UC San Diego Health

The Axilla: How far we've come and where we're headed to next..

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Topics to cover:

1. **Quick review of the evolution of axillary management**
2. **Current statuses of axillary management for select groups**
3. **Updates on ongoing trials or recently presented interesting papers**

The Evolution (de-escalation) of axillary management

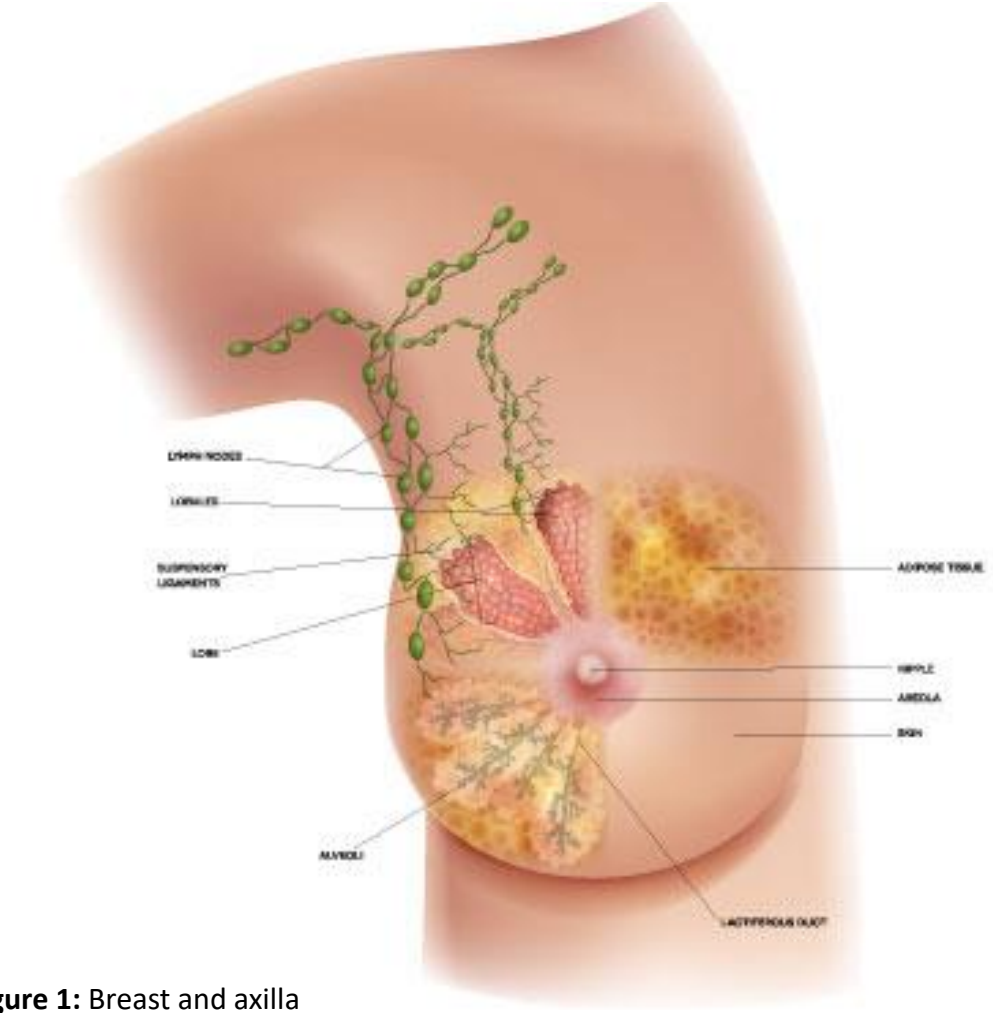
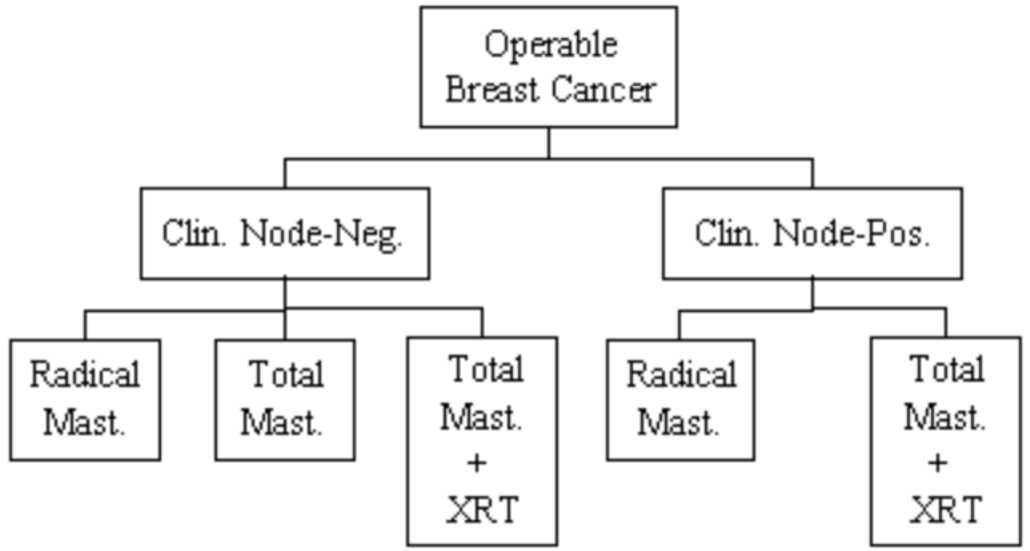


Figure 1: Breast and axilla
Image courtesy of https://www.pristyncare.com/cms/wp-content/uploads/2022/09/How-does-accessory-breast-tissue-form.jpg

Axilla – transit point between the breast and rest of the body

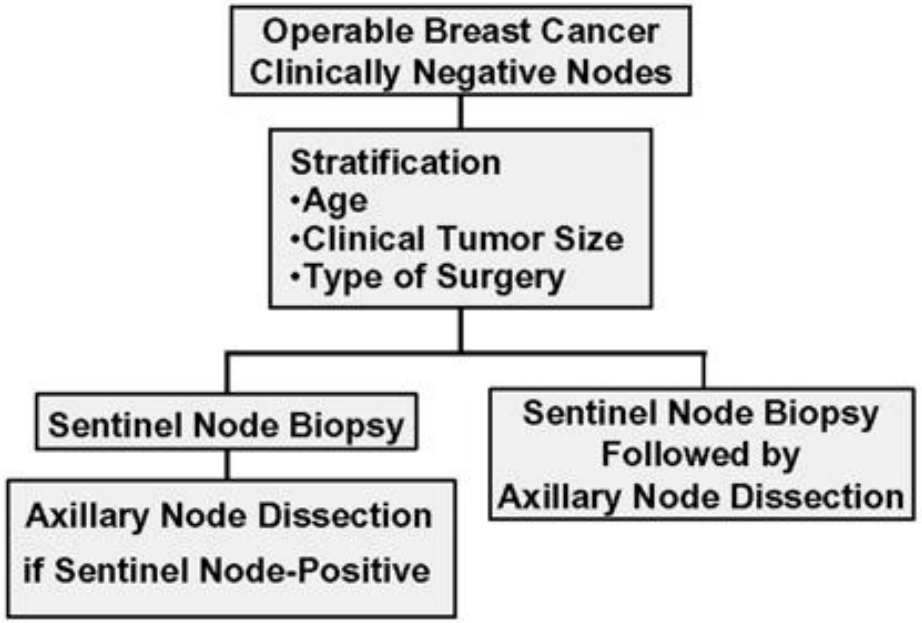
Halsted radical mastectomy = mandatory lymph node dissection to Prevent distant spread of disease

NSABP-04 (1971): Bigger isn't always better
- 25 year follow-up for cN0 patients showed no diff in OS or DFS[1]



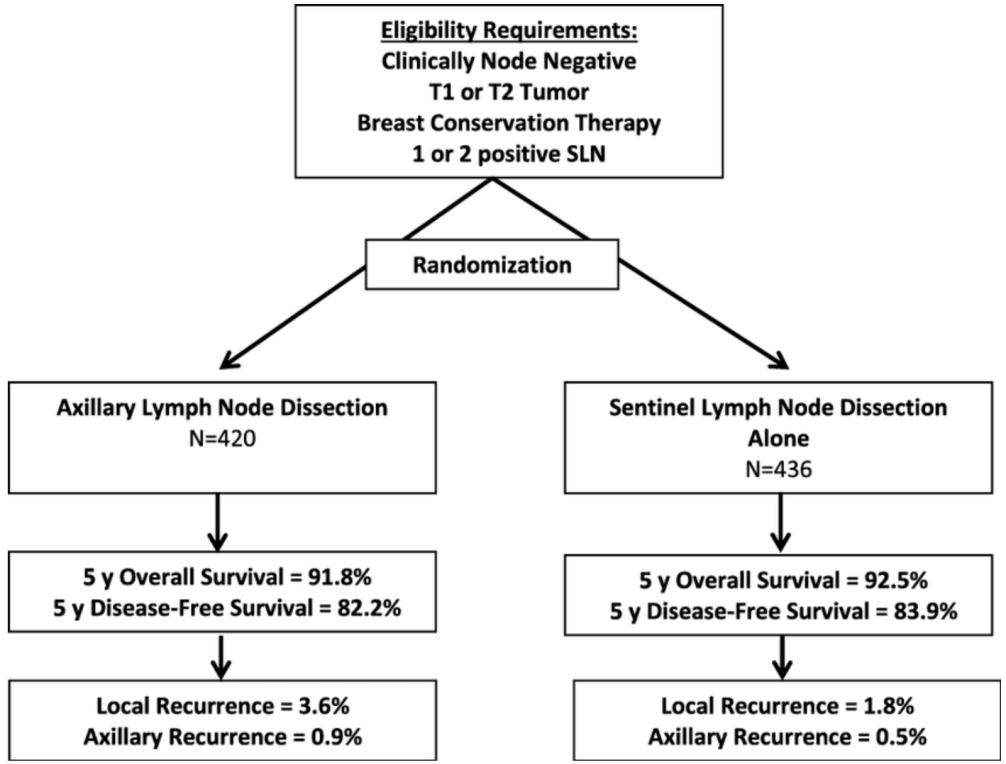
The Evolution of axillary management: The rise of SNLB

NSABP 32 (1999-2005)[2]



Bottom Line: For patients with cN0, there was no Diff in OS, DFS, or regional control between ALND Vs. SNLB. Regional recurrence <1% for both groups

ACOSOG Z011 (1999-2004)[3]



Bottom Line: No diff in OS and both groups had low locoregional recurrences

The Evolution of axillary management: updated NCCN guidelines integrating Z11 preoperatively for image-detected limited LN met

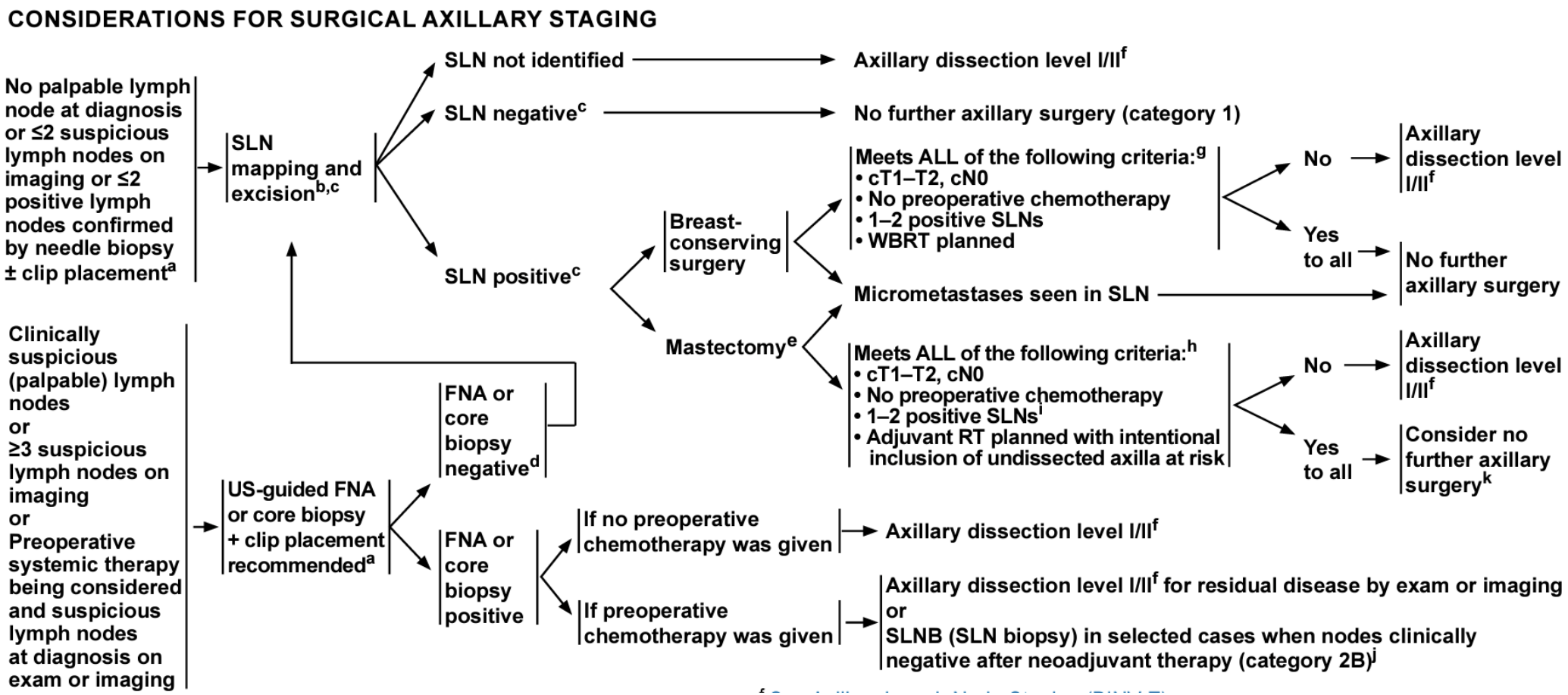
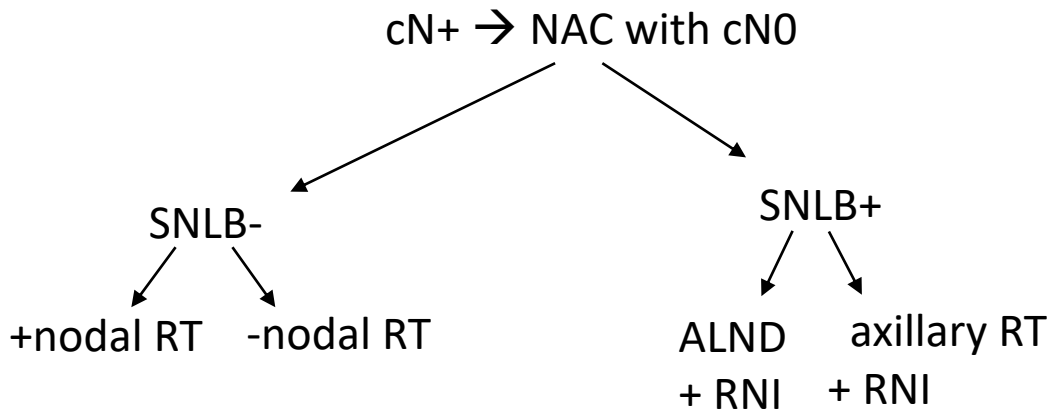


Figure 2: Axillary management per National Comprehensive Cancer Network. Breast Cancer Screening and Diagnosis (Version 1.2023)[4]

Axillary management in the post-neoadjuvant group

Multiple feasibility studies (ACOSOG Z1071, SENTINA, SN FNAC and GANEA) demonstrated SNLB after neoadjuvant chemo can be performed with FNR <10% if dual tracer, 2+ lymph nodes removed and +/- clipping the biopsy proven positive node



NSABP 51
(est trial completion 8/2028)
Post-NAC patients who convert to ypN0

Alliance 011202 (est trial completion 1/2024)
cT1-3N1M0 disease who will undergo post-NAC SNLB
Endpts: DFSS, OS, LRR

Figure 3: Schema for axillary management following neoadjuvant chemotherapy (adapted from Dr. Giuliano's fellows lecture "SLN surgery" ASBrS Fellows Lecture, September 8 2022

Axillary management in the post-neoadjuvant group

Is SLNB enough for patients who were cN+ and then convert to ypN0? **So far -- YES**

JAMA Oncology | Brief Report

Nodal Recurrence in Patients With Node-Positive Breast Cancer Treated With Sentinel Node Biopsy Alone After Neoadjuvant Chemotherapy—A Rare Event

Andrea V. Barrio, MD; Giacomo Montagna, MD, MPH; Anita Mamtani, MD; Varadan Sevilimedu, MBBS, DrPH; Marcia Edelweiss, MD; Deborah Capko, MD; Hiram S. Cody III, MD; Mahmoud El-Tamer, MD; Mary L. Gemignani, MPH, MD; Alexandra Heerdt, MD; Laurie Kirstein, MD; Tracy-Ann Moo, MD; Melissa Pilewskie, MD; George Plitas, MD; Virgilio Sacchini, MD; Lisa Sclafani, MD; Audree Tadros, MD; Kimberly J. Van Zee, MS, MD; Monica Morrow, MD

Ann Surg Oncol (2021) 28:2621–2629
https://doi.org/10.1245/s10434-020-09211-0

Annals of SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – BREAST ONCOLOGY

Oncologic Safety of Sentinel Lymph Node Biopsy Alone After Neoadjuvant Chemotherapy for Breast Cancer

Stephanie M. Wong, MD, MPH[1,2], Mark Basik, MD[1,2,3], Livia Florianova, MD[4], Richard Margolese, MD[1,3], Sinziana Dumitra, MD, MSc[1,3], Thierry Muanza, MD[2,3,5], Annie Carbonneau, MD[5], Cristiano Ferrario, MD[2,3], and Jean Francois Boileau, MD, MSc[1]

[1]Department of Surgical Oncology, McGill University Medical School, Montreal, QC, Canada; [2]Lady Davis Institute for Medical Research, Sir Mortimer B. Davis Jewish General Hospital, Montreal, Canada; [3]Department of Oncology, McGill University Medical School, Montreal, QC, Canada; [4]Department of Pathology, McGill University Medical School, Montreal, QC, Canada; [5]Department of Radiation Oncology, McGill University Medical School, Montreal, QC, Canada

MSK Study: 234 patients converted to ypN0 after chemo and Treated with SLNB only.[5]

- 62% HER2+; 18% TNBC. Majority received postop RT (70%)
- 1 nodal recurrence (<0.5%) over F/U period 3.5 yrs

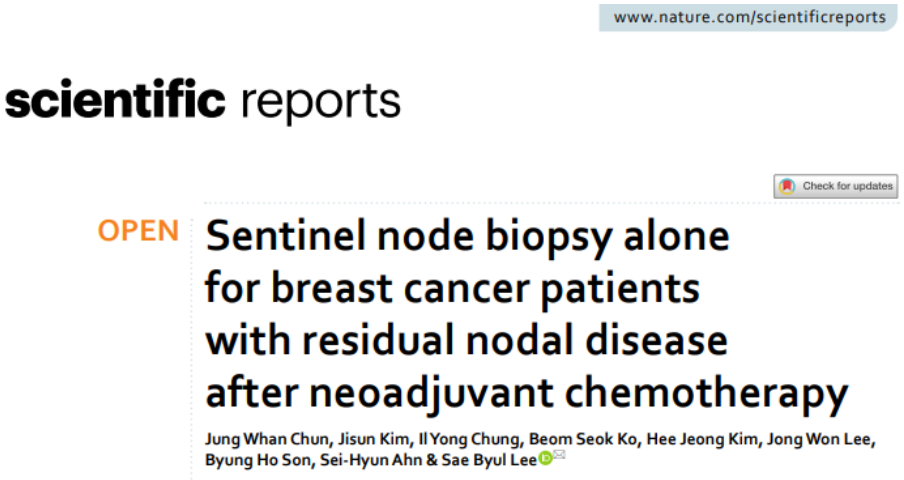
McGill Study: 60 pts cT1-2 → ypN0 and treated with SNLB/XRT
- No axillary recurrences at 5 yrs follow-up[6]

Axillary management in the post-neoadjuvant group

Is SLNB enough for patients who were cN+ and persist as ypN1? Alliance 011202 will answer this but in the meantime…

Single institution study, 324 pts with ypN1
Propensity matched 98 pts with ypN1 who underwent SNLB only to 98 ALND pts
Follow-up 71 mts
No diff in 5-yr OS, BCSS, regional recurrence

Authors conclude: SNLB might be an option for pts with limited axillary nodal disease after chemo without Compromising survival outcomes.[7]



Axillary management in the post-neoadjuvant group

Is SLNB enough for patients who were cN+ and persist as ypN1? Alliance 011202 will answer this but in the meantime…

Ann Surg Oncol (2021) 28:930–940
https://doi.org/10.1245/s10434-020-08928-2

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – BREAST ONCOLOGY

Omission of Axillary Lymph Node Dissection is Associated with Inferior Survival in Breast Cancer Patients with Residual N1 Nodal Disease Following Neoadjuvant Chemotherapy

Muayad F. Almahariq, MD, PhD[1], Ronald Levitin, MD[1], Thomas J. Quinn, MD[1], Peter Y. Chen, MD[1], Nayana Dekhne, MD[2], Sayee Kiran, MD[2], Amita Desai, MD[2], Pamela Benitez, MD[2], Maha S. Jawad, MD[1], Gregory S. Gustafson, MD[1], and Joshua T. Dilworth, MD, PhD[1]

[1]Department of Radiation Oncology, Beaumont Health, Royal Oak, MI; [2]Department of Surgery, Beaumont Health, Royal Oak, MI

Cohort study with pt population from NCBD Database 2006-2014[8]

- cT1-3N1 with residual disease -> grouped into SNLB + RNI (<4 nodes removed) or ALND+RNI
- 1313 ALND pts vs 304 SNLB pts
- 5yr OS SNLB vs. ALND: 71% vs. 77% (p=0.01)

Axillary management in the post-neoadjuvant group

Meeting Abstract | 2023 ASCO Annual Meeting I

BREAST CANCER—LOCAL/REGIONAL/ADJUVANT

Can axillary lymph node dissection (ALND) be omitted in patients with breast cancer with persistent axillary disease after neoadjuvant chemotherapy?

Callie Hlavin, Zainab Balogun, Daniel R. Lavage, Michael S. Cowher, Kristin Lupinacci, Quratulain Sabih, Atilla Soran, Jennifer G. Steiman, Priscilla F. McAuliffe, Emilia J. Diego

University of Pittsburgh, Pittsburgh, PA; University of Pittsburgh School of Medicine, Pittsburgh, PA

Single institution, retrospective study[9]
156 pts, ypN1 → ALND or TAD
- No diff in OS, DFS based on type of axillary surgery at 3yrs
- 19 pts had distant recurrence and majority had ALND
- Distant recurrences suggest tumor biology as a major factor
Rather than extent or type of axillary surgery

Meeting Abstract | 2023 ASCO Annual Meeting I

BREAST CANCER—LOCAL/REGIONAL/ADJUVANT

Axillary surgery efficacy for patients with breast cancer receiving neoadjuvant chemotherapy on NSABP B40 and B41.

Raymond Mailhot Vega, Adeline M. Deladisma, Erin Michele Mobley, Shu Wang, Christopher G. Morris, Oluwadamilola Temilade Oladeru, ...

Obtained data from NSABP 40 and 41[10]
- 3 separate groups: SNLB only, SNLB + ALND, ALND only
- Looked at association of axillary surgery type with LRR, distant Recurrence, DFS, OS
- Combined multivariate analyses showed SNLB only was NOT Associated with higher likelihood of recurrence

Axillary management in the elderly: Choosing Wisely

(2016) Don’t routinely use sentinel node biopsy in clinically node negative women >70 years of age with hormone receptor positive, HER2-negative invasive breast cancer.[11]

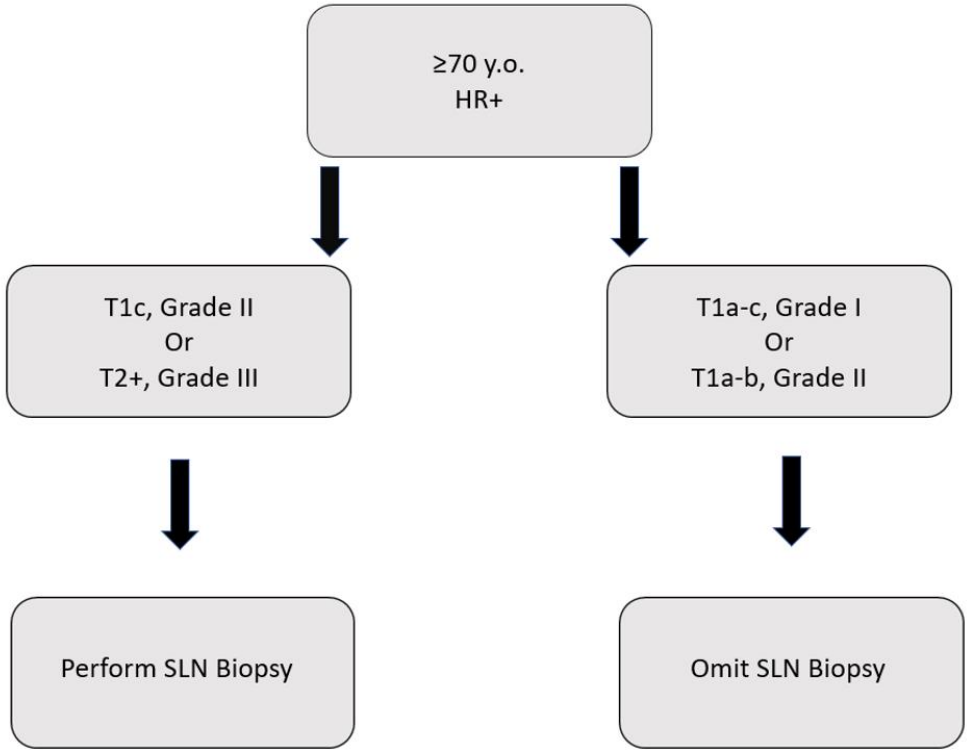
Axillary management in the elderly: How are we applying this?

> Ann Surg Oncol. 2017 Oct;24(10):2881-2888. doi: 10.1245/s10434-017-5932-1.
Epub 2017 Aug 1.

Predicting Nodal Positivity in Women 70 Years of Age and Older with Hormone Receptor–Positive Breast Cancer to Aid Incorporation of a Society of Surgical Oncology Choosing Wisely Guideline into Clinical Practice

Jessemae L Welsh [1], Tanya L Hoskin [2], Courtney N Day [2], Elizabeth B Habermann [1 2 3], Matthew P Goetz [4], Judy C Boughey [5]

Mayo Clinic Study to develop a risk Stratification model to predict which patients the Guideline can be applied to.[12]



Axillary management in the elderly: SOUND trial

JAMA Oncology

RCT: Sentinel Lymph Node Biopsy vs No Axillary Procedure in Small Node-Negative Breast Cancer

POPULATION

1463 Women

Adult women with breast cancer smaller than 2 cm and negative preoperative axillary ultrasound

Median (IQR) age, 60 (52-68) y

INTERVENTION

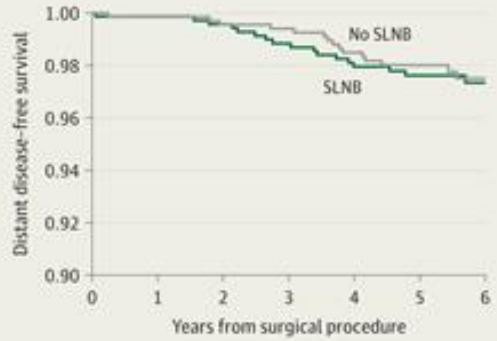
1463 Patients randomized and analyzed

727 Sentinel node biopsy (SLNB)
SLNB was performed (control group)

736 No SLNB
SLNB was omitted (experimental group)

FINDINGS

Omission of SLNB was noninferior to SLNB in patients with breast cancer smaller than 2 cm and a negative ultrasound of the axillary lymph nodes



SETTINGS / LOCATIONS

18 Hospitals in 4 countries

PRIMARY OUTCOME

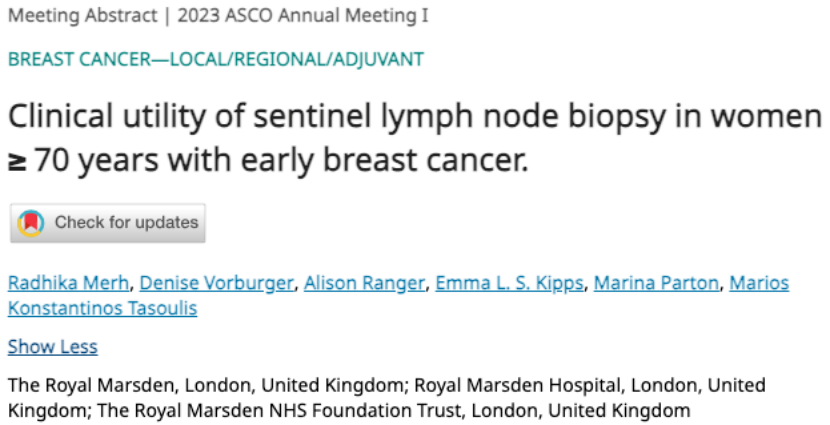
The protocol-specified primary end point was distant disease-free survival (DDFS) at 5 y

SLNB: 5-y DDFS, 97.7%
No SLNB: 5-y DDFS, 98.0%
(log-rank test, $P = .67$; hazard ratio, 0.84; 90% CI, 0.45-1.54; noninferiority $P = .02$)

Gentilini OD, Botteri E, Sangalli C, et al; SOUND Trial Group. Sentinel lymph node biopsy vs no axillary surgery in patients with small breast cancer and negative results on ultrasonography of axillary lymph nodes: SOUND randomized clinical trial. *JAMA Oncol.* Published online September 21, 2023. doi:10.1001/jamaoncol.2023.3759

	SNLB	No SNLB
Locoregional recurrence	1.7%	1.6%
Distant met	1.8%	2%
Deaths	3%	2.6%

Axillary management in the elderly



Meeting Abstract | 2023 ASCO Annual Meeting I

BREAST CANCER—LOCAL/REGIONAL/ADJUVANT

Clinical utility of sentinel lymph node biopsy in women ≥ 70 years with early breast cancer.

Check for updates

Radhika Merh, Denise Vorburger, Alison Ranger, Emma L. S. Kipps, Marina Parton, Marios Konstantinos Tasoulis

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The Royal Marsden, London, United Kingdom; Royal Marsden Hospital, London, United Kingdom; The Royal Marsden NHS Foundation Trust, London, United Kingdom

BREAST CANCER—LOCAL/REGIONAL/ADJUVANT

Long-term oncologic outcomes after omitting axillary surgery in older women with early stage, node-negative breast cancer: A systematic review and meta-analysis.

Check for updates

Mariam Rana, Soyon Lee, Alistair Lindsay, Juan Carlos Silva Godinez, Erik Vakil, Evelyn Waugh

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Harvard T.H. Chan School of Public Health, Boston, MA

Subgroup analysis of 294 patients cT1N0 HR+HER2-[13]
- 31 had +SNLB -> 5 received ALND; 16 had axillary RT
- 11 with + SNLB were recommended AC
- SNLB = $6505/pt, potential cost savings $1.9 mil over 5 yrs

Meta-analysis of randomized/obs studies [14]
- Risk reduction of axillary recurrence with SNLB though not Statistically significant RR 0.59, p = 0.21
- No diff in DFS, BCSS
- Protective effect on mortality when pts received SNLB (RR = 0.55; p=0.03)

Summary

#1 - De-escalation of axillary surgery continues to evolve from NSABP-04 in the 1970s, especially with the shift to focus on tumor biology as a driver of outcome and lymph node sampling as more of a prognostic indicator.

#2 - The optimal axillary surgery following neoadjuvant chemotherapy with residual disease burden continues to be explored as we await trials results of Alliance 011202.
- Some preliminary studies demonstrate that TAD or SNLB is not associated with increased locoregional recurrence or worsened outcomes.

#3 - The Choosing Wisely guideline for omission of SNLB continues to be explored for applicability.
- Careful consideration of patient factors (including size/grade, comorbidities and impact on adjuvant care) are integral to physician-patient discussion of SNLB omission.

Questions?

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