Localized Therapy: Updates From a Surgery Perspective

2023 SABCS Review

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Disclosures

- Founder and Minority Stock Owner – Elucent Medical
- Principal Investigator/No Salary Support – Perimeter Medical

Neither of these devices will be discussed or are relevant to the data presented

- Did not attend SABCS this year due to a foot surgery!

Key Themes

- Benign Breast Disease and Cancer Risk
- Surgical Options for BRCA 1 mutation carriers
- The Axilla – every permutation!

- Breast Cancer Surveillance Consortium (BCSC)
  "A collaborative network of breast imaging registries conducting research to assess and improve the delivery and quality of breast cancer screening and related patient outcomes in the United States"

- ***Proliferative changes without atypia***
  - *Papilloma or papillomatosis*
  - *Usual ductal hyperplasia*
  - *Radial scar*
  - *Columnar cell hyperplasia*
  - *Hyperplasia NOS, complex fibroadenoma, flat epithelial atypia, blunt duct adenosis*

Objectives

- Estimate the future risk of invasive breast cancer associated with specific BBD diagnoses typically combined into the broad category of proliferative lesions without atypia (PWoA)
- Evaluate whether these associations differ by breast density categories or by presence of calcifications

Methods

Study population

1. Women in the BCSC without prior history of breast cancer (follow-up started 6 months after each mammogram)
2. Age: 40-79 years
3. Period: 1996-2019
4. 5.3 million mammograms from 1.3 million women

Statistical analysis

1. Cox proportional hazards model
2. Classification trees

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Results: Classification trees, dense breasts

PWoA diagnosis	Calcification	BI-RADS density[c]	% Women	5-year invasive cancer rate per 100: Without specific PWoA diagnosis[a]	5-year invasive cancer rate per 100: With specific PWoA diagnosis[a]	Risk Difference[b]
60 -79 years						
Papillomas (multiple, single); radial scar	With or without	c,d	0.4%	3.66	4.52	
Usual ductal hyperplasia	With or without	c,d	1.3%	3.66	3.92	
Columnar cell hyperplasia; PWoA NOS	With or without	c,d	0.9%	3.66	3.01	
No prior biopsy; Papillomatosis	With or without	c,d	97.5%	1.88	1.83	
40-59 years						
Papillomas (multiple, single); Usual Ductal Hyperplasia; Columnar cell hyperplasia; PWoA NOS	With calcifications	c,d	0.5%	2.02	2.58	
PWoA NOS	No calcifications	c,d	1.1%	2.02	2.08	
Usual ductal hyperplasia	No calcifications	c,d	0.5%	2.02	1.67	
No prior biopsy; Papillomatosis; Radial Scar	With or without	d	15.7%	1.45	1.43	
Papillomas (multiple, single); Columnar cell hyperplasia	No calcifications	c,d	0.2%	2.02	1.22	
No prior biopsy; Papillomatosis; Radial Scar	With or without	c	81.9%	1.13	1.12	

PWoA: Proliferative Lesions without Atypia

[a]5-year risk	Low (<1.0)	Average (1.0-1.66)	Intermediate (1.67-2.49)	High (2.5-3.99)	Very high (≥4.0)

Results: Classification trees, non-dense breasts

PWoA diagnosis	Calcification	BI-RADS density[c]	% Women	5-year invasive cancer rate per 100: Without specific PWoA diagnosis[a]	5-year invasive cancer rate per 100: With specific PWoA diagnosis[a]	Risk Difference[b]
60 -79 years						
Papillomas (multiple, single); radial scar	With or without	b	0.3%	3.2	3.64	↑
Usual ductal hyperplasia; PWoA NOS	With or without	b	1.3%	3.2	3.13	↓
Papillomas (multiple, single); Usual Ductal Hyperplasia; PWoA NOS	With or without	a	0.2%	2.12	2.16	↑
No prior biopsy; Papillomatosis; Columnar cell hyperplasia	With or without	b	81.1%	1.63	1.6	↓
No prior biopsy; Papillomatosis; Radial Scar; Columnar cell hyperplasia	With or without	a	17.1%	1.06	1.05	↓
40-59 years						
Papillomas (multiple, single)	With or without	b	0.2%	1.57	2.04	↑
Usual ductal hyperplasia; PWoA NOS	With calcifications	b	0.3%	1.57	1.83	↑
Usual ductal hyperplasia; PWoA NOS	No calcifications	b	1.0%	1.57	1.42	↓
No prior biopsy; Papillomatosis; Radial Scar; Columnar cell hyperplasia	With or without	b	85.9%	0.9	0.89	↓
Any BBD or no prior biopsy	With or without	a	12.6%	0.45	0.45	—

- Women with a PWoA BBD diagnosis and calcifications had elevated risk for breast cancer in all levels of breast density
- Specific BBD diagnoses and the presence of calcifications can change a woman's predicted 5-year breast cancer risk compared to broad BBD categories alone
- **This information could be incorporated into risk prediction models to improve model accuracy**

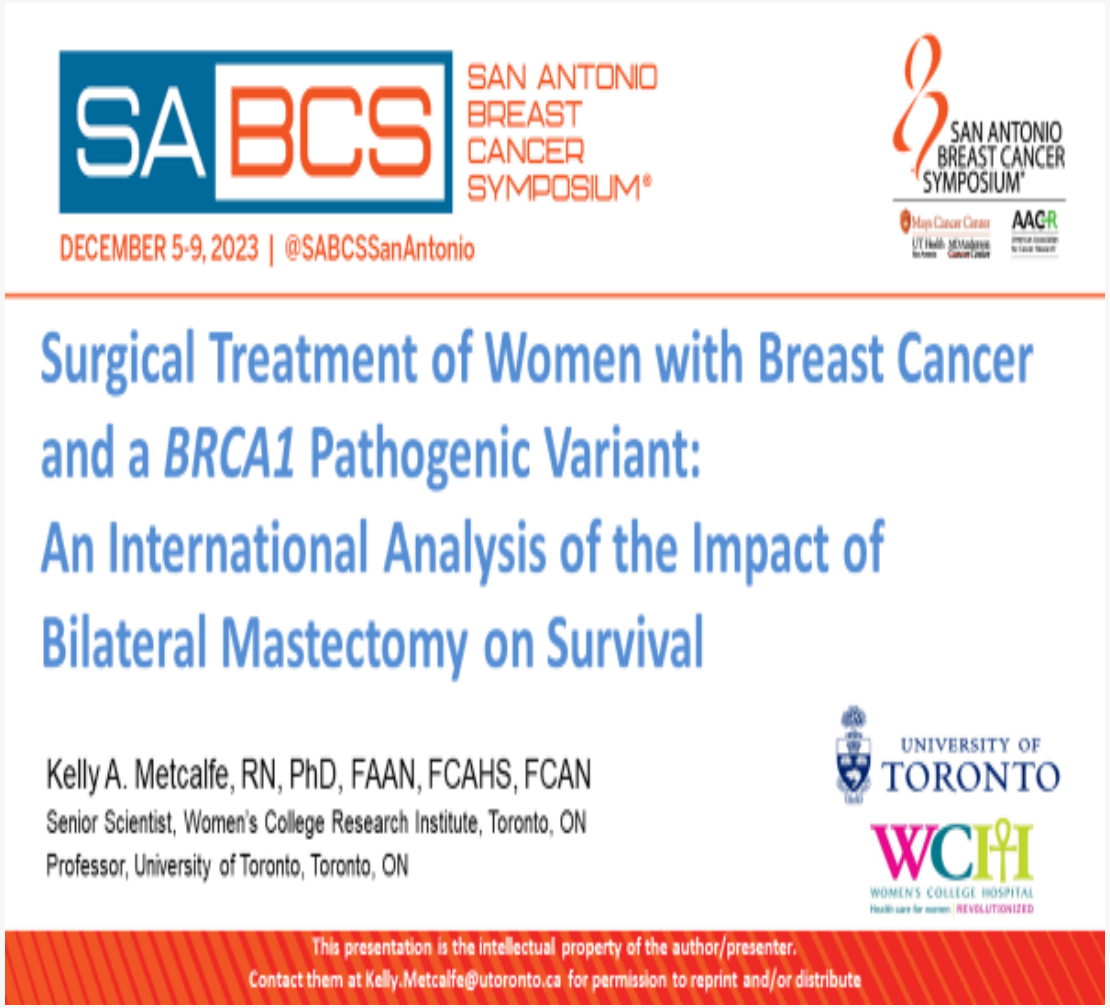
[a]5-year risk	Low (<1.0)	Average (1.0-1.66)	Intermediate (1.67-2.49)	High (2.5-3.99)	Very high (≥4.0)

Olivia Sattayapiwat, SABCS 2023

Changes to our Practices?

- Consider risk discussion in women with non-proliferative biopsy results with calcifications; especially those with an additional family history of breast malignancy

- Emphasis in this population for annual mammograms as a “minimal” approach to screening (vs every other year)



- Objective: Risk of Contralateral breast cancer and breast cancer specific mortality by primary surgical therapying women with BRCA 1 and Stage 1-3 breast cancer

- 2482 eligible individuals – 26 centers; 11 countries; retrospective chart review and patient questionnaire

1995-2021 (age 43) ER pos 25-27%	Mean or %	Follow – up (p <0.0001)	Tumor Size (cm) (<0.0001)	Node positive (p=0.03)
BCT	34% (852)	9.2 years	2.1 (0-20)	21.9
Mastectomy	46% (1141)	9.6 years	3.0 (0-40)	37.6
Bilateral Mastectomy	19.7% (489)	6.5 years	2.2 (0-27)	24.4

Contralateral Breast Cancer

- 11.5% of participants diagnosed with contralateral breast cancer

Variable	BCT N=852	Unilateral mastectomy N=1141	Bilateral Mastectomy N=489	P-value
Contralateral BC				
No	760 (89.2)	1011 (88.6)	485 (99.2)	
Yes	92 (10.8)	130 (11.4)	4 (0.8)	<0.0001

Breast Cancer Mortality

- 285 (11.5%) died of breast cancer

Variable	BCT N=852	Unilateral mastectomy N=1141	Bilateral Mastectomy N=489	P-value
Died of BC				
No	667 (78.3)	968 (84.8)	453 (92.6)	
Yes	76 (6.9)	173 (15.2)	36 (7.4)	<0.0001

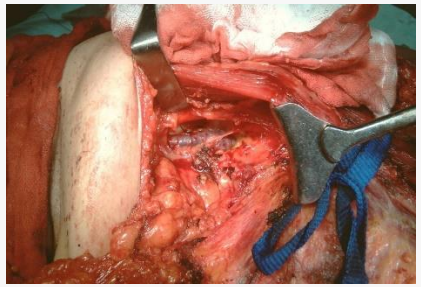
Changes to our Practices?

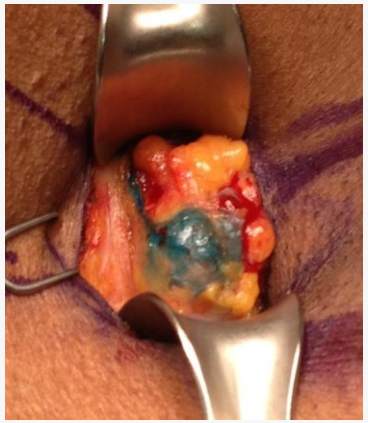
- Bilateral mastectomy was not significantly associated with reduction in mortality compared to BCT (HR 0.83)
- Women with BRCA 1 and bilateral mastectomy have a lower risk of contralateral breast cancer
- Women in this study with unilateral mastectomy had greater node positive disease and larger tumor size
  - Bilateral Mastectomy patients had greater BSO rates (64.6% vs 58.3 and 50.6%)
  - BCT patients had greater use of chemotherapy (84.5% vs 76.9% (UM) vs 47.1% (BM))

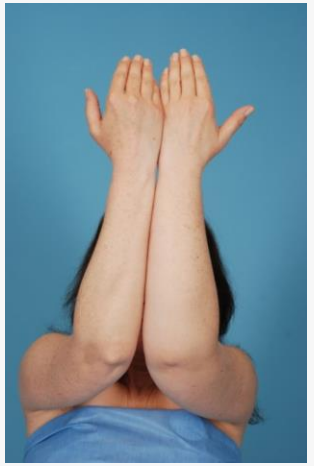
- Further study is needed to determine
  - Benefit of oophorectomy
  - Comparison with modern therapy - Olarparib

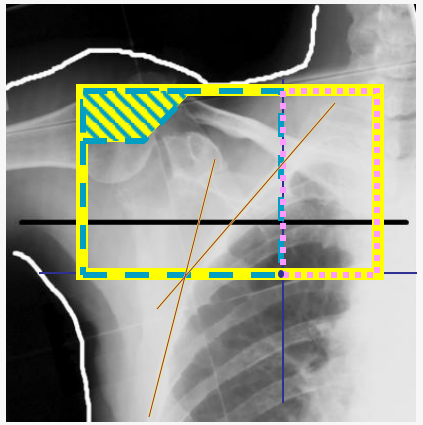
Evolution of Axillary Surgery

1960-1980s	1990s	2000s	2010s
ALND	SLNB for cN0	SLNB ± RT for 1-2+ SLN	SLNB for cN1 after NAC









Adapted from T King, MD; M Morrow MD and E Mittendorf, MD

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EBCTCG Overview of Axillary Management in Early Breast Cancer GS02-05

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History of Axillary Treatment Trials

Year	Randomised trials	
1950s - 1990s	More *vs* Less axillary treatment	Pre-SLNB era
1970s – 1990s	Axillary dissection *vs* Axillary radiotherapy	
1990s - 2010s	More *vs* Less axillary treatment	SLNB era
2000s - 2010s	Axillary dissection *vs* Axillary radiotherapy	
2012+	SLNB *vs* No SLNB	Post-SLNB era

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Thanks to 20,285 women randomised 1000 collaborating trialists and our funders

CANCER RESEARCH UK

OXFORD POPULATION HEALTH

NHS England

Outcome data for the following trial was provided by NHS Digital, or its predecessors:
1958B Addenbrooke's trial

EBCTCG Collaborating Trialists

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Comparisons of Axillary Treatment

	Comparison more vs. less	Trials	Women
Pre-SLNB era (1958-1995)			
AD vs no AD	Yes	4	1558
AD vs no AD*	Yes	1	773
Axillary/SCF RT vs no axillary/SCF RT	Yes	2	652
More vs less surgery to axilla	Yes	1	161
More vs less surgery to axilla*	Yes	3	4516
Axillary/SCF RT + AD vs Axillary/SCF RT *	Yes	1	233
AD vs axillary/SCF RT*	No	3	460
SLNB era (1998-2004)			
SLNB+AS/AD vs SLNB: (cN0/sN-)	Yes	10	8010
SLNB+AD vs SLNB: (sN+)	Yes	3	2023
AD vs Axillary RT: (sN+)	No	2	1899
Total		**30†**	**20285**

*confounded by extent of breast surgery
AD: axillary dissection, AS: axillary sampling, SCF: supraclavicular fossa, SLNB: sentinel lymph node biopsy, RT: radiothera py
†3 trials contributes to two comparisons. Data for ~1000 women from 5 trials not available.

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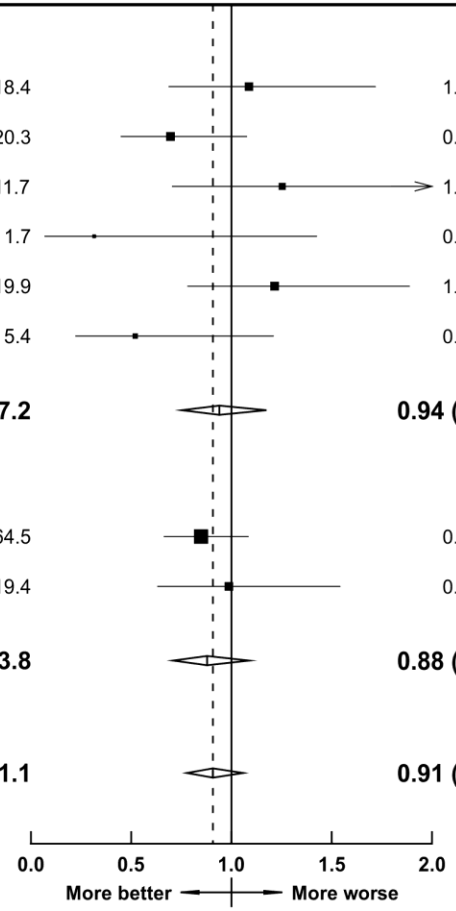
Mittendorf SABCS update Brigham

More vs Less Axillary Treatment: LRR

Treatment era and comparison (n trials)	Events/Woman-years: Allocated More	Events/Woman-years: Allocated Less	More events: Logrank O−E	More events: Variance of O−E	Rate Ratio (95% CI)
(a) Pre−SLNB era (1958−1995)					
AD vs no AD (n=4)	41/4466 (0.9%/y)	38/4512 (0.8%/y)	1.5	18.4	1.09 (0.69−1.72)
AD vs no AD∗ (n=1)	35/4044 (0.9%/y)	49/3753 (1.3%/y)	−7.3	20.3	0.70 (0.45−1.08)
Axi/SCF RT vs no axi/SCF RT (n=2)	25/3089 (0.8%/y)	26/3073 (0.8%/y)	2.6	11.7	1.25 (0.71−2.23)
More vs less surgery to axi (n=1)	1/1149 (0.1%/y)	6/1426 (0.4%/y)	−2.0	1.7	0.32 (0.07−1.42)
More vs less surgery to axi∗ (n=3)	45/19725 (0.2%/y)	43/19256 (0.2%/y)	3.9	19.9	1.22 (0.78−1.89)
Axi/SCF RT + AD vs Axi/SCF RT ∗ (n=1)	7/1203 (0.6%/y)	15/1210 (1.2%/y)	−3.5	5.4	0.52 (0.22−1.21)
■ **(a) Subtotal**	**154/ 33676 (0.5%/y)**	**177/ 33230 (0.5%/y)**	**−4.8**	**77.2**	**0.94 (0.75−1.17)** p = 0.59
(b) SLNB era (1998−2004)					
SLNB+AS/AD vs SLNB (cN0/sN−) (n=10)	126/28773 (0.4%/y)	143/28932 (0.5%/y)	−10.6	64.5	0.85 (0.66−1.08)
SLNB+AD vs SLNB (sN+) (n=3)	39/7822 (0.5%/y)	40/7997 (0.5%/y)	−0.2	19.4	0.99 (0.63−1.54)
■ **(b) Subtotal**	**165/ 36595 (0.5%/y)**	**183/ 36929 (0.5%/y)**	**−10.8**	**83.8**	**0.88 (0.71−1.09)** p = 0.24
■ **Total**	**319/ 70271 (0.5%/y)**	**360/ 70159 (0.5%/y)**	**−15.6**	**161.1**	**0.91 (0.78−1.06)** p = 0.22

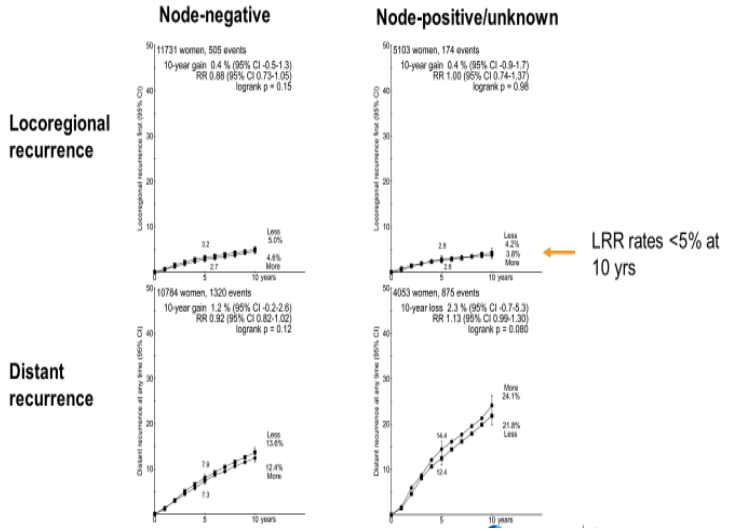
Ratio of annual event rates: More : Less



■ 95% or ◇ 95% confidence intervals

Difference between treatment effects in 2 subtotals: $\chi^2_1 = 0.2$; **p = 0.67**
Heterogeneity within subtotals: $\chi^2_6 = 8.7$; **p = 0.19**
Heterogeneity between 8 trials: $\chi^2_7 = 8.9$; **p = 0.26**

More vs Less Axillary Treatment by Nodal Status



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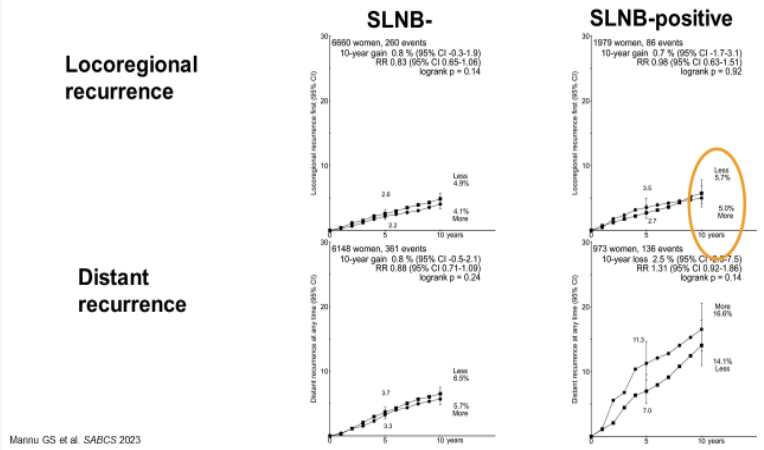
More vs Less Axillary Treatment by Nodal Status in SLNB Trials



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Axillary dissection *vs* Axillary radiotherapy

Summary of outcomes

Outcome	Events/Women: Allocated AD	Events/Women: Allocated AxRT	AD events: Logrank O−E	AD events: Variance of O−E	Ratio of annual event rates AD : AxRT	Rate Ratio* (95% CI)
Recurrence and mortality						
Locoregional recurrence	59/1235	58/1124	−1.5	27.9		0.95 (0.65–1.37)
Distant recurrence	252/1235	229/1124	3.3	108.6		1.03 (0.85–1.24)
Breast cancer mortality	227/1235	197/1124	1.7	93.4		1.02 (0.83–1.25)
Any death	323/1235	286/1124	4.2	134.3		1.03 (0.87–1.22)
Morbidity						
Any lymphoedema	263/612	174/592	40.5	69.3		1.79 (1.42–2.27)

* odds ratio for lymphoedema

Conclusions

- Risk of LRR is low (≈5% at 10 years)
- Axillary recurrences are rare (≈1%)
- No oncologic benefit to more surgery
- More surgery significantly ↑ risk of lymphedema

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Mays Cancer Center UT Health San Antonio MD Anderson Cancer Center
AACR American Association for Cancer Research

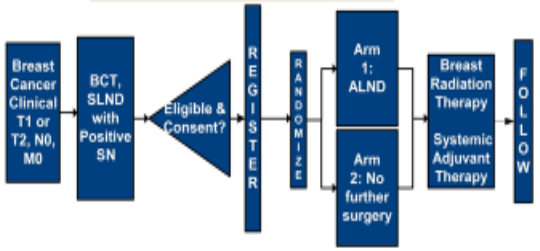
Recurrence-free survival following sentinel node-positive breast cancer without completion axillary lymph node dissection – first results from the international randomized SENOMAC trial

Jana de Boniface, M.D., Ph.D., Associate Professor
Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden
Breast Unit, Capio St. Göran's Hospital, Stockholm Sweden

Karolinska Institutet

SLNB Nodal RT for Limited Nodal Metastasis

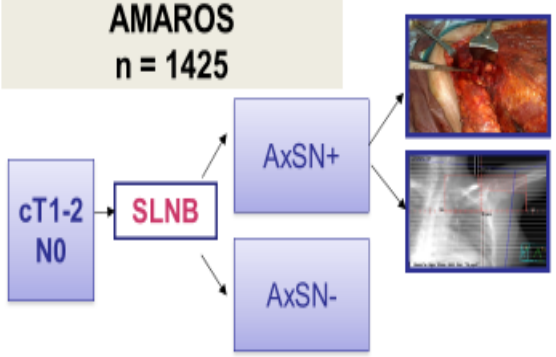
ACOSOG Z00011
n = 856



All BCT

10-year axillary recurrence:
0.5% ALND vs 1.5% SLNB

AMAROS
n = 1425



17% Mastectomy

10-year axillary recurrence:
0.93% ALND vs 1.82% AxRT

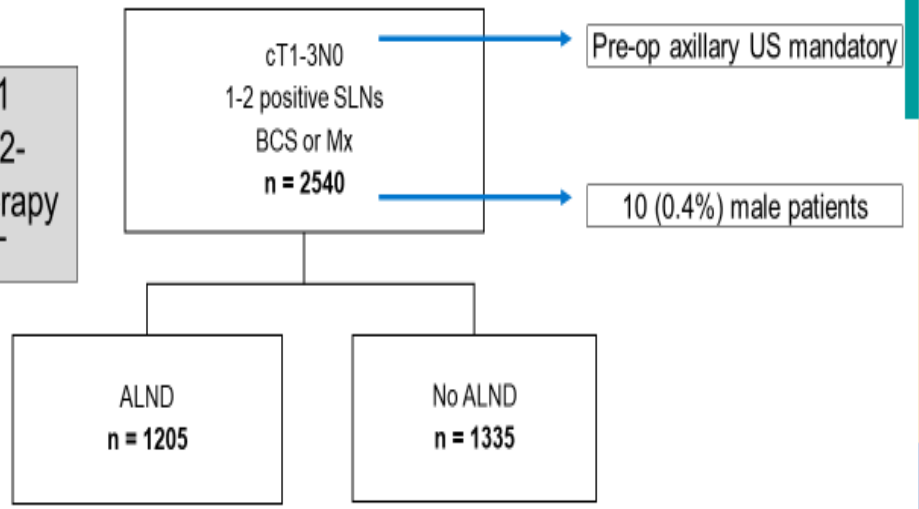
Criticisms of trials related to statistical power, low-risk patient population, uncertain radiotherapy fields, and small number of mastectomy patients

Giuliano A et al. *Ann Surg*, 2016;264:413-420
Bartels SAL et al. *J Clin Oncol*, 2023;41:2159-2165

Slide courtesy A. Barrio MD

SENOMAC

Median age 61
87% HR+/HER2-
99% systemic therapy
88% nodal RT

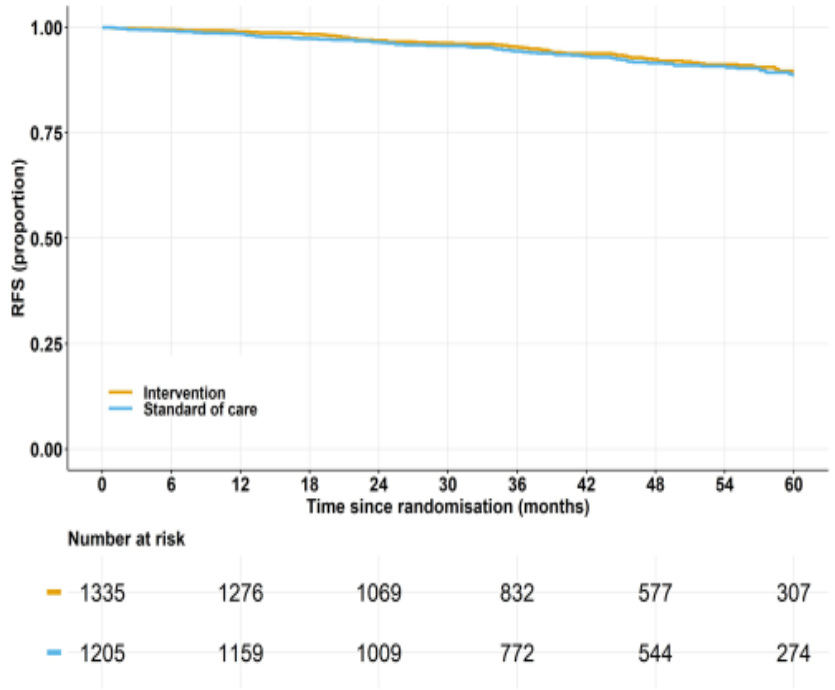


- 1:1 randomized non-inferiority trial
- Primary endpoint: OS
  - Non-inferiority margin 2.5% (HR upper limit of CI below 1.44)
- Secondary endpoint: RFS

deBoniface J et al. *SABCS* 2023

Note – 34.3% had microscopic ENE; 36% were mastectomy

Recurrence-Free Survival



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Conclusion

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- SLN biopsy alone non-inferior to axillary dissection
  - High proportion of nodal irradiation & systemic treatment
- Clinically relevant subgroups well represented
  - Mastectomy
  - Patients aged ≥ 65 years
  - Larger tumors
- Next step is to evaluate omission of nodal RT in the ongoing randomized T-REX trial

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The OPBC05/EUBREAST-14R/ICARO study

Are nodal isolated tumor cells (ITCs) after neoadjuvant chemotherapy an indication for axillary dissection?

ONCOPLASTIC BREAST CONSORTIUM

Speaker: **Giacomo Montagna, MD, MPH**
Breast Service, Department of Surgery, Memorial Sloan Kettering Cancer Center

Giacomo Montagna MD, MPH, Alison Laws MD, MPH, Massimo Ferrucci MD, PhD, Mary M. Mrdutt MD, MS, Susie X. Xun MD, Sung Gwe Ahn MD, PhD, Mariacarla Andreozzi PhD, Suleyman Bademler MD, Hakan Balbaloglu MD, Nora Balint-Lahat MD, Maggie Banys-Paluchowski MD PhD, Daniel Moreiras Barbalho MD, PhD, Andrea V. Barrio MD, Nusan Bese MD, Joan François Boileau MD, MSc, Judy Boughey MD, Marissa Boyle MD, Flavia Vidal Cabero MD, MSc, Daniela Cocco MD, Pablo Corsi MD, Angelene Crown MD, Elco de Bree MD, PhD, Mariadel Mar Vernet-Tomas MD, Christine Deutschmann MD, Emilia J. Diego MD, Nina Ditsch MD, Claire Eden MD, Ruth Eller MD, Emanuele Esposito MD, PhD, Oluwadamilola Fayanju MD, MPHS, Franziska Fick MD, Florian Fitzal MD, Meghan R. Flanagan MD, MPH, Damiano Gentile MD, Oreste D. Gentilini MD, Maite Goldschmidt MSc, Mehmet Ali Gulcelik MD, Celile Havin, MD, MPH, Martin Heidinger MD, Jörg Heil MD, PhD, Justyna Jelinska MD, PhD, Güldeniz Karadeniz Cakmak MD, FEBS, Susan Kesmodel MD, Natalia Krawczyk MD, Henry M. Kuerer MD, PhD, Thorsten Kühn MD, PhD, Sherko Kümmel MD PhD, Cornelia Leo MD, Julie Lorsch MD, Francesco Milardi MD, David Murawa MD, PhD, Tracy Ann Moo MD, Tehillah S. Menes MD, Valentina Nekljudova PhD, Lisa A. Newman MD MPH, Daniele Passeri MD, PhD, Jessica M. Pastorza MD, Andrea Pathaveo MD, PhD, Melissa Pilewskie MD, Nina Pislar MD, Natália Polidorio MD, PhD, Florita Poulakaki MD, PhD, Anne Rami, Fabian Riedel MD, Nicolla Rocco MD PhD, Jai Min Ryu MD, PhD, Freya R. Schnabel MD, Alexandra Schulz MSc, Emily L. Siegel MD, Colin Simonson MD, Christian Singer MD, PhD, Leonardo Soares MD, PhD, Varadan Sevilimedu, MBBS, DrPH, Christoph Tausch MD, Ekaterini Christina Tampaki MD, PhD, Athanasios Tampakis MD, PhD, Marios Konstantinos Tasoula MD, PhD, M. Umit Uguralp MD, Cihan Uras MD, Cicero Urban, MD, PhD, Astrid Botty Van den Bruele MD, Annemiek van Hemert MSc, Glenn Vergauwen MD, PhD, Denise Vorburger MD, Fredrik Wärnberg, Anna Weiss MD, Austin D. Williams MD, MSEd, Kerstin Wimmer MD, PhD, Stephanie M Wong MD, MPH, Steven G. Woodward MD, Tae-Kyung Robyn Yoo MD, Jennifer Q. Zheng MD, Pirdos M. Ziauddin MD, Tari King MD, Hasan Karanlik MD, Nesilhan Cabioğlu MD, Marie-Jeanne Vrancken Peeters MD, PhD, Monica Morrow MD, Walter P. Weber, MD

Study Population

Inclusion criteria

- T1-4 N0-3 BC patients
- Surgery after NAC with detection of ITCs [ypN0(i+)] at frozen section or final pathology
- SLNB performed with dual-tracer mapping *or* TAD *or* MARI for N+ and with single tracer for N0
- Detection of ITCs by H&E or IHC

Exclusion criteria

- No SLNB/TAD
- Inflammatory breast cancer
- Stage IV
- NET
- Detection by OSNA (quantitative measurement of target mRNA) due to lack of standardized cut-off

Residual Isolated Tumor Cells

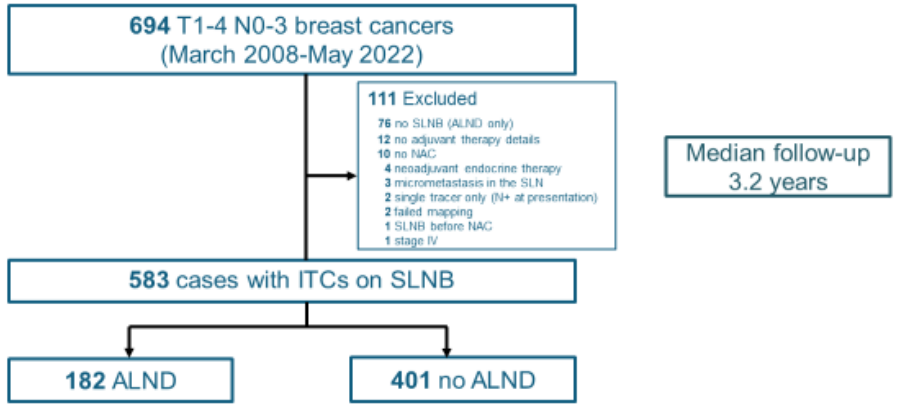
- Residual isolated tumor cells (ITCs) are found in ~1.5% of patients undergoing neoadjuvant chemotherapy
- Data on the likelihood of finding additional positive lymph nodes in patients with residual ITCs are scarce, and the benefit of ALND is unclear

	ACOSOG Z1071	SN FNAC	MSKCC	OVERALL
ITCs	4/11	4/7	1/6	**9/24 (37.5%)**

- As a consequence, surgical management of the axilla in these patients is not standardized

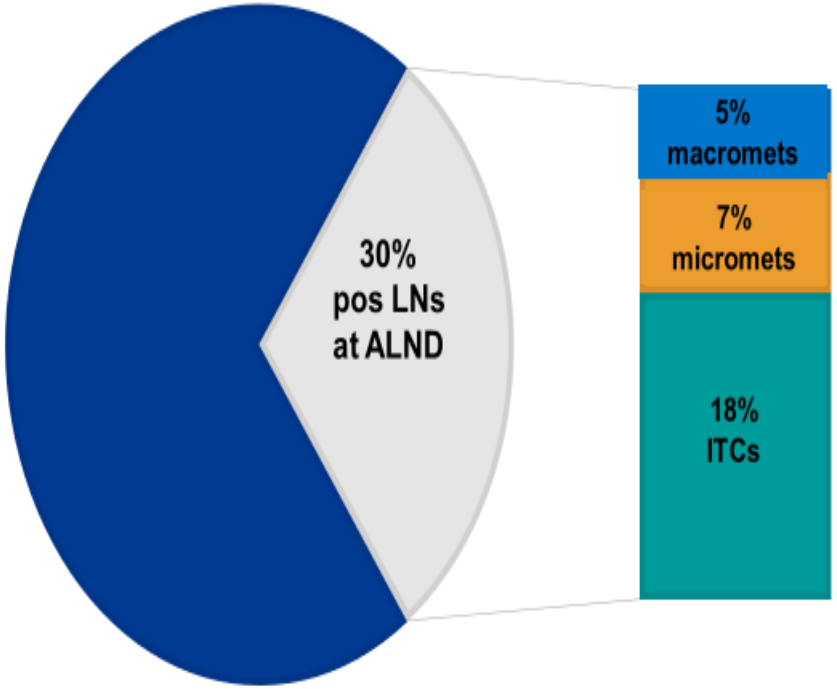
Wong SM et al. ASO 2019
Burstein HJ et al. Ann Onc 2021

Flow Diagram



Data were collected in 62 centers, in 18 countries
The majority of centers are within the oncoplastic breast consortium and the EUBREAST networks

Additional Positive Nodes



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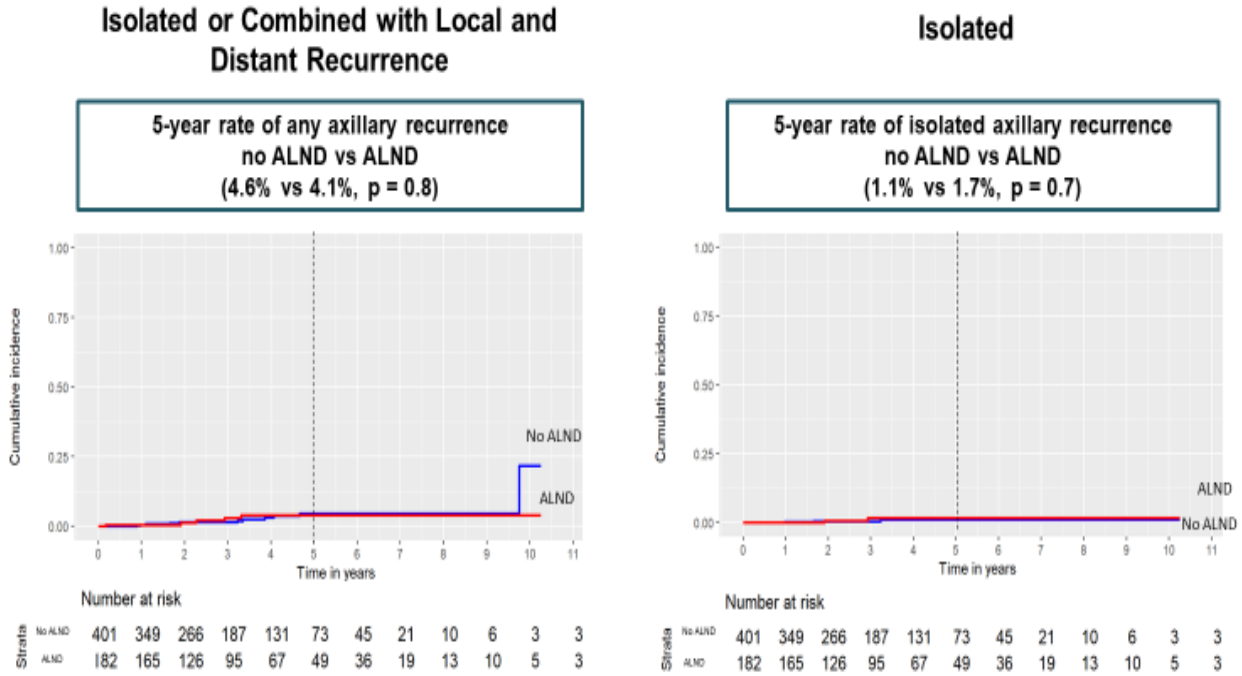
Axillary Recurrence



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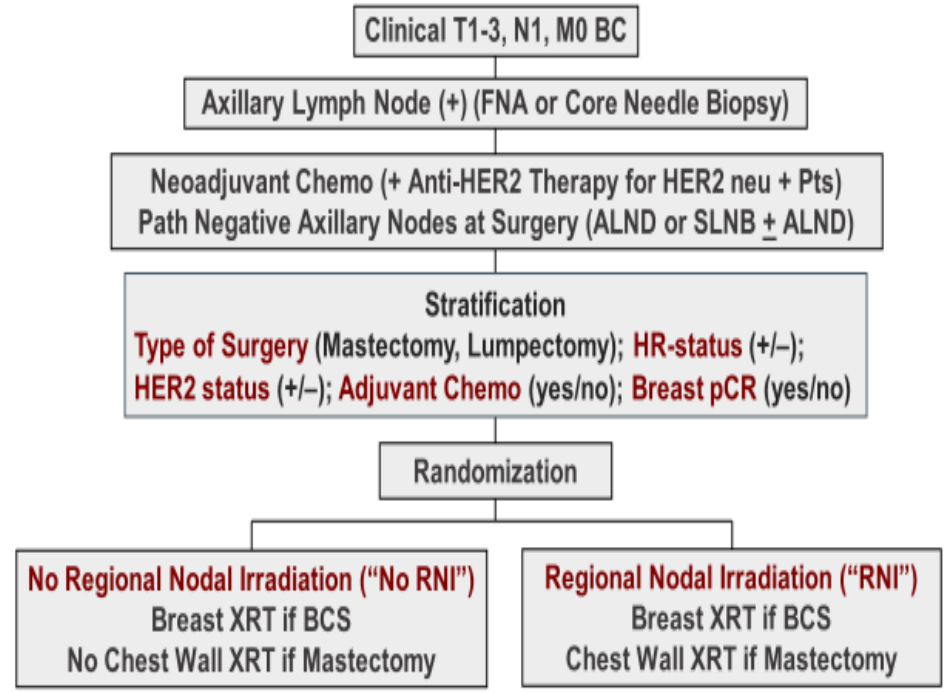
DEC 5-9, 2023
SAN ANTONIO BREAST CANCER SYMPOSIUM

Loco-regional Irradiation in Patients with Biopsy-proven Axillary Node Involvement at Presentation Who Become Pathologically Node-negative After Neoadjuvant Chemotherapy: Primary Outcomes of NRG Oncology/NSABP B-51/RTOG 1304

Eleftherios P. Mamounas[1*], Hanna Bandos[2], Julia R. White[3*], Thomas B. Julian[4], Atif J. Khan[5], Simona F. Shaitelman, Mylin A. Torres[7], Frank A. Vicini[8], Patricia A. Ganz[9], Susan A. McCloskey[10], Peter C. Lucas[11,12], Nilendu Gupta[3], X. Allen Li[13], Beryl McCormick[5], Saumil Gandhi[6], Rahul D. Tendulkar[14], Vivek S. Kavadi,[15], Masahiko Okamoto[16], Samantha Andrews Seaward[17], William J. Irvin, Jr.[18], Jolinta Lin [7], Robert Mutter[19], Thierry M. Muanza[20], Andrew A Muskovitz[21], Reshma Jagsi[22], Anna C. Weiss[23,24], Walter J. Curran, Jr.[7], and Norman Wolmark[12]

*These authors contributed equally.

Study Schema



FNA: Fine Needle Aspiration; ALND: Axillary Lymph Node Dissection; SLNB: Sentinel Lymph Node Biopsy; XRT: Radiation; BCS: Breast Conserving Surgery

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Carbone Cancer Center
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SCHOOL OF MEDICINE AND PUBLIC HEALTH

Baseline Characteristics (1)

Characteristic		No RNI (%) n=821	RNI (%) n=820
Age	Median	52 years	52 years
	≤ 49 yrs	40	41
	50-59 yrs	32	33
	≥ 60 yrs	28	26
Race	Asian	8	6
	Black/African American	17	18
	White	69	69
	Unknown/Other	6	6
Ethnicity	Hispanic or Latino	14	14
	Not Hispanic or Latino	83	82
	Unknown	3	3
Clinical Tumor Size	T1	21	21
	T2	59	61
	T3	20	18

Baseline Characteristics (2)

Characteristic		No RNI (%) n=821	RNI (%) n=820
Tumor Subtype	Triple-negative	21	23
	ER+ and/or PR+/HER2-	22	20
	ER- and PR-/HER2+	25	24
	ER+ and/or PR+/HER2+	31	33
Breast Surgery	Lumpectomy	58	58
	Mastectomy	42	42
Axillary Surgery	SLNB	55	56
	ALND (+/-SLNB)	45	44
pCR in Breast	No	22	21
	Yes	78	79
Adjuvant Chemotherapy	No	100	99
	Yes	<1	1

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Primary Endpoint

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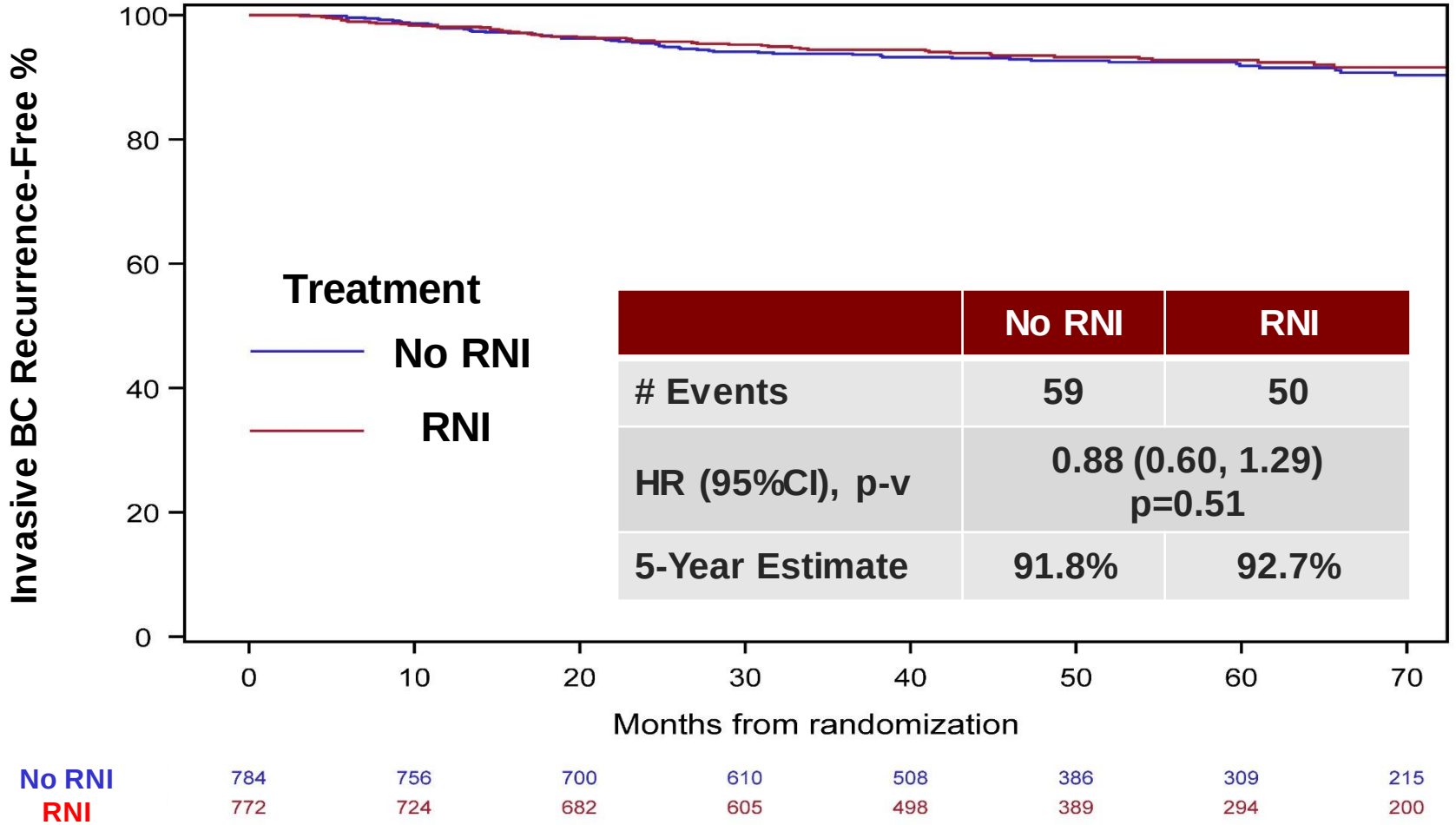
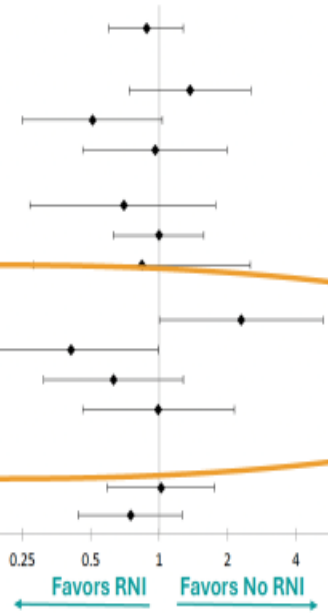
Invasive Breast Cancer Recurrence-free Interval (IBCRFI)



	No RNI	RNI
# Events	59	50
HR (95%CI), p-v	0.88 (0.60, 1.29) p=0.51	
5-Year Estimate	91.8%	92.7%

IBCRFI – Exploratory Subgroup Analysis

Variable		No RNI (D/N)	No RNI 5-y est (%)	RNI (D/N)	RNI 5-y est (%)	HR (95% CI)	P-interaction
	All patients	59/784	91.8	50/772	92.7	0.88 (0.60,1.28)	
Age	<=49	18/311	92.8	24/312	92.0	1.37 (0.74,2.54)	0.09
	50-59	25/257	90.4	12/254	94.4	0.51 (0.25,1.03)	
	>= 60	16/216	92.4	14/206	91.7	0.96 (0.46,1.99)	
Race	Black	11/135	92.6	8/140	93.4	0.70 (0.27,1.77)	0.69
	White	40/543	91.6	36/533	92.1	1.00 (0.63,1.57)	
	Other	8/106	91.8	0/55	95.3	0.84 (0.28,2.52)	
Tumor Subtype	Triple-negative	8/169	95.0	19/188	88.4	2.30 (1.00,5.25)	0.037
	ER/PR+/HER2-	17/173	90.5	7/155	94.0	0.41 (0.17,0.99)	
	ER/PR-/HER2+	20/198	88.8	12/183	92.4	0.63 (0.31,1.28)	
	ER/PR+/HER2+	14/244	93.3	12/246	95.7	0.99 (0.46,2.14)	
Axillary Surgery	Axil +/- SLNB	27/357	92.0	25/338	91.8	1.02 (0.59,1.75)	0.42
	SLNB alone	32/427	91.5	25/434	93.5	0.75 (0.44,1.26)	



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Conclusions

- In patients who present with biopsy-proven axillary node involvement (cN+) and convert their axillary nodes to ypN0 after NAC, CWI+RNI after mastectomy, or WBI+RNI after lumpectomy, did not improve the 5-year IBCRFI, LRRFI, DRFI, DFS, or OS
- These findings suggest that downstaging involved axillary nodes with neoadjuvant chemotherapy can optimize adjuvant radiotherapy use without adversely affecting oncologic outcomes
- Follow-up of patients for long-term outcomes continues

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What Can We Change in our Practices?

- **EBCTCG** – for clinically node negative patients with sentinel node positive disease an axillary dissection is not needed. The risk of local regional and axillary recurrence is at or below 5% and an axillary dissection provides only an increase in lymphedema risk
- **SENOMAC** – ALND should not be considered standard in individuals with cT1-3N0 patients with 1-2 positive sentinel nodes (even with microscopic ENE) having a primary lumpectomy or mastectomy (with anticipation that most will get PMRT)
- **ICARO** – Routine ALND not indicated for SLN positive ITCs post Neoadjuvant Chemotherapy
- **B-51 -** Patients experiencing pCR (to include pN0i+) after Neoadjuvant chemotherapy have an excellent prognosis ± RT and supports NO further surgery for these patients

Key perspectives from the Masters

No method detects axillary metastases as effective as axillary surgery!

Sentinel Node Biopsy is not for all patients but is essential for some.

Nodal Status and Adjuvant Therapies

- Nodal status usually does not influence systemic therapy for:

  Age > 50 cN0 T1,T2 ER(+)HER2(-)

  Women with serious comorbidities

- Nodal staging (SNB) usually influences therapy for other subtypes.

Axillary Staging (SNB) is Necessary

- Premenopausal women
- HER2(+) cN0 ≤3cm
- All subtypes post NAC (even cN0!)

Giuliano; SABCS; clinical controversies; 12/7/2023

Add: Triple negative breast cancer

Key perspectives from the Masters

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Are We Ready to Stop Staging the Axilla?

Monica Morrow, MD
Chief, Breast Surgery Service
Anne Burnett Windfohr Chair of Clinical Oncology
Memorial Sloan Kettering Cancer Center

SOUND Trial

cT1N0 cancer
Negative axillary US

RANDOMIZE

- No axillary surgery n = 736
- SLNB n = 727

81% ≥ 50 years of age
Median 60 years
78% ductal cancer
50% T1c
93% ER+, 93% HER2-

14% positive SLNs
9% macrometastases
0.6% > 3 positive nodes

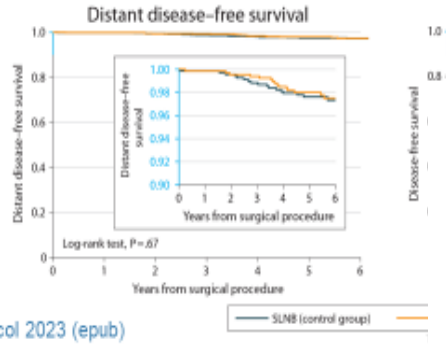
Gentilini O, JAMA Oncol 2023 (epub)

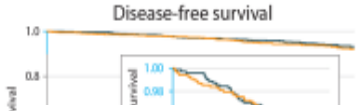
SOUND Trial

Median follow-up: 5.7 years

	No Axillary Surgery	SLNB	p value
Axillary recurrence	0.4%	0.4%	p = NS
Locoregional recurrence	1.6%	1.7%	p = NS
5 year DDFS	98%	97.7%	p = NS

Primary Endpoint: Non-Inferiority 5 year DDFS
HR 0.84; 90% CI 0.45-1.54 p = 0.024





Gentilini O, JAMA Oncol 2023 (epub)

Conclusions

- In cN0, postmenopausal patients with HR+/HER2- cancers, axillary staging:
  - Adds morbidity
  - Does not provide a survival benefit
  - Is not needed for local control
  - Influences systemic therapy decisions in a very small minority of patients

For those having BCS, axillary staging can be safely eliminated, but we need to determine if the RT tradeoffs in those < 70 years of age make this the least morbid approach

Morrow, SABCS; clinical controversies; 12/7/2023

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When NOT to place an incision in the axilla?

Clinical n0 patients

- post-menopausal (NOT peri-menopausal)
- cT1/2
- Estrogen positive; HER 2 negative
- ? Grade of cancer – i.e., should no SLN be done in Grade 3

Thank you and Questions ?