早期乳癌放射治療的新境界：手術中單一劑量放射治療〈INTRAOPERATIVE RADIOTHERAPY〉

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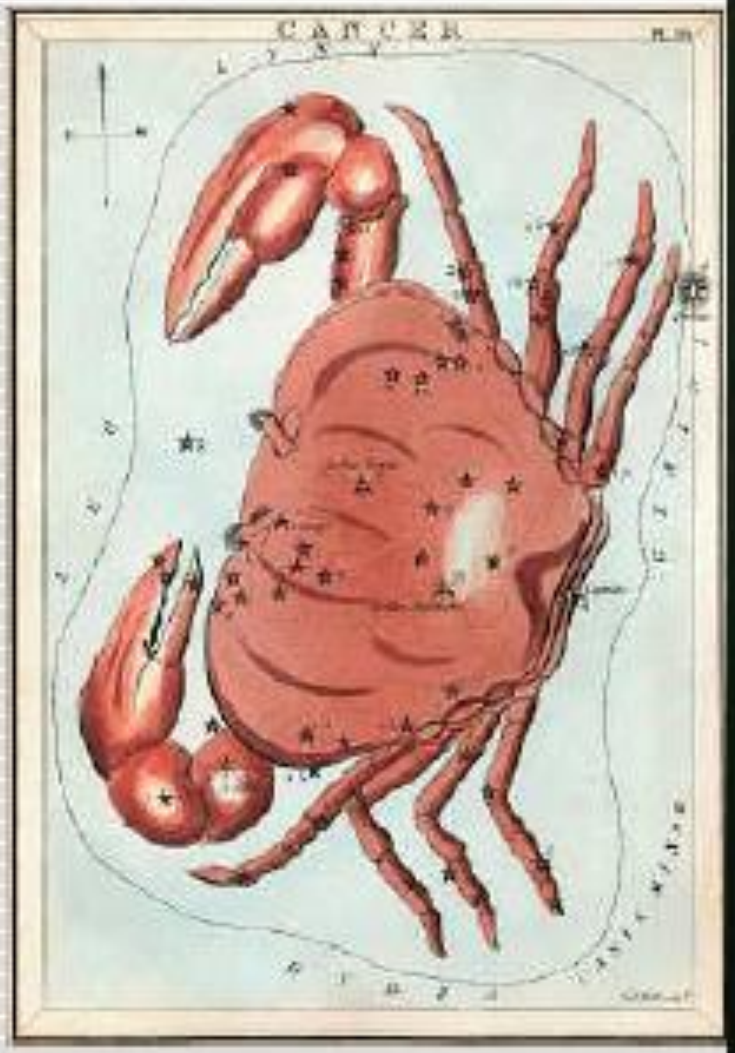
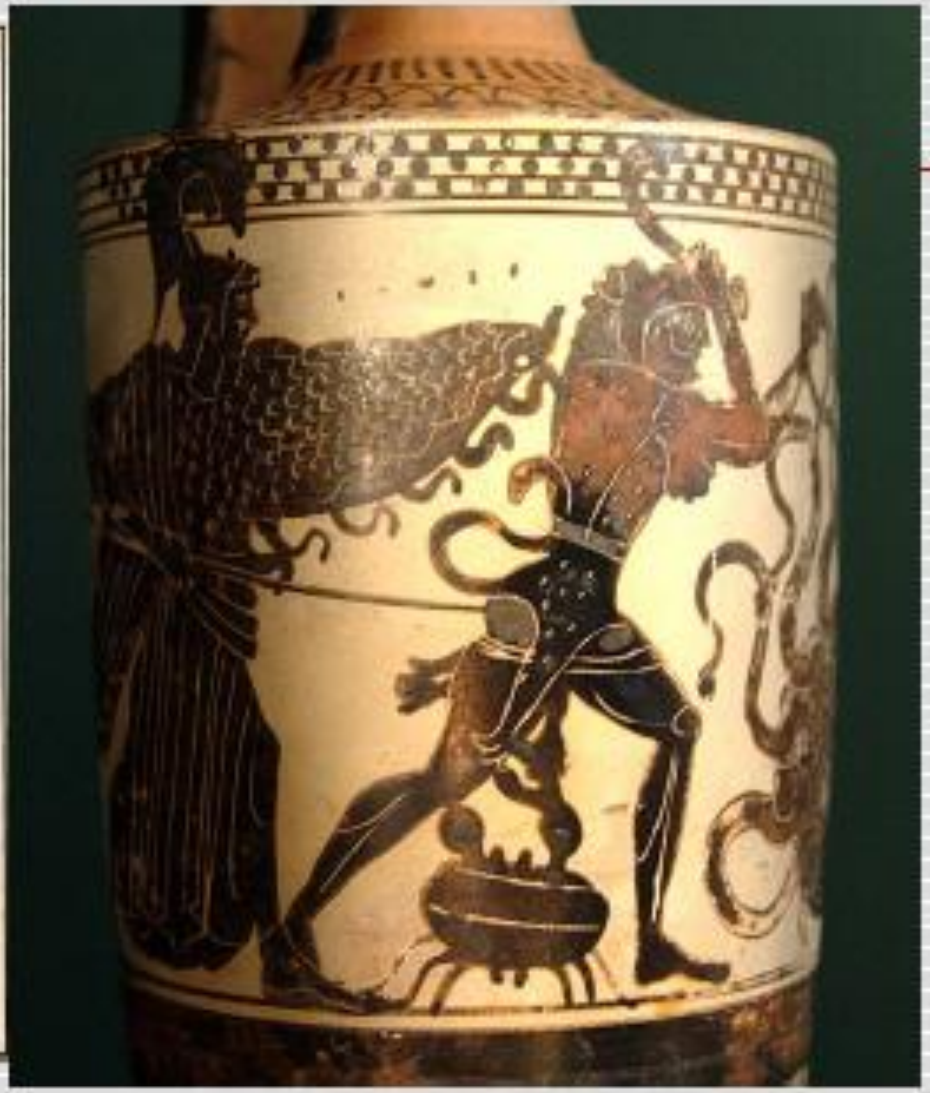
一般外科

Cancer (Karkinos)





99年癌登年報

期別	臨床期別	
	申報數	%
合 計	10124	100.00
0 期	1350	13.33
I 期	2976	29.4
II 期	3569	35.25
III 期	780	7.7
IV 期	573	5.66
不 詳	876	8.65

表八之二　乳癌 -94 年~96 年發生人數按整併期別*分類

期別	94 年		95 年		96 年	
	申報數	%	申報數	%	申報數	%
合計	5775	100.00	6102	100.00	7058	100.00
0 期	573	9.92	599	9.82	721	10.22
I 期	1559	27.00	1640	26.88	1971	27.93
II 期	2189	37.90	2281	37.38	2549	36.12
III 期	1051	18.20	1150	18.85	1222	17.31
IV 期	249	4.31	333	5.46	413	5.85
不詳	154	2.67	99	1.62	182	2.58

篩檢發現的個案，早期所佔比率較高

	早期所佔%		
	篩檢發現個案	非篩檢發現個案	差異
子宮頸癌(0-1期)	90.8	69.5	21.3
乳癌(0-2期)	82.8	69.8	13.0
口腔癌(0-1期)	33.6	28.5	5.1
大腸癌(0-2期)	55.1	43.0	12.1

資料來源：
- 台灣癌症登記資料庫(含原位癌)
- 子宮頸癌篩檢資料係取為98-99年資料，其他三癌則取97-99年資料
- 子宮頸癌與口腔癌則界定為第0-1期，乳癌及大腸癌早期個案定界為第0-2期

- Mammogram screening in 2012, **582000 screened,2838 breast cancer**, Most of them are early stage Breast Cancer

- We will be facing more and more early stage breast cancer in the future

TWENTY-YEAR FOLLOW-UP OF A RANDOMIZED TRIAL COMPARING TOTAL MASTECTOMY, LUMPECTOMY, AND LUMPECTOMY PLUS IRRADIATION FOR THE TREATMENT OF INVASIVE BREAST CANCER

BERNARD FISHER, M.D., STEWART ANDERSON, PH.D., JOHN BRYANT, PH.D., RICHARD G. MARGOLESE, M.D., MELVIN DEUTSCH, M.D., EDWIN R. FISHER, M.D., JONG-HYEON JEONG, PH.D., AND NORMAN WOLMARK, M.D.

N Engl J Med, Vol. 347, No. 16 · October 17, 2002

23% vs 5.8%

Radiotherapy after breast-conserving surgery in small breast carcinoma: Long-term results of a randomized trial

U. Veronesi,[1] E. Marubini,[2] L. Mariani,[2] V. Galimberti,[1] A. Luini,[1] P. Veronesi,[1] B. Salvadori[3] & R. Zucali[4]

Annals of Oncology **12**: 997–1003, 2001.

24% vs 8.5%

10-Year Results After Sector Resection With or Without Postoperative Radiotherapy for Stage I Breast Cancer: A Randomized Trial

By G. Liljegren, L. Holmberg, J. Bergh, A. Lindgren, L. Tabár, H. Nordgren, H.O. Adami, and the Uppsala-Örebro Breast Cancer Study Group

Current Practice in Early Breast CA

Negative axillary nodes	→	Radiation therapy to whole breast with or without boost[o] (by photons, brachytherapy, or electron beam) to tumor bed or consideration of partial breast irradiation (PBI) in selected patients.[o,q] Radiation therapy should follow chemotherapy when chemotherapy indicated.[r]

Surgery → C/T → Radiotherapy

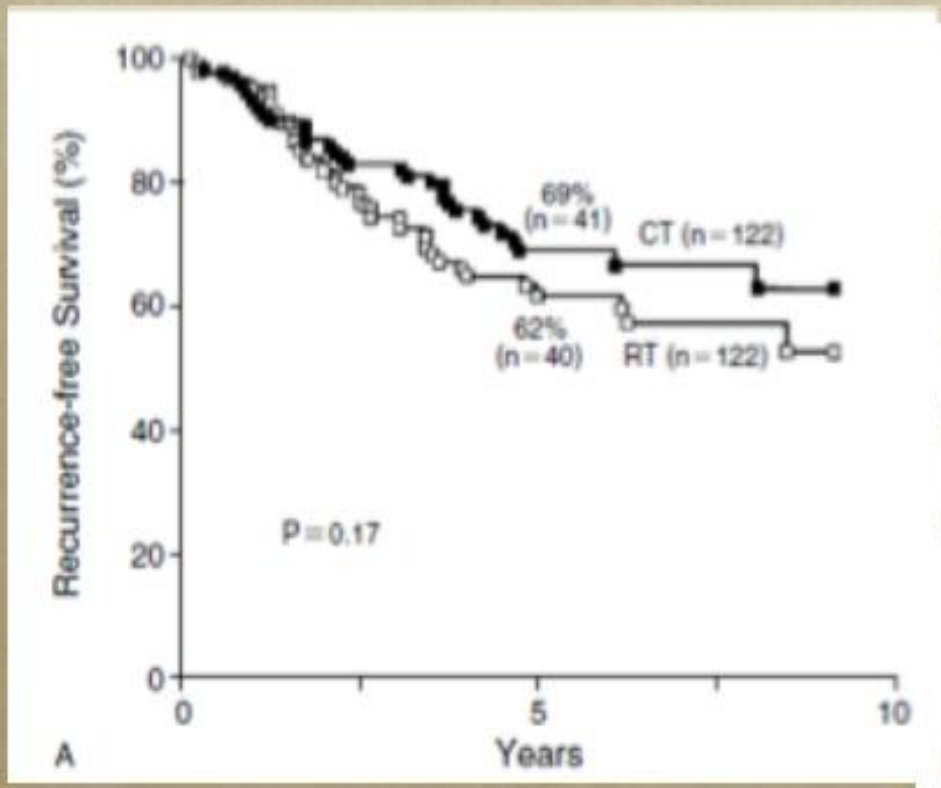
~4 Months **~1.5 Months**

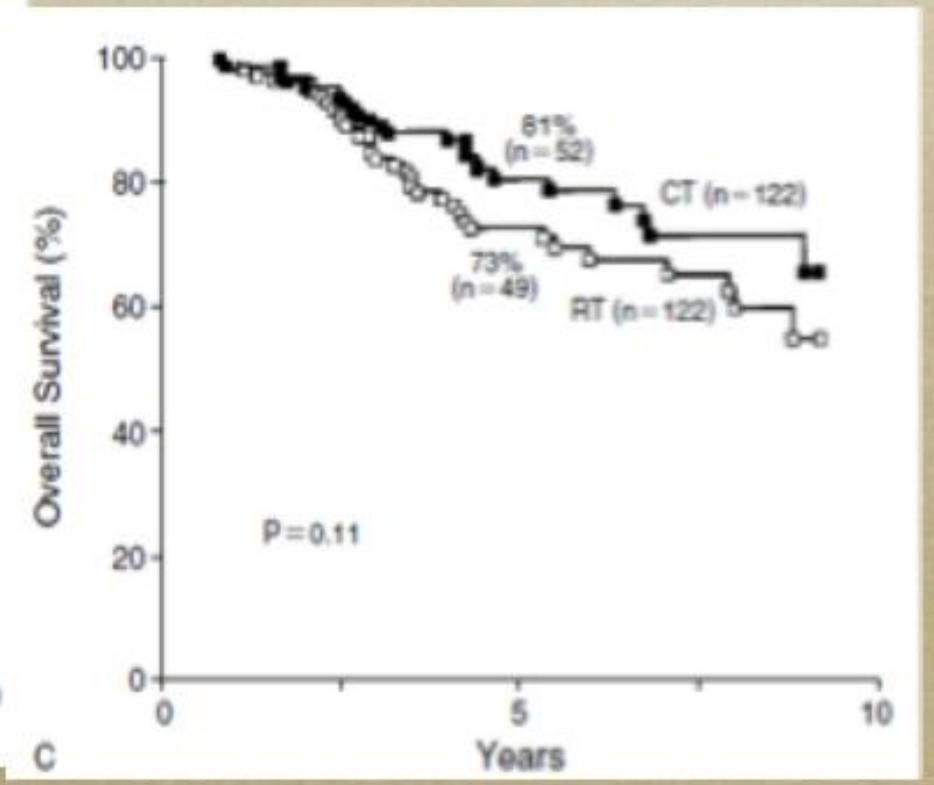
Treatment is Delayed for 4 months

IS IT OK TO DELAY RADIOTHERAPY?

THE SEQUENCING OF CHEMOTHERAPY AND RADIATION THERAPY AFTER CONSERVATIVE SURGERY FOR EARLY-STAGE BREAST CANCER

ABRAM RECHT, M.D., STEVEN E. COME, M.D., I. CRAIG HENDERSON, M.D., REBECCA S. GELMAN, PH.D., BARBARA SILVER, B.A., DANIEL F. HAYES, M.D., LAWRENCE N. SHULMAN, M.D., AND JAY R. HARRIS, M.D.





Delay C/T Decrease Survival

Recht *et al.* Trial (n=244)

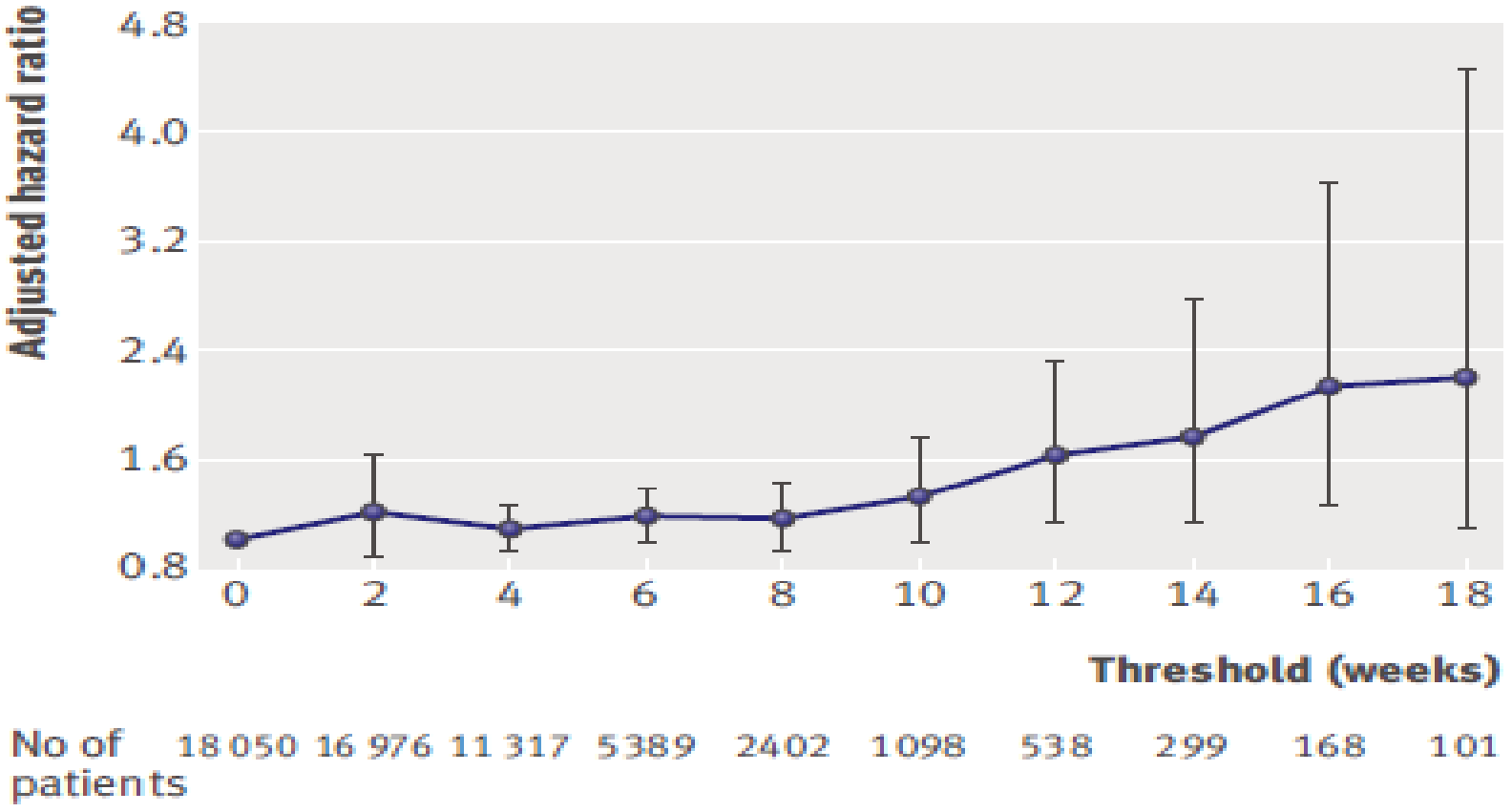
	Site of First	
	5 years	
	Local	Distant
RT→CT	5%	32%
CT→RT	14%	20%

Recht *et al.* (1996) N Engl J Med 334:1356

Delay RT, Probably is not the Best Choice

Impact of interval from breast conserving surgery to radiotherapy on local recurrence in older women with breast cancer: retrospective cohort analysis

Rinaa S Punglia, assistant professor,[1] Akiko M Saito, research fellow,[2] chief,[3] Bridget A Neville, programmer,[2] Craig C Earle, associate professor,[2] senior scientist,[4] Jane C Weeks, professor[2]



BMJ 2010;340:c845

DELAY C/T = HIGHER DISTANT METASTASIS

DELAY RT = HIGHER LOCAL RECURRENCE

兩全其美?

IORT, PBI

RISK OF SECONDARY CANCER

Whole Breast RT Irradiates Large Volume of Normal Organs

100%
50%
10%
5%
1%

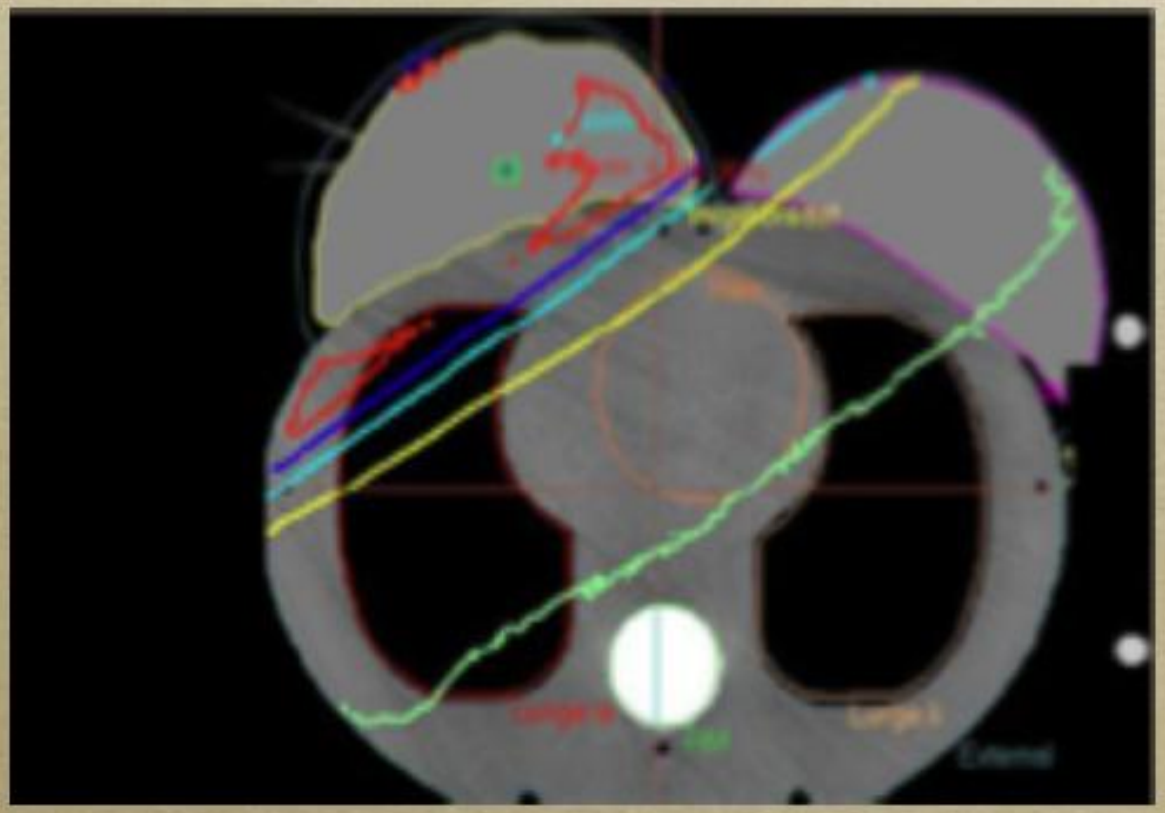
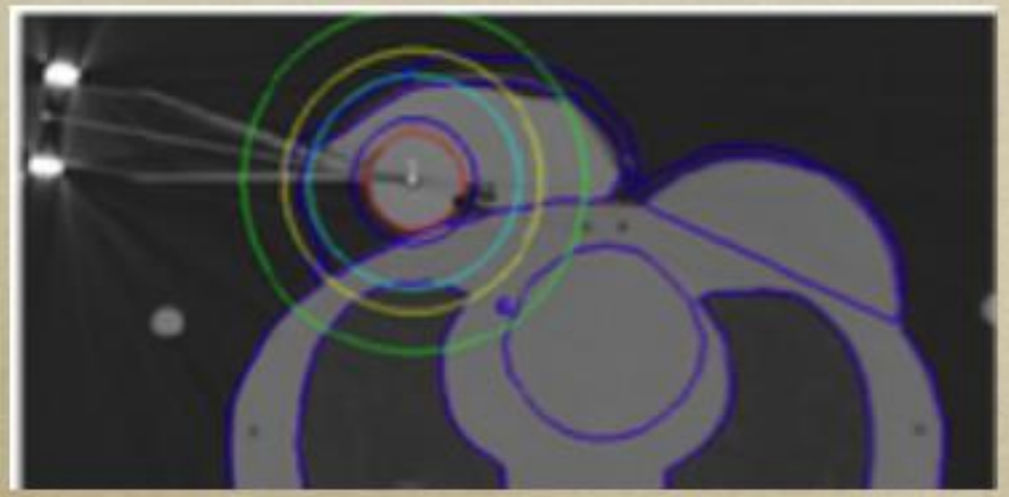


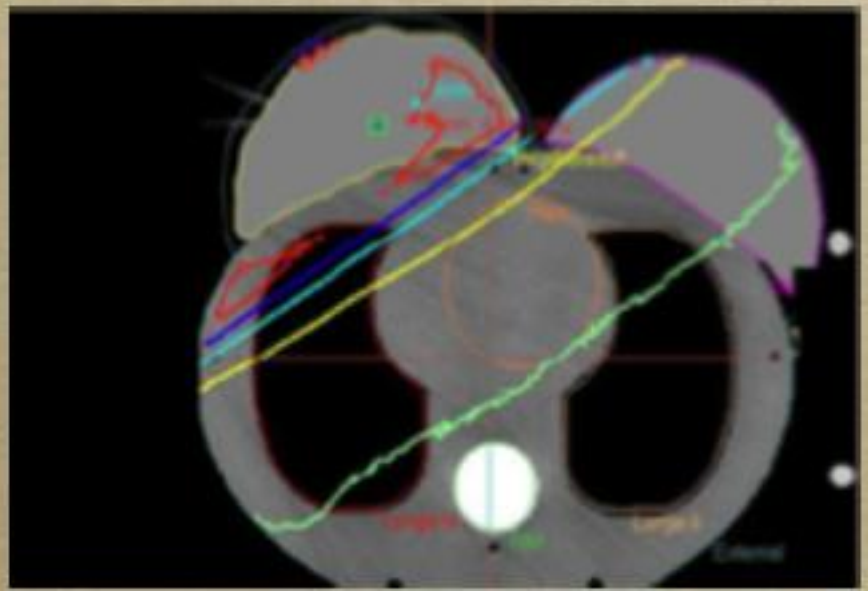
Table 4 Secondary cancer risk after radiotherapy for breast cancer

Authors, journal, year	No. of patients	Follow up time	organs	Risk for secondary cancer
Berrington de Gonzalez Br J Cancer (2010) [22]	182,057 69,181 treated with radiotherapy	13 years	Lung, oesophagus, pleura, bone and soft tissue Contralateral breast	RR = 1.38 (95% CI 1.26-1.51) RR = 1.09 (95% CI 1.04-1.15)
Kirova Int J Radiat Oncol Biol Phys (2007) [53]	16,705 13,472 treated with radiotherapy	10 years	Lung Contralateral breast	RR = 3.09 (95% CI 1.12-8.53) RR = 1.1 (95% CI 0.96-1.27)
Roychoudhuri Br J Cancer (2004) [54]	64,782 33,763 received radiotherapy	> 10 years	Lung	RR = 1.65 (95% CI 1.05-2.54)
Zablotska Cancer (2003) [31]	260,541 76,467 treated with radiotherapy	10 years	lung	0.30% RR = 2.06 (95% CI 1.53-2.78)
Prochazka Eur J Cancer (2002) [55]	141,053 141,053 treated with radiotherapy	> 10 years	lung	RR = 2.3 (95% CI 1.97-2.63)
Fowble Int J Radiat Oncol Biol Phys (2001) [28]	1,253 977 treated with radiotherapy	10 years	Contralateral breast	7%
Obedian J Clin Oncol (2000) [29]	2,416 1,029 treated with radiotherapy	15 years	Contralateral breast	10%

PBI Spares Normal Organs



100%
50%
10%
5%
1%



COMPLICATION & COSMETIC RESULT

乳房保留手術後的全乳房放射治療

- 療程通常需5至7週，每天一次，每週五次，每次治療約5~10分鐘，若含報到、姿勢擺設等時間，約半小時，總治療次數約25~33次。
- 這對患者的生活造成一定的不便，尤其對部分住在偏遠地區，交通不便或行動不便之患者有可能因無法接受放射治療而被迫選擇接受全乳房切除手術。

POTENTIAL PROBLEMS WITH CURRENT EARLY STAGE BREAST CANCER TREATMENT

- ***Treatment is Delayed for 4 months***
- ***Risk for second cancer, Lung, Contralateral breast, Heart…..***
- ***Risk for RT complications, fibrosis, contracture, swelling….***
- ***Long Protracted , daily trip to hospital***

BREAST SURGERY AND RADIOTHERAPY?

I have them done in the morning

And I don't want to miss lunch at home

PBI, IORT

- PBI
  - **Intra-operative RT (IORT)**
  - ~20 Gy x1
  - **Accelerated Partial Breast Irradiation**
  - ~34Gy / ~10Fx
- **Whole Breast RT**
  - 50Gy/25~28Fx Plus Local boost 1600/8 Fx

HOW TO DO PBI

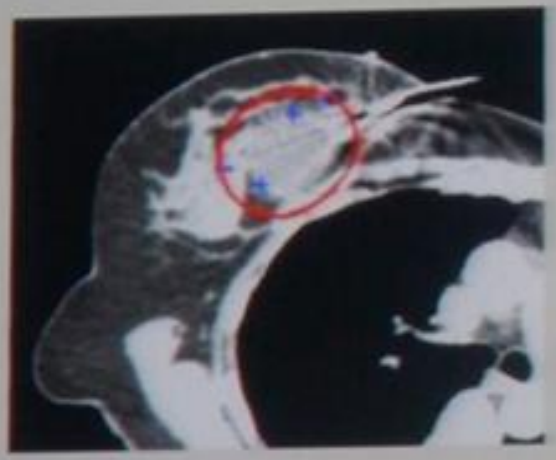
- APBI (34Gy, 10 Fractions /1 Week, Post-OP)
  - External Beam Radiotherapy
  - Brachytherapy
  - 50 kv X-ray
- IORT (Single Fraction 20 Gy)
  - Electron Beam
  - 50 kv X-ray

部分性乳房加速放射線治療 (ACCELERATED PARTIAL BREAST IRRADIATION, APBI)

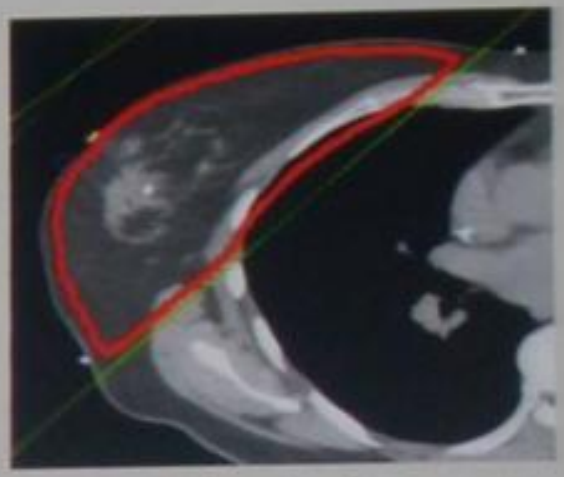
- 組織插種近接治療（Interstitial implant）:當局部乳房切除手術後將可讓放射性射源進入的細管或細針直接插種到乳房腫瘤區域，待術後再進行放射治療。
- MammoSit乳房腔內近接治療（Intracavitary brachytherapy）:當局部乳房切除手術後將可讓放射性射源進入之球型MammoSite裝置器(applicator)直接放入乳房術後的空腔內，待術後再進行放射治療。
- 體外放射治療(External beam radiotherapy):使用直線加速器進行強度調控放射治療或順形放射治療來執行APBI，通常照射範圍侷限於原發腫瘤附近。
- 手術中放射治療 (Intraoperative radiotherapy,IORT):在外科手術過程中同時採用放射療法，使早期乳癌婦女在腫塊切除的同時，完成放射治療

- Novac 7,ELIOT (NRT, Inc.) 採用4-10 百萬電子伏特(MeV)電子射束進行單次高劑量21格雷(Gy)放射治療。
- INTRABEAM (Carl Zeiss Meditec)，採用低能量50仟伏特(Kv) X射線進行單次高劑量20格雷(Gy)放射治療治療。
- Mobetron (IntraOp Medical Inc.)，採用6-12百萬電子伏特(MeV)電子射束進行單次高劑量21格雷(Gy)放射治療。
- Axxent eBx(Xoft Inc.) 採用低能量50仟伏特(Kv) X射線進行單次高劑量20格雷(Gy)放射治療

Brachytherapy vs Whole Breast Irradiation



A. Brachytherapy



B. Whole breast

Breast brachytherapy:

- Irradiates less tissue
- Focuses treatment to highest-risk portion of breast

Brachytherapy vs Whole Breast Irradiation

Breast brachytherapy:

- Delivers radiation through catheter(s)
- Requires 1 wk treatment (vs. 3 to 7 wks)

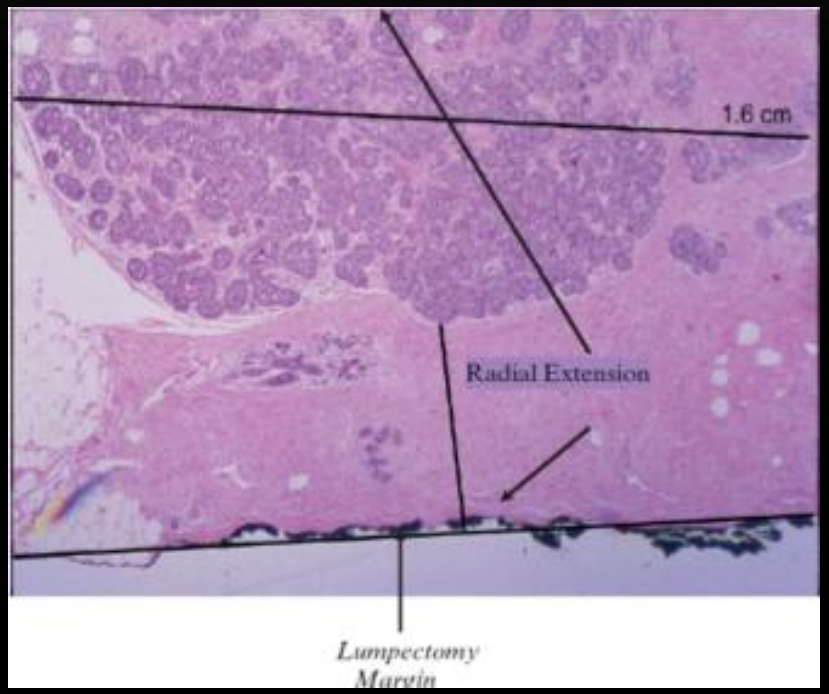
RATIONALES FOR DOING IORT/PBI

- Irradiate Partial Breast
- Large Fraction Size, Lower Total Dose
- Why Irradiate the Whole Breast?
- Radiobiological Rationale

ARE THERE TUMORS BEYOND LUMPECTOMY MARGIN?

Yes, But How Far

Can They Extend?



FOR MARGIN NEGATIVE EARLY BREAST CANCER, THE RESIDUAL TUMORS ARE MOSTLY WITHIN 1 CM

- **Vicini FA,**
  - **Int J Radiat Oncol Biol Phys, 2004**
- **Imamura H,**
  - **Breast Cancer Res Treat 62:177-184,2000**
- **Ohtake T,**
  - **Cancer 76:32-45, 1995**

- 133 cases, In more than 90% of cases, Residual tumor was limited to <10 mm
- 324 cases , >40 years, the maximum extension was < 9mm in all cases
- For Patients > 50 years Maximum distance of DCIS extension < 8 mm

PATTERN OF RECURRENCE AFTER BCS

- **Same Quadrant Recurrences**: ~90%
- **Elsewhere failure** : ~ 4-5%
- **Contra-Lateral Tumor Recurrence: ~ 4-5%**

Kurtz et al. (1990), Veronesi et al. 2002; Clark et al. 1992; Uppsala-, Oreboro Breast Cancer Study Group 1990

Dose Whole Breast RT Reduce Elsewhere Failure?

Trial	% Elsewhere failures	
	CS alone	CS + RT
NSABP B06 (Fisher et al. 2002)	2.7 (17/636)	3.8 (24/629)
Ontario (Clark et al. 1992)	3.5 (15/421)	0.9 (4/416)
Milan (Veronesi et al. 2002)	2.8 (8/280)	0.6 (2/299)
Finland	5.5 (4/72)	5.0 (4/80)
Sweden (Liljegren et al. 1994)	1.5 (3/194)	0.5 (1/187)
Range	1.5–5.5	0.5–5.0

Whole Breast RT dose not Reduce Elsewhere Failure

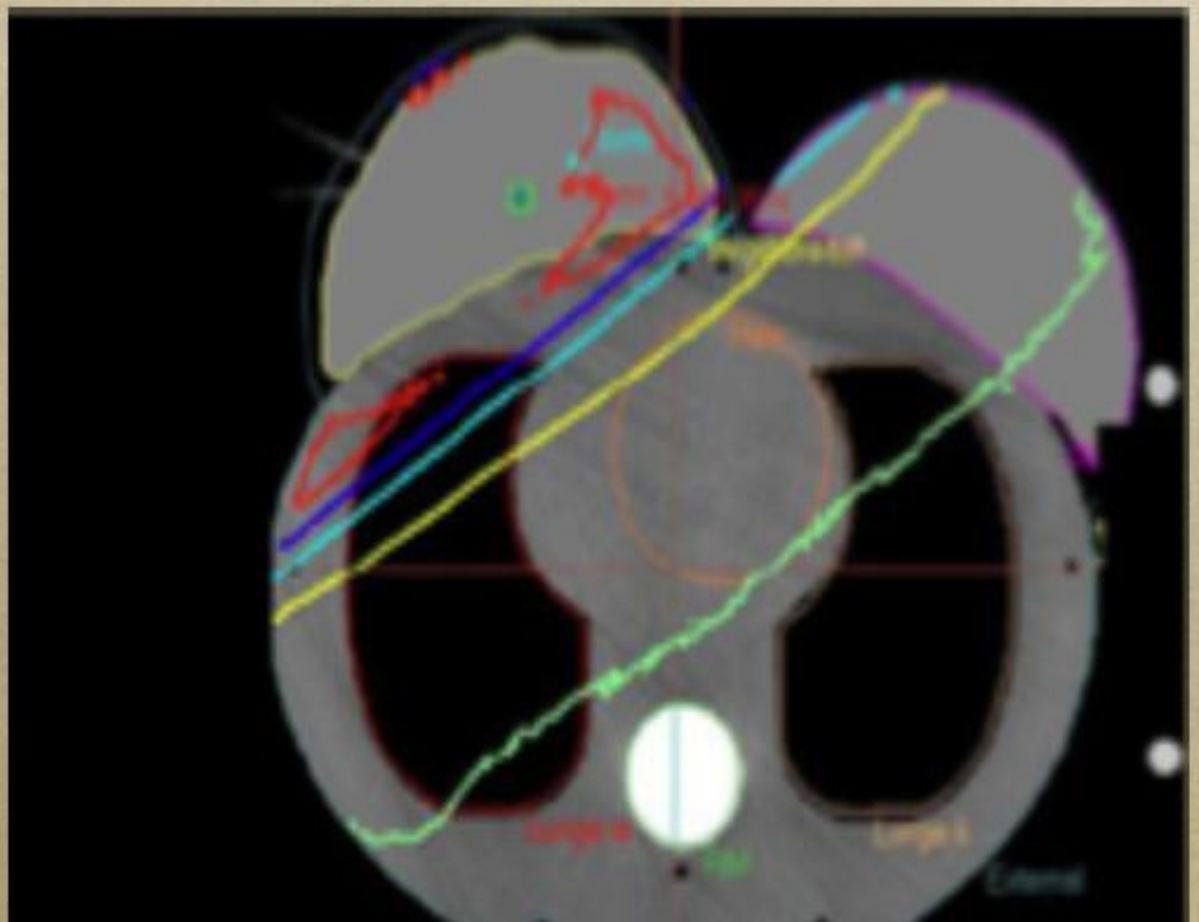
Investigator	Year	Number of patients	Percent of patients with elsewhere local recurrence*
With radiation			
Fourquet et al[1]	1989	518	5.8
Boyages et al[2]	1990	783	2.2
Kurtz et al[3]	1990	1593	2.4
Fowble et al[4]	1990	1093	1.7
Clark et al[5]	1992	416	0.9
Gage et al[6]	1995	974	2.8
Liljegren et al[7]	1999	184	5.0[Δ]
Touboul et al[8]	1999	528	4.2
Smith et al[9]	2000	1152	6.0
Veronesi et al[10]	2001	299	0.6
Huang et al[11]	2002	1339	3.6
Without radiation			
Clark et al[5]	1992	421	3.5
Liljegren et al[7]	1999	184	5.0[Δ]
Veronesi et al[10]	2001	280	2.9
Total		**9764**	**3.3**

IS IT REALLY NECESSARY TO DO WHOLE BREAST RADIATION?

There are no data that unequivocally show that whole breast radiation is required for local control

Whole Breast RT Irradiates Large Volume of Normal Organs

100%
50%
10%
5%
1%



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 14, 2013 VOL. 368 NO. 11

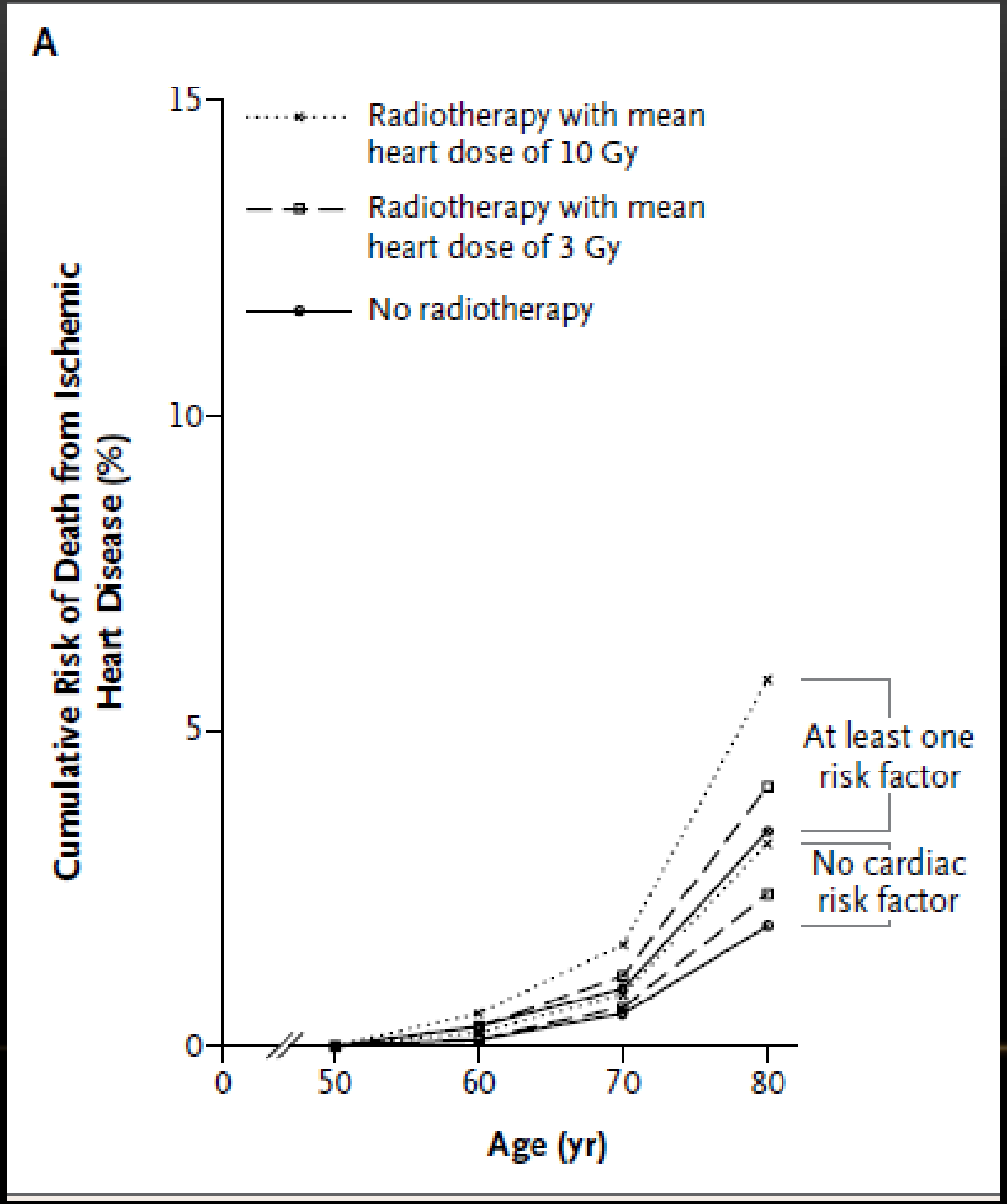
Risk of Ischemic Heart Disease in Women after Radiotherapy for Breast Cancer

RESULTS

The overall average of the mean doses to the whole heart was 4.9 Gy (range, 0.03 to 27.72). Rates of major coronary events increased linearly with the mean dose to the heart by 7.4% per gray (95% confidence interval, 2.9 to 14.5; P<0.001), with no apparent threshold. The increase started within the first 5 years after radiotherapy and continued into the third decade after radiotherapy. The proportional increase

Table 3. Percentage Increase in the Rate of Major Coronary Events per Gray, According to Time since Radiotherapy.

Time since Radiotherapy*	No. of Case Patients	No. of Controls	Increase in Rate of Major Coronary Events (95% CI)†
			% increase/Gy
0 to 4 yr	206	328	16.3 (3.0 to 64.3)
5 to 9 yr	216	296	15.5 (2.5 to 63.3)
10 to 19 yr	323	388	1.2 (–2.2 to 8.5)
≥20 yr	218	193	8.2 (0.4 to 26.6)
0 to ≥20 yr	963	1205	7.4 (2.9 to 14.5)


A
15
10
5
0
Radiotherapy with mean heart dose of 10 Gy
Radiotherapy with mean heart dose of 3 Gy
No radiotherapy
Cumulative Risk of Death from Ischemic Heart Disease (%)
At least one risk factor
No cardiac risk factor
0
50
60
70
80
Age (yr)

COMPLICATION AND QUALITY OF LIFE

Targit A N= 2232

	Targeted intraoperative radiotherapy (n=1113)	External beam radiotherapy (n=1119)	p value
Haematoma needing surgical evacuation	11 (1·0%)	7 (0·6%)	0·338
Seroma needing more than three aspirations	23 (2·1%)	9 (0·8%)	0·012
Infection needing intravenous antibiotics or surgical intervention	20 (1·8%)	14 (1·3%)	0·292
Skin breakdown or delayed wound healing*	31 (2·8%)	21 (1·9%)	0·155
RTOG toxicity grade of 3 or 4†	6 (0·5%)	23 (2·1%)	0·002
Major toxicity‡	37 (3·3%)	44 (3·9%)	0·443

Data are number of patients (%). RTOG=Radiation Therapy Oncology Group. *Some of the patients in the first three rows (haematoma needing surgical evacuation, seroma needing more than three aspirations, infection needing intravenous antibiotics or surgical intervention) could be included in the fourth row (skin breakdown or delayed wound healing). †No patient had grade 4 toxicity. ‡Defined as skin breakdown or delayed wound healing and RTOG toxicity grade of 3 or 4).

Table 5: **Clinically significant complications**

Late radiation toxicity after intraoperative radiotherapy (IORT) for breast cancer: results from the randomized phase III trial TARGIT A

Elena Sperk · Grit Welzel · Anke Keller · Uta Kraus-Tiefenbacher · Axel Gerhardt · Marc Sütterlin · Frederik Wenz

Breast Cancer Res Treat (2012) 135:253–260

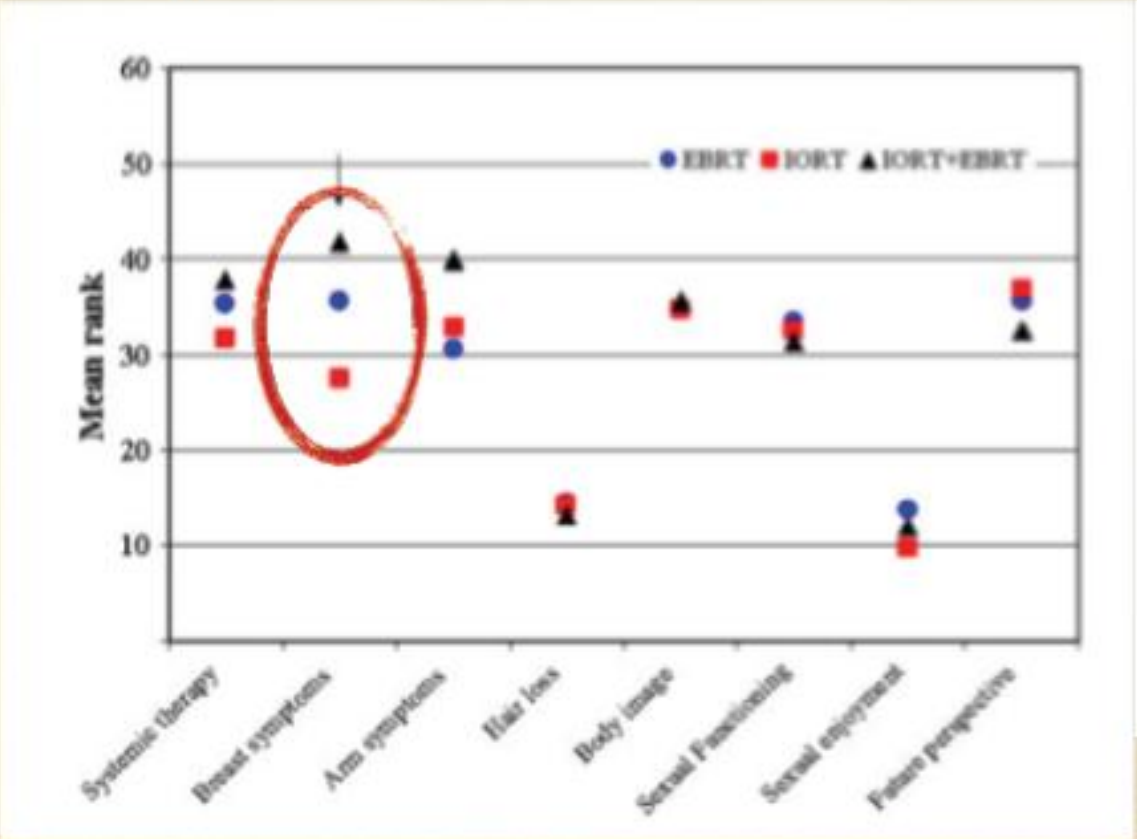
N= 305

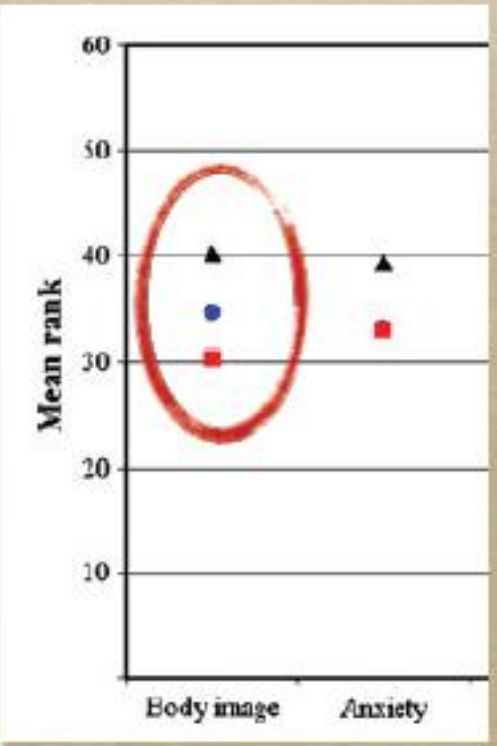
	IORT	*EBRT*	
Fibrosis	*5.9%*	*18.4%*	
Telangictasis	*0*	*17.7%*	

Health-Related Quality of Life After Breast-Conserving Surgery and Intraoperative Radiotherapy for Breast Cancer Using Low-Kilovoltage X-rays

Grit Welzel[1], Frank Hofmann[1], Elena Blank[1], Uta Kraus-Tiefenbacher[1], Brigitte Hermann[1], Marc Sütterlin[2], and Frederik Wenz[1]

Ann Surg Oncol (2010) 17:S359–S367





COSMETIC RESULT?

Yes, They're Fake
The Real Ones
Tried to
KILL ME
ustomize it!

Breast enlargement without surgery!

BREAST-CONSERVING TREATMENT WITH PARTIAL OR WHOLE BREAST IRRADIATION FOR LOW-RISK INVASIVE BREAST CARCINOMA—5-YEAR RESULTS OF A RANDOMIZED TRIAL

CSABA POLGÁR, M.D., PH.D.,* JÁNOS FODOR, M.D., PH.D., D.SC.,* TIBOR MAJOR, M.SC., PH.D.,* GYÖRGY NÉMETH, M.D., PH.D., D.SC.,* KATALIN LÖVEY, M.D.,* ZSOLT OROSZ, M.D., PH.D.,† ZOLTÁN SULYOK, M.D.,‡ ZOLTÁN TAKÁCSI-NAGY, M.D., PH.D.,* AND MIKLÓS KÁSLER, M.D., PH.D.*

Departments of *Radiotherapy, †Human and Experimental Tumor Pathology, and ‡General and Thoracic Surgery, National Institute of Oncology, Budapest, Hungary

Int. J. Radiation Oncology Biol. Phys., Vol. 69, No. 3, pp. 694–702, 2007

N = 258

	PBI	WBRT
Good Cosmetic Result	77.6%	62.9%

Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial

Jayant S Vaidya, PhD, Frederik Wenz, MD, Max Bulsara, PhD, Jeffrey S Tobias, FRCR, David J Joseph, FRACR, Mohammed Keshtgar, PhD, Henrik L Flyger, MD, Samuele Massarut, MD, Michael Alvarado, MD, Christobel Saunders, FRACS, Wolfgang Eiermann, MD, Marinos Metaxas, PhD, Elena Sperk, MD, Marc Sütterlin, MD, Douglas Brown, FRCS, Laura Esserman, MD, Mario Roncadin, MD, Alastair Thompson, FRCS, John A Dewar, FRCR, Helle M R Holtveg, MD, Steffi Pigorsch, MD, Mary Falzon, FRCPath, Eleanor Harris, MD, April Matthews, BSc, Chris Brew-Graves, MSc, Ingrid Potyka, PhD, Tammy Corica, BSc, Norman R Williams, PhD, Michael Baum, MD and on behalf of the TARGIT trialists' group

The Lancet
Volume 383, Issue 9917, Pages 603-613 (February 2014)
DOI: 10.1016/S0140-6736(13)61950-9

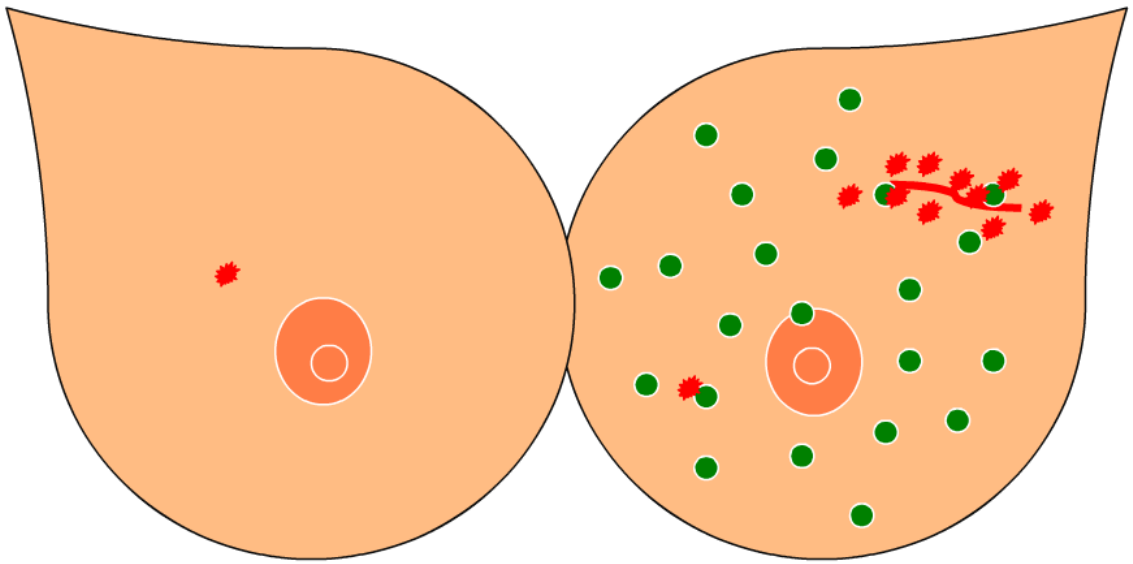
ELSEVIER

Scientific rationale for TARGIT

Br J Cancer 1996;74:820-824

Multicentricity of breast cancer: whole-organ analysis and clinical implications

J S Vaidya, J S Vyas, R F Chinoy, N Merchant, O P Sharma and I Mittra



Breast cancer is frequently multicentric…

But most recurrences occur near the primary tumour

So, it makes sense to target radiotherapy to the tumour bed

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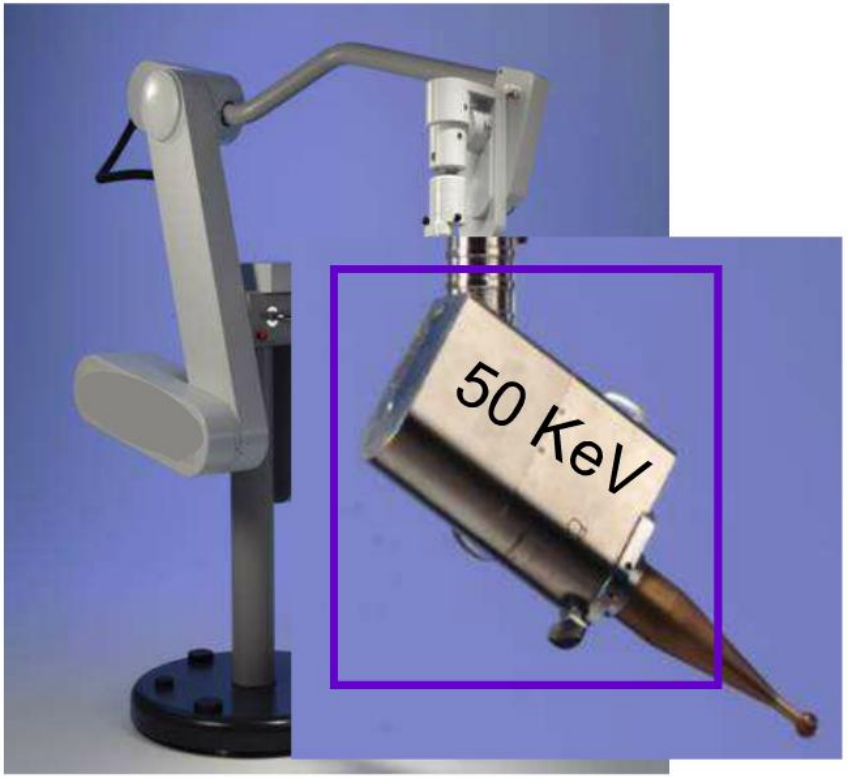
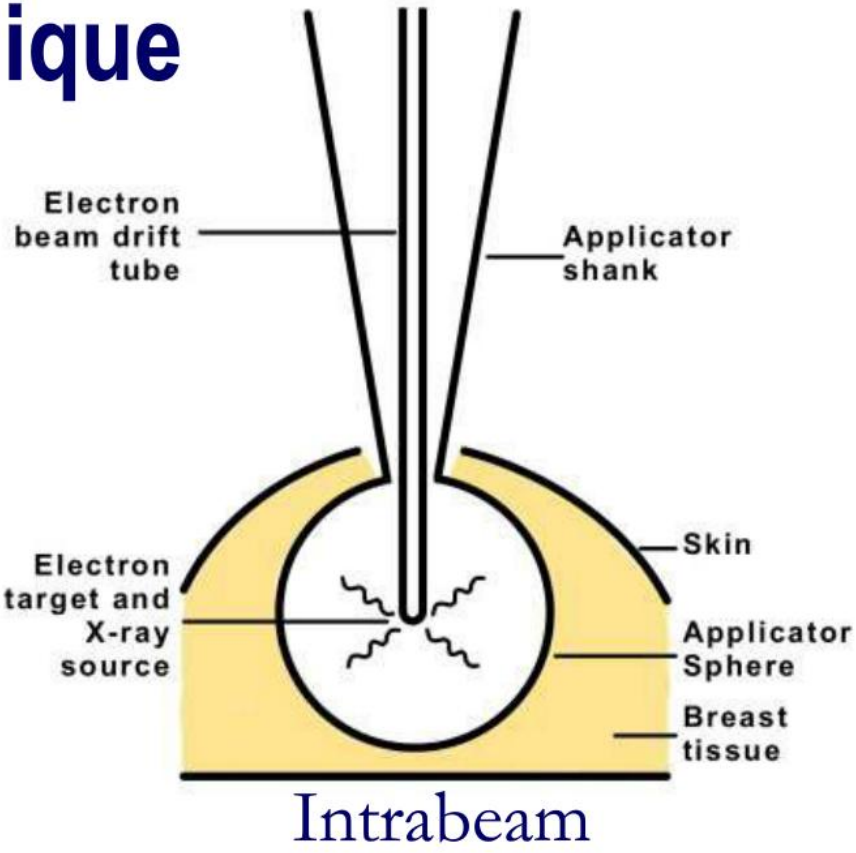
The TARGIT Technique





Intrabeam

The dose corresponds to tumour cell density

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Breast cancer patient (>=45 years) suitable for breast conserving surgery

RANDOMISE

TARGIT group (A)

Individualised-Risk-Adjusted Radiotherapy

A single dose of TARGIT with Intrabeam (in ~85%)

+

if high risk*
add EBRT (45-50Gy, no boost)

*prespeficied criteria e.g., unsuspected lobular carcinoma, lymphovascular invasion, etc.

EBRT group (B)

One-size-fits-all Radiotherapy

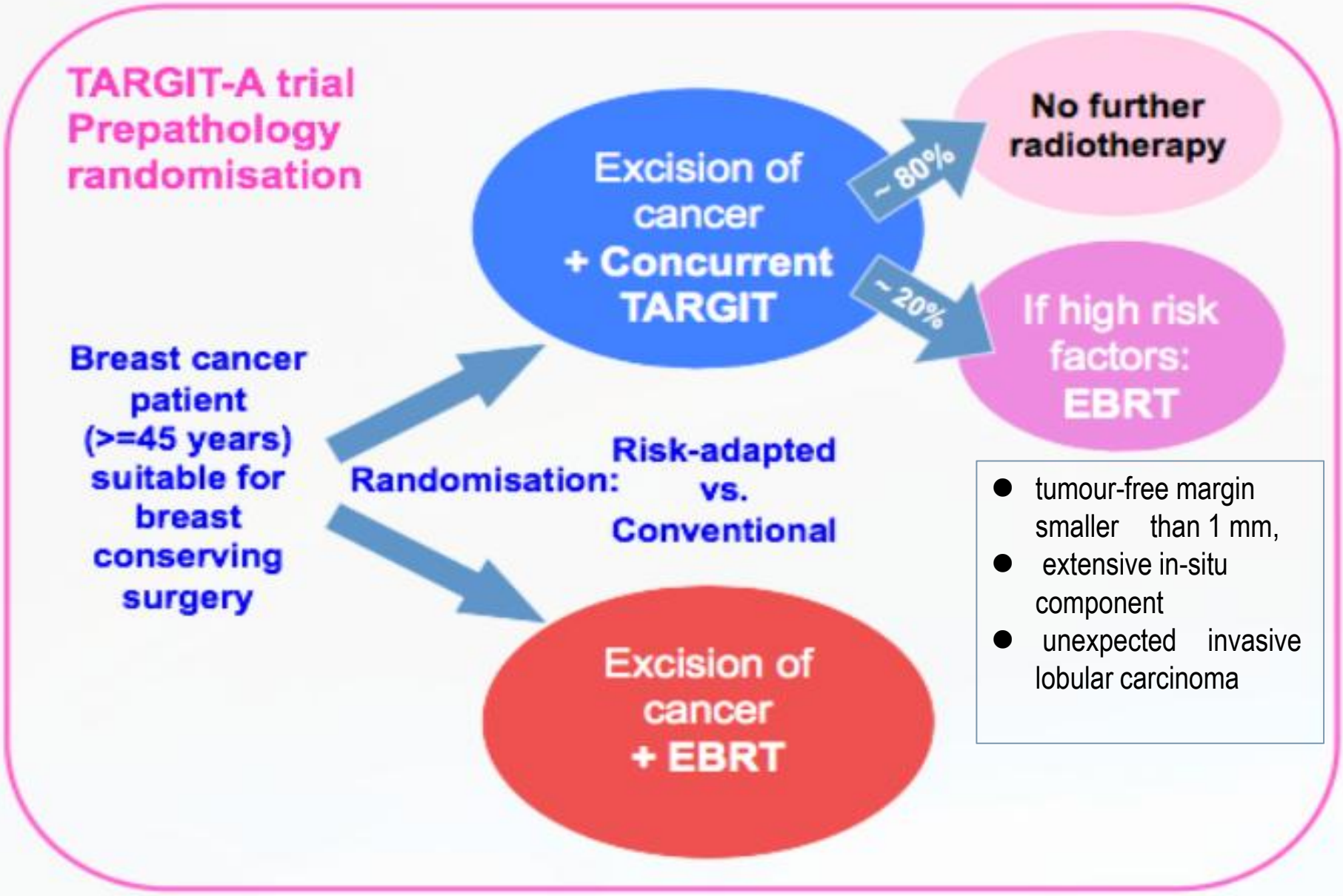
Standard 4-6 week course of external beam radiotherapy (EBRT)

40-56Gy in 15-25 fractions

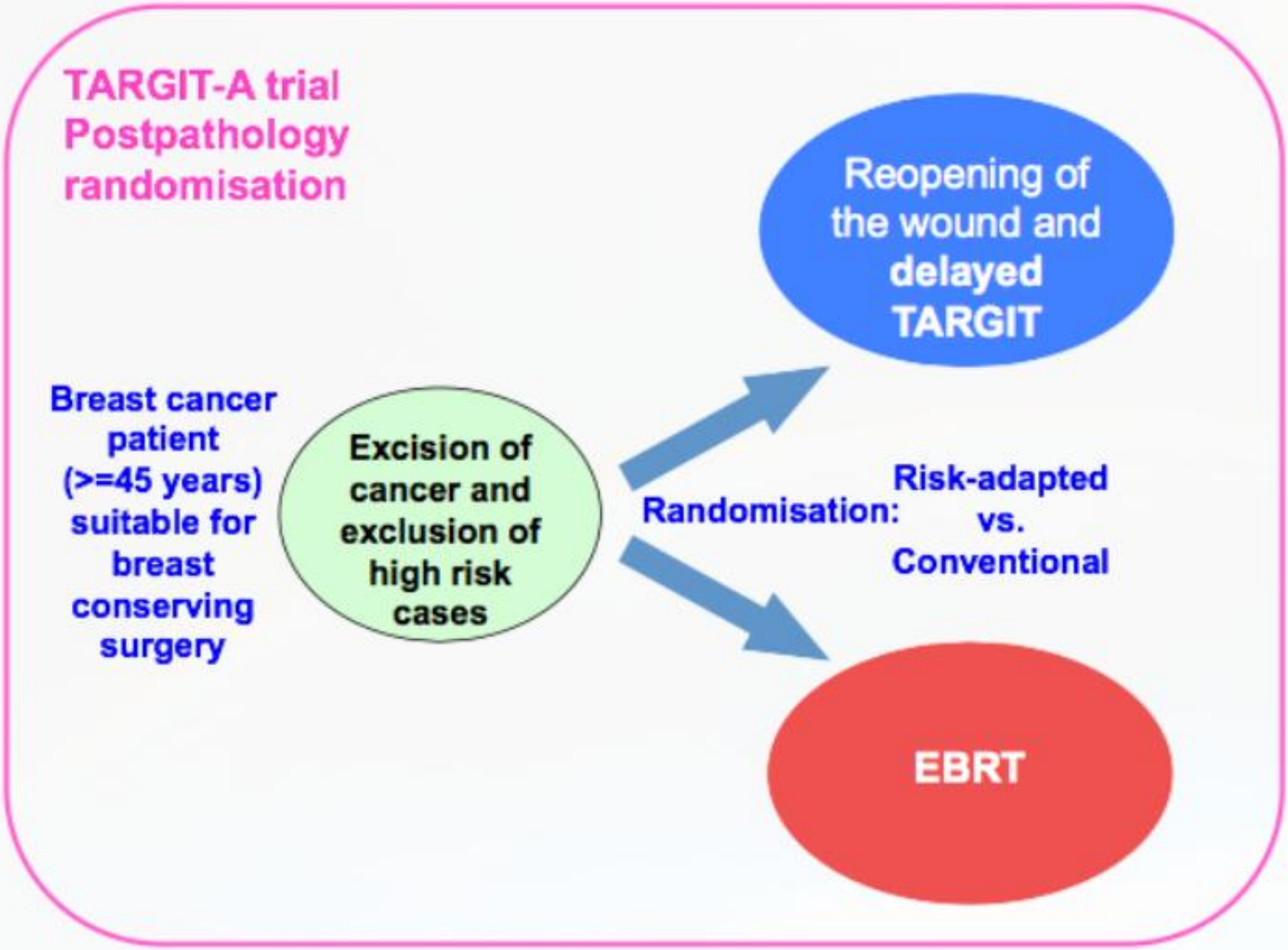
+/-

Tumour bed boost
10-16 G y in 5-8 fractions

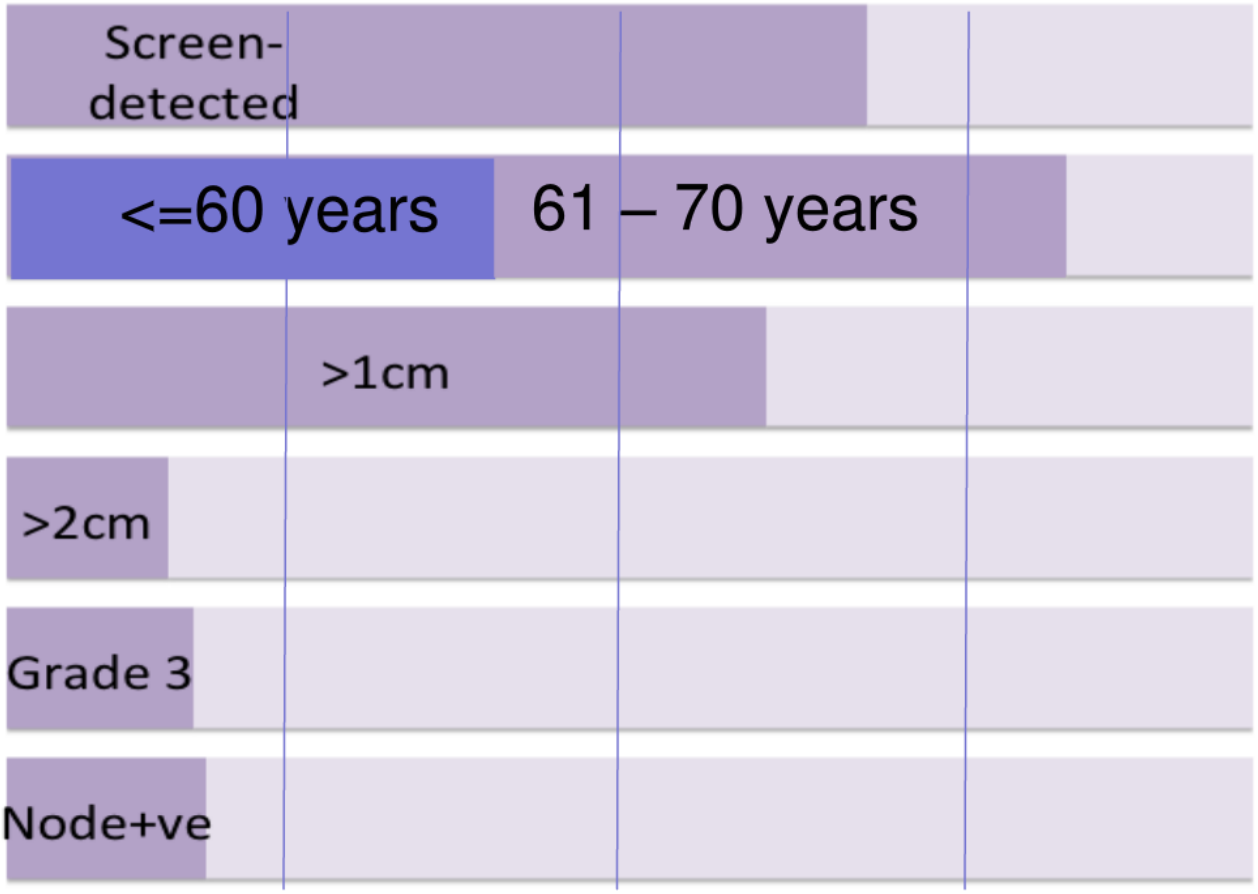
Eligible patients were recruited at two stages of their treatment in the pragmatic Targit trial:



After the primary surgery (Postpathology randomisation)


TARGIT-A trial
Postpathology randomisation
Reopening of the wound and delayed TARGIT
Breast cancer patient (>=45 years) suitable for breast conserving surgery
Excision of cancer and exclusion of high risk cases
Randomisation:
Risk-adapted
vs.
Conventional
EBRT

Patient characteristics (n=3451)



Good prognosis

BUT

Not elderly

Substantial number of adverse prognosis patients

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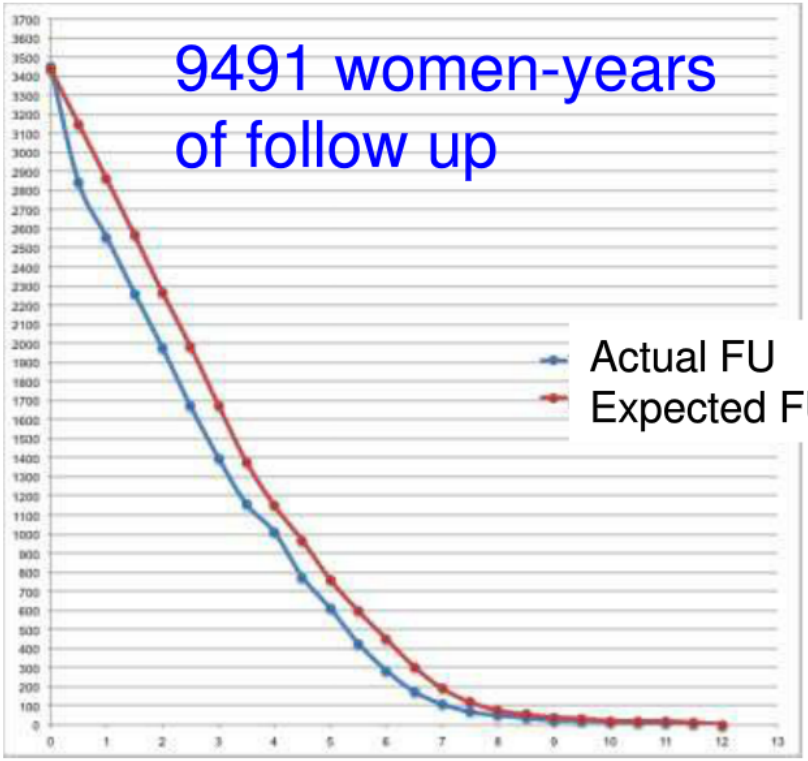
Follow up

1222 patients - median follow up of 5 years

2020 patients - median follow up of 4 years

3451 patients - median follow up of 2 yrs 5 months

93.7% patients seen for 5 years or within the preceding year



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Outcomes and number of events

- Total number of patients 3451
- Primary outcome:
  - Ipsilateral Breast recurrence 34
- Secondary outcome:
  - Deaths 88
    - Breast cancer deaths 36
    - Non Breast cancer deaths 52
- Exploratory outcome:
  - Loco-regional recurrence 42
  - All recurrences (Breast + axilla + contralateral + distant) 117
  - Distant recurrence 63

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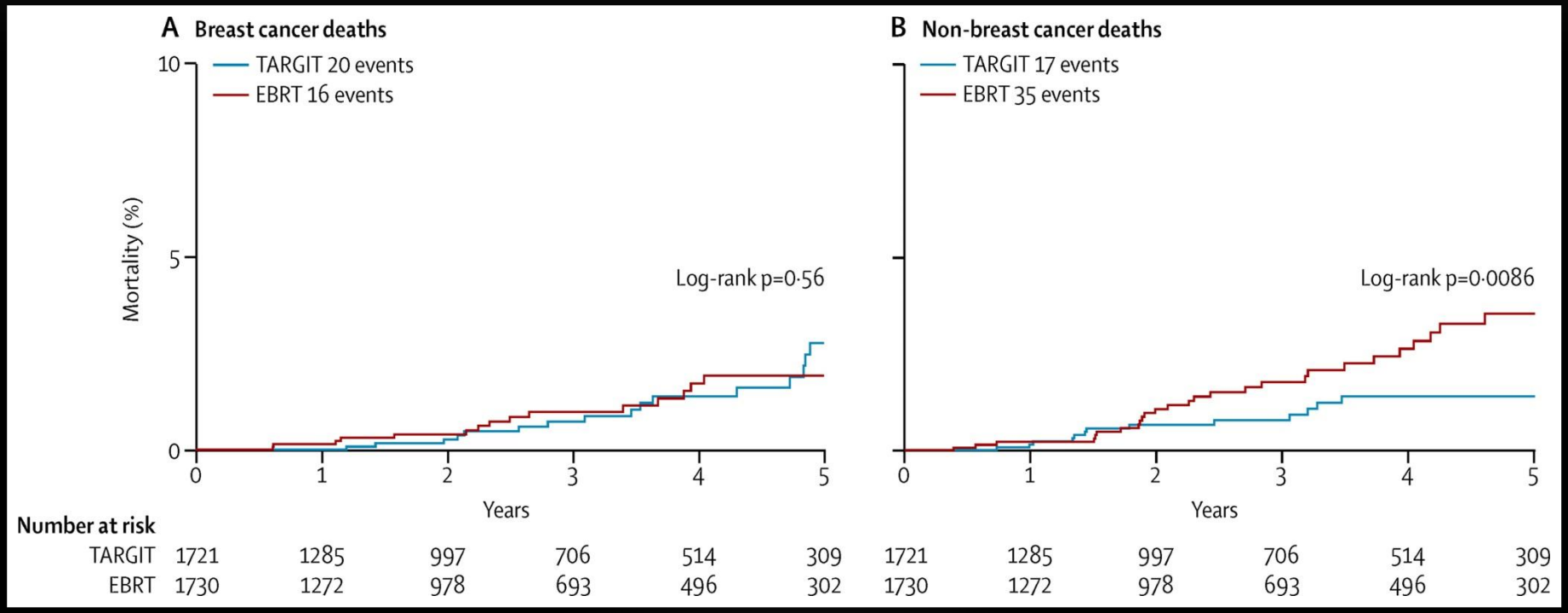
	Events; 5-year cumulative risk (95%CI)		Absolute difference*
	TARGIT	EBRT	
All patients			
Local recurrence (n=3375)	23; 3·3% (2·1–5·1)	11; 1·3% (0·7–2·5)	12 (2·0%)
Any other recurrence (n=3375)	46; 4·9% (3·5–6·9)	37; 4·4% (3·0–6·4)	9 (0·5%)
Death (n=3451)	37; 3·9% (2·7–5·8)	51; 5·3%(3·9–7·3)	–14 (–1·4%)
Prepathology†			
Local recurrence (n=2234)	10; 2·1% (1·1–4·2)	6; 1·1% (0·5–2·5)	4 (1·0%)
Any other recurrence (n=2234)	29; 4·8% (3·1–7·3)	25; 4·7% (3·0–7·4)	4 (0·1%)
Death (n=2298)	29; 4·6% (1·8–6·0)	42; 6·9% (4·3–9·6)	–13 (–2·3%)
Postpathology‡			
Local recurrence (n=1141)	13; 5·4% (3·0–9·7)	5; 1·7%(0·6–4·9)	8 (3·7%)
Any other recurrence (n=1141)	17; 5·2% (3·0–8·8)	12; 3·7% (1·9–7·0)	5 (1·5%)
Death (n=1153)	8; 2·8% (1·3–5·9)	9; 2·3% (1·0–5·2)	–1 (0·5%)

TARGIT=targeted intraoperative radiotherapy. EBRT=external beam radiotherapy. *In Kaplan-Meier point estimate at 5 years (TARGIT minus EBRT). †TARGIT given at same time as lumpectomy. ‡TARGIT given after lumpectomy, as separate procedure.

Table 1: **Results of primary (local recurrence in the conserved breast), secondary (death), and exploratory (any other recurrence) outcomes for all patients and the two strata as per timing of randomisation and delivery of TARGIT**

BREAST CANCER DEATHS AND NON-BREAST-CANCER DEATHS



	TARGIT	EBRT
Other cancers	8	16
Cardiovascular causes		
Cardiac*	2	8
Stroke	0	2
Ischaemic bowel	0	1
Other†	7	8
Total	17	35

5-year risk 1·4% for TARGIT versus 3·5% for EBRT; log-rank p=0·0086.
TARGIT=targeted intraoperative radiotherapy. EBRT=external beam radiotherapy.
*Included one "sudden death at home" in EBRT group. †TARGIT: two diabetes, one renal failure, one liver failure, one sepsis, one Alzheimer's disease, one unknown; EBRT: one myelopathy, one perforated bowel, one pneumonia, one old age, four unknown

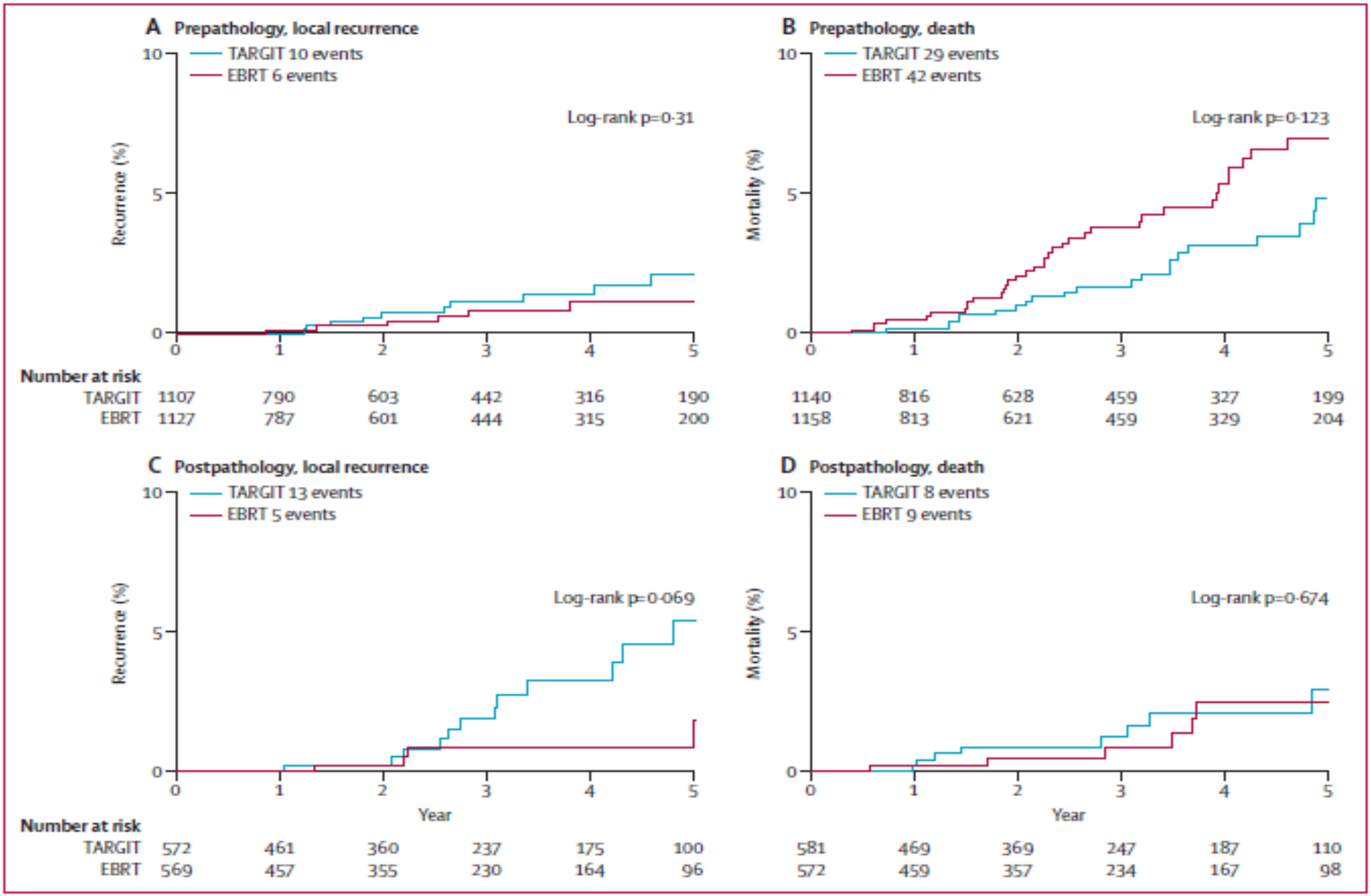
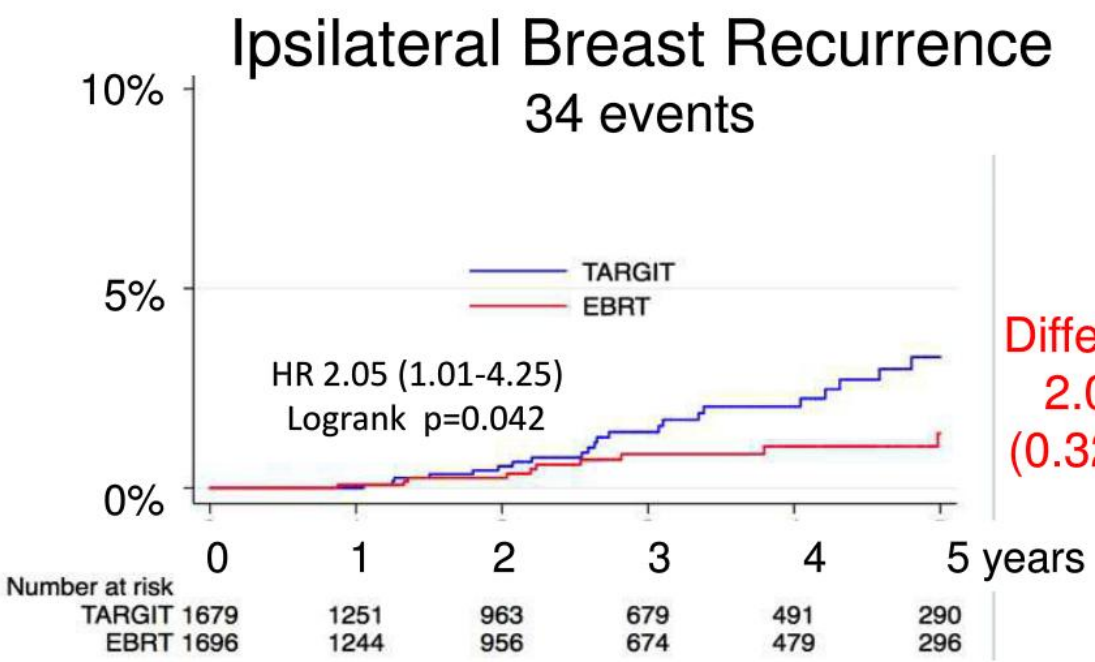
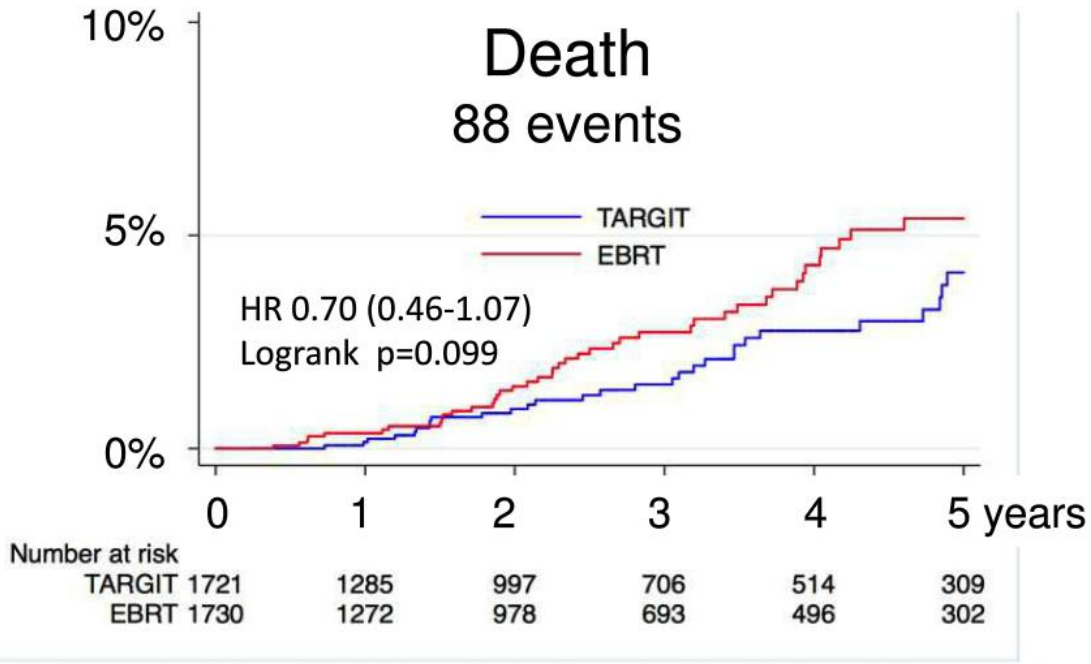


***Figure 3*: Kaplan-Meier analysis of local recurrence in the conserved breast and death for the two strata as per timing of randomisation and delivery of TARGIT (prepathology *vs* postpathology)**

Local recurrence was the primary outcome, death was a secondary outcome. Prepathology (n=2298), randomised before lumpectomy and TARGIT given concurrently with lumpectomy. Postpathology (n=1153), randomised after lumpectomy and TARGIT given by reopening the wound. (A) Local recurrence in prepathology stratum. (B) Deaths in prepathology stratum. (C) Local recurrence in postpathology stratum. (D) Deaths in postpathology stratum. TARGIT=targeted intraoperative radiotherapy. EBRT=external beam radiotherapy.

Blue = TARGIT
Red = EBRT





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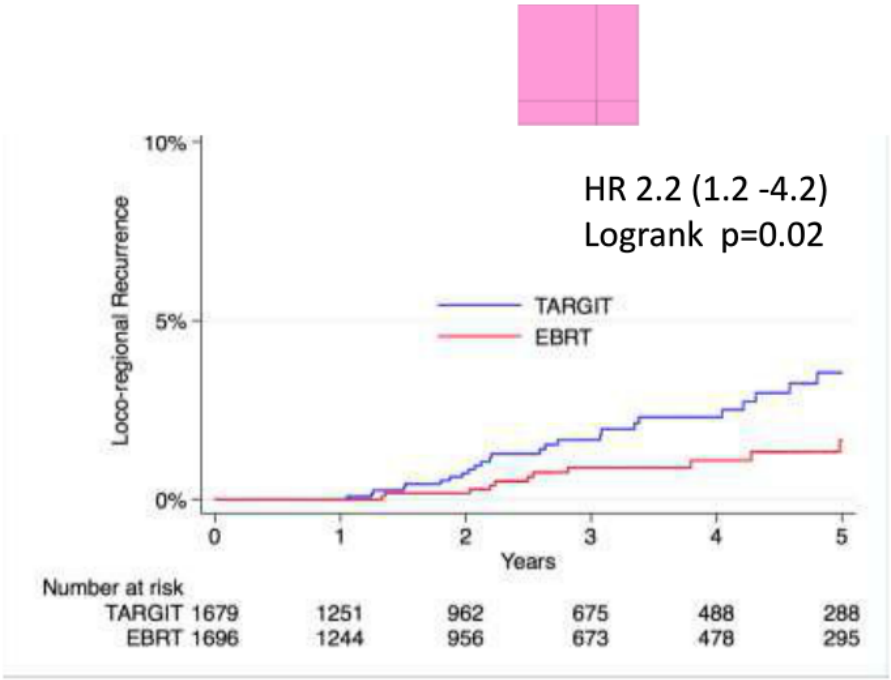
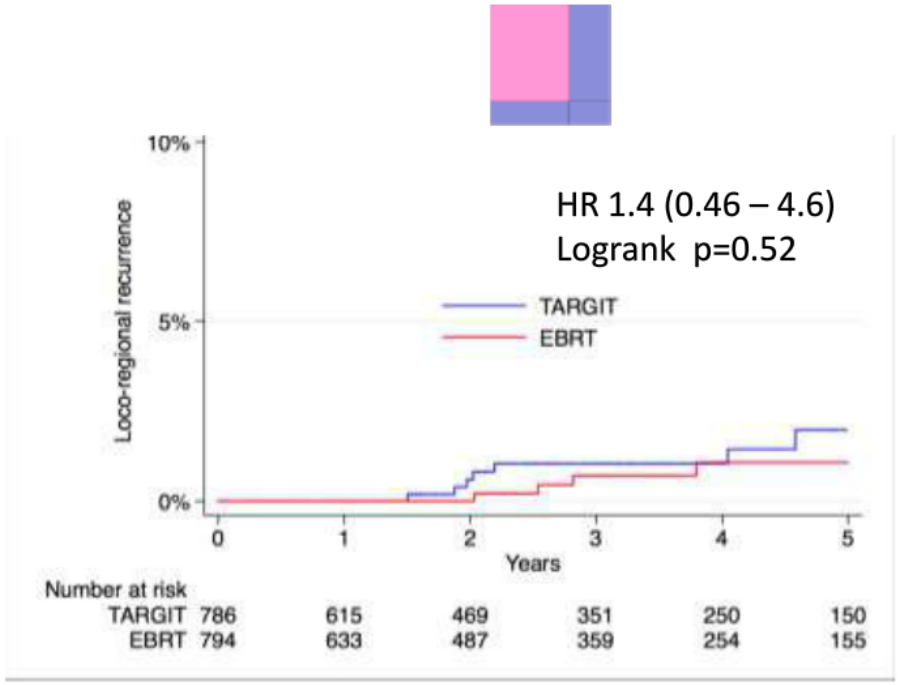
Blue = TARGIT
Red = EBRT

Loco-regional recurrence

All patients



Prepathology PgR+ve



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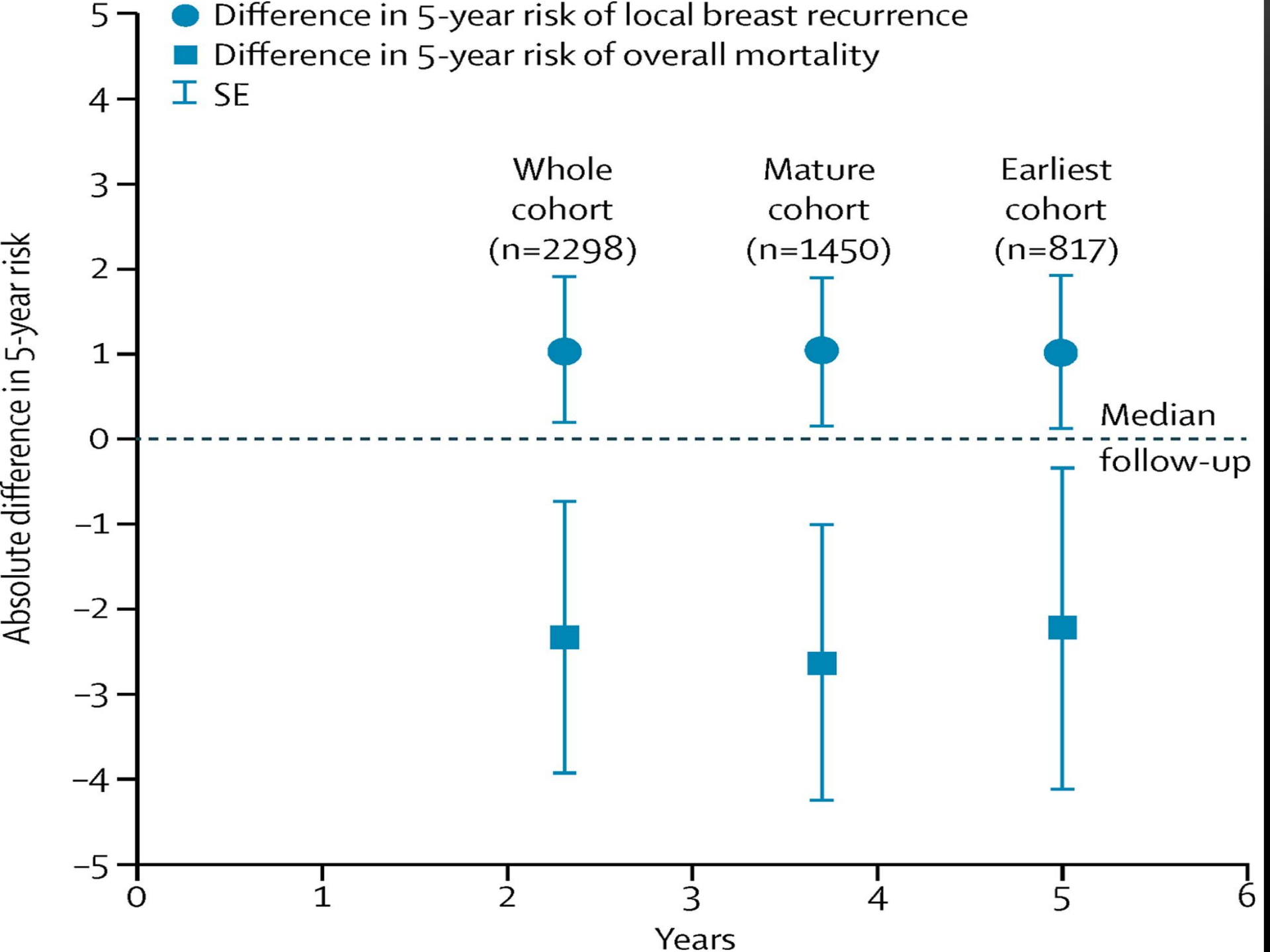
Difference in 5-year risk of local breast recurrence
Difference in 5-year risk of overall mortality
SE
Whole cohort (n=2298)
Mature cohort (n=1450)
Earliest cohort (n=817)
Median follow-up
Absolute difference in 5-year risk
5
4
3
2
1
0
−1
−2
−3
−4
−5
0
1
2
3
4
5
6
Years

	Median follow-up	Number of events	Absolute difference (90% CI) in the binomial proportions of local recurrence* in the conserved breast (TARGIT minus EBRT)	Z score	$p_{\text{non-inferiority}}$
Whole trial					
All patients (n=3451)	2 years 5 months	34	0·72% (0·2 to 1·3)	-5·168	<0·0001
Mature cohort (n=2232)	3 years 7 months	32	1·13% (0·3 to 2·0)	-2·652	0·0040
Earliest cohort (n=1222)	5 years	23	1·14% (-0·1 to 2·4)	-1·750	0·0400
Prepathology†					
All patients (n=2298)	2 years 4 months	16	0·37% (-0·2 to 1·0)	-5·954	<0·0001
Mature cohort (n=1450)	3 years 8 months	14	0·6% (-0·3 to 1·5)	-3·552	0·0002
Earliest cohort (n=817)	5 years	9	0·76% (-0·4 to 2·0)	-2·360	0·0091
Postpathology‡					
All patients (n=1153)	2 years 4 months	18	1·39% (0·2 to 2·6)	-1·503	0·0664
Mature cohort (n=782)	3 years 7 months	18	2·04% (0·3 to 3·8)	-0·429	0·3339
Earliest cohort (n=405)	5 years	14	1·8% (-1·2 to 4·8)	-0·382	0·3511

Conclusion 1

Primary end point

The absolute difference in ipsilateral breast recurrence between TARGIT and EBRT is:

	TARGIT *minus* EBRT difference (95%CI)
For unselected patients	2.0% (0.32 – 3.7)
Prepathology PgR +ve	0.18% (-1.62 –1.98)

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Conclusion 2

Secondary end point

Compared with EBRT, TARGIT results in:

- A trend for reduced mortality
  (Difference -1.4% p=0.1)
- Fewer non breast-cancer deaths
  (Difference -2.1% p=0.009)

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PARTIAL BREAST IRRADIATION

- Non-inferior to Whole breast RT (in selected patients)
- Results in better cosmetic result
- And has favorable complication profile
- Trend for reduced mortality
- Less non-breast cancer death

WHO ARE CANDIDATES FOR PBI?

Breast cancer being treated with Breast Conserving Surgery

Age>=45 years

Unifocal invasive duct carcinoma - MRI not required

Size preferably < 3.5cm

Randomisation

TARGIT	EBRT
Risk-Adapted Radiotherapy	**One-size-fits-all Radiotherapy**
Single dose of TARGIT with Intrabeam If high risk factors are found, add EBRT (in ~15%)	Standard fractionated External Beam Radiotherapy (EBRT)

2000 – 2012: 3451 patients randomised

Thank You for Your Attention