

# DBCG-IMN

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Effect of adjuvant radiotherapy to the internal  
mammary lymph nodes in patients with early  
node-positive breast cancer

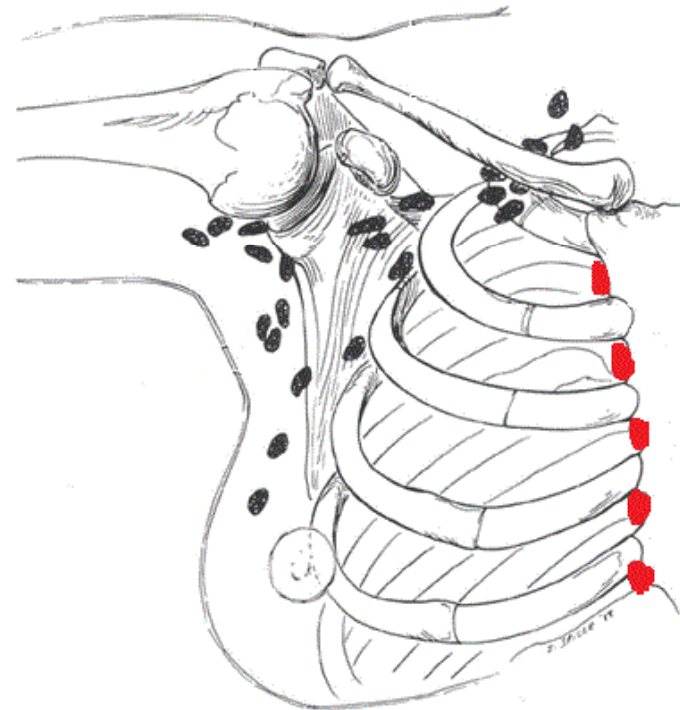
Lise B J Thorsen

On behalf of the DBCG Radiotherapy Committee

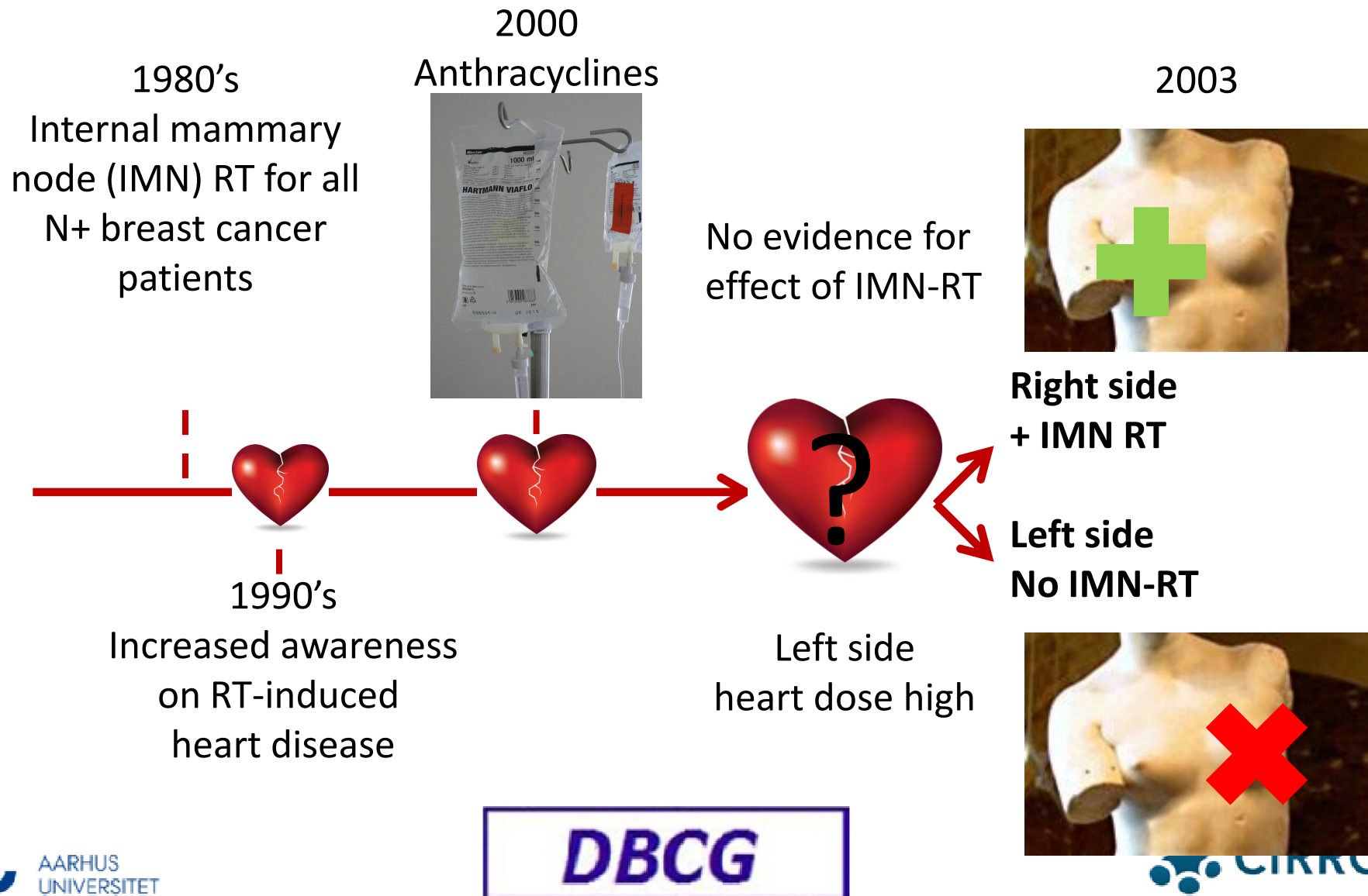
# DBCG-IMN

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- IMN metastasis
  - Often w. medial tumor/N+ disease
  - A poor prognostic sign
- Surgical studies: no beneficial effect IMN dissection
- IMN-RT: increased toxicity with earlier techniques
- No consensus on whether IMN-RT is useful



# DBCG-IMN

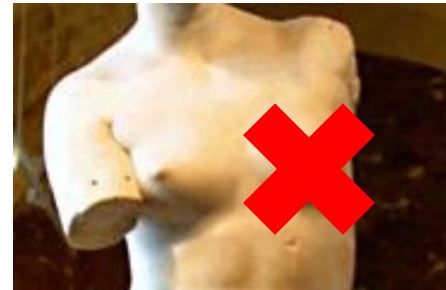


# DBCG-IMN

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Right side  
+ IMN RT



Left side  
No IMN-RT

↑ Breast cancer death

↓ Heart death

# Hypotheses

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In patients with early node positive breast cancer, IMN-RT

- Improves overall survival
- Prevents distant recurrence
- Decreases breast cancer mortality

# DBCG-IMN: Design

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- Nation-wide population based cohort study
- Inclusion: 2003-2007
  - operable unilateral early BC
  - one or more macrometastatic axillary lymph nodes
  - no prior malignancies
  - age < 70 years
  - Treated with standard RT after introduction of new internal mammary node guidelines
  - No recurrence earlier than 30 days after RT

# DBCG-IMN: Design

		N	
	Ineligible		
	No or non-standard RT	134	ion criteria et (n=306)
	Early recurrence	52	
Right-sided b	Micrometastases	33	(n=1586)
	Stage 4 disease at diagnosis	38	

**Primary endpoint: Overall Survival**

**Secondary endpoints: Metastatic disease, Breast cancer death**

Multivariate model adjusting for known prognostic factors: age, menopausal status, pT, pN, and grade, tumor location, stratified for receptor status and histological type

# Patient and tumor characteristics

	IMN RT (n=1485)	No IMN RT (n=1586)
Median age (range)	56 (23-70)	57 (27-70)
Pre-menopausal	611 (41%)	646 (40%)
Estrogen receptor positive (%)	1202 (81%)	1274 (80%)
Invasive ductal carcinoma	1305 (88%)	1346 (85%)*
Invasive lobular carcinoma	134 (9%)	163 (10%)
Other	46 (3%)	77 (5%)
Grade I	307 (19%)	307 (19%)
Grade II	710 (48%)	743 (47%)
Grade III	414 (28%)	456 (29%)
pT1	527 (36%)	556 (35%)
pT2	830 (56%)	905 (57%)
pT3	126 (9%)	124 (8%)
pN1	867 (58%)	949 (60%)
pN2	396 (27%)	412 (26%)
pN3	222 (15%)	225 (14%)
Lateral	904 (61%)	943 (60%)
Medial/central	578 (39%)	640 (40%)

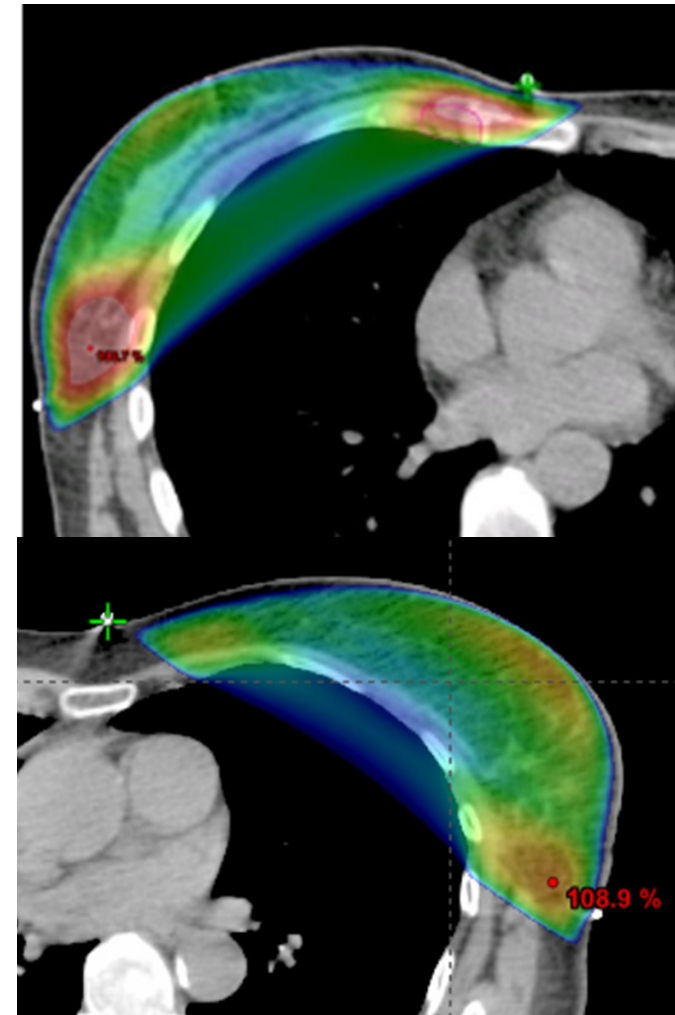


# DBCG-IMN: Treatment

	IMN RT (n=1485)	No IMN RT (n=1586)
Radiotherapy: 48 Gy/24 F IMN-RT (%)	1431 (96%)	161 (10%)
Axillary level II-III (%)	1213 (82%)	1294 (82%)
Axillary level I-II-III (%)	272 (18%)	292 (18%)
Boost after BCS (%)	176 (33%)	164 (30%)
Type of surgery		
Mastectomy + AC(%)	959 (65%)	1048 (66%)
Breast conserving +AC(%)	526 (35%)	538 (34%)
Systemic treatment		
Anti-hormonal therapy (%)	697 (47%)	741 (47%)
Chemotherapy (%)	274 (19%)	304 (19%)
Both (%)	514 (35%)	541 (34%)

# DBC-G-IMN: QA RT-techniques

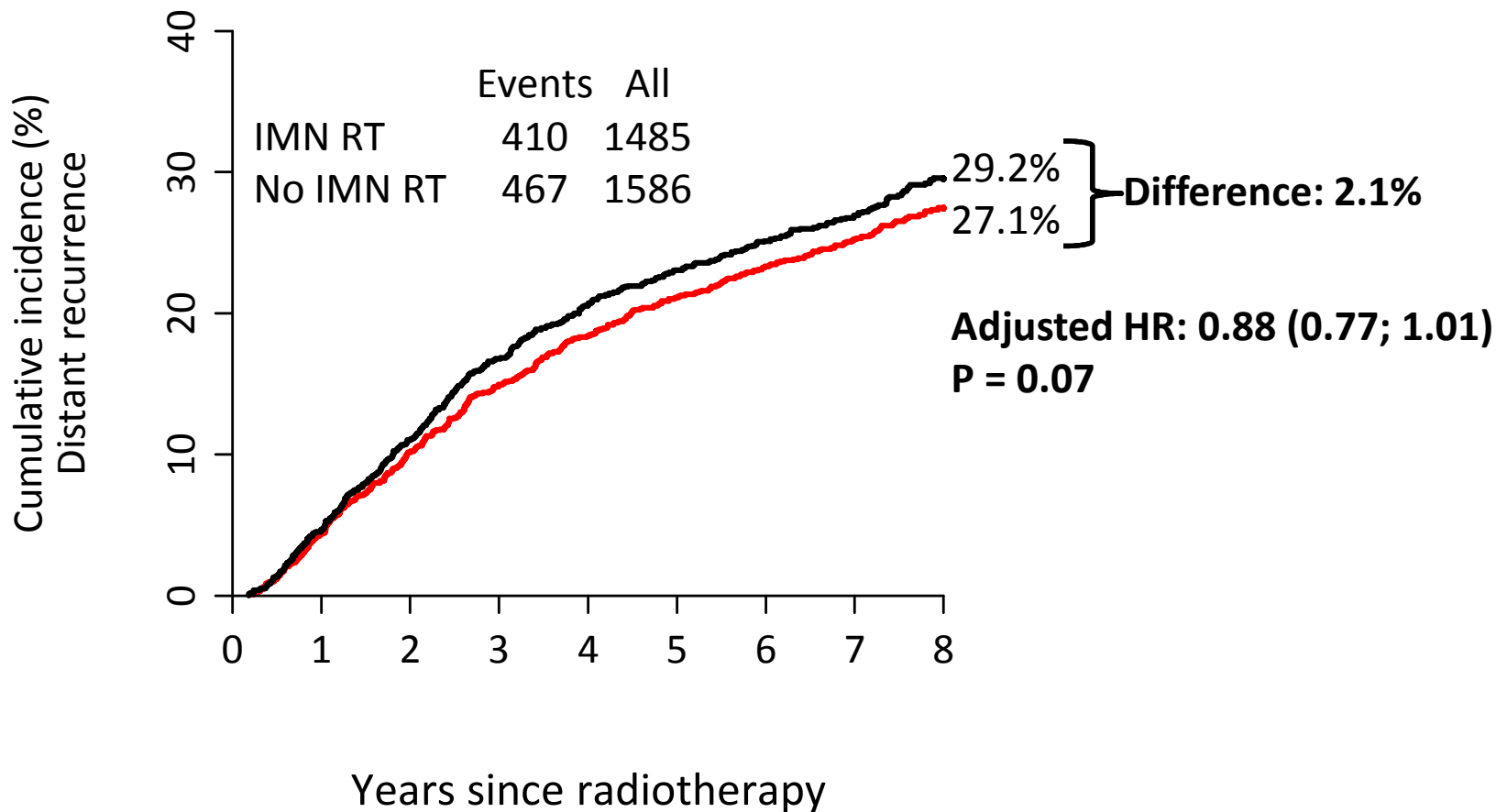
- Doses to normal tissues acceptable
- IMN-RT intended: Some underdosage
- IMN-RT NOT intended: Some dose unavoidable
- ->Possible dilution of measurable IMN-RT effect!



# Pattern of recurrence

Pattern of recurrence Median FU= 8.0 years	IMN RT (n=1485)	No IMN RT (n=1586)
Local recurrence	29 (2.0 %)	21 (1.3 %)
Regional lymph node recurrence	10 (0.7 %)	15 (0.9 %)
Contralateral breast cancer	39 (2.6 %)	36 (2.3 %)

# Distant recurrence



At risk

IMN RT	1485	1322	1193	1043	521	<span style="color: red;">—</span>
No IMN RT	1586	1401	1229	1075	500	<span style="color: black;">—</span>

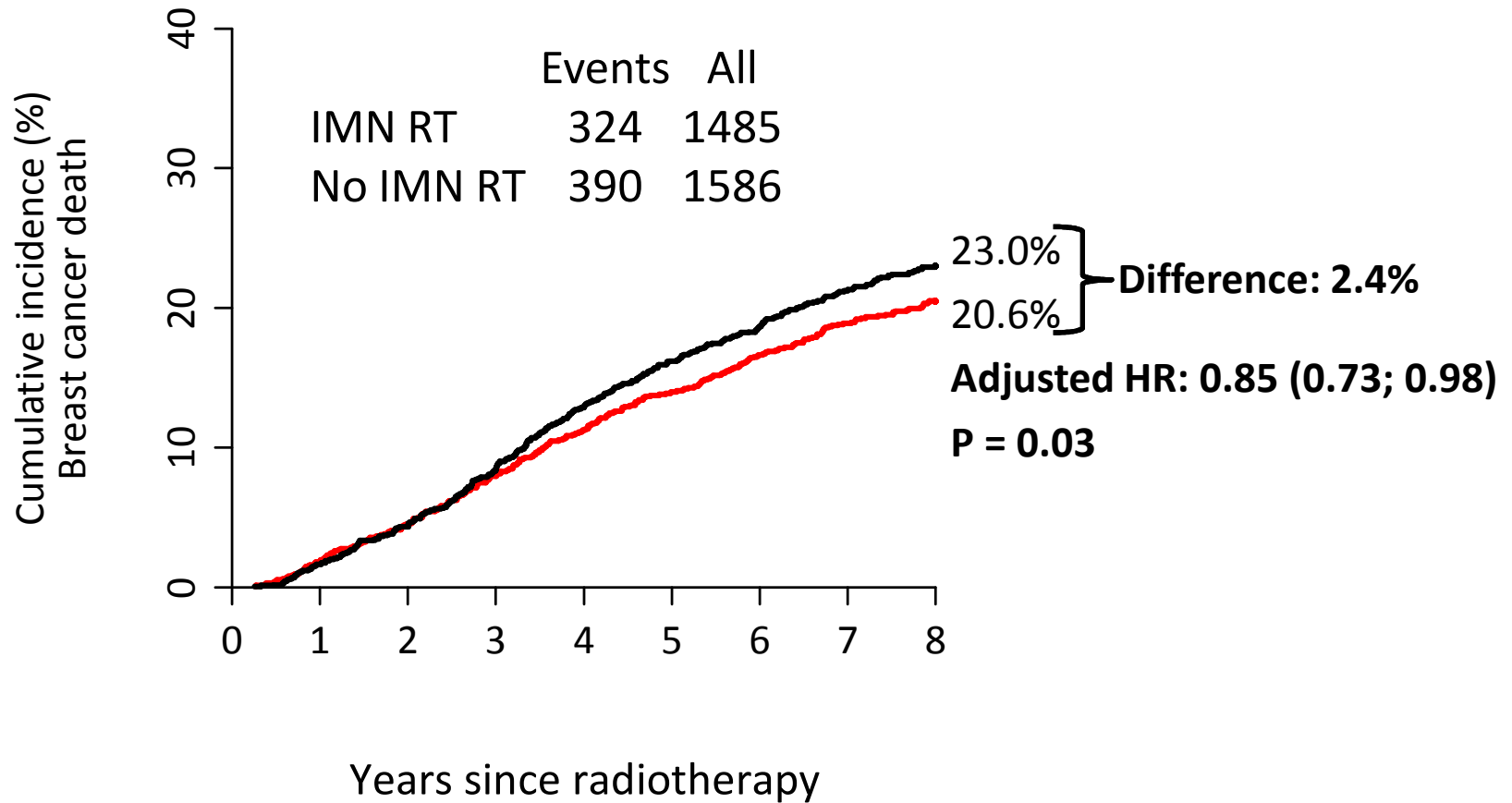
# Secondary endpoint

## Breast cancer mortality

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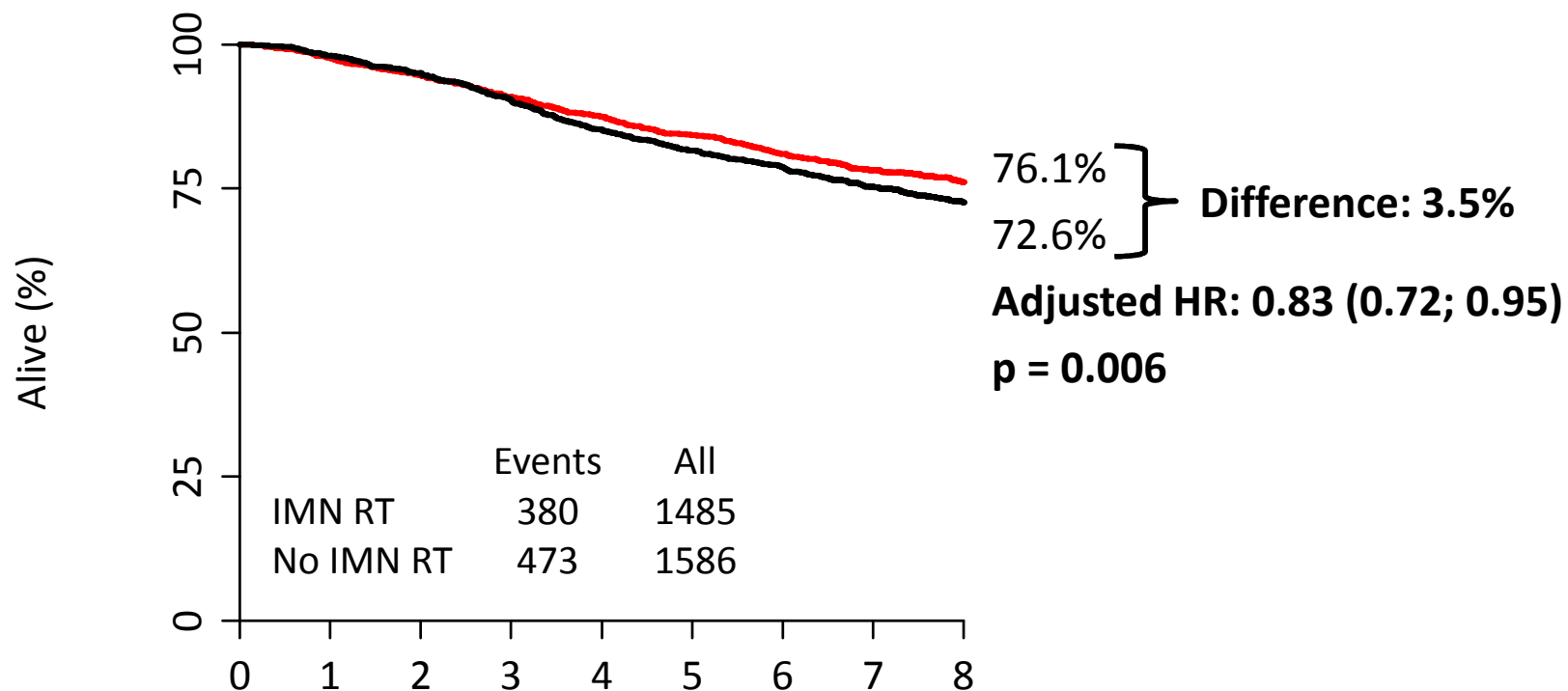
Cause of death Median FU= 8yrs	IMN RT (n=1485)	No IMN RT (n=1586)
Breast cancer	<b>324</b>	<b>390</b>
Cardiovascular	<b>9</b>	<b>9</b>
Other malignancy	26	39
Other	21	32
Unknown	0	3

# Breast cancer mortality



At risk	0	1	2	3	4	5	6	7	8
IMN RT	1485	1406	1299	1203	782	—	—	—	—
No IMN RT	1586	1507	1352	1246	790	—	—	—	—

# Primary endpoint: Overall Survival



At risk

IMN RT	1485	1406	1299	1203	782
No IMN RT	1586	1507	1352	1246	790



**DBCG**



# Association: ✓ - Causality?

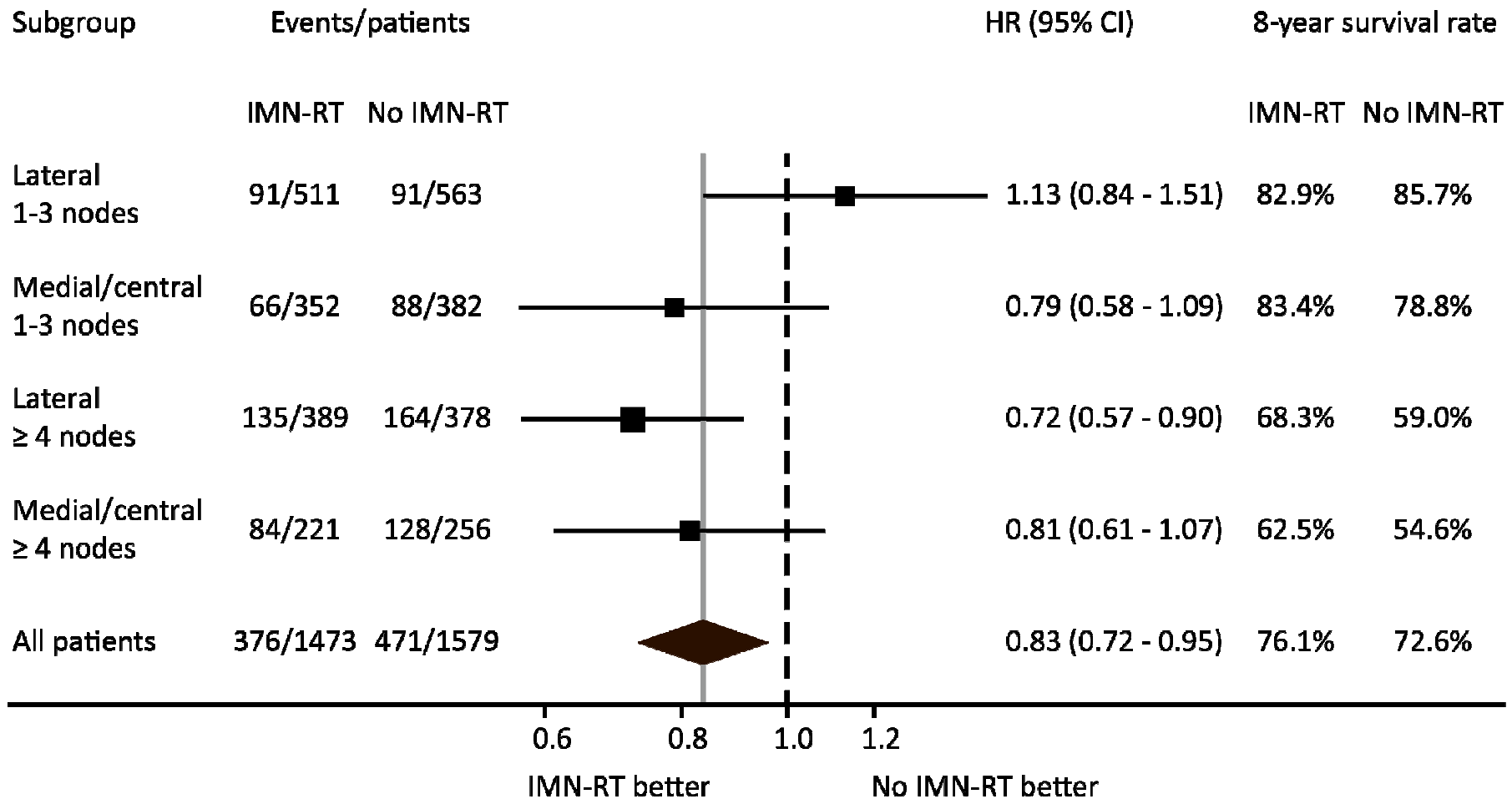
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- Increasing risk of IMN metastasis with:
  - Increasing number of positive axillary lymph nodes
  - Medial/central tumor location



# Subgroup analysis

## Endpoint: Overall survival



# DBCG-IMN: Conclusion

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- Overall survival improved with IMN-RT
- Risk of metastatic disease decreased with IMN-RT
- Risk of breast cancer death decreased with IMN-RT

# DBCG-IMN: Conclusion

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Benefit increased with

- Increasing number of lymph nodes involved
- Medial or central tumor location

# Acknowledgements

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- The Breast Friends Cancer Campaign
- Max and Inger Wørzners Memorial Foundation

# Evidence 2013-14

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- **EBCTCG meta-analysis**
  - RT after mastectomy+axillary dissection
  - 20 years results: RT reduced breast cancer mortality (BCM) for all (n=3086) N+ patients, effect both in pts with 1-3 and 4+ positive nodes
- **EORTC 22922-10925**
  - 4004 pts. with medial/central tumor and/or N+ disease randomised to medial supraclavicular (MS) and IMN-RT
  - 10 year results: Improved DFS and D-DFS with MS+IMN-RT, OS borderline significant
- **MA.20**
  - 1832 pts. randomised to whole breast irradiation (WBI) versus WBI + regional RT, 85 % of patients with 1-3 nodes positive
  - 5 year results: Improved DFS and D-DFS with addition of regional RT, OS borderline significant

**The Role of Irradiation of the Internal Mammary Lymph Nodes in High-Risk Stage II to IIIA Breast Cancer Patients After High-Dose Chemotherapy: A Prospective Sequential Nonrandomized Study**

**Long-term effect of internal mammary chain treatment. Results of a multivariate analysis of 1195 patients with operable breast cancer and positive axillary lymph nodes**

Retrospective and non-randomized: Bias and confounding  
Small: Insufficient power to detect an effect  
Old: Surgical and systemic treatment (if any) are outdated

to treat?

**Invasive Breast Carcinoma**

**Influence of internal mammary node irradiation on long-term outcome and contralateral breast cancer incidence in node-negative breast cancer patients**

**Long-term Survival Outcomes Following Internal Mammary Node Irradiation in Stage II-III Breast Cancer: Results of a Large Retrospective Study With 12-Year Follow-up**