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MD Anderson Cancer Center
Making Cancer History®

A NEW ERA OF AXILLARY MANAGEMENT

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Ochsner Breast Surgery

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Disclosures

We have no disclosures

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OUTLINE

- Historical Context
- Upfront Surgery (cN0)
- Positive Sentinel Lymph Nodes
- Neoadjuvant Therapy Pathway
- Residual Disease after Neoadjuvant Treatment
- Special Populations

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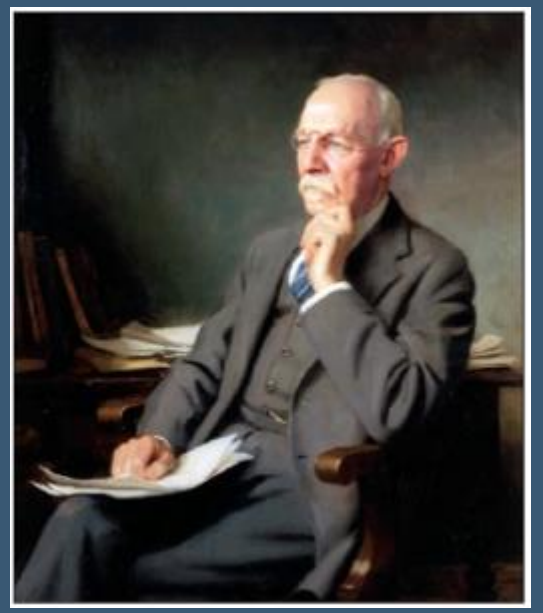
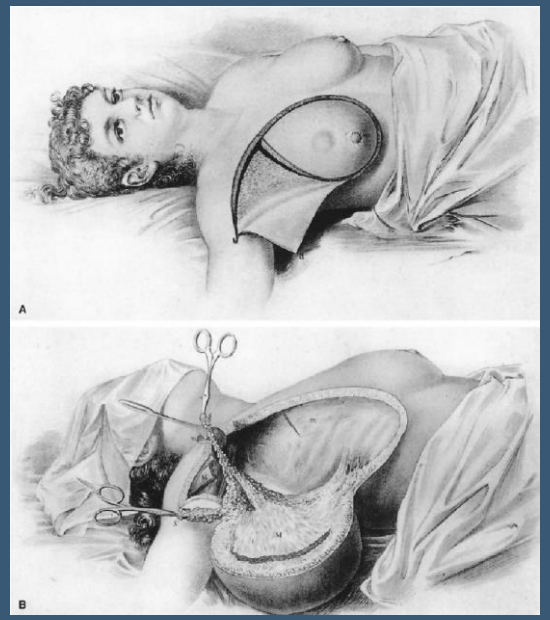
Historical Management Of The Axilla



- Axillary lymph node dissection was the standard for staging and local control
- First described by Dr. William Halsted in 1894
- “Results of the Cure of Cancer of the Breast”
  - Removal of skin, breast tissue, pec major/minor, levels I-III axillary dissection en bloc
- High morbidity
  - Lymphedema
  - Nerve injury
  - Shoulder dysfunction



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Upfront Surgery (cN0)

- **SOUND** (*JAMA Onc 2023*)

Sentinel Lymph Node Biopsy vs No Axillary Surgery in Patients With Small Breast Cancer and Negative Results on Ultrasonography of Axillary Lymph Nodes
The SOUND Randomized Clinical Trial

Oreste Davide Gentilini, MD[1,2]; Edoardo Botteri, PhD[3,4]; Claudia Sangalli, BSc[5] ; et al

- **INSEMA** (*NEJM 2024*)

Axillary Surgery in Breast Cancer — Primary Results of the INSEMA Trial

Authors: Toralf Reimer, Ph.D., Angrit Stachs, Ph.D., Kristina Veselinovic, M.D., Thorsten Kühn, Ph.D., Jörg Heil, Ph.D. , Silke Polata, M.D., Frederik Marmé, Ph.D., +15 , and Bernd Gerber, Ph.D. Author Info & Affiliations

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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

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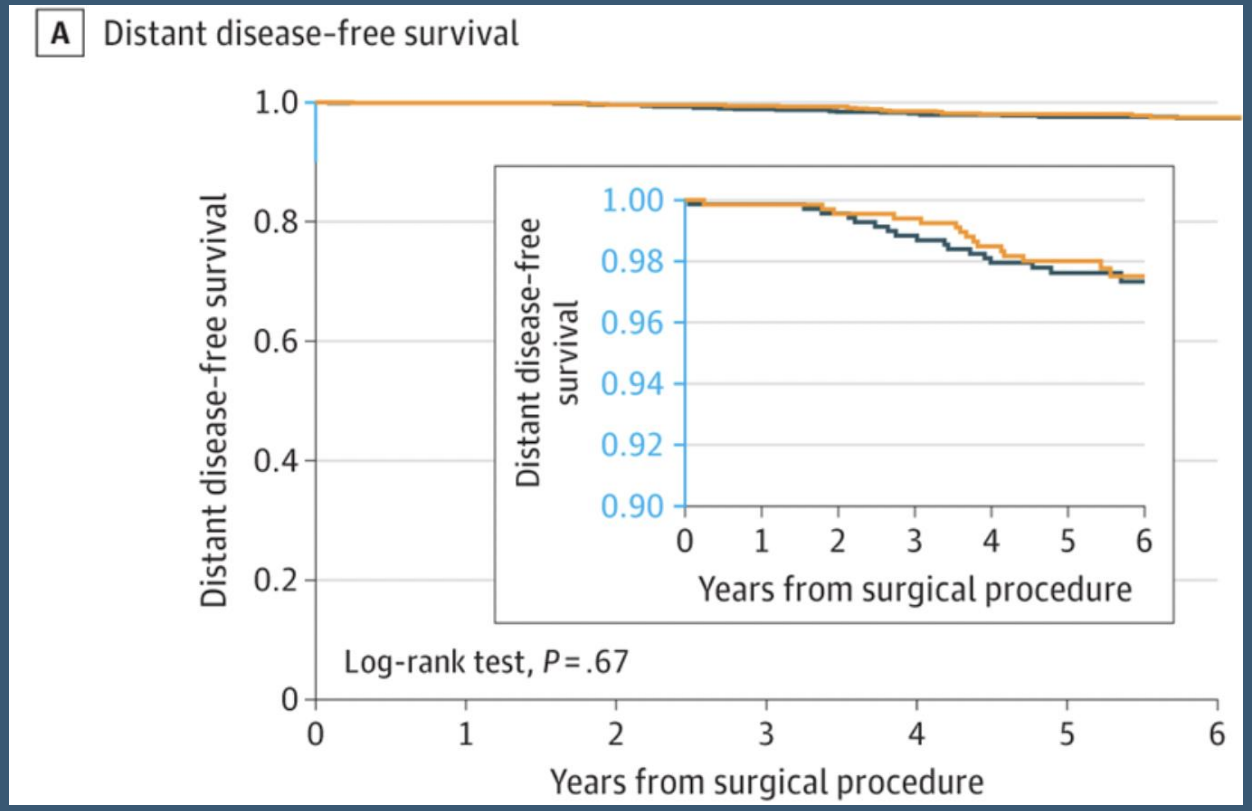
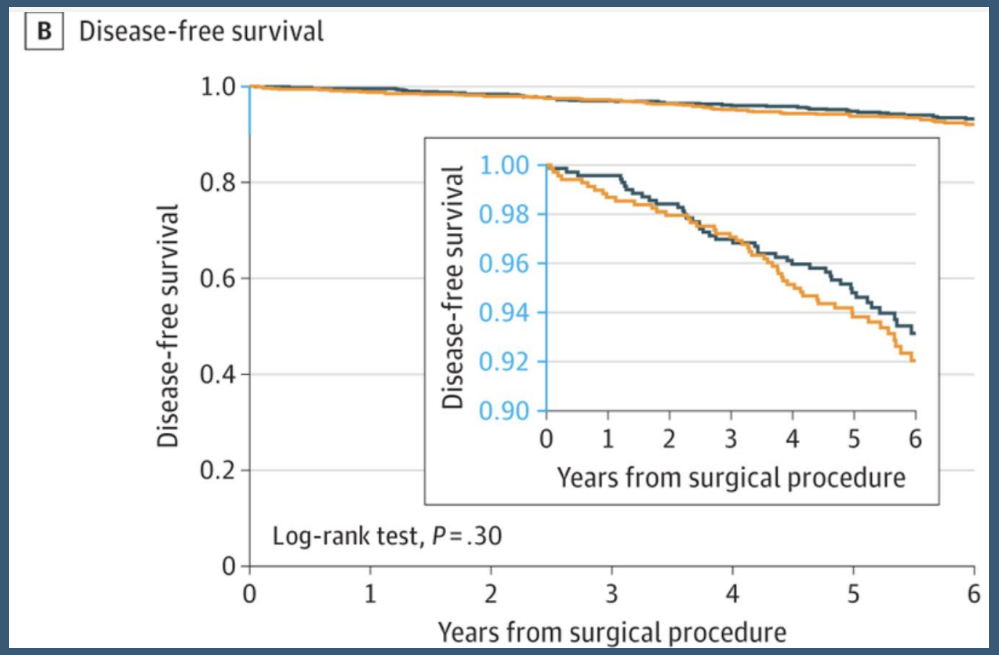
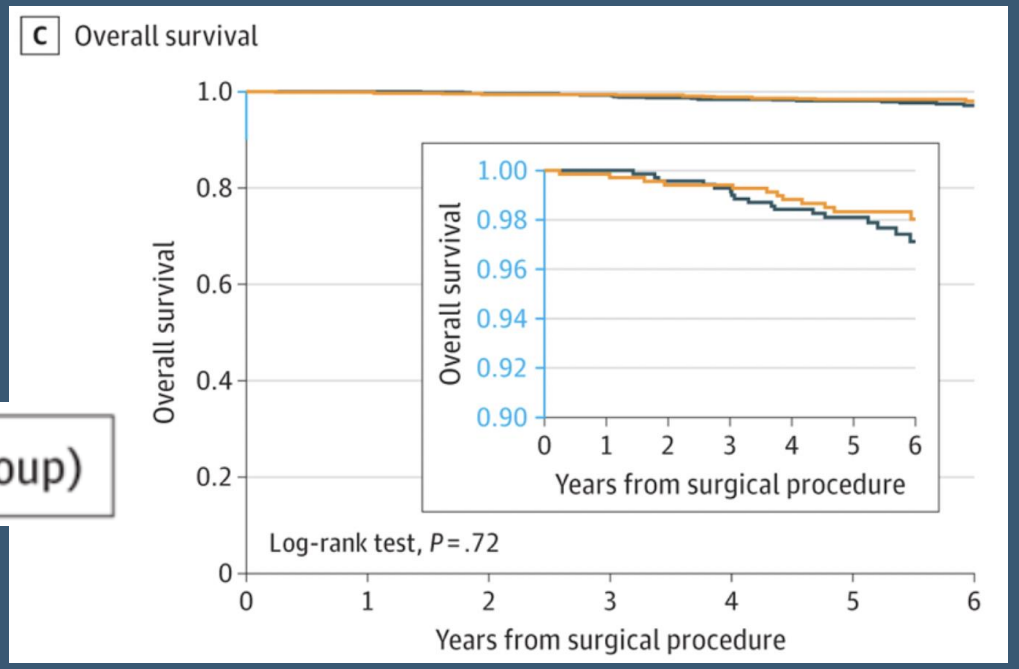
SOUND Trial







SLNB (control group) No SLNB (experimental group)

SOUND Trial- Results and Conclusions

- Median tumor size 1.1 cm
- 87.8% estrogen-receptor positive
- 5.7 year follow-up
- 5-year distant disease free survival:
  - 97.7% in SLNB group
  - 98.0% in no axillary surgery group
- 12 locoregional (1.7%) relapses, 13 (1.8%) distant metastases, and 21 (3.0%) deaths were observed in the SLNB group, and 11 (1.6%) locoregional relapses, 14 (2.0%) distant metastases, and 18 (2.6%) deaths were observed in the no axillary surgery group

Omission of axillary surgery noninferior to SLNB in patients with small tumors and clinically node negative

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INSEMA Trial

- Can axillary surgery be omitted without compromising survival?
- T1-T2 (<5cm) cN0 breast cancer undergoing breast conservation
  - Adjuvant whole breast radiation
- Primary outcome: invasive disease free survival
- 5502 pts (90% cT1, 79% pT1)
- Randomization 1:4, no axillary surgery to sentinel lymph node biopsy
- Median follow-up 73.6 months
- 5-year iDFS 91.9% in no surgery versus 91.7% surgery group
- Axillary occurrences rare

Omission of surgical axillary staging was noninferior to sentinel-lymph-node biopsy after a median follow-up of 6 years

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Practice Point: Sentinel lymph node biopsy can be omitted if nodal status would not change systemic therapy

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Positive Sentinel Lymph Nodes

- Z0011
- AMAROS
- SENOMAC

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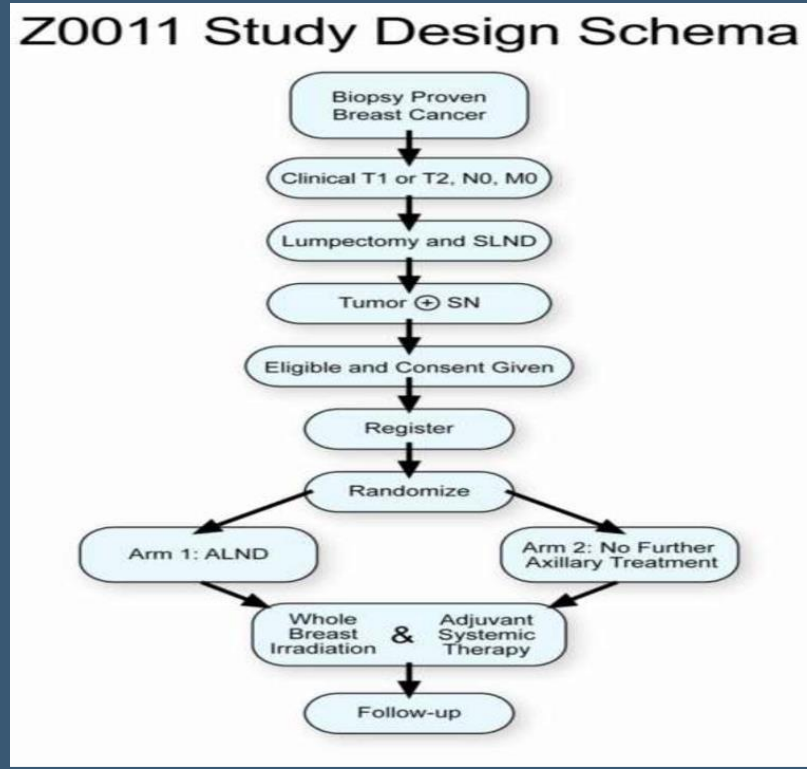
Z0011 Trial

- Randomized trial of ALND vs no ALND in women with positive SN
- Primary endpoint: Overall survival
  - Key secondary: Locoregional recurrence (current analysis)
- Hypothesis: Selected SN+ patients can safely omit completion ALND without compromising control
- 891 pts >18YO T1-2 cN0M0 undergoing breast conservation
  - Adjuvant whole breast radiation
- Randomized to completion ALND or no further axillary surgery

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

The American College of Surgeons Oncology Group Z0011 Randomized Trial

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



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Z0011 Trial

Locoregional Recurrence Intent-to-Treat

Median follow-up: 6.3 years; total LRR: 29/856 (3.4%).
Local recurrence: 8 (1.8%) SLND-only vs 15 (3.6%) ALND.
5-yr local recurrence: 1.6 % SLND-only vs 3.1 % ALND (P = 0.11).
Regional (axillary) recurrence: 4 (0.9%) SLND-only vs 2 (0.5%) ALND.
Median local- and regional-recurrence–free survival not reached; no statistical difference between arms.

Locoregional Recurrence As-Treated

ALND received (n = 388) vs SLND-only received (n = 425).
Total LRR: 16 (4.1%) ALND-treated vs 12 (2.8%) SLND-treated.
Local recurrence: 14 (3.6%) vs 8 (1.9%); Regional recurrence: 2 (0.5%) vs 4 (0.9%).
Locoregional recurrence-free survival curves did not differ significantly

At 5 years, there were no differences in terms of overall survival (92.5% observation vs. 91.8% ALND; HR 0.79), disease-free survival (83.9% vs. 82.2%), or locoregional recurrence-free survival (96.7% vs. 95.7%).

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Z0011 Limitations

- Low axillary tumor burden: pts with ≥3 positive SNs largely excluded
- 41 % had micromets/ITCs; staging manual at time did not stratify by volume
- Early closure (891/1900 pts) & few events; may limit power for rare outcomes
- >95 % received adjuvant systemic therapy (chemo ± endocrine) → reduces LRR
- Whole-breast tangential RT fields cover much of level I–II axilla; may sterilize residual disease
- Thus, omission of formal axillary RT did not equate to zero axillary radiation

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Z0011 Clinical Implications

- Low cT1–T2, N0 pts undergoing BCT & systemic therapy, completion ALND can be safely omitted when 1–2 H&E-positive SNs
- Particularly relevant for micrometastases/ITCs
- Not applicable to mastectomy, palpable nodes, or ≥3 positive SNs—ongoing trials addressing these gaps
- Long-term survival impact still maturing; vigilance in follow-up essential

Reduces morbidity without compromising early disease control

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AMAROS

- Q: Can axillary radiation replace ALND?
- 4823 pts with cT1-2 with positive SLN
- 82% underwent breast conservation, 17% mastectomy
- Randomization 1:1 ALND or axillary radiation (25fx of 2 Gy)
- Primary endpoint = noninferiority of 5-year axillary recurrence
- Median follow up 6.1 years
- 5-year axillary recurrence was 0.43% after axillary lymph node dissection versus 1.19% after axillary radiotherapy
- No significant differences between treatment groups in DFS and overall survival
- Confirmed by 10 year data - ART preferred for patients with SN positive cT1-2 breast cancer

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Practice Point: Axillary lymph node dissection no longer routine in limited positive sentinel lymph nodes, even with mastectomy

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Neoadjuvant Therapy Pathway

- Goal: Downstage the axilla to avoid ALND if ypN0
- Technique: SLNB + Targeted Axillary Dissection (TAD)
  - Dual tracer, >3 nodes, clipped node retrieval
- Key data: JAMA Surg 2023

Targeted axillary dissection safe if ypN0

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Residual Disease after Neoadjuvant Therapy

- Current standard: ALND required if residual nodal disease.
- Ongoing trials
  - Alliance A011202 (ALND vs RT)
  - OPBC-03/TAXIS.
- Practice Point: Awaiting trial data; for now, ALND remains standard

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ACOSOC Z1071 (Alliance)

Sentinel Lymph Node Surgery After Neoadjuvant Chemotherapy in Patients With Node-Positive Breast Cancer
The ACOSOG Z1071 (Alliance) Clinical Trial

- SLN surgery reliable in cN0, but FNR post-chemo in cN1 uncertain.
- Goal: evaluate SLN accuracy after chemo in biopsy-proven node-positive breast cancer.
- Inclusion:
  - Women ≥18 y, T0-T4, N1-N2, M0 invasive breast cancer
  - Biopsy-proven nodal metastasis before chemo (FNA or core).
- Primary: Determine false-negative rate (FNR) of SLN surgery after neoadjuvant chemo in cN1 pts with ≥2 SLNs excised.
- Secondary: Pathologic complete nodal response (pCR) rate.

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ACOSOC Z1071 (Alliance)

Sentinel Lymph Node Surgery After Neoadjuvant Chemotherapy in Patients With Node-Positive Breast Cancer
The ACOSOG Z1071 (Alliance) Clinical Trial

- cN1 Results (≥2 SLNs, n=525)
- Nodal pCR: 41.0 % (215/525)
- Residual nodal disease distribution:
  - 20.6 % SLN only
  - 7.4 % ALND only (false-negatives)
  - 31.1 % both SLN & ALND
- False-negatives: 39/310 => FNR = 12.6 % (90 % BCI 9.9-16.1)

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ACOSOC Z1071 (Alliance)

Sentinel Lymph Node Surgery After Neoadjuvant Chemotherapy in Patients With Node-Positive Breast Cancer
The ACOSOG Z1071 (Alliance) Clinical Trial

- Overall FNR 12.6 % exceeded prespecified 10 % threshold → SLN alone not sufficiently accurate for routine use in cN1 post-chemo.
- Technique matters: dual mapping & ≥3 SLNs improve accuracy.
- Patient selection crucial—avoid SLN surgery when residual nodal disease likely or poor chemo response.
- Approximately 41 % achieved nodal pCR, potentially sparing ALND if better selection/technique implemented.

ACOSOG Z1071: SLN surgery post-chemo in cN1 breast cancer had FNR 12.6 %
Dual mapping & ≥3 SLNs bring FNR closer to acceptable level

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Consensus Guidelines

- ASCO 2025
  - SLNB can be omitted in select postmenopausal, HR+/HER2-
- ASBrS Consensus Statements
  - Stepwise algorithms for upfront versus NAT pathways

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Special Populations

- Mastectomy: SENOMAC broadens ALND omission
- Elderly populations: ASCO 2025 supports omission SLNB
- Pregnancy: SLNB data limited
  - Blue dye contraindicated
  - Case-by-case approach

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Summary

- De-escalation is safe in carefully selected patients
- Sentinel lymph node biopsy omission supported by SOUND/INSEMA
- Axillary lymph node dissection omission validated in limited SLN+ disease (Z0011, AMAROS, SENOMAC)
- Post-neoadjuvant therapy: Targeted axillary dissection if ypN0
- Residual nodal disease: ALND remains standard until RCTs report

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QUESTIONS?

THANK YOU!

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