



Where **Science** Becomes **Hope**

# IS PMRT NEEDED IN PATIENTS WITH NODAL PCR FOLLOWING NEOADJUVANT CHEMOTHERAPY?

## PRO

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**EMORY**  
**WINSHIP**  
**CANCER**  
**INSTITUTE**

National Cancer Institute-Designated  
Comprehensive Cancer Center

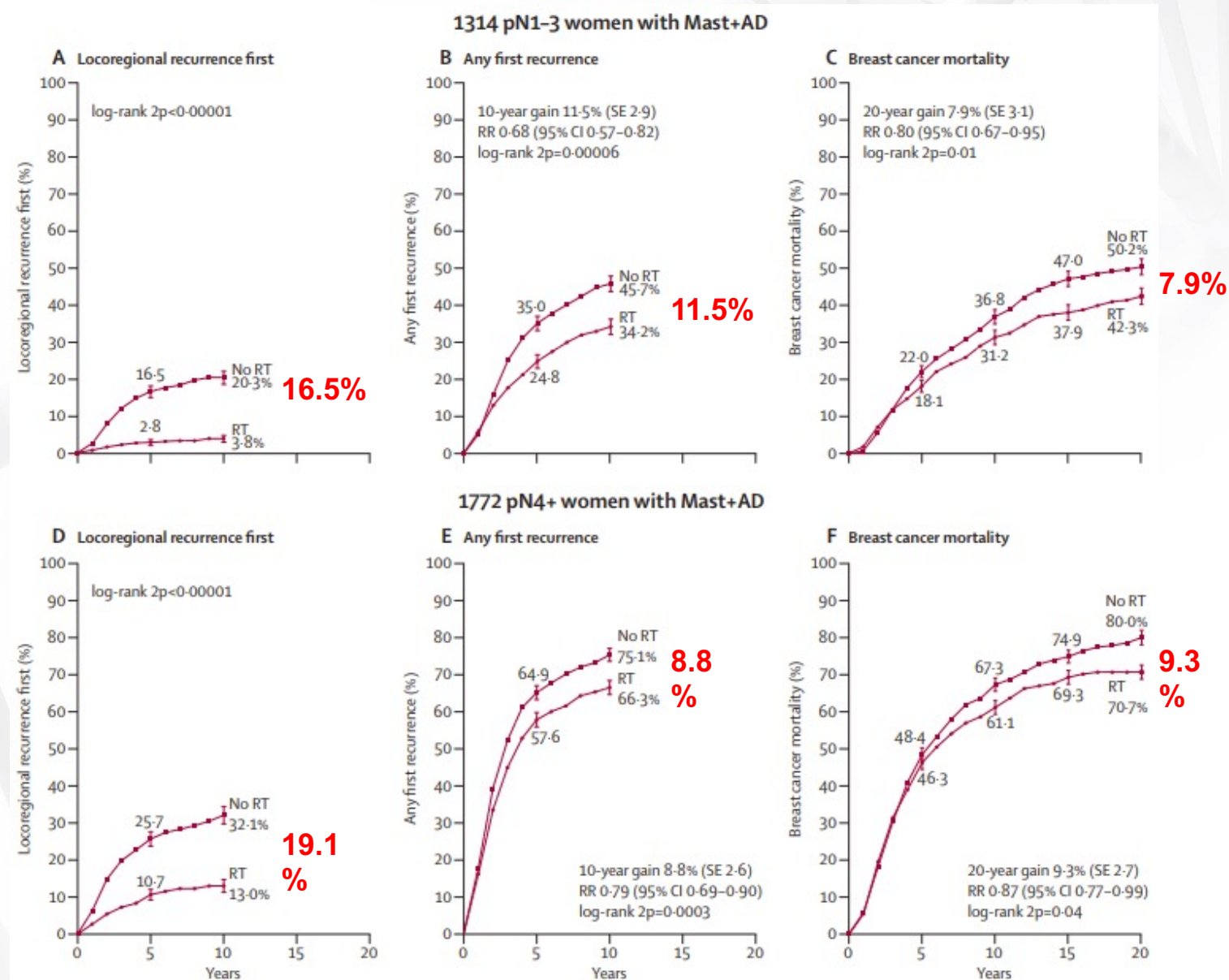
**NCI**

Designated  
Comprehensive  
Cancer Center

# BENEFIT OF PMRT

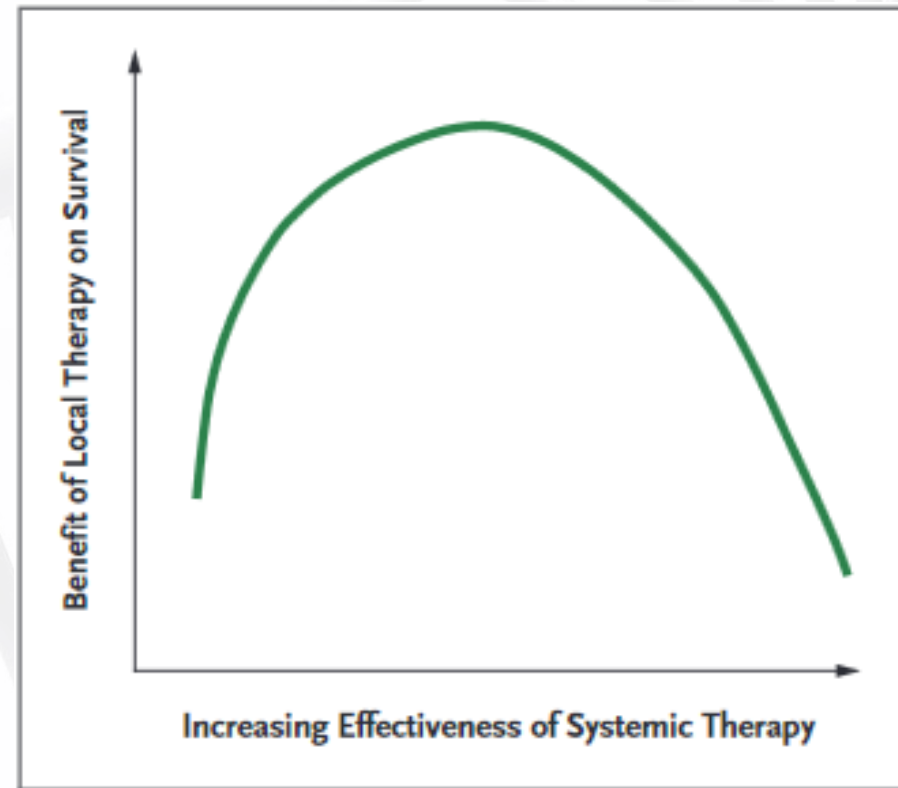
Landmark trials

EBCTCG, Lancet 2014; 383:2127-35





# HYPOTHETICAL BENEFIT OF LOCAL TUMOR CONTROL ON SURVIVAL WITH INCREASING EFFECTIVENESS OF SYSTEMIC THERAPY



Punglia RS et al. *N Engl J Med*. 2007;356(23):2399-2405.

## 2023 EBCTCG META-ANALYSIS

17 “randomized trials” starting before 2009 had been conducted worldwide in which the only difference between the 2 treatment groups involved irradiation of regional lymph nodes in 1 or more of 3 sites: the IMC, SC fossa, and axilla

- 1 not RCT: DBCG study where laterality used to determine RNI to the IMN (only administered for right-sided disease)
- Surgery, any RT to chest wall or breast, & systemic therapy same for both study arms (unconfounded comparisons)
- EBCTCG was able to collect individual pt data from all but one (165 patients)
- 8 older trials where RT technique was direct anterior photon beams alone
  - Usually these patients did not receive chest wall RT
  - Comparison=RNI vs no RT
  - Only 1.6% of patients received BCS, 20% chemo, 0 endocrine therapy
- 8 newer trials where RT technique was more tailored to spare heart & lung
  - Usually these patients did receive breast or chest wall RT
  - Comparison=more vs less RT
  - 57.7% of patients received BCS, 62% chemo, 61% endocrine therapy

# FINDINGS

In the 8 newer trials (12 167 patients), which started 1989-2008:

RNI significantly reduced recurrence (rate ratio 0.88, 95% CI, 0.81-0.95; P=.0008).

The main effect was on distant recurrence as few regional node recurrences were reported.

RNI significantly reduced breast cancer mortality (RR 0.87, 95% CI, 0.80-0.94; P=.0010), with no significant effect on non-breast-cancer mortality (0.97, 0.84-1.11; P=.63) or on heart disease mortality, contralateral breast cancer incidence, or other second cancer incidence, leading to significantly reduced all-cause mortality (0.90, 0.84-0.96; P=.0022).

Early Breast Cancer Trialists' Collaborative Group (EBCTCG). *Lancet*. 2023;402(10416):1991-2003.

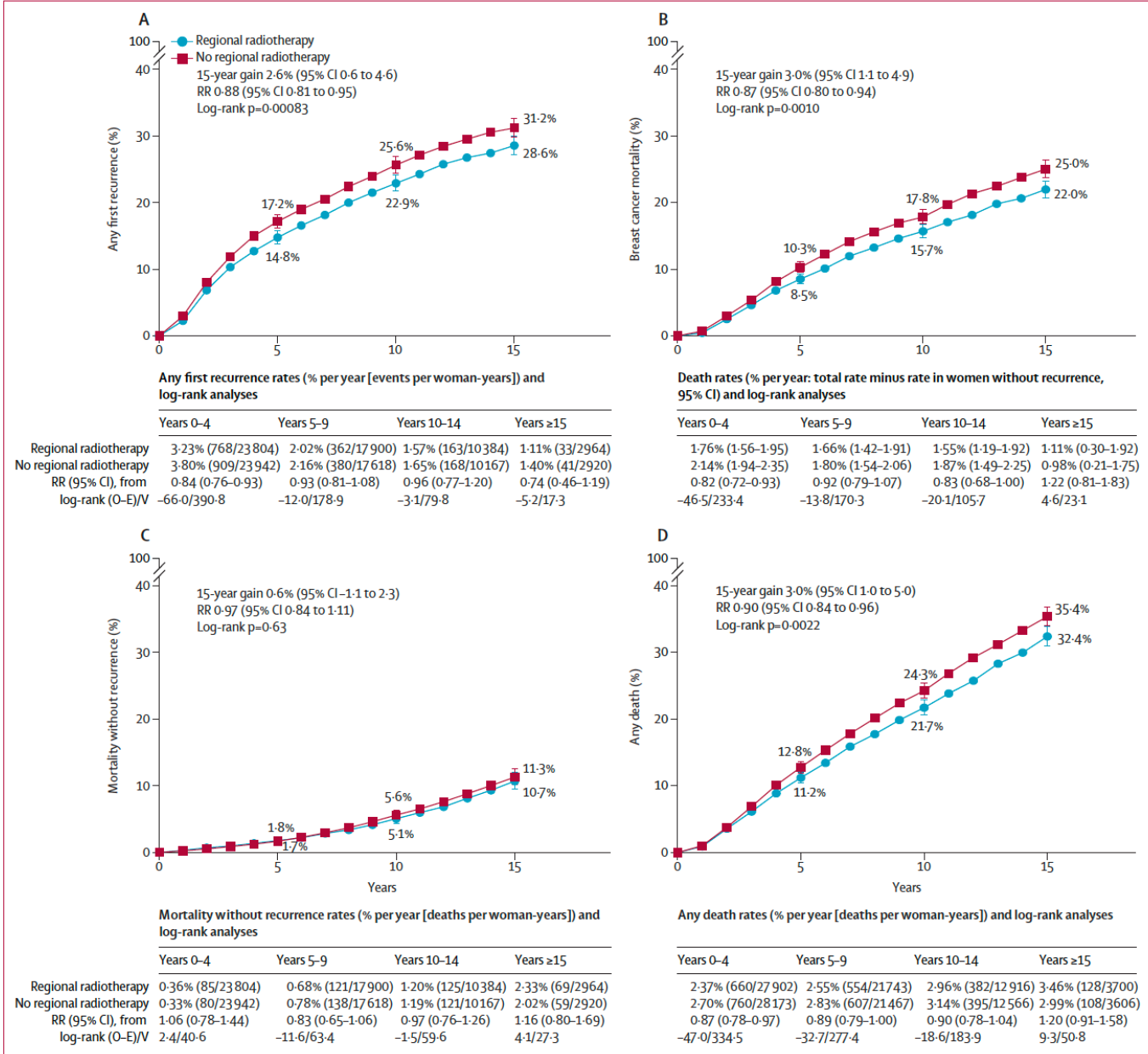


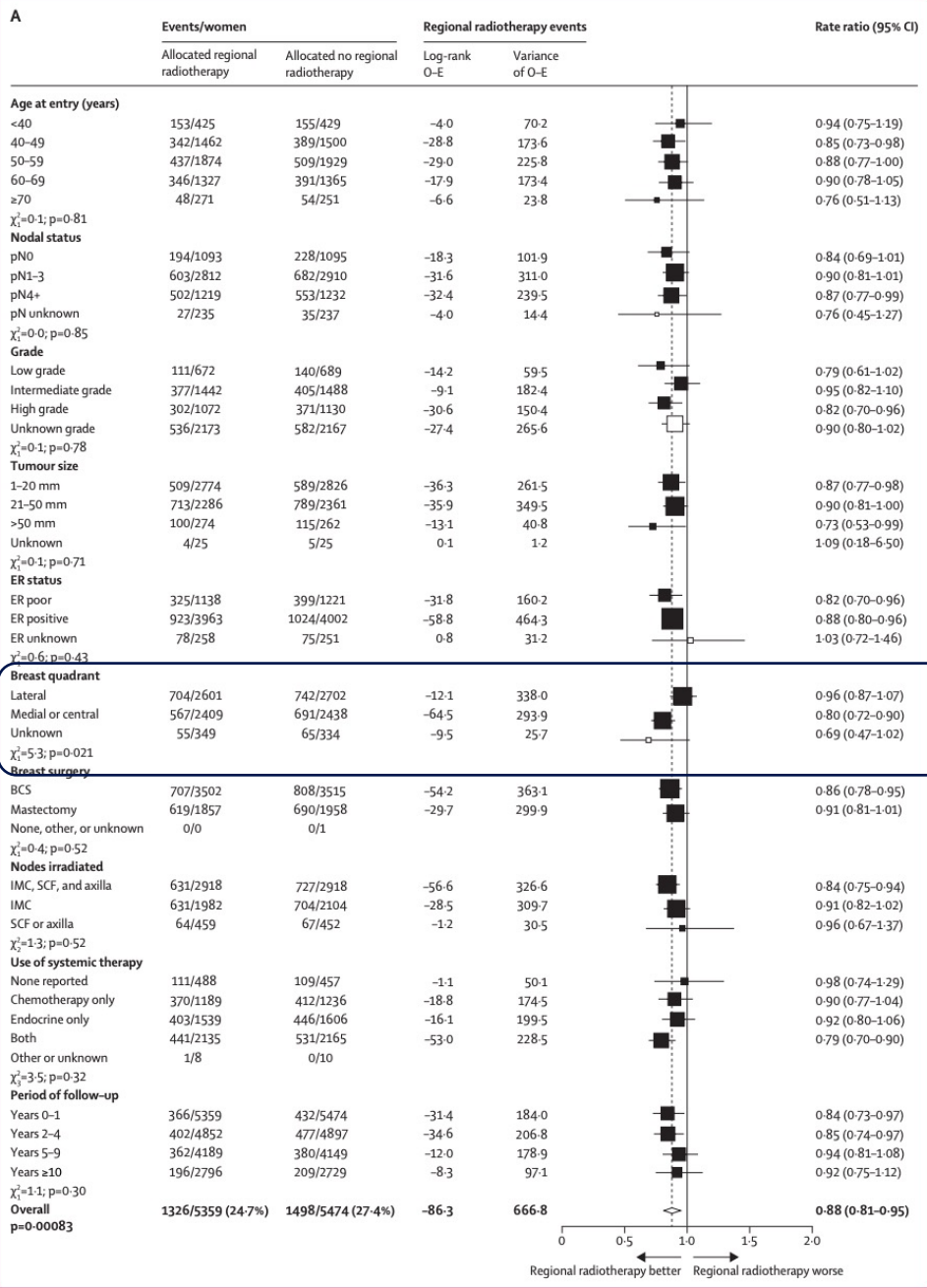
Figure 2: Effect of regional node radiotherapy in the eight newer trials on (A) any recurrence, (B) breast cancer mortality, (C) non-breast-cancer mortality, and (D) any death. One newer trial of 1334 women that reported only all-cause mortality is included only in graph D. RR=rate ratio.

# HETEROGENEITY TESTING

Proportional reductions in recurrence and breast cancer mortality did not vary significantly according to most treatment or patient or tumor characteristics, including age, nodal status, grade, tumor size, and ER status.

Some evidence to support a previous hypothesis that the proportional effects of RNI were greater for women with medial or central tumors than for women with lateral tumors (P value for heterogeneity of effect for medial or central vs lateral: any recurrence .021; distant recurrence .052; breast cancer mortality .069; overall mortality .40).

Early Breast Cancer Trialists' Collaborative Group (EBCTCG). *Lancet*. 2023;402(10416):1991-2003.





# ABSOLUTE BENEFITS

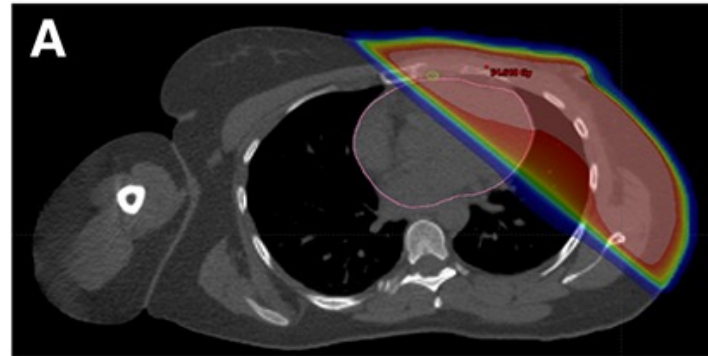
	Regional radiotherapy	No regional radiotherapy	Gain from regional radiotherapy
<b>Any recurrence</b>			
pN0	19.0%	21.3%	2.3%
pN1-3	25.6%	28.5%	2.9%
pN4+	46.8%	51.1%	4.3%
<b>Breast cancer mortality</b>			
pN0	10.9%	12.5%	1.6%
pN1-3	20.3%	23.0%	2.7%
pN4+	40.5%	45.0%	4.5%

Data are 15-year cumulative risks. The overall rate ratios (RRs) for any recurrence (RR=0.88; figure 3) and breast cancer mortality (0.87; figure 3) were applied to annual rates of any recurrence and breast cancer mortality in the trials, averaged over treatment groups (there was no significant heterogeneity in the proportional reductions [RRs] for any recurrence and breast cancer mortality). pN0=pathologically node negative. pN1-3=one to three involved axillary lymph nodes. pN4+=four or more involved axillary lymph nodes.

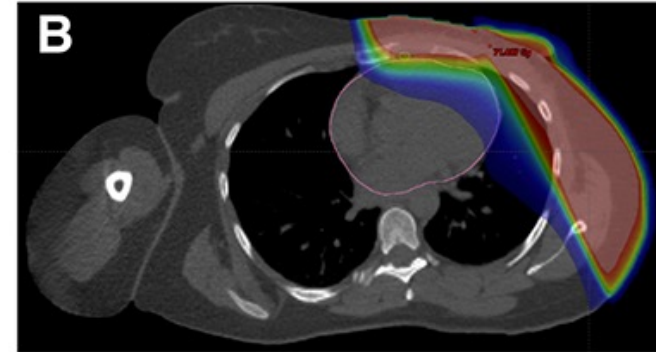
**Table 2: Absolute effect of regional node radiotherapy on 15-year risk of any recurrence and breast cancer mortality by nodal status in 10 833 women in the seven newer trials with data on recurrence**

Early Breast Cancer Trialists' Collaborative Group (EBCTCG). *Lancet*. 2023;402(10416):1991-2003.

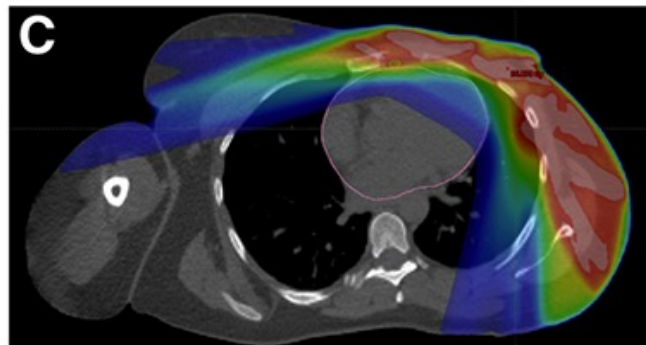
# DECLINING TOXICITY FROM MODERN RT: EXAMPLE OF CARDIAC SPARING



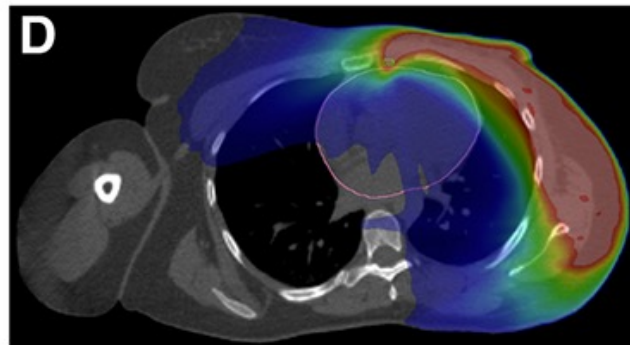
3DCT Photon Tangents



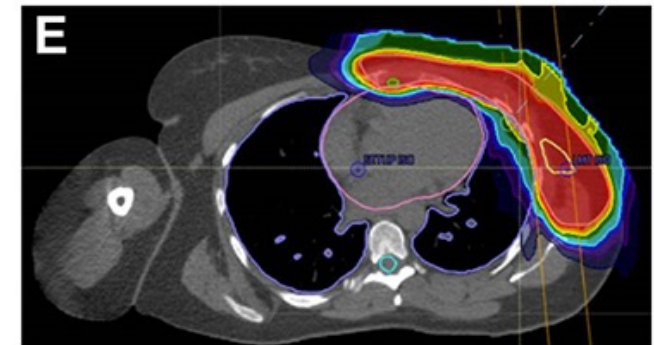
Electron/Photon Matched Fields Plan



IMRT Photon Plan



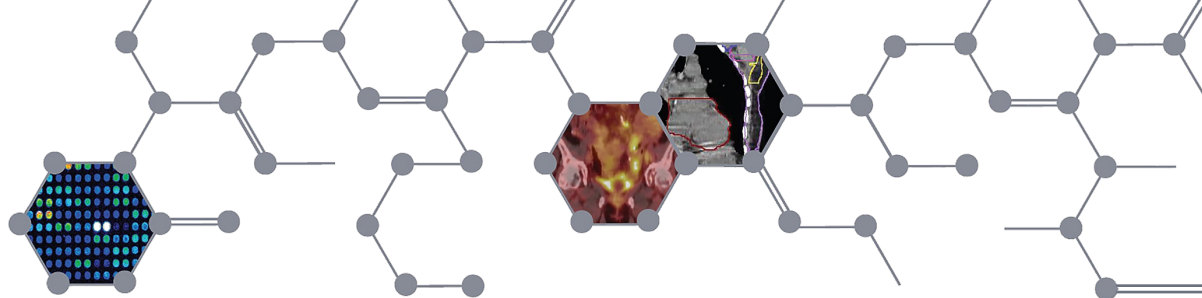
VMAT Photon Plan



Proton Plan

Torres MA et al. *J Clin Oncol*. 2020;38(20):2299-2309.





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

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

\*These authors contributed equally.

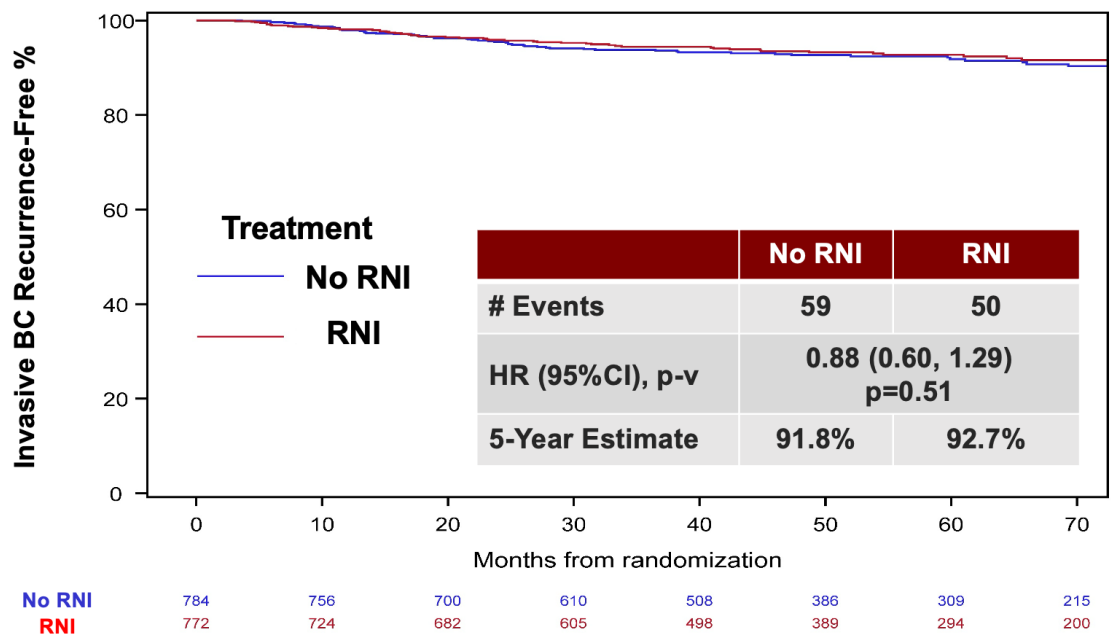
# LISTEN CAREFULLY & CONTINUE TO REFER PATIENTS FOR DISCUSSION: THIS IS A NUANCED STORY AND IT IS NOT COMPLETE...

Median Follow-up Time: 59.5 months (IQR 40.7-74.1)

53% ER+

N=1641

## Invasive Breast Cancer Recurrence-free Interval (IBCRFI)



## Isolated Loco-Regional Recurrence-free Interval (ILRRFI)\*

