

# Focused updates in the Surgical Management of Breast Cancer

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# Recent Focus in Breast Surgery

- Improve accuracy and efficiency
- Reduce morbidity, De-escalation of axillary surgery
- Emphasis on cosmesis



# Topics in Breast Surgery

- Localization of non palpable breast lesions
- Lumpectomy margins
- Sentinel Node biopsy and axillary management
- Oncoplastic breast conservation surgery
- Nipple sparing mastectomy

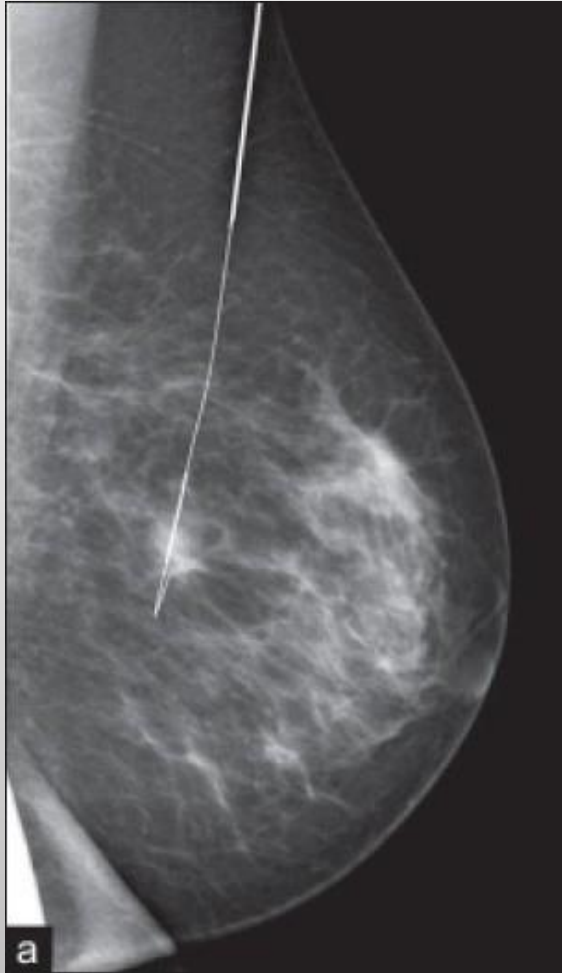
# Non palpable breast lesions

- Over 30-40% of breast cancers are not palpable and require localization for the surgeon to find the lesions in the OR
- Localization of lesions requires cooperation with the Radiologist and Surgeon and imaging confirmation of removal

Ahmed, M. *et al.* (2015) Surgical treatment of nonpalpable primary invasive and *in situ* breast cancer  
*Nat. Rev. Clin. Oncol.* doi:10.1038/nrclinonc.2015.161

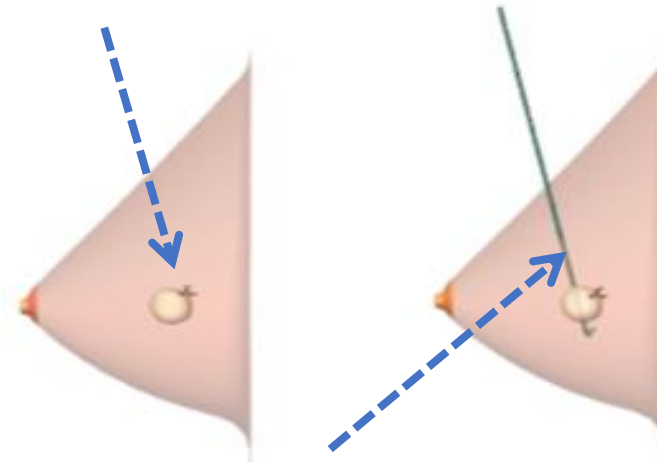
# Wire Localization Approach

Wire Loc was formerly the most commonly used method of locating tumors at time of lumpectomy



## Wire Localization Technique

- Marker is left in the biopsy site



- Hook-wire placed by radiologist the morning of surgery

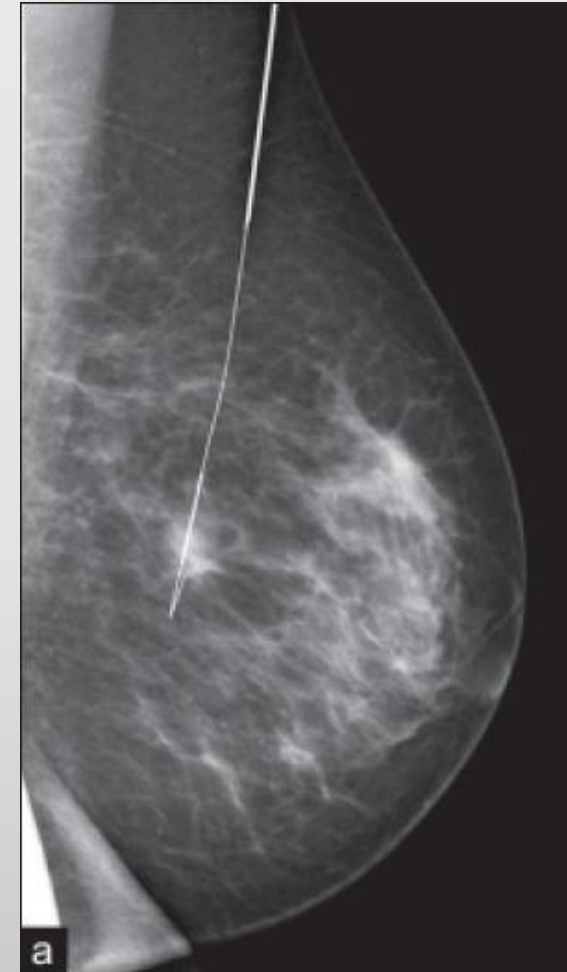
# Wire Localization Challenges

## Workflow Challenges

- Coordinate radiology and surgery department schedules
- Often results in delayed operating room start times
- Special Handling/Transport to Prevent Migration/Delay/Discomfort
- Proximity of Mammography suite to the OR

## Procedural Challenges

- Radiology often must consider surgical approach rather than placing in most convenient approach
- Tip of wire can be difficult to pinpoint
- Wire migration can contribute to positive margins



# Alternative methods for localization

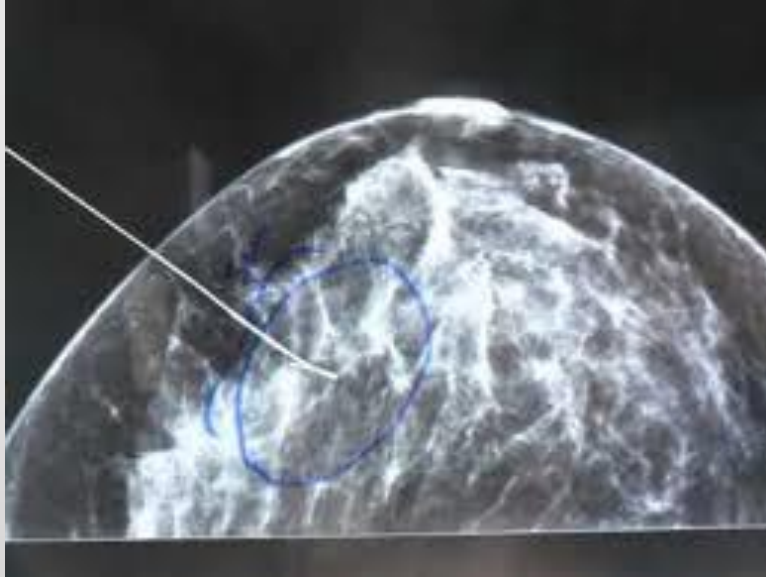
- Radioactive Seed localization
  - SAVI Scout surgical guidance system
  - Magseed
  - RFD
- 
- Intraoperative ultrasound
  - Ink marking

# Radioactive Seed Localization

- Small radioactive seed (titanium with Iodine 125) is placed into lesion
- Can be performed days before surgery
- Locate lesion in surgery by probe ( most sentinel node probes for Technetium also have Iodine 125 setting)

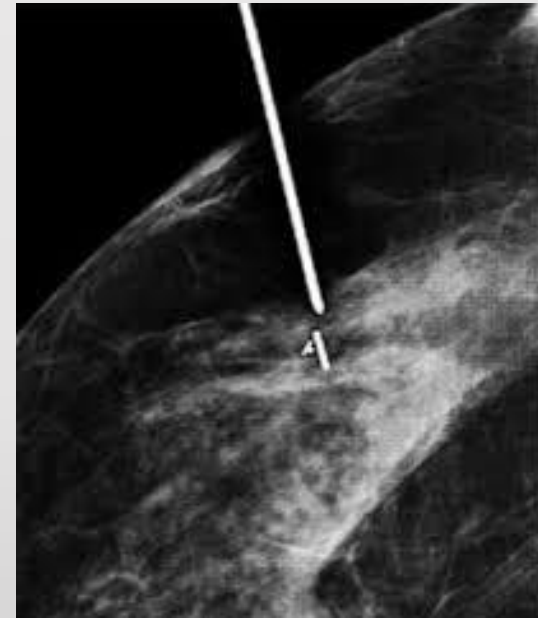


# Localization Radiographs



Wire localization

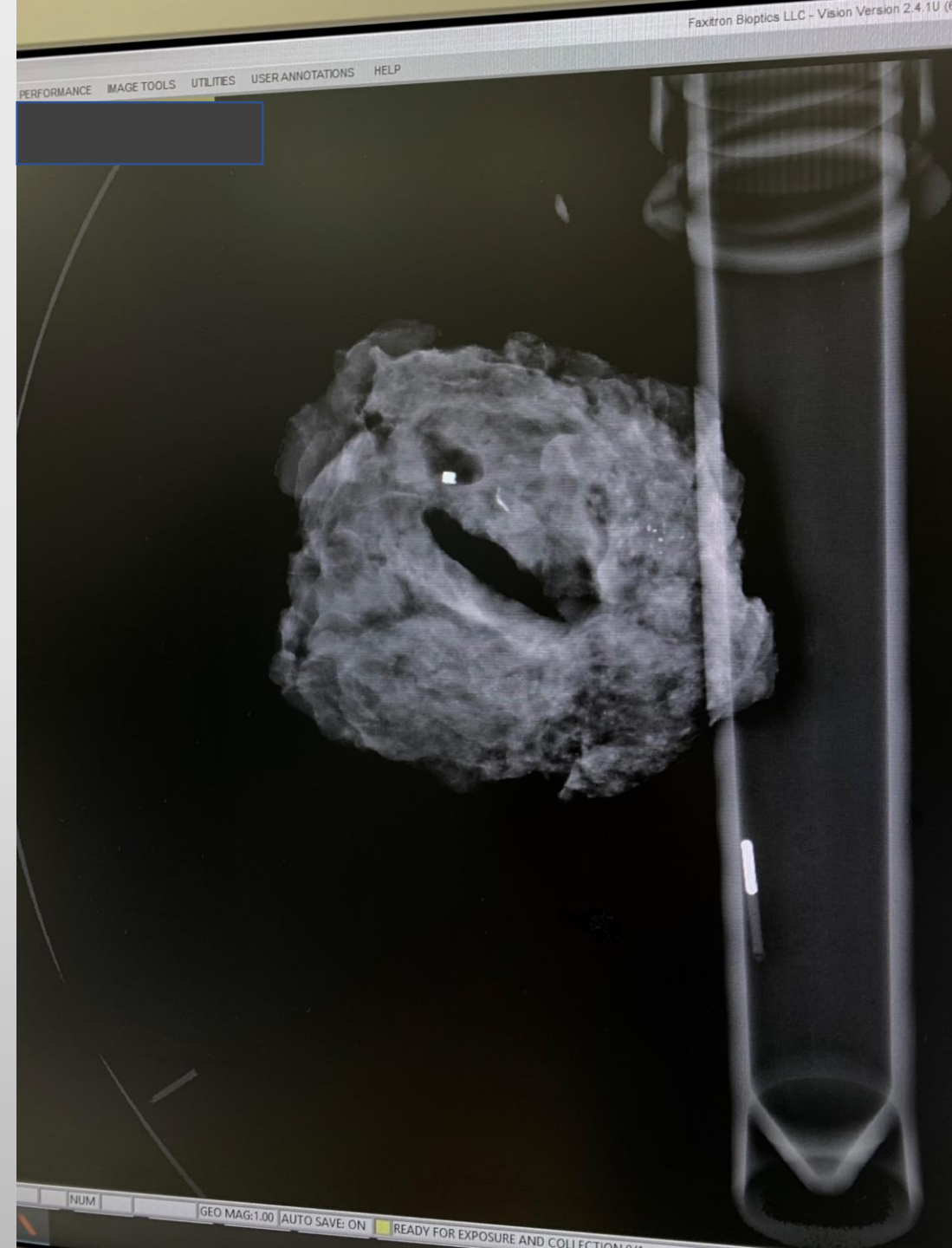
Seed localization



# Problems with Radioactive seed localization

- Radioactive sources
- Stringent regulations
- Facility must have license for therapeutic radiation
- Fear of handling radioactive materials
- Strict chain of command handling of seeds





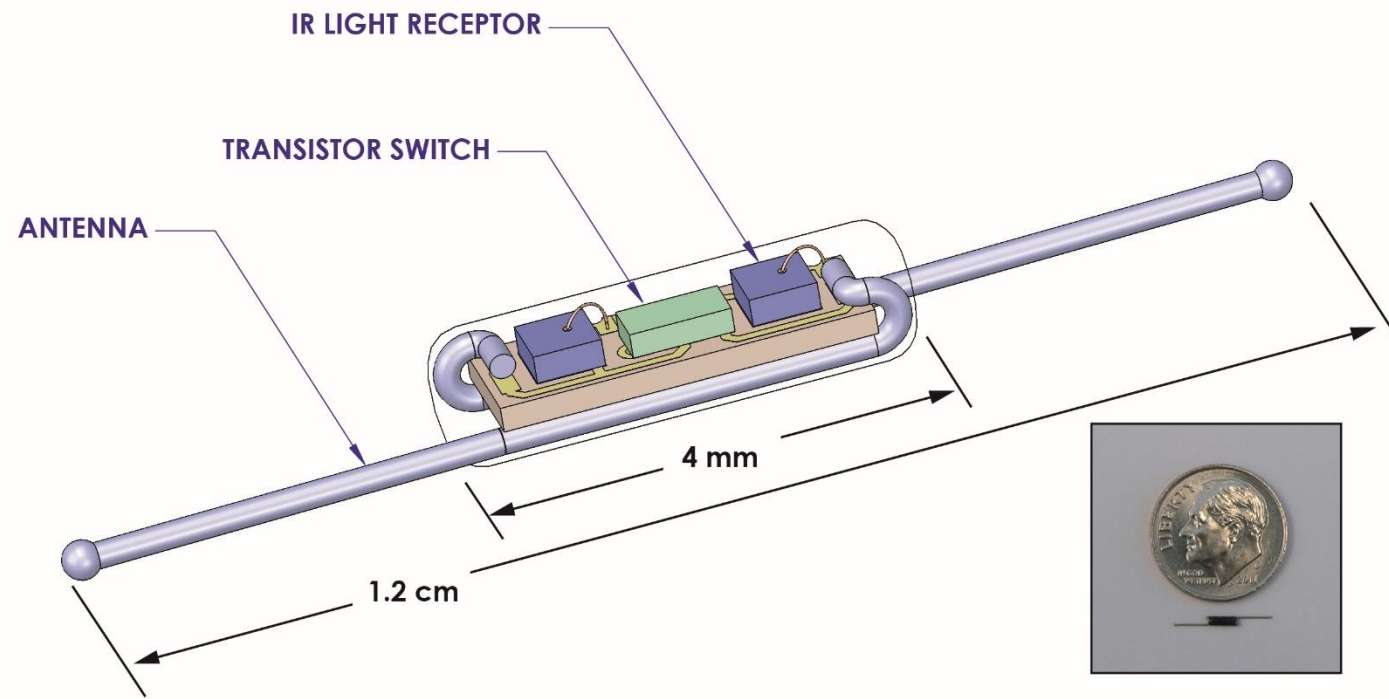


# SCOUT Surgical Guidance System

- ❑ No Wires
  - ❑ Non-Radioactive
  - ❑ Not a wire, marker, pellet or seed
- Unique technology that is reimbursed differently
  - Electromagnetic Wave Technology
    - Similar to Radar
    - Infrared activated



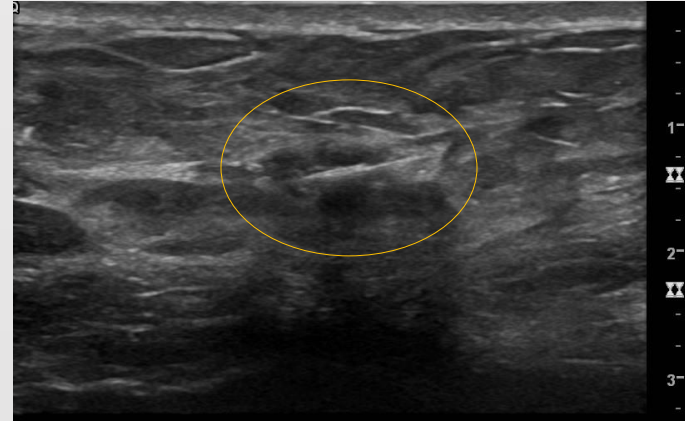
# SCOUT Reflector



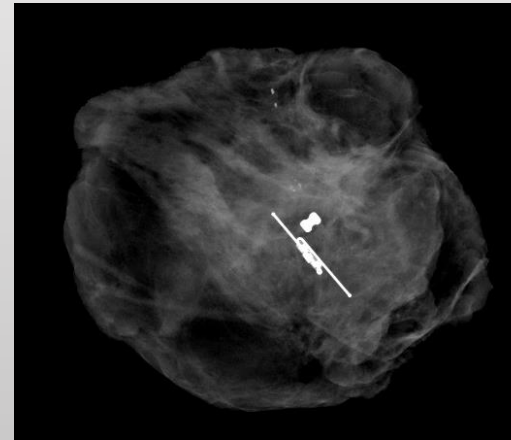
# Clinical Views – Reflector



Mammogram



Ultrasound



Specimen radiograph

## SAVI Surgical Guidance intraop

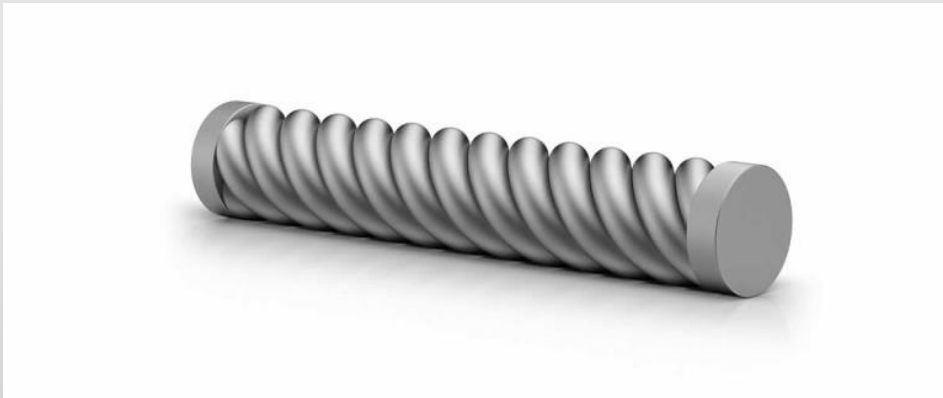


# Advantages of SAVI

- Not radioactive
- No special handling needed
- Can be placed anytime before surgery
- Localizes lesions without wires
- Can be used with MRI with no imaging problem



# Magseed localization

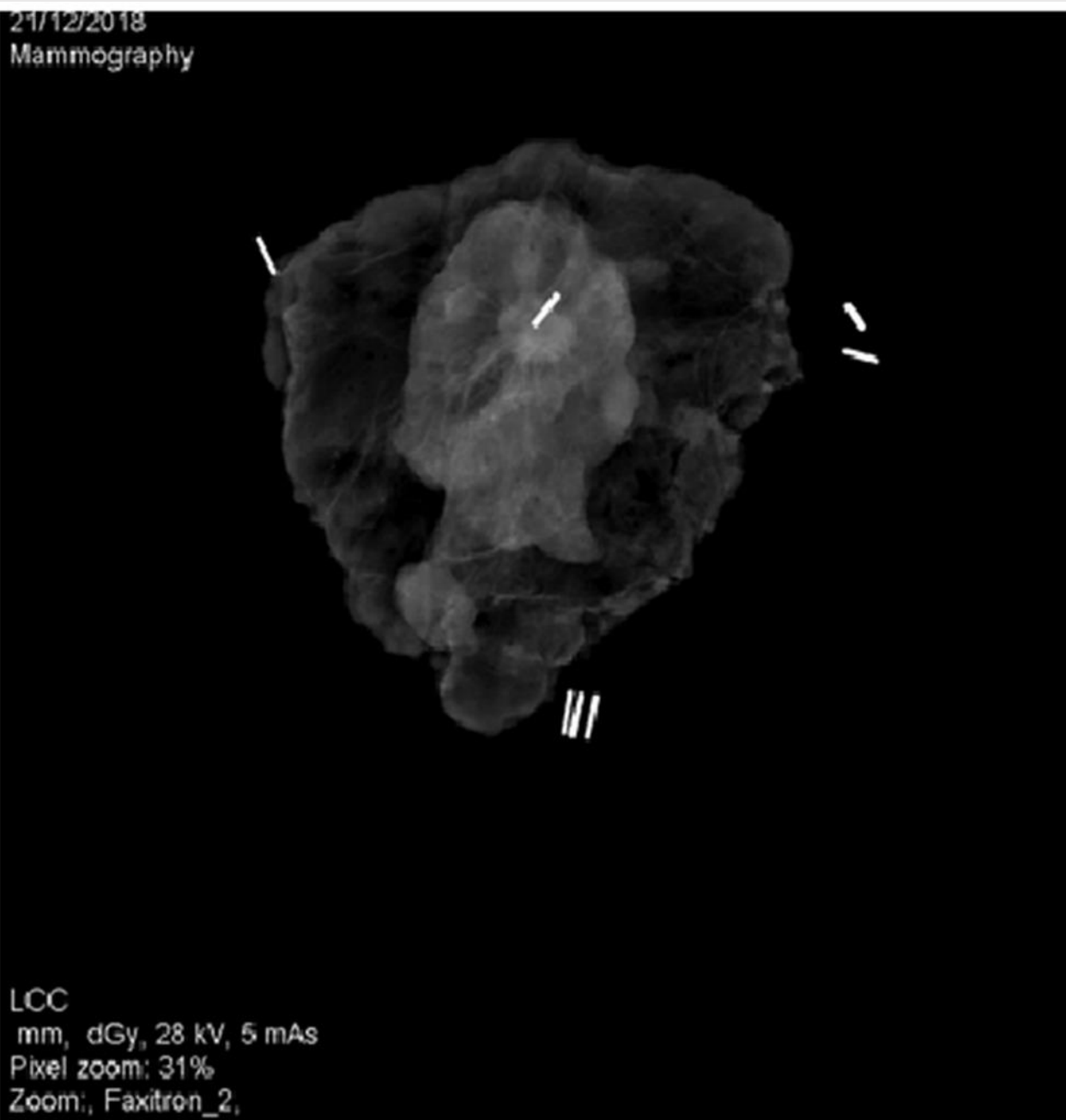


018  
Mammogram Lt



ton  
0.016 dGy, 31 kV, 87 mAs  
om: 32%  
GE-CR-03, alk

21/12/2018  
Mammography



LCC  
mm, dGy, 28 kV, 5 mAs  
Pixel zoom: 31%  
Zoom: Faxitron\_2,

# Advantages and disadvantages of Magseed

- Non radioactive
- No special handling
- Can be placed anytime before surgery
- Metal instruments interfere with signal
- Interferes with MRI imaging

# Newer localization procedures vs Wire Loc

- All of the techniques have been shown in initial feasibility trials to be as effective in localizing lesions compared to wire localization
- Current data on margin status, cosmesis, procedure time and recurrence rate are insufficient to judge RSL or others as superior to WL
- **Uncoupling of the localization procedure from the surgical procedure is the major advantage.**

# Margins ?!



# Lumpectomy margins

- Positive margins = higher risk of local recurrence
  - Local breast cancer recurrence can influence patient survival
  - 1 life saved for every 4 local recurrences prevented at 10 year follow up
- Positive margin rate 9-35%

# Consensus Guideline for Margins - Invasive Breast Cancer

Multidisciplinary expert panel convened in 2013 examine the relationship between margin width and IBTR - define optimal margin width

- 33 Studies

- 28,162 patients

- 1,506 recurrences

Negative margin = No ink on tumor

- ink on tumor margin - at least 2 x increase in IBTR

- wider margins do not significantly lower risk

# Guideline for Margins - DCIS

- Multidisciplinary consensus panel metanalysis of margin width and IBTR  
20 studies  
7883 patients

**Conclusion** : 2mm margin minimizes risk of IBTR compared to smaller margins

More widely clear margins do not lower rate of IBTR

Morrow et al, *Journal of Clinical Oncology* 2016 34:33, 4040-4046

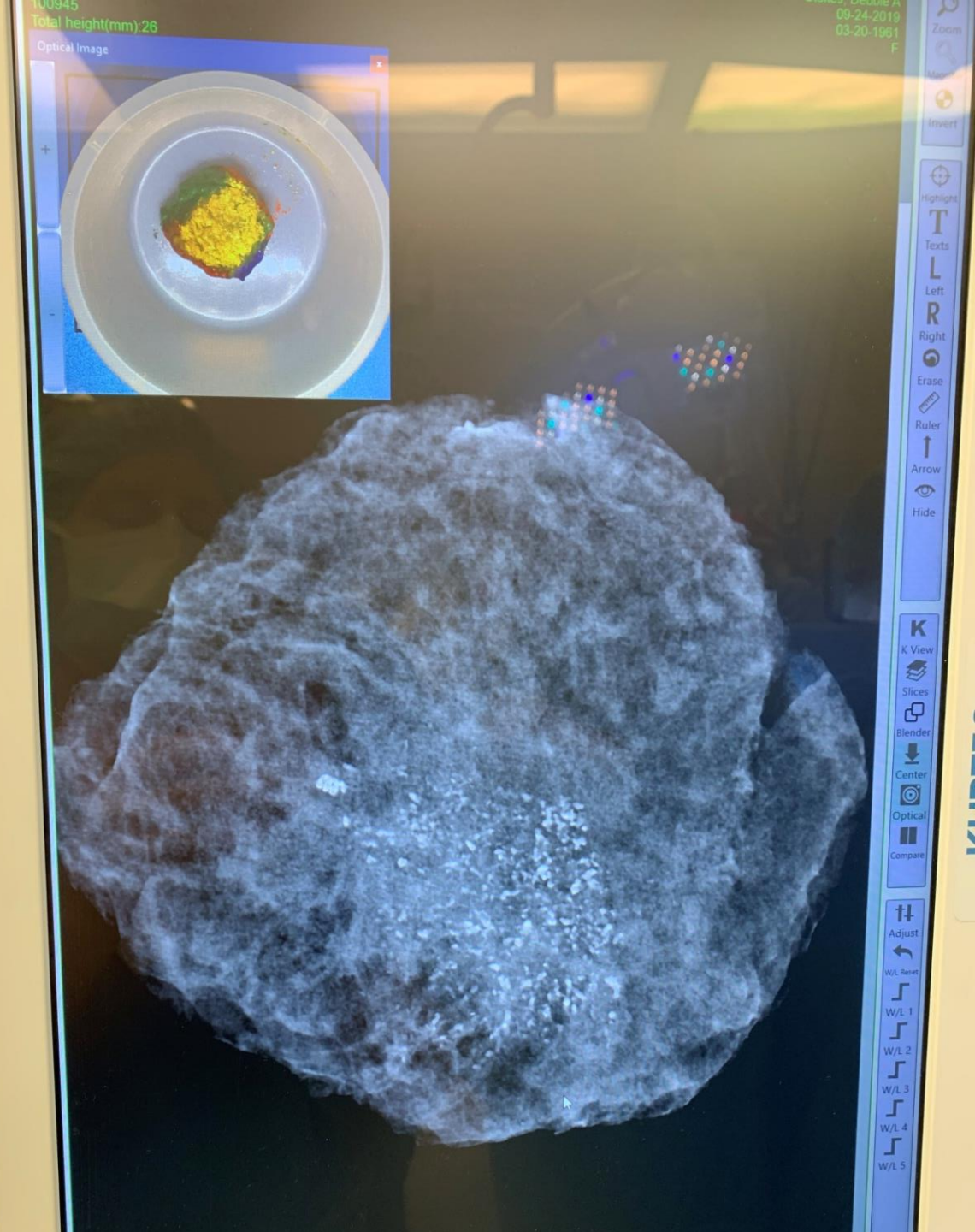


# Assessment of Margins

- Intraoperative assessment
  - Evaluation of tissue removed
  - Evaluation of surgical cavity
- Permanent/ fixed tissue margin evaluation
  - Ink on specimen
  - Cavity margins

# Assessment of margins intraoperatively

- Frozen section or touch prep analysis
  - Time consuming and labor intensive
- Intraoperative specimen imaging
  - Faxitron
  - Tomosynthesis (Mozart)
  - Ultrasound



# Intraoperative Margin Assessment

- Newer methods of tissue assessment

Margin probe, Clear Edge, Intelligent knife

- Cavity assessment – LUM Imaging system (Lumicell, Inc)
  - LUM 015 dye = intravenously injected protease – activated fluorescent imaging agent
  - hand held wide field detector device
  - special tumor detection software.

Dumitru et al, *ecancer* 2018

Smith, B.L., Gadd, M.A., Lanahan, C.R. et al. Breast Cancer Res Treat (2018) 171: 413.  
<https://doi.org/10.1007/s10549-018-4845-4>





Abstract No. 2178 - Poster No. OT3-06-02

## RESULTS FROM THE EXPANSION INTO MULTIPLE INSTITUTIONS FOR TRAINING IN THE USE OF THE LUM IMAGING SYSTEM FOR INTRAOPERATIVE DETECTION OF RESIDUAL CANCER IN THE TUMOR BED OF FEMALE SUBJECTS WITH BREAST CANCER CLINICAL TRIAL

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MASSACHUSETTS  
GENERAL HOSPITAL  
CANCER CENTER

### BACKGROUND

- 15% of lumpectomy patients have positive margins that require a second surgery, and most patients receive radiation following lumpectomy to reduce the risk of local cancer recurrence.
- These positive margins are poorly predictive (35% PPV) of cancer left in the cavity, so most second surgeries find no residual cancer.
- Tools are needed to identify residual cancer in real time during the first lumpectomy to reduce the amount of second surgeries and radiation that are used to manage the risk of local recurrence.
- The LUM Imaging System consists of (1) an intravenously injected protease-activated fluorescent imaging agent (LUM015), (2) a hand-held wide field detector device and (3) a proprietary tumor detection software.
- The LUM Imaging System allows the surgeon to identify residual cancer intraoperatively in the lumpectomy cavity after the resection of the main lumpectomy specimen.

### OBJECTIVES

- Optimize the tumor detection algorithm that will be used in the upcoming pivotal study to evaluate the safety and efficacy of the LUM imaging system
- Train clinical staff and surgeons on integrating the LUM Imaging System into surgical practice, and establish site-specific workflows for labeling tissue shaves by orientation
- Correlate LUM System images with histopathology results from excisions
- Collect usability feedback on system design
- Collect safety data

### INTERIM RESULTS

- 234 patients were enrolled. 230 had complete data for analysis.
- Median age 61 years (37-83)
- 69% Post menopausal and 31% Pre/Peri menopausal.
- 64% IDC +/- DCIS, 11% ILC, 21% DCIS alone
- 1 SAE anaphylactic reaction occurred.
- Tumor detection algorithm was optimized based on data collected during the investigation.

Metric	All patients (n=230)
Positive Margin Rate after SoC	17.8% of patients (41/230)
Average # LUM-guided excisions per patient	1.1
Average volume of LUM-guided excisions	3.6 cc
Sensitivity and Specificity (compared to histopathology of excision)	Sensitivity: 80% of excisions (37/46) Specificity: 71% of excisions (1098/1550)
Positive margin detection rate (LUM system indicated positive signal in the cavity for all SoC positive margins)	29.3% of patients (12/41)
Conversion rate of positive to negative margins	19.5% of patients (8/41)
Rate of removal of residual cancer after SoC	10.9% of patients (25/230)
Rate of cancer found in re-excision surgery	48.1% of patients (13/27)

### METHODS

- Non-randomized, prospective, multi-center feasibility study.
- Adult female breast cancer patients undergoing lumpectomies were enrolled at 16 community based and academic medical centers across the U.S.
- All patients were injected with LUM015 prior to surgery.
- Surgeons performed standard of care (SoC) lumpectomy, and then the cavity was scanned with the LUM Imaging System to guide further excision based on detection of fluorescent signal (see below).



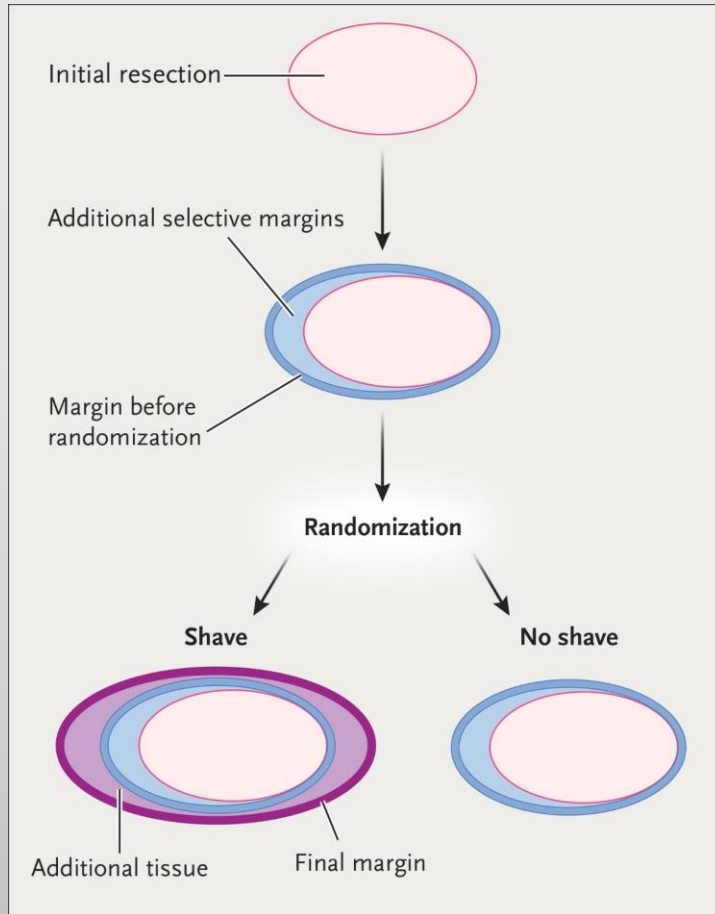
### DISCUSSION

- Data from previous clinical trials support that using the LUM Imaging System may identify cancerous tissue that may have otherwise been missed during routine lumpectomy
- LUM Imaging System training is intended to improve the quality and integrity of the data collected in the upcoming pivotal clinical trial to evaluate the safety and efficacy of the LUM Imaging System.
- The LUM System is currently being evaluated in other cancer indications including gastrointestinal cancers, prostate cancer, peritoneal surface malignancies, pancreatic cancer, and brain cancer

# Margin assessment – post surgery tissue evaluation

- Cavity Shave Margins
- Specimen orientation
- Specimen inking

# Cavity shaved margins



Randomized controlled trial of 235 patients with Stage 0-3 Breast Cancer undergoing lumpectomy/breast conserving surgery

Cavity shaved margins resulted in significant reduction in the reoperation rate to achieve clear margins ( 10% vs 21%)

Statistically significant reduction in positive margins 19% vs 34%

No significant difference in specimen weight or final cosmesis

# Intraoperative Inking of Lumpectomy margins performed by Surgeon

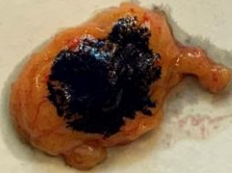

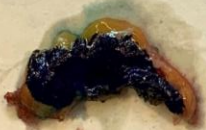
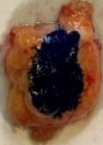


- More effective at guiding re-excision of positive margins
- Can reduce cost

Botty Van Den Bruele et al, *Journal of Surgical Research* 2018

Altman, et al, *Breast J.* 2019: 00:1-7





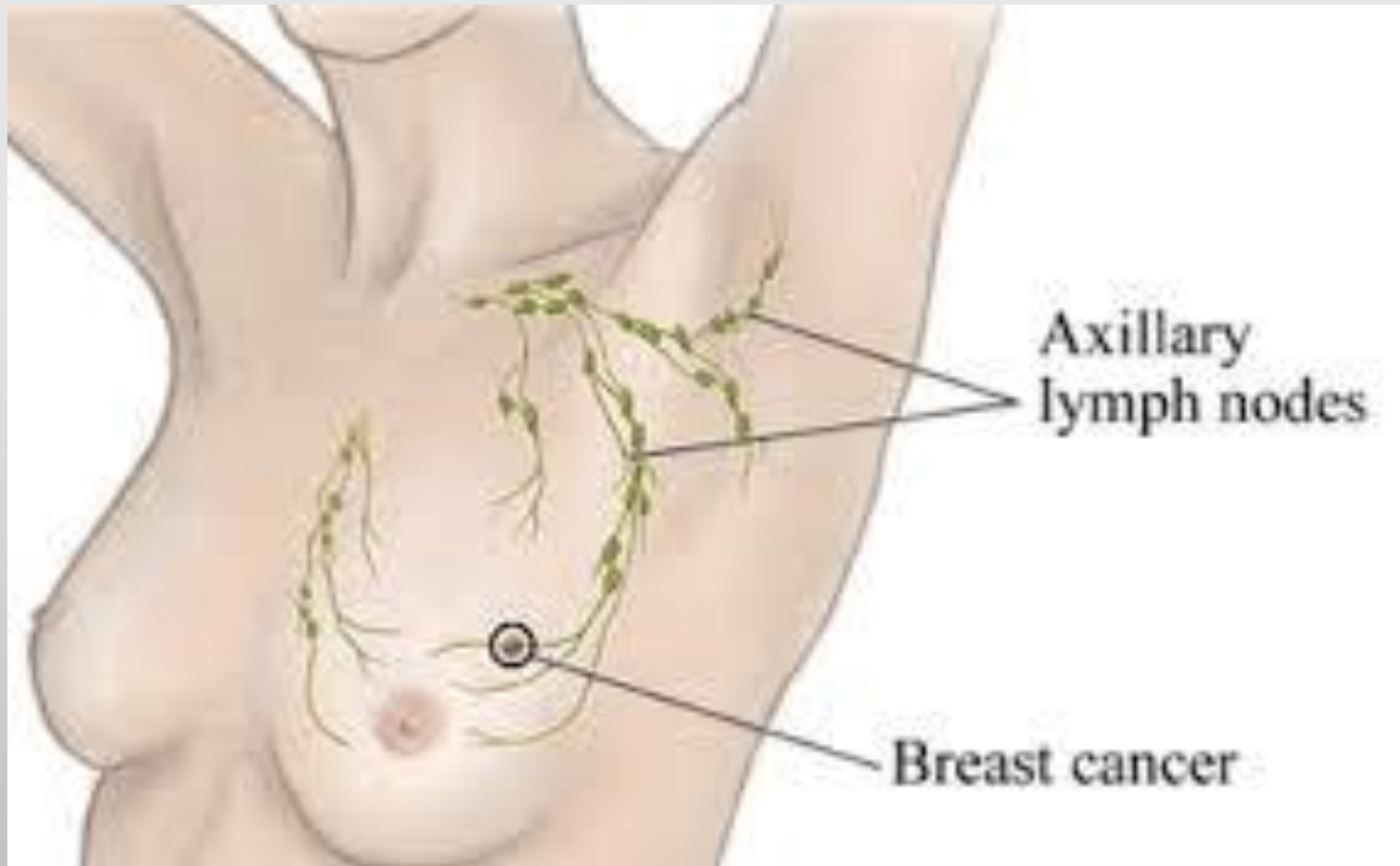
Breast Specimen		Margin Sheet	
SUPERIOR		LATERAL	
INFERIOR		MEDIAL	
POSTERIOR/ DEEP		ANTERIOR/ SUPERFICIAL	



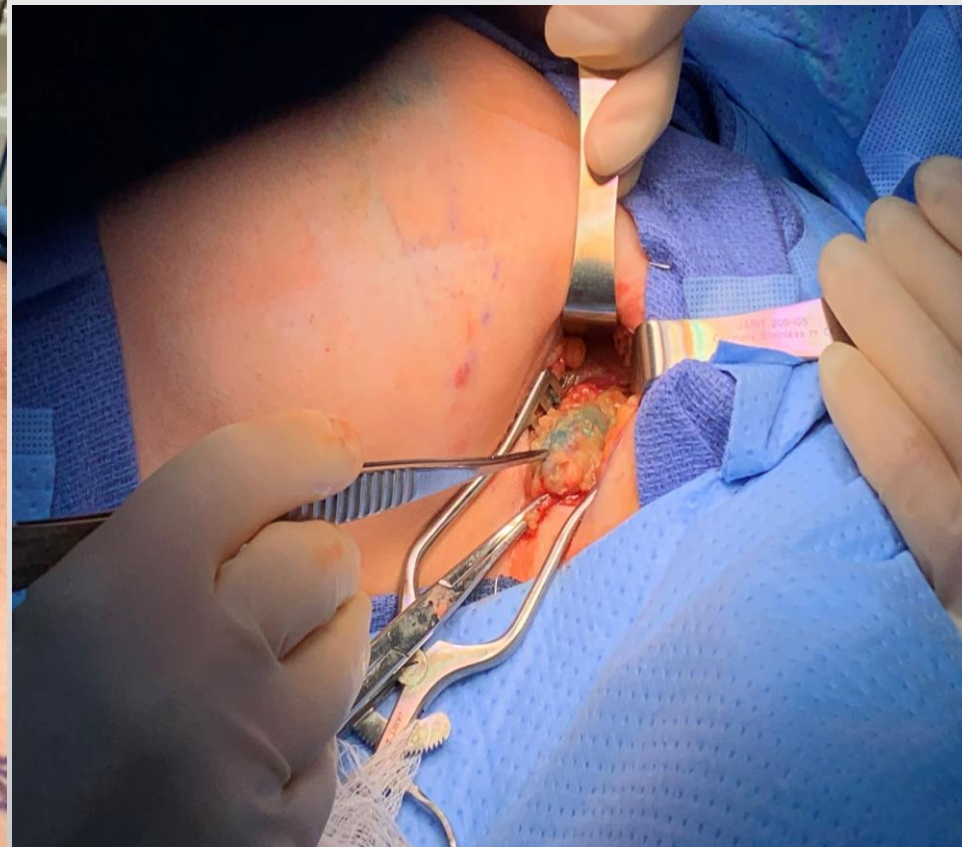
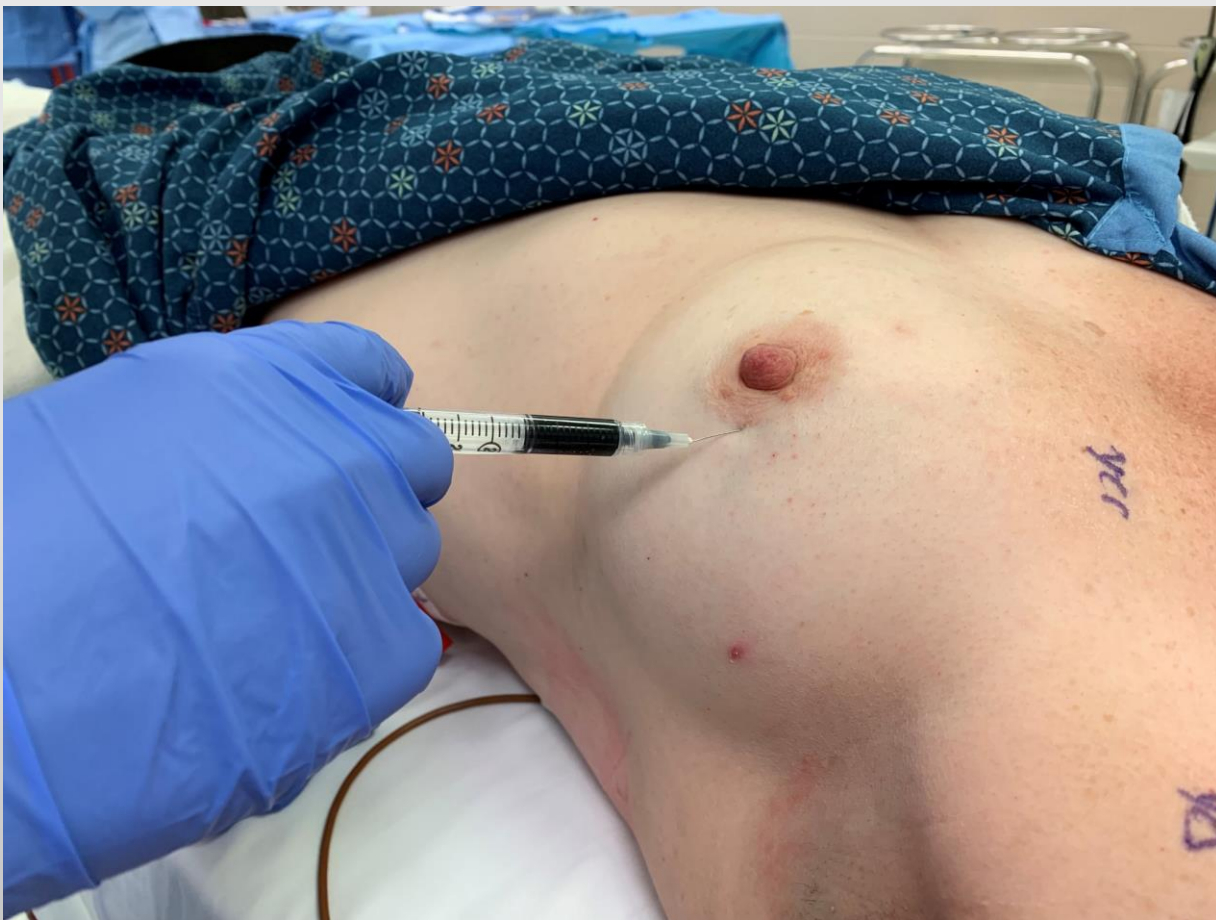




# Surgical Management of Axillary Lymph Nodes



# Sentinel Lymph Node Biopsy



# Sentinel Node Biopsy in patients presenting with clinically negative nodes

- ACOSOG Z0011 trial
- AMAROS trial
- No axillary dissection is indicated in most patients who have clinically negative nodes at diagnosis even if the sentinel node is positive for metastatic cancer

There is usually no need for frozen section pathology on the sentinel node in patients who present with clinically negative lymph nodes

Giuliano et al, *JAMA* 2011 and *JAMA* 2017

Donker et al, *Lancet Oncol* 2014

# What about patients who present with clinically positive lymph node(s) ?

- Patients with Estrogen receptor negative or Her-2 positive cancer will be referred for neoadjuvant chemotherapy
- Patients with Er positive, node positive breast cancer are more challenging for the Surgeon and Oncologist

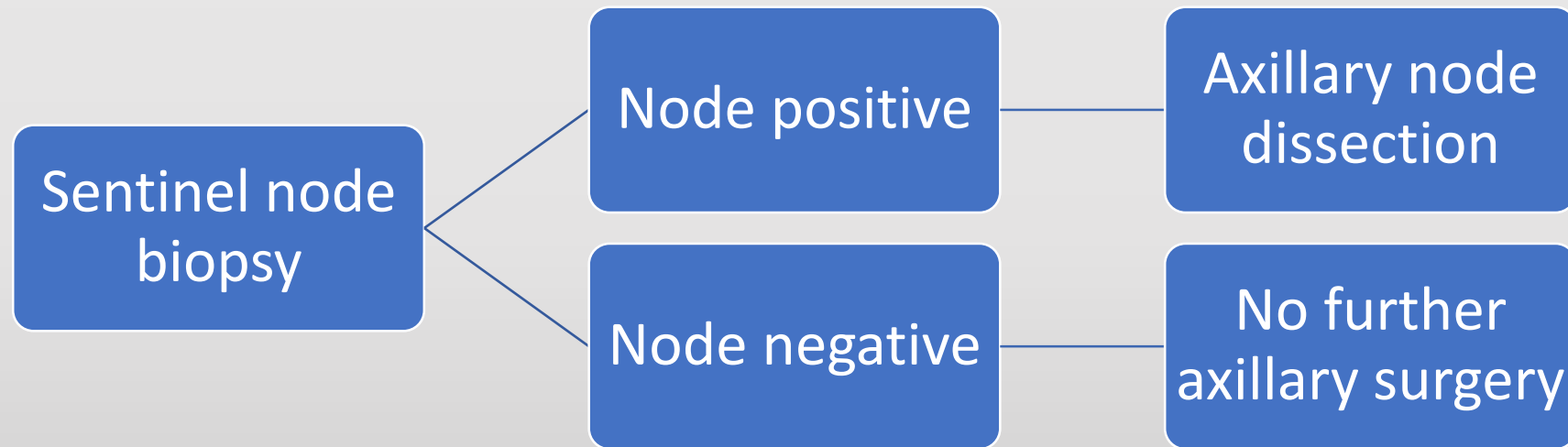
# Sentinel Node Biopsy after Neoadjuvant Chemotherapy

- ACOSOG 1071

- Patients were biopsy proven node positive before chemotherapy
- Sentinel node biopsy completed at the time of definitive surgery
- SLN biopsy was accurate with false negative rate 10.8 % if over 3 SLNs removed AND if both radioactive tracer and blue dye were used
- If clipped node if found, FNR is 6.8%

# Axillary Management After Neoadjuvant Chemotherapy

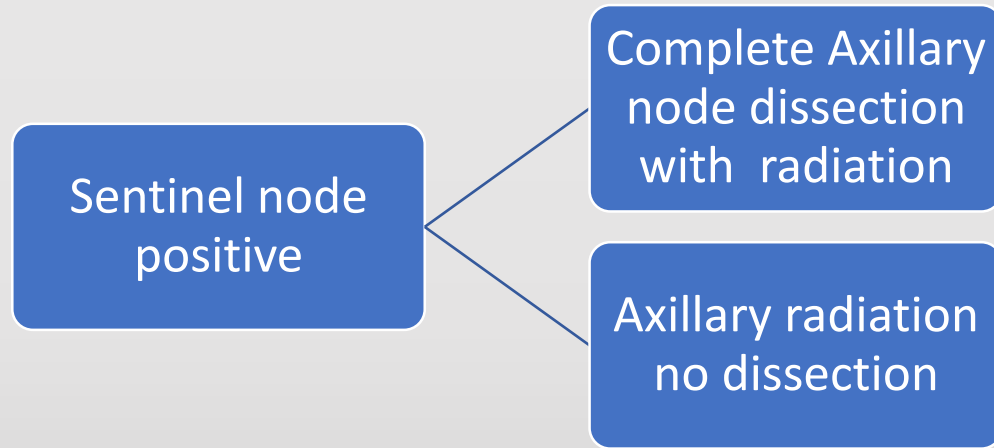
## Current Standard of Care



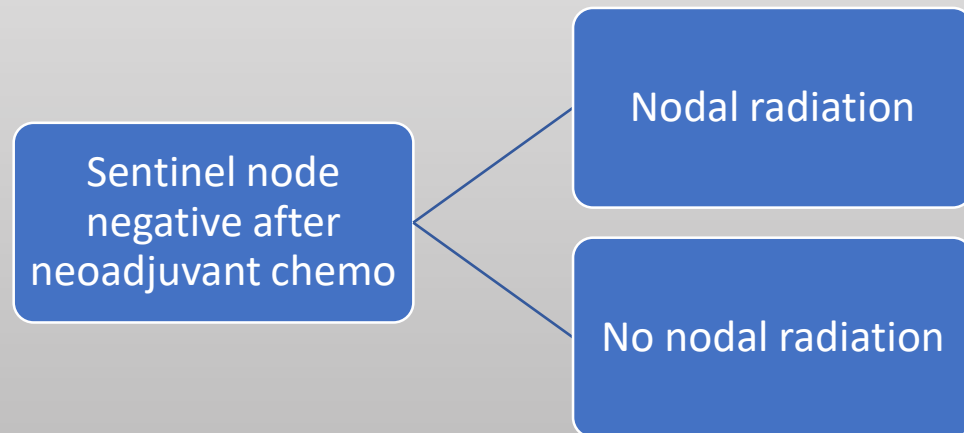


# Future of Axillary Management

- Alliance 11202 trial



- NSABP 51



Axillary dissection may soon be.....



# Oncologic Surgical techniques for optimal cosmesis

- Oncoplastic lumpectomies
- Oncoplastic reduction
- Nipple sparing mastectomies

Breast conserving surgery can result in poor cosmetic result



# Oncoplastic Breast Surgery

- **Oncoplastic surgery** combines the latest plastic **surgery** techniques with **breast surgical** oncology. When a large lumpectomy is required that will leave the **breast** distorted, the remaining tissue is sculpted to realign the nipple and areola and restore a natural appearance to the **breast** shape.
- any surgery that aims to maintain quality of life and an acceptable breast appearance whilst at the same time being uncompromising on oncological effectiveness.

# Benelli or “donut” mastopexy

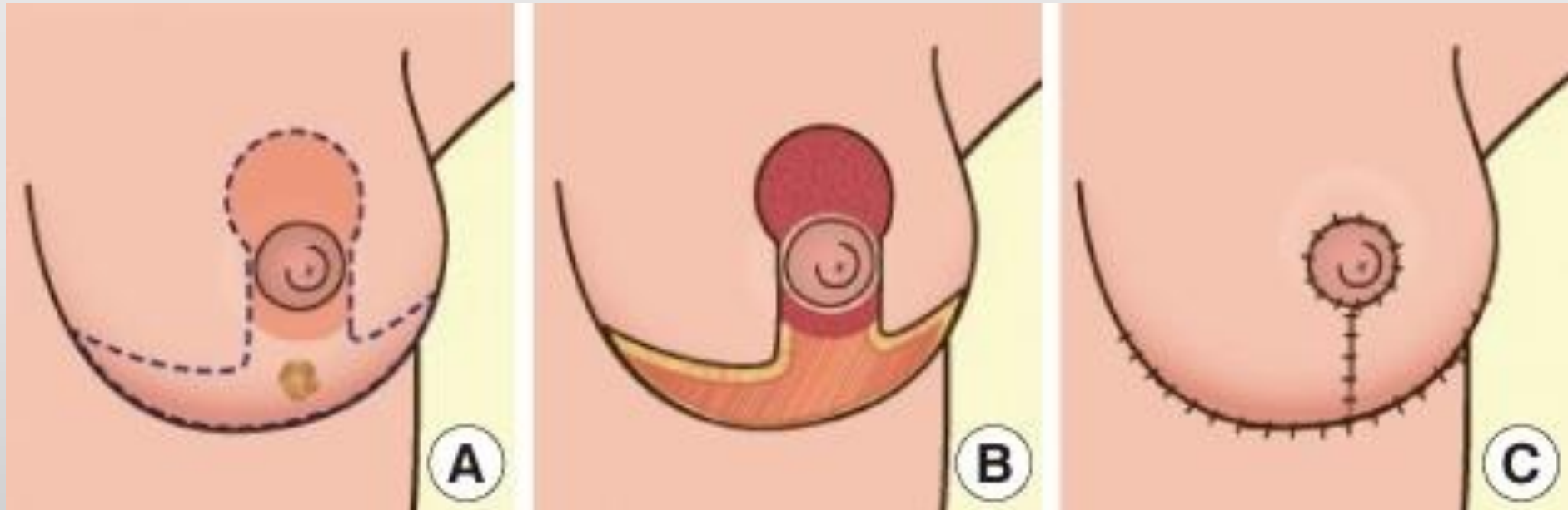


2 weeks post op, lumpectomy with  
mastopexy





# Oncoplastic Reductions





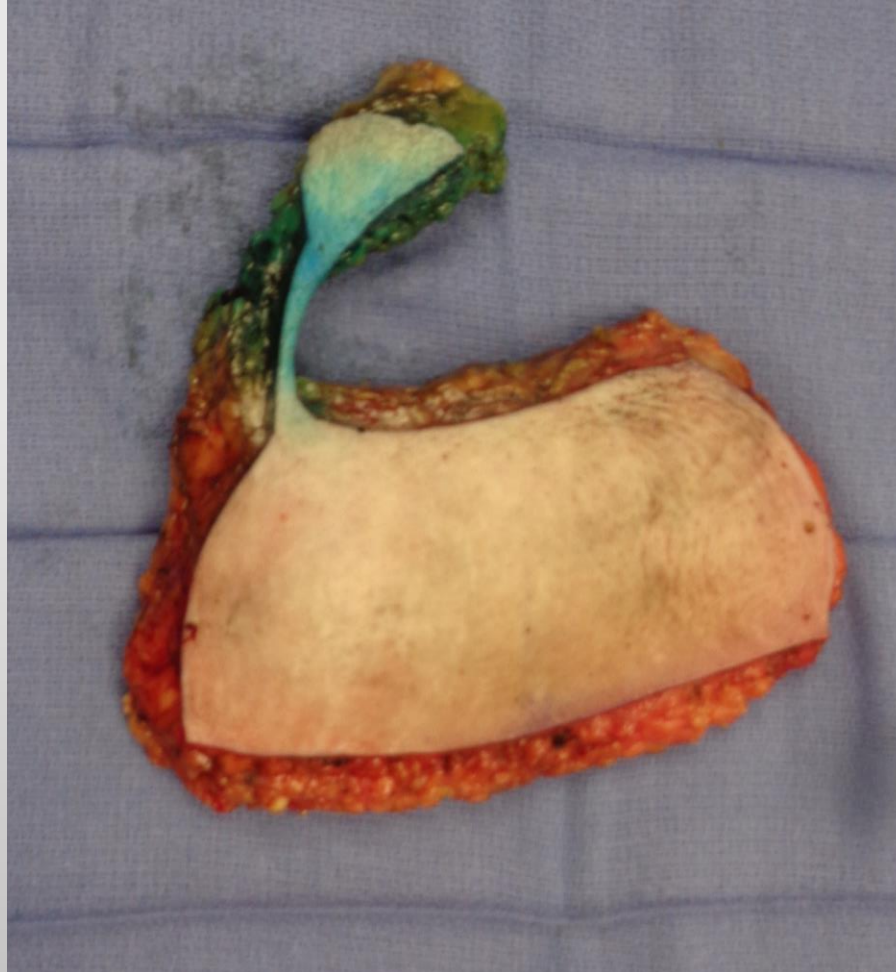
# Oncoplastic Reductions



# Oncoplastic Reductions



# Oncoplastic Reductions



# Oncoplastic Reductions





# Oncoplastic Reductions



# Oncoplastic Reductions





# Oncoplastic Reductions



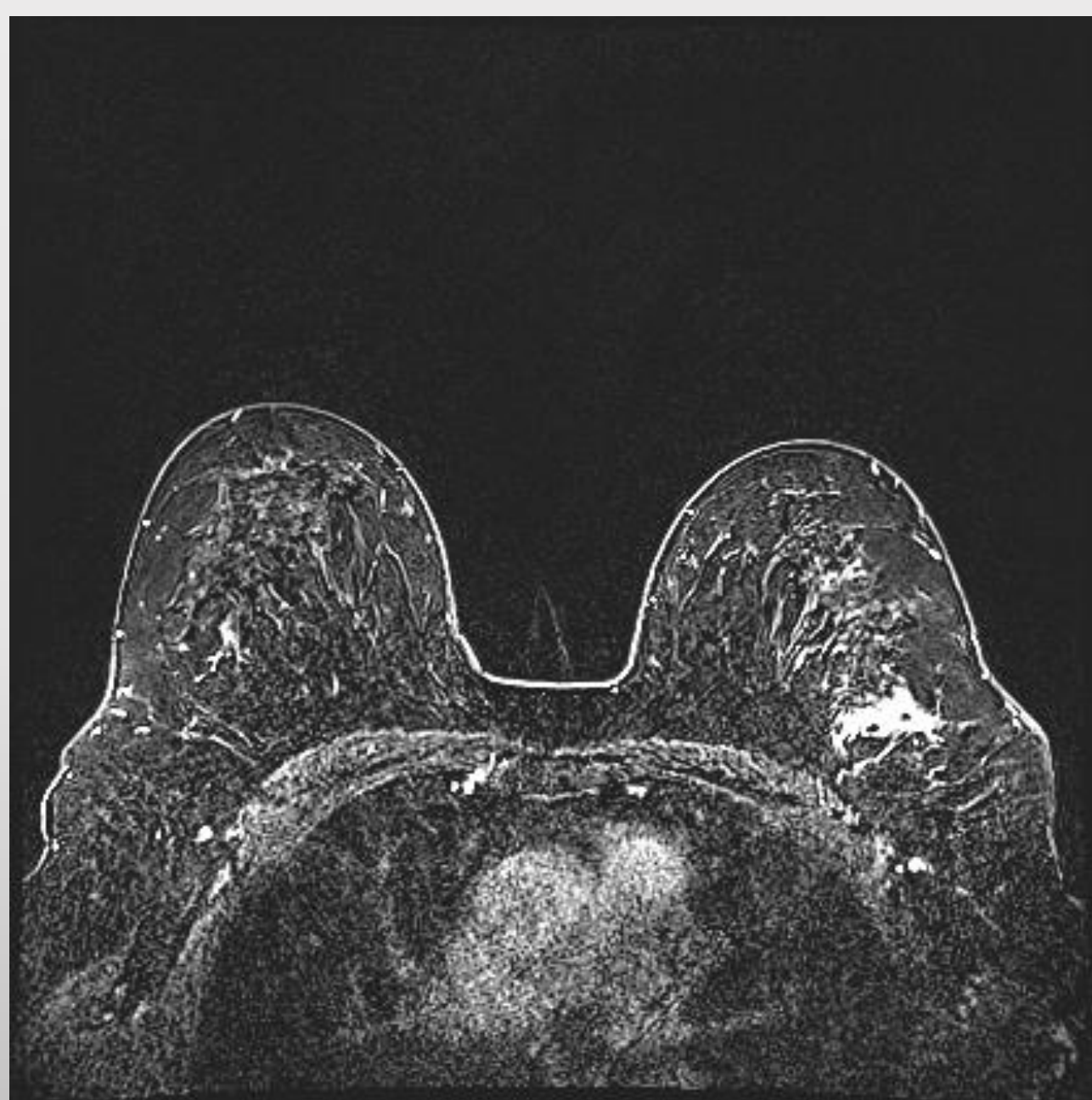
# Oncoplastic Reductions



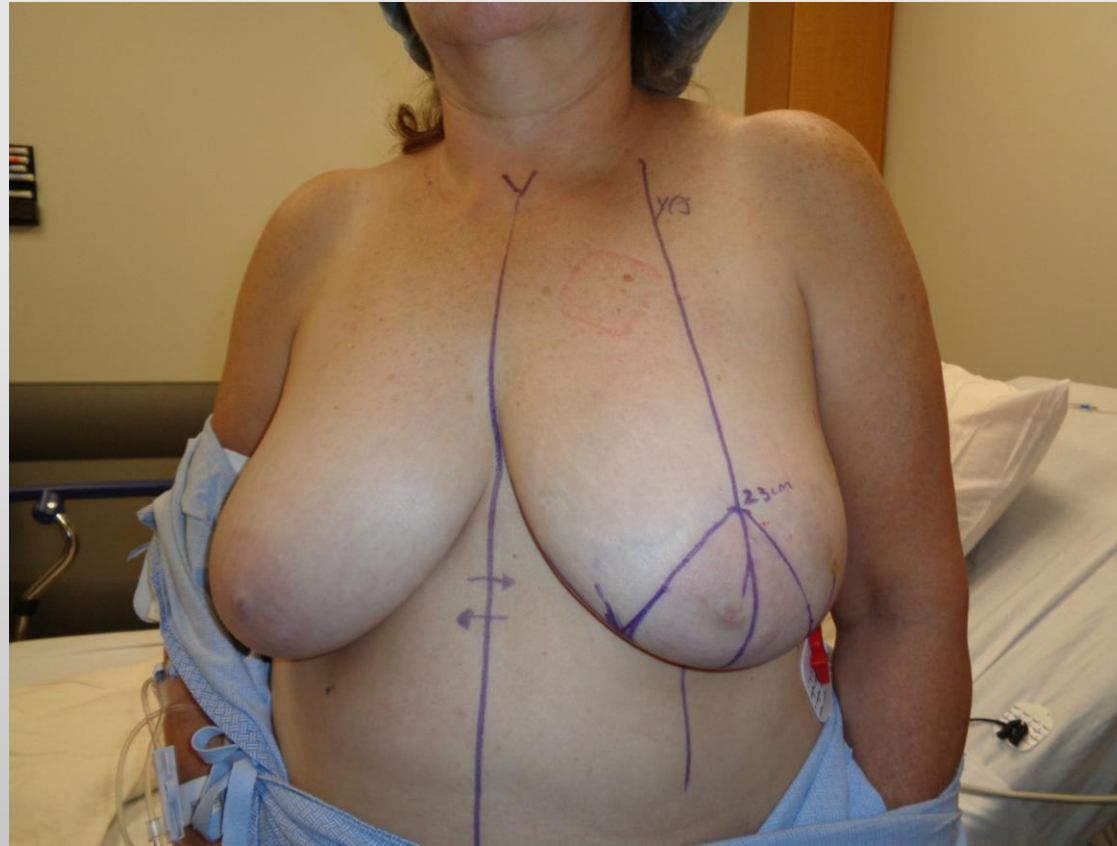
# Oncoplastic Reductions





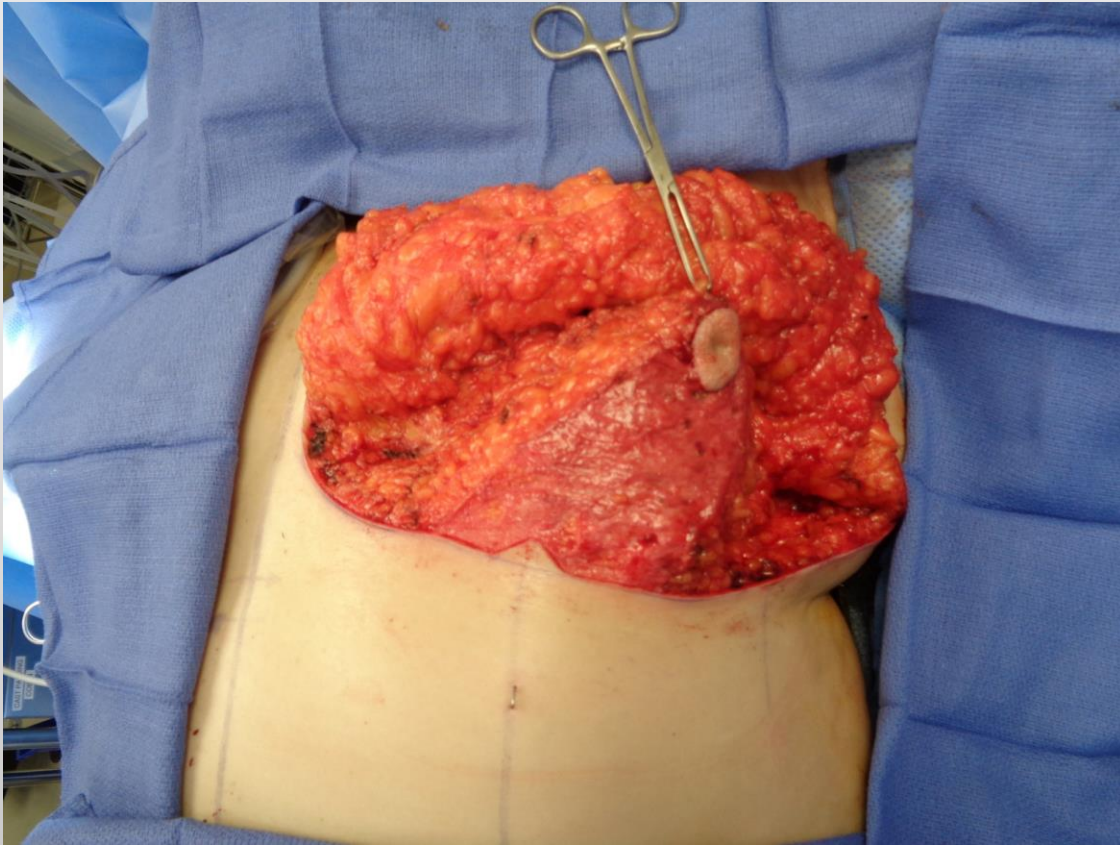


# Pre op planning for oncoplastic resection





# Oncoplastic lumpectomy with reduction mammoplasty





# Post op Oncoplastic lumpectomy with reduction



# Oncoplastic Reductions

## The Oncoplastic Reduction Approach to Breast Conservation Therapy: Benefits for Margin Control

Albert Losken, MD; Ximena Pinell-White, MD;  
Alexandra M. Hart, MD; Alessandrina M. Freitas, MD;  
Grant W. Carlson, MD; and Toncred M. Styblo, MD

Table 2. Comparison of Pathologic and Clinical Outcomes

Outcome	Procedure		P Value
	Oncoplastic Reduction (n = 83)	Lumpectomy (n = 139)	
Mean lumpectomy weight, g (range)	161.0 (25-1200)	57.3 (6-246)	<.001 <sup>a</sup>
Mean total resection weight, g (range)	394.9 (40-1200)	57.3 (6-246)	<.001 <sup>a</sup>
Mean width of margin to in situ cancer, mm (range)	4.7 (0-20)	3.2 (0-16)	.04 <sup>a</sup>
Mean margin width to invasive cancer, mm (range)	5.3 (0-20)	3.3 (0-14.5)	.01 <sup>a</sup>
Closest margin to any cancer, mm	4.3 (0-20)	2.8 (0-14.5)	.01 <sup>a</sup>
Positive margins, n (%)			
0 mm (+ if cancer transected)	7 (8.4)	22 (15.8)	.11
≤1 mm	20 (24.1)	57 (41.0)	.01 <sup>a</sup>
Re-excision for positive margins, n (%)	10 (12.0)	36 (25.9)	.01 <sup>a</sup>
1 re-excision	10 (12.0)	33 (23.7)	
2 re-excisions	0	3 (2.2)	
Completion mastectomy, n (%)	2 (2.4)	13 (9.4)	.05 <sup>a</sup>

<sup>a</sup>Denotes significance, defined as  $P \leq .05$ .

# Oncoplastic Reductions

## Long-term Results After Oncoplastic Surgery for Breast Cancer A 10-year Follow-up

Krishna B. Clough, MD,\* Raquel F. D. van la Parra, MD, PhD,\* Helene H. Thygesen, PhD,† Eric Levy, MD,\*  
Elisabeth Russ, MD,\* Najeeb M. Halabi, PhD,‡ Isabelle Sarfati, MD,\* and Claude Nos, MD\*

*Annals of Surgery* • Volume 268, Number 1, July 2018

- 12.6% had positive margins
- 92% overall breast conservation rate
- 8.9% postoperative complications
  - 4.6% had delay in postoperative treatments
- The cumulative 5 year incidences for recurrence
  - Local 2.2%
  - Regional 1.1%
  - Distant 12.4%

TABLE 3. Margin Status and Histology

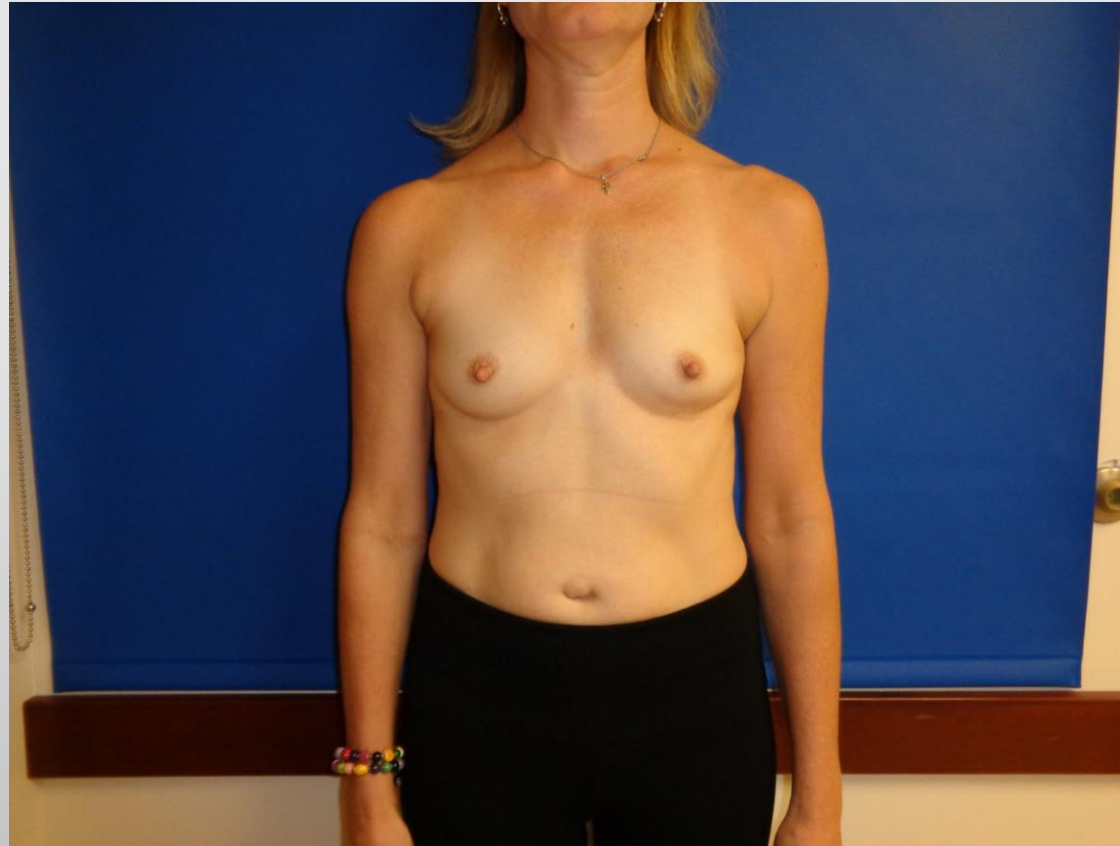
Margin status	Overall	IDC	DCIS	ILC
Clear	306	214	58	34
Involved	44 (12.6%)	25 (10.5%)	10 (14.7%)	9 (20.9%)
Total	350	239	68	43

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

# Nipple sparing mastectomy

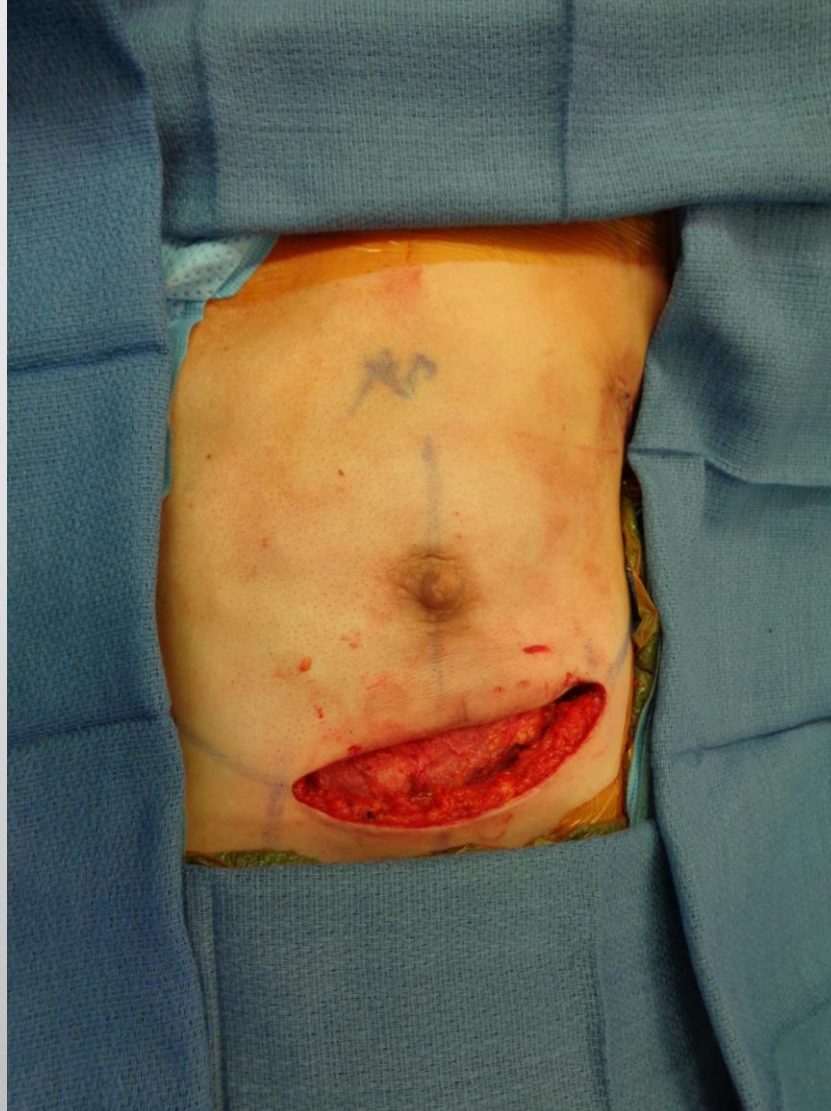
- Remove all breast tissue and leave all of skin and nipple and areola
- Driven by need to improve cosmetic results of breast surgery

# Before surgery

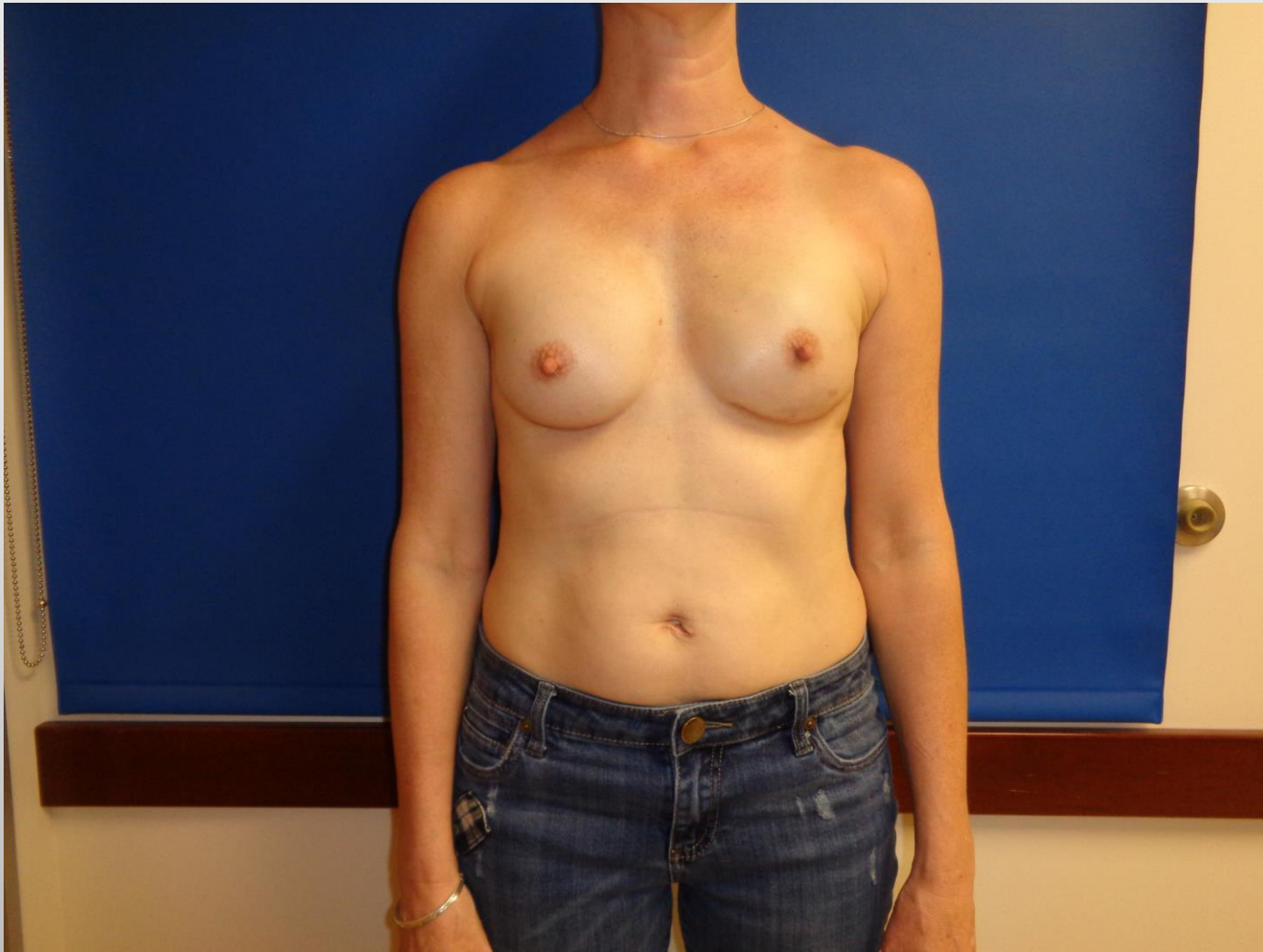




# Inframammary incision with nipple sparing mastectomy



after nipple sparing mastectomy and  
reconstruction



# Nipple sparing mastectomy – Oncologic outcomes

- Metanalysis of 20 studies with 5594 patients - No statistically significant difference in DFS, OS or LR in NSM vs MRM/ SSM
- Nipple areolar recurrence 1.2%
- Most Recurrences in superior breast and in location of primary tumor, not in nipple
- Local recurrence rate 3.7 - 3.9% NSM vs 3.3% SSM
- No adverse oncologic outcomes of NSM in carefully selected women with early stage breast cancer

DeLaCruz et al, [Ann Surg Oncol](#). 2015 Oct;22(10):3241-9. doi: 10.1245/s10434-015-4739-1. Epub 2015 Aug 5.

R. A. Agha, Y. Al Omran, G. Wellstead, H. Sagoo, I. Barai, S. Rajmohan et al , *BJS Open* 2019; 3: 135–145

Smith, et al , *JACS* 2017

Oncologic Safety of Nipple Sparing Mastectomy in Women with Breast Cancer, *Journal of the American College of Surgeons*. DOI: <http://dx.doi.org/10.1016/j.jamcollsurg.2017.06.013>.

# Nipple and skin sparing mastectomy - concerns

- Higher local recurrence in skin sparing mastectomies in high risk patients
  - Er negative
  - Young
  - Extensive DCIS, high grade disease
  - Close margins

Rashtian et al, *Int J Radiation Oncology, Biol. Phys*, 2008

Timbrell et al, *Ann Surg Oncol* (2017) 24:1071–1076

# Nipple Sparing Mastectomy – technical considerations

- Best outcomes in patients with lower BMI, B cup or smaller, non smokers, no prior radiation
- Incisions away from and not involving nipple areolar complex lower rates of nipple necrosis
- Best cosmesis with inframammary incisions or inferior incision

Ashikari AY, Kelemen PR, Tastan B, Salzberg CA, Ashikari RH. Nipple sparing mastectomy techniques: a literature review and an inframammary technique. *Gland Surg.* 2018;7(3):273–287. doi:10.21037/gs.2017.09.02



# Updates in Breast Surgery

Breast surgery is evolving

- improvements in efficiency and accuracy
- reduce morbidity
- cosmetic results





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