Young boost randomized phase III trial of high vs low boost radiation in young breast cancer patients: 10-year results

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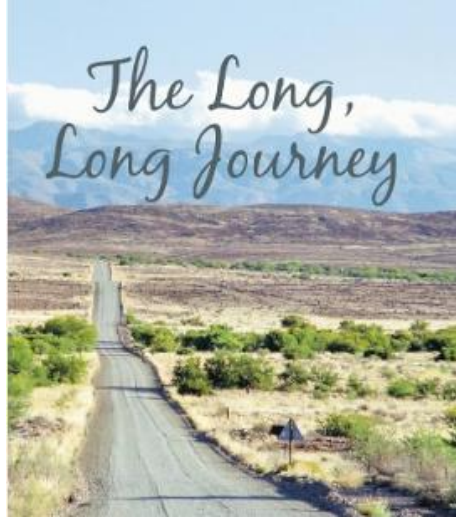
No disclosures

How it started..



The New England Journal of Medicine

RECURRENCE RATES AFTER TREATMENT OF BREAST CANCER WITH STANDARD RADIOTHERAPY WITH OR WITHOUT ADDITIONAL RADIATION

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Bartelink H, Horiot JC, Poortmans P, Struikmans H, Van den Bogaert W, Barillot I, Fourquet A, Borger J, Jager J, Hoogenraad W, Collette L, Pierart M; European Organization for Research and Treatment of Cancer Radiotherapy and Breast Cancer Groups. Recurrence rates after treatment of breast cancer with standard radiotherapy with or without additional radiation. **N Engl J Med. 2001** Nov 8;345(19):1378-87. doi: 10.1056/NEJMoa010874. PMID: 11794170.

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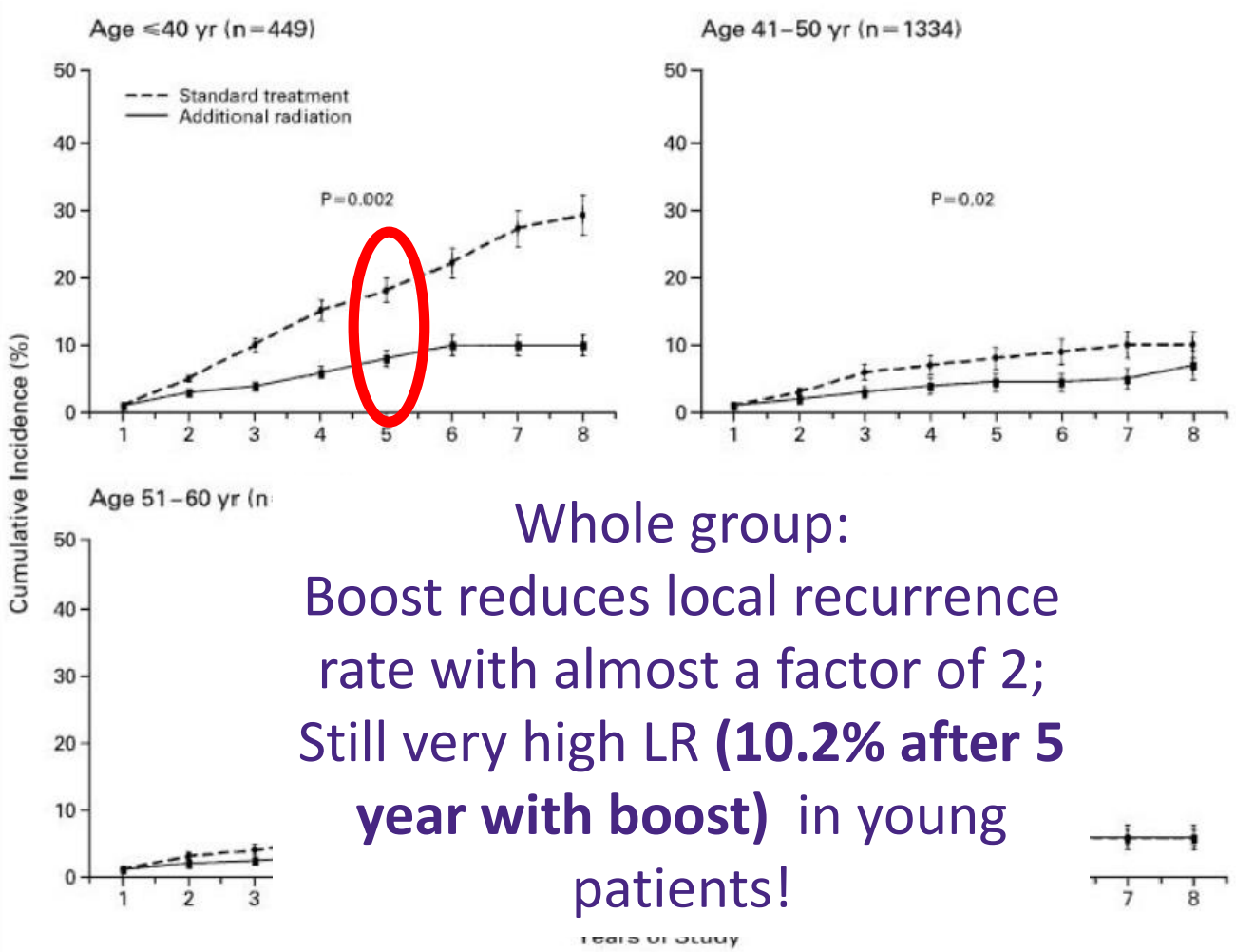
How it started: 5-year results of boost no boost trial

Breast conserving therapy for early breast cancer in 2001:

Breast conserving surgery + whole breast RT 25 x 2 Gy

Boost-no-Boost trial EORTC 22881/10882:

Randomisation between 8 x 2 Gy boost to tumor bed vs no boost



Whole group:
Boost reduces local recurrence rate with almost a factor of 2;
Still very high LR **(10.2% after 5 year with boost)** in young patients!

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Key question:

Can we improve local control in young breast cancer patients, by increasing the boost dose to 26 Gy ?

youngBoost

The Intergroup Trial of the BOOG

"The Young Boost Trial"

BOOG 2004-01; CKTO 2003-13

Radiation dose intensity study in breast cancer in young women: a randomized phase III trial of additional dose to the tumor bed

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How it started..: the FLIMS workshop in 2002

Conferences & Courses involving EORTC

Methods in Clinical Cancer Research (FLIMS)

June 2002

Venue: Waldhaus, flims, Switzerland

Organised by EORTC, ESMO, and AACR
Has provided training to over 1900 investigators from all over the world since its' inception in 1999.

One-week workshop:
You come with an concept protocol;

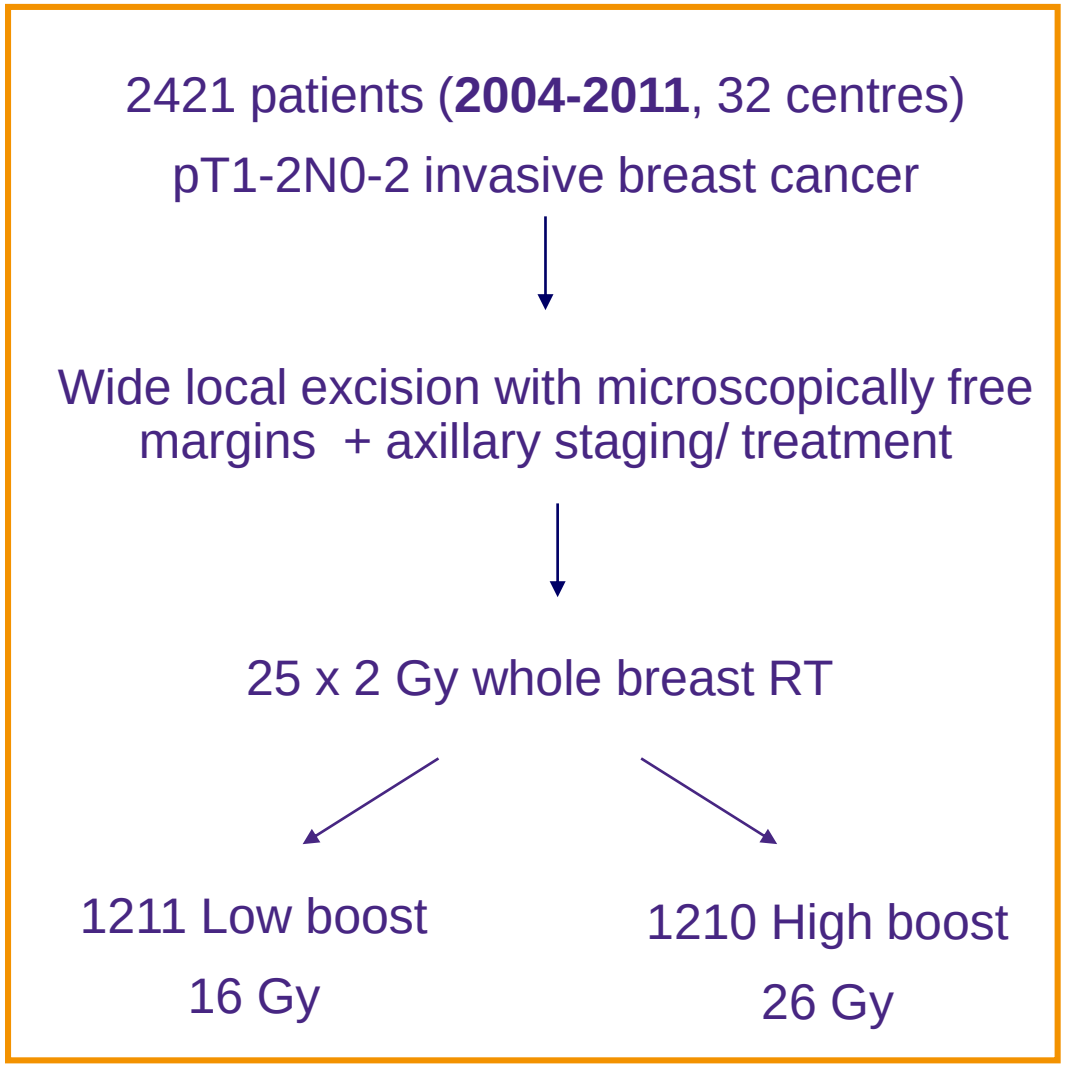
You leave with a full protocol!

First year after residency in AvL, Amsterdam…

Material & Methods

- Main endpoint: local control at **10 years**
- Design 3.5% difference (92% → 95,5%)

- Secondary endpoints
  - Fibrosis
  - Cosmetic outcome*



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** Brouwers et al R&0 2016; 2018*

Baseline characteristics

	16 Gy (n=1211)	26 Gy (n=1210)	Total (n = 2421)
Age, median	45 (19-51)	45 (21-51)	45 (19-51)
pT-stage			
T1	822 (68%)	837 (70%)	1659 (69%)
T2	382 (32%)	361 (30%)	743 (31%)
pN-stage			
N0	849 (70%)	844 (70%)	1693 (70%)
N+	356 (30%)	361 (30%)	717 (30%)
Grade			
1	152 (17%)	166 (18%)	318 (18%)
2	399 (45%)	418 (46%)	817 (45%)
3	340 (38%)	328 (36%)	668 (37%)
Subtype			
ER+HERneu-	538 (68%)	525 (66%)	1063 (67%)
HERneu+	106 (13%)	107 (13%)	213 (13%)
TNBC	150 (19%)	169 (21%)	319 (20%)

Final margin
97% complete
3% foc incomplete

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Treatment

	16 Gy (n=1211)	26 Gy (n=1210)	Total (n = 2421)
Boost technique			
X-ray beams	882 (74%)	895 (76%)	1777 (75%)
Electrons	264 (22%)	214 (18%)	478 (20%)
Other	50 (4%)	69 (6%)	119. (5%)
SIB			
Yes	416 (35%)	416 (35%)	832 (35%)
No	783 (65%)	768 (65%)	1551 (65%)
Systemic treatment			
Yes	934 (79%)	899 (77%)	1833 (78%)
No	247 (21%)	263 (23%)	510 (22%)
Type of treatment			
Chemo and hormo	477 (41%)	460 (40%)	937 (40%)
Chemo	238 (21%)	229 (20%)	467 (20%)
Hormo	191 (17%)	192 (17%)	383 (17%)

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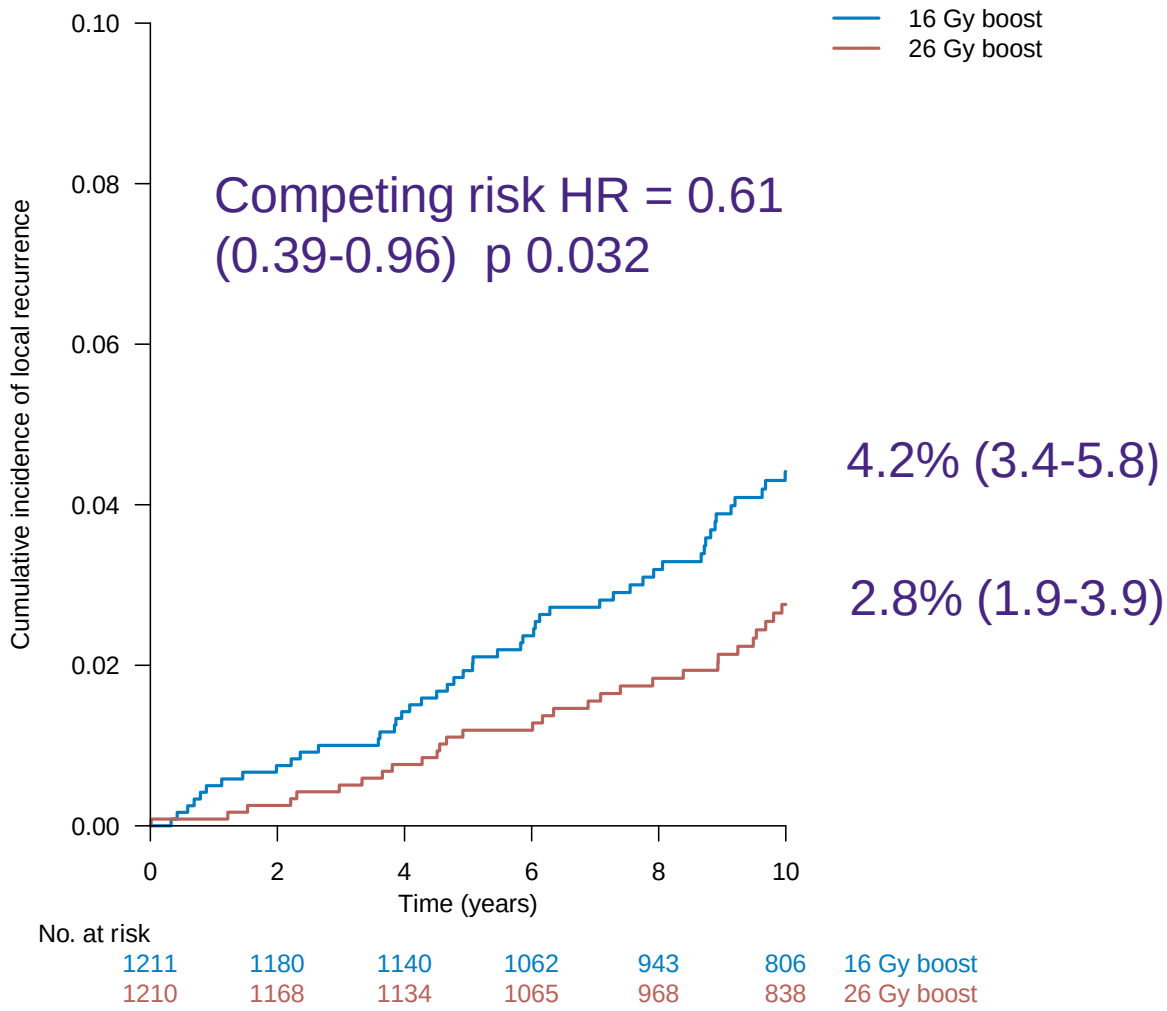
10- year local recurrence risk

- All new tumors ipsilateral breast counted as LR
- Median FUP 11.7 yrs; n = 109 LR
  - 61 low boost (1st event 42)
  - 48 high boost (1st event 23)
- Death competing risk (n = 200)



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Multivariable model

Variable	Level	HR (95% CI)	P-value
Randomized treatment	1= 16 Gy 2 = 26 Gy	1 0.39 (0.20-0.76)	 **0.006**
Age		0.96 (0.91-1.02)	0.15
Final margin status	Complete Focally incomplete	1 4.14 (1.24-13.86)	 **0.021**
Subtype	ER+HER2- HER+ TNBC	1 0.50 (0.12-2.19) 2.64 (1.06-6.57)	 0.36 **0.037**
In situ component	None DCIS	1 1.48 (0.77-2.83)	 0.24
Chemotherapy	No Yes	1 0.27 (0.12-0.60)	 **0.0013**
Hormonal treatment	No Yes	1 0.73 (0.34-1.59)	 0.43

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Cosmetic outcome

	Number of patients (%) with satisfactory cosmesis					
	Baseline			**4 yrs**		
	16 Gy	26 Gy	*p-value*	16 Gy	26 Gy	*p-value*
BCCT.core	741/831 (89%)	745/82 (90%)	0.52	265/397 (67%)	225/408 (55%)	**0.009**
Physician	774/970 (80%)	771/988 (78%)	0.35	484/749 (65%)	391/753 (52%)	**<0.0001**
Patients	415/604 (69%)	406/604 (67%)	0.62	**361/577 (63%)**	**307/584 (53%)**	**0.0007**

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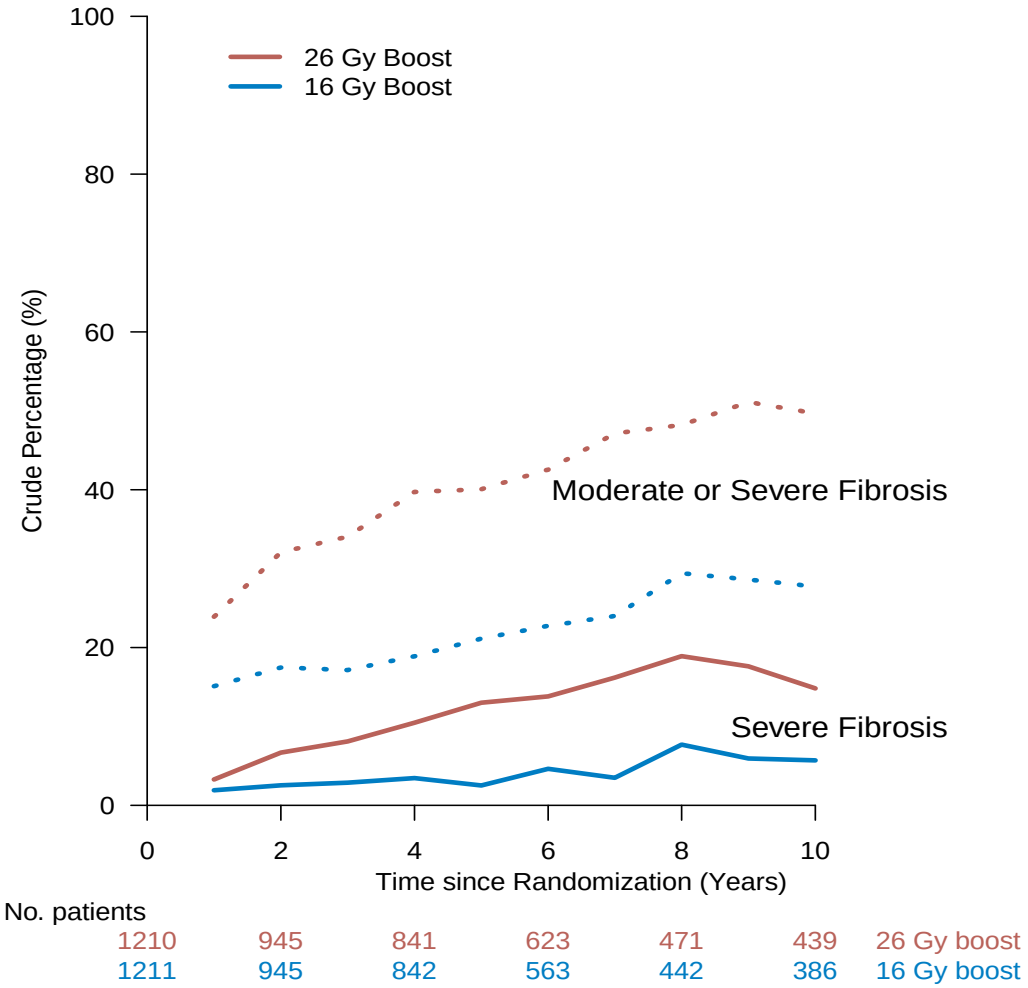
** Brouwers et al R&O 2016; 2018*

Fibrosis



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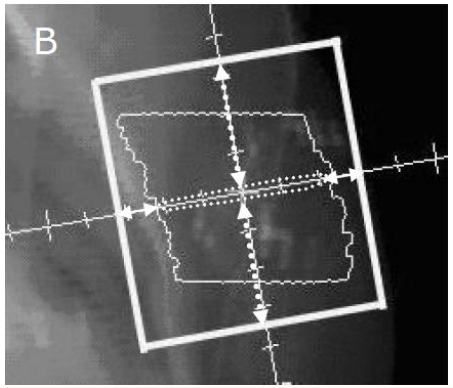
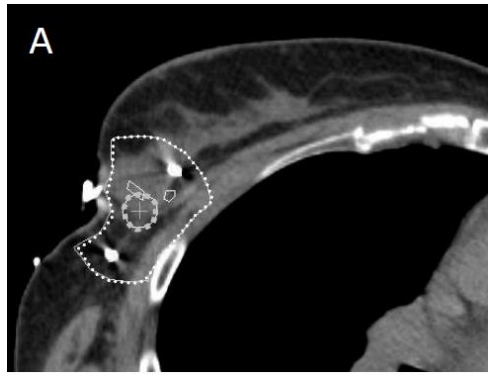
Comparison boost-no boost trial vs Young Boost

1989-1996



Simulator based RT fields

2004-2011



CT-based RT plans

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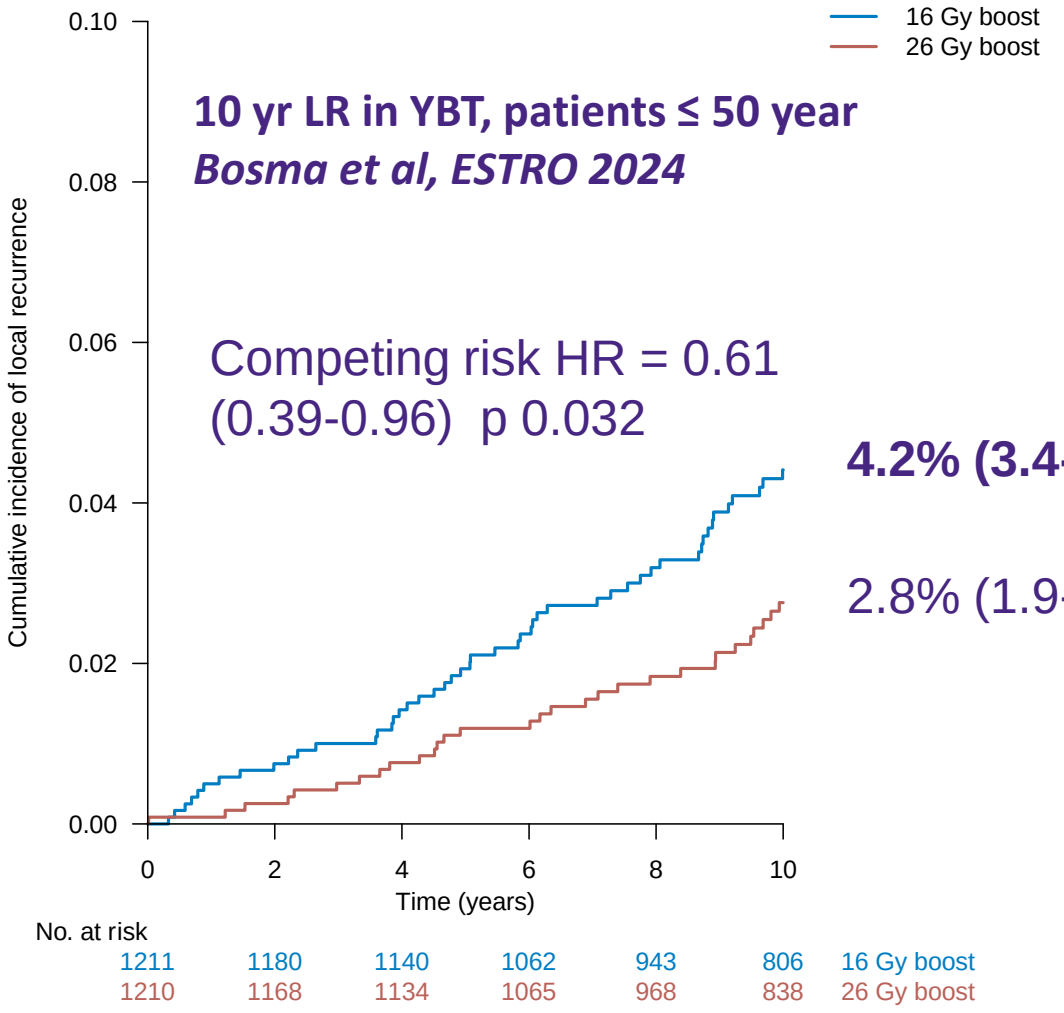
Comparison local control Young Boost vs boost-no boost trial



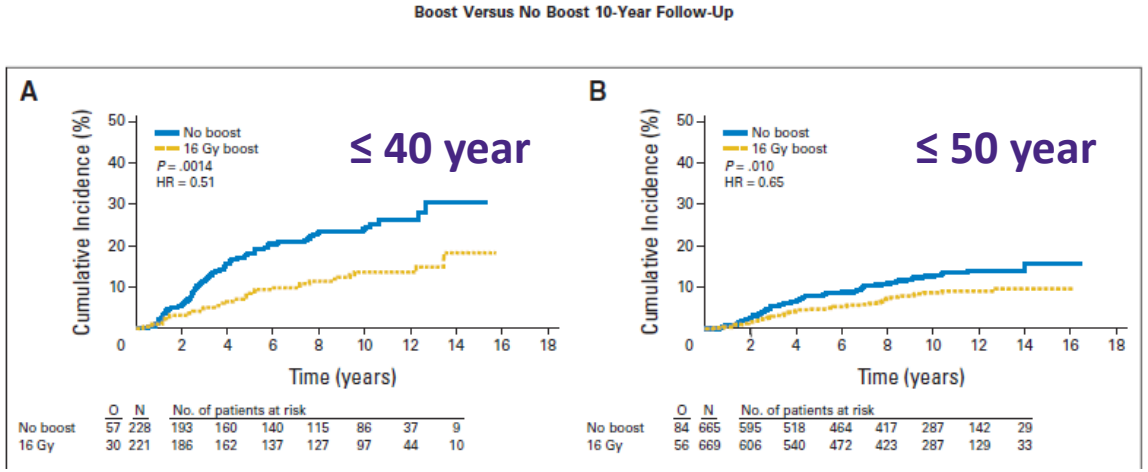
10 yr LR in YBT, patients ≤ 50 year

Bosma et al, ESTRO 2024

Competing risk HR = 0.61
(0.39-0.96) p 0.032

4.2% (3.4-5.8)

2.8% (1.9-3.9)



10 yr LR in boost arm ≤ 50 year ≈10%

Bartelink et al JCO 2007

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Local recurrence rate in historical perspective

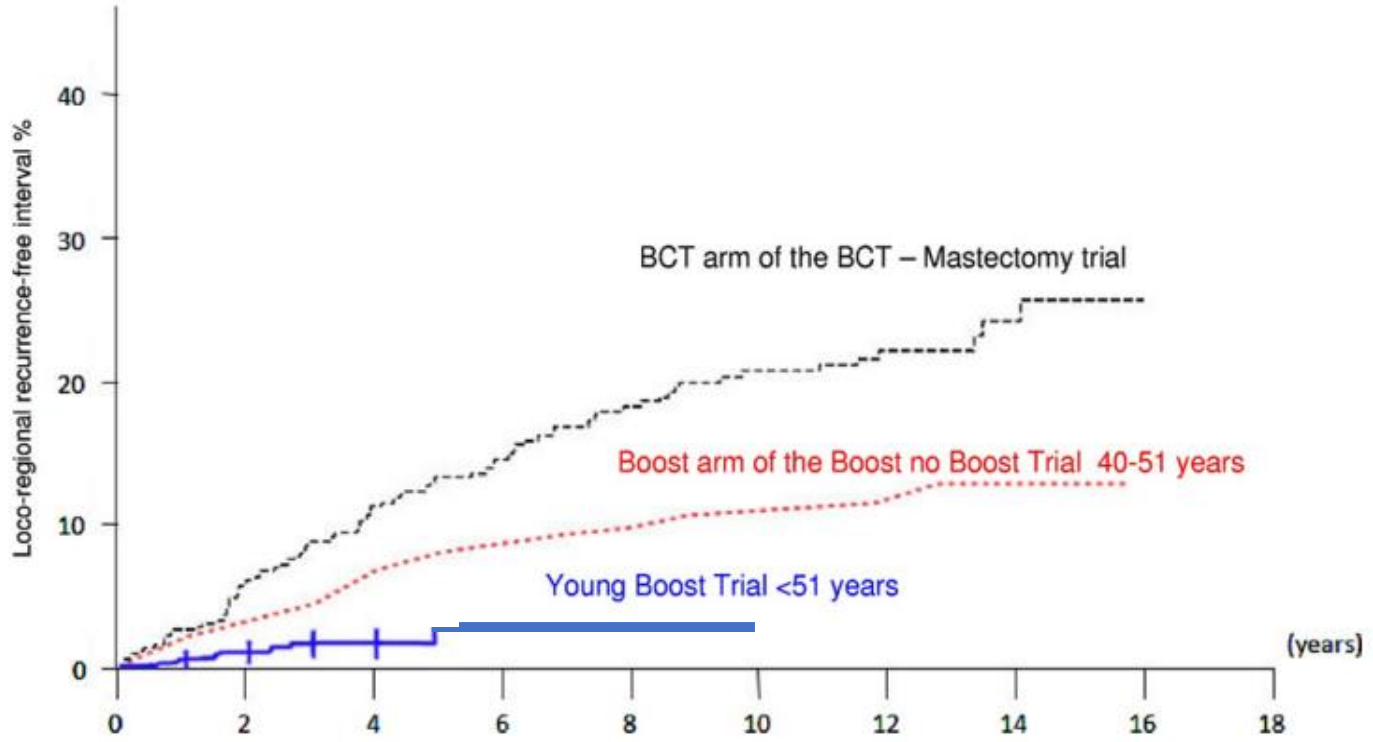

Figure 4 The local recurrence rate in the consecutive EORTC 10801, EORTC 22881-10882, and the Young Boost trials.[14]

Adapted from Poortmans et al 2012

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No effect of (low) boost on 10 yr overall survival compared to no boost

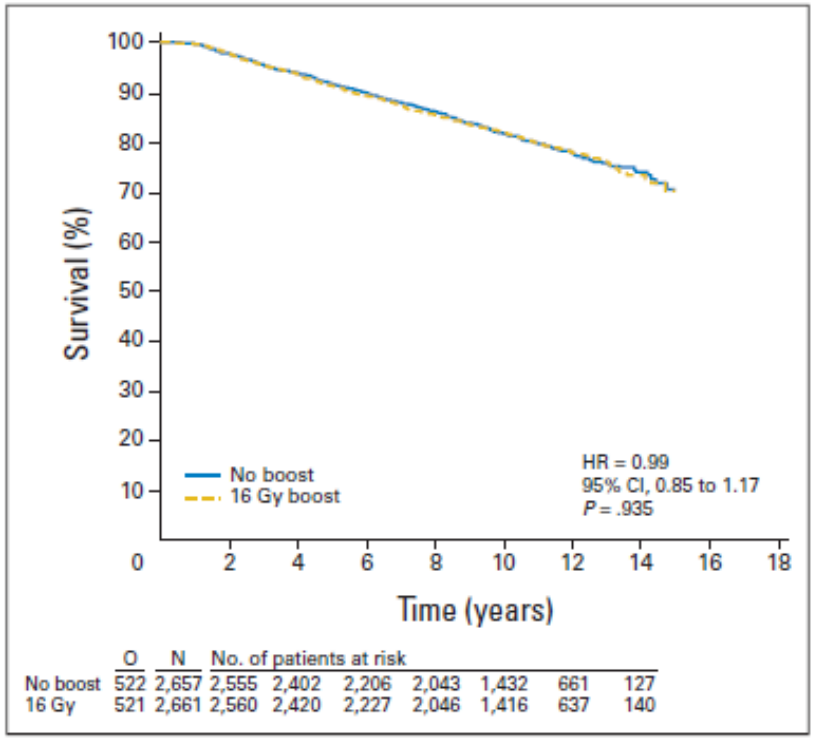
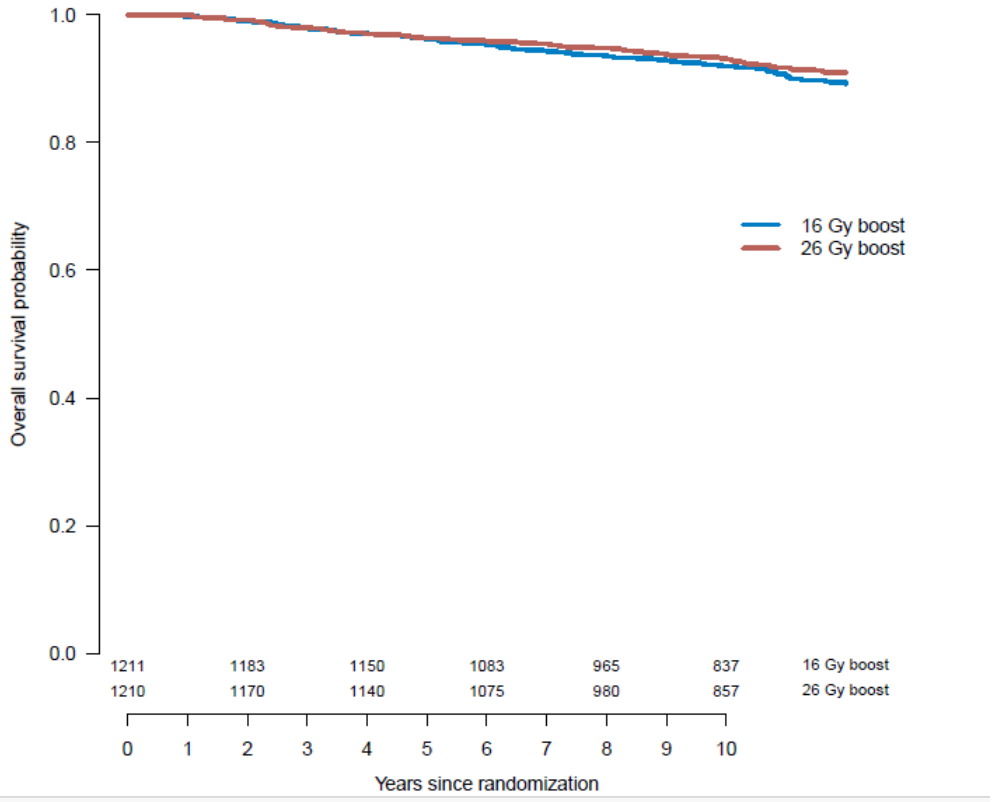


Fig 5. Survival after 50 Gy irradiation of the breast or 50 Gy irradiation and a boost. HR, hazard ratio; O, occurrences; N, number of patients at risk.

Bartelink et al 2007

No effect of (high) boost on 10 yr overall survival – compared to low boost



Bosma et al ESTRO 2024

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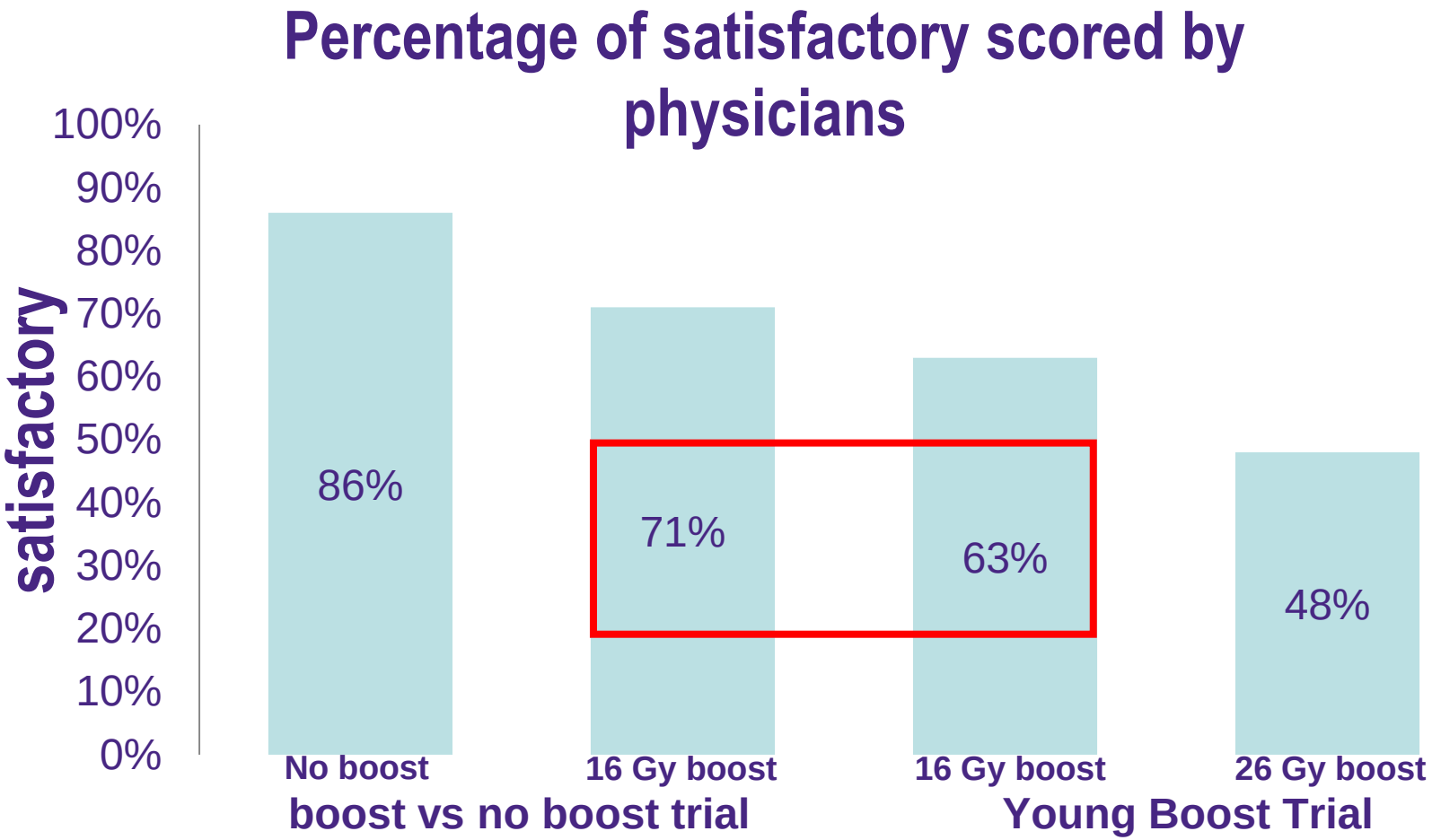
Comparison cosmetic outcome Young Boost vs boost-no boost trial



Probably due to larger boost volume in YBT due to CT-planning…

Al Uwini, Boersma et al 2009

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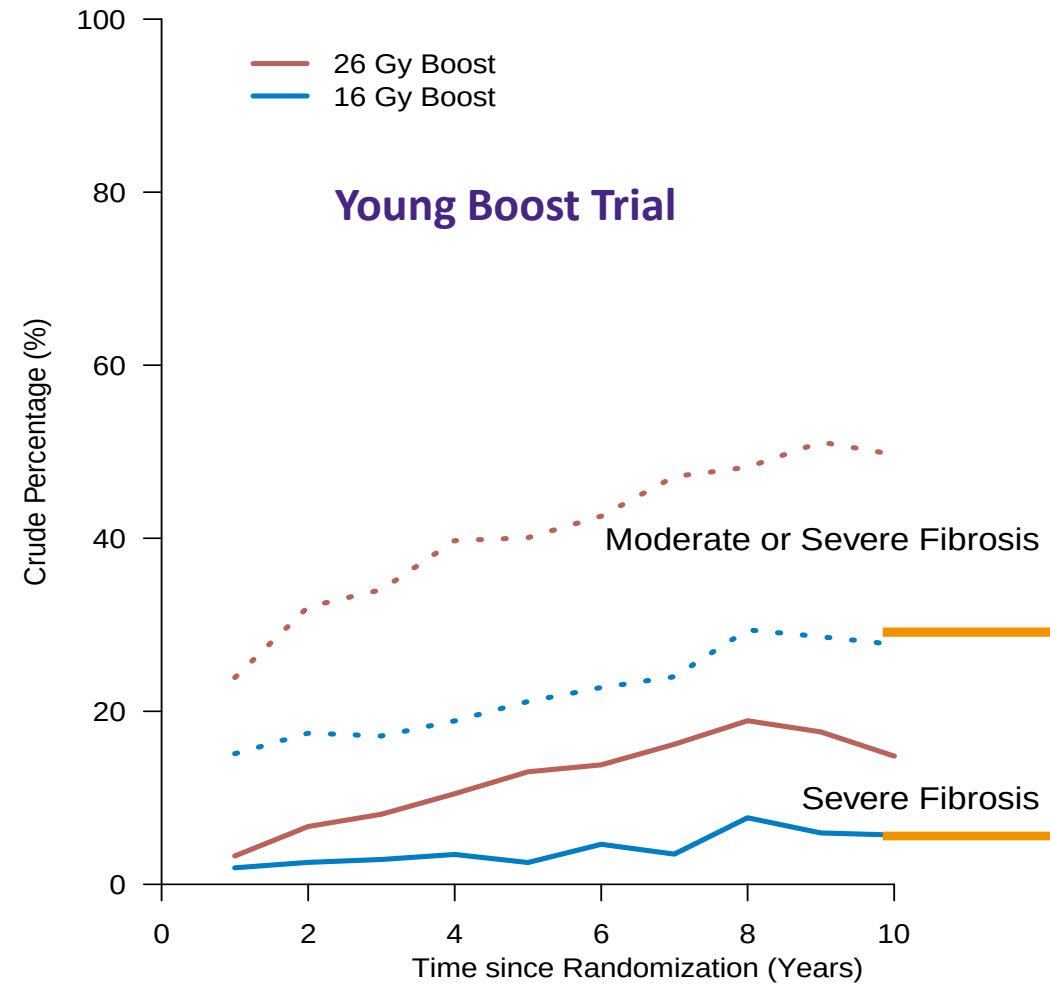
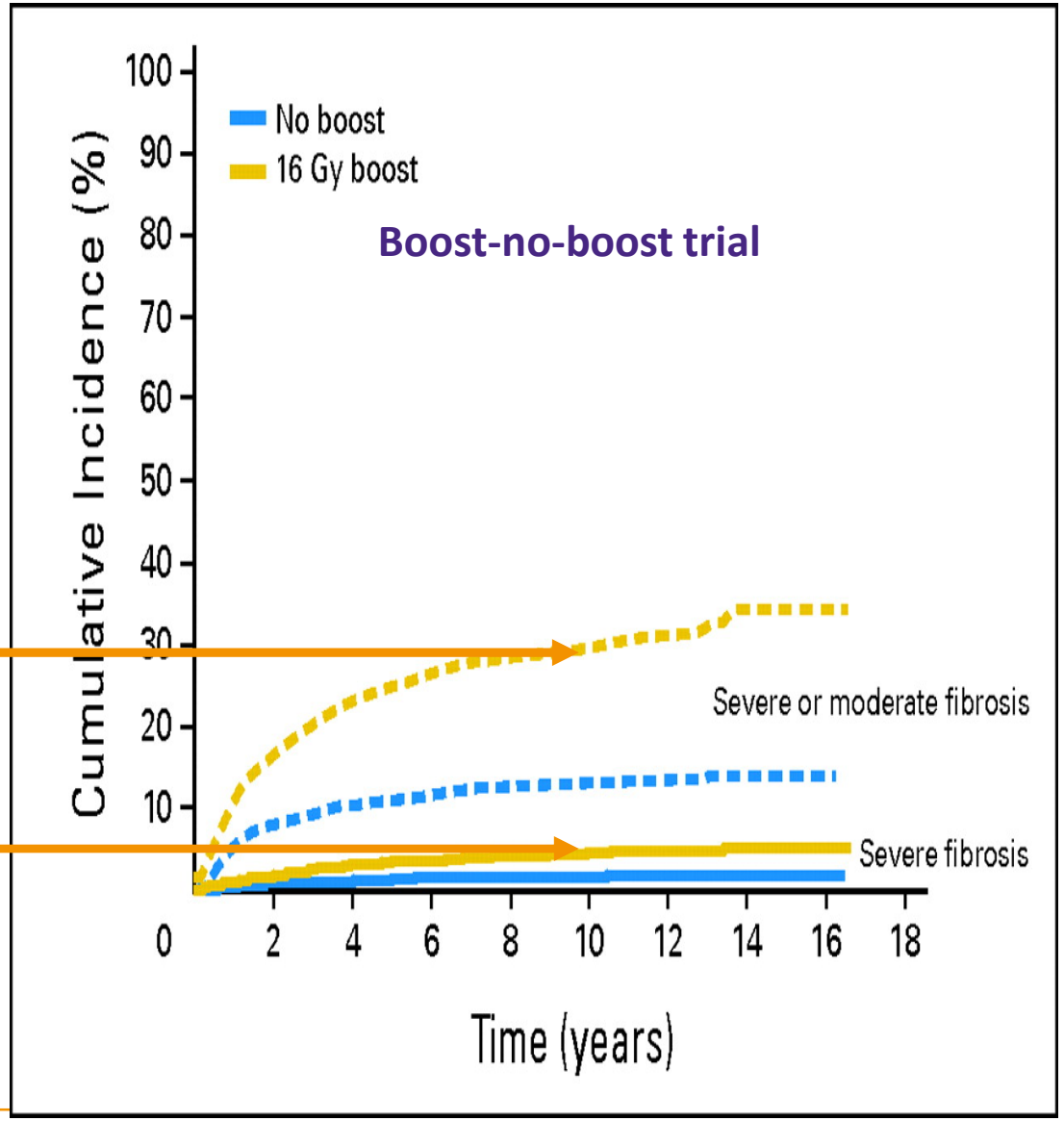
Comparison fibrosis Young Boost vs boost-no boost trial



No. patients

1210	945	841	623	471	439	26 Gy boost
1211	945	842	563	442	386	16 Gy boost



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Conclusions from the Young Boost Trial

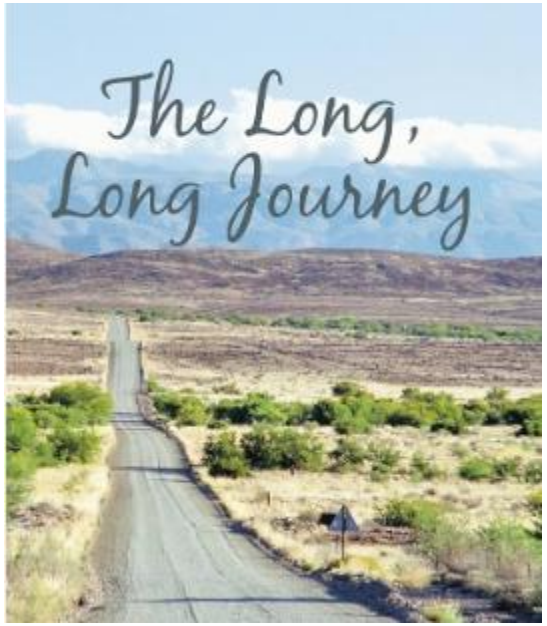
- Local control has improved considerably; even in young BC patients LC is excellent after Breast Conserving Therapy!

- A high boost (26 Gy):
  - Improves local control (< 3.5%)
  - Increases risk of fibrosis
  - Increases risk of poor cosmetic outcome
  - No effect on overall survival expected

- Thus: the small significant benefit does not justify increase in side-effects

Conclusions from a long long journey

- Even if the result of this RCT is not practice changing, we can learn a lot, e.g.:
  - Even > 66 Gy, a dose-effect relation for local control is present
  - The YBT yields valuable opportunities for obtaining insight in the dose-volume-effect relationships for:
    - Fibrosis
    - Cosmetic outcome
    - Ribfractures
  - Translational research is ongoing
- We need an early surrogate endpoint in RCTs for breast cancer..!
- ***Current studies: aimed at in whom a boost can be omitted***



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