

TARGET-IORT

TARGETed Intraoperative radiotherapy



Jayant S Vaidya, Max Bulsara, Michael Baum, Frederik Wenz, Samuele Massarut, Steffi Pigorsch, Michael Alvarado, Michael Douek, Christobel Saunders, Henrik Flyger, Wolfgang Eiermann, Chris Brew-Graves, Norman Williams, Ingrid Potyka, Nicholas Roberts, Marcelle Bernstein, Douglas Brown, Elena Sperk, Siobhan Laws, Marc Sütterlin, Tammy Corica, Steinar Lundgren, Dennis Holmes, Lorenzo Vinante, Fernando Bozza, Montserrat Pazos, Magali Le Blanc-Onfroy, Günther Gruber, Wojciech Polkowski, Konstantin J Dedes, Marcus Niewald, Jens Blohmer, David McCready, Richard Hoefler, Pond Kelemen, Gloria Petralia, Mary Falzon, David Joseph, Jeffrey S Tobias.

Acknowledgements



University College London Hospitals
NHS Foundation Trust

University of Dundee
NHS Tayside

Hampshire Hospitals
NHS Foundation Trust

Royal Free London
NHS Foundation Trust

Whittington Health
NHS

Guy's and St Thomas'
NHS Foundation Trust



ST. OLAVS HOSPITAL
TRONDHEIM UNIVERSITY HOSPITAL



UNIVERSITY OF COPENHAGEN



Herlev Hospital
Rigshospitalet



FUNDED BY

NIHR | National Institute for Health Research



Government of Western Australia
Department of Health
Sir Charles Gairdner Hospital



THE UNIVERSITY OF
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AUSTRALIA



UNIVERSITY OF NEBRASKA
MEDICAL CENTER



Sentara Surgery Specialists
SENTARA MEDICAL GROUP



International Steering Committee



Trial Steering Committee 2019





More info at
targit.org.uk



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The TARGIT-A trial investigators / authors



Professor Max Bulsara

Potential conflict of Interest

- I receive grant funding for UCL from Dept of Health – NIHR HTA
- I receive honoraria / travel reimbursement from Carl Zeiss



YOU HAVE BREAST CANCER

“Can you come to the hospital every day for 6 weeks for radiotherapy?”

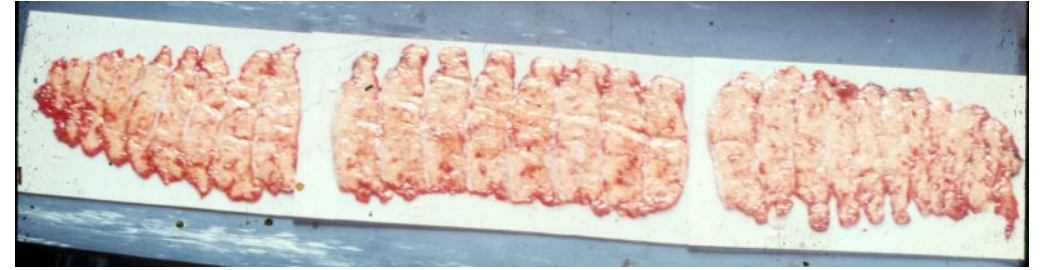


YES
we can
conserve your
breast
3 miles from UCSF, USA

NO
we need to do
a mastectomy

Concern about patients and curiosity about breast cancer

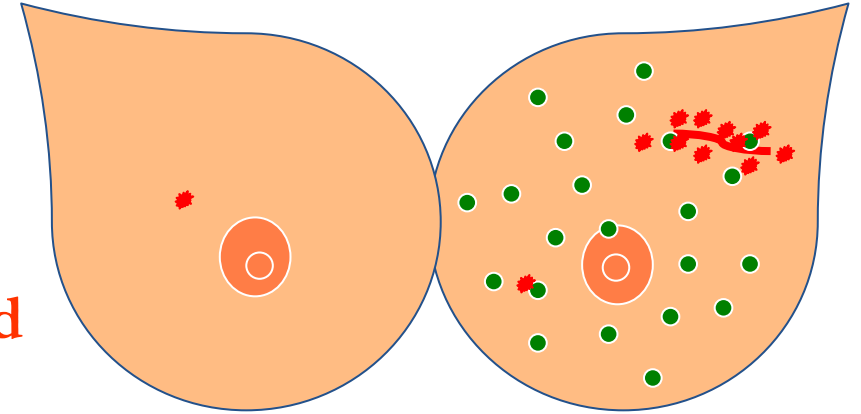
Whole organ analysis of mastectomy specimens



The breast has many other microscopic cancers

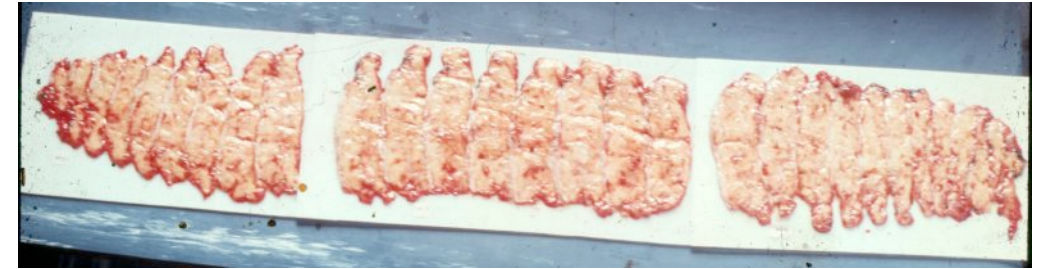
BUT >90% recurrences occur in the index quadrant.

Sensible to target radiotherapy just to the tumour bed



Concern about patients and curiosity about breast cancer

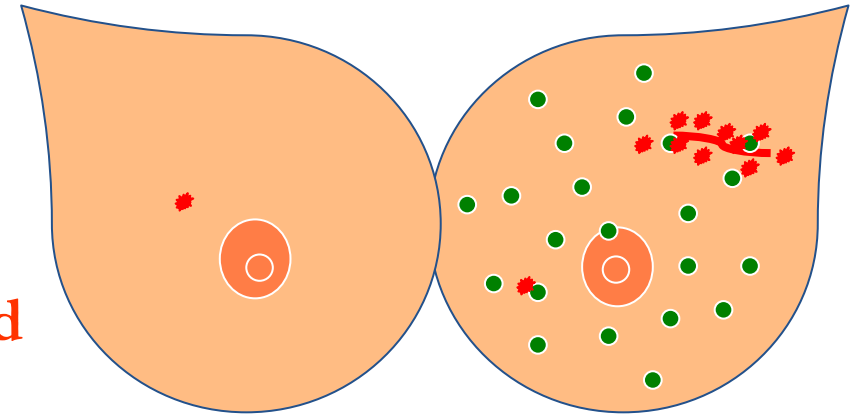
Whole organ analysis of mastectomy specimens



The breast has many other microscopic cancers

BUT >90% recurrences occur in the index quadrant.

Sensible to target radiotherapy just to the tumour bed



Br J Cancer 1996;74:820-824

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

JS Vaidya¹, JJ Vyas², RF Chinoy², N Merchant³, OP Sharma³ and I Mitra¹

THE LANCET

1997 Jan 18;349(9046):208

Multicentricity and recurrence of breast cancer

Michael Baum, *Jayant S Vaidya, Indraneel Mitra

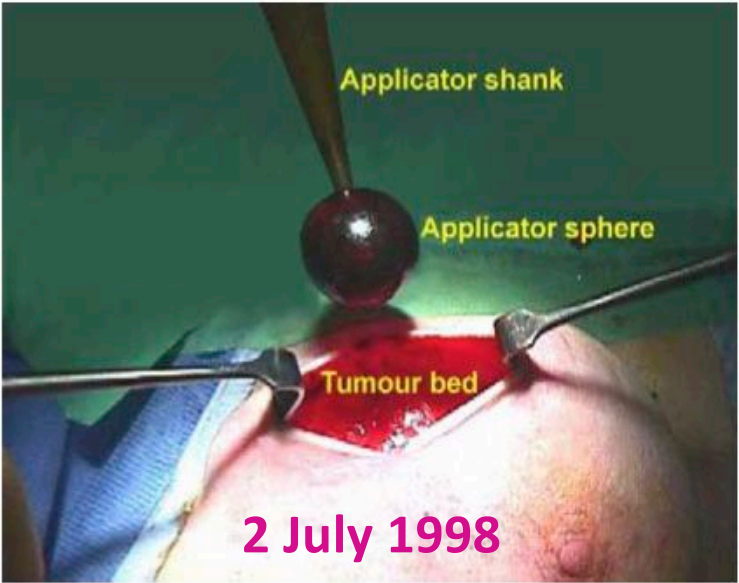
*Department of Surgery, Institute of Surgical Studies, University College London, London W1P 7LD, UK; and Department of Surgery, Tata Memorial Hospital, Bombay, India

Hong Kong
International
Cancer Congress,
Nov 1995

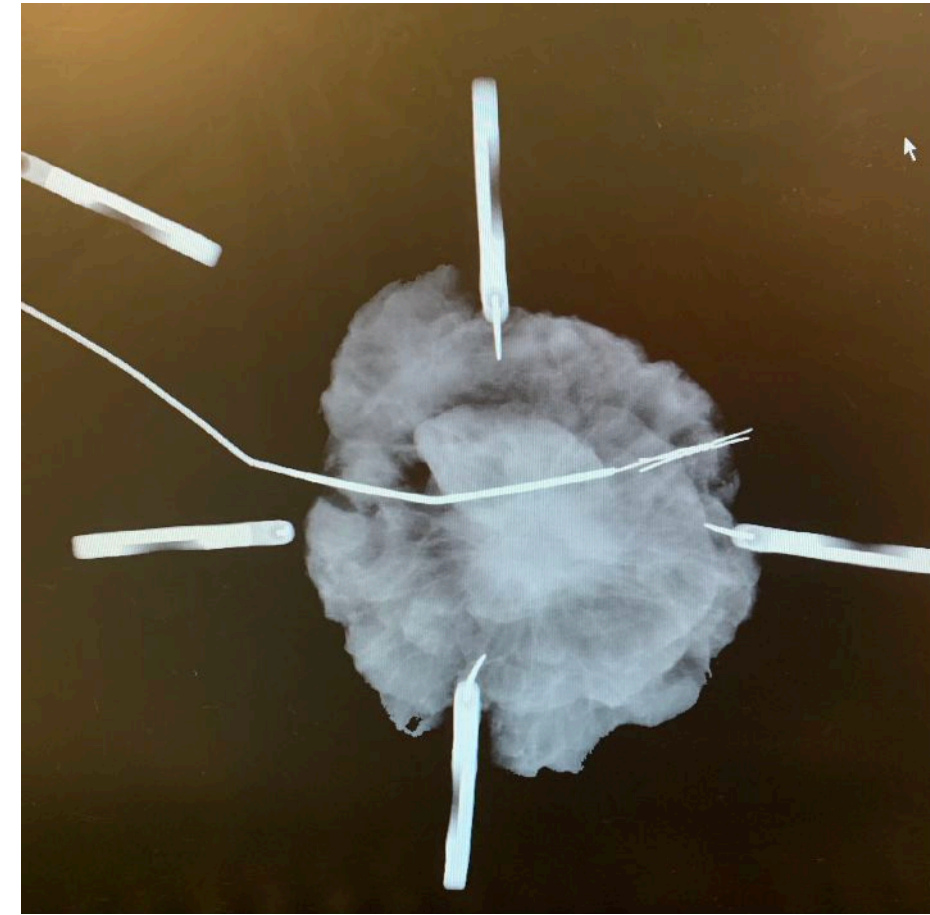
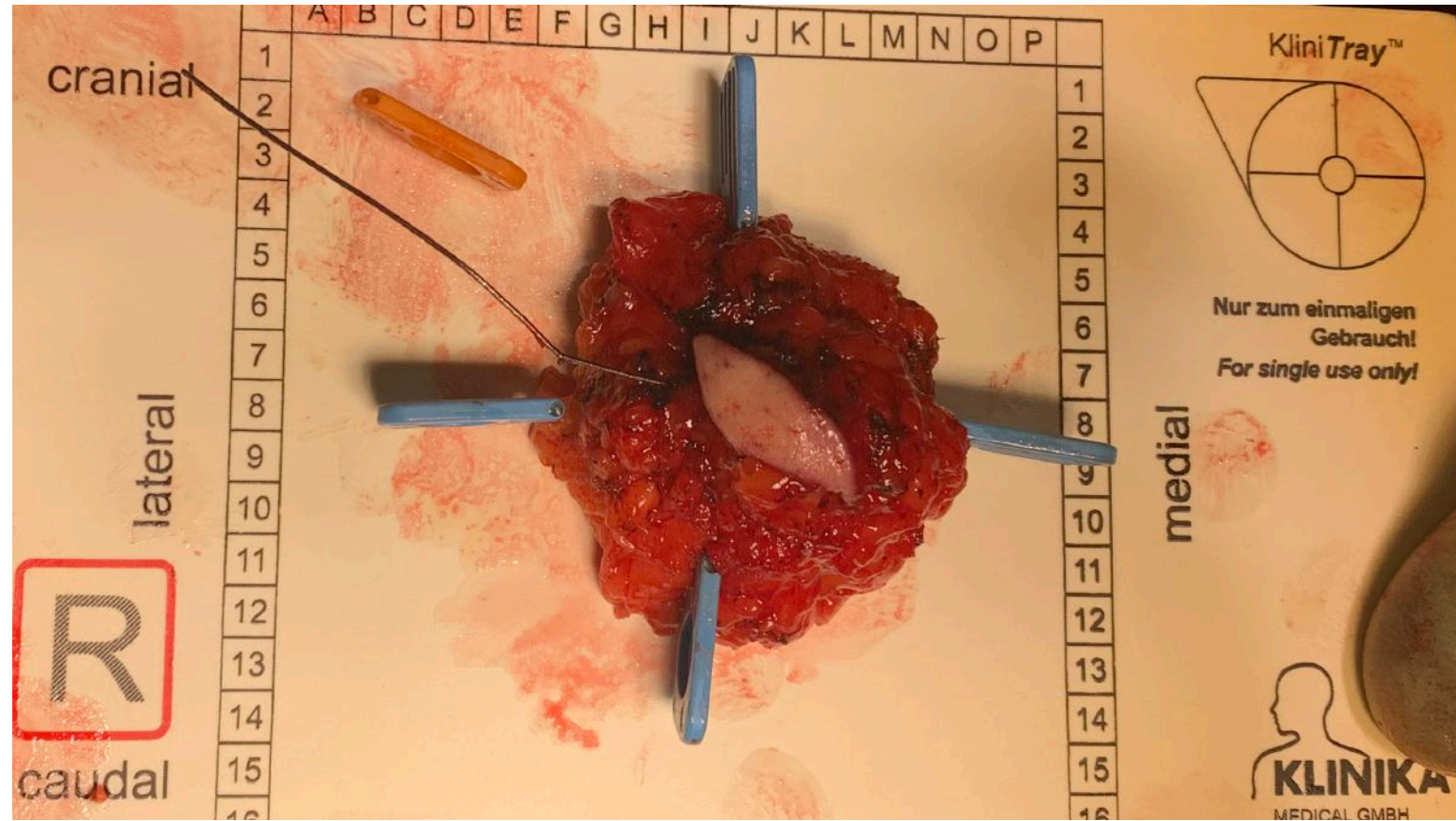
44.4
Multicentricity and its Influence on Conservative Breast Cancer Treatment Strategy.
Vaidya J S, Vyas J J, Mitra I, Chinoy R F Tata Memorial Hospital, Bombay, India

the basis of a clinical trial to test whether giving RT to only the quadrant of primary tumour makes a difference in the incidence of local recurrence.

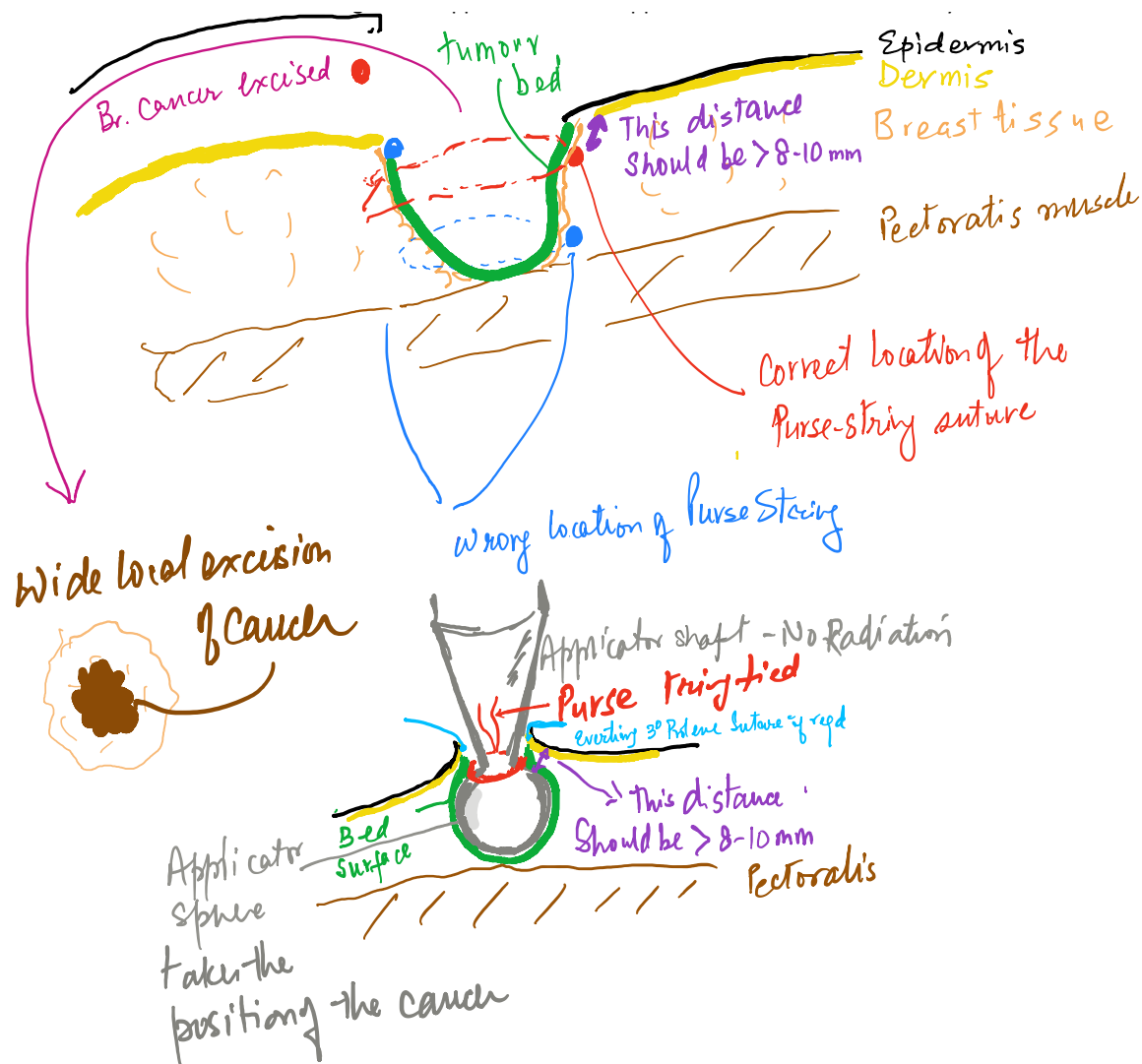
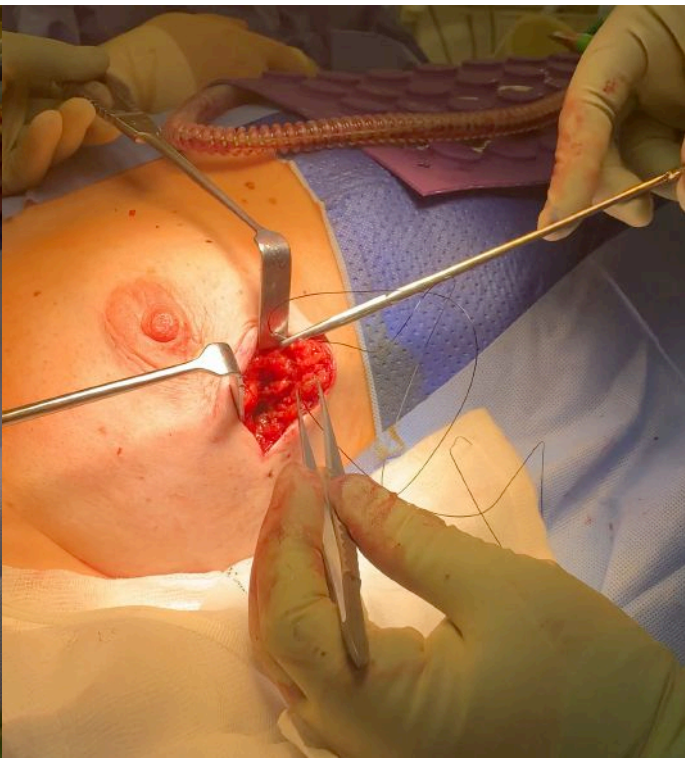
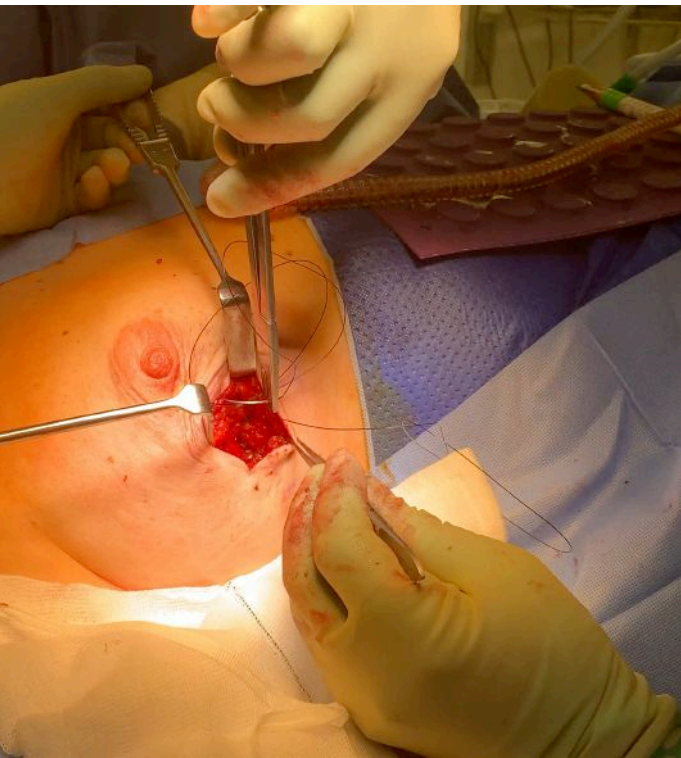
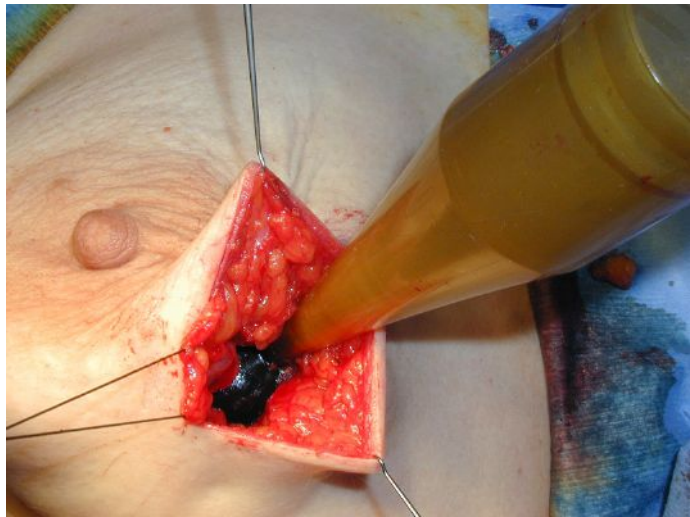
The TARGIT technique

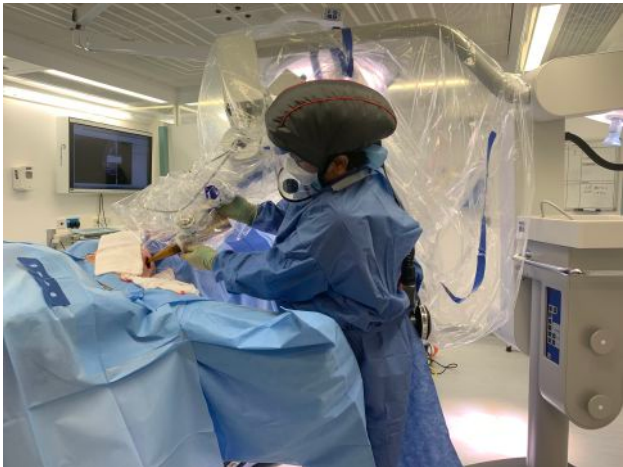


Most breast cancer treatment is completed by the surgeon!!



How to give intraoperative radiotherapy TARGET-IORT



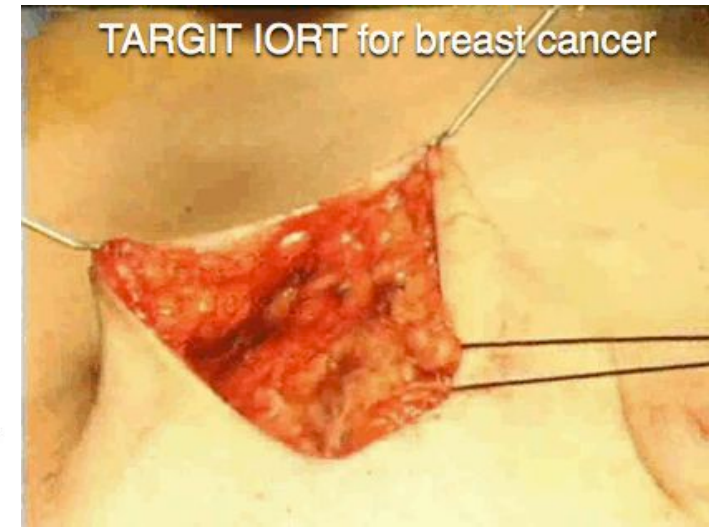
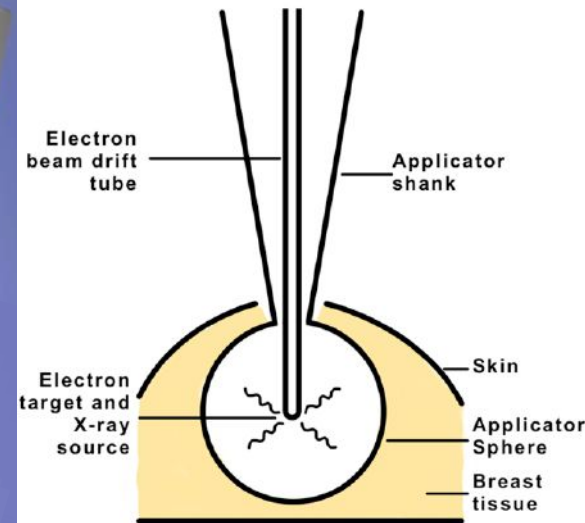
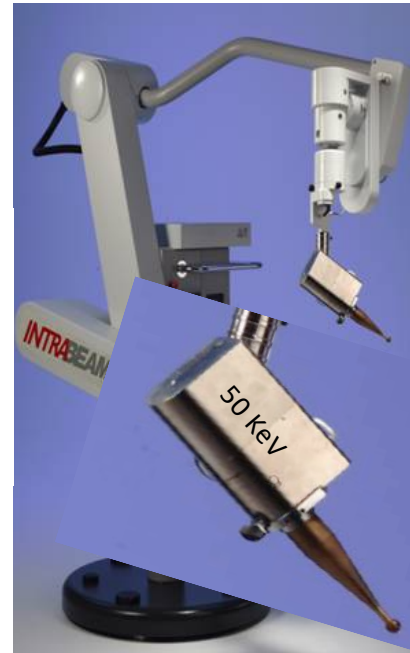


The TARGIT-IORT Technique

Developed in UCL/Middlesex Hospital 1996-98



X-ray source and applicator



Choose the applicator (1.5 to 5cm) according to size of the patient's tumour bed

- Radiotherapy delivered immediately after lumpectomy
- Focused radiation to the tumour bed:
 - Targets tissues at highest risk of relapse
 - Avoids normal structures eg heart and lungs

PRECISION and IMMEDIACY

The surgical technique

EJSO 2002; **28**: 447–454

doi:10.1053/ejs.2002.1275, available online at <http://www.idealibrary.com> on **IDEAL**[®]

EJSO
European Journal of Surgical Oncology

EDUCATIONAL SECTION

The novel technique of delivering targeted intraoperative radiotherapy (Targit) for early breast cancer

**Jayant S. Vaidya, Michael Baum, Jeffrey S. Tobias*,
Steven Morgan† and Derek D'Souza†**

The first 25 patients' results

Annals of Oncology **12**: 1075–1080, 2001.
© 2001 Kluwer Academic Publishers. Printed in the Netherlands.

Original article

Targeted intra-operative radiotherapy (Targit): An innovative method of treatment for early breast cancer

J. S. Vaidya,¹ M. Baum,¹ J. S. Tobias,² D. P. D'Souza,³ S.V. Naidu³ S. Morgan,³ M. Metaxas,³
K. J. Harte,⁴ A. P. Sliski⁴ & E. Thomson⁴

¹Department of Surgery, ²Department of Radiation Oncology, ³Department of Medical Physics, University College London, UK; ⁴Photoelectron Corporation, Lexington, Massachusetts, USA

TARGIT- A randomised trial

Can risk-adapted single-dose TARGIT-IORT during lumpectomy for breast cancer effectively replace the 3-6 weeks' course of daily post-operative whole breast radiotherapy?

Recruitment: March 2000 – July 2012

www.targit.org.uk

TARGET-A trial

Started in
year 2000

2298 Breast cancer patients
due to have a lumpectomy



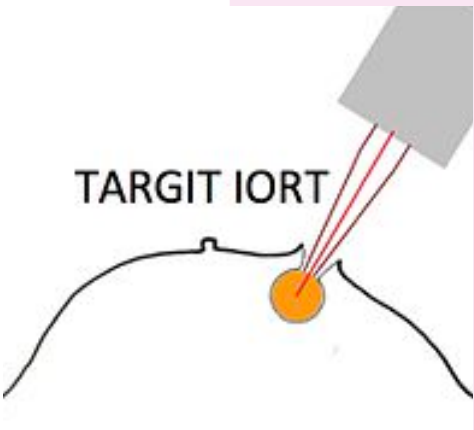
10
countries

Random allocation

TARGET-IORT

Lumpectomy

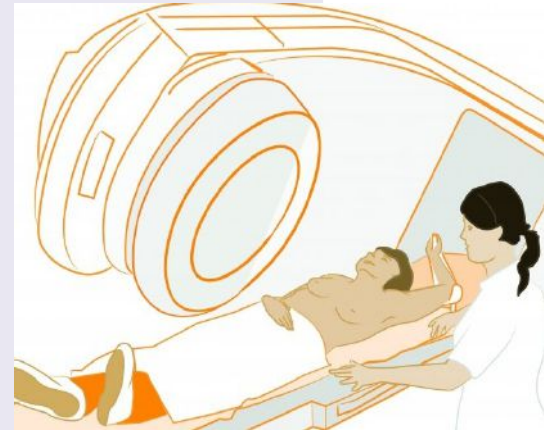
Single-dose TARGET-IORT
under the same
anaesthetic*



EBRT

Lumpectomy

Daily radiation dose
to the whole breast
over 3-6 weeks



*20% will be recommended EBRT
as well

The publication of first results July 2010

Lancet 2010; 376: 91–102

2010

Targeted intraoperative radiotherapy versus whole breast radiotherapy for breast cancer (TARGIT-A trial): an international, prospective, randomised, non-inferiority phase 3 trial

Jayant S Vaidya, David J Joseph, Jeffrey S Tobias, Max Bulsara, Frederik Wenz, Christobel Saunders, Michael Alvarado, Henrik L Flyger, Samuele Massarut, Wolfgang Eiermann, Mohammed Keshtgar, John Dewar, Uta Kraus-Tiefenbacher, Marc Sütterlin, Laura Esserman, Helle M R Holtveg, Mario Roncadin, Steffi Pigorsch, Marinos Metaxas, Mary Falzon, April Matthews, Tammy Corica, Norman R Williams, Michael Baum

THE LANCET

Articles

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



2013

11 Nov 2013

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



Summary

Background The TARGIT-A trial compared risk-adapted radiotherapy using single-dose targeted intraoperative radiotherapy (TARGIT) versus fractionated external beam radiotherapy (EBRT) for breast cancer. We report 5-year

Lancet 2014; 383: 603-13

Published Online

November 11, 2013

Breast cancer has a long natural history

So, long-term outcomes are important

The first patient randomised – 24 Mar 2000
Data lock for long-term outcomes – 3 Jul 2019

Follow up was considered complete only if

- 95% patients had at least 5-year complete follow up

AND

- 90% patients had either 10-year follow up or had been seen within previous year



**Teams from all over the world helped to
bring the completeness of follow-up data
to 95%**

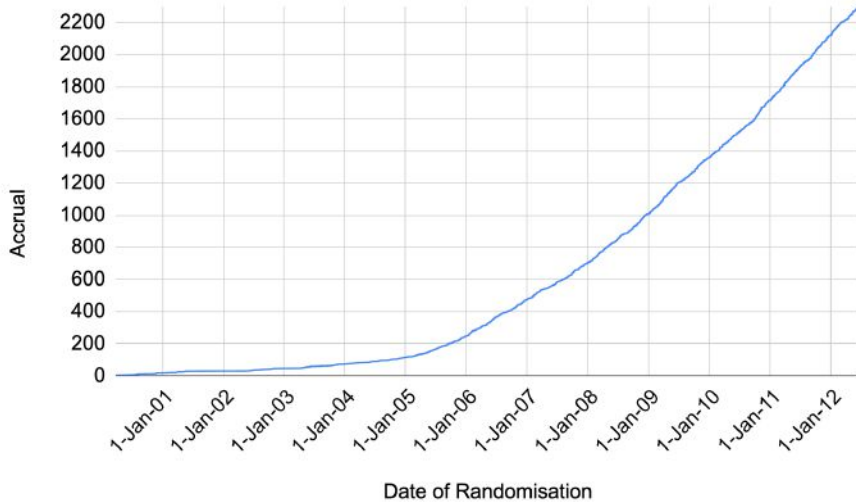


The SITU team at UCL

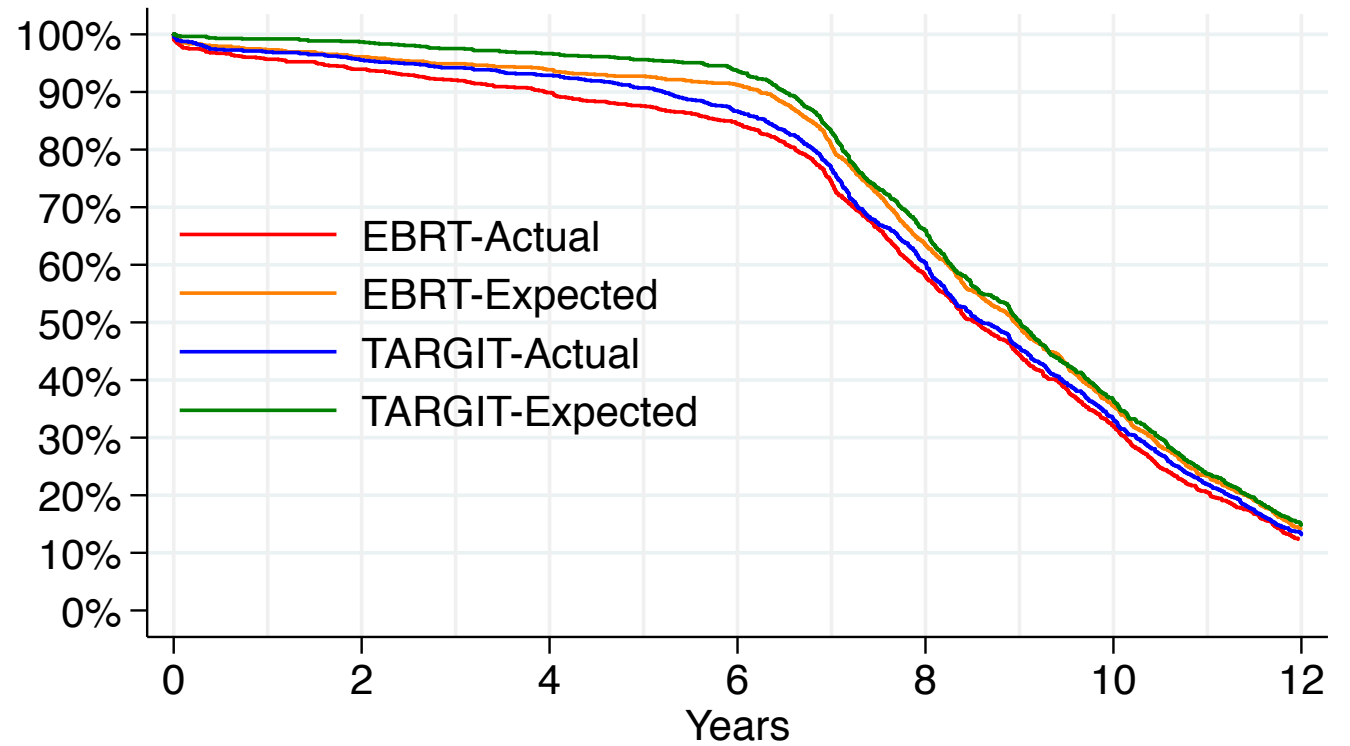


After follow up was complete, the database was unblinded

Trial accrual



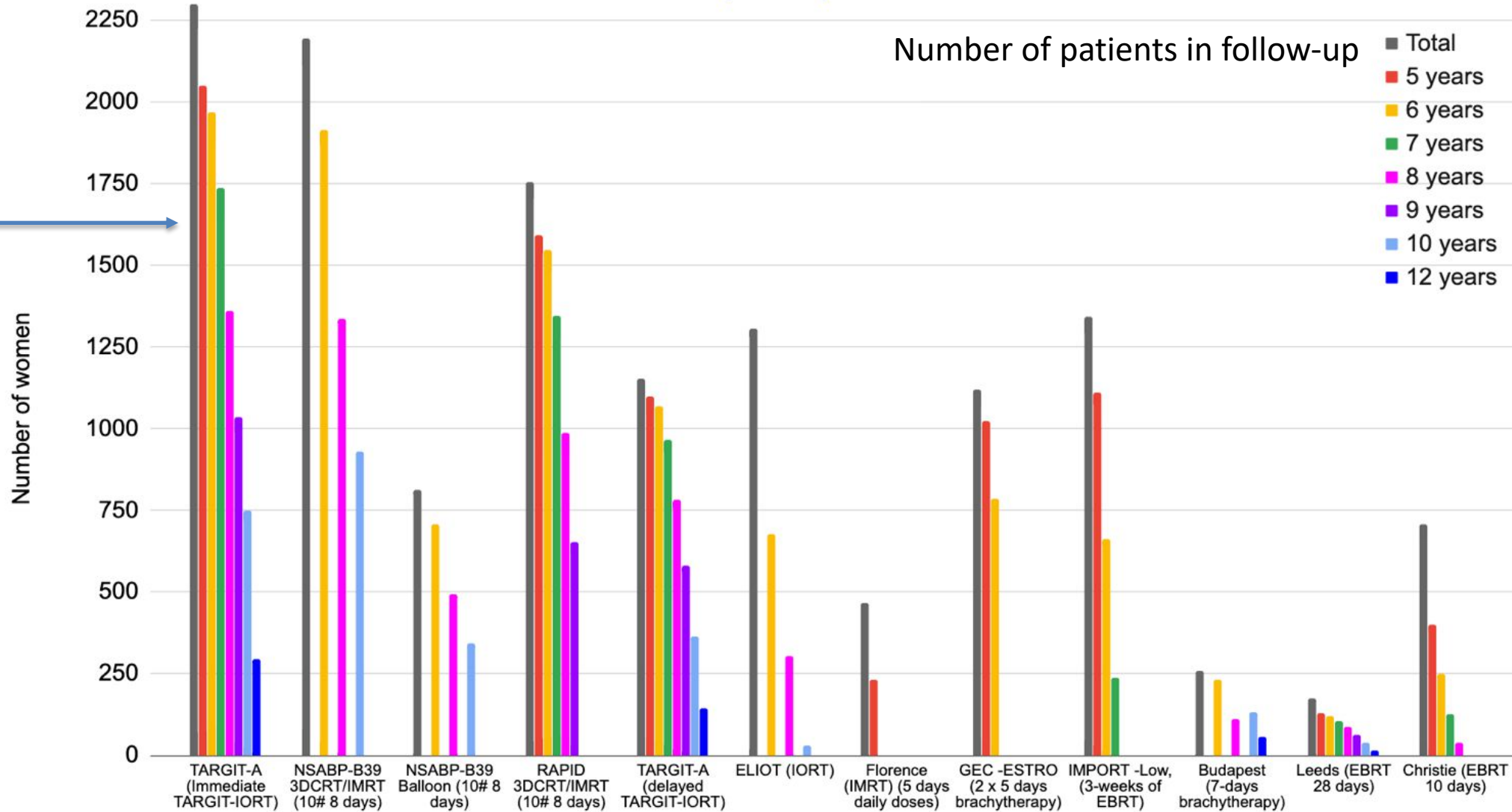
Actual and Expected follow up



	0	2	4	6	8	10	12
Number at risk							
EBRT-Actual	1158	1088	1041	978	672	371	143
EBRT-Expected	1158	1113	1087	1056	735	411	164
TARGIT-Actual	1140	1089	1059	988	688	378	152
TARGIT-Expected	1140	1125	1102	1068	752	415	169

TARGIT-A has the largest amount of follow up data amongst Partial Breast Irradiation (PBI) trials for *invasive* breast cancer

TARGIT-A trial



Breast cancer patients eligible for breast conserving surgery

- ≥ 45 years, with unifocal invasive duct carcinoma
- Tumour size preferably $< 3.5\text{cm}$ (MRI not required)

Randomisation

n=2298

TARGIT

Single dose TARGIT-IORT with Intrabeam during lumpectomy, under the same anaesthetic

Risk-adapted radiotherapy:
EBRT added if high risk factors found later (in ~20%)

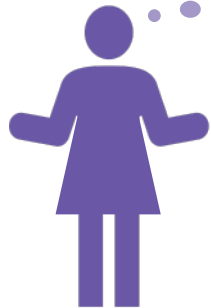
EBRT

Multiple daily doses of radiation over 3-6 weeks

Whole breast external beam radiotherapy for every patient

Advantages of TARGIT-IORT

- ✓ Surgery and radiotherapy completed at the same time
- ✓ Less travel
- ✓ Good cosmetic outcome
- ✓ Less pain
- ✓ Fewer complications
- ✓ Lower toxicity

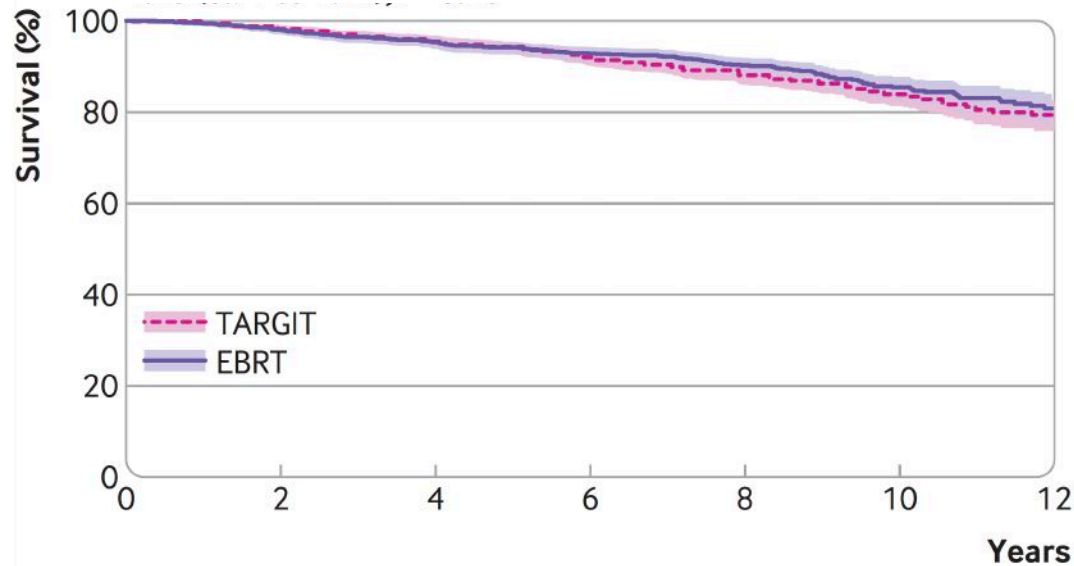


What is my chance of living without the cancer coming back?

Results

Long-term outcomes of the TARGIT-A trial: TARGIT-IORT during lumpectomy vs Whole breast radiotherapy

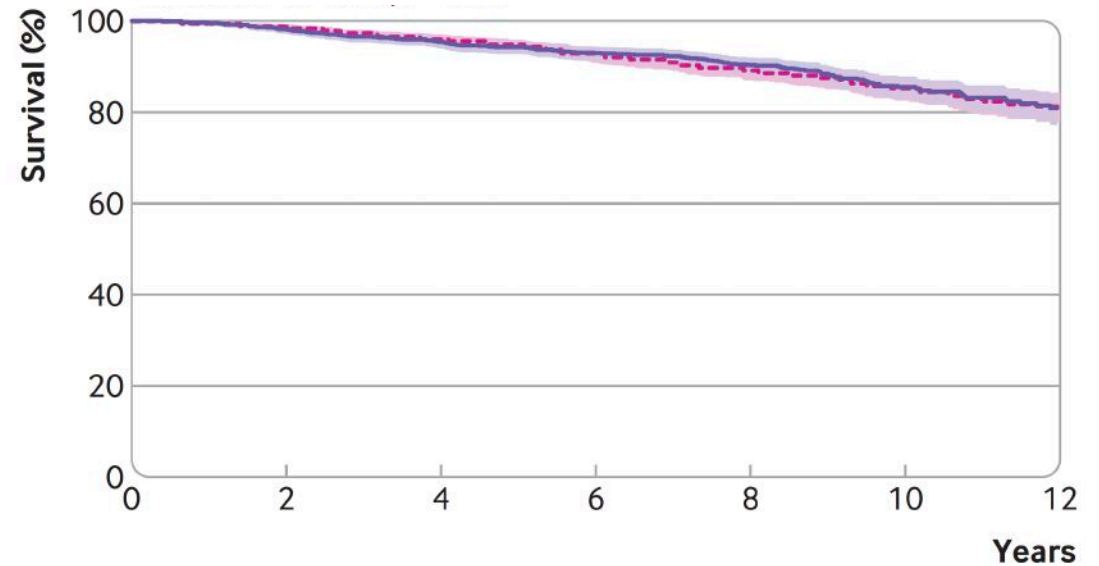
Local recurrence-free survival
HR 1.13 (0.91 to 1.41), P=0.28



No at risk

Years	0	2	4	6	8	10	12
TARGIT	1140	1081	1043	960	662	363	144
EBRT	1158	1086	1034	972	666	366	139

Invasive local recurrence-free survival
HR 1.04 (0.83 to 1.31) P=0.70

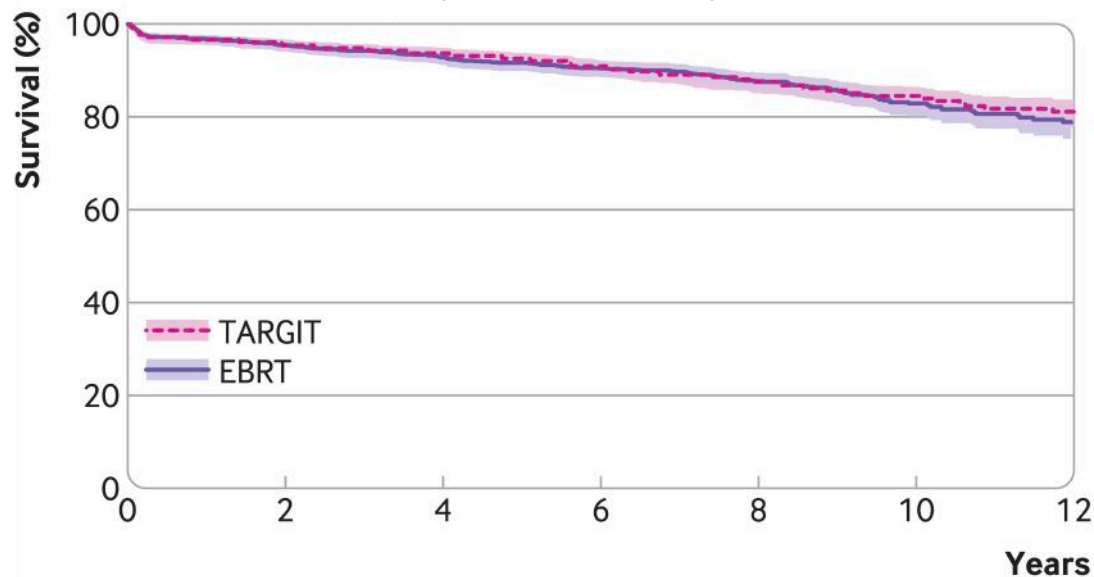


No at risk

Years	0	2	4	6	8	10	12
TARGIT	1140	1084	1047	966	668	365	145
EBRT	1158	1086	1034	972	666	366	139

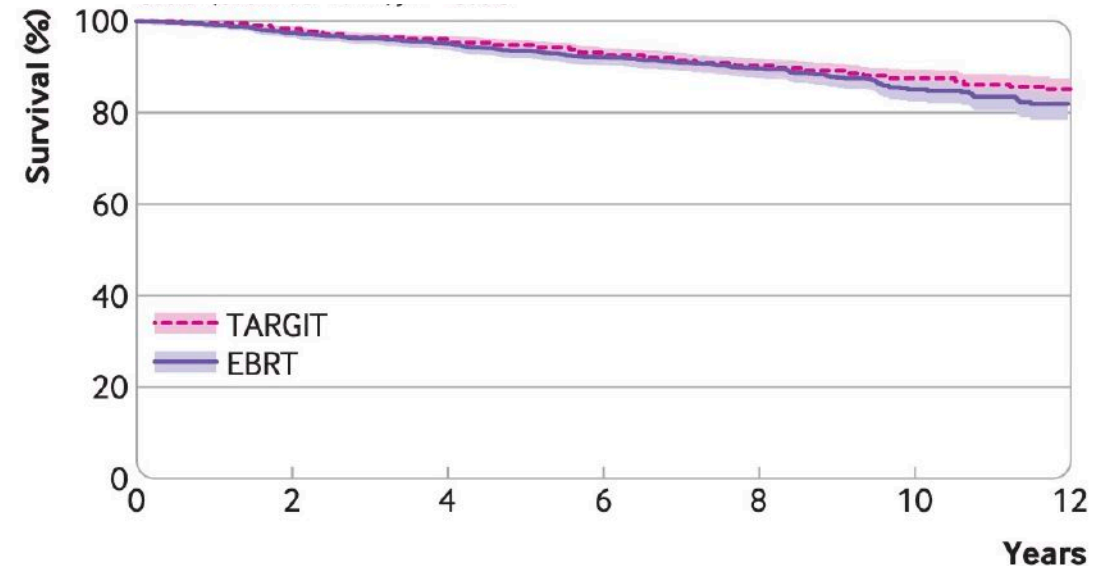
Long-term outcomes of the TARGIT-A trial: TARGIT-IORT during lumpectomy vs Whole breast radiotherapy

Mastectomy-free survival
HR 0.96 (0.78 to 1.19), P=0.74



No at risk								
TARGIT		0	2	4	6	8	10	12
TARGIT		1140	1049	1020	948	650	362	144
EBRT		1158	1058	1009	949	645	356	139

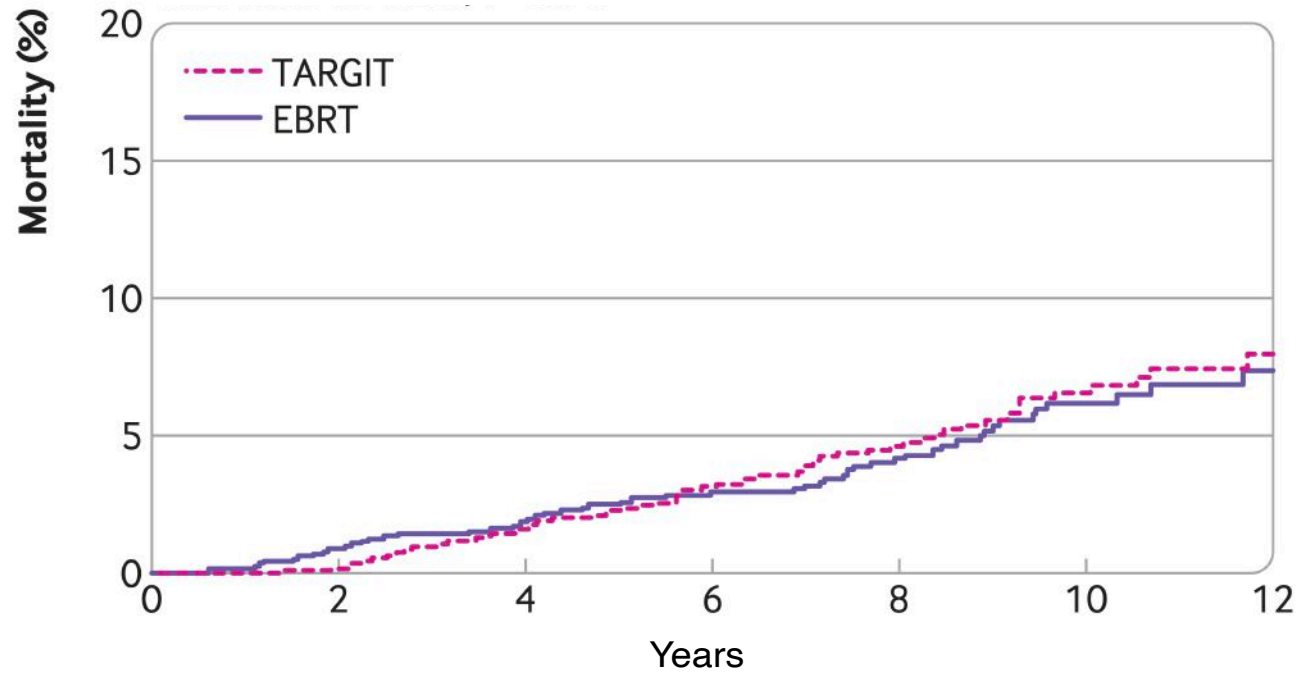
Distant disease-free survival
HR 0.88 (0.69 to 1.12) P=0.30



No at risk								
TARGIT		0	2	4	6	8	10	12
TARGIT		1140	1077	1042	969	674	369	148
EBRT		1158	1079	1031	964	658	361	139

Long-term outcomes of the TARGIT-A trial: TARGIT-IORT during lumpectomy vs Whole breast radiotherapy

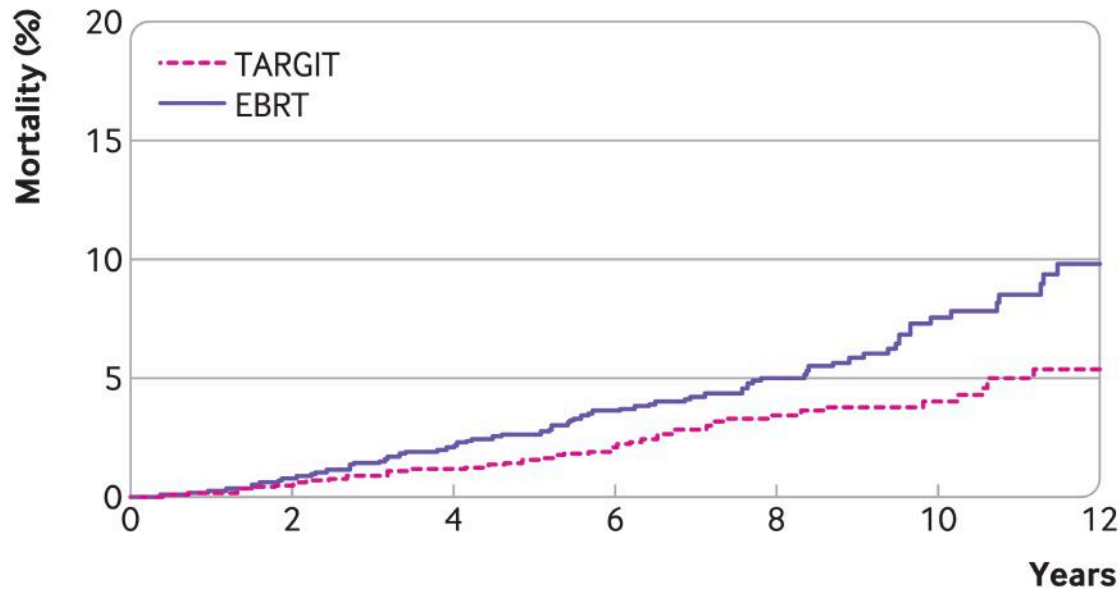
Breast cancer mortality
HR 1.12 (0.78 to 1.60), P=0.54



Number at risk							
TARGIT	1140	1089	1059	989	689	378	152
EBRT	1158	1088	1041	978	672	371	143

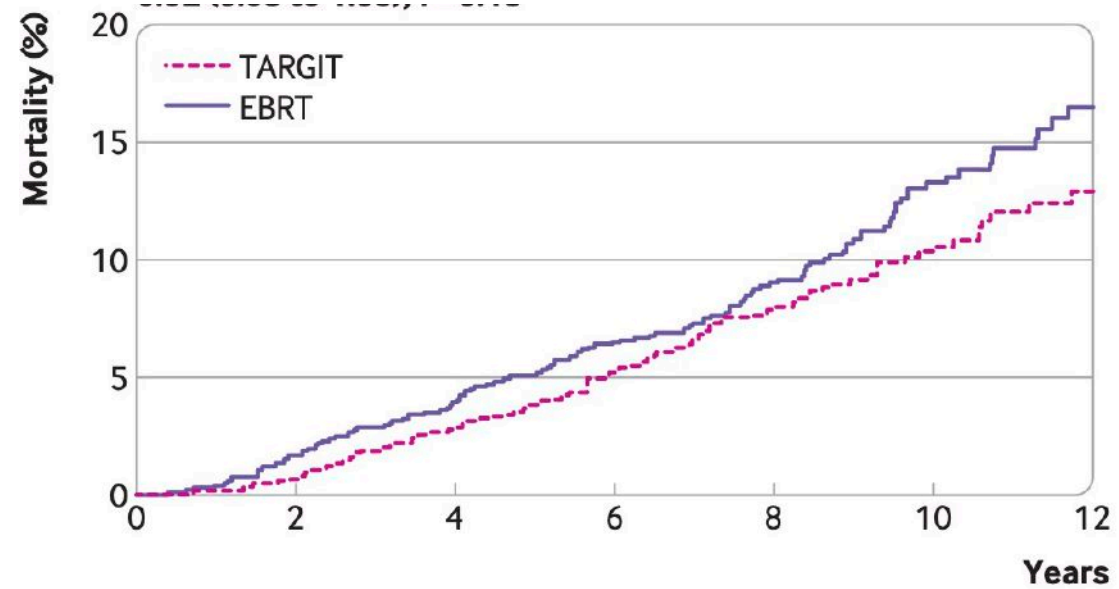
Long-term outcomes of the TARGIT-A trial: TARGIT-IORT during lumpectomy vs Whole breast radiotherapy

Non-breast-cancer mortality
HR 0.59 (0.40 to 0.86), P=0.005



No at risk								
TARGIT		1140	1089	1059	989	689	378	152
EBRT		1158	1088	1041	978	672	371	143

Overall mortality
HR 0.82 (0.63 to 1.05), P=0.13

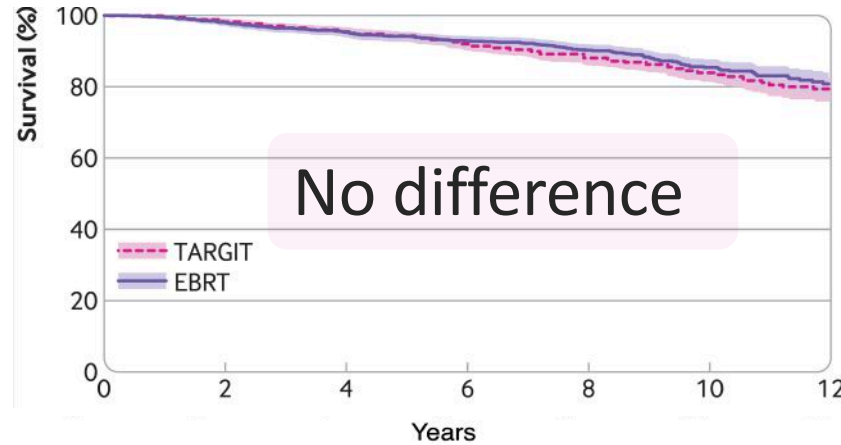


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Results

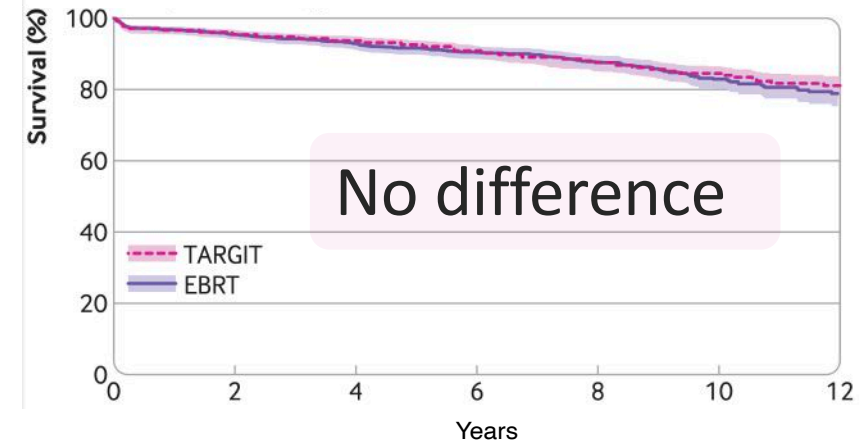
Long-term outcomes of the TARGIT-A trial

Local recurrence-free survival
HR 1.13 (0.91 to 1.41), P=0.28



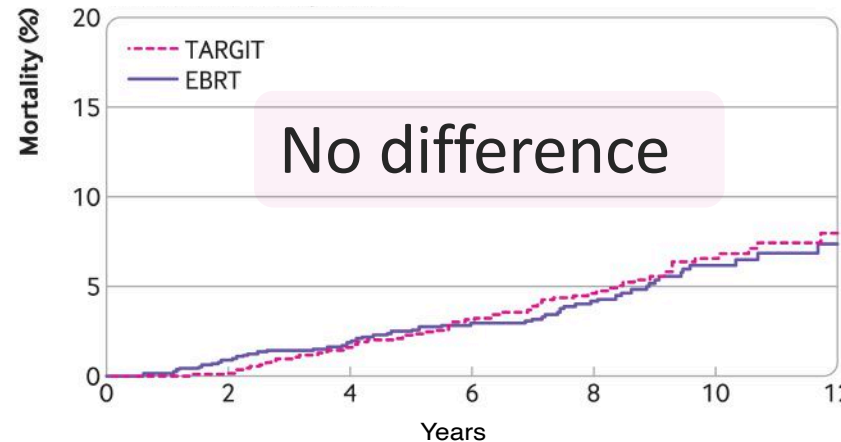
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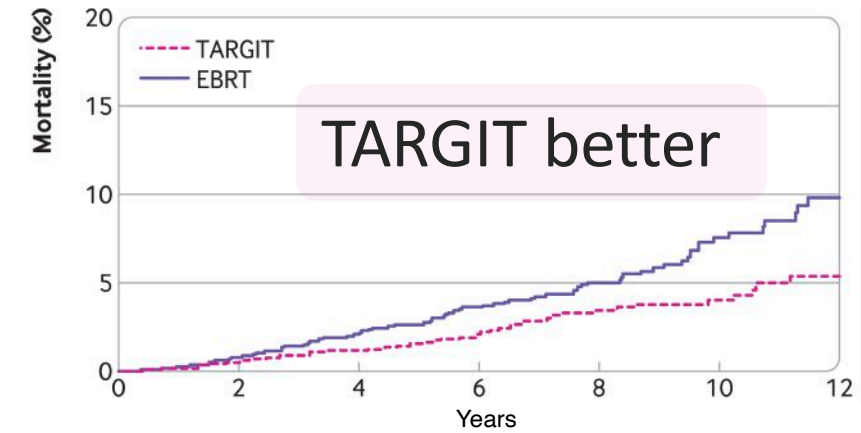
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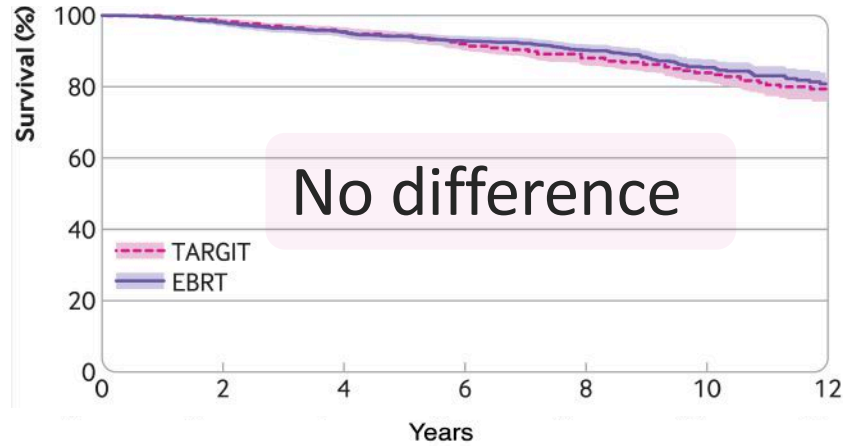
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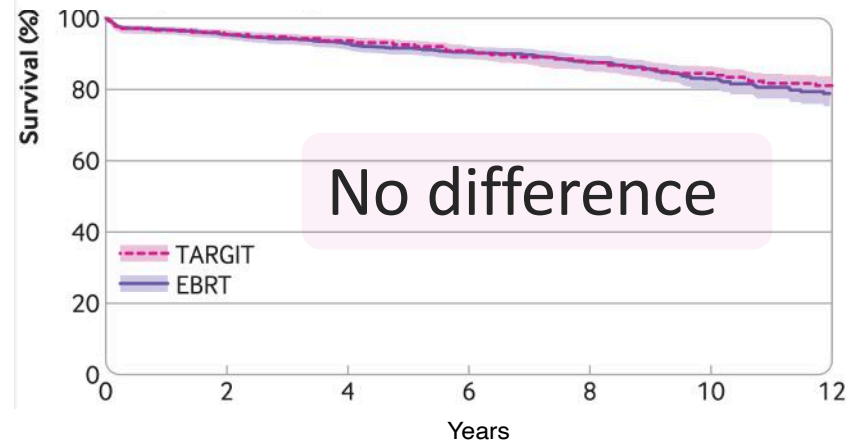
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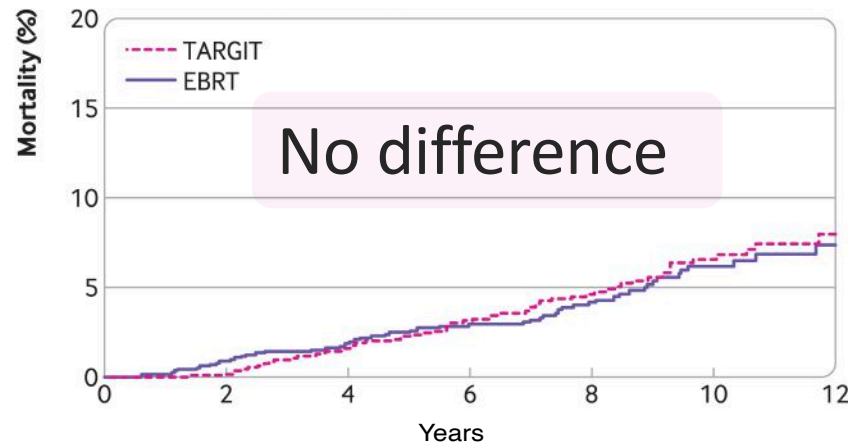
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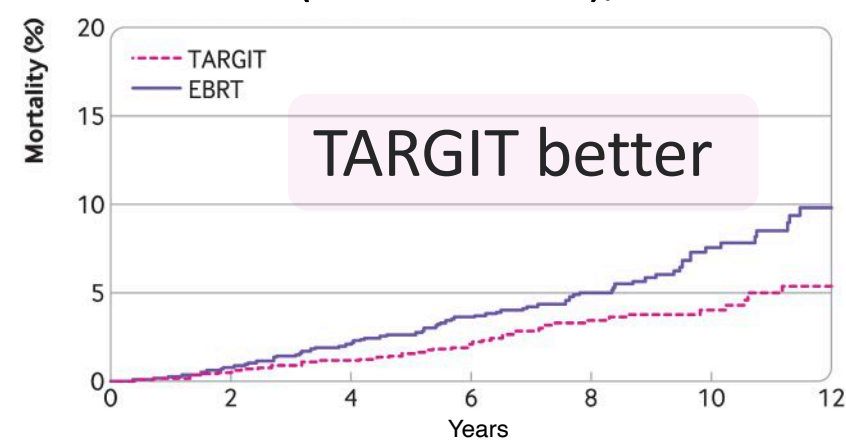
**Long-term
results of the
TARGIT-A trial**

Breast cancer mortality
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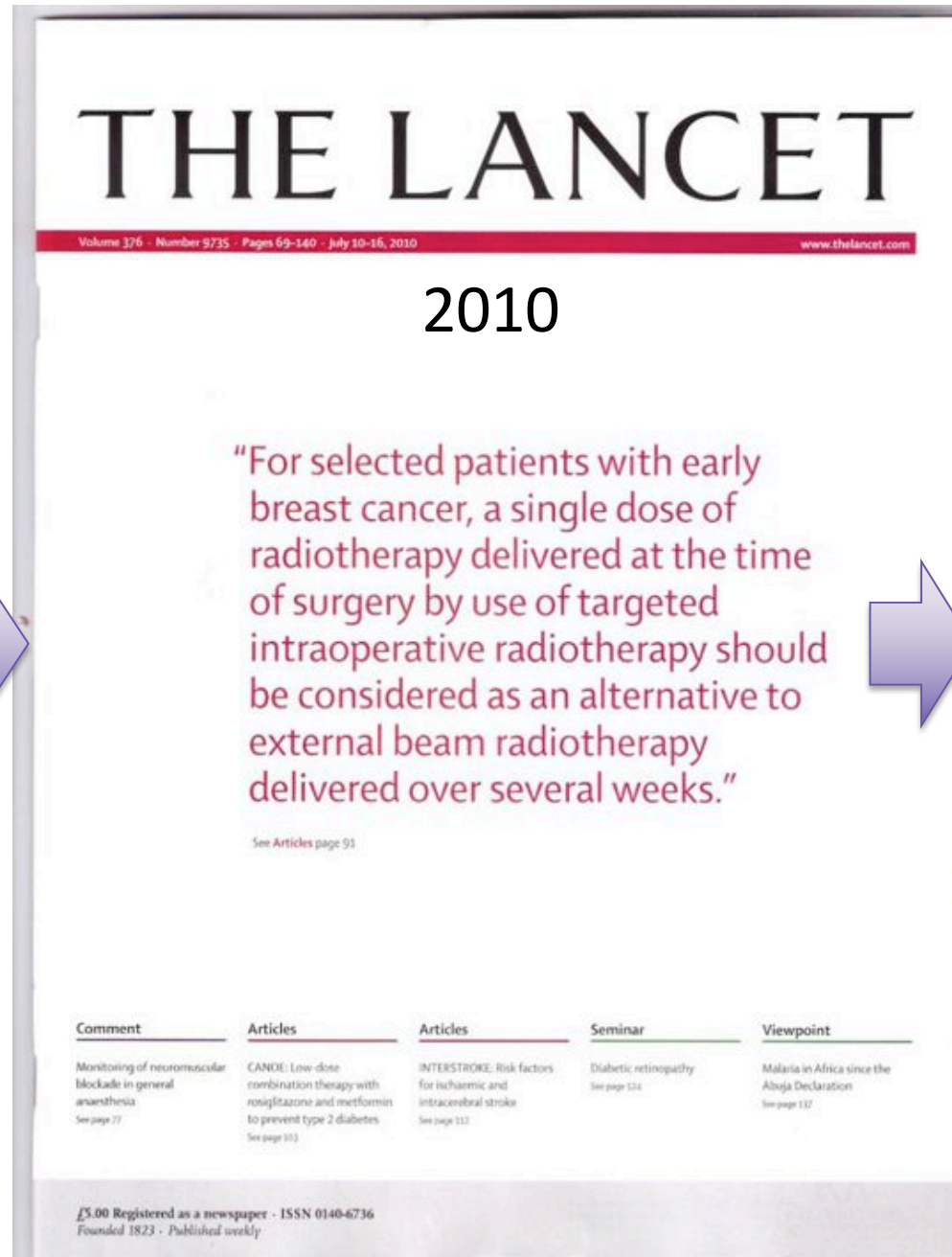
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9.85%
5.41%
**A difference of
4.4% at 12 years**

2000
1st patient
randomised



2020

TARGET-A long-term results:
median follow-up 9 years (IQR 7-11)

- Breast cancer control comparable to EBRT
- Reduced non-breast-cancer mortality compared with EBRT



Bend it like a banker

From Goldman Sachs to the yoga mat

INSIDE TIMES?



Deborah Ross

If dogs could write the law

New treatment heralds breakthrough for breast cancer patients

Kat Lay Health Correspondent

A single dose of radiotherapy delivered from inside the body in only 30 minutes is as effective for breast cancer as weeks of the treatment, according to a long-term study.

Doctors at University College London have developed a technique in which the therapy is given immediately

after a tumour is removed, while the patient is still under anaesthetic.

A small ball-shaped "Intrabeam" device is placed inside the breast where the cancer had been. Once the radiotherapy dose has been delivered, the ball is removed and the surgical wound closed up. It allows women to avoid multiple hospital visits over weeks for traditional radiotherapy. The new

study, published in the *BMJ*, concluded that there was no significant difference between the two methods in either survival chances or the cancer returning.

The treatment, called Targeted Intraoperative Radiotherapy (Targit Iort), was given cautious NHS approval in 2018 for centres that already had the equipment and trained staff, pending further results. However, many clini-

cians have been waiting for longer follow-up data on patients.

Jayant Vaidya, the lead author, said that the new results should prompt wider use, adding: "In these terrible times it is one good news story. There is less pain, a better cosmetic outcome and better quality of life.

"With Targit Iort, women can have their surgery and radiation treatment

for breast cancer all at the same time. This reduces the amount of time spent in hospital and enables women to recover more quickly, meaning they can get back to their lives more quickly.

"With publication of these very positive long-term results, it is now clear that this treatment should be made much more freely available. It

Continued on page 2, col 3

Williamson was warned about risk of exam fiasco

Education secretary informed six weeks ago

Steven Swinford Deputy Political Editor

Gavin Williamson was warned directly that the A-level and GCSE grading system could lead to hundreds of thousands of students being given the wrong results but decided to push ahead, *The Times* can reveal.

A senior source at the Department for Education disclosed that Sir Jon Coles, a former director-general there, wrote to Mr Williamson early last month to express concerns about the algorithm used by Ofqual.

He said that, at best, the model being applied to A-level and GCSE grading would be only 75 per cent accurate, meaning that hundreds of thousands of students would get the wrong grades. In the event Ofqual's own tests on its algorithm, which were published last week, found that it was 60 per cent accurate.

In his letter, Sir Jon also raised particular concerns about using teachers' predicted grades for small groups of pupils but leaving larger groups reliant on the algorithm. He said that this would lead to unfairness in the system.

The issue proved one of the central problems as it meant that private schools, which typically can afford to have smaller classes, saw their results improve significantly more than state schools.

The *Times* understands that Mr Williamson held a video conference with Mr Coles in mid-July to discuss his concerns. He decided to push ahead with the algorithm amid worries about

grade inflation and the risk that results could be significantly delayed. Sir Jon, who helped to found Ofqual when he served at the Department for Education, did not respond to requests for comment.

A government source said that the education secretary had raised the concerns expressed by Sir Jon directly with Ofqual within days of the meeting and had been given reassurances.

The revelation that detailed concerns were put to Mr Williamson last month appears at odds with his claim that the full scale of the problem with the grading system became clear only at the weekend.

On Friday he told *The Times* that there would be "no U-turn" and that abandoning the algorithm in favour of teachers' predictions would risk "rampant grade inflation". On Monday he abandoned the algorithm in favour of teachers' predictions and apologised to pupils, parents and schools.

"Over the weekend it became clearer to me the number of students who were getting grades that frankly they shouldn't have been getting," he said.

The education select committee also raised concerns about the grading system on July 11 in a report warning that some pupils risked being "systematically disadvantaged by calculated grades".

Mr Williamson repeatedly refused earlier this week to express confidence in Sally Collier, the head of Ofqual. He bowed to pressure from his officials

Continued on page 2, col 3



Jill and Joe Biden

United state Jill and Joe Biden at the Democrat convention. The candidate's second wife said that he would reconcile the country as he had rebuilt his family. Page 30

Teen migrant drowns as he paddles across the Channel

Richard Ford Home Correspondent
Charles Bremner Paris

A 16-year-old Sudanese migrant who could not swim drowned in the Channel after trying to reach Britain in a tiny makeshift boat using shovels as oars.

The body of the teenager washed up on a French beach yesterday as about 150 migrants arrived in Dover after making the crossing aboard rigid hulled inflatable dinghies.

A beach walker found the body after dawn at Sangatte, near the mouth of the Channel tunnel. The coastguard and police had been searching during the night after the rescue of the boy's friend, also 16. The survivor, who was found suffering hypothermia at sea, said that the pair had attempted to reach England but their small craft had foundered in the waves and his friend did not know how to swim.

The dead youth was identified by his friend and from his passport, which was on his body. His death was the first known to have occurred this year among the more than 4,800 migrants who have made the crossing on small craft. Last year four bodies of migrants were found in the Channel and one was washed up on a French beach.

About 150 migrants arrived in Kent yesterday while the French authorities rescued 41 who had run into difficulties after setting sail from France.

Priti Patel, the home secretary, who has promised to make the cross-Channel route "unviable", said that the death of the teenager was an upsetting and tragic loss of a young life. She added: "This horrendous incident serves as a brutal reminder of the abhorrent criminal gangs and people-smugglers who exploit vulnerable people."

Marlene Schiappa, the French citizenship minister, also said that the death highlighted the need to tackle people-smugglers. She tweeted her "immense sadness" at the boy's death.

British and French officials will meet in Paris today to discuss how to tackle cross-Channel migration.

France attacks 'inhumane' Britain, page 5

Some important points!

Reduced mortality with TARGIT-IORT is plausible



Int. J. Radiation Oncology Biol. Phys., Vol. 55, No. 4, pp. 914–920, 2003
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0360-3016/03/\$—see front matter

doi:10.1016/S0630-3016(02)04156-1

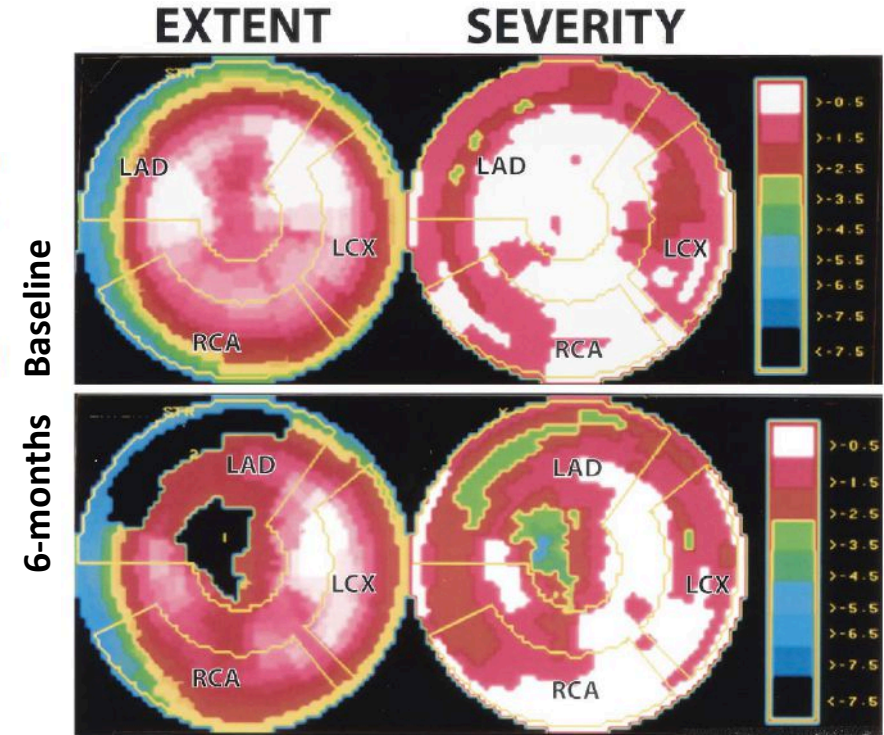
The Red Journal, 2003

CLINICAL INVESTIGATION

Breast

MYOCARDIAL PERFUSION CHANGES IN PATIENTS IRRADIATED FOR LEFT-SIDED BREAST CANCER AND CORRELATION WITH CORONARY ARTERY DISTRIBUTION

PEHR A. LIND, M.D., PH.D.,*† ROBERT PAGNANELLI,‡ LAWRENCE B. MARKS, M.D.,*
SALVADOR BORGES-NETO, M.D., PH.D.,‡ CAROLINE HU,* SU-MIN ZHOU, PH.D.,* KIM LIGHT,* AND
PATRICIA H. HARDENBERGH, M.D.*



EBRT is shown to cause cardiac perfusion defects within 6 months

Reduced mortality with TARGIT-IORT compared with WBI is consistent with other PBI trials

Vaidya JS, Bulsara M, Wenz F, et al. Targeted radiotherapy for early breast cancer. *Lancet* 2018; **391**: 26–27.

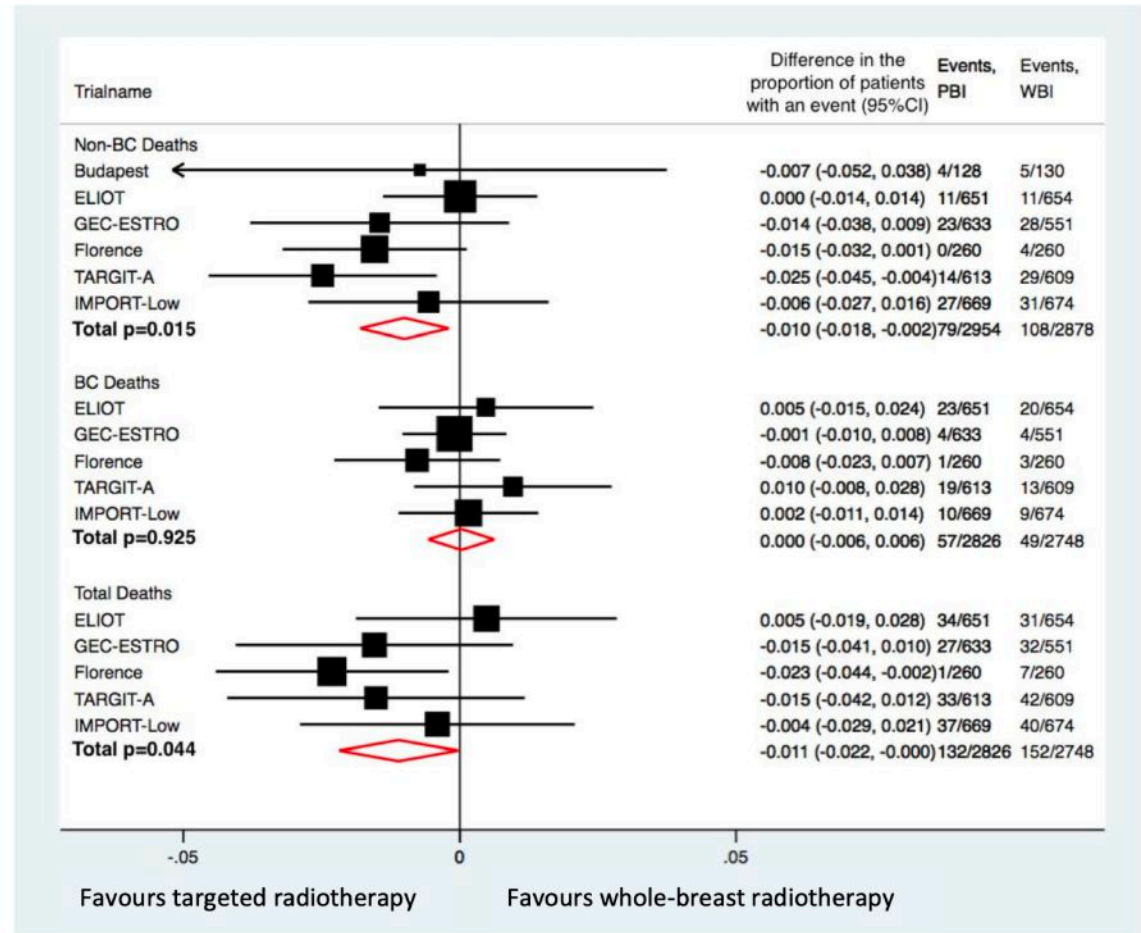


Figure 1: Meta-analysis of mortality in six randomised trials of targeted radiotherapy

Forest plots representing meta-analysis of nearly 6000 patients in randomised trials of PBI showing the difference in mortality between PBI and WBI.

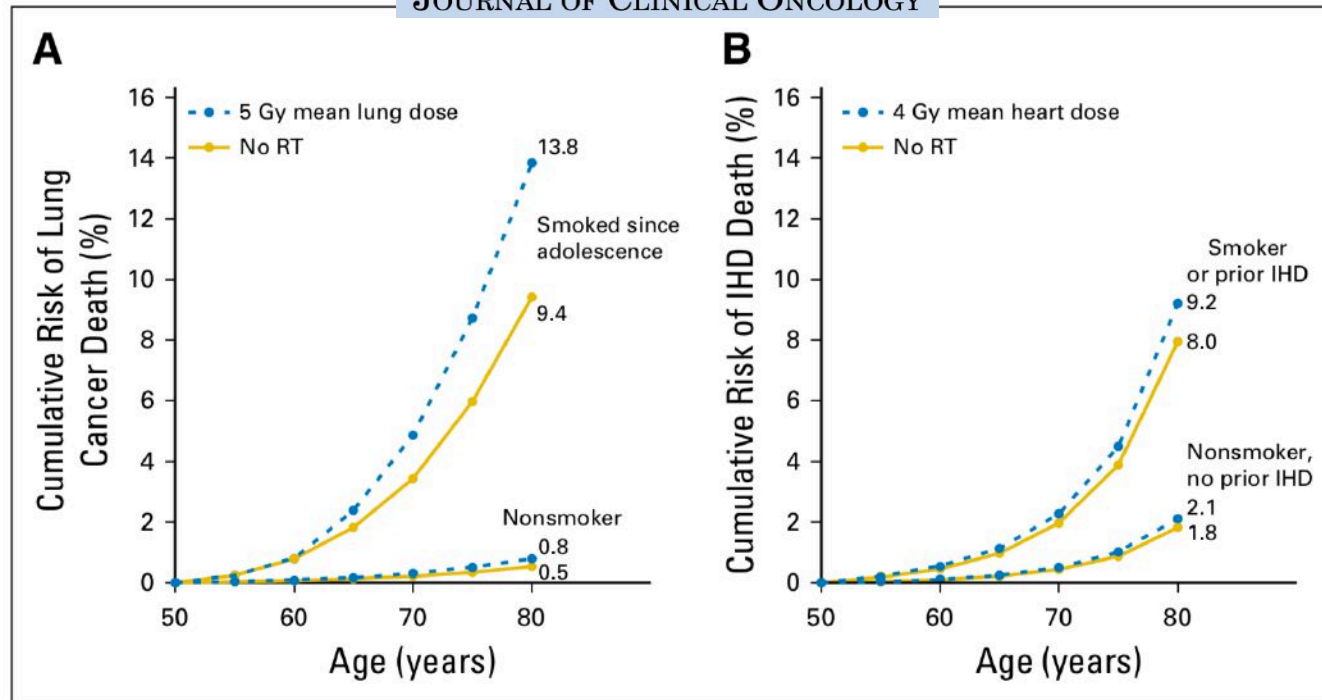
In smokers, the increased mortality with EBRT is very high

Estimating the Risks of Breast Cancer Radiotherapy: Evidence From **Modern Radiation Doses** to the Lungs and Heart and From Previous Randomized Trials

Carolyn Taylor, Candace Correa, Frances K. Duane, Marianne C. Aznar, Stewart J. Anderson, Jonas Bergh, David Dodwell, Marianne Ewertz, Richard Gray, Reshma Jagsi, Lori Pierce, Kathleen I. Pritchard, Sandra Swain, Zhe Wang, Yaochen Wang, Tim Whelan, Richard Peto, and Paul McGale, for the Early Breast Cancer Trialists' Collaborative Group

Doi: 10.1200/JCO.2016.72.0722

JOURNAL OF CLINICAL ONCOLOGY



23% smokers who have external beam radiotherapy for breast cancer will die because of heart attacks or lung cancer = **A 6% increase**

Giving TARGIT-IORT to smokers will reduce overall mortality by 6%

It is unethical to not offer TARGIT-IORT to eligible patients who are smokers.

TARGIT-A had a substantial 'high-risk' population

...typical of cohort seen in our breast clinics

- 1958 (**85%**) patients were ≤ 70 years
- 443 (**20%**) patients had grade 3 cancers
- 488 (**22%**) patients had involved nodes
- 426 (**19%**) patients had ER/PgR negative tumours

Not 'low-risk'

**Much higher
risk than trials
of no
radiotherapy**

PRIME-2: No radiation vs WBI

- 1326 patients. Median FU 7.3yrs
- No patients under 65 years
- 2% grade 3
- None node positive
- None ER negative

- Local control much worse than WBI
10-yr Local recurrence
9.8% with no-radiotherapy vs 0.9% with WBI

- Was the reduction in non-BC mortality nullified by an increase in breast cancer mortality in PRIME-II?

TARGET-A: TARGET-IORT during lumpectomy vs WBI

- 2298 patients. Median FU 8.6yrs
- 60% patients under 65
- 20% grade 3
- 20% node positive
- 19% ER or PgR negative

- Local control same as WBI

- BC mortality same as WBI
- Significant reduction of non-breast cancer mortality reduced by 4.4% to 5.41% from 9.85% at 12 years

Fast-Forward

Whole breast irradiation

- Medium-risk patients
(28%Gr3, 19% node positive)
- 7 to 15 extra visits
- BC control comparable to 3-wk EBRT
- Scattered irradiation to vital organs

No reduction in mortality

- **Higher toxicity**
 - 25% patients report having a hardened/firm breast
 - Breast induration 19 times higher by physician assess.
- Long term follow-up not available

TARGET-IORT

Partial breast irradiation

- Medium risk patients
(20%Gr3, 22% node positive)
- No extra visits in 80% (15-20% WBI)
- BC control comparable to 3-wk EBRT
- No scattered irradiation to vital organs

Significantly fewer cardiovascular and other cancer deaths

9.85% reduced to 5.41% at 12 years

- **Lower toxicity**
 - Less travel
 - Better quality of life
 - Less pain
- Median follow up 8.6y (max 19y)

Brachytherapy (eg GEC-ESTRO)

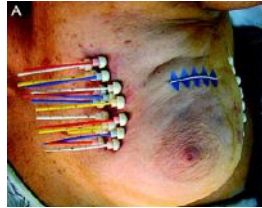
- Low-risk patients only
- N@6 years = 784
- BC outcomes similar (5y)

• Wire entry scarring

• Additional procedure

• Lead lined walls

• 10 fractions / 5d



• Scattered irradiation to vital organs

• **No reduction in mortality**

External beam PBI (eg RAPID, IMPORT low)

- Low-risk patients only
- N@6 years = 1915
- BC outcomes similar (10y)

• Higher toxicity

• Planning visit

• Lead lined bunker

• 10 fractions x 5-8 d

• 15 fractions x 3 wks



• Scattered irradiation to vital organs

• **No reduction in mortality**

TARGIT-IORT during lumpectomy (TARGIT-A) 🍌

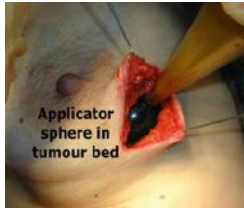
- Medium risk (20% Gr3, 22%Node pos)
- N@6 years = 1967
- BC outcomes similar(12y)

• Lower toxicity, better QOL, less pain

• No extra visits in 80%

• Routine operation theatre/room

• Delivered during initial cancer surgery



• No scattered irradiation to vital organs

• **Significant reduction in non-breast cancer deaths**
9.85% reduced to 5.41% at 12y

TARGIT-Retrospective - S. Valente..... S. Grobmyer

Conclusion: “These data support the idea that IORT with Intrabeam is a rational option for selected patients with early stage breast cancer.”

“Comparing multi center retrospective data to a prospective RTC is scientifically completely invalid, and should never be done except when naysayers are trying to support their own position of bias.”

-Dr Stephen Grobmyer

-senior author of TARGIT-R paper

TARGIT-A: TARGIT-IORT during lumpectomy vs WBI

A 'real world' randomised trial – *the highest level of evidence*

- 95% complete 5-year follow up
- 90% patients seen for 10 years or in the previous year

Patients typical of standard breast clinic

- 66% patients ≤ 65
- 20% grade 3
- 22% node positive
- 19% ER / PgR negative

Excellent outcomes compared to control

- Local control same as WBI
- Distant control same as WBI
- BC mortality same as WBI
- Significant reduction by 4.4% of non-breast cancer mortality (9.85% to 5.41% at 12 years)



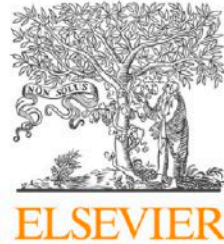
2298 patients in 32 centres from 10 countries participated in the TARGIT-A trial

TARGIT-A: TARGIT-IORT use in the 'real world'



45,000 patients in 260 centres from 38 countries worldwide have been treated with TARGIT-IORT

Real world data

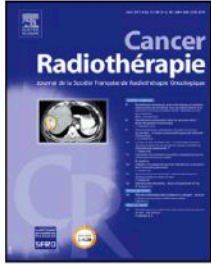


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Original article

Intraoperative partial irradiation for highly selected patients with breast cancer: Results of the INTRA OBS prospective study

Claire Lemanski^a, Celine Bourgier^{a,b}, Roxanna Draghici^a, Simon Thezenas^c,
Aurélie Morel^d, Philippe Rouanet^e, Pierre-Emmanuel Colombo^e, Anne Mourregot^e,
Laure Delmond^e, Pascal Fenoglio^d, Norbert Ailleres^d, David Azria^{a,b,*},
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^d Radiophysics Unit, ICM-Val d'Aurelle, université Montpellier, Montpellier, France

^e Department of Surgical and Reconstructive Oncology, ICM-Val d'Aurelle, université Montpellier, Montpellier, France



200 patients – from single-centre Montpellier, France

5-year **Local recurrence 2.5%**



ORIGINAL ARTICLE

The Breast Journal WILEY

Outcomes with intraoperative radiation therapy for early-stage breast cancer

Elizabeth Obi BS¹ | Martin C. Tom MD¹ | Bindu V. Manyam MD¹  |
Stephen R. Grobmyer MD² | Zahraa Al-Hilli MD² | Stephanie Valente MD² |
Alicia Fanning MD² | Diane M. Radford MD² | Sheen Cherian MD¹ |
Rahul D. Tendulkar MD¹ | Chirag Shah MD¹ 

¹Department of Radiation Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland, Ohio

²Section of Breast Surgery, Department of Surgery, Cleveland Clinic, Cleveland, Ohio

Abstract

Adjuvant radiation therapy has been associated with improved local control following breast-conserving surgery. Traditionally, treatment has been delivered with whole breast irradiation over 3-6 weeks or partial breast irradiation over 1-3 weeks.

201 patients – in single-centre in USA

3-year Local recurrence 1.5%

Real world data



All-inclusive!

Suitable for breast
conservation with
tumour <5cm

No exclusions based on
ER, Grade, Nodes

Targeted Intraoperative Radiotherapy Is Non-inferior to Conventional External Beam Radiotherapy in Chinese Patients With Breast Cancer: A Propensity Score Matching Study

Yin Mi¹, Pengwei Lv², Fang Wang², Lin Li², Mingzhi Zhu², Yanyan Wang²,
Yingying Zhang², Lele Liu¹, Qinchen Cao¹, Meilian Dong¹, Yonggang Shi¹, Ruitai Fan¹,
Jingruo Li², Yuanting Gu² and Xiaoxiao Zuo^{1*}

OPEN ACCESS

Edited by:
Francesco Cellini,
University of Turin, Italy

¹ Department of Radiation Oncology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China, ² Department of Breast Surgery, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China

82 + 199 (control) patients – in single-centre in China

5-year Local recurrence 3.2% in TARGIT-IORT v 3.1% in control

Real world data

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BREAST CANCER—TRIPLE-NEGATIVE/CYTOTOXICS/LOCAL THERAPY

Mid-term results of INTRABEAM intraoperative radiotherapy in St. Petersburg, Russia.



[Alexey Manikhas](#), [Armen Oganesyn](#), [Ivan Grinev](#), [Sergey Chekrizov](#), [Vitaly Skvortsov](#), [Leonid Li](#), [Roman Babeshkin](#), [Georgiy Manikhas](#)

City Clinical Oncological Dispensary, St. Petersburg, Russian Federation; City Clinical Oncology Dispensary, St. Petersburg, Russian Federation; City Clinical Oncology Dispensary, St. Petersburg, Russia; City Clinical Oncology Center, St. Petersburg, Russia

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ARTICLE CITATION

129 patients – from single centre in St Petersburg, Russia

Follow up 3 years

Local recurrence 1.5%

They have now treated over 1200 patients

Real world data

ORAL SCIENTIFIC SESSION | [VOLUME 105, ISSUE 1, SUPPLEMENT , S8, SEPTEMBER 01, 2019](#)



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First per Protocol Analysis of the Prospective Phase II Study of Intraoperative Radiotherapy (IORT) in Elderly Patients with Small Breast Cancer: Targit E(Ilderly)

[E. Sperk](#)

DOI: <https://doi.org/10.1016/j.ijrobp.2019.06.393>



Check for updates

PROSPECTIVE
Real-World study

PlumX Metrics



541 patients – 28 centres in Germany, France, Denmark, Switzerland

5-year Local recurrence 1.5%

5-year Overall survival 91.4%



The actual benefit of intraoperative radiation therapy using 50 kV x-rays in early breast cancer: A retrospective study of 676 patients

Agnès Tallet MD^{1,2}  | Séverine Racadot MD³ | Jean-Marie Boher PhD^{4,5} |
Monique Cohen MD⁶ | Julien Barrou MD^{5,6} | Gilles Houvenaeghel MD, PhD^{2,5,6}  |
Marian Gutowski MD⁷ | Laure Delmond MD⁷ | Claire Lemanski MD⁸

676 patients – from 3 centres in France

Median follow up 54 months

5-year **Local recurrence 1.7%** (11 local recurrences)

5-year Overall survival 96.5%

Review Article

Intraoperative Boost Radiotherapy during Targeted Oncoplastic Breast Surgery: Overview and Single Center Experiences

Wolfram Malter,¹ Verena Kirn,^{1,2} Lisa Richters,^{1,2} Claudius Fridrich,^{1,2} Birgid Markiefka,³ Rudolf Bongartz,⁴ Robert Semrau,⁴ Peter Mallmann,² and Stefan Kraemer¹

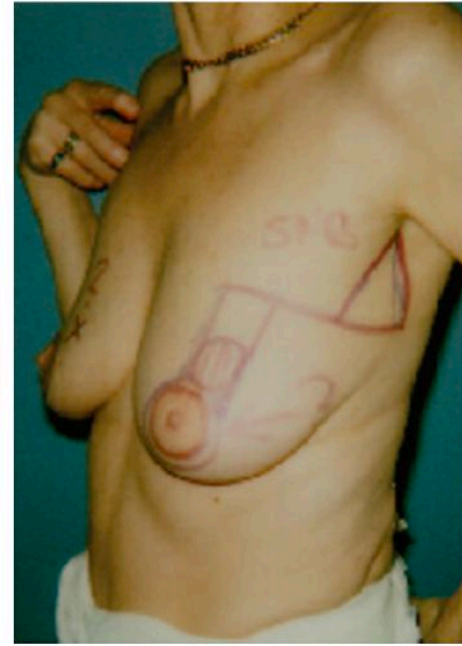
¹*Breast Center, University Hospital of Cologne, Kerpenerstrasse 34, 50931 Cologne, Germany*

²*Department of Obstetrics and Gynaecology, University Hospital of Cologne, Kerpenerstrasse 34, 50931 Cologne, Germany*

³*Department of Pathology, University Hospital of Cologne, Kerpenerstrasse 34, 50931 Cologne, Germany*

⁴*Department of Radiotherapy, University Hospital of Cologne, Kerpenerstrasse 34, 50931 Cologne, Germany*

149 patients – excellent results



TARGIT-IORT during oncoplastic surgery will ensure high precision and immediacy of radiotherapy



FIGURE 1: Combination of IORT boost irradiation with targeted oncoplastic breast-conserving surgery (dermoglandular rotation).

Strahlenther Onkol (2017) 193:62–69

DOI 10.1007/s00066-016-1072-y



CrossMark

ORIGINAL ARTICLE

Targeted intraoperative radiotherapy tumour bed boost during breast-conserving surgery after neoadjuvant chemotherapy

Hans-Christian Kolberg¹  · Gyoergy Loevey² · Leyla Akpolat-Basci¹ · Miltiades Stephanou¹ · Peter A Fasching³ · Michael Untch⁴ · Cornelia Liedtke⁵ · Max Bulsara^{6,7} · Jayant S Vaidya⁷

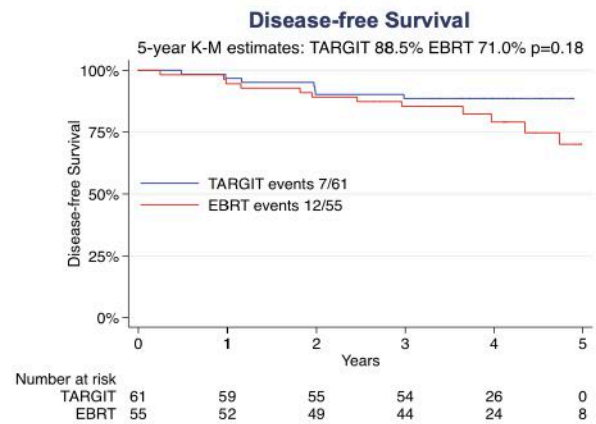
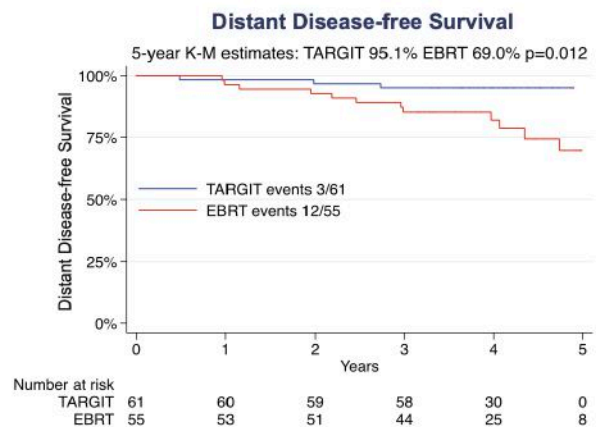
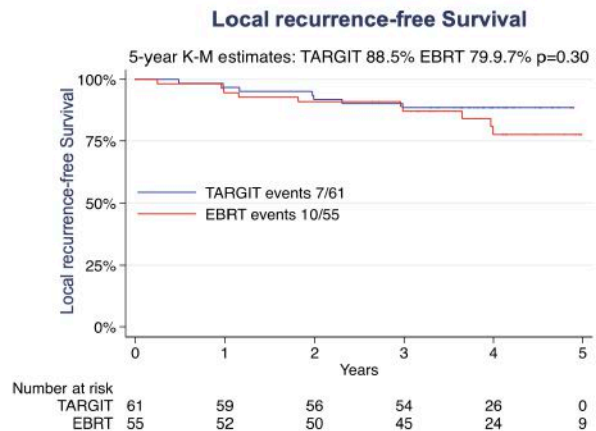


Fig. 1 Local recurrence-free survival, disease-free survival and distant disease-free survival (*TARGIT* targeted intraoperative radiotherapy boost; *EBRT* external beam radiotherapy boost)

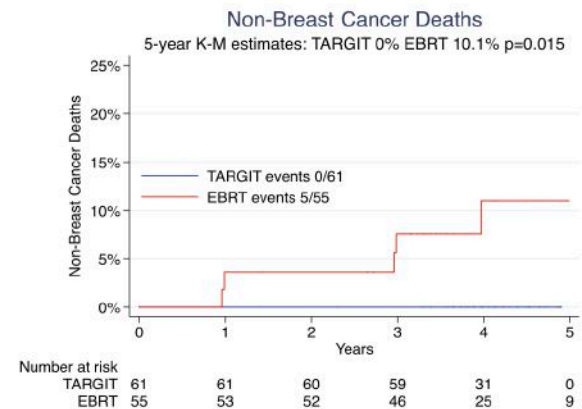
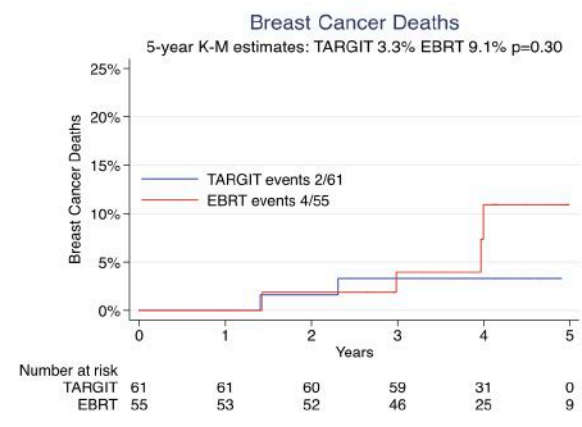
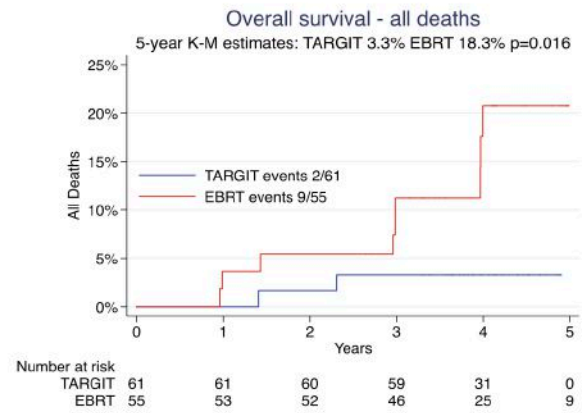


Fig. 2 Overall survival, breast cancer deaths and non-breast cancer deaths (*TARGIT* targeted intraoperative radiotherapy boost, *EBRT* external beam radiotherapy boost)

TARGIT-IORT Boost after neoadjuvant chemotherapy and oncoplastic surgery seems to improve oncological and survival outcomes

TARGIT-B trial for young veryhigh-risk patients currently recruiting in China, S Korea, S Aftrica, Middle-East, Europe, USA

Conclusions

Long-term outcomes of the TARGIT-A Trial

Risk-adapted TARGIT-IORT given during lumpectomy

- achieved comparable long-term cancer control to EBRT
- reduced non-breast-cancer mortality compared with EBRT

TARGIT-IORT has substantial advantages:

- better quality of life, cosmetically superior, less pain
- more convenient for the patient, less travel time
- lower cost to the patient and healthcare system

Eligible patients should be offered TARGIT-IORT as a one-stop treatment option during their lumpectomy for breast cancer

UK NICE recommends TARGIT IORT

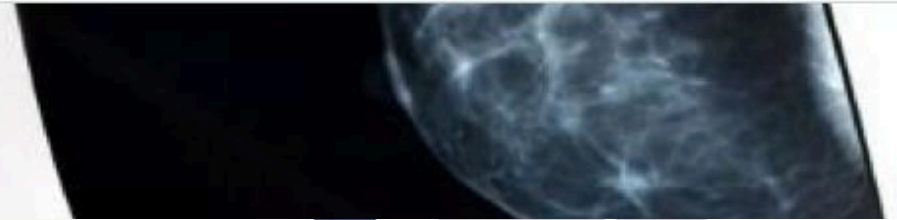
in centres which have the equipment and expertise



NICE @NICEcomms

15/02/2017

We've recommended the Intrabeam Radiotherapy System for people with early breast cancer: nice.org.uk/news/article/n...



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Single-dose radiotherapy eases breast cancer stress



Chris Smyth Health Correspondent
Last updated at 12:01AM, July 25 2014

Trials show women found quicker and I

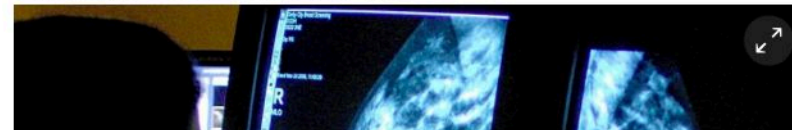
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Breast cancer

Single-dose radiotherapy could transform breast cancer treatment

Intrabeam radiotherapy, which has go-ahead for NHS use, is given during surgery, eliminating need for additional hospital trips



THE INDEPENDENT 25 Feb 2015

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Life > Health & Families > Health News

NHS approves one-shot breast cancer therapy treatment

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Is this spooky apparition the Grey An unspeakable obscenity, a End of the line for cold callers: New How your credit card turned into a

Half-hour breast cancer treatment can replace weeks of radiotherapy: Thousands of women could benefit from treatment given during surgery

- Intrabeam radiotherapy will be given to breast cancer patients in surgery
- Treatment has been given provisional go-ahead for use on NHS by NICE
- Up to 36,000 women with early breast cancer could benefit from technique

By JENNY HOPE FOR THE DAILY MAIL
PUBLISHED: 23.03, 24 July 2014 | UPDATED: 13.53, 25 July 2014

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2016 1st US user meeting



2016 Mannheim user meeting



Dec 2016 Bangkok user meeting



May 2017 1st US TARGIT collaborative group



2018 Mannheim user meeting



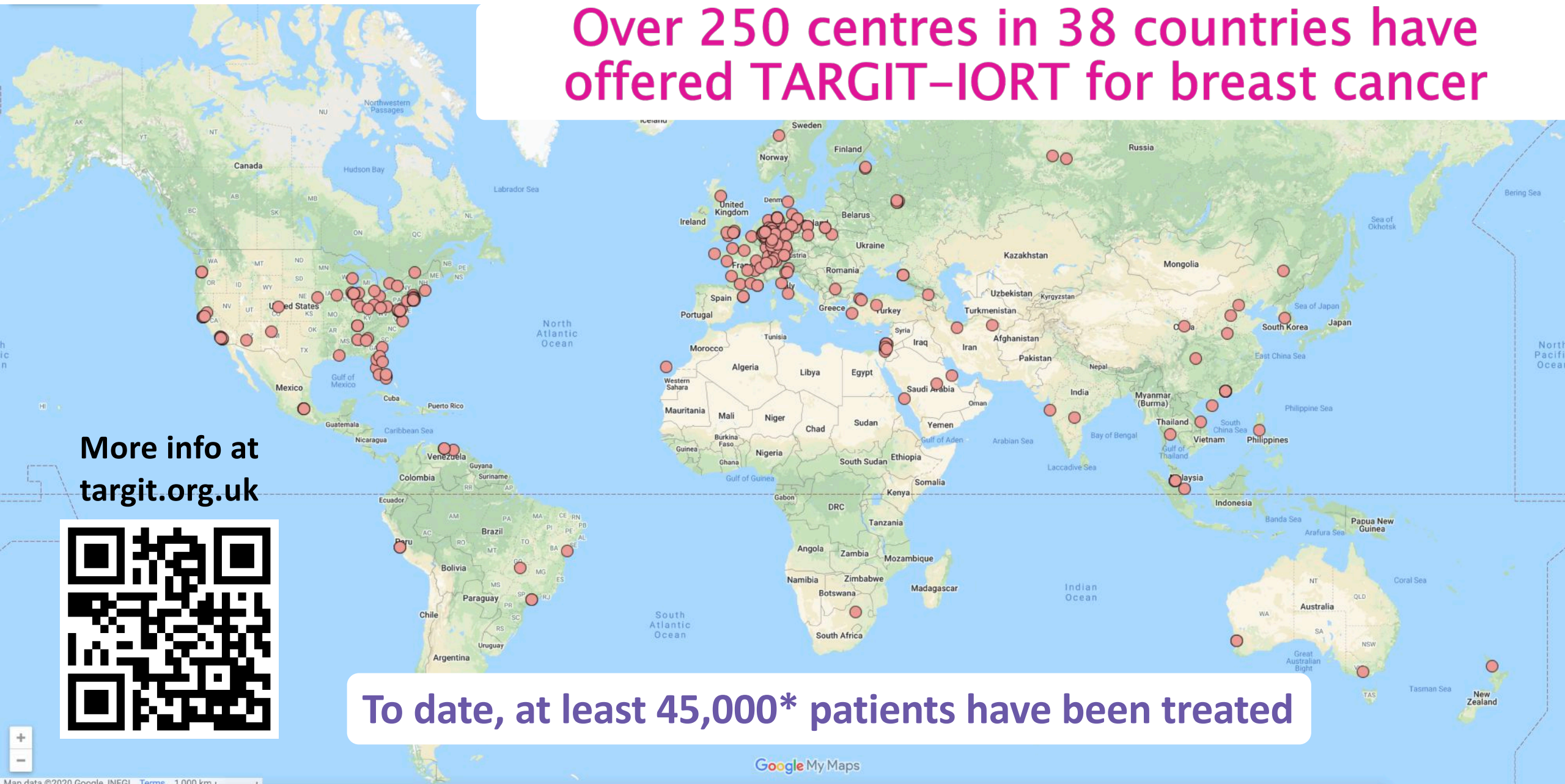
Over 250 centres in 38 countries have offered TARGIT-IORT for breast cancer

More info at
targetit.org.uk



To date, at least 45,000* patients have been treated

*Data from 260 centres (updated late 2019- early 20)





4 Aug

**TARGET-IORT has now been used in
>45,000 women around the world**

**It should be available to every
suitable patient**

**More info at
targetit.org.uk**

THANK YOU

