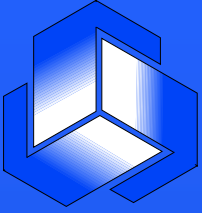


Joint 22881/10882 trial of the Radiation Oncology and Breast groups

Impact of the boost dose on local control and survival in patients with early breast cancer after a microscopically incomplete lumpectomy: 10 year results of the randomised EORTC boost trial.

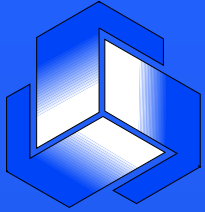
Poortmans P, Collette L, Horiot JC, Van den Bogaert W, Fourquet A, Kuten A, Noordijk E, Hoogenraad W, Mirimanoff RO, Pierart M, Bartelink H.

EORTC



Joint trial of the Radiation Oncology and Breast groups


- Introduction and trial design
- Results on local control and fibrosis
- Conclusions



Trial design


Complete excision

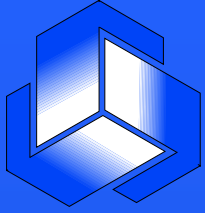
tumours: 0 - 5 cm
completely excised
external irradiation of 50 Gy

randomisation:  no boost
16 Gy boost

Incomplete excision

tumours: 0 - 5 cm
incompletely excised
external irradiation of 50 Gy

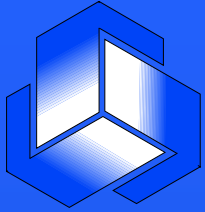
randomisation:  10 Gy boost
26 Gy boost



Accrual

- 5569 patients entered in total
 - 251 (4.5%) with incomplete resection
 - 126 to 'Low boost' and 125 to 'High boost'
- Median follow-up 11.3 years

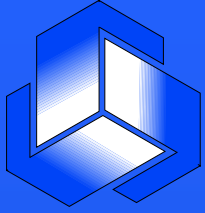
Results are given for the group with incomplete resection



Accrual - remarks

Time period = 1989 - 1996

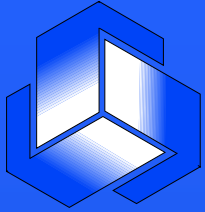
- No detailed information on DCIS
 - Presence
 - Radicality
- No discrimination for “grade” of incompleteness
 - Focal
 - Extensive
- Limited use of adjuvant systemic treatment (39%)
 - 14% chemotherapy
 - 19% tamoxifen
 - 7% both



Accrual - remarks

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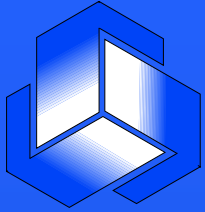
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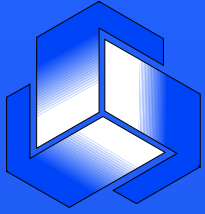
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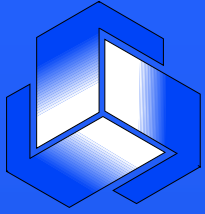
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Baseline Characteristics

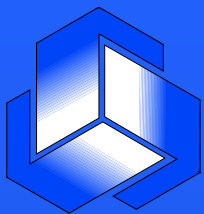
	Low Boost	High Boost	
Age (years)	54 (31 – 73)	61 (31 – 71)	55
Menopausal status			
Pre		40%	
Post		58%	
Artificial	0%	2%	
Tumour location			
Lateral	54%	46%	
Central/Superior	14%	18%	
Medial	16%	14%	
Inferior	15%	21%	

Well balanced



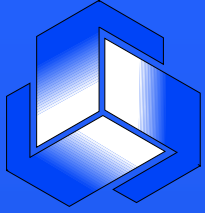
Baseline Characteristics

	Low Boost	High Boost
Pathological T1	66%	72%
T2	29%	26%
Unknown	5%	2%
Pathological N0	63%	66%
N+ (1-3)	25%	26%
N+ (>3)	11%	7%
Unknown	1%	1%



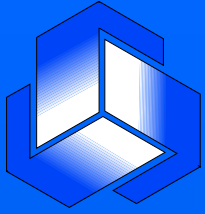
Boost Characteristics

	Low Boost	High Boost
Boost received ?		
No Boost	3%	0%
External boost	87%	72%
Interstitial boost	10%	28%
External boost technique		
Electron	75%	78%
Co-60	14%	10%
X-ray	11%	12%



Joint trial of the Radiation Oncology and Breast groups

- Introduction
- **Results on local control and fibrosis**
- Conclusions

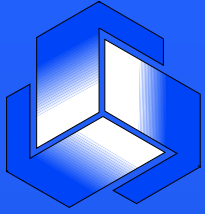


Local Failures *first event*

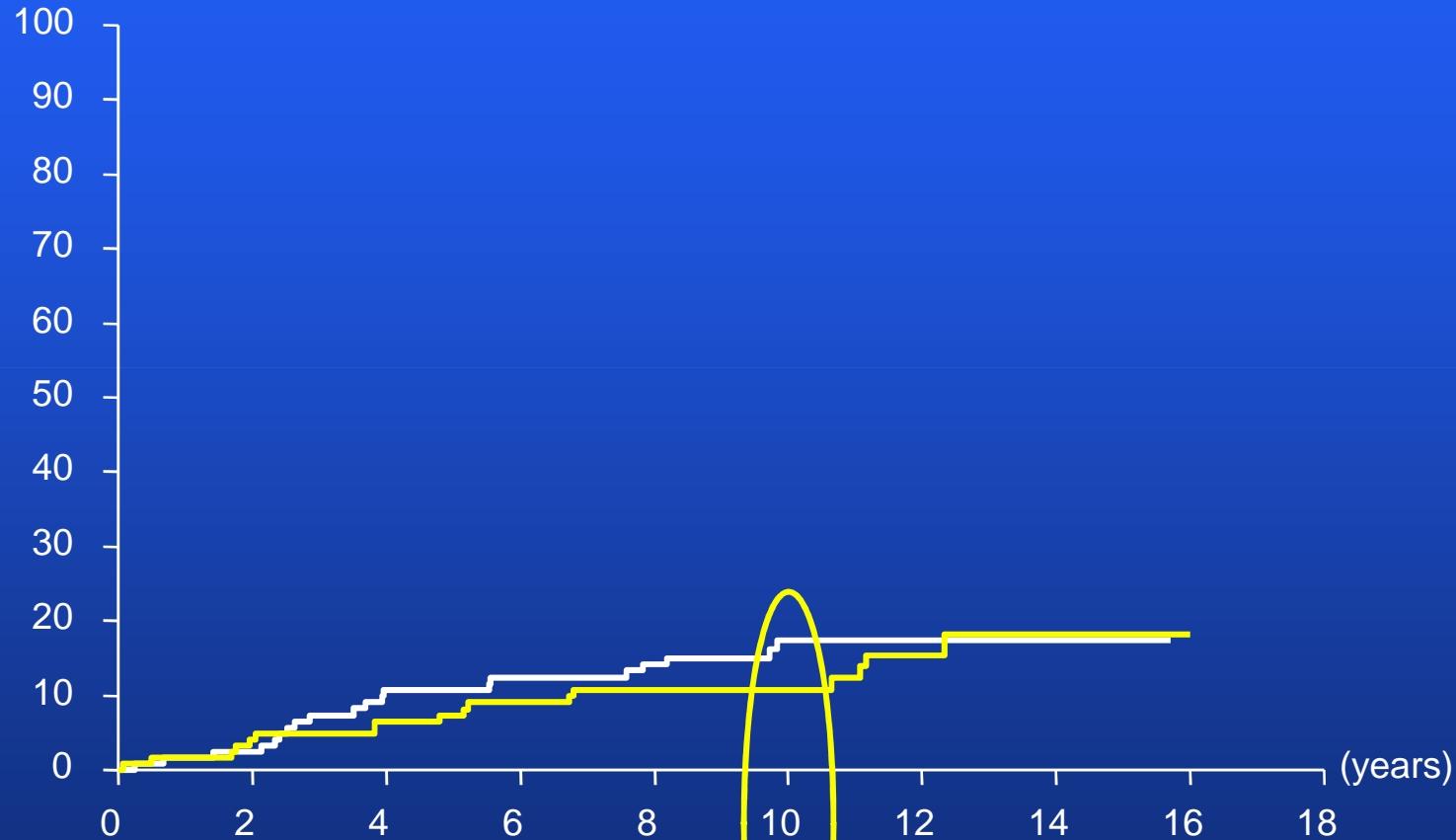
	Low Boost	High Boost	Radical
Absolute (11.3y):	N=20	N=17	N=44
Actuarial (5y):	10.7%	7.3%	4.8%
Actuarial (10y):	17.5%	10.8%	8.2%

$p > 0.1$

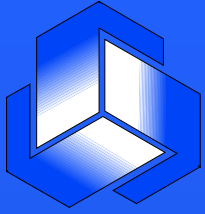
EORTC



Cumulative incidence of local failure (as first event)

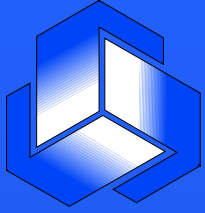


O	N	Number of patients at risk :										
20	126	120	96	84	78	64	32	11	3			— IR 10 GY
17	125	118	99	89	73	66	39	10	2			— IR 25 GY



Local Failures

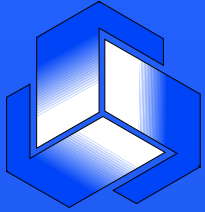
	Low Boost (N=21)	High Boost (N=19)	(
Primary tumour bed	10 (48%)	10 (53%)	
Scar	2 (10%)	2 (11%)	
Skin outside scar	2 (10%)	1 (5%)	
In breast tissue outside boost area	2 (10%)	4 (21%)	
Outside irradiated volume, within glandular tissue	2 (10%)	0 (0%)	
Diffuse	1 (5%)	2 (11%)	
Unknown site	2 (10%)	0 (0%)	



Local Failures

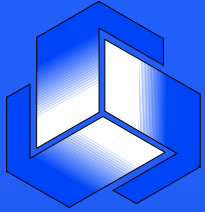
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No difference



All Failures \leq 10 years *first event*

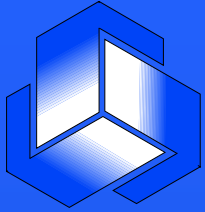
	Low Boost	High Boost	Radical
	45 (36%)	42 (34%)	1666 (31%)
Local	20 (44%)	13 (31%)	407 (24)
Regional	1 (2%)	5 (12%)	113 (7)
Distant	19 (42%)	21 (50%)	627 (38)
Contralateral BC	3 (7%)	3 (7%)	224 (13)



Causes of death

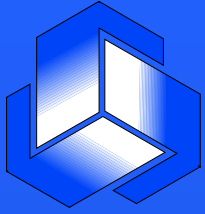
	Low Boost	High Boost	Radical
	33 (26%)	1043 (20%)	
Breast cancer	24 (73%)	24 (77%)	690 (66%)
Other cancer	1 (3%)	1 (3%)	103 (10%)
Cardiovascular	2 (6%)	1 (3%)	76 (7%)
Complication	0 (0%)	0 (0%)	7 (1%)
Other	3 (9%)	3 (10%)	87 (8%)

No difference



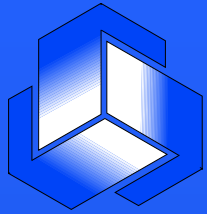
Fibrosis in whole breast

	Low Boost	High Boost	Radical
None	56 (46%)	38 (31%)	2372 (46%)
Minor	46 (37%)	42 (34%)	2057 (40%)
Moderate	12 (10%)	34 (28%)	558 (11%)
Severe	1 (1%)	6 (5%)	66 (1%)
Unknown	8 (6%)	3 (2%)	148 (3%)

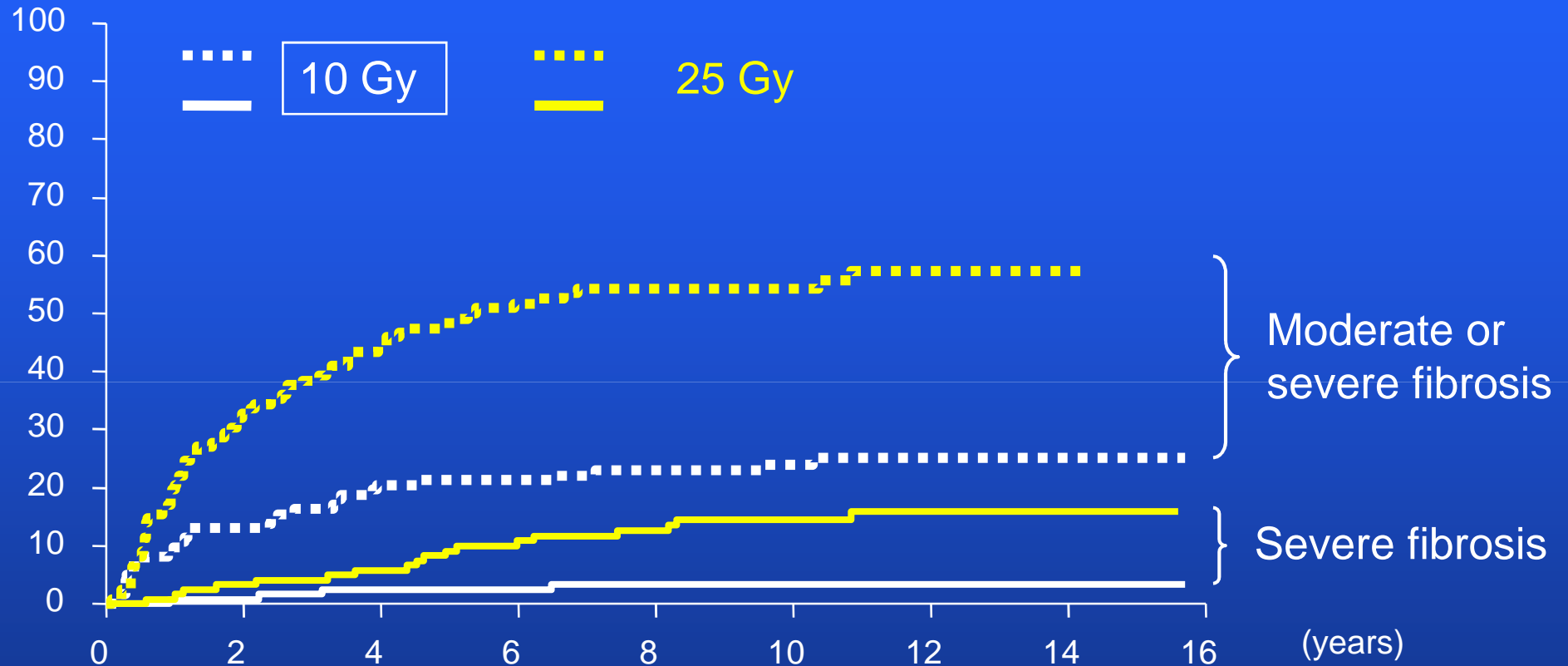


Fibrosis in boost area

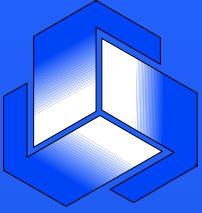
	Low Boost	High Boost	Rad
None	38 (32%)	20 (16%)	801 (
Minor	44 (37%)	32 (26%)	1022 (
Moderate	25 (21%)	51 (42%)	610 (
Severe	4 (3%)	17 (14%)	112 (
Unknown	8 (7%)	3 (2%)	72 (



Cumulative incidence of moderate or severe fibrosis (boost or WB)

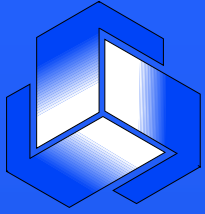


O	N	Number of patients at risk :								Treatment	
30	123	103	84	76	66	50	26	6	-----	10 Gy boost - Mod+Sev	
68	123	81	61	48	42	28	14	1	-----	25 Gy Boost - Mod+Sev	
4	123	118	106	99	89	66	37	8	_____	10 Gy boost - Sev	
18	123	117	102	88	77	54	29	5	_____	25 Gy Boost - Sev	



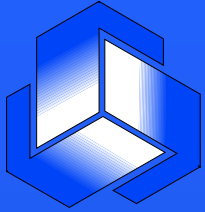
Joint trial of the Radiation Oncology and Breast groups

- Introduction
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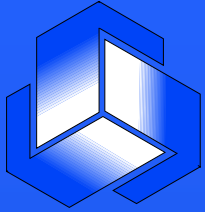
Conclusions low vs. high dose

- At 10 years, the cumulative incidence of local recurrence was 17.5% vs. 10.8 % for the low and high boost, respectively.
- Overall, 64 patients have died (25.5%), 3/4 of them due to breast cancer.
- None of the endpoints on efficacy differed significantly between the 2 groups..
- More patients in the high boost group received an interstitial boost (28% vs. 10%).



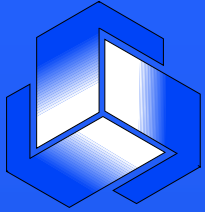
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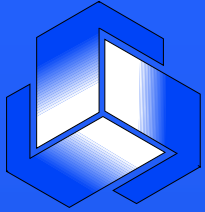
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- At 10 years, the cumulative incidence of local recurrence was 17.5% vs. 10.8 % for the low and high boost, respectively.
- This difference was not statistically significant ($p > 0.1$) but the sample size and the number of events are small and thus the statistical power is low for detecting any realistic difference.
- Overall, 64 patients have died (25.5%), 3/4 of them due to breast cancer.
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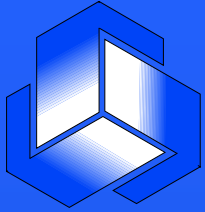
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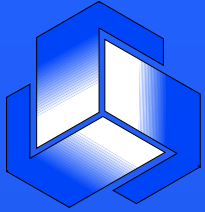
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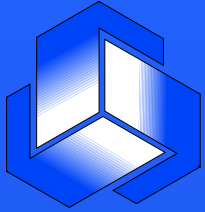
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 - 33% versus 11 % in the breast



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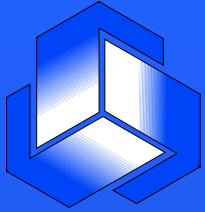
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- By year 10, the incidence of moderate/severe fibrosis was higher in the high boost group:
 - 33% versus 11 % in the breast
 - 54% versus 23 % in the boost area



Conclusions irradiated vs. radical

Compared to the 5318 patients who had a microscopically complete tumour resection:

- The pathological tumour size was larger (28% vs. 20% T2).
- More patients had involved lymph nodes (35% vs. 21%).
- More patients received an interstitial (18% vs. 9%) boost.
- The local recurrence risk was nearly doubled (15% vs. 8% absolute risk, first event).
- More fibrosis was reported for the high boost dose.



Conclusions irradiated vs. radical

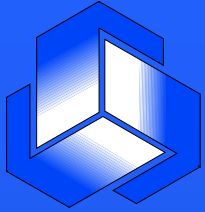
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28% vs. 20% T2

- More patients had involved lymph nodes:

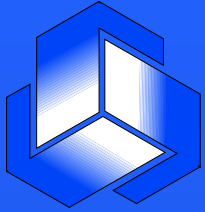
35% vs. 21% pN+

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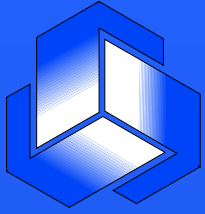
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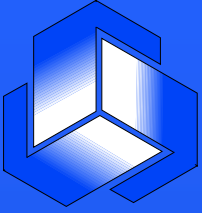
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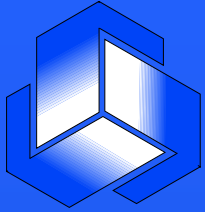
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Practical advises

BCT might be offered after a microscopically incomplete tumour resection, but:

- It should be avoided if possible: optimal surgery
- It should be well documented: pathology
- The local control rate is lower – although patient selection might play a role (age & systemic treatment)
- Further research is needed to
 - ◆ Increase the local control rate
 - ◆ Limit the late toxicity (fibrosis)



Participation EORTC 22881/10882

- Amsterdam, NL Borger
- Heerlen, NL Jager
- Leiden, NL Noordijk
- Nijmegen, NL Hoogenraad
- Rotterdam, NL Koper
- Tilburg, NL Poortmans
- Utrecht, NL Struikmans
- Creteil, F Calitchi
- Dijon, F Horiot
- Grenoble, F Boll
- Montpellier, F
- Paris, F
- Vannes, F
- Antwerp, B v. d. Weyngaert
- Brussels, B Storme
- La Louviere, B Renaud
- Leuven, B v. d. Bogaert
- Namur, B Salamon
- Berlin, D Budach
- Cologne, D Muller
- Dusseldorf, D Roth
- Barcelona, ES Schultz
- Madrid, ES Casas
- Pamplona, ES Calvo
- Pamplona, ES Dominguez
- Geneva, CH Kurtz
- Lausanne, CH Mirimanoff
- Haifa, IS Kuten
- Tel Aviv, IS Kovner
- Brisbane, AUS Poulsen
- Nottingham, GB Morgan

Thank you all!