

Best of SABCS 2022



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COUNTRY
DATE



Innovations in Surgery



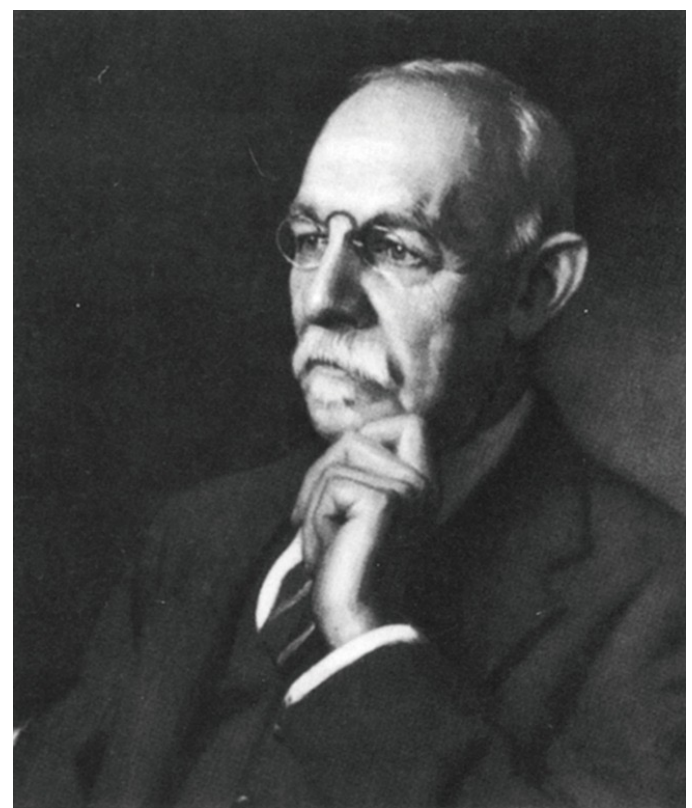
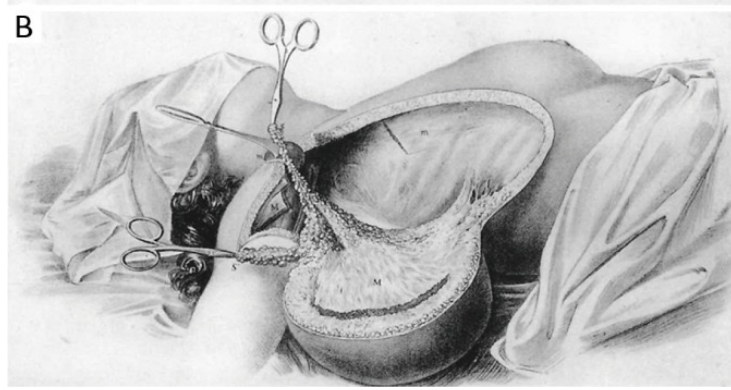
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Financial Disclosure

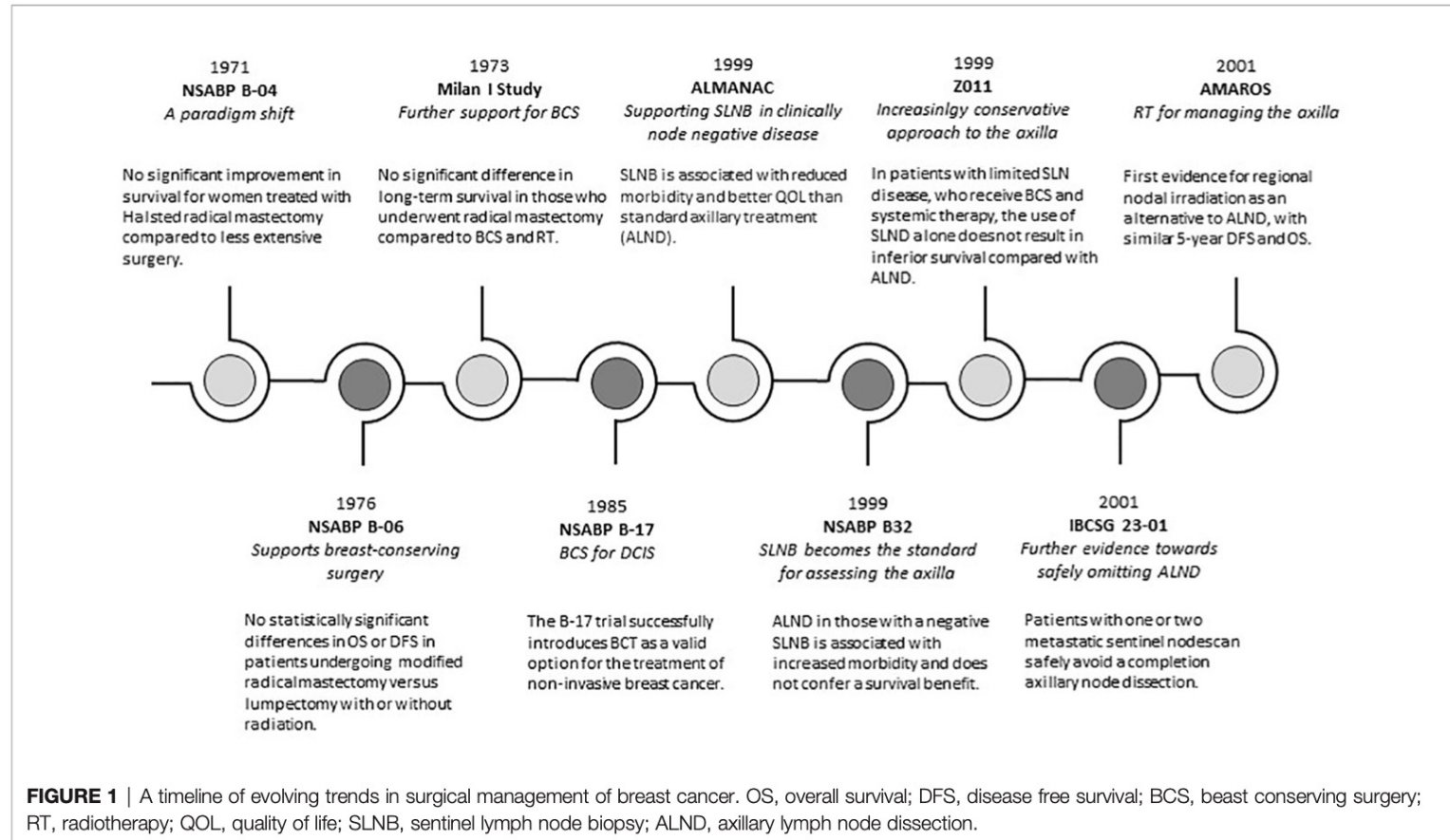
- No disclosures

Introduction: A bit of history



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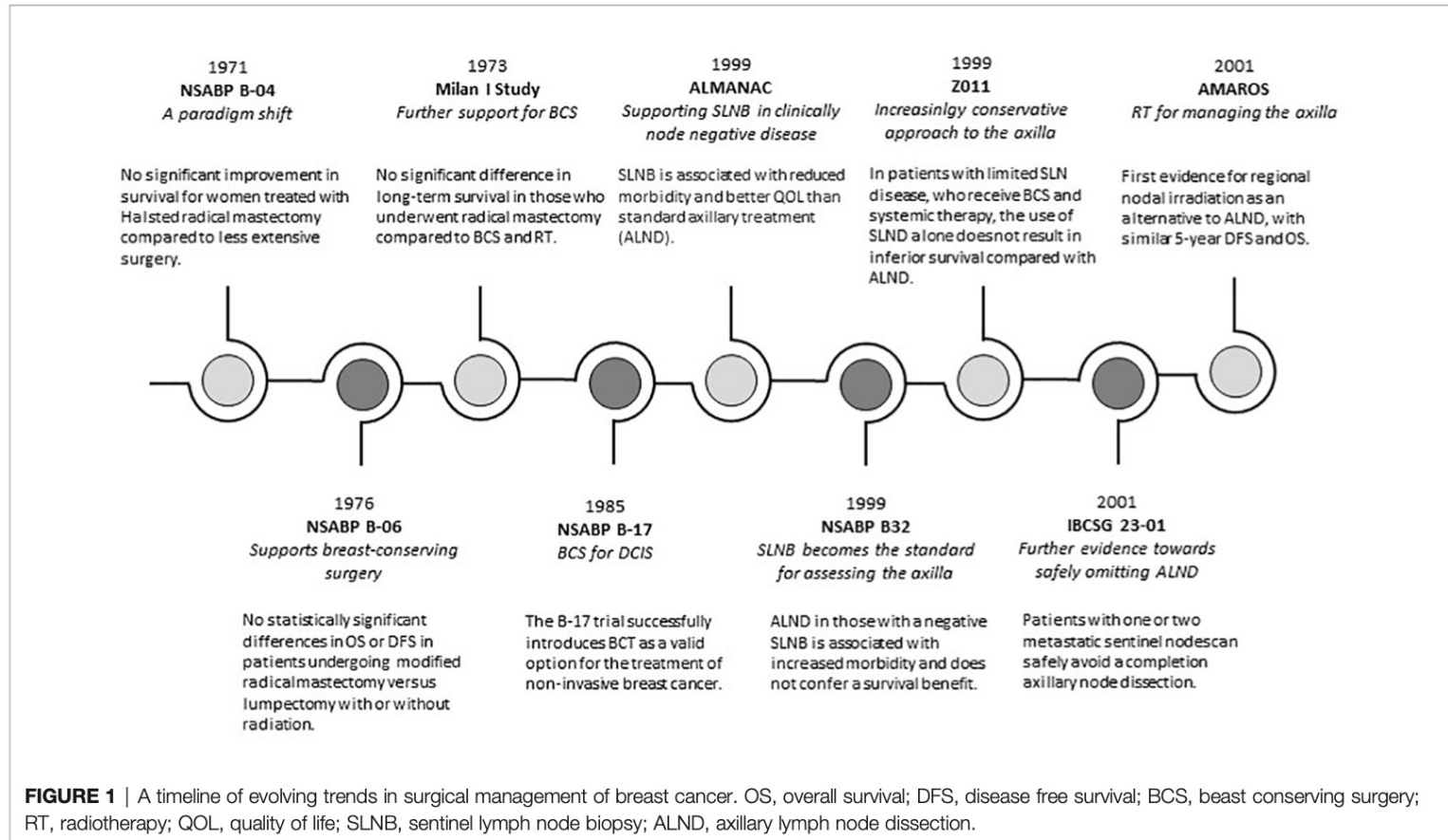
- Surgical studies: de-escalation
 - Cosmesis
 - QoL
 - Oncological outcomes



Keelan et al., *Frontiers in oncology*, 2021

Introduction: innovations in surgery at SABCS 2022

- 1. BCT
multicentric disease
- 2. Axillary surgery
patients receiving NACT



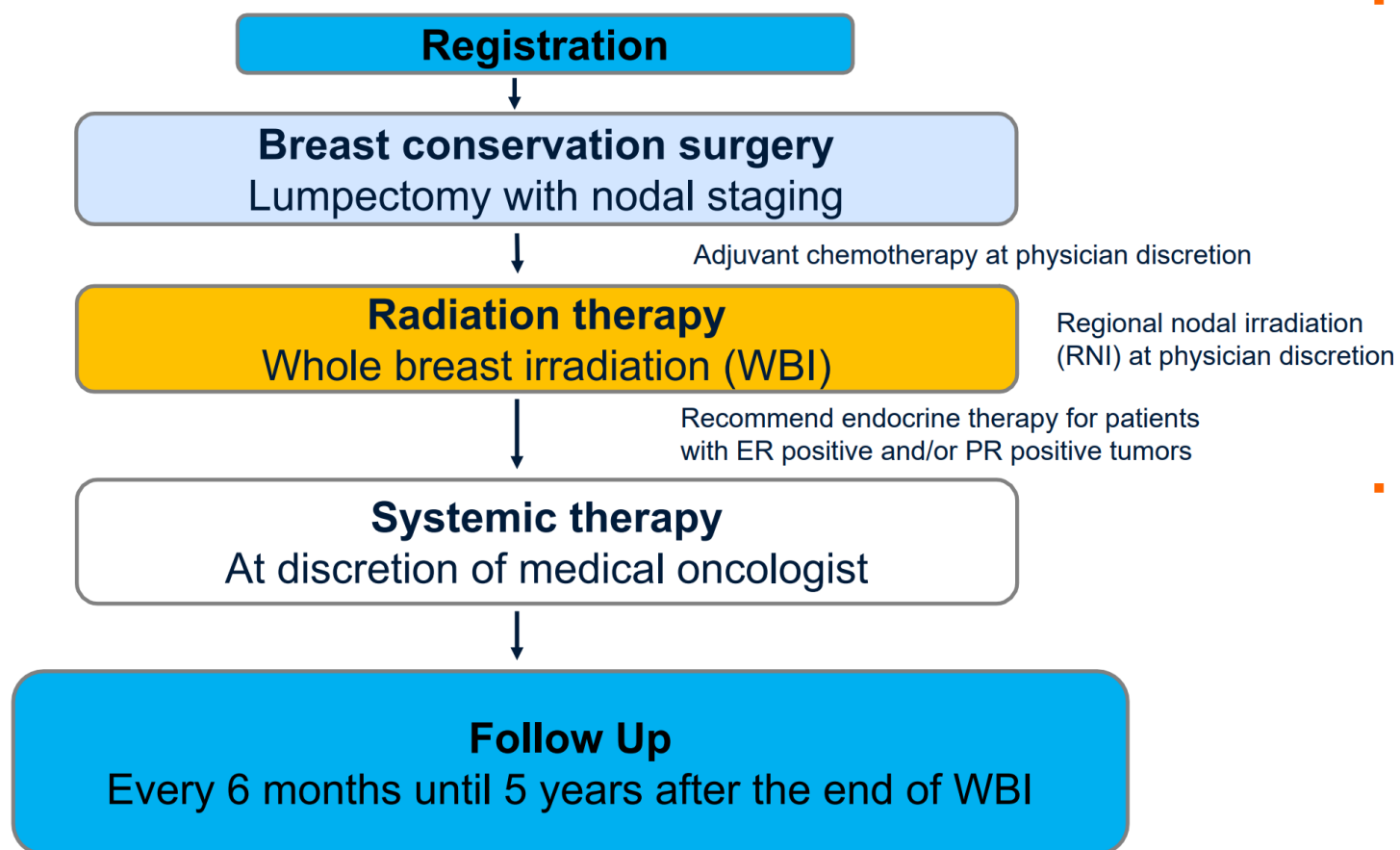
Keelan et al., *Frontiers in oncology*, 2021

ACOSOG Z11102 (GS4—01)

- **Impact of Breast Conservation Therapy on Local Recurrence in Patients with Multiple Ipsilateral Breast Cancer (ACOSOG Z11102) presented by JC. Boughey et al.**
- Increased diagnosis of multiple ipsilateral breast cancer (MIBC) because of improved imaging.
- Historical, retrospective studies showing high rates of local recurrence (LR) with BCT.
- Recent, retrospective institutional studies demonstrated acceptable LR rates.

→ Prospective single arm phase II trial to assess the LR rate with breast conservation in women with two or three lesions in the breast (MIBC)

ACOSOG Z11102: PROTOCOL



■ Inclusion Criteria

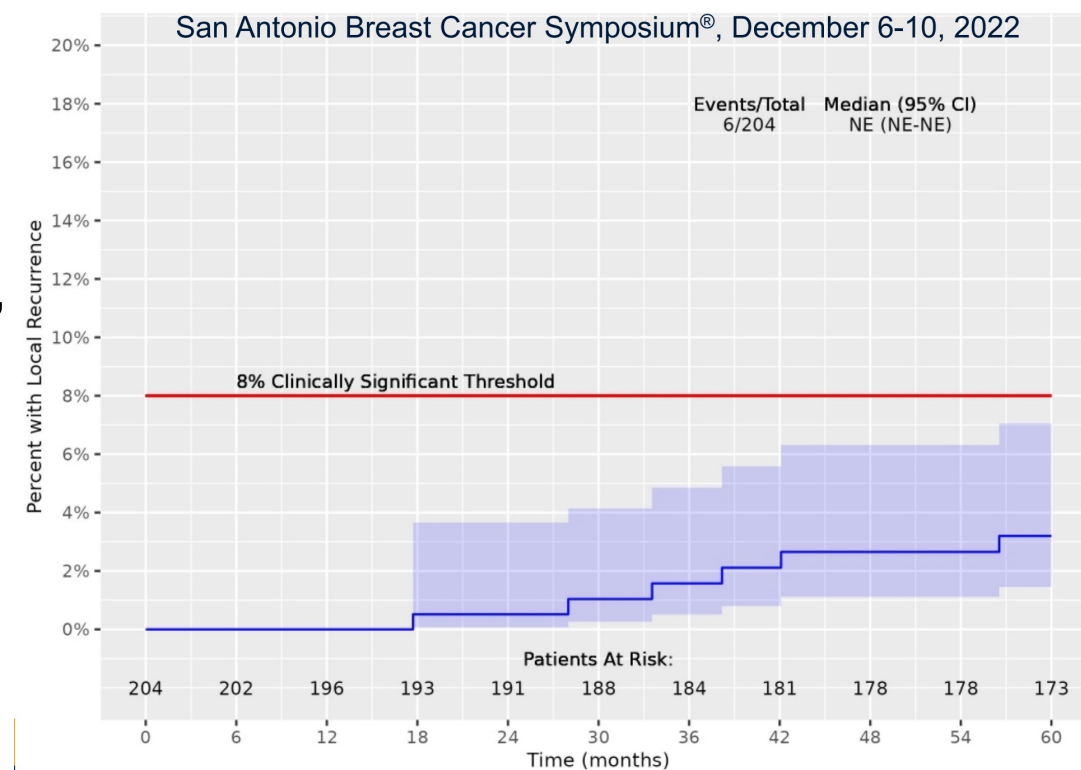
- Women age ≥ 40
- 2 or 3 foci of breast cancer
- At least one foci of invasive disease
- ≥ 2 cm normal tissue between lesions
- **No more than 2 quadrants**
- cN0 or cN1 disease

■ Exclusion Criteria

- Focus of disease > 5 cm on imaging
- Bilateral breast cancer
- Prior ipsilateral breast cancer
- Known BRCA 1/2 mutations
- **Neoadjuvant therapy**

ACOSOG Z11102: PRIMARY ENDPOINT

- 270 Patients enrolled and **204 eligible** to evaluate LR
 - 66 not evaluable (14 converted to mastectomy)
- All patients underwent BCT+ WBRT + boost
- Postmenopausal (mean: 61.1y) , ER⁺/HER2⁻ (83.5%), N⁻ (77.5%) disease with **only 2 foci (96.6%)**
- Median follow-up of 66.4 months (1.3 – 90.6 months)
- **6 out of 204** patients have developed LR
- CI of LR at 5 years: **3.1% (95% CI: 1.3 - 6.4)**
- **Outcomes:**
 - 6 local recurrence
 - 6 contralateral BC
 - 4 distant recurrence
 - 3 new non-BC primaries



ACOSOG Z11102: PRIMARY ENDPOINT

- **Breast MRI**
 - Initially required, 2015 amended to allow patients without MRI
 - 189 patients (92.6%) had MRI, 15 patients (7.4%) no MRI
 - Local Recurrence: 3/189 with MRI and 3/15 without MRI (HR: 13.5 (2.7 – 66.9), P= 0.002)
- **Endocrine therapy**
 - 195 patients with at least 1 ER+ laesion
 - Adjuvant Endocrine Therapy (n=3/175) vs. No Adjuvant Endocrine Therapy (n=2/20)
 - HR: 7.7 (1.3 – 46.3), P= 0.025
- No other clinicopathological parameters were associated with LR

ACOSOG Z11102: SECONDARY ENDPOINTS

- Previously presented
- **Rate of conversion to mastectomy:**
 - **7.1%** (14 patients converted due to positive margins)
 - 67.6% achieved margin-negative excision in a single operation
- **Cosmetic outcome:** good or excellent in **70.6% at 2 years**
- **Adherence to protocol directed radiation:** Increasing radiation boost volume associated with acute dermatitis, but not associated with worse overall cosmesis.

Rosenkranz et al. Ann Surg Oncol. 2018 Oct;25(10):2858-2866

Rosenkranz et al. Ann Surg Oncol. 2020 Nov;27(12):4650-4661

Cuttino et al. Int J Radiat Oncol Biol Phys. 2022 Mar 1;112(3):636-642

ACOSOG Z11102: CONCLUSION

- BCS followed by RT (with lumpectomy site boosts) has a low LR rate:
3.1% at 5 years
- Local recurrence was impacted by:
 - Preoperative MRI to evaluate disease extent
 - Adjuvant endocrine therapy (ER+ disease)

ACOSOG Z11102: STRENGTH & LIMITATIONS

STRENGTHS

- Patients that would previously be considered for mastectomy (based on “multicentricity”) might also be offered BCT with good oncologic and esthetic outcomes

LIMITATIONS

- Single arm study
- Small subset of patients with
 - no preop MRI
 - HER2+ or TN disease
 - 3 disease foci
- “Multicentricity” ? Vs. 2 quadrants and > 2 cm apart
- ER+ disease needs longer FU

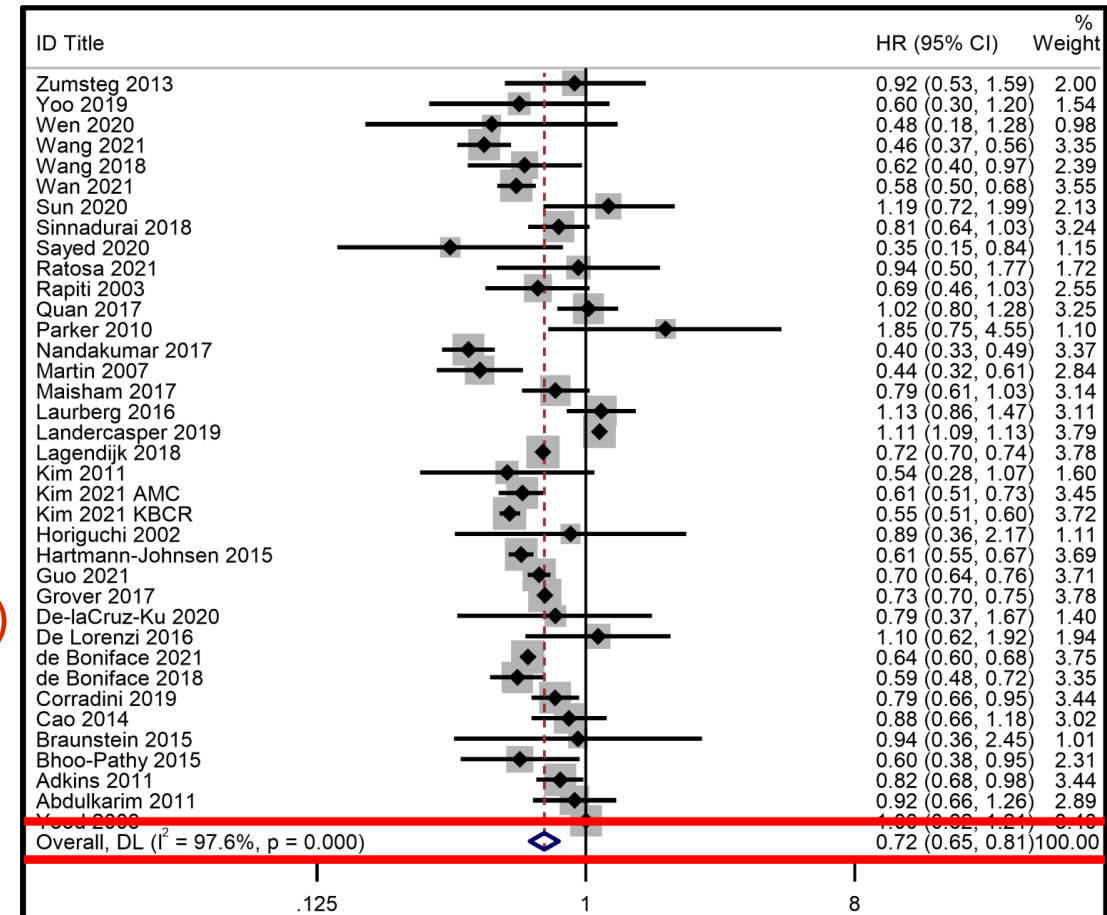
BREAST MRI?

- **PD15-08**: Brazilian Randomized Study - BREAST-MRI Trial - Impact of Preoperative Magnetic Resonance in the Evaluation for Breast Cancer Conservative Surgery: Local recurrence and surgical outcomes
Mota et al.
 - 524 patients: 257 in the MRI group, 267 in the control group.
 - A 6-year LRFS: 99.2% vs. 98.9%, $p=0.702$
 - OS: 95.3% vs. 96.3%, $p=0.481$.
 - Re-operation rates: 22 (8.7%) vs. 23 (8.7%), $p= 0.85$
 - Surgical management changed: 21 (8.3%) had mastectomies vs 1, $p < 0.01$

Houssami N et al., Ann Surg. 2013;257(2):249.

SURVIVAL OUTCOMES AFTER BCT

- PD15-04:** Overall survival following breast conserving surgery and adjuvant radiotherapy compared with mastectomy for early stage breast cancer: a systematic review and meta-analysis - *Rajan et al.*
 - 37 studies reported OS >1.3 million pat.
 - 729,789 BCS+RT vs. 591,502 mastectomy
 - Pooled HR: 0.73 (95% CI 0.65 – 0.81, p<0.001)
 - CAVE: treatment bias



OPBC-04/EUBREAST-06/OMA Study (GS4—02)

- **Oncological Outcomes Following Sentinel Lymph Node Biopsy (SLNB) or Targeted Axillary Dissection (TAD) in Breast Cancer Patients Downstaging From Node Positive To Node Negative with Neoadjuvant Chemotherapy presented by G. Montagna et al.**
- To evaluate rates of axillary, locoregional, and any invasive recurrence in a large, real-world cohort of node-positive patients who achieved nodal pCR with NAC, after omission of ALND
- To compare rates of axillary recurrence after SLNB with dual-tracer mapping versus TAD

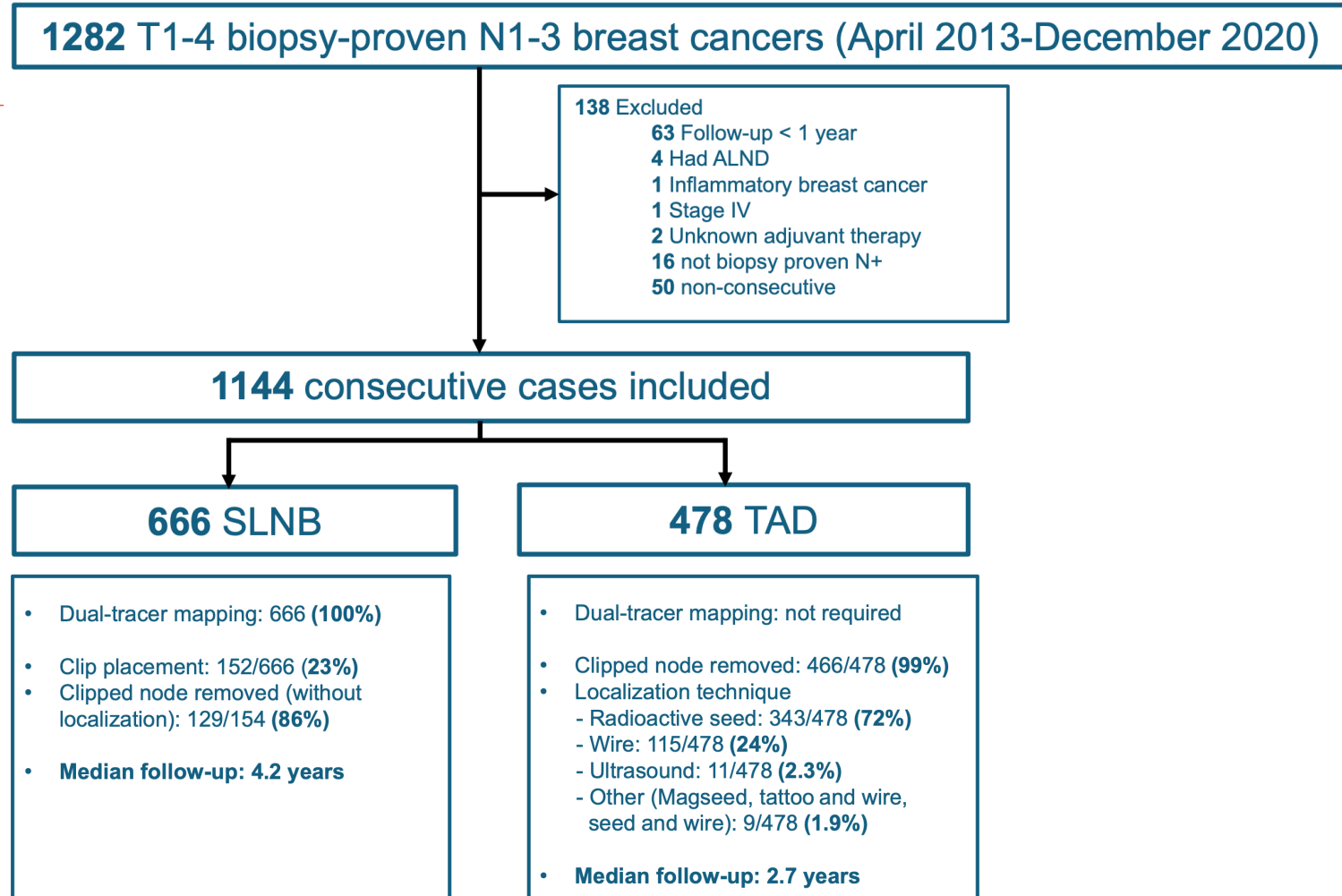
OPBC-04: PROTOCOL

■ Inclusion criteria

- T1-4
- Biopsy-proven nodal metastases (N1-3)
- Nodal pCR
- SLNB (dual-tracer mapping) or TAD
- A minimum of 10 cases per institution

■ Exclusion criteria

- ALND
- Inflammatory breast cancer
- Stage IV
- < 1-year follow-up



OPBC-04: RESULTS

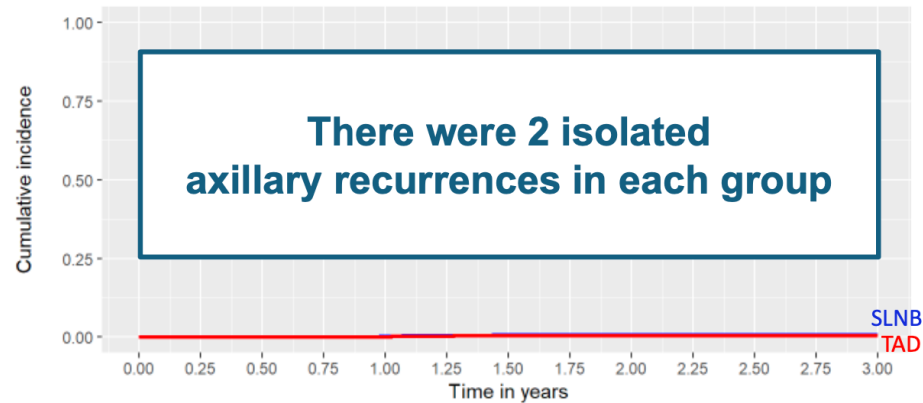
- Significant differences between the 2 cohorts:
 - Race (P < 0.001)
 - Differentiation (P < 0.001)
 - NACT regimen (P < 0.001)
 - # (S)LN removed (P < 0.001)
 - Nodal RT (P = 0.005)
 - Adjuvant CT (P = 0.005)

Treatment Characteristics				
	Overall n = 1144	SLNB n = 666	TAD n = 478	p value
# of SLNs removed (median, IQR)	3 (3, 5)	4 (3, 5)	3 (2, 4)	< 0.001
# of total LNs removed (mean, SD)	4.2 (2.03)	4.4 (2.04)	3.9 (1.97)	< 0.001
Radiation therapy (RT)				
Breast (n = 615)	98%	98%	98%	> 0.9
Chest wall (n = 522)	80%	79%	80%	0.8
Nodal RT				
Yes	81%	78%	85%	0.005
Adjuvant chemotherapy				
Yes	6.2%	4.5%	8.6%	0.005
HR+				
Adjuvant endocrine therapy				0.6
Yes	91%	90%	92%	
HER2+				
Adjuvant HER2 therapy				> 0.9
Yes	97%	96%	98%	

OPBC-04: RESULTS

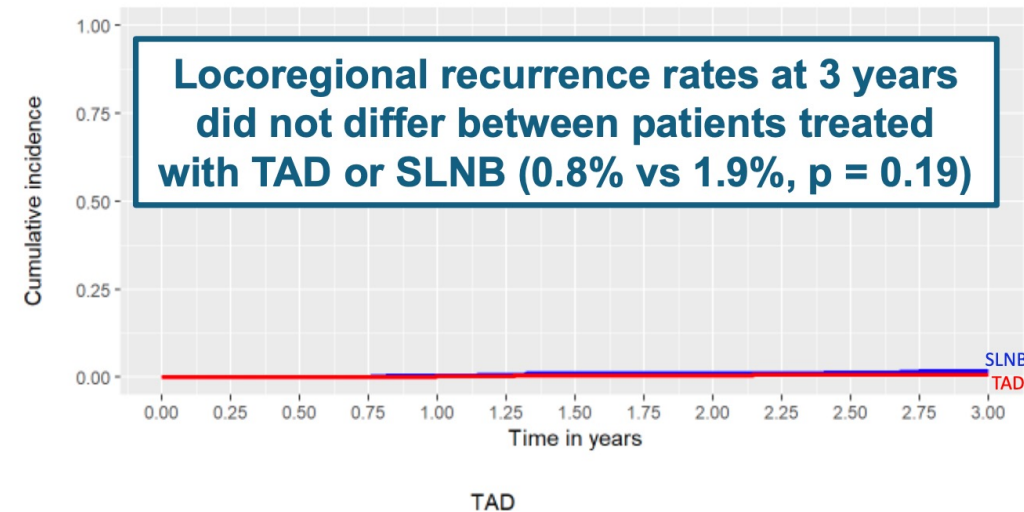
- 5 year rate of axillary recurrence:
 - 1.0 %, 95% CI: 0.49 – 2.0 %

3-year rate of any axillary recurrence TAD vs SLNB (0.5% vs 0.8%, p = 0.55)



		Number at risk												
Strata		0	0.25	0.5	0.75	1	1.25	1.5	1.75	2	2.25	2.5	2.75	3
SLNB	666	664	660	653	641	615	600	572	540	511	481	448	420	
TAD	478	477	471	462	439	401	366	336	308	271	250	230	213	

- 5 year of locoregional recurrence:
 - 2.7%, 95% CI: 1.6 – 4.1 %



		Number at risk												
Strata		0	0.25	0.5	0.75	1	1.25	1.5	1.75	2	2.25	2.5	2.75	3
SLNB	666	664	660	653	641	614	599	571	539	510	480	447	419	
TAD	478	477	471	462	439	401	366	336	308	271	250	230	213	

OPBC-04: CONCLUSIONS

- **Early axillary recurrence** after omission of ALND in N+ patients who downstage to N- after NACT is a **very rare event (1% after 5 years)**.
- **No difference between TAD and SLNB**
 - Despite more TAD patients receiving nodal RT
 - TAD allows removal of fewer lymphnodes (median: -1)

OPBC-04: STRENGTH & LIMITATIONS

STRENGTHS

- Results support omission of ALND in patients who downstage to N- disease after NACT
- First study comparing outcomes after SLNB and TAD
- Large number of consecutive patients
- Multicenter (intercontinental)

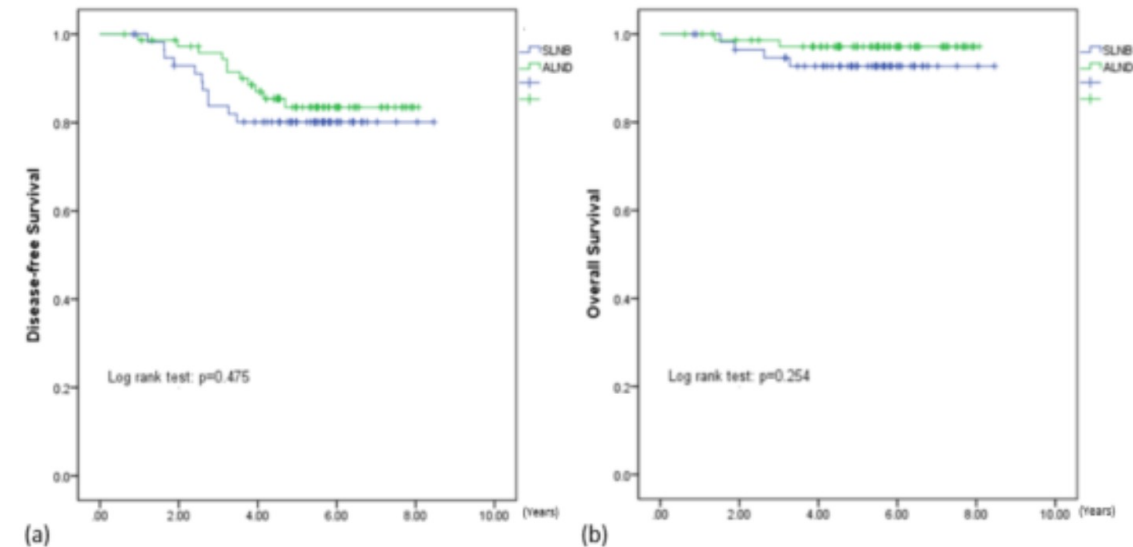
LIMITATIONS

- Retrospective
- Difference in median follow-up
- Longer follow-up is needed
- Multicenter study -> regional differences
- Pre-operative evaluation? How much ycN0 -> ypN+ disease?

OMISSION OF ALND?

- PD15-02:** Long Term Outcome in Patients with Nodal-Positive Breast Cancer Treated with Sentinel Lymph Node Biopsy Alone After Neoadjuvant Chemotherapy - *Lim et al.*
 - Retrospective study, 1/2014-12/2018, 902 patients, T1-4, cN1 → cN0 after NACT
 - 477 ypN0 (52.9%), 425 ypN+(47,1%) of which 133 ypN0i or ypN1mi (14,7%)
 - No difference in DFS and OS for SLNB vs. ALND YpN0i/ypN1mi, p=0.475 & 0.254

	N	Axillary recurrence N (%)	P-value
ypN0 (N=477)			
SLNB	314	10 (3.2%)	0.39
ALND	136	3 (1.8%)	
ypN0i, ypN1mi (N=133)			
SLNB	58	7 (12%)	0.09
ALND	75	3 (4%)	



OMISSION OF ALND?

- **PD15-11**: Axillary dissection to determine nodal burden to inform systemic therapy recommendations in patients with clinically node-positive breast cancer - *Weber et al.*
 - N=500, cN+, TAD (removal of suspicious palpable nodes and SLNs), HR+/HER 2- 80%
 - Randomized to ALND vs. Axillary RT
 - ALND significantly increased the number of positive nodes removed
 - Type of axillary surgery did not impact adjuvant systemic therapy
- **PD15-01**: Axillary Nodal Recurrence is Rare in patients with node-positive Breast Cancer Undergoing SLNB following neoadjuvant chemotherapy: Early results of the NEOSENTITURK trial/MF18-03. - *N Cabioğlu et al.*
 - Very low rates of LR (0.6%, n=14/2358) 3 years after surgery in cN+ patients after NACT
 - No difference between SLNB (1433) and ALND (957) groups regardless ypN status.

OMISSION OF ALND: ONGOING TRIALS

- OT1-06-01: Preservation of axillary lymph nodes in breast cancer patients undergoing mastectomy with 1-2 metastatic sentinel lymph nodes: The current status and future perspectives of the multicenter randomized clinical trial SINODAR-ONE
- OT1-07-01: Omission of SLNB in triple-negative and HER2-positive breast cancer patients with radiologic and pathologic complete response in the breast after NAST: a single-arm, prospective surgical trial (EUBREAST-01 trial, GBG 104)
- OT1-08-01: AXSANA – EUBREAST3: An international prospective multicenter cohort study to evaluate different surgical methods of axillary staging in clinically node-positive breast cancer patients treated with neoadjuvant chemotherapy
- OT1-09-02: ATNEC: A multicentre, randomized trial investigating whether axillary treatment can be avoided in T1-3N1M0 breast cancer patients with no residual cancer in the axillary lymph nodes after neoadjuvant chemotherapy



SABCS 2022: CONCLUSIONS

- Patients that would previously be considered for mastectomy, based on “multicentricity”, might also be offered BCT with good oncologic and esthetic outcomes.
- Early axillary recurrence after omission of ALND in N+ patients who downstage to N- after NACT is a very rare event. These results support omission of ALND in patients who downstage to N-disease after NACT and underwent SLN (dual-mapping) or TAD.

INTERESTING POSTERS

- **P1-09-05**: Effect of Wire vs Magnetic Seed Localization on Lumpectomy Cavity Size, *Dykstra et al.*
 - Retrospective review, 387 patients
 - No difference in positive margins ($p = 0.81$), CT cavity size ($p = 0.38$) or boost delivery ($p = 0.14$)
- **P2-14-07**: Omission of Sentinel Lymph Node Biopsy in Patients with Early Stage Breast Cancer: Looking Beyond the Choosing Wisely Guidelines for Age < 70, *Carleton et al.*
 - Natural language understanding (NLU) technology to extract relevant data in 591 pts with early stage ER+, cN0 breast cancer
 - Low rates of SLN positivity (specifically T1a and T1b)
- **P4-02-06**: Clinical and biological predictors of lymph node involvement in patients with early breast cancer for adjuvant treatment personalization, *Pivetta et al.*
 - Gradient boosting machine learning algorithm (GBM). AUC: 0.77
 - Features with the highest RI: SLN+, tumor size ≥ 3 cm and LVI

n = 591 patients who underwent SLNB			
	Rate of SLN Positivity		p-value
	< 70yo	≥ 70 yo	
T1a	10.4% (5 / 48)	6.7% (1 / 15)	0.99
T1b	6.8% (5 / 74)	5.9% (1 / 17)	0.99
T1c	17.3% (29 / 168)	13.2% (5 / 38)	0.64
T2	30.4% (45 / 148)	27.8% (10 / 36)	0.84
T3	58.5% (24 / 41)	33% (2 / 6)	0.39

INTERESTING POSTERS

- **P2-14-05**: Comparison of RFS according to axillary surgery extent for cN0, sentinel node(s) positive, primary breast cancer patients who underwent total mastectomy, *Chun et al.*
 - Retrospective, 208 patients, cT1/2N0 and pN1 (1-3+), mastectomy, SLN vs. subsequent ALND
 - mean number of metastatic nodes: 1.2 for SLNB group and 1.7 for ALND group
 - No difference between SLNB and ALND for LRR and DFS
 - For SLNB alone group: post-mastectomy radiation: less LRR (P= 0.026)
- **P5-01-06**: Single cell profile of tumor and immune cells in primary triple-negative breast cancer and different sites in the axillary lymph nodes, *Liao et al.*
 - Single-cell sequencing analysis suggested that the sentinel lymph node was the initial meeting site of tumor infiltration and immune response
 - Some T lymphocytes perform anti-tumor activity while other T cells exhibit an exhaustion state.

Breast Cancer (2023) 30:77–87
<https://doi.org/10.1007/s12282-022-01400-x>

ORIGINAL ARTICLE



Single-cell profile of tumor and immune cells in primary breast cancer, sentinel lymph node, and metastatic lymph node

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