

In Which Patients Can Radiotherapy Be Omitted After Breast Conserving Surgery?

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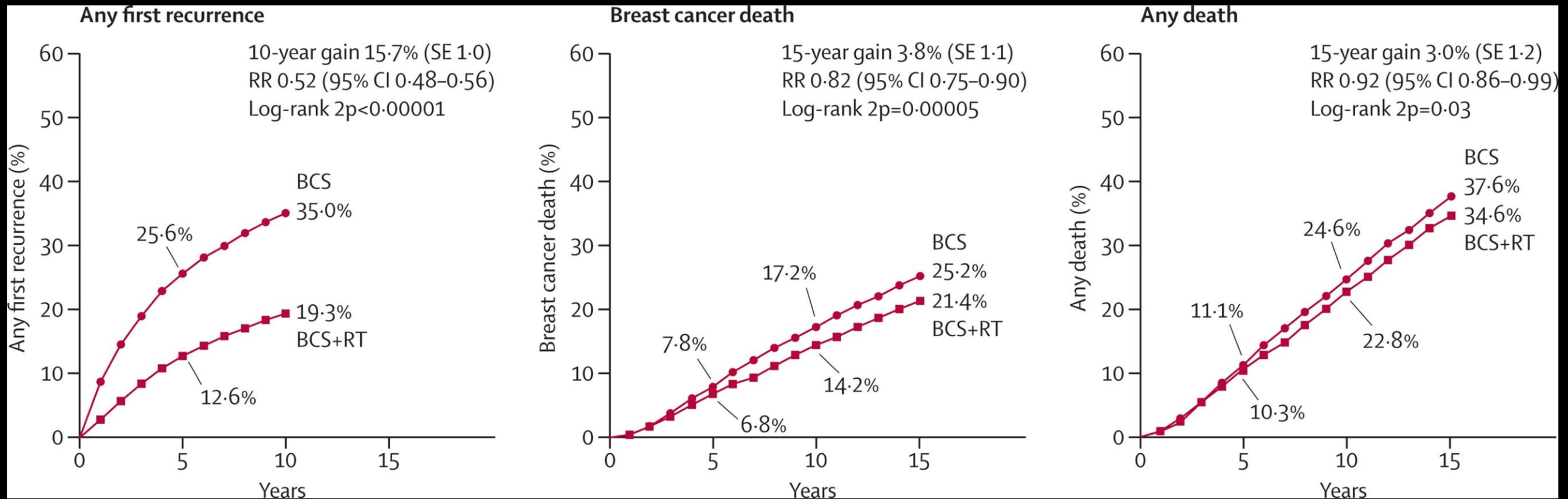


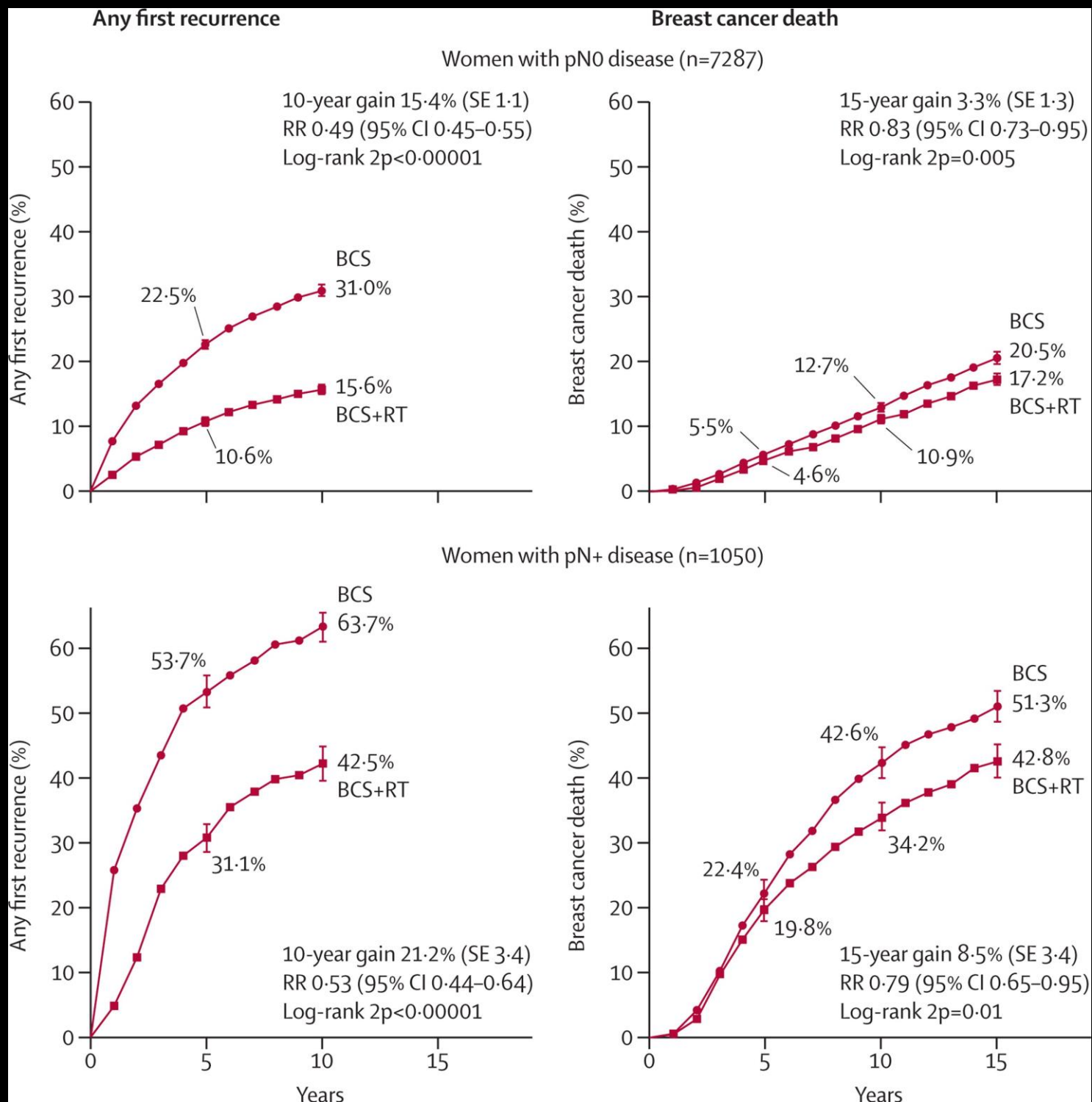
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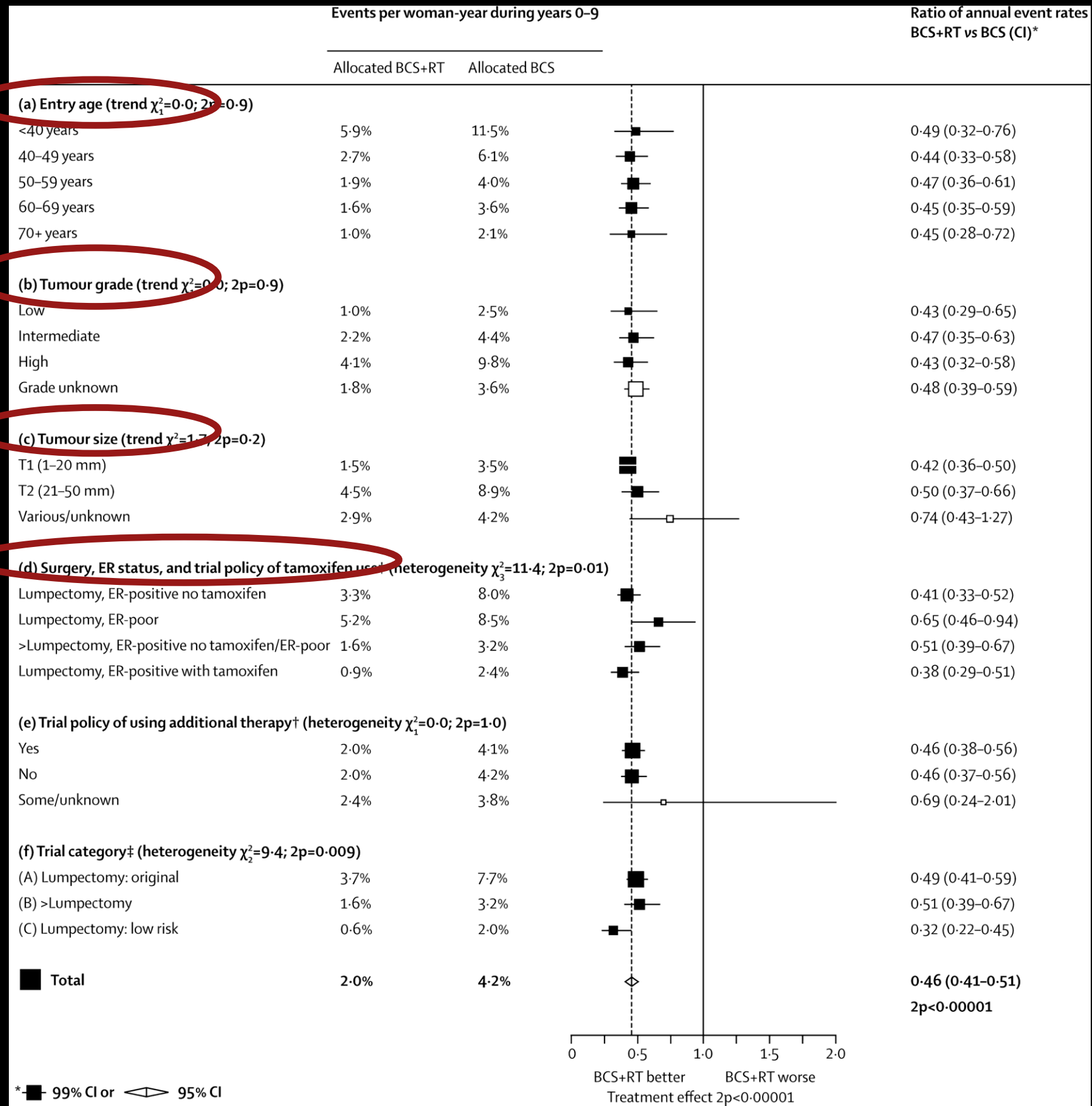


Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10 801 women in 17 randomised trials

Early Breast Cancer Trialists' Collaborative Group (EBCTCG)










Guidelines

Practical Radiation Oncology (2018) 8, 145-152

 
www.practicalradonc.org

Special Article

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



clinical practice guidelines

Annals of Oncology 26 (Supplement 5): v8-v30, 2015
doi:10.1093/annonc/mdv298

Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up[†]

E. Senkus¹, S. Kyriakides², S. Ohno³, F. Penault-Llorca^{4,5}, P. Poortmans⁶, E. Rutgers⁷,
S. Zackrisson⁸ & F. Cardoso⁹, on behalf of the ESMO Guidelines Committee*

BreastCare

Review Article

Breast Care 2017;12:102-107
DOI: 10.1159/000475698

Published online: April 26, 2017

St. Gallen/Vienna 2017: A Brief Summary of the Consensus Discussion about Escalation and De-Escalation of Primary Breast Cancer Treatment

Michael Gnant^a Nadia Harbeck^b Christoph Thomssen^c

 National
Comprehensive
Cancer
Network[®]

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®])

Breast Cancer

Version 1.2018 — March 20, 2018

NCCN.org

NCCN Guidelines for Patients[®] available at www.nccn.org/patients

However.....



Is there a group of low risk patients where XRT can be omitted?

- Small size tumours
- Low grade
- Node Negative
- ER +ve
- Clear Margins
- Elderly patients

Randomised Studies in Low Risk Population Groups

Author	Number of patients	Age	Tumour size	ER status
Fyles et al <i>NEJM 2004</i>	769	>50yrs	<5cm	+ve
Pötter et al ABC SG <i>Int J Rad Onc Bio Phisi 2007</i>	869	>50yrs	<3cm	+ve
Hughes et al CALGB 9394 <i>JCO 2013</i>	636	>70yrs	<2cm	+ve
Blamey et al BASO II <i>Eur J Cancer 2013</i>	1135	>50yrs	<2cm	+ve
Kunkler et al PRIME II <i>Lancet Oncol 2015</i>	1326	>65yrs	<3cm	+ve

Risk of Local Recurrence

Author	Follow up	Hormonal Blockade	Hormonal Blockade + XRT	HR	p
Fyles et al NEJM 2004	5yrs	7,7%	0,6%	9,02	<0.001
Pötter et al ABCSG Int J Rad Onc Bio Phisi 2007	5yrs	5,1%	0,4%	10.2	0.002
Hughes et al CALGB 9394 JCO 2013	10yrs	10,0%	2,0%	5.5	<0.001
Blamey et al BASO II Eur J Cancer 2013	10yrs	10,2%	3,9%	7.34	0.006
Kunkler et al PRIME II Lancet Oncol 2015	5yrs	4,1%	1,3%	5.19	0.0002

Time to Local Recurrence

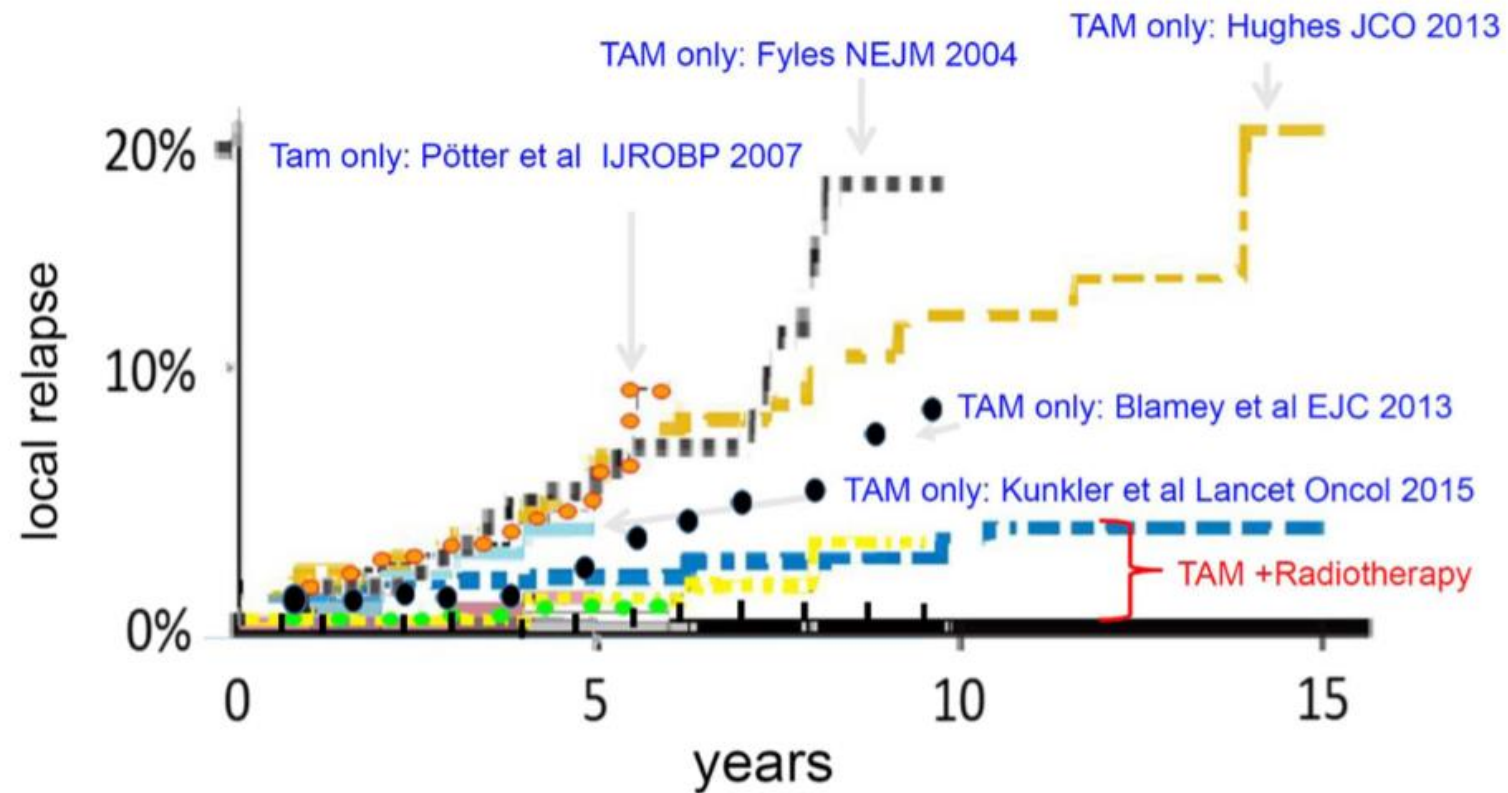
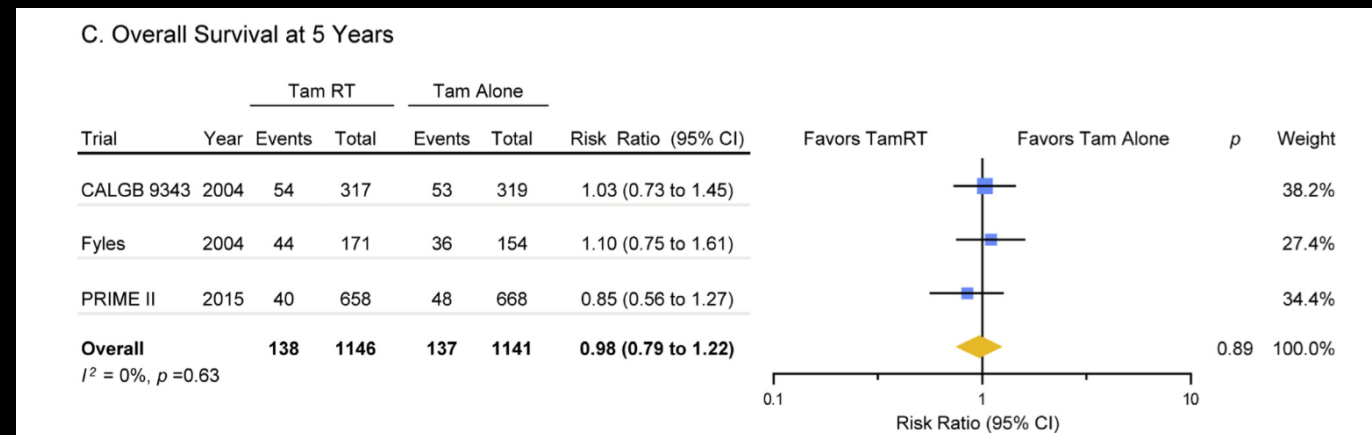
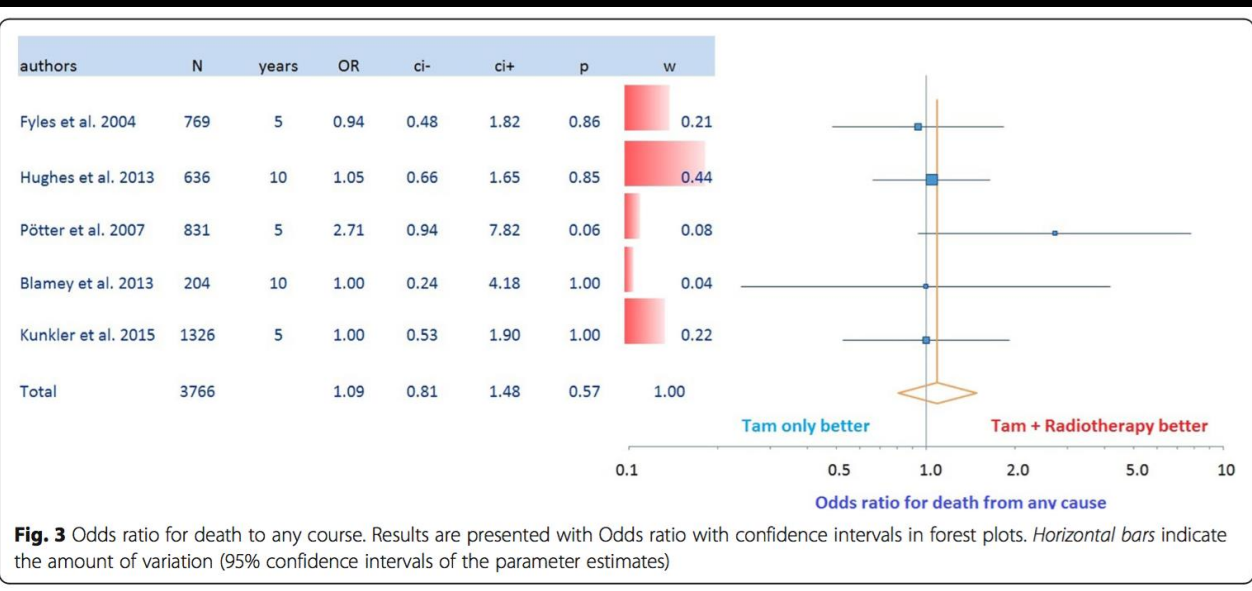


Fig. 2 Time to local recurrence. *Blue letters:* treatment arm with Tamoxifen (Tam) only without RT. *Red letters:* TAM + RT

Overall Survival



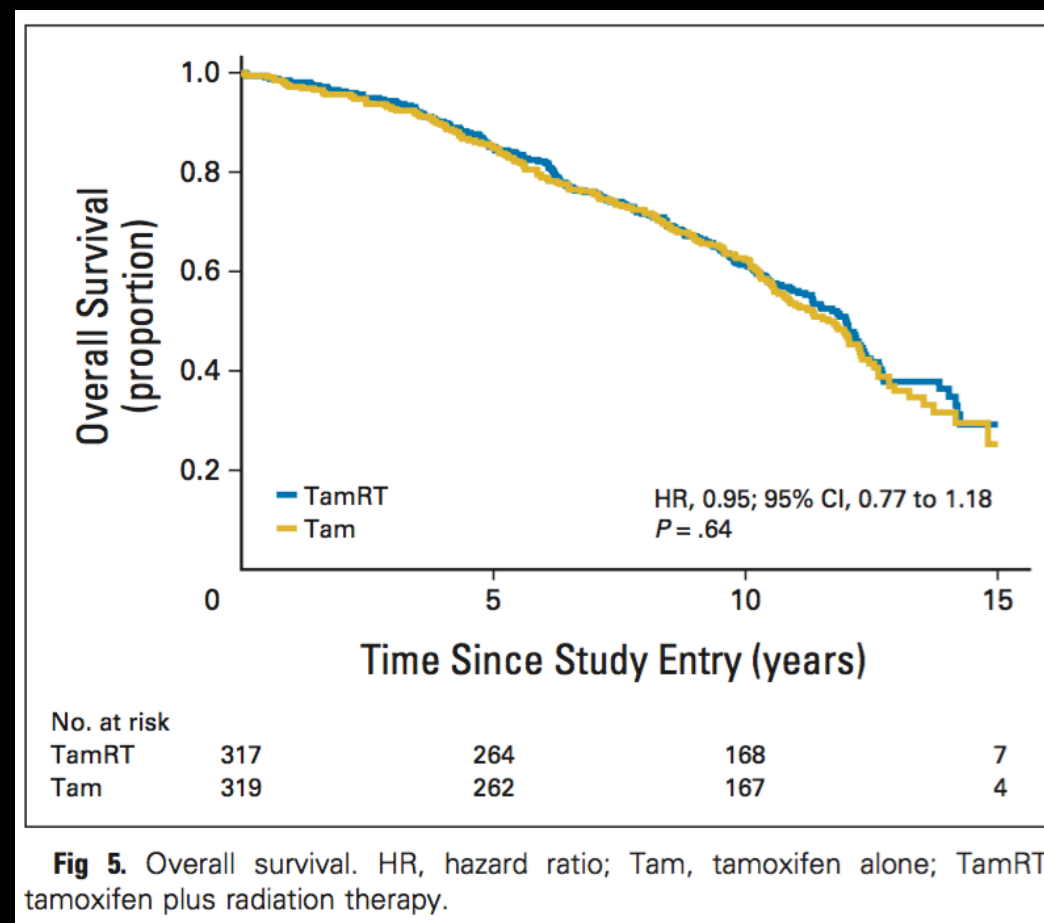
Matuschek et al. Radiation Oncology (2017) 12:60

T.R. Chesney et al. / Radiotherapy and Oncology 123 (2017) 1–9

Overall Survival

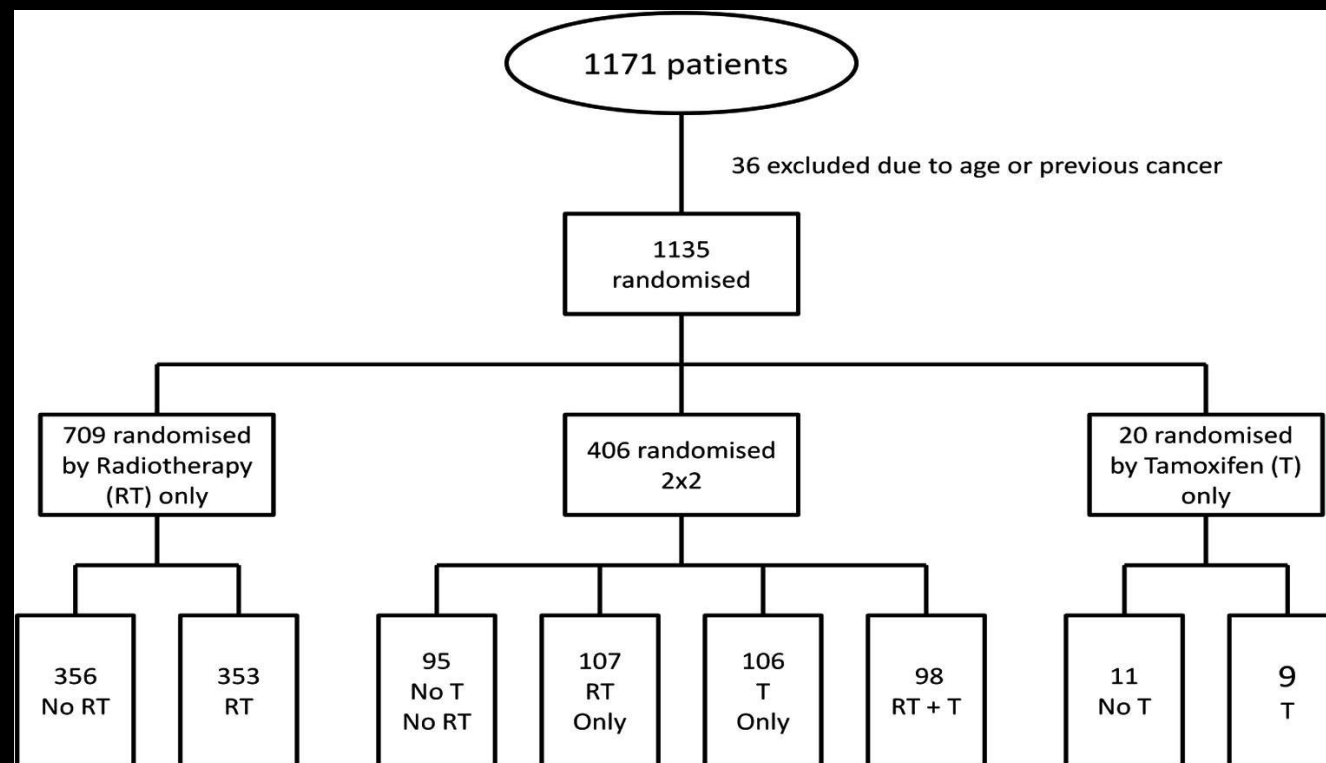
CALGB 9343

Only 6% deaths were due to Breast Cancer



Radiotherapy or tamoxifen after conserving surgery for breast cancers of excellent prognosis:

British Association of Surgical Oncology (BASO) II trial

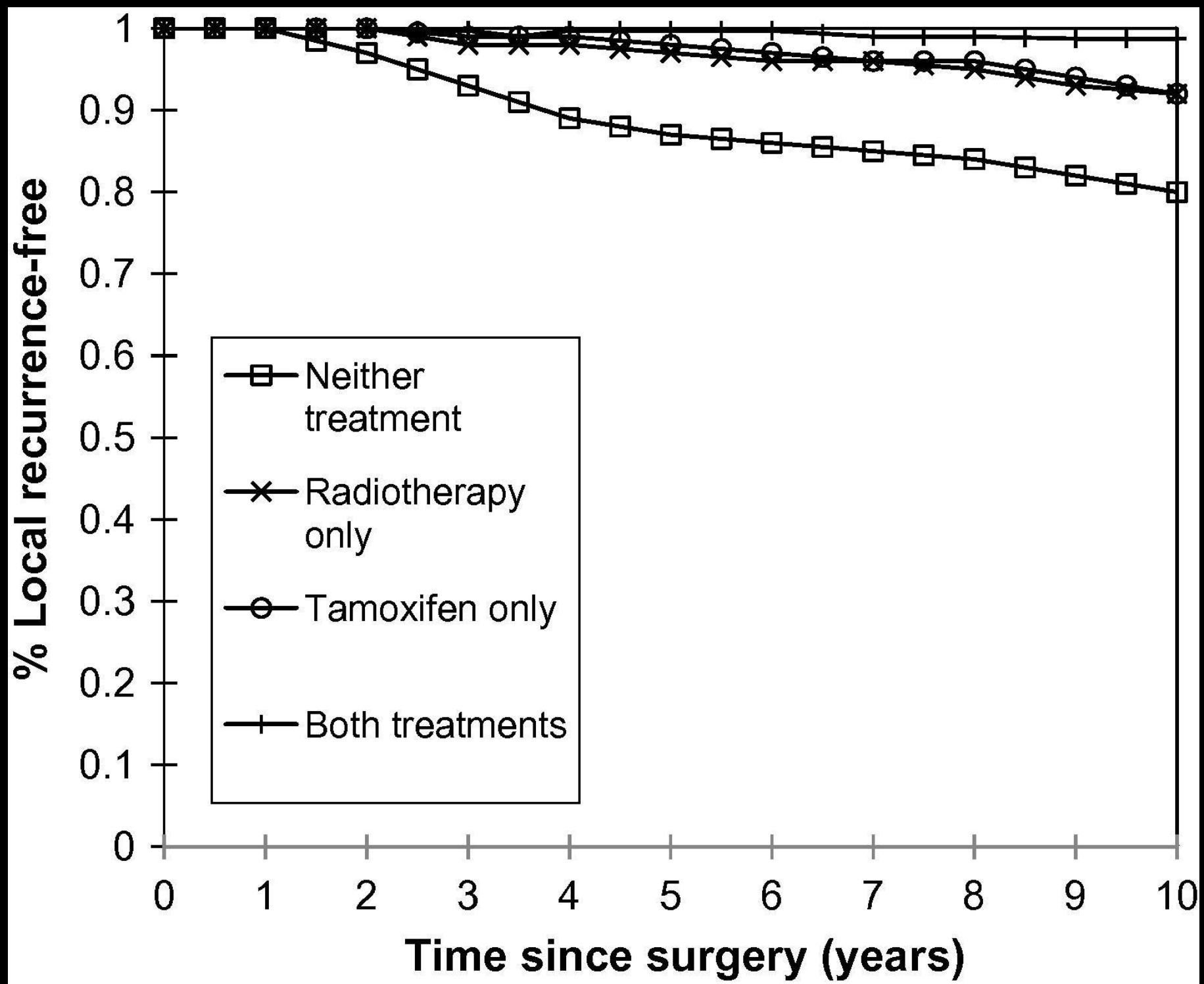


R.W. Blamey, T. Bates, U. Chetty, S.W. Duffy, I.O. Ellis, D. George, E. Mallon, M.J. Mitchell, I. Monypenny, D.A.L. Morgan, R.D. Macmillan, J. Patnick, S.E. Pinder

European Journal of Cancer

Volume 49, Issue 10, Pages 2294-2302 (July 2013)

DOI: 10.1016/j.ejca.2013.02.031



Toxicities

- Only 2 of these studies reported on side effects
- Subgroup analyses of PRIME and Canadian Studies showed no significant impact of Radiotherapy on QOL
- With modern 'hypo fractionated' radiotherapy, minimal toxicity is anticipated but radiation dermatitis; fibrosis and lymphoedema can occur
- Tamoxifen also has toxicities and compliance in this group of patients may be suboptimal

Toxicities

- Also need to factor in the anxiety associated with an increased risk of recurrence and the toxicities of further treatments, if recurrence was to occur

Toxicities of XRT

South African Context

- **Availability**
 - ▶ Resource restrictions
 - ▶ Geographical restrictions
- **Cost**

Future Directions

Genomic Profiling

- IDEA study (Oncotype Dx)
- PRECISION trial (Prosigna)
- LUMINA trial (IHC)
- PRIMETIME trial (IHC4)

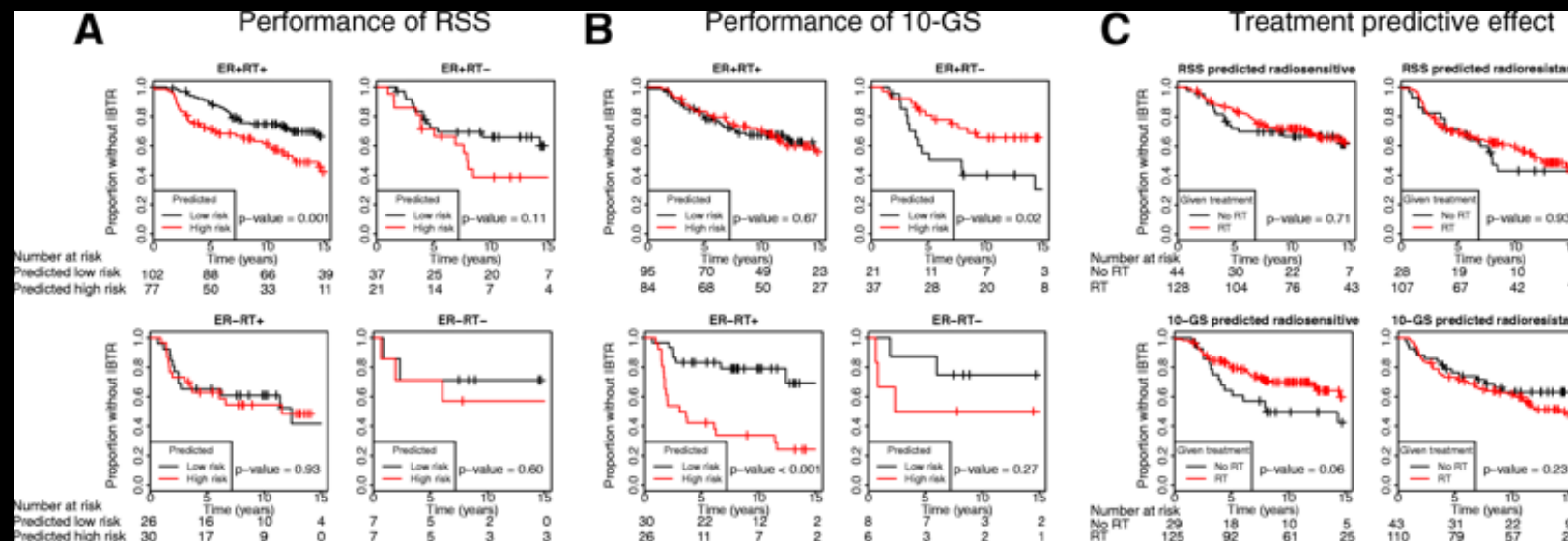
Future Directions

Genomic Profiling

- Radiosensitivity Signature (RSS)
- Radiosensitivity Index (RSI)
- Genomic Adjusted Radiation Dose (GARD)
- 10 Gene Score

Future Directions

Genomic Profiling - 10 GS



- 1) Those that don't benefit from XRT due to low risk of recurrence
- 2) Those that don't benefit from XRT due to radio resistance (and, therefore, require mastectomy)
- 3) Those that have radiosensitive tumours, that will benefit from XRT

- Tjöström et al Breast Cancer Research 2018 20:64

Future Directions




Radiogenomics

Predictor of Radiation Toxicity in patients based on SNPs

- RTOG 1005
- REQUITE study
- RAPPER study

Future Directions

Circulating Tumour Cells

   More ▾

This Issue Views **4,371** | Citations **1** | Altmetric **154**

Original Investigation ONLINE ONLY

August 9, 2018

Association of Circulating Tumor Cell Status With Benefit of Radiotherapy and Survival in Early-Stage Breast Cancer

Chelain R. Goodman, MD, PhD¹; Brandon-Luke L. Seagle, MD²; Thomas W. P. Friedl, PhD³; [et al](#)

» [Author Affiliations](#)

JAMA Oncol. 2018;4(8):e180163. doi:10.1001/jamaoncol.2018.0163

DCIS

- EBCTCG Meta-analysis showed a 50% reduction in the risk of recurrence at 10yrs
- No trials have shown an impact on mortality
- 1/2 of the recurrences will be invasive breast carcinomas

DCIS

- Clinico-Pathological features unable to define a group of patients with DCIS that don't benefit from XRT
- There are, however, patients where the risk of recurrence is so low that radiotherapy can be omitted

DCIS

Nomograms

Table 1

Scoring system for University of Southern California/Van Nuys Prognostic Index

Score	1	2	3
Size	≤15 mm	16–40	>40
Margin	≥10 mm	1–9	<1
Class	Grade 1/2 without necrosis	Grade 1/2 with necrosis	Grade 3
Age	>60	40–60	<40

Memorial Sloan Kettering Cancer Center. [Prediction Tools](#) > [Breast Cancer Nomograms](#) > [Ductal Carcinoma Recurrence](#) mskcc.org PREDICTION TOOLS

Breast Cancer Nomogram: Ductal Carcinoma In Situ (DCIS) Recurrence TEXT SIZE

In consultation with a physician, this tool can be used by patients who have had breast-conserving surgery to treat ductal carcinoma in situ (DCIS) to predict the likelihood that their breast cancer will return in the same breast that was originally treated. Patients can use this information to make decisions regarding various treatment options, such as radiation therapy and anti-estrogen therapy.

Enter Your Information

Age at Diagnosis
Enter age at the time of diagnosis. years old (25 to 90)

Family History?
Select YES if there are first- (e.g., mother or sister) or second-degree (e.g., paternal aunt or grandmother) relatives with breast cancer. YES

Presentation
Select Clinical if there was an abnormality on physical examination; select Radiologic if an abnormality was seen only on breast imaging studies (e.g., mammography).

Adjuvant Radiation Therapy?
Select YES if radiation therapy is given after breast-conserving surgery. YES

Adjuvant Endocrine Therapy?
Select YES if anti-estrogen treatment (e.g., tamoxifen, raloxifene). YES


Nuclear Grade

Your Results

[Learn more](#) about your results below.

Probability of Recurrence	5 Year	6%
	10 Year	10%

Make an Appointment

Call us to schedule an appointment or contact us online 

[Contact Us](#)

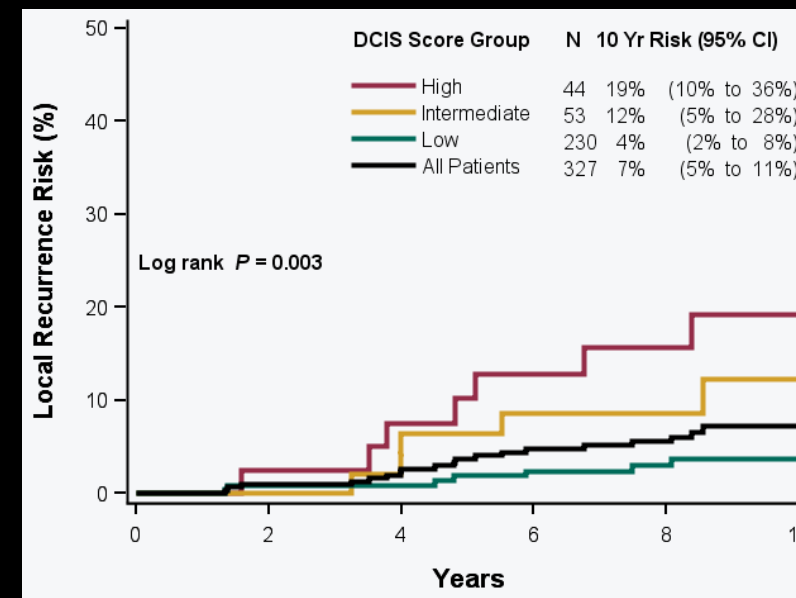
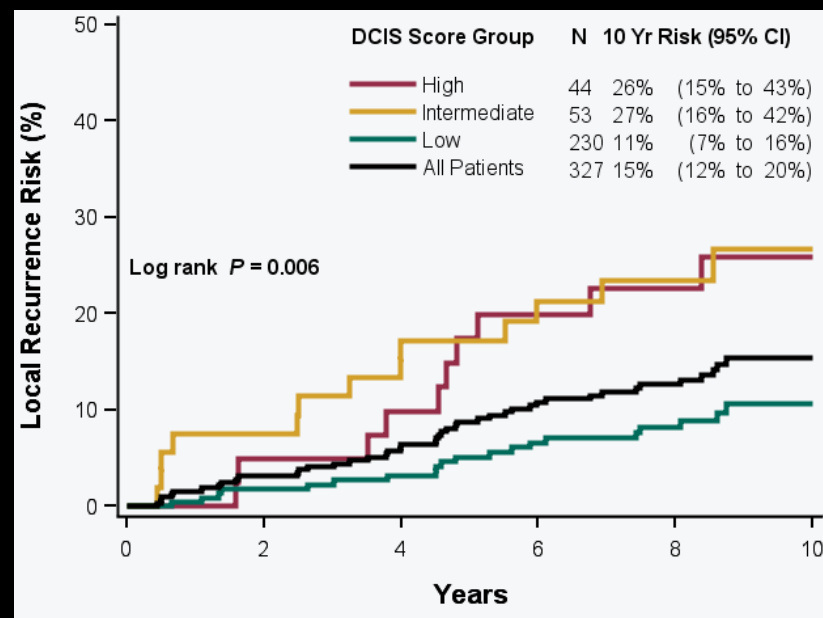
DCIS

Genomic Predictors



Any Local Recurrence

Invasive Local Recurrence



ECOG E5194: 10-Year Local Recurrence by Risk Group for the Breast DCIS Score™

Older (≥ 50 y.o.) Patient with Smaller Tumor (≤ 1 cm)

Page 1 and 2: Risk Assessment and Single Gene Results

Breast DCIS Score Report

PATIENT, SAMPLE
 Date of Birth: 01-Jan-1950 Gender: Female Report Number: OR000123456-01 Report Date: 17-Aug-2017
 Ordering Physician: Dr. First-Name I. Ordering-Physician-Last-Name

Breast DCIS Score™ Result

10

What does a Breast DCIS Score of 10 mean?

Based on your patient's age, tumor size and Breast DCIS Score result of 10, your patient's risk of any local recurrence within 10 years is 6%, if treated with breast-conserving surgery alone.

10-Year Risk of Local Recurrence (PROGNOSIS)
 Age Category ≥ 50 years old, Tumor Size ≤ 1.0 cm

The Breast DCIS Score validation was derived from two studies, E5194 with 327 patients and the Ontario DCIS Cohort Study with 571 patients. The studies consisted of diverse DCIS patient populations treated with breast-conserving surgery alone. The results below reflect a meta-analysis with 773 patients of the two studies incorporating patient age and tumor size with the Breast DCIS Score result to estimate 10-year risk. The meta-analysis excluded patients whose tumors were multifocal and/or had positive margins.¹⁻³

123456-01 Report Date: 17-Aug-2017

east/SP-16_0123456
ical Center

elow. These results may differ from ER or

Risk of Any Local Recurrence (DCIS or Invasive)

6% 95% CI: 4% - 10%

Risk of Invasive Local Recurrence

4% 95% CI: 3% - 7%

ASCO. 2017.

Joseph, MD

or approved by the FDA, nor is it currently required to be
 poses. It should not be regarded as investigational or for

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 act

10.8

≥ 6.5

≥ 12.5

9.5

≥ 5.5

≥ 10.0

Information on the Breast DCIS Score and clinical experience is available upon request.

COX-8001 Rev009

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Page 2 of 3

Patient's 10-year risk of local recurrence, based on patient's age, tumor size, and DCIS Score result

Assay results clearly displayed

Refined risk of recurrence—any local recurrence (DCIS or invasive) and invasive local recurrence

Older (≥ 50 y.o.) Patient with Smaller Tumor (≤ 1 cm)


Page 3: Patient Summary

Breast DCIS Score Report oncotype^{DX}
Breast DCIS Score

PATIENT, SAMPLE
Date of Birth: 01-Jan-1950 Gender: Female Report Number: OR000123456-01 Report Date: 17-Aug-2017
Ordering Physician: Dr. First-Name I. Ordering-Physician-Last-Name

Patient Educational Summary
What does your result mean?

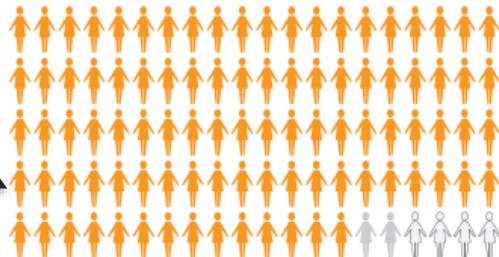
10



Your Breast DCIS Score result of 10, combined with information about your age and tumor size, indicates a **6%** risk of your tumor returning as DCIS or invasive cancer in the same breast within 10 years, if treated only with breast-conserving surgery.

By measuring the activity of certain genes in your breast tumor tissue, the Oncotype DX[®] test predicts the risk of disease returning in the same breast, as either DCIS or invasive cancer - a key factor in deciding your treatment following DCIS surgery.





What are the chances of your breast cancer returning?



If 100 women with a Breast DCIS Score result of 10 are treated with only breast-conserving surgery:

- 94 women** will **not** have their disease return in the same breast as either DCIS or invasive cancer within 10 years.
- 6 women** will have their disease return in the same breast as either DCIS or invasive cancer within 10 years. 4 women will have their disease return in the same breast as invasive cancer within 10 years.

What are your treatment options? (For doctor/patient discussion)

 SURGERY	 RADIATION	 ENDOCRINE THERAPY	 MONITORING
_____	_____	_____	_____
_____	_____	_____	_____

Join other DCIS patients to learn about genomics and help transform patient care: MyOncotype.com

This Patient Educational Summary is a brief explanation of your Oncotype DX test results. It is being provided by your doctor for discussion purposes. More information at www.OncotypeIQ.com or www.MyBreastCancerTreatment.org.

ODX-B001 Rev009 Page 3 of 3

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Patient-friendly language to help explain the results to patients

Visual representation of patient's personalized risk of local recurrence

Notes section to facilitate patient discussions and treatment decisions

Conclusions

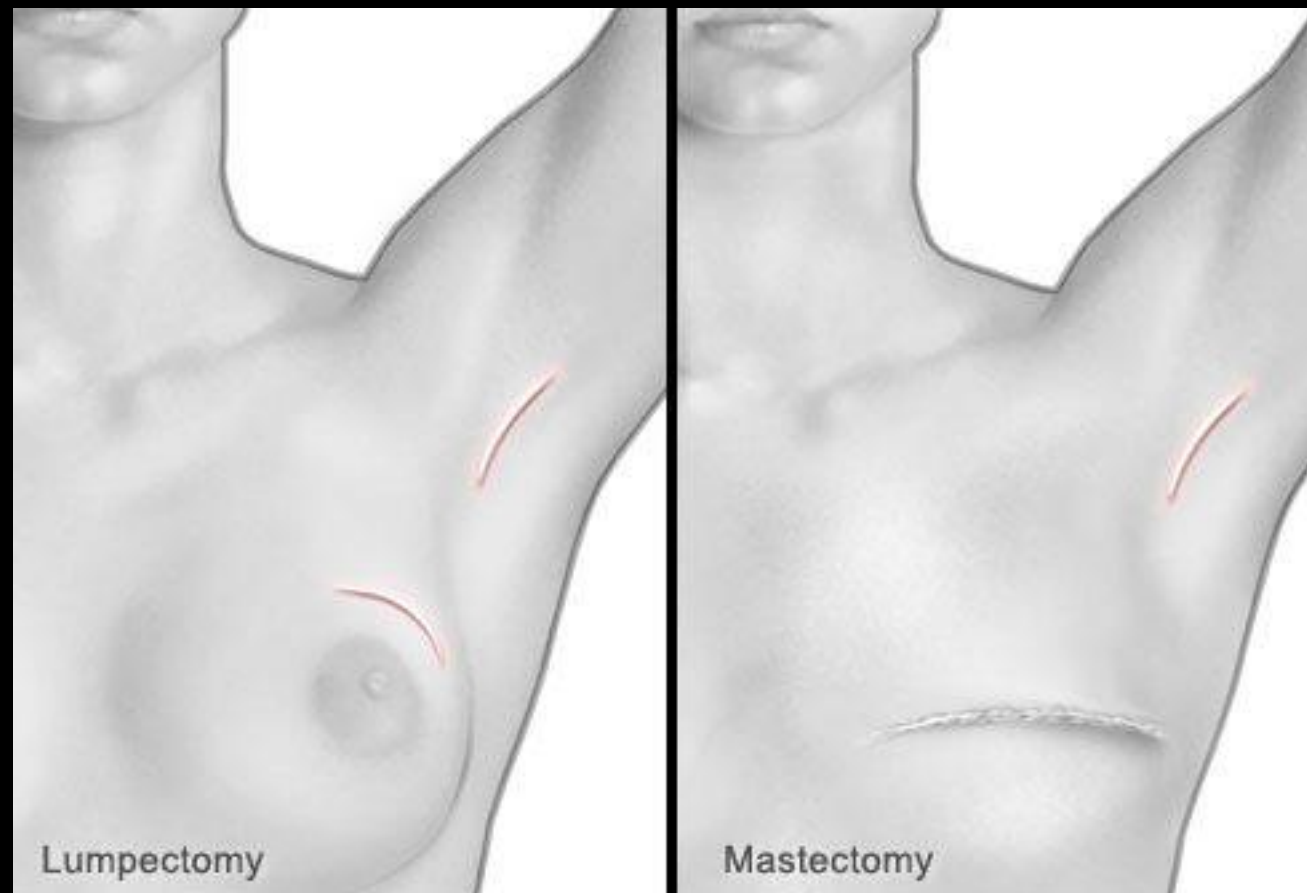
- Currently, there are no clinical, pathological or genomic biomarkers that identifies a group of patients that don't benefit from adjuvant radiotherapy in terms of local control
- There are, however, groups of low risk patients that have a very low (absolute) risk of recurrence, in which adjuvant radiotherapy doesn't impact on overall survival

Conclusions

- This same profile of patients can be treated with abbreviated XRT protocols, which are associated with very little radiation related toxicity
- Where radiotherapy resources are available (and affordable) I would still consider radiotherapy in most patients treated with breast conserving surgery.

Conclusions

In patients (with low risk features), where adjuvant radiotherapy is not available, affordable or desired by the patient, breast conserving surgery alone is certainly a reasonable option.



Thank you