

Hipofracionamento no Câncer de Mama

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Introdução

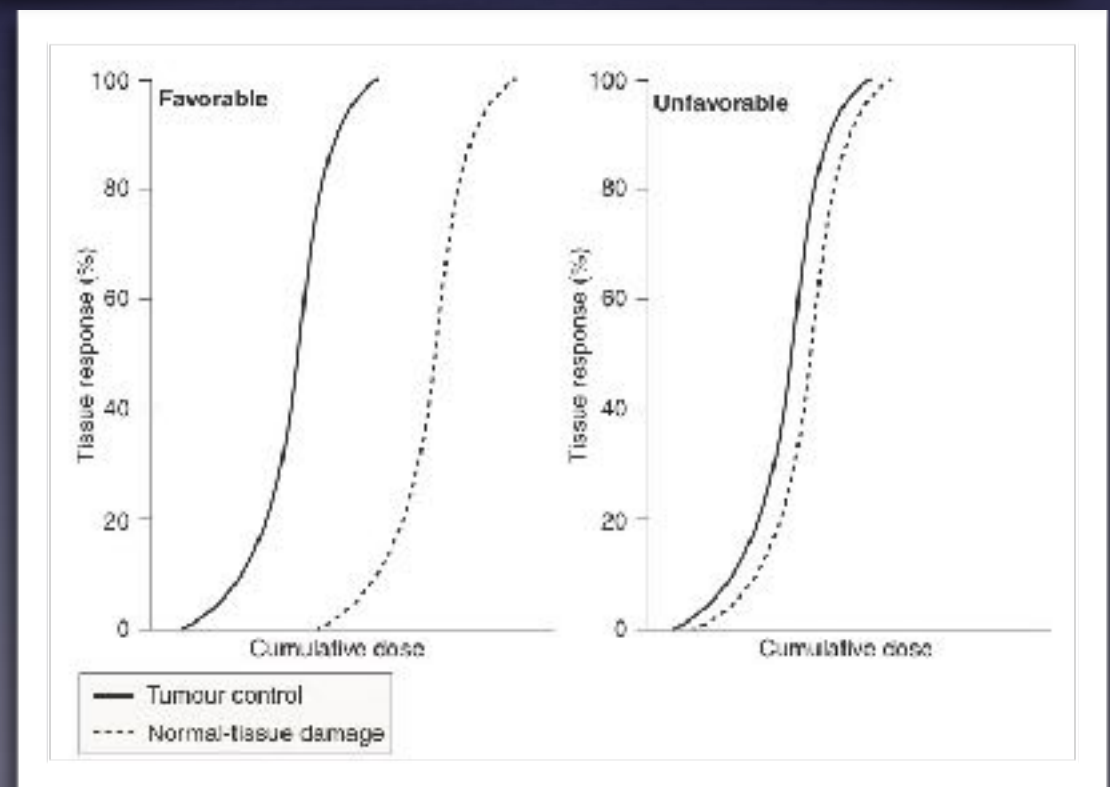
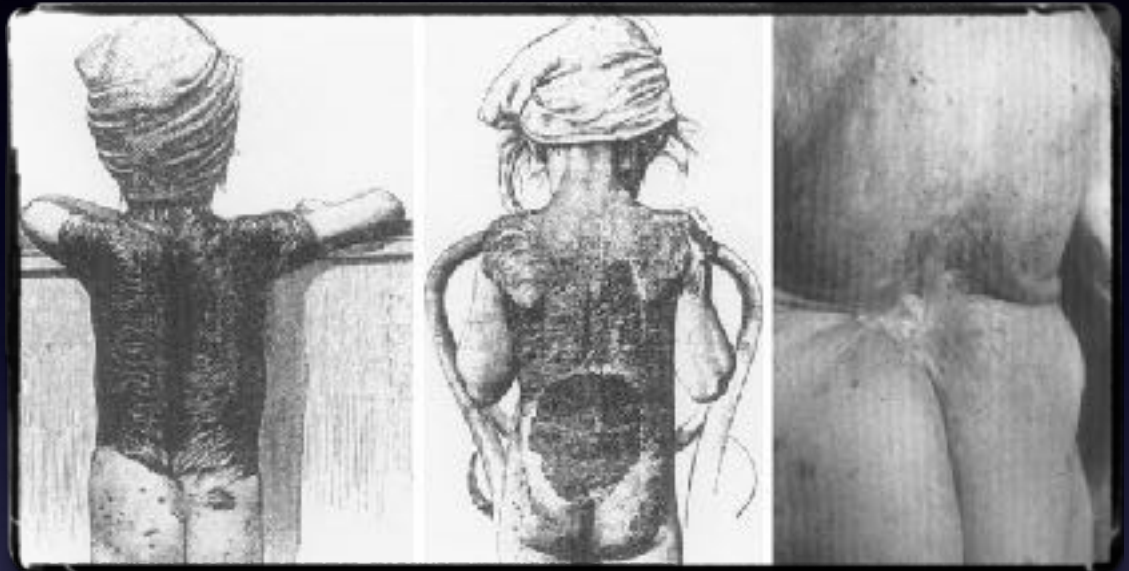
- O câncer de mama representa 29.7% de todos os tipos de câncer no Brasil.

<https://www.inca.gov.br/estimativa>

- Radioterapia (RT) é uma parte importante no tratamento do câncer de mama.
- O fracionamento convencional (1.8-2 Gy/dia) foi usado como padrão nas últimas décadas.
- Radioterapia hipofracionada é uma técnica de RT em que a dose total é administrada em um intervalo de tempo menor com doses fracionadas superiores às doses convencionais.

Introdução

- O hipofracionamento extremo era usado nos primeiros 30 anos do século XX.
- Controle tumoral pobre e complicações severas nos tecidos normais.



Introdução

- Graças ao avanço da tecnologia nos últimos anos há tratamentos altamente conformados.
- Em termos de biologia do hipofracionamento ainda há muito a ser aprendido.



ORIGINAL ARTICLE

Long-Term Results of Hypofractionated Radiation Therapy for Breast Cancer

pT1-pT2pN0

50 Gy (25fx) vs 42.5 Gy (16fx)

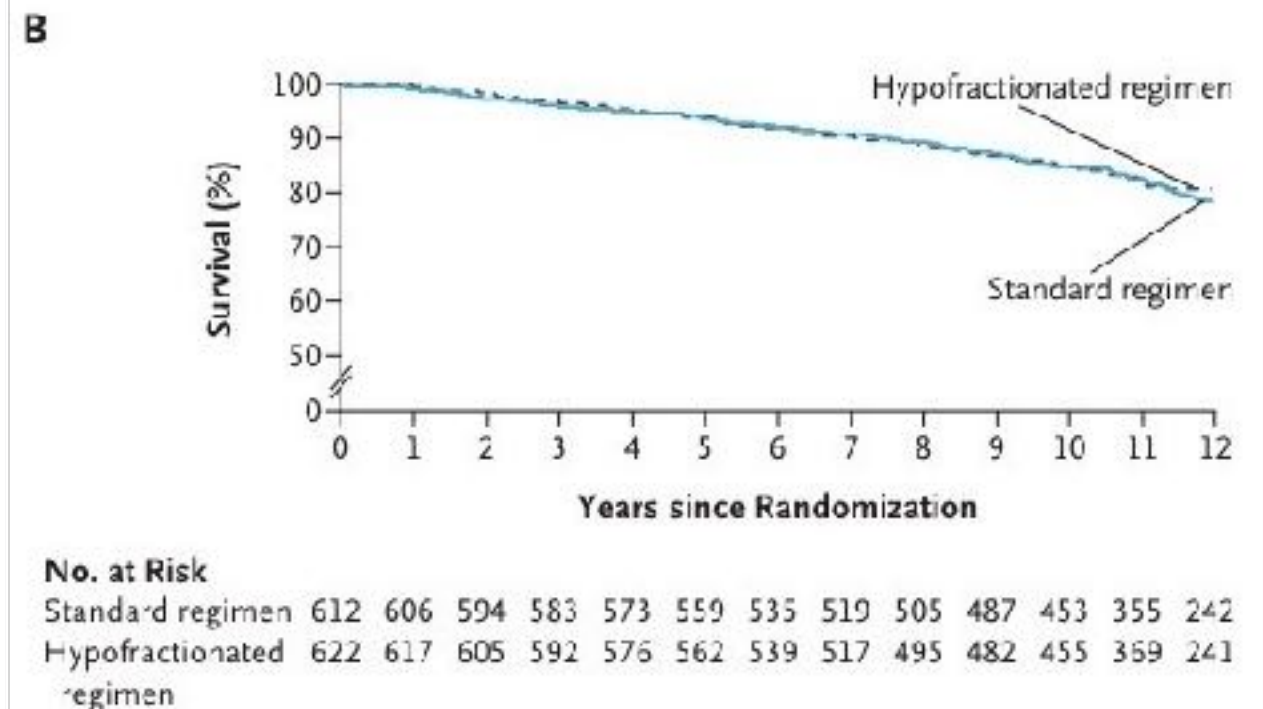
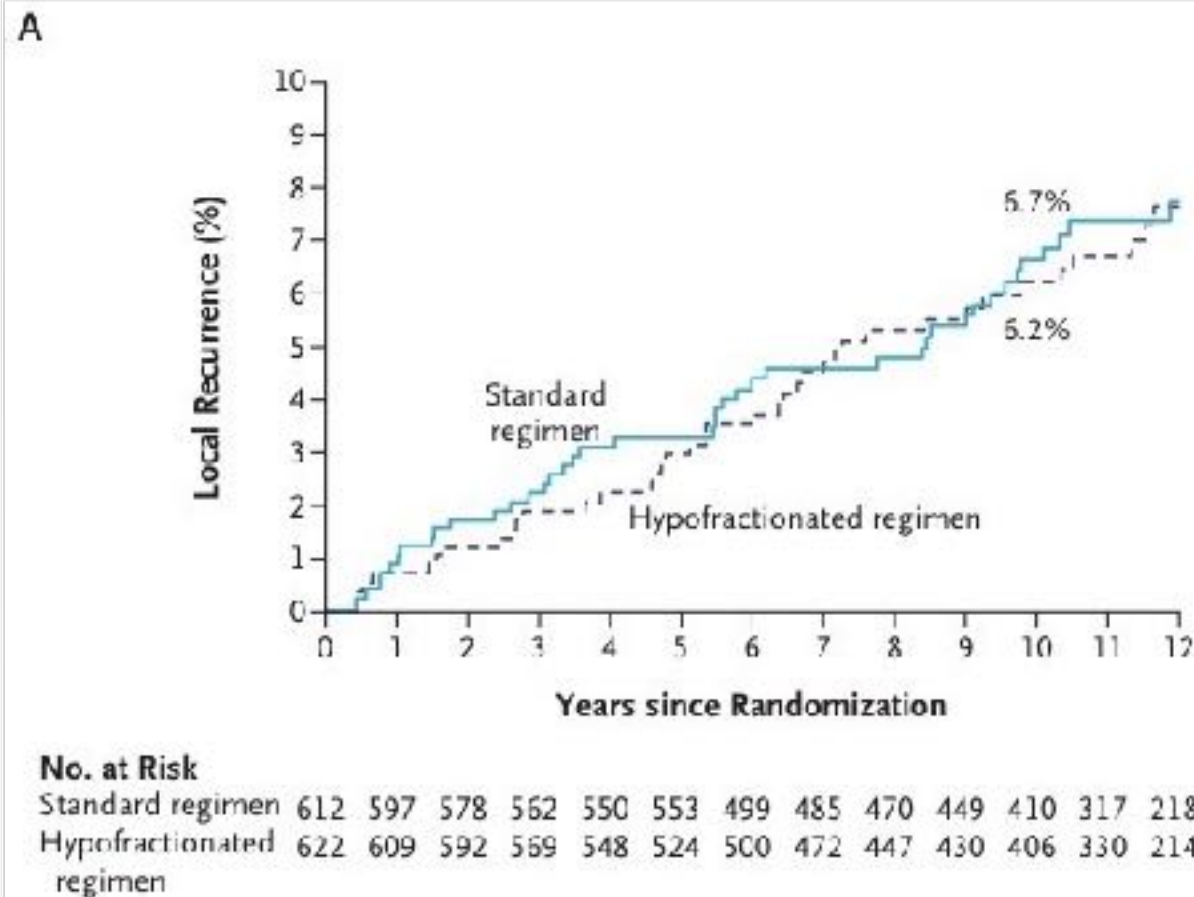


Table 1. Late Toxic Effects of Radiation, Assessed According to the RTOG–EORTC Late Radiation Morbidity Scoring Scheme.*

Site and Grade	5 Yr		10 Yr	
	Standard Regimen (N=424)	Hypofractionated Regimen (N=449)	Standard Regimen (N=220)	Hypofractionated Regimen (N=235)
	percent of patients			
Skin				
0†	82.3	86.1	70.5	66.8
1	14.4	10.7	21.8	24.3
2	2.6	2.5	5.0	6.4
3	0.7	0.7	2.7	2.5
Subcutaneous tissue				
0†	61.4	66.8	45.3	48.1
1	32.5	29.5	44.3	40.0
2	5.2	3.8	6.8	9.4
3	0.9	0.9	3.6	2.5



**The UK Standardisation of Breast Radiotherapy (START)
trials of radiotherapy hypofractionation for treatment of
early breast cancer: 10-year follow-up results of two
randomised controlled trials**

Joanne S Hawford, J Roger Owen, John A Dewar, Rajiv K Agrawal, Jane Barrett, Peter J Barrett-Lee, H Jane Dabbs, Penelope Hopwood, Pat A Lawton, Brian J Magee, Judith Mills, Sandra Simmons, Mark A Sydenham, Karen Venables, Judith M Bliss, John R Yarnold*, on behalf of the START Trialists' Group†*

- **START A** N=2236, pT1-3, N0-1. 77% >50 anos.
29% N+, 15% mastectomia.

Braço 1: 39 Gy/13; Braço 2: 41.6 Gy/13; Braço 3: 50 Gy/25.
Todos tratamentos em 5 semanas. 61% receberam boost.

- **START B** N=2215, pT1-3, pN0-1. 79% >50 anos.
23% N+, 8% mastectomia

Braço 1: 40 Gy/15 (3 semanas); Braço 2: 50 Gy/25. 43%
receberam boost.

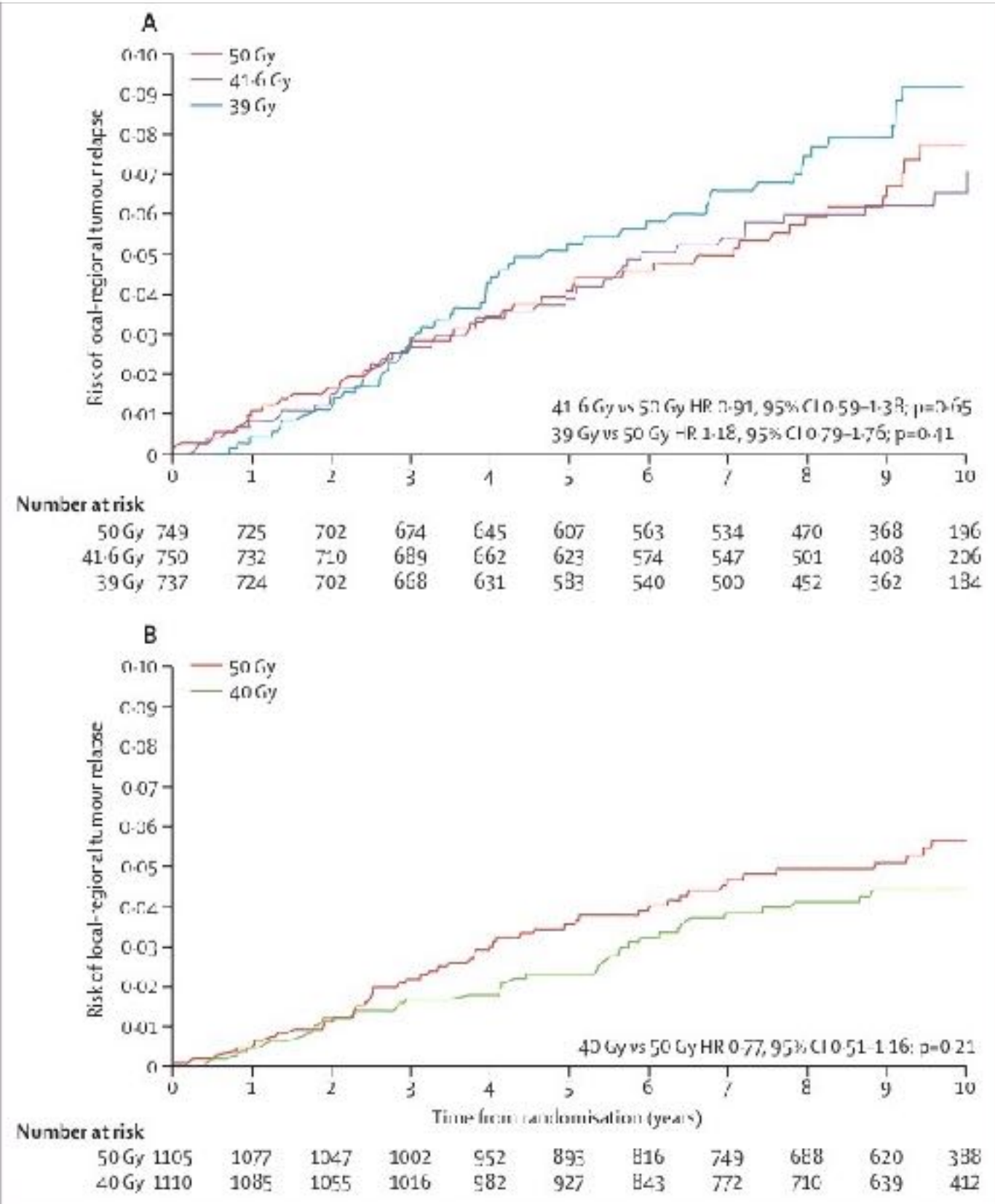


Figure 1: Cumulative risk of local-regional tumour relapse in START-A (A) and START-B (B).

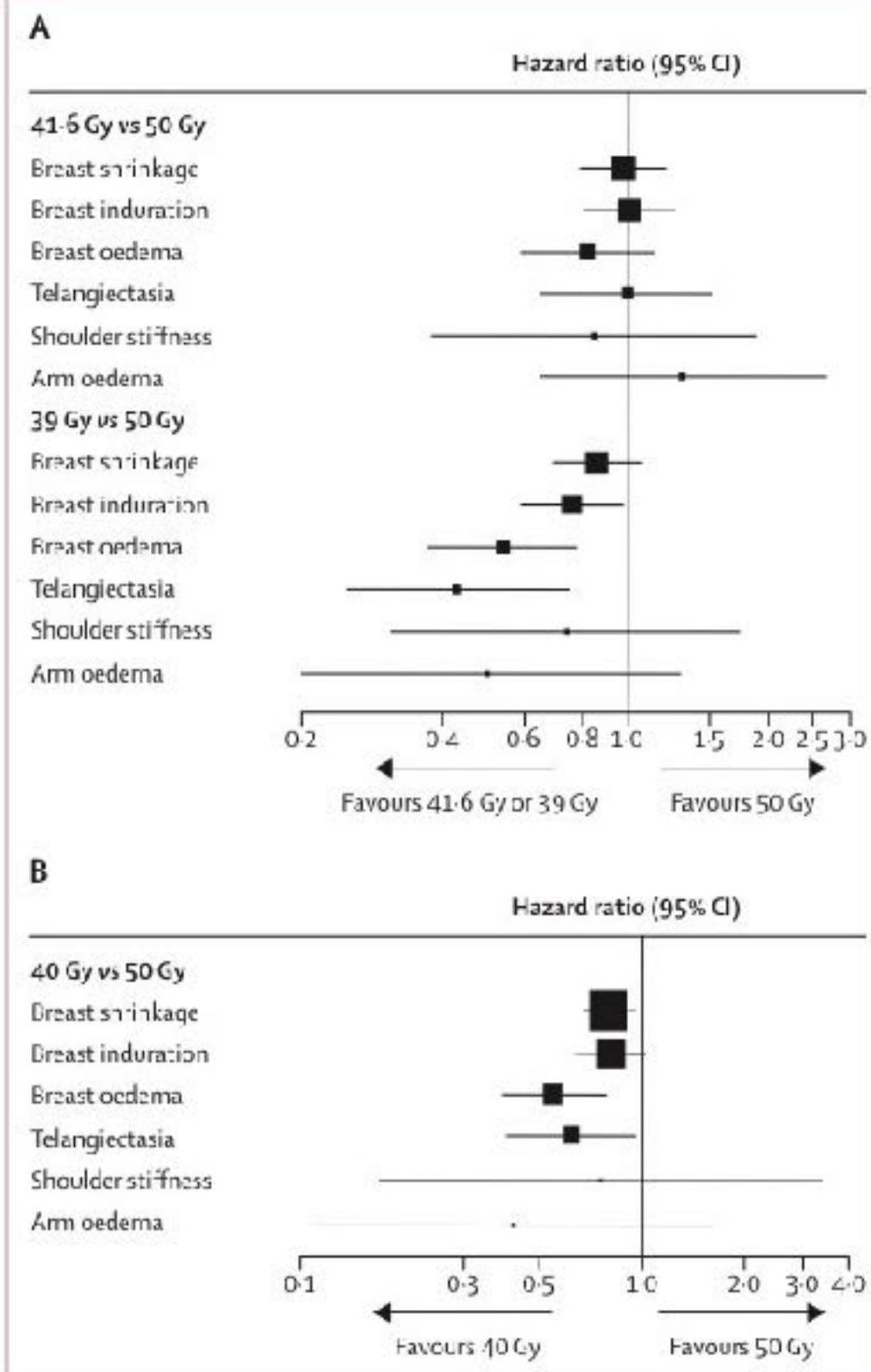


Figure 3: Late normal tissue effects

In START-A (A) and START-B (B). Assessed as moderate or marked by physicians

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



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

Table 1 Patients for whom consensus supports use of HF-WBI: A comparison of the 2011 and 2018 ASTRO Guidelines *

Factor	2011 Guideline	2018 Guideline
Age	≥50 years	Any
Stage	T1-2 N0	Any stage provided intent is to treat the whole breast without an additional field to cover the regional lymph nodes
Chemotherapy	None	Any chemotherapy
Dose homogeneity	±7% in the central axis	Volume of breast tissue receiving >105% of the prescription dose should be minimized regardless of dose-fractionation

Dose homogeneity
Chemotherapy

±7% in the central axis
None

should be minimized regardless of dose-fractionation
Volume of breast tissue receiving >105% of the prescription dose
Any chemotherapy

Recommendations for hypofractionated whole-breast irradiation

Author: SBRT, Brazilian Society of Radiotherapy

Participants:  Nilceana Mayo Aires Freitas¹, Arthur Accioly Rosa²,  Gustavo Nader Marta^{3,4}, Samir Abdalla Hanra⁴, Rodrigo de Moraes Hanriot⁵, Allisson Bruno Barcelos Borges⁶, Guilherme Rocha Melo Gondim^{5,7}, Antonio Cassio Assis Pellizzon⁷, Igor Moreira Veras⁸, Wilson José de Almeida Júnior⁹, Claudia Regina Scaramello Hadlich Willis Fernandez¹⁰, Eronides Salustiano Bataíha Filho¹¹, Marcus Simões Castilho¹², Felipe Quirino Kuhn¹³, Rosa Maria Xavier Faria Najas¹⁴, Renato José Affonse Júnior⁶, André Campana Correia Leite¹⁵, Homero Lavieri Martins Ribeiro¹⁶,  Ruffo Freitas-Junior¹⁷,  Harley Francisco de Cliveiro¹⁸.

Final version: July 8, 2018

HYPOFRACTIONATED RT FOR BREAST CANCER TREATMENT (AGREEMENT > 75% AMONGST PANEL MEMBERS)

Variable	Level of agreement (%)	Level of evidence
Surgery		
Conservative	100	Strong
Mastectomy		
Without reconstruction	100	Moderate
Age		
>40 years	100	Strong
Stage of the tumor		
T1 – T2	100	Strong
T3	77	Weak
Histological grade		
G1 – G2 – G3	100	Strong
Histology		
Invasive carcinoma of no special type	100	Strong
DCIS	100	Moderate
Regardless of IHC	100	Strong

Axillary lymph nodes		
Absent	100	Strong
Breast size		
Any size	100	Strong
Systemic treatment		
After adjuvant CT	100	Strong
After neoadjuvant CT	94	Weak
Concurrent with anti-HER2 drugs	89	Weak
Boost	100	Strong

Hypofractionated versus conventional fractionated postmastectomy radiotherapy for patients with high-risk breast cancer: a randomised, non-inferiority, open-label, phase 3 trial

Shu-Lian Wang^{*}, Hui Fang^{*}, Yong-Wen Song, Wei-Hu Wang, Chen Hu, Yue-Ping Liu, Jing Jin, Xin-Fan Liu, Zi-Hao Yu, Hua Ren, Ning Li, Ning-Ning Lu, Yu Tang, Yuan Tang, Shu-Nan Qi, Guang-Yi Sun, Ran Peng, Shuai Li, Bo Chen, Yong Yang, Ye-Xiong Li

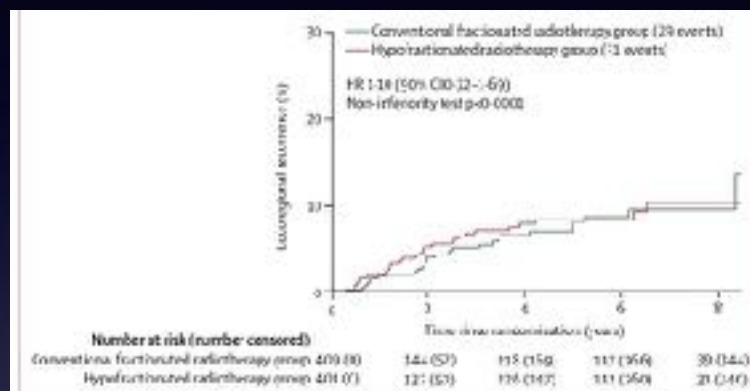


Figure 2: Kaplan-Meier plot of cumulative locoregional recurrence. HR=hazard ratio.

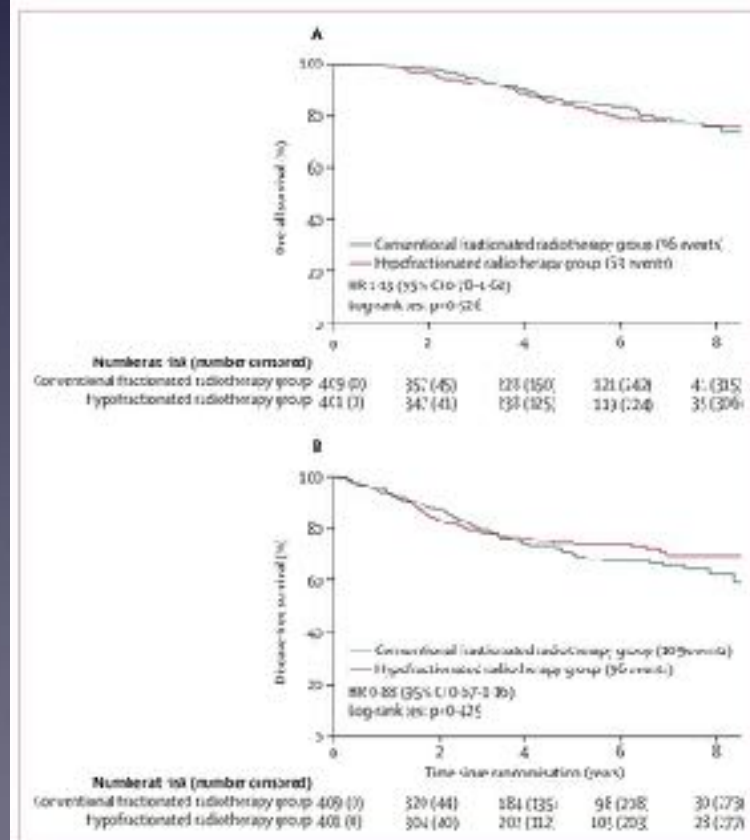


Figure 3: Kaplan-Meier plots of overall survival (A) and disease-free survival (D). HR=hazard ratio.

	Conventional fractionated radiotherapy group (n=409)	Hypofractionated radiotherapy group (n=401)	p value
Acute toxicity			
Skin toxicity			<0.0001
Grade 1-2	357 (87%)	351 (89%)	
Grade 3	32 (8%)	14 (3%)	
Pneumonitis			0.278
Grade 1	62 (15%)	61 (15%)	
Grade 2	7 (2%)	14 (3%)	
Grade 3	..	..	
Late toxicity			
Skin toxicity			0.669
Grade 1-2	90 (22%)	85 (21%)	
Grade 3	0	1 (<1%)	
Lymphoedema			0.961
Grade 1-2	81 (20%)	78 (20%)	
Grade 3	3 (1%)	3 (1%)	
Shoulder dysfunction			0.734
Grade 1-2	13 (3%)	7 (2%)	
Grade 3	1 (<1%)	1 (<1%)	
Lung fibrosis			0.081
Grade 1-2	42 (10%)	62 (25%)	
Grade 3	0	0	
Ischaemic heart disease			0.506
Grade 1-2	1 (<1%)	3 (1%)	
Grade 3	3 (1%)	4 (1%)	

Data are n (%). The χ^2 test was used to calculate p values. No grade 4 events or deaths due to adverse effects were reported.

Table 2: Adverse events

Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial

Adrian Murray Brent¹, Joanne S Haviland², Duncan A Whaites³, Mark A Sydes⁴, Abdulh Alhussayn⁵, David J Bloomfield⁶, Charlie Chua⁷, Mark Chua⁸, Susan Cleator⁹, Charlotte E Coles¹⁰, Andrew Goodman¹¹, Adrian Harcourt¹², Penelope Hopwood¹³, Anna M Kirby¹⁴, Cliona C Kirwan¹⁵, Carolyn Morris¹⁶, Zohair Naji¹⁷, Eleanor Sawyer¹⁸, Navita Sennin¹⁹, Liha Stones²⁰, Robert Sydes²¹, Judith M Bliss²², John R Yarnold²³, on behalf of the FAST-Forward Trial Management Group

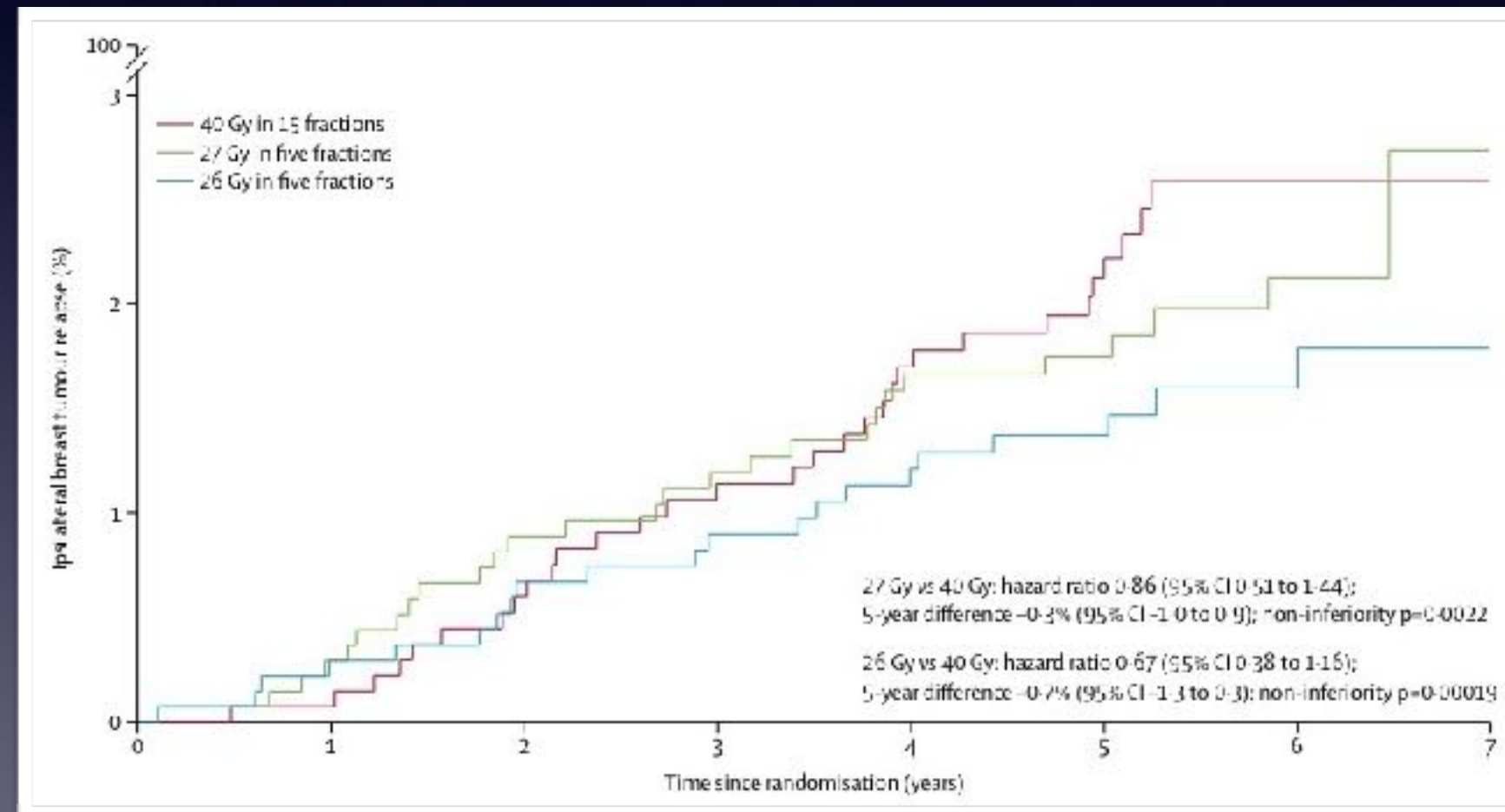
- N=4096, pT1-3, pN0-N1, M0

- Fracionamento

40 Gy em 15 frações (3 semanas)

27 Gy em 05 frações (1 semana)

26 Gy em 05 frações (1 semana)



	Number of moderate or marked events/total number of assessments over follow-up
Any adverse event in the breast or chest wall*	..
40 Gy	651/6121 (10.6%)
27 Gy	1004/6303 (15.9%)
26 Gy	774/6327 (12.2%)
Breast distortion†	..
40 Gy	232/5724 (4.0%)
27 Gy	363/5953 (6.1%)
26 Gy	299/5945 (5.0%)
Breast shrinkage†	..
40 Gy	330/5728 (5.8%)
27 Gy	503/5944 (8.5%)
26 Gy	369/5943 (6.2%)
Breast induration (tumour bed)†	..
40 Gy	185/5713 (3.2%)
27 Gy	304/5948 (5.1%)
26 Gy	235/5937 (4.0%)
Breast induration (outside tumour bed)†	..
40 Gy	45/5712 (0.8%)
27 Gy	137/5943 (2.3%)
26 Gy	97/5930 (1.6%)
Telangiectasia	..
40 Gy	63/6087 (1.0%)
27 Gy	100/6272 (1.6%)
26 Gy	102/6300 (1.6%)
Breast or chest wall oedema	..
40 Gy	83/6037 (1.5%)
27 Gy	217/6287 (3.4%)
26 Gy	155/6318 (2.4%)
Breast or chest wall discomfort	..
40 Gy	234/6086 (3.8%)
27 Gy	269/6285 (4.3%)
26 Gy	250/6309 (4.0%)

- 26 Gy foi equivalente a 40 Gy em todas as avaliações de toxicidade, exceto:

1- Enduração da mama: 0,8% vs 1.6%

2-Telangiectasia: 1% vs 1.6%

3- Edema da mama: 1.5% vs 2.4%

ESTRO 2020

- “ Existem benefícios óbvios para os pacientes e os sistemas de saúde com os tratamentos mais curtos, particularmente no momento atual, e de fato, a pandemia do COVID acelerou a adoção do cronograma de 26 Gy em todo o mundo”. Joane S. Haviland, MSc, of Institute of Cancer Research in London.
- “ Este é um trabalho muito importante. Acho que este é um dos ensaios mais importantes dos últimos anos. Realmente mudou a prática” . Ben Slotman, MD, PhD, do Vrije Universiteit Medical Center, Amsterdam.





- 2019

55.4% Fraccionamiento
Convencional

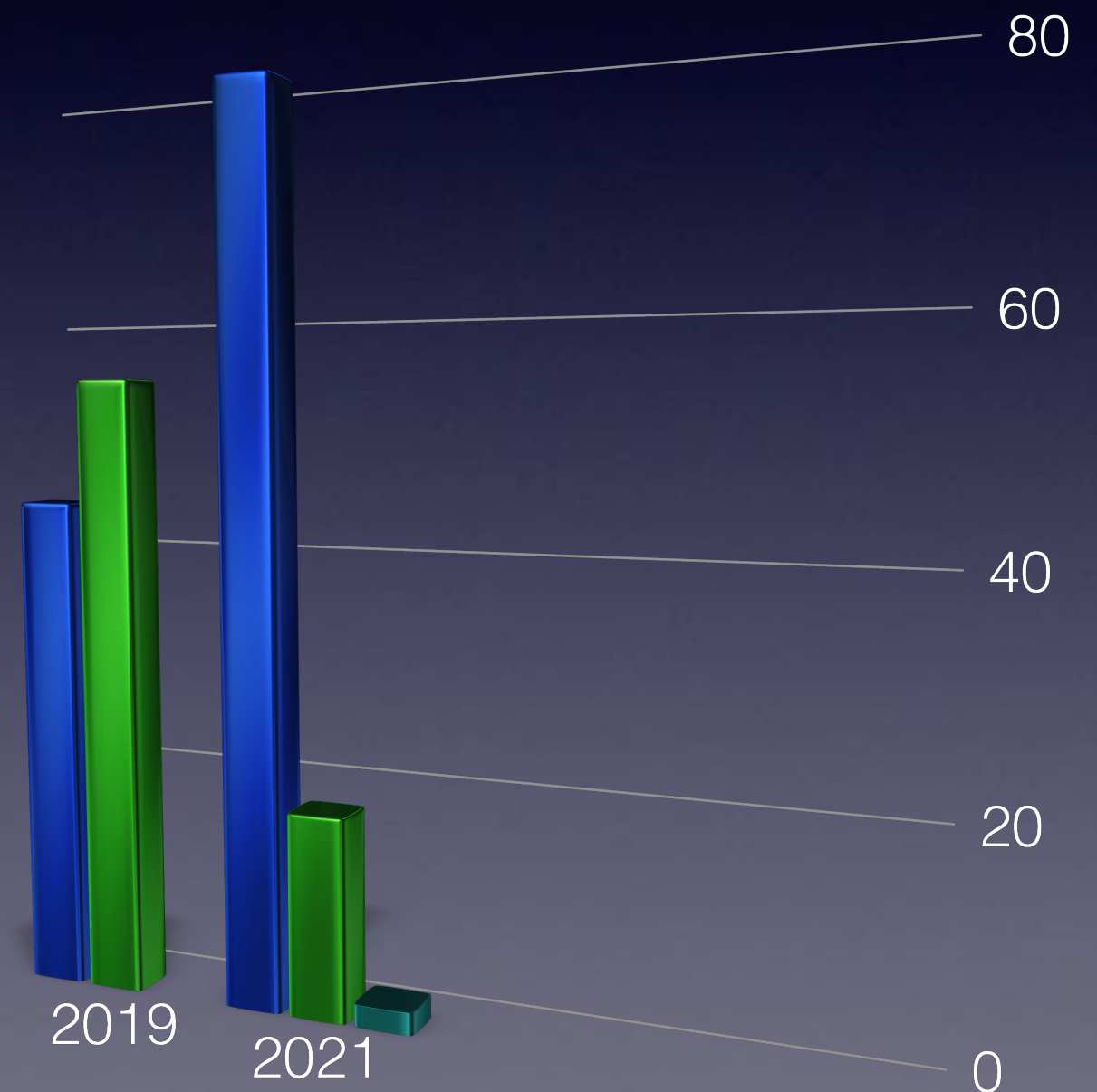
44.5% Hipofraccionamiento

- 2021

80% Hipofraccionamiento

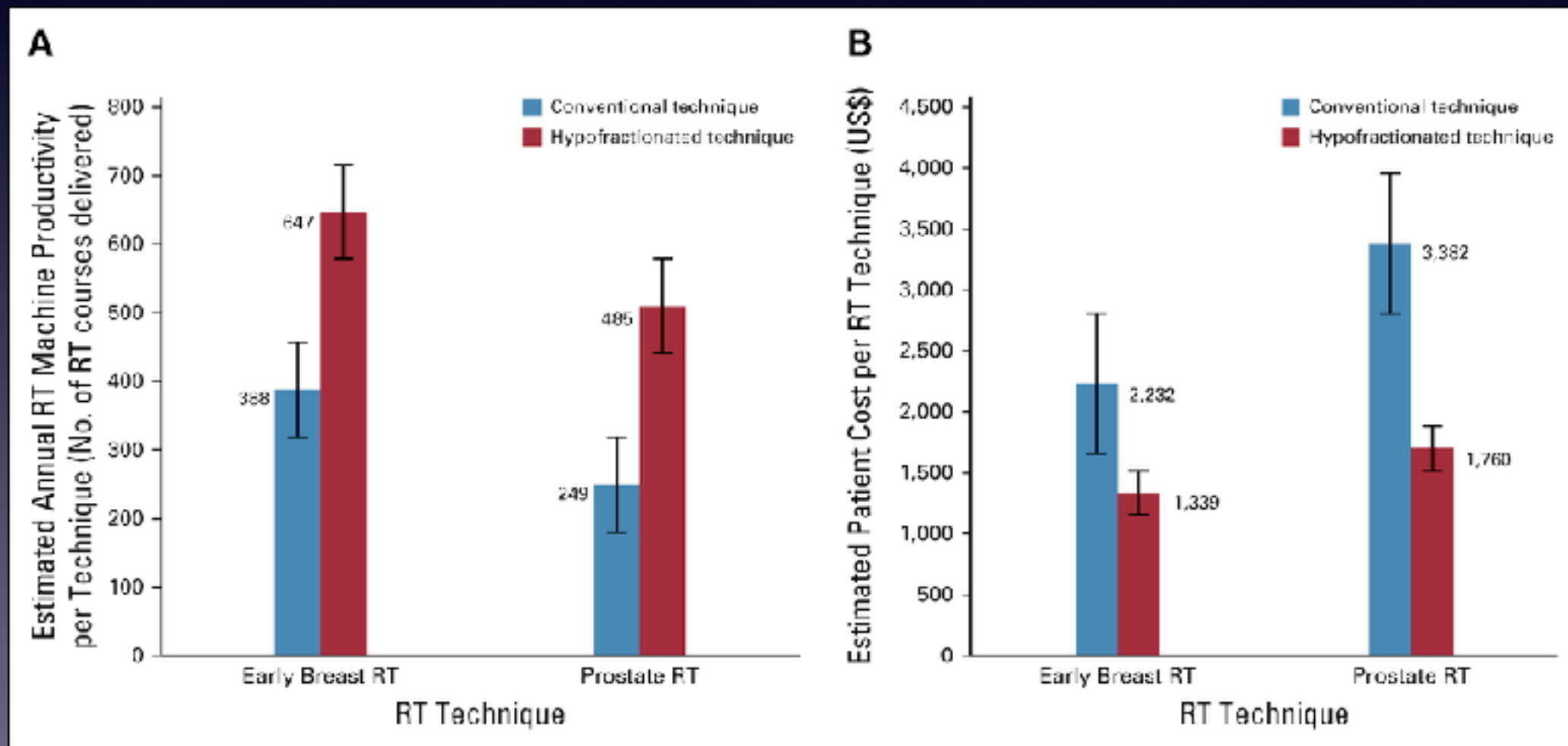
18% Fraccionamiento
Convencional

2% Ultra-Hipofraccionamiento

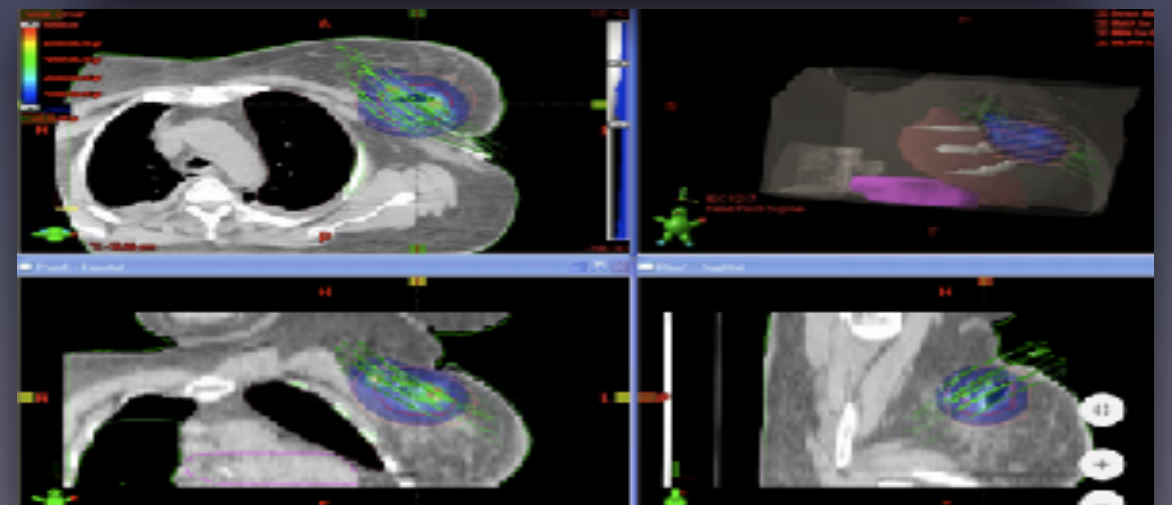


Can the Adoption of Hypofractionation Guidelines Expand Global Radiotherapy Access? An Analysis for Breast and Prostate Radiotherapy

Omoruyi Credit Irabor, MBBS, MPH^{1,2}; William Swanson, MS^{1,3}; Fiza Shaukat, BS⁴; Johanna Wirtz^{1,5}; Abba Aji Mallum, MD⁶; Twalib Ngoma, MD⁷; Ahmed Elzawawy, MD⁸; Paul Nguyen, MD²; Luca Incrocci, MD, PhD⁹; and Wilfred Ngwa, PhD^{1,2,3}

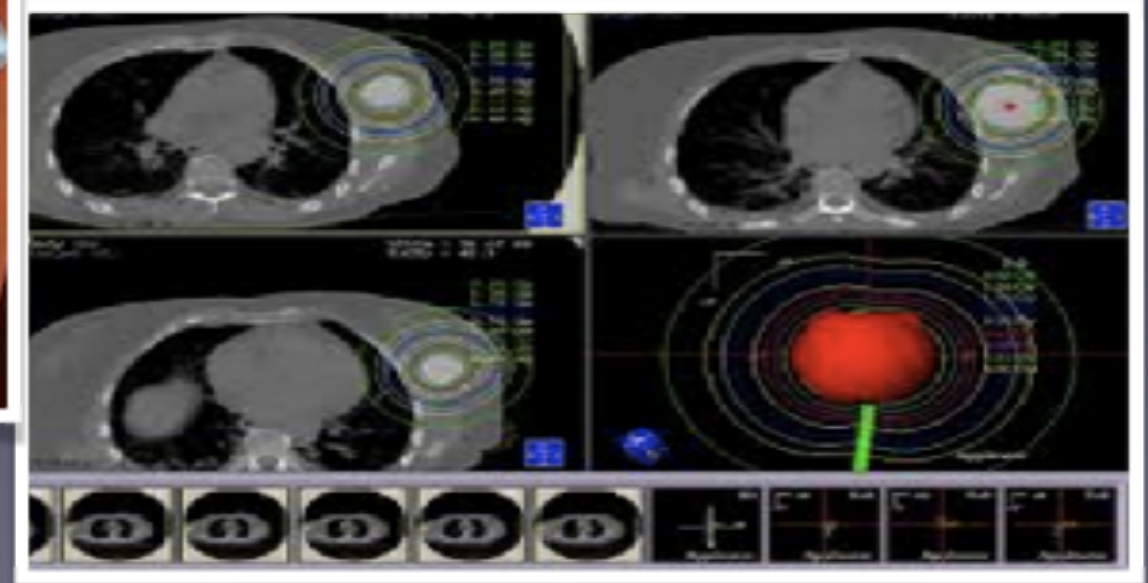
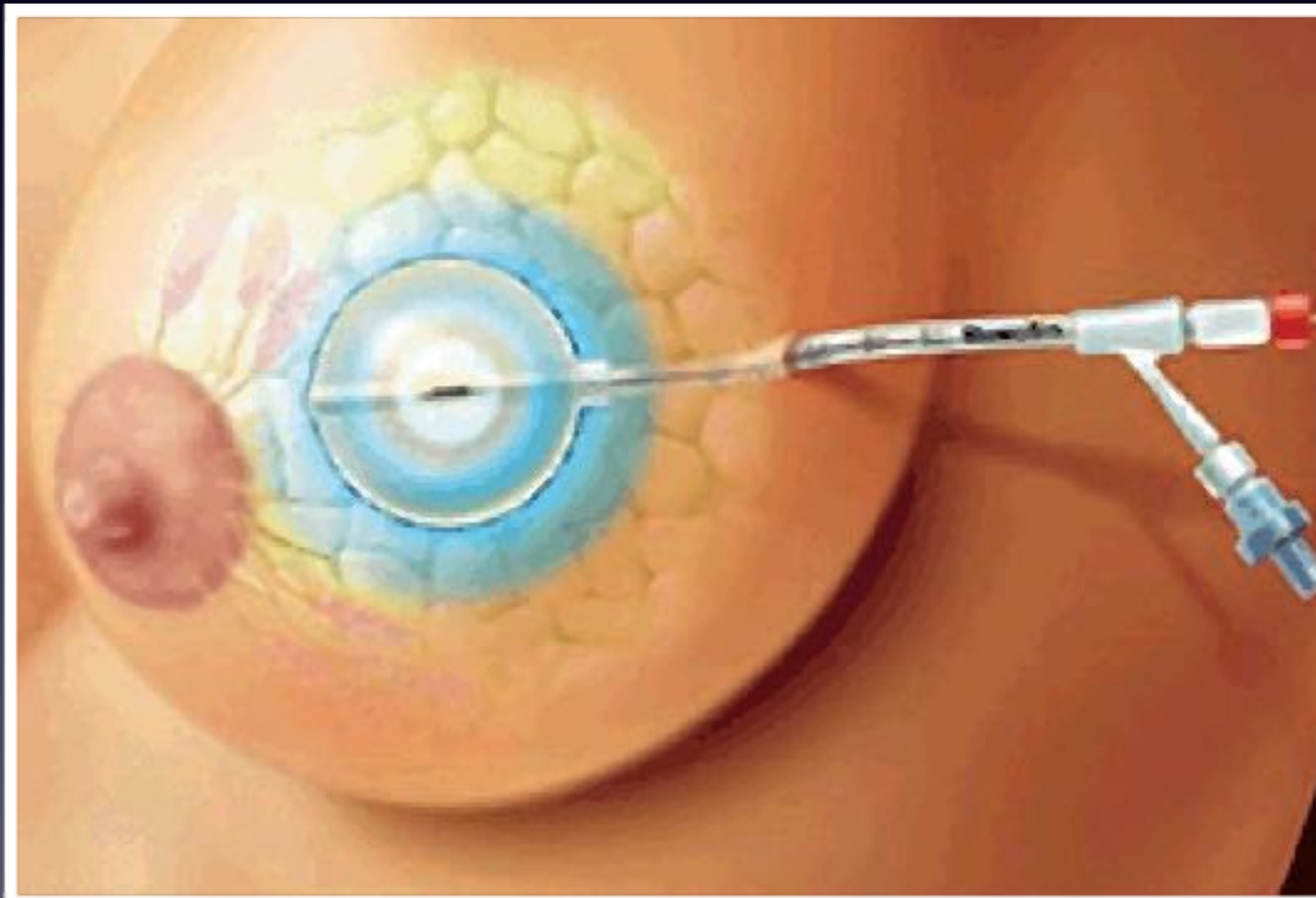


Braquiterapia de Mama



Hypofractionated and Stereotactic Radiation,
A Practical Guide. 2018

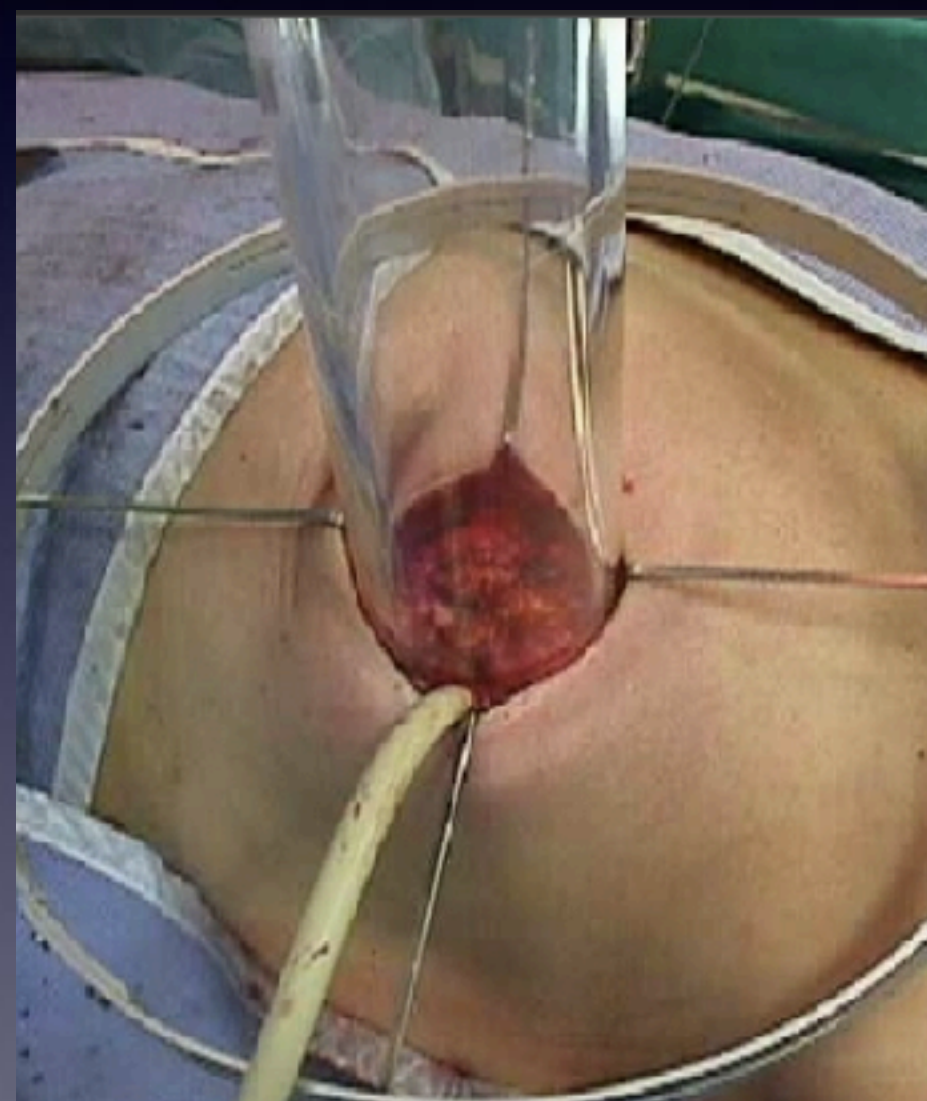
Braquiterapia de Mama



Intraoperative irradiation for early breast cancer (ELIOT): long-term recurrence and survival outcomes from a single-centre, randomised, phase 3 equivalence trial

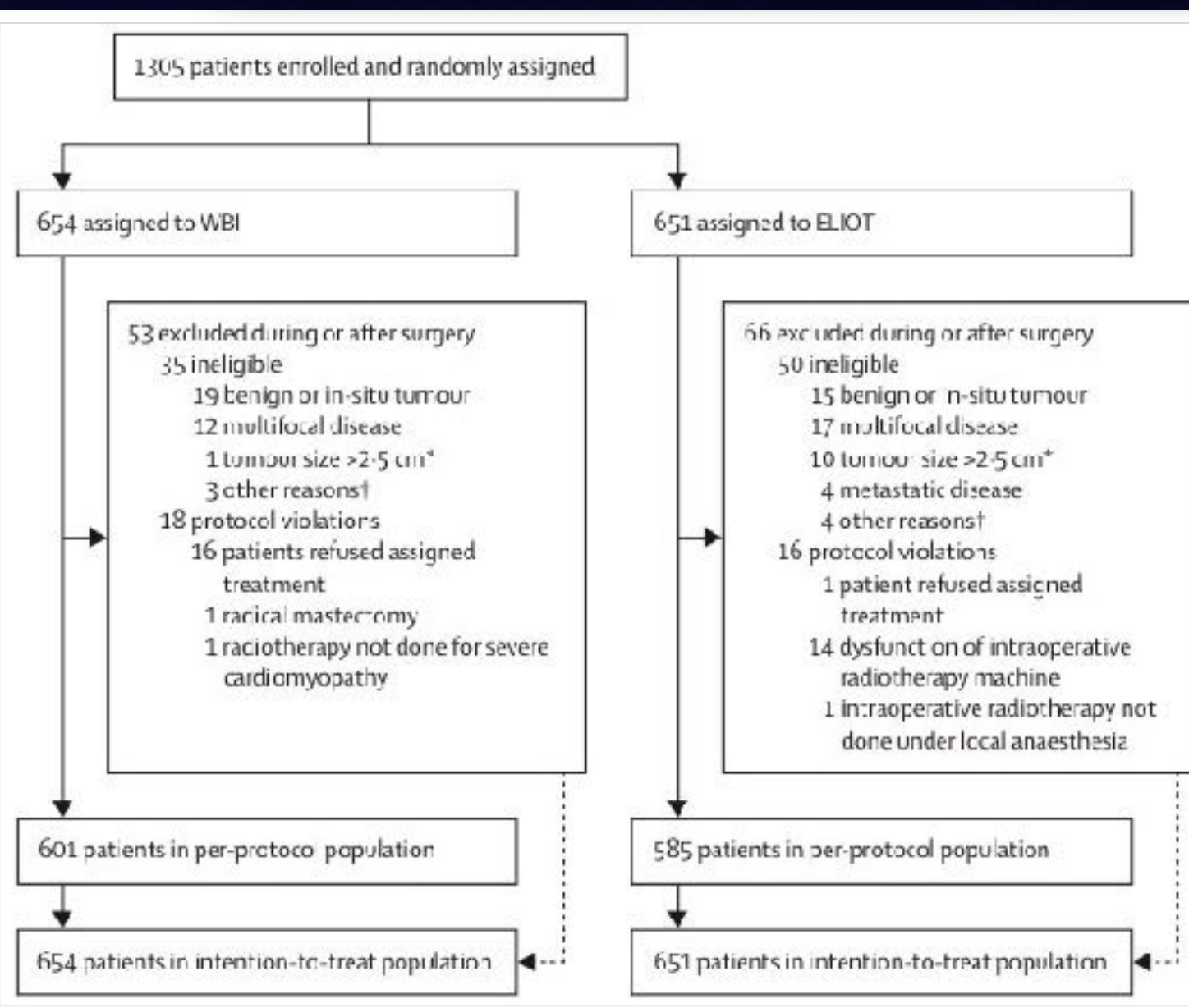
Roberto Orecchia, Umberto Veronesi*, Patrick Maisonneuve, Viviana Enrica Galimberti, Roberto Lazzari, Paolo Veronesi, Barbara Alicja Jereczek-Fossa, Federica Cattani, Claudia Sangalli, Alberto Luini, Pietro Caldarella, Marco Venturino, Daniele Sances, Stefano Zurrida*, Giuseppe Viale, Maria Cristina Leonardi†, Mattia Intra†

- 48-75 anos.
- Carcinoma unicentrico medindo até 2.5 cm.
- LN axilar negativo.
- 50 Gy(25fx) + 10 Gy(5fx) vs Dose Única 21 Gy (ELIOT).
- Objetivo Primário: Recorrência ipsilateral.

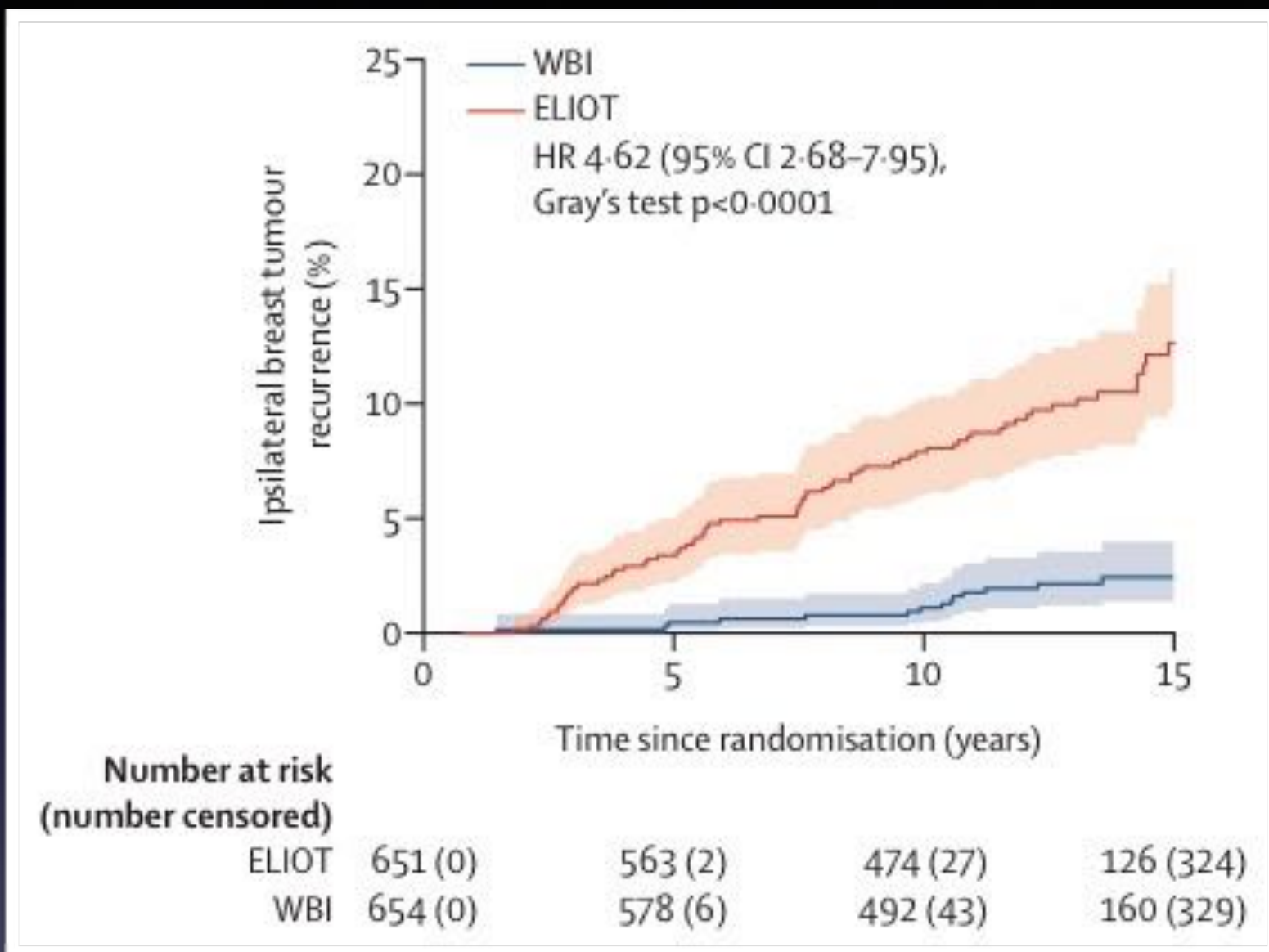


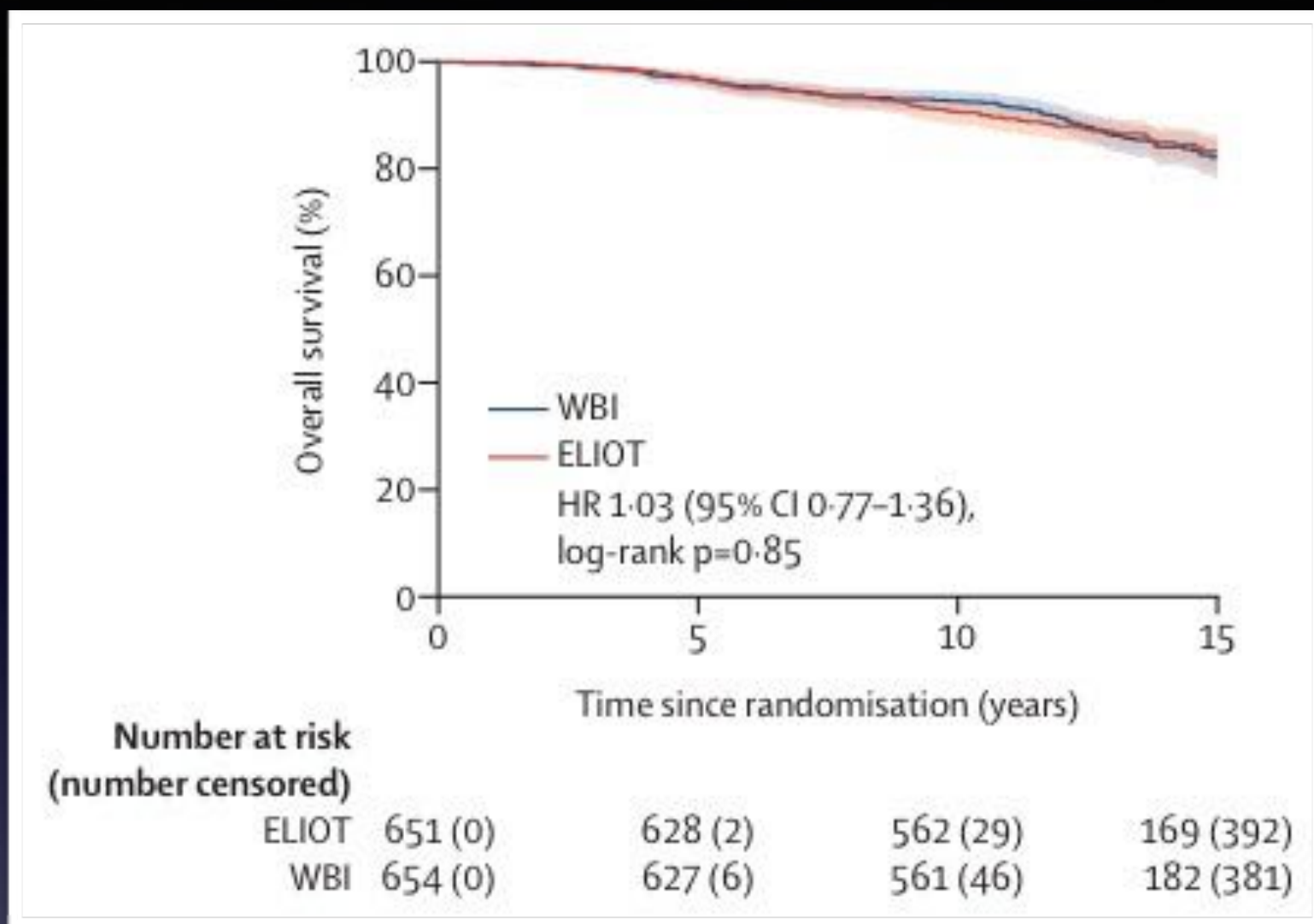
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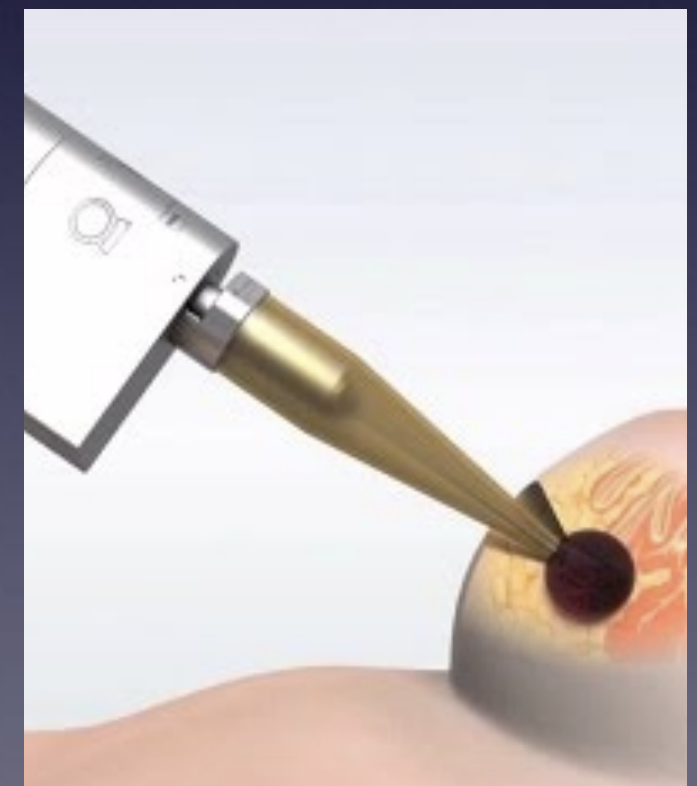
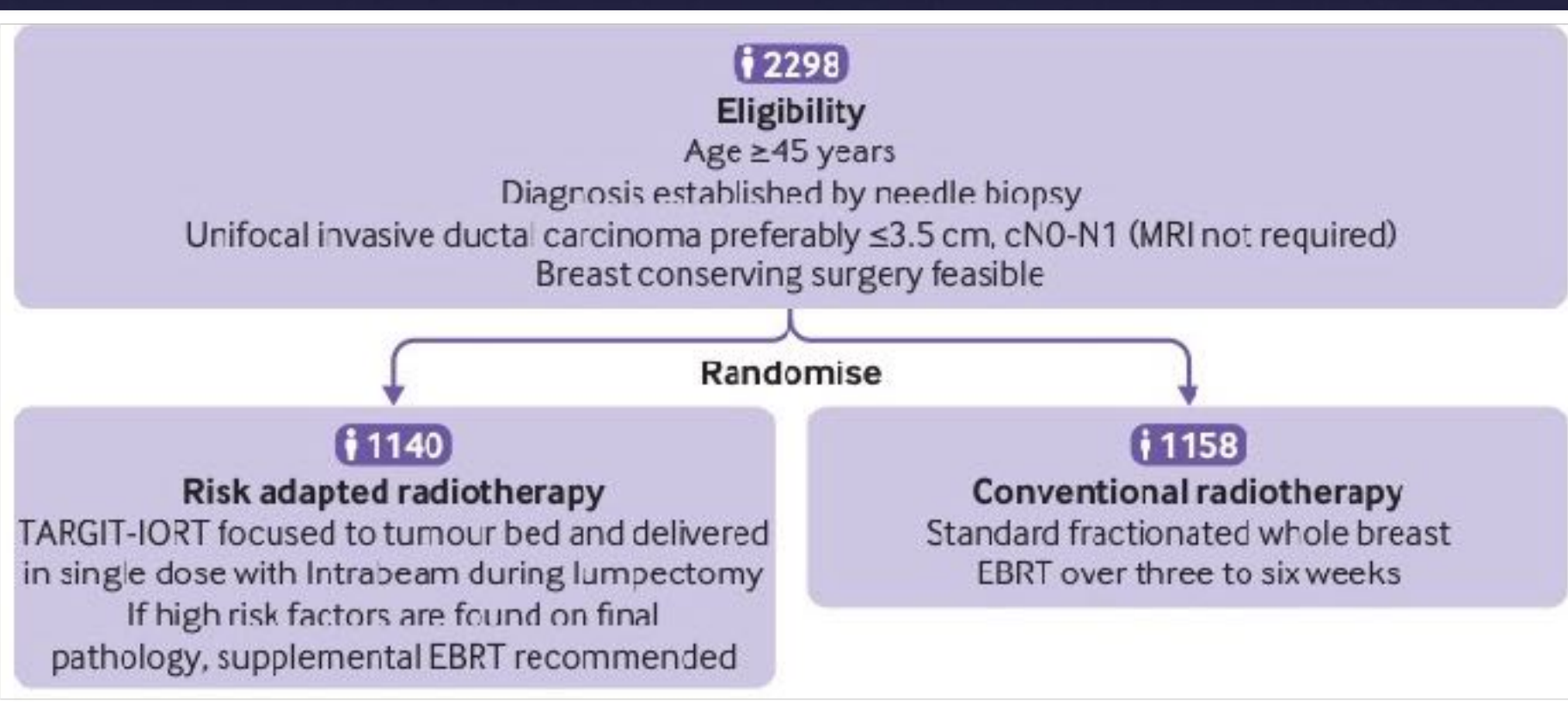
- A pele mantém-se intacta e cirurgia plástica pode ser facilmente realizada se necessário.
- Aplicação única ao invés de 6 semanas.
- Não existe atraso na administração da radioterapia, caso seja necessário quimioterapia.
- Completa proteção em pulmão e mama contralateral.





Long term survival and local control outcomes from single dose targeted intraoperative radiotherapy during lumpectomy (TARGIT-IORT) for early breast cancer: TARGIT-A randomised clinical trial

Jayant S Vaidya,¹ Max Bulsara,² Michael Baum,¹ Frederik Wenz,³ Samuele Massarut,⁴ Steffi Pigorsch,⁵ Michael Alvarado,⁶ Michael Douek,⁷ Christobel Saunders,⁸ Henrik L Flyger,⁹ Wolfgang Eiermann,⁵ Chris Brew-Graves,¹ Norman R Williams,¹ Ingrid Potyka,¹ Nicholas Roberts,¹ Marcelle Bernstein,¹⁰ Douglas Brown,¹¹ Elena Sperk,³ Siobhan Laws,¹² Marc Sütterlin,¹³ Tammy Corica,¹⁴ Steinar Lundgren,^{15,16} Dennis Holmes,¹⁷ Lorenzo Vinante,¹⁸ Fernando Bozza,¹⁹ Montserrat Pazos,²⁰ Magali Le Blanc-Onfroy,²¹ Günther Gruber,²² Wojciech Polkowski,²³ Konstantin J Dedes,²⁴ Marcus Niewald,²⁵ Jens Blohmer,²⁶ David McCready,²⁷ Richard Hofer,²⁸ Pond Kelemen,²⁹ Gloria Petralia,³⁰ Mary Falzon,³¹ David J Joseph,¹⁴ Jeffrey S Tobias³²



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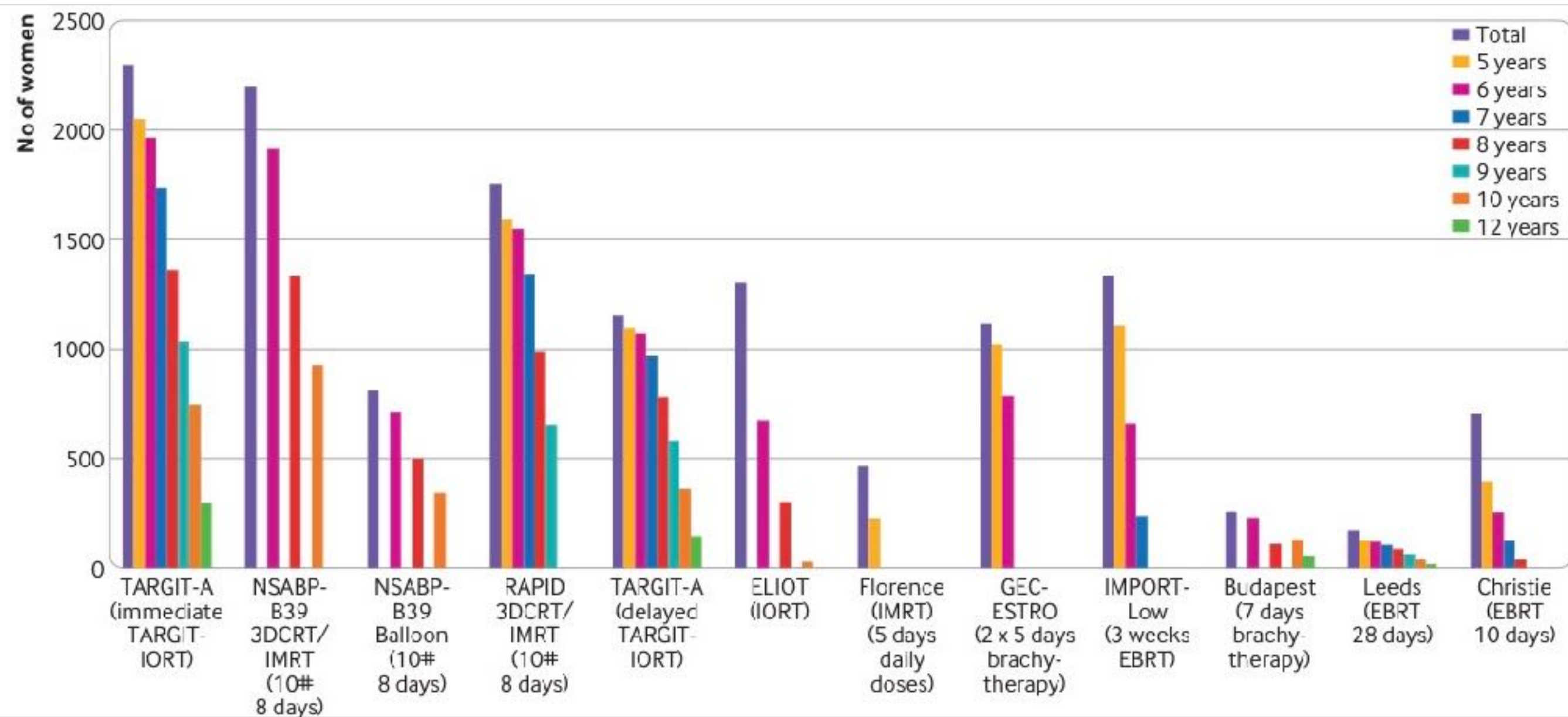
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Seguimento Médio de 8.6 anos

Sem diferença significativa foi encontrada:

- Sobrevida Livre de Recorrência Local.
- Sobrevida Livre de Mastectomia.
- Sobrevida Livre de Doença a Distância.
- Sobrevida Global.
- Mortalidade por Câncer de Mama.
- Mortalidade por outras causas foi significativamente menor.





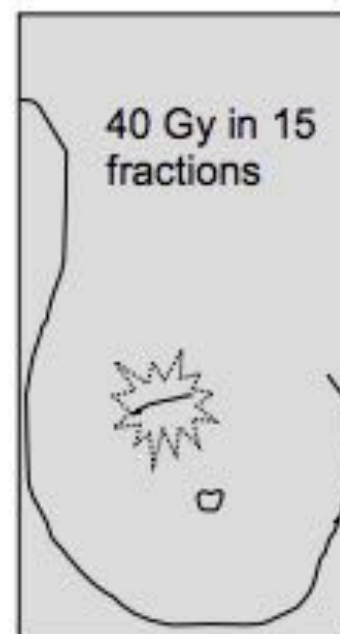
Partial-breast radiotherapy after breast conservation surgery for patients with early breast cancer (UK IMPORT LOW trial): 5-year results from a multicentre, randomised, controlled, phase 3, non-inferiority trial



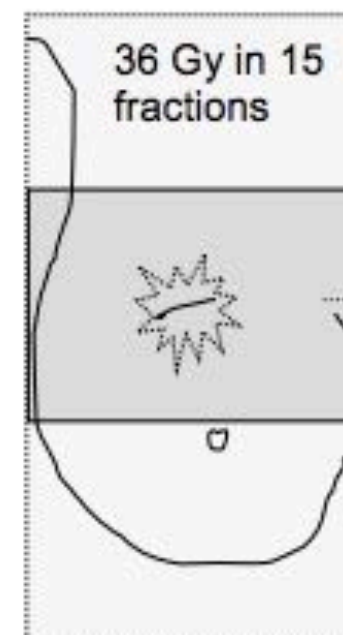
Charlotte E Coles, Clare L Griffin, Anna M Kirby, Jenny Titley, Rajiv K Agrawal, Abdulla Alhassan, Indrani S Bhattacharya, Adrian M Brunt, Laura Ciurlionis, Charlie Chan, Ellen M Donovan, Marie A Emson, Adrian N Harnett, Joanne S Haviland, Penelope Hopwood, Monica L Jefford, Ronald Kaggwa, Elinor J Sawyer, Isabel Syndikus, Yat M Tsang, Duncan A Wheatley, Maggie Wilcox, John R Yarnold*, Judith M Bliss*, on behalf of the IMPORT Trialists†



Control

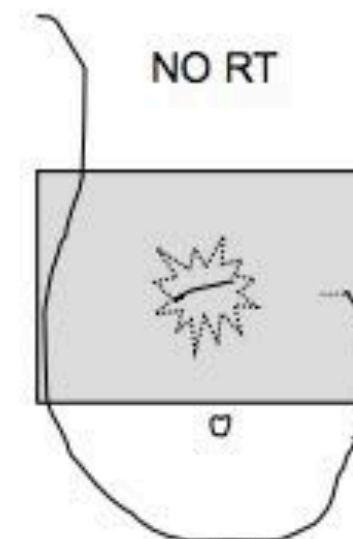


Test arm 1



40 Gy in 15 fractions

Test Arm 2



40 Gy in 15 fractions

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



Charlotte E Coles, Clare L Griffin, Anna M Kirby, Jenny Titley, Rajiv K Agrawal, Abdulla Alhassa, Indrani S Bhattacharya, Adrian M Brunt, Laura Ciurlionis, Charlie Chan, Ellen M Donovan, Marie A Emson, Adrian N Harnett, Joanne S Haviland, Penelope Hopwood, Monica L Jefford, Ronald Kaggwa, Elinor J Sawyer, Isabel Syndikus, Yat M Tsang, Duncan A Wheatley, Maggie Wilcox, John R Yarnold*, Judith M Bliss*, on behalf of the IMPORT Trialists†



Critério de inclusão

- Mulheres de 50 anos ou mais.
- Realizaram cirurgia conservadora para doença invasiva unifocal.
- Grau 1-3.
- Tumores com 3 cm ou menos.
- 0-3 linfonodos.
- Terapia endócrino foi permitida.
- Margens cirúrgicas de 2 mm ou mais.

Critérios de Exclusão

- Metástase à distância.
- Malignidade prévia de qualquer tipo.
- Realizaram mastectomia.
- Receberam quimioterapia neoadjuvante ou adjuvante.

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



Charlotte E Coles, Clare L Griffin, Anna M Kirby, Jenny Tittley, Rajiv K Agrawal, Abdulla Alhassan, Indrani S Bhattacharya, Adrian M Brunt, Laura Ciurlionis, Charlie Chan, Ellen M Donovan, Marie A Emson, Adrian N Harnett, Joanne S Haviland, Penelope Hopwood, Monica L Jefford, Ronald Kaggwa, Elinor J Sawyer, Isabel Syndikus, Yat M Tsang, Duncan A Wheatley, Maggie Wilcox, John R Yarnold*, Judith M Bliss*, on behalf of the IMPORT Trialists†



	Cumulative number of events, n/N (%)	5-year cumulative incidence, % (95% CI)	Hazard ratio* (95% CI)	p value†
Local relapse				
Whole breast	9/674 (1%)	1.1% (0.5–2.3)	1	..
Reduced dose	3/673 (<1%)	0.2% (0.02–1.2)	0.33 (0.09–1.20)	0.077
Partial breast	6/669 (1%)	0.5% (0.2–1.4)	0.65 (0.23–1.84)	0.420
Local-regional relapse				
Whole breast	9/674 (1%)	1.1% (0.5–2.3)	1	..
Reduced dose	3/673 (<1%)	0.2% (0.02–1.2)	0.33 (0.09–1.21)	0.077
Partial breast	8/669 (1%)	0.8% (0.3–1.8)	0.88 (0.34–2.27)	0.761
Distant relapse				
Whole breast	13/674 (2%)	1.4% (0.7–2.6)	1	..
Reduced dose	10/673 (1%)	1.5% (0.8–2.8)	0.77 (0.34–1.75)	0.525
Partial breast	12/669 (2%)	1.6% (0.8–2.9)	0.92 (0.42–2.03)	0.838
Any breast-cancer-related event				
Whole breast	33/674 (5%)	3.7% (2.5–5.4)	1	..
Reduced dose	24/673 (4%)	3.4% (2.2–5.1)	0.72 (0.43–1.22)	0.223
Partial breast	33/669 (5%)	4.0% (2.8–5.9)	1.00 (0.62–1.62)	0.982
All-cause mortality				
Whole breast	40/674 (6%)	5.0% (3.6–7.0)	1	..
Reduced dose	39/673 (6%)	4.1% (2.8–5.9)	0.97 (0.62–1.50)	0.883
Partial breast	37/669 (6%)	3.7% (2.5–5.4)	0.91 (0.58–1.42)	0.693

	Whole breast (n=674)	Reduced dose (n=673)	Partial breast (n=669)	Total (n=2016)
Local relapse	9* (1%)	3† (<1%)	5 (1%)	18 (1%)
Within radiotherapy field‡	9 (1%)	1 (<1%)	4 (1%)	14 (1%)
Borderline with radiotherapy field	0	0	1 (<1%)	1 (<1%)
Not documented	0	2 (<1%)	1 (<1%)	3 (<1%)
Contralateral breast second primary	12 (2%)	13 (2%)	13 (2%)	38 (2%)
Invasive	10 (1%)	11 (2%)	11 (2%)	32 (2%)
DCIS	2 (<1%)	2 (<1%)	2 (<1%)	6 (<1%)
Non-breast second primary	35 (5%)	37 (5%)	24 (4%)	96 (5%)
Colorectal	105 (1%)	7 (1%)	3 (<1%)	20 (1%)
Lung	115 (2%)	4 (1%)	4 (1%)	19 (1%)
Gynaecological	5 (1%)	8 (1%)	4 (1%)	17 (1%)
Other¶	4 (1%)	3 (<1%)	1 (<1%)	8 (<1%)
Oesophagus	0	3 (<1%)	3 (<1%)	6 (<1%)
Pancreas	1 (<1%)	2 (<1%)	3 (<1%)	6 (<1%)
Lymphoma	0	2 (<1%)	3 (<1%)	5 (<1%)
Genitourinary	3 (<1%)	1 (<1%)	0	4 (<1%)
Head and neck	1 (<1%)	2 (<1%)	0	3 (<1%)
Liver	0	2 (<1%)	1 (<1%)	3 (<1%)
Cancer of unknown primary	0	0	2 (<1%)	2 (<1%)
Peritoneal	0	2 (<1%)	0	2 (<1%)
Sarcoma	1 (<1%)	1 (<1%)	0	2 (<1%)
Deaths	40 (6%)	39 (6%)	37 (6%)	116 (6%)
Breast cancer	9** (1%)	7†† (1%)	10††† (1%)	26 (1%)
Second cancer	14 (2%)	16 (2%)	12 (2%)	42 (2%)
Cardiac	5 (1%)	2 (<1%)	2 (<1%)	9 (<1%)
Cerebrovascular accident	1 (<1%)	2 (<1%)	1 (<1%)	4 (<1%)
Pulmonary embolism	0	2 (<1%)	0	2 (<1%)
Other	11 (2%)	10 (1%)	10 (1%)	31 (2%)
Unknown	0	0	2 (<1%)	2 (<1%)

	Cumulative number of adverse events			Adverse events at 5 years	
	n/N (%)	5-year cumulative incidence*, % (95% CI)	HR (95% CI), p value†	n/N (%)	p value‡
Protocol-specific items					
Breast appearance changed					
Whole breast	158/411 (38%)	47.7% (41.1–54.8)	1	80/295 (27%)	..
Reduced dose	123/433 (28%)	36.7% (30.6–43.6)	0.74 (0.54–1.00), p=0.051	66/325 (20%)	0.047
Partial breast	113/421 (27%)	35.1% (28.7–42.5)	0.64 (0.46–0.89), p=0.007	49/331 (15%)	<0.0001
Breast smaller					
Whole breast	119/411 (29%)	37.3% (30.9–44.4)	1	66/294 (22%)	..
Reduced dose	110/433 (25%)	31.9% (26.3–38.4)	0.83 (0.59–1.16), p=0.280	63/326 (19%)	0.373
Partial breast	104/421 (25%)	34.7% (27.5–43.0)	0.78 (0.54–1.11), p=0.162	56/331 (17%)	0.086
Breast harder or firmer					
Whole breast	115/411 (28%)	35.3% (28.4–43.3)	1	27/292 (9%)	..
Reduced dose	74/433 (17%)	21.0% (16.2–26.9)	0.53 (0.36–0.79), p=0.002	23/325 (7%)	0.376
Partial breast	58/421 (14%)	15.3% (12.0–19.5)	0.47 (0.32–0.71), p<0.0001	15/330 (5%)	0.024
Shoulder stiffness					
Whole breast	56/411 (14%)	19.3% (14.0–26.5)	1	12/295 (4%)	..
Reduced dose	56/433 (13%)	19.3% (13.9–26.4)	0.93 (0.64–1.35), p=0.701	22/328 (7%)	0.161
Partial breast	58/421 (14%)	15.3% (12.0–19.5)	1.06 (0.73–1.54), p=0.756	13/331 (4%)	0.999
Skin appearance changed					
Whole breast	63/411 (15%)	21.0% (15.5–27.9)	1	22/294 (7%)	..
Reduced dose	59/433 (14%)	17.9% (13.2–24.0)	1.07 (0.68–1.68), p=0.775	23/325 (7%)	0.878
Partial breast	49/421 (12%)	14.6% (10.4–20.5)	0.87 (0.54–1.40), p=0.569	12/330 (4%)	0.051
EORTC QLQ-BR23					
Arm or shoulder pain					
Whole breast	98/411 (24%)	32.6% (26.3–39.9)	1	33/297 (11%)	..
Reduced dose	104/433 (24%)	30.1% (24.7–36.4)	0.94 (0.71–1.25), p=0.678	43/329 (13%)	0.465
Partial breast	97/421 (23%)	27.2% (21.9–33.6)	0.97 (0.73–1.28), p=0.809	24/331 (7%)	0.097
Swollen arm or hand					
Whole breast	21/411 (5%)	6.2% (4.1–9.5)	1	5/295 (2%)	..
Reduced dose	26/433 (6%)	9.8% (6.2–15.3)	1.19 (0.67–2.11), p=0.558	15/330 (5%)	0.066
Partial breast	16/421 (4%)	4.4% (2.7–7.3)	0.59 (0.30–1.15), p=0.123	2/330 (1%)	0.264
Difficulty raising arm					
Whole breast	42/411 (10%)	13.6% (9.2–19.8)	1	10/297 (3%)	..
Reduced dose	45/433 (10%)	14.0% (9.8–19.8)	0.98 (0.64–1.50), p=0.913	17/328 (5%)	0.326
Partial breast	47/421 (11%)	13.5% (10.1–18.0)	1.08 (0.71–1.64), p=0.726	15/331 (5%)	0.542

(Table 4 continues on next page)

	Cumulative number of adverse events			Adverse events at 5 years	
	n/N (%)	5-year cumulative incidence*, % (95% CI)	HR (95% CI), p value†	n/N (%)	p value‡
Worst normal-tissue effects					
Whole breast	134/674 (20%)	27.6% (22.5–33.6)	1	60/457 (13%)	..
Reduced dose	108/673 (16%)	21.1% (17.2–25.7)	0.77 (0.60–0.99), p=0.043	48/480 (10%)	0.152
Partial breast	94/669 (14%)	20.0% (15.6–25.4)	0.69 (0.53–0.90), p=0.006	49/474 (10%)	0.221
Breast shrinkage					
Whole breast	79/674 (12%)	18.4% (13.7–24.5)	1	41/452 (9%)	..
Reduced dose	70/673 (10%)	13.6% (10.6–17.5)	0.86 (0.62–1.18), p=0.345	37/478 (8%)	0.480
Partial breast	61/669 (9%)	13.9% (10.1–19.0)	0.78 (0.56–1.08), p=0.134	33/472 (7%)	0.276
Breast induration (index)					
Whole breast	63/674 (9%)	12.7% (9.5–16.8)	1	21/453 (5%)	..
Reduced dose	43/673 (6%)	8.4% (6.0–11.6)	0.66 (0.45–0.98), p=0.040	13/474 (3%)	0.161
Partial breast	48/669 (7%)	10.8% (7.7–15.1)	0.77 (0.53–1.12), p=0.165	24/471 (5%)	0.762
Breast induration (outside index)§					
Whole breast	15/674 (2%)	2.3% (1.4–3.8)	1	2/450 (<1%)	..
Reduced dose	10/673 (1%)	2.1% (1.0–4.1)	0.66 (0.30–1.48), p=0.310	2/464 (<1%)	>0.999
Telangiectasia					
Whole breast	8/674 (1%)	1.6% (0.8–3.3)	1	3/445 (1%)	..
Reduced dose	8/673 (1%)	3.0% (1.3–6.8)	0.96 (0.36–2.57), p=0.976	6/468 (1%)	0.507
Partial breast	5/669 (1%)	0.6% (0.2–1.7)	0.62 (0.21–1.92), p=0.401	4/465 (1%)	>0.999
Breast oedema					
Whole breast	24/674 (4%)	4.0% (2.6–6.2)	1	4/446 (1%)	..
Reduced dose	18/673 (3%)	3.2% (2.0–5.3)	0.74 (0.40–1.37), p=0.338	2/468 (<1%)	0.441
Partial breast	11/669 (2%)	1.7% (0.9–3.0)	0.46 (0.23–0.94), p=0.029	0/468	0.056
Other radiotherapy related					
Whole breast	11/674 (2%)	1.7% (1.0–3.1)	1	3/457 (1%)	..
Reduced dose	9/673 (1%)	1.4% (0.7–2.6)	0.81 (0.34–1.97), p=0.646	0/480	0.263
Partial breast	6/669 (1%)	0.9% (0.4–2.0)	0.55 (0.20–1.49), p=0.234	0/474	0.221
HR=hazard ratio. *Estimated at 5 years and 3 months. †Log-rank test. ‡Fisher's exact test. §No cases of moderate or marked breast induration (outside index) were reported in the partial-breast group.					

Table 5: Clinician assessment of moderate or marked late adverse events

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



Charlotte E Coles, Clare L Griffin, Anna M Kirby, Jenny Titley, Rajiv K Agrawal, Abdulla Alhasso, Indrani S Bhattacharya, Adrian M Brunt, Laura Ciurlionis, Charlie Chan, Ellen M Donovan, Marie A Emson, Adrian N Harrett, Joanne S Haviland, Penelope Hapwood, Monica L Jefford, Ronald Kaggwa, Elinor J Sawyer, Isabel Syndikus, Yat M Tsang, Duncan A Wheatley, Maggie Wilcox, John R Yarnold*, Judith M Bliss*, on behalf of the IMPORT Trialists†



- A simplicidade do IMPORT LOW é um ponto forte!
- A maioria das pacientes tinham tumores de pequeno tamanho, baixo grau, RH +, linfonodos negativos.
- Mas independente da baixa proporção de pacientes com alto risco, esses pacientes tiveram 8 das 18 falhas locais.
- **RADIOTERAPIA PARCIAL DE MAMA PODE SER CONSIDERADA EM MULHERES COM 50 ANOS OU MAIS, GRAU 1-2, TUMOR COM 3 CM OU MENOS, RH +, HER2 NEGATIVO, N0, MARGEM CIRÚRGICA COM MÍNIMO DE 1 MM.**

Dr Duncan Wheatley
Royal Cornwall Hospital, UK

First results of FAST-Forward phase III RCT nodal substudy: 3-year normal tissue effects

Duncan Wheatley, Jo Haviland, Jaymini Patel, Mark Sydenham, Abdulla Alhasso, Charlie Chan, Suzy Cleator, Charlotte Coles, Ellen Donovan, Anna Kirby, Cliona Kirwan, Zohal Nabi, Elinor Sawyer, Navita Somaiah, Isabel Syndikus, Karen Venables, John Yarnold, Murray Brunt, Judith Bliss on behalf of the FAST-Forward Trial Management Group

FAST-Forward Nodal Sub-study: Conclusions

- At 2-3 years' follow-up no early indication that levels of arm / shoulder NTEs different for 26 Gy/5Fr compared with 40 Gy/15Fr
- Definitive assessment of non-inferiority will await 5-year formal primary analysis
- Efficacy outcomes will be assessed in meta-analysis with FAST-Forward main trial (N~4000) at 5 years' follow-up

Obrigado!



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OUTUBRO ROSA
MOVIMENTO DE CONSCIENTIZAÇÃO
SOBRE O CÂNCER DE MAMA

Obrigado!

