

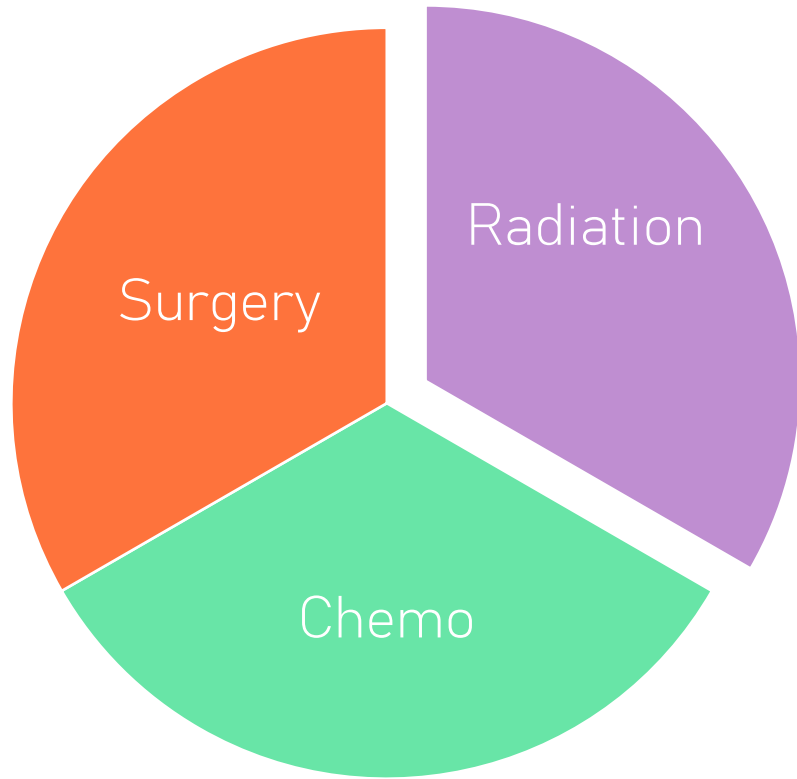


Adjuvant Radiotherapy in Breast Cancer : Indications, Evolving Evidence, and Controversies

DR. A.RAMYA

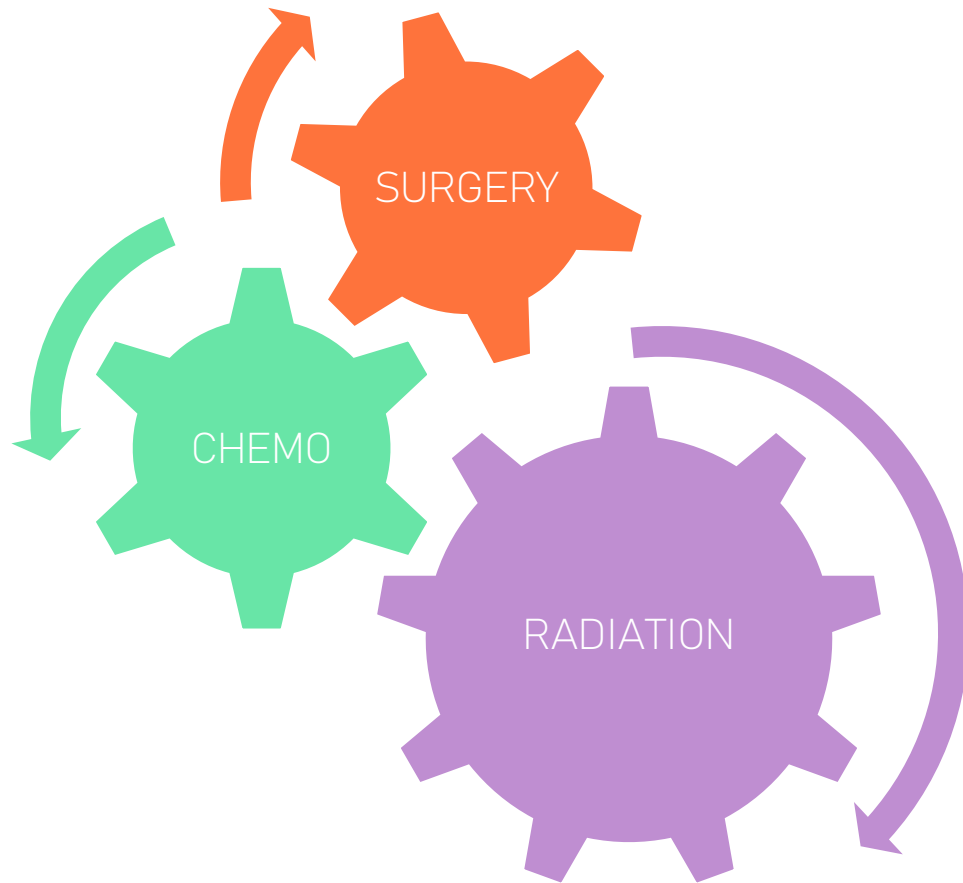
ASSOCIATE PROFESSOR

TNGMSSH, CHENNAI



- **FISHER HYPOTHESIS**

- Breast ca is systemic in onset
- Eradication of microscopic residual disease after surgery.
- Locoregional recurrence ? Marker of metastatic disease
- Radiation improves local control not survival (NSABP 04 & 06)



- **HELLMAN SPECTRUM MODEL**

Disease exists on a spectrum.

Locoregional recurrence = independent source of metastases.

Coined Oligomets

RT prevents distant relapse → survival benefit.

EBCTCG - meta-analysis confirmed: every 4 local recurrences prevented ~1 breast cancer death avoided

AJCC –TNM

Table 1. Definitions for T, N, M

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis (DCIS)*	Ductal carcinoma <i>in situ</i>
Tis (Paget)	Paget disease of the nipple NOT associated with invasive carcinoma and/or carcinoma <i>in situ</i> (DCIS) in the underlying breast parenchyma. Carcinomas in the breast parenchyma associated with Paget disease are categorized based on the size and characteristics of the parenchymal disease, although the presence of Paget disease should still be noted
T1	Tumor ≤20 mm in greatest dimension
T1mi	Tumor ≤1 mm in greatest dimension
T1a	Tumor >1 mm but ≤5 mm in greatest dimension (round any measurement >1.0–1.9 mm to 2 mm)
T1b	Tumor >5 mm but ≤10 mm in greatest dimension
T1c	Tumor >10 mm but ≤20 mm in greatest dimension

T2	Tumor >20 mm but ≤50 mm in greatest dimension
T3	Tumor >50 mm in greatest dimension
T4	Tumor of any size with direct extension to the chest wall and/or to the skin (ulceration or macroscopic nodules); invasion of the dermis alone does not qualify as T4
T4a	Extension to the chest wall; invasion or adherence to pectoralis muscle in the absence of invasion of chest wall structures does not qualify as T4
T4b	Ulceration and/or ipsilateral macroscopic satellite nodules and/or edema (including peau d'orange) of the skin that does not meet the criteria for inflammatory carcinoma
T4c	Both T4a and T4b are present
T4d	Inflammatory carcinoma

*Note: Lobular carcinoma *in situ* (LCIS) is a benign entity and is removed from TNM staging in the AJCC Cancer Staging Manual, 8th Edition.

[Continued](#)

Table 1. Definitions for T, N, M (continued)

Regional Lymph Nodes (N)

Clinical (cN)

cNX*	Regional lymph nodes cannot be assessed (e.g., previously removed)
cN0	No regional lymph node metastases (by imaging or clinical examination)
cN1	Metastases to movable ipsilateral level I, II axillary lymph node(s)
cN1mi**	Micrometastases (approximately 200 cells, larger than 0.2 mm, but none larger than 2.0 mm)
cN2	Metastases in ipsilateral level I, II axillary lymph nodes that are clinically fixed or matted; or in ipsilateral internal mammary nodes in the absence of axillary lymph node metastases
cN2a	Metastases in ipsilateral level I, II axillary lymph nodes fixed to one another (matted) or to other structures
cN2b	Metastases only in ipsilateral internal mammary nodes in the absence of axillary lymph node metastases
cN3	Metastases in ipsilateral infraclavicular (level III axillary) lymph node(s) with or without level I, II axillary lymph node involvement; or in ipsilateral internal mammary lymph node(s) with level I, II axillary lymph node metastases; or metastases in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement
cN3a	Metastases in ipsilateral infraclavicular lymph node(s)
cN3b	Metastases in ipsilateral internal mammary lymph node(s) and axillary lymph node(s)
cN3c	Metastases in ipsilateral supraclavicular lymph node(s)

Pathologic (pN)

pNX	Regional lymph nodes cannot be assessed (e.g., not removed for pathological study or previously removed)
pN0	No regional lymph node metastasis identified or ITCs only
pN0(i+)	ITCs only (malignant cells clusters no larger than 0.2 mm) in regional lymph node(s)
pN0(mol+)	Positive molecular findings by reverse transcriptase polymerase chain reaction (RT-PCR); no ITCs detected
pN1	Micrometastases; or metastases in 1–3 axillary lymph nodes; and/or in clinically negative internal mammary nodes with micrometastases or macrometastases by sentinel lymph node biopsy
pN1mi	Micrometastases (approximately 200 cells, larger than 0.2 mm, but none larger than 2.0 mm)
pN1a	Metastases in 1–3 axillary lymph nodes, at least one metastasis larger than 2.0 mm
pN1b	Metastases in ipsilateral internal mammary sentinel nodes, excluding ITCs
pN1c	pN1a and pN1b combined.
pN2	Metastases in 4–9 axillary lymph nodes; or positive ipsilateral internal mammary lymph nodes by imaging in the absence of axillary lymph node metastases
pN2a	Metastases in 4–9 axillary lymph nodes (at least one tumor deposit larger than 2.0 mm)
pN2b	Metastases in clinically detected internal mammary lymph nodes with or without microscopic confirmation; with pathologically negative axillary nodes

pN3	Metastases in 10 or more axillary lymph nodes; or in infraclavicular (level III axillary) lymph nodes; or positive ipsilateral internal mammary lymph nodes by imaging in the presence of one or more positive level I, II axillary lymph nodes; or in more than three axillary lymph nodes and micrometastases or macrometastases by sentinel lymph node biopsy in clinically negative ipsilateral internal mammary lymph nodes; or in ipsilateral supraclavicular lymph nodes
pN3a	Metastases in 10 or more axillary lymph nodes (at least one tumor deposit larger than 2.0 mm); or metastases to the infraclavicular (level III axillary lymph) nodes
pN3b	pN1a or pN2a in the presence of cN2b (positive internal mammary nodes by imaging); or pN2a in the presence of pN1b
pN3c	Metastases in ipsilateral supraclavicular lymph nodes

Note: (sn) and (f) suffixes should be added to the N category to denote confirmation of metastasis by sentinel node biopsy or FNA/core needle biopsy respectively, with NO further resection of nodes

Distant Metastasis (M)

M0	No clinical or radiographic evidence of distant metastases*
cM0(i+)	No clinical or radiographic evidence of distant metastases in the presence of tumor cells or deposits no larger than 0.2 mm detected microscopically or by molecular techniques in circulating blood, bone marrow, or other nonregional nodal tissue in a patient without symptoms or signs of metastases
cM1	Distant metastases detected by clinical and radiographic means
pM1	Any histologically proven metastases in distant organs; or if in non-regional nodes, metastases greater than 0.2 mm

The Anatomic Stage Group table should only be used in global regions where biomarker tests are not routinely available.

Cancer registries in the U.S. must use the Clinical and Pathological Prognostic Stage Group tables for case reporting.

Stage 0	Tis	N0	M0	Stage IIIA	T0	N2	M0
Stage IA	T1	N0	M0		T1	N2	M0
Stage IB	T0	N1mi	M0		T2	N2	M0
	T1	N1mi	M0		T3	N1	M0
Stage IIA	T0	N1	M0		T3	N2	M0
	T1	N1	M0	Stage IIIB	T4	N0	M0
	T2	N0	M0		T4	N1	M0
Stage IIB	T2	N1	M0		T4	N2	M0
	T3	N0	M0	Stage IIIC	Any T	N3	M0
				Stage IV	Any T	Any N	M1

Notes:

1. T1 includes T1mi.
2. T0 and T1 tumors with nodal micrometastases (N1mi) are staged as Stage IB.
3. T2, T3, and T4 tumors with nodal micrometastases (N1mi) are staged using the N1 category.
4. M0 includes M0(i+).
5. The designation pM0 is not valid; any M0 is clinical.
6. If a patient presents with M1 disease prior to neoadjuvant systemic therapy, the stage is considered Stage IV and remains Stage IV regardless of response to neoadjuvant therapy.
7. Stage designation may be changed if postsurgical imaging studies reveal the presence of distant metastases, provided the studies are performed within 4 months of diagnosis in the absence of disease progression, and provided the patient has not received neoadjuvant therapy.
8. Staging following neoadjuvant therapy is designated with "yc" or "yp" prefix to the T and N classification. There is no anatomic stage group assigned if there is a complete pathological response (pCR) to neoadjuvant therapy, for example, ypT0ypN0cM0.

[Continued](#)

MOLECULAR SUBTYPES

Intrinsic subtypes (GEP)	IHC classification (St Gallen)	Agreement IHC/GEP
Luminal A	'Luminal A' ER and/or PR positive HER2 negative Ki-67 < 14%	73%–100%
Luminal B	'Luminal B (HER2 negative)' ER and/or PR positive HER2 negative Ki-67 ≥ 14% 'Luminal B (HER2 positive)' ER and/or PR positive Any Ki-67 HER2 over-expressed or amplified	73%–100%
HER2-enriched	'HER2 positive (non-luminal)' HER2 over-expressed or amplified ER and PR absent	41%–69%
Basal-like	'Triple negative' ER and PR absent HER2 negative	80%



GEP, gene expression profiling; IHC, immuno-histochemical; ER, oestrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2.



PRINCIPLES OF BIOMARKER TESTING
HER2 TESTING BY VALIDATED IMMUNOHISTOCHEMISTRY (IHC) ASSAY
 For HER2 (*ERBB2*) testing validated by dual-probe ISH assay, see [BINV-A 3 of 4](#).

Result Category	Score/Pattern	Criteria	Clinical Relevance
Negative ^b	0/absent membrane staining	No staining observed	HER2 protein not detected in sample Not included in DESTINY-Breast04 (DB-04) and DESTINY-Breast06 (DB-06) trials Considered "HER2 Null"
Negative	0+/with membrane staining	Membrane staining that is incomplete and is faint/barely perceptible and within ≤10% of tumor cells	Treat as HER2-negative disease Considered "HER2 Ultralow" in DB-06
Negative	1+	Incomplete membrane staining that is faint/barely perceptible and within >10% of tumor cells	Treat as HER2-negative disease Considered "HER2 Low" in DB-04/-06
Equivocal	2+	Weak to moderate complete membrane staining in >10% of tumor cells ^c or Complete membrane staining that is intense but within ≤10% of tumor cells ^{c,d}	Reflex to in situ hybridization (ISH) testing to determine if HER2 (<i>ERBB2</i>) gene amplification present (see BINV-A 3 of 4) If ISH+ : HER2 (<i>ERBB2</i>) positive If ISH- : HER2 (<i>ERBB2</i>) negative (considered "HER2 Low" in DB-04/-06)
Positive	3+	Complete membrane staining that is intense and >10% of tumor cells ^d	HER2 protein overexpression present Treat as HER2-positive disease Eligible for various HER2-targeted treatments

1970s

NSABP B-06 / Milan I trials
BCS + RT equivalent to mastectomy

1990s

EBCTCG meta-analyses
RT reduces local recurrence and mortality

2000s

Canadian / START A&B trials
Hypofractionation (40 Gy/15 fr) equivalent to conventional fractionation

2010s

Z0011 / MA.20 / PRIME II / AMAROS
Omit axillary dissection if 1-2 SN+
RNI benefit confirmed; RT omission acceptable in elderly low-risk pts

2020s

FAST-Forward / ongoing trials
26 Gy/5 fr non-inferior; de-escalation trials in genomically low-risk disease

Current practice pillars

WBI after BCS
Standard; hypo/ultra-hypo preferred

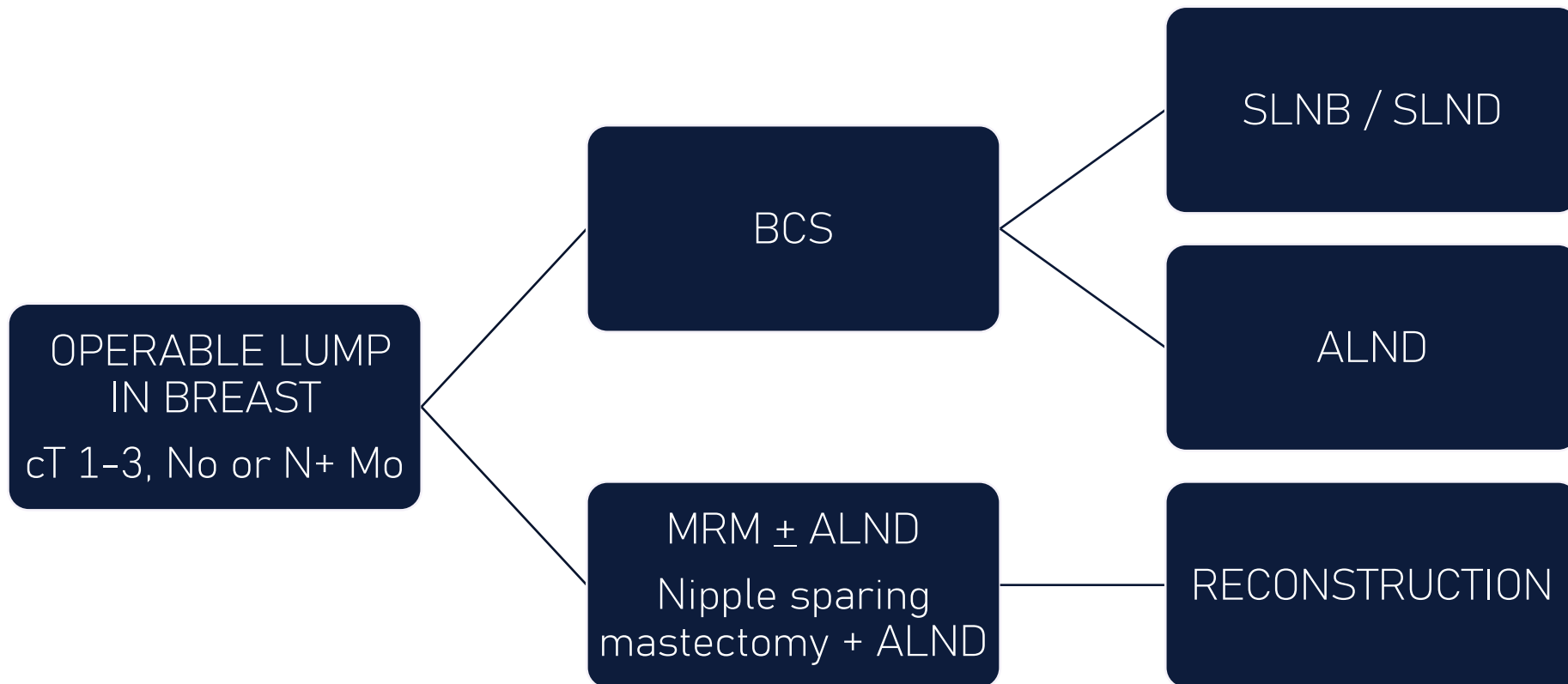
PMRT
T3/T4, ≥ 4 nodes, +ve margins

Regional nodal RT
Node-positive; high-risk node-negative

Partial breast RT (PBI/APBI)
Selected low-risk, age ≥ 50 , small ER+

RT omission
Age ≥ 70 , T1, ER+, node-neg, on ET

Active controversies
PMRT in 1-3 node+; RT after pCR;
IMN RT; protons; NAC restaging





ADJUVANT RADIATION – where do we stand?

- Reduces locoregional recurrence
- Improves disease control
- Selected survival benefit
- Integral component of breast-conserving therapy

BCS INDICATIONS FOR ADJUVANT RT

DCIS – after BCS and RT- Reduces IBTR 50-70%



Invasive breast carcinoma –
c T1-3, ? T4 c No/N+, Mo disease



All patients post BCS – Whole breast RT is indicated.





CONTRAINDICATIONS FOR BCS AND RT

- **ABSOLUTE**

- Inflammatory Breast Cancer
- DIFFUSE SUSPICIOUS MICROCALCIFICATIONS
- Inability to clear multiple positive pathologic margins after multiple attempts.
- Homozygous ATM mutation
- BRCA1 and BRCA 2 PV carrier
- PREGNANCY
- Multicentric disease

- **RELATIVE**

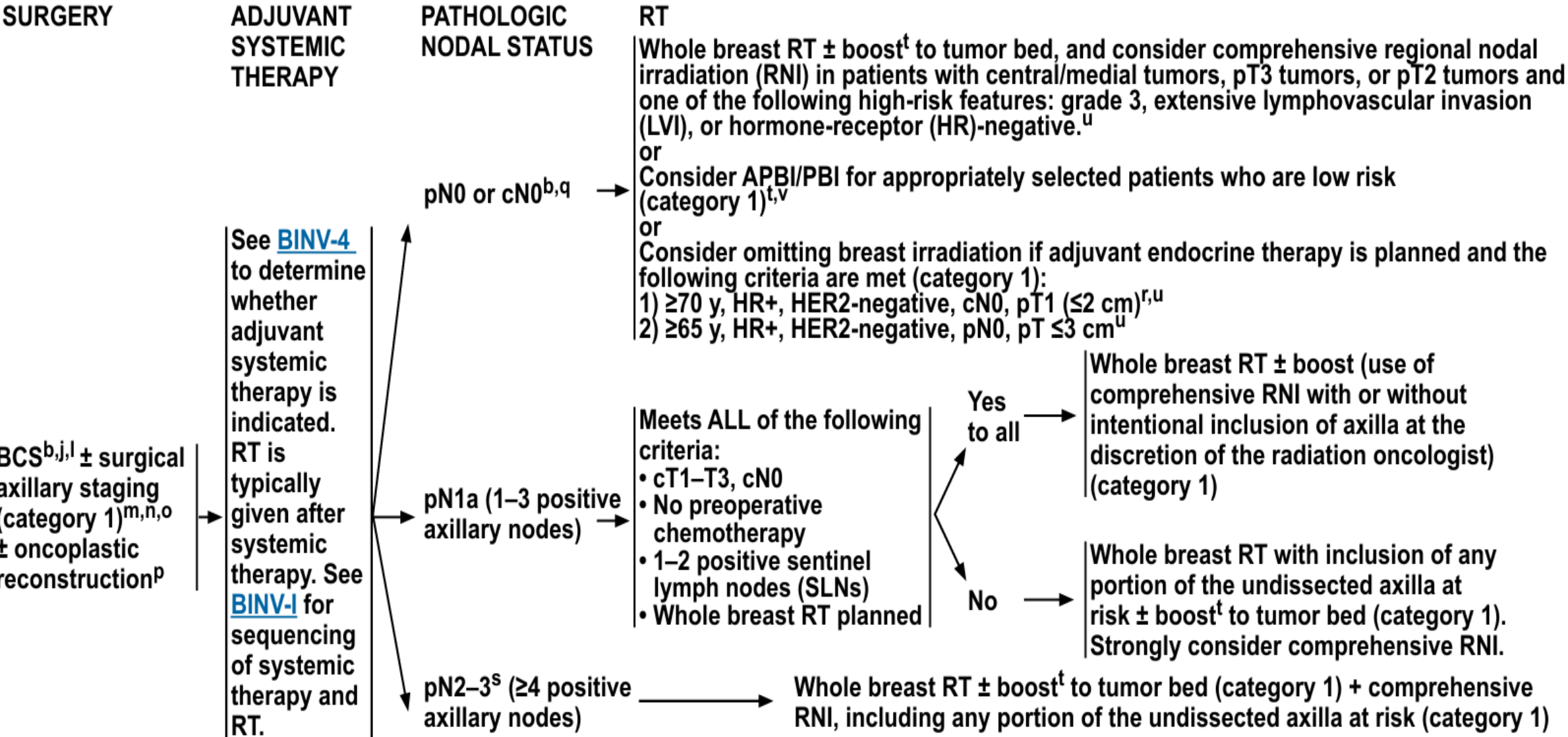
- Genetic predisposition to cancer
- TP53 PV
- Active connective tissue disorders
- History of prior RT

NCCN 2026

Absolute Contraindications for BCS (mastectomy is recommended)

- Inflammatory breast cancer or invasive breast cancer with extensive skin or dermal lymphatic involvement
- Diffuse suspicious or malignant-appearing microcalcifications
- Inability to clear multiple positive pathologic margins after one or more re-excision attempts, see [BINV-F](#)
- Homozygous *ATM* mutation (often leads to ataxia-telangiectasia syndrome) (category 2B)^a
- Patients diagnosed with gestational breast cancer (not receiving systemic chemotherapy) who cannot receive RT within 12–16 weeks
- Multicentric disease with any of the following criteria (mandate mastectomy)^{1,b}:
 - ▶ Receipt of neoadjuvant chemotherapy or endocrine therapy
 - ▶ Age ≤40
 - ▶ Triple-negative breast cancer (ER-, PR-, and HER2-negative)
 - ▶ More than 2 lesions involving more than 2 quadrants by MRI evaluation
 - ▶ Any individual lesion ≥5 cm
 - ▶ *BRCA1* and/or *BRCA2* PV carrier
 - ▶ Multicentric pure DCIS
 - ▶ Inability to achieve negative margins (defined as no ink on tumor for invasive cancers ± DCIS), see [BINV-F](#)
 - ▶ cN2–N3
 - ▶ Any reason for precluding the delivery of adjuvant whole breast RT + boost

LOCOREGIONAL TREATMENT OF cT1–3, cN0 or cN+, M0 DISEASE^{a,k}: BREAST-CONSERVING SURGERY (BCS) ± RT



1. What is the margin status for DCIS-M

- A. No margins
- B. 3mm
- C. 5mm
- D. 2mm

	No ink on tumor	2-mm margin	No margin necessary
Invasive breast cancer	X		
Invasive breast cancer + DCIS	X		
Invasive breast cancer + extensive DCIS	X		
Invasive breast cancer (treated with neoadjuvant chemotherapy followed by breast-conservation therapy) ^{4,5}	X		
Pure DCIS		X	
DCIS-M		X	
Classic LCIS* at surgical margin			X
Atypia at surgical margin			X

CAN WE OMIT ADJUVANT RT IN BCS

- RTOG 9804 criteria - DCIS

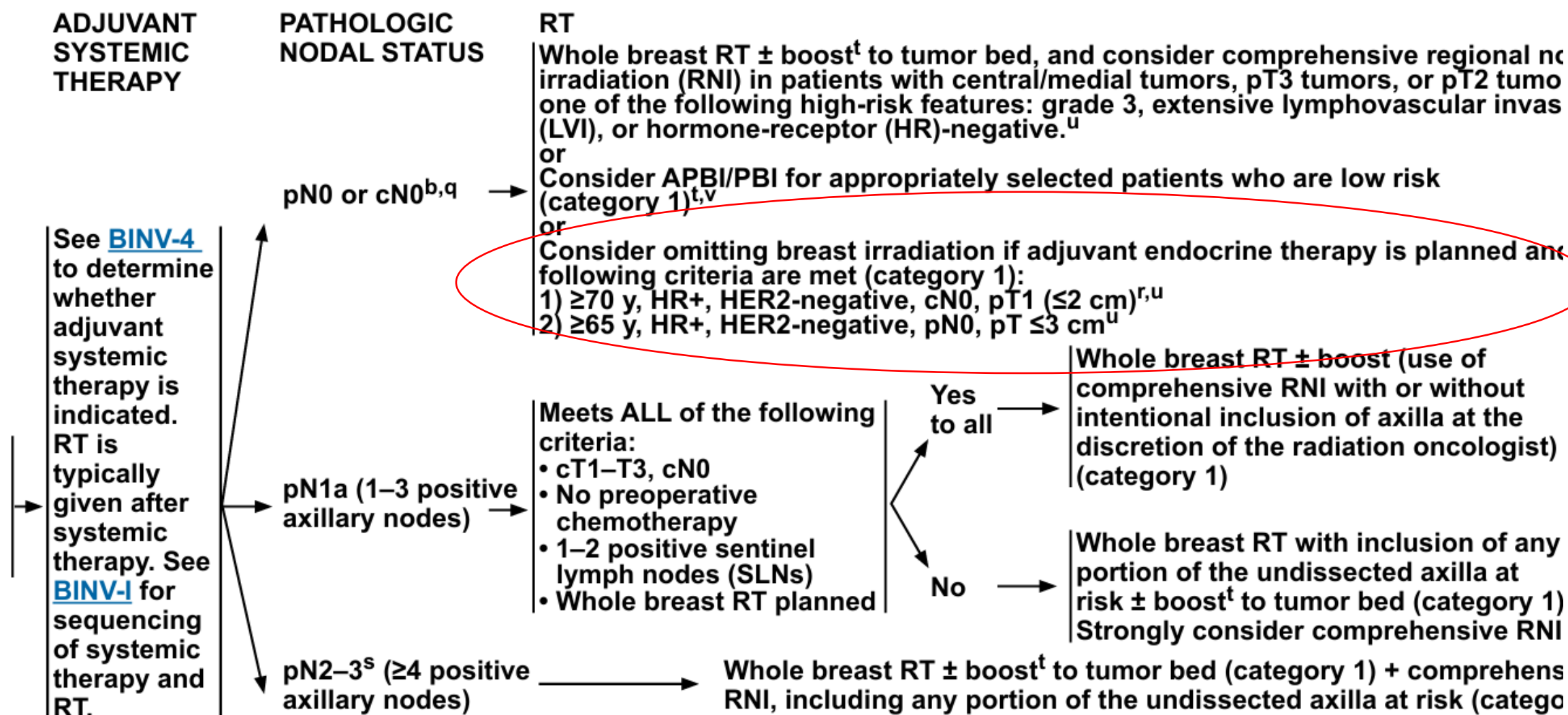
- Mammogram detected
- DCIS Grade 1 or 2
- Size ≤ 2.5 cm
- Margins ≥ 3.5 mm

Follow up of 7 yrs – local failure observed more in observation arm.

- Invasive cancer- Post BCS

- Endocrine therapy – NO RT
- Age > 70 yrs
- HR + and Her 2 negative
- Tumor pT1 ≤ 2 cm and N0

TREATMENT OF cT1–3, cN0 or cN+, M0 DISEASE^{a,k}: BREAST-CONSERVING SURGERY (BCS) ± RT



PRIME II



The NEW ENGLAND
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ORIGINAL ARTICLE



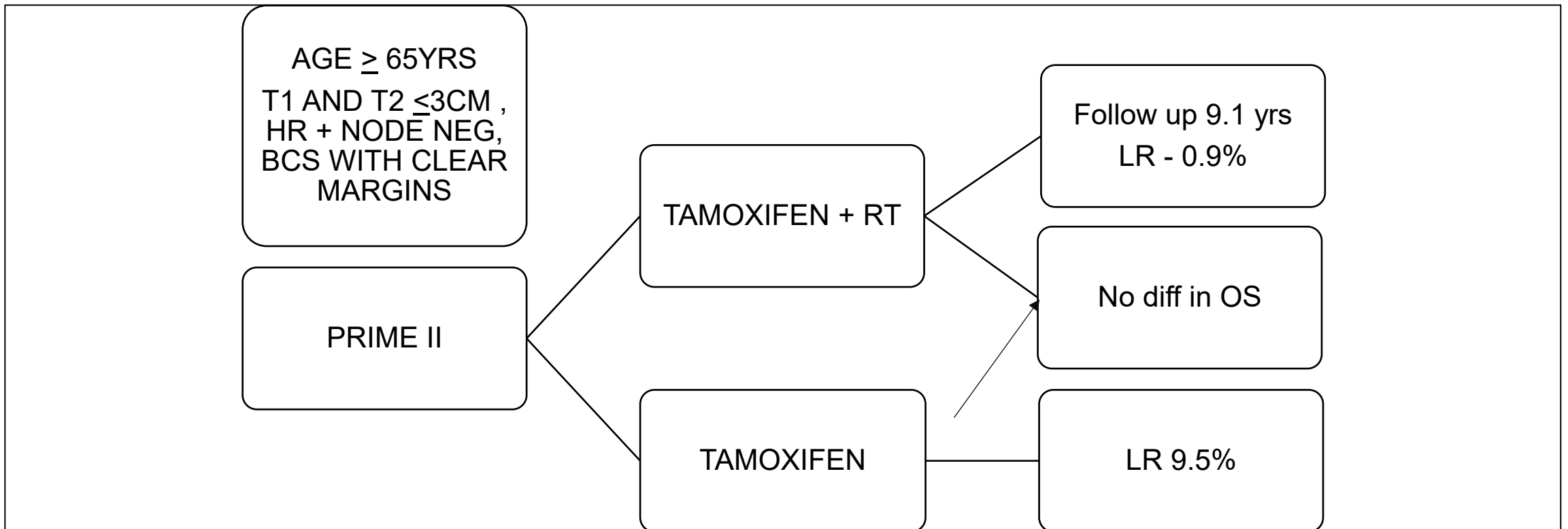
Breast-Conserving Surgery with or without Irradiation in Early Breast Cancer

Authors: Ian H. Kunkler, M.B., B.Chir., Linda J. Williams, Ph.D., Wilma J.L. Jack, M.B., Ch.B., David A. Cameron, M.D., and J. Michael Dixon, M.D. [Author Info & Affiliations](#)

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CONCLUSION: Omission of radiotherapy was associated with an increased incidence of local recurrence but had no detrimental effect on distant recurrence as the first event or overall survival among women 65 years of age or older with low-risk, hormone receptor– positive early breast cancer.



ARTICLES · [Volume 26, Issue 1](#), P37-50, January 2025

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Single-modality endocrine therapy versus radiotherapy after breast-conserving surgery in women aged 70 years and older with luminal A-like early breast cancer (EUROPA): a preplanned interim analysis of a phase 3, non-inferiority, randomised trial

[Icro Meattini, MD](#) ^{a,b} [✉](#) · [Maria Carmen De Santis, MD](#) ^c · [Luca Visani, MD](#) ^b · [Prof Marta Scorsetti, MD](#) ^d · [Alessandra Fozza, MD](#) · [Bruno Meduri, MD](#) ^f · et al. [Show more](#)

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EBRT better preserved HRQOL in elder woman with low-risk, early-stage breast cancer & endocrine therapy was associated with a greater reduction in HRQOL compared with EBRT

No difference in IBTR, LRR OR DISTANT METS.

ORIGINAL ARTICLE

Omitting Radiotherapy after Breast-Conserving Surgery in Luminal A Breast Cancer

T.J. Whelan, S. Smith, S. Parpia, A.W. Fyles, A. Bane, F.-F. Liu, E. Rakovitch, L. Chang, C. Stevens, J. Bowen, S. Provencher, V. Th  berge, A.M. Mulligan, Z. Kos, M.A. Akra, K.D. Voduc, T. Hijal, I.S. Dayes, G. Pond, J.R. Wright, T.O. Nielsen, and M.N. Levine, for the LUMINA Study Investigators*

- Age ≥ 55 years, IDC
- Underwent BCS + ALND/ SLND
- pT1N0, Margin > 1 mm
- Luminal A - ER+ ($\geq 1\%$), PR+ ($> 20\%$),
- Her2 (-)
- Ki67 13.25% or less

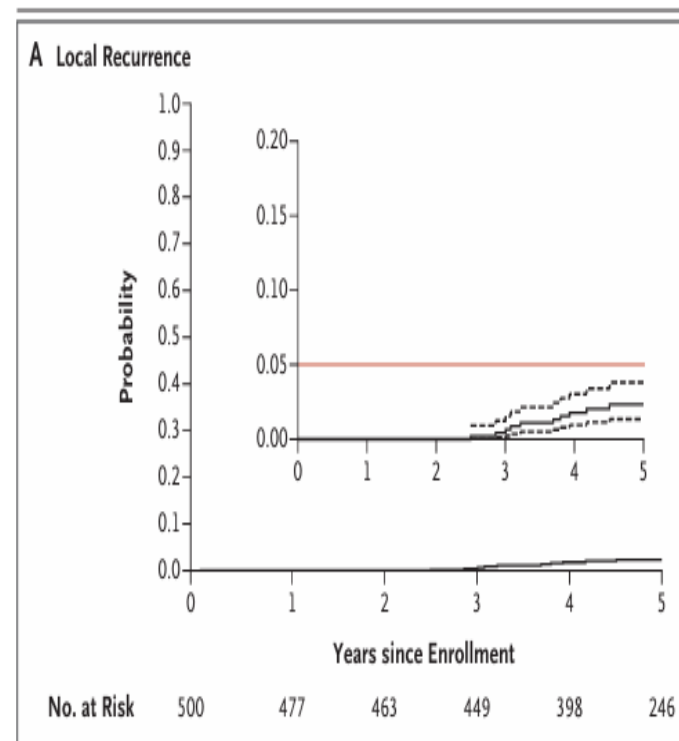


Figure 1. Cumulative Incidence of Local Recurrence, Cancer in the Contralateral Breast, and Any Recurrence.

Shown are the probabilities of local recurrence in the ipsilateral breast (Panel A), contralateral breast cancer (Panel B), and any recurrence (Panel C) among the 500 patients with luminal A breast cancer who were enrolled in the study. The red horizontal line at 5% (Panel A) represents the prespecified boundary for an acceptable incidence of local recurrence at 5 years. Dashed lines indicate the 90% confidence interval, and the insets show the same data on an expanded y axis.

47 overall and 5-year disease-free survival of 89.9% (90% CI, 87.5 to 92.2). A total of 13 deaths oc-



LUMINA A

- CONCLUSION :
- age ≥ 55 yrs or more, low-risk breast ca (pT1N0, Gr 1-2, Luminal A) treated with BCS & endocrine therapy alone,
- 5-yrs LR(2.3%) was low with omission of RT.



2.The EORTC boost trial demonstrated that tumor bed boost:

- A. Improves overall survival significantly
- B. Reduces ipsilateral breast tumor recurrence
- C. Reduces distant metastases
- D. Eliminates need for endocrine therapy

Whole-breast irradiation with or without a boost for patients treated with breast-conserving surgery for early breast cancer: 20-year follow-up of a randomised phase 3 trial

Harry Bartelink ¹, Philippe Maingon ², Philip Poortmans ³, Caroline Weltens ⁴, Alain Fourquet ⁵, Jos Jager ⁶, Dominic Schinagel ⁷, Bing Oei ⁸, Carla Rodenhuis ⁹, Jean-Claude Horiot ¹⁰, Henk Struikmans ⁹, Erik Van Limbergen ⁴, Youlia Kirova ⁵, Paula Elkhuis ¹¹, Rudolf Bongartz ¹², Raymond Miralbell ¹³, David Morgan ¹⁴, Jean-Bernard Dubois ¹⁵, Vincent Remouchamps ¹⁶, René-Olivier Mirimanoff ¹⁷, Sandra Collette ¹⁸, Laurence Collette ¹⁸;
European Organisation for Research and Treatment of Cancer Radiation Oncology and Breast Cancer Groups

- **EORTC trial 22881-10882** concludes that tumor bed boost improves locoregional recurrence in young, invasive breast cancer patients, DCIS in margins --- but no improvement in OS in Early breast cancer patients post BCS.

APBI AND PBI

Partial Breast Irradiation for Patients With Early-Stage Invasive Breast Cancer or Ductal Carcinoma In Situ: An ASTRO Clinical Practice Guideline

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Janice A. Lyons, MD^s





ASTRO 2024 GUIDELINES

- PBI is recommended for patients
- Early-stage invasive breast cancer
- **With all the following factors:**
- Age ≥ 40 years
- Grade 1-2 disease
- ER-positive histology
- Tumor size ≤ 2 cm
- Margins negative
- No nodes and no LVSI

- CONDITIONALLY RECOMMENDED
- SIZE $>2\text{CM}$ - $\leq 3\text{CM}$
- ER NEGATIVE
- GRADE 3

IF MULTIPLE FACTORS ARE PRESENT
THEN **NOT RECOMMENDED**

Table 3 Indications for PBI as an alternative to WBI

KQ1 Recommendations	Strength of Recommendation	Quality of Evidence (refs)
Early-stage invasive breast cancer*		
1. PBI is recommended for patients with early-stage invasive breast cancer with all of the following factors: • Grade 1-2 disease • ER-positive histology • Age ≥ 40 years • Tumor size ≤ 2 cm	Strong	High (for grade, histology, & age ≥ 50 years) Moderate (for age 40-49 years & size) 7-9,12-15,18
2. PBI is conditionally recommended for patients with early-stage invasive breast cancer with the following factors: • Grade 3 disease or • ER-negative histology or • Size >2 - ≤ 3 cm <u>Implementation remark:</u> PBI may not be appropriate when multiple of these factors are present, given the possibility of a higher recurrence risk.	Conditional	Low 7-9,12-15,18
3. PBI is conditionally not recommended for patients with early-stage invasive breast cancer with any of the following factors: • HER2-positive tumors not receiving anti-HER2 therapy • Lymphovascular invasion • Lobular histology <u>Implementation remark:</u> Given low patient numbers accrued to RCTs, higher risk of recurrence with PBI is possible.	Conditional	Expert Opinion
4. PBI is not recommended for patients with early-stage invasive breast cancer with any of the following factors: • Positive lymph nodes • Positive surgical margins • Known germline BRCA1/2 mutation • Age <40 years	Strong	Expert Opinion



APBI FOR DCIS

- RECOMMENDED

- Low-to-intermediate grade
- Age ≥ 40 years
- Size ≤ 2 cm

- CONDITIONALLY RECOMMENDED

- SIZE $> 2\text{CM} - \leq 3\text{CM}$
- GRADE 3

IF BOTH FACTORS ARE PRESENT THEN
NOT RECOMMENDED



APBI TECHNIQUES

- Brachytherapy 34Gy / 10# - 3.4Gy bid
- Multi-catheter interstitial
- SAVI
- Balloon catheterization (Mammosite, Contura)
- Permanent breast seed implant (PBSI)
- Electronic breast brachytherapy (EBB)
- Non-invasive image guided breast brachytherapy (NIBB)
- External beam (EBRT)
- 3D-CRT/IMRT
- Protons
- Electrons
- Single-dose intraoperative radiotherapy (IORT)
- Intraoperative radiotherapy with electrons (ELIOT)
- Targeted intraoperative radiotherapy (TARGIT)

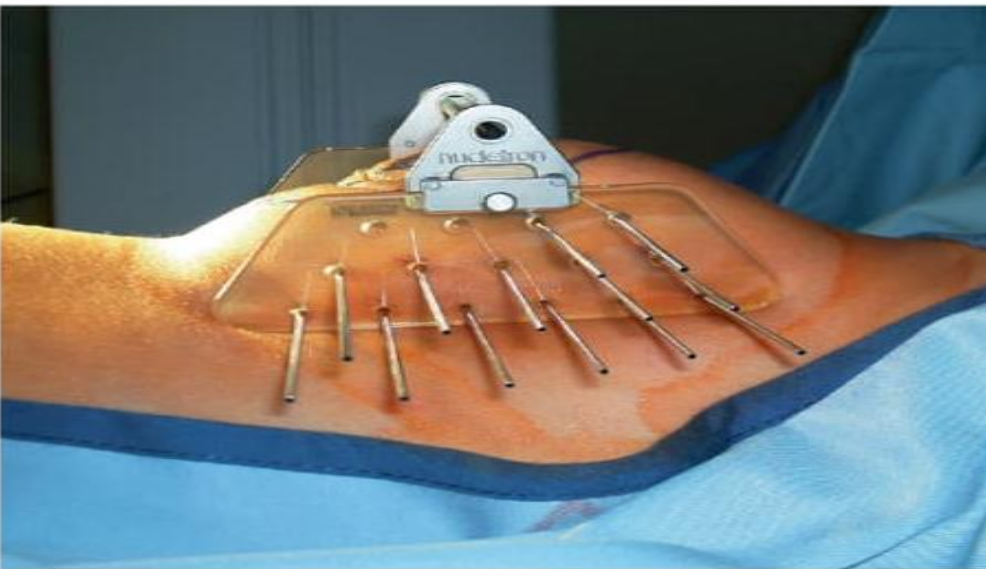


Fig. 11.2 Template-guided insertion of steel needles into the left breast



Fig. 11.3 Interstitial multicatheter breast implant in the same patient as shown in Fig. 11.2. The steel needles have been replaced by 14 flexible afterloading tubes

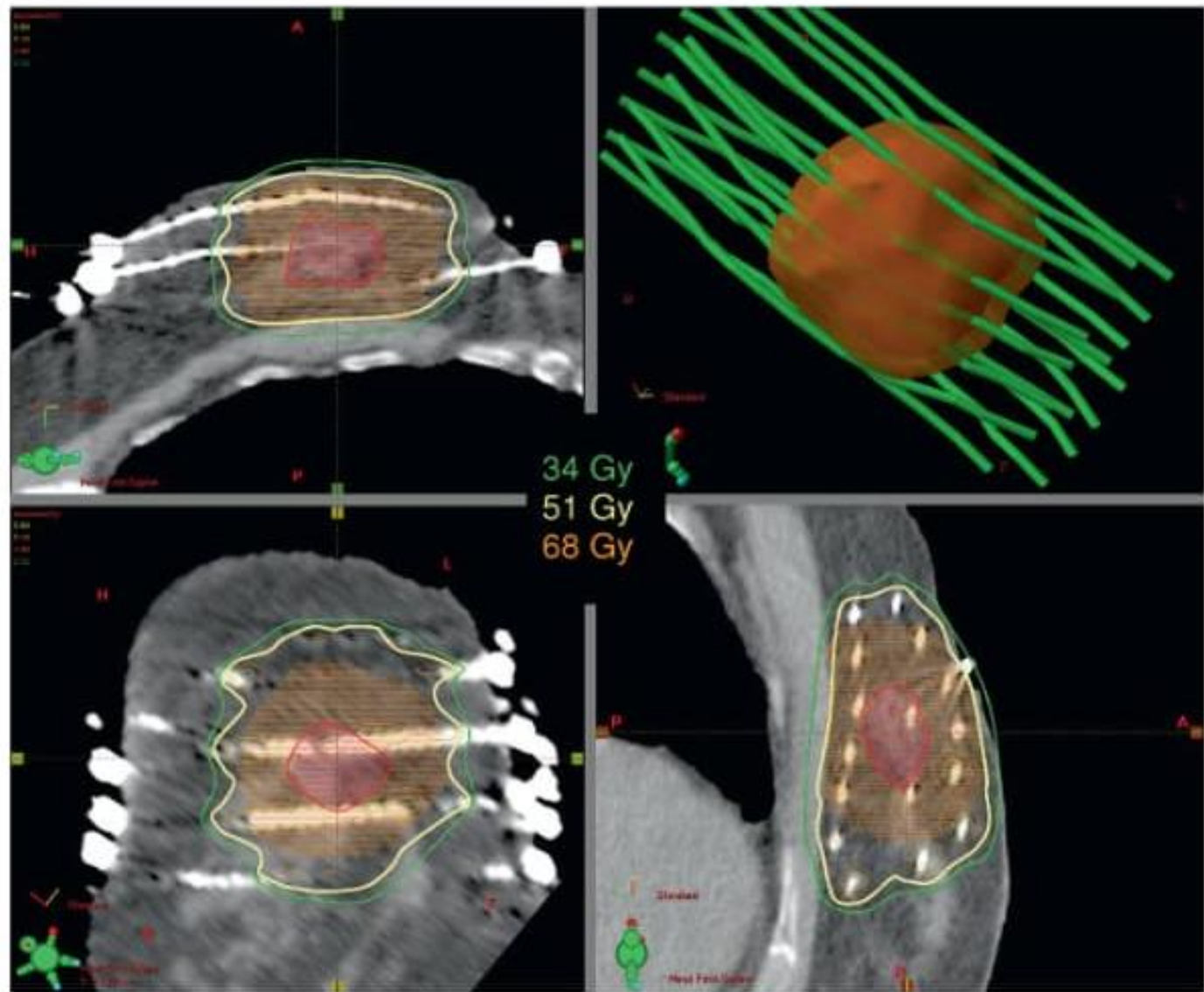
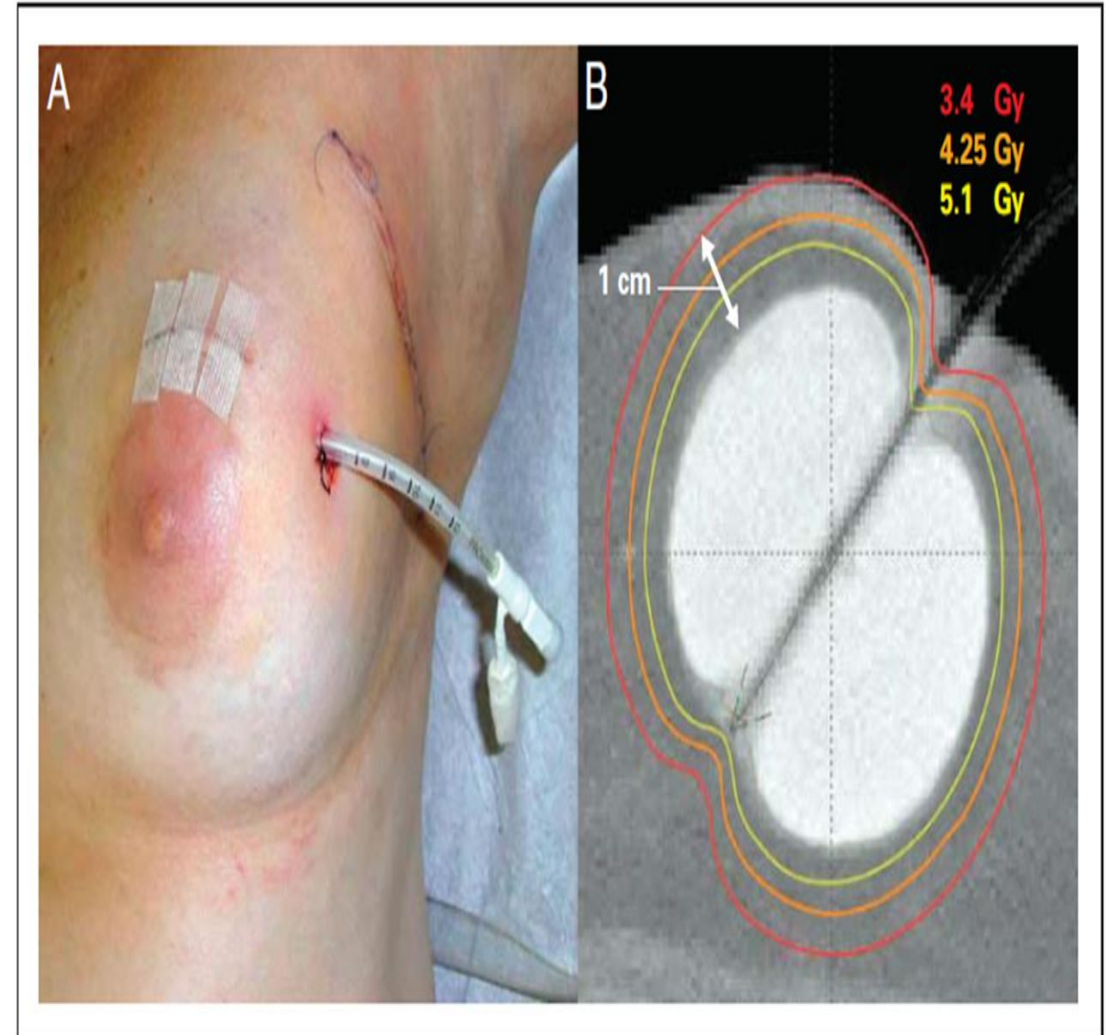
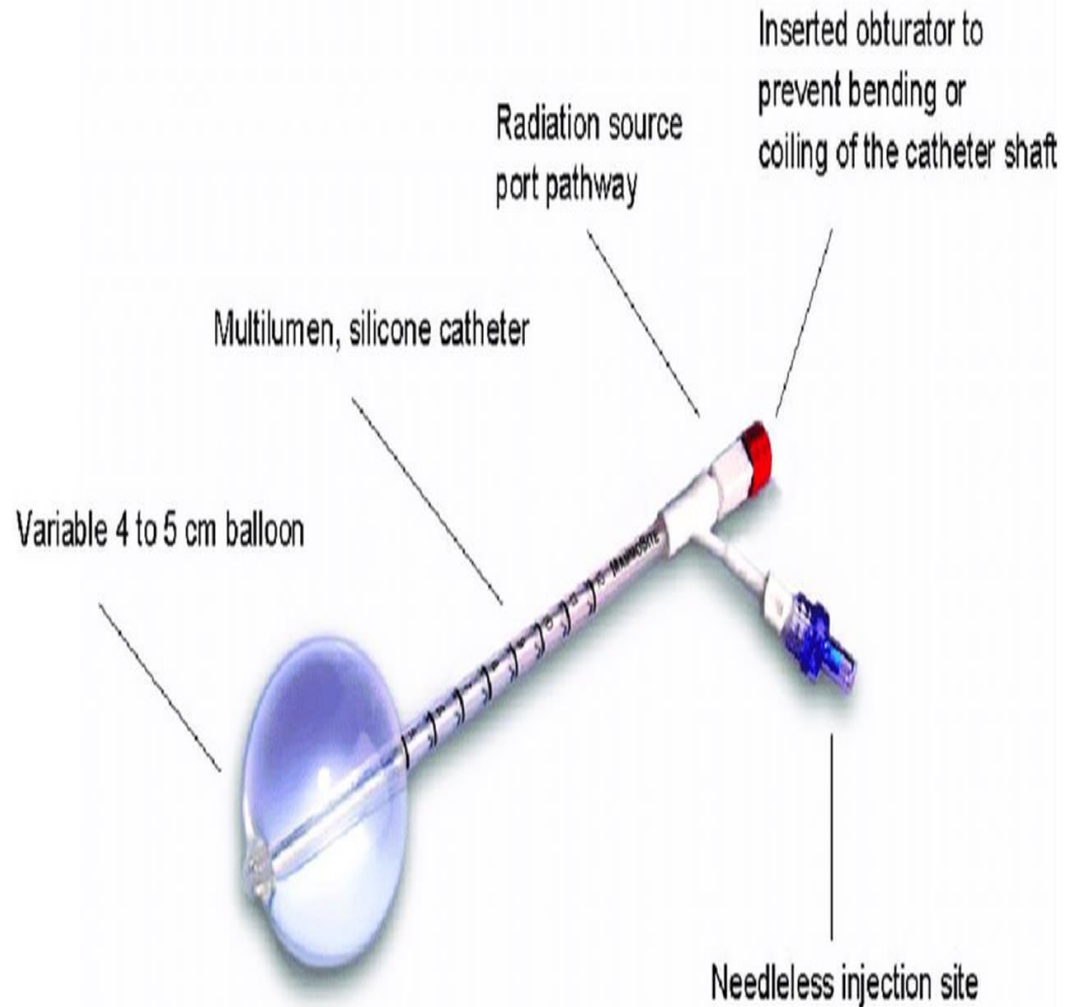


Fig. 11.9 CT-based 3D treatment planning for multicatheter interstitial brachytherapy. The lumpectomy cavity is outlined in red, and the target is shaded in orange (target is defined as the lumpectomy cavity with a 1.5 cm expansion)

MAMMOSITE



STRUT ADJUSTED VOLUME IMPLANT (SAVI) :



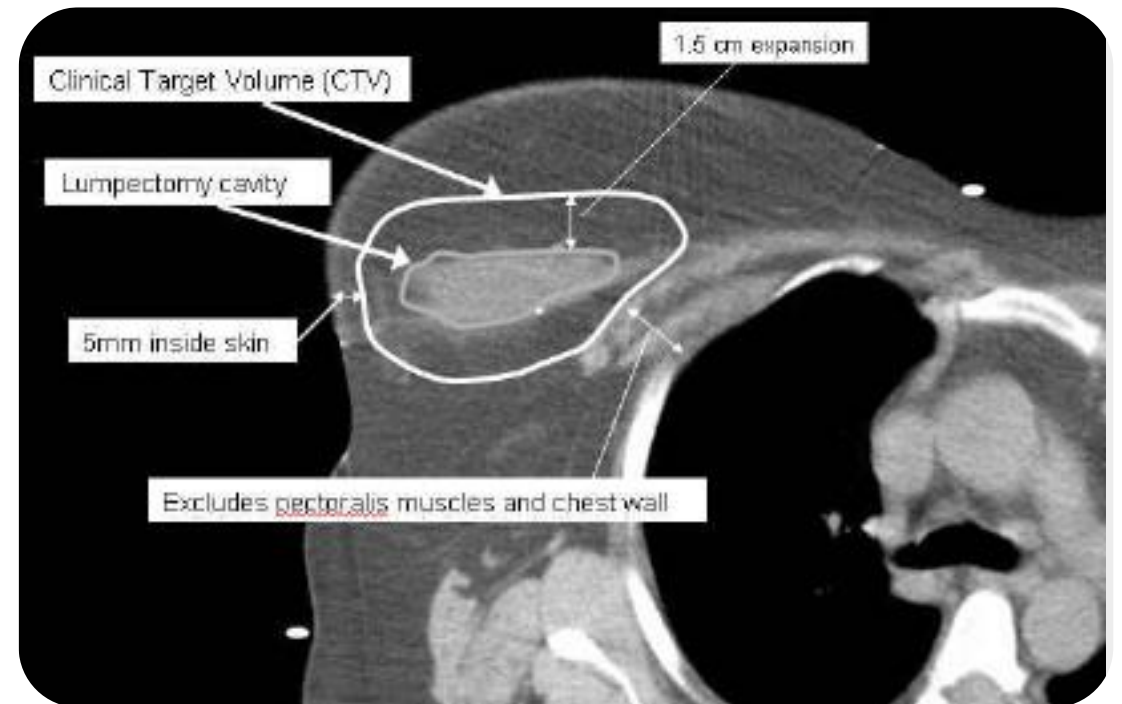
CONTURA



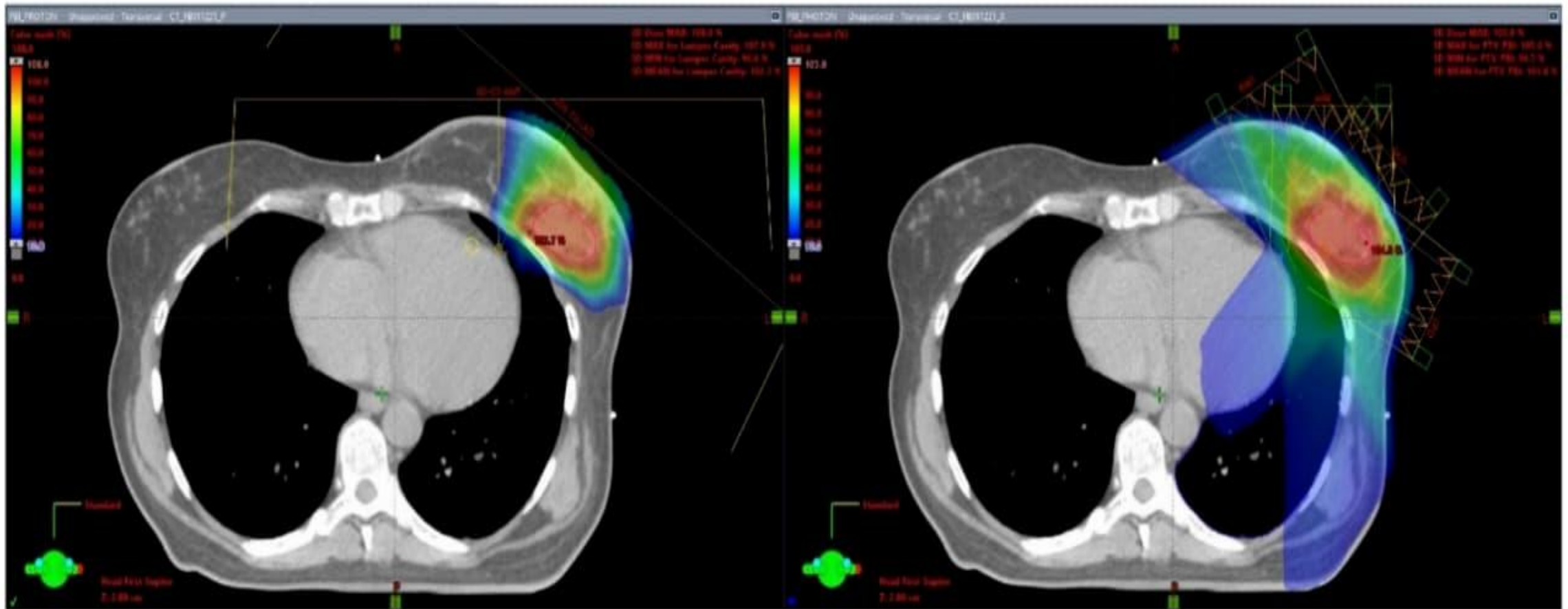
EBRT

- 3.85Gy bid 10# 38Gy
- NSABP B39/RTOG 04-13: Phase III trial
- RAPID: Phase III trial
- FLORENCE TRIAL – IMRT 30Gy in 5#
- Better cosmesis and toxicity

Poor cosmesis



PROTON Vs PHOTON IN PBI



NCCN 2026

PRINCIPLES OF RADIATION THERAPY

Accelerated Partial Breast Irradiation (APBI)/Partial Breast Irradiation (PBI)

- The NCCN Panel endorses APBI/PBI for any patient without germline *BRCA1/2* PVs who meets the criteria outlined in the 2024 ASTRO guidelines. Patients aged ≥ 40 years are recommended for APBI/PBI if they have:
 - Invasive ER-positive ductal carcinoma measuring ≤ 2 cm (pT1 disease), grade 1–2, with negative margin widths, no LVSI, and negative nodes
 - Or
 - DCIS measuring size ≤ 2 cm with low-intermediate grade with negative margins
- APBI offers comparable local control and comparable or improved cosmesis to whole breast RT when delivered with the following dose regimens. The APBI regimens have not been compared directly but 30 Gy/5 fractions is preferred based on the highest rated cosmesis outcomes.
- RT dosing:

Dose	Regimen
EBRT APBI	
30 Gy/5 fractions QOD (preferred); IMRT/VMAT protocol mandated	• Livi L, Meattini I, Marrazzo L, et al. Accelerated partial breast irradiation using intensity-modulated radiotherapy versus whole breast irradiation: 5-year survival analysis of a phase 3 randomised controlled trial. <i>Eur J Cancer</i> 2015;51:451-463. • Meattini I, Marrazzo L, Saieva C, et al. Accelerated partial-breast irradiation compared with whole-breast irradiation for early breast cancer: Long-term results of the randomized phase III APBI-IMRT-Florence Trial. <i>J Clin Oncol</i> 2020;38:4175-4183. • Franceschini D, Loi M, Chiola I, et al. Preliminary results of a randomized study on postmenopausal women with early stage breast cancer: Adjuvant hypofractionated whole breast irradiation versus accelerated partial breast irradiation (HYPAB Trial). <i>Clin Breast Cancer</i> 2021;21:231-238. • Lo Faro L, Fogliata A, Franceschini D, et al. Adjuvant hypofractionated whole breast irradiation (WBI) vs. accelerated partial breast irradiation (APBI) in postmenopausal women with early stage breast cancer: 5 years update of the HYPAB trial. <i>Clin Breast Cancer</i> 2024;24:253-260.
40 Gy/15 fractions	• Coles CE, Griffin CL, Kirby AM, et al. Partial-breast radiotherapy after breast conservation surgery for patients with early breast cancer (UK IMPORT LOW trial): 5-year results from a multicentre, randomised, controlled, phase 3, non-inferiority trial. <i>Lancet</i> 2017;390:1048-1060.
Brachytherapy APBI (including balloon/interstitial)	
34 Gy/10 fractions BID; 32 Gy/8 fractions BID; 30.1 Gy/7 fractions BID	• Vicini FA, Cecchini RS, White JR, et al. Long-term primary results of accelerated partial breast irradiation after breast-conserving surgery for early-stage breast cancer: a randomised, phase 3, equivalence trial. <i>Lancet</i> 2019;394:2155-2164. • Strnad V, Ott OJ, Hildebrandt G, et al. 5-year results of accelerated partial breast irradiation using sole interstitial multicatheter brachytherapy versus whole-breast irradiation with boost after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: a randomised, phase 3, non-inferiority trial. <i>Lancet</i> 2016;387:229-238. • Polgár C, Ott OJ, Hildebrandt G, et al. Late side-effects and cosmetic results of accelerated partial breast irradiation with interstitial brachytherapy versus whole-breast irradiation after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: 5-year results of a randomised, controlled, phase 3 trial. <i>Lancet Oncol</i> 2017;18:259-268.

Postmastectomy Radiation Therapy: An ASTRO-ASCO-SSO Clinical Practice Guideline

Rachel B. Jimenez, MD¹ ; Yara Abdou, MD² ; Penny Anderson, MD³; Parul Barry, MD⁴; Lisa Bradfield, BA⁵; Julie A. Bradley, MD⁶; Lourdes D. Heras, MPH⁷; Atif Khan, MD, MS⁸ ; Cindy Matsen, MD⁹ ; Rachel Rabinovitch, MD¹⁰ ; Chantal Reyna, MD, MHA¹¹; Kilian E. Salerno, MD¹²; Sarah E. Schellhorn, MD¹³ ; Deborah Schofield, PhD¹⁴; Kekoa Taparra, MD, PhD, MPH¹⁵; Iman Washington, MD¹⁶ ; Jean L. Wright, MD¹⁷ ; Youssef H. Zeidan, MD, PhD¹⁸ ; Richard C. Zellars, MD¹⁹; and Kathleen C. Horst, MD²⁰

DOI <https://doi.org/10.1200/JCO-25-01747>



Postmastectomy Radiation Therapy

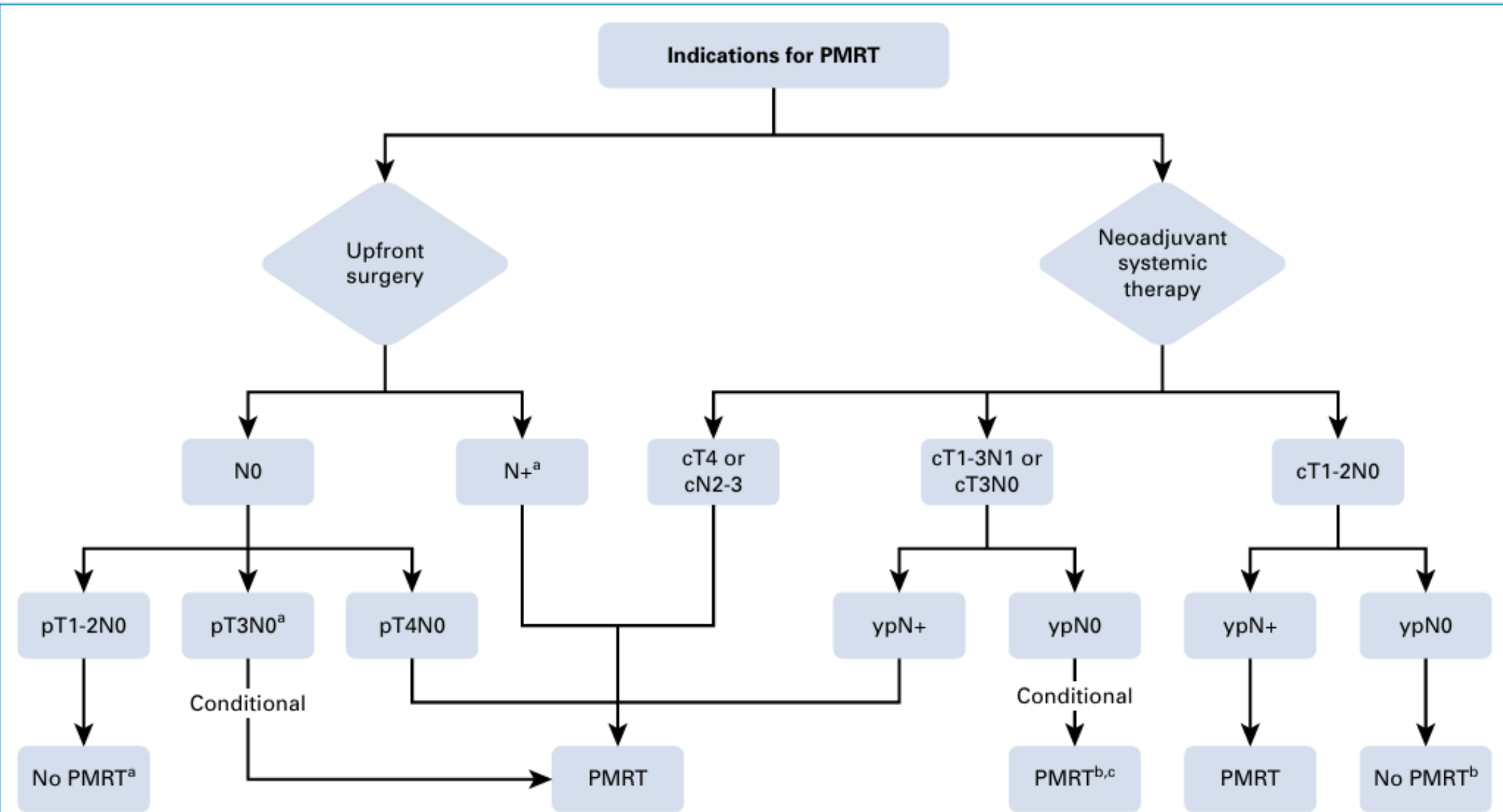
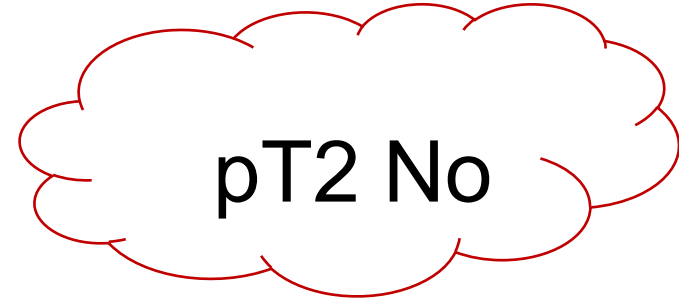


TABLE 3. Indications for PMRT With Mastectomy as Initial Treatment

KQ1 Recommendation	Strength of Recommendation	Quality of Evidence (refs)
1. For patients with node-positive (pN+) breast cancer, PMRT is recommended <i>Implementation remarks:</i> Omission of PMRT may be appropriate for select patients with pN1mic or low nodal burden pN1a disease following ALND who have favorable clinicopathologic features. Favorable clinicopathologic features include pT1-2 disease, low-to-intermediate grade HR-positive/HER2-negative subtype, postmenopausal status, absence of LVI, and a low 21-gene recurrence score.	Strong	High ^{2,8-12}
2. For patients with any pT4 breast cancer, PMRT is recommended even in the absence of any other risk factors.	Strong	High ^{2,8}
3. For patients with pT3N0 breast cancer, PMRT is conditionally recommended. <i>Implementation remark:</i> PMRT may be omitted or treatment volumes reduced (eg, chest wall alone) for patients with favorable clinicopathologic features including low-to-intermediate grade, HR-positive/HER2-negative subtype, postmenopausal status, absence of LVI, and a low 21-gene recurrence score.	Conditional	High ^{2,8,10}
4. For patients with pT1-2N0 breast cancer, PMRT is not recommended. <i>Implementation remark:</i> Select patients with pT1-2N0 breast cancer who have multiple unfavorable clinicopathologic features (eg, triple-negative, high histologic grade, LVI, young age, and/or central/medially located tumors) may benefit from PMRT.	Strong	Low ^{2,13,14}
5. For patients with positive surgical margins after mastectomy and no other indication for PMRT, RT to the chest wall/reconstructed breast alone is conditionally recommended.	Conditional	Expert opinion

ASTRO ASCO pT3No

- NO RT
- Postmenopausal
- Low or intermediate grade
- HR+ and Her negative
- Absence of LVI
- Low 21 gene recurrence score



- Consider RT - High risk recurrence factors
- Central / medial tumor
- Grade 3
- ER NEG (Triple negative)
- Young age / longevity
- LVI

-
- pT2No
 - Consider RT - High risk recurrence factors
 - Central / medial tumor
 - Grade 3
 - ER NEG (Triple negative)
 - Young age / longevity
 - LVI
 - Inadequate lymphnode dissection

	LRR AFTER 10 YEARS
LRR	6%
1 RISK FACTOR	10%
2 RISK FACTORS	18%
3 OR MORE	40%

3. Which famous actress underwent bilateral prophylactic mastectomy

- A. Anna Hathaway
- B. Jennifer Lawrence
- C. Angelina Jolie
- D. Sandra Bullock

LOCOREGIONAL TREATMENT OF cT1–3, cN0 or cN+, M0 DISEASE^{a,k}: MASTECTOMY ± PMRT

SURGERY

ADJUVANT SYSTEMIC THERAPY

PATHOLOGIC NODAL STATUS

RT

Nipple-sparing, skin-sparing, or total mastectomy with surgical axillary staging^{m,n} (category 1) ± reconstruction^w

See [BINV-4](#) to determine whether adjuvant systemic therapy is indicated. RT is typically given after systemic therapy. See [BINV-1](#) for sequencing of systemic therapy and RT.

Negative axillary nodes (pN0/pN0[i+]) and ≤pT2 (≤5 cm) and negative margins

→ No RT^y

Negative axillary nodes and pT3 (>5 cm)

Consider PMRT^t to chest wall ± comprehensive RNI (including any portion of the undissected axilla at risk).^z

1–3 positive axillary nodes^x

Strongly consider PMRT^t to chest wall + comprehensive RNI (including any portion of the undissected axilla at risk).

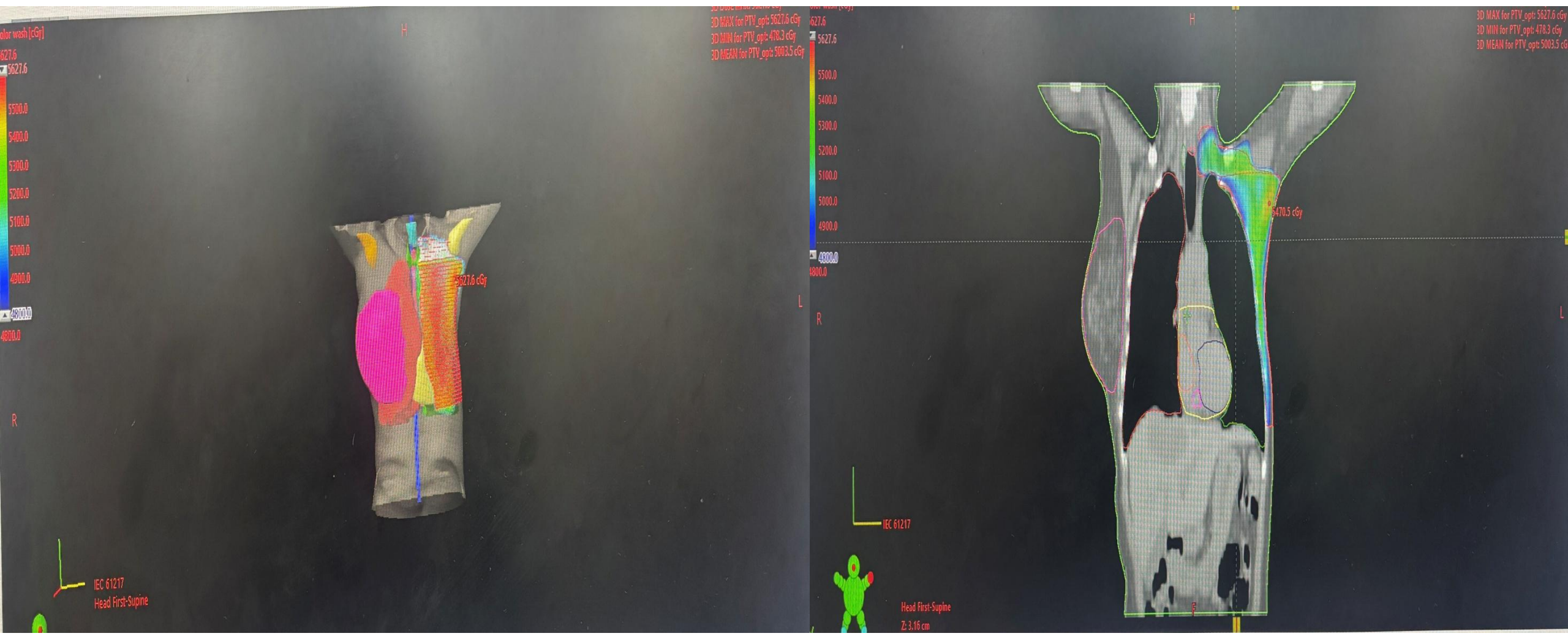
≥4 positive axillary nodes^s

PMRT^t to chest wall + comprehensive RNI (including any portion of the undissected axilla at risk) (category 1).

Any pT/pN with positive margins

Re-excision to negative margins is preferred. If not feasible, then strongly consider PMRT^t to chest wall ± comprehensive RNI (including any portion of the undissected axilla at risk).

PMRT





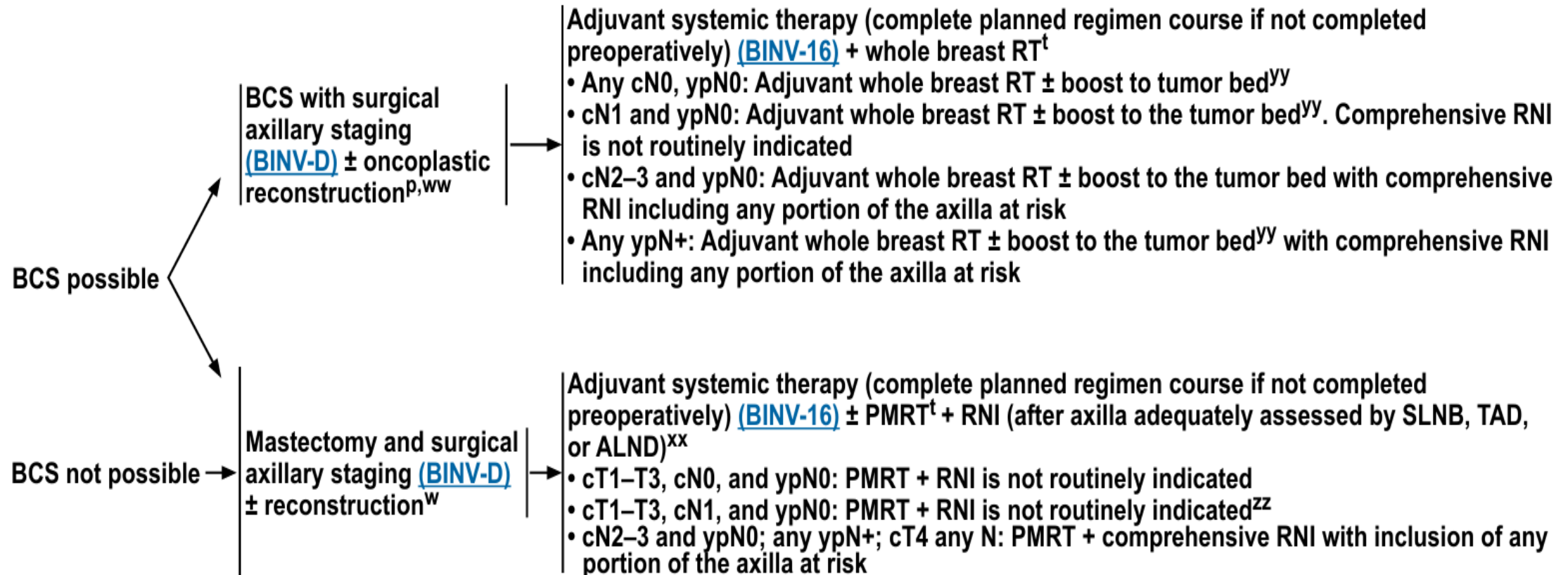
Operable disease after neoadjuvant chemo

OPERABLE DISEASE:

SURGICAL TREATMENT AND ADJUVANT THERAPY AFTER PREOPERATIVE SYSTEMIC TREATMENT^{ww}

SURGICAL TREATMENT

ADJUVANT SYSTEMIC THERAPY^k AND RT

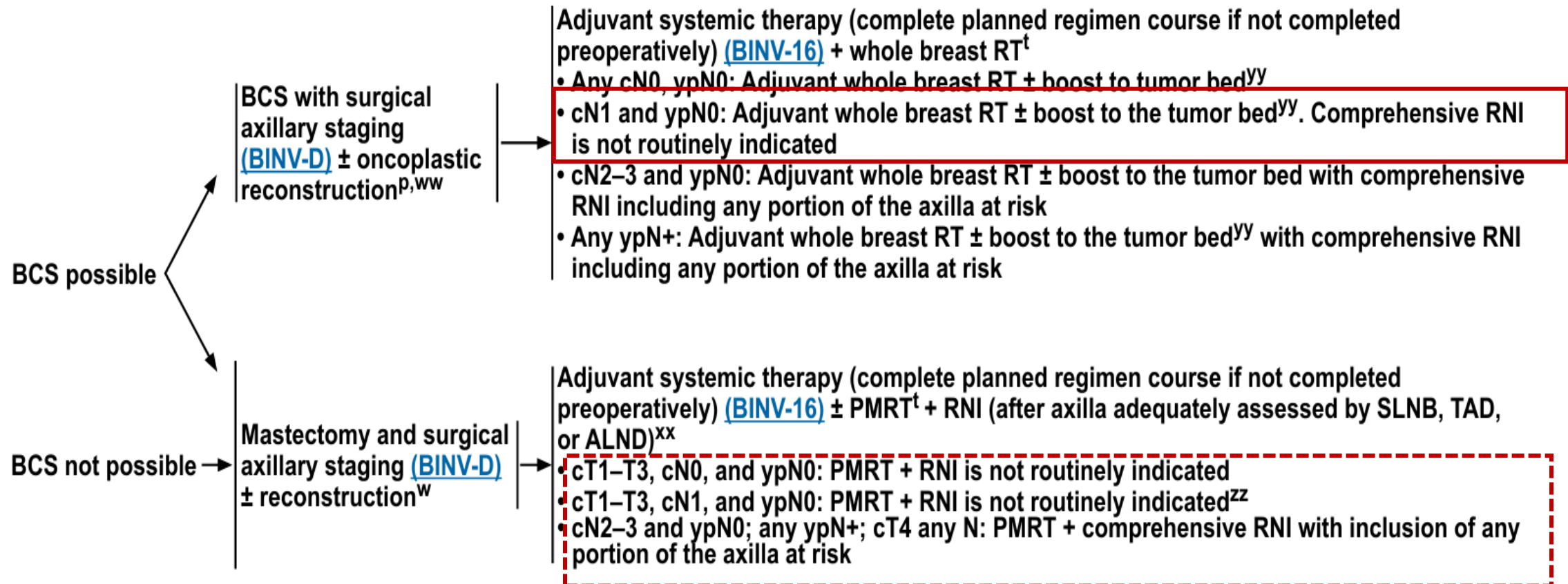


OPERABLE DISEASE:

SURGICAL TREATMENT AND ADJUVANT THERAPY AFTER PREOPERATIVE SYSTEMIC TREATMENT^{ww}

SURGICAL TREATMENT

ADJUVANT SYSTEMIC THERAPY^k AND RT



4. What is the optimal strategy for axillary management in patients with residual node-positive/negative disease after neoadjuvant chemotherapy?"

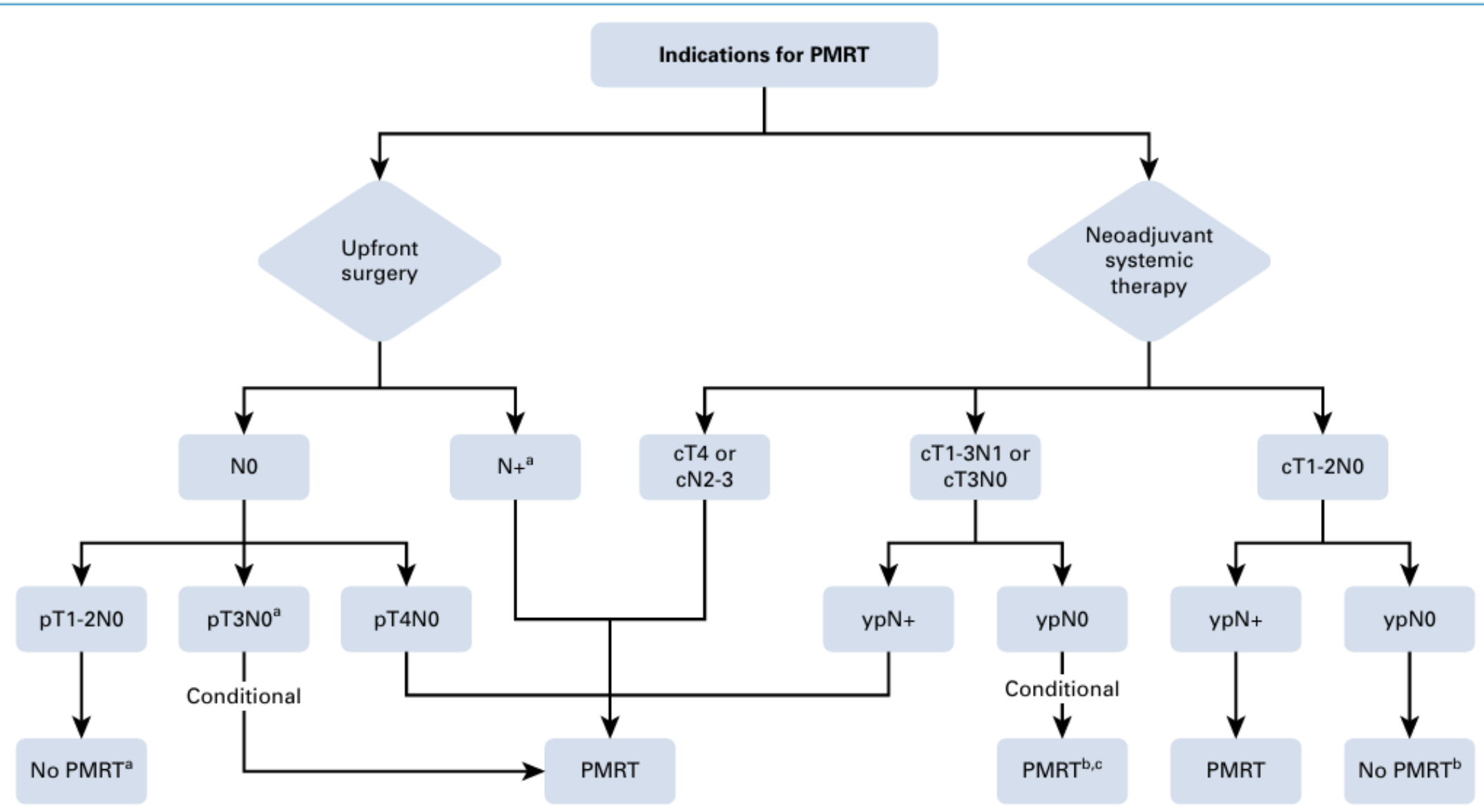
A. SLND

B. ALND

C. TAD

D. SLNB

Postmastectomy Radiation Therapy



NSABP 51

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Omitting Regional Nodal Irradiation after Response to Neoadjuvant Chemotherapy

E.P. Mamounas,¹ H. Bandos,^{2,3} J.R. White,⁴ T.B. Julian,⁵ A.J. Khan,⁶ S.F. Shaitelman,⁷ M.A. Torres,⁸ F.A. Vicini,⁹ P.A. Ganz,^{10,11} S.A. McCloskey,¹² P.C. Lucas,¹³⁻¹⁶ N. Gupta,¹⁷ X.A. Li,¹⁸ B. McCormick,⁶ B. Smith,⁷ R.D. Tendulkar,^{19,20} V.S. Kavadi,²¹ K. Matsumoto,²² S.A. Seaward,²³ W.J. Irvin, Jr.,²⁴ J.Y. Lin,⁸ R.W. Mutter,²⁵ T.M. Muanza,²⁶ J. Stromberg,²⁷ R. Jagsi,⁸ A.C. Weiss,²⁸ W.J. Curran, Jr.,²⁹ and N. Wolmark^{14,15,30}

Clinical group — no. (%)		
Hispanic or Latino	118 (14.4)	114 (13.9)
Not Hispanic or Latino	675 (82.3)	682 (83.1)
Unknown	27 (3.3)	25 (3.0)
Type of surgery — no. (%)		
Lumpectomy	473 (57.7)	474 (57.7)
Mastectomy	347 (42.3)	347 (42.3)
Clinical tumor stage — no. (%)‡		
T1	170 (20.7)	171 (20.8)
T2	499 (60.9)	484 (59.0)
T3	151 (18.4)	166 (20.2)
HR status — no. (%)		
Negative	386 (47.1)	382 (46.5)
Positive	434 (52.9)	439 (53.5)
HER2 status — no. (%)		
Negative	355 (43.3)	356 (43.4)
Positive	465 (56.7)	465 (56.6)
Tumor subtype — no. (%)		
Triple negative	191 (23.3)	175 (21.3)
HR positive and HER2 negative	164 (20.0)	181 (22.0)
HR negative and HER2 positive	195 (23.8)	207 (25.2)
HR positive and HER2 positive	270 (32.9)	258 (31.4)
Adjuvant chemotherapy — no. (%)		
No	813 (99.1)	817 (99.5)
Yes	7 (0.9)	4 (0.5)
Pathological complete response in breast — no. (%)		
Absent	176 (21.5)	182 (22.2)
Present	644 (78.5)	639 (77.8)

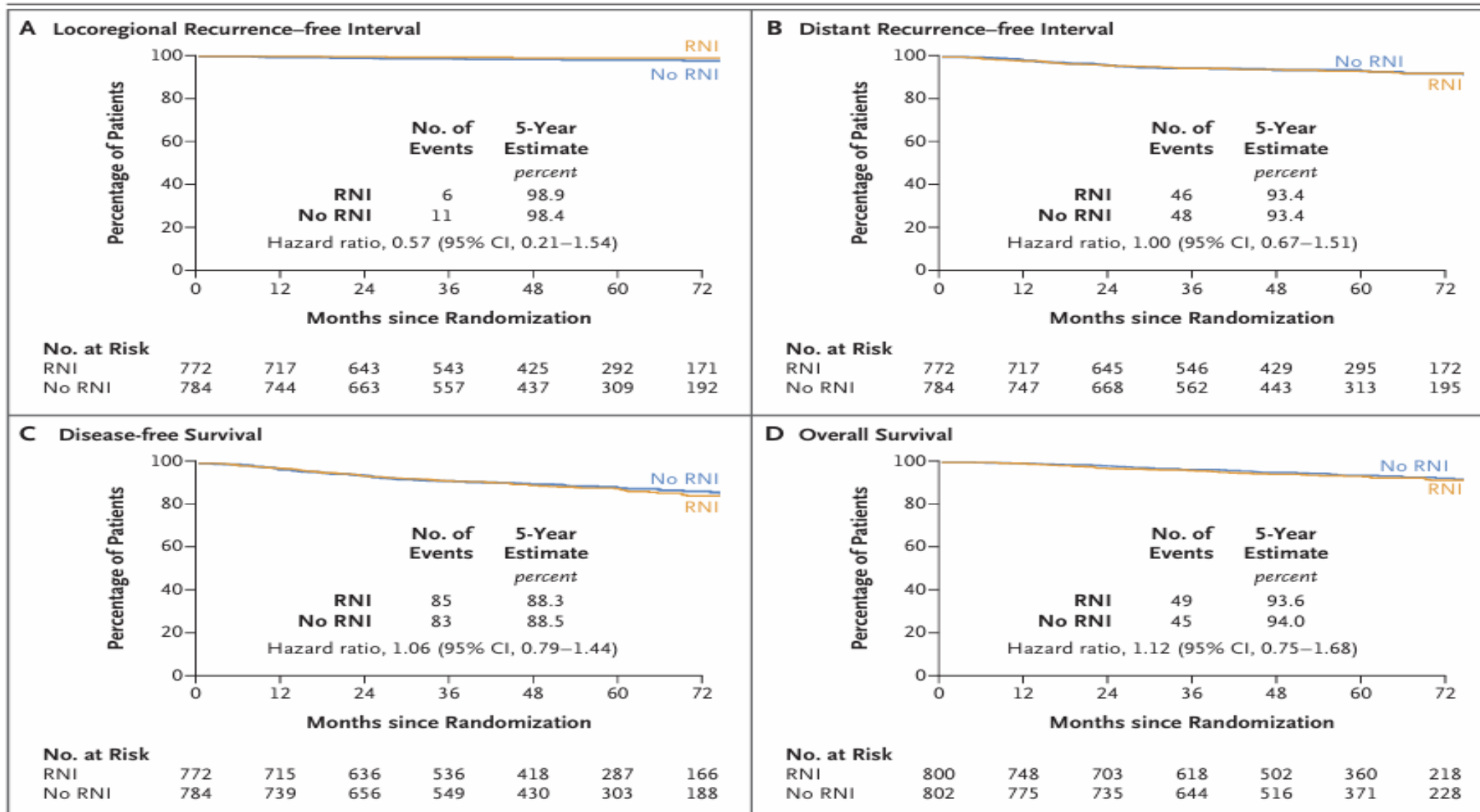
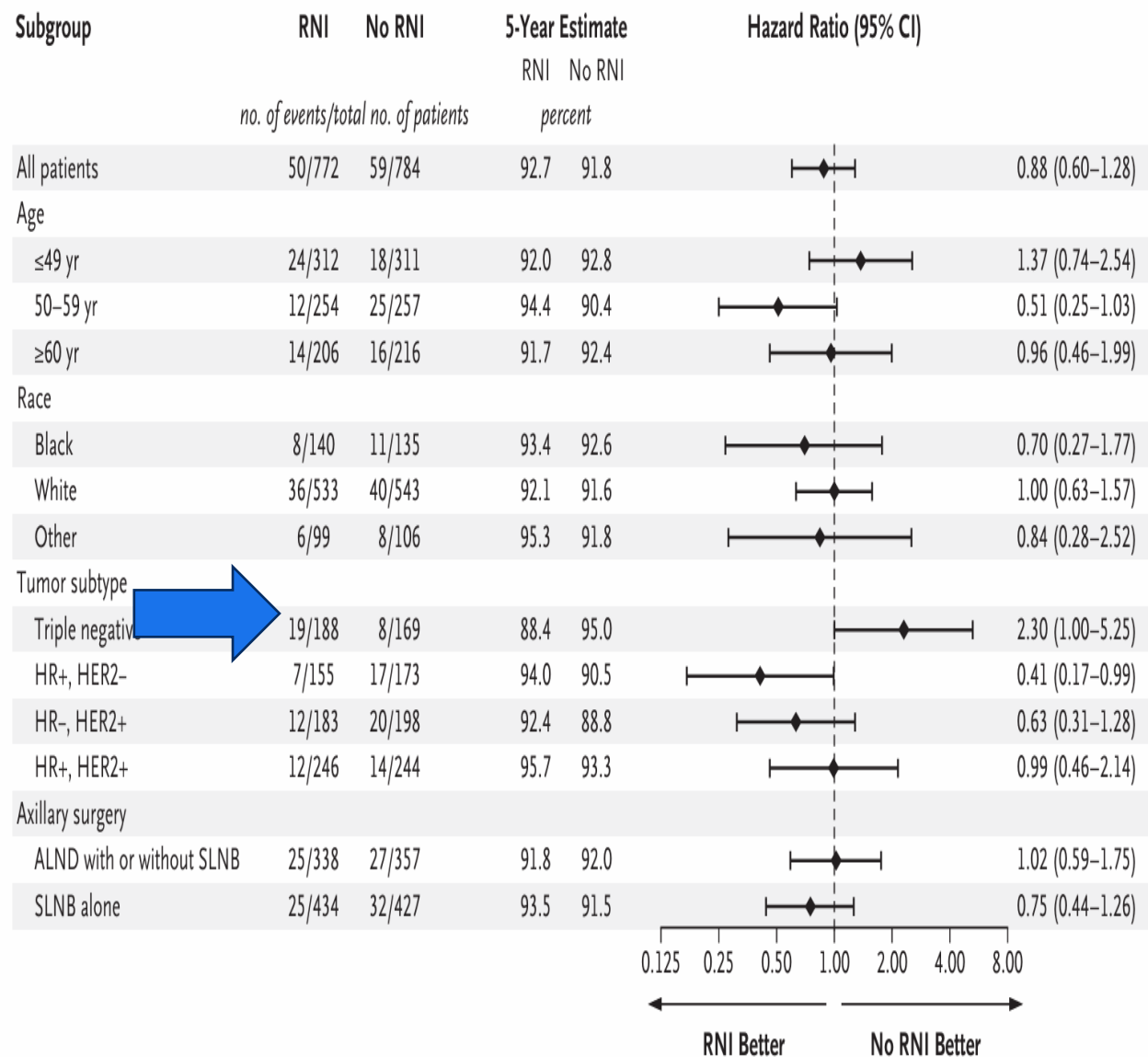


Figure 2. Effects of Regional Nodal Irradiation on Secondary End Points.

Shown are effects of regional nodal irradiation on the locoregional recurrence-free interval (Panel A), the distant recurrence-free interval (Panel B), disease-free survival (Panel C), and overall survival (Panel D).

B Exploratory Analysis



CONCLUSION:
 patients with positive axillary lymph nodes(N1) who reach stage ypN0 after neoadjuvant chemotherapy have low rates of disease recurrence and do not receive a statistically significant benefit from regional nodal irradiation at 5 years.

NO RNI FOR ypNo



The EORTC 22922/10925 trial investigating regional nodal irradiation in stage I-III breast cancer: Outcomes according to locoregional and systemic therapies

Orit Kaidar-Person^{a b c}  , Liesbeth J. Boersma^c, Peter De Brouwer^d, Caroline Weltens^e, Carine Kirkove^f, Karine Peignaux-Casasnovas^g, Volker Budach^h, Femke van der Leijⁱ, Max Peters^j, Nicola Weidner^k, Sofia Rivera^l, Geertjan van Tienhoven^m, Alain Fourquetⁿ, Georges Noel^o, Mariacarla Valli^p, Matthias Guckenberger^q, Eveline Koiter^r, Severine Racadot^s, Roxolyana Abdah-Bortnyak^t, Harry Bartelink^u...Philip M. Poortmans^{d x y}

Long-term EORTC trial challenges assumptions about lymph node radiation therapy in breast cancer

— 17 May 2026

Stockholm, Sweden, 17 May 2026 — Final results from a landmark EORTC randomised trial with more than 20 years of follow-up show that irradiation of the internal mammary and medial supraclavicular lymph nodes reduces breast cancer mortality but does not improve overall survival. The findings highlight the importance of very long-term follow-up when evaluating cancer treatments, particularly in patients with otherwise favourable prognosis.



ESTRO 2026

Regional Nodal Irradiation in Early-Stage Breast Cancer

Authors: Timothy J. Whelan, B.M., B.Ch., Ivo A. Olivotto, M.D., Wendy R. Parulekar, M.D., Ida Ackerman, M.D., Boon H. Chua, M.B., B.S., Ph.D., Abdenour Nabid, M.D., Katherine A. Vallis, M.B., B.S., Ph.D., [+16](#), for the MA.20 Study Investigators* [Author Info & Affiliations](#)

Published July 23, 2015 | N Engl J Med 2015;373:307-316 | DOI: 10.1056/NEJMoa1415340 | [VOL. 373 NO. 4](#)
[Copyright © 2015](#)

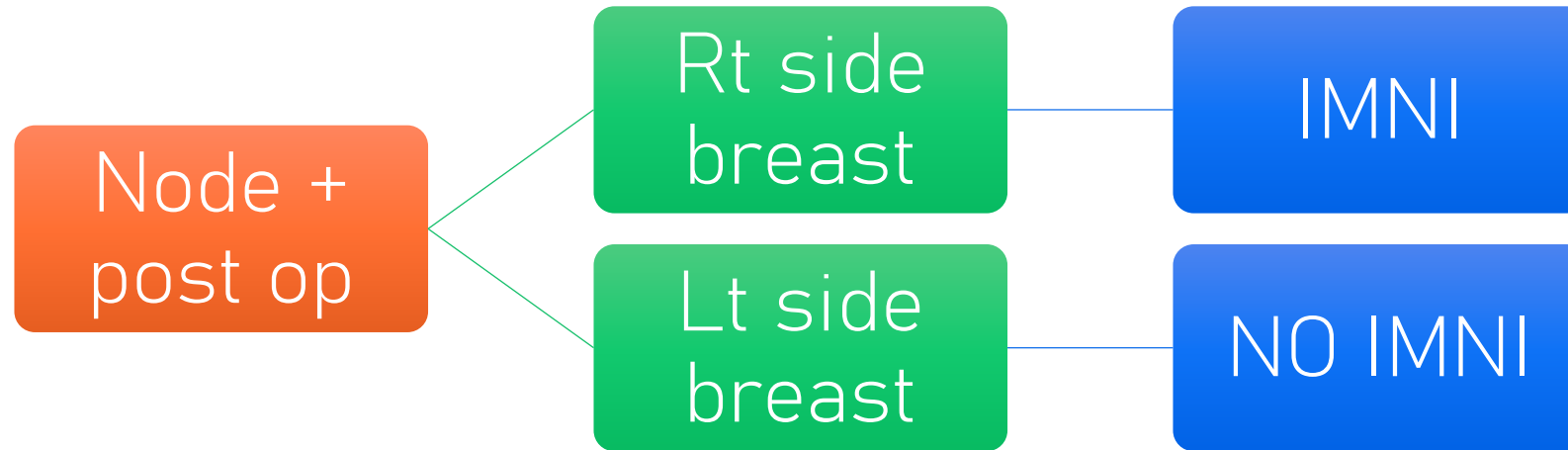
- MA 20 TRIAL (2000- 2007)
- No improvement in OS but reduction in LR recurrence.

Internal mammary node irradiation in 4541 node-positive breast cancer patients treated with newer systemic therapies and 3D-based radiotherapy (DBCG IMN2): a prospective, nationwide, population-based cohort study

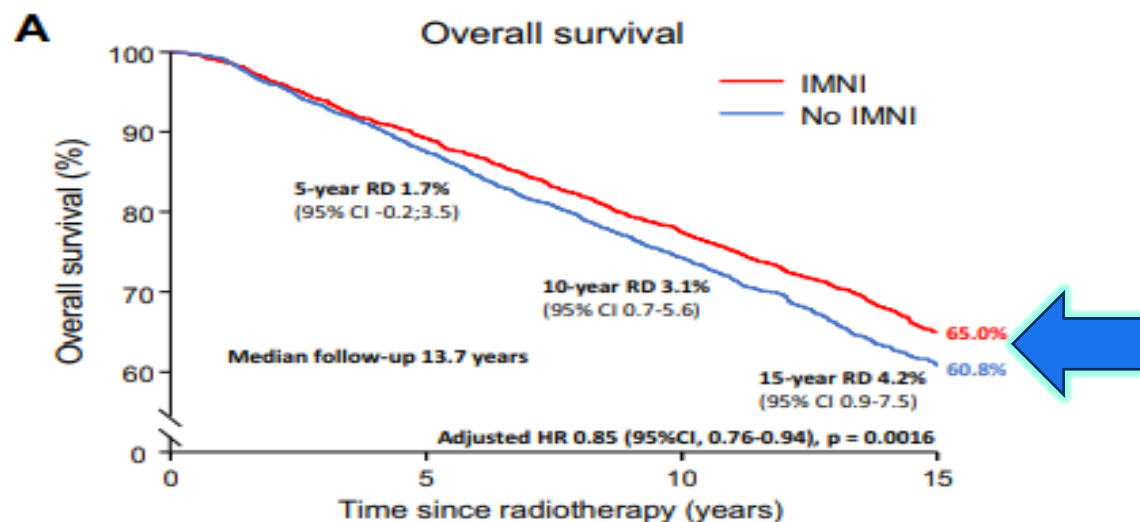
Anders W. Mølby Nielsen,^{a,b,*} Lise B. J. Thorsen,^{a,b,c} Demet Özcan,^{a,d} Louise W. Matthiessen,^e Else Maae,^f Marie L. H. Milo,^g Mette H. Nielsen,^h Trine Tramm,^{a,d} Jens Overgaard,^{a,b} and Birgitte V. Offersen,^{a,b,c,i} on behalf of the DBCG RT Committee

^aDepartment of Experimental Clinical Oncology, Aarhus University Hospital, Aarhus, Denmark

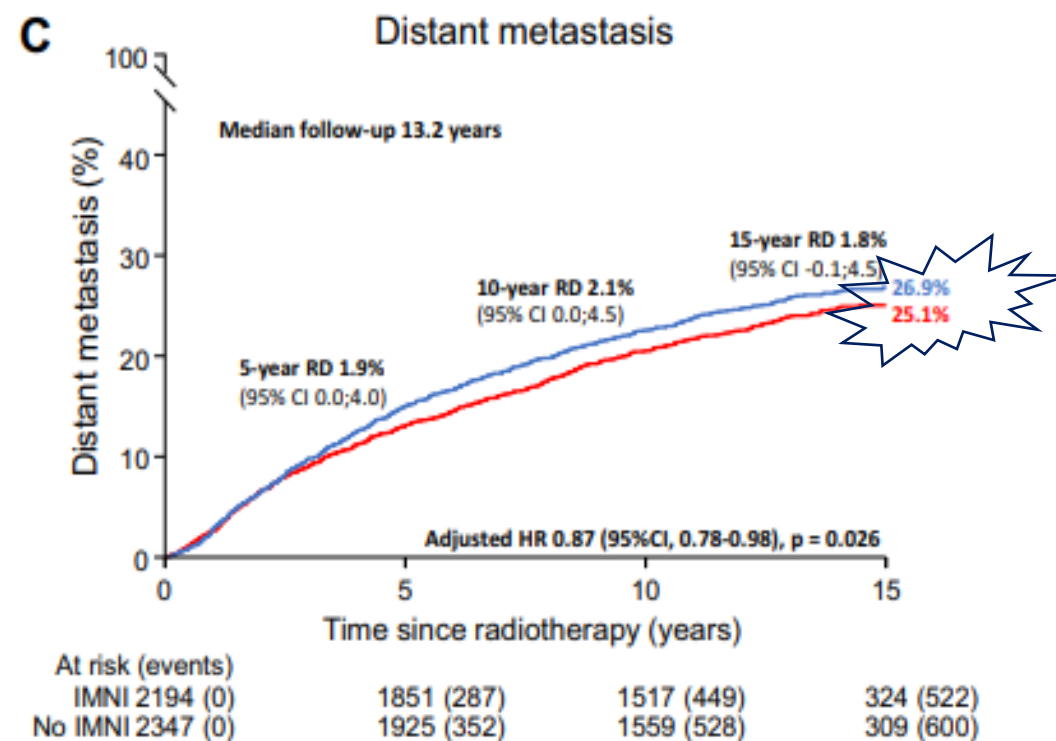
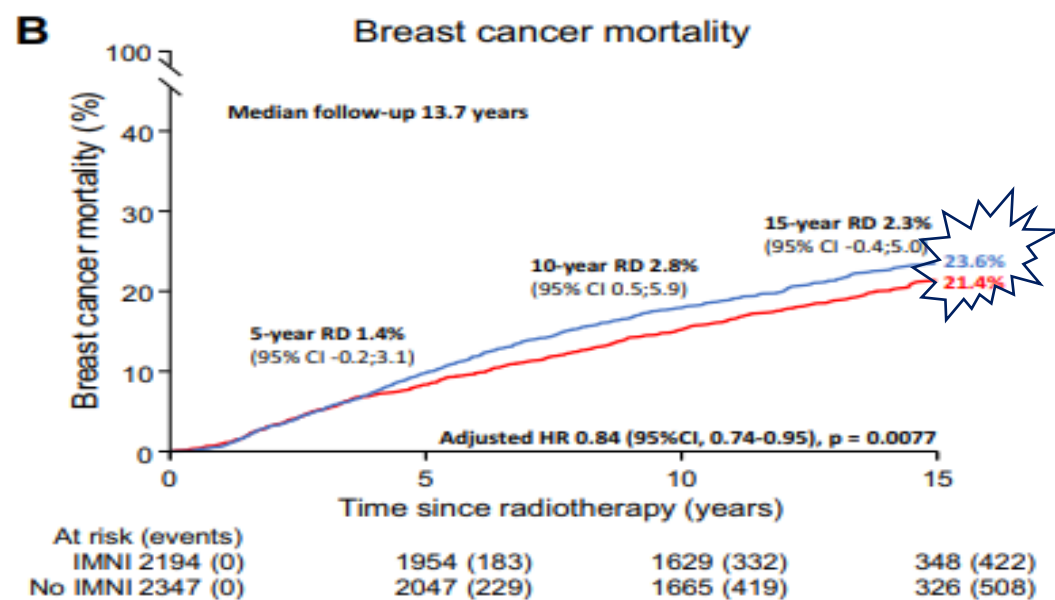
- Largest study to evaluate the effect of IMN RT in high-risk breast cancer patients treated with 3D-based RT & newer systemic therapies(from 2007-2014) •
- To see the efficacy of IMN RT in the lowest nodal burden of 1–3 positive axillary nodes.
- Node + breast cancer ; post BCS/ Mastectomy



Endpoint Primary : OS
Secondary: 1.Breast cancer mortality
2.Distant mets



IMNI improves OS.
Added benefit in modern
systemic therapy and RT
techniques.....

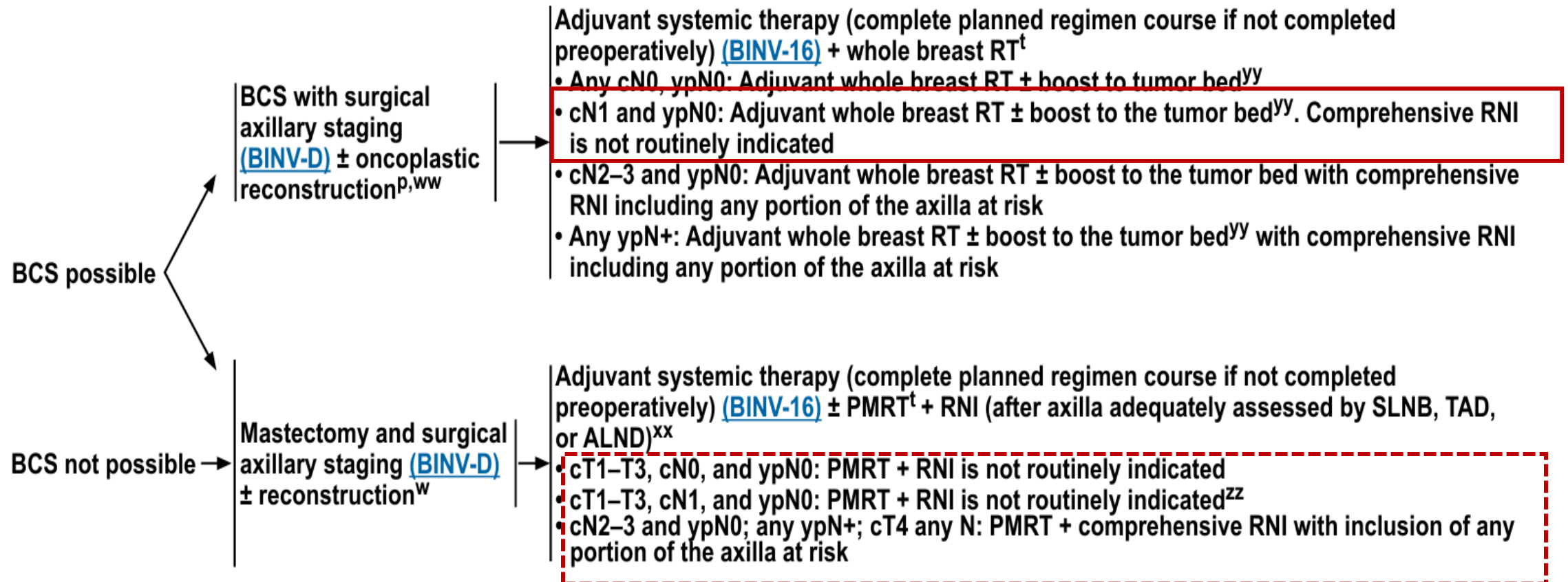


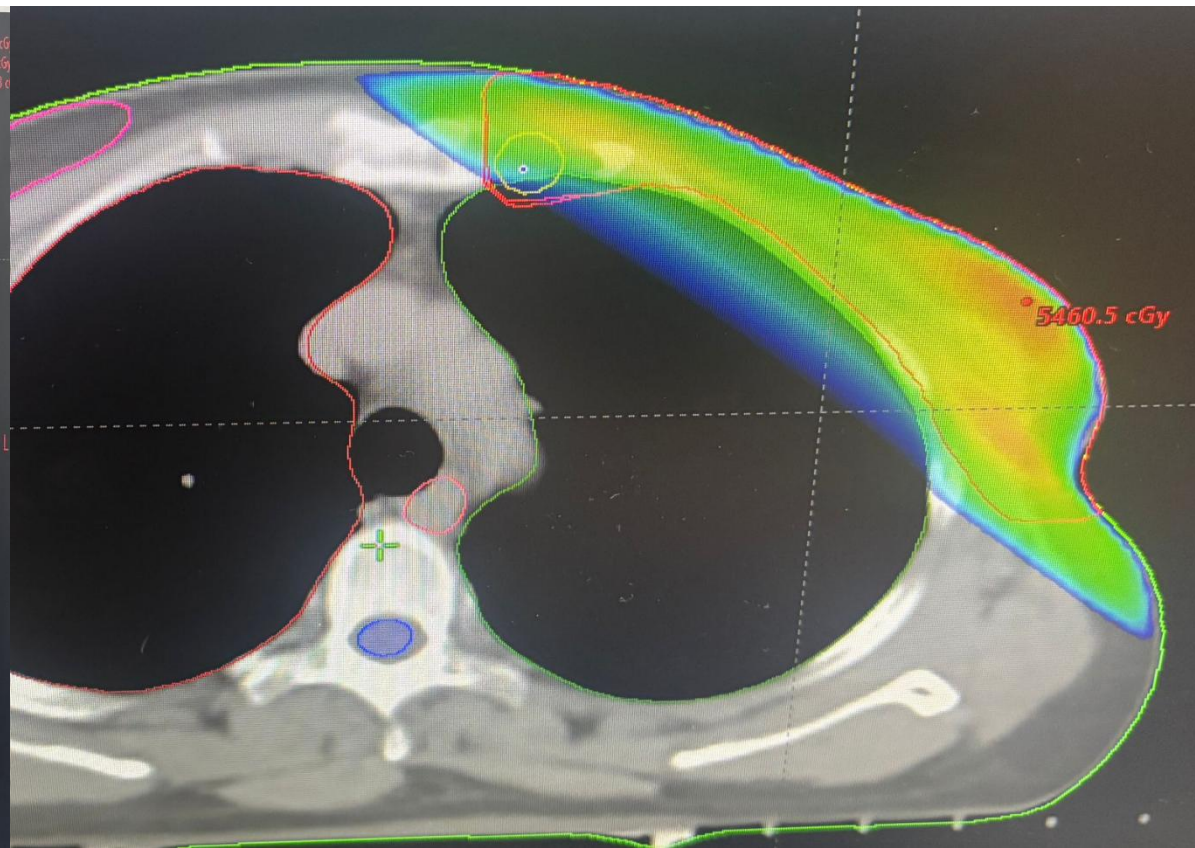
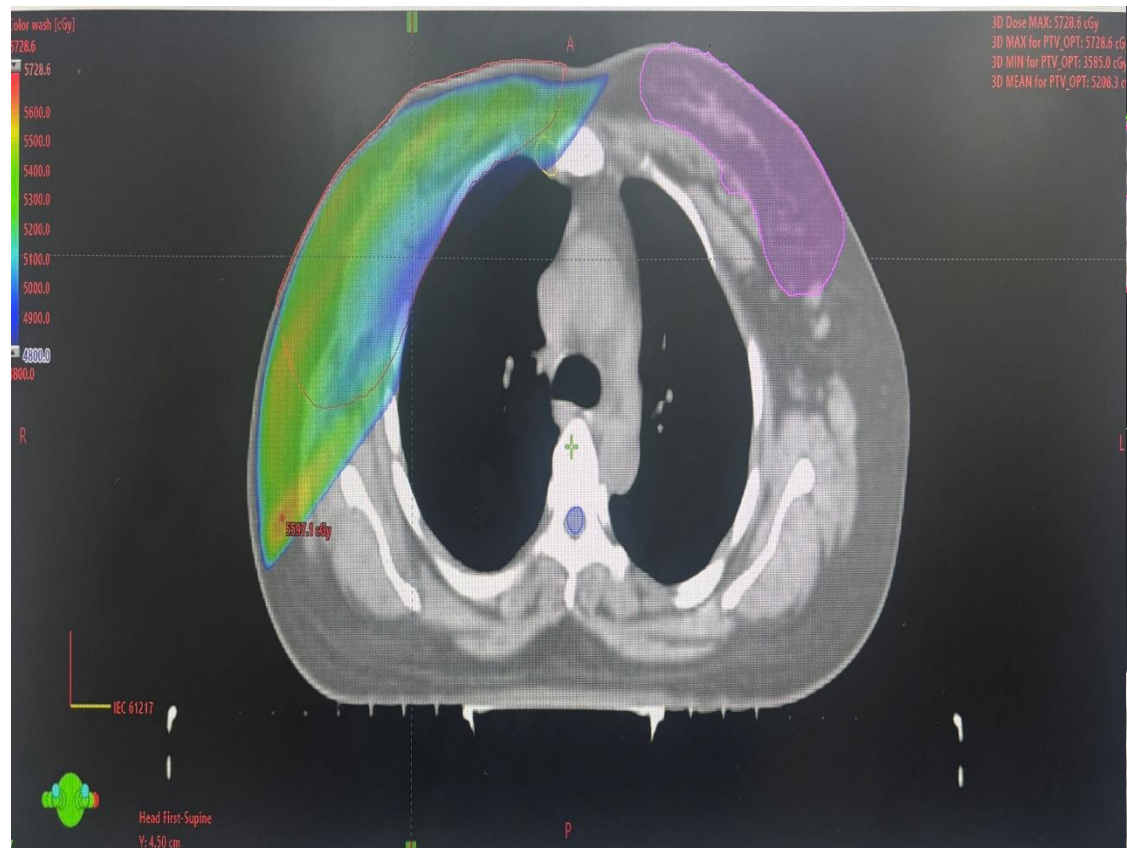
OPERABLE DISEASE:

SURGICAL TREATMENT AND ADJUVANT THERAPY AFTER PREOPERATIVE SYSTEMIC TREATMENT^{ww}

SURGICAL TREATMENT

ADJUVANT SYSTEMIC THERAPY^k AND RT



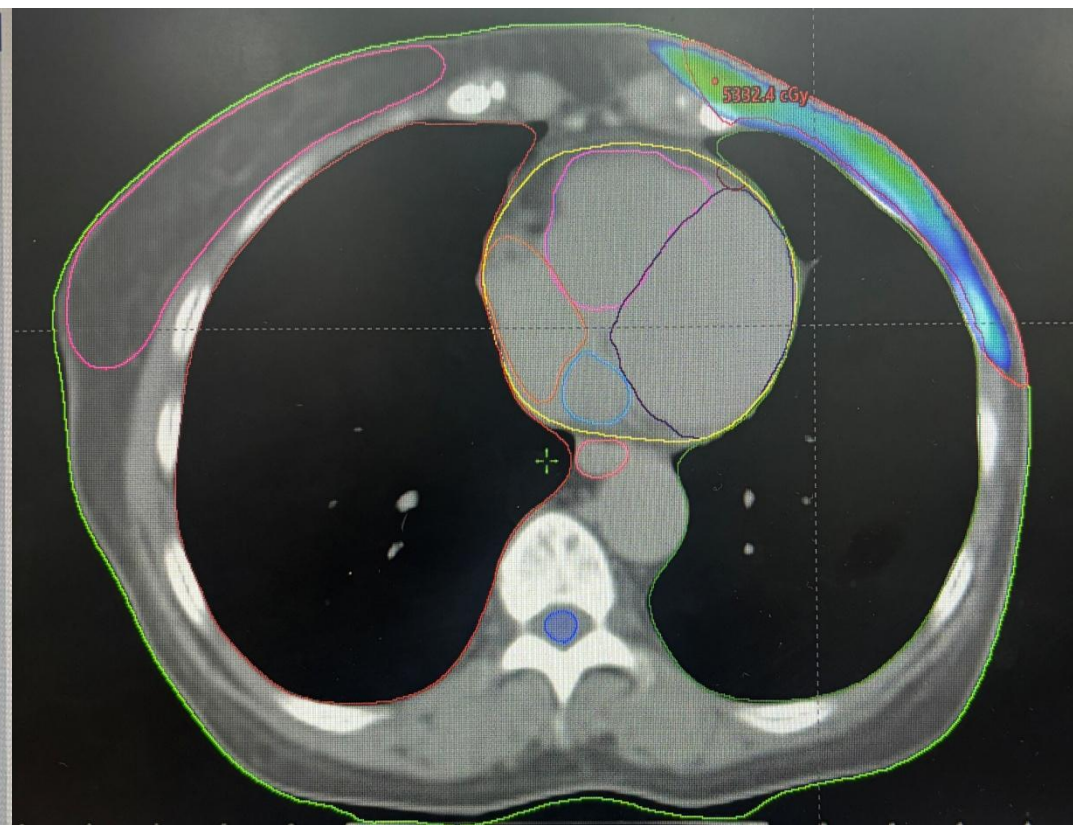
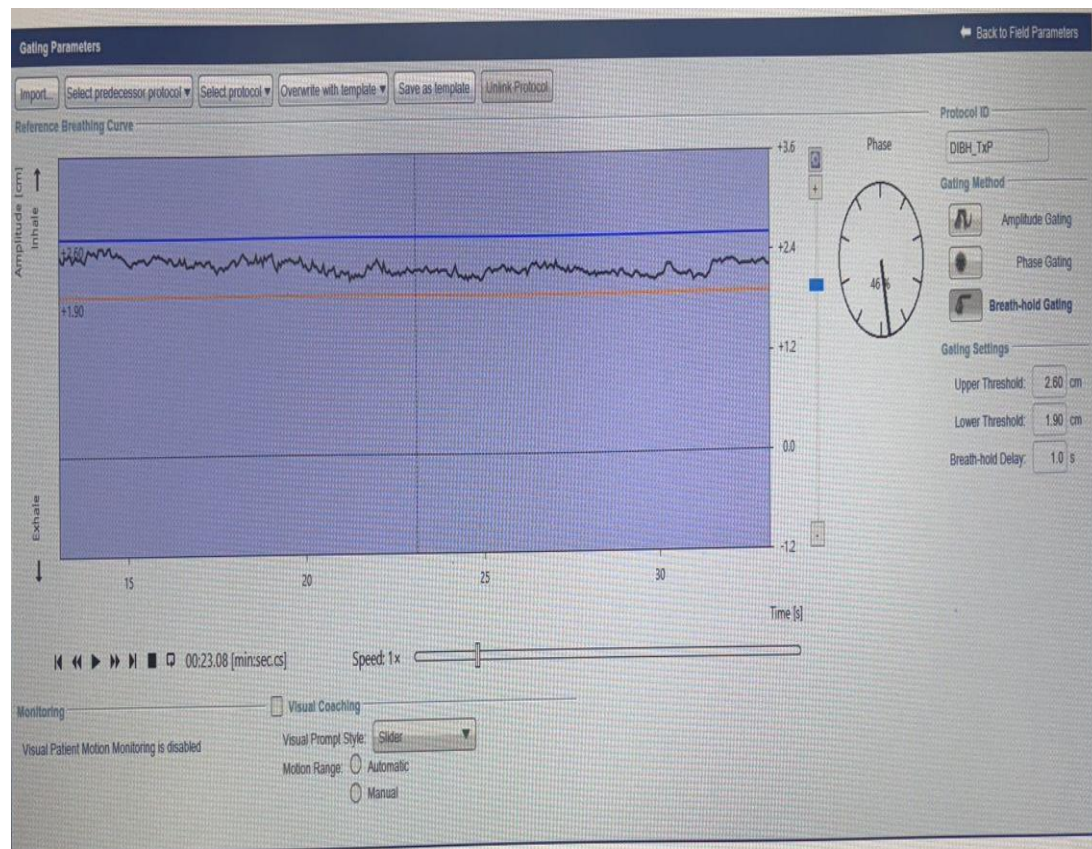


5. Heart V25Gy volume should be below–

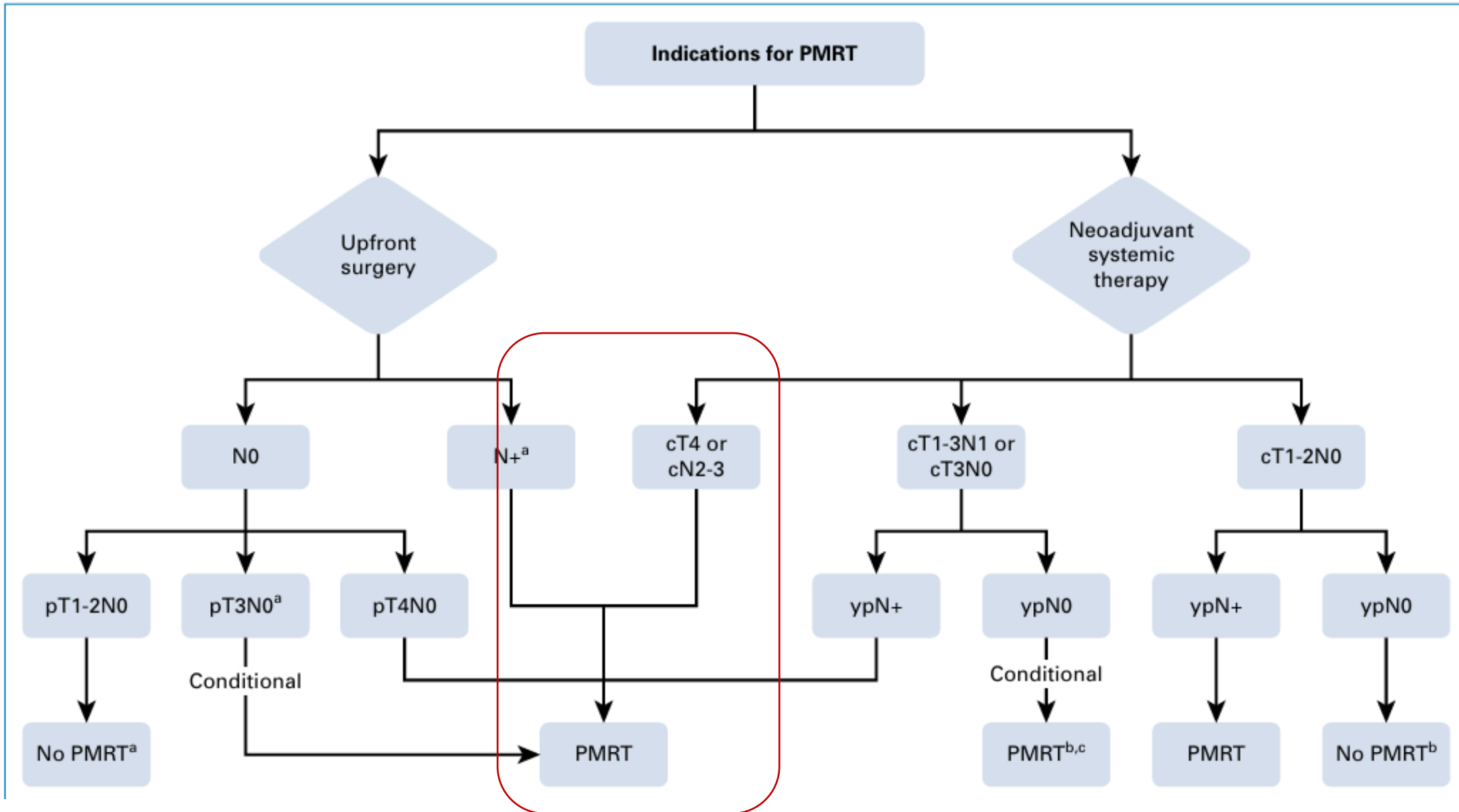
- A. 20%
- B. 25%
- C. 10%
- D. 15%

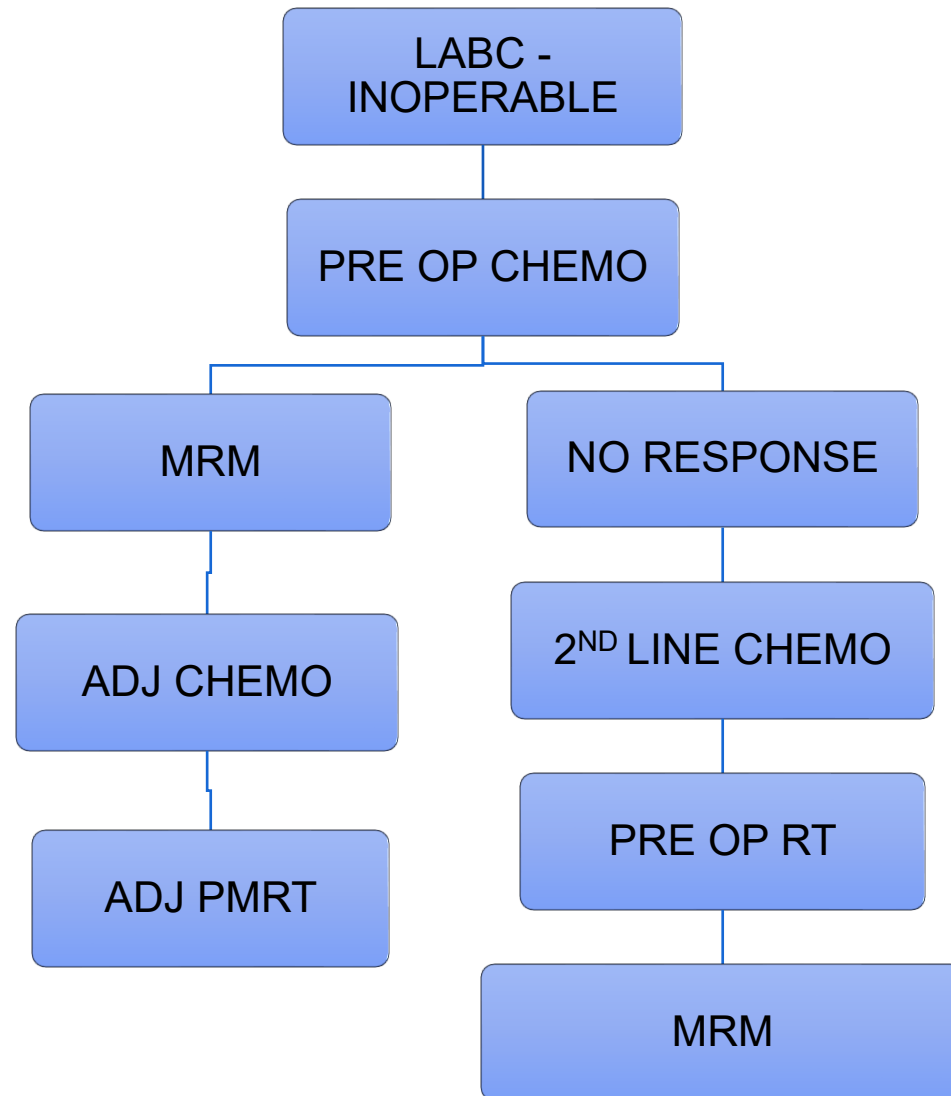
For 1Gy increase in mean heart dose – 7.4% increase in MCE

DIBH



Postmastectomy Radiation Therapy





Neoadjuvant radiotherapy in the approach of locally advanced breast cancer

[Cláudia Sousa](#)^{1,✉}, [Mafalda Cruz](#)¹, [Ana Neto](#)¹, [Kayla Pereira](#)¹, [Marta Peixoto](#)², [Joana Bastos](#)³, [Mónica Henriques](#)¹, [Domingos Roda](#)¹, [Rui Marques](#)¹, [Cristina Miranda](#)¹, [Gilberto Melo](#)¹, [Gabriela Sousa](#)², [Paulo Figueiredo](#)⁴, [Paula Alves](#)¹

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PMCID: PMC7082639 PMID: [32152044](#)

Neoadjuvant Radiation Therapy in the Treatment of Breast Cancer

[H. Kristofovicova](#)  · [C. Cifuentes](#) · [C. Carvajal](#) · [V. Lopez](#) · [V. Salvador](#) · [C. Osorio](#)

[Affiliations & Notes](#) ▼ [Article Info](#) ▼

CONCLUSION:

- Improves operability rates - MRM
- Achieves meaningful pCR,
- survival outcomes increased.
- With acceptable toxicity

Effect of Neoadjuvant Concurrent Chemoradiation on Operability and Survival in Locally Advanced Inoperable Breast Cancer

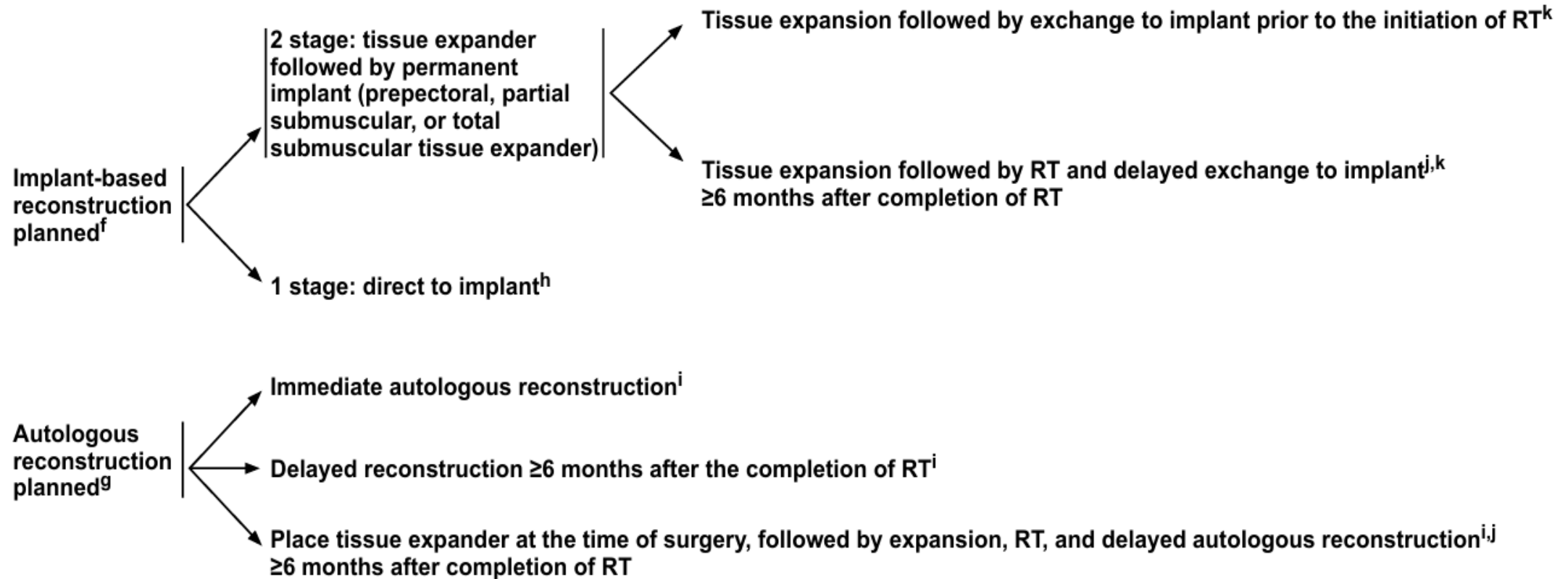
Priya Iyer ¹, Arvind Krishnamurthy ², Sridevi Velusamy ², Shirley Sundersingh ³, Swaminathan Rajaram ⁴, Ananthi Balasubramanian ⁵, Venkatraman Radhakrishnan ⁶

- May 2017 - December 2021,
- Stage III inoperable LABC.
- After 4 cycles of doxorubicin and cyclophosphamide and 4 cycles of paclitaxel, along with concurrent radiation therapy to a total dose of 46 Gy.
- Operability achieved in 91.6%
- •pCR rate: 36.5%
- HR+: 16%
- TNBC: 45.6%
- **HER2+: 60.7%**
- The 4-year event-free survival – 63.4%
Overall survival rate - 71.5%
- HER2-positive patients increased pCR , OS...

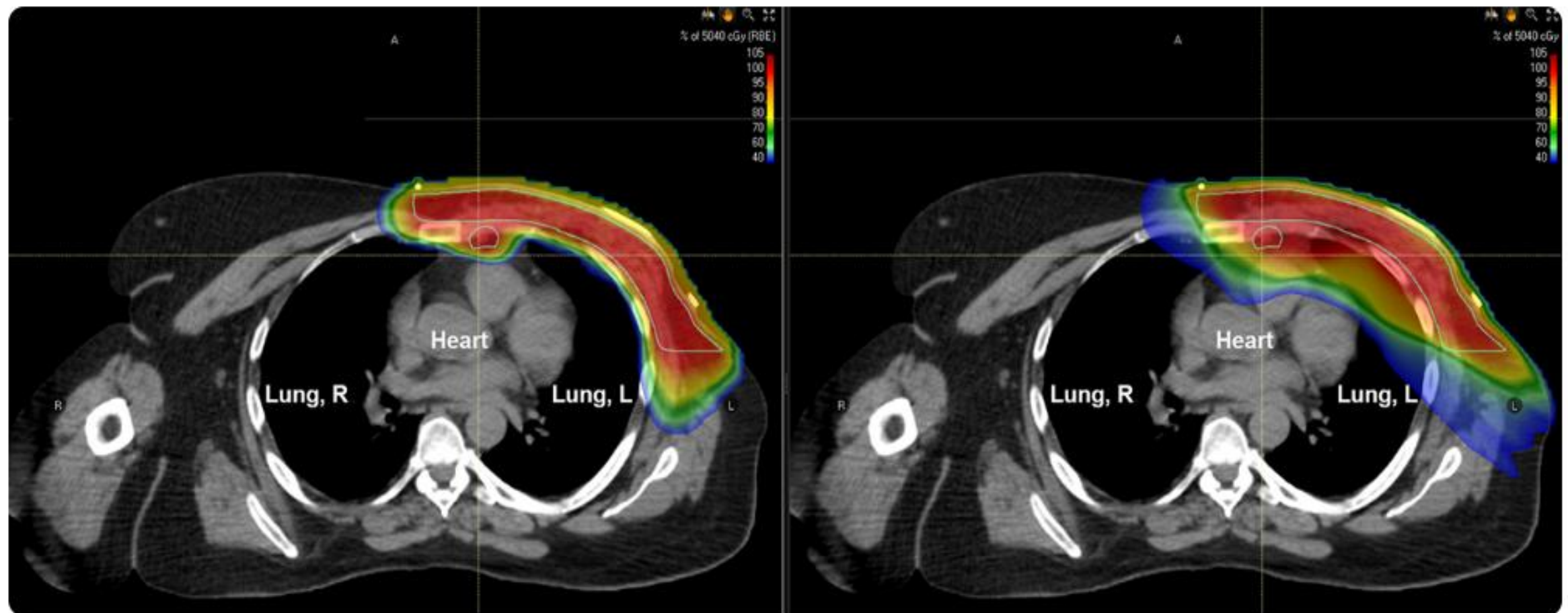
BREAST RECONSTRUCTION AFTER SURGERY

PRINCIPLES OF BREAST RECONSTRUCTION AFTER SURGERY

RECONSTRUCTION BASED ON PLANNED ADJUVANT RT^{a,b}



PROTON IN BREAST CANCER – Affordability???



FUTURE GOALS

A phase III randomized trial of radiotherapy optimization for low-risk HER2-positive breast cancer (HERO): NRG-BR008.

Authors: [Lior Zvi Braunstein](#), [Melissa Mitchell](#), [Hanna Bandos](#), [William M. Sikov](#), [Atif J. Khan](#), [Peter Y. Chen](#), [Patricia A. Ganz](#), ... [SHOW ALL](#) ... , and [Norman](#)

[Wolmark](#) | [AUTHORS INFO & AFFILIATIONS](#)

J Clin Oncol 43, TPS1120(2025) • [Volume 43, Number 16 suppl](#) • [DOI: 10.1200/JCO.2025.43.16 suppl.TPS1120](#)

Meeting Abstract: 2019 ASCO Annual Meeting I

FREE ACCESS | Breast Cancer—Local/Regional/Adjuvant | May 26, 2019



Cctg MA.39 tailor RT: A randomized trial of regional radiotherapy in biomarker low-risk node-positive breast cancer (NCT03488693).

Authors: [Wendy R. Parulekar](#), [Tanya Berrang](#), [Iwa Kong](#), [Eileen Rakovitch](#), [Valerie Theberge](#), [Karen A. Gelmon](#), [Stephen K. L. Chia](#), ... [SHOW ALL](#) ... , and

[Timothy Joseph Whelan](#) | [AUTHORS INFO & AFFILIATIONS](#)

J Clin Oncol 37, TPS602(2019) • [Volume 37, Number 15 suppl](#) • [DOI: 10.1200/JCO.2019.37.15 suppl.TPS602](#)



FRACTIONATION SCHEDULE

- CONVENTIONAL FRACTIONATION: 50Gy / 25#/ 2Gy
- HYPOFRACTIONATION : 40Gy / 15# /2.67 Gy.
- WBI tumor bed boost – 10-16Gy in 4-8 fractions.
- ULTRAHYPOFRACTIONATION: 26Gy in 5 fractions



TAKE HOME MESSAGE

- BASED ON GENOMIC, MOLECULAR PROFILE OF THE PATIENT
- RISK ADAPTED STRATEGY.
- EACH AND EVERY PATIENT TREATMENT – INDIVIDUALISED.
- is there a pathological complete response after systemic therapy ?
- De-escalate RNI in carefully selected patients.
- Omit RT in LOW-risk early-stage breast cancer.

THANK
YOU



—