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CONFERÊNCIA BRASILEIRA
DE CÂNCER DE MAMA 2018

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LATIN AMERICAN
COOPERATIVE
ONCOLOGY GROUP

Radioterapia Acelerada Parcial de Mama Atualizações do Consenso da ASTRO

Rodrigo Hanriot

Radioterapeuta - Hospital Alemão Oswaldo Cruz

“Declaro que não há conflito de interesses relacionados com esta apresentação”

Em acordo com as normas do Conselho Federal de Medicina (número 1595/2000) e de Vigilância Sanitária RDC 102/2000

Dois conceitos diferentes de irradiação parcial de mama:

1. RT em dose única (intraoperatória)
2. RT fracionada

Racional da irradiação parcial de mama

Técnicas de irradiação parcial de mama

RT intraoperatória (IORT – elétrons ou IntraBeam™)

Braquiterapia (LDR ou HDR)

Mammosite™

RT externa hipofracionada

Racional da irradiação parcial de mama

Técnicas de irradiação parcial de mama - DOSE ÚNICA

RT intraoperatória (IORT – elétrons ou IntraBeam™)

Braquiterapia (LDR ou HDR)

Mammosite™

RT externa hipofracionada



Racional da irradiação parcial de mama

Técnicas de irradiação parcial de mama - FRACIONADA

RT intraoperatória (IORT – elétrons ou IntraBeam™)

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RT externa hipofracionada



Racional da irradiação parcial de mama

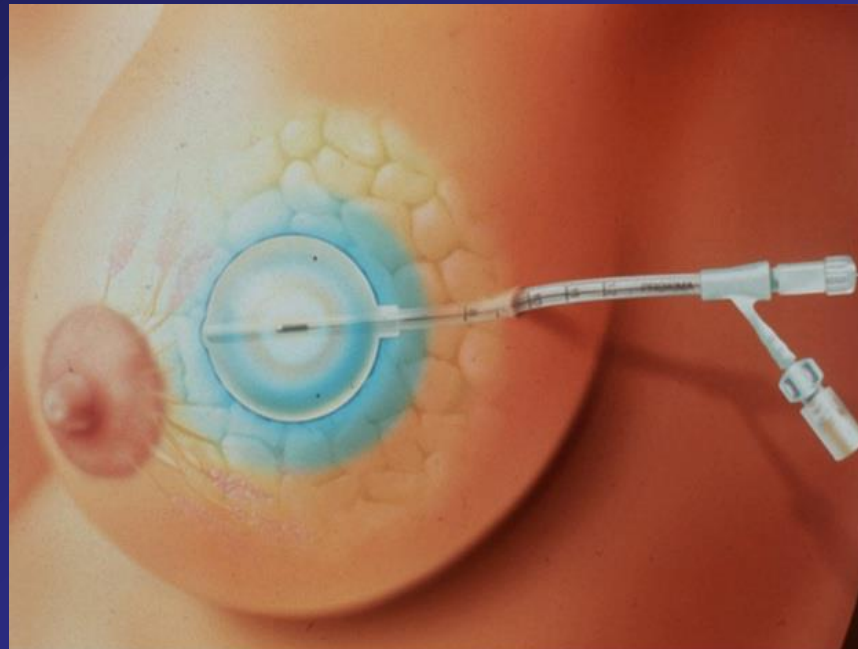
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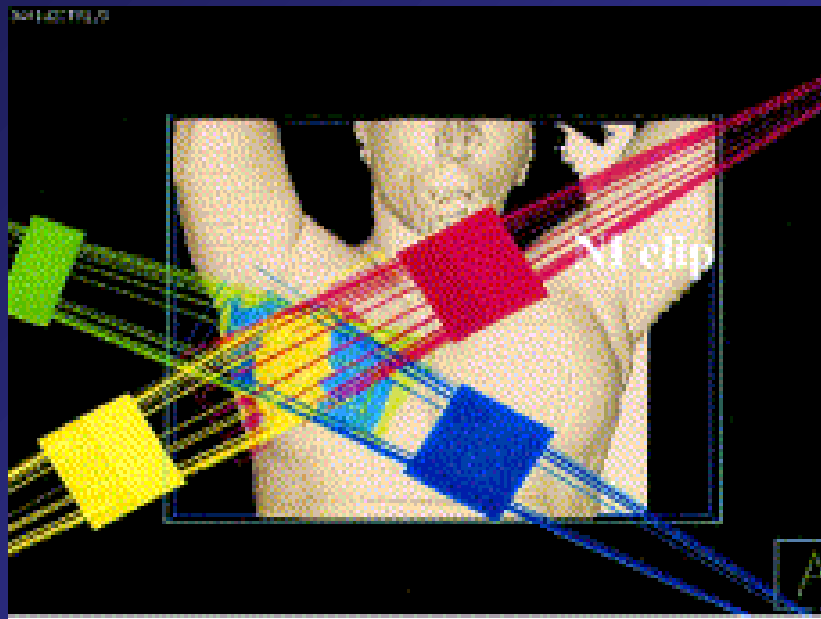
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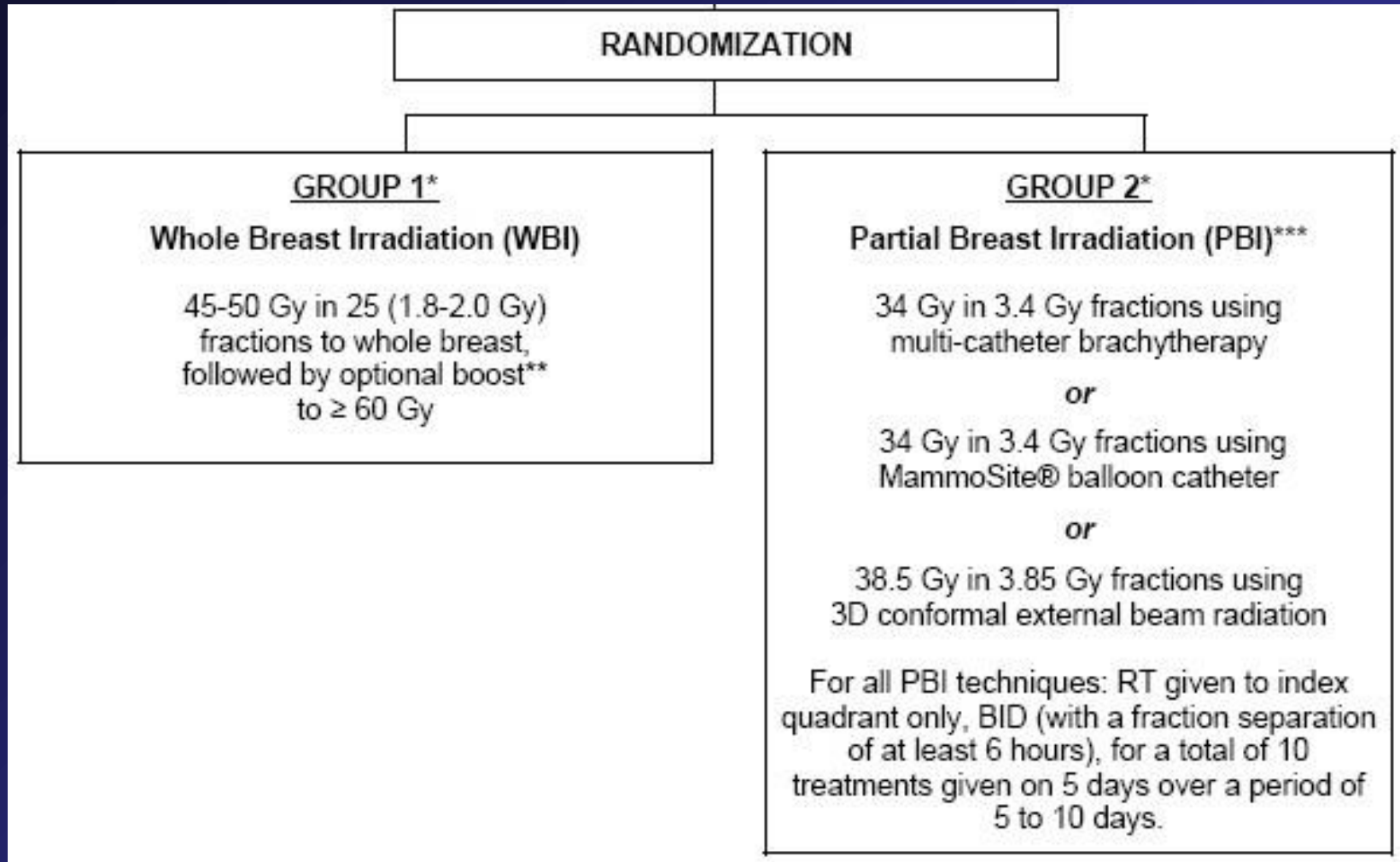
Mammosite™

RT externa hipofracionada



Irradiação parcial de mama

NSABP B-39 / RTOG 0413 – fase III



**ACCELERATED PARTIAL BREAST IRRADIATION: CAUTION AND CONCERN FROM
AN ASTRO TASK FORCE**

LEONARD R. PROSNITZ, M.D., F.A.S.T.R.O., F.A.C.R.,* JANET HORTON, M.D.,*
AND PAUL E. WALLNER, D.O., F.A.S.T.R.O., F.A.C.R., F.A.O.C.R., F.A.C.R.O.†

Categorias para pacientes “off-protocol”

Adequado: ≥ 60 a., N0, T1, RE+, sem IV, margem > 2mm; (Her2 -)

Restrição (1 fator +): <60a. / T2 / CDIS < 3 cm / margem < 2mm / IV focal /
/ RE negativo / multifocal / lobular invasivo

Inadequado (1 fator +): idade < 50 anos / ca. > 3cm / margem + / N1 ou Nx /
IV extensa / CDIS > 3 cm / BRCA1 ou 2 mutados

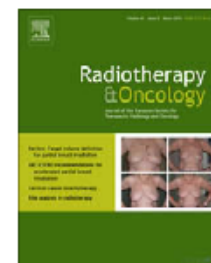


ELSEVIER

Contents lists available at ScienceDirect

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journal homepage: www.thegreenjournal.com



GEC-ESTRO Recommendations

Patient selection for accelerated partial-breast irradiation (APBI) after breast-conserving surgery: Recommendations of the Groupe Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) breast cancer working group based on clinical evidence (2009)

GEC-ESTRO recommendations on patient selection for accelerated partial-breast irradiation.

Characteristic	A/low-risk group – good candidates for APBI	B/intermediate-risk group – possible candidates for APBI (em protocolo clínico)	C/high-risk group – contraindication for APBI
Patient age ✓	>50 years	>40–50 years	≤40 years
Histology ✓	IDC, mucinous, tubular, medullary , and colloid cc.	IDC, ILC, mucinous, tubular, medullary, and colloid cc	–
ILC	Not allowed	Allowed	–
Associated LCIS	Allowed	Allowed	–
DCIS ✓	Not allowed	Allowed	–
HG ✓	Any	Any	–
Tumour size ✓	pT1–2 (≤30 mm)	pT1–2 (≤30 mm)	pT2 (>30 mm), pT3, pT4
Surgical margins	Negative (≥2 mm)	Negative, but close (<2 mm)	Positive
Multicentricity	Unicentric	Unicentric	Multicentric
Multifocality	Unifocal	Multifocal (limited within 2 cm of the index lesion)	Multifocal (>2 cm from the index lesion)
EIC	Not allowed	Not allowed	Present
LVI	Not allowed	Not allowed	Present
ER, PR status ✓	Any	Any	–
Nodal status ✓	pN0 (by SLNB or ALND ^a)	pN1mi, pN1a (by ALND ^a)	pNx; ≥pN2a (4 or more positive nodes)
Neoadjuvant chemotherapy	Not allowed	Not allowed	If used

APBI = accelerated partial-breast irradiation; IDC = invasive ductal carcinoma; ILC = invasive lobular carcinoma; LCIS = lobular carcinoma in situ; DCIS = ductal carcinoma in situ; HG = histologic grade; EIC = extensive intraductal component; LVI = lympho-vascular invasion; ER = estrogen receptor; PR = progesterone receptor; SLNB = sentinel lymph node biopsy.

^a ALND = axillary lymph node dissection (at least 6 nodes pathologically examined).

Clinical Investigation: Breast Cancer

How Do the ASTRO Consensus Statement Guidelines for the Application of Accelerated Partial Breast Irradiation Fit Intraoperative Radiotherapy? A Retrospective Analysis of Patients Treated at the European Institute of Oncology

Maria Cristina Leonardi, M.D.,* Patrick Maisonneuve, Ing.,[†]
Mauro Giuseppe Mastropasqua, M.D.,[‡] Anna Morra, M.D.,* Roberta Lazzari, M.D.,*
Nicole Rotmensz, M.Sc.,[†] Claudia Sangalli, D.M.,[§] Alberto Luini, M.D.,[§]
Umberto Veronesi, M.D.,[¶] and Roberto Orecchia, M.D.*,^{||}

Avaliação das 1822 pctes. tratadas “*off protocol*” com ELIOT

Table 3 Five-year clinical outcomes for breast cancer patients treated with full-dose intraoperative radiotherapy with electrons categorized according to the American Society for Radiation Oncology (ASTRO) consensus statement

	ASTRO consensus statement						
	<u>Suitable</u>		Cautionary		Unsuitable		
Patients	294		691		812		
Person-years	1,009		2,416		2,837		
Outcome	Events	Rate* (%)	Events	Rate* (%)	Events	Rate* (%)	Log-rank <i>p</i>
Ipsilateral breast tumor recurrence	3	1.5	21	4.4	50	8.8	0.0003
Regional lymph node failure	3	1.5	9	1.9	6	1.1	0.55
Distant metastases	3	1.5	8	1.7	22	3.9	0.047
Breast cancer related event	14	6.9	46	9.5	87	15.3	0.0025
Progression free survival	17	91.6	58	88.0	109	80.8	0.0005
Cause-specific survival	2	99.1	7	98.7	22	96.5	0.026
Overall survival	3	98.6	13	97.5	30	95.2	0.039

ASTRO group was not assessable for 25 patients.

* Five-year rate (%) assuming constant rate during the first 5 years.

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Accelerated Partial Breast Irradiation: Executive summary for the update of an ASTRO Evidence-Based Consensus Statement

Candace Correa MD ^a, Eleanor E. Harris MD ^b, Maria Cristina Leonardi MD ^c, Benjamin D. Smith MD ^d, Alphonse G. Taghian MD PhD ^e, Alastair M. Thompson MD ^f, Julia White MD ^g, Jay R. Harris MD ^{h,*}

Revisão dos critérios de indicação após dados mais maduros

Atualização de duas *key questions*:

- 1) Quais pctes. podem fazer APBI fora de protocolo?
- 2) Quais pctes. podem fazer APBI no intraoperatório?

Table 1 Comparison of patient groups in original and updated consensus statements

Patient group	Risk factor	Original	Update
Suitability	Age	≥60 y	≥50 y
	Margins	Negative by at least 2 mm	No change
	T stage	T1	Tis or T1
	DCIS	Not allowed	If all of the below: <ul style="list-style-type: none"> • Screen-detected • Low to intermediate nuclear grade • Size ≤2.5 cm • Resected with margins negative at ≥3 mm
Cautionary	Age	50-59 y	<ul style="list-style-type: none"> • 40-49 y if all other criteria for "suitable" are met • ≥50 y if patient has at least 1 of the pathologic factors below and does not have any "unsuitable" factors <i>Pathologic factors:</i> <ul style="list-style-type: none"> • Size 2.1-3.0 cm^a • T2 • Close margins (<2 mm) • Limited/focal LVSI • ER(-) • Clinically unifocal with total size 2.1-3.0 cm^b • Invasive lobular histology • Pure DCIS ≤3 cm if criteria for "suitable" not fully met • EIC ≤3 cm
	Margins DCIS	Close (<2 mm) ≤3 cm	No change ≤3 cm and does not meet criteria for "suitable"
Unsuitable	Age	<50 years	<ul style="list-style-type: none"> • <40 y • 40-49 y and do not meet the criteria for cautionary
	Margins	Positive	No change
	DCIS	>3 cm	No change

^a The size of the invasive tumor component.^b Microscopic multifocality allowed, provided the lesion is clinically unifocal (a single discrete lesion by physical examination and ultrasonography/mammography) and the total lesion size (including foci of multifocality and intervening normal breast parenchyma) falls between 2.1 and 3.0 cm.

Table 1 Comparison of patient groups in original and updated consensus statements

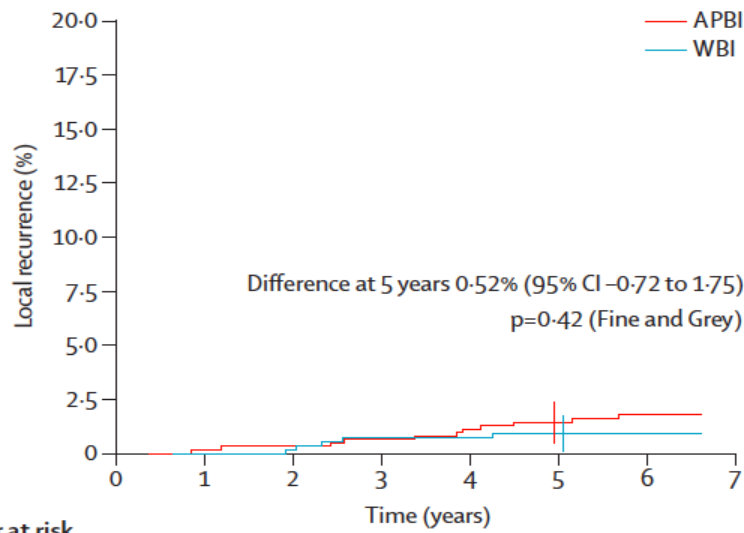
Patient group	Risk factor	Original	Update
<u>Suitability</u>	Age	≥60 y	≥50 y ✓
	Margins	Negative by at least 2 mm	No change
	T stage	T1	Tis✓ or T1
	DCIS	Not allowed	If all of the below: <ul style="list-style-type: none"> • Screen-detected • Low to intermediate nuclear grade • Size ≤2.5 cm • Resected with margins negative at ≥3 mm
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	Margins	Positive	No change
	DCIS	>3 cm	No change

^a The size of the invasive tumor component.

^b Microscopic multifocality allowed, provided the lesion is clinically unifocal (a single discrete lesion by physical examination and ultrasonography/mammography) and the total lesion size (including foci of multifocality and intervening normal breast parenchyma) falls between 2.1 and 3.0 cm.

5-year results of accelerated partial breast irradiation using sole interstitial multicatheter brachytherapy versus whole-breast irradiation with boost after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: a randomised, phase 3, non-inferiority trial

Lancet 2016; 387(10015)229–38



Number at risk	0	1	2	3	4	5	6	7
APBI	633	626	616	606	601	573	429	
WBI	551	543	535	522	511	490	381	

1184 ptes.

Recidiva GEC-ESTRO BT X RT

1,44% X 0,92%

(p=0,42)

Lancet 2016; 387(10015)229–38

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, 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

Lancet 2014;383(9917)603-13

Intraoperative radiotherapy versus external radiotherapy for early breast cancer (ELIOT): a randomised controlled equivalence trial

Umberto Veronesi, Roberto Orecchia, Patrick Maisonneuve, Giuseppe Viale, Nicole Rotmensz, Claudia Sangalli, Alberto Luini, Paolo Veronesi, Viviana Galimberti, Stefano Zurrada, Maria Cristina Leonardi, Roberta Lazzari, Federica Cattani, Oreste Gentilini, Mattia Intra, Pietro Caldarella, Bettina Ballardini

Lancet Oncol 2013;14(13)1269-77

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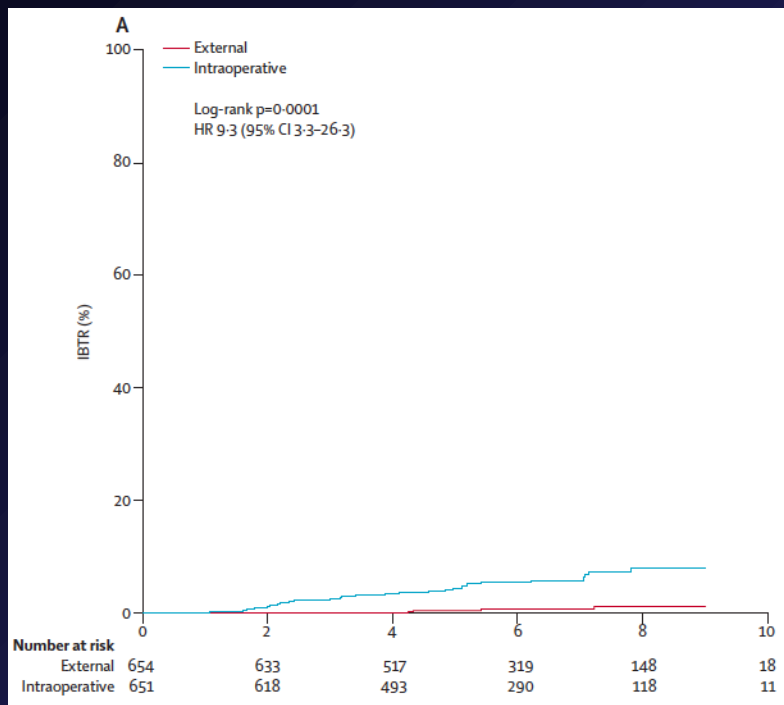
Umberto
Viviana G
Bettina B



y versus external radiotherapy for
a randomised controlled

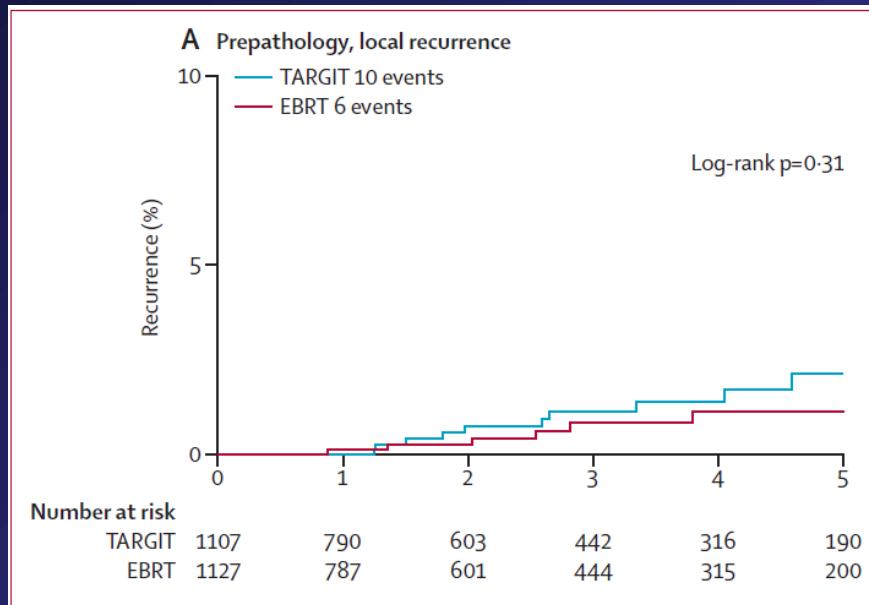
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berta Lazzari, Federica Cattani, Oreste Gentilini, Mattia Intra, Pietro Caldarella,

Lancet Oncol 2013;14(13)1269-77



1305 ptes.
Recidiva ELIOT X RT
4,4% X 0,4%
(2,5% local e 1,9% ipsilateral)
($p<0,0001$)

Lancet Oncol 2013;14(13)1269-77



2298 ptes.
Recidiva Targit A X RT
2,1% X 1,1%
($p=0,31$)
21% receberam IORT+RT
(recidiva local 0,9% / 5a.)

Lancet 2014;383(9917)603-13

ELIOT - Recidiva ipsilateral

	Patients (n/N)	IBTR 5-year event rate (95% CI)	Log-rank p value*
Total	35/651	4.4% (2.7-6.1)	..
Age			
48-49 years	0/44	0	..
50-59 years	21/286	5.6% (2.7-8.5)	..
60-69 years	10/259	3.1% (0.8-5.4)	..
≥70 years	4/62	7.2% (0.4-14.1)	0.11
Histology			
Ductal	28/524	4.5% (2.6-6.5)	..
Lobular	3/53	4.6% (0.0-10.8)	..
Ductal and lobular	2/17	6.3% (0.0-18.1)	..
Other	2/53	2.1% (0.0- 6.1)	0.69
Pathological size			
≤1 cm	5/199	1.9% (0.0-4.0)	..
1-1.5 cm	13/243	4.2% (1.5-6.9)	..
1.5-2.0 cm	7/120	4.7% (0.7-8.8)	..
>2.0 cm	10/83	10.9% (3.7-18.1)	0.006
Number of positive nodes			
None	21/478	3.5% (1.7-5.3)	..
1-3	10/138	5.3% (1.5-9.2)	..
≥4	4/31	15.0% (1.4-28.7)	0.06
Overall p value	

Tumour grade			
G1	5/196	1.1% (0.0-2.7)	..
G2	15/305	3.8% (1.5-6.1)	..
G3	15/129	11.9% (5.7-18.2)	0.0003
Oestrogen receptor			
Absent	8/63	14.9% (5.2-24.5)	..
Present	21/583	3.3% (1.8- 4.9)	0.004
Overall p value	
Progesterone receptor			
Absent	12/158	7.4% (2.9-11.8)	..
Present	23/487	3.5% (1.7- 5.2)	0.17
Proliferative index (Ki-67)			
<14%	8/263	1.8% (0.0-3.5)	..
14-20%	5/138	1.5% (0.0-3.6)	..
>20%	22/244	9.1% (5.1-13.1)	0.002
Molecular subtype			
Luminal A	7/256	1.4% (0.0-3.0)	..
Luminal B	20/327	4.9% (2.4-7.4)	..
HER2-positive (non-luminal)	1/20	5.9% (0.0-17.1)	..
Triple negative	7/43	18.9% (6.1-31.7)	0.001
Characteristics suggesting subsequent whole breast irradiation			
No	14/452	1.5% (0.3-2.7)	..
Yes†	21/199	11.3% (6.4-16.1)	<0.0001

TARGET A

Mortalidade câncer específica

Não câncer

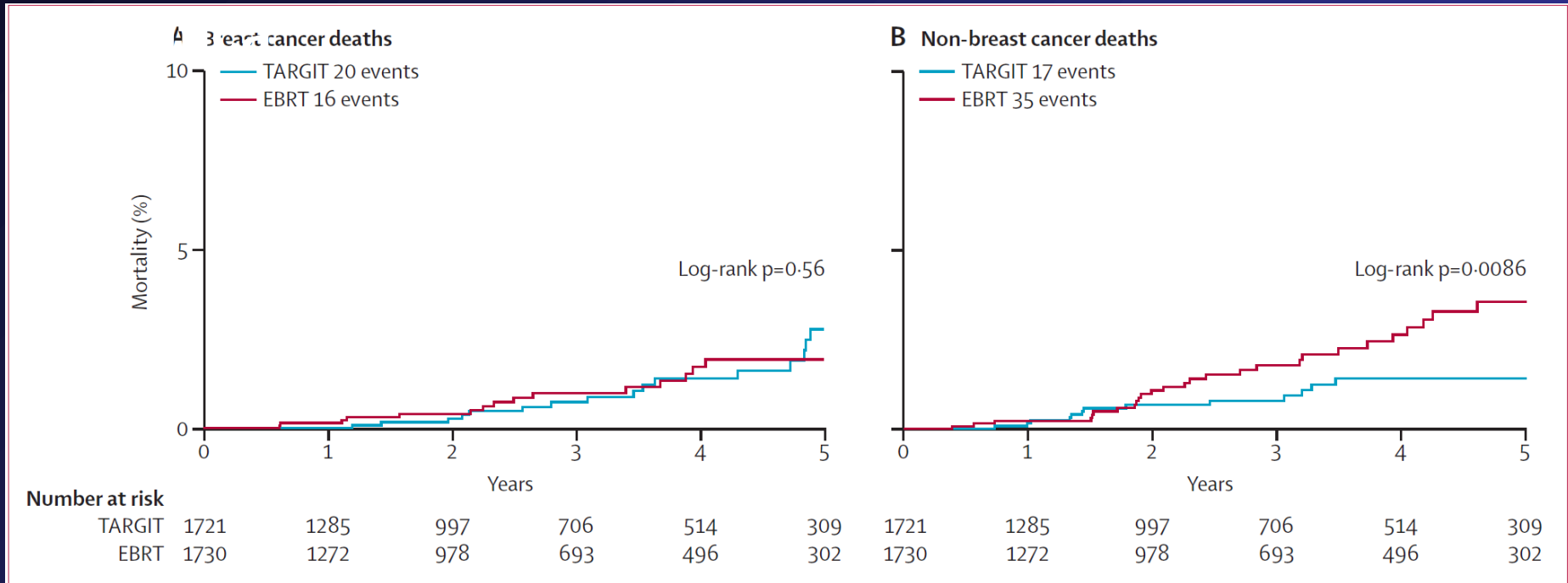


Figure 1: Kaplan-Meier analysis of breast cancer deaths and non-breast-cancer deaths

(A) Breast cancer. (B) Non-breast-cancer. TARGIT=targeted intraoperative radiotherapy. EBRT=external beam radiotherapy.

Causas de morte “não câncer de mama”

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

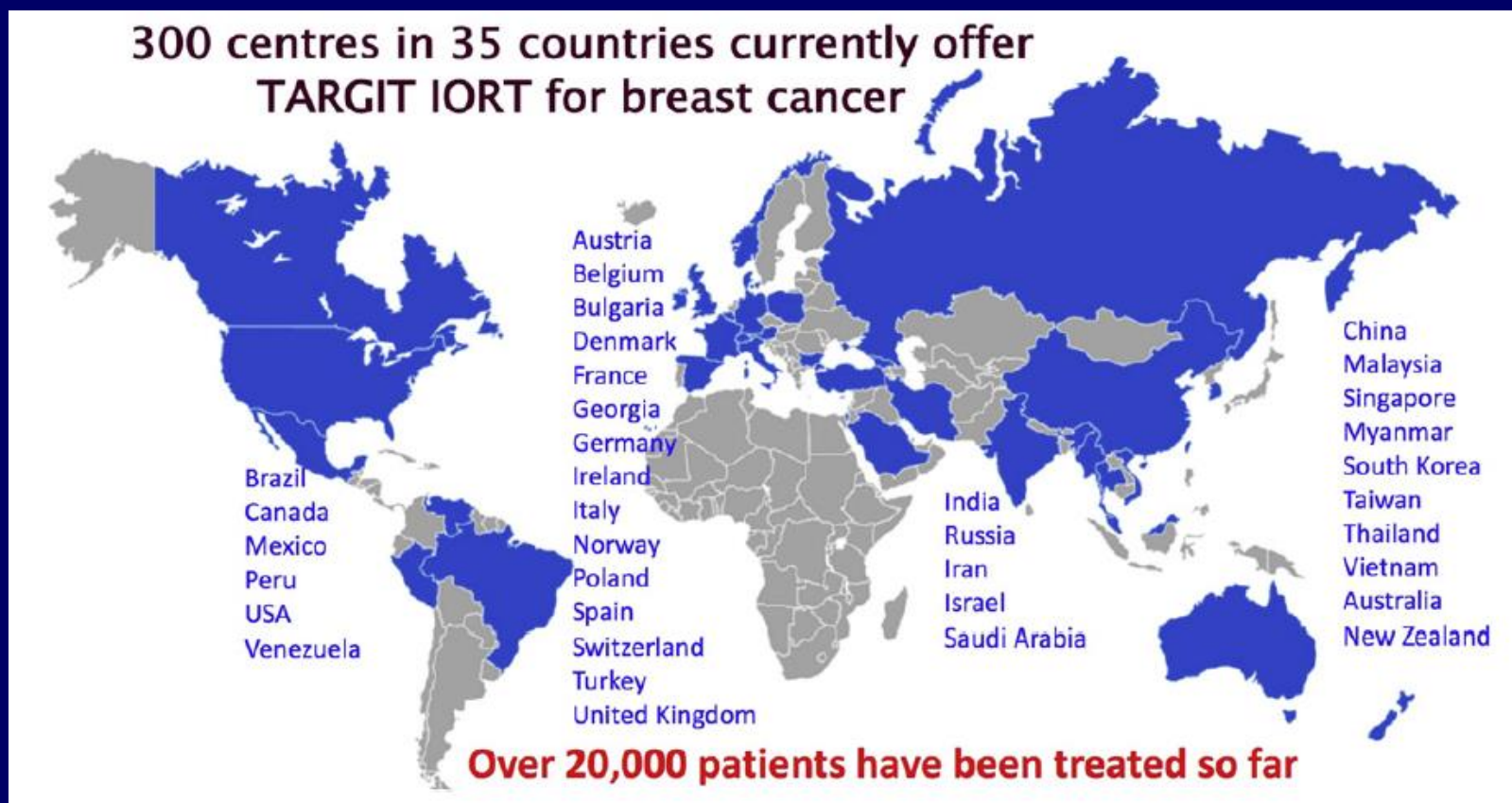
5-year risk 1.4% for TARGIT versus 3.5% for EBRT; log-rank $p=0.0086$.

TARGIT=targeted intraoperative radiotherapy. EBRT=external beam radiotherapy.

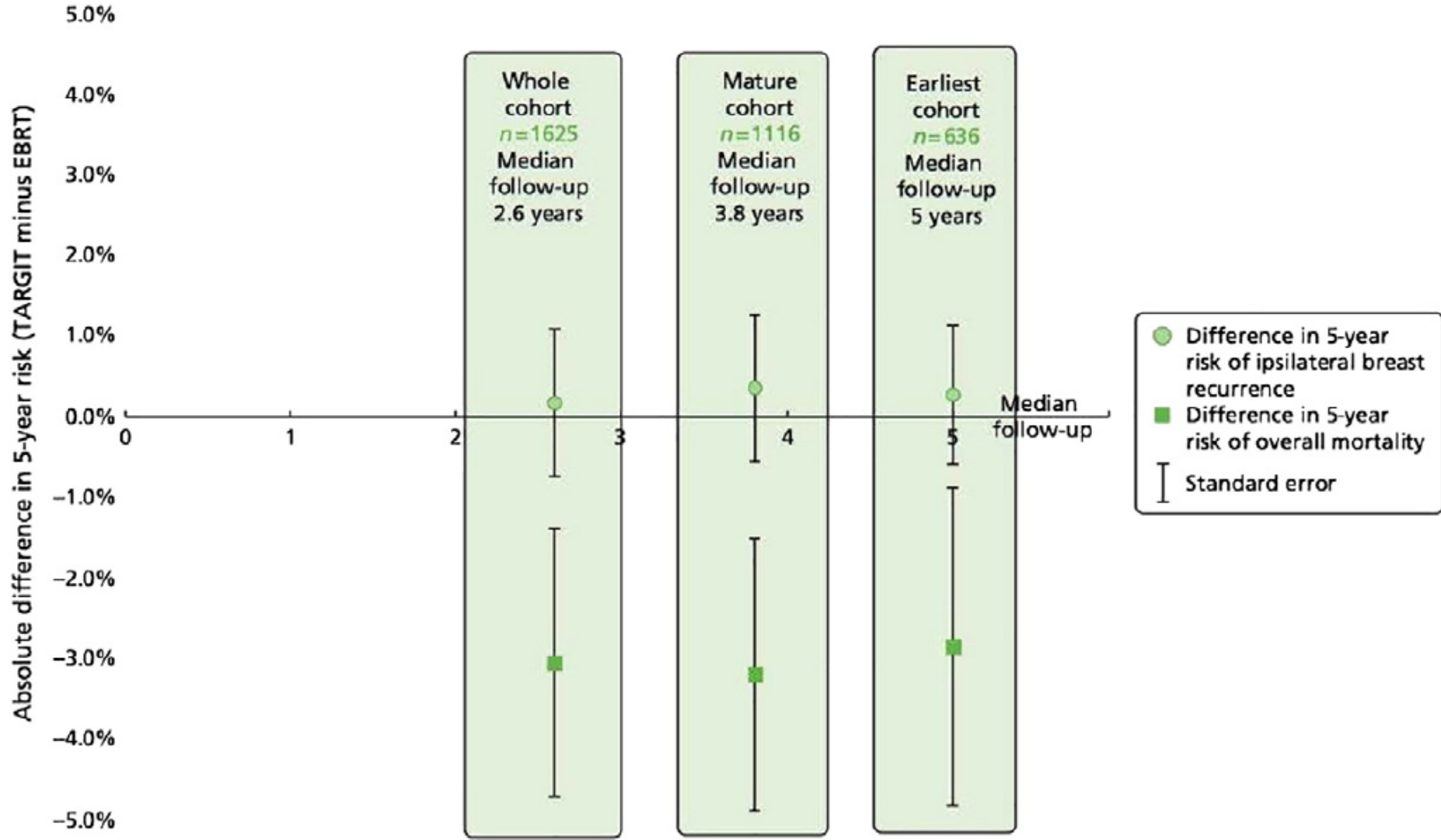
*Included one “sudden death at home” in EBRT group. †TARGIT: two diabetes, one renal failure, one liver failure, one sepsis, one Alzheimer’s disease, one unknown; EBRT: one myelopathy, one perforated bowel, one pneumonia, one old age, four unknown.

Table 2: Causes of death other than breast cancer in all patients

Commentary on "Accelerated partial breast irradiation consensus statement: Update of an ASTRO Evidence-Based Consensus Statement"

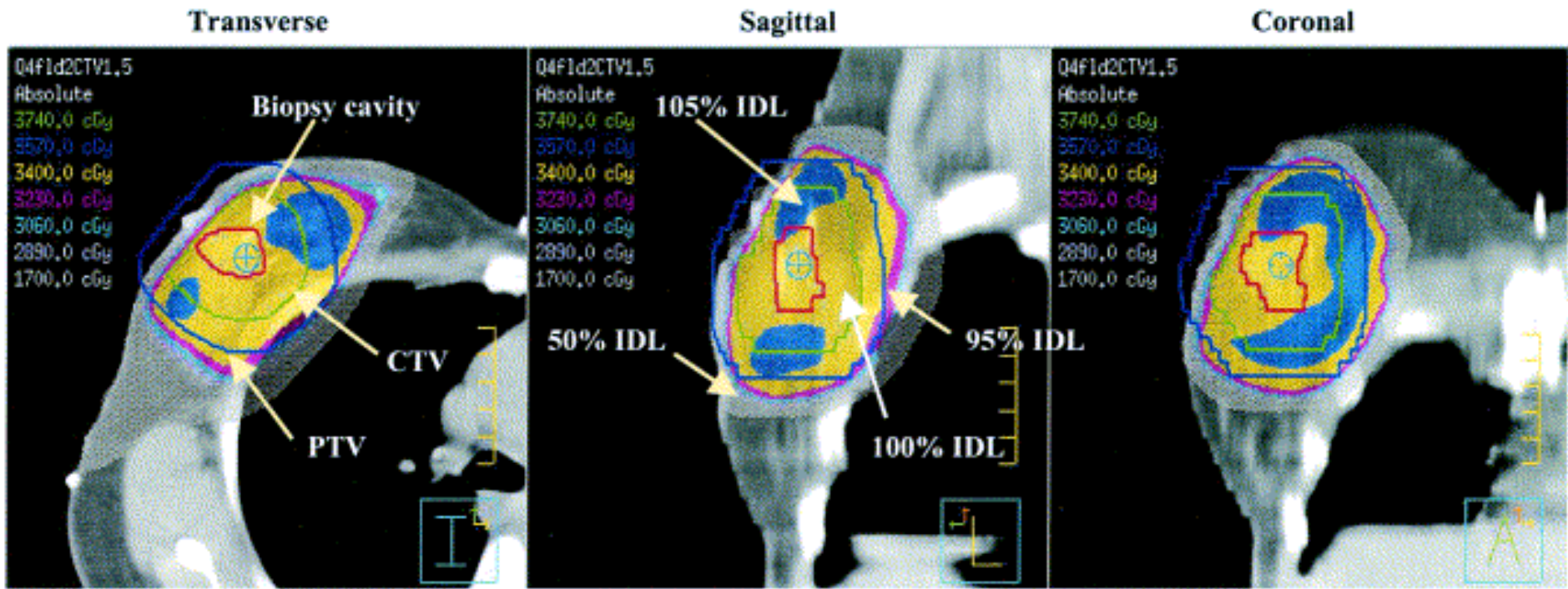


Diferença TARGIT x RT (SLR e SG)



patients to benefit from the best available options. The ASTRO statement should include the high-quality evidence that indicates that low-energy IORT is an excellent option for suitable patients.

Irradiação parcial de mama – NSABP B-39



Dose de 34Gy em 10 frações de 3,4Gy BID

Partial-breast radiotherapy after breast conservation surgery for patients with early breast cancer (UK IMPORT LOW trial): 5-year results from a multicentre, randomised, controlled, phase 3, non-inferiority trial

Trial UK / NHS com 2.018 ptes. CDI mama baixo risco (≥ 50 anos, pT1-2pN0M0, qualquer grau; RT com IMRT

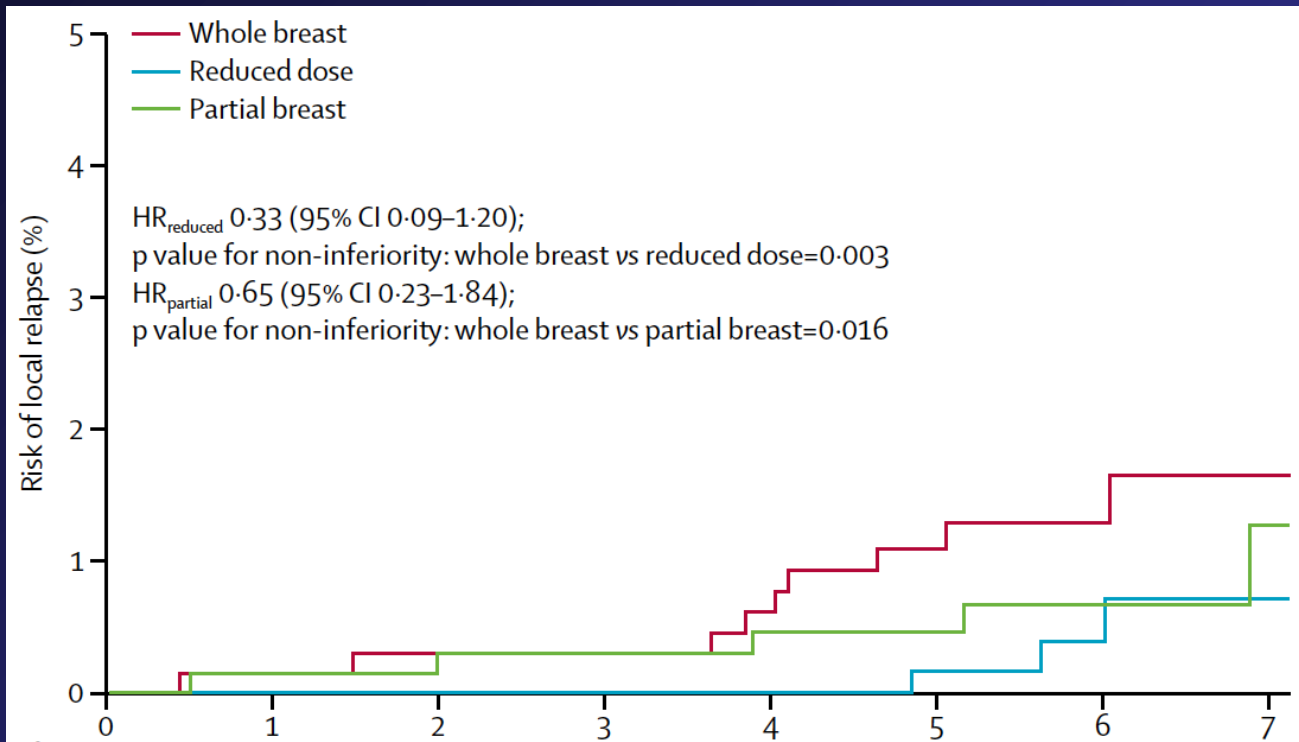
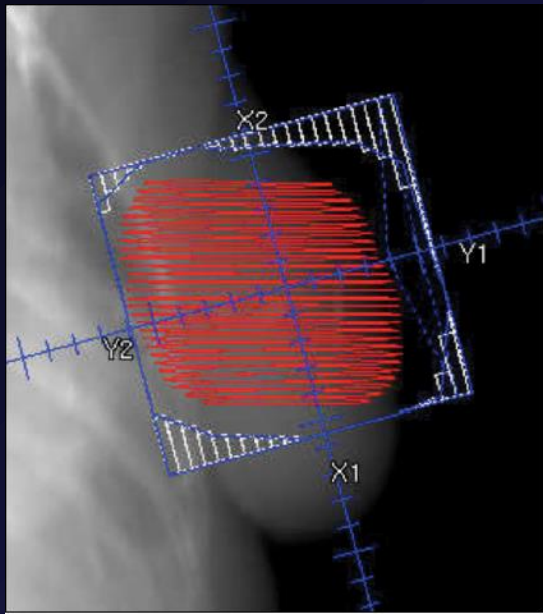
Conduzido entre 2007 – 2010 em 30 centros no UK

Hipofracionamento:

40Gy@2,67Gy mama

36Gy@2,4Gy mama @ 40Gy@2,67Gy quadrante acometido

40Gy@2,67Gy no quadrante acometido



Seguimento mediano – 68,3 meses

Resultados de controle local:

40Gy toda mama – 1,1%

36Gy mama + 40Gy quadrante – 0,2%

40Gy quadrante – 0,5%

Pcte. tratada com o *Import Low* Hipofracionamento com IMRT

Dia da alta



Retorno em 1 mês

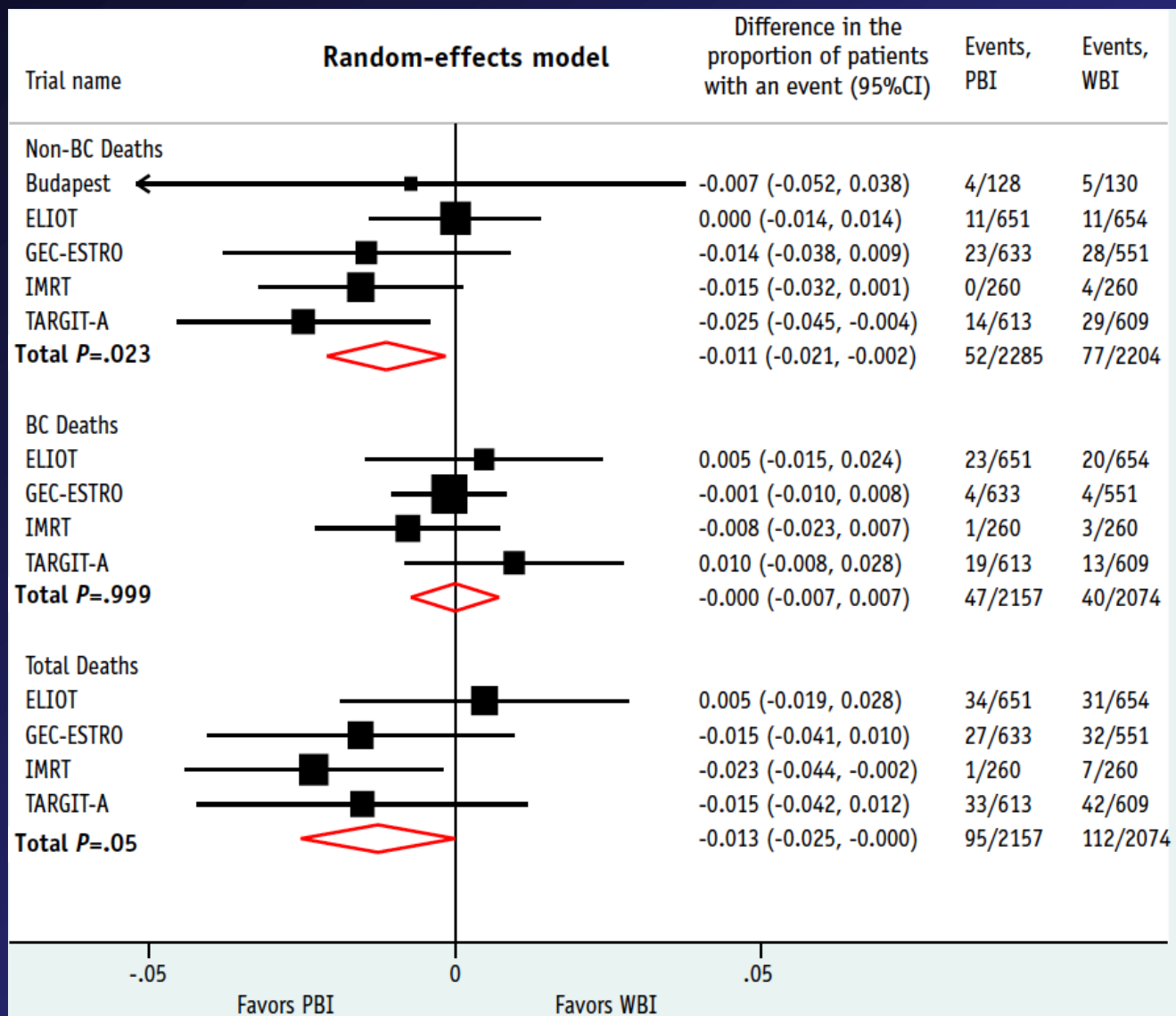


Reduced Mortality With Partial-Breast Irradiation for Early Breast Cancer: A Meta-Analysis of Randomized Trials

Jayant S. Vaidya, MBBS, MS, DNB, FRCS, PhD,^{*,†,‡} Max Bulsara, PhD,
Frederik Wenz, MD,^{||} Nathan Coombs, BSc, BM, FRCS,[¶]
Julian Singer, MBBS, MRCP, FRCR,[#] Stephen Ebbs, MD, FRCS,^{**}
Samuele Massarut, MD,^{††} Christobel Saunders, FRCS,^{‡‡}
Michael Douek, MBBS, MD, FRCS,^{§§}
Norman R. Williams, BSc, PhD, CSci, MICR, FIBMS,^{*}
David Joseph, MD, FRCR,^{|||} Jeffrey S. Tobias, MD, FRCS,^{¶¶}
and Michael Baum, MBBS, MD, FRCS^{*}

Meta-análise de 9 *trials* prospectivos de irradiação parcial *versus* radioterapia externa

8720 pctes. (4489 mortalidade não ca.-mama específica e 4231 mortalidade ca. específica e SG)



Redução de 1,3% na mortalidade global

Environmental and social benefits of the targeted intraoperative radiotherapy for breast cancer: data from UK TARGIT-A trial centres and two UK NHS hospitals offering TARGIT IORT

Seguimento de 485 pctes. no UK – 249 Targit / 236 RT

Cálculo de gastos de tempo no deslocamento, distância, combustível e geração de CO2

Centros de RT no UK

Circulo vermelho – diâmetro 40Km

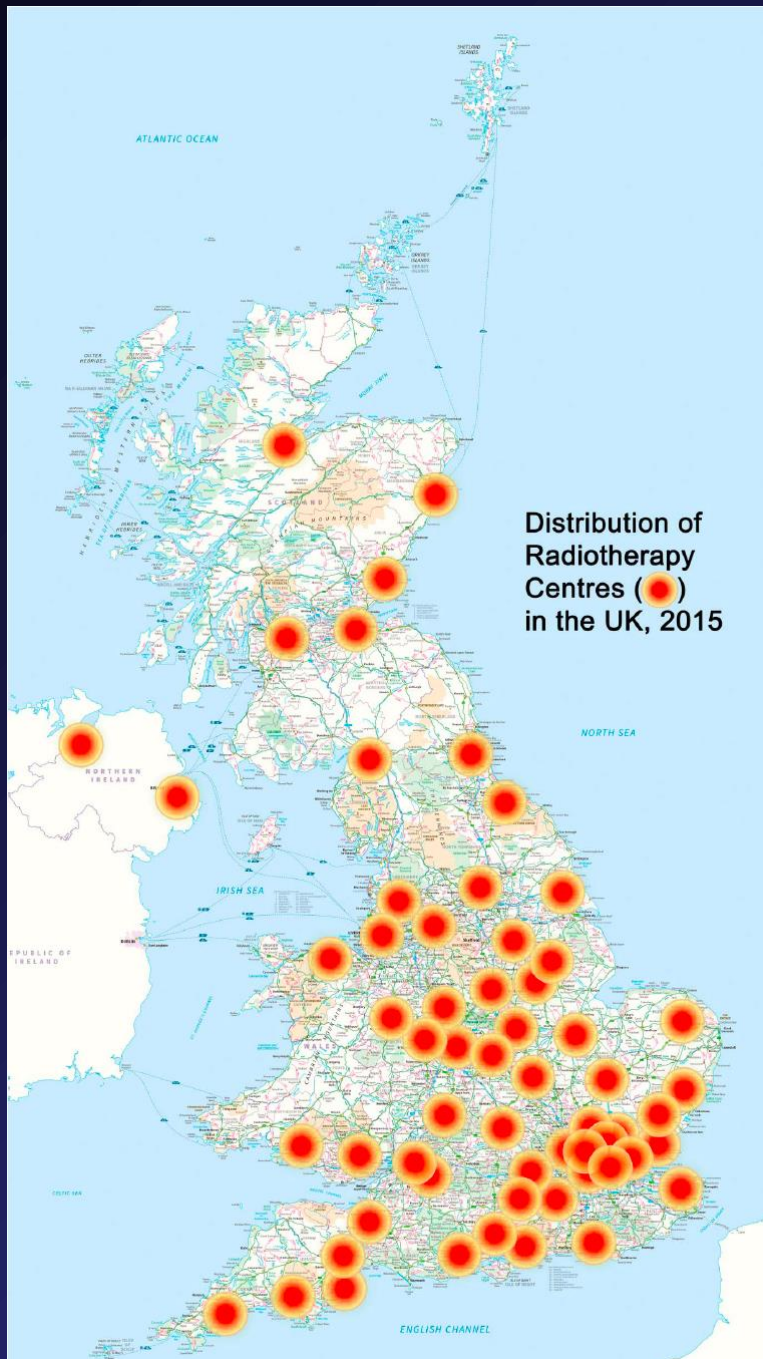
63% população UK vive fora de cidades com serviços de RT

Tto aprovado pelo NHS

Custo Intrabeam - £2170

Custo RT externa - £9700

Economia 8.000.000 Km, 170.000 horas/mulher e 1.200 Ton CO2 (equivalente floresta 100 hectares)



Accelerated partial breast irradiation: the new standard?

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Obrigado!



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