NCCN 2021 Virtual Congress: Breast Cancer
with Updates from the 2020 San Antonio Breast Cancer Symposium

Friday, February 12, 2021
12:25 PM – 1:10 PM EST

Surgical and Radiation Treatment Updates to Management of Breast Cancer, Including SABCS Updates

Doreen M. Agnese, MD
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Background

- Optimal breast cancer care requires a multidisciplinary approach
  - Surgery
  - Radiation therapy
  - Systemic therapy (adjuvant or neoadjuvant)
  - Supportive care
- For those with early stage cancer, surgery is often the first therapy
  - Care of the primary tumor with breast conservation or mastectomy
  - Axillary staging
- Locoregional treatment strategies have evolved over the years to maximize effectiveness and minimize morbidity

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Axillary Staging, clinically node negative

- Key prognostic predictor with significant impact on treatment planning
- Historically, axillary node dissection was required for staging of the axilla
  - Significant morbidity, including lymphedema
- Sentinel lymph node biopsy
  - Allowed accurate staging and avoidance of completion nodal dissection when sentinel node was negative
  - When first introduced, was followed by completion nodal dissection in those who had positive SLN
  - More recent studies have demonstrated node positive populations where axillary node dissection is not required

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Is there a population in whom SLN can be avoided?

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Omission of SLN

VOLUME 24 · NUMBER 3 · JANUARY 20 2006

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

Randomized Trial Comparing Axillary Clearance Versus No Axillary Clearance in Older Patients With Breast Cancer: First Results of International Breast Cancer Study Group Trial 10-93

International Breast Cancer Study Group

From the International Breast Cancer Study Group. Appendix lists the names and affiliations of the writing committee, and participants and authors of Trial 10-93.

Submitted February 14, 2005; accepted June 13, 2005.

Supported in part by the Swiss Group for Clinical Cancer Research, Frontier Science and Technology Research Foundation, The Cancer Council Australia, Australian New Zealand Breast Cancer Trials Group (National Health Medical Research Council), National Cancer Institute (Grant No. CA-75362), Swedish Cancer Society, Cancer Association of South Africa, and Foundation for Clinical Research of Eastern Switzerland.

Presented at the 40th Annual Meeting of the American Society of Clinical Oncology, New Orleans, LA, June 5-8, 2004.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

Address reprint requests to Carl-Magnus Rudenstam, MD, West Swedish Breast Cancer Study Group, Sahlgrenska University Hospital/Mölndal, Göteborgsvägen 31, 431 80 Mölndal, Sweden; e-mail:

A B S T R A C T

Purpose
Axillary clearance in early breast cancer aims to improve locoregional control and provide staging information but is associated with undesirable morbidity. We therefore investigated whether avoiding axillary surgery in older women would result in improved quality of life (QL) with similar disease-free survival (DFS) and overall survival (OS).

Patients and Methods
Between 1993 and 2002, women ≥ 60 years old with clinically node-negative operable breast cancer in whom adjuvant tamoxifen was considered indicated regardless of pathologic nodal status were randomly assigned to primary surgery plus axillary clearance (Sx + Ax) followed by tamoxifen (Tam) versus Sx without Ax followed by Tam for 5 consecutive years. The primary end point was QL reported by the patient and by physician assessment.

Results
A total of 473 patients (234 to Sx + Ax, 239 to Sx) were randomly assigned. The median age was 74 years; 80% had estrogen receptor–positive disease. In both the patients' subjective assessment of their QL and the physicians' perception of the patients' QL, the largest adverse QL effects of Ax were observed from baseline to the first postoperative assessment, but the differences tended to disappear in 6 to 12 months. At a median follow-up of 6.6 years, results for Sx + Ax and Sx yielded similar DFS (6-year DFS, 67% *v* 66%; hazard ratio [HR] Sx + Ax/Sx, 1.06; 95% CI, 0.79 to 1.42; $P = .69$) and OS (6-year OS, 75% *v* 73%; HR Sx + Ax/Sx, 1.05; 95% CI, 0.76 to 1.46; $P = .77$).

Conclusion
Avoiding axillary clearance for women ≥ 60 years old who have clinically node-negative disease and receive Tam for endocrine-responsive disease yields similar efficacy with better early QL.

J Clin Oncol 24:337-344. © 2006 by American Society of Clinical Oncology

- RCT of women ≥ 60
  - Clinically node negative
  - Adjuvant tamoxifen
- 473 patients randomly assigned to surgery and tamoxifen with and without axillary clearance

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Omission of SLN

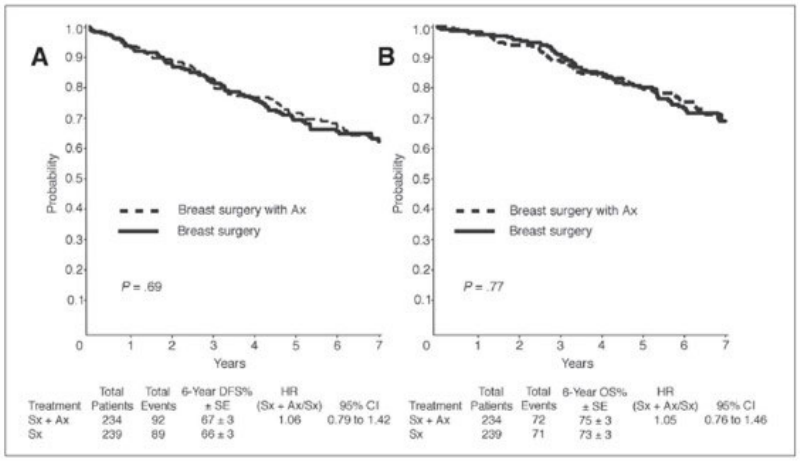

Fig 3. (A) Disease-free survival (DFS) and (B) overall survival (OS) according to treatment group. The median follow-up was 6.6 years. Ax, axillary clearance; Sx, primary surgery; HR, hazard ratio.

- With median follow-up of 6.6 years, no significant difference in DFS or OS

J Clin Oncol 2006; 24: 337-344

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Omission of SLN

Ann Surg Oncol (2011) 18:125–133
DOI 10.1245/s10434-010-1217-7

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – BREAST ONCOLOGY

Axillary Dissection Versus No Axillary Dissection in Elderly Patients with Breast Cancer and No Palpable Axillary Nodes: Results After 15 Years of Follow-Up

Gabriele Martelli, MD[1], Rosalba Miceli, PhD[2], Maria Grazia Daidone, PhD[3], Gaetano Vetrella, MD[4], Anna Maria Cerrotta, MD[5], Domenico Piromalli, MD[1], and Roberto Agresti, MD[1]

[1]Breast Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [2]Unit of Clinical Epidemiology and Trial Organization, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [3]Unit of Biomolecular Determinants in Prognosis and Therapy, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [4]Unit of Preventive Gynecology, Melegnano Hospital, Melegnano, Italy; [5]Unit of Radiotherapy, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

- Retrospective analysis of 671 women aged ≥ 70 with clinically negative axilla treated with and without axillary clearance with 15 year follow-up

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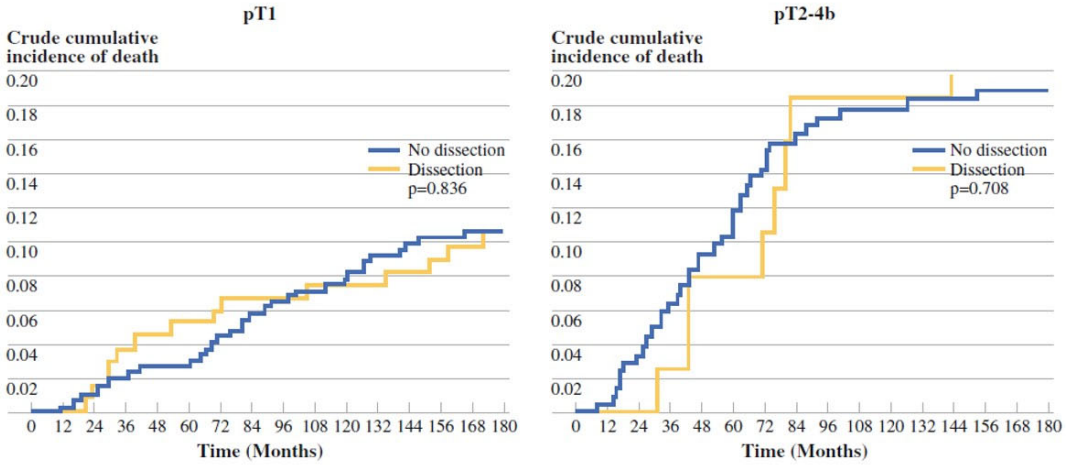

FIG. 1 Crude cumulative incidence curves of breast cancer death for patients given and not given axillary dissection. pT1 (*left*); pT2–4b (*right*)

- No significant difference in breast cancer mortality
- Low cumulative incidence of axillary recurrence in no axillary dissection group

Martelli Ann Surg Oncol 2011; 18: 125-133

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Choosing Wisely Campaign

- Society of Surgical Oncology statement (released July 2016, updated June 2019)
- **Don’t routinely use sentinel node biopsy in clinically node negative women ≥70 years of age with early stage hormone receptor positive, HER2 negative invasive breast cancer.**

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Do all patients with positive SLN need completion AND?

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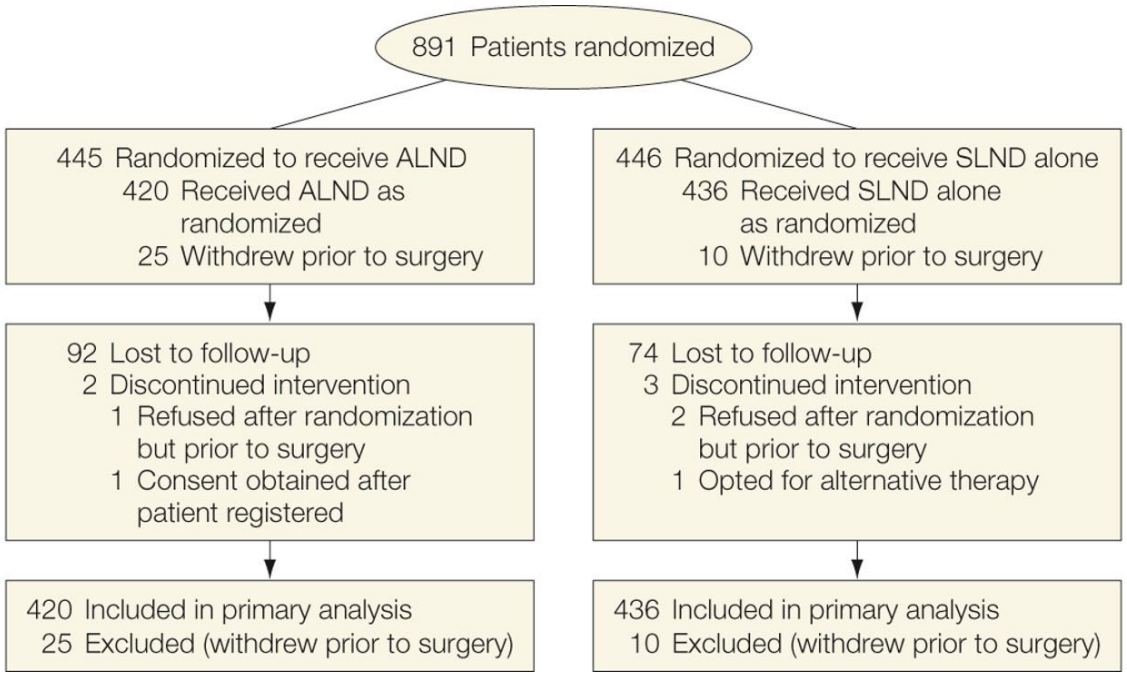
ACOSOG Z11

- Phase 3 non-inferiority trial conducted at 115 sites and enrolling patients from May 1999 to December 2004.
- 891 women with clinical T1-T2 invasive breast cancer, BCT, no palpable adenopathy, and 1 to 2 SLNs containing metastases were randomized



Giuliano *JAMA.* 2011;305(6):569–575. doi:10.1001/jama.2011.90

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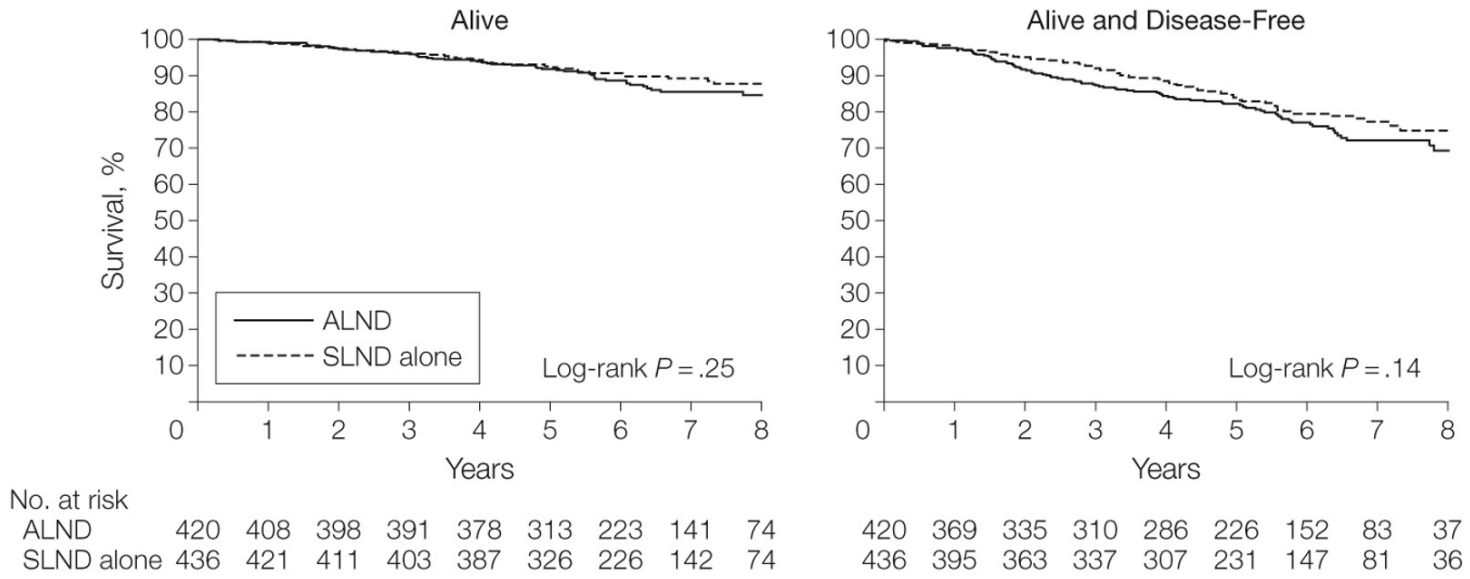
ACOSOG Z11



- The use of SLN alone did not result in inferior survival or local control

Giuliano *JAMA.* 2011;305(6):569–575. doi:10.1001/jama.2011.90

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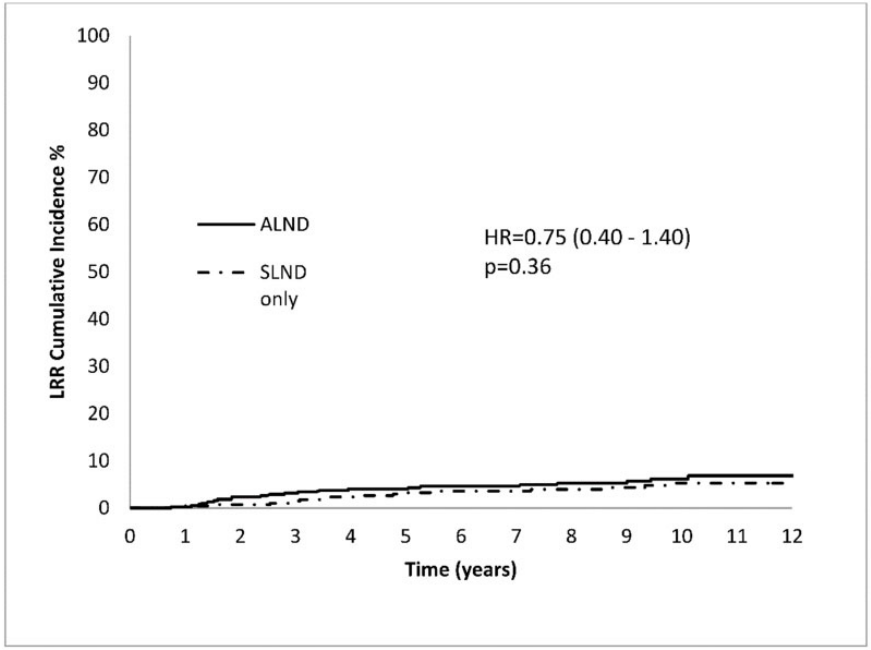
ACOSOG Z11 extended follow-up



Giuliano Ann *Surg*. 2016 Sep: 264(3): 413-420.

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AMAROS Trial

- Multicenter prospective randomized trial
- 4823 patients with T1-2 tumors and clinically negative nodes were randomized to either axillary node dissection or radiation therapy in the setting of a positive sentinel node
  - 82% had lumpectomy, 17-18% had mastectomy

Donker The Lancet Oncology 2014; 15 (12): 1303-1310

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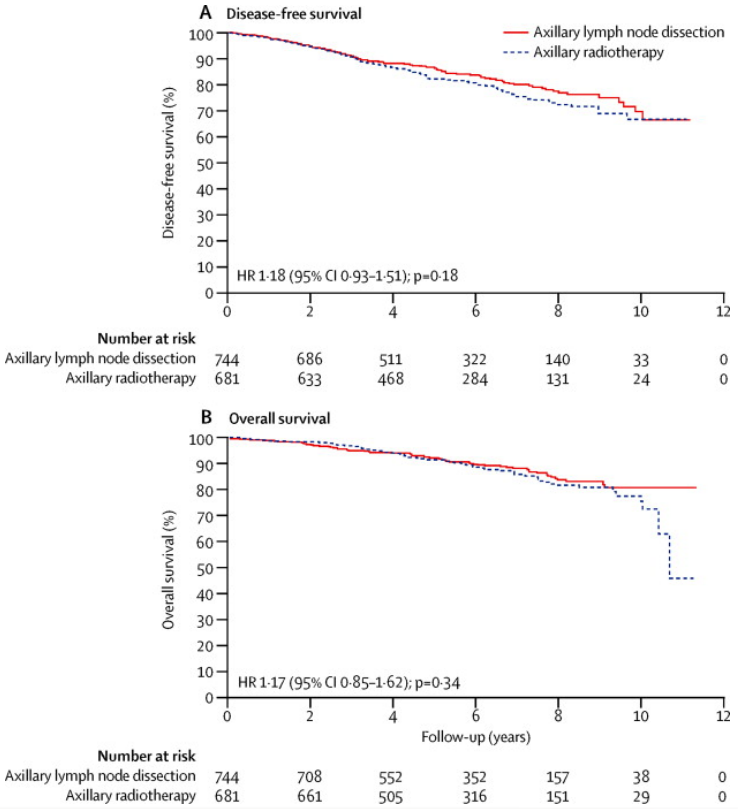
AMAROS Trial



- Axillary lymph node dissection and axillary radiotherapy provided equivalent local control
- Morbidity was decreased with radiation therapy

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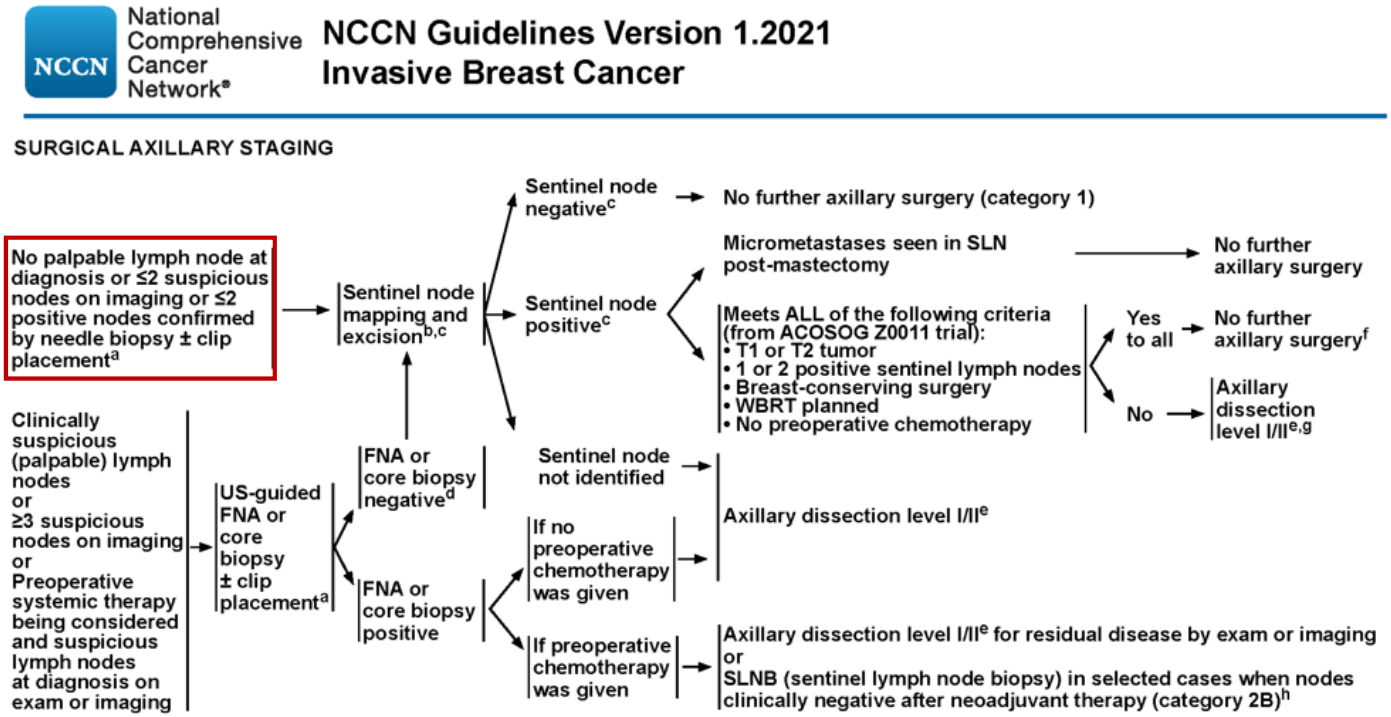
Axillary management



Clinically negative axilla with abnormal ultrasound

- Some centers perform axillary ultrasound even when no nodes are clinically palpable
- If biopsy performed and positive, patient may still meet Z11 criteria and can still be offered SLN
- Efforts should be made to clip the sampled node at the time of biopsy and remove at the time of SLN to assure accuracy of axillary staging

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Axillary management

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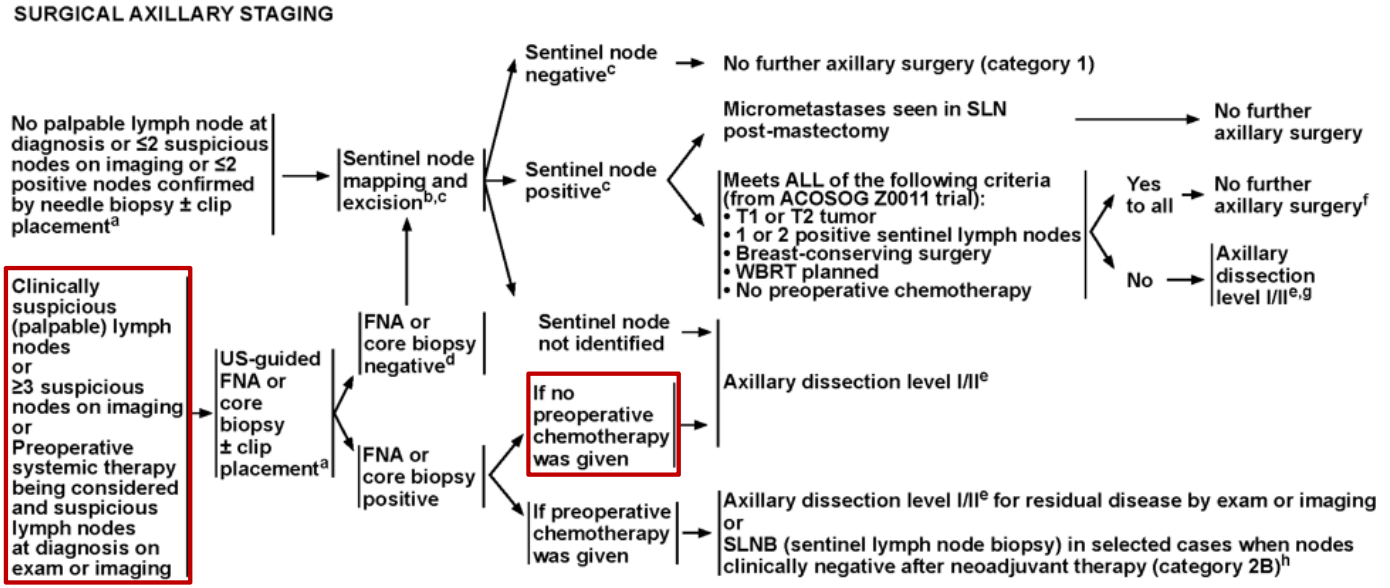
NCCN Guidelines Version 1.2021
Invasive Breast Cancer



BINV-D

Do all patients with positive nodes require axillary dissection after neoadjuvant chemotherapy?

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Axillary assessment after neoadjuvant therapy

- Historically, axillary node dissection was required for all patients with positive nodes prior to neoadjuvant chemotherapy regardless of response
- SLN after neoadjuvant therapy
  - Identification rate of about 89%
  - False negative rate >10%
  - Negative predictive value of 56-87%

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Targeted Axillary Dissection

VOLUME 34 · NUMBER 10 · APRIL 1, 2016

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Improved Axillary Evaluation Following Neoadjuvant Therapy for Patients With Node-Positive Breast Cancer Using Selective Evaluation of Clipped Nodes: Implementation of Targeted Axillary Dissection

Abigail S. Caudle, Wei T. Yang, Savitri Krishnamurthy, Elizabeth A. Mittendorf, Dalliah M. Black, Michael Z. Gilcrease, Isabelle Bedrosian, Brian P. Hobbs, Sarah M. DeSnyder, Rosa F. Hwang, Beatriz E. Adrada, Simona F. Shaitelman, Mariana Chavez-MacGregor, Benjamin D. Smith, Rosalind P. Candelaria, Gildy V. Babiera, Basak E. Dogan, Lumarie Santiago, Kelly K. Hunt, and Henry M. Kuerer

- Prospective study of patients with biopsy proven positive nodes with clip placed at biopsy
- After neoadjuvant therapy, patients had SLN and removal of the clipped node with iodine-125 seed localization

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TAD

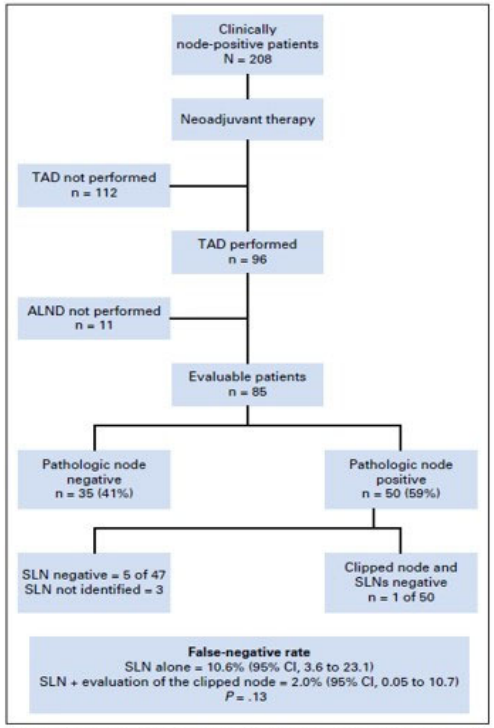

Fig 4. Ability of targeted axillary dissection (TAD) to predict nodal response after neoadjuvant therapy. Pathologic results of nodes removed from TAD were compared with other lymph nodes in patients who underwent axillary lymphadenectomy (ALND) to determine the false-negative rate of TAD. SNL, sentinel lymph node.

- False negative rate SLN alone 10.6%
- False negative rate SLN + evaluation of clipped node 2.0%

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Axillary management

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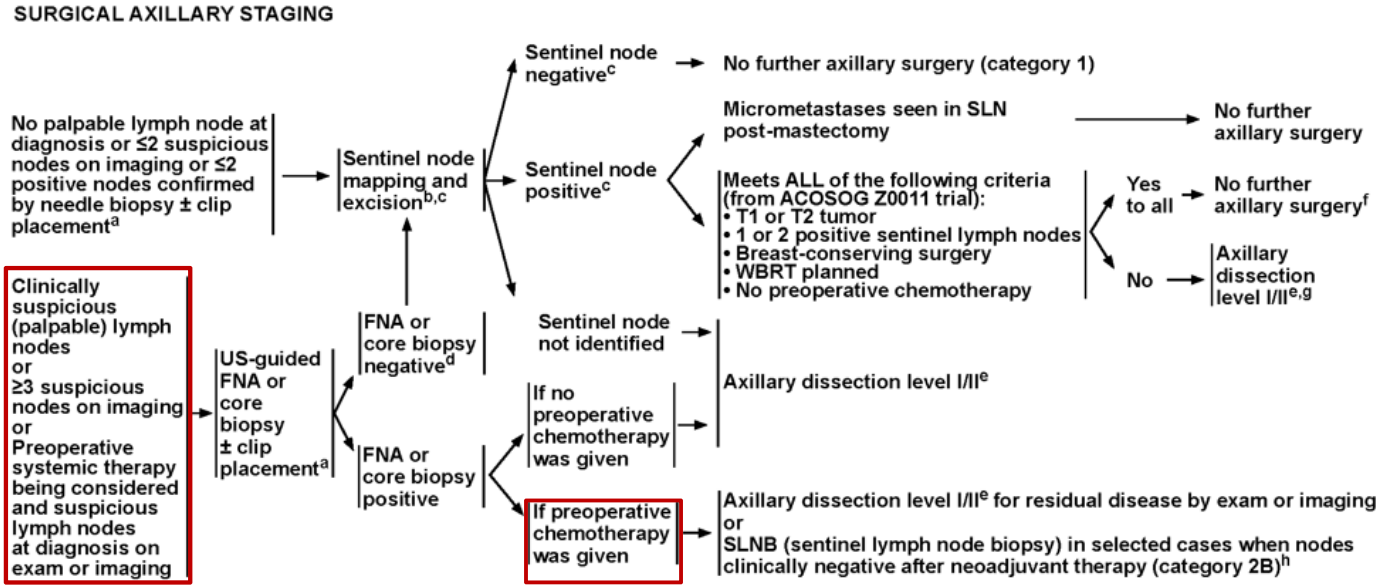

BINV-D

RISAS Trial-presented at SABCS 2020

- Radioactive Iodine Seed localization in the Axilla in axillary node positive breast cancer combined with a Sentinel node procedure.
- Prospective multicenter trial in which patients underwent RISAS procedure followed by axillary node dissection
  - 223 patients had successful identification of at least one lymph node
  - 79 had pathologic complete response
  - 144 had residual nodal disease
  - 5 patients had false negative RISAS procedure (FNR 3.4%, NPV 93.6%)
    - Of the 5 false negatives, 4/5 occurred within the 1st 10 procedures performed at the institution

RISAS trial- Abstract Number: GS1-10; SABCS 2020

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Summary

- Routine SLN should can be omitted in select patients ≥ 70 with early stage HR+, Her-2 negative breast cancer
- SLN is recommended for axillary staging in clinically node negative patients
- Completion nodal dissection can be avoided in patients who meet Z11 criteria
- There is growing evidence that modifications of SLN with addition of TAD may allow de-escalation of axillary surgery after neoadjuvant chemotherapy

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Radiation Treatment Updates to Management of Breast Cancer, Including SABCS Updates

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Learning Objectives

- Develop an evidence-based approach for the management of the axilla in patients with early stage breast cancer
- Individualize radiation therapy recommendations based on patient and tumor characteristics
- Discuss new and emerging data in the management of patients with early-stage breast cancer and integrate key findings into clinical practice

Definitions of Margins after BCT in 2014:
Variations by Current Consensus Groups

Consensus Group	Recommended Negative Margin Width
National Comprehensive Cancer Network (NCCN)	>1 mm
European Society for Medical Oncology (ESMO)	≥2 mm
New Zealand Guidelines Group (NZGG)	≥2 mm
German Cancer Society	≥1 mm

JOURNAL OF CLINICAL ONCOLOGY

SPECIAL ARTICLE

Society of Surgical Oncology–American Society for Radiation Oncology Consensus Guideline on Margins for Breast-Conserving Surgery With Whole-Breast Irradiation in Stages I and II Invasive Breast Cancer

Moran MS et al. 2014

*Guidelines simultaneously published in JCO, Int J. Radiat Bio Phy/PRO, & Annals Surg Onc

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NCCN Guidelines Version 1.2015
Invasive Breast Cancer

BCT is defined as complete removal of the tumor with a negative margin[1], followed by whole breast RT (WBRT)

- Negative margin for invasive cancers (or DCIS associated with invasive cancers):
- The NCCN Panel has adopted the definition of a negative margin as "No ink on tumor" from the SSO/ASTRO Guideline on Margins
- In cases where there is a positive margin, additional surgery (either re-excision to achieve a negative margin, or mastectomy) should be performed

1. **Moran MS,** JCO 2014 SSO/ASTRO Margin Guideline; The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Breast Cancer (Version 1.2015).

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NCCN Guidelines Version 2.2017
Ductal Carcinoma in Situ (DCIS)

MARGIN STATUS IN DCIS

- Substantial controversy over definition of a negative pathologic margin in DCIS
- Margins greater than 10 mm are widely accepted as negative (but may be excessive and may lead to a less optimal cosmetic outcome)
- Margins less than 1 mm are considered inadequate
- With pathologic margins between 1–10 mm, wider margins are generally associated with ↓IBTR

JOURNAL OF CLINICAL ONCOLOGY | SPECIAL ARTICLE

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JOURNAL OF CLINICAL ONCOLOGY | SPECIAL ARTICLE

Society of Surgical Oncology–American Society for Radiation Oncology–American Society of Clinical Oncology Consensus Guideline on Margins for Breast-Conserving Surgery With Whole-Breast Irradiation in Ductal Carcinoma In Situ

Morrow M et al. 2016

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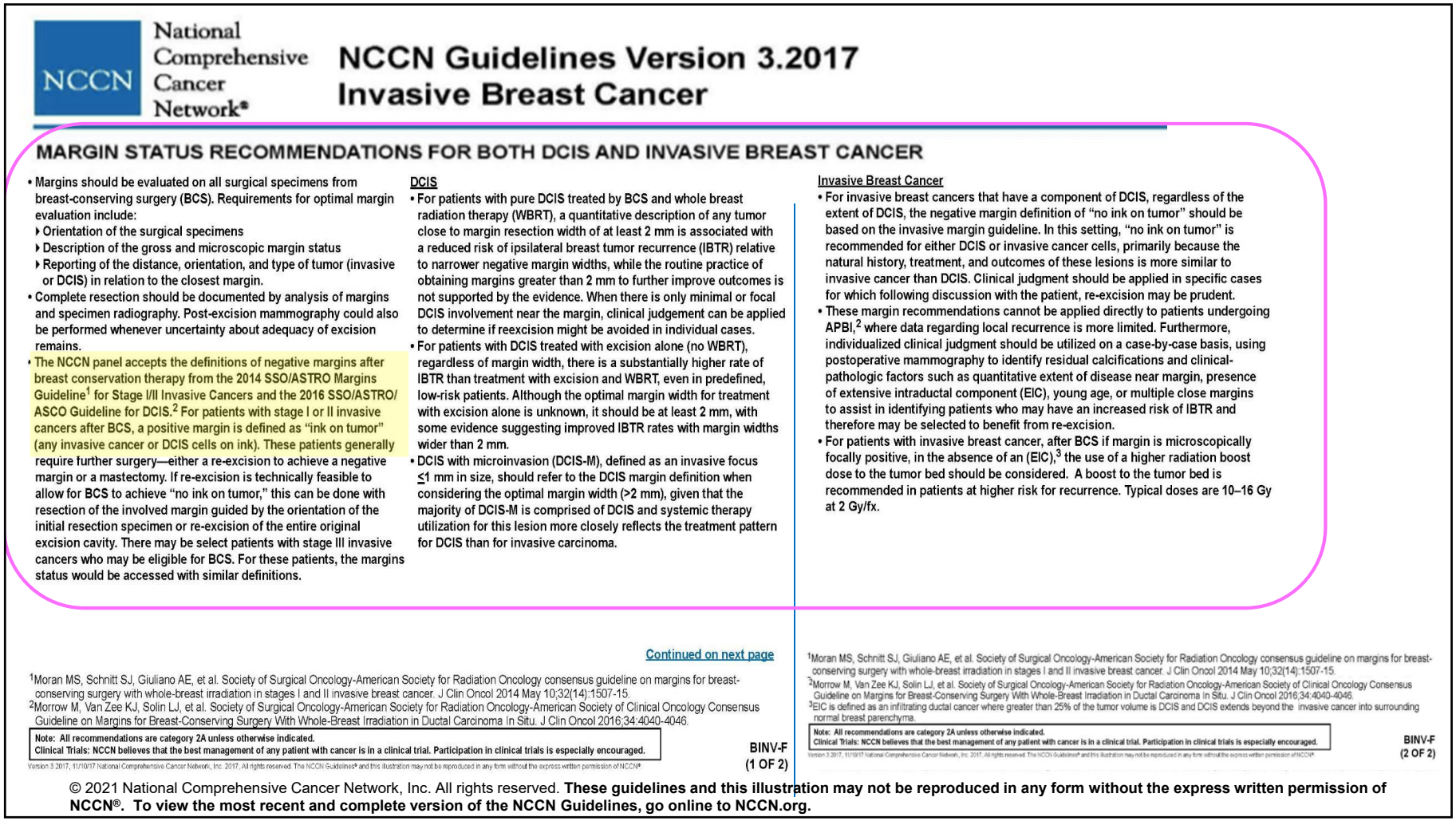

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NCCN Guidelines Version 3.2017
Invasive Breast Cancer

MARGIN STATUS RECOMMENDATIONS FOR BOTH DCIS AND INVASIVE BREAST CANCER

- Margins should be evaluated on all surgical specimens from breast-conserving surgery (BCS). Requirements for optimal margin evaluation include:
  - Orientation of the surgical specimens
  - Description of the gross and microscopic margin status
  - Reporting of the distance, orientation, and type of tumor (invasive or DCIS) in relation to the closest margin.
- Complete resection should be documented by analysis of margins and specimen radiography. Post-excision mammography could also be performed whenever uncertainty about adequacy of excision remains.
- The NCCN panel accepts the definitions of negative margins after breast conservation therapy from the 2014 SSO/ASTRO Margins Guideline[1] for Stage I/II Invasive Cancers and the 2016 SSO/ASTRO/ASCO Guideline for DCIS.[2] For patients with stage I or II invasive cancers after BCS, a positive margin is defined as "ink on tumor" (any invasive cancer or DCIS cells on ink). These patients generally require further surgery—either a re-excision to achieve a negative margin or a mastectomy. If re-excision is technically feasible to allow for BCS to achieve "no ink on tumor," this can be done with resection of the involved margin guided by the orientation of the initial resection specimen or re-excision of the entire original excision cavity. There may be select patients with stage III invasive cancers who may be eligible for BCS. For these patients, the margins status would be accessed with similar definitions.

DCIS

- For patients with pure DCIS treated by BCS and whole breast radiation therapy (WBRT), a quantitative description of any tumor close to margin resection width of at least 2 mm is associated with a reduced risk of ipsilateral breast tumor recurrence (IBTR) relative to narrower negative margin widths, while the routine practice of obtaining margins greater than 2 mm to further improve outcomes is not supported by the evidence. When there is only minimal or focal DCIS involvement near the margin, clinical judgement can be applied to determine if reexcision might be avoided in individual cases.
- For patients with DCIS treated with excision alone (no WBRT), regardless of margin width, there is a substantially higher rate of IBTR than treatment with excision and WBRT, even in predefined, low-risk patients. Although the optimal margin width for treatment with excision alone is unknown, it should be at least 2 mm, with some evidence suggesting improved IBTR rates with margin widths wider than 2 mm.
- DCIS with microinvasion (DCIS-M), defined as an invasive focus ≤1 mm in size, should refer to the DCIS margin definition when considering the optimal margin width (>2 mm), given that the majority of DCIS-M is comprised of DCIS and systemic therapy utilization for this lesion more closely reflects the treatment pattern for DCIS than for invasive carcinoma.

Invasive Breast Cancer

- For invasive breast cancers that have a component of DCIS, regardless of the extent of DCIS, the negative margin definition of "no ink on tumor" should be based on the invasive margin guideline. In this setting, "no ink on tumor" is recommended for either DCIS or invasive cancer cells, primarily because the natural history, treatment, and outcomes of these lesions is more similar to invasive cancer than DCIS. Clinical judgment should be applied in specific cases for which following discussion with the patient, re-excision may be prudent.
- These margin recommendations cannot be applied directly to patients undergoing APBI,[2] where data regarding local recurrence is more limited. Furthermore, individualized clinical judgment should be utilized on a case-by-case basis, using postoperative mammography to identify residual calcifications and clinical-pathologic factors such as quantitative extent of disease near margin, presence of extensive intraductal component (EIC), young age, or multiple close margins to assist in identifying patients who may have an increased risk of IBTR and therefore may be selected to benefit from re-excision.
- For patients with invasive breast cancer, after BCS if margin is microscopically focally positive, in the absence of an (EIC),[3] the use of a higher radiation boost dose to the tumor bed should be considered. A boost to the tumor bed is recommended in patients at higher risk for recurrence. Typical doses are 10–16 Gy at 2 Gy/fx.

Continued on next page

[1]Moran MS, Schnitt SJ, Giuliano AE, et al. Society of Surgical Oncology-American Society for Radiation Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in stages I and II invasive breast cancer. J Clin Oncol 2014 May 10;32(14):1507-15.
[2]Morrow M, Van Zee KJ, Solin LJ, et al. Society of Surgical Oncology-American Society for Radiation Oncology-American Society of Clinical Oncology Consensus Guideline on Margins for Breast-Conserving Surgery With Whole-Breast Irradiation in Ductal Carcinoma In Situ. J Clin Oncol 2016;34:4040-4046.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

BINV-F (1 OF 2)

[1]Moran MS, Schnitt SJ, Giuliano AE, et al. Society of Surgical Oncology-American Society for Radiation Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in stages I and II invasive breast cancer. J Clin Oncol 2014 May 10;32(14):1507-15.
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[3]EIC is defined as an infiltrating ductal cancer where greater than 25% of the tumor volume is DCIS and DCIS extends beyond the invasive cancer into surrounding normal breast parenchyma.

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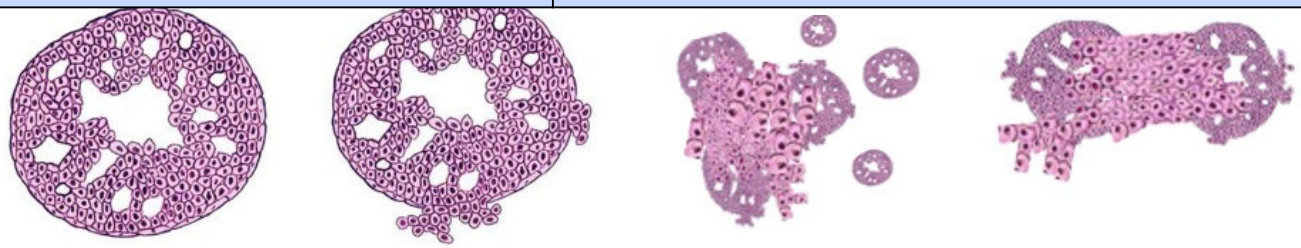
BINV-F (2 OF 2)

Which Guideline to Use?

DCIS guideline	DCIS w/Invasive Cancer guideline
2 mm	No ink on tumor



Pure DCIS

DCIS with micro-invasion*

Invasive Cancer with DCIS**

Invasive Cancer

*Defined as: DCIS w/ invasive focus <1mm

Non-invasive

Non-invasive/ Minor invasive

Invasive Minor DCIS

Invasive

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NCCN Guidelines Version 1.2021
Invasive Breast Cancer

MARGIN STATUS RECOMMENDATIONS AFTER BREAST-CONSERVING SURGERY FOR INVASIVE CANCERS AND DCIS

Invasive Breast Cancer

- **For invasive breast cancers that have a component of DCIS, regardless of the extent of DCIS, the negative margin definition of "no ink on tumor" should be based on the invasive margin guideline. In this setting, "no ink on tumor" is recommended for either DCIS or invasive cancer cells, primarily because the natural history, treatment, and outcomes of these lesions are more similar to invasive cancer than DCIS. For specifically challenging cases, clinical judgment and discussion with the patient should precede routine re-excision.**
- **These margin recommendations cannot be applied directly to patients undergoing APBI,[1] where data regarding local recurrence are more limited. Furthermore, individualized clinical judgment should be utilized on a case-by-case basis, using postoperative mammography to identify residual calcifications and clinical-pathologic factors such as quantitative extent of disease near margin, presence of extensive intraductal component (EIC),[3] young age, or multiple close margins to assist in identifying patients who may have an increased risk of IBTR and therefore may be selected to benefit from re-excision.**
- **For patients with invasive breast cancer after BCS, with microscopically focally positive margins (in the absence of an EIC),[3] the use of a higher radiation boost dose to the tumor bed may be considered, since generally a boost to the tumor bed is recommended for patients at higher risk of recurrence. See BINV-I.**

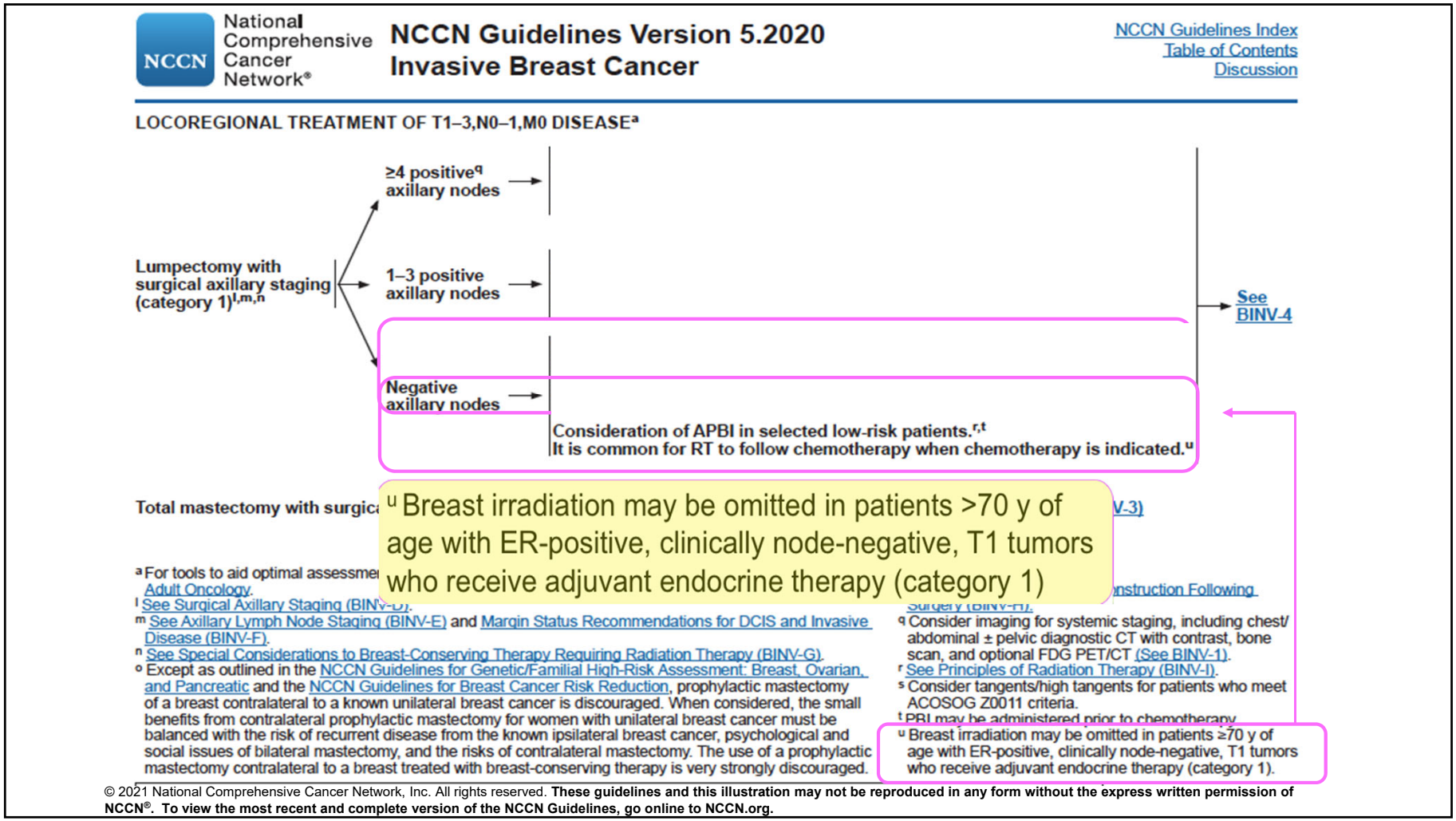
	No ink on tumor	2-mm margin	No margin necessary
Invasive breast cancer	X		
Invasive breast cancer + DCIS	X		
Invasive breast cancer + extensive DCIS	X		
Pure DCIS		X	
DCIS with microinvasion		X	
Pure LCIS* at surgical margin			X
Atypia at surgical margin			X

*For pleomorphic LCIS, the optimal width of margins is not known.

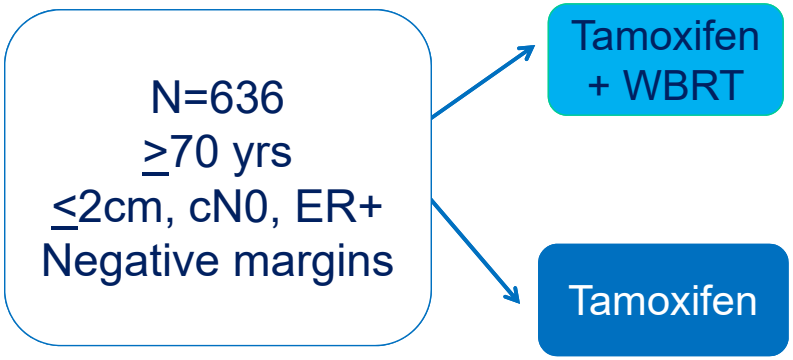
[1] Moran MS, Schnitt SJ, Giuliano AE, et al. Society of Surgical Oncology-American Society for Radiation Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in stages I and II invasive breast cancer. J Clin Oncol 2014 May 10;32(14):1507-1515.

[3] EIC is defined as an infiltrating ductal cancer where >25% of the tumor volume is DCIS and DCIS extends beyond the invasive cancer into surrounding normal breast parenchyma.

BINV-2: Modifications to Local Regional Management



CALGB 9343



12 yr Outcomes*	No RT	RT
	All p values NS >0.05*	
Axillary Rec	1%	0%
Mastectomy Rate	2%	4%
Distant Mets	5%	5%
10 yr BCSS	98%	97%

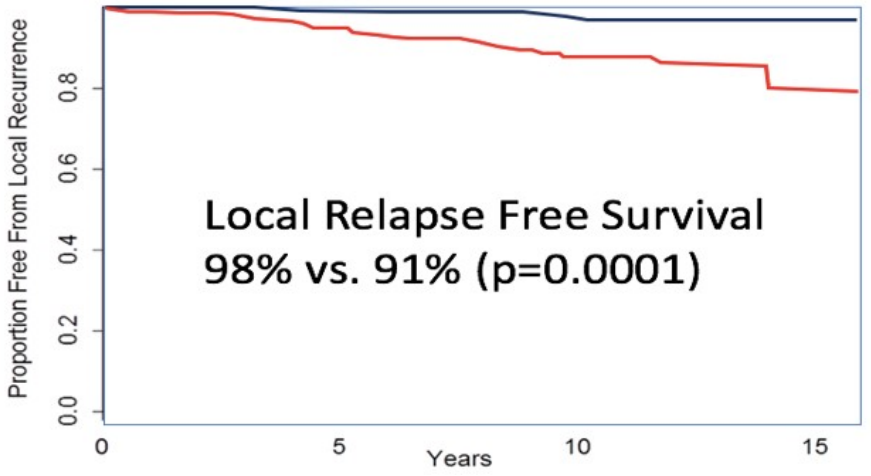
Hughes KS, J Clin Oncol, 2013

CALGB 9343

N=636
≥70 yrs
≤2cm, cN0, ER+
Negative margins

→ Tamoxifen + WBRT

→ Tamoxifen



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10 yr BCSS	98%	97%

Local Relapse	5 yr	8 yr	12 yr
		All p values <0.05*	
Tam + RT	1%	1%	2%
Tam alone	4%	7%	9%

Hughes KS, J Clin Oncol, 2013

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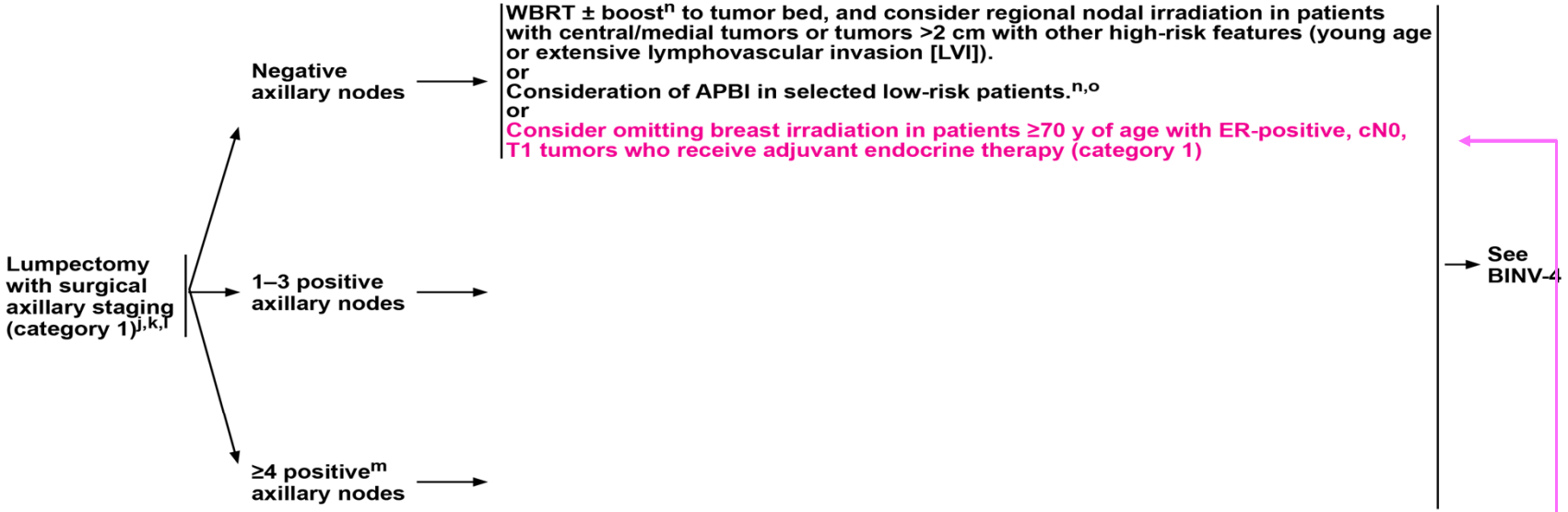
Invasive Breast Cancer

LOCOREGIONAL TREATMENT OF cT1–3, cN0 or cN+, M0 DISEASE:[a]
BREAST-CONSERVING THERAPY



[a] For tools to aid optimal assessment and management of older adults, see NCCN Guidelines for Older Adult Oncology.
[j] See Surgical Axillary Staging (BINV-D).
[k] See Axillary Lymph Node Staging (BINV-E) and Margin Status Recommendations After Breast-Conserving Surgery for Invasive Cancers and DCIS (BINV-F).
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[m] Consider imaging for systemic staging, including chest/abdominal ± pelvic diagnostic CT with contrast, bone scan, and optional FDG PET/CT.
[n] See Principles of Radiation Therapy (BINV-I).
[o] APBI may be administered prior to chemotherapy.

PRIME II Trial: 5 yr. Follow-up

N=1370
≥65 yrs age
≤3cm,
pN0,
ER+
Margins ≥1mm

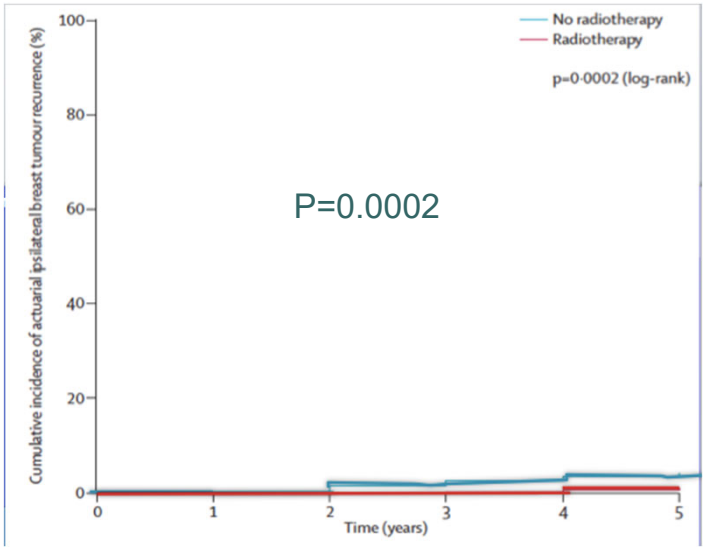
→ Tamoxifen + WBRT

→ Tamoxifen

Endpoints:

1°= IBTR rates

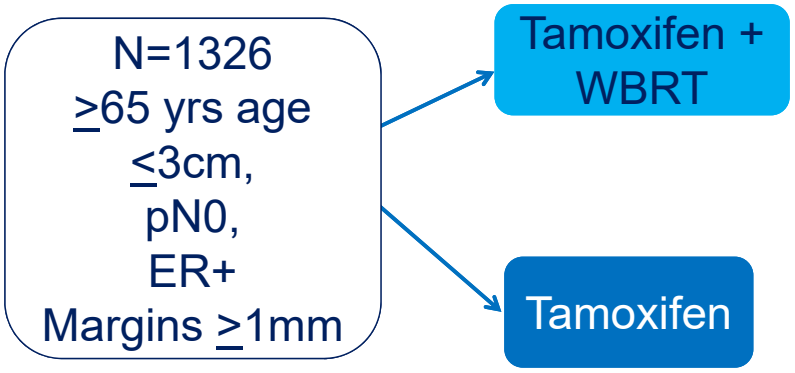
2°= Regional failures, contralat BC distant rec, DFS, OS



Outcomes		P value
Median Follow up 5 years		
Local Relapse	4.1% vs 1.3%	0.0002
Overall Survival	94% vs 94%	0.34

Kunkler et. al. Lancet Onc 2015

(SABC 2020) PRIME II Trial: 10 yr. Follow-up



Characteristic (%)	No RT (%)	+RT (%)
Mean age, yrs (SD)	71.12 (4.96)	70.78 (4.74)
Tumor size, mm		
▪ 0-10.0	38.6	40.3
▪ 10.1-20.0	48.8	48.5
▪ 20.1-30.0	12.6	11.2
Grade		
▪ 1	40.9	44.4
▪ 2	55.6	54.6
▪ 3	3.5	2.0
LVI	4.8	4.1
Preop Endocrine	9.1	8.3

Kunkler et. al. SABC Dec 2020 . Abstr GS2-03

PRIME II 10 yr. Update: Outcomes

Characteristic, %	No RT	+ RT	*p* Value
Local control at 10 yrs actuarial n (%)	43 (9.8)	5(0.9)	.00008
Recurrence, n (%)			
▪ Regional	13 (2.3)	3 (0.5)	.014
▪ Distant	8 (1.9)	15 (3.6)	.07
▪ Contralateral breast cancer	7 (1.2)	11 (2.2)	.20
▪ New (nonbreast) cancer	49 (10.2)	40 (8.7)	.41
Deaths, n	89	81	.68
▪ 10-yr actuarial rate, %	80.4	81.0	
10-yr metastasis-free survival, % (95% CI)	98.1 (96.7-99.6)	96.4 (94.5-98.4)	.28
Cause of death, n (%)			
▪ Cancer	35 (39)	29 (37)	

Median follow-up: 7.3 yrs

Kunkler et. al. SABC Dec 2020 . Abstr GS2-03

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Cause of death, n (%)			
▪ Cancer	35 (39)	29 (37)	

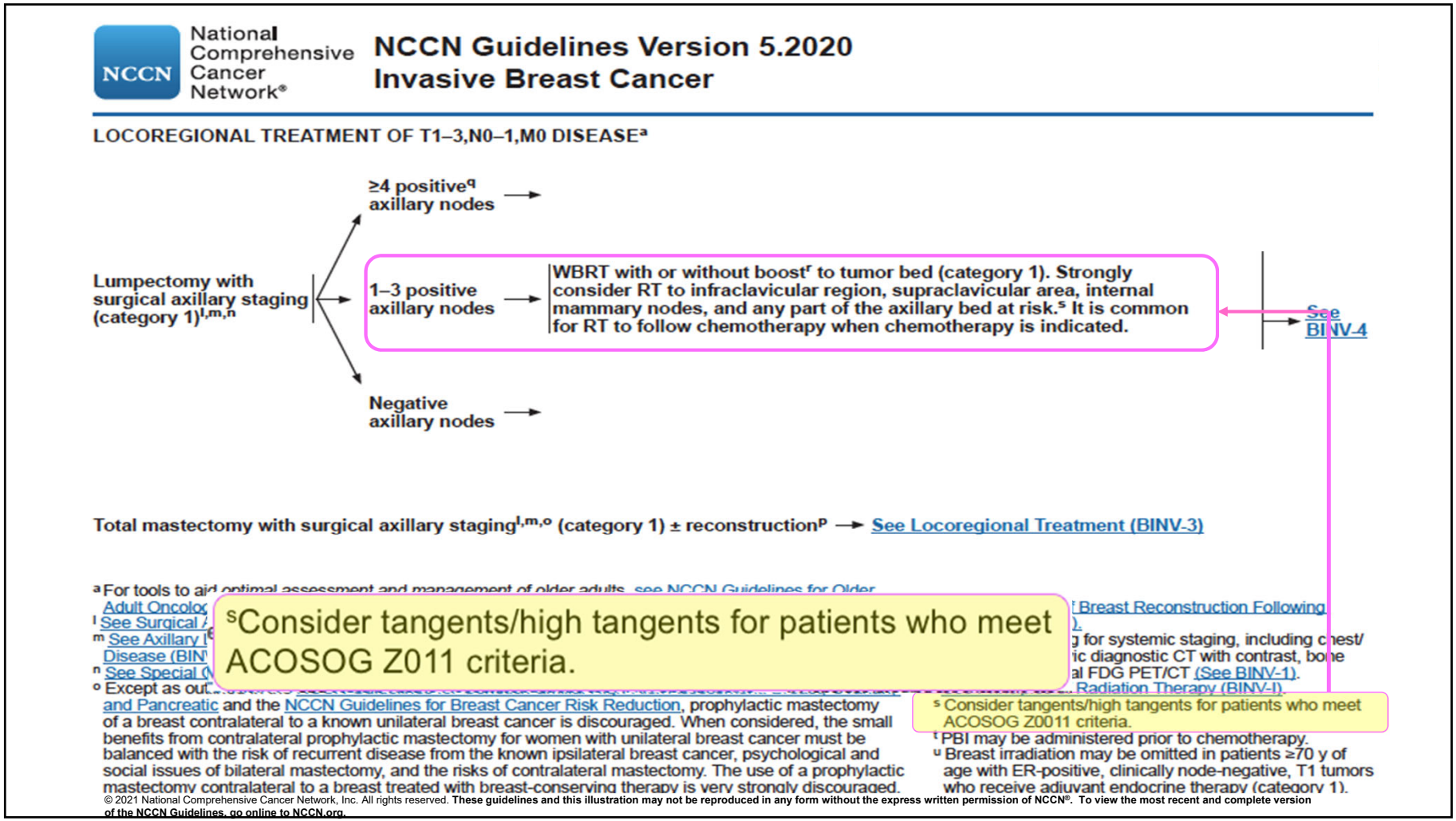
Patient selection criteria for observation may be expanded in near future

Median follow-up: 7.3 yrs

Kunkler et. al. SABC Dec 2020 . Abstr GS2-03

BINV-2: 1-3+ Nodes

- Recommendation to ‘Strongly consider regional nodal RT with WBRT’ based on 2 phase III trials, MA-20 and EORTC that have demonstrate improved distant metastatic event free survival when RT is delivered to regional nodes
- Regional nodes defined as supra/infraclavicular, internal mammary, and undissected axilla
- The algorithm doesn’t address lower risk patients with 1-3+ nodes



ACOSOG Z0011 10 yr. Outcomes

cN0➔T1/T2
Up to 2+ SLN

SLN + WBRT + ALND

*Protocol: Tangents only

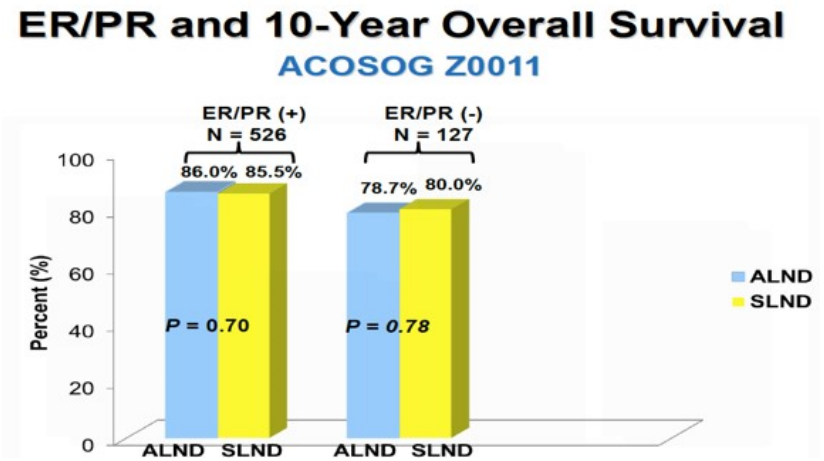
SLN alone + WBRT

Primary Endpoints:

- Overall Survival
- Morbidity
- LR and nodal rec

10 yr LR recurrence: (p = 0.36)
6.2% ALND vs. 5.3% SLND

10 yr nodal recurrences: (p = 0.28)
0.5% ALND vs. 1.5% in the SLND



Giuliano et. al., JAMA, 2017

ACOSOG Z0011 10 yr. Outcomes

- Despite criticisms of this trial:
  - Major deviations in the protocol: +SC Field: >20%; High Tangents:>50%; >10% did not get any WBRT
  - Not powered to show statistically significant differences; incomplete accrual
- Nodal relapses very rare (<2%) & LR relapses similarly low (<7%) @ 10 yrs
- Findings strongly suggest in this Z0011 population:
  - Irrespective of axillary adjuvant therapy (RT to axilla /completion ALND/no tx) axillary rec are rare
  - This population does not warrant more aggressive axillary treatment
  - ER negative dx (in and of itself) should not be an indication for more aggressive axillary tx

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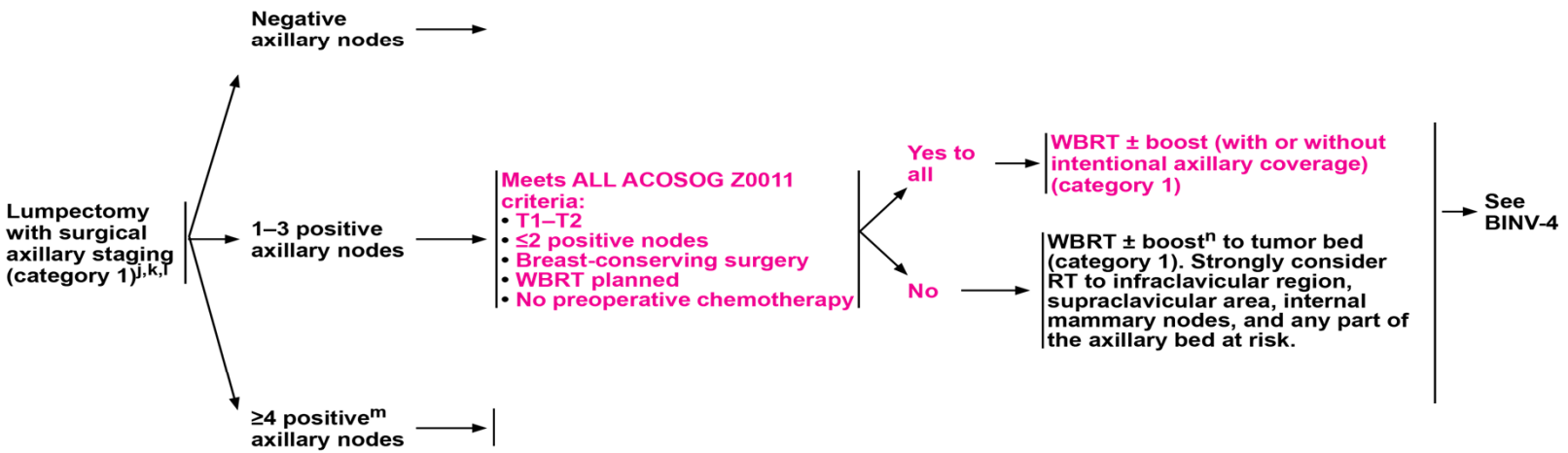
Invasive Breast Cancer

LOCOREGIONAL TREATMENT OF cT1–3, cN0 or cN+, M0 DISEASE:[a]
BREAST-CONSERVING THERAPY



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[n] See Principles of Radiation Therapy (BINV-I).
[o] APBI may be administered prior to chemotherapy.

BINV-I:
Principles of Radiation Therapy:

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Invasive Breast Cancer

PRINCIPLES OF RADIATION THERAPY

Optimizing Delivery of Individual Therapy
- It is important to individualize RT planning and delivery.
  - CT-based treatment planning is encouraged to delineate target volumes and adjacent organs at risk.
  - Radiation to the breast/chest wall and nodal regions is generally delivered with photons ± electrons.
  - Greater target dose homogeneity and sparing of normal tissues can be accomplished using compensators such as wedges, forward planning using segments, and intensity-modulated RT (IMRT).
  - Respiratory control techniques including deep inspiration breath-hold and prone positioning may be used to try to further reduce dose to adjacent heart and lung and adjacent normal tissue.
  - Boost treatment in the setting of breast conservation can be delivered using enface electrons, photons, or brachytherapy. Chest wall scar boost when indicated is typically treated with electrons or photons.
  - Verification of daily setup consistency is done with weekly imaging. When using certain techniques (ie, prone breast), more frequent imaging may be appropriate. Routine use of daily imaging is not recommended.

Whole Breast Radiation
- Target definition is the breast tissue in entirety.
- RT dosing:
  - The whole breast should receive a dose of 45–50.4 Gy in 25–28 fractions or 40–42.5 Gy in 15–16 fractions (hypofractionation is preferred).
  - A boost to the tumor bed is recommended in patients at higher risk for recurrence. Typical boost doses are 10–16 Gy in 4–8 fractions.
- All dose schedules are given 5 days per week.

Chest Wall Radiation (including breast reconstruction)
- The target includes the ipsilateral chest wall, mastectomy scar, and drain sites when indicated.
  - Depending on whether or not the patient has had breast reconstruction, several techniques using photons and/or electrons are appropriate.
  - CT-based treatment planning is encouraged in order to identify lung and heart volumes and minimize exposure of these organs.
  - Special consideration should be given to the use of bolus material to ensure that the skin dose is adequate.
  - RT dosing:
    - Dose is 45–50.4 Gy in 25–28 fractions to the chest wall ± scar boost, at 1.8–2 Gy per fraction, to a total dose of approximately 60 Gy.
- All dose schedules are given 5 days per week.

Regional Nodal Radiation
- Target delineation is best achieved by the use of CT-based treatment planning.
  - For the paraclavicular and axillary nodes, prescription depth varies based on the patient anatomy.
  - For internal mammary node identification, the internal mammary artery and vein can be used as a surrogate for the nodal location (as the nodes themselves are not usually visible on planning imaging). Based on the post-mastectomy radiation randomized studies and recent trials, RT of the internal mammary nodal chain to include the first 3 intercostal spaces should be strongly considered when delivering regional nodal irradiation. When treating the internal mammary nodes, dose-volume histograms (DVHs) should be used to evaluate dose constraints, dose to normal tissues (ie, heart, lung), and planned target volumes (PTVs).
  - RT dosing:
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Accelerated Partial Breast Irradiation (APBI)
- Studies of APBI suggest that rates of local control in selected low-risk patients with early-stage breast cancer may be comparable to those treated with standard WBRT. However, compared to standard WBRT, several studies document an inferior cosmetic outcome with APBI. Follow-up is limited and studies are ongoing.
  - Patients are encouraged to participate in clinical trials.
  - The NCCN Panel accepts the updated 2016 version of the ASTRO APBI guideline, which now defines patients "suitable" for APBI to be one of the following:
    - 1) ≥50 years with invasive ductal carcinoma measuring ≤2 cm (T1 disease) with negative margin widths of ≥2 mm, no LVI, ER-positive, and *BRCA* negative; or
    - 2) low/intermediate nuclear grade, screening-detected DCIS measuring size ≤2.5 cm with negative margin widths of ≥3 mm.
  - RT dosing:
    - A course of 34 Gy in 10 fractions delivered twice per day with brachytherapy or 38.5 Gy in 10 fractions delivered twice per day with external beam photon therapy is typically prescribed to the tumor bed.
    - Other fractionation schemes are currently under investigation.

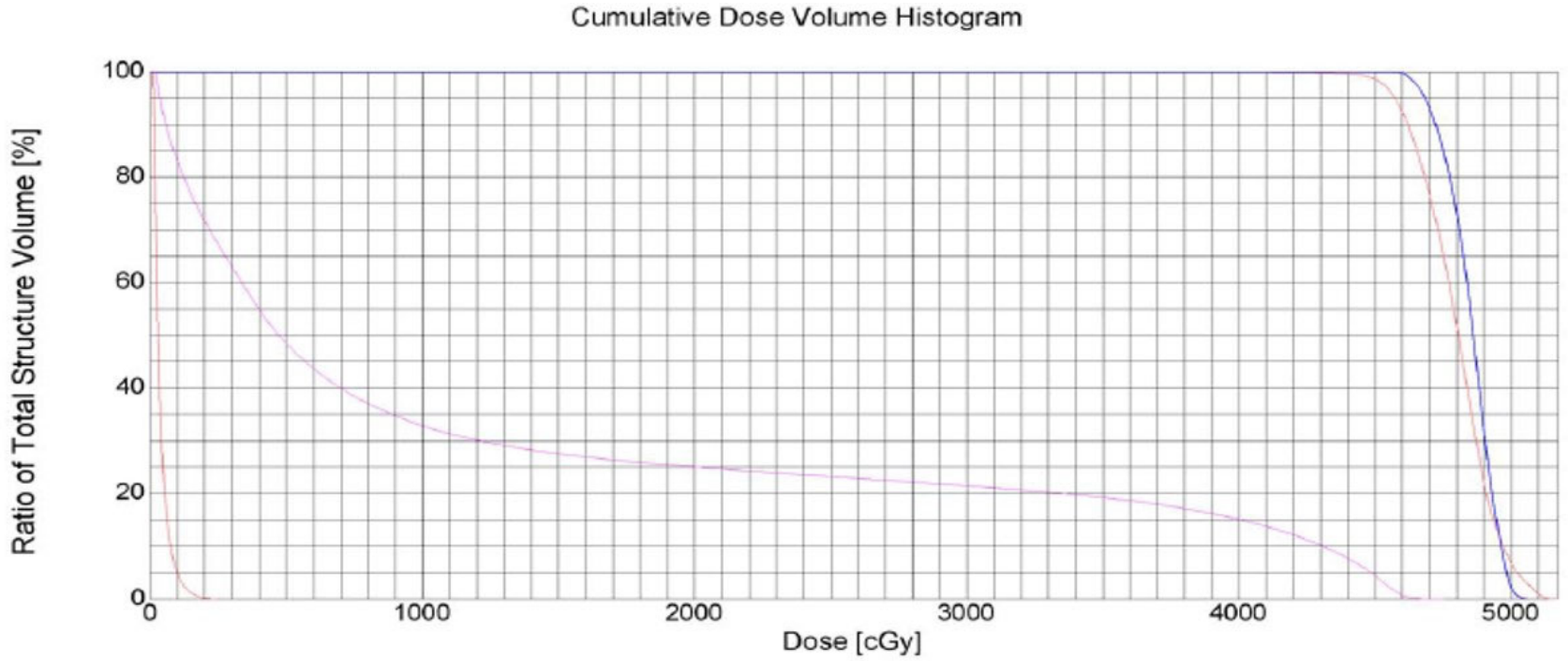
Preoperative Systemic Therapy
- In patients treated with preoperative systemic therapy, adjuvant RT is based on the maximal disease stage (ie, clinical stage, pathologic stage, tumor characteristics) at diagnosis (before preoperative systemic therapy) and pathology results after preoperative systemic therapy.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Optimizing Delivery of Individual Therapy

- It is important to individualize RT planning and delivery.
  - CT-based treatment planning should be routinely utilized to delineate target volumes and adjacent organs at risk.
  - Radiation to the breast/chest wall and nodal regions is generally delivered with single energy or mixed energy photons ± electrons.
  - Improved homogeneity of the target dose and sparing of normal tissues can be accomplished using compensators such as wedges, forward planning using segments, and intensity-modulated RT (IMRT).
  - Additional techniques such as respiratory control (deep inspiration breath-hold), prone positioning, cardiac blocks may also be used to try to further reduce dose to heart, lung, and adjacent normal tissue.
  - Verification of treatment setup consistency is done with weekly imaging. When using certain techniques (ie, prone breast), more frequent imaging may be appropriate. Standard utilization of daily imaging is not recommended.
  - When treating the internal mammary nodes, dose-volume histograms (DVHs) should be used to evaluate dose constraints, dose to normal tissues (ie, heart, lung), and planning target volumes (PTVs).
- It is common for RT to follow chemotherapy when chemotherapy is indicated.

Dose Volume Histogram



Some structures are unapproved or rejected

	Structure Status	Coverage [%/%]	Volume	Min Dose	Max Dose	Mean Dose	Modal Dose	Median Dose	Std Dev
IM Nodes	Unapproved	100.0 / 100.0	481.3 [cm³]	3769.1 cGy	5172.9 cGy	4798.6 cGy	4808.8 cGy	4805.3 cGy	136.2 cGy
CTV	Unapproved	100.0 / 100.0	42.1 [cm³]	4544.3 cGy	5060.0 cGy	4850.2 cGy	4862.8 cGy	4860.3 cGy	90.0 cGy
Lung	Unapproved	100.0 / 100.0	1193.4 [cm³]	14.4 cGy	4752.1 cGy	1301.5 cGy	29.9 cGy	473.8 cGy	1589.4 cGy
Heart	Unapproved	100.0 / 100.0	370.8 [cm³]	7.4 cGy	245.4 cGy	37.4 cGy	15.0 cGy	27.8 cGy	29.9 cGy

Choosing Wisely®

An initiative of the ABIM Foundation

American Society for Radiation Oncology

ASTRO

TARGETING CANCER CARE

Five Things Physicians and Patients Should Question

Don't initiate whole breast radiotherapy as a part of breast conservation therapy in women age ≥50 with early stage invasive breast cancer without considering shorter treatment schedules.

National Comprehensive Cancer Network®

NCCN Guidelines Version 5.2020
Invasive Breast Cancer

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ASTRO hWBRT Consensus 2011

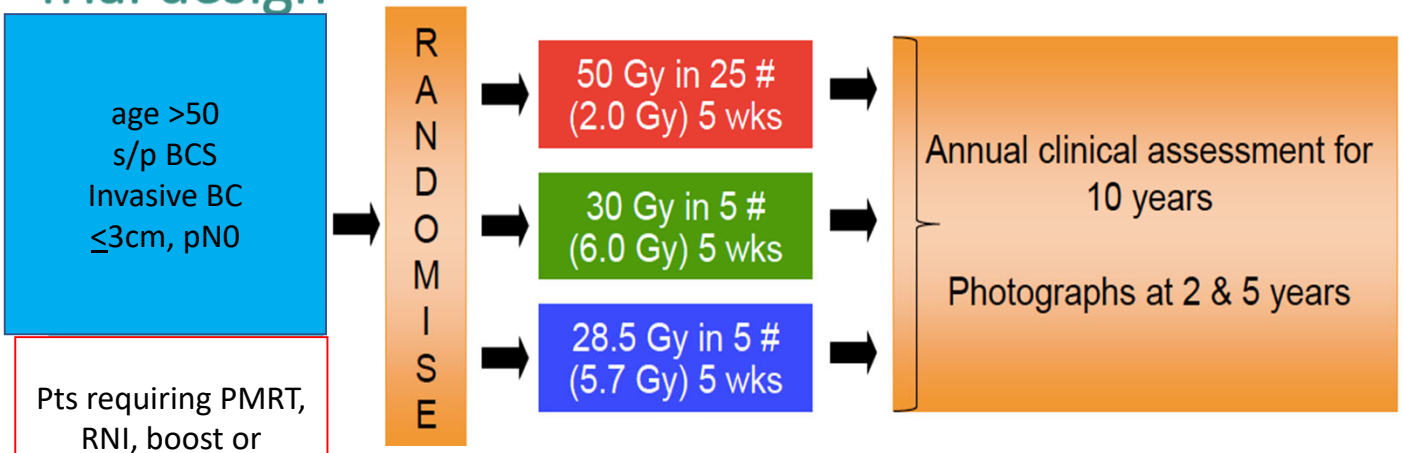
Factor	2011 Guideline	2018 Guideline
Age	>50 years	Any
Stage	T1 or T2, N0	Any, provided only WBRT
Chemotherapy	No	Yes
Dose homogeneity	+/- 7% of the central axis	Volume >105% should be minimized
	Smith B, Int J Radiat Bio Phy 2011	Smith B, PRO, 2018

Almost all patient receiving WBRT alone (without regional nodal radiation) are eligible for moderately hWBRT

FAST Trial

FAST Trial (CRUKE/04/015)

Trial design



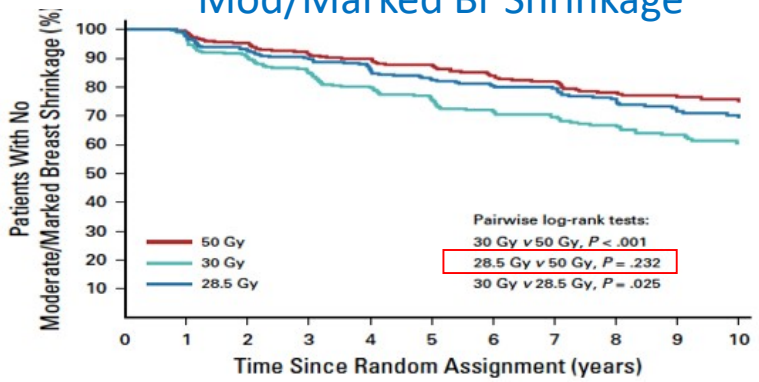
Primary Cosmesis End-point:

3-yr physician assessed moderate to severe breast adverse effects:

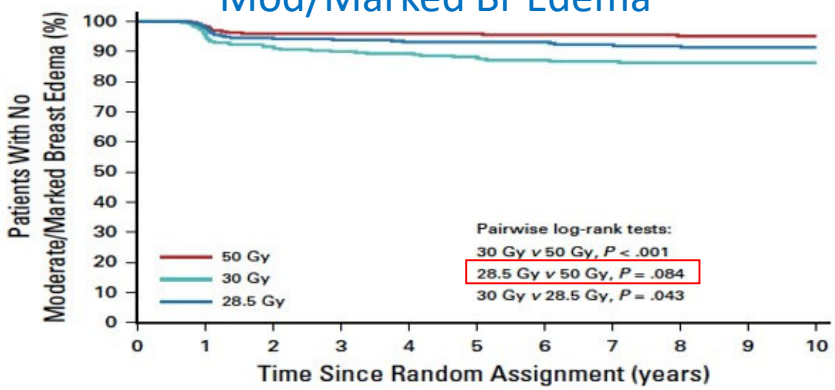
Agarwal, et al. Radiother Oncol. 2011 Jul;100(1):93-100
Brunt AM, et al JCO July 2020

FAST Trial: 10 yr. Follow-up

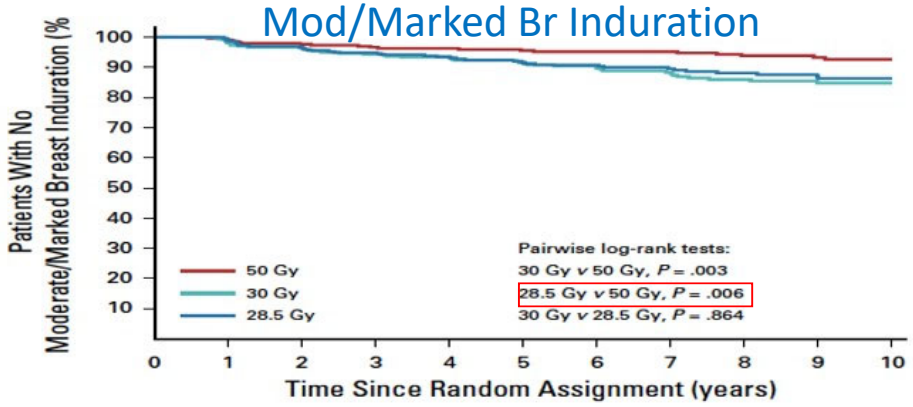
Mod/Marked Br Shrinkage



Mod/Marked Br Edema



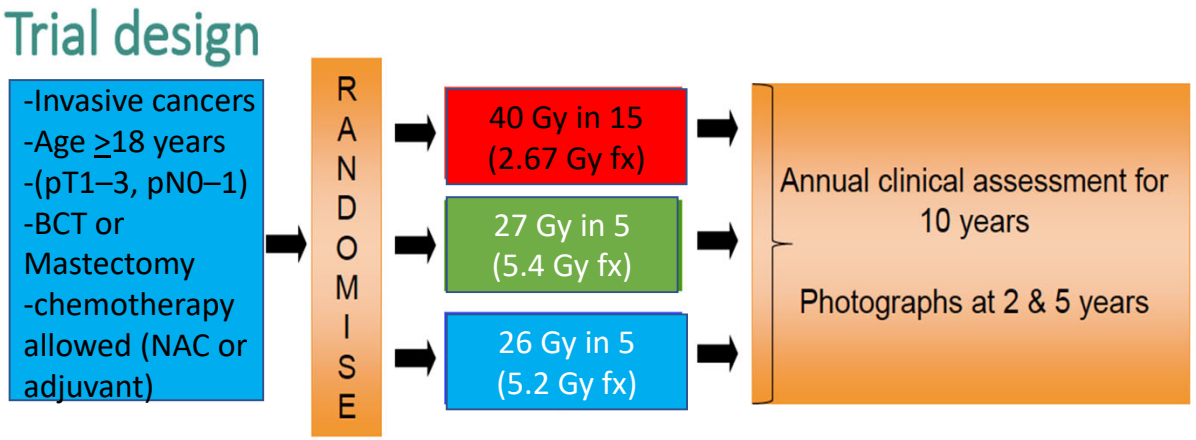
Mod/Marked Br Induration



10 Year Cum
LR 1.3%

Brunt AM, et al JCO July 2020

FAST-Forward Trial: 5 yr Follow-up



- Breast or CW
- Protocol mandated 3D-CT planning

Dose constraints (5 fx):

PTV: 95% of PTV should get 95% prescribed dose

$V_{8\,Gy}$ ipsilateral lung: ≤15%

$V_{7\,Gy}$ heart: ≤5 % and $V_{1,5\,Gy}$ heart: ≤ 30%

Dmax of ≤ 110%

Brunt AM, et al Lancet April 2020

FAST-Forward Trial: 5 yr. Outcomes

	40 Gy in 15 fractions (n=1361)	27 Gy in five fractions (n=1367)	26 Gy in five fractions (n=1368)
Local tumour control event (primary endpoint)*	31 (2·3%)	27 (2·0%)	21 (1·5%)
Local relapse	23 (1·7%)	22 (1·6%)	17 (1·2%)
Ipsilateral breast, new primary	6 (0·4%)	3 (0·2%)	4 (0·3%)
Cannot differentiate	2 (0·1%)	2 (0·1%)	0
Regional relapse	13 (1·0%)	11 (0·8%)	10 (0·7%)
Distant relapse	59 (4·3%)	69 (5·0%)	76 (5·5%)

- Local relapse: Non-inferiority bt 3 arms
- No detectable dose response bt 26 Gy and 27 Gy arms
- Patient & clinician-assessed normal tissue effects:
  - 26 Gy/5.2 Gy fx = 40 Gy/15
  - 26 Gy/5.2 Gy fx better than 27 Gy/5.4 Gy
  - 26Gy less mod/severe toxicity

Brunt AM, et al Lancet April 2020

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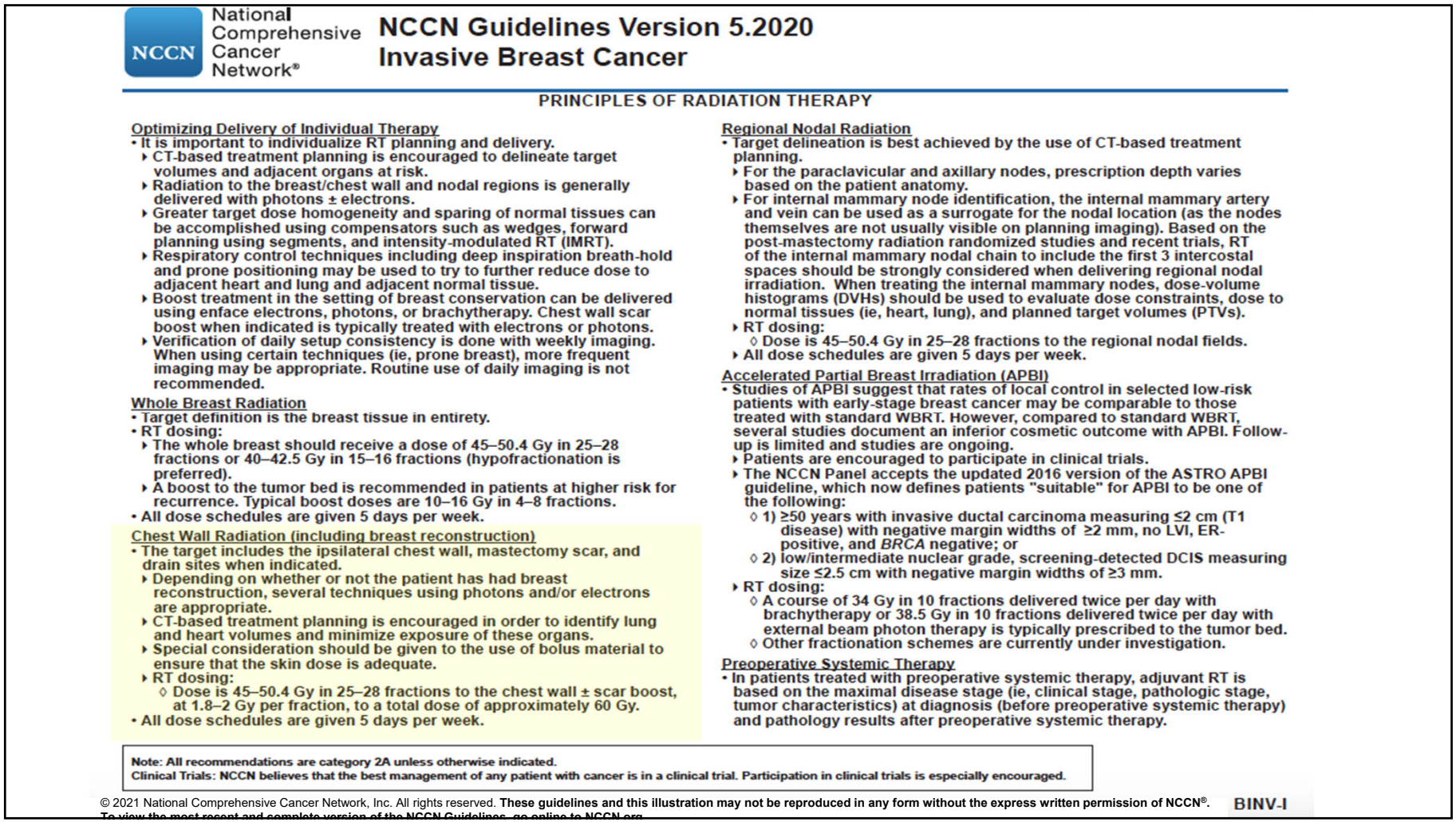
Invasive Breast Cancer

Whole Breast Radiation

- Target definition is the breast tissue in entirety.
- 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. Typical boost doses are 10–16 Gy in 4–8 fractions.
- Lumpectomy cavity boost can be delivered using enface electrons, photons, or brachytherapy.
- For patients who require a more limited number of treatment visits for WBRT delivery, ultra-hypofractionated WBRT of 28.5 Gy delivered as 5 (once-a-week) fractions, may be considered in selected patients aged ≥50 years following BCS with pTis/T1/T2/N0 tumors. However, late toxicity effects beyond 10 years are not currently defined.[1]
  - The optimal fractionation for the delivery of a boost is not known for this regimen.
  - 3-D planning to minimize inhomogeneity and exposure to heart and lung is essential when using this regimen.

[1] Brunt AM, Haviland JS, Sydenham M, et al. Ten-year results of FAST: A randomized controlled trial of 5-fraction whole-breast radiotherapy for early breast cancer. J Clin Oncol 2020;38(28):3261-3272.



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NCCN Guidelines Version 5.2020
Invasive Breast Cancer

PRINCIPLES OF RADIATION THERAPY

Optimizing Delivery of Individual Therapy
- It is important to individualize RT planning and delivery.
  - CT-based treatment planning is encouraged to delineate target volumes and adjacent organs at risk.
  - Radiation to the breast/chest wall and nodal regions is generally delivered with photons ± electrons.
  - Greater target dose homogeneity and sparing of normal tissues can be accomplished using compensators such as wedges, forward planning using segments, and intensity-modulated RT (IMRT).
  - Respiratory control techniques including deep inspiration breath-hold and prone positioning may be used to try to further reduce dose to adjacent heart and lung and adjacent normal tissue.
  - Boost treatment in the setting of breast conservation can be delivered using enface electrons, photons, or brachytherapy. Chest wall scar boost when indicated is typically treated with electrons or photons.
  - Verification of daily setup consistency is done with weekly imaging. When using certain techniques (ie, prone breast), more frequent imaging may be appropriate. Routine use of daily imaging is not recommended.

Whole Breast Radiation
- Target definition is the breast tissue in entirety.
- RT dosing:
  - The whole breast should receive a dose of 45–50.4 Gy in 25–28 fractions or 40–42.5 Gy in 15–16 fractions (hypofractionation is preferred).
  - A boost to the tumor bed is recommended in patients at higher risk for recurrence. Typical boost doses are 10–16 Gy in 4–8 fractions.
- All dose schedules are given 5 days per week.

Chest Wall Radiation (including breast reconstruction)
- The target includes the ipsilateral chest wall, mastectomy scar, and drain sites when indicated.
  - Depending on whether or not the patient has had breast reconstruction, several techniques using photons and/or electrons are appropriate.
  - CT-based treatment planning is encouraged in order to identify lung and heart volumes and minimize exposure of these organs.
  - Special consideration should be given to the use of bolus material to ensure that the skin dose is adequate.
  - RT dosing:
    - Dose is 45–50.4 Gy in 25–28 fractions to the chest wall ± scar boost, at 1.8–2 Gy per fraction, to a total dose of approximately 60 Gy.
- All dose schedules are given 5 days per week.

Regional Nodal Radiation
- Target delineation is best achieved by the use of CT-based treatment planning.
  - For the paraclavicular and axillary nodes, prescription depth varies based on the patient anatomy.
  - For internal mammary node identification, the internal mammary artery and vein can be used as a surrogate for the nodal location (as the nodes themselves are not usually visible on planning imaging). Based on the post-mastectomy radiation randomized studies and recent trials, RT of the internal mammary nodal chain to include the first 3 intercostal spaces should be strongly considered when delivering regional nodal irradiation. When treating the internal mammary nodes, dose-volume histograms (DVHs) should be used to evaluate dose constraints, dose to normal tissues (ie, heart, lung), and planned target volumes (PTVs).
  - RT dosing:
    - Dose is 45–50.4 Gy in 25–28 fractions to the regional nodal fields.
  - All dose schedules are given 5 days per week.

Accelerated Partial Breast Irradiation (APBI)
- Studies of APBI suggest that rates of local control in selected low-risk patients with early-stage breast cancer may be comparable to those treated with standard WBRT. However, compared to standard WBRT, several studies document an inferior cosmetic outcome with APBI. Follow-up is limited and studies are ongoing.
  - Patients are encouraged to participate in clinical trials.
  - The NCCN Panel accepts the updated 2016 version of the ASTRO APBI guideline, which now defines patients "suitable" for APBI to be one of the following:
    - 1) ≥50 years with invasive ductal carcinoma measuring ≤2 cm (T1 disease) with negative margin widths of ≥2 mm, no LVI, ER-positive, and *BRCA* negative; or
    - 2) low/intermediate nuclear grade, screening-detected DCIS measuring size ≤2.5 cm with negative margin widths of ≥3 mm.
  - RT dosing:
    - A course of 34 Gy in 10 fractions delivered twice per day with brachytherapy or 38.5 Gy in 10 fractions delivered twice per day with external beam photon therapy is typically prescribed to the tumor bed.
    - Other fractionation schemes are currently under investigation.

Preoperative Systemic Therapy
- In patients treated with preoperative systemic therapy, adjuvant RT is based on the maximal disease stage (ie, clinical stage, pathologic stage, tumor characteristics) at diagnosis (before preoperative systemic therapy) and pathology results after preoperative systemic therapy.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

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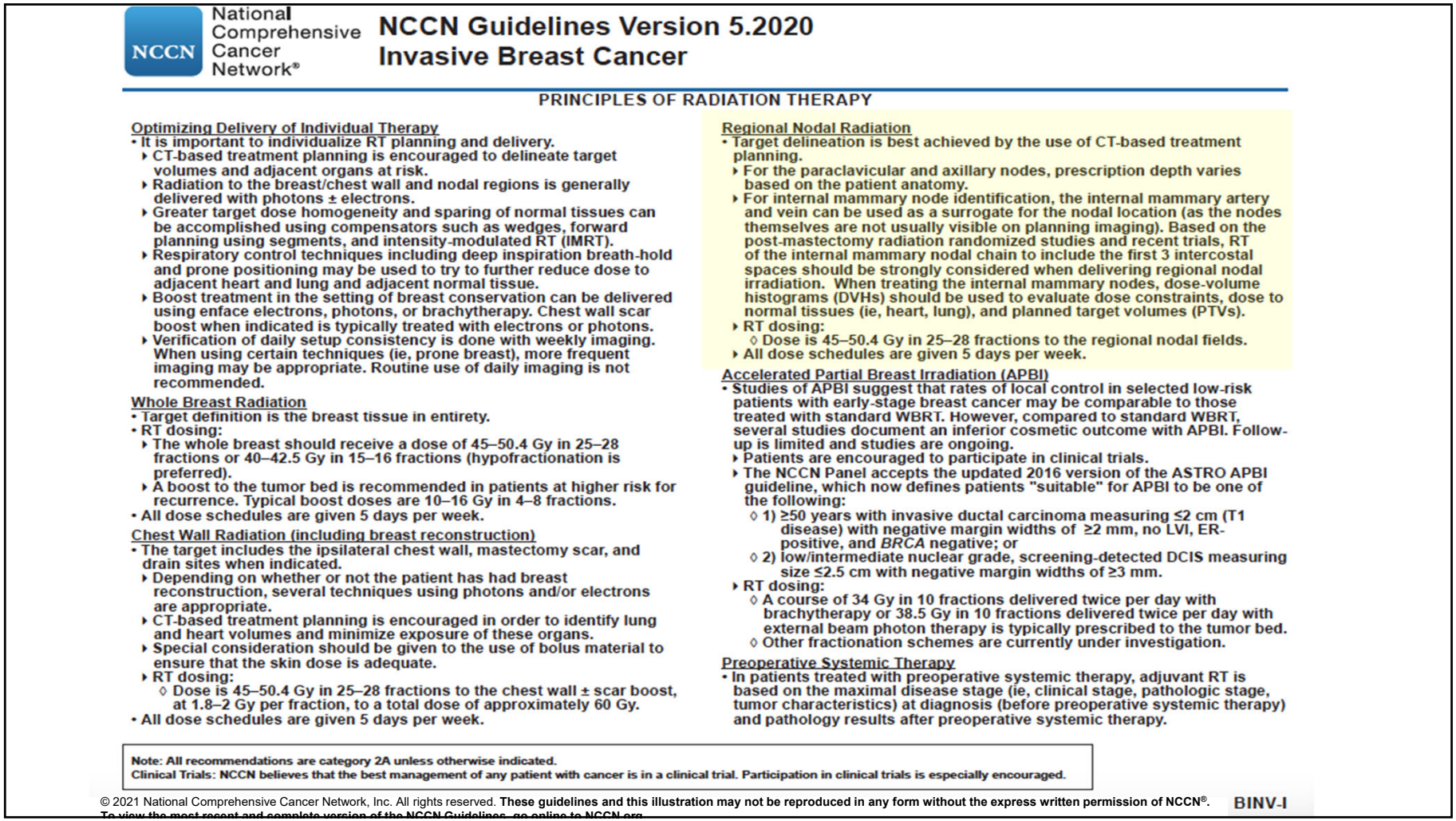
PRINCIPLES OF RADIATION THERAPY

Chest Wall Radiation (including breast reconstruction)

- The target includes the ipsilateral chest wall, mastectomy scar, and drain sites when indicated.
  - Depending on whether or not the patient has had breast reconstruction, several techniques using photons and/or electrons are appropriate.
  - Special consideration should be given to the use of bolus material to ensure that the skin dose is adequate, particularly in the case of inflammatory breast cancer.
  - RT dosing:
    - Dose is 45–50.4 Gy in 25–28 fractions to the chest wall ± scar boost, at 1.8–2 Gy per fraction, to a total dose of approximately 60–66 Gy.
- Chest wall scar boost may be delivered with or without bolus using electrons or photons.



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Invasive Breast Cancer

PRINCIPLES OF RADIATION THERAPY

Optimizing Delivery of Individual Therapy
- It is important to individualize RT planning and delivery.
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  - Radiation to the breast/chest wall and nodal regions is generally delivered with photons ± electrons.
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Whole Breast Radiation
- Target definition is the breast tissue in entirety.
- RT dosing:
  - The whole breast should receive a dose of 45–50.4 Gy in 25–28 fractions or 40–42.5 Gy in 15–16 fractions (hypofractionation is preferred).
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- All dose schedules are given 5 days per week.

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  - Special consideration should be given to the use of bolus material to ensure that the skin dose is adequate.
  - RT dosing:
    - Dose is 45–50.4 Gy in 25–28 fractions to the chest wall ± scar boost, at 1.8–2 Gy per fraction, to a total dose of approximately 60 Gy.
- All dose schedules are given 5 days per week.

Regional Nodal Radiation
- Target delineation is best achieved by the use of CT-based treatment planning.
  - For the paraclavicular and axillary nodes, prescription depth varies based on the patient anatomy.
  - For internal mammary node identification, the internal mammary artery and vein can be used as a surrogate for the nodal location (as the nodes themselves are not usually visible on planning imaging). Based on the post-mastectomy radiation randomized studies and recent trials, RT of the internal mammary nodal chain to include the first 3 intercostal spaces should be strongly considered when delivering regional nodal irradiation. When treating the internal mammary nodes, dose-volume histograms (DVHs) should be used to evaluate dose constraints, dose to normal tissues (ie, heart, lung), and planned target volumes (PTVs).
  - RT dosing:
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- Studies of APBI suggest that rates of local control in selected low-risk patients with early-stage breast cancer may be comparable to those treated with standard WBRT. However, compared to standard WBRT, several studies document an inferior cosmetic outcome with APBI. Follow-up is limited and studies are ongoing.
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  - RT dosing:
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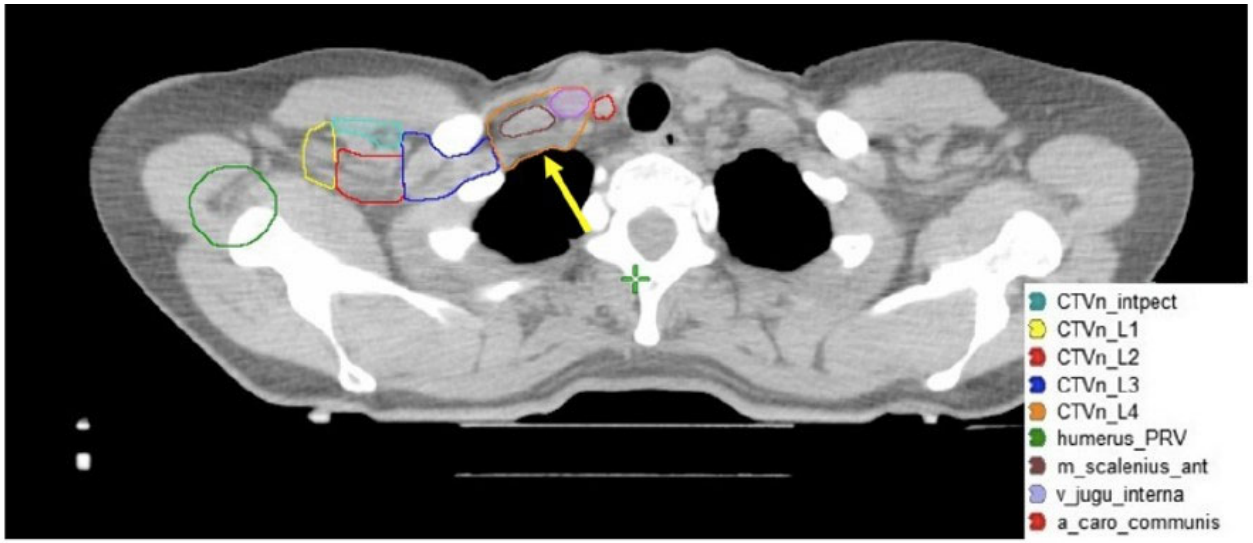
Multiple Breast Atlases Available to Contour Nodes at Risk



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Regional Nodal Radiation

- For paraclavicular and axillary nodes, prescription depth varies based on the patient anatomy.
- Regional nodes should be contoured when considering regional nodal RT. Refer to breast atlases for contouring guidelines.[2,3]
- RT dosing:
  - Dose is 45–50.4 Gy in 25–28 fractions to the regional nodal fields.
  - A supplemental boost of RT can be delivered to grossly involved or enlarged lymph nodes (ie, internal mammary or clavicular) that have not been surgically addressed.

[2] Offersen BV, Boersma LJ, Kirkove C, et al. ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer. Radiother Oncol 2015;114(1):3-10.

[3] Gentile MS, Usman AA, Neuschler EI, et al. Contouring guidelines for the axillary lymph nodes for the delivery of radiation therapy in breast cancer: Evaluation of the RTOG Breast Cancer Atlas. Int J Radiat Oncol Biol Phys 2015;93(2):257-265.

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Invasive Breast Cancer

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ASTRO APBI Consensus "Suitable" 2009 vs. 2016 Criteria

Factor	2009 Guideline	2016 Guideline
Age	>60 years	>50
Margins	Negative by at least 2mm	Negative by at least 2mm
Stage	T1 only	T1 or Tis
Histology	IDC	IDC
LVI	No	No
DCIS	Not Allowed	If following criteria are met: • Screen detected • GI or GII • Size <2.5 cm • Margins >3mm

Smith B,Int J Radiat Bio Phy 2011

Correa PRO, 2016

Florence APBI-IMRT Trial: 10 yr Follow-up

N=520

- WBRT (50 Gy)
- APBI-IMRT (30 Gy/6 Gy qod)

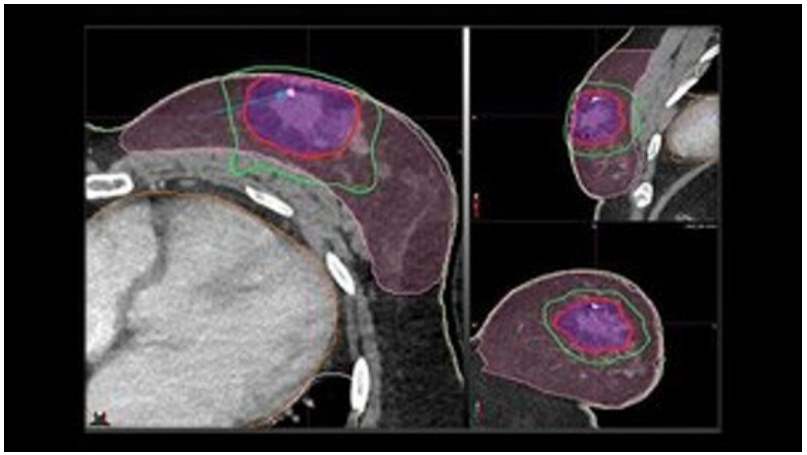
Treatment Details:

- Co-planar VMAT/IMRT plan
- ~2-cm around surgical clips
- 5 step and shoot fields

Primary Endpoints:

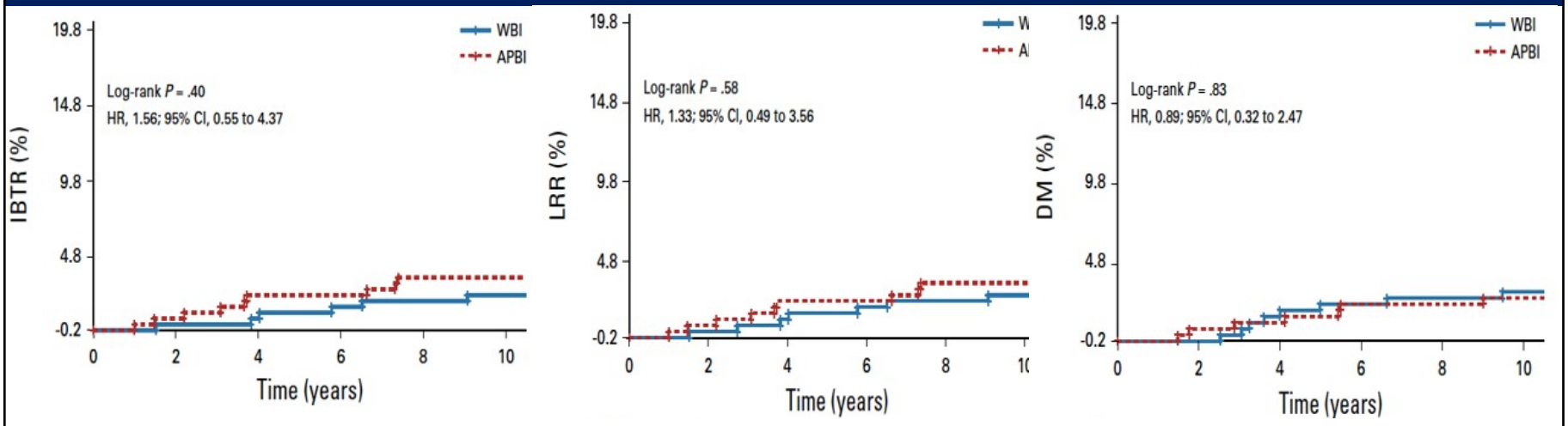
- IBTR

ASTRO Risk class		
suitable	133 (51.2)	113 (43.5)
cautionary	74 (28.5)	79 (30.4)
unsuitable	53 (20.3)	68 (26.1))



Meattini, I 2020 JCO

Florence APBI-IMRT Trial 10 yr.



Very low risk <5% for IBTR, LRR and DM in both arms
No difference in cosmetic outcomes
Benefits of this regimen:

- Once per day, every other day x 5 (others are BID)
- Some data suggest EBRT-based APBI have suggest worse cosmetic outcomes delivered BID
- QOD-no difference in cosmesis at 10 years

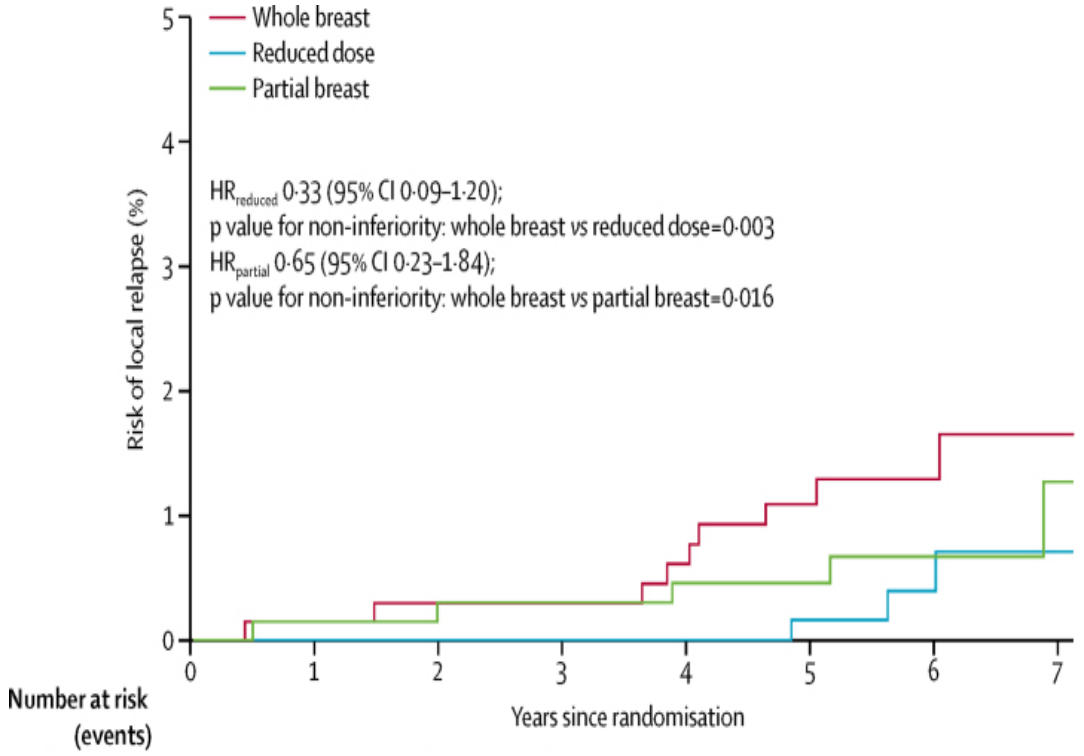
Meattini, I 2020 JCO

IMPORT-Low Trial

40 Gy/15 Whole Breast RT

40 Gy/15 Partial Breast RT

36Gy /40Gy Reduced dose



Coles, C 2017 Lancet

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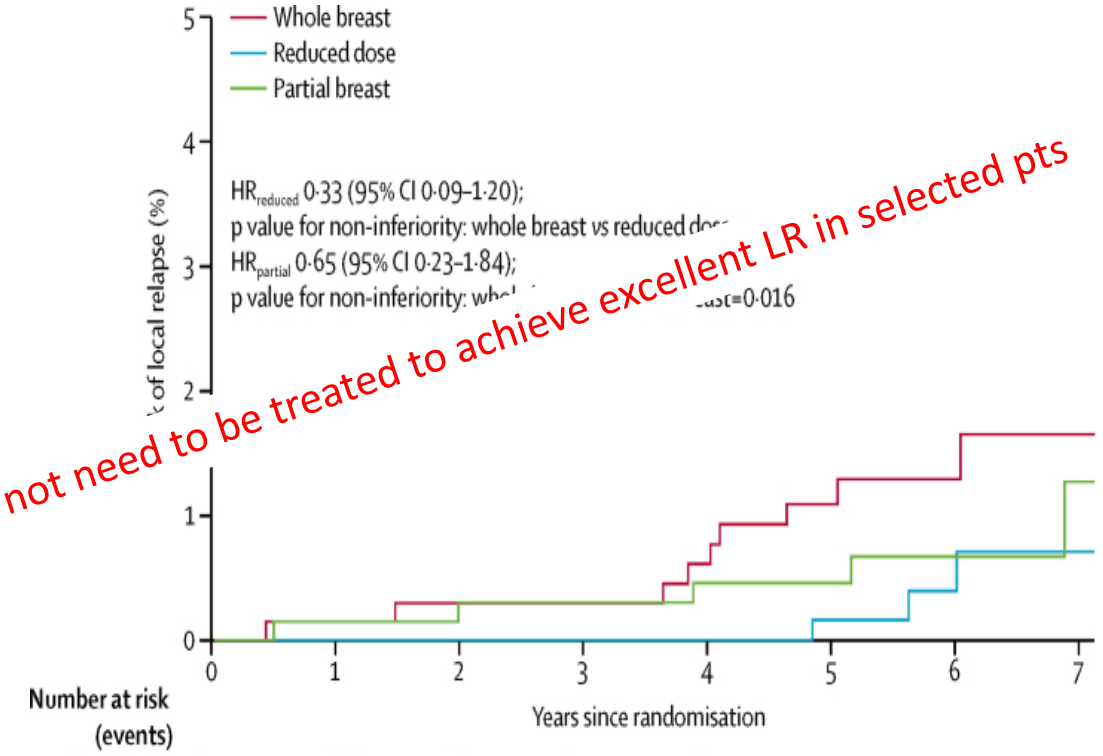

Confirms that the whole breast does not need to be treated to achieve excellent LR in selected pts

Coles, C 2017 Lancet

RAPID	NSABP B-39
8-year cumulative results: APBI: strictly external beam 3.0% APBI vs. 2.8% WBRT non-inferior Worse cosmetic outcomes with EBRT	10-year cumulative outcomes IBTR: APBI: external beam single-entry catheter multi-entry catheter techniques 4.6% APBI vs. 3.9% cf WBRT Not non-inferior Not worse cosmetic outcomes w/EBRT APBI
Whelan T, 2019 Lancet	Vicini F, 2019 Lancet

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Invasive Breast Cancer

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Accelerated Partial Breast Irradiation (APBI)

- **Studies of APBI suggest that rates of local control in selected low-risk patients with early-stage breast cancer may be comparable to those treated with standard WBRT. However, compared to standard WBRT, several studies document an inferior cosmetic outcome with external beam delivery methods of APBI. Follow-up is limited and studies are ongoing.**
  - **Patients are encouraged to participate in clinical trials.**
  - **The NCCN Panel accepts the updated 2016 version of the ASTRO APBI guideline consensus statement, which now defines patients age ≥50 years to be considered "suitable" for APBI if:**
    - ◊ **Invasive ductal carcinoma measuring ≤2 cm (pT1 disease) with negative margin widths of ≥2 mm, no LVI, ER-positive, and BRCA negative; or**
    - ◊ **Low/intermediate nuclear grade, screening-detected DCIS measuring size ≤2.5 cm with negative margin widths of ≥3 mm.**
- **RT dosing**

Regimen	Method	Reference
30 Gy/5 fractions QOD (preferred)	**External beam RT (EBRT)[a]**	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. Eur J Cancer 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. J Clin Oncol 2020;38:4175-4183.
40 Gy/15 fractions	**EBRT**	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. Lancet 2017;390:1048-1060.
34 Gy/10 fractions BID	**Balloon/ Interstitial**	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. Lancet 2019;394:2155-2164.
38.5 Gy/10 fractions BID	**EBRT**	Whelan TJ, Julian JA, Berrang TS, et al. External beam accelerated partial breast irradiation versus whole breast irradiation after breast conserving surgery in women with ductal carcinoma in situ and node-negative breast cancer (RAPID): a randomised controlled trial. Lancet 2019;394:2165-2172.

[a] The protocol mandated IMRT.

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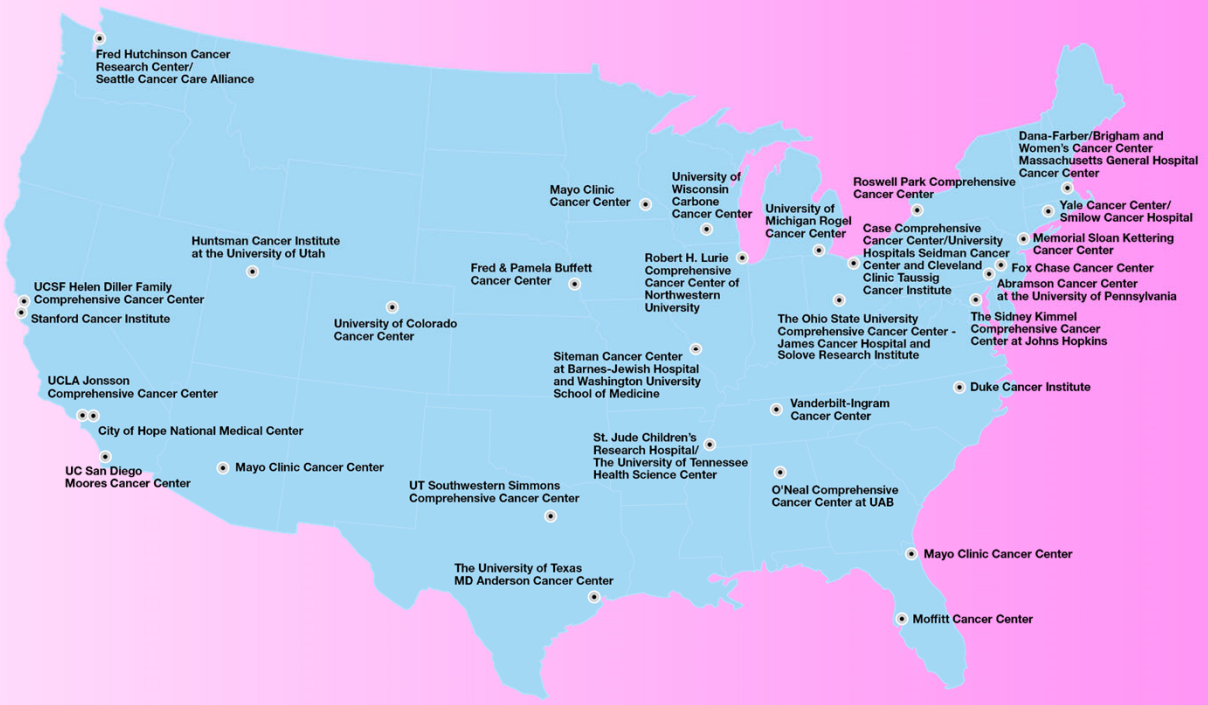
NCCN Member Institutions

- **Who We Are**
  An alliance of leading cancer centers devoted to patient care, research, and education
- **Our Mission**
  To improve and facilitate quality, effective, efficient, and accessible cancer care so patients can live better lives
- **Our Vision**
  To define and advance high-quality, high-value, patient-centered cancer care globally



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