National Comprehensive Cancer Network®

Updates to Radiation Therapy for Invasive Breast Cancer with SABCS Updates

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Summary NCCN Updates

1

26 Gy in 5 once daily fractions can be offered for whole breast irradiation.

Optimal strategy for boost unknown.

2

26 Gy in 5 once daily fractions is an emerging, non-standard treatment for adjuvant RT with RNI.

Internal mammary nodes excluded.

3

Omission of RNI/PRMT can be offered to patients with cN1 → ypN0 breast cancer.

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Breast Cancer (Version 1.2026).

Case for polling

45-year-old woman with T1 N0 TNBC presents to discuss adjuvant radiation therapy after breast conserving surgery.

What do you recommend?

A) Accelerated partial breast irradiation (30 Gy in 5 fractions)

B) Whole breast irradiation (40 Gy in 15 fractions) + boost (10 Gy in 5 fractions).

C) Whole breast irradiation (26 Gy in 5 fractions) without boost.

D) Whole breast irradiation (26 Gy in 5 fractions) + boost (10 Gy in 5 fractions).

E) Something else.

Ultrahypofractionated WBI without RNI

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2026
Invasive Breast Cancer

NCCN Guidelines Index
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Discussion

PRINCIPLES OF RADIATION THERAPY

Whole Breast RT

- Target definition is the breast tissue at risk.
- RT dosing:
  - The whole breast should receive a hypofractionated dose of 40–42.5 Gy in 15–16 fractions; in selected cases 45–50.4 Gy in 25–28 fractions may be considered.
  - A boost to the tumor bed is recommended in patients at higher risk for recurrence. The boost can be given sequentially after whole breast RT or as a simultaneous integrated boost. Typical boost doses when given sequentially are 10–16 Gy in 4–8 fractions. When given concurrently, the whole breast should receive 40 Gy in 15 fractions and the lumpectomy site should receive 48 Gy in 15 fractions.[a,b]
  - Available data support the use of ultra-hypofractionated regimens (28.5 Gy in 5 once-a-week fractions or 26 Gy in 5 daily fractions). The optimal way to incorporate a tumor bed boost and the long-term toxicity associated with its delivery in the ultrahypofractionated setting is yet to be established. Lumpectomy cavity boost can be delivered using enface electrons, photons, or brachytherapy.

BINV-I
1 OF 3

UK Fast Forward: 10-year update presented at ESTRO 2025 (Murray-Brunt et al, E25-607)

UK Fast Forward

Brunt *et al* Lancet 2020; ESTRO 2025

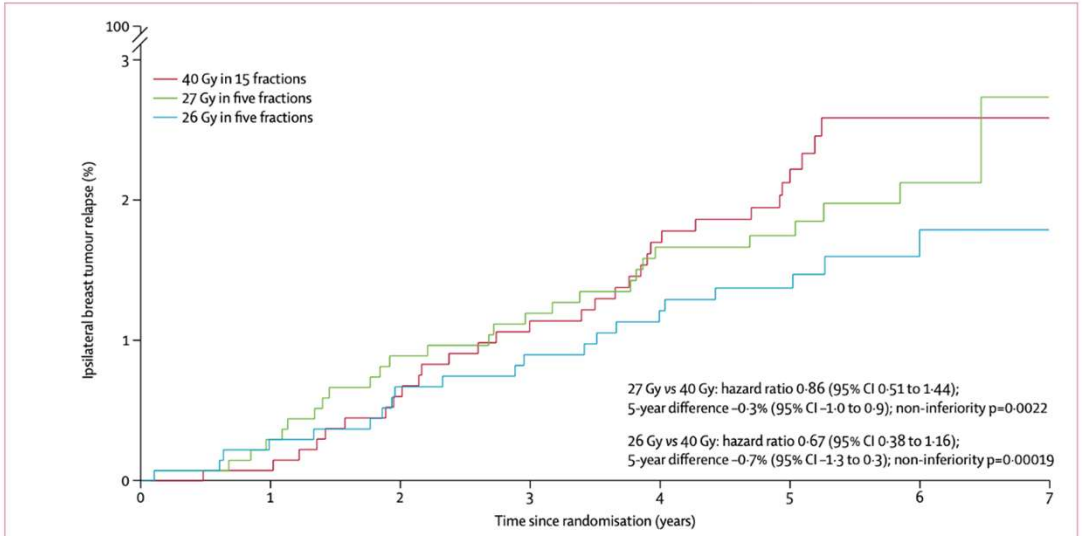
- 4,096 patients age ≥18 with pT1-T3 pN0-1 breast cancer who underwent BCS (94%) or mastectomy (6%) randomized to WBI (or chest wall RT) at **40 Gy in 15 fractions, 26 Gy in 5 fractions, or 27 Gy in 5 fractions**.
- Primary endpoint = IBTR
- Secondary endpoints = late normal tissue effects assessed by clinicians, patients & photographs, LRR, DM, DFS, OS
- 80% power to exclude an absolute increase of 1·6% in 5-year ipsilateral breast tumour relapse incidence for a five-fraction schedule compared with control.

Murray Brunt *et al*, Lancet 2020; 395:1613-1626.
Murray Brunt *et al*, Rad Onc 2025; vol 207, 110915.

UK Fast Forward
IBTR

No difference in IBTR at 5 years (published) or 10 years (presented).

No difference in other cancer control outcomes.



40 Gy								
Number at risk	1361	1347	1307	1281	1230	1045	486	91
Censored	0	13	46	65	109	289	844	1239
Events	0	1	8	15	22	27	31	31
27 Gy								
Number at risk	1367	1352	1328	1303	1255	1066	508	90
Censored	0	11	27	48	90	278	833	1250
Events	0	4	12	16	22	23	26	27
26 Gy								
Number at risk	1368	1347	1325	1302	1257	1070	524	89
Censored	0	17	34	54	95	280	824	1258
Events	0	4	9	12	16	18	20	21

Figure 2: **Cumulative risk of ipsilateral breast tumour relapse by fractionation schedule**

Murray Brunt *et al*, Lancet 2020; 395:1613-1626.
Murray Brunt *et al*, Rad Onc 2025; vol 207, 110915.

UK Fast Forward

Late normal tissue effects

	Number of moderate or marked events/total number of assessments over follow-up	Odds ratio for schedule (95% CI)	p value for comparison with 40 Gy	p value for comparison between 27 Gy and 26 Gy	Odds ratio for years of follow-up (95% CI); p value
Any adverse event in the breast or chest wall*	..	..	..	..	0·98 (0·96–1·00); 0·055
40 Gy	651/6121 (10·6%)	1 (ref)	..	..	..
27 Gy	1004/6303 (15·9%)	1·55 (1·32–1·83)	<0·0001	..	..
26 Gy	774/6327 (12·2%)	1·12 (0·94–1·34)	0·20	0·0001	..

- 26 Gy comparable to 40 Gy; 27 Gy worse.
- 5-year results: a few very minor statistically significant differences between 26 Gy and 40 Gy:
  - Breast harder or firmer 24.7% vs 20.4% (p = 0.048)
  - Breast induration outside tumor bed 1.6% vs 0.8% (p = 0.013)
  - Breast or chest wall edema 2.4% vs 1.5% (p = 0.032)
- 10-year results: 26 Gy still similar to 40 Gy (patient-reported and clinician-reported)
- **Important caveat: boost (10 or 16 Gy in 5 or 8 fractions) only given to 25% of patients**

45 yof with TNBC…?

Murray Brunt *et al*, Lancet 2020; 395:1613-1626.
Murray Brunt *et al*, Rad Onc 2025; vol 207, 110915.

Ultrahypofractionated PMRT or WBI + RNI

PRINCIPLES OF RADIATION THERAPY

PMRT (including breast reconstruction)

- The target includes the ipsilateral chest wall and the clinically relevant mastectomy scar ± drain sites.
  - Regional nodal RT is typically delivered with the chest wall. See below.
- Based on anatomic considerations and presence of reconstruction, various 3D-, intensity-modulated RT [IMRT], or volumetric modulated arc therapy (VMAT) techniques using photons and/or electrons are appropriate.
- PMRT details and dosing:
  - The routine use of bolus is not recommended. Bolus should be used for inflammatory breast cancer and considered in clinically relevant situations where the dose to the skin may not be adequate.[d]
  - Chest wall RT dose may be delivered in conventional dosing of 45–50.4 Gy in 25–28 fractions or moderately hypofractionated dosing of 40–42.5 Gy in 15–16 fractions.[e]
  - In patients who are at high risk for local recurrence, a chest wall scar boost may be considered of approximately 10 Gy delivered in 4-5 fractions with or without bolus.
- For patients with positive surgical margins after neoadjuvant systemic therapy, re-excision to negative margins is preferred. If not feasible, then strongly consider PMRT to chest wall ± comprehensive RNI (including any portion of the undissected axilla at risk).

RNI

- For supra/infraclavicular and axillary nodes, prescription depth varies based on the patient anatomy.
- Regional nodes should be contoured when RNI is indicated. Refer to breast atlases for contouring guidelines.[f,g]
- RNI generally includes supraclavicular, infraclavicular, internal mammary, and axillary nodes at risk. Coverage of the internal mammary nodes may be individually determined based on tumor location (medial/central), tumor size, extent of nodal involvement, and dose to the OAR.
- RT dosing:
  - RT doses to the regional nodes of 46–50 Gy (conventional fractionation) or 39–42.56 Gy (moderately fractionated) dosing schedules are similar to PMRT and whole breast.[e]
  - A supplemental boost of RT can be delivered to grossly involved or enlarged lymph nodes (ie, internal mammary, supra/infraclavicular) that have not been surgically removed.

[e] Preliminary data show similar normal tissue toxicity at 5 years with 26 Gy in 5 fractions, for patients receiving regional nodal irradiation without inclusion of internal mammary nodes. Longer-term toxicity and efficacy data are not yet available, and limited data are available in the context of reconstruction (UK FF Nodal Sub-study; Murray Brunt AM, et al. Rad Onc 2025).

BINV-I
2 OF 3

UK Fast Forward Nodal Sub-study

- **469 patients** age ≥18 with pT1-T3 pN1-N3a breast cancer treated with BCS (~54%) or mastectomy (~46%) +/- reconstruction (~10%) being treated with whole breast or chestwall RT + "level 1-4 lymph nodes (or a subset thereof)" **without IM node RT**. **Randomized to 40/15, 26/5, 27/5*.** Sequential boost permitted. *Arm suspended at 3Y results of main UK FF trial (underpowered, looks worse).

Nodal areas irradiated	40 Gy/15Fr All randomised N = 181 (%)		26 Gy/5Fr N = 182 (%)		40 Gy/15Fr (Randomised concurrently with 27 Gy/5Fr) N = 108 (%)		27 Gy/5Fr N = 104 (%)	
Axilla level I	82	(46)	91	(51)	47	(44)	46	(44)
Axilla level II	91	(51)	95	(53)	52	(49)	51	(49)
Axilla level III	123	(69)	126	(70)	76	(71)	66	(63)
Axilla level IV (SCF)	161	(91)	164	(91)	94	(88)	95	(91)
IMN	0	(0)	1	(<1)	0	(0)	0	(0)
Missing on form	1		2		1		1	

Murray Brunt *et al*, Rad Onc 2025; Jun 207:110915.

UK Fast Forward Nodal Sub-study

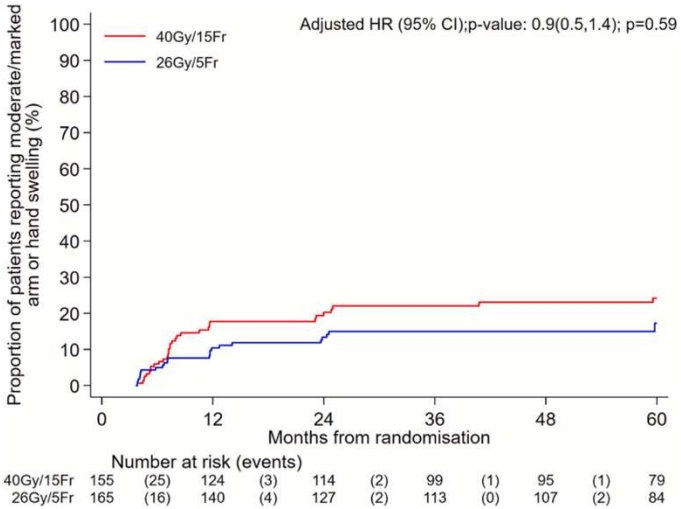
- **Primary endpoint = patient-reported moderate/marked arm/hand swelling at 5 years** (EORTC QLQ-BR23).
- Secondary endpoints = patient & clinician-reported adverse effects.
- **Not powered to assess efficacy**; will be reported separately.

Median follow-up 6 years.

300 patients provided 5-year questionnaire data for primary endpoint (107 pts 40/15, **116 pts 26/5**, 77 pts 27/5).

Patient-reported arm or hand swelling up to 5 years (Primary endpoint).

Visit	40 Gy/15Fr n	(%)	n (%) moderate or marked	26 Gy/5Fr n	(%)	n (%) moderate or marked	Absolute difference in moderate/marked events (%) (90 % CI); p-value[a]
Baseline	**180**			**181**			
Not at all	144	(80)		140	(77)		
A little	29	(16)		26	(14)		
Quite a bit	4	(2)		8	(4)		
Very much	3	(2)	7 (4)	7	(4)	15 (8)	
1 year	**130**			**141**			
Not at all	98	(75)		95	(67)		
A little	22	(17)		35	(25)		
Quite a bit	6	(5)		8	(6)		
Very much	4	(3)	10 (8)	3	(2)	11 (8)	
2 year	**127**			**134**			
Not at all	93	(73)		102	(76)		
A little	21	(17)		22	(16)		
Quite a bit	7	(6)		7	(5)		
Very much	6	(5)	13 (10)	3	(2)	10 (8)	
5 year	**107**			**116**			
Not at all	75	(70)		79	(68)		
A little	21	(20)		24	(21)		
Quite a bit	6	(6)		8	(7)		
Very much	5	(5)	11 (10)	5	(4)	13 (11)	1 (−6, 8); p = 0.41
Analysis using per protocol population[b]							
5 year	**105**			**114**			
Not at all	73	(70)		77	(68)		
A little	21	(20)		24	(21)		
Quite a bit	6	(6)		8	(7)		
Very much	5	(5)	11 (11)	5	(4)	13 (11)	1 (−7, 8); p = 0.41

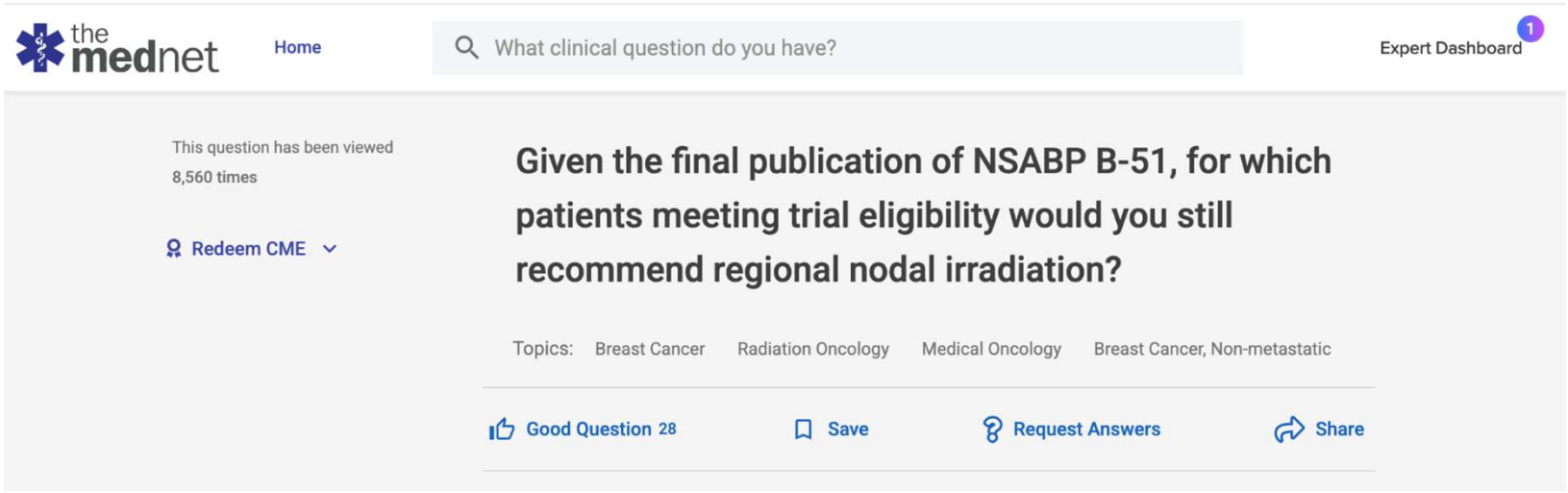


Murray Brunt *et al*, Rad Onc 2025; Jun 207:110915.

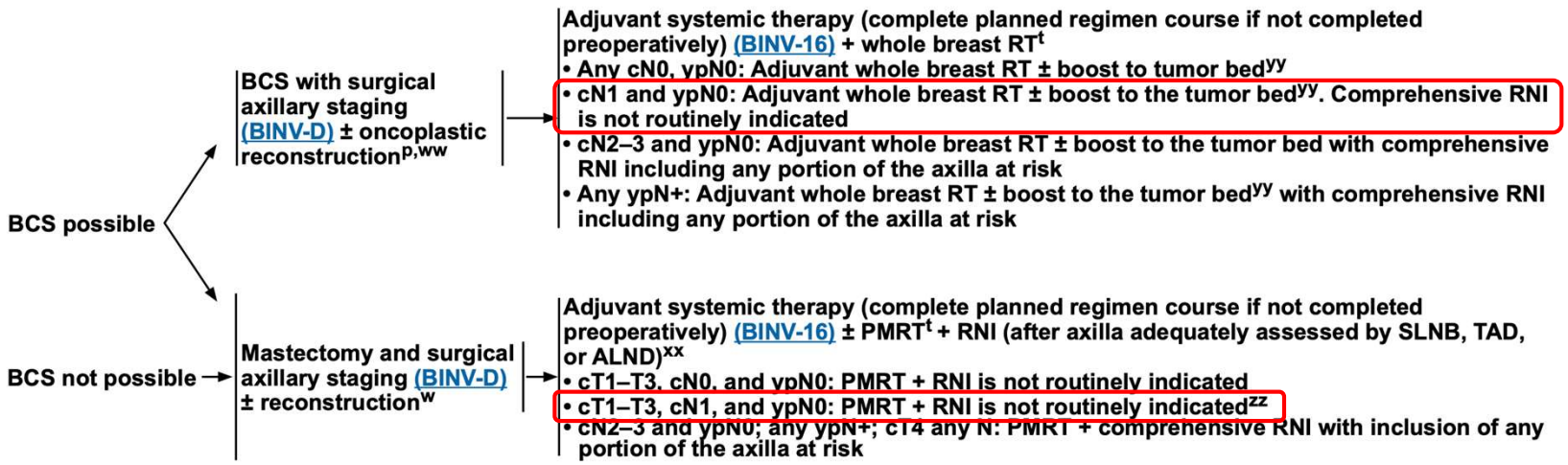
UK Fast Forward Nodal Sub-study

- No brachial plexopathy in any arm.
- Incidences of symptomatic rib fracture, ischaemic heart disease, and symptomatic lung fibrosis were very low at five-year follow-up across groups.
- "The results suggest that use of 26 Gy in five daily fractions for irradiating the chest wall or breast could safely be extended to include patients requiring axillary radiotherapy, without IMN irradiation. Based on the FAST-Forward trial primary results, efficacy is expected to be non-inferior to a 15-fraction schedule. The main trial will produce 10-year **efficacy data** later in 2025, the nodal sub-study contributes to this, and it may be prudent to await reassurance from this data before any widespread change in practice."

Murray Brunt *et al*, Rad Onc 2025; Jun 207:110915.



OPERABLE DISEASE:
SURGICAL TREATMENT AND ADJUVANT THERAPY AFTER PREOPERATIVE SYSTEMIC TREATMENT[ww]



[k] Special Considerations for Breast Cancer in Males (Sex Assigned at Birth) (BINV-J).
[p] Includes techniques such as local tissue rearrangement, local flaps, regional flaps, breast reduction, and mastopexy to allow for greater volumes of resection while optimizing aesthetic outcomes in patients undergoing BCS.
[t] Principles of Radiation Therapy (BINV-I).
[w] Principles of Breast Reconstruction Following Surgery (BINV-H).
[ww] The accurate assessment of in-breast tumor or regional lymph node response to preoperative systemic therapy is difficult, and should include physical examination and performance of imaging studies (mammogram and/or breast ultrasound and/or breast MRI) that were abnormal at the time of initial tumor staging. Selection of imaging methods prior to surgery should be determined by the multidisciplinary team. MRI is more accurate than mammography for assessing tumor response to preoperative therapy.
[xx] Among patients shown to be N+ prior to preoperative systemic therapy, SLNB has a >10% false-negative rate when performed after preoperative systemic therapy, which can be improved by marking the most suspicious biopsied node prior to treatment, and at the time of surgery, using dual tracers, obtaining ≥3 sentinel lymph nodes nodes and removal of the marked node (Targeted Axillary Dissection [TAD]).
[yy] Strongly consider RT boost for high-risk features (eg, central/medial tumors, tumors ≥2 cm with ≥1 of the following: grade 3, ER-negative, LVI, high residual cancer in the breast, or young age/longevity).
[zz] When considering PMRT + RNI for cN1 that has become ypN0 (after preoperative therapy), based on limited followup duration of NSABP B-51 study (Mamounas EP, et al. N Engl J Med 2025;392:2113-2124) and the inability to demonstrate long-term non-inferiority for this subgroup, a discussion of potential risks of under-treatment should be weighed against the previously established long-term survival benefits of PMRT+RNI, particularly for patients of younger age/longevity with ER-positive tumors, residual disease in the breast, and/or those with multiple traditional clinical pathologic high-risk features.

NSABP B51

- 1,641 patients with cT1-T3 cN1 breast cancer treated with neoadjuvant chemo (at least 8 weeks; anthracycline and/or taxane-based, HER2+ directed therapy if applicable) followed by BCS (58%) or mastectomy (42%) + SLNB (55%) or ALND (45%) showing ypN0. **Randomized to WBI +/- RNI or +/-PMRT.**
- Median age 52 (25% <50 years)
- ~20% cT3
- ~22% did not have pCR in breast
- ~53% ER/PR-
- ~57% HER2+

Mamounas *et al*, NEJM June 2025:392;21:2113-2124

NSABP B51

- Primary endpoint: **invasive breast cancer recurrence-free interval** (time from randomization to invasive LRR, DM or death from breast cancer)
- Secondary endpoints: OS, locoregional recurrence free interval, DM recurrence free interval, DFS.
- The trial was designed to have 80% power to test the hypothesis that treatment with regional nodal irradiation would reduce the annual hazard rate of primary end-point events by 35%.
- Published with median f/u time of 5 years.
- The observed 5-year cumulative incidence of invasive breast cancer recurrence or death from breast cancer (8.2%) was approximately 40% lower than projected on the basis of the combined analysis of the NSABP B-18 and B-27 trials. As a result of the low incidence of events, we conducted a **time-driven analysis** as specified in the protocol, but the number of primary end-point events included was considerably less than the number that would have been included in an event-driven analysis (**109 vs. 172**). Patient follow-up continues, and we expect to report updated analyses when the number of events specified for the **event-driven analysis** is reached.

Mamounas *et al*, NEJM June 2025:392;21:2113-2124

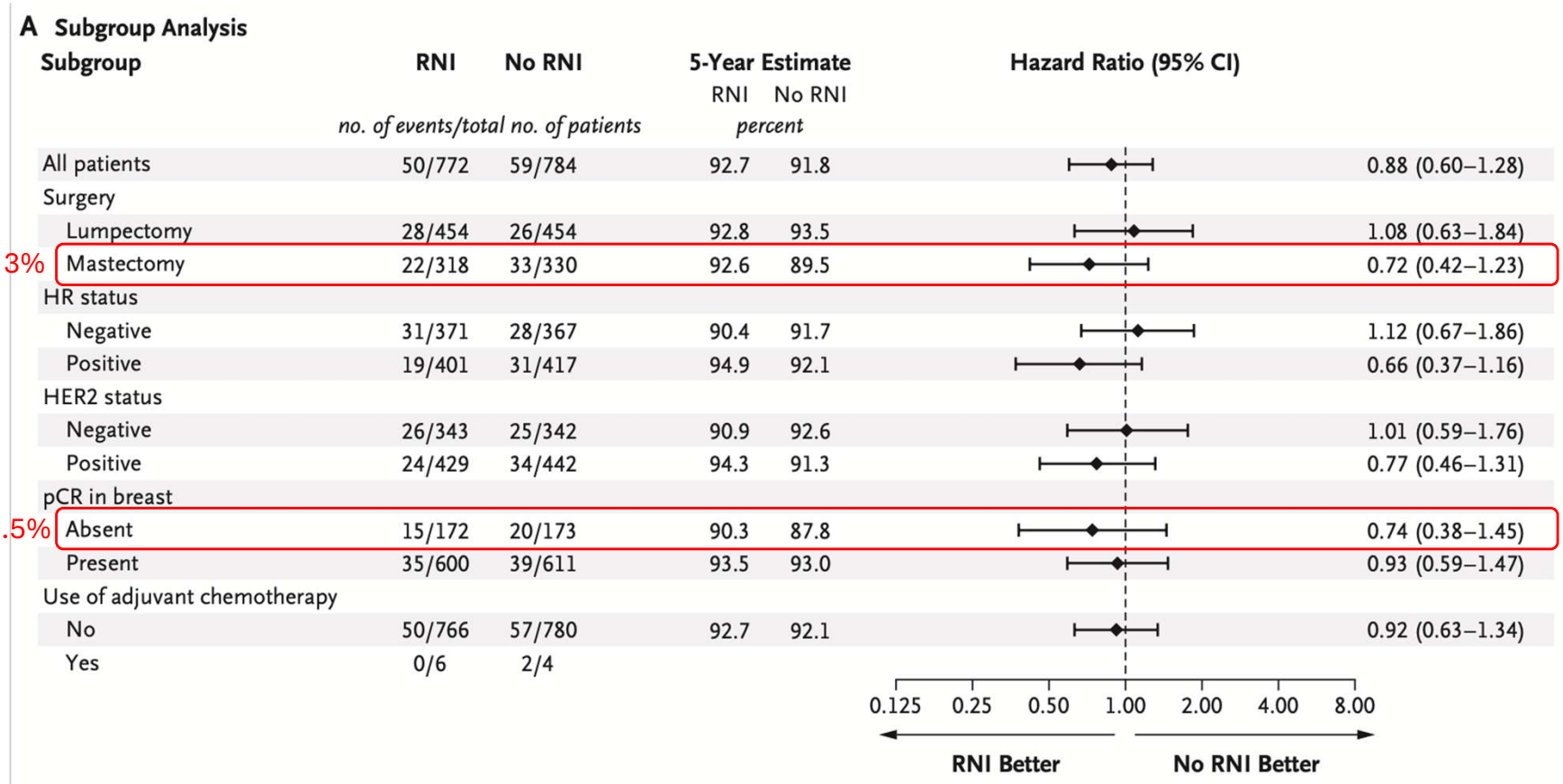
Median f/u 5 years.
No difference in any endpoint.

Mamounas *et al*, NEJM June 2025:392;21:2113-2124

Table 2. Primary and Secondary End-Point Events.*

Event	Regional Nodal Irradiation (N=772)	No Regional Nodal Irradiation (N=784)
	number (percent)	
Primary end point		
Invasive breast cancer recurrence or death from breast cancer	50 (6.5)	59 (7.5)
Distant recurrence†	41 (5.3)	36 (4.6)
Synchronous locoregional recurrence and distant recurrence‡	2 (0.3)	9 (1.1)
Isolated locoregional recurrence	4 (0.5)	11 (1.4)
Death from breast cancer	3 (0.4)	3 (0.4)
Secondary end points		
Locoregional recurrence	6 (0.8)	11 (1.4)
Local recurrence§	6 (0.8)	2 (0.3)
Regional recurrence¶	0	8 (1.0)
Locoregional recurrence‖	0	1 (0.1)
Distant recurrence or death from breast cancer	46 (6.0)	48 (6.1)
Distant recurrence	43 (5.6)	45 (5.7)
Death from breast cancer	3 (0.4)	3 (0.4)
Disease recurrence or death	85 (11.0)	83 (10.6)
Distant recurrence	43 (5.6)	45 (5.7)
Locoregional recurrence	6 (0.8)	11 (1.4)
Second primary cancer	19 (2.5)	16 (2.0)
Death from any cause	17 (2.2)	11 (1.4)

Invasive Breast Cancer Recurrence-free Interval

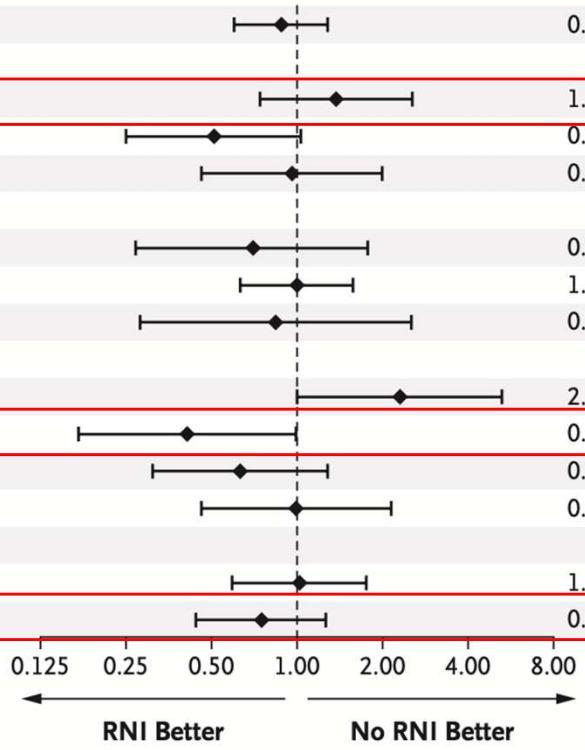


Mamounas *et al*, NEJM June 2025:392;21:2113-2124

Invasive Breast Cancer Recurrence-free Interval

B Exploratory Analysis

Subgroup	RNI	No RNI	5-Year Estimate RNI	5-Year Estimate No RNI	Hazard Ratio (95% CI)
	no. of events/total no. of patients		*percent*		
All patients	50/772	59/784	92.7	91.8	0.88 (0.60–1.28)
Age					
okay ≤49 yr	24/312	18/311	92.0	92.8	1.37 (0.74–2.54)
50–59 yr	12/254	25/257	94.4	90.4	0.51 (0.25–1.03)
≥60 yr	14/206	16/216	91.7	92.4	0.96 (0.46–1.99)
Race					
Black	8/140	11/135	93.4	92.6	0.70 (0.27–1.77)
White	36/533	40/543	92.1	91.6	1.00 (0.63–1.57)
Other	6/99	8/106	95.3	91.8	0.84 (0.28–2.52)
Tumor subtype					
Triple negative	19/188	8/169	88.4	95.0	2.30 (1.00–5.25)
3.5% HR+, HER2–	7/155	17/173	94.0	90.5	0.41 (0.17–0.99)
HR–, HER2+	12/183	20/198	92.4	88.8	0.63 (0.31–1.28)
HR+, HER2+	12/246	14/244	95.7	93.3	0.99 (0.46–2.14)
Axillary surgery					
ALND with or without SLNB	25/338	27/357	91.8	92.0	1.02 (0.59–1.75)
2% SLNB alone	25/434	32/427	93.5	91.5	0.75 (0.44–1.26)



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Optimal strategy for boost unknown.

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26 Gy in 5 once daily fractions is an emerging, non-standard treatment for adjuvant RT with RNI.

Internal mammary nodes excluded.

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Omission of RNI/PRMT can be offered to patients with cN1 → ypN0 breast cancer.

Case for polling

45-year-old woman with T1 N0 TNBC of the left breast presents to discuss adjuvant radiation therapy after breast conserving surgery.

What do you tell her regarding cardiac risks?

A) For each Gy of mean heart dose delivered, there is a 7% absolute risk for major cardiac events.

B) There is a higher risk of major cardiac events for women receiving left vs right whole breast radiation in the modern era.

C) There may not be a significant difference in major cardiac events for women after left vs right whole breast irradiation in the modern era.

D) Something else.

Summary SABCS Abstracts

RadComp found no association between cardiac radiation dose volume metrics and cardiac-specific HRQOL.

Ontario database found no association between WBI and long-term cardiac outcomes.

Radiotherapy compliance high on INSEMA; favorable local control results with SLNB omission are NOT due to routine irradiation of level II-III axilla.

Only 15% of patients with pN1mic on SWOG 1007 (TailoRx) received regional nodal irradiation; keep accruing to MA.39!

Associations Between Cardiac Radiation Dose Volume Metrics and Cardiac Specific Health Related Quality of Life for Patients with Breast Cancer Randomized to Proton versus Photon Radiation on the RadComp Trial

Jean L. Wright, Kyunga Ko, Walter Kenworthy, Walter Bosch, William Straube, Wei Zou, Nicholas Remmes, Mark Pankuch, Eva Berlin, D. Hunter Boggs, Lior Braunstein, Oren Cahlon, Ashish Chawla, Victoria Croog, Marcio Fagundes, L. Christine Fang, Ashley Feriozzi, Gary Freedman, Erin Gillespie, Karen Hoffman, Rachel B. Jimenez, Janice Kim, Hien Lu, Shannon MacDonald, Teresa Meier, Mark Mishra, Robert Mutter, Nisha Ohri, Stephanie Pugh, Lane Rosen, Neil Taunk, Alphonse Taghian, Arpi Thukral, James Urbanic, Justin Bekelman, Alexander Lin, Bonnie Ky

RadComp
PATIENT POWERED
A study at the heart of breast cancer treatment

Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.

Background and Objectives

- Proton therapy has the potential to lessen the morbidity of radiation therapy compared to photon therapy by reducing the volume of heart & other tissues exposed to radiation.
- A large, prospective, pragmatic randomized trial in patients requiring comprehensive radiation is needed to evaluate morbidity and effectiveness of proton vs photon therapy. (n = 1,239)
- **Primary Objective:** To assess the effectiveness of proton vs. photon therapy in reducing major cardiovascular events (MCE)
- **Secondary Objective:** To develop predictive models to examine the association of radiation dose distribution to heart/substructures and MCE and HRQOL outcomes.

Internal mammary nodes treated. Conventional fractionation.

Hypothesis: 10Y MCE rate reduced from 6.3% to 3.8%.

Wright, et al. RadComp Trial. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.

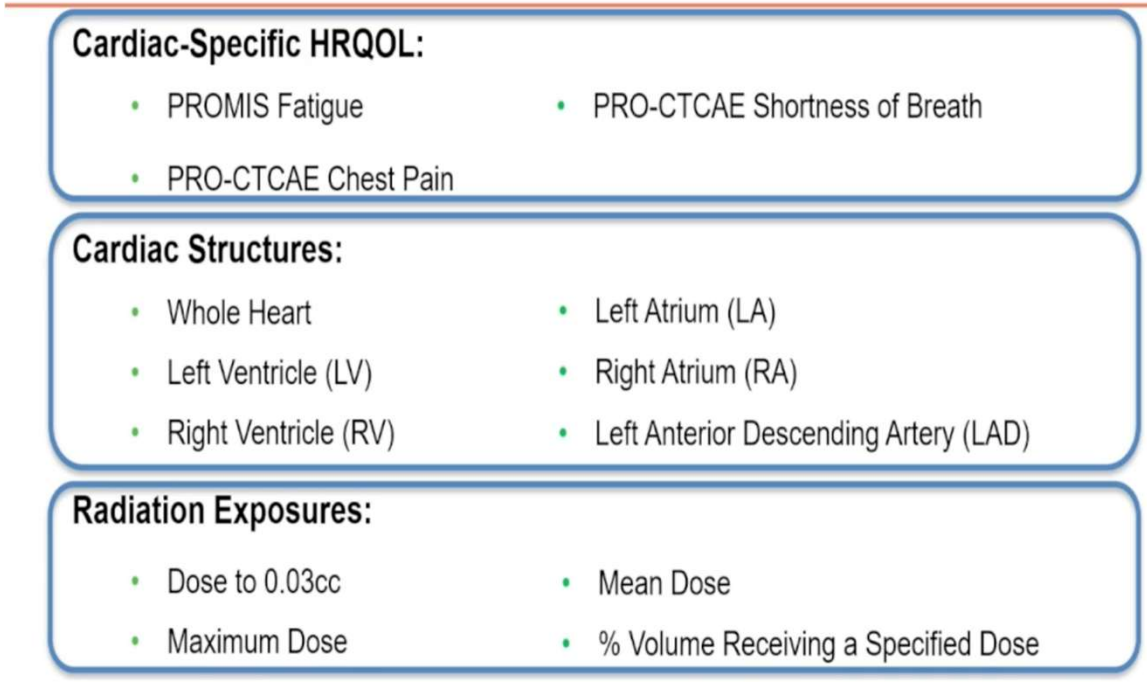
Cardiac HRQOL Objectives

- To compare radiation dose to cardiac substructures in patients treated with proton versus photon RT
- To evaluate changes in cardiac-specific HRQOL outcomes from baseline to 6 months following RT for all participants (not protons vs photons).
- To determine the associations between radiation dose volume histogram (DVH) parameters and changes in cardiac-specific HRQOL across all participants

(n = 1,160)

Wright, et al. RadComp Trial. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.

Methods: Measures of Interest



Wright, et al. RadComp Trial. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.

Cardiac Dosimetry by Modality: Whole Heart

Radiation Exposure	Total, N = 1,160	Photon, N = 574	Proton, N = 586	p-value
Heart Dmean (Gy(RBE))	1.47 (0.80, 3.13)	2.99 (1.60, 4.61)	0.88 (0.49, 1.39)	< 0.001
Heart Dmax (Gy(RBE))	39.58 (25.80, 48.76)	30.70 (17.17, 43.31)	47.17 (36.55, 51.50)	< 0.001
Heart D0.03cc (Gy(RBE))	36.26 (22.97, 47.27)	27.37 (15.31, 40.00)	44.56 (32.77, 50.02)	< 0.001

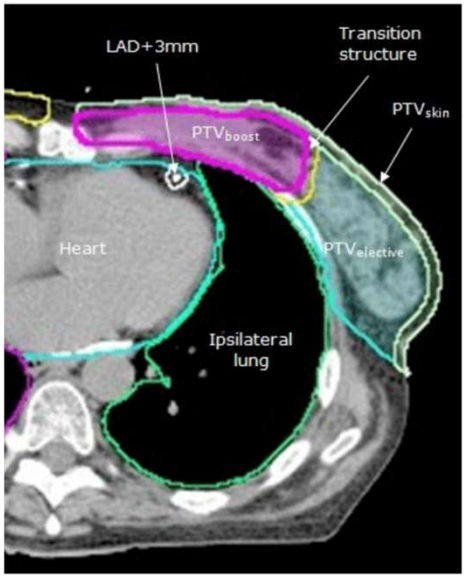
- Mean heart dose lower with protons
- Dmax and D0.03cc lower with photons

Wright, et al. RadComp Trial. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.

Cardiac Dosimetry by Modality: LAD

LAD Exposure	Total, N = 1,160	Photon, N = 574	Proton, N = 586	p-value
LAD Dmean (Gy(RBE))	2.93 (0.42, 6.05)	4.56 (2.02, 7.88)	0.99 (0.03, 3.57)	< 0.001
LAD Dmax (Gy(RBE))	10.00 (1.19, 22.98)	10.93 (2.91, 22.12)	8.26 (0.22, 23.40)	< 0.001
LAD D0.03cc (Gy(RBE))	7.42 (0.98, 17.34)	8.71 (2.77, 18.25)	4.89 (0.16, 16.51)	< 0.001

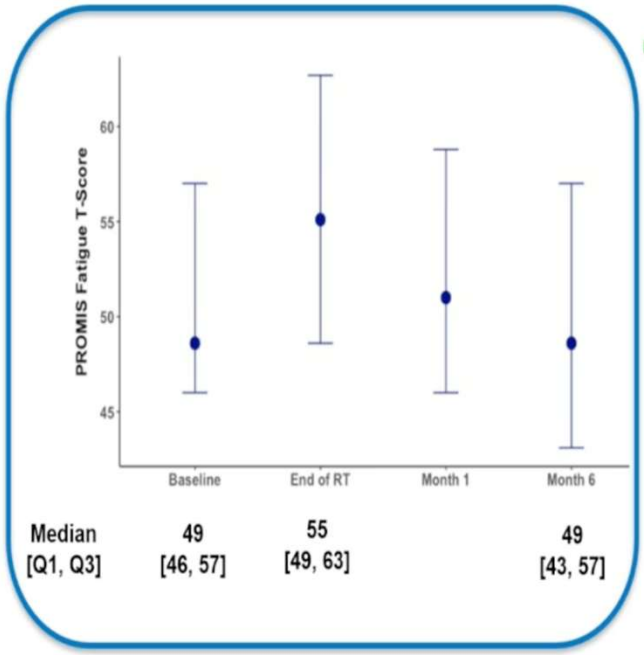
- Mean LAD dose lower with protons
- Dmax and D0.03cc lower with protons



Jeulink *et al*, J Applied Clin Med Phys 2015;16(3):5266.

Wright, et al. RadComp Trial. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.

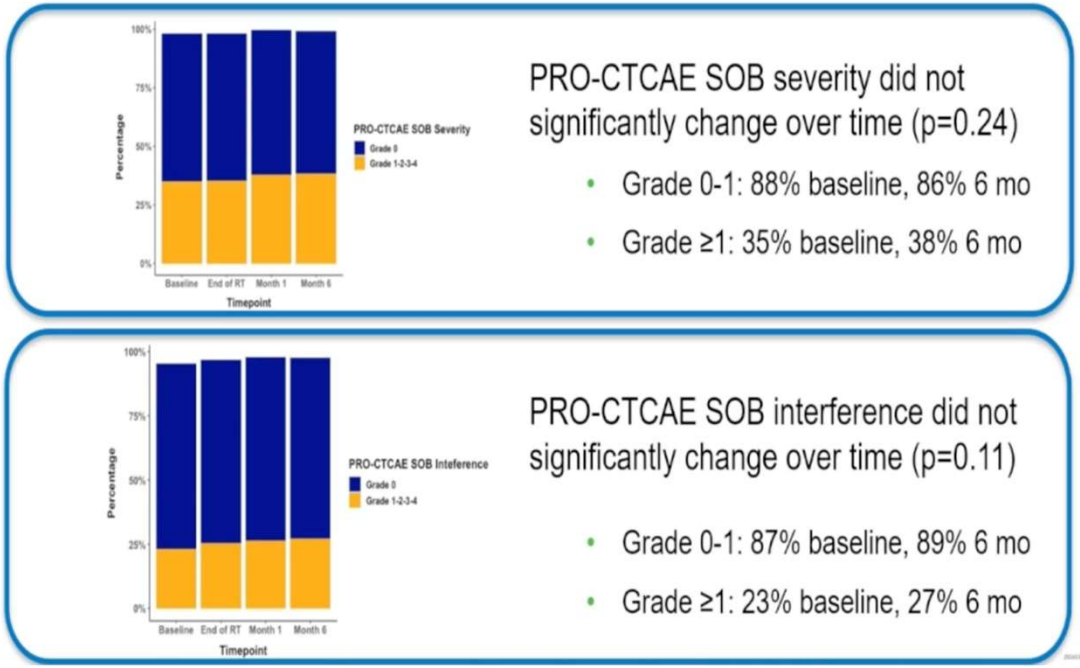
Changes in HRQOL over Time



- Median PROMIS Fatigue T-Score
  - Increased from baseline to end of RT ($p<0.001$)
  - Returned to baseline at month 6
  - Changes were small in effect size and transient.

Wright, et al. RadComp Trial. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.

Changes in HRQOL over Time



Wright, et al. RadComp Trial. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.

Changes in HRQOL over Time

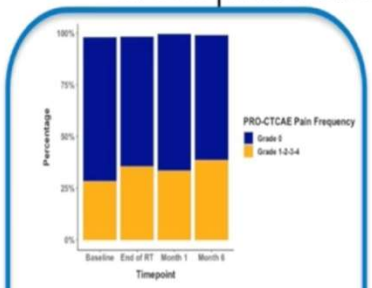
RadComp PATIENT POWERED A study at the heart of breast cancer treatment

SAN ANTONIO BREAST CANCER SYMPOSIUM®

UT Health San Antonio Mays Cancer Center

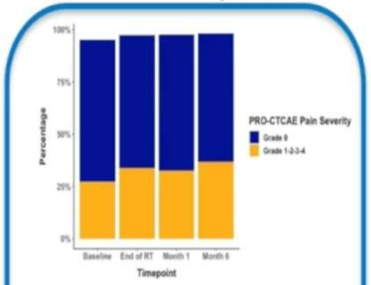
AACR American Association for Cancer Research

Chest pain increased over time, absolute differences small



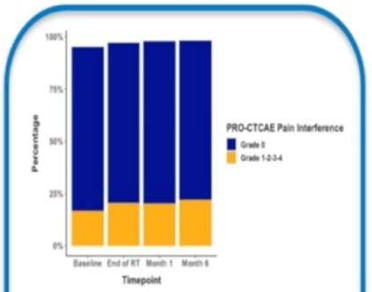
Frequency (p<0.001)

- Grade 0-1:
  - 85% baseline
  - 80% 6m
- Grade ≥1:
  - 29% baseline
  - 39% 6m



Severity (p<0.001)

- Grade 0-1:
  - 87% baseline
  - 84% 6m
- Grade ≥1:
  - 27% baseline
  - 37% 6m



Interference (p<0.008)

- Grade 0-1:
  - 89% baseline
  - 90% 6m
- Grade ≥1:
  - 17% baseline
  - 22% 6m

Wright, et al. RadComp Trial. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.

Associations: HRQOL and DVH Parameters

- No DVH metrics were significantly associated with HRQOL outcomes.
- The results were similar when the HRQOL measures were analyzed as ordinal values
- There were no significant differences between the as-treated and intention-to-treat analyses (data not shown).

Wright, et al. RadComp Trial. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.

SEP
29

PL 01 - Plenary

LBA 01 - PHASE III RANDOMIZED TRIAL OF PROTON VS. PHOTON THERAPY FOR PATIENTS WITH NON-METASTATIC BREAST CANCER RECEIVING COMPREHENSIVE NODAL RADIATION: A RADIOTHERAPY COMPARATIVE EFFECTIVENESS (RADCOMP) CONSORTIUM TRIAL: HEALTH-RELATED QUALITY OF LIFE OUTCOMES

01:30pm - 01:40pm PT

San Francisco Ballroom

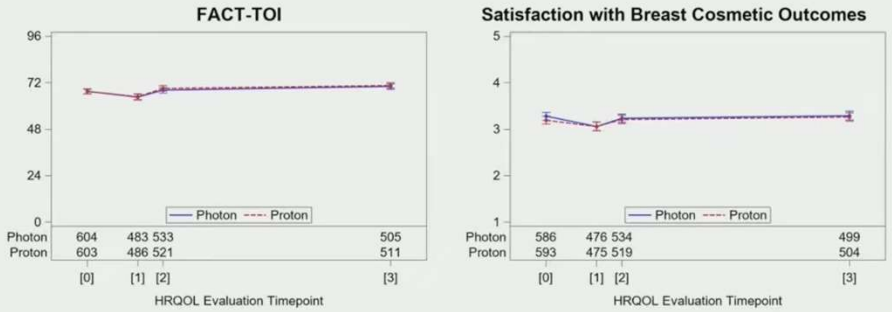
PRESENTER(S)

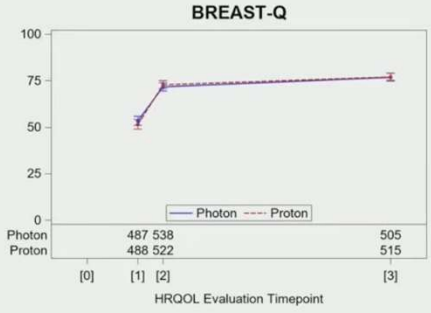
Shannon MacDonald, MD, FASTRO - Southwest Florida Proton Center, Estero, Florida

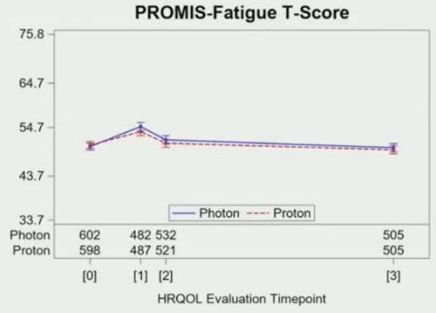
Presented at ASTRO's 67th Annual Meeting. September 27 – October 1, 2025. San Francisco, California.

Results

- There were no clinically meaningful differences by treatment arm in:
  - PROMIS Fatigue total score
  - Satisfaction with Breast Cosmetic Outcomes score
  - BREAST-Q total score
  - FACT-B trial outcome index score







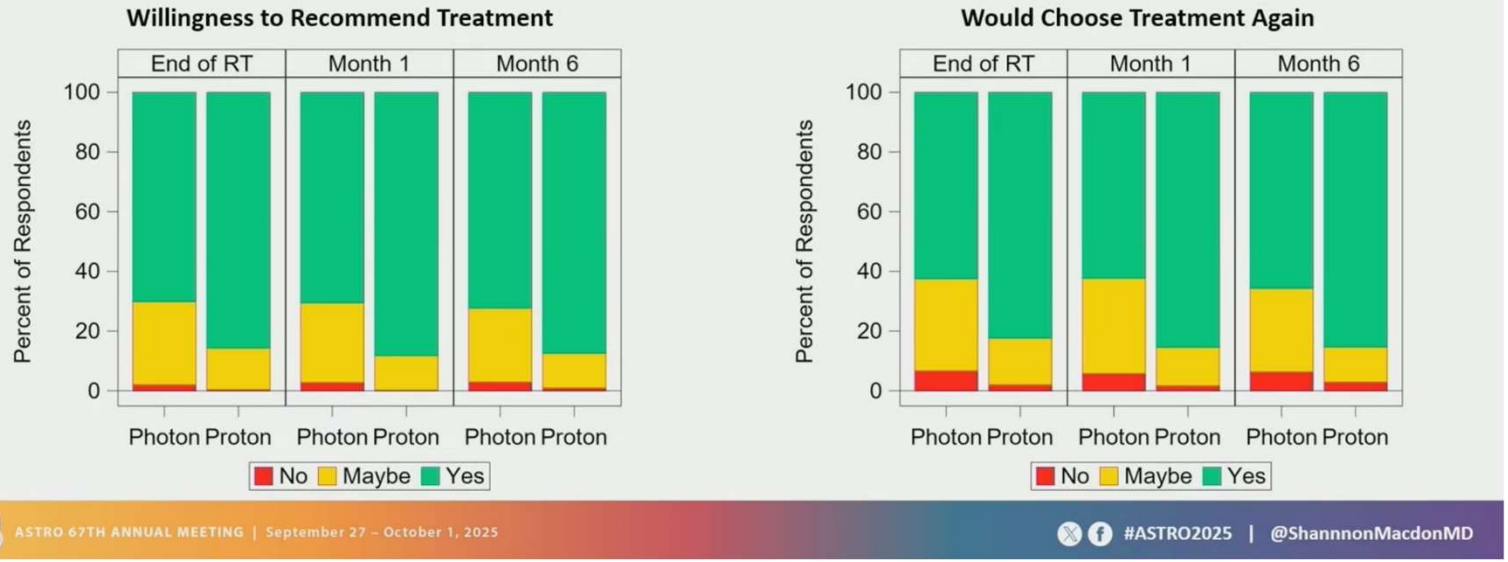
[0]=Baseline, [1]=End of RT, [2]=Month 1, [3]=Month 6

ASTRO 67TH ANNUAL MEETING | September 27 – October 1, 2025 #ASTRO2025 | @ShannnonMacdonMD

MacDonald, S. Presented at ASTRO's 67th Annual Meeting. September 27 – October 1, 2025. San Francisco, California.

Results

- Five FACIT items were statistically significant in favor of protons including willingness to recommend treatment OR=0.13, 95% CI: 0.08-0.22, p<0.001 or choose treatment again OR=0.11, 95% CI: 0.07-0.18, p<0.001 ;maintained significance after multiplicity analyses



MacDonald, S. Presented at ASTRO's 67th Annual Meeting. September 27 – October 1, 2025. San Francisco, California.

RadComp Conclusion (SABCS & ASTRO):

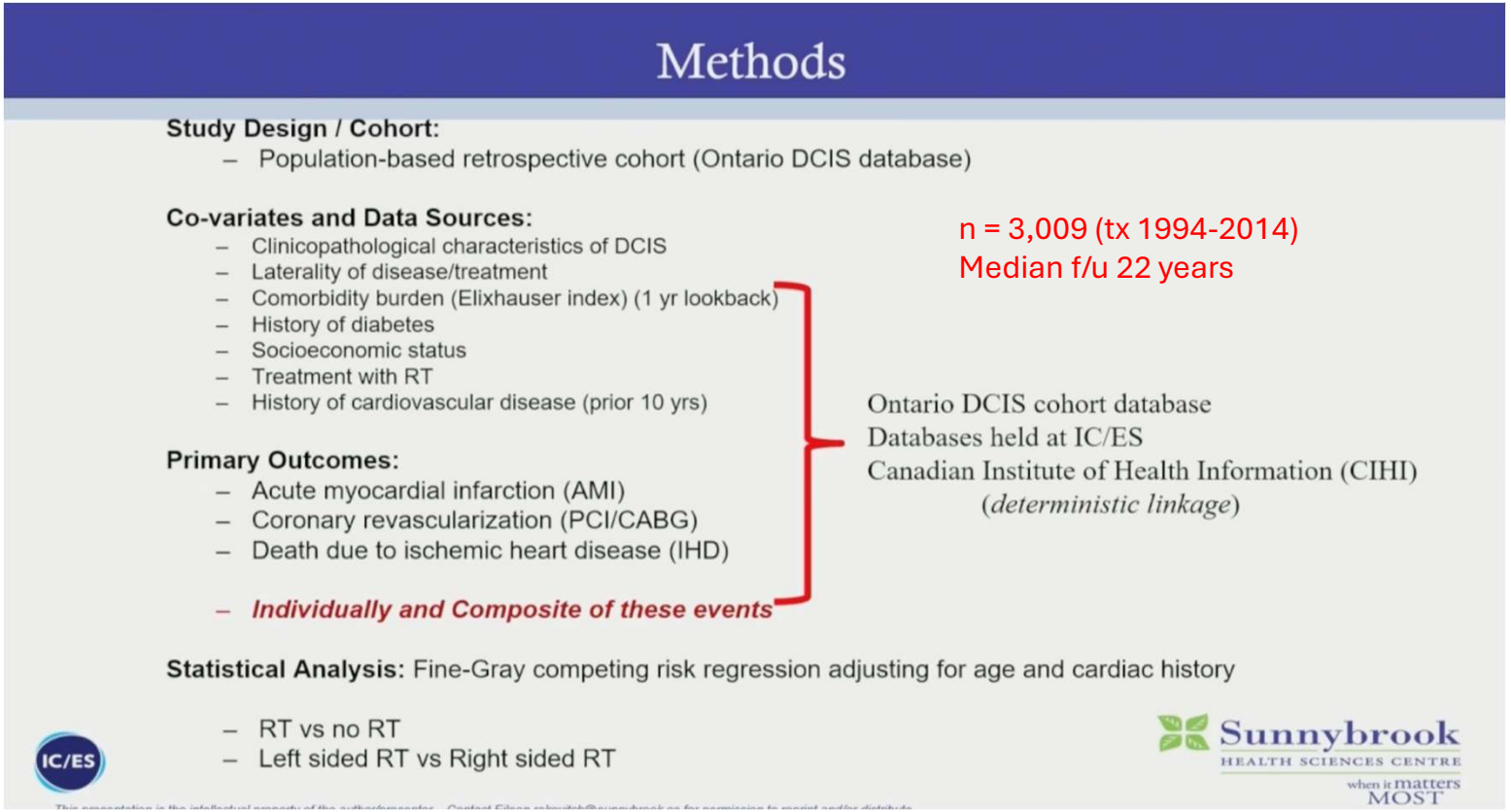
- Mean whole heart dose for comprehensive RNI (including IM node coverage) higher with photons, but low overall in the modern era (2.99 Gy vs 0.88 Gy).
- Maximum whole heart dose higher with PROTONS.
- LAD dose lower with PROTONS.
- No correlation between cardiac dosimetry and HRQOL.
- No correlation between radiotherapy modality and QOL/cosmesis.
- **Primary endpoint (10-year major coronary event rate) not yet reported.**

Impact of Breast Irradiation on Long-Term Risk of Cardiac Events Following Breast-Conserving Surgery for DCIS

Eileen Rakovitch MD MSc FRCPC

Professor, Department of Radiation Oncology
LC Campbell Chair in Breast Cancer Research
Sunnybrook Health Sciences Centre
Institute for Clinical Evaluative Sciences
Toronto, Canada

PD12-10. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.



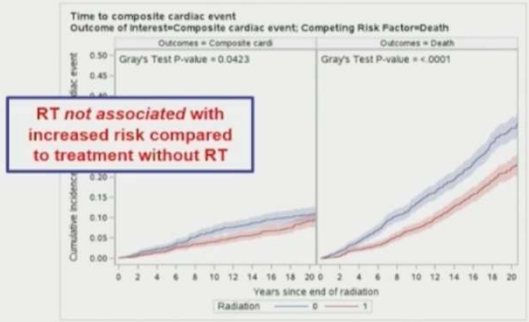
Rakovitch, E. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.

Results: *Multivariable Analyses (Composite Outcome)*

- RT was not associated with increased risk of any cardiac event

- Any cardiac event (composite outcome)

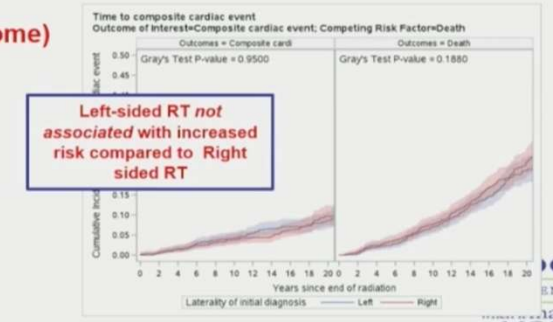
	HR	UCL	LCL	P value
Radiation (yes/no)	0.97	0.76	1.24	0.80
Age >60 vs <= 60	2.97	2.26	3.89	<0.001
Cardiac history (yes/no)	2.87	1.96	4.19	<0.001



RT *not associated* with increased risk compared to treatment without RT

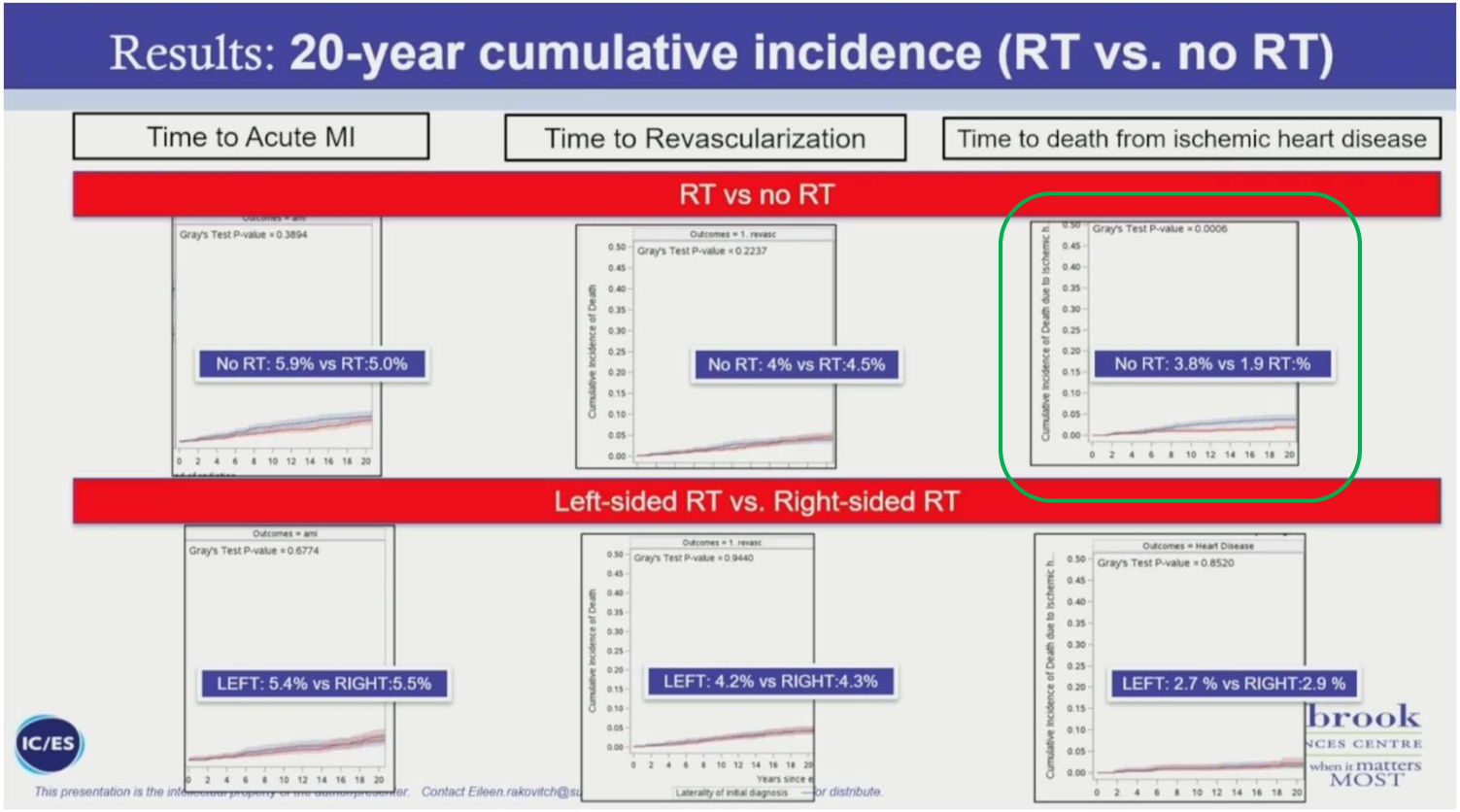
- Left sided radiation vs. Right sided radiation (Composite outcome)

	HR	UCL	LCL	P value
Radiation (left vs. right)	0.99	0.70	1.42	0.97
Age >60 vs <= 60	3.10	2.12	4.52	<0.001
Cardiac history (yes/no)	4.94	2.95	8.28	<0.001

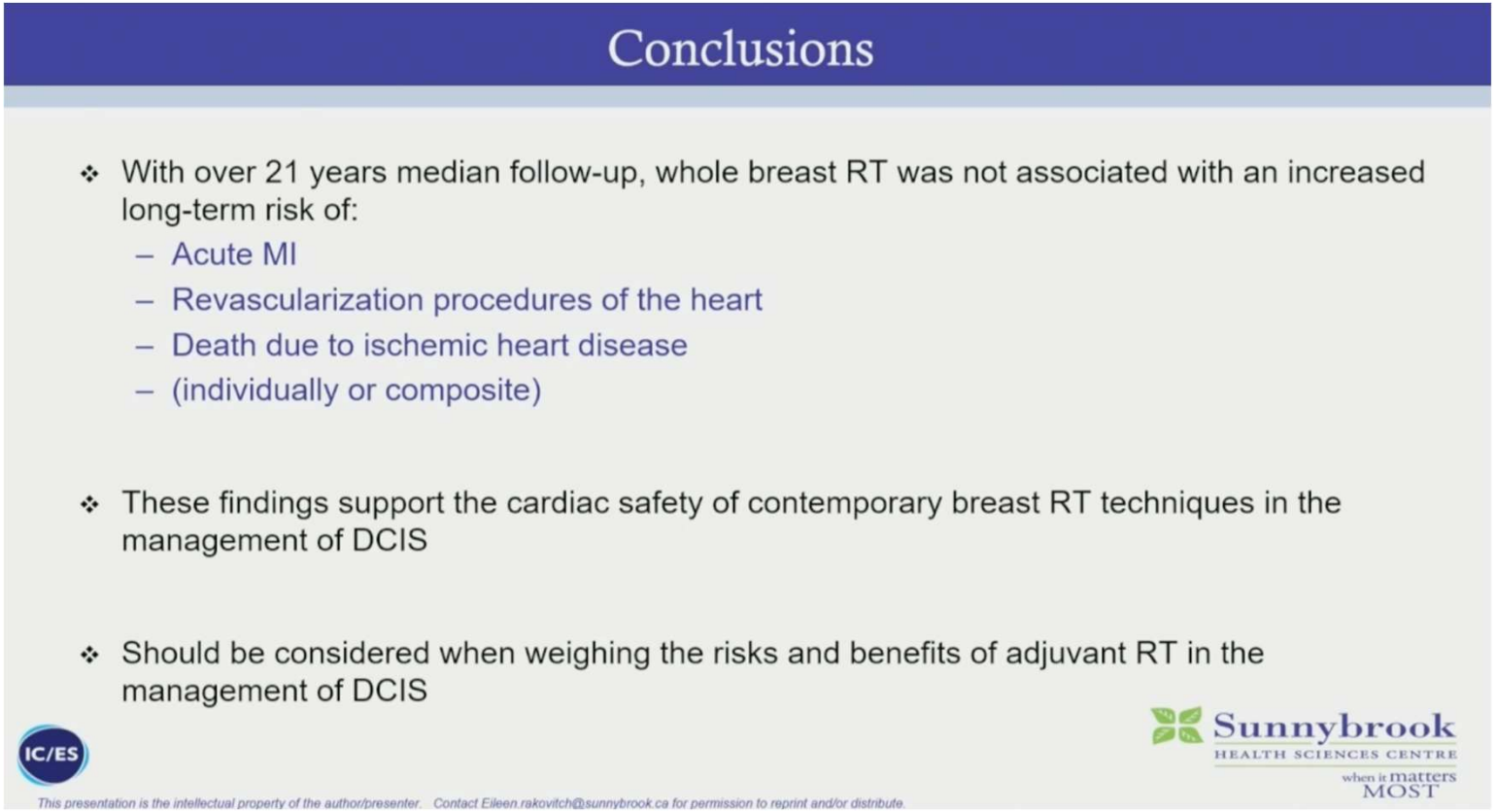


Left-sided RT *not associated* with increased risk compared to Right sided RT

Rakovitch, E. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.



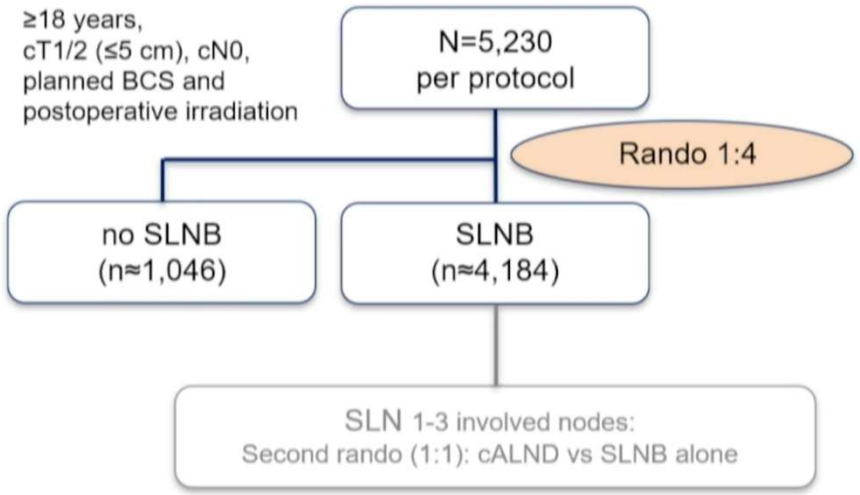
Rakovitch, E. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.



Rakovitch, E. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.

San Antonio Breast Cancer Symposium®, December 9-12, 2025

Study Design INSEMA Trial



iDFS, invasive disease-free survival; BCS, breast-conserving surgery;
SLNB, sentinel lymph node biopsy; cALND, completion axillary lymph node dissection

In 4 patients (both ITT and PP set) SLNB result is missing

Primary objective:

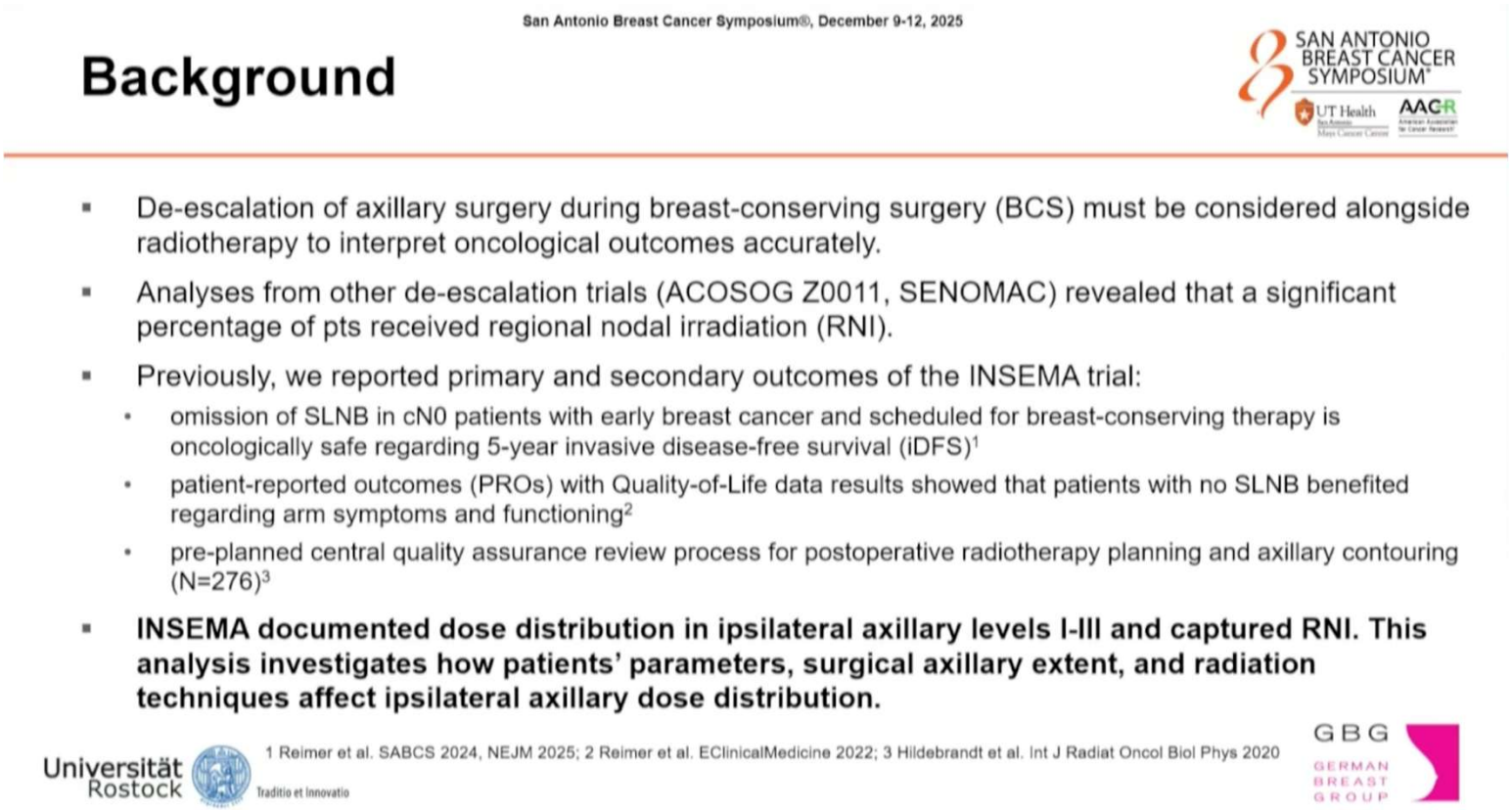
- To compare iDFS after BCS (non-inferiority question) between no axillary surgery and SLNB patients (first randomization)

Secondary objective:

- Determination of the actually applied radiotherapy doses at the respective axillary levels I-III (QA of RT)

- Recruitment in Germany and Austria (09/2015-04/2019), **n=108 RT facilities**

Hildebrant, et al. INSEMA Trial. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.



Hildebrant, et al. INSEMA Trial. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.

San Antonio Breast Cancer Symposium®, December 9-12, 2025

Methods

- The INSEMA protocol mandated whole-breast irradiation (WBI ± tumor bed boost)
- RNI was only permitted in patients with 4 or more involved lymph nodes (≥ pN2a; *after amend. #4 (Sep 2016)*)
- Contouring of the ipsilateral axilla (level I-III) followed the Radiation Therapy Oncology Group (RTOG) consensus definitions

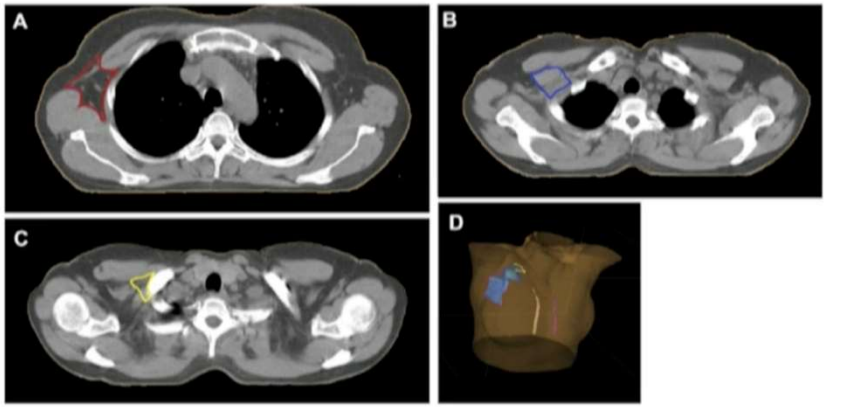


Fig. 2. Representative example of detailed radiation therapy planning record that was classified as receiving standard tangents with acceptable contouring of axillary levels I-III. A: contour level I (red); B: contour level II (blue); C: contour level III (yellow); D: contouring levels I-III (3D illustration).[1]

- Dose parameters are presented as relative doses (in % of the prescribed breast dose) to allow biological interpretation since absolute physical doses differ between conventionally and hypofractionated cases.

1 Hildebrandt et al. Int J Radiat Oncol Biol Phys 2020

Hildebrant, et al. INSEMA Trial. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.

San Antonio Breast Cancer Symposium®, December 9-12, 2025

Conclusion

- Approximately 50% of all INSEMA pts received a potentially therapeutic dose in axillary level I *(defined as median dose of ≥ 85% of the prescribed breast dose)*.
- A higher incidental axillary dose and an increased use of RNI were observed in the SLNB arm compared to no SLNB pts.
  - level I 91.3% vs. 86.3% (p<0.001)
  - level II 37.8% vs. 23.3% (p<0.001)
  - level III 5.2% vs. 4.5% (p=0.002)
- In the no SLNB arm, RNI was applied in <1% of patients.
  - RNI 4.0% vs. 0.6% (p<0.001)
- For pts without postoperative RT, the iDFS did not differ significantly between the arms
  - HR for no SLNB to SLNB = 1.47 [95% CI: 0.75-2.85](p=0.26)
- **Clinical implication: omission of SLNB during BCS does not need compensation by escalated axillary RT concepts (RT volume & RT dose).**

...beyond whole breast radiation

Hildebrant, et al. INSEMA Trial. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.

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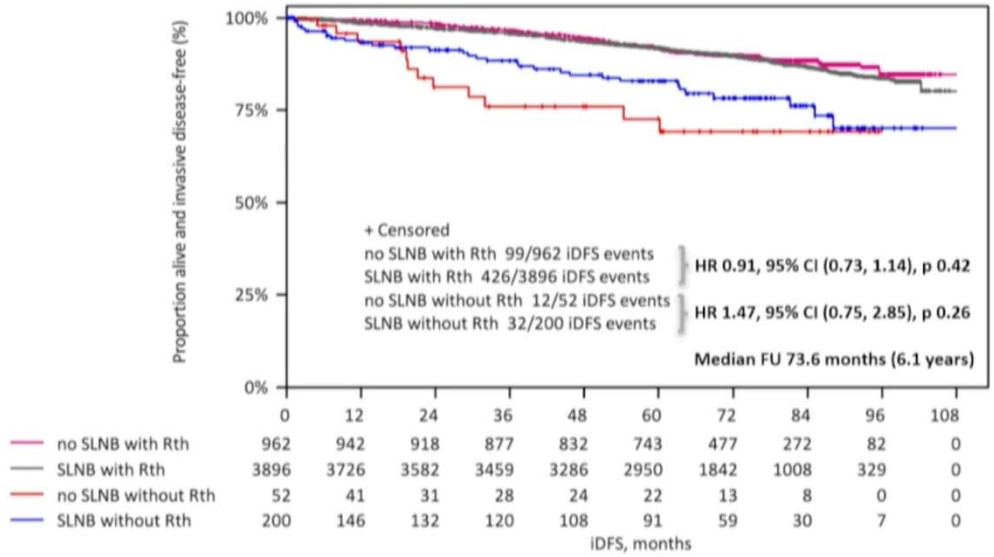
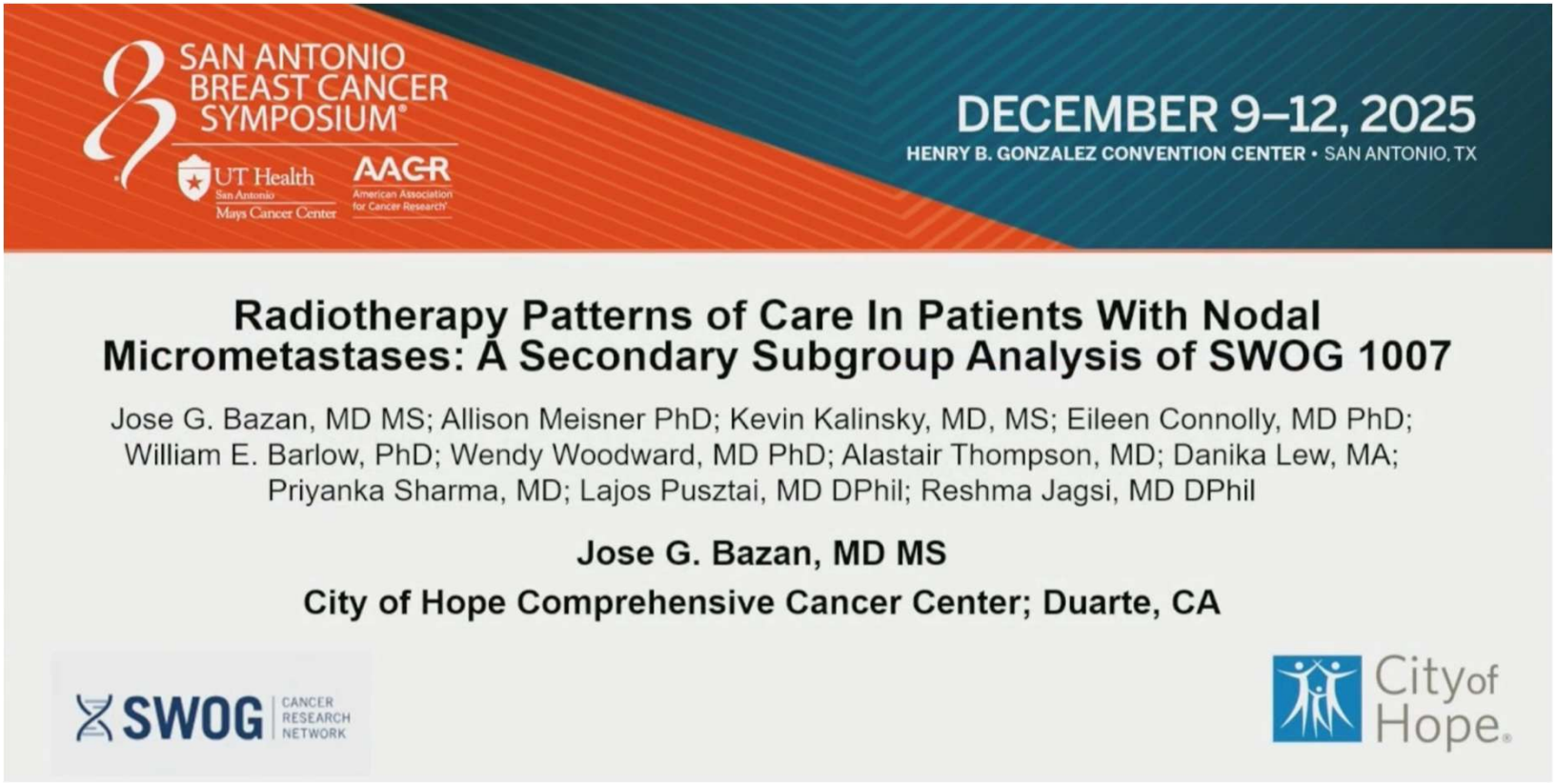
iDFS: per-protocol analysis: with RT (N=4858) / without RT (N=252)*



First iDFS event	with RT N=4858 N(%)	no RT* N=252 N(%)
Total	525 (10.8)	44 (17.5)
Invasive LRR	**72 (1.5)**	**13 (5.2)**
- Axillary	22 (0.5)	3 (1.2)
- ipsilateral breast	50 (1.0)	10 (4.0)
Invasive contralateral BC	35 (0.7)	2 (0.8)
Distant relapse	130 (2.7)	10 (4.0)
Secondary malignancy	182 (3.7)	4 (1.6)
Death	106 (2.2)	15 (6.0)

*(*post hoc analysis, only pts who would be included in PP set, if they had Rth)*

Hildebrant, et al. INSEMA Trial. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.



Background

- Regional nodal irradiation (RNI) targeting the breast/chestwall and undissected axillary, supraclavicular and internal mammary nodes is the standard of care for the majority of patients with breast cancer and axillary nodal macrometastases
- The benefit of RNI for patients with axillary nodal micrometastases (pN1mi) is less clear, and there are wide variations in radiation therapy (RT) practice patterns for these patients.
- The SWOG 1007 (RxPonder) trial included patients with pN1mi disease and provides an opportunity to learn how these patients were treated with regards to RT

Bazan, et al. SWOG 1007. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.

Methods

- Reviewed pathology reports of patients enrolled on S1007 from 2011-2014 prior to amendment) and then used the RT forms captured during the study to classify patients into 1 of 4 groups:
  - No RT
  - Breast/Chestwall + low axillary RT (level I/II only)
  - Breast/Chestwall RT alone
  - RNI (inclusion of at least a SCL field to treat axillary apex+SCL nodes)
- Analysis is primarily descriptive with multivariable logistic regression analysis performed for the association of individual factors with RNI use.

Bazan, et al. SWOG 1007. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.

Results

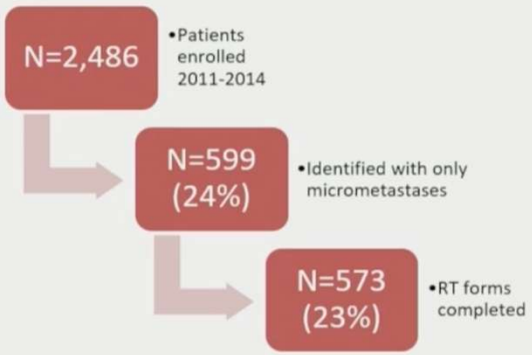


Table 1: Pt Characteristics	
Type of Surgery	
Lumpectomy	371 (65%)
Mastectomy	202 (35%)
Menopausal Status	
Premenopausal	192 (34%)
Postmenopausal	381 (66%)
Number of Positive Nodes	
1	500 (87%)
2-3	73 (13%)
Tumor Size, median (IQR)	1.7 cm (1.2-2.4 cm)
Lymphovascular Invasion	118 (21%)
Multifocal/Multicentric	104 (18%)
Grade	
1	152 (27%)
2	353 (62%)
3	54 (9%)
Unknown	14 (2%)
Histology	
ILC	72 (13%)
Mixed IDC/ILC	18 (3%)
IDC	483 (84%)
Received Chemotherapy	226 (39%)
Oncotype RS, median (IQR)	15 (11-19)

Bazan, et al. SWOG 1007. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.

Results: RT delivery for patients with pN1mic

Table 2: RT Delivery	
No Radiation	**163 (29%)**
Lumpectomy	15 (4%)
Mastectomy	148 (73%)
Breast/CW+Low Axilla	**59 (10%)**
Lumpectomy	52 (14%)
Mastectomy	7 (4%)
Breast/CW Only	**267 (47%)**
Lumpectomy	252 (68%)
Mastectomy	15 (7%)
RNI	**84 (15%)**
Lumpectomy	52 (14%)
Mastectomy	32 (16%)

Table 3: Logistic Regression for RNI	Odds Ratio (95% CI), p-value
Post-menopausal v Pre-menopausal	0.84 (0.52-1.36), p=0.48
Mastectomy vs. Lumpectomy	1.16 (0.72-1.86), p=0.55
2-3 nodes+ vs. 1 node+	**2.36 (1.31-4.22), p=0.004** **Adj OR: 2.34 (1.94-4.24), p=0.005**
Grade 3 vs. Grade 1-2/Unk	0.86 (0.37-1.96), p=0.71
Lymphovascular Invasion (Y vs. N)	**1.80 (1.07-3.03), p=0.03** Adj. OR: 1.63 (0.96-2.77), p=0.07
Multifocal/centric vs. Unifocal	0.80 (0.43-1.51), p=0.49
Pure ILC vs. Other	1.06 (0.53-2.10), p=0.87
T2-3 vs. T1	**1.98 (1.24-3.16), p=0.004** **Adj. OR: 1.93 (1.20-3.11), p=0.007**
Chemotherapy (yes vs. no)	0.88 (0.55-1.42), p=0.61
Oncotype RS (continuous)	0.98 (0.94-1.03), p=0.41

Bazan, et al. SWOG 1007. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.

Conclusions

- Practice patterns analysis suggests de-escalation of RT occurred on S1007 in patients with pN1mic disease
  - Only 15% of all patients received RNI
  - 75% of patients that underwent mastectomy had NO radiation
- Factors associated with receipt of RNI included >1+ node and larger tumors (T2-3 vs. T1)
- The impact of this de-escalated RT on cancer control outcomes in this cohort is ongoing
- Practice patterns variations observed on S1007 support enrollment of patients with pN1mic disease on TAILOR RT

Bazan, et al. SWOG 1007. Presented at 2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.

Summary SABCS Abstracts

RadComp found no association between cardiac radiation dose volume metrics and cardiac-specific HRQOL.

Ontario database found no association between WBI and long-term cardiac outcomes.

Radiotherapy compliance high on INSEMA; favorable local control results with SNLB omission are NOT due to routine irradiation of level II-III axilla.

Only 15% of patients with pN1mic on SWOG 1007 (TailoRx) received regional nodal irradiation; keep accruing to MA.39!

2025 Breast Cancer Symposium. December 9-12, 2025. San Antonio, Texas.

National Comprehensive Cancer Network®

NCCN Member Institutions

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To define and advance quality, effective, equitable, and accessible cancer care and prevention so all people can live better lives

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Access to high-quality, high-value, patient-centered cancer care for all people globally

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