Update on Local Therapy Research 2009

Barbara L. Smith, MD, PhD
Division of Surgical Oncology
Massachusetts General Hospital
Harvard Medical School

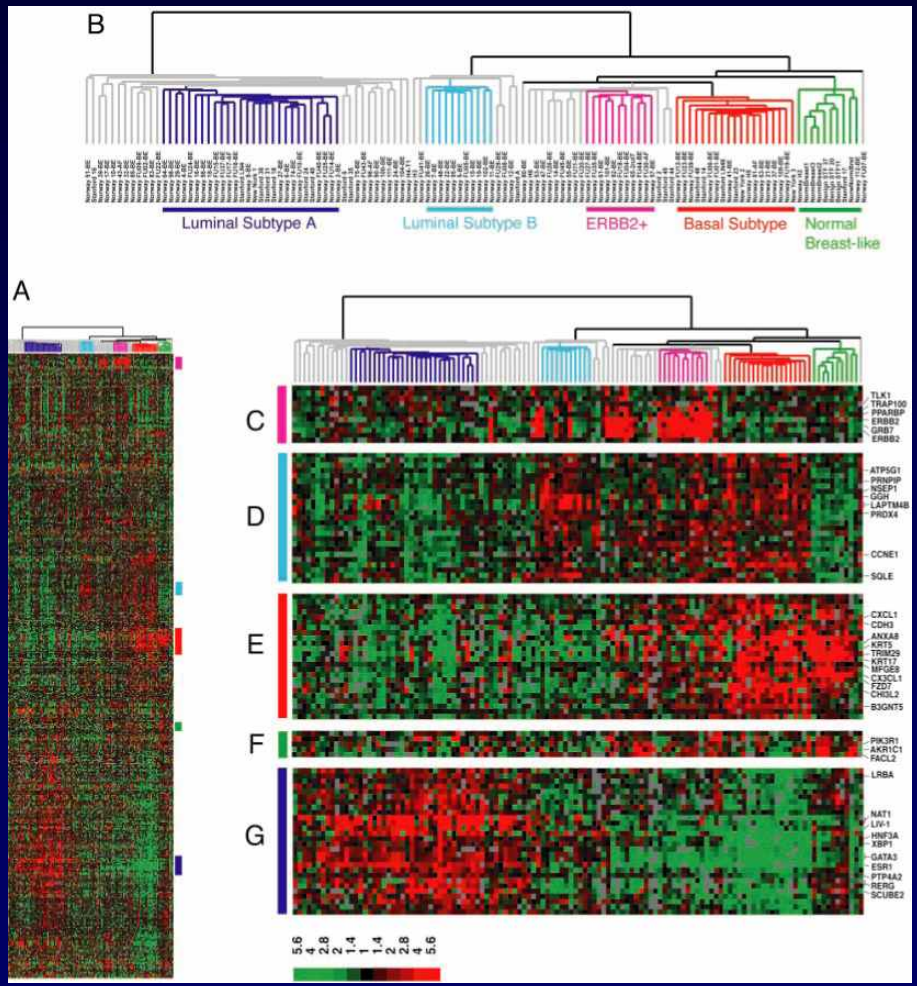
Local Therapy Research: Goals

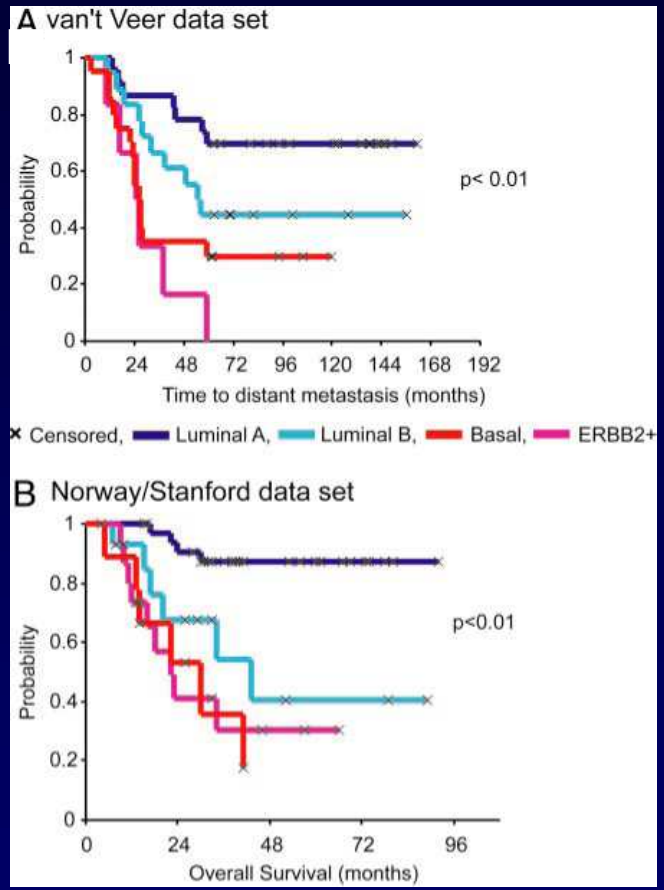
- Reduce local recurrence
- Reduce the extent of surgery and radiation
- Reduce treatment complications
- Best cosmetic result

Recent Advances in Local Therapy Breast Conserving Therapies

- Predicting risk of local recurrence
- Oncoplastic surgery techniques
- Partial breast irradiation
- Margin Assessment
- Non-surgical tumor ablation

Gene Expression Subtypes and Clinical Outcome





Sorlie et al. PNAS 2003,100:8418-8423

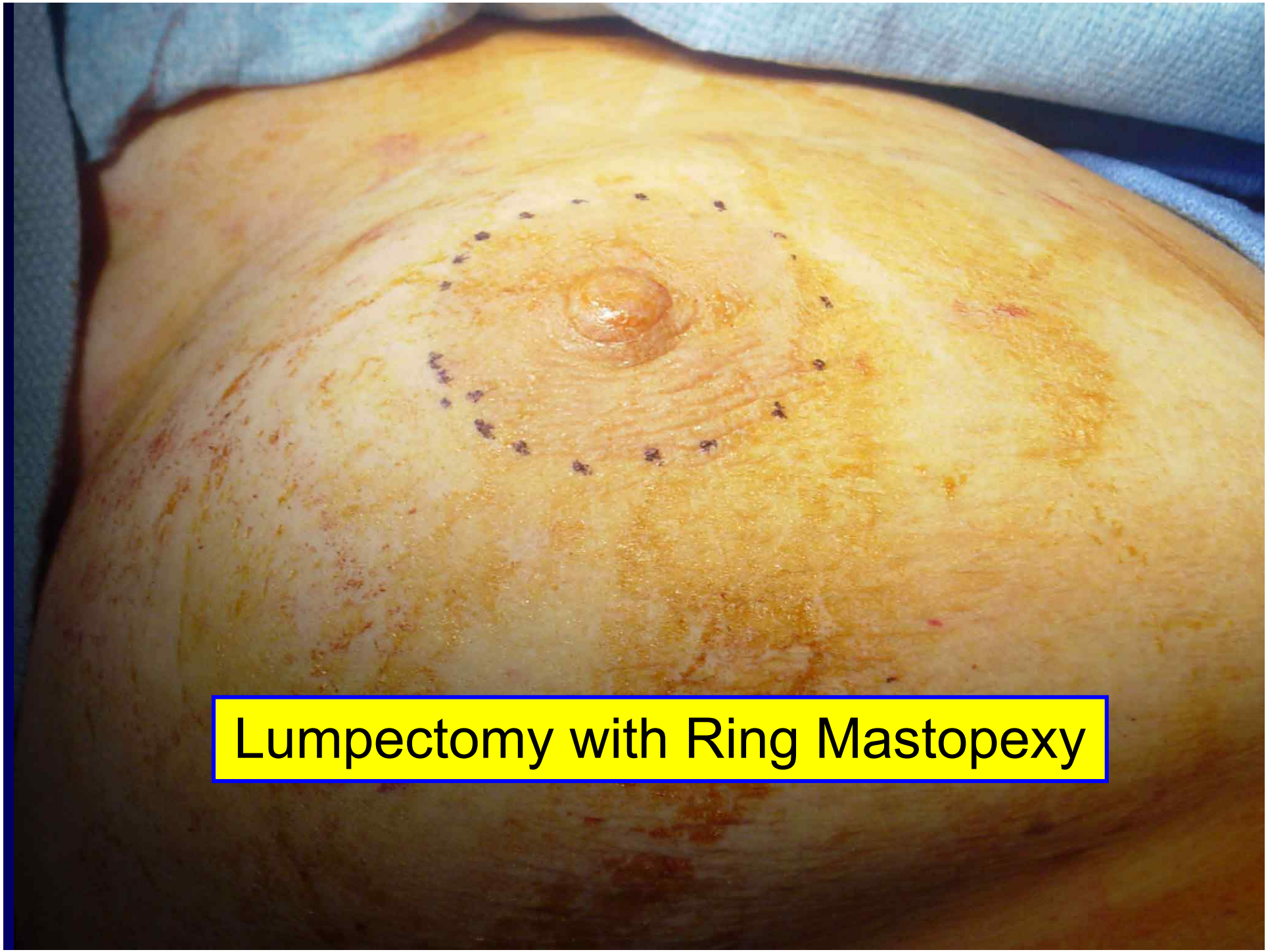
Local and Distant Recurrence Rates by Subtype

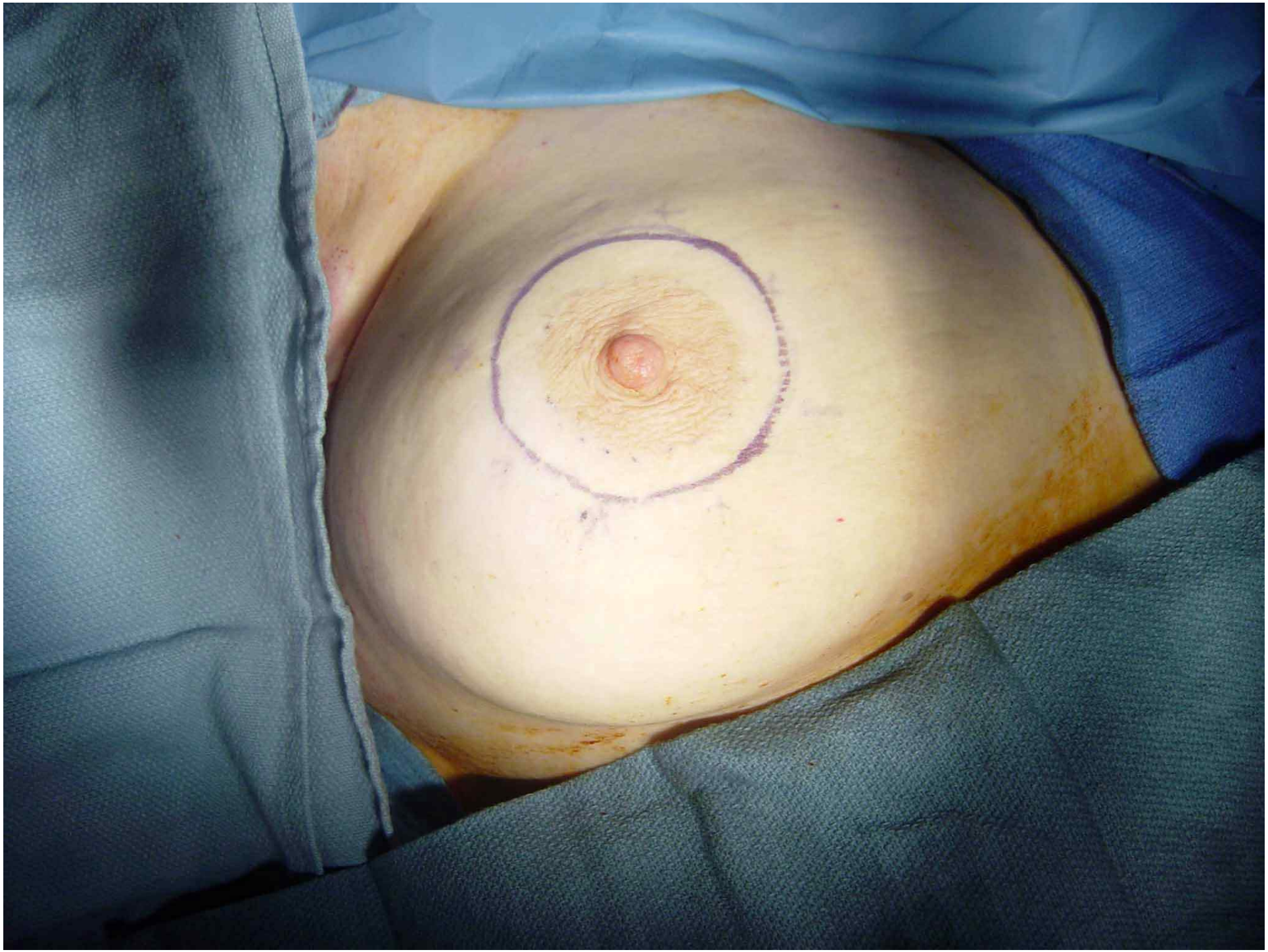
Nguyen JCO 2008 - 799 patients

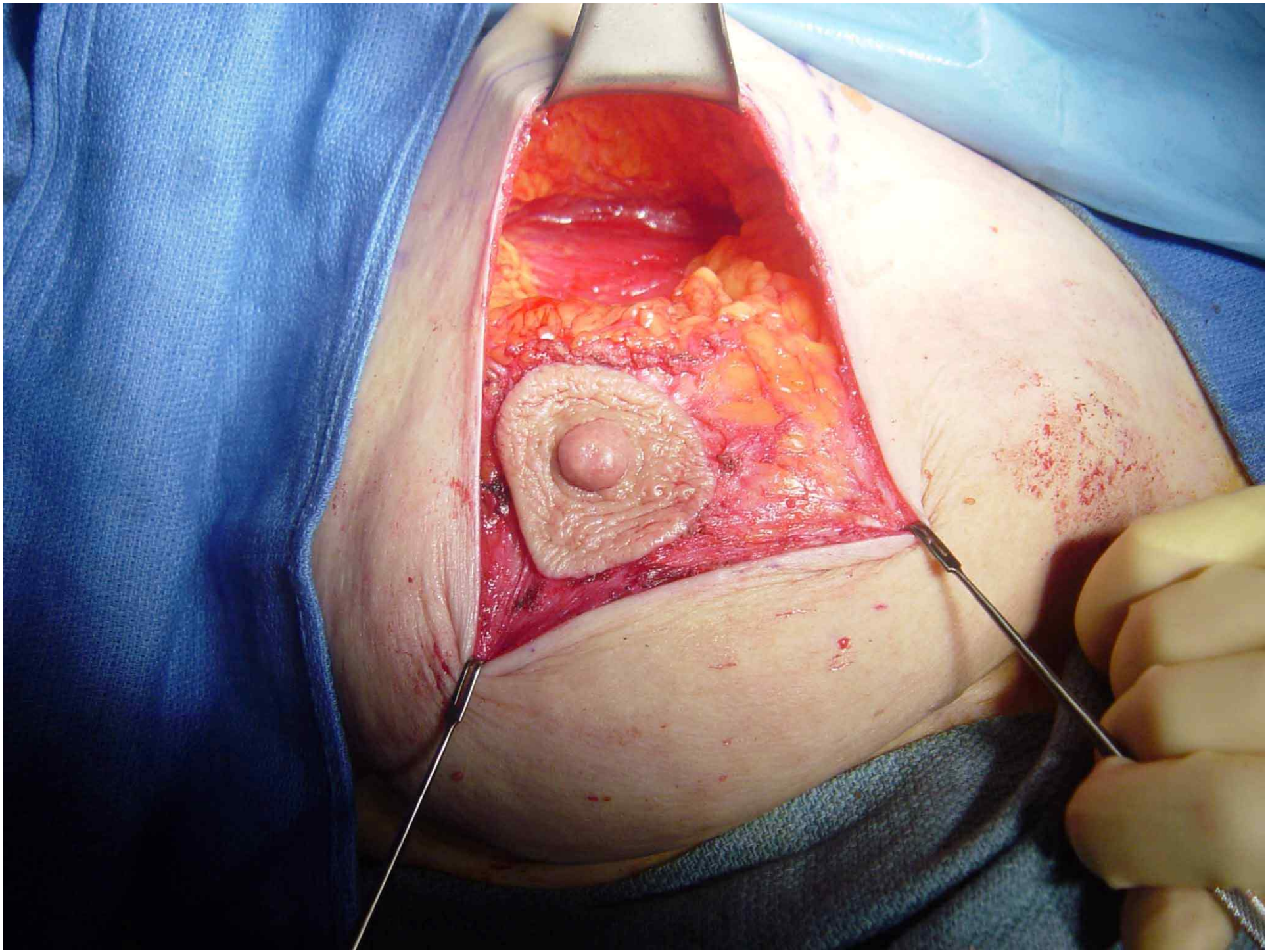
Group	Receptors	5-yr local regional failures	Adjusted HR (95%CI) p-value	5-yr Distant Mets
LumA n=599	ER/PR+, HER2-	0.7%	Baseline	3.0%
LumB n=78	ER/PR+, HER2+	1.3%	NS	11.5%
HER2+ n=33	ER/PR- HER2+	12.4%	6.7 (1.7-26.7) p=0.007	15.2%
Basal n=89	ER/PR-, HER2-	6.8%	3.9 (1.1-13.7) p=0.036	14.8%

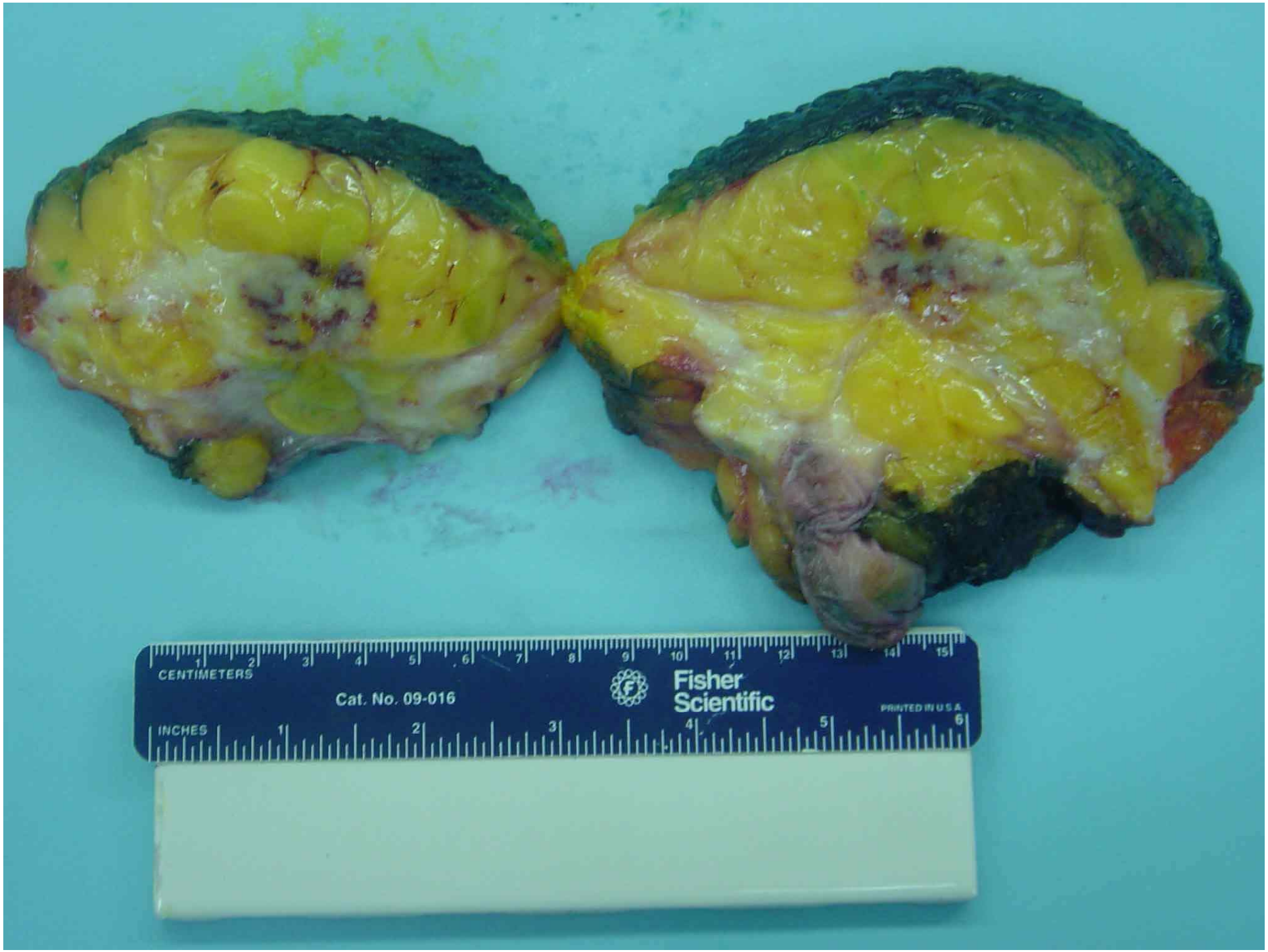
Oncoplastic Surgery:
Better Cosmesis for Large lesions

- Extensive tissue mobilization after lumpectomy to recreate breast contour
- Addition of mastopexy or reduction mammoplasty to lumpectomy – single or 2-stage procedure
- Cosmetic skin closure


Lumpectomy with Ring Mastopexy






CENTIMETERS
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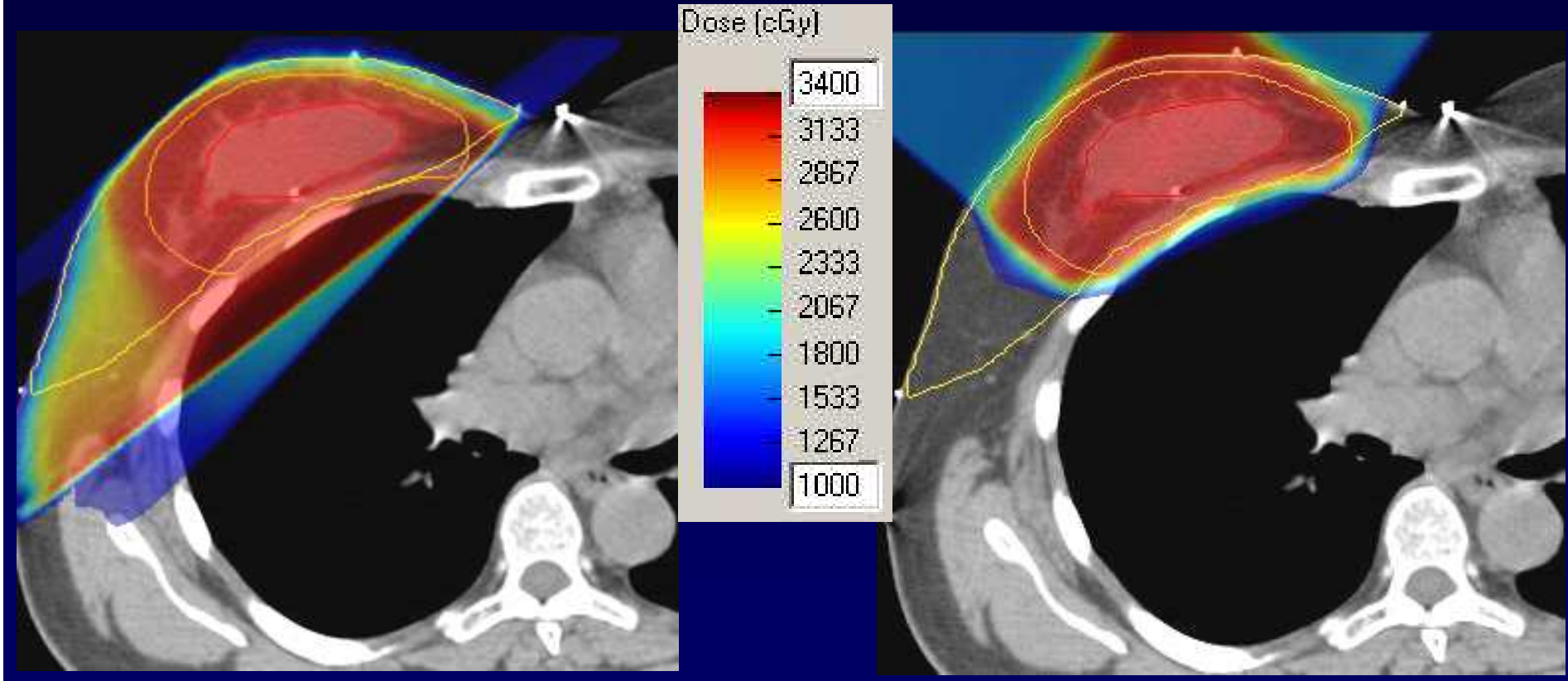
Partial Breast Irradiation: Rationale

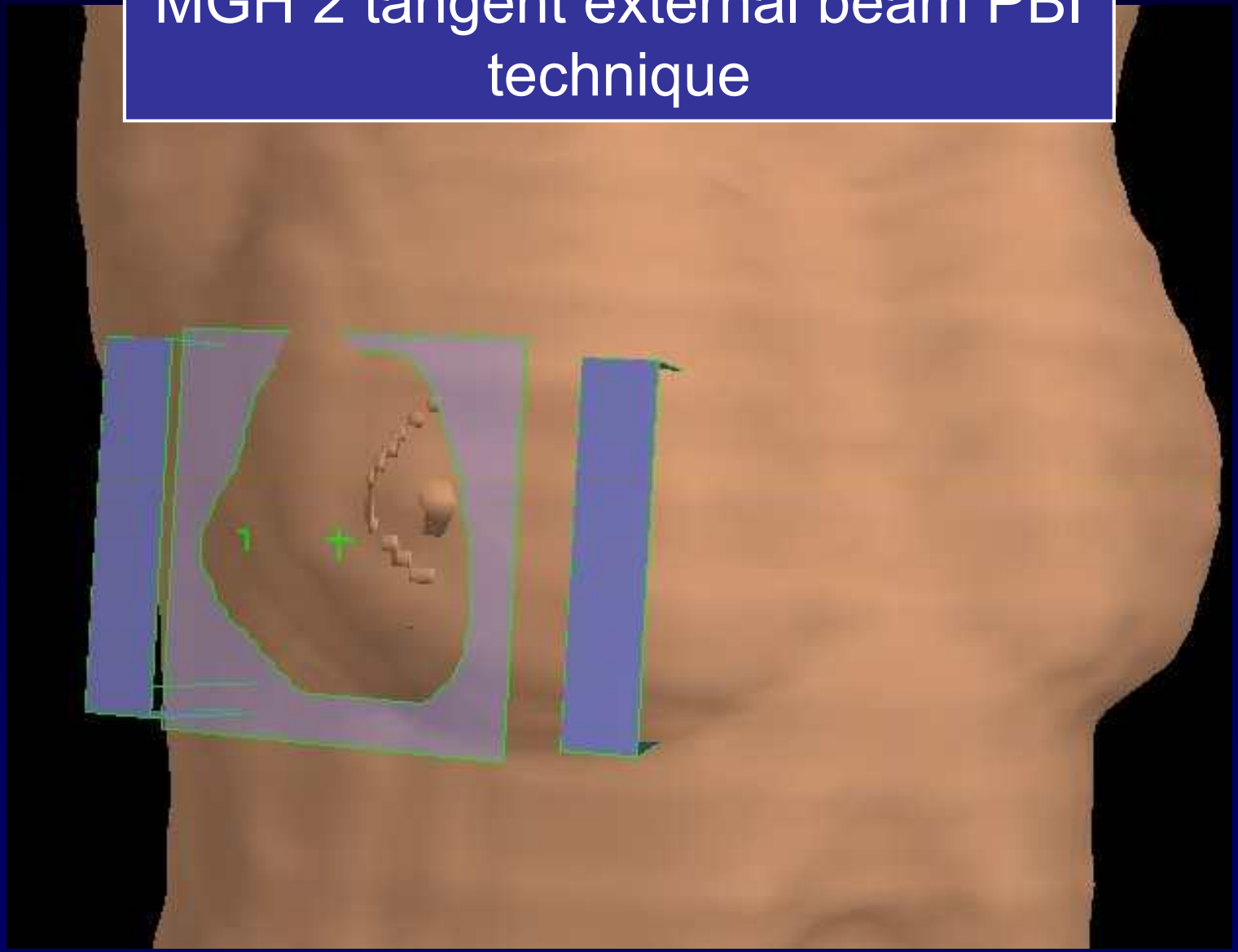
- Lumpectomy without radiation: recurrences close to primary tumor site
- Radiate only region of primary?
  - Reduces dose to non target tissue, heart, lung
  - Shorter treatment time
  - Lower cost with some techniques
  - Potential for re-irradiation for new primary

Standard whole breast irradiation

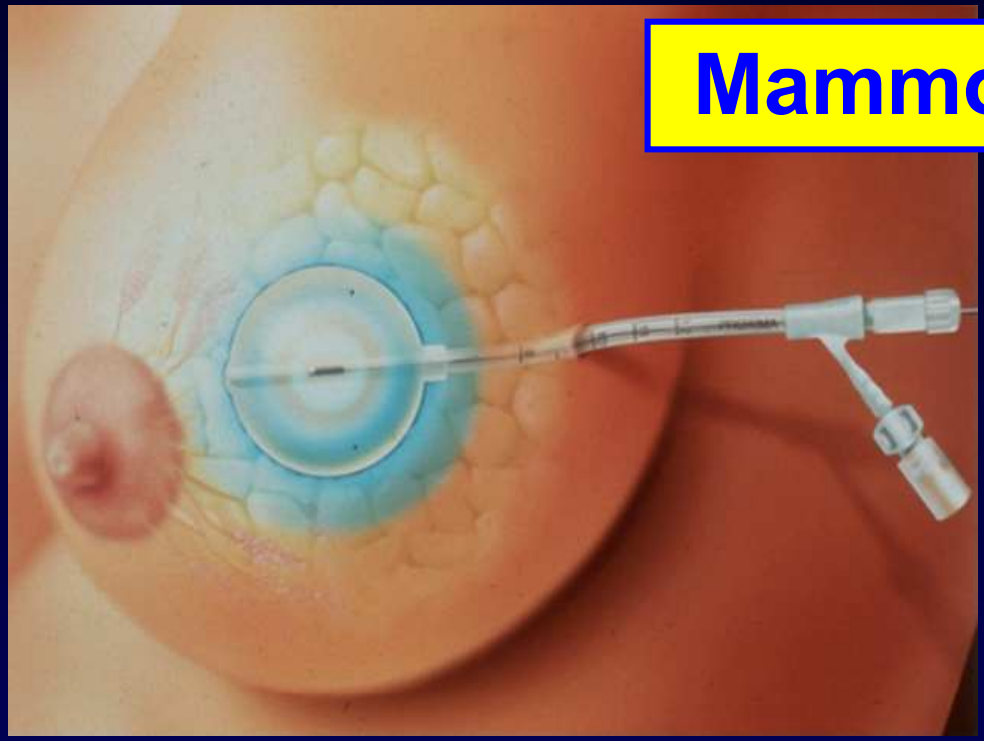
Partial breast irradiation

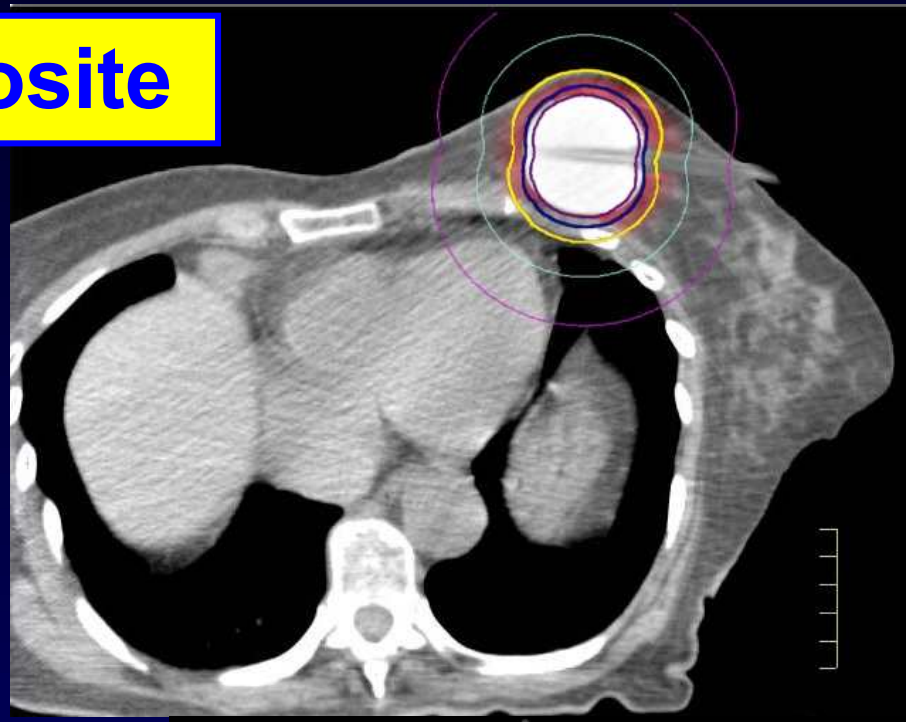


MGH 2 tangent external beam PBI technique

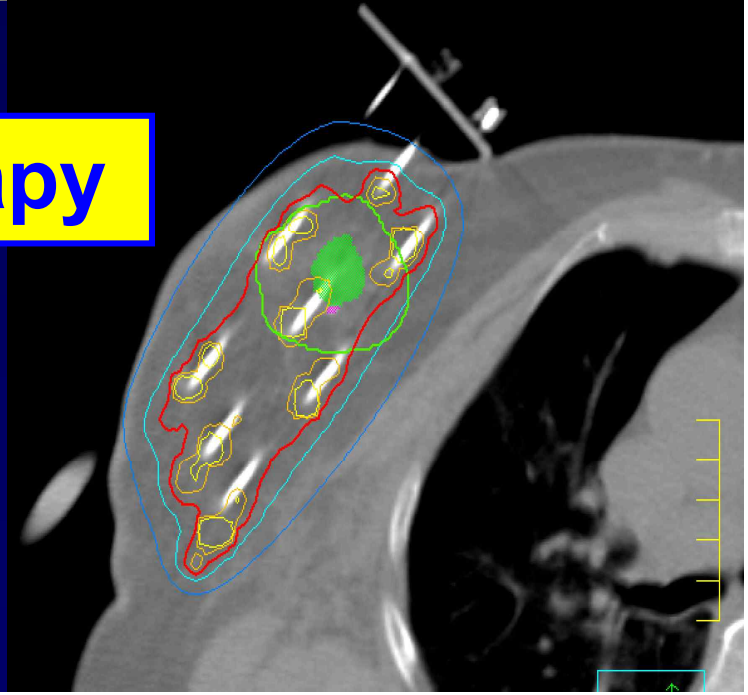


Mammosite





Brachytherapy



Brachytherapy and Mammosite

- Catheter placed during surgery or as separate procedure
  - 10 fractions over 5 days
- Mammosite: dose to 0.5-1.0 cm margin
  Brachytherapy: dose to 1-1.5 cm margin
- Early data good local control
- Limitations of placement, skin spacing, infections, cavity conformity, **fibrosis**

Proton PBI (2 fields) after Lumpectomy

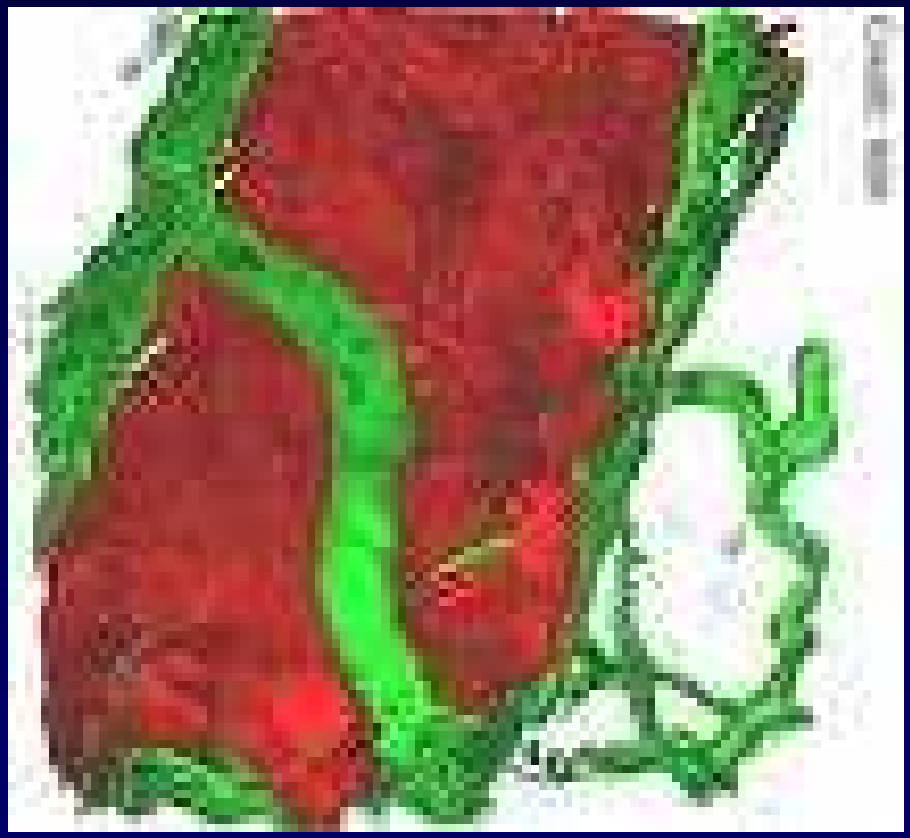
Kozak Int J Radiat Oncol Biol Phys; 66:691, 2006

Lumpectomy Margin Assessment

- Positive margins require re-excision in 20-60% of patients
- Frozen section slow, unreliable
- Touch prep not widely available, inaccurate
- Search for accurate intraoperative margin assessment

Early Data: Ramen Spectroscopy

Quantitative chemical information from unique laser light scattering patterns of tissue components

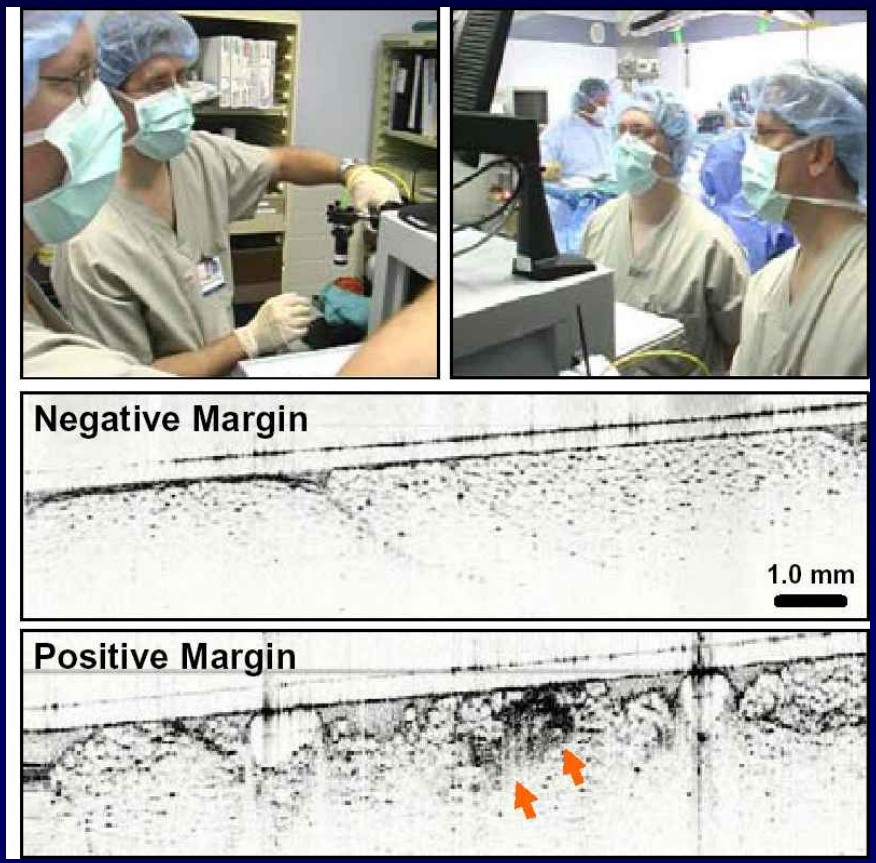


- 31 margins in 9 patients
- 1 second per margin
- 100% sensitivity, 100% specificity malignant vs. benign

Haka Cancer Res 66: 3317, 2006

Early Data: Optical Coherence Tomography

Hsiung Radiology 244:865, 2007



- Measures reflection of near infrared light
- Micron level resolution
- Only few mm depth
- Real time imaging
- 119 specimens 35 women could distinguish normal, invasive, DCIS

Better Lumpectomies: Multiple localizing wires reduce re-excision for larger mammographic lesions

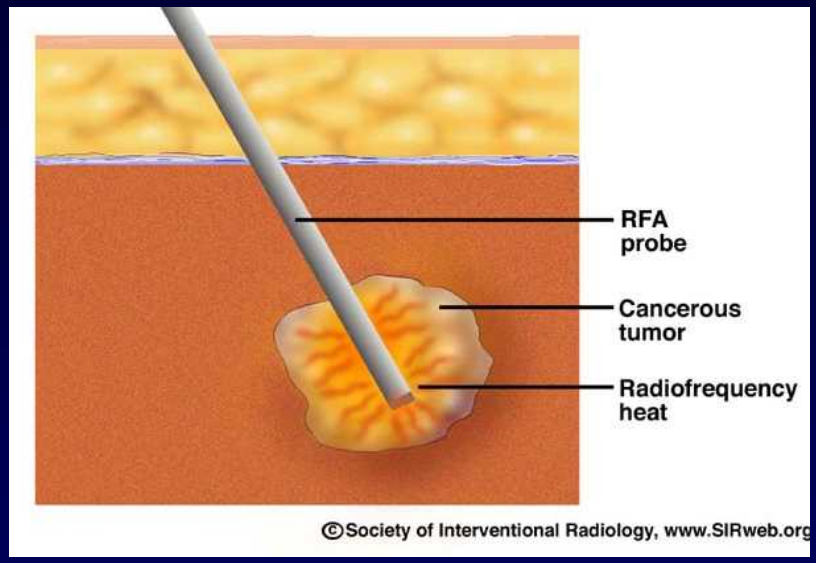
	N	Specimen volume cc	BCS success	Re-excision required	Local failure 24 mo
≥ 2 wires	153	76	77%	20%	1%
1 wire	196	53	90%	34%	1%

L Kirstein, J Am Coll Surg 207:342, 2008

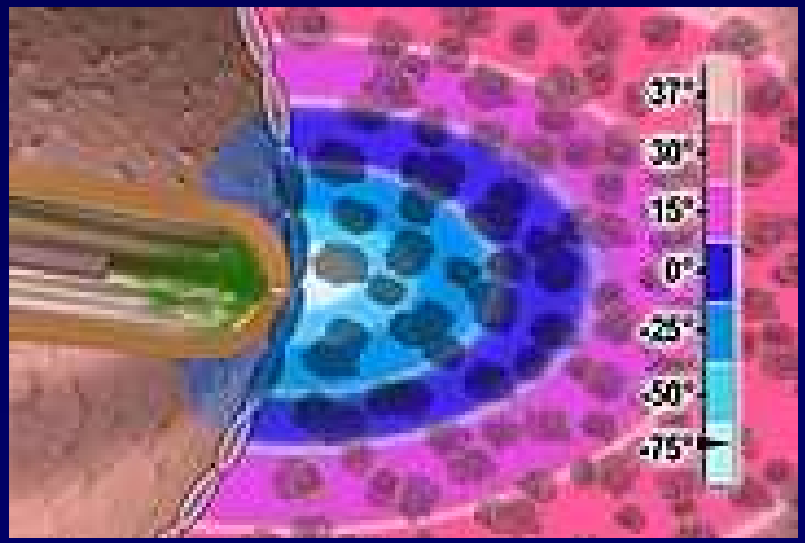
Non-Surgical Tumor Ablation

- Goal: eliminate tumor without surgery
- Used in hepatic metastases
- Breast approaches:
  - Most promising: radiofrequency ablation, cryoablation, laser ablation
  - Focused ultrasound, microwave – limited killing
- 78-96% of tumors complete killing

Tumor ablation techniques



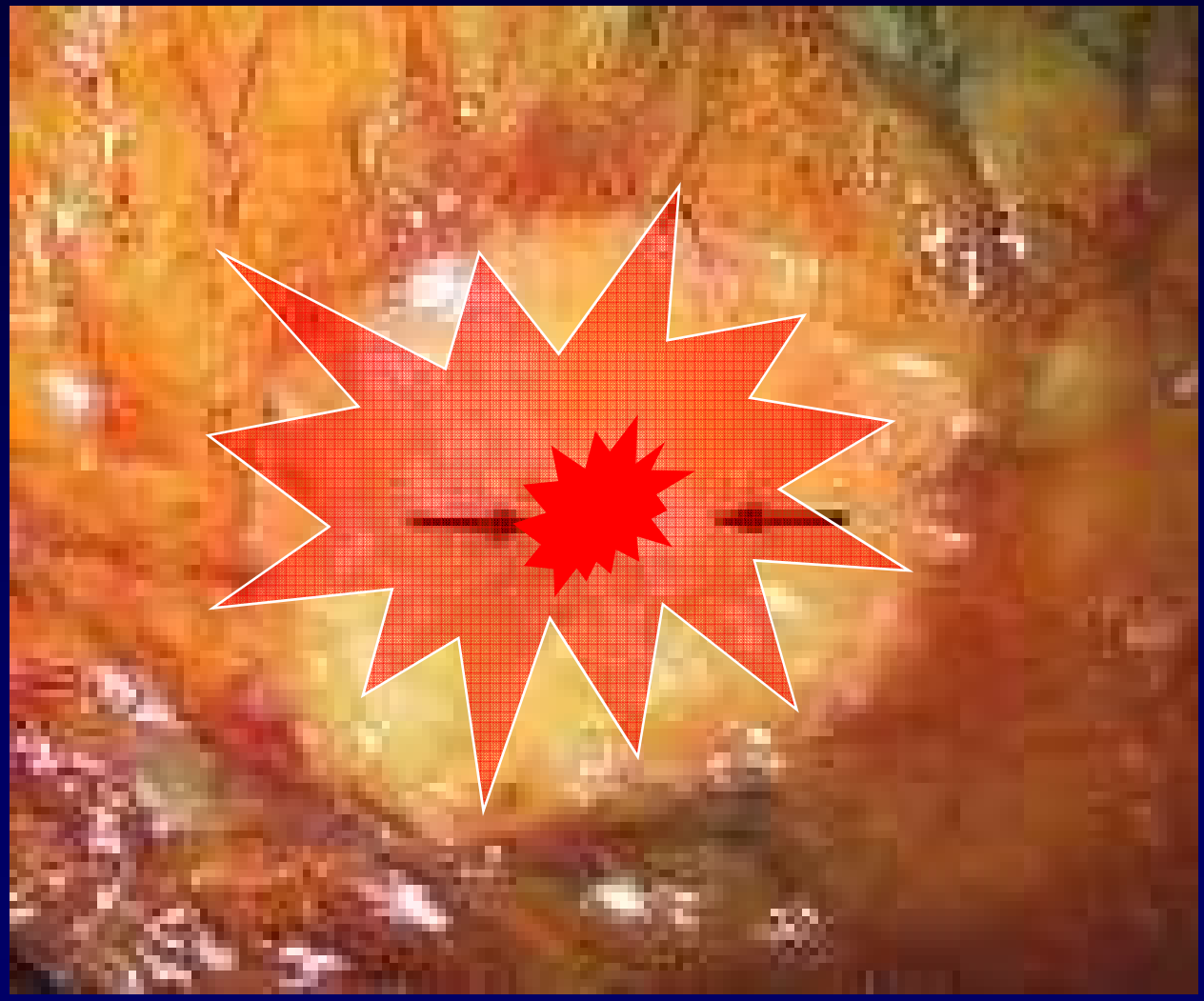
- Radiofrequency probe kills tumors by localized tissue heating
  - 60˚ C x 15 minutes



- Cryoablation kills tumors by localized tissue freezing
  - Liquid nitrogen iceball

Tumor (arrows) and surrounding tumor ablation

BUT – What about additional tumor foci or DCIS beyond central tumor mass targeted?



Local control with ablation alone

	Method	N	f/u (mo)	Local control
Marcy 2007	RF	5 T1-2	29	4/5 1 abscess All: 4-5 cm mass
Akimov 1998	laser	7		5/7

Limitations of ablation techniques

- Imaging limitations prevent precise ablation
  - Early local recurrence 20-30% in pilot series
  - No data on ablation plus radiation
- Fat necrosis at ablation site
  - Persistent mass
  - Imaging abnormalities
- Skin and muscle burns

Conclusion: Breast surgeons are still needed (for now)

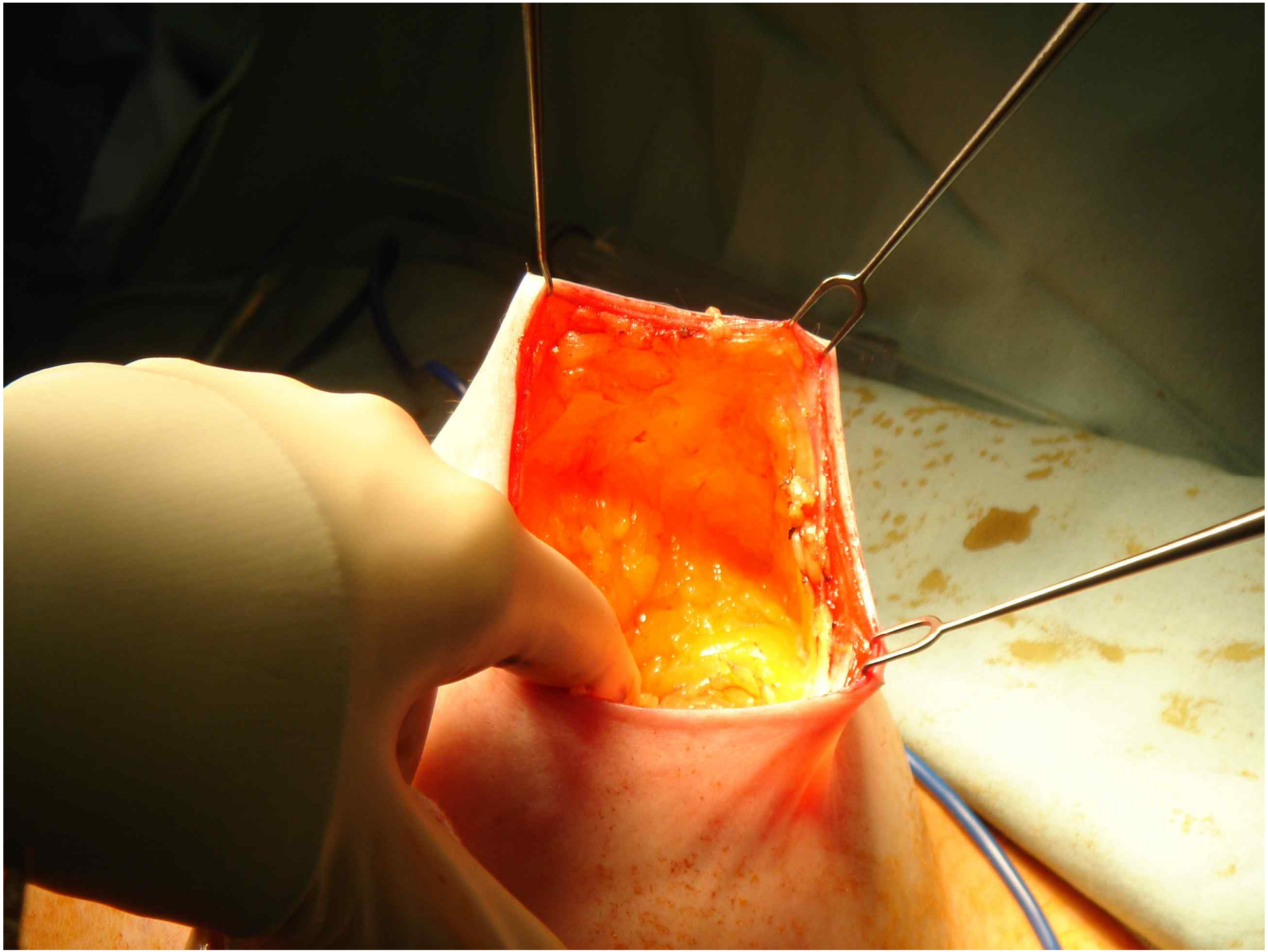
Impact of New Imaging Modalities on Local Therapies

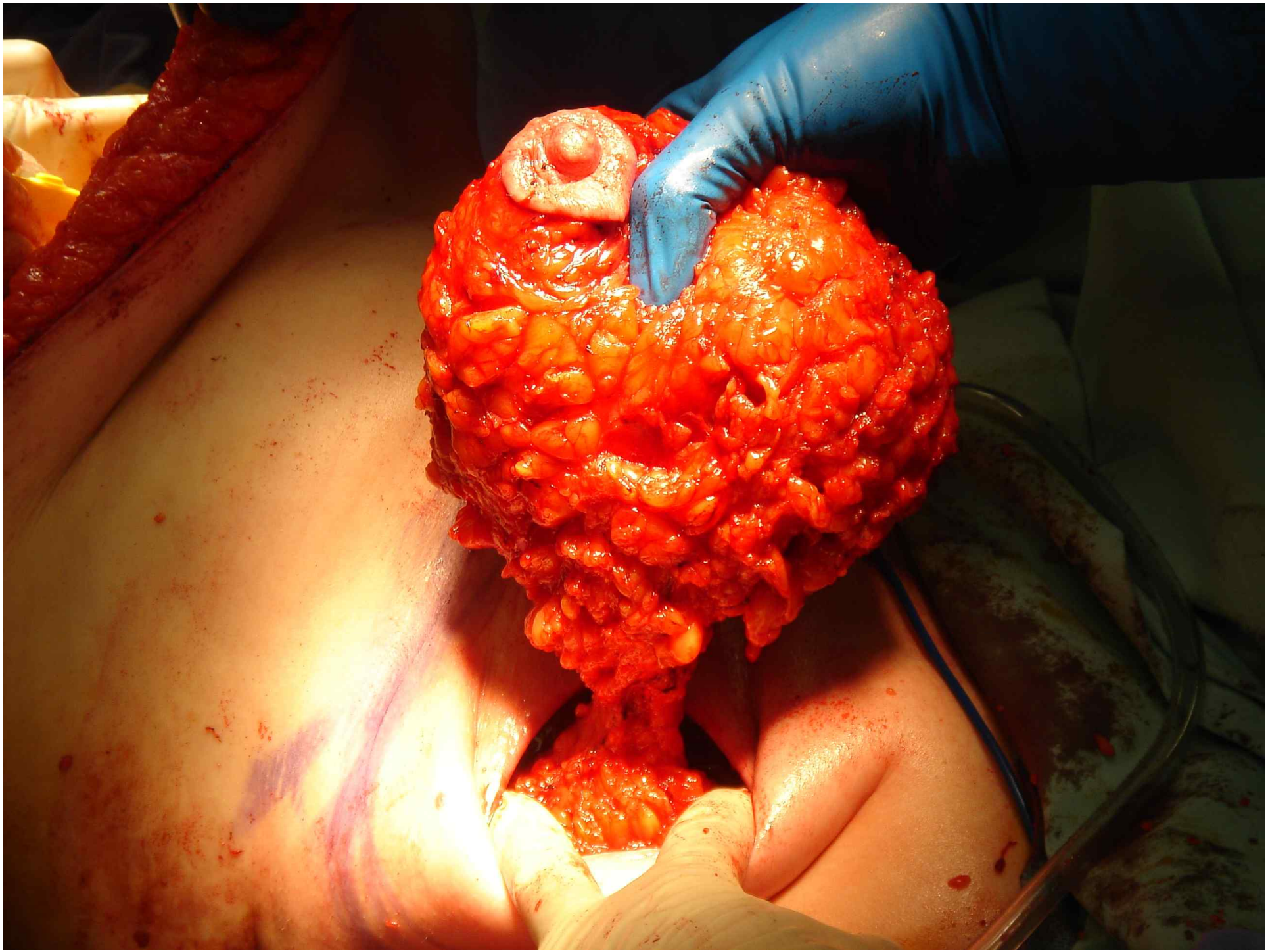
- Better imaging to guide surgery, ? ablation
  - Digital mammography
  - MRI advances
  - Digital Tomosynthesis
  - BSGI
- Imaging for non-surgical axillary staging

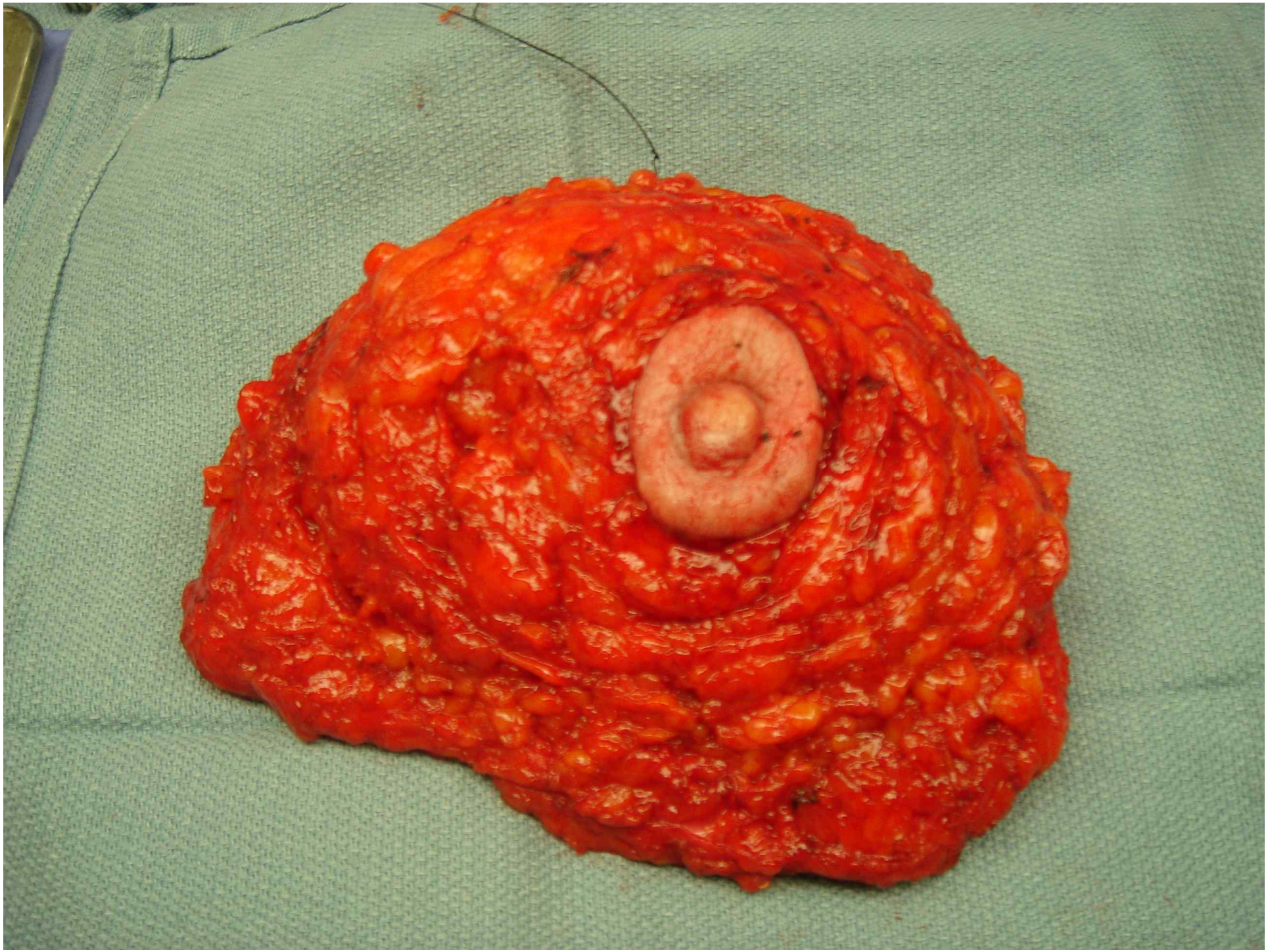
Recent Advances in Local Therapy Mastectomy Innovations

- Immediate reconstruction – more options
  - Single stage implants, expanders, TRAM, DIEP, latiissimus dorsi, gracilis, etc.
- Skin-sparing mastectomy
- Areola-sparing mastectomy
- Nipple sparing mastectomy


Skin-sparing Mastectomy Incision







Nipple Sparing Mastectomy Issues

- Oncologic safety
  - Low risk of clinical nipple involvement
  - Proper margin assessment
- Technical issues
  - Remove ducts but preserve vessels
- Cosmetic issues
  - Incision placement
  - Nipple location

DCIS Involving Nipple Ducts

Patient Selection

- Acceptably low risk of nipple involvement
  - Prophylactic mastectomies
  - Tumor >2 cm from nipple, negative imaging
- Patient informed that positive margin will require nipple resection
- Small to moderate-sized breast, minimal ptosis
  - Options for concurrent mastopexy
- Well vascularized skin

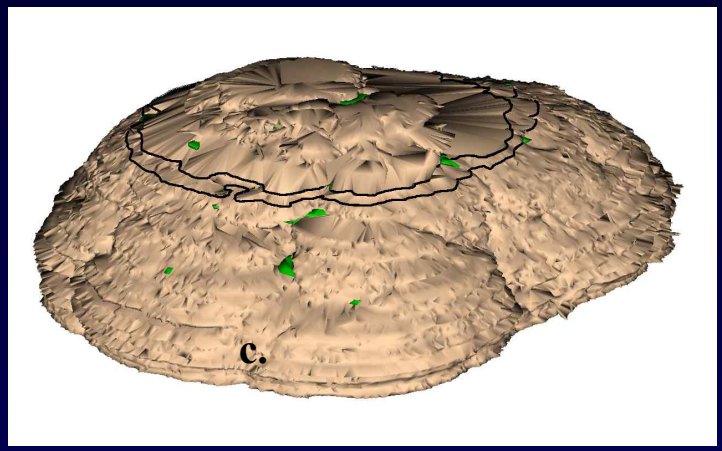
Occult Nipple Involvement MGH Series: 319 consecutive mastectomies Brachtel JCO 2009

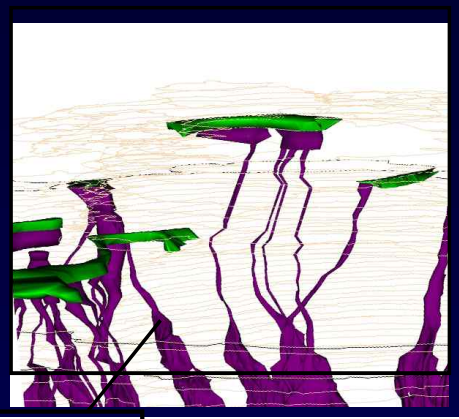
Nipple involvement by tumor:

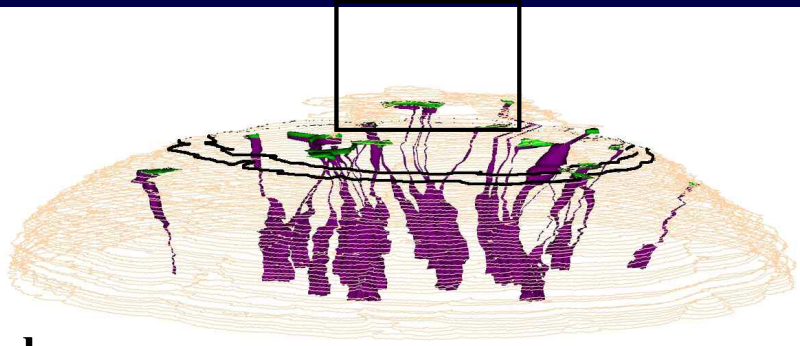
- 0/84 nipples from prophylactic mastectomies
- 52/235 (22%) nipples from cancer-bearing mastectomies contained tumor:
  - 39 Ductal carcinoma in-situ (DCIS)
  - 6 Invasive ductal carcinoma (IDC)
  - 5 Invasive lobular carcinoma (ILC)
  - 8 Lymphovascular invasion (LVI)

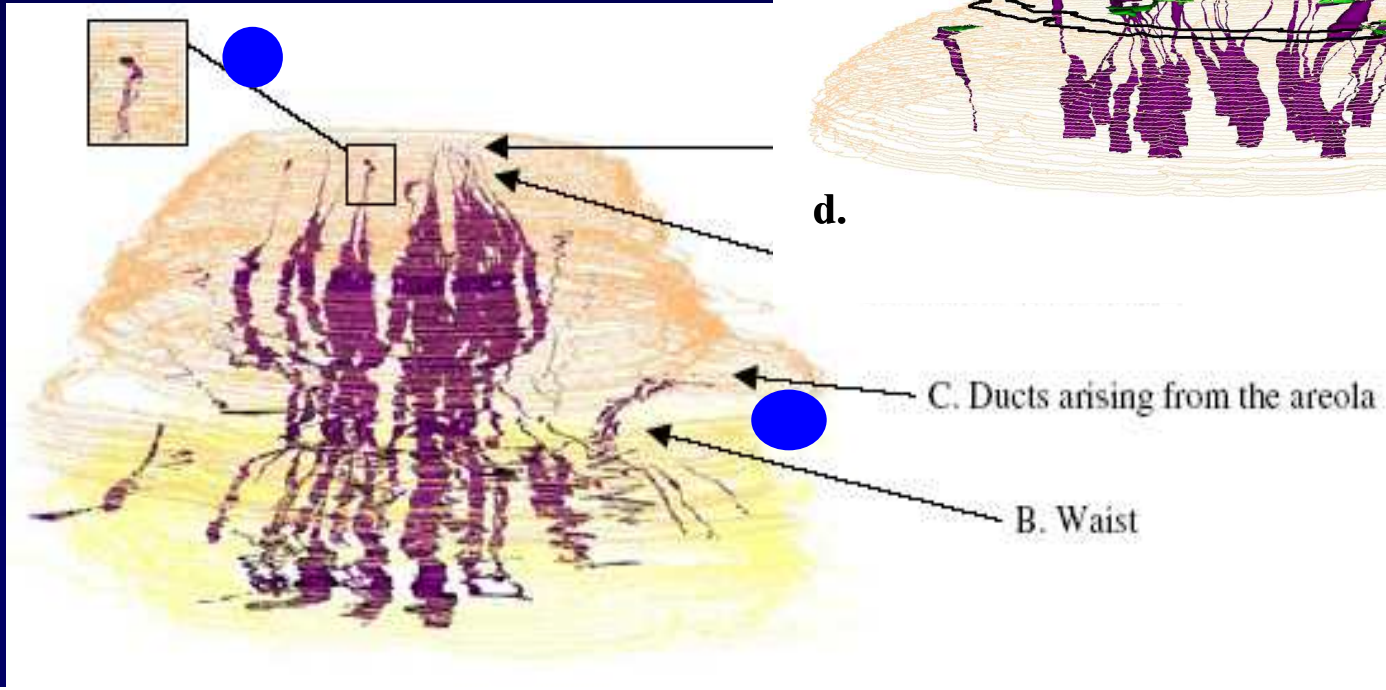
3-D Nipple Anatomy

Rusby et al. Breast Cancer Res Treat 106:171-9 2007









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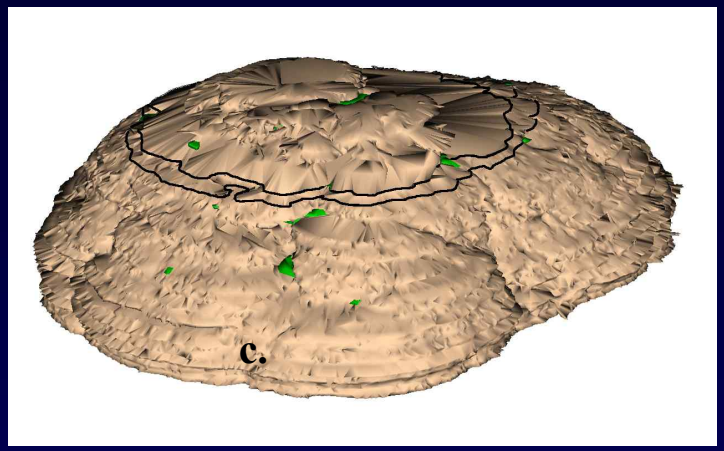

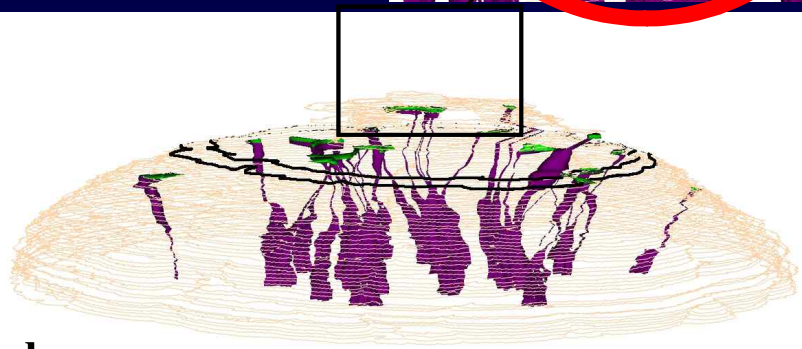

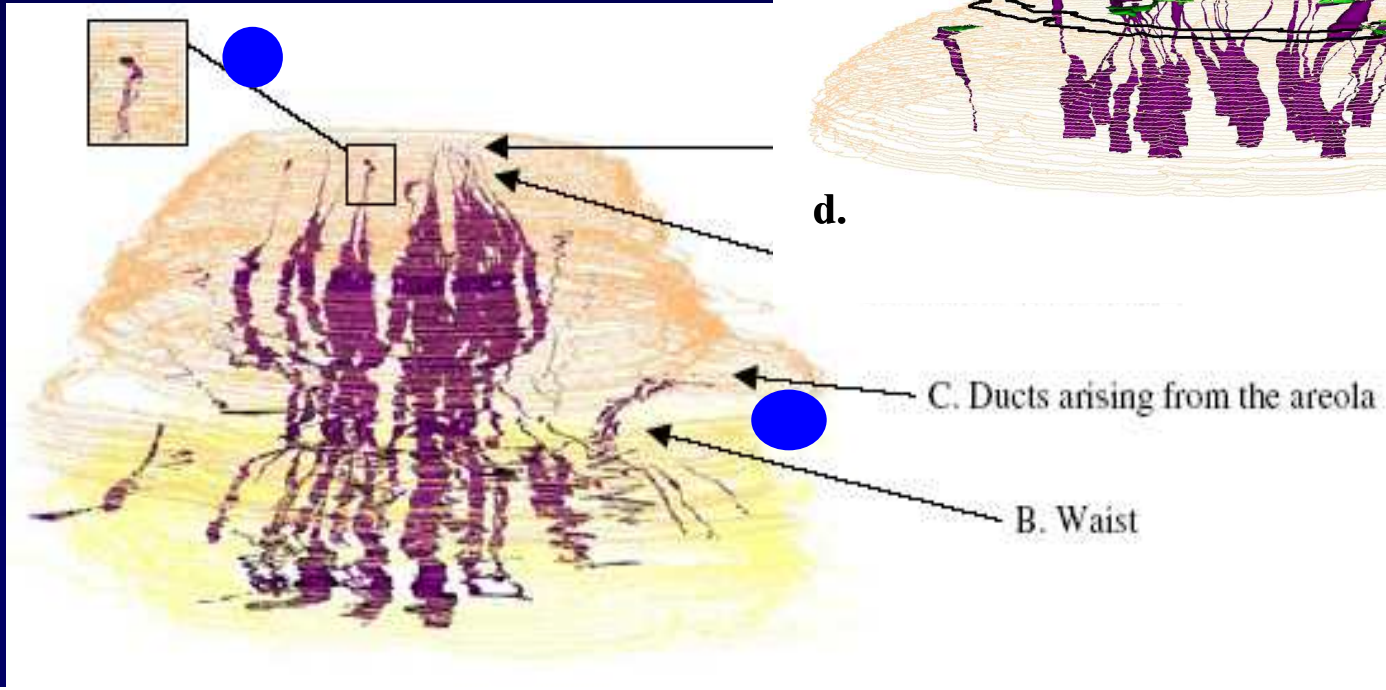

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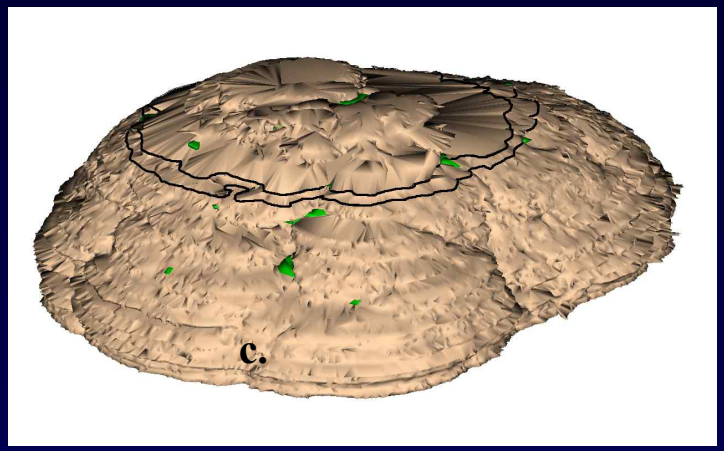
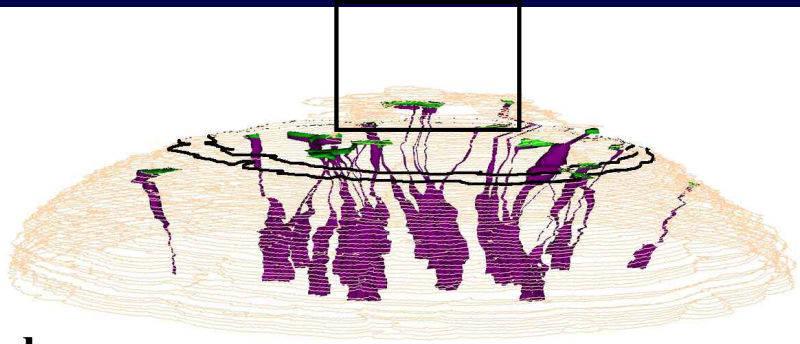
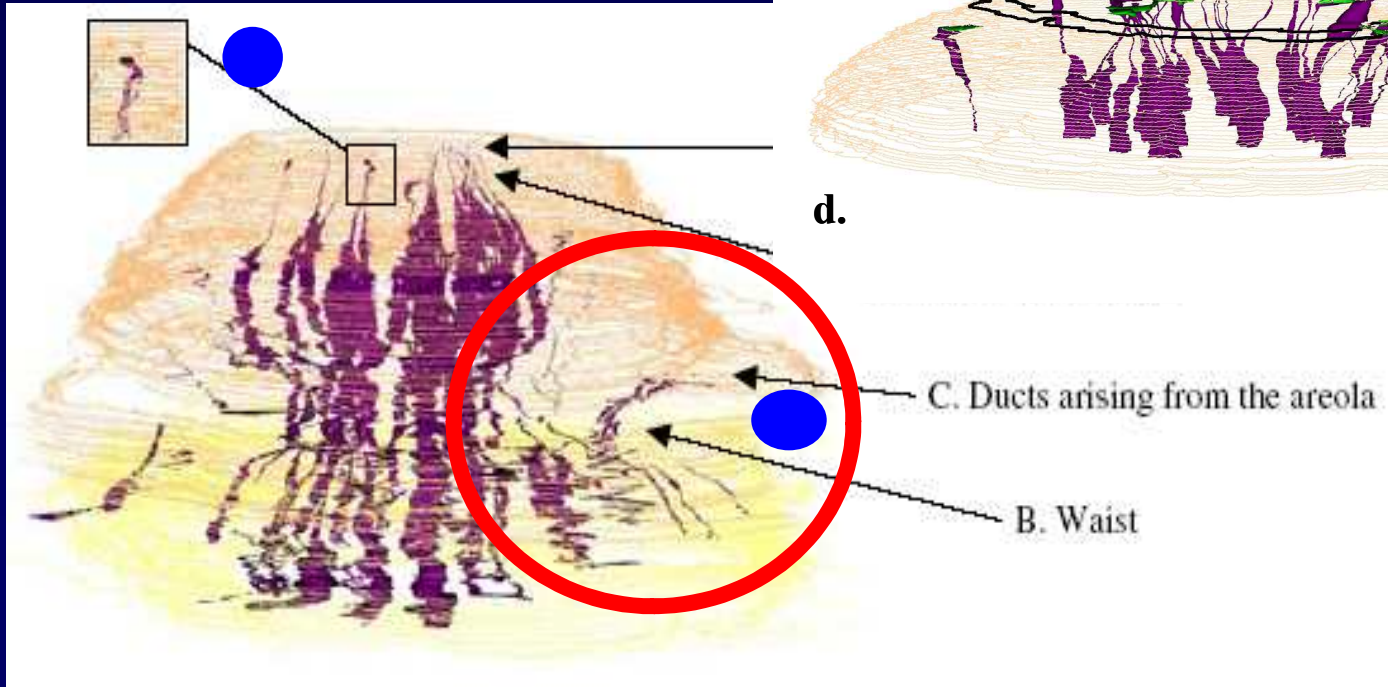
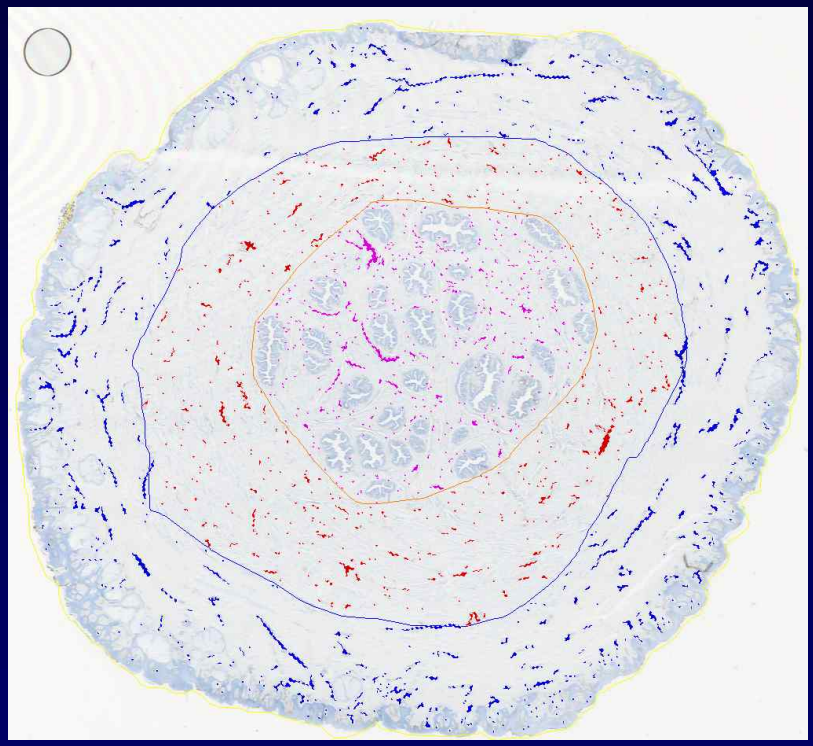


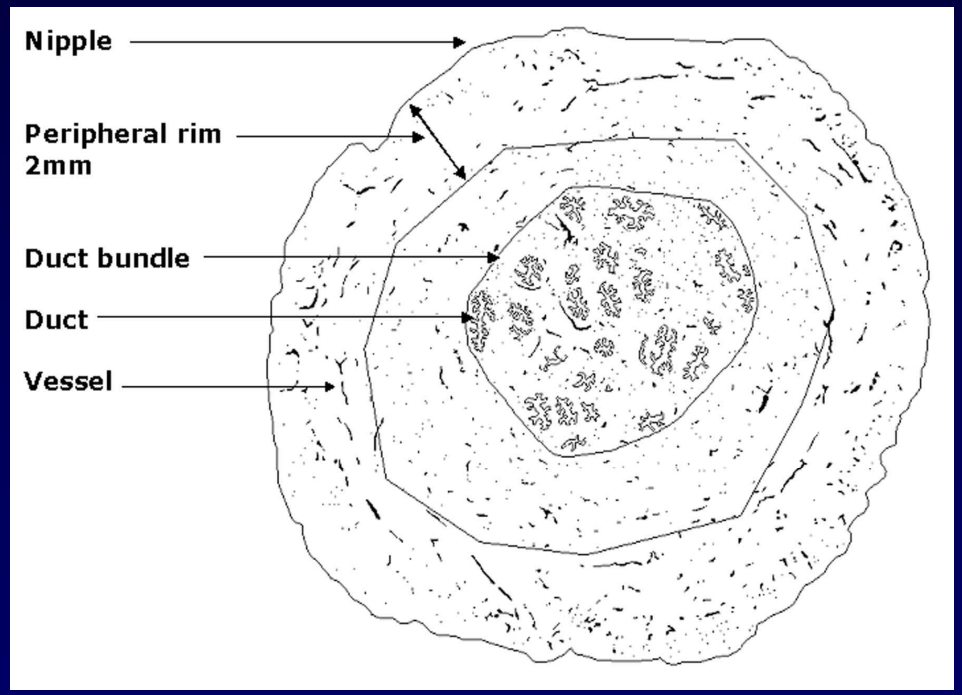




Distribution of vascular structures

Rusby et al. Am J Surg 194:433, 2007

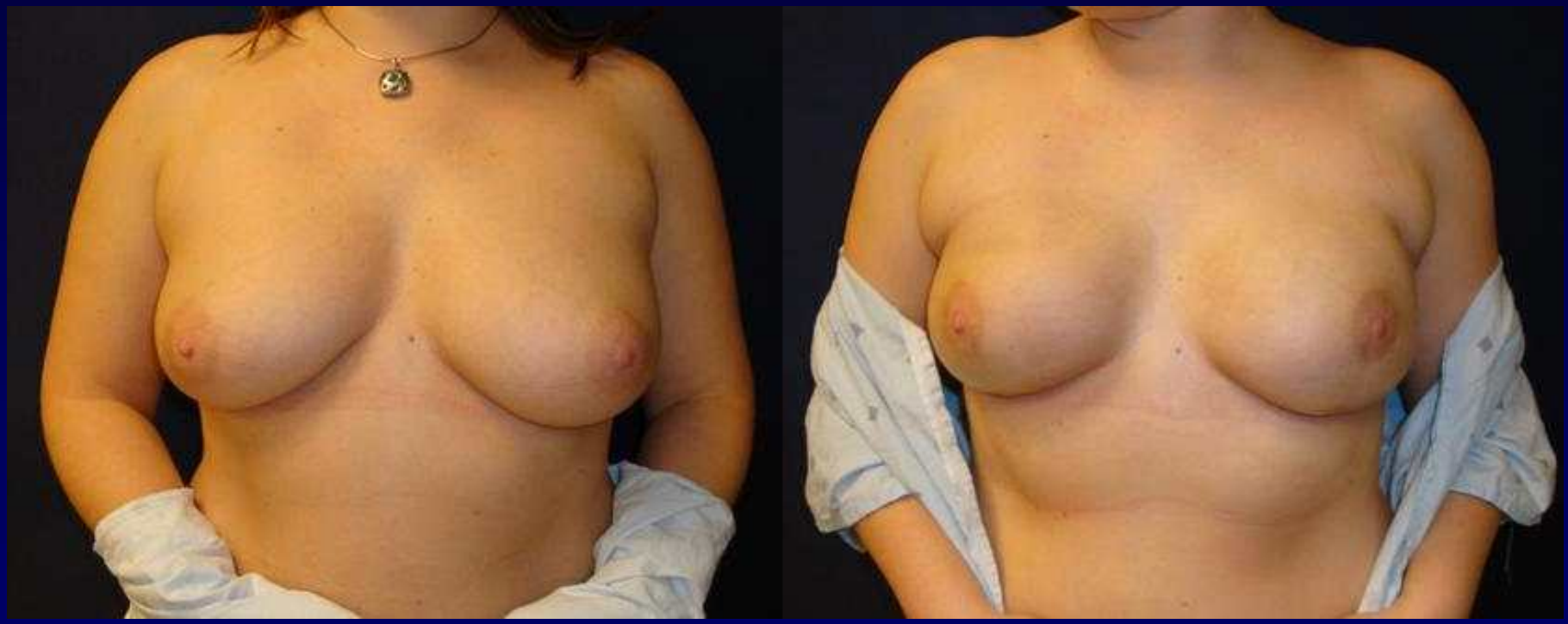




BRCA gene mutation, L UOQ cancer scar, old R bx scar

Bilateral nipple sparing, UOQ incisions, 3 mo postop

BRCA gene mutation, left cancer
Bilateral nipple sparing, implants
lateral inframammary incision



Pre-op **1 month post op**

Right lumpectomy and radiation, local recurrence

Right nipple sparing mastectomy, lateral incision, 6 wks post-op

Other Important Areas in Local Therapy Research

- Role of local therapy in patients with Stage IV breast cancer – Dr. Mehra Golshan
- Sentinel node biopsy – Dr. Wonshik Han