CRPT : Workshop Agli Estremi Dello Screening
L’ APPROCCIO CHIRURGICO ALL’ ASCELLA

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Ospedale Santa Croce e Carle

Cuneo

De-escalation meaning

Cambridge Dictionary

de- escalate: To (cause to) become less dangerous or difficult

In surgery: to cause less harm

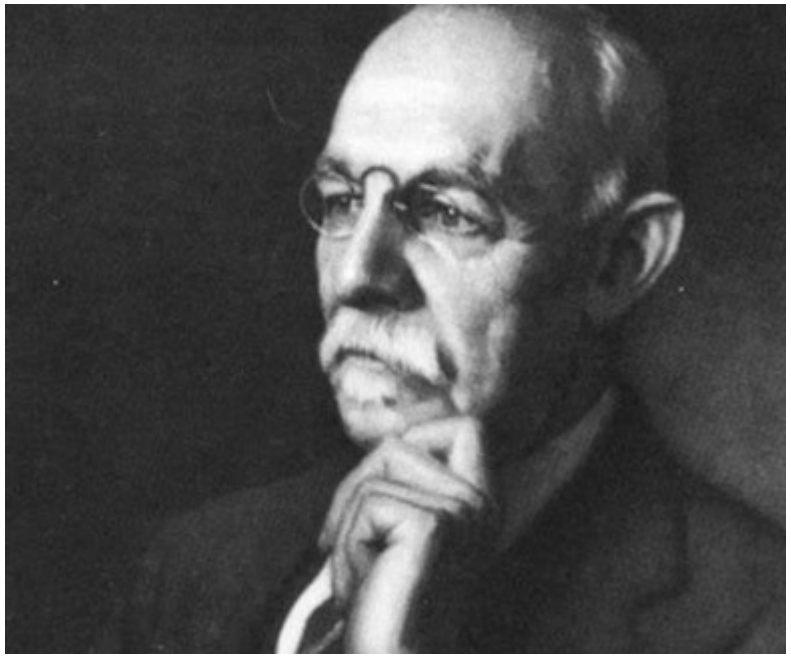
In the axillary surgery: to cause less lymphedema, nerve damage, reduced mobility in the shoulder and arm, and chronic pain

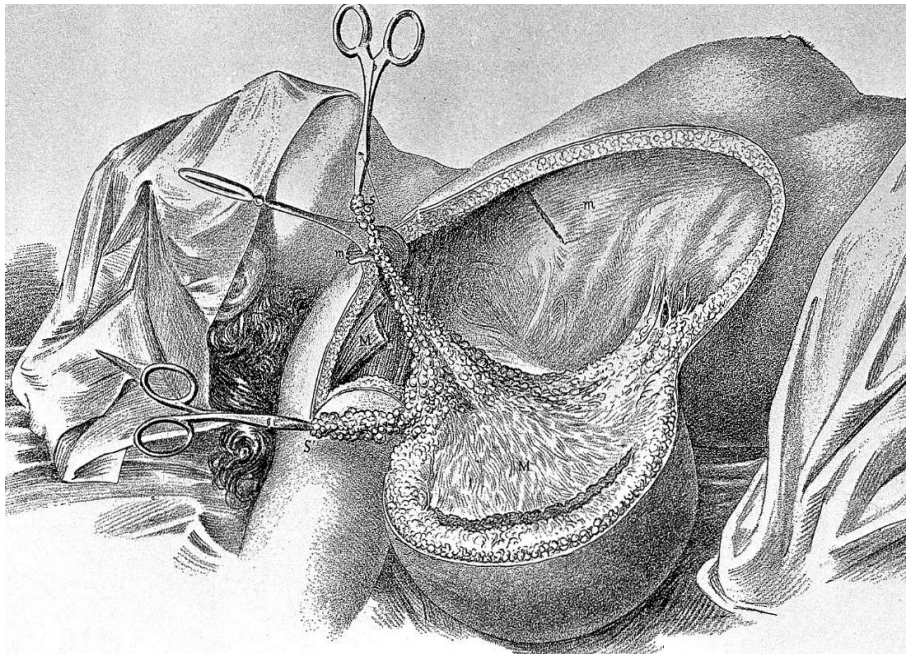
THE RESULTS OF OPERATIONS FOR THE CURE OF CANCER OF THE BREAST PERFORMED AT THE JOHNS HOPKINS HOSPITAL FROM JUNE, 1889, TO JANUARY, 1894.

By WILLIAM S. HALSTED, M.D.,

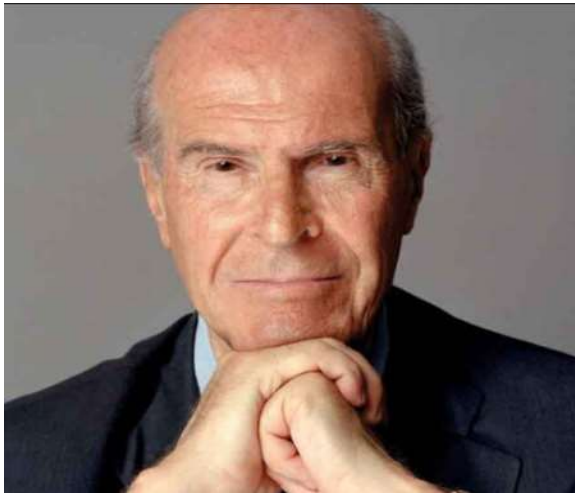
OF BALTIMORE,

PROFESSOR OF SURGERY IN JOHNS HOPKINS UNIVERSITY.





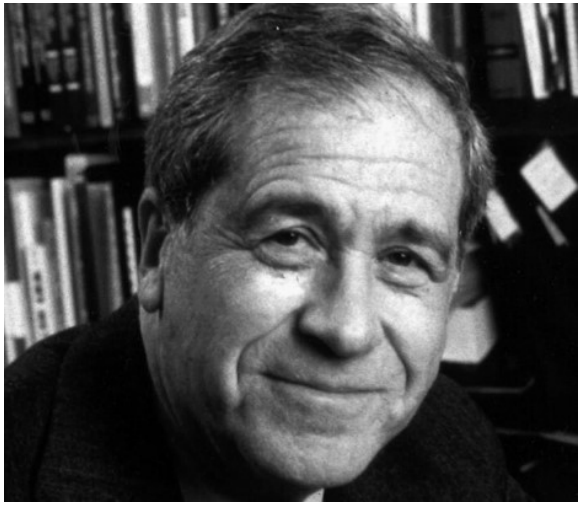
minor disabilities caused by a radical mastectomy are trivial because no disability is worse than dying. He further defends the results of his procedure by reasoning that because most of the patients are older, averaging fifty-five years of age, they are no longer very active members of society and so slight disabilities do not matter.



Twenty-Year Follow-up of a Randomized Study Comparing Breast-Conserving Surgery with Radical Mastectomy for Early Breast Cancer

Authors: Umberto Veronesi, M.D., Natale Cascinelli, M.D., Luigi Mariani, M.D., Marco Greco, M.D., Roberto Saccozzi, M.D., Alberto Luini, M.D., Marisel Aguilar, M.D., and Ettore Marubini, Ph.D. Author Info & Affiliations

Published October 17, 2002 | N Engl J Med 2002;347:1227-1232 | DOI: 10.1056/NEJMoa020989 | VOL. 347 NO. 16



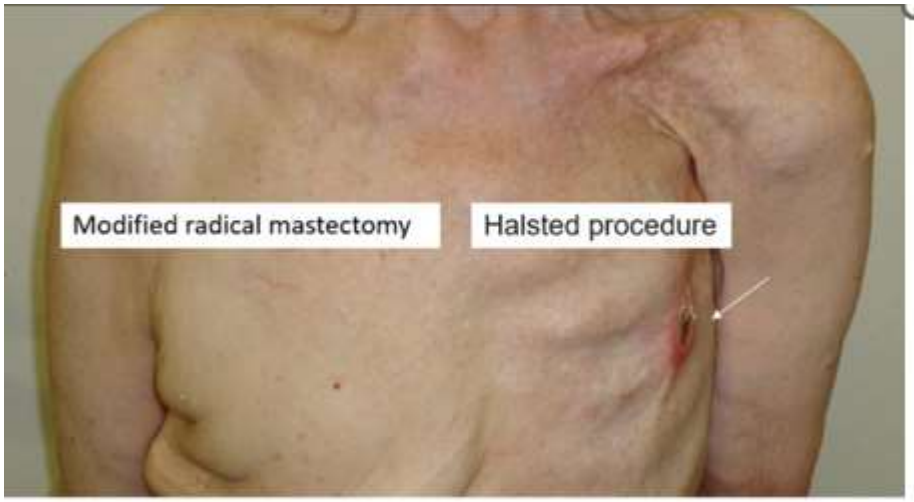
Comparative Study > N Engl J Med. 2002 Oct 17;347(16):1233-41. doi: 10.1056/NEJMoa022152.

Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer

Bernard Fisher [1], Stewart Anderson, John Bryant, Richard G Margolese, Melvin Deutsch, Edwin R Fisher, Jong-Hyeon Jeong, Norman Wolmark

Evolution in Breast Surgery

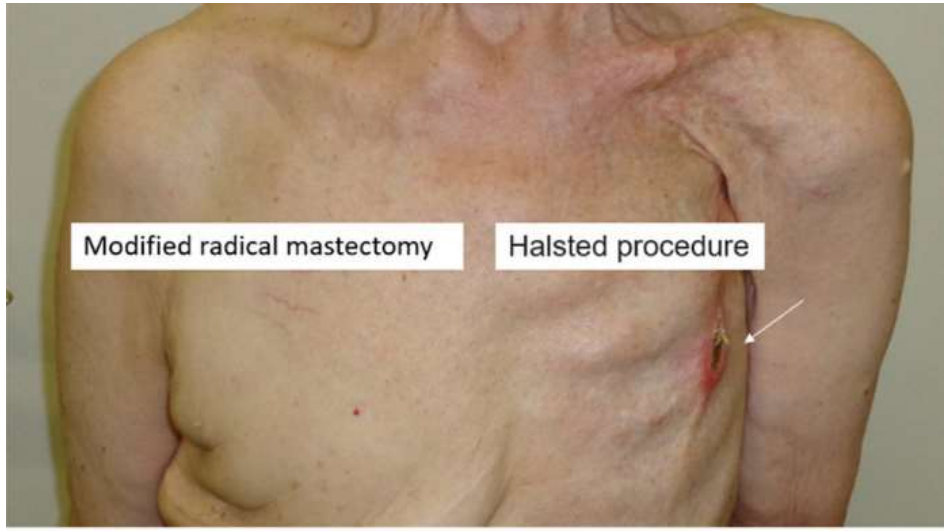
Mastectomy to Oncoplastic Breast Surgery



Past

Present

Evolution in Breast Surgery
Mastectomy to Nipple Sparing Mastectomy



Past

Present

De-escalation of Breast Cancer Treatment

In surgery

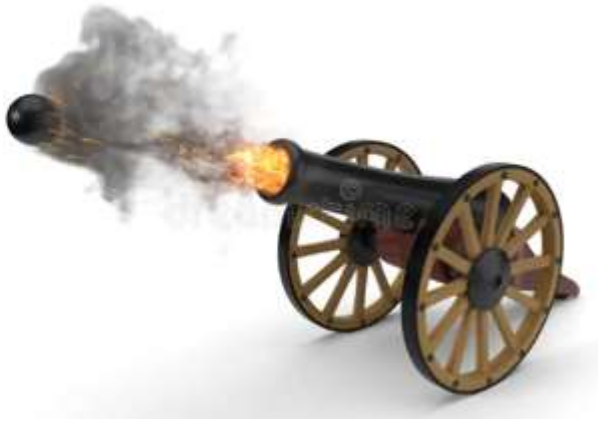
- Conservative surgery + radiotherapy instead of mastectomy (Veronesi and Fischer)
- Sentinel node biopsy instead of axillary clearance (Giuliano. Veronesi, Mansel)
- Nipple sparing mastectomy with reconstruction instead of simple mastectomy
- Omitting ALND in SNB+ Pt in BCS with Radiotherapy (ACOSOG Z0011)
- Avoiding SLNB in Low-risk patients (Sound trial)

In radiotherapy

- Radiotherapy instead of ALND (AMAROS trial)
- DIBH technique

In oncology

- More targeted treatment
- Less chemotherapy: Oncotype DX, MammaPrint, EndoPredict, Prosigna Breast Cancer Assay, BCI responder, tailor x



Pioneers in de-escalation of axillary surgery in Breast Cancer Treatment

Ann Surg 2000 Jul;232(1):1-7. doi: 10.1097/00000658-200007000-00001.

Breast cancer patients treated without axillary surgery: clinical implications and biologic analysis

M Greco[1], R Agresti, N Cascinelli, P Casalini, R Giovanazzi, A Maucione, G Tomasic, C Ferraris, M Ammatuna, S Pilotti, S Menard

401 pt clinically node-negative, who underwent breast surgery without axillary dissection (01/1986 to 06/1994).

The 5-year follow-up: low rate of nodal relapses (6.7%), particularly for T1a and T1b patients (2% and 1.7%, respectively), whereas T1c and T2 patients showed a 10% and 18% relapse rate,

Avoidance of axillary dissection has a negligible effect on the outcome of T1 patients, particularly in T1a and T1b tumors with no palpable nodes

Pioneers in de-escalation of axillary surgery in Breast Cancer Treatment

1946 - 2009

Eur J Surg Oncol. 2006 Sep;32(7):733-7. doi: 10.1016/j.ejso.2006.04.016. Epub 2006 Jun 30.

Axillary staging in women with small invasive breast tumours

G Q della Rovere[1], R Bonomi, S Ashley, J R Benson

Eur J Surg Oncol. 2016 Jul;42(7):942-8. doi: 10.1016/j.ejso.2016.03.027. Epub 2016 Apr 13

Long term results of treatment of breast cancer without axillary surgery - Predicting a SOUND approach?

R L O'Connell[1], J E Rusby[2], G F W Stamp[3], A Conway[3], N Roche[4], P Barry[3], K Khabra[5], R Bonomi[6], I F Rapisarda[6], G Q Della Rovere[3]

Aim of the study: assess long term outcomes of Pt with 'low-risk' breast cancers who did not undergo any axillary surgery. 'Low-risk': postmenopausal, <20 mm G 1 or <15 mm G 2, LVI-, ER +.

	5 years	10 years
Axillary recurrence (cumulative incidence	0.8%	1.9%
DDFS	99.2%	97%
DFS	96.6%	91.2%
OS	90.3%	75.5%

Conclusion: Axillary recurrence and DDFS in this low-risk cohort is favourable. In the modern era of breast cancer management it is possible to define a group of women in whom axillary surgery can be omitted.

De-escalation of the treatment of the axilla

In Patients having surgery upfront

studies on de-escalation in patients having ITC or micrometastasis in the sentinel node

studies on de-escalation in patients having macrometastasis in the sentinel node

In patients having neoadjuvant chemotherapy

studies investigating the false negative rates of SNB after neoadjuvant chemo

studies investigating the recurrence rate in TAS (TAD) or ALND

studies investigating the omission of regional nodal irradiation

In patients with early breast cancer

studies investigating the omission of axillary staging

De-escalation on micrometastasis in patients who are having surgery first

Study	Type of trial	Eligibility criteria	Patient groups	Primary endpoint	Results	Status
IBCSG 23-01 Lancet Oncol. 2013;14(4):297-305.	Phase III RCT	cT1–T2, N0 with 1 or + micromet SN	AD 464 Pt No AD 467 Pt	DFS 5 years	AD 84.4% No AD 87.8%	C
ACOSOG0010 Ann Surg. 2012;256(3):428-36.	Multicenter prognostic study	cT1–T2, N0, who had BCS, SNB, and BM aspiration	5,184 sn 23.9% sn+ on histo 10.5% sn+ on IHC 3.0% BM+	OS 5 years	1- No ≠ In pt with micro on IHC. 2- BM mets by IHC > death Risk Both no independent predictors	C
AATRM Ann Surg Oncol. 2013 Jan;20(1):120-7	Multicenter Randomized clinical study	T<3.5, cN0 with SN micromets	ALND 112 No ALND 121	DFS 5 years	No ≠ between the groups	C

De-escalation on macromets in patients who are having surgery first

Study	Type	Eligibility criteria	Patient groups	Primary endpoint	Results	Status
ACOSOG Z0011 Giuliano et al JAMA. 2017 Sep 12;318(10):918-926.	RCT	cT1–T2, N0, with 1 or 2 SN macro +, BCS and breast RT	• SN alone • ALND	OS non inferiority (HR) of 1.3 DFS	At 10 years no difference	C
SINODAR-ONE Tinterri et al Ann Surg Oncol. 2022 Sep;29(9):5732-5744.	RCT	T1–T2, BCS or mastectomy, with 1 or2 macro + SN	• ALND + adjuvant therapy • SN alone + adjuvant therapy	Overall survival	5-year OS rates 98.9% ALND 98.8%, SNLB-only	O
POSNOC trial Goyal a et al BMJ Open. 2021 Dec 2;11(12)	RCT	T ≤5 cm, with one or two SN with macrometastases + or- extracapsular spread	• Adjuvant therapy alone • Adjuvant therapy plus ALND or axillary RT	5 y axillary rec. rate		O

De-escalation on macromets in patients who are having surgery first

Study	Type of trial	Eligibility criteria	Patient groups	Primary endpoint	Results	Status
AMAROS - Donker M, et al Lancet Oncol 20214 - Sanne AL Bartels et al J clin Oncol 2023	RCT	cT1–T2, N0, with positive SN	ALND 2402 pt (744 ln +) Axillary RT 2404 pt (681 ln +)	Five-year axillary recurrence	At 5 years non inferior. At 10 years no difference in OS, DFS, and locoregional control.	C
OTOASOR Sávolt Á et al EJSO 2017	RCT	cT <3cm, N0, with positive SNB	• ALND 244 pt • RNI 230 Pt	Axillary recurrence OS DFS	At 8 Years ALND vs RNI Ax Rec: 2% vs 1.7% OS:77.9% vs84.8% DFS:72.1% vs 77.4%	C

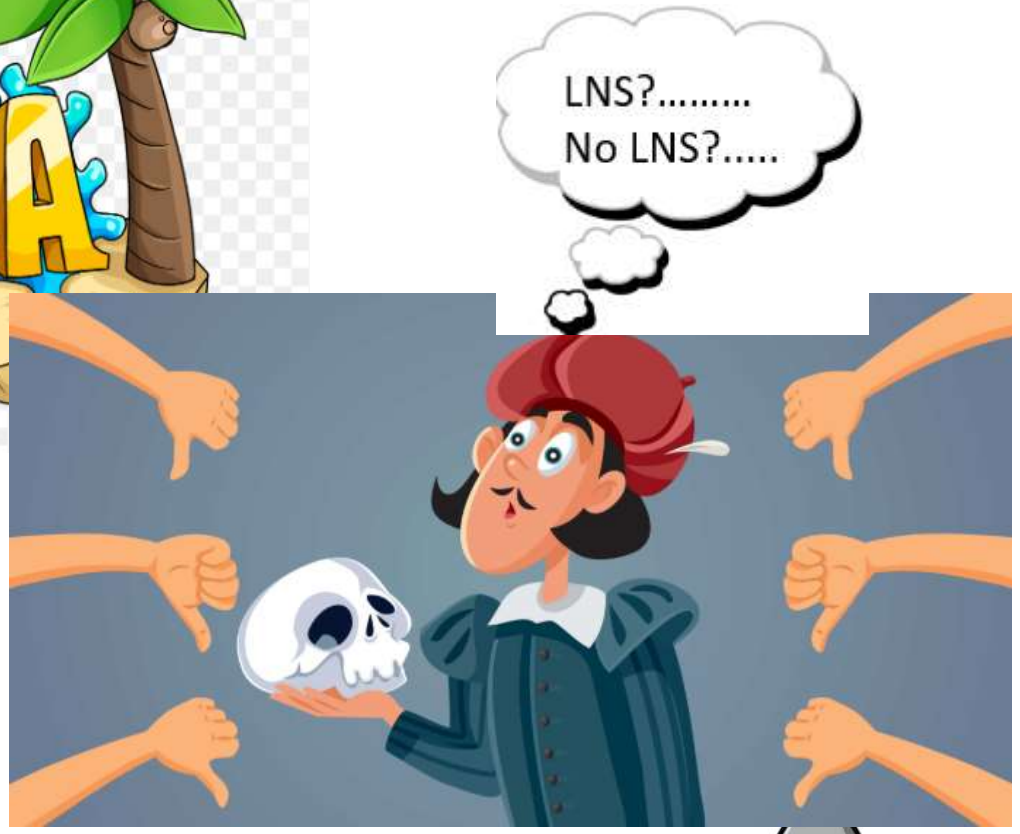
De-escalation in Patients having neoadjuvant chemotherapy Studies investigating FNR

Study	Type of trial	Eligibility criteria	Patient groups	Primary endpoint	Results	Status
ACOSOG Z1071 JAMA 2013 ;310(14):1455-61	prospective non RCT	T0–4 N1–2, M0 NAC	663 Pt had SNB and ALND	FNR in SLNB after CHEMO in Pt with node+	FNR of 12.6%	C
Sentina Lancet Oncol . 2013;14(7): 609-18	four-arm, prospective, multicentre cohort study. 103 institution in Austria and Germany	Invasive BC requiring NAC, cN0–1,	Arm A: cN0 had SNB pre NAC Arm B: if SNB + Chemo + SNB and ALND Arm C: ycN0 had SNB + ALND Arm D: ycN+ had ALND	FNR in SNB after NAC for patients who converted from cN1 to ycN0	FNR Arm B: 51.6% Arm C: 24.3% (1 node) 18.5% (2 nodes) After chemo SNB has lower detection rate and high FNR	C
SN FNAC study J Clin Oncol 2015;33:258-	Prospectic multicentric trial	T0–3, N1–2, NAC	153 Pt had SNB and ALND	FNR in SLNB after CHEMO in Pt with node+	FNR 8.4% with mandatory use of IHC potential for avoiding ALND was around 30%	C

De escalation after NAC

Study	Type of trial	Eligibility criteria	Patient groups	Primary endpoint	Results	Status
OPBC-03/ TAXIS Ann Surg Onc 2023 30;31(1):344–355	Randomized Controlled Trial	BC, N+ NAC or upfront surgery	• TAS with IGL followed by ALND • TAS without IGL followed by ALND	quantify the extent of residual disease after TAS.	IGL did not change the performance of TAS or the volume of residual nodal tumor burden.	O
Alliance A011202	Phase III randomized controlled study	T1–3, N1, NAC	Positive SNB • ALND and regional nodal radiation • Axillary and regional nodal radiation alone	8years IBC recurrence-free interval - OS - ILR-REC lymphoedema		O
ADARNAT	Phase III randomized study	Invasive BC, positive SNB, NAC	• Axillary RT alone • ALND alone	5-year axillary recurrence rate		O
NSABP B-51 San Antonio 2023	Phase III randomized study	T1–3, N1, NAC→ypN0	• Post-BCS: = WBI only -WBI with RNI • Post-mastectomy: - Chest wall RT only - Chest wall rt +RNI	-invasive breast cancer recurrence-free survival - OS	follow-up of 59.5 5-year IBC RFS rate 92.7% in pt with RNI vs 91.8% in pT no RNI	O


ERESIA


LNS?.....
No LNS?.....

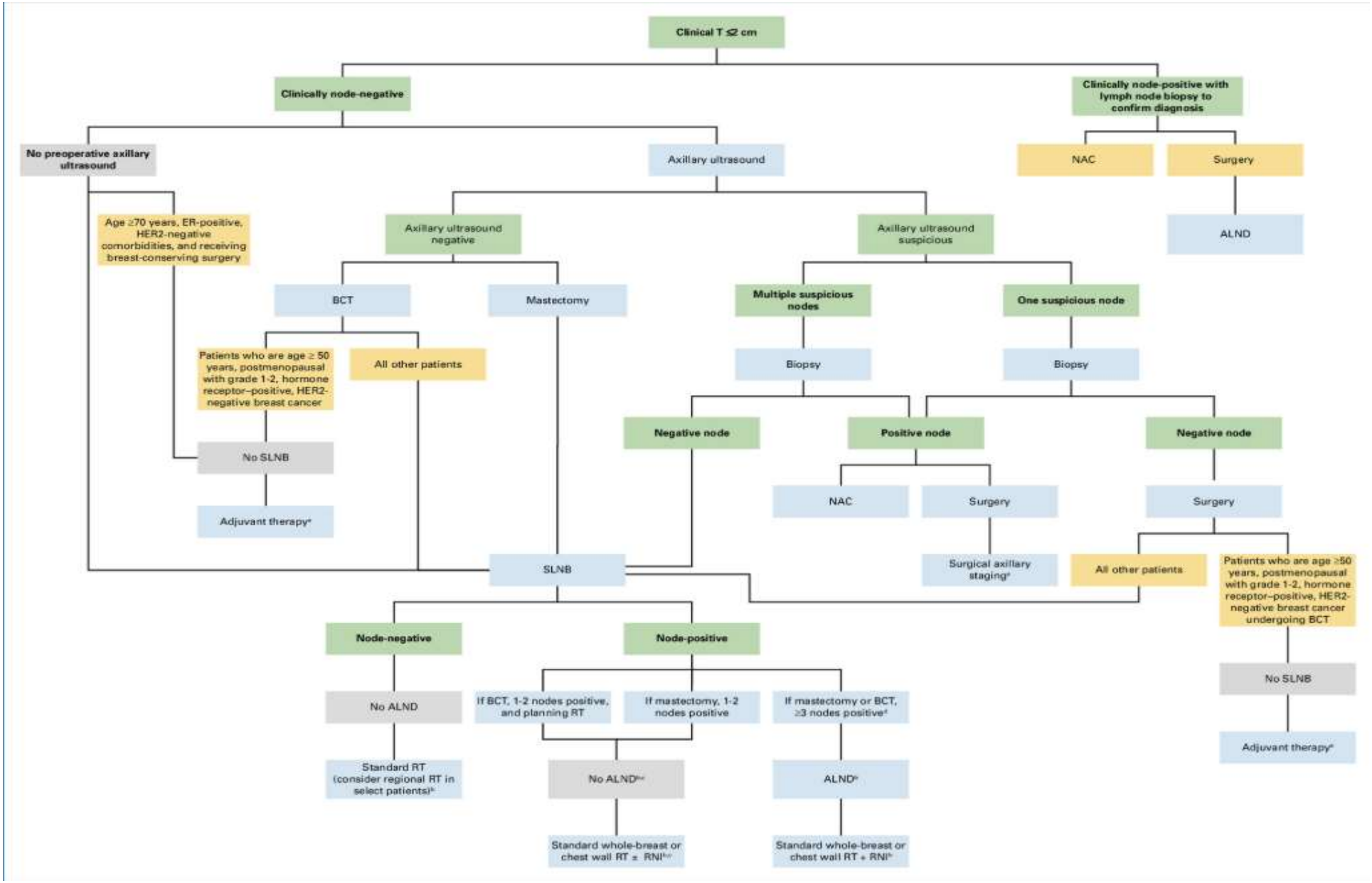
Omission of axillary surgery in patients with early stage invasive breast cancer

Study	Type of trial	Eligibility criteria	Patient groups	Primary endpoint	Results	Status
Insema N Engl J Med 2025;392:1051-1064	Prospective, randomized, non-inferiority trial 2015 – 2019 San Antonio 2024	cT1–2 cN0, BCS	• No axillary surgery 962 pt • SNB 3896 pt (if 1–2 positive SNB, randomization: SNB alone vs. ALND)	Invasive disease-free survival	5 years snb no snb Loc rec 1.4% 1.9% Ax rec 0.3% 1.0% Mets 2.7% 2.7% Death 2.4% 1.4%	ongoing
SOUND JAMA Oncol. 2023;9(11):1557-1564.	noninferiority phase 3 randomized clinical trial 2012-2027	cT1N0, US-neg axilla, BCS	• SNB 708 pt • No axillary surgery 697pt	DDFS OS	5 years snb no snb DDFS 97.7% 98.0% Loc rec 1.7% 1.6% Mets 1.8% 2.0% Death 3.0% 2.6%	closed
BOOG 13-08	Dutch prospective non-inferiority randomized multicentre trial	cT1–2N0, BCT	• SNB • No axillary surgery	5 and 10 year regional recurrence rate		ongoing

Omission of axillary surgery in patients with invasive breast cancer

Study	Type of trial	Eligibility criteria	Patient groups	Primary endpoint	Results	Status
SOAPET Sentinel Node Biopsy Vs Observation After Axillary PET (SOAPET)	two phase study target number of N = 1528 Pt	target number of N = 1528 Pt node negative at presentation	In the first stage, the NPV in patients with negative preoperative axillary assessment, including axillary PET In the second stage omission SNB	NPV of Lymph PET DDFR LRFS		ongoing
NAUTILUS	Phase III randomized controlled trial	cT1–2N0, US-negative axilla, BCS	• SNB • No axillary surgery	5-year invasive disease-free survival		Recruitment closedd

ASCO GUIDELINES 2025
Management of the axilla for patients with clinical T ≤2 cm



THANK YOU