

CHANGING ROLE OF SURGERY IN EARLY BREAST CANCER

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Necessity for change

- The ability of surgery to cure breast cancer has not changed over time
- The cancers we see in the screening era are more likely to be amenable to surgical care
 - **Smaller**
 - **Lower Nodal disease burden**

The overall 5-year survival rate improved in the past 3 decades:

1.Improvements in systemic treatment: (ie, chemotherapy, hormone therapy, targeted therapy).

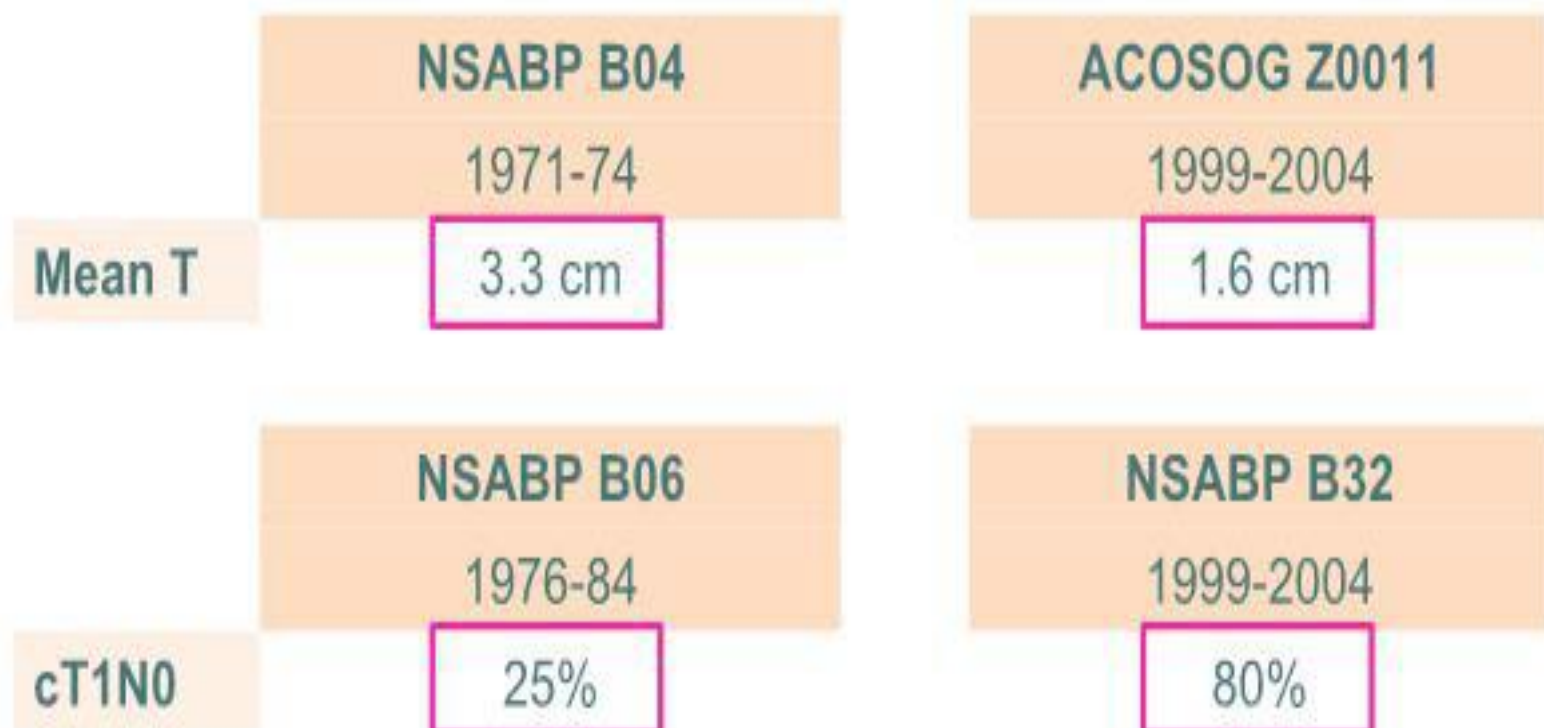
Today the estimated relative survival rates for breast cancer are :

- ❖ 5-years : 89%
- ❖ 10-years: 83%
- ❖ 15-years: 78%

2. Earlier detection: through increased **awareness**, widespread use of **screening mammography**, highly specific diagnostic approaches (**MRI, tomosynthesis**). This led to a higher incidence of non-palpable tumors, DCIS and early, small and N0 tumors



Changes in Breast Cancer Presentation Over Time



Fisher B, Cancer 1977;39:2827
Fisher B, N Engl J Med 1989;320:822

Giuliano A, JAMA 2011;305:569
Krag D, Lancet Oncol 2007;8:881

Changing role of breast cancer surgery

-De-escalating surgery

- 1) **Margin width** in patients with Ductal Carcinoma in situ (**DCIS**) and early invasive breast cancer decreasing
- 2) Even the **necessity for surgical treatment** in selected low risk dcis started to be under consideration.
- 3) **Axillary management** in clinically N-, SLN +, BCS
- 4) **Neoadjuvant chemotherapy (NAC)** followed by SN biopsy for patients presenting with **node-positive breast cancer. Minimizing the use of ALND: initial surgery or NAC?**

-Escalating surgery

- 1) **Bilateral mastectomy** rates rise
- 2) **Oncoplastic** procedures

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1. Overtreatment of DCIS. Are we doing more?

- Several large studies demonstrate specific survival rates greater than 95% in patients with DCIS regardless of the type of surgical treatment : **Overtreatment of DCIS** ¹
- Is any low risk DCIS subgroup where even omission of surgical treatment can be considered?

1. Bleyer A, Welch HG. Effect of three decades of screening mammography on breast-cancer incidence. N Engl J Med 2012;367:1998e2005.

2. Narod SA, Iqbal J, Giannakeas V, Sopik V, Sun P. Breast cancer mortality after a diagnosis of ductal carcinoma in situ. JAMA Oncol 2015;

3. Elshof LE, Tryfonidis K, Slaets L, van Leeuwen-Stok AE, Skinner VP, Dif N, et al. Feasibility of a prospective, randomised, open-label, international multicentre, phase III, non-inferiority trial to assess the safety of active surveillance for low risk ductal carcinoma in situ e the LORD study. Eur J Cancer 2015;51:1497e510

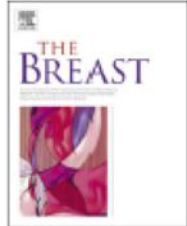


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Finding the balance between over- and under-treatment of ductal carcinoma in situ (DCIS)

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✓ Prospective trials: Active surveillance vs surgical treatment

Comparison of the designed and initiated prospective, randomised, open-label, phase III, non-inferiority trials to test whether less intensive treatment of low risk DCIS is safe. The information provided is based on literature for the LORIS and LORD trial [19,96] and on personal communication for the COMET and LARRIKIN trial.

Trial name	LORD	LORIS	COMET	LARRIKIN
Clarification acronym/ trial name	Low risk DCIS	Low risk DCIS	Comparison of operative versus medical endocrine therapy for low risk DCIS	The Australian slang word 'larrikin' is associated with the Australian identity: a bloke who refuses to stand on ceremony.
Trial status	Recruitment will start in 2016	Recruiting from July 2014	Not yet recruiting	Funding request submitted
Setting and locations	Mainland Europe (n > 30)	United Kingdom (n > 20)	United States (n = 100)	Australia and New Zealand (n ≥ 12)
Inclusion criteria	Women ≥ 45 years with asymptomatic, pure low-grade DCIS based on representative vacuum-assisted biopsies (at least 6) of unilateral, calcifications only of any size detected by population-based or opportunistic screening mammography.	Women ≥ 46 years with asymptomatic pure, non-high grade DCIS (e.g. low grade DCIS and intermediate grade DCIS with low grade features) based on vacuum assisted core biopsies of screen-detected or incidental calcifications only of any size (uni-/bilateral).	Women ≥ 40 years with pure, non-mass forming low-risk DCIS, e.g. ER + and/or PR + and HER-2 receptor-negative grade I or II DCIS based on a core biopsy without evidence of other breast disease on physical examination and breast imaging within 6 months of registration.	Women ≥ 55 years with pure, asymptomatic and low risk DCIS (low and intermediate grade) based on either a core biopsy and/or vacuum-assisted biopsy or open diagnostic surgical biopsy of screen detected or incidental calcifications (uni/bilateral but unifocal) ≤ 20 mm.
Exclusion criteria	No prior history of DCIS or invasive breast cancer, a BRCA 1/2 gene mutation present in family, no bilateral DCIS, synchronous contralateral invasive breast cancer, lobular carcinoma in situ, Paget's disease, or invasive breast disease on cytology/histology	No prior history or current diagnosis of invasive breast cancer or ipsilateral DCIS and no high risk group for developing breast cancer	Not known.	No previous or current diagnosis of invasive cancer, previous ipsilateral DCIS, Paget's disease or LCIS, pregnancy/lactation or a known BRCA1/2 mutation
Central review	No central review of pathology.	Real time central review of histological slides by expert DCIS pathologists.	Not known.	No central review planned.
Interventions	Randomisation between standard treatment according to local policy (wide local excision with/without radiotherapy, mastectomy and possibly hormonal therapy by Tamoxifen) and active surveillance. Both study arms will be monitored with annual digital mammography for 10 years.	Randomisation between standard surgical and adjuvant treatment according to local policy and active surveillance, with specific notification that patients in the latter group should not receive anti-oestrogen treatment. Both study arms will be monitored with annual mammography for 10 years. Anti-oestrogen treatment is not allowed in the active surveillance arm.	Randomisation between standard treatment including surgery and radiation and active surveillance. Patients in both groups are free to decide whether to choose endocrine therapy. Both study arms will be carefully monitored with mammograms and physical exams every 6 months for 5 years.	Randomisation between standard treatment according to physician and patient choice (surgery with/without radiotherapy) and active surveillance. Patients in both groups are free to decide whether to opt for endocrine therapy for 5 years. Both groups will be monitored with annual mammography for at least 10 years and regular clinical examinations or at patient's request for 5 years then annually.



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Feasibility of a prospective, randomised, open-label, international multicentre, phase III, non-inferiority trial to assess the safety of active surveillance for low risk ductal carcinoma in situ – The LORD study



Lotte E. Elshof^{a,b,c}, Konstantinos Tryfonidis^d, Leen Slaets^e,
A. Elise van Leeuwen-Stok^f, Victoria P. Skinner^a, Nicolas Dif^g, Ruud M. Pijnappel^h,
Nina Bijkerⁱ, Emiel J.Th. Rutgers^a, Jelle Wesseling^{b,j,*}



Feasibility of a prospective, randomised, open-label, international multicentre, phase III, non-inferiority trial to assess the safety of active surveillance for low risk ductal carcinoma in situ – The LORD study



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Nina Bijkerⁱ, Emiel J.Th. Rutgers^a, Jelle Wesseling^{b,j,*}

Eligibility criteria

- >46 years
- **Pure** Low grade DCIS
- in VACBiopsy
- No mass detection radiologically
- Any Size

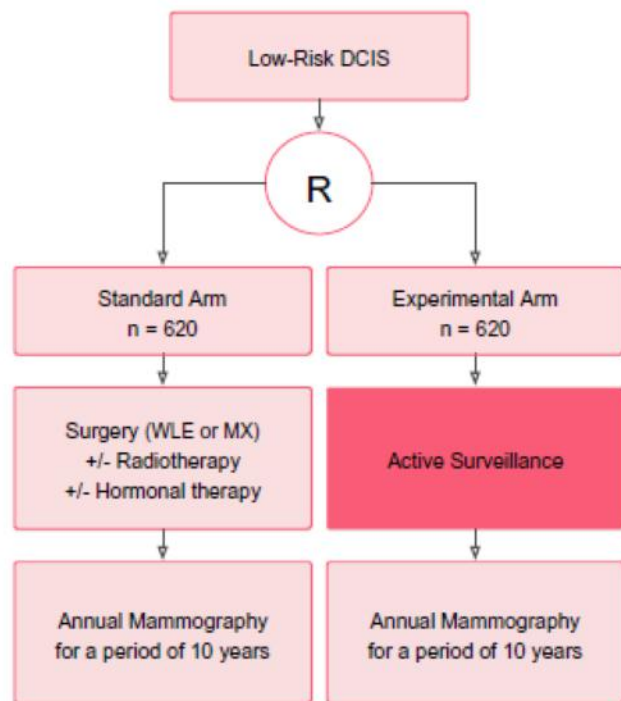


Fig. 2. Flow chart of study design. R = randomisation. WLE = wide local excision. MX = mastectomy.



Feasibility of a prospective, randomised, open-label, international multicentre, phase III, non-inferiority trial to assess the safety of active surveillance for low risk ductal carcinoma in situ – The LORD study



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iBC-free rate in the active surveillance arm, in relation to the expected iBC-free rate in the standard treatment arm, is **clinically acceptable**. If low-grade DCIS progresses to iBC, this is most likely to be low-grade iBC . After an active surveillance strategy of a low-grade DCIS lesion, multiple treatment options of the subsequent low-grade iBC will still be feasible and excellent long-term survival outcomes can be preserved.



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Addressing overtreatment of screen detected DCIS; the LORIS trial



Adele Francis^{a,*}, Jeremy Thomas^b, Lesley Fallowfield^c, Matthew Wallis^d,
John M.S. Bartlett^e, Cassandra Brookes^f, Tracy Roberts^g, Sarah Pirrie^f, Claire Gaunt^f,
Jennie Young^f, Lucinda Billingham^f, David Dodwell^h, Andrew Hanbyⁱ,
Sarah E. Pinder^j, Andrew Evans^k, Malcolm Reed^l, Valerie Jenkins^c, Lucy Matthews^c,
Maggie Wilcox^m, Patricia Fairbrother^m, Sarah Bowden^f, Daniel Rea^f

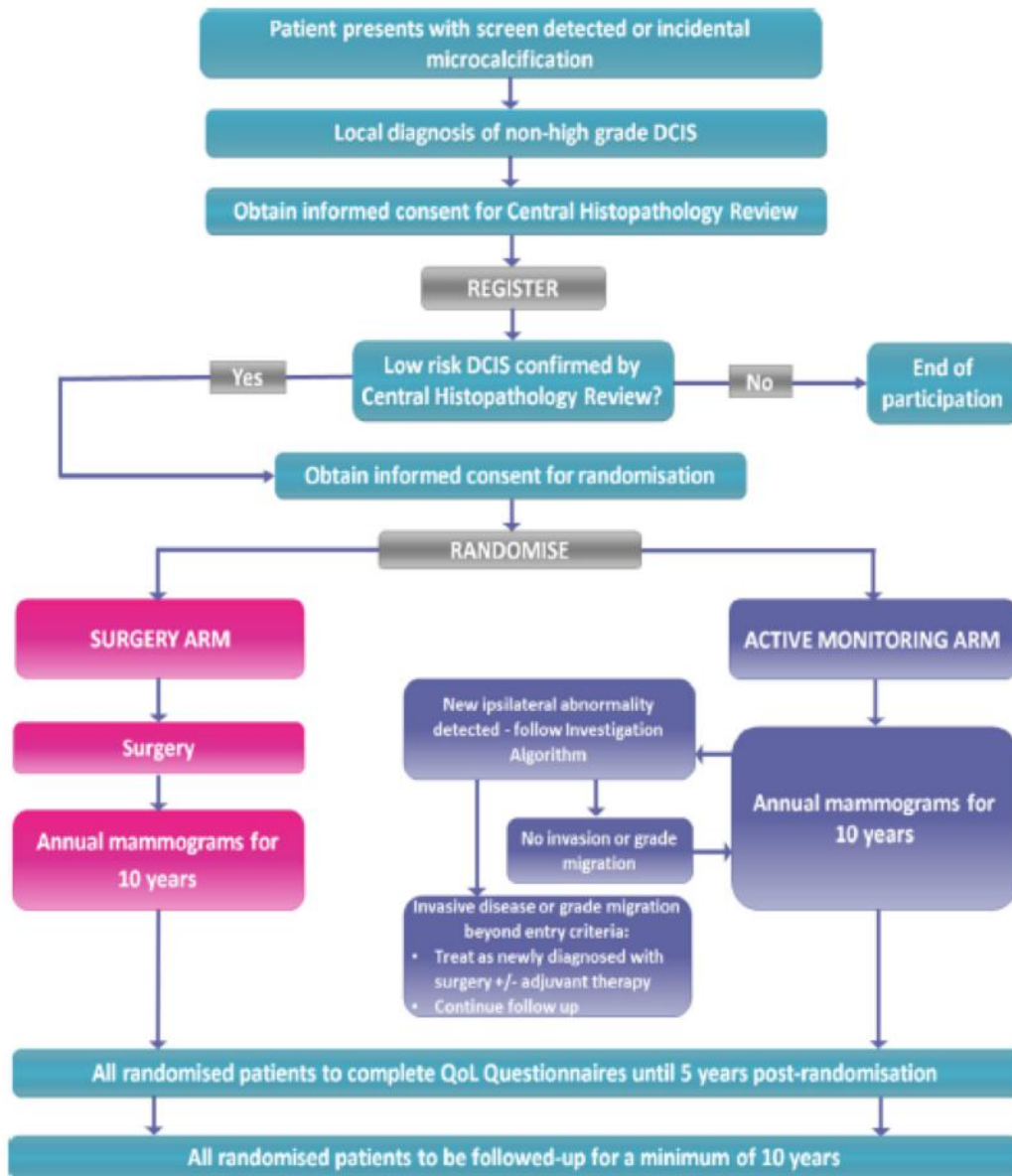


Fig. 1. Low risk DCIS (LORIS) trial flow diagram.

European Journal of Cancer (2015) 51, 2296–2303

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Addressing overtreatment of screen detected DCIS: the LORIS trial

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Adele Francis^{a,*}, Jeremy Thomas^b, Lesley Fallowfield^c, Matthew Wallis^d, John M.S. Bartlett^e, Cassandra Brookes^f, Tracy Roberts^g, Sarah Pirrie^h, Claire Gauntⁱ, Jennie Young^f, Lucinda Billingham^f, David Dodwell^h, Andrew Hanby^j, Sarah E. Pinder^l, Andrew Evans^k, Malcolm Reed^l, Valerie Jenkins^c, Lucy Matthews^c, Maggie Wilcox^m, Patricia Fairbrother^m, Sarah Bowden^l, Daniel Rea^l

Eligibility criteria

- >46ετών
- Low and Intermediate grade VACBiopsy
- No mass detection radiologically
- Any Size



Addressing overtreatment of screen detected DCIS: the LORIS trial



Adele Francis^{a,*}, Jeremy Thomas^b, Lesley Fallowfield^c, Matthew Wallis^d, John M.S. Bartlett^e, Cassandra Brookes^f, Tracy Roberts^g, Sarah Pirrie^f, Claire Gaunt^f, Jennie Young^f, Lucinda Billingham^f, David Dodwell^h, Andrew Hanbyⁱ, Sarah E. Pinder^j, Andrew Evans^k, Malcolm Reed^l, Valerie Jenkins^c, Lucy Matthews^c, Maggie Wilcox^m, Patricia Fairbrother^m, Sarah Bowden^f, Daniel Rea^l

Is active surveillance safe in screen-detected low/intermediate-risk DCIS

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••••••

-Primary endpoint :
invasiveBC-free rate 10-year

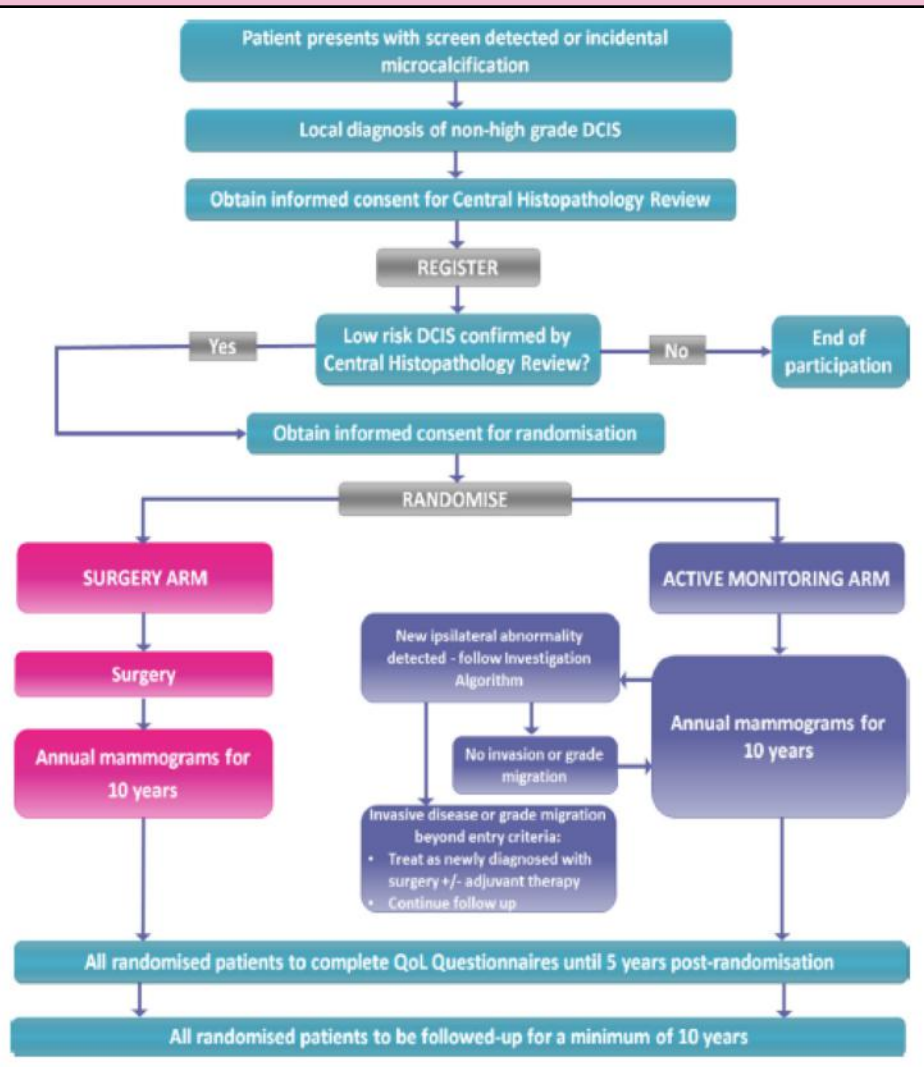


Fig. 1. Low risk DCIS (LORIS) trial flow diagram.

2. Decreasing Re-excision in DCIS with a standardized margin definition

- Society of Surgical Oncology (SSO), the American Society of Radiation Oncology (ASTRO), and the American Society of Clinical Oncology (ASCO) to convene a multi-disciplinary panel to develop an evidence-based consensus on **margin width** for DCIS patients treated with **lumpectomy and whole breast irradiation**

1. Morrow M, et al Society of surgical oncology-american society for radiation oncology-american society of clinical oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in ductal carcinoma in situ. Ann Surg Oncol 2016;23:3801e10.

2. Morrow M, et al. Society of surgical oncology-american society for radiation oncology- american society of clinical oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in ductal carcinoma in situ. Pract Radiat Oncol 2016;6:287e95.

3. Morrow M, et al. Society of surgical oncology-american society for radiation oncology- american society of clinical oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in ductal carcinoma in situ. J Clin Oncol 2016;34(33):4040e6

2. Decreasing Re-excision in DCIS with a standardized margin definition

-Meta-analysis of **20** studies that included **8651** patients and 865 local recurrences served as a primary evidence base for the consensus.

-Screen-detected DCIS was present in 86% of patients, 71% received a boost dose of radiation, and 21% received endocrine therapy, primarily tamoxifen.

Primary question : **Threshold negative margin width** associated with a **reduced risk of local recurrence** in patients undergoing BCT and receiving whole-breast irradiation ?

1. Marinovich ML, Azizi L, Macaskill P, Irwig L, Morrow M, Solin LJ, et al. The association of surgical margins and local recurrence in women with ductal carcinoma in situ treated with breast-conserving therapy: a meta-analysis. *Ann Surg Oncol* 2016;23:3811e21.

Impact of negative margin width on local recurrence: Bayesian network meta-analysis.

	Threshold Negative Margin Distance			
	>0–1 mm	2 mm	3 mm	10 mm
Number of Patients	2230	2412	289	1963
Odds Ratio	0.45	0.32	0.30	0.32
95% Credible Interval	0.32–0.61	0.21–0.48	0.12–0.76	0.19–0.49

Data from Marinovich M. et al. [9].

-Comparison of **2 mm to smaller negative margins demonstrated a significant benefit for the 2 mm margin** (odds ratio 0.51, 95% confidence interval (CI) 0.31e0.85; $p = 0.01$).

-**No significant differences were seen when comparing margins of 2 mm, 3 mm, and 10 mm** ($p > 0.40$)

.Marinovich ML, Azizi L, Macaskill P, Irwig L, Morrow M, Solin LJ, et al. The association of surgical margins and local recurrence in women with ductal carcinoma in situ treated with breast-conserving therapy: a meta-analysis. *Ann Surg Oncol* 2016;23:3811e21.

2. Decreasing Re-excision in DCIS with a standardized margin definition

-Obtaining negative margin widths greater than 2 mm was not supported by the evidence

-Margins of at least **2 mm** were associated with a **reduced risk of local recurrence** relative to narrower margin widths in patients receiving whole-breast irradiation.

- **Clinical judgment** is necessary to determine whether patients with negative margin widths < 2 mm require **re-excision** based on the long-term rates of local control seen NSABP trials, which used the negative margin definition of **no ink on tumor** and on the results of the large single-institution study of Van Zee et al.

Factors to decide Re-excision

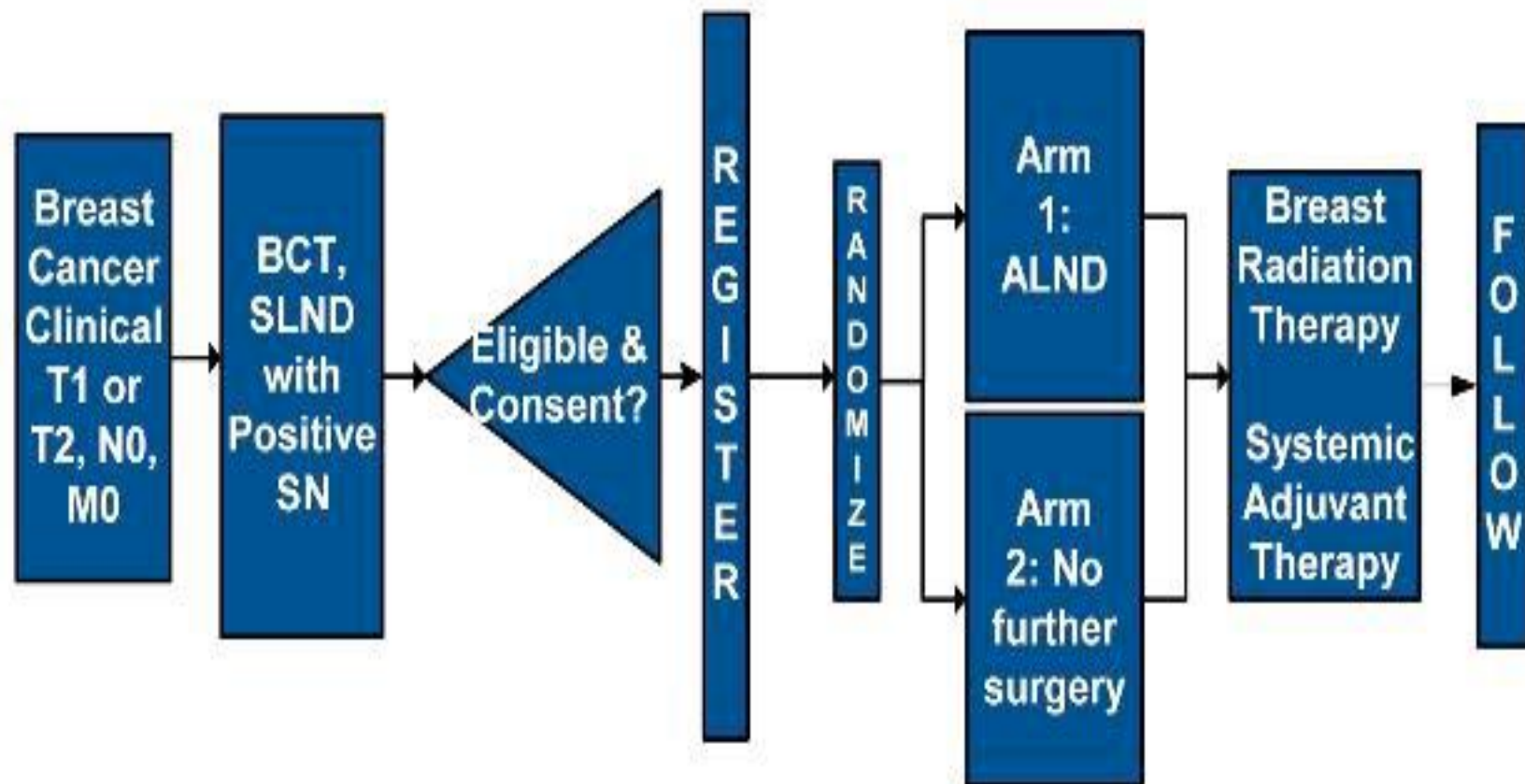
-Re-excise a negative margin < 2 mm or not?

- ✓ Extent of DCIS in proximity to the margin
- ✓ Which margin is close
- ✓ The presence of residual calcifications on mammogram
- ✓ The cosmetic impact of re-excision
- ✓ The patient's life expectancy.

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**3. Reducing axillary dissection
(ALND) rates in patients having
BCT**

2011 Study Design Schema



Outcomes of ACOSOG Z0011

Median f/u 6.3 yrs

- No difference in nodal recurrence between the ALND and SN groups (0.5% vs 0.9% , $p=0.45$)
- No difference in DFS or OS
- Morbidity significantly decreased with SN only
 - Wound infection $p = .0016$
 - Paresthesia $p < .0001$
 - Lymphedema (pt report) $p < .0001$

Concerns Regarding ACOSOG Z0011

- Follow-up too short
ER+ population at risk for late LRR
- Highly favorable, selected population—results not generally applicable
- Not safe for high risk patients

Locoregional Recurrence After Sentinel Lymph Node Dissection With or Without Axillary Dissection in Patients With Sentinel Lymph Node Metastases

Long-term Follow-up From the American College of Surgeons Oncology Group (Alliance) ACOSOG Z0011 Randomized Trial

Armando E. Giuliano, MD,* Karla Ballman, PhD,† Linda McCall, MS,‡ Peter Beitsch, MD,§
Pat W. Whitworth, MD,¶ Peter Blumencranz, MD,|| A. Marilyn Leitch, MD,** Sukamal Saha, MD,††
Monica Morrow, MD,‡‡ and Kelly K. Hunt, MD§§

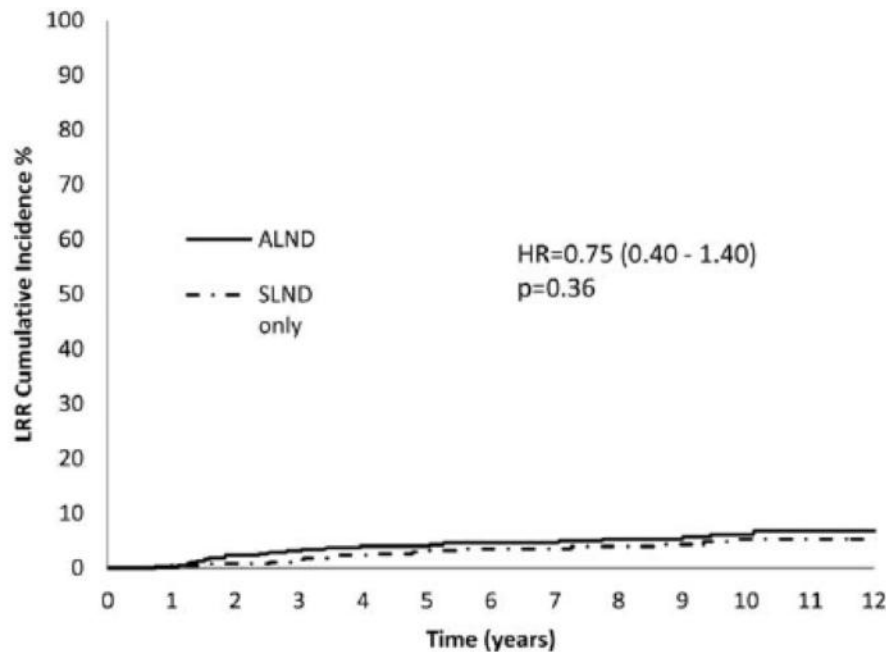







FIGURE 2. Cumulative incidence of locoregional recurrence by treatment arm.

- Despite the potential for residual axillary disease after SLN+,
SLN without ALND offers excellent regional control for selected patients with early metastatic breast cancer

3. Reducing axillary dissection (ALND) rates in patients having BCT

- 10-year results of the ACOSOG Z0011 trial continue to demonstrate **no difference in the risk of locoregional recurrence** between treatment arms.
- Nodal recurrence was seen in 1.1% of the sentinel node-only group and 0.5% of the ALND group (p 1/4 0.45) with a median follow-up of 9.25 years, and only one nodal recurrence was seen in the sentinel node-only group after the initial 76- month follow-up.
- Even in ER positive patients, nodal recurrence is an early event. **Survival outcomes do not differ significantly between groups with longer follow-up.**

How Many N+ Patients Are Spared ALND Using ACOSOG Z0011 Criteria?

Author		# Patients	% No ALND
Ngui		119	22%
Verhuevel		916	61%
Delpech		125	70%
Yi		488	75%
Guth		55	9%

Ngui N, ANZ J Surg 2013;83:924

Verhuevel W, Eur J Surg Oncol 2016;42:1162

Delpech Y, Ann Surg Oncol 2013;20:2556

Yi M, J Am Coll Surg 2013;216:105

Guth U, Eur J Surg Oncol 2012;38:645

MSKCC Study Aims

- To determine how often ALND can be avoided in a consecutive, unselected series of patients meeting ACOSOG Z0011 eligibility criteria
- To determine the incidence of LRR after SN biopsy alone in this group

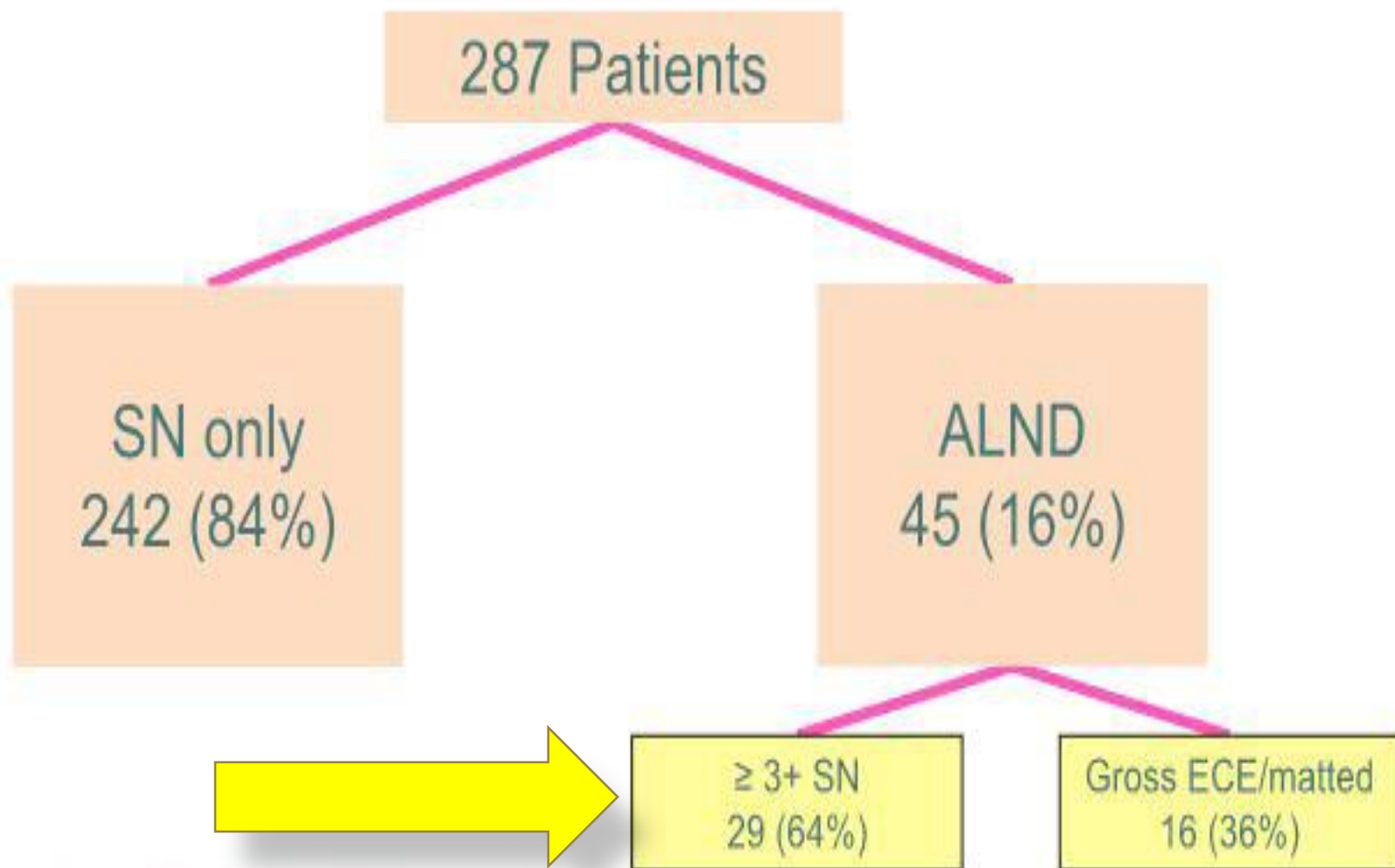
Initiated August 2010

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Morrow M, Van Zee KJ, Pilewskie M, El-Tamer M, Barrio A, Plitas G, et al. Axillary dissection, nodal recurrence and extent of RT in Z0011 eligible breast cancer patients: a prospective study (abstract No. 54).

Ann Surg 2017 (In press).

Intention to Treat Outcome



How Many Patients Can Avoid ALND With the ACOSOG Z0011 Approach?

MSKCC Experience
T1/2 cN0 BCS
Positive SN

Initial Cohort
8/10-11/12

287
Eligible

242 (84%)
SN ONLY

Total Cohort
8/10-9/16

774
Eligible

658 (85%)
SN ONLY

Exclusions
NAC, micromets,
mastectomy



Can Axillary Dissection Be Avoided in High Risk Subsets?

High Risk: Age < 50
TNBC
HER2+

	High Risk	Average Risk
# Patients	251	472
Completion ALND	39 (15.1%)	75 (15.9%)
Median # additional positive nodes	3.5	3.0

- **ALND necessity the same**
- **Nodal disease burden did not differ significantly between groups**

Outcomes: MSKCC Series

Median f/u 33 months (12-68)

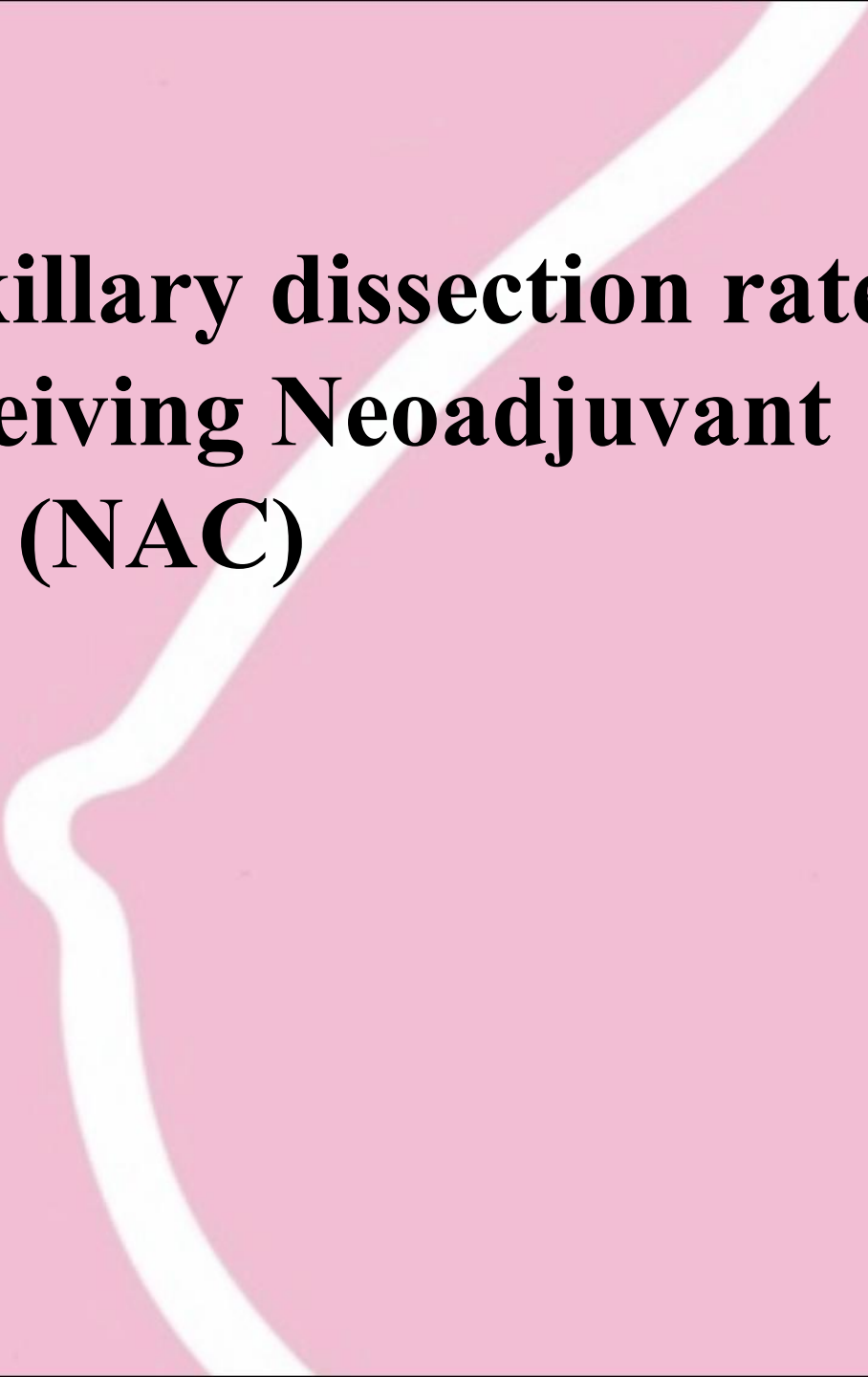
- No axillary first failures
- 3 Breast + axilla
- 2 Axilla + distant

5 yr KM nodal recurrence-free rate: 98% (95% CI 96-99)

Reducing axillary dissection (ALND) rates in patients having BCT in:

- Clinically node-negative women undergoing BCT
- **Age, ER, and HER2 status should not be used as selection criteria.**
- Avoidance of ALND in women meeting ACOSOG Z0011 eligibility criteria represents a **major step forward in de-escalating surgery to reduce the burden of treatment.**

Morrow M, Van Zee KJ, Pilewskie M, El-Tamer M, Barrio A, Plitas G, et al. Axillary dissection, nodal recurrence and extent of RT in Z0011 eligible breast cancer patients: a prospective study (abstract No. 54). Ann Surg 2017 (In press).

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4. Reducing axillary dissection rates in patients receiving Neoadjuvant chemotherapy (NAC)

4. Reducing axillary dissection rates in patients receiving Neoadjuvant chemotherapy (NAC)

- Large prospective trials : Sentinel node can be identified in more than 90% of patients after NAC with a false-negative rate less than 10%.
- Studies of NAC in patients presenting with biopsy-proven nodal metastases have reported nodal pathologic complete response (pCR) rates of **35%- 49%**

Could these patients be identified with sentinel node biopsy after NAC and spared ALND ?

- Classe JM, et al. Sentinel lymph node biopsy after neoadjuvant chemotherapy for advanced breast cancer: results of Ganglion Sentinelle et Chimiotherapie Neoadjuvante, a French prospective multicentric study. J Clin Oncol 2009;27:726e32.
- Hunt KK, et al. Sentinel lymph node surgery after neoadjuvant chemotherapy is accurate and reduces the need for axillary dissection in breast cancer patients. Ann Surg 2009;250:558e66.
- Boileau JF, et al. Sentinel node biopsy after neoadjuvant chemotherapy in biopsy-proven node-positive breast cancer: the SN FNAC study. J Clin Oncol 2015;33: 258e63.

4. Reducing axillary dissection rates in patients receiving Neoadjuvant chemotherapy (NAC)

-Three prospective, single-arm studies have investigated the feasibility of sentinel node biopsy after NAC in patients presenting with nodal metastases and reported **overall false-negative rates for sentinel node biopsy of 8%-14%** in this group. In the

- ACOSOG Z1071 trial and the SENTINA study, the false-negative rate was **less than 10%** only when **3** or more sentinel nodes were retrieved.

-Boileau JF et al. Sentinel node biopsy after neoadjuvant chemotherapy in biopsy-proven node-positive breast cancer: the SN FNAC study. J Clin Oncol 2015;33: 258e63.

-Boughey JC et al. Sentinel lymph node surgery after neoadjuvant chemotherapy in patients with node-positive breast cancer: the ACOSOG Z1071 (Alliance) clinical trial. JAMA 2013;310:1455e61.

-Mamtani A, et al. How often does neoadjuvant chemotherapy avoid axillary dissection in patients with histologically confirmed nodal Metastases? Results of a prospective study. Ann Surg Oncol 2016;23:3467e74.

-Boughey JC, et al. Tumor biology correlates with rates of breastconserving surgery and pathologic complete response after neoadjuvant chemotherapy for breast cancer findings from the ACOSOG Z1071 (alliance) prospective multicenter clinical trial. Ann Surg 2014;260:608e16.

Sentinel-lymph-node biopsy in patients with breast cancer before and after neoadjuvant chemotherapy (SENTINA): a prospective, multicentre cohort study



Thorsten Kuehn, Ingo Bauerfeind, Tanja Fehm, Barbara Fleige, Maik Hausschild, Gisela Helms, Annette Lebeau, Cornelia Liedtke, Gunter von Minckwitz, Valentina Nekjudova, Sabine Schmatloch, Peter Schrenk, Annette Staebler, Michael Untch

Lancet Oncol 2013; 14: 609–18

False negative rate (FNR): 14%
but....

-Arm C : clinically node positive who converted to clinically node negative after chemotherapy.

-FNR: 1 SLN 24.3 % removed,

2 18.5 %

3 <10 %

-FNR was lower (8.6 %) for patients who underwent dual mapping with radioisotope and blue dye.

4. Reducing axillary dissection rates in patients receiving Neoadjuvant chemotherapy (NAC)

-The likelihood of identifying 3 or more sentinel nodes and having a nodal pCR was investigated in a prospective study of 128 patients receiving NAC at Memorial Sloan Kettering Cancer Center.

-Three or more sentinel nodes were retrieved in 110 patients, and 62 had a nodal pCR, meaning that **ALND was avoided in 48%** of those who were clinically eligible for a sentinel node biopsy after NAC. Rates of nodal pCR in this study ranged from **21% in ER positive HER2 negative patients** to **97% in ER negative HER2 positive patients** ($p < 0.0001$).

Management algorithm to minimize the use of ALND is presented

M. Morrow / The Breast xxx (2017) 1–4

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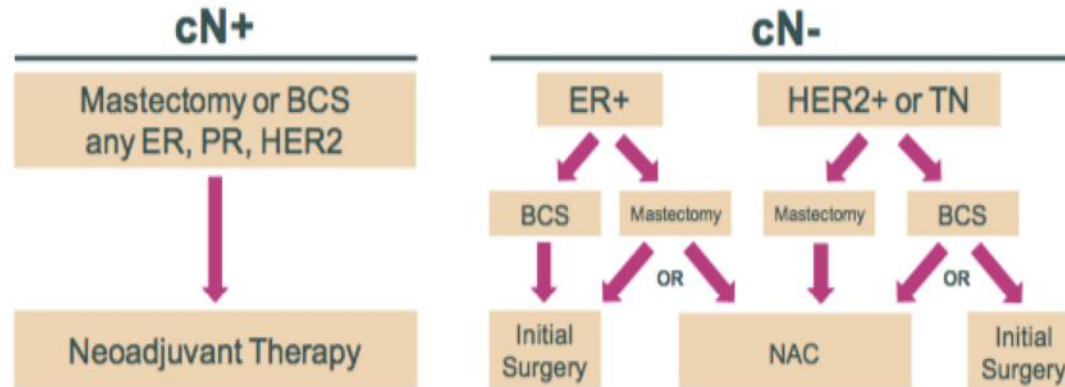


Fig. 1. Algorithm for Minimizing the Need for Axillary Node Dissection. Patients presenting with palpable, biopsy-proven nodal disease (cN+) have no option other than neoadjuvant therapy to avoid axillary dissection. Patients who are clinically node negative and ER positive having breast conservation should have initial surgery, while those who are ER negative or HER2 positive having mastectomy should receive neoadjuvant therapy. For triple-negative or HER2 positive patients having breast conservation, the likelihood of ALND does not differ for initial surgery versus neoadjuvant therapy, and the same is true for ER positive patients having mastectomy. cN+, clinically node positive; cN-, clinically node negative; BCS, breast-conserving surgery; ER, estrogen receptor; PR, progesterone receptor; TN, triple negative; NAC, neoadjuvant chemotherapy.

- **cN+ : NAC only chance to spare ALND**
- **cN- : Approach based on surgery type NAC only for mastectomy candidates**

Management algorithm to minimize the use of ALND is presented

M. Morrow / *The Breast* xxx (2017) 1–4

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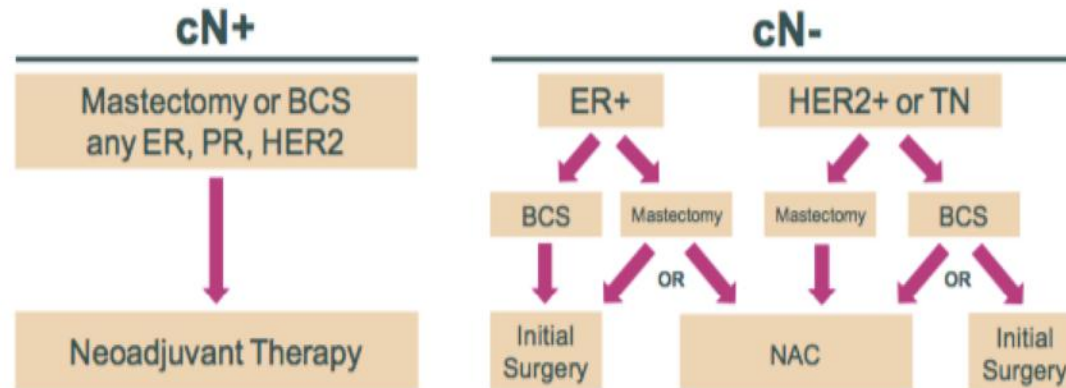


Fig. 1. Algorithm for Minimizing the Need for Axillary Node Dissection. Patients presenting with palpable, biopsy-proven nodal disease (cN+) have no option other than neoadjuvant therapy to avoid axillary dissection. Patients who are clinically node negative and ER positive having breast conservation should have initial surgery, while those who are ER negative or HER2 positive having mastectomy should receive neoadjuvant therapy. For triple-negative or HER2 positive patients having breast conservation, the likelihood of ALND does not differ for initial surgery versus neoadjuvant therapy, and the same is true for ER positive patients having mastectomy. cN+, clinically node positive; cN-, clinically node negative; BCS, breast-conserving surgery; ER, estrogen receptor; PR, progesterone receptor; TN, triple negative; NAC, neoadjuvant chemotherapy.

When comparing rates of ALND in patients having mastectomy to those receiving NAC, **NAC significantly reduced the need for ALND in HER2 positive (8% vs 36%; $p < 0.001$) and triple-negative cancers (7% vs 25%; $p \leq 0.001$), but not in ER positive cancers (34% vs 37%; $p = 0.62$)**

Morrow M., *Breast*. 2017 Aug;34 Suppl 1:S1-S4

De-escalation of surgery:

Reducing axillary dissection rates in patients receiving NAC is a viable strategy for avoiding ALND in patients presenting with nodal metastases.

One threat to the de-escalation of surgery is *patient acceptance*. After years of steadily increasing rates of BCT, mastectomy rates, particularly bilateral mastectomy rates, began to rise.....

ESCALATING SURGERY

...patients, not physicians,
are primarily responsible
for mastectomy rise

–Escalating surgery

- 1) **Oncoplastic** procedures
- 2) **Bilateral mastectomy** rates rise

Types of Oncoplastic procedures

- ✓ Immediate and delayed reconstruction.
- ✓ Autologous or Implant/expander techniques
- ✓ Oncoplastic techniques all levels to obtain a good shape of the affected breast.
- ✓ Reduction mammoplasty procedures to the affected or/and to the contralateral breast to obtain symmetry

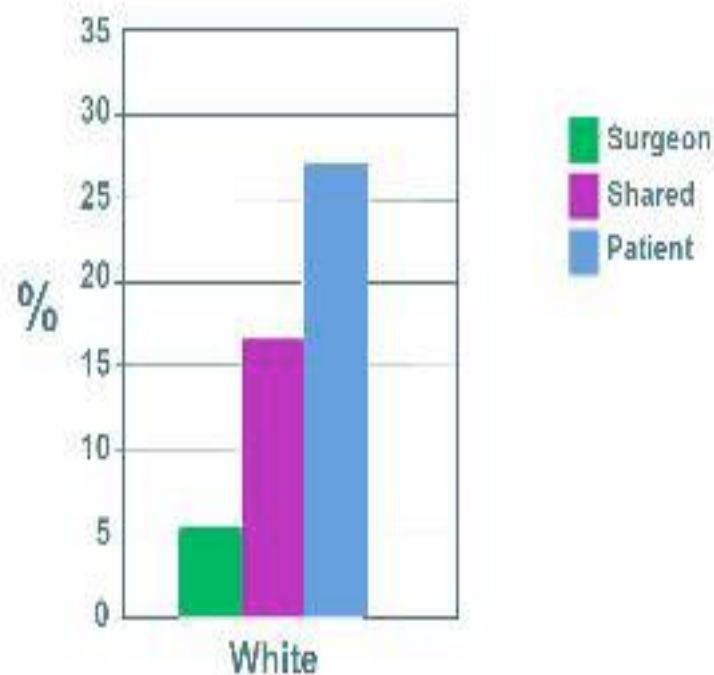
Pitfalls of Oncoplastic procedures

- ✓ Increase the duration of operation
- ✓ Increase the postoperative complications which may delay adjuvant therapies.
- ✓ Technically demanding
- ✓ Often require plastic surgeon's contribution.

But...

- ✓ Offer excellent cosmetic result
- ✓ Psychological positive effect to the patient.

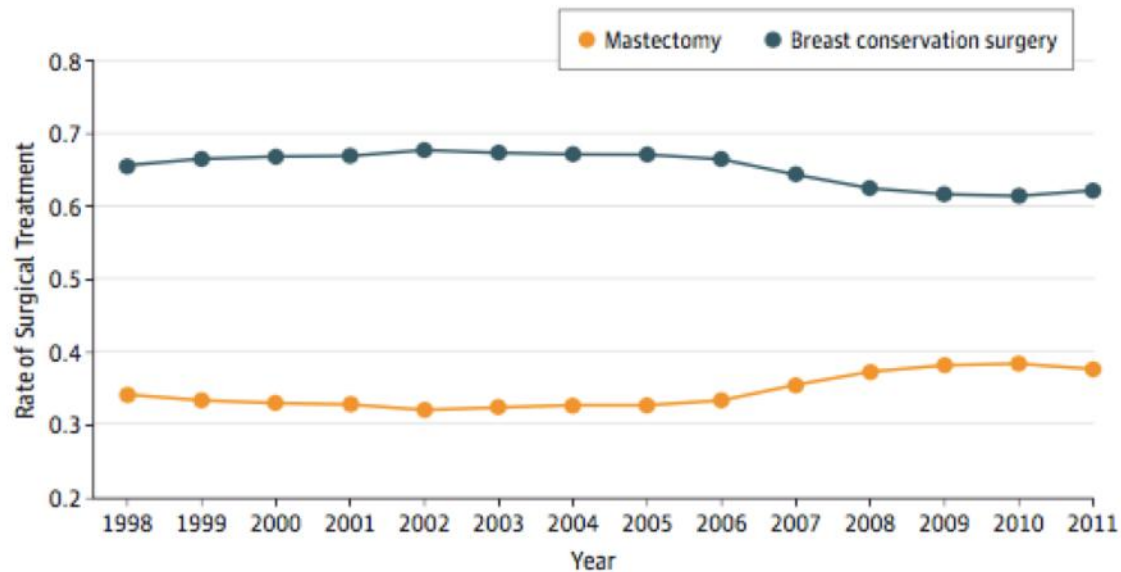
Factors Responsible for Rising Mastectomy Rates



Adjusted for age, marital status, # surgeons visited, comorbidity, tumor size, grade, SEER site

Proportion of women for each surgical approach by year of diagnosis

Figure 1. Temporal Trends in Surgical Treatment of Early Breast Cancer

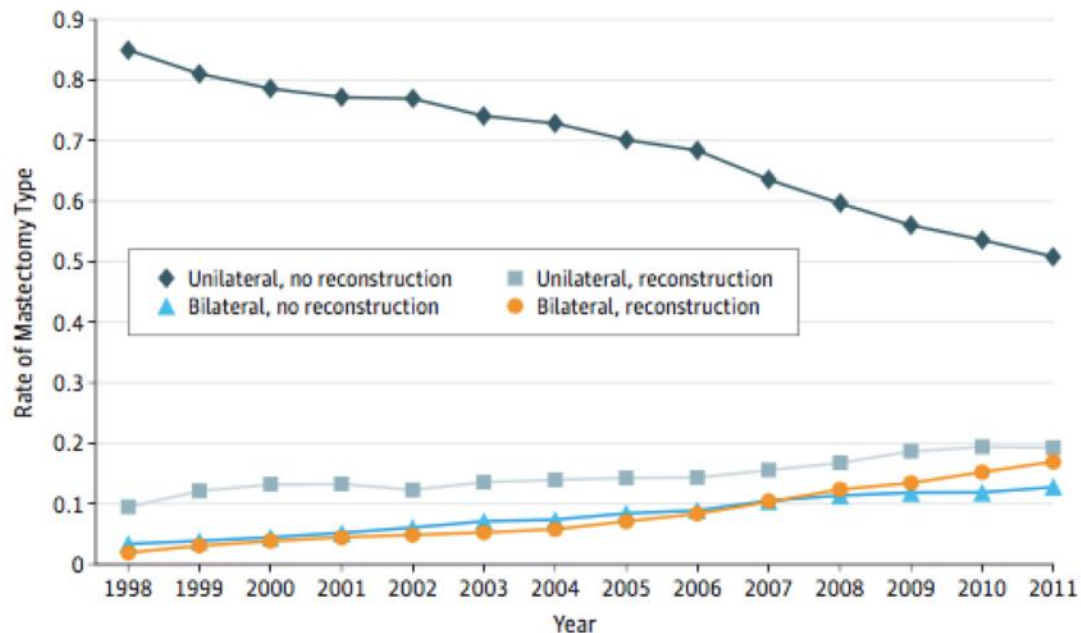


BCS

MASTECTOMY

Proportion of women with early breast cancer who underwent mastectomy (orange line) and breast conservation surgery (blue line) by year of diagnosis in the National Cancer Data Base. All trends are significant ($P < .001$).

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



Proportion of mastectomies for early breast cancer that were unilateral without reconstruction (dark blue line with diamonds), unilateral with reconstruction (light blue line with squares), bilateral without reconstruction (bright blue line with triangles), and bilateral with reconstruction (orange line with circles) by year of diagnosis in the National Cancer Data Base. Operative categories determined based on definitive operation for each breast cancer case (includes staged approaches). Reconstruction categories include tissue, implant, and combined reconstructive approaches. All trends are significant ($P < .001$).

- **Increase in breast reconstruction and bilateral mastectomy** starting in the mid-2000s, with a continued increasing trend over time.
- **Reconstruction** in women undergoing mastectomy increased from 11.6% in 1998 to 36.4% in 2011.
- **Bilateral mastectomy for unilateral disease also increased** significantly, from 1.9% of all BCS-eligible women in 1998 to 11.2% in 2011.
- Among women undergoing any type of mastectomy for unilateral disease, **bilateral mastectomy increased from 5.4% in 1998 to 29.7% in 2011.**

Bilateral mastectomy rates rise

- **No evidence that bilateral mastectomies with Contralateral Prophylactic Mastectomies prolong survival** for women with sporadic breast cancer.
- Greater use of mastectomy, (and particularly CPM), have been associated with **younger age at diagnosis, greater educational attainment and socioeconomic status, race, higher histologic grade and *in situ* cancer (stage 0).**

Albornoz CR, et al, *Plast Reconstr Surg.* 2015 June ; 135(6): 1518–1526.

f. poufakaki

The Perfect Storm

↓ Tumor Burden

Better systemic rx

↓ LRR

Surgery

Systemic rx indications expanding

Longer duration therapy

RT indications/fields expanding

Patient choice of bigger surgery

Net Result: Incremental addition of therapies has resulted in a greater burden of treatment for patients



Thank you for your attention