

Cardiotoxic effects of breast conserving therapy in patients with left-sided breast cancer treated with tangential fields. A retrospective multicenter study

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Purpose of the study

To investigate long-term risk of cardiotoxic events after tangential breast irradiation (left vs right)

To examine the impact of irradiated heart volume (MHD) accounting for cardiac risk factors

Patients

- BCT with tangential breast fields (1980-1993)
- No additional radiation fields
- No lymph node metastases/ no distant metastases
- No adjuvant chemotherapy/ no adjuvant hormonal therapy
- No pre-existing second cancer
- No bilateral breast cancer

Patients

Institutes	N	%
Catharina ZH Eindhoven	470	29.4
Erasmus/DDHK Rotterdam	399	24.9
MAASTRO Maastricht	340	21.2
NKI/AVL Amsterdam	199	12.4
Universiteits ZH Leuven	193	12.1
Total	1601	

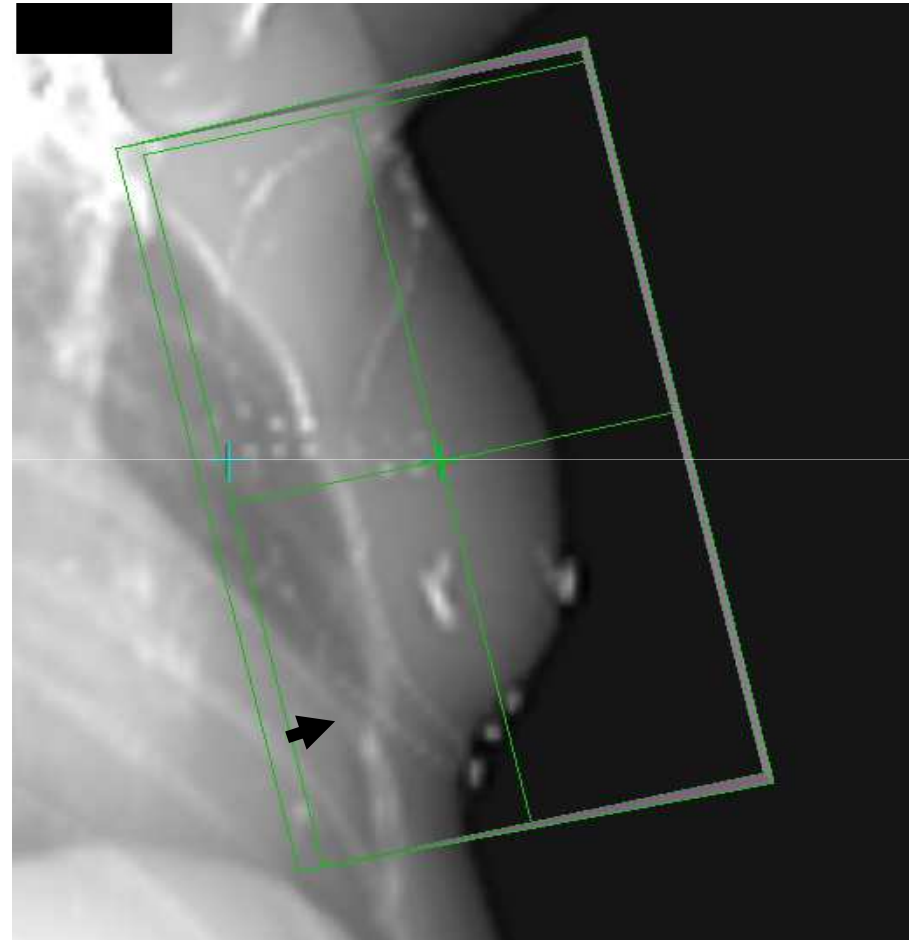
Methods

- Retrospective analysis of medical records
- Questionnaire to general practitioners
Cardiac risk factors: smoking, hypertension, DM
- Statistical analysis
Multivariate regression analysis (Cox)
Left/right comparison; analysis of MHD

Methods

Measurements of
Maximum Heart Distance
(MHD)

Two independent
observers/ cross check
(disagreement > 3 mm)

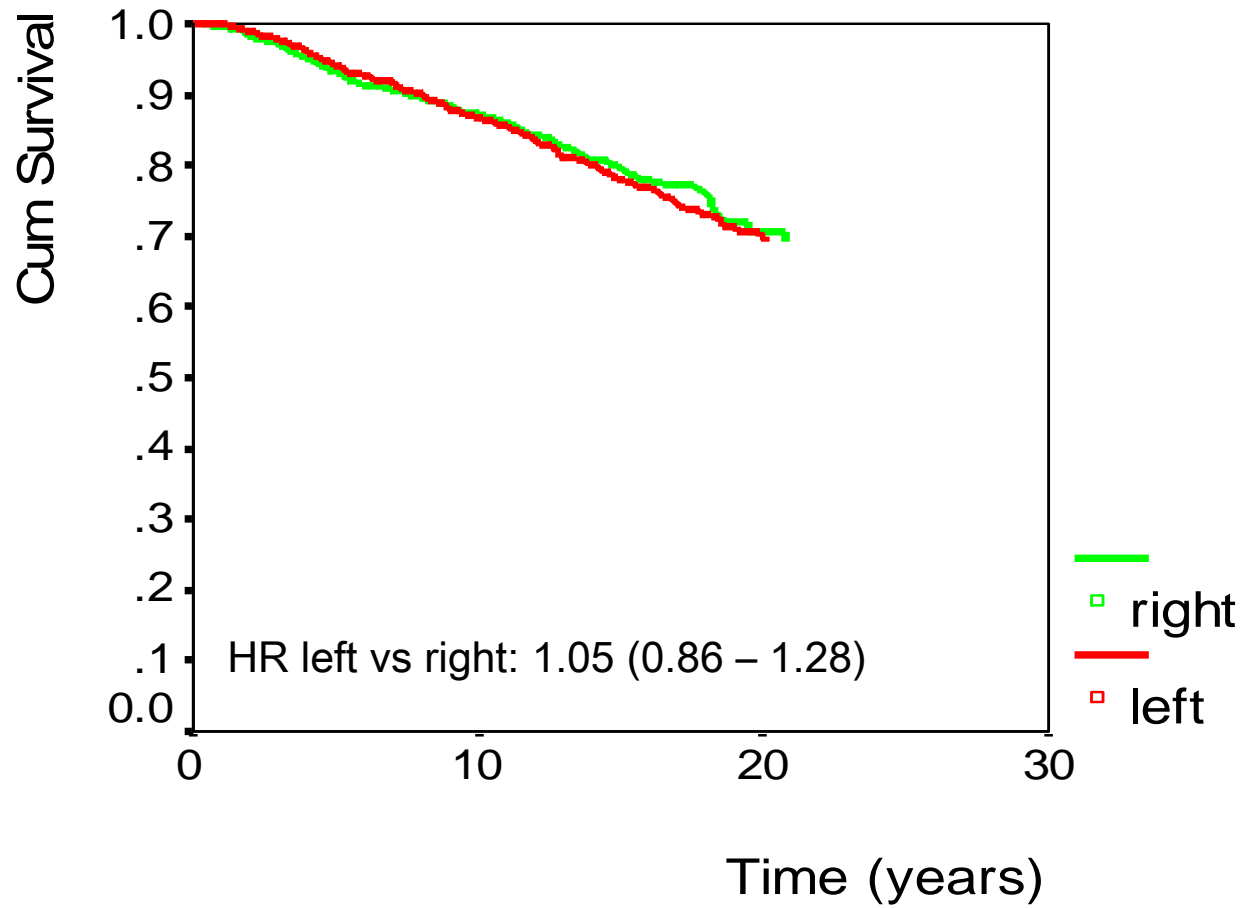


Patient characteristics

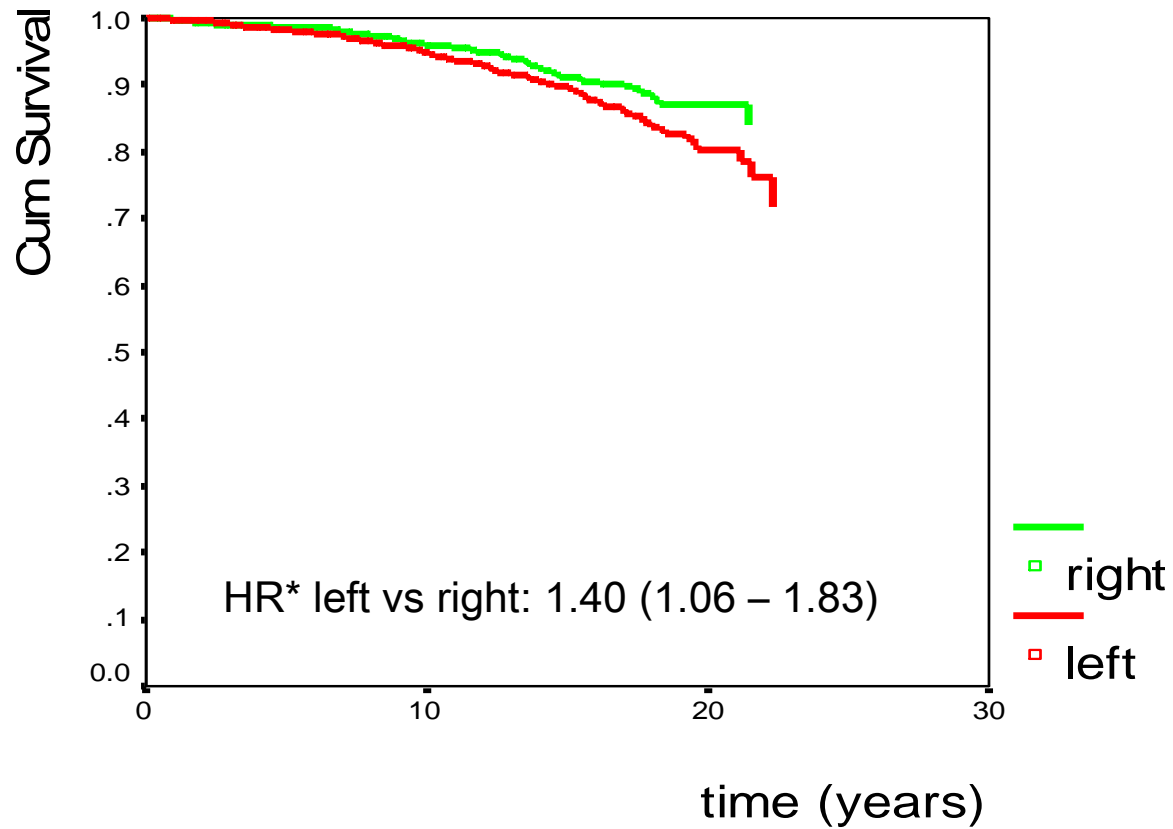
	Left	Right
Number of patients	870	731
MHD known	796	
Median age (yrs)	49	48
Median FUP (yrs)	16	16
Smoking no (%)	37.2	38.2
Smoking yes (%)	18.8	19.7
Smoking unknown (%)	43.9	42.1
Hypertension (%)	23.8	21.2
Diabetes mellitus (%)	5.4	8.3*
Hypercholesterolemia(%)	13.4	15.4
Cardiovascular disease history (%)	2.0	1.0

*P=0.02

Overall survival by Laterality



Cardiovascular disease-free survival



Patients at risk:

Left	870	695	70
Right	731	581	66

*adjusted for age, DM

Cardiovascular Events

	Left (%)	Right (%)
Cardiovascular disease	139 (16)	85 (11.6)
Ischemic heart disease	73 (8.4)	44 (6.0)
Other heart disease	94 (10.8)	53 (7.3)

*CVD 22/139 no MHD available
IHD 11/73 no MHD available

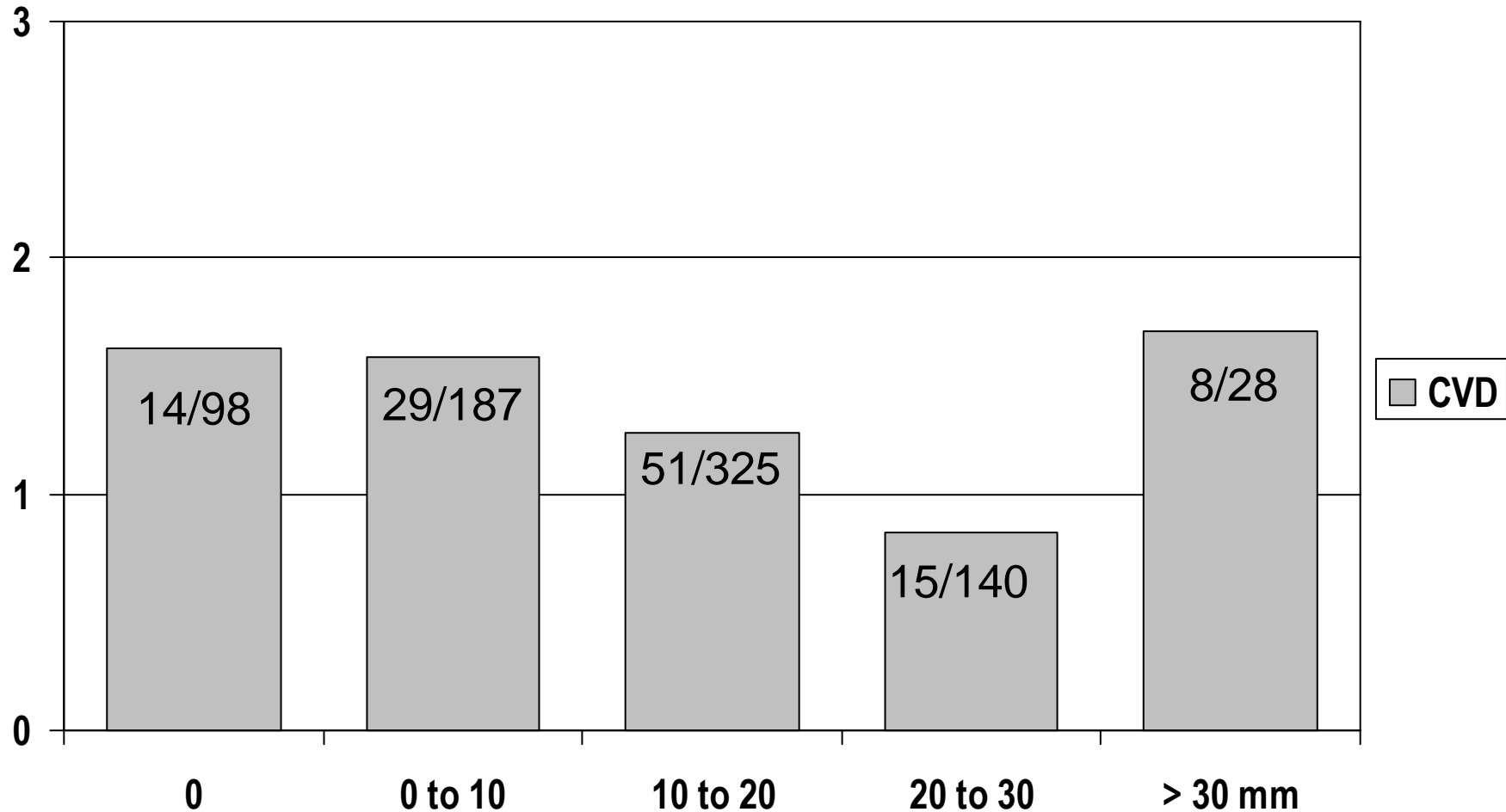
Cardiovascular Disease by Laterality

	HR (95% CI)
Ischemic HD right	1.0
Ischemic HD left	1.41 (0.97-2.05)
Other HD right	1.0
Other HD left	1.53 (1.09-2.15)
Cardiovascular D right	1.0
Cardiovascular D left	1.40 (1.06-1.83)

Cardiovascular Risk Factors (Cox model)

	HR(95% CI)
Radiotherapy right	1.0
Radiotherapy left	1.39 (1.06-1.82)
Hypertension	1.70 (1.30-2.23)
Diabetes mellitus	2.13 (1.14-3.07)
Smoking current	1.48 (0.96-2.30)
Smoking stopped	1.35 (0.86-2.12)

Hazard Ratios of Cardiac Events by MHD



Conclusions

- A significantly higher incidence of cardiovascular disease was seen in patients irradiated for left-sided breast cancer compared to right-sided cancer.
- We could not determine a significant trend for larger heart volumes being irradiated
- Nevertheless we think that heart sparing techniques should be used for irradiation of patients with left-sided breast cancer

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Causes of Death

	Left (%)	Right (%)
Breast cancer	97 (45.3)	81 (47.1)
Other malignancies	19 (8.9)	17 (9.9)
Ischemic heart disease	14 (6.5)	5 (2.9)
Other heart disease	15 (7.0)	9 (5.2)
Sudden death	5 (2.3)	5 (2.9)
Complications	2 (0.9)	
Other causes	33 (15.4)	38 (22.1)
Unknown	29 (13.6)	17 (9.9)
Total	214	172

Cardiovascular Events by MHD (Cox)

MHD (mm)	IHD: HR (CI)	OHD: HR (CI)	CVD: HR (CI)
Right	1.0	1.0	1.0
Left (0)	1.11 (0.44-2.82)	2.10 (1.09-4.06)	1.62 (0.91-2.86)
0-10	1.52 (0.84-2.74)	1.73 (1.02-2.94)	1.58 (1.03-2.42)
10-20	1.38 (0.86-2.21)	1.24 (0.79-1.93)	1.26 (0.89-1.79)
20-30	1.05 (0.51-2.15)	0.79 (0.39-1.61)	0.84 (0.48-1.46)
> 30	1.85 (0.66-5.22)	2.07 (0.88-4.89)	1.69 (0.81-3.53)

Maximum Heart Distance Distribution

