

Breast Surgery: Where Change is the Only Constant and Personalized Care is Key

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Aims:

- **Breast Conservation:** Discuss history & outcomes, newer techniques, and expanded indications
- **Nipple Sparing Mastectomy:** Review outcomes, patient selection, technical considerations, and nerve preservation
- **Axillary Surgery:** When to consider omitting axillary surgery and avoiding axillary lymph node dissection
- **Treatment Order:** How to decide who gets surgery or chemotherapy first considering patient and tumor factors

Breast Conservation Therapy (BCT)

Historical Perspective

Modern Era

Quality of Life

Moving Past Contraindications

History of Breast Conservation

1980s: Randomized controlled trials published showing equivalent survival results of BCT and mastectomy

- **BCT= lumpectomy + radiation**

1990: BCT endorsed by NIH as standard of care for early-stage breast cancer

1998-2005: BCT rates increased

2006: BCT rates started to decline as mastectomy rates increased, especially bilateral mastectomy + reconstruction

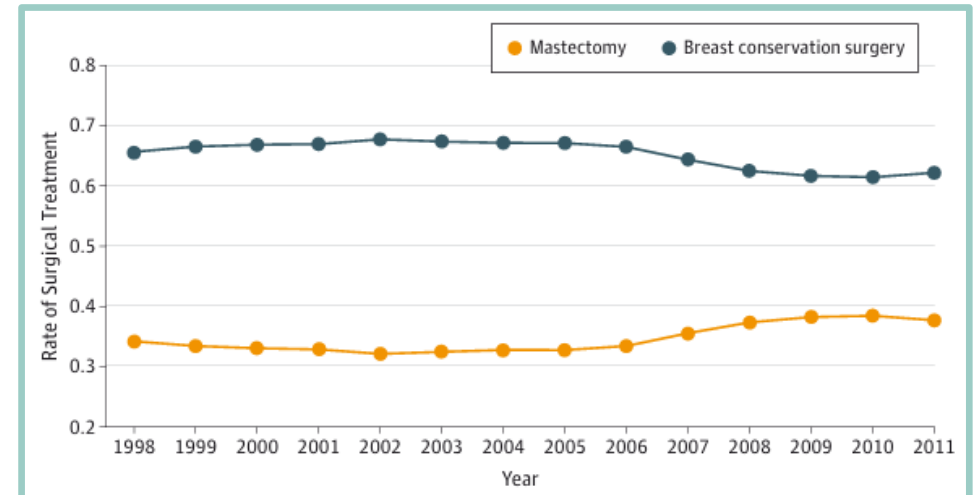
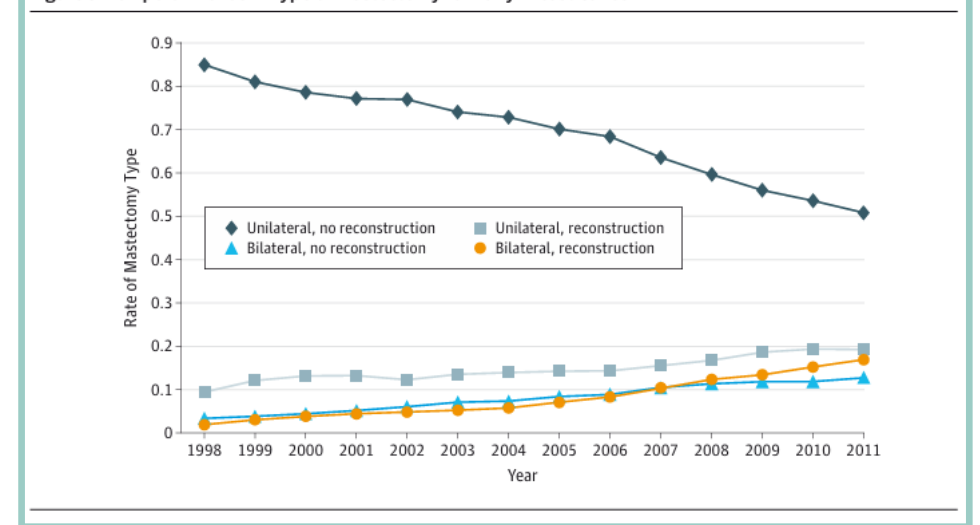


Figure 3. Temporal Trends in Type of Mastectomy for Early Breast Cancer



Pak L, *Expert Rev Anticancer Ther* 2022; 22(5): 535.
Kummerow KL, *JAMASurg* 2015;150(1):9.

Landmark Trial: BCT vs Mastectomy

COMPARING RADICAL MASTECTOMY WITH QUADRANTECTOMY, AXILLARY DISSECTION, AND RADIOTHERAPY IN PATIENTS WITH SMALL CANCERS OF THE BREAST

UMBERTO VERONESI, M.D., ROBERTO SACCOZZI, M.D., MARCELLA DEL VECCHIO, PH.D., ALBERTO BANFI, M.D., CLAUDIO CLEMENTE, M.D., MARIO DE LENA, M.D., GIUSEPPE GALLUS, PH.D., MARCO GRECO, M.D., ALBERTO LUINI, M.D., ETTORE MARUBINI, PH.D., GIUSEPPE MUSCOLINO, M.D., FRANCO RILKE, M.D., BRUNO SALVADORI, M.D., ANNAMARIA ZECCHINI, AND ROBERTO ZUCALI, M.D.

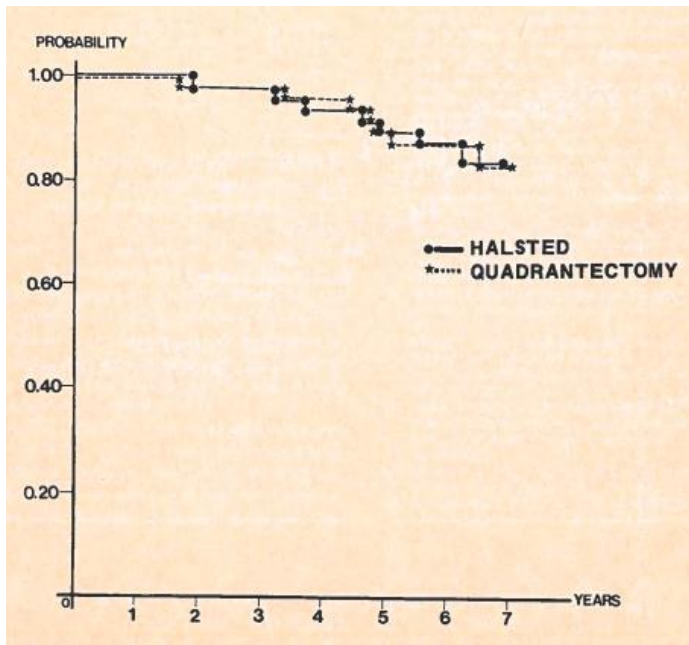


Table 6. Actuarial Five-Year Survival (Mean $\pm$ S.E.M.) in Patients Treated with Halsted Mastectomy or Quadrantectomy.

VARIABLE	TREATMENT	
	HALSTED	QUADRANTECTOMY
	percentage of patients	
Overall survival	90.1 $\pm$ 2.5	89.6 $\pm$ 2.6
Disease-free survival		
All patients	83.0 $\pm$ 2.8	84.0 $\pm$ 2.8
Patients with negative lymph nodes	89.1 $\pm$ 2.4	86.5 $\pm$ 2.98
Patients with positive lymph nodes	62.0 $\pm$ 9.0	77.5 $\pm$ 6.3

- 1973-1980
- Milan Institute Trial
- RCT, clinical T1N0
 - 349 Radical Halsted Mastectomy
 - 352 Quadrantectomy, ALND, Radiation
- **RT: 50 Gy + 10 Gy boost over 6 wks**
- CMF chemo for LN+

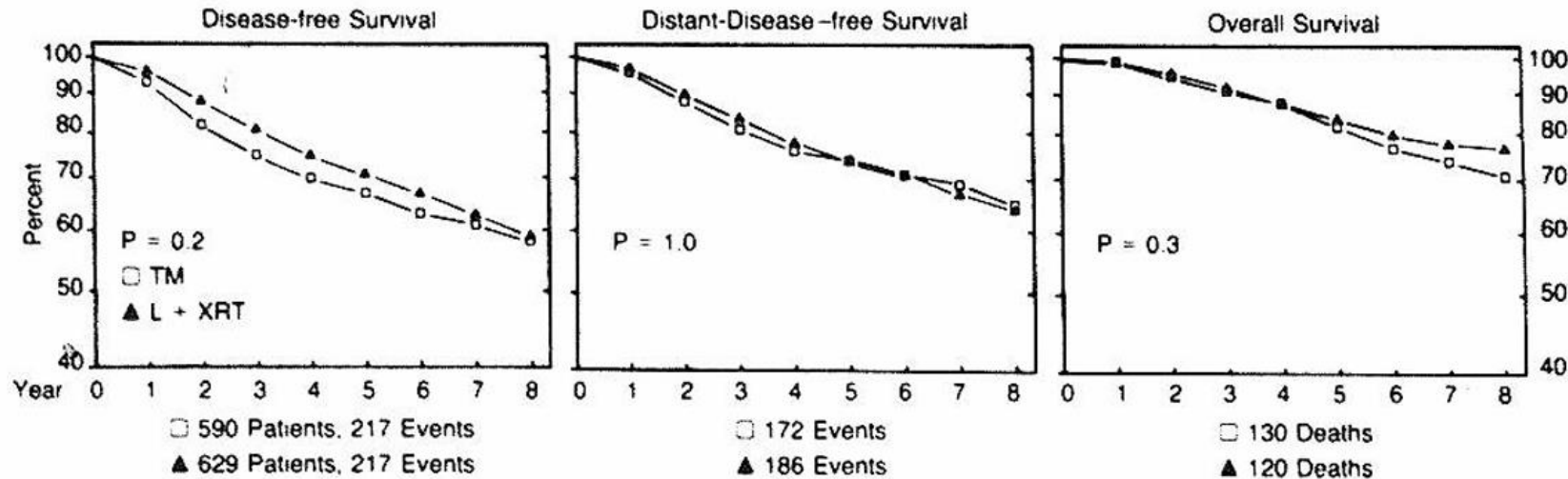
****No Difference in Overall or Disease-Free Survival****

Veronesi U, *N Engl J Med* 1981;305:6.

Landmark Trial: BCT vs Mastectomy

EIGHT-YEAR RESULTS OF A RANDOMIZED CLINICAL TRIAL COMPARING TOTAL MASTECTOMY AND LUMPECTOMY WITH OR WITHOUT IRRADIATION IN THE TREATMENT OF BREAST CANCER

BERNARD FISHER, M.D., CAROL REDMOND, Sc.D., ROGER POISSON, M.D., RICHARD MARGOLESE, M.D., NORMAN WOLMARK, M.D., LAWRENCE WICKERHAM, M.D., EDWIN FISHER, M.D., MELVIN DEUTSCH, M.D., RICHARD CAPLAN, Ph.D., YOSEF PILCH, M.D., ANDREW GLASS, M.D., HENRY SHIBATA, M.D., HARVEY LERNER, M.D., JOSE TERZ, M.D., AND LYNNE SIDOROVICH



- 1976-1984
- NSABP B-06
- RCT, Stage I-II
 - 590 Total Mx + ALND
 - 636 lump + ALND
 - 629 lump + ALND + RT
- **RT: 50 Gy over 5wks**
- All LN+ received chemo

****No Difference in Overall or Disease-Free Survival****

Fisher B, *N Engl J Med* 1989;320:822.

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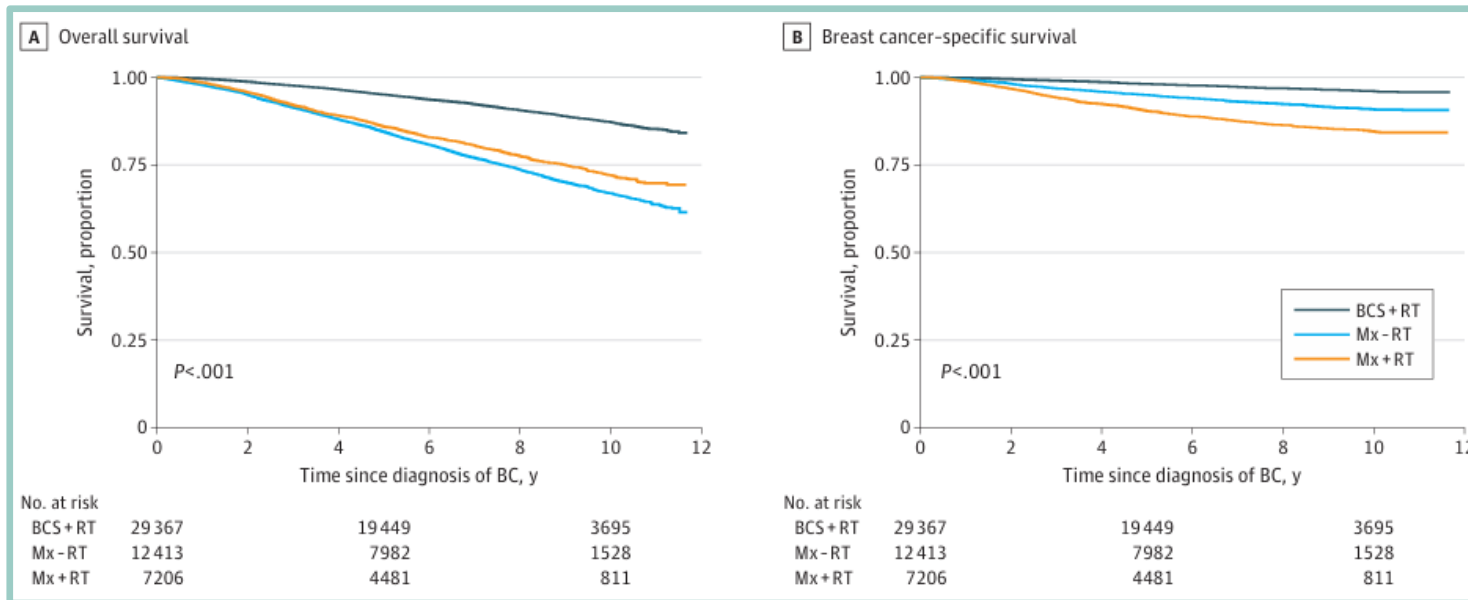
Sept 18, 2026

Outcomes of BCT vs Mastectomy: Modern Era

JAMA Surgery | Original Investigation

Survival After Breast Conservation vs Mastectomy Adjusted for Comorbidity and Socioeconomic Status A Swedish National 6-Year Follow-up of 48 986 Women

Jana de Boniface, PhD; Robert Szulkin, PhD; Anna L. V. Johansson, PhD

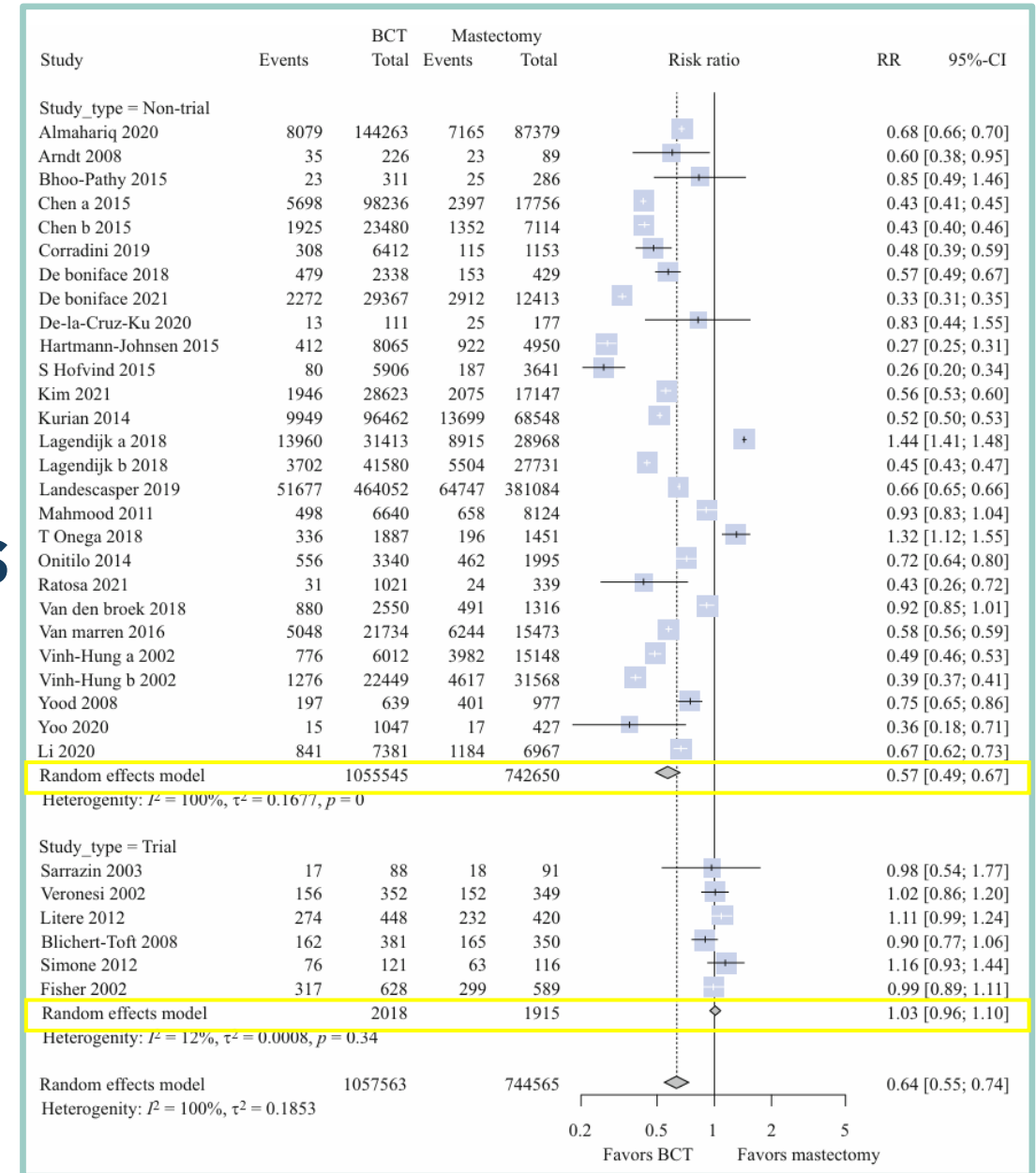


*adjusted for tumor characteristics, treatment, demographics, comorbidity, SES

- 48,986 women, Swedish National Breast Cancer Registry, **2008-2017**
- T1-2 N0-2 breast cancer
- OS and BCSS were better with BCT vs Mastectomy (Mx) +/- Radiation Therapy (RT)*
- **Conclusion:** If both BCT and Mx are options, Mx should NOT be regarded as equal to BCT

Outcomes of BCT vs Mastectomy: Modern Era

- Meta-Analysis, 30 studies, published **2002-2021**
- 1.8 Million Women, Stage I-III breast cancer treated with upfront surgery
- Follow-up ranged from 4-20 yrs
- **BCT was associated with improved OS** compared to mastectomy in both RCT (RR 0.64) and cohort studies (RR 0.57)
- **Conclusion:** "This meta-analysis demonstrates that OS is better in patients who undergo BCT compared to mastectomy"



Proposed Theories for Survival Advantage of BCT over Mastectomy in Modern Era

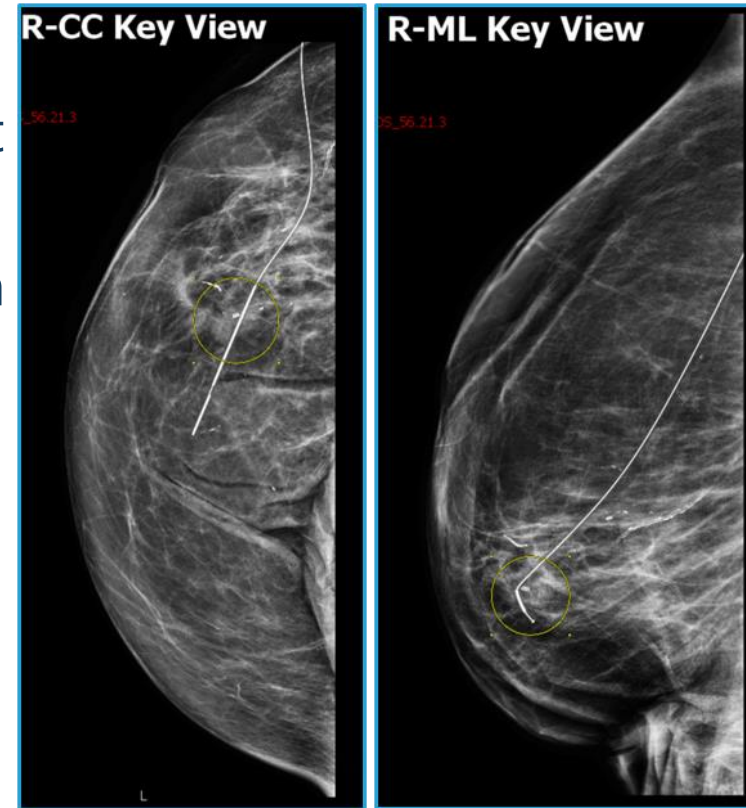
- **Improvements in Radiation Therapy**
 - Better planning and techniques to avoid organ damage
- **Improvements in Systemic Therapy**
 - More effective treatments
 - Less toxicity
- **Improvements in Breast Imaging**
 - 3D mammograms, MRIs, localization techniques, specimen imaging
- **Improvements in Breast Pathology**
 - Better margin assessment

Improvements in Localization Techniques: Original Wire Localization

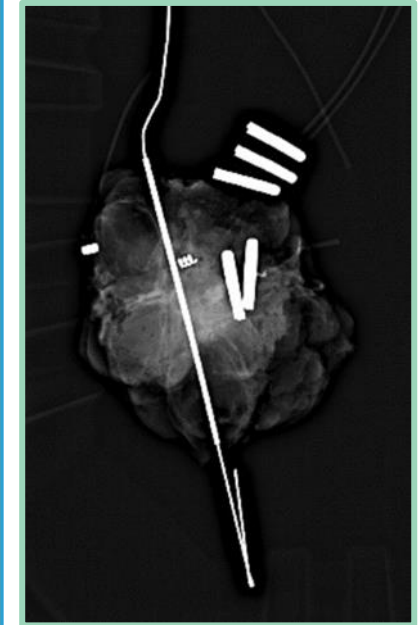
- Developed in the late 1970s to localize non-palpable breast lesions

- **Cons:**

- Proximal wire protrudes from breast
- Must be performed day of surgery
- Risk of wire migration or transection
- Cannot easily localize lymph nodes



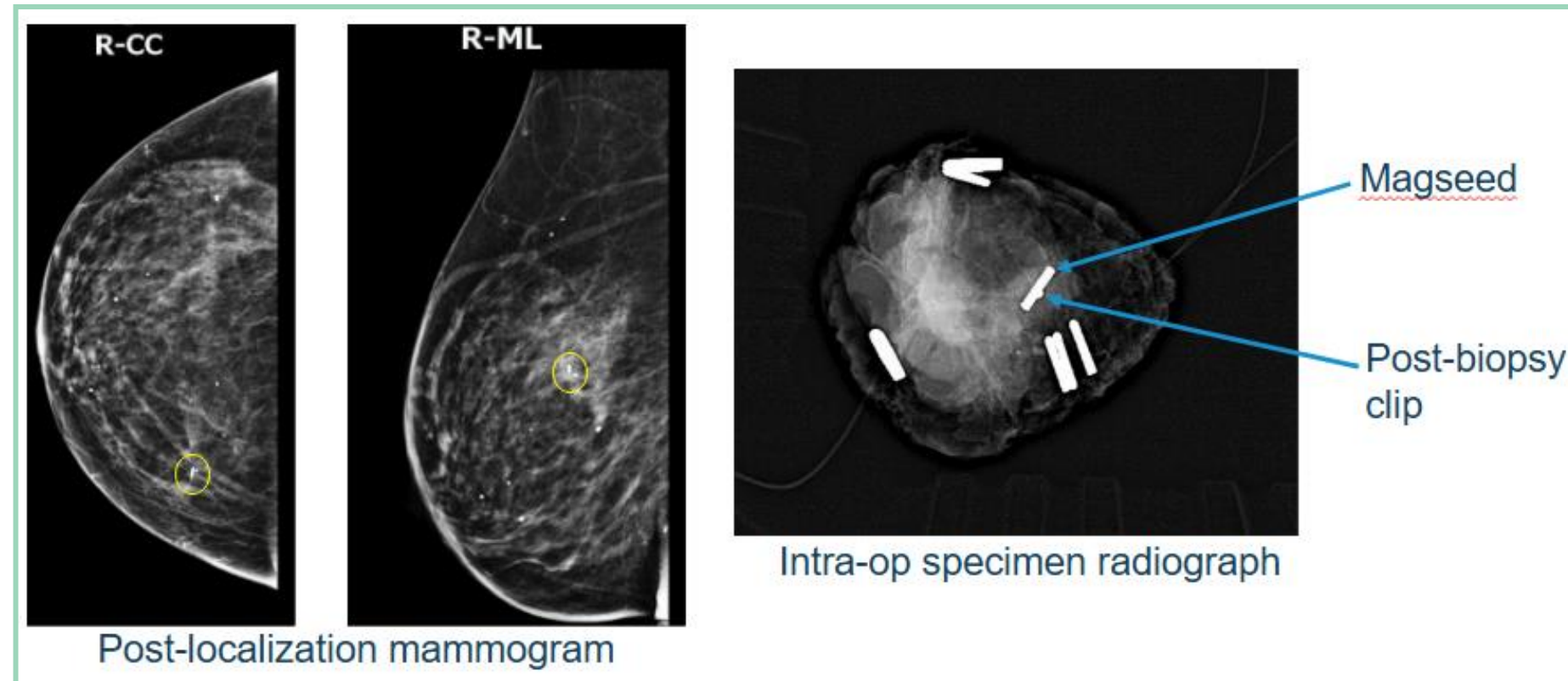
Post-localization mammogram



Intra-op
specimen
radiograph

Improvements in Localization Techniques: Wireless Localization Methods

- 2001: Radioactive Seed, ^{125}I -labeled 5mm titanium implant
- 2015: Infrared Radar Reflector Seed
- 2016: Magnetic Seed
- 2017: Radiofrequency ID Seed



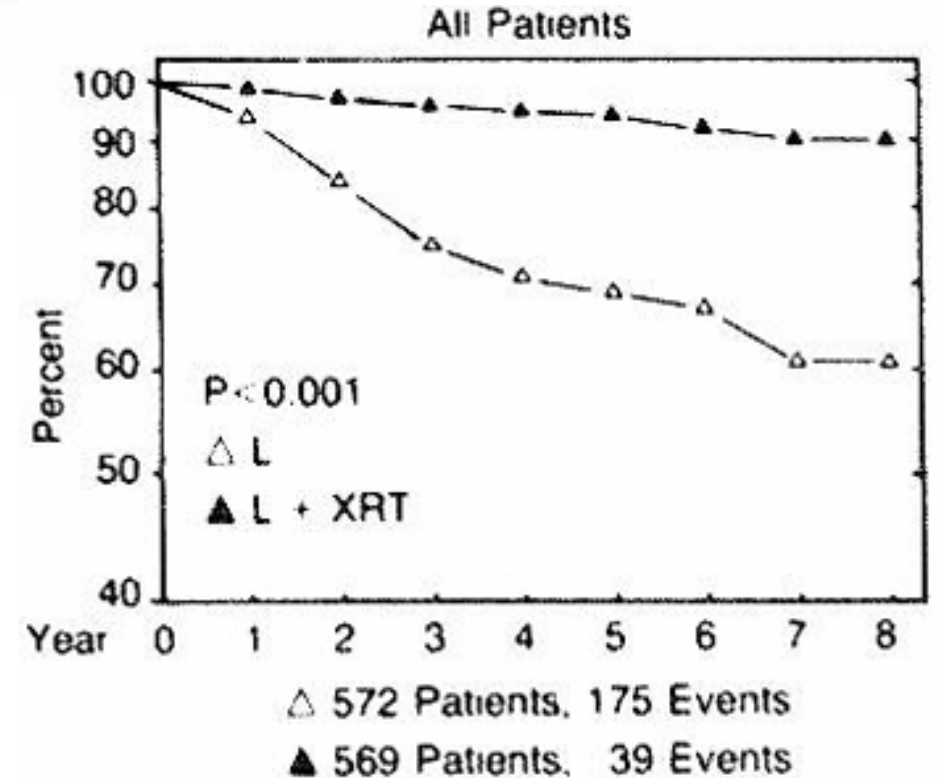
Kapoor MM, *RadioGraphics* 2019; 39:1886.

Landmark Trial: Lumpectomy vs Lumpectomy + RT

EIGHT-YEAR RESULTS OF A RANDOMIZED CLINICAL TRIAL COMPARING TOTAL MASTECTOMY AND LUMPECTOMY WITH OR WITHOUT IRRADIATION IN THE TREATMENT OF BREAST CANCER

BERNARD FISHER, M.D., CAROL REDMOND, Sc.D., ROGER POISSON, M.D., RICHARD MARGOLESE, M.D., NORMAN WOLMARK, M.D., LAWRENCE WICKERHAM, M.D., EDWIN FISHER, M.D., MELVIN DEUTSCH, M.D., RICHARD CAPLAN, Ph.D., YOSEF PILCH, M.D., ANDREW GLASS, M.D., HENRY SHIBATA, M.D., HARVEY LERNER, M.D., JOSE TERZ, M.D., AND LYNNE SIDOROVICH

- NSABP B-06, 1976-1984
- RCT, Stage I-II
 - 636 lump + ALND
 - 629 lump + ALND + RT
- RT: 50 Gy over 5wks
- **In-breast tumor recurrence at 8 years:**
 - **10% with RT vs 29% with no RT**



Fisher B, *N Engl J Med* 1989;320:822.

Risk of In-Breast Tumor Recurrence with BCT

- Systematic Review, 16 Studies, Pts Diagnosed **1979-2009**

First author (year)	Number of women that developed a recurrence	Number of women included in study	Cumulative Recurrence Rate	Median follow-up (years)	Annual Incidence Rate
Isolated ipsilateral breast tumor recurrence (n = 16 studies)					
Kim (2011)	40	2102	1.9%	5.1	0.4%
Tinterri (2014)	28	749	3.7%	9.0	0.4%
Panet-Raymond (2011)	289	6020	4.8%	11.4	0.4%
Arvold (2011)	44	1434	3.1%	7.1	0.4%
Mansell (2009)	94	3614	2.6%	5.0	0.5%
Metzger-Filho (2013)	133	1951	6.8%	12.5	0.6%
Whelan (2010)	83	1234	6.7%	12.0	0.6%
van Hezewijk (2013)	270	9231	2.9%	5.2	0.6%
Nottage (2006)	98	1540	6.4%	10.9	0.6%
Taghian (2006)	28	313	8.9%	15.1	0.6%
Goulart (2011)	6	100	6.0%	10.0	0.6%
Bartelink (2015)	591	5318	11.1%	17.2	0.7%
Christiansen (2008)	698	8850	7.9%	12.0	0.7%
van der Hage (2003)	314	3648	8.6%	11.0	0.8%
Diaz (2014)	5	116	4.3%	5.3	0.8%
Gujral (2011)	150	1410	10.6%	10.1	1.1%
			Median: 6.2%	Median: 10.5 year	Median: 0.6%

Spronk I, *The Breast* 2018;39:70.

Risk of In-Breast Tumor Recurrence with BCT: Partial Breast Irradiation

Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial

	Cumulative number of events	Estimated cumulative incidence by 5 years (95% CI)	Hazard ratio (95% CI); p value	Estimated absolute difference vs 40 Gy at 5 years (95% CI)
Ipsilateral breast tumour (local) relapse*				
40 Gy (n=1361)	31 (2.3%)	2.1% (1.4 to 3.1)	1 (ref)	..
27 Gy (n=1367)	27 (2.0%)	1.7% (1.2 to 2.6)	0.86 (0.51 to 1.44); 0.56	-0.3% (-1.0 to 0.9)
26 Gy (n=1368)	21 (1.5%)	1.4% (0.9 to 2.2)	0.67 (0.38 to 1.16); 0.15	-0.7% (-1.3 to 0.3)

- 4096 pts, pT1-3,N0-1
- 97 hospitals in UK, **2011-2014**
- **Annual Incidence IBRT:**
 - **40 Gy:** 0.42%
 - **27 Gy:** 0.34%
 - **26 Gy:** 0.28%

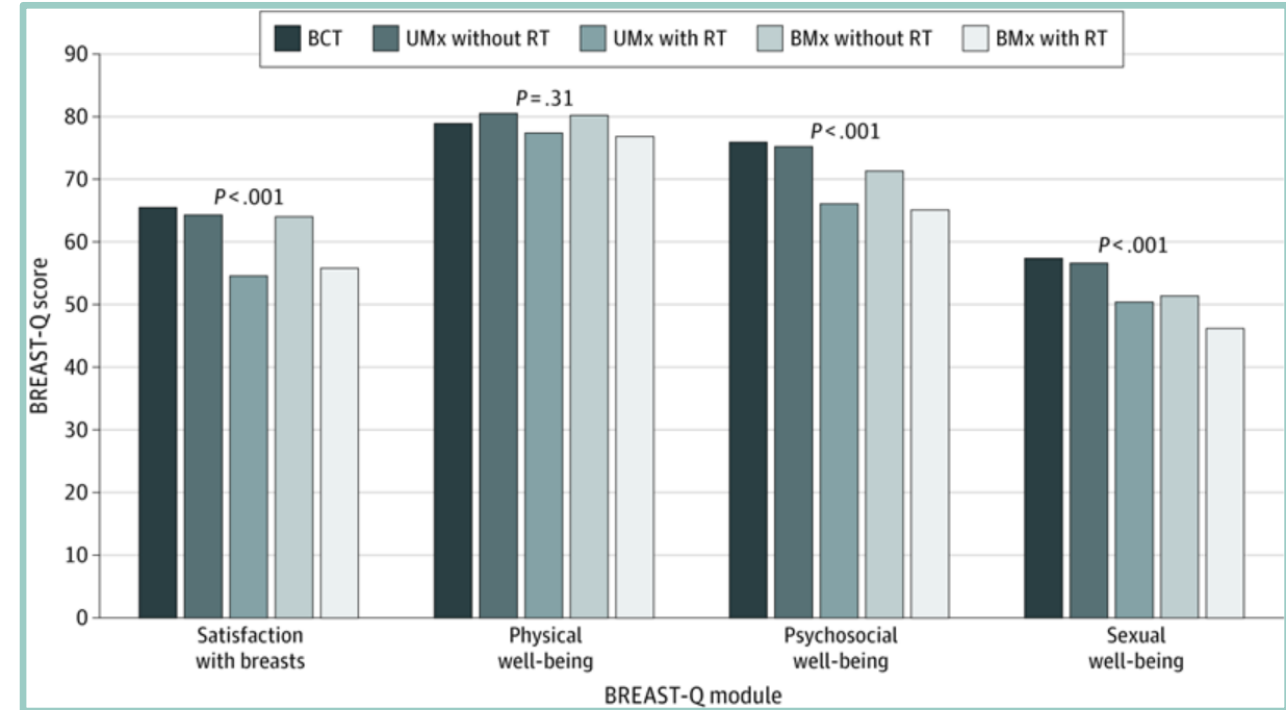
Brunt AM, *Lancet* 2020;396:1613.

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Association of Local Therapy with Quality of Life in Young Women with Breast Cancer

- Young Women's Breast Cancer Study, Age ≤ 40 , Stage 0-III, **2006-2016**
- 52% BMx, 20% UMx, 28% BCT
 - Mx pts: 89% Recon, 45% RT
- **Higher scores with BCT for:**
 - Satisfaction with Breasts
 - Psychosocial Well-being
 - Sexual Well-being
- Lowest scores for Mastectomy + RT



Dominici L, *JAMA Surg* 2021;156(10):e213758.

Historical Contraindications to BCT Are Being Challenged

- **Multicentric tumors**

- ACOSOG Z11102 Trial

- **History of prior breast radiotherapy**

- NRG Oncology/RTOG 1014 Trial

- **Large tumor size to breast ratio**

- Neoadjuvant therapy to downstage
 - Oncoplastic surgery

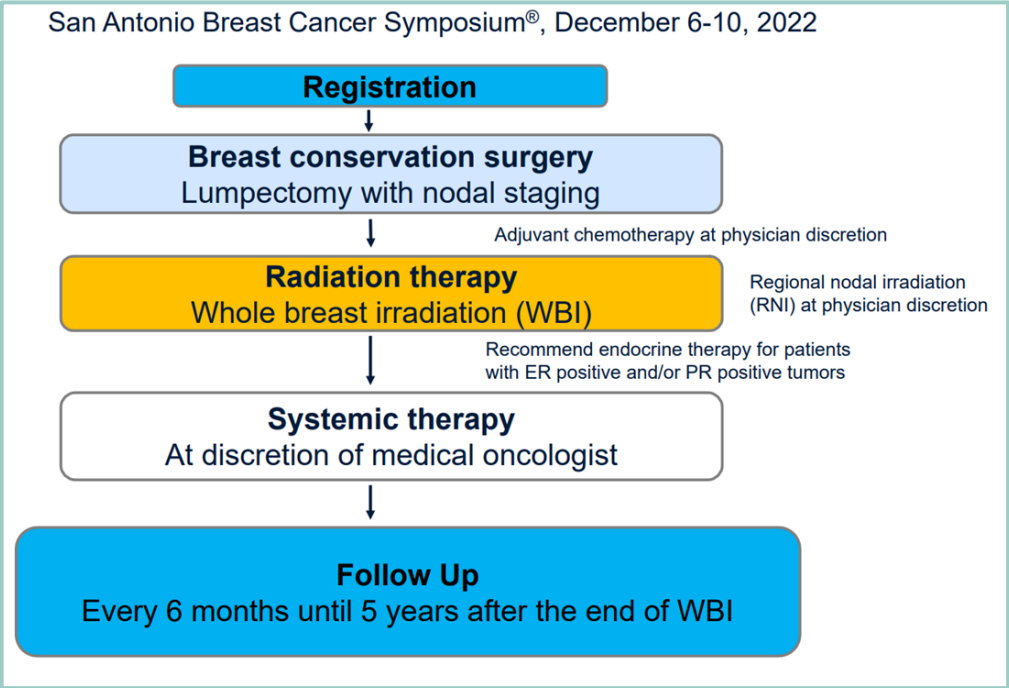
Pak L, *Expert Rev Anticancer Ther* 2022; 22(5): 535.

Local Recurrence After Breast-Conserving Therapy in Patients With Multiple Ipsilateral Breast Cancer: Results From ACOSOG Z11102 (Alliance)

Judy C. Boughey, MD¹; Kari M. Rosenkranz, MD²; Karla V. Ballman, PhD³; Linda McCall, MS⁴; Bruce G. Haffty, MD⁵; Laurie W. Cuttino, MD⁶; Charlotte D. Kubicky, MD⁷; Huong T. Le-Petross, MD⁸; Armando E. Giuliano, MD⁹; Kimberly J. Van Zee, MS, MD¹⁰; Kelly K. Hunt, MD⁸; Olwen M. Hahn, MD¹¹; Lisa A. Carey, MD¹²; and Ann H. Partridge, MD, MPH

- Prospective, Single Arm Phase II Multicenter Study

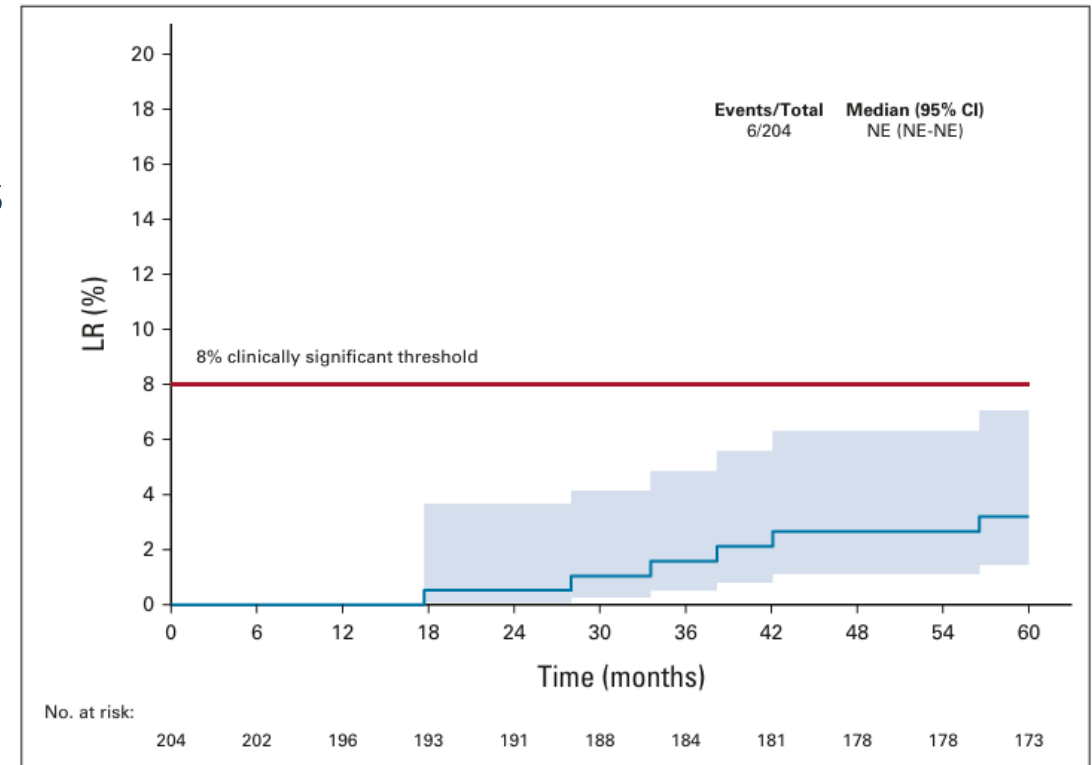
Inclusion Criteria:	Exclusion Criteria:
Women ≥ Age 40	Focus of disease > 5cm on imaging
2 or 3 foci of breast cancer	Bilateral breast cancer
At least 1 foci of invasive disease	Prior ipsilateral breast cancer
≥ 2cm normal tissue between lesions	Known BRCA 1/2 mutations
No more than 2 quadrants of disease	Neoadjuvant therapy
cN0 or cN1 disease	Men



- Lumpectomies with negative margins
- Whole breast irradiation with boost to all lumpectomy beds

BCT with Multiple Ipsilateral Breast Cancers

- 204 eligible patients, 78 sites
- Enrolled 2012-2016
- **Primary Endpoint:** Local Recurrence at 5 yrs
 - Acceptable 5-yr LR Rate defined as < 8%
- 5-yr Local Recurrence: 3.1%
- **Factors impacting LR:**
 - Pre-op MRI
 - Endocrine therapy



Boughey JC, *J Clin Oncol* 2023;41:3184.

Effectiveness of Breast-Conserving Surgery and 3-Dimensional Conformal Partial Breast Reirradiation for Recurrence of Breast Cancer in the Ipsilateral Breast

The NRG Oncology/RTOG 1014 Phase 2 Clinical Trial

Douglas W. Arthur, MD¹; Kathryn A. Winter, MS²; Henry M. Kuerer, MD, PhD³; [et al](#)

- Enrolled 58 pts, **in-breast recurrence $\leq$ 3cm, clinically node negative, unicentric on MRI, no skin involvement, negative staging**
- Median time from 1st RT: 13.4 yrs, all prior WBI, 80% boost to lumpectomy site
- 3D-conformal PBI of 1.5 Gy twice per day for total dose 45 Gy in 30 fractions (15 days)
- **3-yr LR: 3.4%, 5-yr LR: 5.2%, 5-yr incidence of mastectomy: 10%**
- **5-yr Distant-Mets Free Survival and OS: 95%**

Table 3. The 3- and 5-Year Efficacy Results (Median Follow-up of 5.5 Years)

End Points	No. of Events	3 y	No. at Risk	5 y	No. at Risk
		Estimate, % (95% CI)		Estimate, % (95% CI)	
IBR ^a	4	3.4 (0.6-10.7)	52	5.2 (1.4-13.2)	46
MF ^b	7	5.2 (1.3-13.1)	51	10.5 (4.2-20.1)	43
DMFS	3	94.8 (84.8-98.3)	53	94.8 (84.8-98.3)	48
OS	3	94.8 (84.8-98.3)	53	94.8 (84.8-98.3)	48

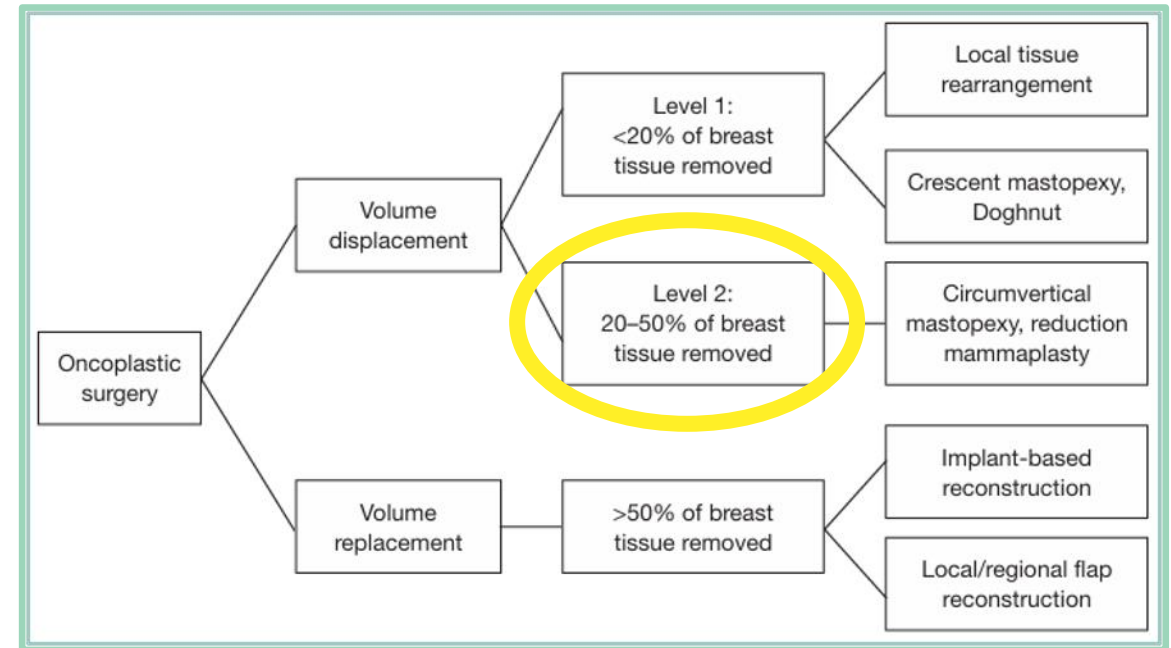
Conversion of Patients who are BCT Ineligible to BCT after Neoadjuvant Systemic Therapy

- National Breast Cancer Surgery Snapshot, Netherlands:
 - 467 neoadjuvant systemic therapy, March-May 2022
 - Conversion rate from mastectomy to BCT based on breast cancer subtype:
 - Triple Negative: 68%
 - ER- HER2+: 66%
 - ER+ HER2+: 63%
 - ER+ HER2-: 33%

Kramer G, *Clin Breast Cancer* 2026;26(1):64.

Oncoplastic Surgery Increases Eligibility for BCT

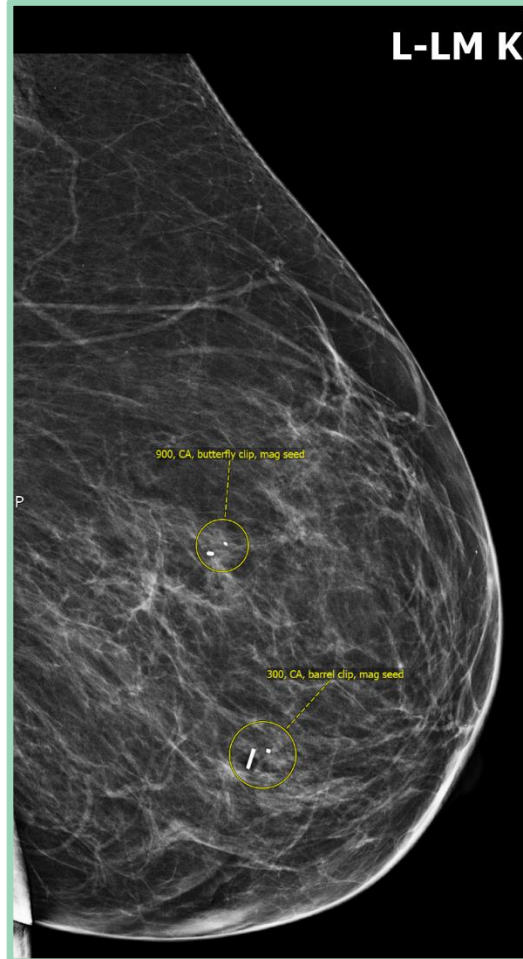
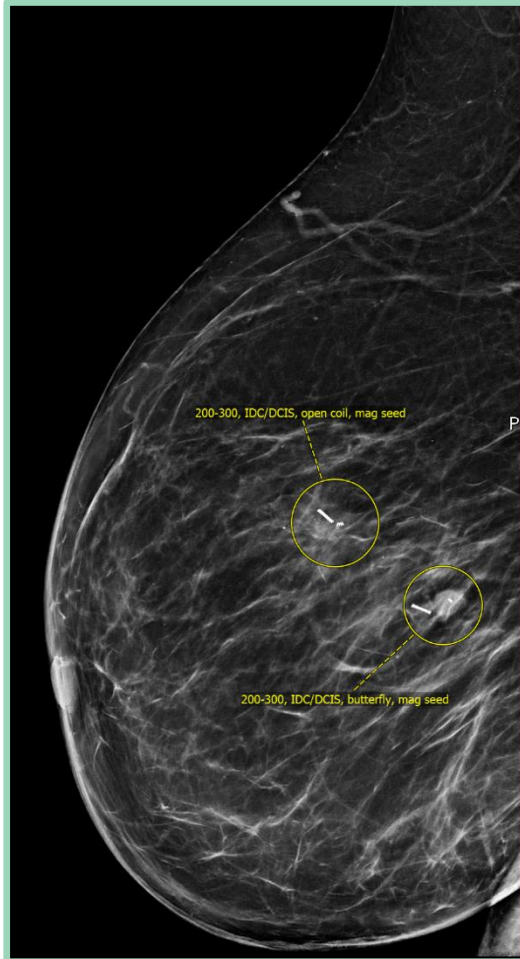
- **2006:** Aims of oncoplastic surgery defined
 - Complete excision of tumor with free margins
 - Minimal aesthetic compromise
 - Breast re-shaping if needed
- **2014:** Oncoplastic breast conservation surgery “The New Paradigm”



Torres I, *Gland Surg* 2024;13(3):412.

Silverstein MJ, *J Surg Oncol* 2014;110:82.

Oncoplastic Surgery



- 60 yo F with R T2N0 multifocal ER+ HER2+ and L multicentric T1N0 ER+ HER2- and DCIS
- Good response to neoadjuvant chemo
- R bracketed lumpectomy, L 2 site lumpectomy with oncoplastic reduction



1 month post-op

Oncoplastic Surgery

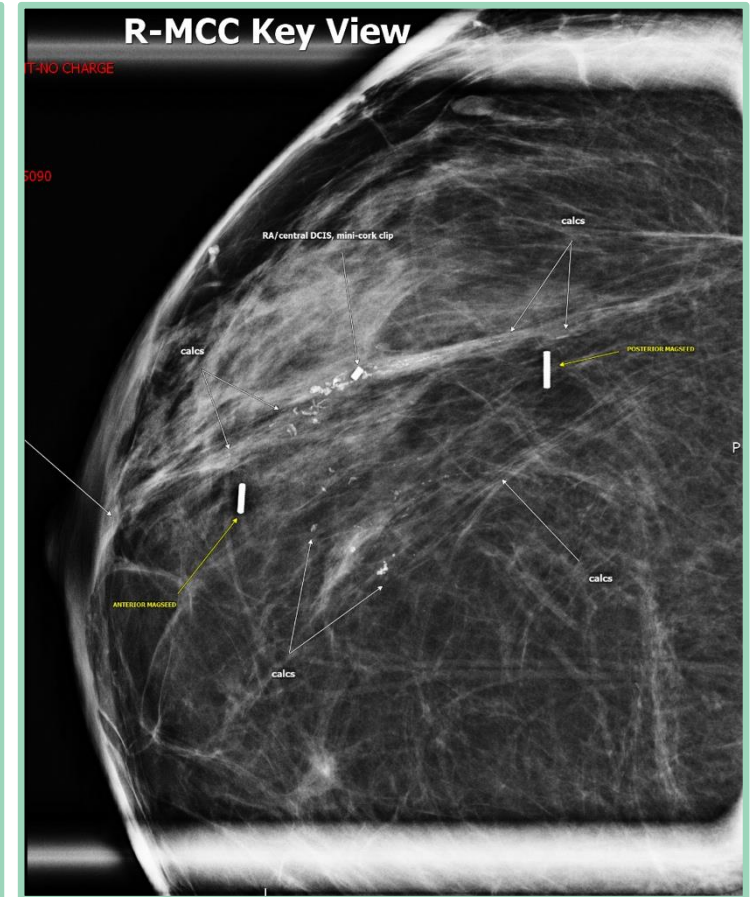
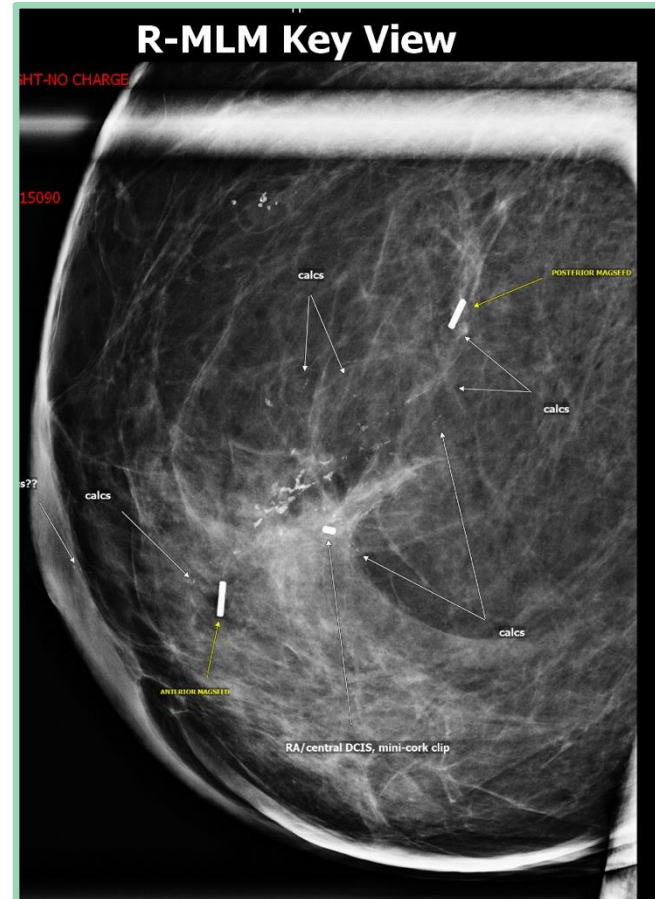
- 63 yr old R breast DCIS, calcs spanning 5.5cm at the 9:00 and central breast
- Prior breast reduction



Pre-op



4 days post-op

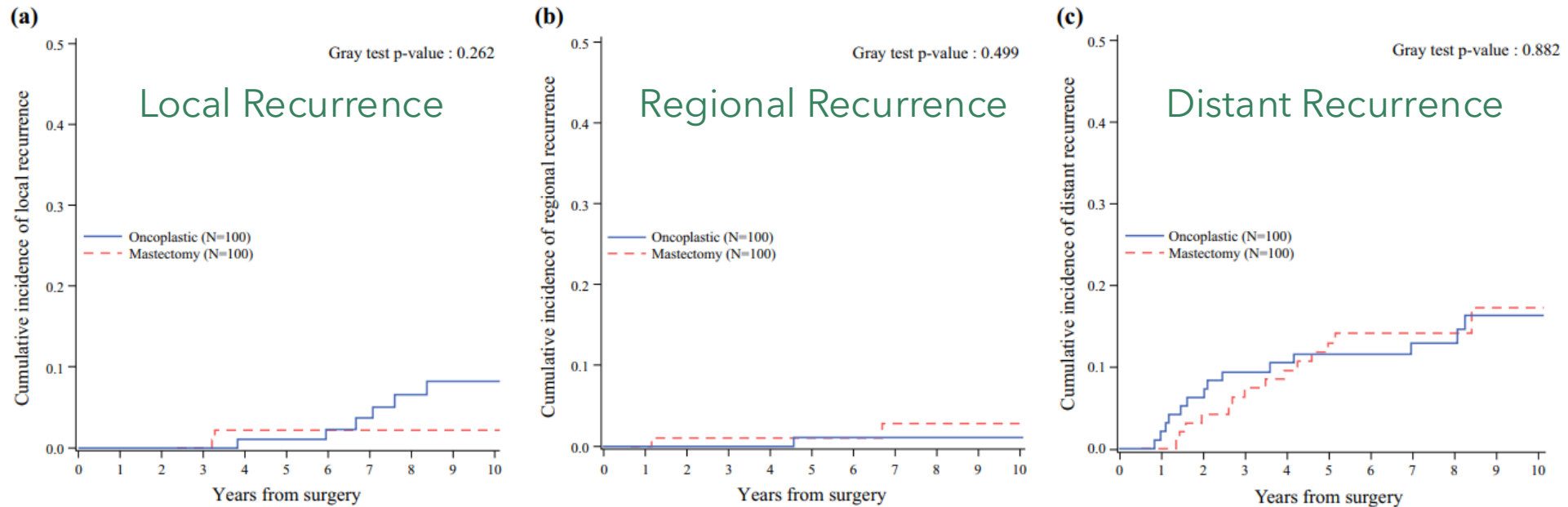


Oncoplastic Surgery Outcomes

Oncoplastic Breast-Conserving Surgery for Synchronous Multicentric and Multifocal Tumors: Is It Oncologically Safe? A Retrospective Matched-Cohort Analysis

Francesca De Lorenzi, MD, PhD¹, Francesco Borelli, MD¹ , Eleonora Pagan, MSc², Vincenzo Bagnardi, PhD², Nickolas Peradze, MD³, Barbara Alicia Jereczek-Fossa, MD, PhD⁴, Cristina Leonardi, MD⁴, Giovanni Mazzarol, MD⁵, Giorgio Favia, MD¹, Giovanni Corso, MD, PhD³, Emilia Montagna, MD⁶, Mario Rietjens, MD, PhD¹, and Paolo Veronesi, MD, PhD³

- 100 consecutive oncoplastic surgery pts, 2000-2015, all received WBI + boost
- European Inst of Oncology
- Matched by yr, age, tumor & compared to Mastectomy pts



- Higher LR with oncoplastic, higher RR with Mx, similar distant recurrence
- No difference in 10-Yr Disease-Free Survival

Nipple Sparing Mastectomy (NSM)

Evolution of Mastectomy

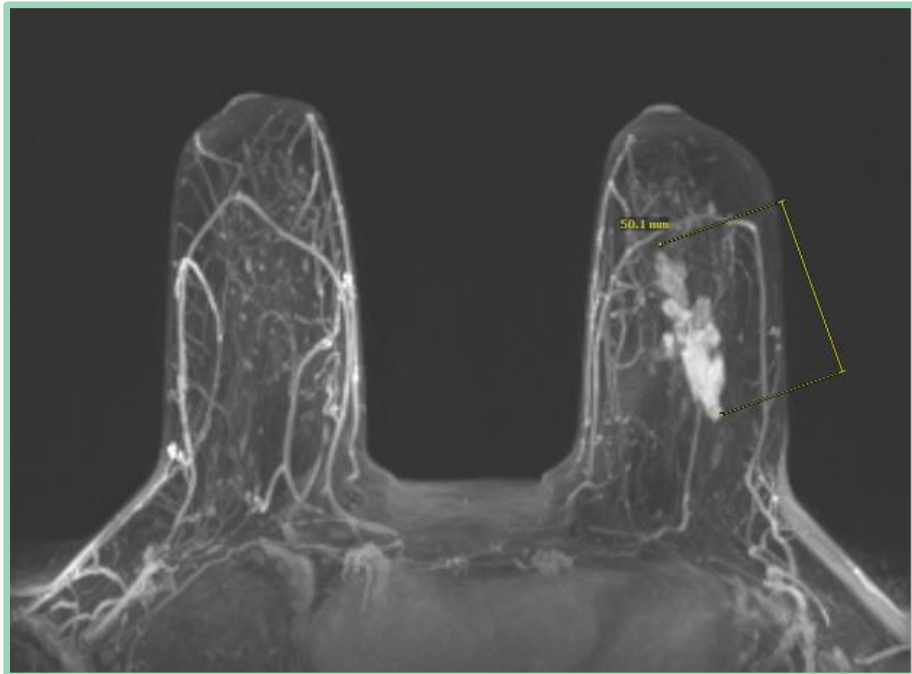
Oncologic Safety

Patient Selection

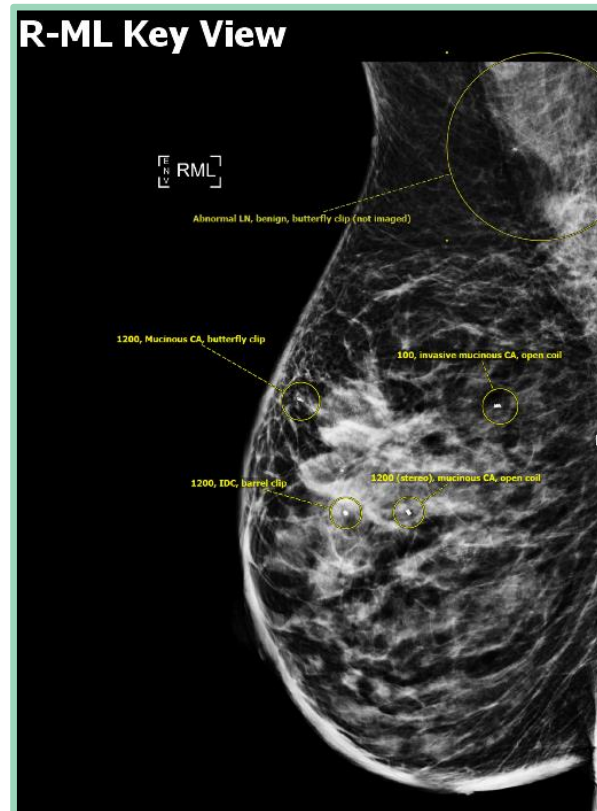
Re-sensation

When Extent of Disease Mandates Mastectomy

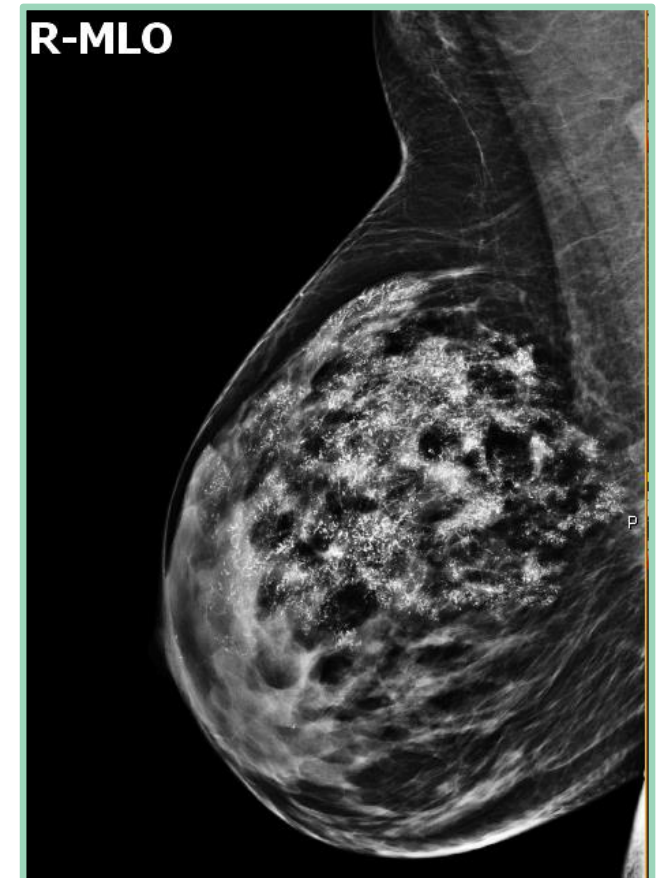
- Unfavorable tumor-to-breast size ratio
- Extensive Ductal Carcinoma in Situ
- Multicentric disease with more than 2-3 foci
- Persistently + margins



67 yo with ~6cm of ILC, gr 1, ER+ HER2-
AHN



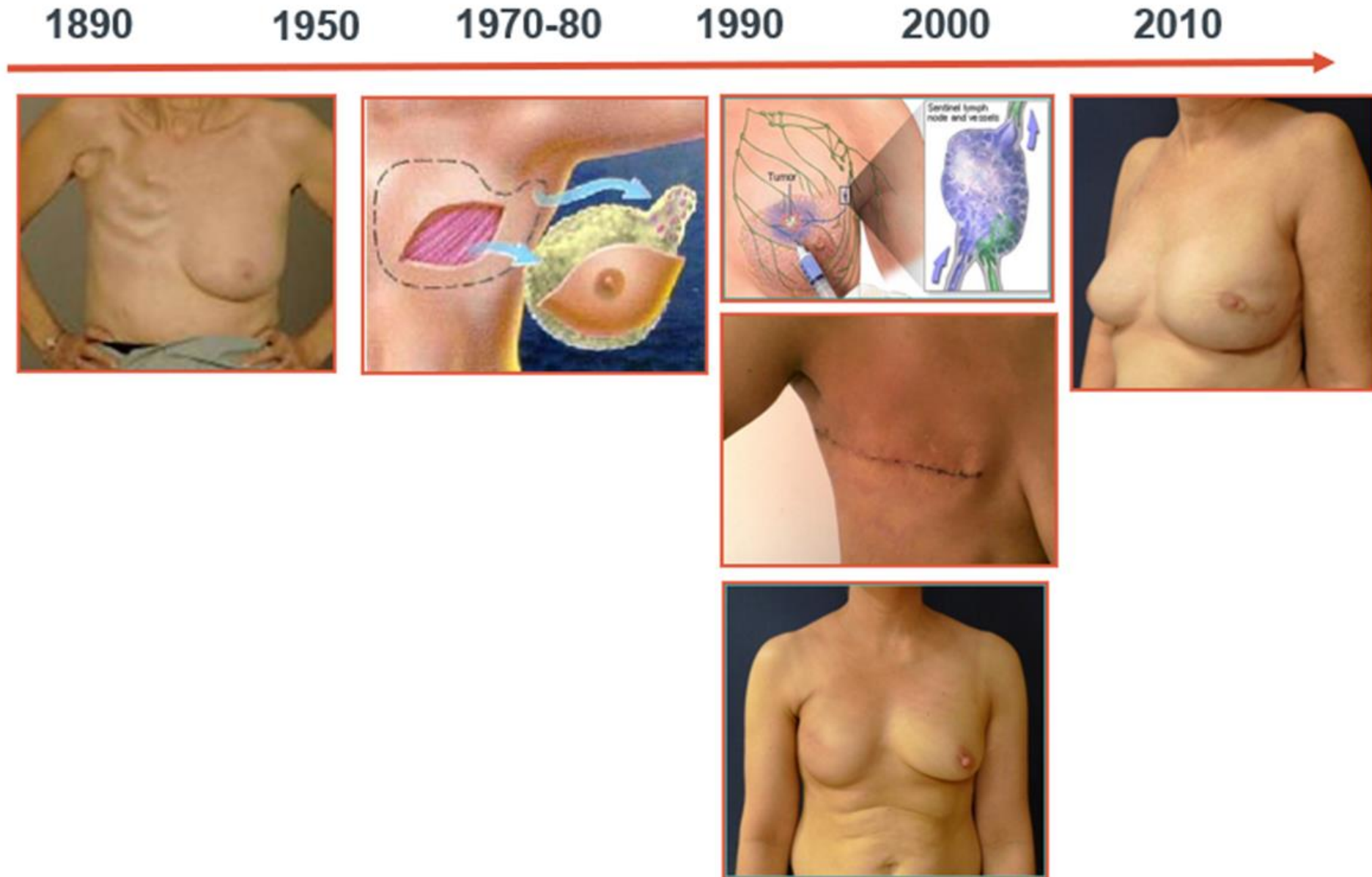
44 yo with 4 foci of IDC
spanning > 5cm



22 yo extensive DCIS +
HER2+ breast cancer

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Evolution of Mastectomy



Benefits of Nipple Sparing Mastectomy

- Single Stage Surgery
- Superior Cosmetic Outcome
- Higher Psychosocial Well-being & Better Body Image
 - Compared to skin sparing mastectomy patients

Colwell AS, *Plast Reconstr Surg* 2014;133:496.

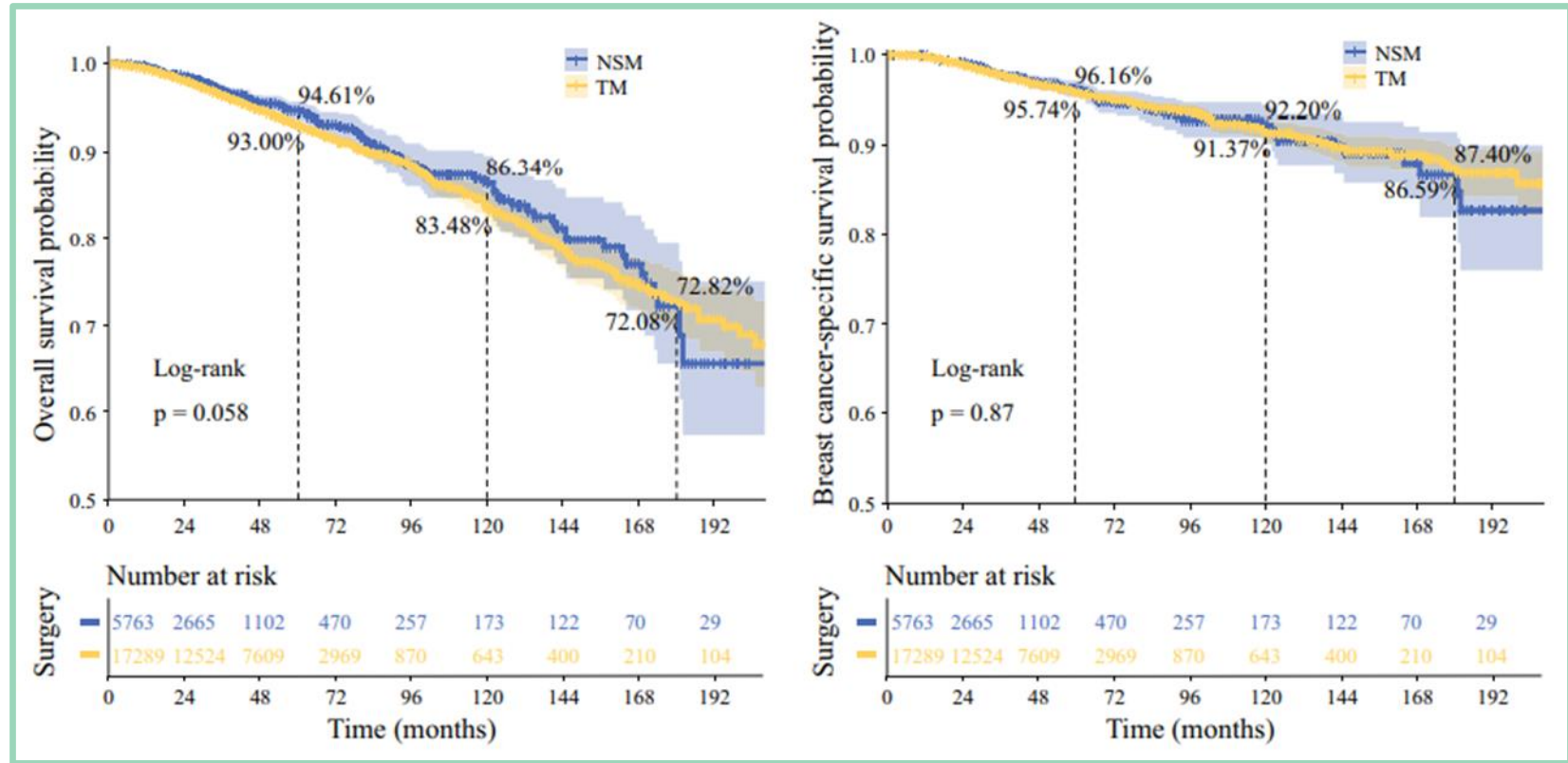
Metcalfe KA, *Ann Surg Oncol* 2015;22:3324.

Howard MA, *J Surg Oncol* 2016;114: 416.



Safety of Nipple Sparing Mastectomy

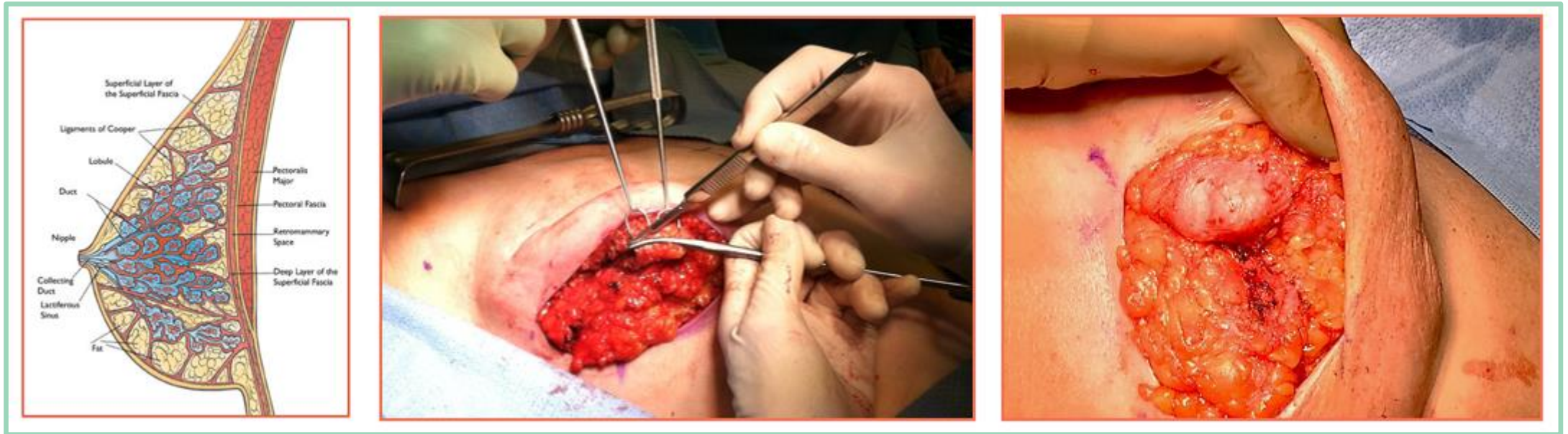
- No difference in 5-yr, 10-yr, 15-yr Overall Survival & Breast Cancer Specific-Survival between NSM and total mastectomy



Fu M, *Ann Surg Oncol* 2021;28(8):4284

Safe Nipple Preservation Essentials

1. Clearing ducts within nipple
2. Adequate sampling of tissue
3. Pathologic analysis of this “nipple margin”



NSM Patient Selection: Absolute Contraindications

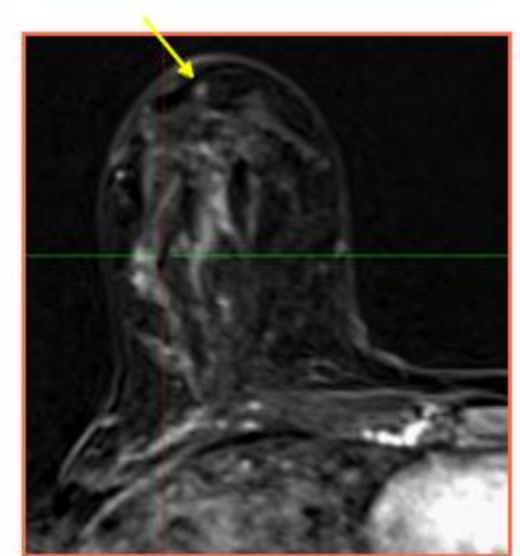
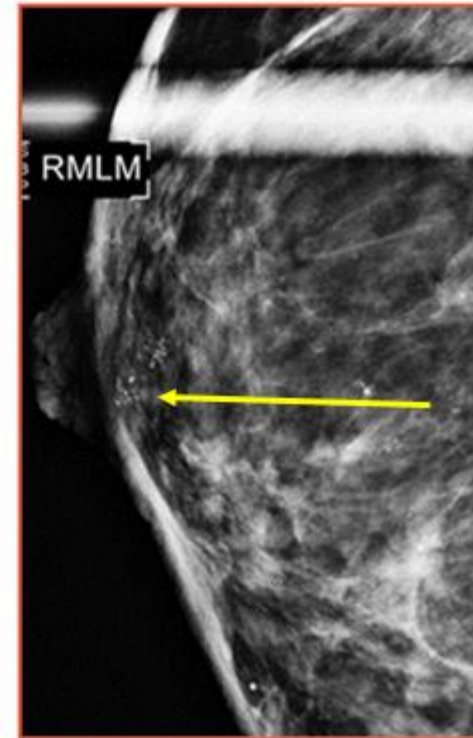
- Clinical or imaging evidence of direct nipple involvement
- Pathologic nipple discharge
- Inflammatory breast cancer



Paget's Disease

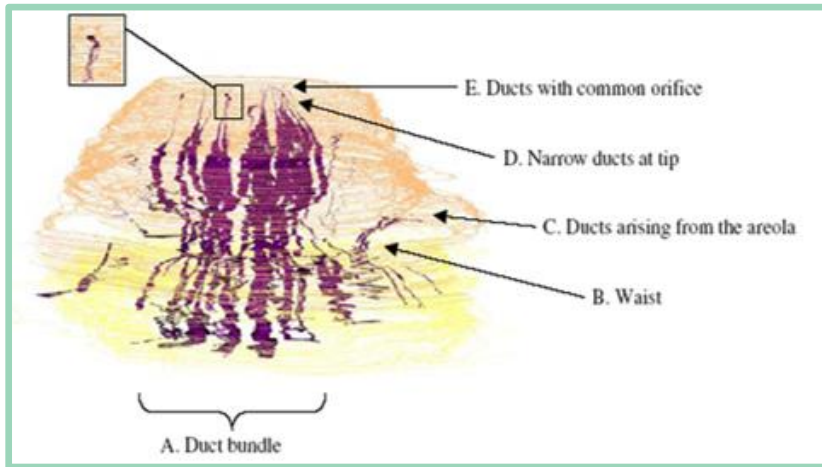


Invasive Cancer



Areola Sparing Mastectomy

- Option for patients with imaging evidence of disease involving base of nipple (calcs on mammo, enhancement MRI), those with bloody nipple discharge
 - Minority of ducts arise from areola
 - DCIS spreads by contiguous extension into nipple papilla



Brachtel EF, *J Clin Oncol* 2009;27:4948
Rusby JE, *Breast Cancer Res Treat* 2007;106(2):171

40 yo F with R DCIS extending to nipple, 3 months s/p R ASM, L NSM, and prepectoral implants

Skin Sparing Mastectomy with Reduction Pattern

- For patients with large volume breasts and/or significant ptosis



Pre-op: 49 yo F L TNBC

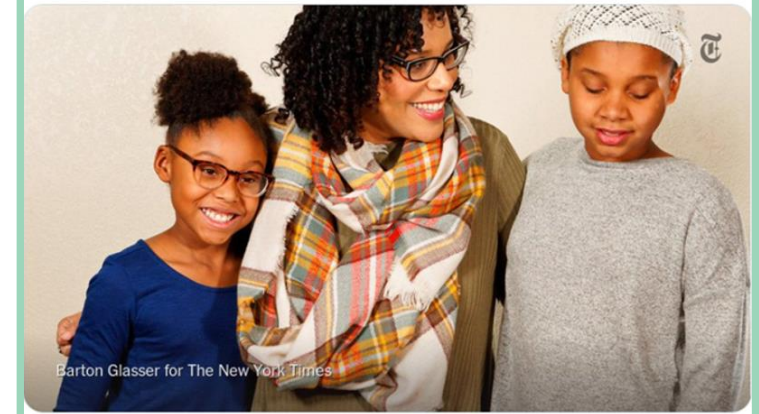


6 Months Post-op: 49 yo s/p B SSM with immediate implants

Nerve Sparing Mastectomy

- NSM generally leads to numbness of nipple areola complex (NAC)
- National attention in 2017
- Early results of Nerve Preservation & Allografting of NAC during NSM & Immediate Implant Reconstruction 2019-2020

After Mastectomies, an Unexpected Blow: Numb New Breasts [nyti.ms/2jJVsfW](https://www.nytimes.com/2017/01/30/health/after-mastectomies-an-unexpected-blow-numb-new-breasts.html)



3:16 PM · Jan 30, 2017 · SocialFlow

OPEN



IDEAS AND INNOVATIONS

Breast

Nerve Preservation and Allografting for Sensory Innervation Following Immediate Implant Breast Reconstruction

Anne Warren Peled, MD*
Ziv M. Peled, MD†

Summary: While newer breast reconstruction approaches utilizing nipple-sparing

IDEAS AND INNOVATIONS

Neurotization of the Nipple-Areola Complex during Implant-Based Reconstruction: Evaluation of Early Sensation Recovery

Risal Djohan, M.D.
Isis Scomacao, M.D.
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Cleveland, Ohio

Summary: The concept of sensate autologous breast reconstruction is not novel, and prior literature has focused mainly on sensate abdominally based breast reconstruction. The goal of this article is to present the authors' results with a novel technique performing sensate implant-based reconstruction. A database was prospectively maintained for patients who underwent implant-based sensate breast reconstruction. The anterior branch of the lateral fourth intercostal is identified and preserved during the mastectomy by the breast sur-

Peled AW, *Plast Reconstr Surg Glob Open* 2019;7:e2332

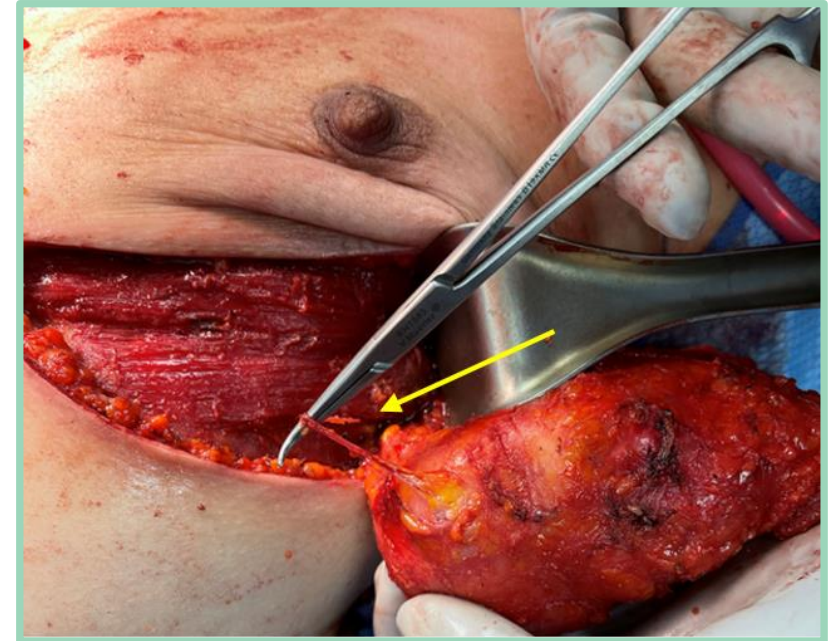
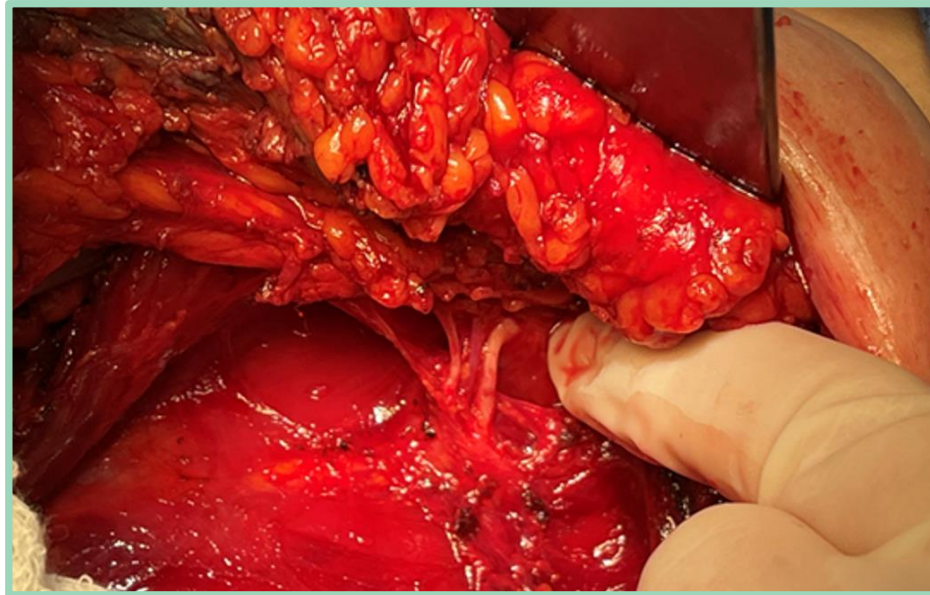
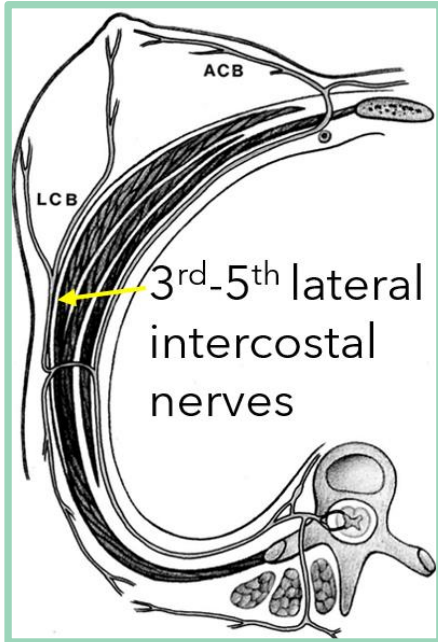
Djohan R, *Plast Reconstr Surg* 2020;146:250

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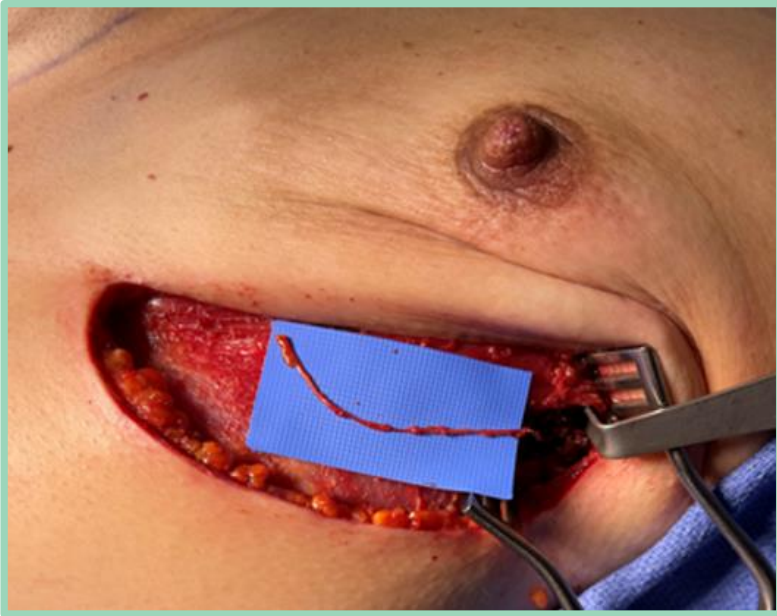
Nerve Sparing Mastectomy

- Innervation to breast comes from 3-5th intercostal nerves through medial and lateral branches
 - Medial branch: usually left intact
 - Lateral branch: exits at the lateral edge of pectoralis muscle or within 2 cm
- Additional length can be obtained by dissecting nerve into breast tissue

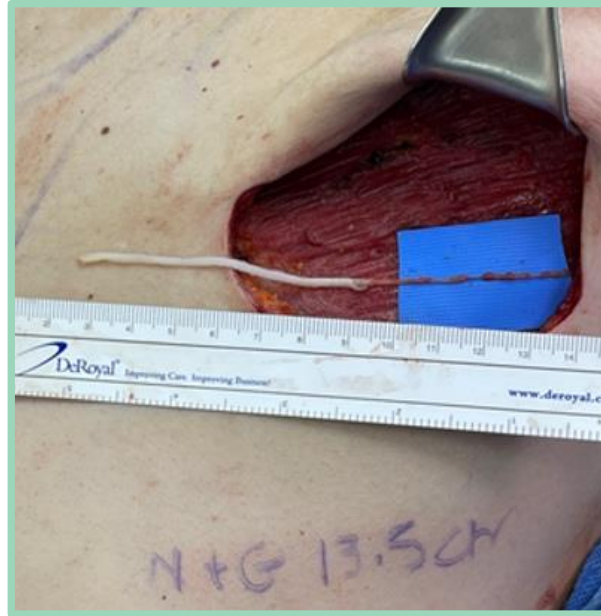


Nerve Sparing Mastectomy

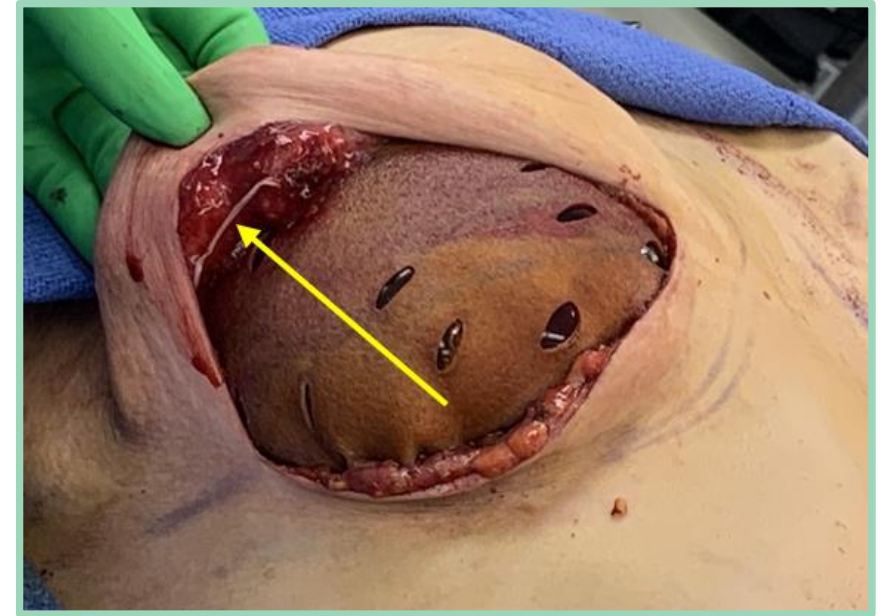
- 1-2mm 7cm nerve allograft is sutured to nerve stump
- Nerve graft is positioned over implant towards NAC
 - If distal nerve stump is identified, end-to-end anastomosis
 - If not, direct neurotization of NAC is performed



Native nerve



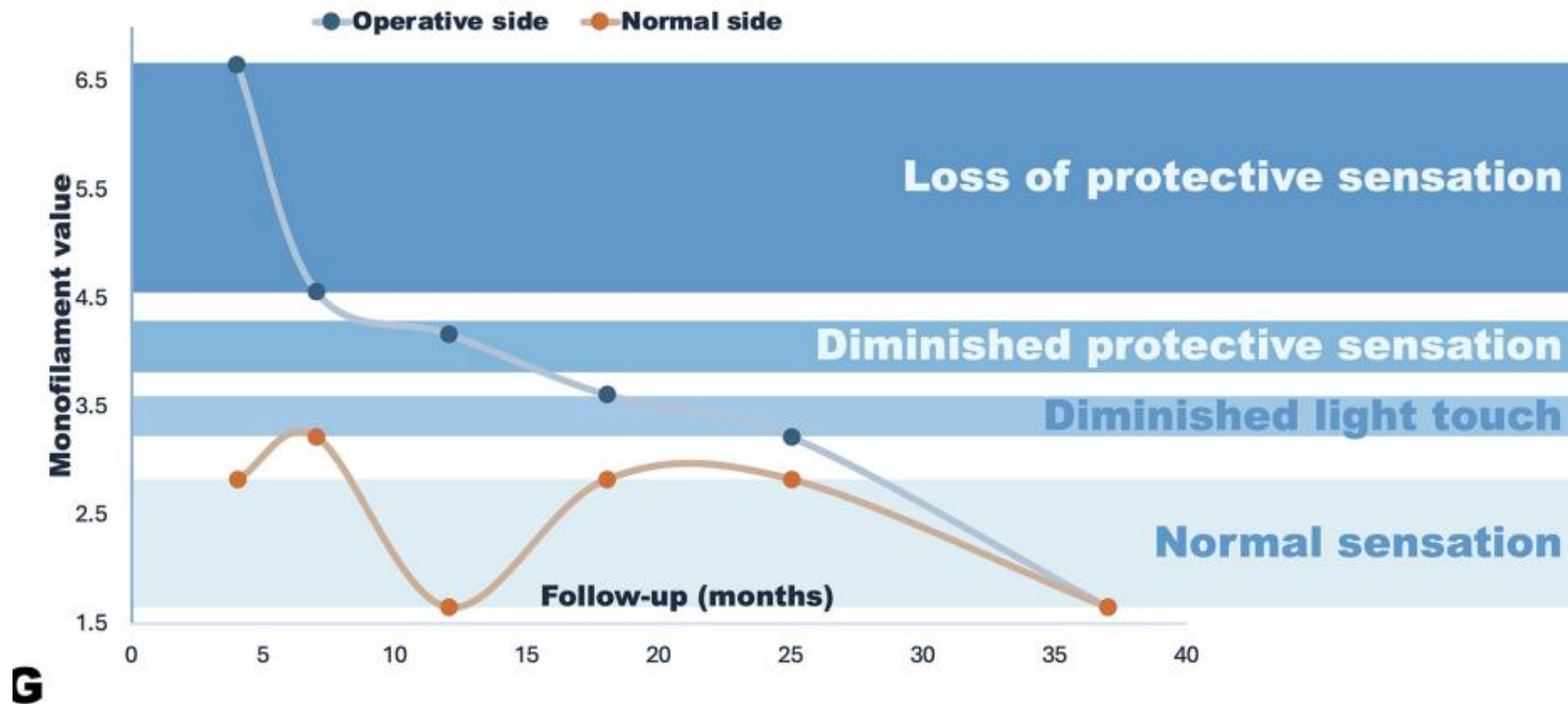
Nerve graft sutured to
nerve stump



Nerve graft sutured to NAC

Nerve Sparing Mastectomy Outcomes

- Early results are promising that nerve grafting improves sensation and quality of life, but limited data...
- May take 3+ years for normal sensation to return



Shyu S, *Int J Surg* 2025;111:3235

De-escalation of Axillary Surgery

Omitting any axillary surgery

Avoiding axillary lymph node dissection

Benefits of Axillary Surgery for Breast Cancer?

Staging & Prognosis:

YES

Locoregional Control:

RARELY

Overall Survival:

NO

Guide Systemic Therapy: LESS & LESS

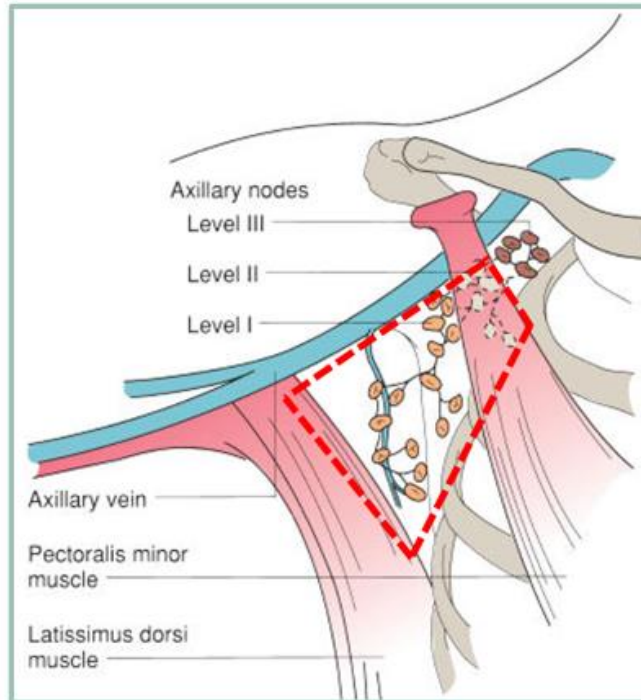
Guide Radiation Therapy:

YES

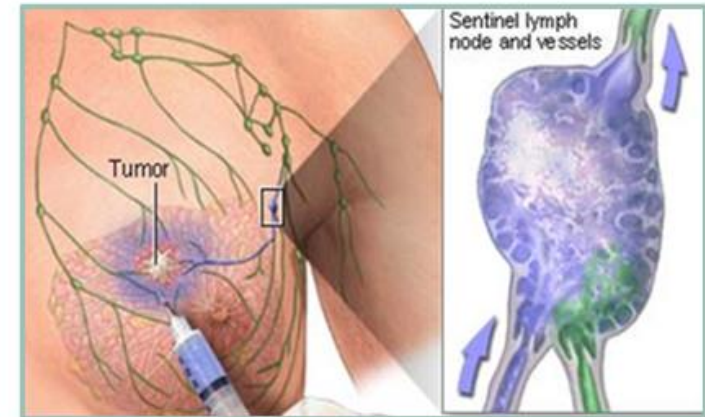


Axillary Lymph Node Dissection (ALND) vs Sentinel Lymph Node Biopsy (SLNB)

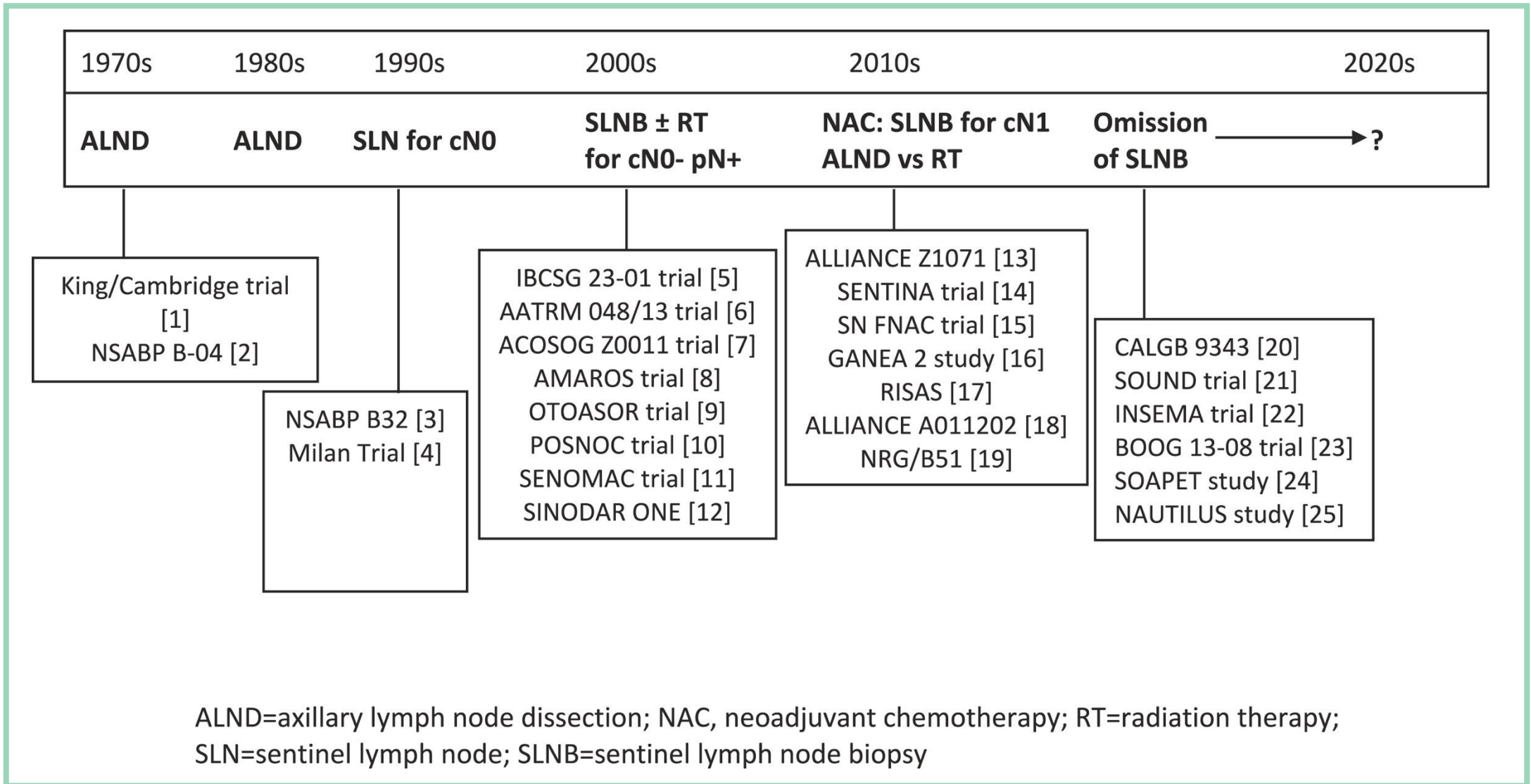
- **ALND (10+ lymph nodes)**
 - Clears nodes within anatomic region



- **SLNB (~1-3 lymph nodes)**
 - Removes main draining lymph node(s)
 - Negative SLN predicts that additional nodes will be negative 90-95% of time
 - Does not increase regional or distant recurrence rates
 - Reduces morbidity of axillary surgery



De-Escalating Axillary Surgery Over Time



Why Avoid ALND?

- Breast cancer-related lymphedema most common cause of lymphedema in the US
- **Biggest risk factors:**
 - #1--Axillary Lymph Node Dissection (ALND)
 - Regional Lymph Node Radiation (XRT)
 - Obesity
 - Cellulitis of Arm
- Incidence ~33% in highest risk group (ALND +XRT)
- Negative impact on quality of life



Taghian NR, *Cr Rev Oncol/Hematol* 2014;92(3):227.

Johnson AR, *Ann Plast Surg* 2019;82:S234.

AHN Ferguson CM, *J Clin Oncol* 2016;34(7):691.

Axillary Surgery Omission in DCIS

- Traditionally SLNB was performed during mastectomy for DCIS
- Superparamagnetic iron oxide (SPIO) is novel tracer for mapping sentinel nodes, detectable up to 30 days
- Allows for delayed SLNB if invasive cancer found on final path
- Avoids any lymph node surgery in ~85% of patients with DCIS undergoing mastectomy (SentiNot Study)

Karakatsanis A, BJS 2019;106:720.

<https://clinicaltrials.gov/ct2/show/NCT04722692>

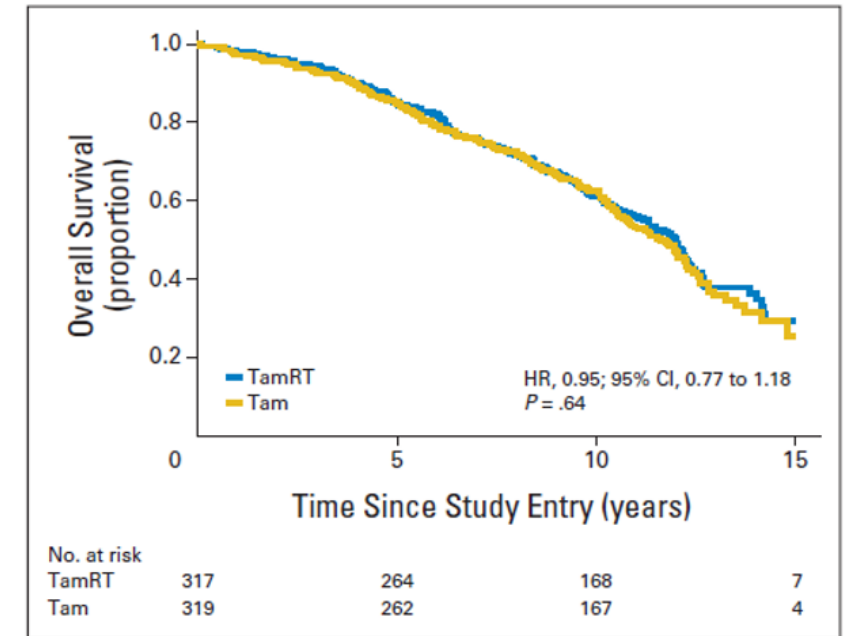
Axillary Surgery Omission Age ≥ 70 Society of Surgical Oncology Choosing Wisely®:

Don't routinely use sentinel node biopsy in clinically node negative women $\geq$ age 70 with early stage, ER+, HER2 - breast cancer

■ Rationale:

- Endocrine therapy is standard of care
- Low risk of axillary recurrence
 - 3% at 12.6 yrs in CALGB 9343 in the 200 pts who had no LNs removed and no RT
- No impact on survival outcomes

❖ Recommended since 2016



CALGB 9343

<https://www.choosingwisely.org/societies/society-of-surgical-oncology/>
Hughes KS, *J Clin Oncol* 2013;31:2382.

Axillary Surgery Omission: SOUND (Sentinel Node vs Observation after Axillary US) Trial

- Prospective, Non-inferiority, Phase 3, RCT
 - ~1400 patients
- Clinical T1N0, undergoing lumpectomy + WBI
 - Median age: 60, 93% ER+
- Any Age
- Negative Axillary US
- Italy, Switzerland, Spain, Chile from 2012-2017
- Randomized 1:1 No SLNB vs SLNB

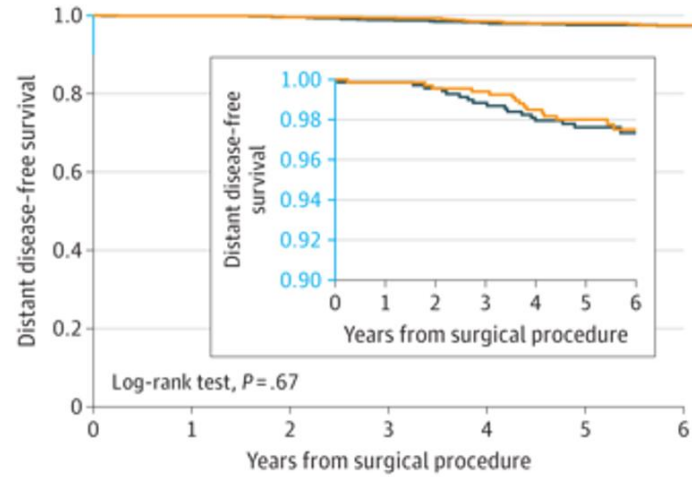
Characteristic	Patients, No. (%)	
	SLNB (n = 708)	No axillary surgery (n = 697)
Pathological node status		
pNx	12 (1.7)	675 (96.8)
pN0	584 (82.5)	12 (1.7)
pN0(i+)	15 (2.1)	0
pN1mi	36 (5.1)	4 (0.6)
pN1	57 (8.1)	5 (0.7)
pN2	4 (0.6)	1 (0.1)

****Enrolled pts who underwent SLNB had minimal nodal involvement**

Gentilini OD, *JAMA Oncol* 2023;9(11):1557.

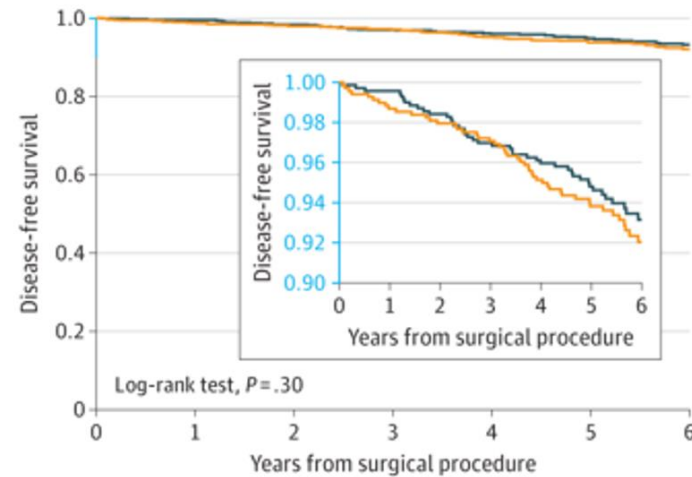
Axillary Surgery Omission: SOUND (Sentinel Node vs Observation after Axillary US) Trial

A Distant disease-free survival



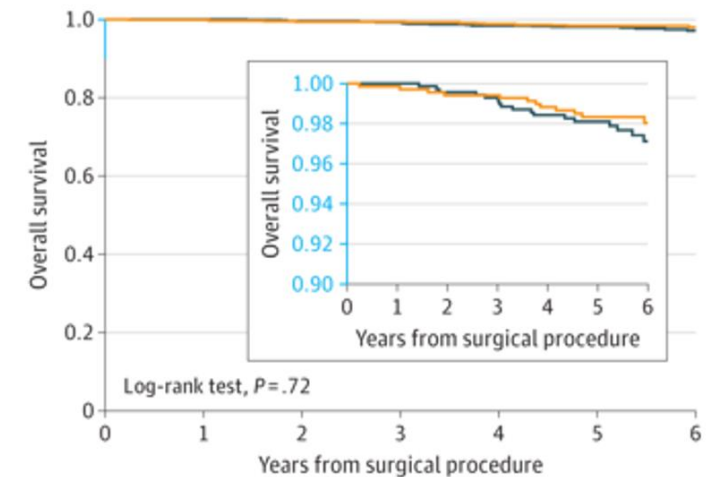
No. at risk	708	702	694	684	657	532	303
SLNB	697	684	675	669	640	512	289
No SLNB							

B Disease-free survival



No. at risk	708	702	694	684	657	532	303
SLNB	697	684	675	669	640	512	289
No SLNB							

C Overall survival



No. at risk	708	705	702	700	673	550	317
SLNB	697	693	688	687	663	531	310
No SLNB							

	SLN surgery	No axillary surgery	
Locoregional relapse	12 (1.7%)	11 (1.6%)	
Distant metastases	13 (1.8%)	14 (2.0%)	
Deaths	21 (3.0%)	18 (2.6%)	
5-year DDFS	97.7%	98.0%	$p = 0.67$
5-year DFS	94.7%	93.9%	$p = 0.30$
5-year OR	98.2%	98.4%	$p = 0.72$

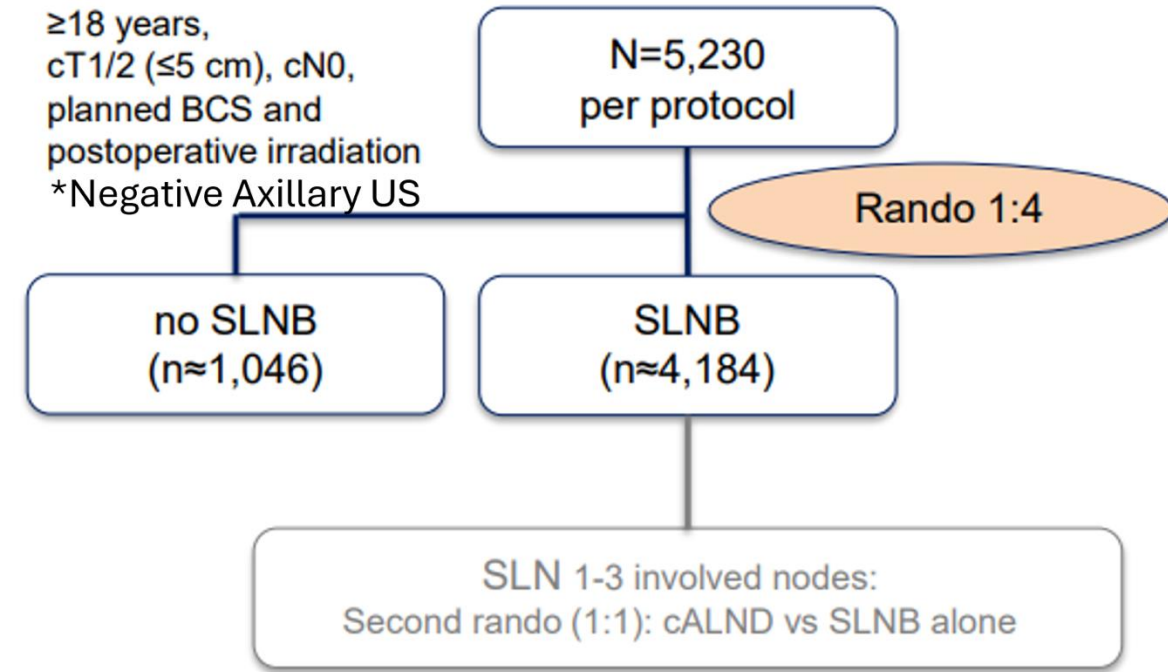
Gentilini OD, *JAMA Oncol* 2023;9(11):1557.

AHN <https://www.breastsurgeons.org/news/?id=100>

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Axillary Surgery Omission: INSEMA (INtergroup SEntinel MAmma Trial)

- Prospective, Randomized, Non-inferiority Trial
- Clinical **T1-T2** N0, undergoing lumpectomy + WBI
 - ~90% age 50+, 95% ER+ HER2-
- Negative Axillary US
- Germany & Australia, 2015-2019
- Randomized 1:4 No SLNB vs SLNB
- **14.9% were node positive**



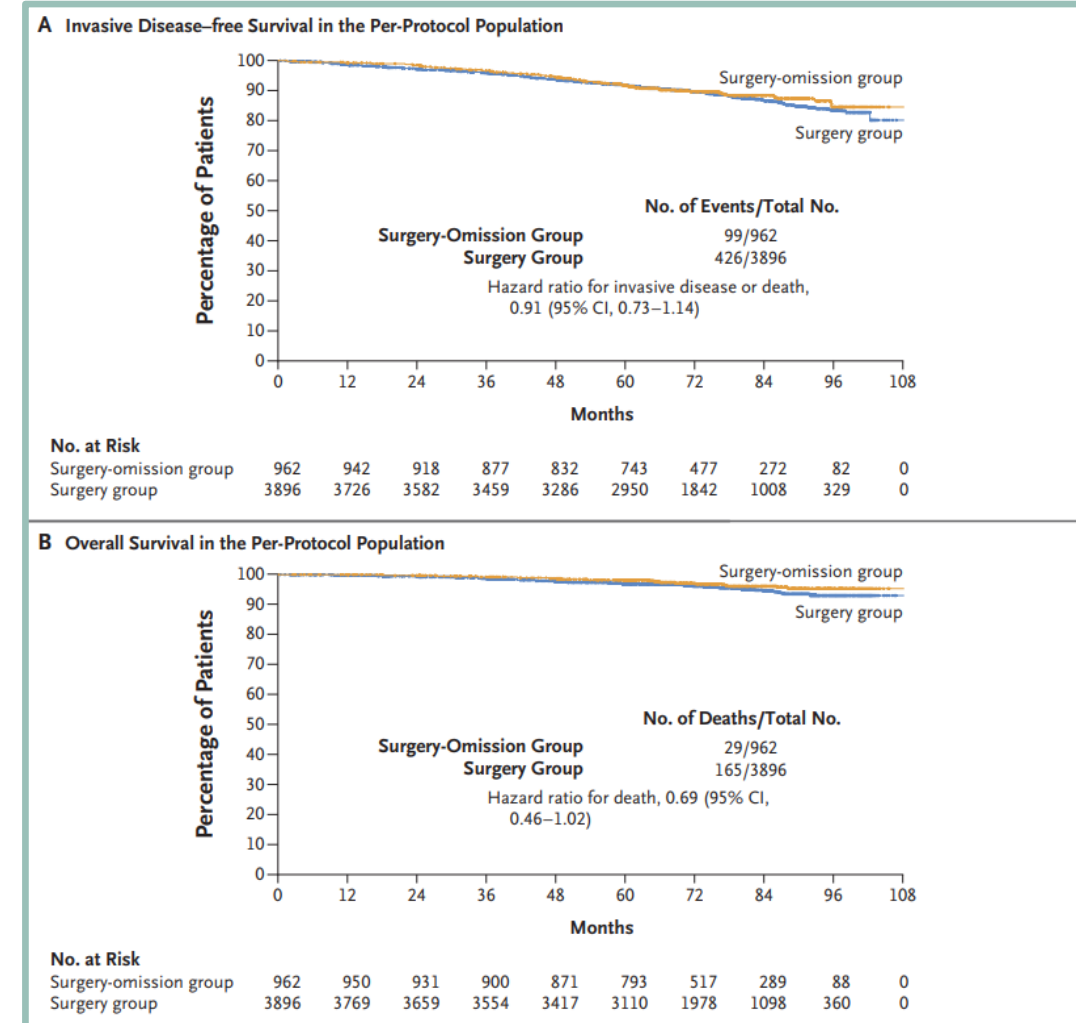
Reimer T, *N Engl J Med* 2025;392:1051.

Axillary Surgery Omission: INSEMA (INtergroup SEntinel MAmma Trial)

- Median Follow-up: 6.1 years
- **Omission of SLNB was NOT inferior to SLNB**
 - Axillary recurrence was 1.0% in no SLNB group vs 0.3% in SLNB group
- **De-escalation Suitable For:**
 - Age 50+
 - ER+ HER2-
 - Grade 1-2 tumors
 - T1 tumors

Reimer T, *N Engl J Med* 2025;392:1051.

AHN

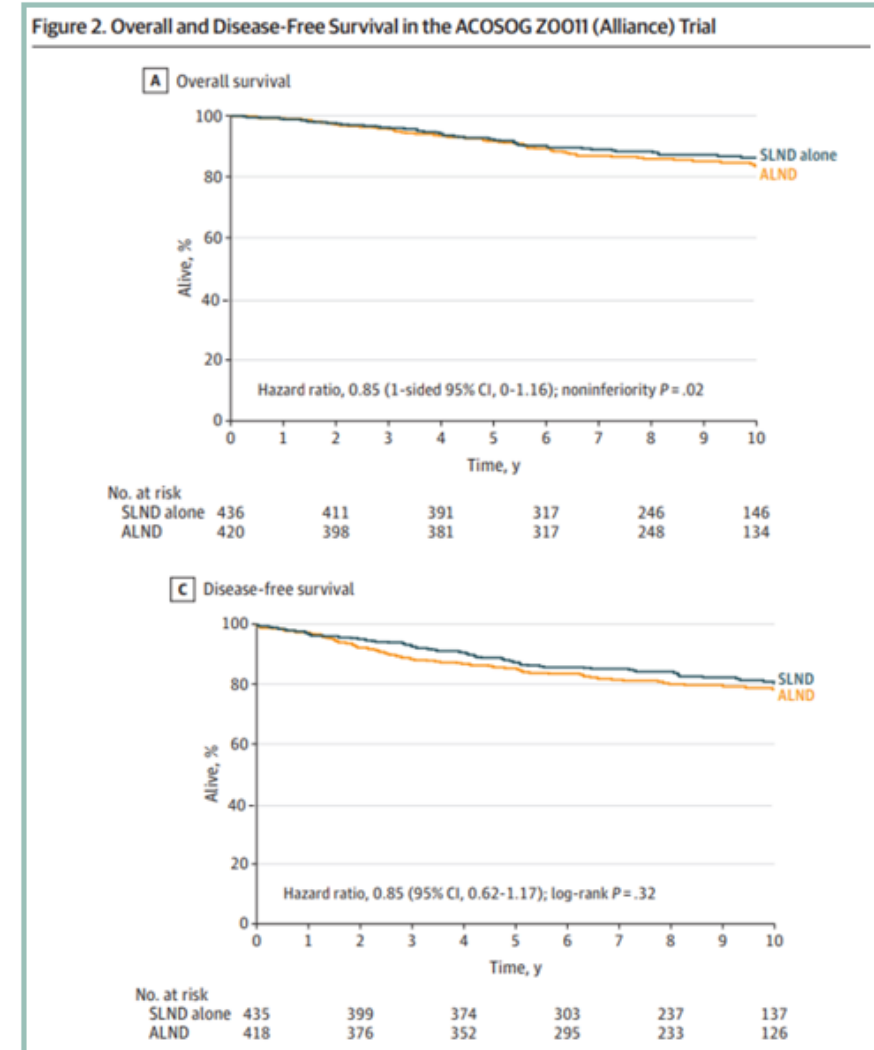


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Axillary De-escalation for Positive Lymph Nodes in Upfront Surgery

- Began in 2010 with ACOSOG Z0011 Trial Publication
- **Z0011:**
 - Clinical T1/T2N0, lumpectomy + WBI
 - 1-2+ SLN, randomized to SLNB alone or ALND
 - No difference in 10-yr OS or DFS with SLNB alone vs ALND
 - 27.4% of ALND contained add'l + nodes, but axillary recurrence rate was only 0.9%
 - 96-97% of patients received systemic therapy

Giuliano AE, *JAMA* 2017;318(10):918.



Axillary De-escalation after Downstaging of Positive Nodes with Neoadjuvant Systemic Therapy

- **ACOSOG Z1071 Trial Publication**

- Clinical T0-T4, biopsy-proven node + (N1-N2)
- After neoadjuvant chemo, SLNB followed by ALND (≥ 2 SLN, dual tracer, clip optional)
- False Negative Rate of SLNB: 12.6% (Pre-defined acceptable threshold 10%)
 - 10.8% with dual tracers
 - 9.1% with removal at least 3 nodes
 - **6.8% with removal of at least 2 nodes, if clipped node removed**

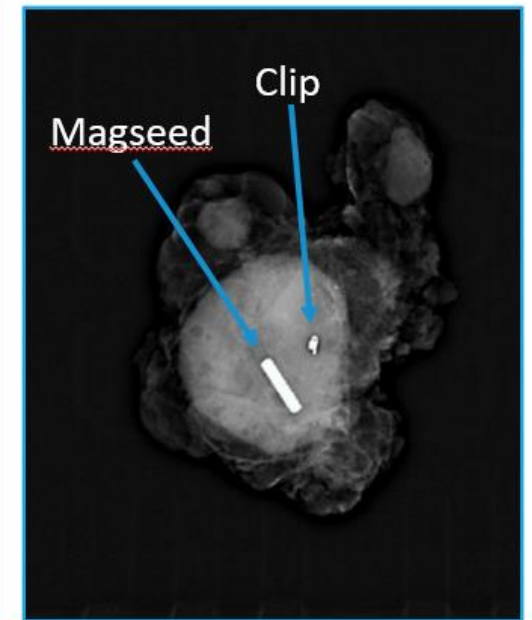
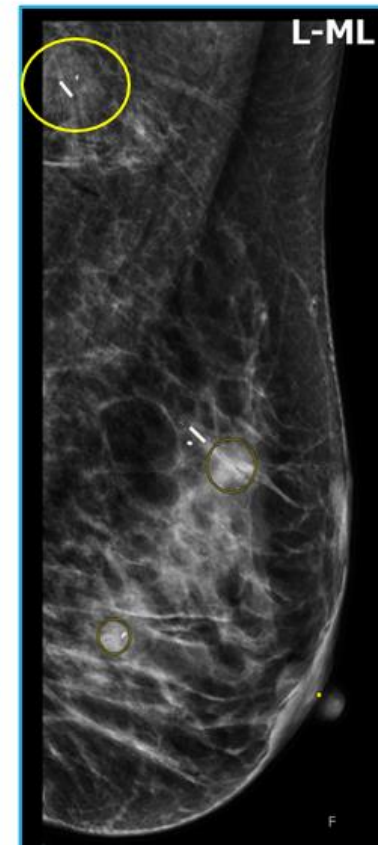
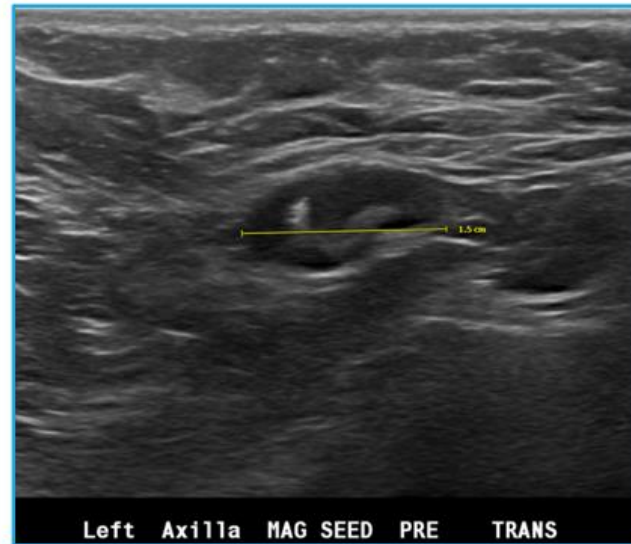
Boughey JC. *JAMA* 2013;310(14):1455.

Boughey JC. *Ann Surg* 2016;263(4):802.

Targeted Axillary Dissection (TAD)

- Localized removal of biopsy-proven node with clip
- Sentinel lymph node biopsy (with dual tracers)
- Removal of at least 2-3 lymph nodes

30 year old F with 4.7cm ER- HER2+ left breast cancer with 1 biopsy proven + lymph node. After chemo, no residual cancer. 0/3 LN positive.



Intra-op specimen radiograph

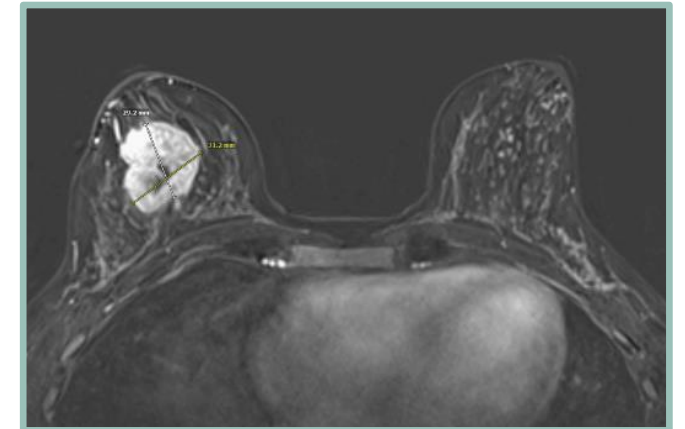
Determining Treatment Order

Who Gets Chemotherapy Prior to Surgery?

- **Inflammatory breast cancer**
- Other **locally advanced** breast cancer which is not operable at diagnosis
- **Triple negative breast cancer** > 1-2cm and/or lymph node +
- **HER2+ breast cancer** > 1-2cm and/or lymph node +
- **High Risk ER+ HER2- breast cancer**



Inflammatory Breast Cancer

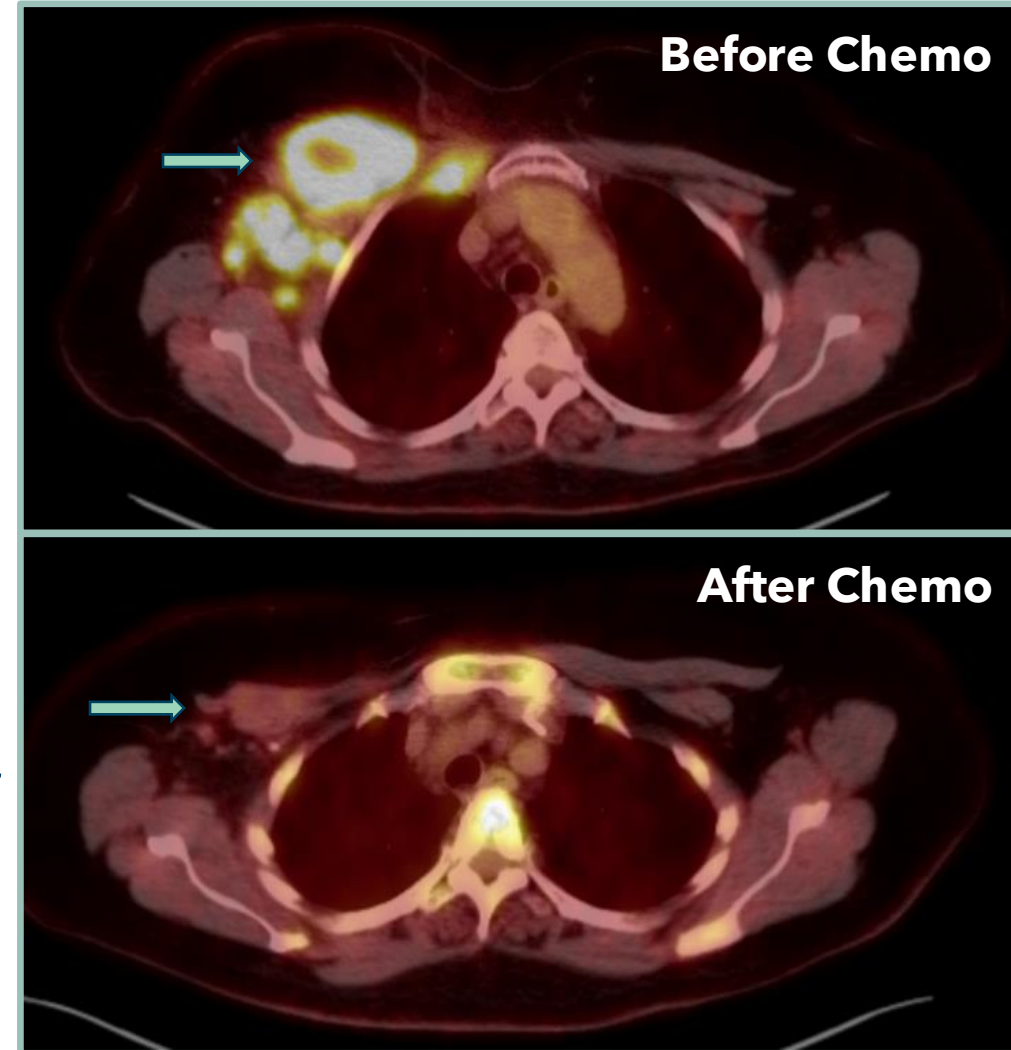


25 yo 3.6cm IDC, multiple nodes +, ER+ HER2-

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Benefits of Preoperative Systemic Therapy

- Facilitates breast conservation therapy (BCT)
- Downstages positive axillary nodes
- Can render inoperable tumors operable
- Prevent distant metastasis & improved survival
- Treatment response provides prognostic information for HER2+ and Triple Negative Breast Cancer (TNBC)
- Identifies patients with residual disease at higher risk for relapse to allow for addition of supplemental adjuvant regimens



NCCN Guidelines Version 4.2025, Invasive Breast Cancer, [nccn.org](https://www.nccn.org)

Pathologic Complete Response (pCR)

- **pCR:** Absence of residual invasive cancer in the breast and lymph nodes
- **pCR Rates:**
 - ~65% with pembrolizumab in TNBC
 - ~80% with dual agent anti-HER2 therapy if ER- HER2+
 - ~50% with dual agent anti-HER2 therapy if ER+ HER2+
- Associated with extremely favorable overall and disease-free survival, especially for TNBC and HER2+ cancers

NCCN Guidelines Version 4.2025, Invasive Breast Cancer, nccn.org
Globus O, *Ann Breast Surg* 2023;7:39.

How can we identify patients with **ER+ HER2-** breast cancer that would benefit from neoadjuvant chemotherapy?

Defining High-Risk ER+ HER2- Breast Cancer

High-Risk = Higher Risk of Recurrence

- High grade
- Larger tumor size
- Positive lymph node(s)
- High Ki-67
- Low level ER expression
- Low/negative PR expression
- High residual cancer burden after neoadjuvant treatment
- High-risk genomic signature

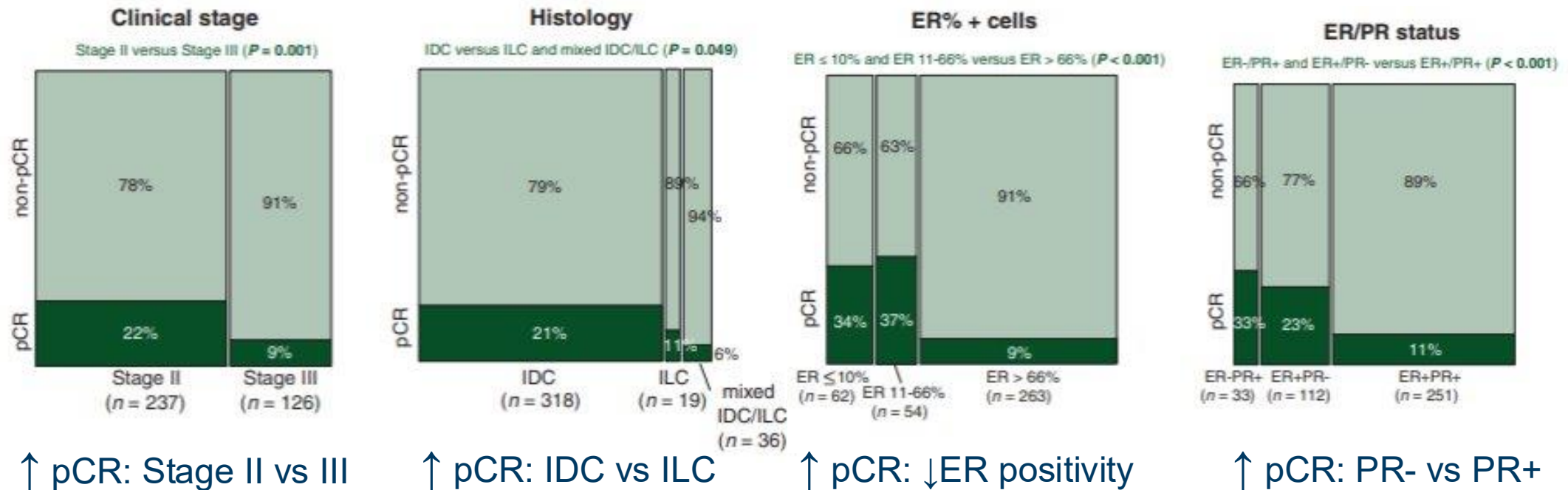
Table 2. Synoptic table of risk factors for disease relapse.

Factor	High Risk	Low Risk
Grade	3	1
Histotype	n/a	Pure tubular, pure mucinous, pure cribriform
Tumor size	T3/4	T1
Nodal status	N2/N3	N0
Ki-67	>30%	<20%
Expression level of hormonal receptors (ER, PgR)	ER <10% and/or PgR <20%	n/a
Residual cancer burden	RCB-III	RCB-0
Genomic signature (Oncotype DX, MammaPrint®, EndoPredict®, PAM50)	High-risk class	Low-risk class

n/a: not available, RCB: residual cancer burden.

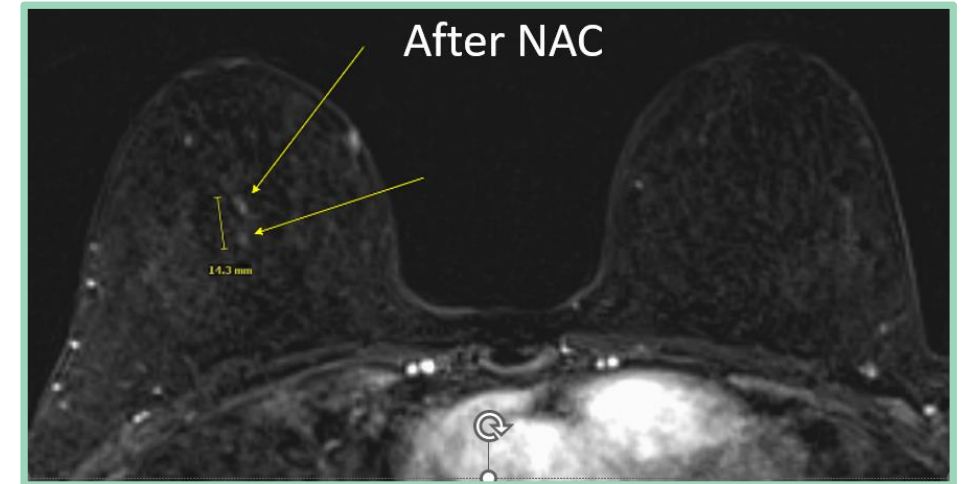
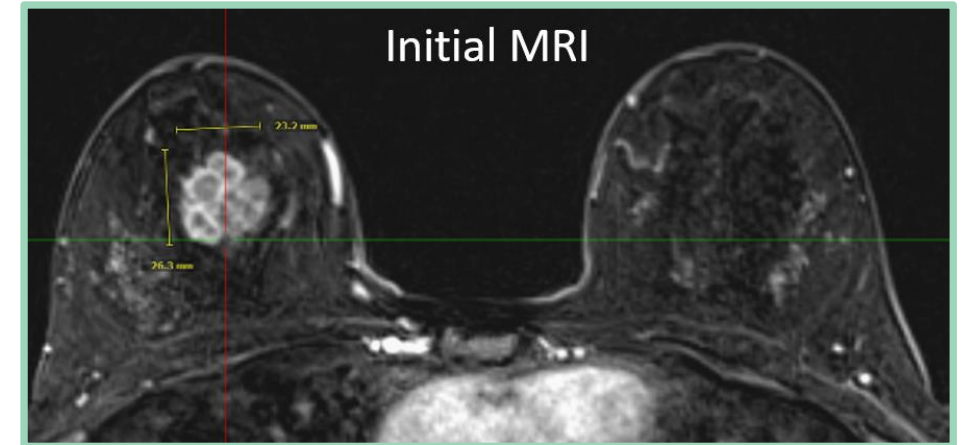
Clinical Features Which Increase pCR in HR+ HER2- Breast Cancer

- 379 pts with Stage II-III HR+ HER2- breast cancer enrolled in I-SPY2 Trial
- Enrolled if high molecular risk on MammaPrint



Likelihood of Downstaging to Breast Conservation with Neoadjuvant Chemo (NAC) in ER+ HER2-

- Petruolo, MSKCC, 196 ER+ HER2- pts
- Ineligible or borderline for BCT due to large tumor-to-breast size ratio
- Undergoing NAC due to high-risk features:
 - 62% became BCT eligible after NAC
 - Very few lobular cancers included



33 yo T2N0 ER+PR+HER2-, Oncotype 28

Petruolo O, *Ann Surg Oncol* 2021;28:287.

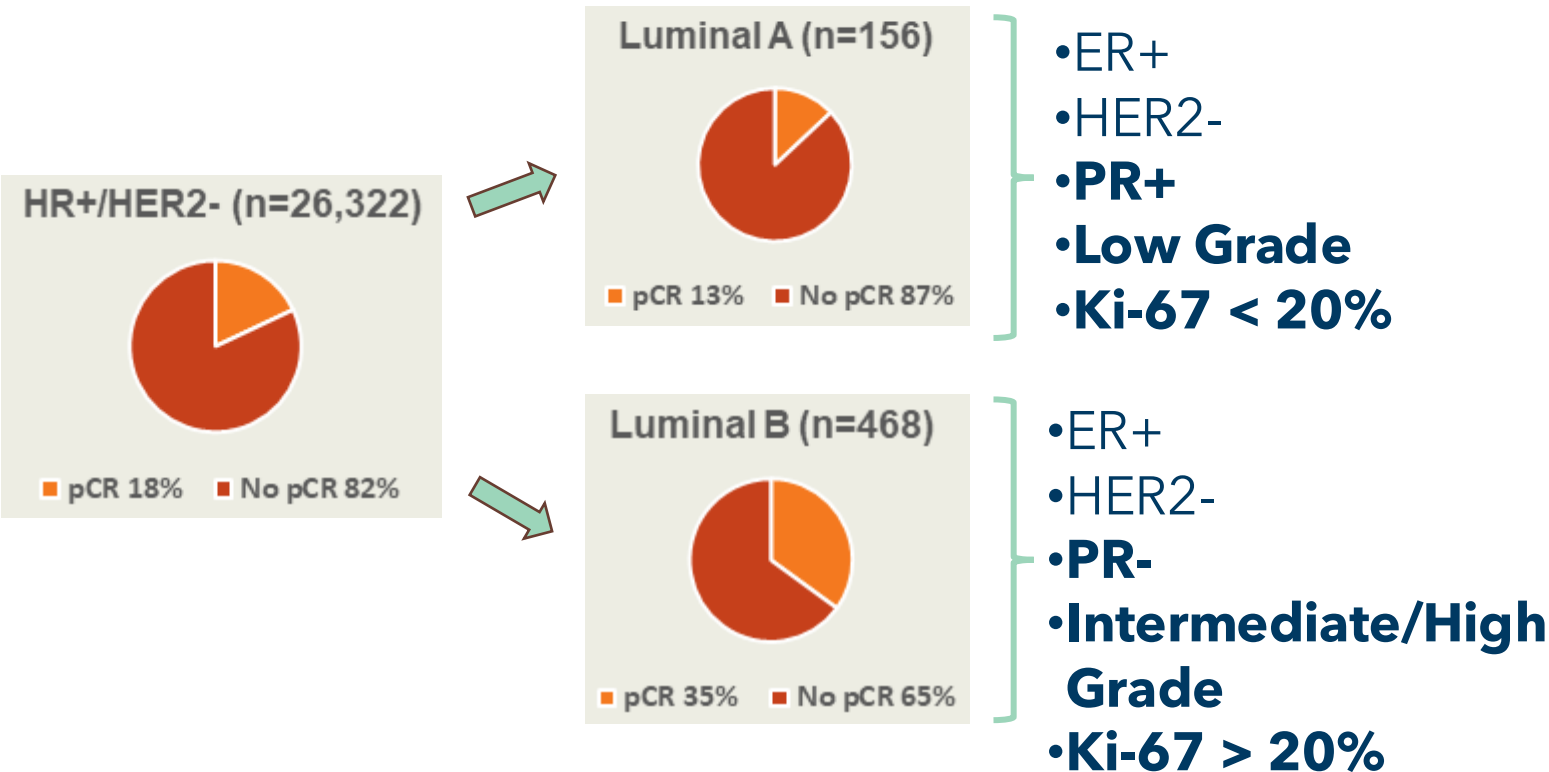
Likelihood of Nodal pCR in ER+ HER2-

JAMA Surgery | Original Investigation

Axillary Pathologic Complete Response After Neoadjuvant Systemic Therapy by Breast Cancer Subtype in Patients With Initially Clinically Node-Positive Disease

A Systematic Review and Meta-analysis

Sanaz Samiei, MD; Janine M. Simons, MD, PhD; Sanne M. E. Engelen, MD, PhD; Regina G. H. Beets-Tan, MD, PhD; Jean-Marc Classe, MD, PhD; Marjolien L. Smidt, MD, PhD; and the EUBREAST Group



- Systematic Review
- 25 studies, 26,322pts
- **Axillary Nodal pCR Rates:**
 - All ER+ HER2-: 18%
 - Luminal A: 13%
 - Luminal B: 35%

Likelihood of Nodal pCR in ER+ HER2-

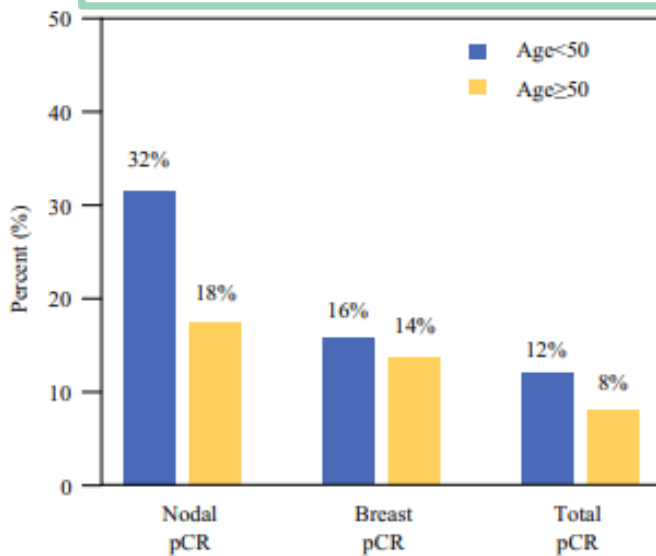
ORIGINAL ARTICLE – BREAST ONCOLOGY

Neoadjuvant Chemotherapy and Nodal Response Rates in Luminal Breast Cancer: Effects of Age and Tumor Ki67

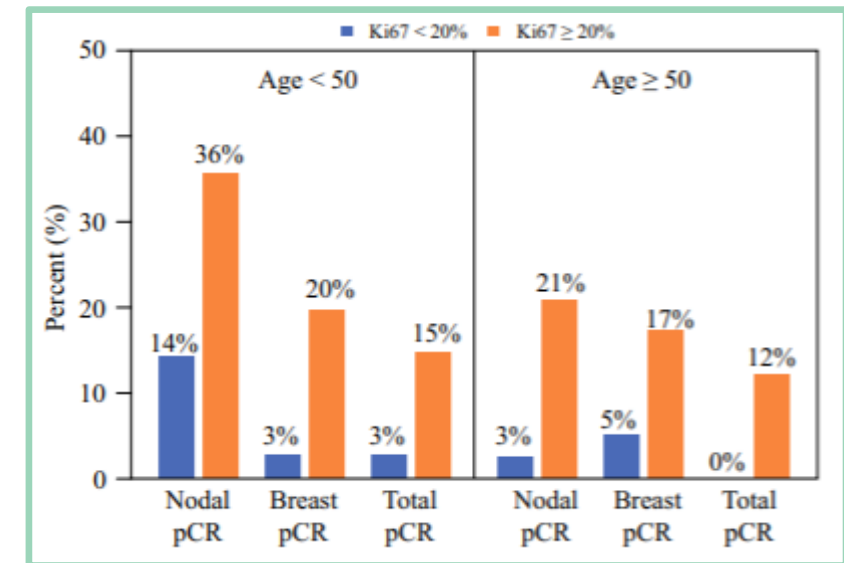
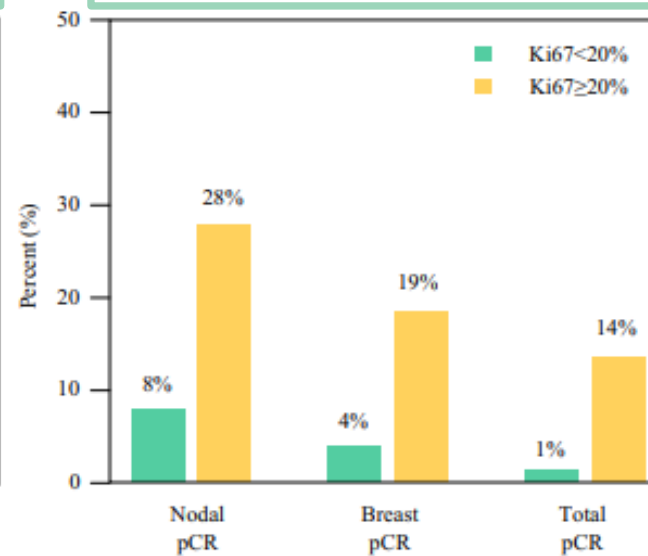
Judy C. Boughey, MD¹ , Tanya L. Hoskin, MS², and Matthew P. Goetz, MD³

- Mayo Clinic, 315 pts, 2012-2021
- ER+ HER2-, node +
- Axillary Nodal pCR Higher in:
 - Age < 50
 - Ki-67 ≥ 20%

Age < 50 vs ≥ 50



Ki67 < 20% vs ≥ 20%



Likelihood of Nodal pCR in ER+ HER2-

ORIGINAL ARTICLE – BREAST ONCOLOGY

The Role of Oncotype DX® Recurrence Score in Predicting Axillary Response After Neoadjuvant Chemotherapy in Breast Cancer

Jaime A. Pardo, MD, Betty Fan, DO, Alessandra Mele, MD, Stephanie Serres, MD PHD, Monica G. Valero, MD, Isha Emhoff, MD MPH, Amulya Alapati, MD, and Ted A. James, MD MHCM

- 158 pts in NCDB 2010-2015, cT1-2N1-2 ER+ HER2- breast cancer
- Received Neoadjuvant Chemo
- Had Oncotype DX® Recurrence Score (RS):
 - Low: < 18
 - Intermediate: 18-30
 - High: > 30

- Conclusion: Oncotype DX® RS was an independent predictor of axillary pCR in pts with ER+ HER2- breast cancer receiving NAC

TABLE 2 Axillary response after neoadjuvant chemotherapy among clinical variables

Characteristic	pCR		No pCR		<i>p</i> Value
	<i>N</i> = 23	%	<i>N</i> = 135	%	
Oncotype					0.0268
Low RS	6	10.7	50	89.3	
Intermediate RS	6	9.7	56	90.3	
High RS	11	27.5	29	72.5	

PCR pathologic complete response, *RS* recurrence score

Multidisciplinary Management Crucial for High-Risk HR+ HER2-

- Refer any ER+ HER2- patient with an indication for chemotherapy for neoadjuvant chemotherapy consideration
 - Possible Benefits: Downstage breast, downstage axilla, assess treatment response
- In the absence of clear neoadjuvant treatment algorithms for ER+ HER2-, decisions are best made with multidisciplinary input

In Summary:

- Breast cancer care continues to evolve and treatments have become more personalized.
- It is essential to work closely with a multidisciplinary team to determine the best care path for each patient.
- From screening through survivorship, there are so many ways we can make a positive difference in each patient's journey.

Thanks to:



suzanne.coopey@ahn.org
cell: 412-266-3010