions. OBS recommendations of the experts participating in the panel are summarized in Table 2. Table 3 shows the panelists, speakers and presidents of the sessions.

Discussion and Conclusion

ORBS techniques demonstrate a significant growth in Turkey. Also, training and certification are very important in ORBS. We should offer patients breasts without defects, not excellent breasts. If the patients do not have very high expectations, it will increase their compliance after surgery. OBS is an approach that treats the patient, not the disease. OBS increases the role of surgeons. There are important efforts concentrated on learning and the implementation of these techniques among surgeons.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - M.E.; Design - B.K., M.E.; Supervision - B.G.; Funding - C.K.; Analysis and/or Interpretation - M.A.G., K.A., A.S.; Literature Review - M.E.; Writing - M.E.; Critical Review - B.G.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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The New Paradigm: Oncoplastic Breast Conservation Surgery

COLLEEN M. O'KELLY PRIDDY, NIRAV B. SAVALIA, AND MELVIN J. SILVERSTEIN

The adoption of breast conserving therapy as an acceptable alternative to mastectomy opened the door to a wide and varied range of partial breast reconstruction techniques. The term *oncoplastic breast surgery,* as suggested by Werner Audretsch in 1993,[1] describes the concept of local tissue rearrangement that would allow for wide resection of tumors while preserving or improving breast cosmesis. Although the term has been used more broadly to include nipple- and skin-sparing mastectomies with immediate reconstruction, this chapter focuses on immediate or delayed partial breast reconstruction with volume-displacing or volume-replacing techniques after wide excision of the primary lesion. In other words, oncoplastic breast conservation. A contralateral mammaplasty or mastopexy is generally required for symmetry due to the loss of volume from removal of the index cancer.

Traditionally, surgical oncologists are trained to remove the cancer at all costs, with little emphasis placed on the importance of the cosmetic result. Many women have simple excisions and appear to have a reasonable cosmetic outcome in the early postoperative period, but the early results are sometimes misleading. The addition of scarring, resolution of the seroma, and radiotherapy ultimately reveals the true esthetic outcome many months or even years later.

Oncoplastic breast conservation surgery is a new paradigm combining sound oncologic principles with plastic surgery techniques, allowing for wide excision of tumors with minimized risk of involved margins and simultaneous prevention of the deformities commonly associated with simple excisions and postradiotherapy fibrosis.[2] It requires a philosophy that the appearance and function of the breast after tumor excision is important; the patient will live with this result for the rest of her life. The goals of oncoplastic breast surgery include complete removal of the lesion with negative margins, a good to excellent cosmetic result, and the definitive procedure at a single operation. Over the past 30 years we have developed a comprehensive multidisciplinary oncoplastic approach for the surgical treatment of breast cancer.[3–6] This requires an approach that includes coordination with the surgical oncologist, radiologist, plastic surgeon, medical oncologist, pathologist, radiation oncologist, and genetic counselor. As improved breast imaging and neoadjuvant chemotherapy allow a larger number of women to be considered for breast conservation, the combination of oncologic and plastic surgery disciplines also increases the number of women who may be treated with breast conserving surgery by allowing larger excisions with more acceptable cosmetic results.[7] These techniques are applicable to patients with both noninvasive (ductal carcinoma in situ [DCIS]) and invasive breast cancers. Furthermore, now that excision without radiation therapy is an accepted treatment for patients with biologically favorable DCIS, widely clear margins are of even greater importance than previously appreciated.[8,9]

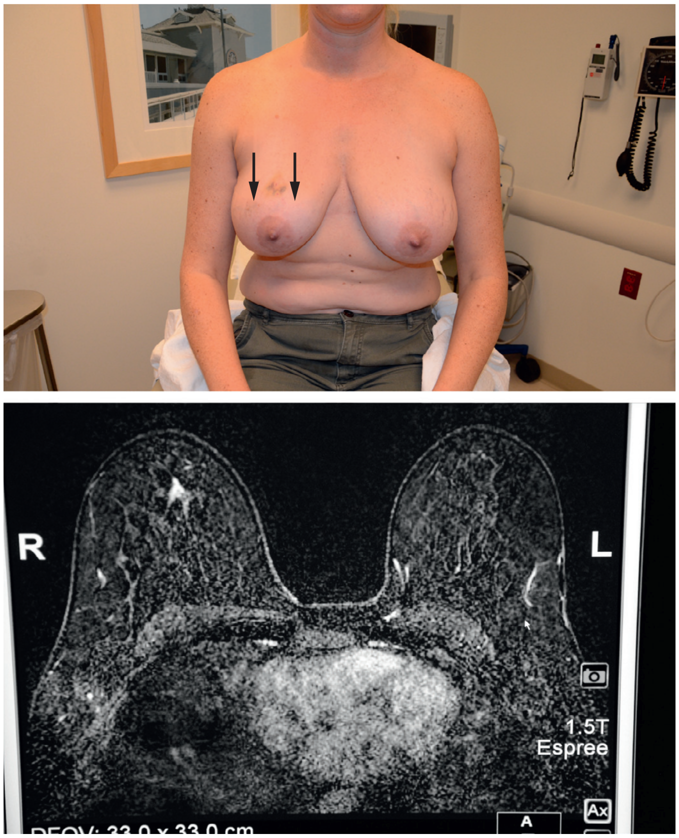
An important goal in caring for a woman with breast cancer is to go to the operating room once and perform a definitive procedure that does not require reoperation. The first attempt to remove a cancer is critical, offering the best chance to remove the entire lesion in a single piece, evaluate its true extent and margin status, and to achieve the best possible cosmetic result. The concept of a one-stage operation is important in the psychological and emotional recovery of a cancer patient.[10] Fewer procedures allow the patient to quickly move on with her life, to the next phase of treatment, if necessary. With this in mind, it is of highest importance to thoroughly stage the cancer preoperatively and carefully plan the operation. This is accomplished by reviewing the patient's full diagnosis, stage, pathology, imaging, risk of recurrence, and risk of developing cancer in the contralateral breast. Whenever possible, the initial breast biopsy should be performed using a minimally invasive percutaneous technique.[11] This usually provides ample tissue for diagnosis and biomarker analysis and should be possible in more than 98% of cases.[12] Preoperative knowledge of tumor biology can sometimes be exploited by using neoadjuvant systemic therapy, which will often downstage a tumor and convert the definitive operation from mastectomy to breast preservation.

General Considerations

Leading the Oncoplastic Team

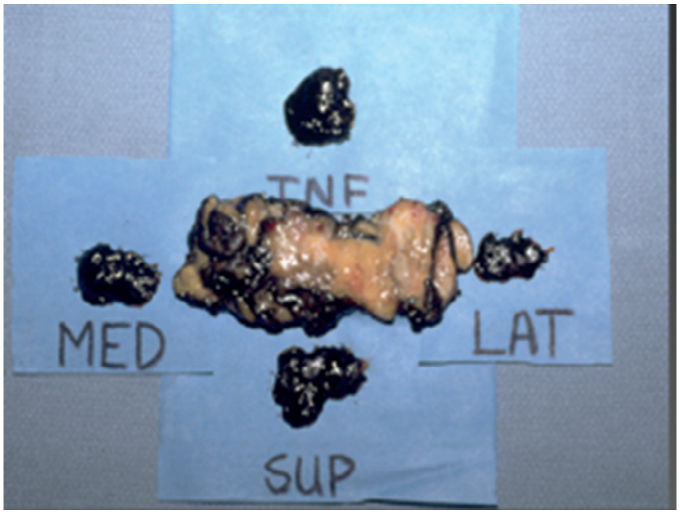
Of utmost importance is a dedicated team approach. At our facility, the oncologic breast surgeon assumes the role of "leader" to guide the team and ensure excellent communication among all team members. During the first visit we generate a "flight plan" that summarizes the diagnosis, includes photos of the patient's chest and relevant imaging, and lists the plan of action leading up to and including the planned operation (Fig. 40.1). The flight plan is given to the patient, distributed to all team members, and updated and revised, if necessary, as the patient moves through the consultation process.

Diagnosis: RIGHT Grade II ductal carcinoma in situ,
ER/PR Positive, 12:00 position, spanning 27 mm on MRI.
12 mm on manno. 5 cm from nipple



1. RIGHT wire guided segmental resection using split reduction
2. LEFT mastopexy for symmetry
3. Plastic surgical consultation with Dr. Davalia 949-759-0980
4. IORT consultation
5. Genetic counseling

• **Fig. 40.1** Example flight plan.



• **Fig. 40.2** The main specimen has been excised with four additional pieces representing the new margins. These additional specimens are clearly smaller than the true margins. Therefore the surgeon cannot be truly certain that the margins are negative. Removal of a single large specimen allows improved confidence in the margin status.

Rationale for Oncoplastic Breast Surgery

The primary goal of breast conservation is to achieve local control with adequate margins while maintaining breast cosmesis.[13] Unfortunately, as many as 36% of simple excisions fail to achieve adequate margins in a single operation, leading to reexcision, worsening cosmesis, and conversions to mastectomy.[14] The benefits of breast conservation compared with mastectomy are preservation of a sense of wholeness, retaining normal breast sensation, and limited morbidity from device-based or autologous reconstruction. The benefits are even greater when adjuvant radiotherapy must be added to postmastectomy reconstruction.[15]

A few of the factors implicated in poor cosmetic results after breast conservation are age greater than 60, tumors larger than 2 cm, small breast size, reexcision for inadequate margins, improper scar orientation, breast tissue resection greater than 100 cm^3 independent of breast size, breast ptosis, tumors located in the central, medial, or lower quadrants, and radiation dose inhomogeneity.[16–20] The common theme among all these limitations is that the removal of tissue without proper reshaping of the breast allows scarring and postradiation fibrosis to reveal an unreconstructed cavity, imbalance in breast tissue distribution, and distortion of the nipple-areola complex (NAC). These limiting factors are largely overcome when an oncoplastic reconstruction is performed. Oncoplastic breast conservation allows rebalancing of the breast. The breast is reconstructed with either a volume displacing or volume replacing technique. This ability to maintain breast balance while reducing breast volume expands the pool of patients who could be considered candidates for breast conservation. This is of particular benefit to the patient with advanced disease who would need adjuvant radiotherapy regardless of mastectomy. These techniques are referred to as extreme oncoplasty or radical breast conservation and are discussed later in this chapter.[21,22]

Currently, because many as 40% to 50% of new breast cancer cases are discovered by modern state-of-the-art imaging.[11] Intraoperatively they are often grossly both nonpalpable and not visible to the surgeon's eye. Under these circumstances, the surgeon essentially operates blindly. Multiple hooked wires can help define the extent of the lesion and guide surgical excision.[23] Using bracketing wires or other newer forms of localization, the surgeon can usually excise the entire lesion within a single piece of tissue, sometimes including overlying skin as well as prepectoral fascia as the anterior and posterior margins. The tissue should be precisely oriented for the pathologist. Intraoperative two-view specimen radiography is extremely useful in localizing the lesion within the specimen, estimating margin distance, and ensuring complete removal.

If the specimen is removed in multiple pieces, rather than a single piece, accurate size and margin assessment may be compromised. Fig. 40.2 shows an excision specimen with four additional pieces that represent the new margins, but clearly the additional specimens do not encompass the full margin, leading to uncertainty about complete excision.

Reconstructive Goals

A common misconception is that the goal of breast reconstruction is to create the "perfect breast." In actuality, the goal should be to achieve an outcome that best suits the *patient's* goals for treatment and desires for final breast appearance. The patient's esthetic goals are often tempered by the complexity of many of the most modern and technically state-of-the-art reconstructive methods. In the same vein, the default reconstructive goal should not be to simply maintain the patient's current appearance. With this in mind, the reconstructive plan can be formulated only after analysis of the tumor size and location, the preoperative breast shape, size, and degree of ptosis, and understanding the patient's oncologic needs and reconstructive desires. The ideal is to minimize the amount of surgery, donor sites, recovery periods, risk of complications, and failure rates, while maximizing the desired esthetic and oncologic outcome.

Many reconstructive options exist, ranging from a simple tissue rearrangement to complex microvascular tissue flap reconstruction. Each step toward a more complex procedure must be carefully weighed against the patient's expectation of results and assessment of the risk to benefit ratio. Reconstructive surgeons may be tempted to use all of their advanced skills and create a complex surgical plan with multiple operations. However, the patient may be satisfied with the reasonable breast shape and symmetry achieved with a simpler course. The decision must be an amalgam of what is oncologically necessary and the simplest reconstructive plan that achieves the patient's goal. Our goal has always been to go to the operating room once, completing the oncologic and reconstructive portions of the case in a single procedure, if possible. The decision to use volume displacement techniques (in other words, to use existing breast volume to reconstruct the defect, versus volume replacement techniques that use regional or distant tissue flaps of varying complexity) depends on the reconstructive needs. Volume displacement techniques offer the simplest solution when there is adequate native breast tissue and the patient accepts a smaller reconstructed breast as well as the need for contralateral surgery to correct asymmetry. Volume replacement allows maintenance of the preoperative breast size but often requires longer operative time, longer recovery, and has associated donor-site morbidity. Our practice is devoted primarily to volume displacement reconstruction and defers to mastectomy only when this is not feasible. In other words, mastectomy (although sometimes appropriate and necessary) is our last choice and never our default option.

To help patients understand the value of oncoplastic breast conservation, they must be educated about their options and the rationale for patient selection and merits of simple excision versus oncoplastic breast conservation. For surgeons, the ability to predict the postlumpectomy deformity leads to understanding the importance of patient selection.

Women with smaller breasts (A/B cup) and minimal ptosis can be challenging. Simple excisions of small tumors are often believed to have little esthetic effect. This is often true when the tumor is in the upper or upper outer breast and a layered glandular repair is performed. However, even the smallest tumor can result in a postlumpectomy deformity if excised from the lower pole of the breast. Postoperative scarring will deform the lower pole and retraction will displace the NAC inferiorly, resulting in the classic "bird's beak" deformity (Fig. 40.3). This can be avoided by recentralizing the NAC over the reshaped breast mound immediately after the resection. With larger tumors, a prediction about the size of the defect will determine eligibility for breast conservation. If the predicted remaining breast is deemed adequate for reconstruction with glandular rearrangement, then oncoplastic breast surgery can be planned. However, if these predictions are inaccurate, then a post lumpectomy deformity will result. In retrospect, these patients may have been better managed with volume replacement techniques or with skin- or nipple-sparing mastectomy. These missteps can only be avoided with experience, and the novice oncoplastic surgeon should be wary.

• **Fig. 40.3** "Bird's beak" deformity after excision of a lower pole tumor from the left breast.

Women with larger breasts (C/D cup and beyond) and ptosis will benefit from oncoplastic breast surgery both oncologically and esthetically. An oncoplastic approach will allow a larger excision with higher probability of obtaining adequate margins as well as correction of breast ptosis and macromastia. Furthermore, the correction of macromastia yields the benefit of better adjuvant radiotherapy dose homogeneity with resultant long-term maintenance of cosmesis.[24]

Preoperative Planning

Preoperative planning requires discussion among, at a minimum, the oncologic surgeon and the radiologist. Usually a plastic surgeon, medical oncologist, radiation oncologist, and others should be included as well. All of the preoperative tests must be carefully evaluated and integrated with information about the pathologic subtype, size and extent of the lesion, size of the breast, lesion position within the breast, patient wishes, among other concerns. Other particular concerns include invasive lobular cancers that may be larger than expected based on initial imaging, extensive in situ components with similar risk for underestimation on imaging, patient desire for symmetry, and timing of the symmetrizing procedure.

Various options for the timing of oncoplastic breast surgery have been suggested.[25,26]

- **Immediate:** Definitive oncoplastic breast surgery at the time of tumor resection. This is a single-stage approach that has the advantage of using surgically naive tissue for reconstruction but may require repeat operations if margins are not clear and may necessitate mastectomy if the proper margins cannot be identified at reexcision.

- **Delayed-immediate:** Delay of oncoplastic breast surgery until final pathologic margins are confirmed to be clear, usually one to 3 weeks later and before the delivery of radiotherapy. This is a staged approach that has the advantage of definitively clearing the margins before committing to oncoplastic breast surgery but the downside of requiring multiple operations.
- **Delayed:** No oncoplastic breast surgery until after completion of adjuvant systemic and radiation therapy, usually 1 to 2 years later. This has the advantage of minimizing the potential delay of initiation of adjuvant therapy from wound-healing complications, but has the highest complication rates and least favorable esthetic outcomes.

In our practice, we have evaluated our postoperative margin status after initial surgery, specifically comparing simple elliptical excisions and Wise-pattern mammaplasty excisions. For tumors spanning 50 mm or more, the elliptical excision group (n = 250) had negative margins (defined as no ink on tumor[27] in 88% of cases. The oncoplastic reduction group (n = 300) had negative margins in 97% of cases. For tumors spanning more than 50 mm in the extreme oncoplastic group (n = 125), the negative margin rate was 87%.[22] As such, we feel justified in routinely performing immediate oncoplastic breast conservation in virtually all patients who are candidates for breast conservation. Even for tumors larger than 50 mm, the positive margin rate is similar to that of simple excisions with margin shaving.[14] In the case of positive margins, early reexcision before scarring has obliterated the dissected planes allows re-creation of the excisional defect for more accurate reexcision. When conversion to mastectomy is indicated, it is of benefit for the macromastia patient to have had the preliminary skin reduction and NAC repositioning. This patient who, before this failed oncoplastic breast conservation, may not have been a good candidate for NAC-sparing mastectomy may now successfully have the procedure after allowing 1 to 2 months of healing for revascularization of the NAC.

The skin overlying the tumor does not always need to be removed as a rule. However, when skin is not removed the anterior margin may be close or involved. We always measure skin-to-tumor distance using all three imaging modalities (mammography, ultrasound, and magnetic resonance imaging). If the skin-to-tumor distance is less than 10 mm, we remove the overlying skin. For patients with DCIS in whom we do not plan to irradiate postoperatively, we generally remove the overlying skin to ensure a negative anterior margin.

It is expected that oncoplastic resection of the index tumor will result in asymmetry. Given that breast asymmetry after breast conservation is known to affect psychosocial functioning and quality of life, the value of contralateral symmetry surgery is not debated.[28] The ideal timing for surgery of the contralateral breast would be after the index breast has been treated and adjuvant radiotherapy has been delivered. It is well accepted that the index breast will respond to radiotherapy with a variable degree of volume loss, fibrosis, and loss of elasticity. At a second operation the contralateral breast can be reduced and lifted for symmetry after these postradiotherapy changes have stabilized. Although ideal symmetry can be achieved in this staged approach, the index breast may continue to slowly shrink for years due to ongoing radiation injury.

When presented with the option of having two separate operations over the span of 1 to 2 years versus having both operations performed in the same setting, albeit with somewhat less accurate symmetry, it is rare that a patient prefers a staged approach. Virtually all are willing to accept the lesser symmetry from a single-stage approach when educated about the long-term effects of radiation therapy. With that in mind, a small fraction of our patients do return 3 to 4 years after surgery to have a secondary procedure for the contralateral breast to maintain symmetry.

Surgical Considerations

On the day of surgery, the patient undergoes wire localization (we do this the afternoon before surgery if the operation is scheduled as a first-start case) and sentinel node mapping by the radiologist. Just before surgery, generally in the preoperative holding area, she is marked in the upright position and counseled one final time. In the operating room, she is positioned on the operating table with her arms secured to the arm boards at 90 degrees. This allows for the head of the bed to be raised 45 to 90 degrees during the operation to assess symmetry. Assuming a bilateral procedure is planned, a two-team approach is used. While the oncologic surgeon is resecting the tumor from the index breast, the plastic surgeon is performing the contralateral breast symmetry procedure. After the tumor has been resected, the index breast is reconstructed, thus minimizing any increase in operative time. Drains are generally not required for these operations. At the conclusion of the procedure, the patient's breasts are wrapped in a compressive dressing for 24 to 48 hours to minimize seroma, ecchymosis, and hematoma.

With the range of oncoplastic approaches, precise and thorough communication between the plastic surgeon and oncologic surgeon is crucial. Proper preoperative planning, combined with knowledge of the blood supply of the breast, will usually allow preservation of a robust pedicle for the NAC and minimize necrosis.

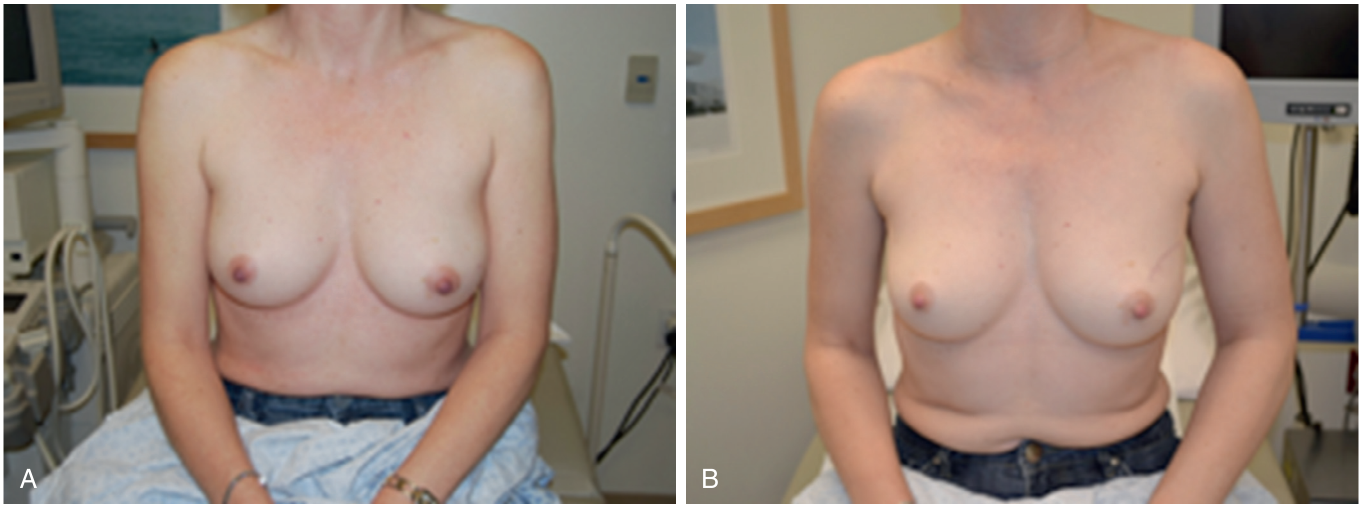
Oncoplastic Techniques

Simple Glandular Flap Techniques

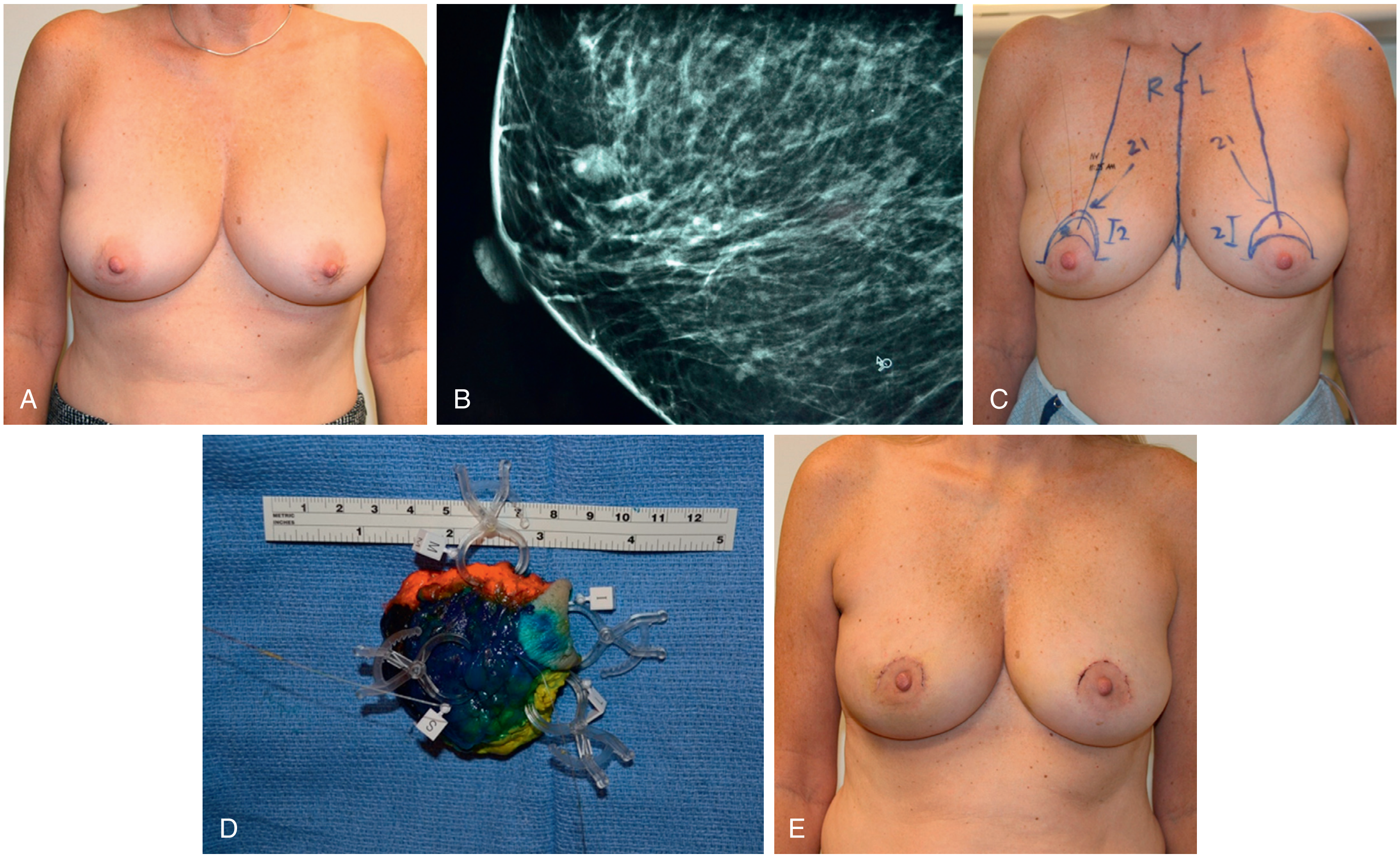
Glandular rearrangement can range from basic undermining and closure of a defect to tissue rearrangement with glandular flaps. The basic technique is to achieve closure of the parenchymal defect independent of the skin. An incision is made for access, often within the periareolar border, but can be anywhere on the breast. Through this incision, skin flaps are elevated (akin to mastectomy flaps) to expose the involved region of the breast. Once the excision is complete the adjacent parenchyma is freed from the underlying chest wall fascia. At this point, if primary closure of the defect is possible without deforming the breast, then it is performed with interrupted sutures. If primary closure is not possible, then the parenchyma can be further freed both from the overlying skin and underlying fascia. Care must be taken to preserve an adequate blood supply. This technique should be avoided in a predominantly fatty breast to avoid fat necrosis. The mobilized flaps of glandular tissue from both sides of the defect can then be rotated or advanced into the defect and sutured into place. Any dimpling of the overlying skin should be conservatively undermined before skin closure (Fig. 40.4).

Crescent, Hemibatwing, and Batwing Techniques

For lesions in the upper hemisphere (generally in the 08:00–04:00 positions going clockwise), crescent, batwing, or hemibatwing excisions may be used. These excisions lift the NAC, and a



• **Fig. 40.4** Radial ellipse technique: preoperative (A) and 6-month postoperative (B) photos. A 2-cm left upper outer quadrant cancer was removed using a radial elliptical incision.



• **Fig. 40.5** Crescent technique: a 56-year-old woman (A) presented with an invasive ductal carcinoma of the right breast spanning 7 mm on mammogram at the 12:00 border of the areola (B). A crescent mastopexy (C) allowed excision of a 44-g specimen including the skin margin (D). A contralateral crescent mastopexy provided symmetry (E). Final pathology revealed a 1.1-cm invasive cancer and 5 cm of ductal carcinoma in situ with all negative margins.

contralateral crescent is often done simultaneously for symmetry. Generally, crescents are only appropriate for breasts with minimal or grade I ptosis that do not require reshaping. We typically limit movement of the NAC to a maximum of 2 cm. The upper hemisphere of the areola is meticulously marked, and an analogous second crescent is marked no more than 2 cm higher. The skin within the crescent is excised and access to the breast is gained. Once again, skin flaps are elevated to expose the breast gland, and the resection is performed. Glandular advancement of the lower pole parenchyma and overlying NAC is performed, and the parenchymal defect is repaired. The incision is then easily closed in layers, resulting in a minor correction of ptosis (Fig. 40.5).

• **Fig. 40.6** Hemibatwing technique: preoperative marking for a hemibatwing excision, which is a combination of a supraareolar crescent and a radial ellipse.

• **Fig. 40.7** Hemibatwing technique: (A) preoperative and (B) 1-month postoperative photos. A lateral invasive ductal carcinoma in the 02:00 position of the left breast was excised with a hemibatwing. A crescent mastopexy was done for symmetry on the right breast.

The batwing technique is essentially a crescent mastopexy with two wings on either side of it.[3] It allows a more aggressive mastopexy to be performed without the need for raising skin flaps or creation of pedicles for the NAC. This method is ideal for an upper pole tumor where a wide area of tissue is involved or in a previously irradiated breast where minimal tissue undermining is critical to avoiding necrosis. This procedure preserves the nipple on an extremely broad inferior pedicle.

A hemibatwing is a combination of a radial elliptical excision and a crescent excision (Fig. 40.6). This achieves dual goals: lifting the NAC while excising a radial segment of the breast. It can be combined with a crescent mastopexy of the contralateral breast for symmetry (Fig. 40.7).

A clamshell technique is also possible, combining two mirror-image batwings with the NAC in between (Fig. 40.8). The center point of these two batwings will determine the final NAC position. The benefit of this technique over a simple batwing is that it allows a larger area of tissue to be excised from an entire hemisphere of the breast. Enough tissue is spared within the clamshell pattern to allow it to be de-epithelialized and advanced into the excavated hemisphere. As with the batwing, this procedure is ideal for patients in whom minimal tissue undermining is important. We commonly use the clamshell pattern in previously irradiated patients who develop a new or recurrent cancer and desire another attempt at breast conservation. In addition, this technique allows for breast conservation in patients with multicentric disease with or without skin involvement.

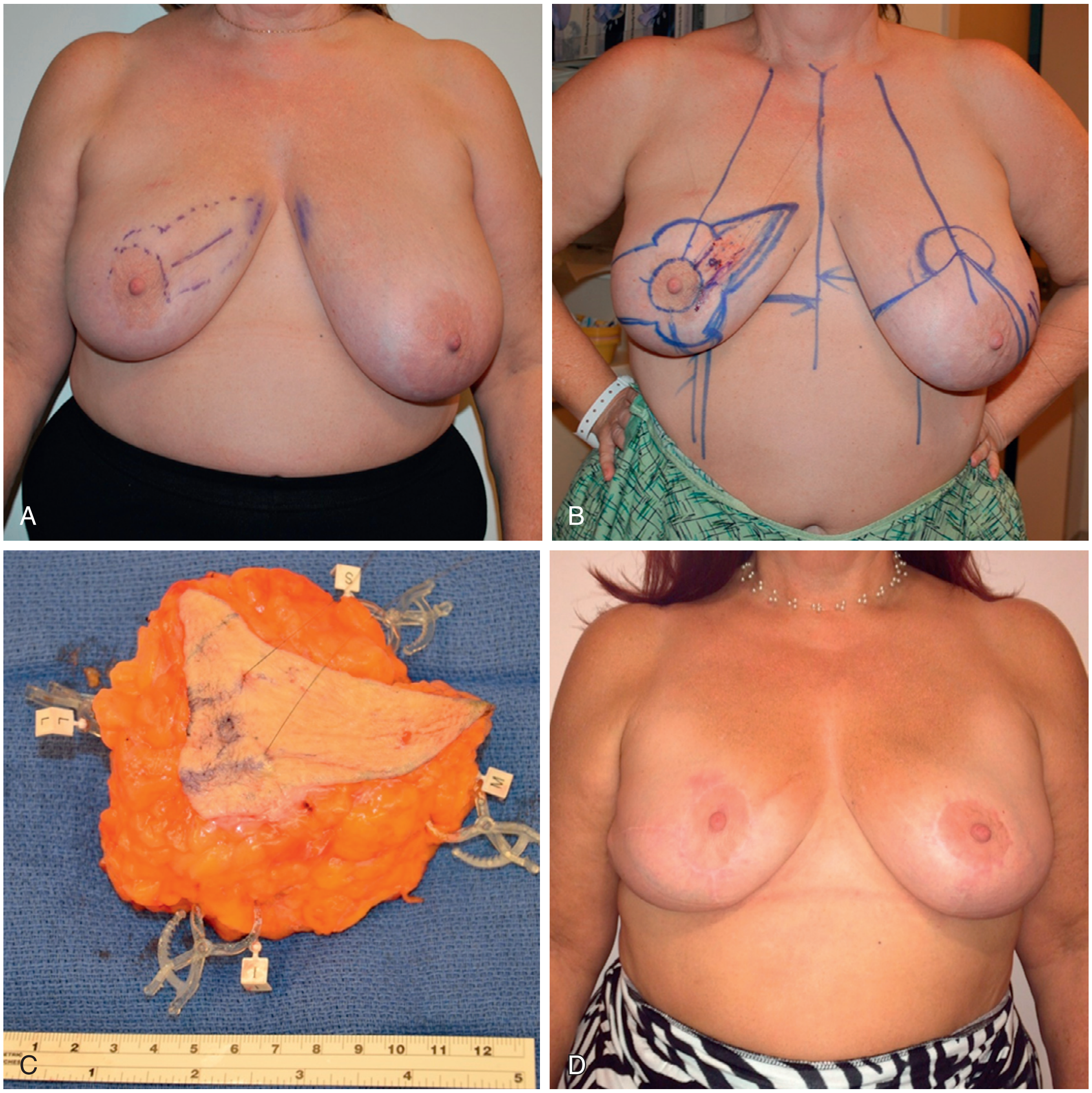
Vertical Mammaplasty, Inframammary Excision, and Central Excision Techniques

The vertical mammaplasty excision removes a triangular-shaped piece of tissue from the lower breast hemisphere. It is ideal for patients with tumors in the 05:00 to 07:00 position who do not want the NAC elevated as it would be with a standard reduction (Fig. 40.9). It leaves an inverted T-shaped scar. A classic vertical mammaplasty relies on liposuction for additional contouring[29]; this is used judiciously or not at all in oncoplastic reconstruction to minimize the potential for seeding of tumor cells. The incision for the inframammary approach is placed just slightly above the inframammary sulcus. In the upright position, this scar is hidden. This incision is an excellent choice for lesions in the posterior inferior position of the breast. It does not remove any skin and generally does not change the size or shape of the breast. Lesions in the upper hemisphere can be reached using this incision.

When the NAC is involved by tumor, the central excision of breast tissue is incorporated into an inverted T mammaplasty that allows for reshaping and immediate NAC reconstruction. This technique takes advantage of breast ptosis to advance an inferiorly based island of tissue into the central defect. It is also feasible to reconstruct a NAC on this island of tissue, which can be tattooed later to complete the reconstruction (Fig. 40.10). Alternatively, the Grisotti technique can be used for smaller defects.[30] It relies on rotation-advancement of a laterally based tissue island with minimal reshaping of the remainder of the breast.

Round Block Mastopexy (Benelli) and Reduction Mammaplasty Techniques

After 30 years of using a range of oncoplastic approaches, it has become clear to us that the best and most consistent results are



• **Fig. 40.8** Clamshell technique: a 60-year-old woman (A) presented with a recurrent ductal carcinoma in situ (DCIS) of the upper inner quadrant of the right breast (treated previously with three excisions and radiation therapy). She had been offered mastectomy and autologous flap reconstruction at an outside institution but declined. Instead, she chose an excision with a clamshell-type reconstruction and contralateral breast reduction for symmetry (B). Final specimen weighed 175 g (C) and contained 2.9 cm of DCIS with negative margins. (D) shows the final postoperative result.

obtained using a round block (Benelli) excision in women with smaller breasts and grade I ptosis and with a reduction mammaplasty in women with medium to large breasts and grade II or III ptosis. An elliptical or triangular extension can be added to either of these approaches, in which case they are called split-Benelli or split-reduction.[31,32]

The round block (Benelli) mastopexy gives excellent results for lesions in small to medium breasts with mild to moderate ptosis (Fig. 40.11).[33] This technique allows 360-degree access to the breast, and the final scar is limited to the circumareolar border. The inner circle is drawn to the desired NAC diameter within the baseline areola. The outer circle is drawn eccentrically, with its center point higher than the current nipple position, allowing elevation of the NAC upon closure. Conversely, if no upward movement of the NAC is desired, the two circles can be drawn concentrically. The diameter of the outer circle should not exceed twice the diameter of the inner circle. The skin within these circles is deepithelialized, and the dermis incised 5 mm inside the outer ring, and access to the breast is gained. The skin flaps can be raised circumferentially down to the chest wall, thus retaining the NAC on a central pedicle. Once the entire gland is exposed in this manner, a pie-shaped wedge of tissue can be resected easily from any location in the breast and the defect closed with minimal undermining off the chest wall. The skin is then redraped and the incision closed with a permanent pursestring closure around the areola. The result is a rounder, lifted breast. Any scalloping or wrinkles that develop after final closure due to size discrepancy between the length of the inner and outer circles will flatten out over the course of a few months.

The workhorse of oncoplastic surgery at our facility is the Wise pattern mammaplasty.[34] This powerful technique owes its versatility to several key features. First, it allows the use of virtually any pedicle for the NAC (superior, lateral, medial, inferior, central, and bipedicle; we generally prefer a superior or medial pedicle).

• **Fig. 40.9** Vertical mammaplasty technique: preoperative (A) and 2-year postoperative (B) photos. This patient underwent excision of a 2-cm invasive cancer in the 06:00 position of the right breast using a triangle excision. This was chosen because she did not want any change in appearance after surgery. A reduction excision was suggested, but she declined. (C) The incision appears as an inverted T.

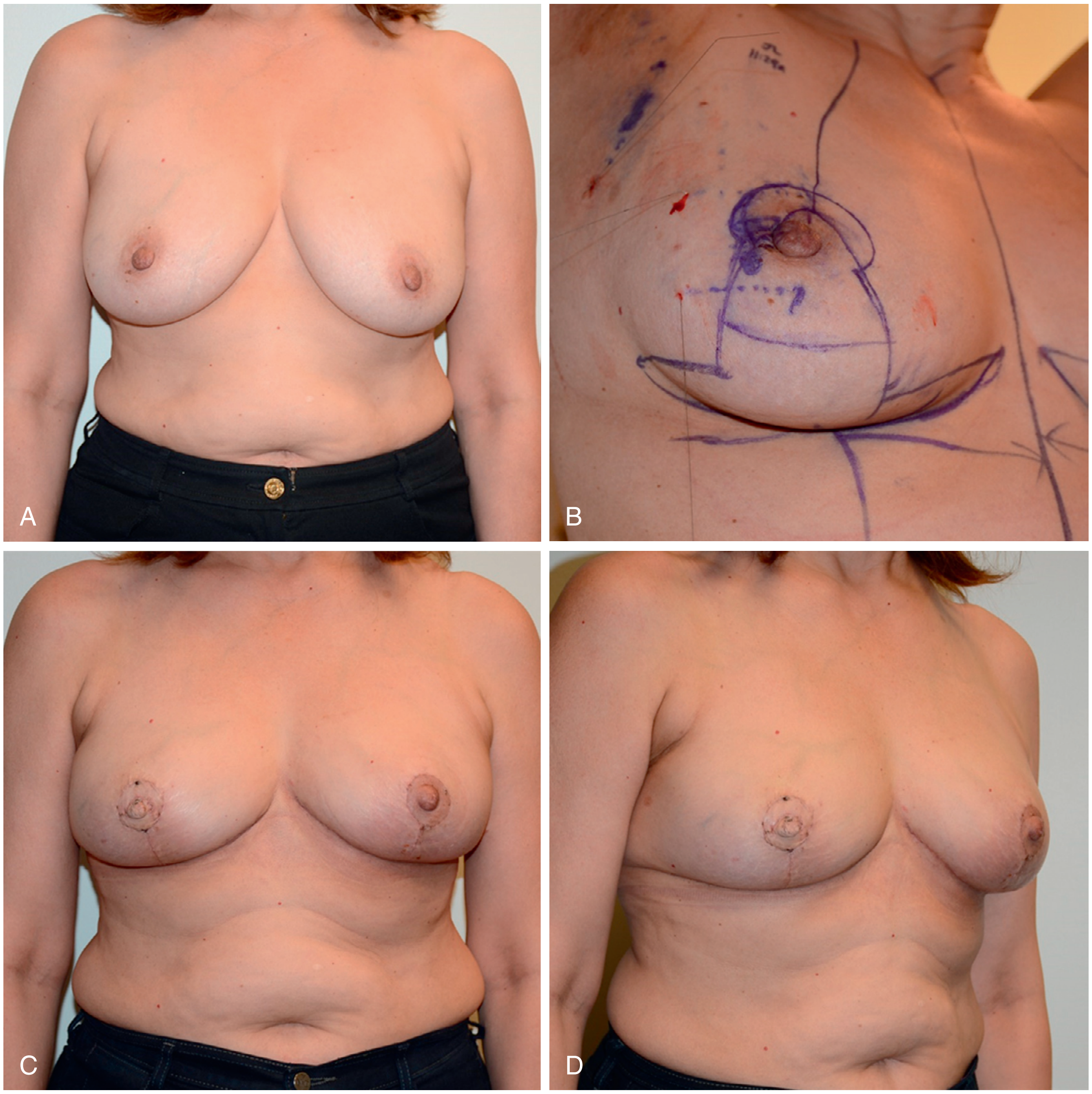
Second, significant tissue rearrangement can be performed with multiple secondary pedicles independent of the NAC. Finally, the wide skin resection allows the most aggressive correction of ptosis. These factors combine to allow exposure to the entire breast, the ability to widely resect tissue from any quadrant, and the opportunity to significantly reduce overall breast volume to aid radiation dose homogeneity.

The Wise pattern mammaplasty requires the creation of three triangles: vertical, medial, and lateral. The inferior borders of all three triangles are incorporated into the inframammary fold incision, limiting the scars to the circumareolar border, the vertical midline of the breast, and the inframammary crease (Fig. 40.12). Tumors located in the inferior pole can be easily incorporated in the incision, with the overlying skin, through a standard Wise pattern. The vertical pillars are then plicated and the NAC inset into the keyhole. If the NAC cannot be saved, a nipple can be re-created immediately or as a delayed procedure. This technique allows the lower pole and central tumors to be easily excised along with the overlying skin to avoid a close or positive anterior margin.

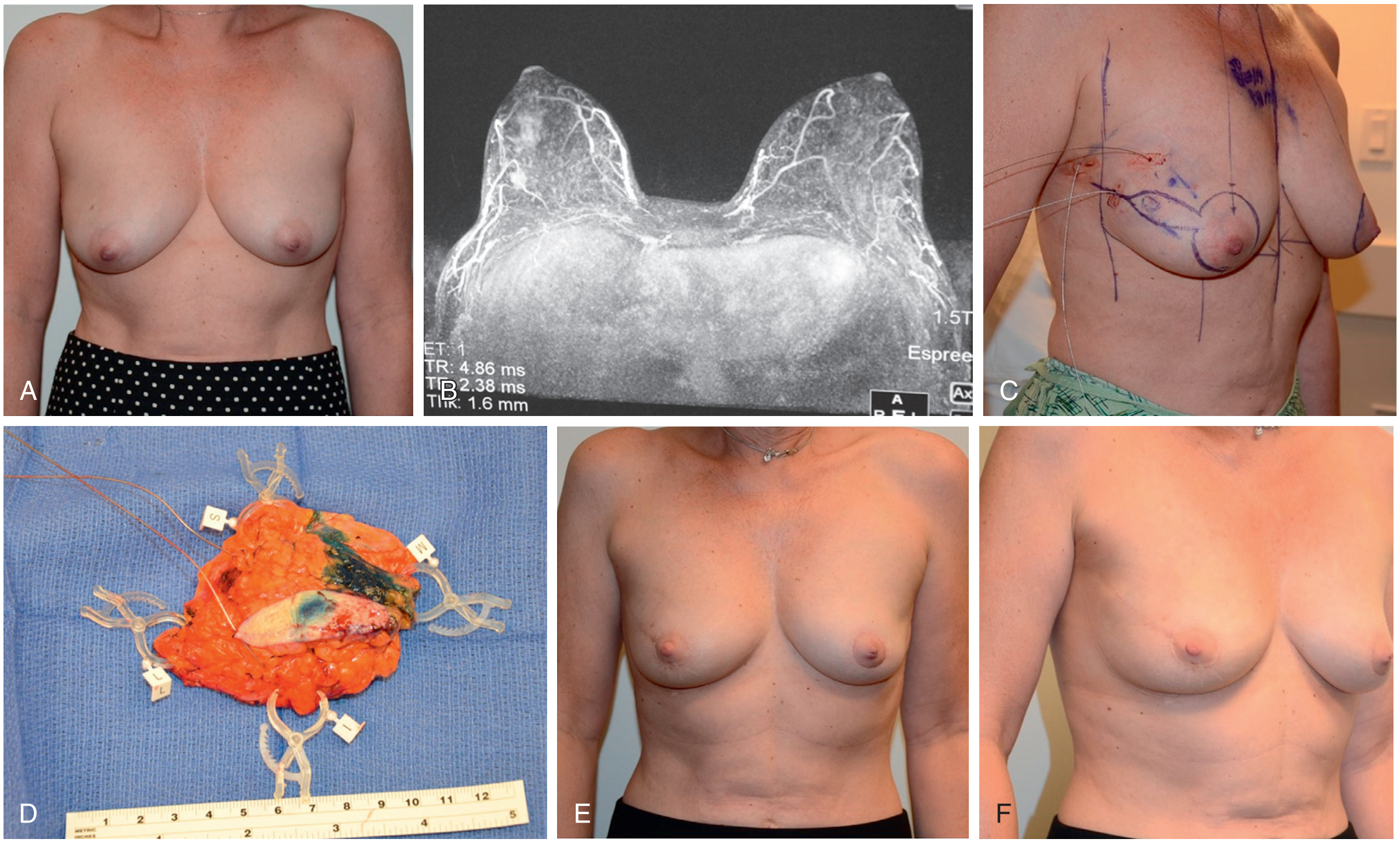
When the tumors are located in areas that do not naturally fall within a standard Wise pattern, two options exist. The first is to perform a standard Wise pattern technique and to tunnel under skin flaps to reach the distant tumor. This is acceptable if the tumor is deep and the anterior margin is not felt to be of concern. However, for most cases when the tumor is located outside the Wise pattern, our preferred alternative is to excise the tumor with the anterior skin margin. For tumors located in the upper outer or upper inner quadrants, the Wise pattern may be reconfigured to include the tumor with the overlying skin, in a split reduction.

When the NAC is involved by tumor, the central excision of breast tissue is incorporated into an inverted T mammaplasty that allows for reshaping and immediate NAC reconstruction. This technique takes advantage of breast ptosis to advance an inferiorly based island of tissue into the central defect. It is also feasible to reconstruct a NAC on this island of tissue that can later be tattooed to complete the reconstruction. Alternatively, the Grisotti technique can be used for smaller defects.[30] This relies on rotation advancement of a laterally based tissue island with minimal reshaping of the remainder of the breast.

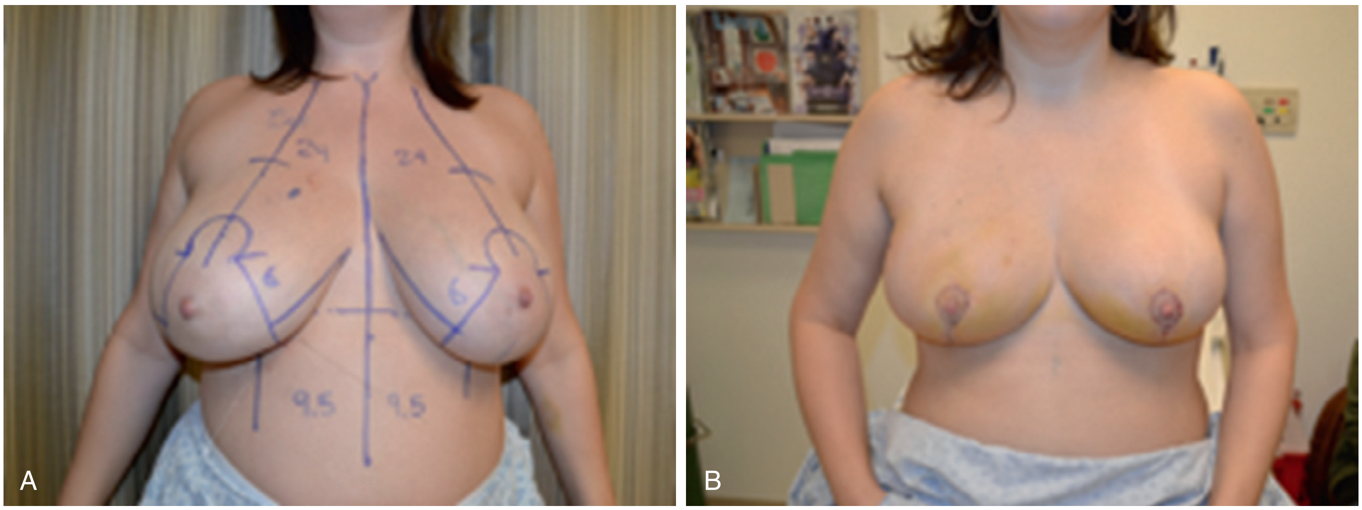
In a split reduction, the lateral or medial triangle of the Wise pattern is not positioned at the base of the breast but advanced



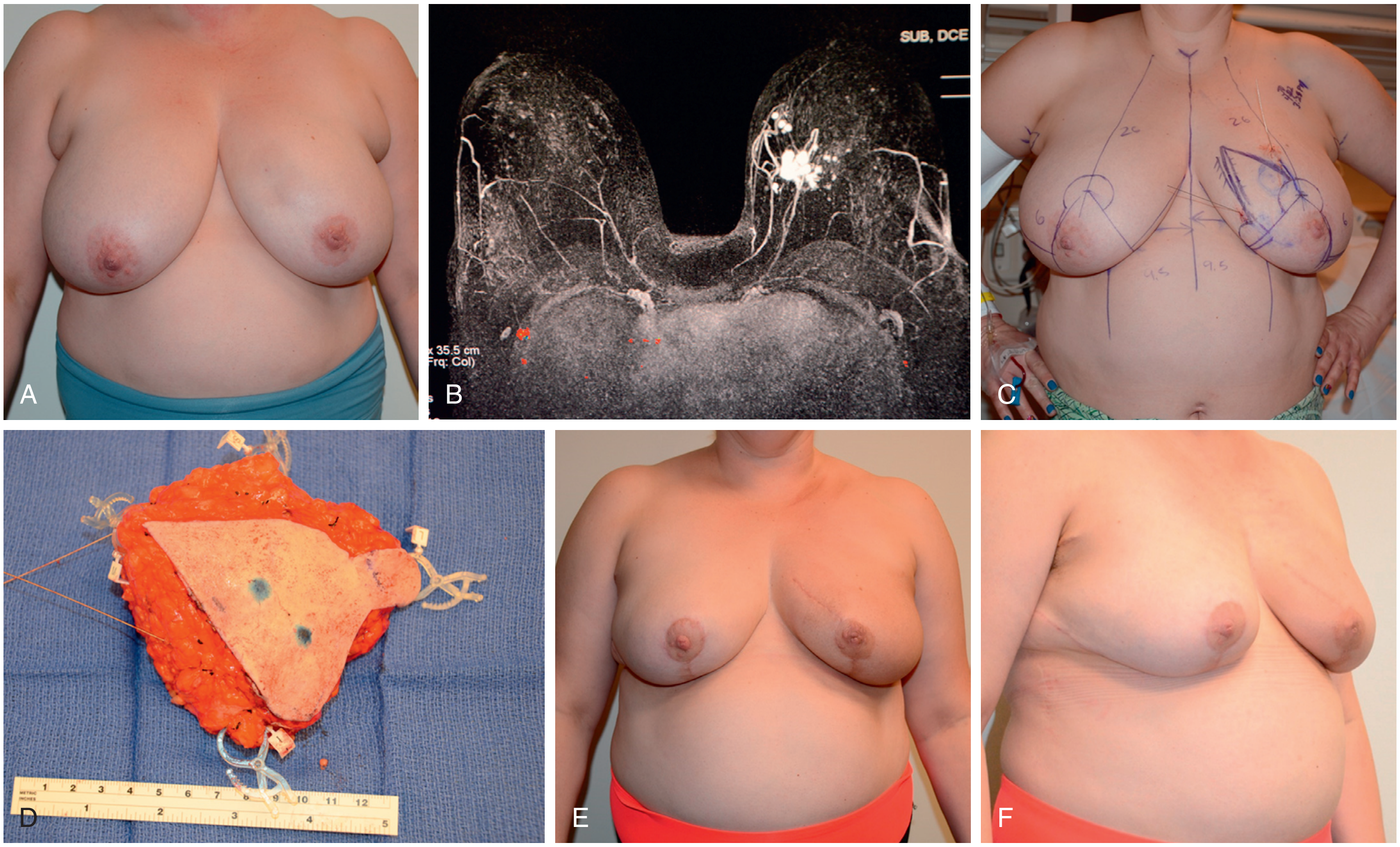
• **Fig. 40.10** Central excision technique: a 60-year-old woman (A) presented with a right breast cancer involving the nipple-areolar complex (NAC). She underwent neoadjuvant chemotherapy followed by a central reduction with excision of the NAC via an inverted-T reduction pattern reconstruction and NAC reconstruction on an inferiorly based parenchymal segment (B). The left breast was reduced with a standard Wise pattern technique for symmetry (C and D).



• **Fig. 40.11** Circumareolar/Benelli technique: a 47-year-old woman (A) presented with an invasive cancer of the right breast at the 10:00 position spanning 25 mm on magnetic resonance imaging (B). After neoadjuvant chemotherapy, a circumareolar/Benelli approach (C) with lateral skin ellipse over the tumor allowed excision of a 75-g specimen (D); final pathology revealed a 1.4-cm invasive ductal carcinoma with negative margins and 3/10 positive axillary lymph nodes. (E and F) Postoperative appearance.



• **Fig. 40.12** Wise-pattern reduction mammaplasty technique: preoperative (A) and 1-week postoperative (B) photos. A 12-mm tumor was removed from the lower inner quadrant of the right breast using a standard Wise pattern reduction.



• **Fig. 40.13** Split reduction technique: a 43-year-old woman (A) presented with a multifocal left breast cancer with ductal carcinoma in situ component in the upper inner breast. There were approximately 20 lesions spanning 74 mm by 72 mm on magnetic resonance imaging (B). After neoadjuvant chemotherapy, she underwent a split reduction of the left breast and contralateral Wise pattern reduction for symmetry (C). The specimen weight was 266 g from the upper inner breast (D) and revealed a 9.5-cm span of multifocal invasive tumors with negative margins. The postoperative photos (E and F) demonstrate the final outcome after adjuvant radiation therapy to the left breast.

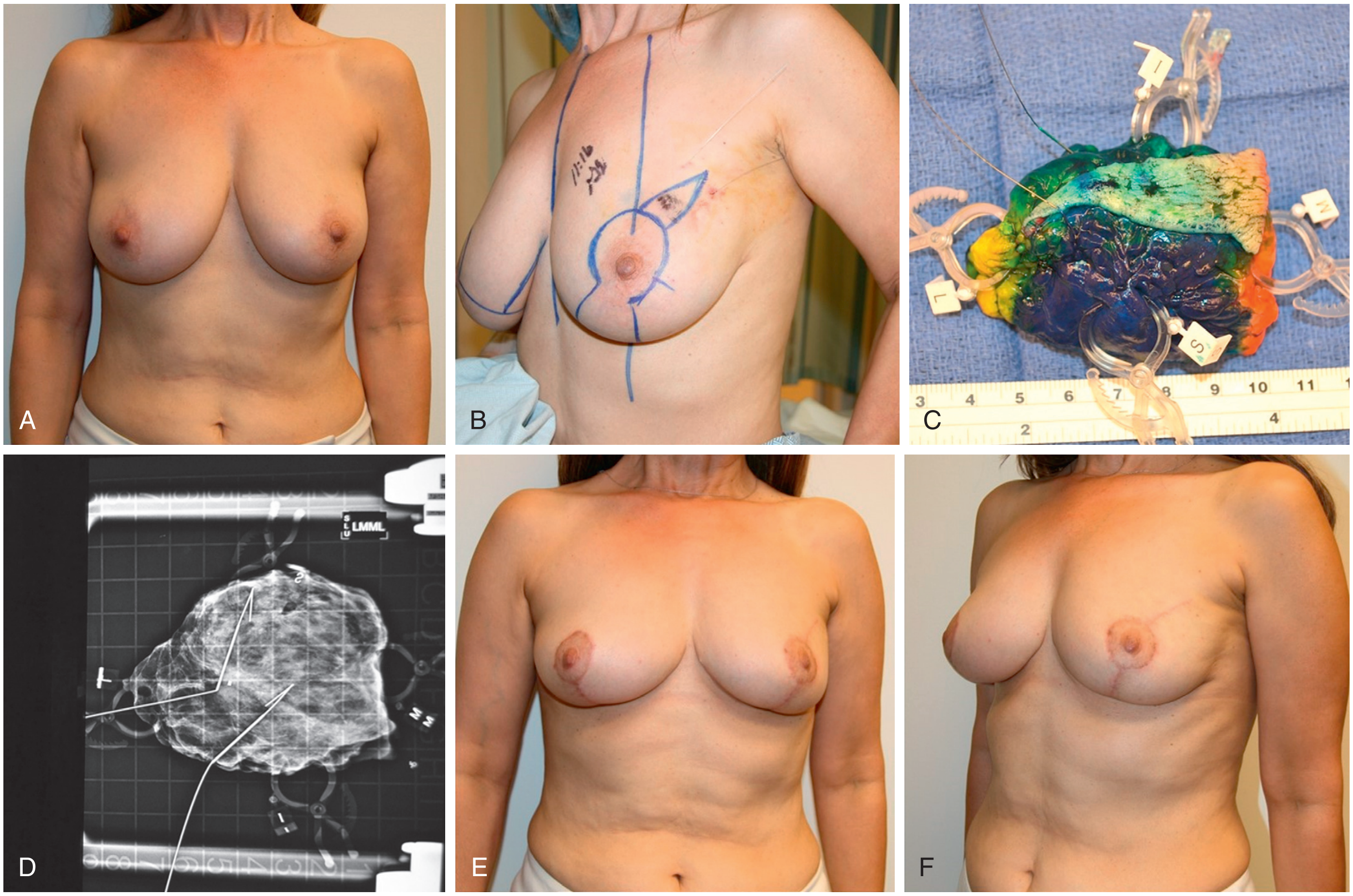
cephalad to a position directly overlying the tumor (Figs. 40.13 through 40.15). The medial or lateral vertical limb of the inverted T is split on the side of the tumor excision to accommodate the higher position of the medial or lateral triangle. When the tumor is located in the 12:00 position, the split occurs at the apex of the keyhole rather than along the vertical limbs of the pattern.

Extreme Oncoplasty

In 2008, we wondered how far we could push the oncoplastic envelope. We had been performing oncoplastic resections for unifocal stage I and II disease for years. We also encountered many patients with larger or multifocal/multicentric tumors who seemed technically amenable to oncoplastic resection, but there were no prospective randomized data to support breast conservation for these patients. We always believed that the relationship between the size of the breast and the span of the tumor was key: a large breast with a large tumor could tolerate a large resection. So we began our “Extreme Oncoplasty Program” to provide second opinions for patients who wanted to save their breast but had been told that they needed a mastectomy.

Extreme oncoplasty is a breast conserving operation using oncoplastic techniques for a patient who, in most physicians’ opinions, requires a mastectomy. Due to the nature of these lesions, most of these patients will also need postmastectomy radiation therapy. Extreme oncoplasty can be considered, if the breast is large enough to support it, for patients with tumors larger than 50 mm, multifocal or multicentric lesions, extensive DCIS or an extensive intraductal component greater than 50 mm, a previously irradiated breast with a new or recurrent cancer within that breast, and locally advanced breast cancers with a limited or partial imaging response to neoadjuvant chemotherapy (Fig. 40.16).[35] Patients such as these have generally not been considered acceptable candidates for breast conservation because the prospective randomized trials on which breast conservation is based only allowed inclusion of unifocal tumors up to 5 cm in extent. There are no prospective randomized data for larger, multifocal, or multicentric lesions, and there are not likely to be any. But what is the difference between a 48-mm cancer that qualifies and a 52-mm cancer that does not? When breast conservation is performed for a patient who turns out to have a 55- or 60-mm cancer on final pathology, most of us will irradiate that breast if the margins are negative and not convert to a mastectomy just because of a size larger than 50 mm. It is important to recognize that we are doing this without the support of any Level I evidence.

The most important reason to consider extreme oncoplasty is that breast conservation yields a better quality of life compared with the combination of mastectomy, reconstruction, and



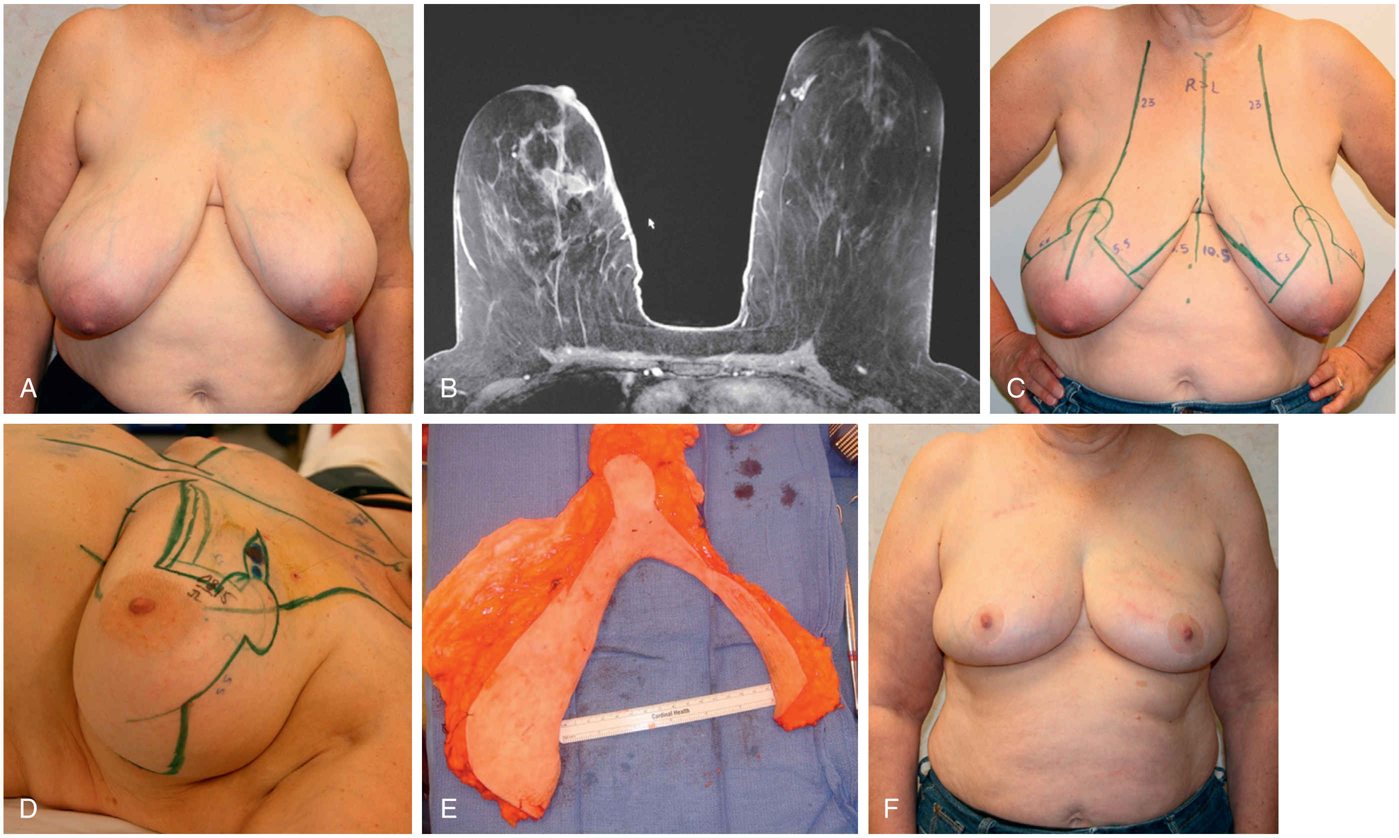
• **Fig. 40.14** Split reduction technique: a 53-year-old woman (A) presented with an invasive lobular carcinoma of the left upper outer breast spanning 2 cm on magnetic resonance imaging. A split reduction pattern was used for the left breast (B), and standard Wise pattern reduction was performed on the right for symmetry. A 62-g specimen was excised (C and D) and revealed a 6-cm invasive lobular carcinoma on final pathology with negative margins. It is likely that this tumor would have required reexcision or conversion to mastectomy with traditional methods of breast conservation. (E and F) Postoperative appearance.

radiation therapy, and survival is likely the same.[36] Consider the quality of life with the combination of mastectomy, reconstruction, and radiation therapy. For most patients, a retropectoral expander will be placed at the time of mastectomy. This causes significant pain. There are drains, a foreign body, the potential for infection, and the additional time required for expansion, all of which can have a significant impact on the patient's life. The final reconstruction requires another operation: the expander to implant exchange or perhaps an autologous flap. If an autologous flap is used it is a longer procedure, with additional operative risks and donor site morbidity. There may be additional operations to adjust the breast and nipple as well as tattoos for the areola. Then there is the opposite breast to consider; many patients will consider prophylactic mastectomy and reconstruction or a reduction for symmetry. The mastectomy or mastectomies will almost always leave insensate breast(s). The final cosmetic result can range from poor to excellent, but our experience in looking at more than 1000 reconstructed patients tells us that fewer than 40% would be rated as excellent by us.

After a mastectomy with reconstruction, most of these high-risk patients need radiation therapy.[37] Currently patients with tumors greater than 5 cm, four or more positive nodes, and sometimes 1 to 3 positive nodes receive radiation therapy.[38,39] Additionally, patients with extensive lymphovascular invasion get radiation therapy, as will patients with close or involved margins after mastectomy. In other words, radiation therapy will be recommended for many patients after mastectomy and certainly for nearly all patients who qualify for extreme oncoplasty. If the patient is going to be given radiation therapy regardless of surgical approach, we generally prefer to save her breast with an acceptable cosmetic result, if it is technically possible and oncologically sound.

Radiation therapy is not friendly to postmastectomy reconstruction.[40] There is a risk of capsular contracture if an implant-based reconstruction is used, or breast shrinkage if autologous tissue is used. Radiation therapy is inconvenient from the patient's perspective, expensive, causes some morbidity, and may interfere with the timing of chemotherapy. Because no mastectomy removes 100% of the breast, if radiation therapy is not given the remaining 5% to 10% of the overall breast tissue and dermal lymphatics are not treated, which may contribute to an increased local recurrence rate.

Compare this to oncoplastic breast conservation with a simultaneous contralateral reduction for symmetry: a single operation,



• **Fig. 40.15** Split reduction technique: a 56-year-old woman (A) presented with a left breast invasive carcinoma and ductal carcinoma in situ of the upper inner quadrant, spanning 19 mm on mammography. (B) Preoperative magnetic resonance imaging. She underwent a split reduction excision of the tumor (C and D) with negative margins (E). In addition, the index breast was significantly reduced, and a contralateral Wise pattern reduction was performed for symmetry. The final results (F) are shown 1 year after adjuvant radiotherapy to the left breast.

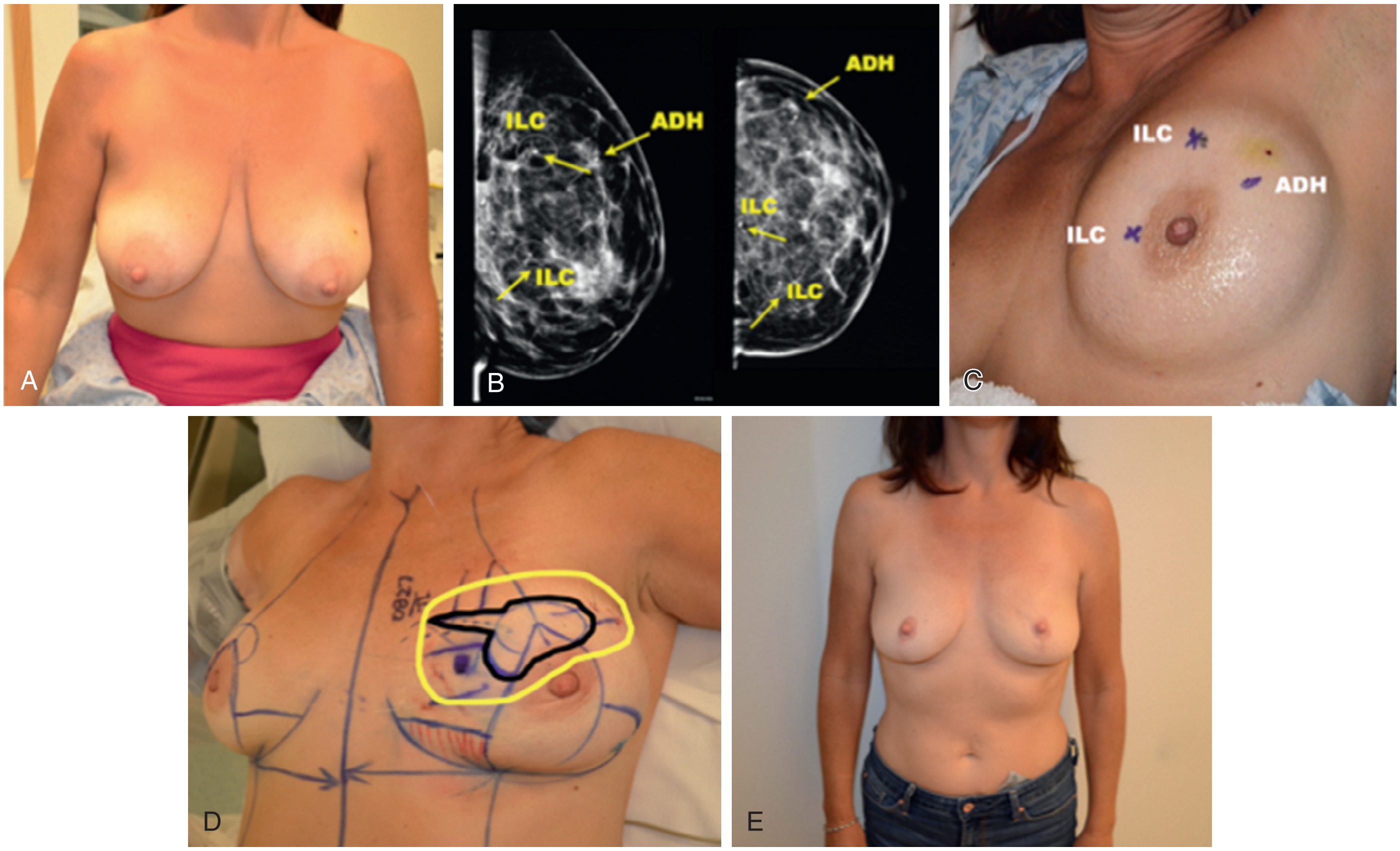
no drains, and better esthetics both immediately and later. There is less pain, less expense, a shorter hospital stay (this is often an outpatient procedure), no foreign body, and no donor site morbidity. The breasts are more functional and sensate. All of this results in better body image and a happier patient.[41] Most importantly, breast conservation with a reduction allows the patient to forget that she had breast cancer—not right away, but at some point in the future. In 6 months or a year, the patient will be getting dressed, and she has two normal reduced breasts. They look good, they are nearly always sensate, and she feels like she is just a normal woman. She will be reminded of breast cancer only when she sees it on television or it is time for an appointment with her doctor. If she had a mastectomy, even with an excellent reconstruction, she will be reminded of her cancer on a daily basis for the rest of her life.

We have followed our extreme oncoplasty patients very carefully.[21] The extreme cases, on average, have cancers about three times the size of our standard oncoplastic cases. The extreme specimens weighed about 70 grams more. No ink on tumor was achieved only 86% of the time during the first excision due to the larger size of the extreme tumors; 12% of patients underwent reexcision, and 5% ultimately underwent mastectomy. The local recurrence rate for the extreme cases is slightly but not significantly higher (1.5% vs. 1.2% over a mean follow-up of 24 months), as would be expected for patients with larger cancers. There are no long-term recurrence or survival data at this point for extreme patients. There was overwhelming patient satisfaction with the oncoplastic program as measured by a patient satisfaction survey.

Summary

The techniques discussed here are our most commonly used methods of oncoplastic breast surgery. The premise of our general techniques is discussed, but each operation must be individualized for the patient at hand. Many patients present to us seeking breast conservation after having been told elsewhere that it would be technically challenging or impossible. A large number of these women have been spared mastectomies by using the carefully selected and designed techniques described. The importance of individualization of these techniques cannot be overstated: we frequently make intraoperative adjustments to the preoperative markings to modify the skin envelope, modify the NAC pedicle if necessary, and often use secondary and tertiary parenchymal pedicles to reconstruct defects. The ability to maintain flexibility is important, and communication between disciplines is critical.

Oncoplastic surgery combines sound oncologic surgical principles with plastic surgical techniques. Coordination of these two disciplines helps avoid poor cosmetic results after wide excision and increases the number of women who can be treated with



• **Fig. 40.16** Extreme oncoplasty: a 48-year-old woman (A) presented with two foci of invasive lobular carcinoma *(ILC)* and an additional focus of atypical ductal hyperplasia *(ADH)* (B and C). The disease spanned nearly half her left breast and was in multiple quadrants. She underwent a wire-localized extreme split reduction excision (D); the black line indicates the skin that was removed and the yellow line the total tissue removed. Final pathology revealed two foci of ILC spanning 42 mm. With the ADH, the total disease spanned 81 mm. All margins were negative. The final results (E) are shown 2.5 years after adjuvant radiotherapy to the breast.

breast conserving surgery by allowing larger breast excisions with more acceptable cosmetic results. Oncoplastic surgery requires cooperation and communication of a large multidisciplinary team. New oncoplastic techniques that allow more extensive excisions can be used to achieve both acceptable cosmesis and widely negative margins, reducing the need for radiation therapy in many cases of DCIS. Extreme oncoplasty is a breast conserving operation using oncoplastic techniques for a patient who, in most physicians' opinions, requires a mastectomy. Because of the size and extent of these lesions, most of these patients will also need postmastectomy radiation therapy. Extreme oncoplasty can be considered, if the breast is large enough to support it, for patients with tumors larger than 50 mm, multifocal or multicentric lesions, extensive DCIS or extensive intraductal component greater than 50 mm, previously irradiated breasts with a new or recurrent ipsilateral cancer, and large locally advanced breast cancer with a partial or complete imaging response to neoadjuvant chemotherapy. Oncoplastic breast surgery and extreme oncoplasty are win-win approaches, allowing removal of the cancer with wide margins while often achieving better cosmesis than before surgery. They both require a philosophy that the appearance, function, and sensation of the breast after cancer surgery are important.

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Training Canadian surgeons in oncoplastic breast surgery: Where do we stand?

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DOI: 10.1503/cjs.001217

Summary

Breast-conserving surgery with adjuvant radiation therapy is widely accepted as a universal standard of care for women with early-stage breast cancer. Oncoplastic breast-conserving surgery (OPS) techniques have emerged in recent years, facilitating the achievement of better cosmetic results while adhering to good oncological principles. Compared with the rest of the international community, Canada has been fairly slow in its clinical uptake of OPS. This commentary discusses how Canada can increase its capacity for OPS.

Breast-conserving surgery with adjuvant radiation therapy is widely accepted as a universal standard of care for women with early-stage breast cancer. Prospective, randomized clinical trials with more than 20 years of follow-up data have reported no difference in mortality and overall survival in women who received breast-conserving surgery compared with women treated with mastectomy.[1] The success of breast conservation depends on 2 goals: the surgery must successfully excise the entire cancer, and the cosmetic result needs to be such that the patient retains a cosmetically pleasing breast contour without deformity. Historically, breast conservation has not always achieved a good cosmetic result, leaving 30% of patients with a visible cosmetic deformity[2] and resulting in negative patient-reported outcomes (body image and quality of life) and postradiation deformities that are severe and difficult to manage by the plastic surgeon.[2]

Oncoplastic breast-conserving surgery (OPS) techniques have emerged in recent years, facilitating the achievement of better cosmetic results while adhering to good oncological principles. The term “oncoplastic” first appeared in 1996,[3] when Audretsch described the technique of reconstructing a partial mastectomy defect as a further refinement of breast conservation based on a basic principal of breast surgery: that it is much easier to prevent a cosmetic deformity than to repair it later. Since its introduction, OPS has enabled surgeons to remove greater volumes of tissue successfully, thus reducing mastectomy and re-excision rates. For the first time, patients with large-volume and multicentric disease are able to undergo breast conservation with superior cosmesis and long-term oncological safety.[4]

Formal Canadian oncoplastic training fellowships

Oncoplastic surgical techniques can be divided into 3 levels according to the extent of skill and training required to perform each of these procedures (Table 1), although the amount of training needed for competency has not yet been standardized. With more and more patients requesting and expecting an optimal postoperative appearance, it should be clear to

Table 1. Classification of oncoplastic breast procedures*

Category	Examples
Level I	Dual plane undermining, nipple undermining, glandular advancement and lumpectomy defect closure
Level II	Glandular rotations, skin excision, de-epithelialization and nipple areolar complex recentralization, round block (Binelli) mastopexy, crescent mastopexy, raquet mastopexy, hemibatwing and batwing
Level III	Reduction mammoplasty procedures with contralateral balancing procedures–wise pattern reduction, vertical mammoplasty, V/J mammoplasty

*Levels I and II can be learned and performed independently by many surgeons; level III techniques involve the contralateral normal breast and are often jointly performed with the plastic surgeon.

breast surgeons that staying relevant in the field must include having an OPS skill set. However, compared with the rest of the international community, Canada has been fairly slow in its clinical uptake of OPS, with a recent study highlighting the lack of available formal training opportunities as a major barrier.[5] Oncoplastic surgery has not traditionally been part of a general surgeon's residency training, nor has it been a formal part of Canadian breast or general surgical oncology fellowship training. These fellowships have traditionally emphasized the development of surgical expertise in the multidisciplinary management of breast disease, with no formal OPS training built into the curriculum. Although fellows do spend time with local plastic surgeons, the scope of training is often limited to postmastectomy breast reconstruction and not methods for performing a cosmetically acceptable breast-conserving surgery while avoiding a mastectomy altogether. As such, Canadian OPS training has traditionally been independent of breast or general surgical oncology training programs.

Recently, owing to increasing demand, Western University and the University of Ottawa developed formal OPS fellowships of 1–2 years with the goal of teaching breast surgical oncology fellows or practising general surgeons to perform a full range of OPS techniques independently. These fellowships also emphasize the necessity of a plastic surgeon as an integral member of the multidisciplinary team in the management of patients with breast cancer. These fellowships, codirected by both breast and plastic surgeons, are the culmination of work on a dedicated OPS curriculum and represent an open collaboration between the 2 surgical specialties. The fellow can tailor the program to meet the demands of current or future academic or community-based positions by increasing training exposure to various plastic surgery techniques of breast reconstruction in order to further increase patient access to such joint surgical procedures (i.e., reduction mammoplasty, immediate prosthetic or autologous reconstruction).

Canadian oncoplastic courses for the practising surgeon

Practising Canadian surgeons currently performing OPS have generally obtained their skills through courses taken internationally,[5] as historically this has been an unmet need in Canada. In partnership with the University of Toronto, University of Ottawa and Western University, the Canadian Breast Surgery Innovations (CBSI) group began offering full-day OPS workshops in late 2016. This group, consisting of expert academic and community OPS surgeons, created the workshop with the goal of raising the standard of breast surgery delivered in Canada. These workshops are currently offered every few months and have been held in conjunction with national or regional general surgery or breast cancer conferences to maximize exposure and enrollment. The workshops include a combination of didactic lectures, comprehensive videos, case discussions and hands-on cadaveric dissections under direct supervision. Participants learn a range of oncoplastic techniques and tips and tricks for effective and efficient collaborations with plastic surgeons, patient selection for OPS, and assessing cosmetic results and patient satisfaction. Workshops are not-for-profit to maximize enrollment and training opportunities. All workshops to date have sold out in 24–72 hours. Further workshops took place in Ottawa and London in October and November, and more are planned throughout Canada (https://oncoplasticpartnershipworkshop.ca).

Conclusion

Historically, most surgeons felt that a postlumpectomy cosmetic defect or contour deformity was a small price to pay for curing breast cancer while avoiding a mastectomy. Today, with recent advances in modern breast cancer management, women can look forward to a long, healthy life after their breast cancer diagnosis. It is more important than ever to offer them a treatment option that preserves their quality of life and their sense of attractiveness and femininity. Oncoplastic surgery techniques allow the surgeon to not only completely excise the disease, but also maintain excellent cosmesis. Hopefully there will be a steady rise in general and breast surgeons embracing OPS as they see the benefits reaped by patients who rightly demand better from us.

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Competing interests: None declared.

Contributors: All authors contributed substantially to the conception, writing and revision of this article and approved the final version for publication.

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Updated Evidence on the Oncoplastic Approach to Breast Conservation Therapy

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Summary: The oncoplastic approach to breast conservation therapy has become a useful and popular option for women with breast cancer who wish to preserve their breast. The initial driving forces were aimed at minimizing the potential for a breast conservation therapy deformity; however, various other benefits have been identified that include broadening the indications for breast conservation therapy in some patients and improved margin control. The various techniques can be categorized into glandular rearrangement techniques such as breast reductions usually in patients with larger breasts or flap reconstruction such as the latissimus dorsi muscle usually in patients with smaller breasts. As the acceptance continues to increase, we are starting to see more outcomes evidence in terms of patient satisfaction, quality of life, complications, and recurrence, to further support the safety and efficacy of the oncoplastic approach. (*Plast. Reconstr. Surg.* 140: 14S, 2017.)

Partial breast reconstruction using the oncoplastic techniques has become an important part of our reconstructive practices. As an option for women with breast cancer who undergo breast conservation therapy, this approach has many proven benefits. It was popularized in Europe and has now expanded and is an accepted option in conjunction with breast conservation surgery in the treatment of breast cancer.[1,2] In a review of 10,607 breast cancer surgeries, the oncoplastic approach was the 1 procedure with the biggest increase of nearly 4-fold from 2007 to 2014.[3] There is some inconsistency in how the oncoplastic approach is offered in various parts of the world. In the United Kingdom, the interest in oncoplastic surgery has increased over the last 5 years with significantly more breast surgeons performing reduction techniques and latissimus dorsi flaps. Seventy five percentage of breast surgeons there have an interest in further oncoplastic training, while plastic surgeons interested in further oncoplastic training dropped from 62% to 27%.[4] A survey in Canada demonstrated that surgeons who did predominantly breast were more likely to use the oncoplastic technique and involve plastic surgeons. Those not performing oncoplastic procedures cited a lack of training and access to plastic surgeons as significant barrier.[5] In a survey in the United States, both breast and plastic surgeons agreed that complex partial reconstructions were best performed using the team approach and that margin concerns were a major concern and aesthetic benefits were a major driving force in both groups.[6]

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Received for publication July 12, 2017; accepted August 10, 2017.

DOI: 10.1097/PRS.0000000000003951

ADVANTAGES AND DISADVANTAGES

Oncoplastic surgery expands the indications for breast conservation allowing the resection of much larger tumors relative to breast size, tumors larger than 4 cm, locally advanced cancers, and prior neoadjuvant chemotherapy that would otherwise only be treated with mastectomy.[7–9] In the United States, given that most breast cancers present in early stage, the optimal breast conservation to mastectomy rate should be at least 60% and ideally at 70% or higher,[10] and oncoplastic surgery in the appropriate patients allow surgeons to reach these goals. The use of this approach also allows additional sampling of ipsilateral breast tissue with a reduction in metachronous breast cancer occurrence by 33% and a diagnosis of synchronous breast cancer on the opposite side of around 4%.[11] One of the initial driving forces behind the oncoplastic technique was the aesthetic benefits. Partial reconstruction prior to radiation therapy will minimize

Disclosure: *Dr. Losken is a speaker for RTI. Drs. Hart and Chatterjee have nothing to disclose.*

the number of breast conservation therapy (BCT) deformities and improve breast shape.[1,12,13] Compared with partial mastectomy alone, there is less deformity long term, especially after radiation with regard to possible nipple eversion volume loss deformity and breast asymmetry.[7] Compared with simple mastectomy with reconstruction, the oncoplastic approach preserves breast tissue and sensation and has been shown to result in lower complication rates and without potential donor-site morbidity.[14] Disadvantages of the oncoplastic surgery can also be divided into oncologic and reconstructive groups. Compared with simple mastectomy, breast-conserving surgery in general still involves a partial mastectomy being done and so locoregional recurrence is still slightly higher (8–10%) compared with simple mastectomy (3–5%) even though there is no survival difference between the 2.[15,16] After oncoplastic surgery for invasive breast cancer, breast radiation is mandatory, whereas after simple mastectomy, it might be avoided.[17] It should be noted that for level II volume displacement oncoplastic surgery (for larger tumors), newer data indicate no difference in locoregional recurrence compared with simple mastectomy likely due to the fact that a large portion of the breast is removed followed by the adjuvant, protective effects of whole breast radiation[18] (Table 1). There have been several recent articles showing the advantages of oncoplastic surgery with regard to oncologic and aesthetic outcomes (15). Reexcision is still possible if indicated and usually performed with the reconstructive surgeon present to help orient the lumpectomy defect. Additional breast scars when local flaps are performed can complicate completion mastectomy if necessary.

INDICATIONS

Poor cosmetic results have been reported in up to 20% of women following BCT alone due to breast shape, tumor size, tumor location, and postoperative radiation.[7] The various indications are listed in Table 2. A recent study of 350 patients demonstrated that the maximal volume of tissue resected with lumpectomy without resulting in unacceptable aesthetic and functional outcomes of decreased quality of life were 18–19 % in the upper-outer quadrant, 14–15% in the lower quadrant, 8–9% in the upper-inner quadrant, and 9–10% in the lower-inner quadrant.[19] When indicated, it is better to perform oncoplastic techniques immediately at the time of tumor resection.[20,21] Reduction techniques prior to radiation therapy results in a significantly lower complication rates when compared with performing reductions after completion of radiation therapy (21% versus 57%; $P < 0.001$) and Kronowitz et al.[22,23] has shown similar results (24% versus 50%).

TECHNIQUES

Volume Displacement Techniques

The breast reshaping oncoplastic procedures all essentially rely on advancement, rotation, or transposition of a large area of breast to fill a small- or moderate-sized defect (Table 1). This absorbs the volume loss over a larger area. Perhaps the most popular and versatile breast-reshaping options are the mastopexy or reduction techniques, which constitute a level 2 oncoplastic volume displacement design (Fig. 1). The ideal patient is one where the tumor can be excised within the expected breast reduction specimen, in medium to large or ptotic breasts where sufficient breast parenchyma remains following resection to reshape the mound.

Larger, more remote defects and defects in smaller breasts can be reconstructed using autoaugmentation flaps during oncoplastic reduction or mastopexy procedures. A recent large series of 333 patients demonstrated the use of

Table 1. Different Techniques in Oncoplastic Surgery

Volume Displacement Techniques	Volume Replacement Techniques
"Parenchymal remodeling, volume shrinkage"	"Adjacent or distant tissue transfer, volume preserving" Implant augmentation—rare
Level 1: complex wound closure; Level 1: local tissue rearrangement, e.g., concentric mastopexy	Local flaps: faciocutaneous, perforator flaps, latissimus dorsi myocutaneous flap
Level 2: reduction/ mastopexy techniques	Distant flaps
Level 2: free nipple grafts with reduction techniques	

Table 2. General Indications for Oncoplastic Surgery

Cosmetic Reasons	Oncological Reasons
High tumor to breast ratio (> 20%)	Concern about clear margins
Tumor location—central, inferior, medial	Wide excision required
Macromastia	Poor candidate for mastectomy and reconstruction (i.e., age, breast size)
Large tumor	Patient desires breast conservation
Patient desires smaller breasts	
Significant ptosis or breast asymmetry	

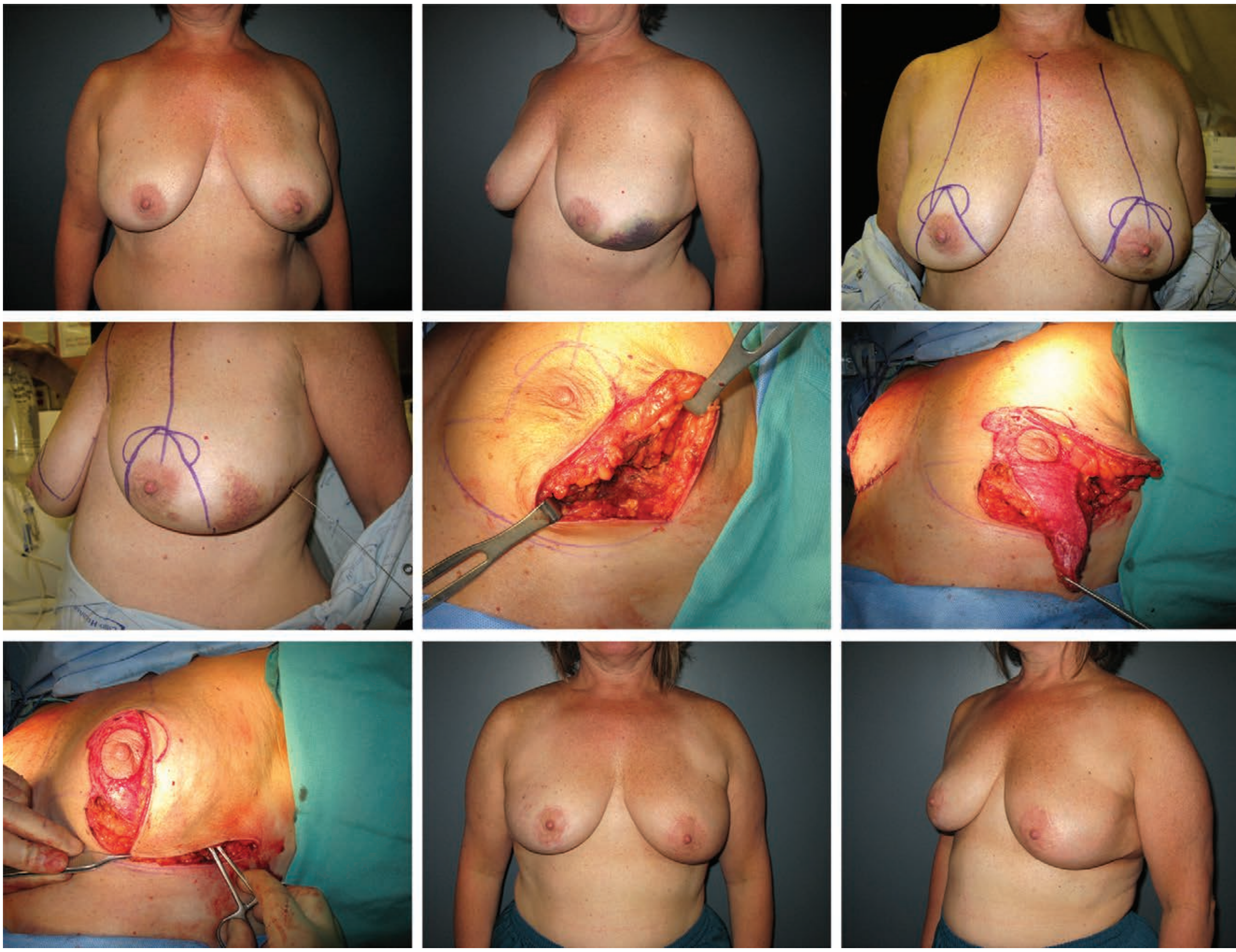

Fig. 1. This is a 51-year-old female with a left lower lateral quadrant DCIS with a left lower lateral quadrant DCIS (*above, left; above center*). She had wire localization and was marked with the Wise pattern (*above, right; middle left*). After a 60 g partial mastectomy, she was left with a large lateral defect (*middle, center*). This was reconstructed with an extended superomedial pedicle and an additional 30 g resection from the left side (*middle, right; below, left*). A contralateral reduction of 120 g was performed. She is shown 1 year following completion of left-sided radiation therapy (*below, center; below, right*). DCIS, ductal carcinoma in situ.

autoaugmentation techniques to be safe and effective and were used 33% of the time.[24] Superomedial was the most common extended pedicle and lateral being the most common tumor location. Inferolateral was the most common secondary pedicle for lateral or upper outer defects. There were no significant differences in the overall complication rate with 15.5% in the regular oncoplastic group, 19.6% in the extended pedicle group, and 20% in the secondary pedicle group. The ipsilateral side is often left about 10% larger in anticipation for radiation fibrosis to improve long-term symmetry and reduce the possible need for reoperation.

Volume Replacement Techniques

Women with large tumor to breast ratios and women with small-to-moderate breasts who have insufficient residual breast tissue for rearrangement require partial reconstruction using nonbreast local or distant flaps. This is now well accepted in the evolution of breast cancer surgery and provides breast symmetry without remodeling the contralateral breast. The usual techniques included (1) rhomboid flaps; (2) subaxillary flap; (3) superior-based lateral thoracodorsal flap (LTDF); (4) inferior-based LTDF; and (5) the extended LTDF. Small lateral defects (less than 10% of breast size) can be closed with local flaps. Other local flaps include the LTDF latissimus dorsi musculocutaneous flap[25] and various perforator flaps[26,27,28] (Fig. 2).

MARGINS

The importance of negative margins in BCT cannot be overstated and has been associated as a

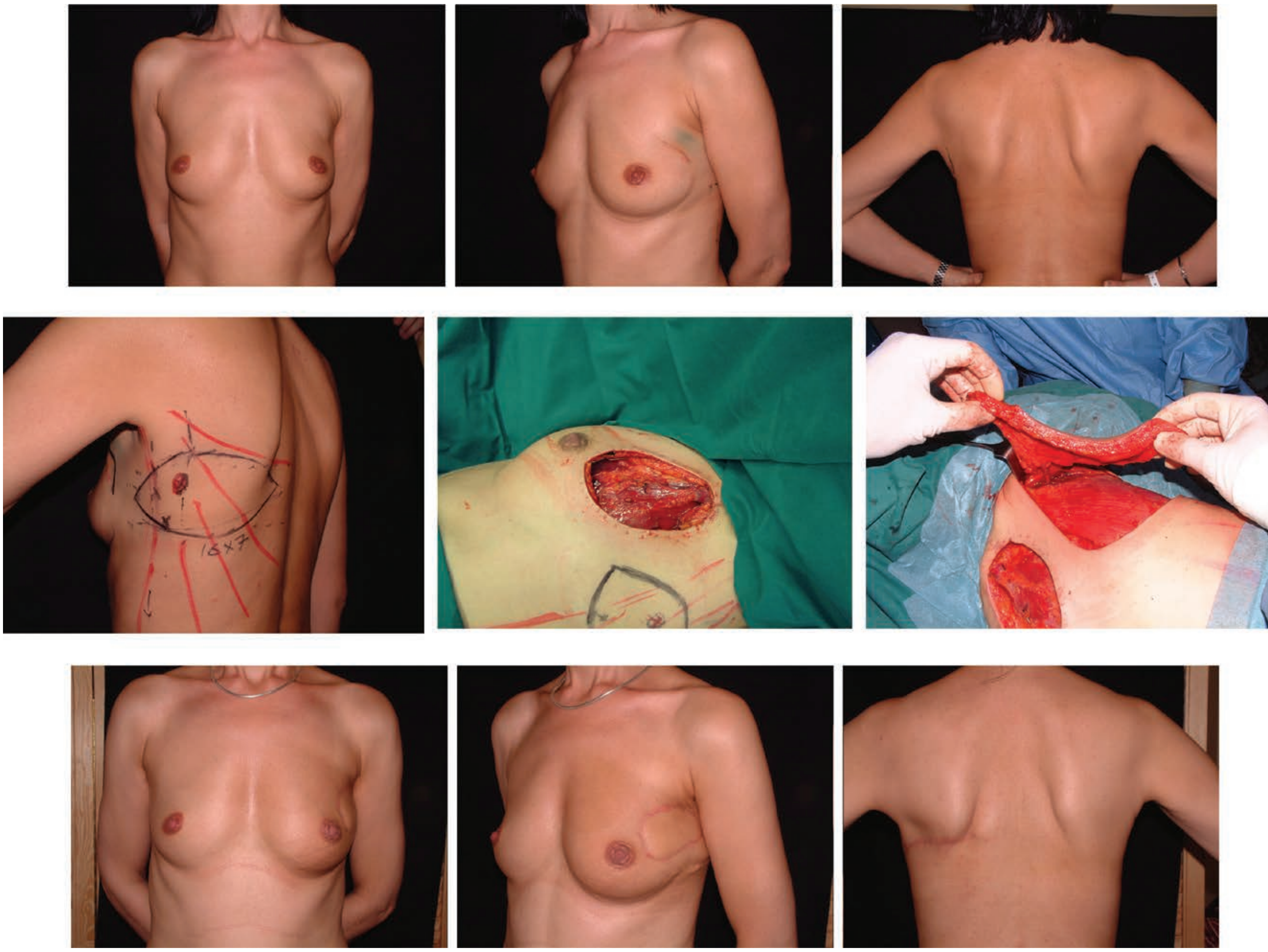

Fig. 2. (*Above*) This is a 44-year-old patient who presented with a T2 tumor in the left breast. An immediate breast reconstruction was planned because of the expected unaesthetic result after tumor resection in such small size breast. Her marking are demonstrated (*middle*) and perforators were mapped preoperatively by unidirectional Doppler. The defect involves skin and parenchyma in the upper-lateral quadrant (*below*) and was reconstructed immediately with a pedicled thoracodorsal artery perforator flap harvested on 1 perforator. Her result is shown 1 year postoperatively. (Used with permission from Losken A, Hamdi M. Partial breast reconstruction: current perspective. *Plast Reconstr Surg*. 2009;124:722–736.)

factor for increased local recurrence.[29,30] Oncological principles should be applied with even greater stringency when reconstructive procedures have been performed since positive margins on final pathology are potentially complicated by altered architecture or elimination of a potential reconstructive option. Positive margins according to the joint guidelines of the American Society of Breast Surgeons/Society of Surgical Oncology/American Society of Radiation Oncology constitute ink on tumor for invasive breast cancer and less than 2 mm margins for ductal carcinoma in-situ.[29,30] In a systematic review of 2,830 oncoplastic patients, the positive margin rate was from 0% to 36%, and local recurrence ranged from 0% to 10%.[31]

Positive margins following oncoplastic surgery range from 1.8% to 19% (Table 3). One of the strengths of the oncoplastic approach is the ability to resect widely and subsequently obtain a lower positive margin rate at 10% compared with 20–40% for standard lumpectomy.[12,32] This translates to far fewer reexcisions and secondary operations and occurs because the breast surgical oncologist has the option to remove a greater section of breast tissue since reconstruction would follow. Fewer secondary operations means that adjuvant treatment in the form of chemotherapy and radiation is not delayed. With the more generous oncoplastic resection, positive margin rates have been shown to be significantly reduced.[33,34] We also showed fewer surgical reexcision (12.0% versus 25.9%; $P = 0.01$) and wider margins from the tumor when oncoplastic surgery was performed (4.3 versus 2.8 mm; $P = 0.01$).[35,36] The recent meta-analysis also found a reduction in the positive margin rate for both invasive and in situ disease from 21% with BCT alone to 12%.[12]

Table 3. Some Recent Evidence and Larger Series

Author	N	Technique	+ Margin Rate (%)	Completion Mastectomy	Complication (%)	Recurrence (%)	F/U
Losken[41], 2017	353	Oncoplastic reduction	6.2	9.9	16	2.8	2 y
De La Cruz et al.[32], 2016		Oncoplastic reduction, local flaps, musculocutaneous flaps (latissimus)	10.8		11.8		50.5 mo
Carter et al.[3]	1,177	Oncoplastic reduction, local flaps	5.8	—	24.6	5.4	3 y
Fitoussi[13], 2016	540	Oncoplastic reduction, flaps	18.9	9.4	16.3	6.8 (local)	49 mo
De Lorenzi[59], 2016	193	Oncoplastic reduction, locoregional flaps, musculocutaneous flaps	2.9		10.3	6.7 (local), 3.1% (regional)	10 y
Munhoz[40], 2006	74	Oncoplastic reduction	9.5		17.6		22 mo
Clough[62], 2017	350	Oncoplastic reduction	12.6	8.0%	8.9	2.2 local/ 12.4 distant	5 y
Mansell[60], 2017	104	Oncoplastic reduction	14.4	12.5		2.0 (local)	56.8 mo
Acea-Nebrill[61], 2017	170	Oncoplastic reduction	8.9	2.9	9.5	5.8 (local)	10 y
Zaha[28], 2017	200	Omental flaps	6.5		12	2	90 mo

Reexcision rate of 30% has been associated with being overweight, microcalcifications, and tumor multifocality.[37] Although it is important to minimize reexcision and positive margins, a recent study has shown that mastectomy rate (34% versus 15%) and reexcision rate (32% versus 18%) are significantly lower in the oncoplastic groups compared with BCT.[38] Positive margins in oncoplastic reductions have been associated with larger biopsy size, larger tumor size (> 2.00 cm), and estrogen receptor positivity were more likely to have positive margins.[36]

OUTCOMES

Complications

It is important that complications resulting from oncoplastic techniques do not interfere with the initiation of adjuvant therapy. A recent meta-analysis compared 1,773 oncoplastic reductions and 1,392 oncoplastic flap reconstructions and 5,494 BCT-alone patients.[12] The average complication rate was 16% and 14% in the oncoplastic reduction and oncoplastic flap reconstruction groups, respectively; however, there was no delay in the initiation of adjuvant therapy. Early complication rates were not routinely reported in the BCT alone group; however, they were on average 25.9% (n = 201/775), compared with 15.5% (386/2482) overall in the oncoplastic group. Some larger series with volume displacement techniques report complications such as delayed wound healing (3–15%), fat necrosis (3–10%), and infection (1–5%).[39,40] Overall complications following volume replacement techniques are slightly higher (range, 2–77%), and this is likely due to the addition of donor-site complications and potential flap loss issues.[25,27] Munhoz et al.[25] recently reported a 33% complication rate using the latissimus dorsi technique for partial mastectomy defects, 65% of which was related to the donor site. The most common complication was dorsal seroma, which occurred in 20% of their patients (50% of their complications). Although complications do exist, they are often managed with conservative treatment and do not delay initiation of adjuvant treatment. In a recent oncoplastic reduction series of 353 patients, we identified an overall complication rate of 16%.[41] These were often minor, and less than 5% required a reoperation. Studies have shown fewer complications in obese women and women with macromastia following oncoplastic reduction compared with mastectomy and immediate reconstruction. Tong et al.[42] demonstrated fewer complications requiring additional surgery (3.8% versus 28%) and fewer complications delaying adjuvant therapy (0.8% versus 14%) in the oncoplastic group for obese patients. In a previous report, we have similarly shown that in patients with macromastia, the oncoplastic approach compared with skin-sparing mastectomy and reconstruction resulted in lower breast complication rate (22% versus 47%), shorter hospital stay (0.8 versus 3.5 days), and fewer trips to the operating room (1.2 versus 2.7).[35] The complication benefits compared with mastectomy are significant and those compared with BCT alone are acceptable. Oncoplastic surgery in 1 study did not delay the time to delivery of adjuvant chemotherapy (29 days) when compared with lumpectomy alone (29.5 days) and mastectomy with immediate reconstruction (31 days).[43] Oncoplastic surgeries have been safely performed for larger tumors too. A recent comparison in

828 patients between oncoplastic resection and lumpectomy alone showed larger tumors in the oncoplastic group (17.5 versus 13.6 mm) with no difference in positive margin rates (22.6% versus 18%), reexcision rates, or complications.[44]

When comparing oncoplastic reduction techniques with lumpectomy alone in large-breasted patients with small (< 3 cm) tumors, despite worse prognostic factors and more surgery in the oncoplastic group, these patients reported slightly better satisfaction and physical functioning and fewer adverse effects of the radiation therapy.[45] A National Surgical Quality Improvement Program evaluation comparing 75,972 BCS patients with 1,363 patients who had oncoplastic surgery with soft-tissue transfer showed no increase risk of complication in the oncoplastic group despite longer operating room time in that group.[46]

Patient-Reported Outcomes

When it comes to patient-reported outcomes and satisfaction, the oncoplastic reduction technique has been shown to fair favorable compared with BCT alone and compared with mastectomy and reconstruction for women with macromastia.[47] Although we often at best wish to preserve satisfaction and quality of life when performing breast reconstruction, this approach does often show improvement. Likely because of the benefit to reduction mammoplasty, these patients in our series reported improvement in body acceptance, feelings of attractiveness, satisfaction with how their breasts looked unclothed, and satisfaction with sex life. Their improvement in emotional health is likely due to the breast cancer being managed and behind them. Veiga et al.[48] showed a positive impact on quality of life and self-esteem when comparing patients who had oncoplastic surgery with those with BCT alone. Hart et al.[47] has similarly shown that oncoplastic reduction patients reported an unexpected increase in their ability to wear sexually provocative clothing and in their partners' perception of them as womanly. Although not typically a driving force behind the selection of the oncoplastic reduction for women with macromastia and breast cancer, the quality of life improvements are a definite benefit of this technique. Others have similarly found that self-reported body image scores and patient-reported outcome measures significantly favored oncoplastic surgery to mastectomy with immediate reconstruction (implant or flap).[49] In a recent large series of oncoplastic patients at over 1 year follow-up, women reported increased emotional health (3.73→4.18; $P = 0.019$), body acceptance (3.41→4.50; $P = 0.050$), feelings of attractiveness (3.07→3.88; $P = 0.064$), satisfaction with how their breasts looked unclothed (2.53→3.38; $P = 0.075$), and satisfaction with sex life (3.16→3.48; $P = 0.068$).[47]

Massa et al.[50] recently reported an aesthetic comparison between BCT alone, oncoplastic surgery, and regular postoperative irradiation therapy and oncoplastic surgery with intraoperative irradiation. They found that all groups gave good oncological and aesthetic results with there being some superiority in the intraoperative radiotherapy group. Other studies have shown comparable results with intraoperative radiotherapy and oncoplastic surgery, without a significant cosmetic advantage.[51] More data on this topic and the type of radiation therapy are needed. Radiation therapy in general remains the unpredictable part of the oncoplastic approach and needs to be evaluated long term.

Outcomes studies have been performed with preliminary results suggesting cost-effectiveness for oncoplastic surgery.[52,53] However, compared with other cancer operations, oncoplastic surgery is relatively young and additional future randomized controlled trials with regard to locoregional recurrence rates, role for adjuvant radiation in certain early-stage cancers, and so on, in addition to patient-centered outcomes data with regard to aesthetic self-perceptions are needed.

Surveillance

Surveillance following oncoplastic surgery has been shown to be just as sensitive despite the additional tissue rearrangement. In a comparative study following oncoplastic reduction techniques and BCT alone, the quantitative mammographic findings at over 6 years follow-up were similar; however, there was a slight trend toward longer times to mammographic stability in the oncoplastic reduction group (25.6 months versus 21.2 months in the BCT alone group).[54] This means that it might take the oncoplastic reduction patients slightly longer to reach the point where any change in mammographic findings might be suspicious for malignancy. Patients who undergo partial breast reconstruction may have an increase in the amount of tissue sampling requirements. In our series, 53% in the oncoplastic group compared with 18% in the BCT-alone group over an average of 7 years required tissue sampling. Contrastingly, in a report by Piper et al.[55], an age-matched comparison of women following BCT versus oncoplastic reduction did not show a significant difference in abnormal mammographic findings prompting biopsy or biopsy rates themselves for up to 5 years postoperatively. Although these are typically benign, additional scarring from the reconstruction might raise clinical suspicion, which is why more biopsies are expected in patients who undergo partial breast reconstruction. Another comparative study between oncoplastic and BCT alone showed that significantly more patients in the oncoplastic group required breast ultrasound (28% versus 15%; *P* = 0.024) and significantly more biopsies in the oncoplastic group (12.6% versus 2.5%; *P* = 0.006).[56] It is important that all members of the team understand the various techniques and imaging differences to ensure accurate postoperative surveillance.

Recurrence

The benefit oncoplastic procedures might have on recurrence are all related to generous resection and wider margins. Longer term follow-up studies have shown local recurrence to be 8.7% at 10 years, and the overall survival rate was 82.2%,[57] and another study of 545 patients had a 6.7 recurrence rate at an average follow-up of 7 years with a comparable survival at 91% compared with BCT alone.[58,59] Whether wider margins truly translate into lower recurrence remains to be seen and has not been demonstrated in the oncoplastic data.[57] In an effort to evaluate the oncological safety of oncoplastic surgery, a recent comparison in 980 patients demonstrated similar 5-year recurrence rates with 3.4% in the lumpectomy group, 2% in the oncoplastic group, and 2.6% in the mastectomy and immediate reconstruction group.[60] The groups all had similar histological variables. Another comparison in 801 patients between oncoplastic reduction and lumpectomy demonstrated longer operating time and higher tissue necrosis in the oncoplastic reduction group, with no difference in reexcision or mastectomy rate.[61] They did report improvement in patient satisfaction and quality of life in the reduction group with equivalent overall 10-year survival. The oncoplastic approach has also been found to be safe compared with mastectomy in tumors larger than 2 cm with similar overall recurrence and survival rates at 10 years.[58]

CONCLUSIONS

The oncoplastic approach has become increasingly accepted as a safe and reliable alternative option in breast conservation surgery. We are now seeing more evidence demonstrating the various techniques as well as favorable outcomes from an aesthetic and oncological perspective.

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^For all patients with HR+/HER2- advanced breast cancer in the first line setting of phase 3 randomized controlled trial, the median PFS was 25.3 months for RIB+ LET vs 16.0 months for PBO + LET (hazard ratio: 0.569; 95% CI: 0.457-0.704; p=9.63x10^{-8})[1,2]

*At the first tumor evaluation (Week 8), decreased tumor size was observed 76% in the RIB + LET arm vs 67% in the PBO + LET arm[3]

**At the first tumor evaluation (Week 8), at least 60% reduction in tumor size was observed in 32% of patients in the RIB + LET arm vs 17% in the PBO + LET arm[3]

#Please refer to the full prescribing information for additional details

Basic Succinct Statement

Presentation: Film-coated tablets (FCT) containing 200 mg of ribociclib.

Indications: Ribociclib is indicated in combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.

Dosage and administration: Adults: The recommended dose of Kryxana is 600 mg (3 x 200 mg FCT) taken orally, once daily for 21 consecutive days followed by 7 days off treatment resulting in a complete cycle of 28 days.

Special populations: •Renal impairment: Mild or moderate: No dose adjustment is necessary. Severe: Caution should be used. •Hepatic impairment: Mild: No dose adjustment is necessary. Moderate or severe: Dose adjustment is required, and the starting dose of 400 mg is recommended. •Geriatrics (≥65 years): No dose adjustment is required. •Pediatrics: Safety and efficacy have not been established.

Contraindications: •Patients with hypersensitivity to the active substance or to any of the excipients.

Warnings and precautions: •Neutropenia was most frequently reported. A complete blood count (CBC) should be performed before initiating therapy. CBC should be monitored every 2 weeks for the first 2 cycles, at the beginning of each of the subsequent 4 cycles, then as clinically indicated. Febrile neutropenia was reported in 1.5% of patients exposed to Kryxana in the phase III clinical study. Based on the severity of the neutropenia, Kryxana may require dose interruption, reduction, or discontinuation. •Increases in ALT and AST have been reported, with the majority of them without concurrent elevations of bilirubin. Concurrent elevations of ALT or AST >3 x ULN and of total bilirubin >2 x ULN, with normal alkaline phosphatase levels and no cholestasis occurred in 1.2% of patients; all patients returned to normal within 154 days after discontinuation of Kryxana. Liver function tests (LFTs) should be performed before initiating therapy with Kryxana. LFTs should be monitored every 2 weeks for the first 2 cycles, at the beginning of each of the subsequent 4 cycles, then as clinically indicated. Based on the severity of transaminase elevations, Kryxana may require dose interruption, reduction, or discontinuation. •QT interval prolongation has been reported with Kryxana. The use of Kryxana should be avoided in patients who have already or who are at significant risk of developing QTc prolongation. The ECG should be assessed prior to initiation of treatment. Treatment with Kryxana should be initiated only in patients with QTcF values <450 msec. The ECG should be repeated at approximately Day 14 of the first cycle and at the beginning of the second cycle, then as clinically indicated. Appropriate monitoring of serum electrolytes (including potassium, calcium, phosphorous, and magnesium) should be performed prior to initiation of treatment, at the beginning of the first 6 cycles, and then as clinically indicated. Any abnormality should be corrected before the start of Kryxana therapy. Based on the observed QT prolongation during treatment, Kryxana may require dose interruption, reduction, or discontinuation. **Pregnancy, lactation, females and males of reproductive potential: Pregnancy:** It is possible that Kryxana can cause fetal harm when administered to a pregnant woman. The patient should be advised of the risk to a fetus if Kryxana is used during pregnancy or if the patient becomes pregnant while taking Kryxana. Lactation: A decision should be made whether to discontinue nursing or to discontinue Kryxana, taking into account the importance of Kryxana to the mother. It is recommended that women taking Kryxana should not breastfeed for at least 21 days after the last dose. **Females and males of reproductive potential:** •Pregnancy testing: For females of reproductive potential the pregnancy status should be verified prior to initiating treatment with Kryxana. •Contraception: Sexually active females of reproductive potential should use effective contraception (methods that result in <1% pregnancy rates) when using Kryxana during treatment and for 21 days after stopping treatment with Kryxana. •Infertility: Based on animal studies, Kryxana may impair fertility in males of reproductive potential. **Adverse drug reactions:** Very common (≥10%): Urinary tract infection, neutropenia, leukopenia, anaemia, lymphopenia, decreased appetite, headache, insomnia, dyspnoea, back pain, nausea, diarrhoea, vomiting, constipation, stomatitis, abdominal pain, alopecia, rash, pruritus, fatigue, peripheral oedema, asthenia, pyrexia, abnormal liver function tests, leukocyte count decreased, neutrophil count decreased, haemoglobin decreased, lymphocyte count decreased, platelet count decreased, alanine aminotransferase increased, aspartate aminotransferase increased, creatinine increased, phosphorous decreased, potassium decreased. **Common (1 to 10%):** Thrombocytopenia, febrile neutropenia, lacrimation increased, dry eye, hypocalcaemia, hypokalaemia, hypophosphataemia, syncope, epistaxis, dysgeusia, dyspepsia, hepatotoxicity, erythema, peripheral oedema, weight decreased, electrocardiogram QT prolonged, bilirubin increased. Interactions: •Concomitant use of strong CYP3A inhibitors should be avoided, including but not limited to clarithromycin, indinavir, itraconazole, ketoconazole, lopinavir, ritonavir, nefazodone, nelfinavir, posaconazole, ritonavir, saquinavir, telaprevir, telithromycin, verapamil, and voriconazole. Alternative medications with less potential to inhibit CYP3A should be considered. Patients should be monitored for ADRs. If concomitant use of a strong CYP3A inhibitor cannot be avoided, the Kryxana dose should be reduced to 200 mg. Pomegranates or pomegranate juice and grapefruit or grapefruit juice should be avoided. •Concomitant use of strong CYP3A inducers should be avoided, including but not limited to phenytoin, rifampin, carbamazepine and St John's Wort (*Hypericum perforatum*). An alternative medication with no or minimal potential to induce CYP3A should be considered. •Caution is advised when Kryxana is administered with CYP3A substrates with narrow therapeutic index (including but not limited to alfentanil, cyclosporine, dihydroergotamine, ergotamine, everolimus, fentanyl, pimozide, quinidine, sirolimus, and tacrolimus), and their dose may need to be reduced. •Co-administration of Kryxana with medications with known potential to prolong the QT interval should be avoided such as anti-arrhythmic medicines (including but not limited to amiodarone, disopyramide, procainamide, quinidine, and sotalol), other medicinal products known to prolong the QT interval including but not limited to chloroquine, halofantrine, clarithromycin, haloperidol, methadone, moxifloxacin, bepridil, pimozide, and ondansetron (i.v.).

Packs: Kryxana strip of 21 film coated tablets

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