

ESMO PRECEPTORSHIP
ON BREAST CANCER

16-17 SEPTEMBER 2016
LISBON, PORTUGAL

Principles of Breast Surgery Oncoplastic Surgery

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Conflict of Interest Disclosure

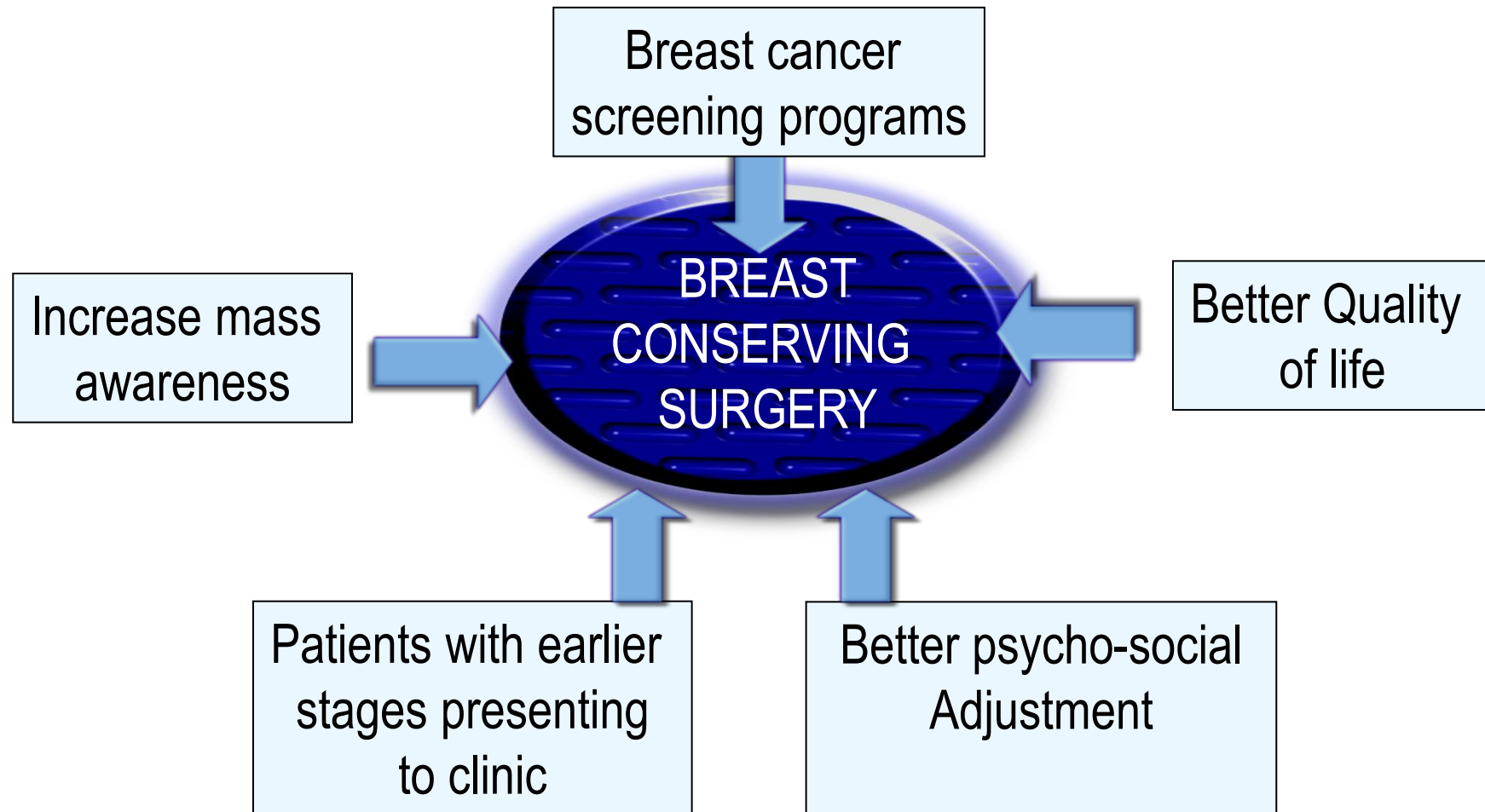
- No financial relationships to disclose



Locoregional therapy for early breast cancer

- Conservative (BCT) vs Mastectomy
- Oncoplastic Surgery
- Delayed Reconstruction vs Immediate Reconstruction
- Total mastectomy vs Skin Sparing Mastectomy
- Surgery after primary systemic treatment (PST)
- Sentinel Node vs Axillary dissection

- Conservative (BCT) vs Mastectomy



- Conservative (BCT) vs Mastectomy



MRM vs BCT

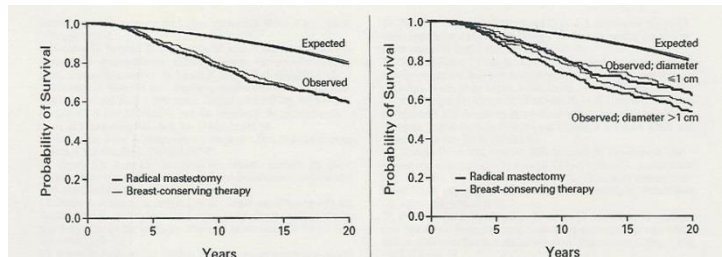
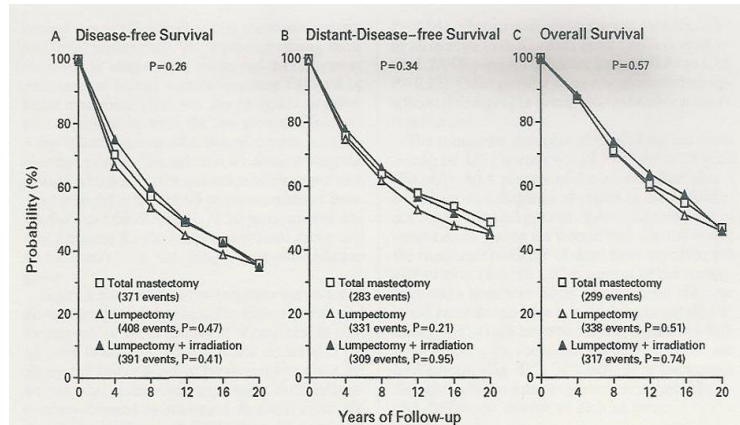
Randomized trials

Meta-analysis

Comparable local control, Overall survival

Better cosmetic outcome

■ Conservative (BCT) vs Mastectomy



Fisher B. et al. (2002).

“Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy and lumpectomy plus irradiation for the treatment of invasive breast cancer.”

N Engl J Med 347(16): 1233-41.

Veronesi U. et al. (2002).

“Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer.”

N Engl J Med 347(16): 1227-32.

.....as long as a good aesthetic outcome is obtained

■ Conservative (BCT) vs Mastectomy



Still 30% of fair/poor results

Ann Surg Oncol. 2011 Jan;18(1):Aesthetics in breast conserving therapy:
do objectively measured results match patients' evaluations?

Heil J1, Dahlkamp J, Golatta M, Rom J, Domschke C, Rauch G, Cardoso MJ,
Sohn C.

■ Conservative (BCT) vs Mastectomy

Original Investigation

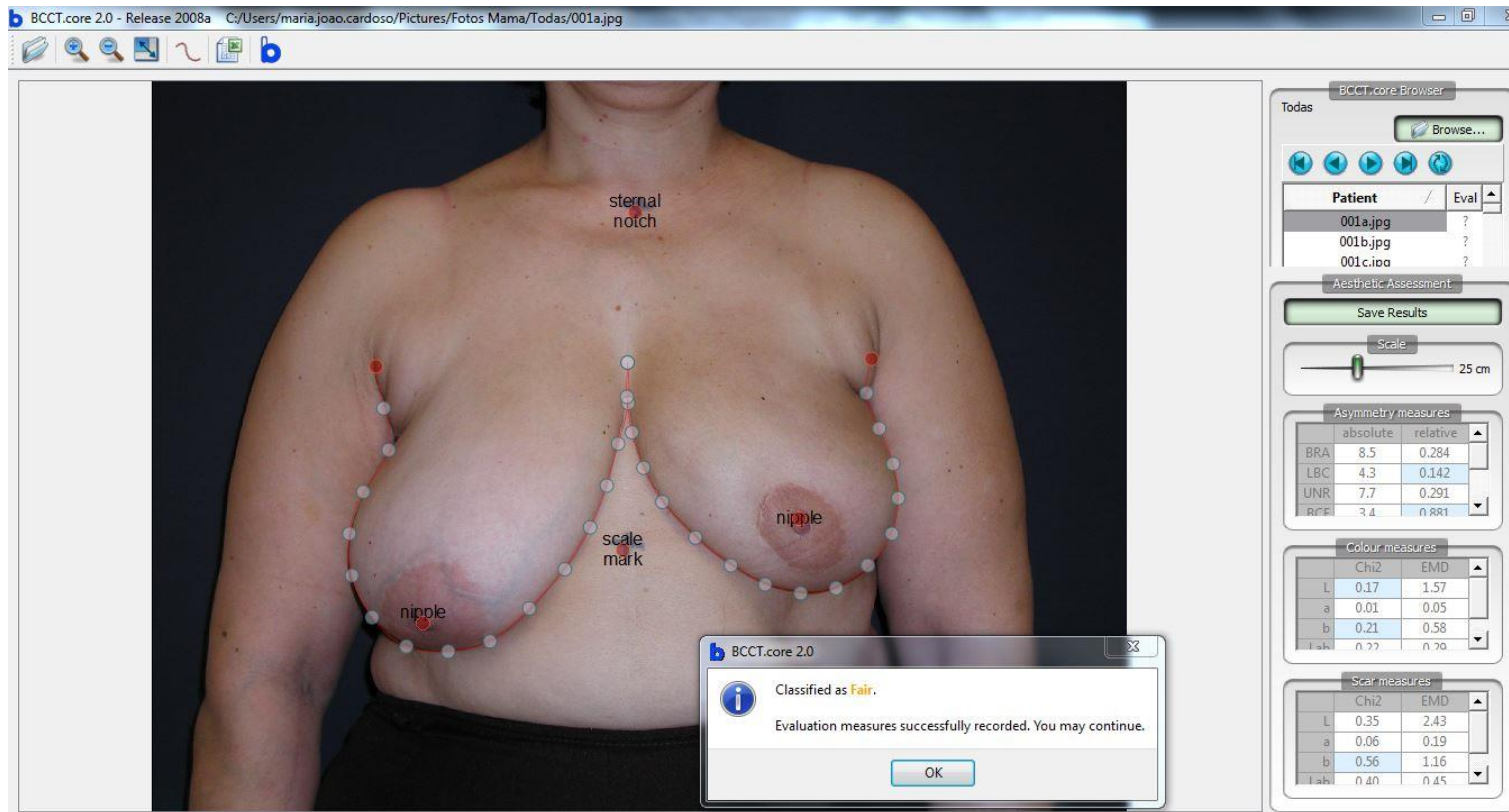
Effect of Breast Conservation Therapy vs Mastectomy on Disease-Specific Survival for Early-Stage Breast Cancer

Shailesh Agarwal, MD; Lisa Pappas, MS; Leigh Neumayer, MD; Kristine Kokeny, MD; Jayant Agarwal, MD

	BCT	Mastectomy	Mastectomy+RT	p value
132 149	70%	27%	3%	
5Y BCSSR	97%	94%	90%	<.001
10Y BCSSR	94%	90%	83%	<.001

CONCLUSIONS AND RELEVANCE Patients who underwent BCT have a higher breast cancer-specific survival rate compared with those treated with mastectomy alone or mastectomy with radiation for early-stage invasive ductal carcinoma. Further investigation is warranted to understand what may be contributing to this effect.

■ Conservative (BCT) vs Mastectomy



<http://medicalresearch.inescporto.pt/breastresearch>

Artif Intell Med. 2007 Jun;40(2):115-26. Epub 2007 Apr 8.

Towards an intelligent medical system for the aesthetic evaluation of breast cancer conservative treatment.

Cardoso JS1, Cardoso MJ.

■ Conservative (BCT) vs Mastectomy

Contra-indications for BCT

In aggregate, in the following clinical situations the increased risk of breast relapse should be extensively discussed with the patient and breast conservation should be executed with caution:

- very young woman (<35 years),
- the presence of extensive DCIS (heralded by extensive microcalcifications) mounting up to one quarter of the breast,
- more than focally incomplete resection of an invasive or in situ cancer,
- and in the case that radiotherapy cannot be given.

In all other clinical situations breast conservation is a safe option, provided complete resections are achieved and good cosmetic outcome is secured.

Breast. 2013 Aug;22 Suppl 2:S110-4.

Who should not undergo breast conservation?

Nijenhuis MV1, Rutgers EJ.

Curr Treat Options Oncol. 2015 Apr;16(4):16.

Breast cancer under age 40: a different approach.

Ribnikar D1, Ribeiro JM, Pinto D, Sousa B, Pinto AC, Gomes E, Moser EC, Cardoso MJ, Cardoso F.

■ Conservative (BCT) vs Mastectomy

Margins

The association of surgical margins and local recurrence in women with early-stage invasive breast cancer treated with breast-conserving therapy: a meta-analysis.

Houssami N1, Macaskill P, Marinovich ML, Morrow M.

Ann Surg Oncol. 2014 Mar;21(3):717-30.

**Society of Surgical Oncology-American Society for Radiation Oncology
consensus guideline on margins for breast-conserving surgery with whole-breast irradiation
in stages I and II invasive breast cancer.**

*Moran MS1, Schnitt SJ, Giuliano AE, Harris JR, Khan SA, Horton J, Klimberg S, Chavez-MacGregor M,
Freedman G, Houssami N, Johnson PL, Morrow M*

Ann Surg Oncol. 2014 Mar;21(3):704-16

J Clin Oncol. 2014 Feb 10

Int J Radiat Oncol Biol Phys. 2014 Mar 1;88(3):553-64

■ Conservative (BCT) vs Mastectomy

1. Positive margins

A positive margin, defined as ink on invasive cancer or ductal carcinoma in situ (DCIS), is associated with at least a 2-fold increase in IBTR. This increased risk in IBTR is not nullified by:

- a) Delivery of a boost dose of radiation
- b) Delivery of systemic therapy (endocrine therapy, chemotherapy, or biologic therapy), or
- c) Favorable biology

2. Negative margin widths

Negative margins (no ink on tumor) minimize the risk of IBTR. Wider margin widths do not significantly lower this risk. The routine practice to obtain negative margin widths wider than no ink on tumor is not indicated.

3. Systemic therapy

The rates of IBTR are reduced with the use of systemic therapy. In the uncommon circumstance of a patient not receiving adjuvant systemic therapy, there is no evidence suggesting that margins wider than no ink on tumor are needed.

4. Biologic subtypes

Margins wider than no ink on tumor are not indicated based on biologic subtype.

■ Conservative (BCT) vs Mastectomy

5. Radiation therapy delivery

The choice of WBRT delivery technique, fractionation, and boost dose should not be dependent on margin width.

6. Invasive lobular carcinoma and lobular carcinoma in situ

Wider negative margins than no ink on tumor are not indicated for invasive lobular carcinoma (ILC). Classic lobular carcinoma in situ (LCIS) at the margin is not an indication for re-excision. The significance of pleomorphic LCIS at the margin is uncertain.

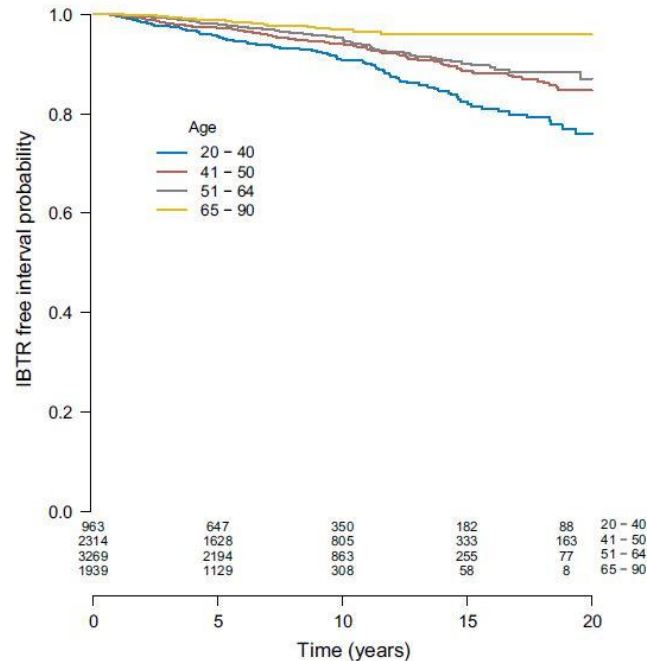
7. Young age

Young age (≤ 40 years) is associated with both increased IBTR after BCT as well as increased local relapse on the chest wall after mastectomy, and is also more frequently associated with adverse biologic and pathologic features. There is no evidence that increased margin width nullifies the increased risk of IBTR in young patients.

8. Lobular carcinoma in situ

A lobular carcinoma in situ (EIC) identifies patients who may have a large residual DCIS burden after lumpectomy. There is no evidence of an association between increased risk of IBTR and EIC when margins are negative.

■ Conservative (BCT) vs Mastectomy



The margin status of invasive carcinoma did not influence IBTR, DM rate, or OS. Between 1980 and 2008, locoregional control after BCT remained stable with low IBTR rates, even in young patients.

Fig. 2 IBTR-free interval by age group

Breast Cancer Res Treat. 2016 Apr;156(2):391-400.

Very low local recurrence rates after breast-conserving therapy: analysis of 8485 patients treated over a 28-year period.

Bosma SC, van der Leij F, van Werkhoven E, Bartelink H, Wesseling J, Linn S, Rutgers E, van de Vijver M, Elkhuisen PH

■ Conservative (BCT) vs Mastectomy



Still 30% of fair/poor results

Can we improve those results

■ Oncoplastic Surgery

When a resection of more than 20% of breast volume is planned oncoplastic techniques are recommended and can prevent major deformities



Current approaches to managing partial breast defects:
the role of conservative breast surgery reconstruction.

Munhoz AM1, Montag E, Filassi JR, Gemperli R.

Anticancer Res. 2014 Mar;34(3):1099-114.

■ Oncoplastic Surgery

- Oncoplastic surgery is **tumor specific immediate breast reconstruction**.
- It represents the **integration of plastic surgery techniques into breast cancer surgery** in order to preserve aesthetical outcomes and quality of life of the patients, without compromising local control of disease.
- It is based on three surgical principles: **ideal breast cancer surgery with free tumour margins, immediate breast reconstruction, and immediate symmetry with the other breast**.
- Although the **word was originally coined by Werner Audrescht** in Germany in the 1990's, plastic surgery techniques were transposed into breast-conserving therapy to avoid late unsatisfactory aesthetic results in the 1980's France by Jean-Yves Petit (Institut Goustave- Roussy), Jean-Yves Bobin (Centre Leon-Berard) and Michel Abbes (Centre Lassagne).

■ Oncoplastic Surgery

Concept background

- At the beginning limited to conservative surgery
- Correction of previous defects
- Use of aesthetic concepts in cancer



■ Oncoplastic Surgery

Concept evolution

- correct oncological surgery
- local reconstruction to correct excision defects
- immediate or delayed reconstruction with access to all techniques
- asymmetry correction on both sides

*Oncoplastic breast surgery--a guide to good practice.
On behalf of BASO, BAPRAS and TIGBS
Eur J Surg Oncol. 2007 Aug;33 Suppl 1:S1-23. Epub 2007 Jul 2*



■ Oncoplastic Surgery

Although oncoplastic surgery is considered to be a major technical improvement it is associated with larger scars, increased complications and an increasing need for contralateral breast surgery



■ Oncoplastic Surgery



The Breast xxx (2010) 1–3



Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst



Viewpoints and Debate

Training in oncoplastic surgery: An international consensus. The 7th Portuguese Senology congress, Vilamoura, 2009

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■ Oncoplastic Surgery

Pros

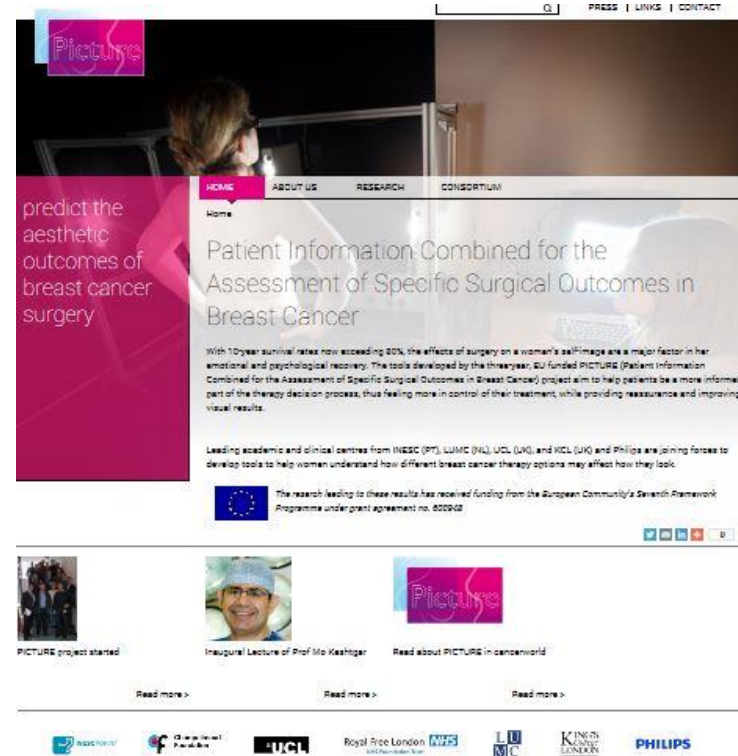
- Wider excisions - Better margins
- Less recurrences
- Overall better cosmetic outcomes

Cons

- Trained teams
- Higher cost
- Higher complication rate
- Possible delay of adjuvant treatments

Which technique to use for each case?

■ Oncoplastic Surgery



<http://www.vph-picture.eu/>

■ Oncoplastic Surgery

TABLE 1. Articles Included in Systematic Review

Reference	Year	Patients/Cases	Mean/Median Follow-up, mo	Oncologic Outcomes Described	Patient or Aesthetic Outcomes Described
Barnea et al ¹	2014	20/22	34.7	No	Yes
Caruso et al ²¹	2008	61/63	68	Yes	No
Caruso et al ²²	2011	50/52	72.6	Yes	No
Chang et al ¹⁰	2004	37/37	NR	Yes	Yes
Chang et al ⁶	2012	79/85	39	Yes	No
Clough et al ⁴	2012	175/175	49	Yes	Yes
Currie et al ²³	2013	20/20	36	Yes	No
Denewer et al ²⁴	2012	50/50	20	Yes	Yes
Eaton et al ³⁵	2014	86/86	54	Yes	No
Grubnik et al ¹⁷	2013	251/251	50	Yes	Yes
Gulcelik et al ²⁰	2013	106/106	33	Yes	No
Imahiyerobo et al ²⁵	2014	64/64	34.6	Yes	No
Losken et al ²⁶	2007	63/63	40	Yes	No
Losken et al ⁹	2014	83/83	NR	No	No
McCulley and Macmillan ¹⁸	2005	50/50	NR	Yes	Yes
Munhoz et al ¹⁵	2011	106/106	47	Yes	Yes
Santanelli et al ¹⁹	2009	11/11	26.5	Yes	Yes

Outcomes Following Oncoplastic Reduction Mammoplasty: A Systematic Review.

Piper ML, Esserman LJ, Sbitany H, Peled AW.

Ann Plast Surg. 2016 May;76 Suppl 3:S222



■ Oncoplastic Surgery

TABLE 2. Articles Reporting Local-Regional and Distant Recurrence Rates

Reference	Patients/Cases	Mean/Median Follow-up, mo	Stages Included	Local-Regional Recurrence Rate	Distant Recurrence Rate
Caruso et al ²¹ (2008)*	61/63	68	I to III	1 (1.6%)	6 (9.8%)
Caruso et al ²² (2011)*	50/52	72.6	0 to IIIB	1 (1.9%)	1 (2%)
Chang et al ¹⁰ (2004)	37/37	NR	NR	0	0
Chang et al ⁶ (2012)	79/85	39	0 to IV	2 (2.3%)	2 (2.3%)
Clough et al ⁴	175/175	49	NR	3 (1.7%)	11 (6.3%)
Currie et al ²³	20/20	36	I and II	0	0
Denewer et al ^{24*}	50/50	20	I and II	0	0
Eaton et al ³⁵	86/86	54	0 to III	6 (7%)	1 (1.2%)
Grubnik et al ^{17*}	251/251	50	NR	6 (2.4%)	3 (1.2%)
Gulcelik et al ²⁰	106/106	33	I to III	1 (0.9%)	NR
Imahiyerobo et al ²⁵	64/64	34.6	0 to III	5 (7.8%)	2 (3.1%)
Losken et al ²⁶	63/63	40	0 to III	2 (3.2%)	0
McCulley and Macmillan ¹⁸	50/50	NR	≥III	0	0
Munhoz et al ^{15*}	106/106	47	NR	7 (6.6%)	NR
Santanelli et al ¹⁹	11/11	26.5	I and II	0	0

*Studies that utilized intraoperative frozen section.

Outcomes Following Oncoplastic Reduction Mammoplasty: A Systematic Review.

Piper ML, Esserman LJ, Sbitany H, Peled AW.

Ann Plast Surg. 2016 May;76 Suppl 3:S222



- Delayed Reconstruction vs Immediate Reconstruction



Is immediate autologous breast reconstruction with postoperative radiotherapy good practice?: a systematic review of the literature.

Schaverien MV, Macmillan RD, McCulley SJ.

J Plast Reconstr Aesthet Surg 2013; 66: 1637-1651.

- Delayed Reconstruction vs Immediate Reconstruction



- Delayed Reconstruction vs Immediate Reconstruction



- **Delayed Reconstruction vs Immediate Reconstruction**
- Reconstruction should be offered to all mastectomy patients and all techniques should be discussed even if not available locally.
- Immediate reconstruction can be performed in the majority of patients and does not reduce radiation efficacy.
- Patients who will probably need radiotherapy should be advised about the possibility of a poorer cosmetic outcome

■ Total mastectomy vs Skin Sparing Mastectomy



Breast Reconstruction following Nipple-Sparing Mastectomy: Predictors of Complications, Reconstruction Outcomes, and 5-Year Trends.

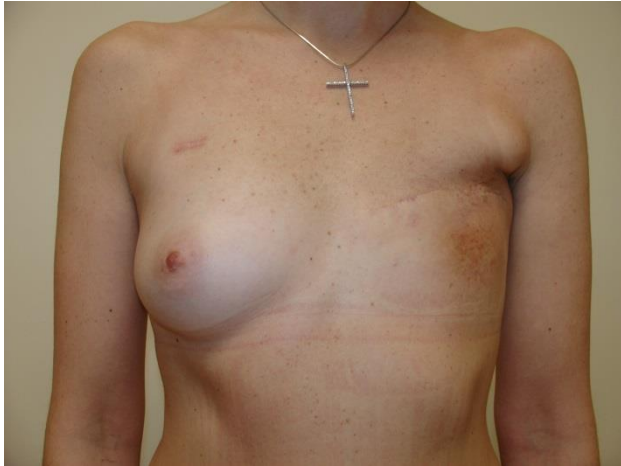
Colwell AS, Tessler O, Lin AM et al.

Plast Reconstr Surg 2014; 133: 496-506.



INTERNATIONAL NIPPLE SPARING MASTECTOMY REGISTRY

■ Total mastectomy vs Skin Sparing Mastectomy



■ Total mastectomy vs Skin Sparing Mastectomy



- Surgery after primary systemic treatment (PST)



.....without ever forgetting the importance of each discipline

■ Surgery after primary systemic treatment (PST)

- Primary systemic treatment (PST) is responsible for a greater percentage of BCT.
- .
- All patients proposed to PST should have their tumor marked before initiating treatment.
- Candidates to PST are those whose tumor breast size ratio doesn't allow conservative treatment with a favorable cosmetic outcome and those with locally advanced breast cancer (LABC).

- Surgery after primary systemic treatment (PST)

- Initial work-up of locoregional disease
- Monitoring response to treatment
- Axillary approach
- BCS after treatment
- Reconstructive surgery

- Surgery after primary systemic treatment (PST)

Pre-treatment work-up

Comparative Accuracy Studies	Number Studies (2050 patients)	P value	AUC
MRI Clinical	11	0.10	0.89 0.83
MRI Ultrasound	10	0.15	0.93 0.90
MRI Mammography	7	0.02	0.90 0.89

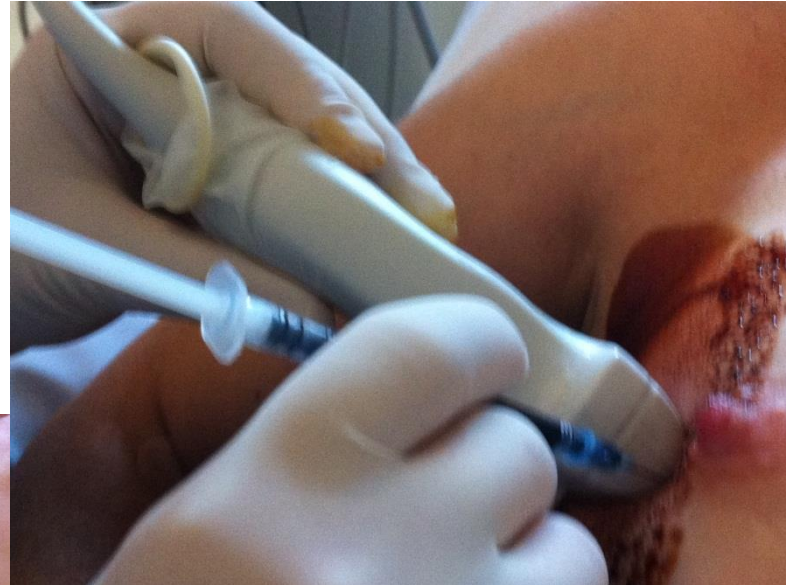
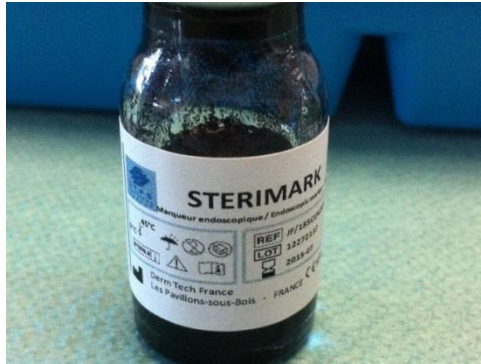
Meta-analysis of Magnetic Resonance Imaging in Detecting Residual Breast Cancer After Neoadjuvant Therapy.

Marinovich ML, Houssami N, Macaskill P, Sardanelli F, Irwig L, Mamounas EP, von Minckwitz G, Brennan ME, Ciatto S.

J Natl Cancer Inst. 2013 Jan 7.

- Surgery after primary systemic treatment (PST)

Tattooing



- Surgery after primary systemic treatment (PST)



- Surgery after primary systemic treatment (PST)



- Surgery after primary systemic treatment (PST)

Table 3. Factors Affecting the Likelihood of a False-Negative Sentinel Lymph Node Finding in the 310 Women With cN1 Disease at Presentation, 2 or More SLNs Examined, and Residual Nodal Disease After Neoadjuvant Chemotherapy

	False-Negative SLN Findings, No. (Total)	FNR (95% CI), %	Fisher Exact Test, P Value
Age, y			
18.0-49.9	20 (150)	13.3 (8.3-19.8)	.73
≥50.0	19 (160)	11.9 (7.3-17.9)	
BMI			
≥25.0	25 (227)	11.0 (7.3-15.8)	.18
<25.0	14 (83)	16.9 (9.5-26.7)	
Clinical T category prior to chemotherapy			
Tis, T0, T1, or T2	32 (225)	14.2 (9.9-19.5)	.18
T3 or T4	7 (85)	8.2 (3.4-16.2)	
Chemotherapy duration, mo			
≤4.0	20 (201)	10.0 (6.2-15.0)	.07
≥4.1	19 (109)	17.4 (10.8-25.9)	
Palpable, fixed, or matted nodes after chemotherapy ^a			
Yes	10 (52)	19.2 (9.6-32.5)	.17
No	28 (247)	11.3 (7.7-16.0)	
Mapping agents used			
Single	12 (59)	20.3 (11.0-32.8)	.05
Dual	27 (251)	10.8 (7.2-15.3)	
Multiple injection sites ^b			
Yes	5 (70)	7.1 (2.4-15.9)	.21
No	30 (225)	13.3 (9.2-18.5)	
No. of SLNs examined			
2	19 (90)	21.1 (13.2-31.0)	.007
≥3	20 (220)	9.1 (5.6-13.7)	

Sentinel lymph node surgery after neoadjuvant chemotherapy in patients with node-positive breast cancer: the ACOSOG Z1071 (Alliance) clinical trial.

Boughey JC, Suman VJ, Mittendorf EA et al.

JAMA 2013; 310: 1455-1461.

■ Surgery after primary systemic treatment (PST)

- For patients with operable BC who are candidates for PST, ultrasound of the axilla and FNA/CB of suspicious lymph nodes should be considered as part of the staging workup.
- SNB before PST does not offer particular clinical advantages and reduces the number of patients who could benefit from the down-staging effect of PST in the axillary nodes.
- SNB after PST is feasible and accurate with similar performance to SNB before PST (bigger samples). Neo-adjuvant protocol.
- By performing SNB after PST, up to 40 percent of patients who present with minimal involvement of axillary nodes may be spared from axillary dissection.
- Caution is however required for patients who present with clinically (or pathologically) involved nodes before PST (until further results of prospective trials are obtained).

- Sentinel Node vs Axillary dissection

Sentinel node biopsy is actually considered standard of care in patients with clinically and ultrasound negative axillae

Sentinel Lymph Node Biopsy for Patients With Early-Stage Breast Cancer:
American Society of Clinical Oncology Clinical Practice Guideline Update.
Lyman GH, Temin S, Edge SB, Newman LA, Turner RR, Weaver DL, Benson AB 3rd,
Bosserman LD, Burstein HJ, Cody H 3rd, Hayman J, Perkins CL, Podoloff DA, Giuliano AE.
J Clin Oncol. 2014 Mar 24. [Epub ahead of print]

■ Sentinel Node vs Axillary dissection

Recommendations

- Recommendation 1: Clinicians should not recommend axillary lymph node dissection (ALND) for women with early-stage breast cancer who do not have nodal metastases. Type: evidence based; benefits outweigh harms. Evidence quality: high. Strength of recommendation: strong.
- Recommendation 2.1: Clinicians should not recommend ALND for women with early-stage breast cancer who have one or two sentinel lymph node metastases and will receive breast-conserving surgery (BCS) with conventionally fractionated whole-breast radiotherapy. Type: evidence based; benefits outweigh harms. Evidence quality: high. Strength of recommendation: strong.
- Recommendation 2.2: Clinicians may offer ALND for women with early-stage breast cancer with nodal metastases found on SNB who will receive mastectomy. Type: evidence based; benefits outweigh harms. Evidence quality: low. Strength of recommendation: weak.
- Recommendation 3: Clinicians may offer SNB for women who have operable breast cancer who have the following circumstances:
 - DCIS/mastectomy
 - Prior breast/axillary surgery
 - PST
- Recommendation 4: There are insufficient data to change the 2005 recommendation that clinicians should not perform SNB for women who have early-stage breast cancer and are in the following circumstances:
 - LABC / Inflammatory
 - DCIS in BCS
 - Pregnancy

