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

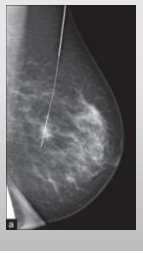
Non palpable breast lesions

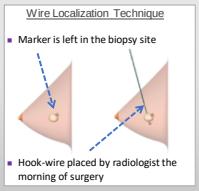
- Over 30-40% of breast cancers are not palpable and require localization for the surgeon to find the lesions in the OR
- Localization of lesions requires cooperation with the Radiologist and Surgeon and imaging confirmation of removal

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





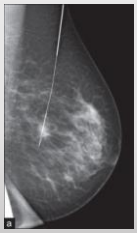
Wire Localization Challenges

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

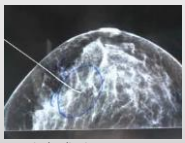
- Radioactive Seed localization
- SAVI Scout surgical guidance system
- Magseed
- RFD

- 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

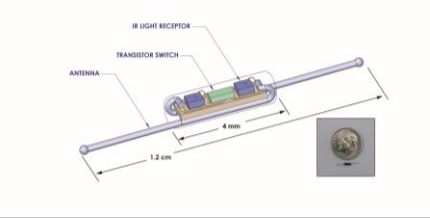
- Radioactive sources
- Stringent regulations
- Facility must have license for therapeutic radiation
- Fear of handling radioactive materials
- Strict chain of command handling of seeds

SCOUT Surgical Guidance System

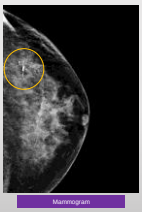
- No Wires
- Non-Radioactive
- Not a wire, marker, pellet or seed

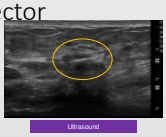
- Unique technology that is reimbursed differently
- Electromagnetic Wave Technology
  - Similar to Radar
  - Infrared activated

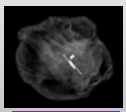
SCOUT Reflector



Clinical Views – Reflector


Mammogram


Ultrasound

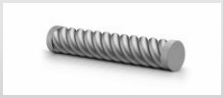

Specimen radiograph

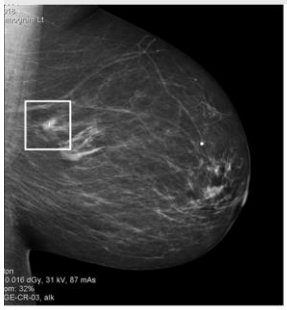
SAVI Surgical Guidance intraop

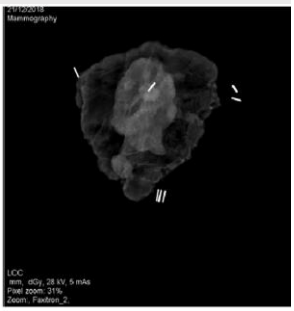
Advantages of SAVI

- 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







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

Int J Radiat Oncol Biol Phys. 2014 March 1; 88(3): 553–564

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

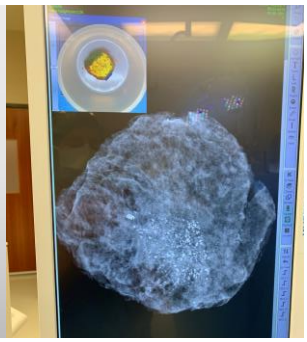
Assessment of Margins

- 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

Dumitru et al, *ecancer* 2018



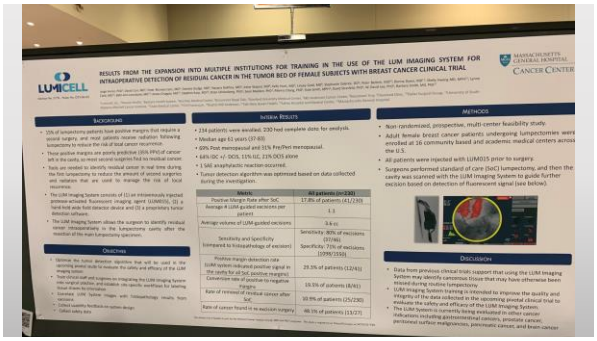
Intraoperative Margin Assessment

- 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

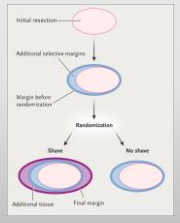
Smith, B.L., Gadd, M.A., Lanahan, C.R. et al. Breast Cancer Res Treat (2018) 171: 413. https://doi.org/10.1007/s10549-018-4845-4



Margin assessment – post surgery tissue evaluation

- Cavity Shave Margins
- Specimen orientation
- Specimen inking

Cavity shaved margins



Randomized controlled trial o f 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%

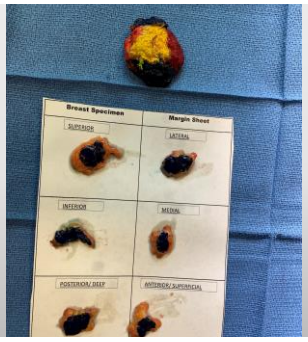
No significant difference in specimen weight or final cosmesis

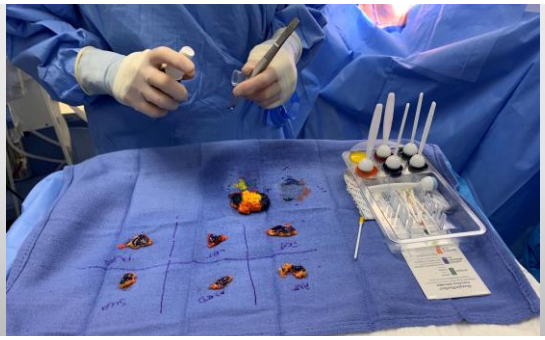
Chagpar, et al
N Engl J Med 2015; 373:503-510

Intraoperative Inking of Lumpectomy margins performed by Surgeon

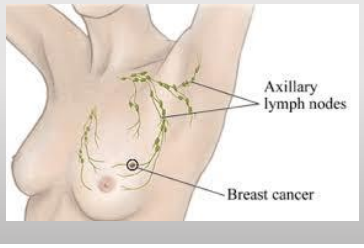
- More effective at guiding re-excision of positive margins
- Can reduce cost

Botty Van Den Bruele et al, *Journal of Surgical Research* 2018
Altman, et al, *Breast J.* 2019: 00:1-7





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

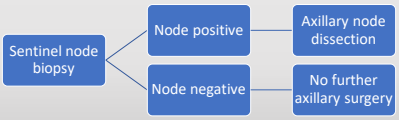
What about patients who present with clinically positive lymph node(s) ?

- 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

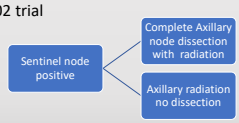
- ACOSOG 1071
  - Patients were biopsy proven node positive before chemotherapy
  - Sentinel node biopsy completed at the time of definitive surgery
  - SLN biopsy was accurate with false negative rate 10.8 % if over 3 SLNs removed AND if both radioactive tracer and blue dye were used
  - If clipped node if found, FNR is 6.8%

Axillary Management After Neoadjuvant Chemotherapy
Current Standard of Care

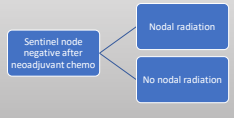


Future of Axillary Management

- 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

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Oncoplastic Reductions

Oncoplastic Reductions

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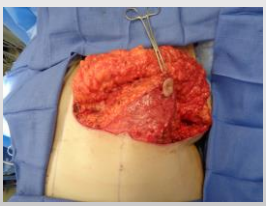
Oncoplastic Reductions

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 Fayeeza M. Styblo, MD

Table 2. Comparison of Pathologic and Clinical Outcomes

	Procedure		
Outcome	Oncoplastic Reduction (n = 63)	Lumpectomy (n = 139)	P Value
Mean lumpectomy weight, g (range)	161.0 (25-1200)	57.3 (6-246)	<.001*
Mean total resection weight, g (range)	394.9 (40-1200)	57.3 (6-246)	<.001*
Mean width of margin to in situ cancer, mm (range)	4.7 (0-20)	3.2 (0-10)	.04*
Mean margin width to invasive cancer, mm (range)	5.3 (0-20)	3.3 (0-14.5)	.01*
Closest margin to any cancer, mm	4.3 (0-20)	2.8 (0-14.5)	.01*
Positive margins, n (%)			
0 mm (= # cancer transected)	7 (8.4)	22 (15.8)	.11
≤1 mm	20 (24.1)	57 (41.0)	.01*
Re-excision for positive margins, n (%)	10 (12.0)	36 (25.9)	.01*
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)	.02*

*Denotes significance, defined as $P \leq .05$.

Oncoplastic Reductions

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

Kristina B. Clough, MD,* Raquel F. D. van la Parra, MD, PhD,* Helene B. Thygesen, PhD,† Eric Levy, MD,* Elisabeth Ross, MD,* Najeeb M. Malahi, PhD,‡ Isabelle Scellat, 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, T. Al Omran, G. Wellstead, H. Sagoo, I. Basit, S. Rajmohan et al., BJS Open 2019; 3: 195–185

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.2017.05.014.

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