Advances in Breast Radiation: Customizing Radiation Delivery

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Breast Cancer: Current State

- 310,720 estimated new invasive breast cases in 2024
- 56,500 new cases of DCIS
- Incidence has increased by 1% per year over the past decade
  - < 50 yo 1.4% increase per yr vs. >50 yo 0.7% per yr
- Breast cancer death rate has dropped by 44% since 1989

Current age	Diagnosed with invasive breast cancer	Dying from breast cancer
20	0.1% (1 in 1,344)	<0.1% (1 in 19,247)
30	0.5% (1 in 198)	<0.1% (1 in 2,192)
40	1.6% (1 in 62)	0.1% (1 in 723)
50	2.5% (1 in 41)	0.3% (1 in 348)
60	3.6% (1 in 28)	0.5% (1 in 217)
70	4.2% (1 in 24)	0.7% (1 in 141)
80	3.1% (1 in 32)	1.0% (1 in 103)
Lifetime risk	**13.1% (1 in 8)**	**2.3% (1 in 43)**

Probability is among those who have not been previously diagnosed with cancer and reflects the likelihood of diagnosis/death within 10 years of current age. Percentages and "1 in" numbers may not be numerically equivalent due to rounding.
Source: DevCan, Version 6.7.5.

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ACS Breast Cancer Facts and Figures 2024-2025

Radiation era y: ere are e going

- Wor in to decrease d ration of radiation treatment co rses
- Incorporatin response to neoad vant chemotherapy into radiation decision ma in
- Inte ratin molec lar profilin into radiation decision ma in

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Decreasing Radiation reatment Duration

- Moderate hypofractionated radiation C rrent standard of care for early sta e breast cancer patients
  - 42.5 y in 16 fractions
  - 40 y in 15 fractions follow by a l mpectomy cavity boost 10 y in 5 fractions
- ood to e cellent cosmesis in 70% of patients Whelan et al. 2010
- 40% mod mar ed late effects at 10 years Haviland et al. 2013

The UK Standardisation of Breast Radiotherapy (START) Trial B of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial

The START Trialists' Group*

ORIGINAL ARTICLE

Long-Term Results of Hypofractionated Radiation Therapy for Breast Cancer

Timothy J. Whelan, B.M., B.Ch., Jean-Philippe Pignol, M.D., Mark N. Levine, M.D., Jim A. Julian, Ph.D., Robert MacKenzie, M.D., Sameer Parpia, M.Sc., Wendy Shelley, M.D., Laval Grimard, M.D., Julie Bowen, M.D., Himu Lukka, M.D., M.D., Anthony Fyles, M.D., Ken Schneider, M.D., lavita, M.D., and Carolyn Freeman, M.D.

Practical Radiation Oncology (2018) 8, 145-152

CME ASTRO pro

Special Article

Radiation therapy for the whole breast: Executive summary of an American Society for Radiation Oncology (ASTRO) evidence-based guideline

Benjamin D. Smith, MD [a,*], Jennifer R. Bellon, MD [b], Rachel Blitzblau, MD, PhD [c], Gary Freedman, MD [d], Bruce Haffty, MD [e], Carol Hahn, MD [f], Francine Halberg, MD [g], Karen Hoffman, MD [a], Kathleen Horst, MD [h], Jean Moran, PhD [i], Caroline Patton, MA [j], Jane Perlmutter, PhD [k], Laura Warren, MD [b], Timothy Whelan, BM, BCh [l], Jean L. Wright, MD [m], Reshma Jagsi, MD, DPhil [i]

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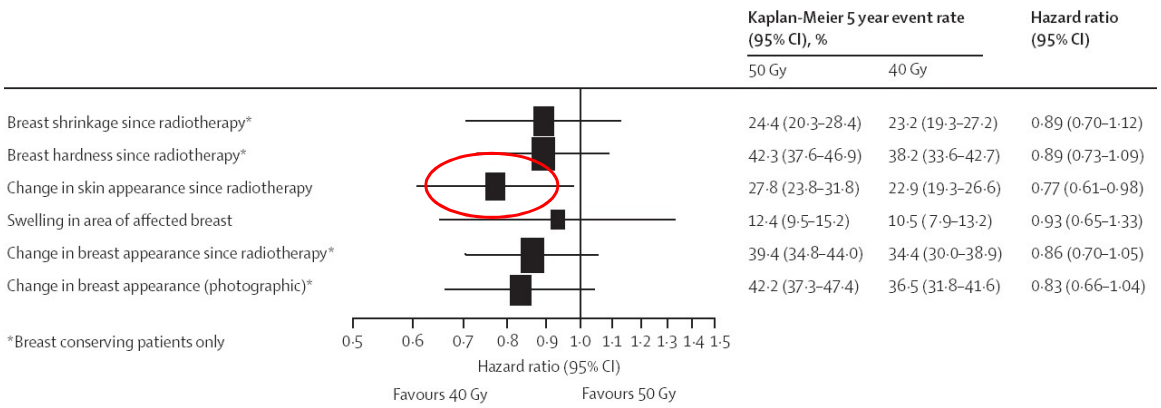

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ltra y o ractionation

- FAST 28.5 y in 5 wee ly fractions vs. 50 y in 25 fractions
- Pts a e 50, t mor si e < 3 cm, L ne ative
- Primary endpoint breast appearance mild increase in breast ind ration and edema

C ange in otogra ic reast a earance at 5 yrs

Gy/fx	No Change (%)	Mild Change (%)	Marked Change (%)
50 y 25	2 5	5	2
2 5 y 5	0		2 4

Brunt et al C 2020

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ltra y o ractionation

- FAST Forward 26 y in 5 daily fractions vs. 40 y in 15 fractions
- Pts A e 18, pT1 3, 0 1
- Primary endpoint ipsilateral breast rec rrence
- At 5 yrs no statistically si nificant difference in IBRT between treatment arms 1.5% vs. 2.3%
- Mar ed or moderate breast ind ration and edema hi her in 1 wee treatment co rse
  - PRO breast firmness also hi her 25% b t no difference in OL metrics

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Brunt et al *Lancet* 2020

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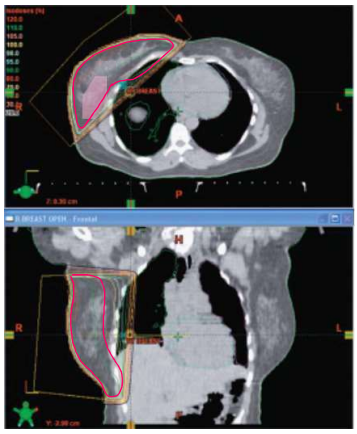
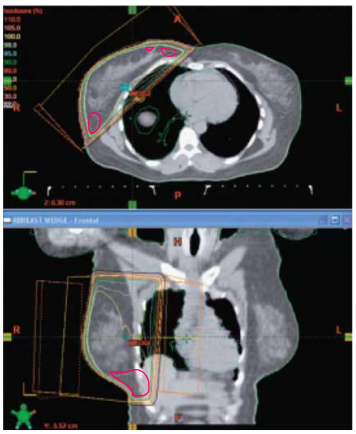
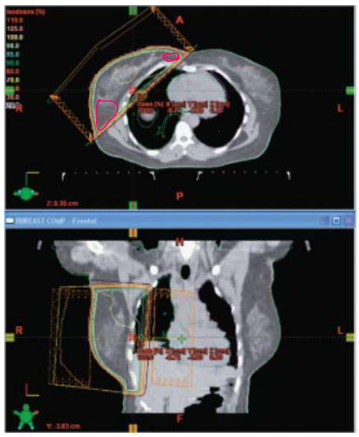


Standard edges



Dynamic edges



Ima es from Halperin, dward C., Carlos A. Pere , and L ther W. Brady. *Perez & Brady's Principles and Practice of Radiation Oncology*. 2008.

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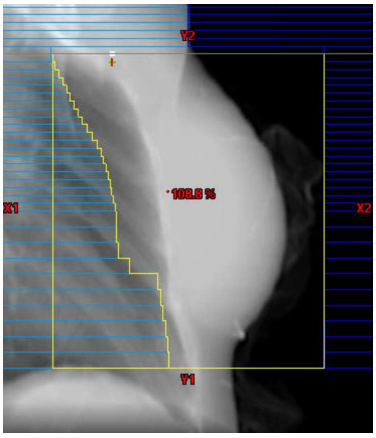

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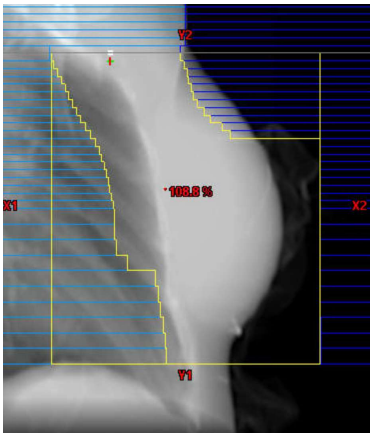

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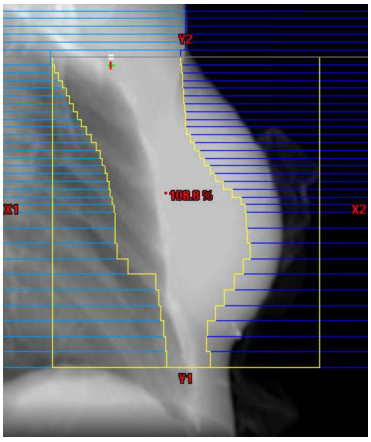

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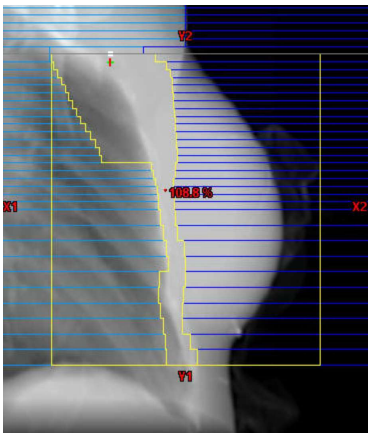

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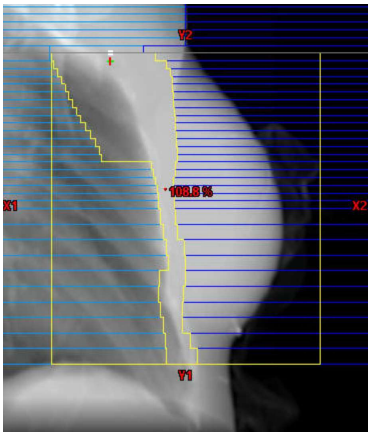

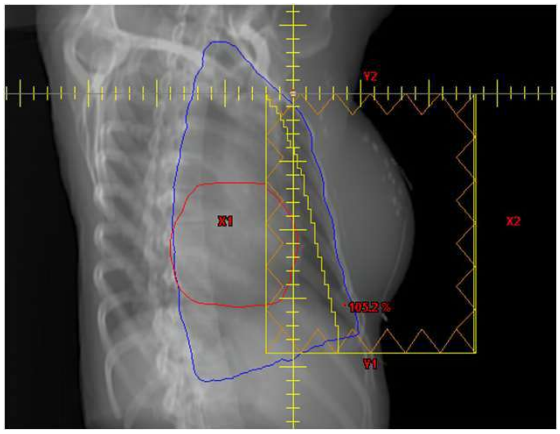

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y o ractionation or MR

- Limited phase III randomi ed clinical trials

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C inese	20 no recon	4 5 y 5	C SC	R no di 5 at 5 yrs S no di	ess grade acute s in to icity
FABR C	400 immediate im lant- ased reconstruction	42 5 y	C SC A - M	t ysical ell eing scores no di	o ic C e ects no di at 5 yrs
R C ARM	25 reconstruction	42 5 y	C SC A M	Recon com lication 2 di at 2 yrs	o di in acute or late to icity at 5 yrs

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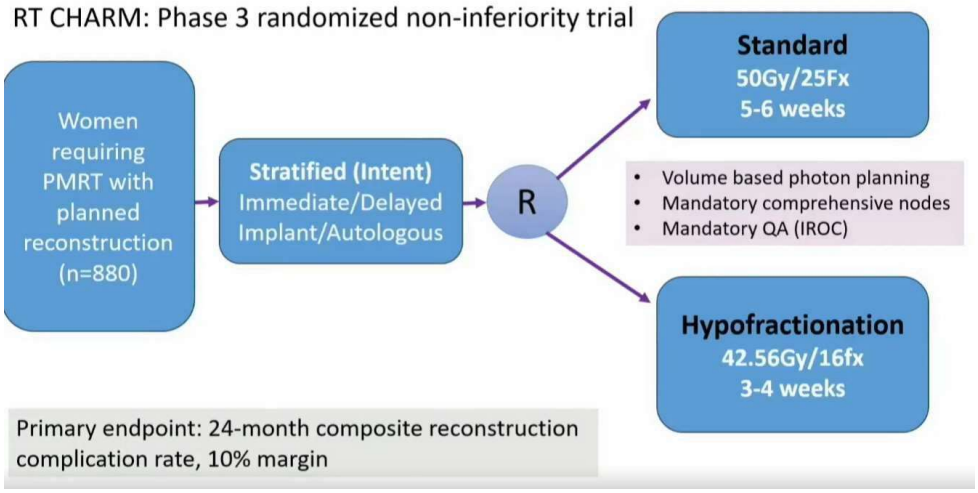

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o e AS R 2024 lenary Session

RT CHARM

- 825 pts in S and Canada, 2 years median follow p

Per Treatment	Conventional	Hypofractionated
Time RT to final Recon (months)	9.3 (0.9-43.8)	9.3 (1.2-58.5)
Temporary TE	225 (65.8%)	243 (66.4%)
Acellular dermal matrix/TE	144 (67.8%)	142 (60.9%)
Implant used	235 (69.1%)	251 (68.8%)
Pre-pec implant	116 (50%)	128 (52.5%)
Sub-pec implant	116 (50%)	117 (48.9%
Autologous (+/- implant)	138 (40.6%)	153 (41.9%)

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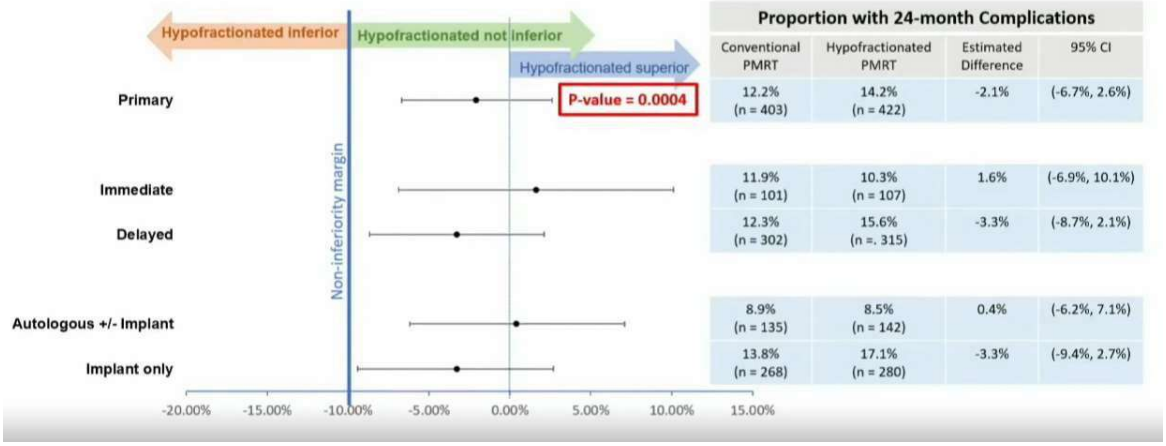
RT CHARM r r d



Proportion with 24-month Complications			
Conventional PMRT	Hypofractionated PMRT	Estimated Difference	95% CI
12.2% (n = 403)	14.2% (n = 422)	-2.1%	(-6.7%, 2.6%)
11.9% (n = 101)	10.3% (n = 107)	1.6%	(-6.9%, 10.1%)
12.3% (n = 302)	15.6% (n =. 315)	-3.3%	(-8.7%, 2.1%)
8.9% (n = 135)	8.5% (n = 142)	0.4%	(-6.2%, 7.1%)
13.8% (n = 268)	17.1% (n = 280)	-3.3%	(-9.4%, 2.7%)

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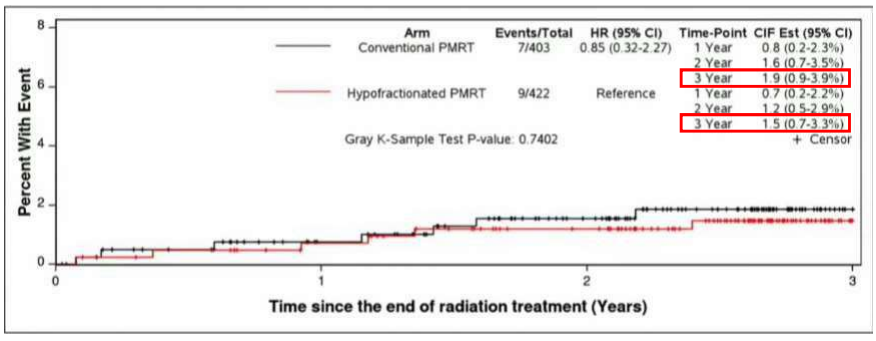

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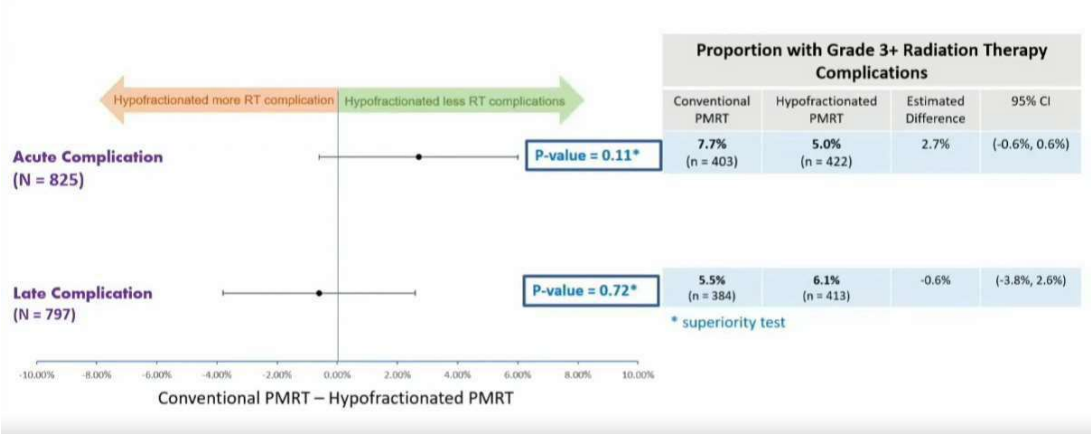

Proportion with Grade 3+ Radiation Therapy Complications			
Conventional PMRT	Hypofractionated PMRT	Estimated Difference	95% CI
7.7% (n = 403)	5.0% (n = 422)	2.7%	(-0.6%, 0.6%)
5.5% (n = 384)	6.1% (n = 413)	-0.6%	(-3.8%, 2.6%)

* superiority test

- m lant only reconstruction trended to ards ig er com lication rate t an autologous reconstruction 20-2 it immediate and delayed im lant

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Future rials

- FAS -For ard odal Su study
  - Radiation to reast c est all level - a illa - SC lym nodes
  - Randomized to 40 y 5 vs 2 y 5 ractions
  - 4 ts interim results:
    - R at 2 yrs: similar rates o arm and s elling most sym toms graded as mild 0 no di erence in moderate-mar ed arm and s elling 0
    - ym edema at yrs: similar et een treatment arms 0
  - rimary results to e re orted at 5 years
- R -Ad uvant
  - Radiation to reast c est all level - a illa SC nodes - M nodes
  - 40 y 5 vs 2 y 5 it S B as needed
  - rimary outcome: local recurrence
- C y o ractionated ocoRegional Radiot era y in Breast Cancer R A
  - Radiation to reast c est all level - a illa SC nodes and M nodes
  - 40 y 5 vs 2 y 5
  - rimary outcome: lym edema

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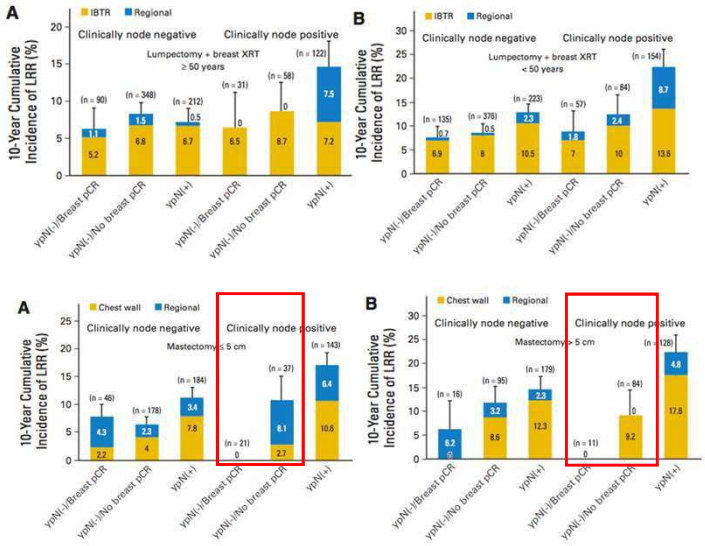
ncor orating AC Res onse in Radiation

- eoad vant chemotherapy trials SABP B18 & B27
- Pts with node positive disease may have low rec rrence rates dependin on response to AC



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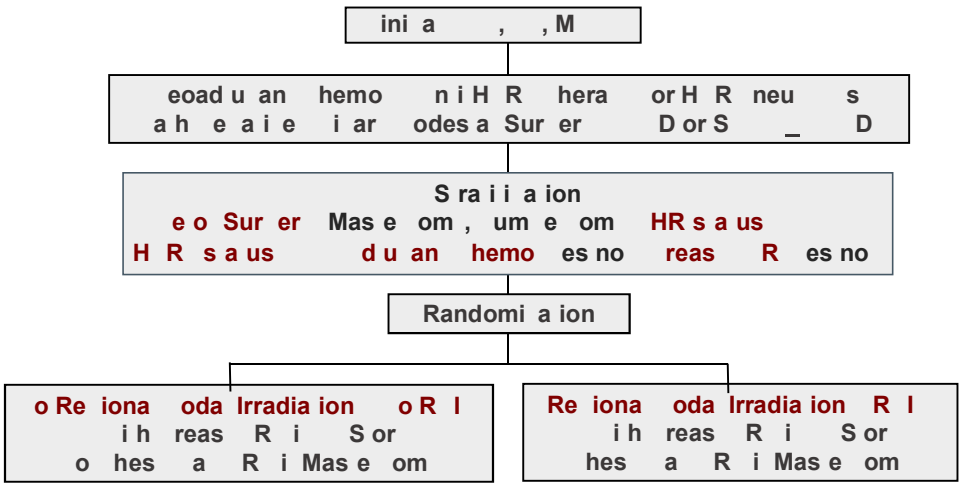
Mamounas et al C 20 0

SAB B5



Mamounas et al SABCS 202

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SAB B5

- 1556 pts, median follow p 59.5 mos
  - 40% of pts< 49 yo
  - 20% of pts triple ne ative
- Primary endpoint 5 yr invasive breast cancer rec rrence free interval IBCRFI
- Final analysis was to occ r after 172 events or 10 yrs after st dy initiation
- *Ti e dri en* analysis performed and presented in abstract form

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SAB B5

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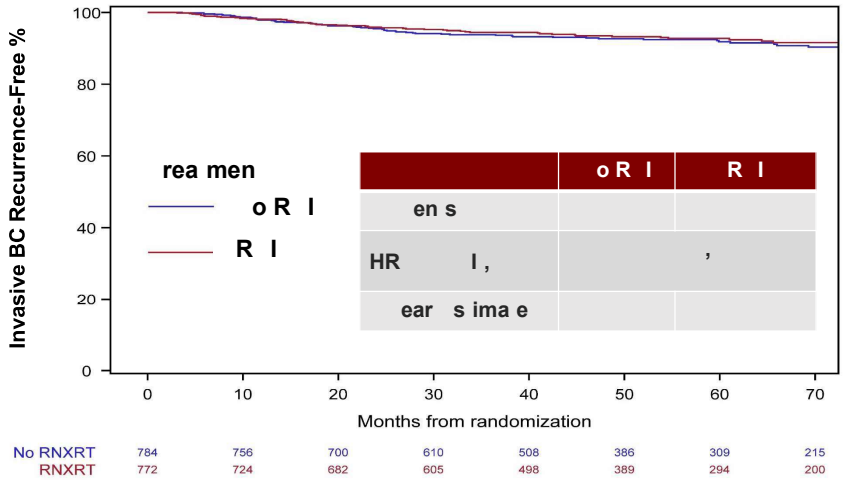

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SAB B5

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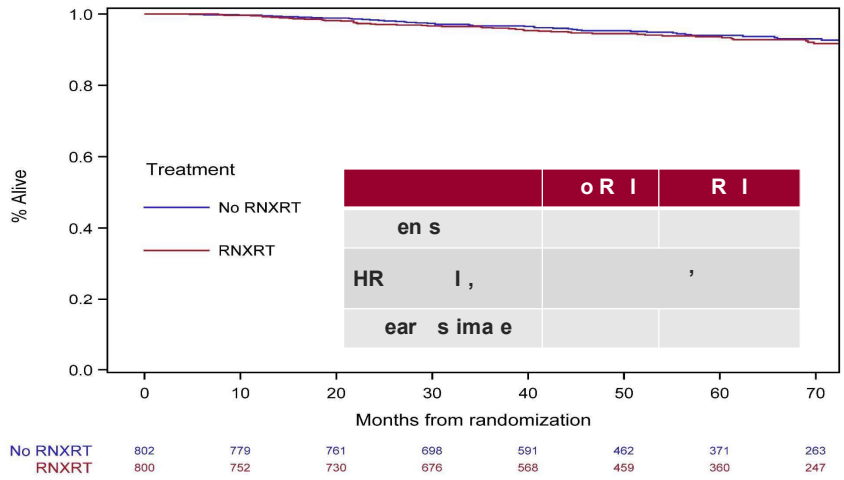

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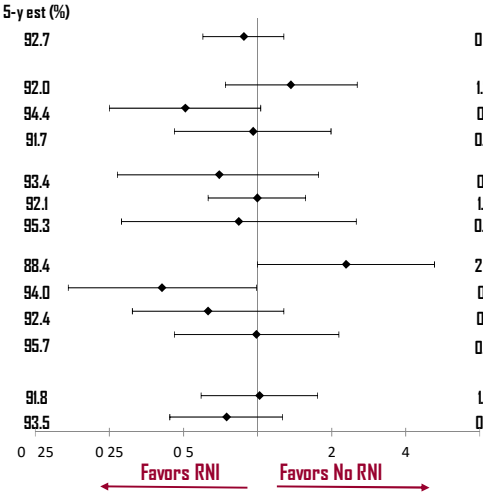
Variable		No RNI (D/N)	No RNI 5-y est (%)	RNI (D/N)	RNI 5-y est (%)	HR (95% CI)	P-interaction
	All patients	59/784	91.8	50/772	92.7	0.88 (0.60,1.28)	
Age	<=49	18/311	92.8	24/312	92.0	1.37 (0.74,2.54)	0.09
	50-59	25/257	90.4	12/254	94.4	0.51 (0.25,1.03)	
	>= 60	16/216	92.4	14/206	91.7	0.96 (0.46,1.99)	
Race	Black	11/135	92.6	8/140	93.4	0.70 (0.27,1.77)	0.69
	White	40/543	91.6	36/533	92.1	1.00 (0.63,1.57)	
	Other	8/106	91.8	6/99	95.3	0.84 (0.28,2.52)	
Tumor Subtype	Triple-negative	8/169	95.0	19/188	88.4	2.30 (1.00,5.25)	0.037
	ER/PR+/HER2-	17/173	90.5	7/155	94.0	0.41 (0.17,0.99)	
	ER/PR-/HER2+	20/198	88.8	12/183	92.4	0.63 (0.31,1.28)	
	ER/PR+/HER2+	14/244	93.3	12/246	95.7	0.99 (0.46,2.14)	
Axillary Surgery	Axil +/- SLNB	27/357	92.0	25/338	91.8	1.02 (0.59,1.75)	0.42
	SLNB alone	32/427	91.5	25/434	93.5	0.75 (0.44,1.26)	



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- imited a lication articularly as inal u lication is ending
  - atients it CR ot in t e reast and in t e lym nodes
    - ts it RCB-2 res onse still get ull regional nodal irradiation
  - R 2 ositive or tri le negative disease
  - Does not a ly to atients it c 2- disease or atients it 4 disease
- uanced s ared decision-ma ing discussion it atient

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enomic ro iling and Radiation

- OncoType D 21 ene panel, invasive breast cancer
  - Predicts for distant rec rrence
  - Role well established for decision ma in for systemic therapy
  - Has not be sed to determine role of radiation therapy, b t increasin data s estin low score may also predict for loco re ional rec rrence

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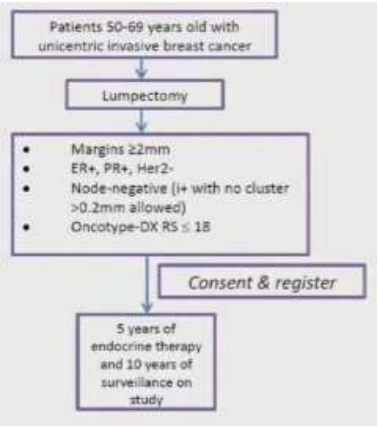
enomic ro iling and Radiation

- ID A Individ ali ed Decisions for _ndocrine therapy Alone
- Prospective phase II, m lticenter cohort trial
- Primary endpoint locore ional rec rrence



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D A trial

- Women 50 69 years, median a e 62 yo
- 200 pts, median follow p 5.21 yrs
- 5 year LRR 50 59yo 3.3%, 60 69yo 3.6%
- 6 pts rec rred after 5 years, 50% noncompliant with endocrine therapy
- 178 pts did not rec r 86.5% complaint with endocrine therapy

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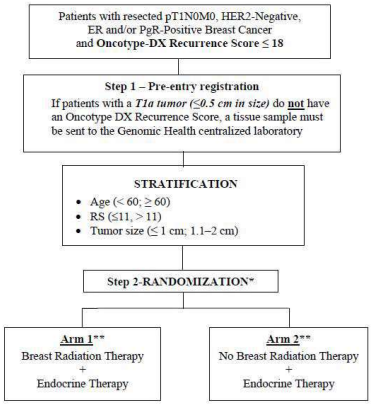
ngoing randomized trials

- D BRA De escalation of Breast Radiation for Conservative Treatment of Sta e I Hormone Sensitive Her2 ne ative, Oncotype Rec rrence score 18 Breast Cancer
- P RT _ aminin Personali ed Radiation Therapy for Low ris arly Breast Cancer
  - PAM 50, L mina A, ROR 60



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→ Strati y:
y e o surgery
A illary dissection
Ad uvant c emot era y

ncoty e D Score

→ ARM : **No N**
ole reast radiation or
no radiation *a tect*

→ ARM2: **N**
B SC undissected
a illary and M nodes or
MR R as a ove

rimary end oint: reast cancer
recurrence ree interval

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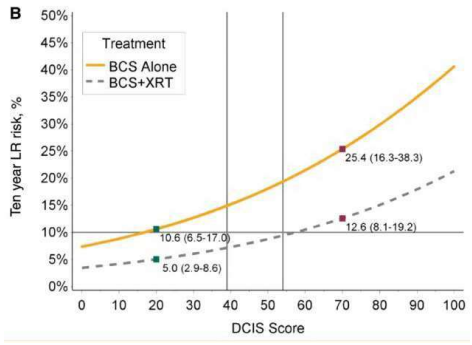

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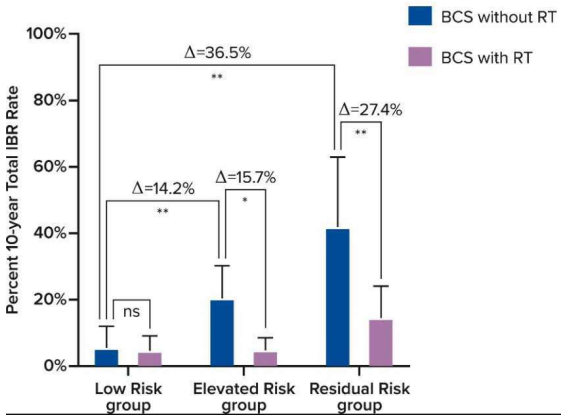

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Summary

- We are contin in to e plore how to red ce treatment times for patients with both early sta e and locally advanced breast cancer
  - 5 fraction treatment co rses reasonable to consider for early sta e patients
  - 3 wee treatment sched les for patients nder oin re ional nodal irradiation can be offered
- For patients with c 1 disease that convert to ypT0 0 disease followin neoad vant chemotherapy, we can consider omittin re ional nodal irradiation
- enomic profilin of breast cancer and DCIS may finally start to infl ence radiation decision ma in in the near f t re

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