Strahlentherapie
Aktuelle Leitlinienempfehlungen beim Mammakarzinom

Wilfried Budach

Klinik für Strahlentherapie und Radioonkologie
Universitätsklinikum Düsseldorf

Strahlentherapie beim Brustkrebs

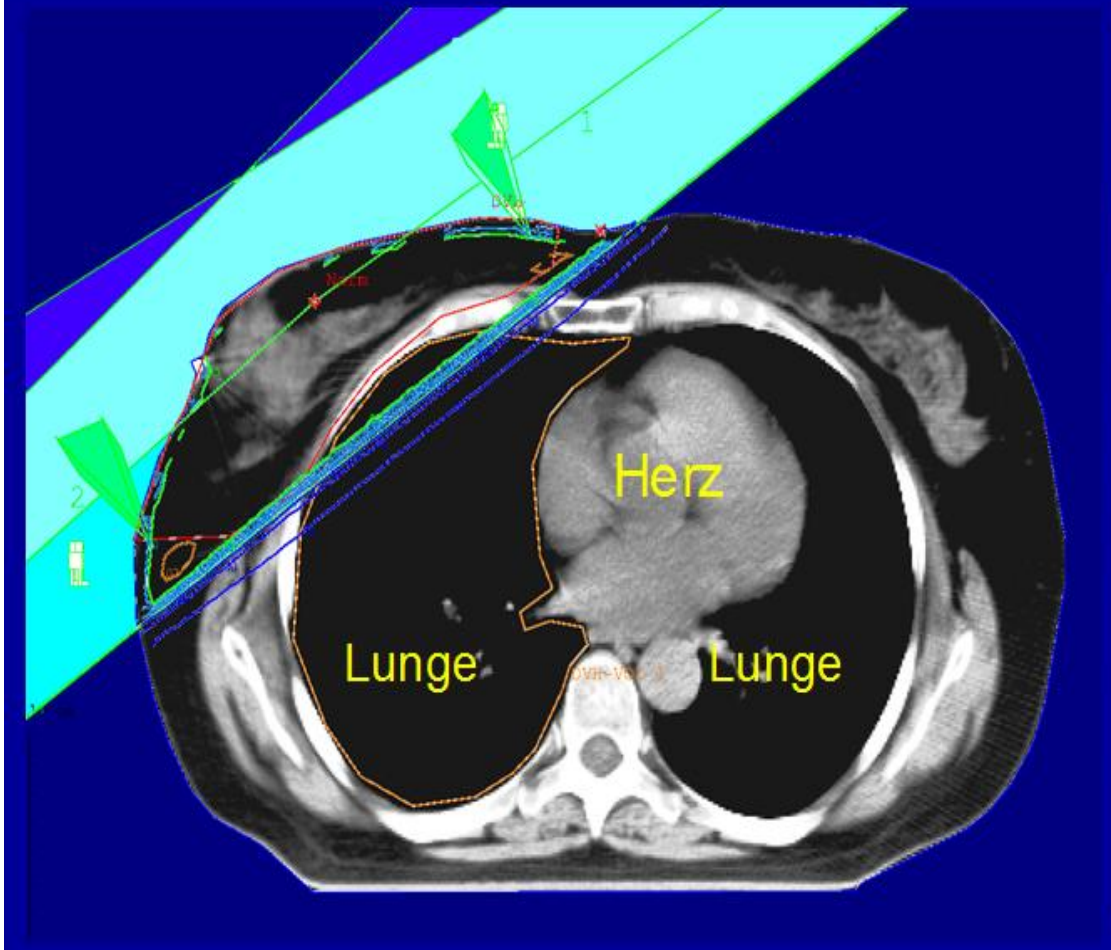
Ziel der Therapie:

- Vernichtung mikroskopisch kleiner Tumorzellnester im Operationsgebiet

Notwendigkeit:

- im Regelfall nach brusterhaltender Operation
- nach operativer Entfernung der Mamma nur wenn große Tumoren vorlagen oder tumorbefallene Lymphknoten in der Achselhöhle gefunden wurden

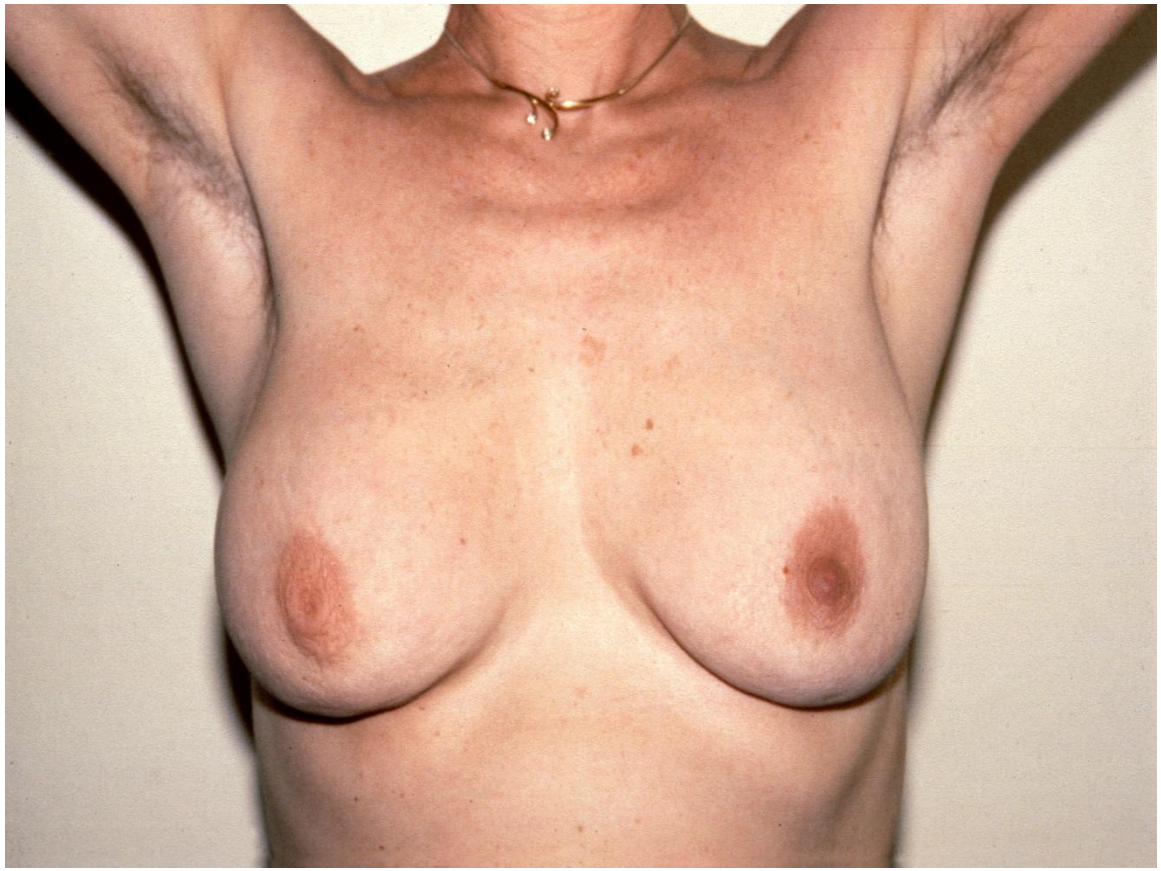
Bestrahlungstechnik bei brusterhaltender Therapie



3D- Bestrahlungsplanung

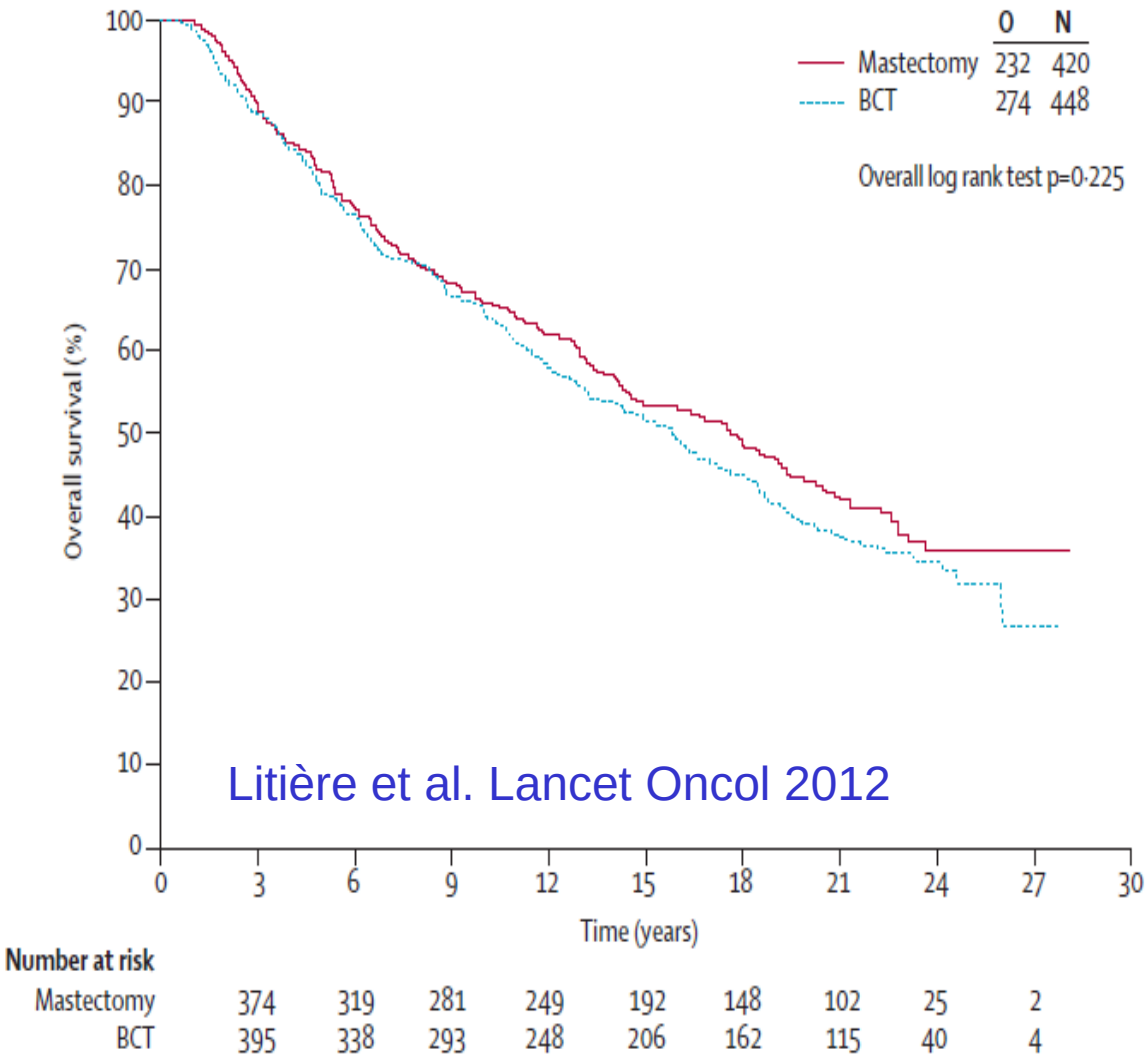
Patientin bei der Bestrahlung

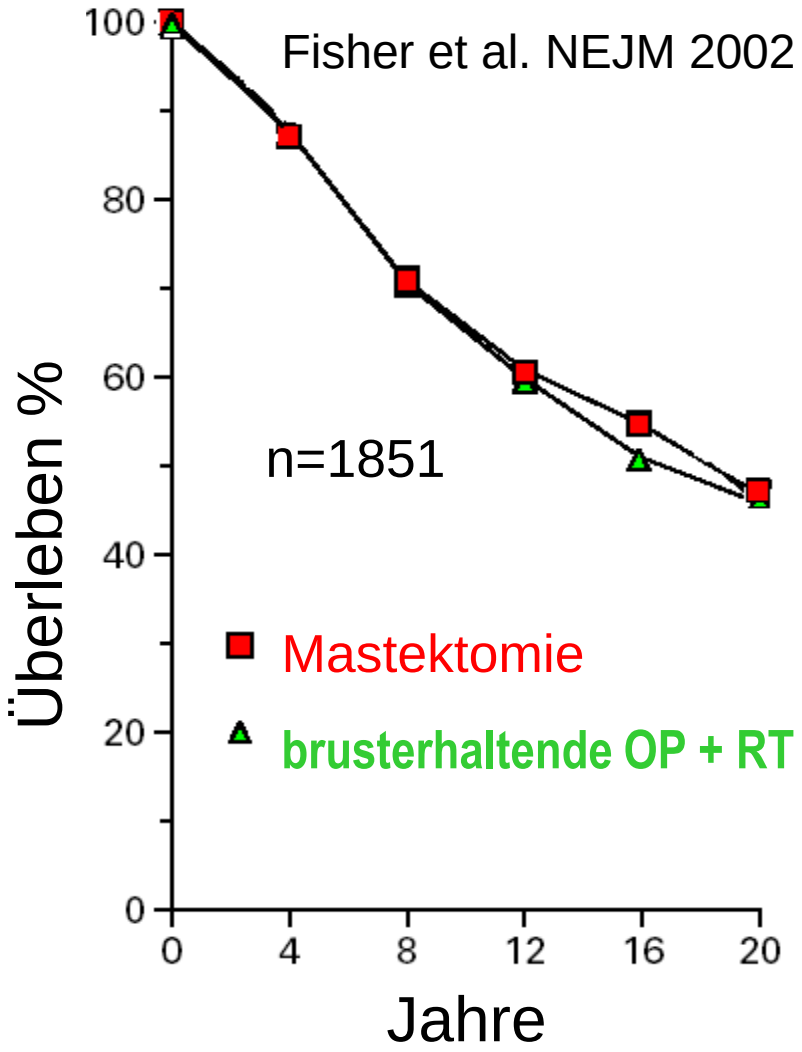
Kosmetisches Ergebnis nach Operation und Strahlentherapie



Brusterhaltende Operation vs. radikale Mastektomie beim Mamma-Ca.

Metaanalyse der EBCTCG, n=3100, NEJM 1995

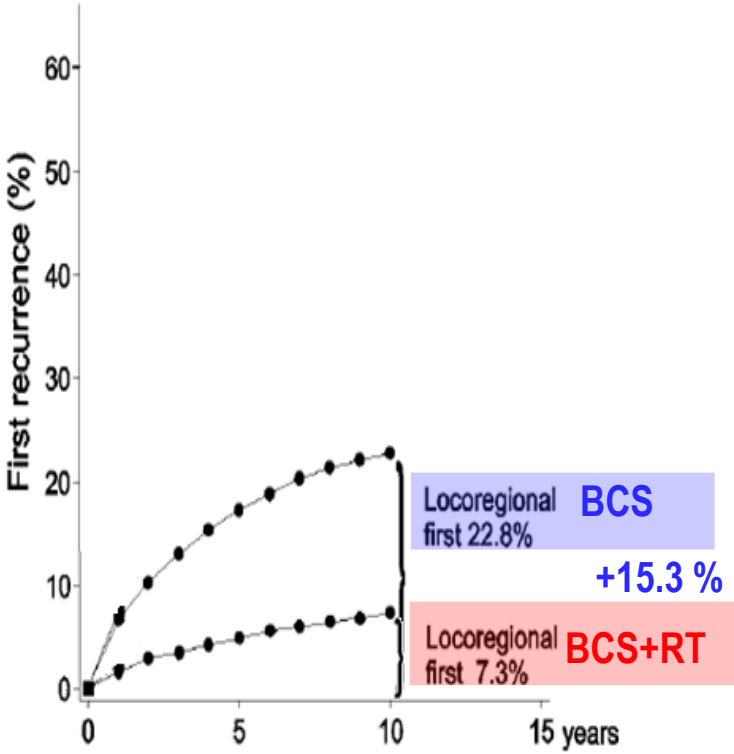




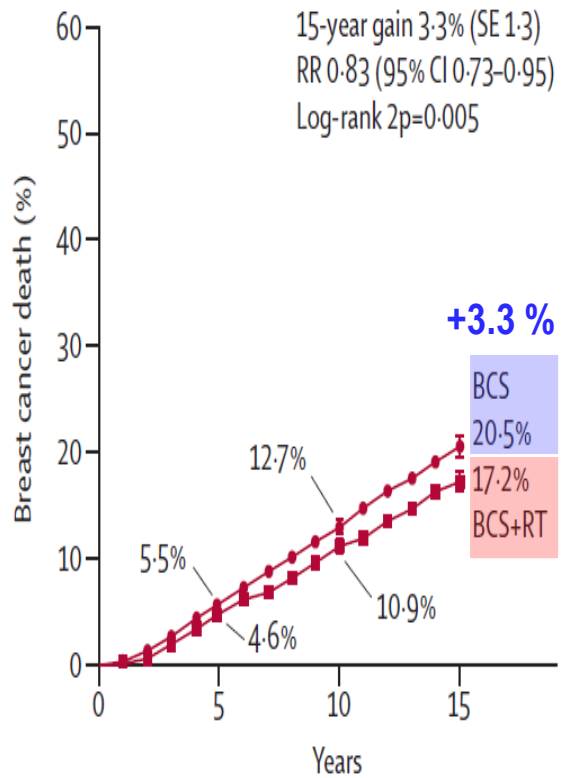
Radiotherapie nach brusterhaltender OP

(7287 Frauen, 10 Jahres-Ergebnisse) EBCTCG Lancet 2011

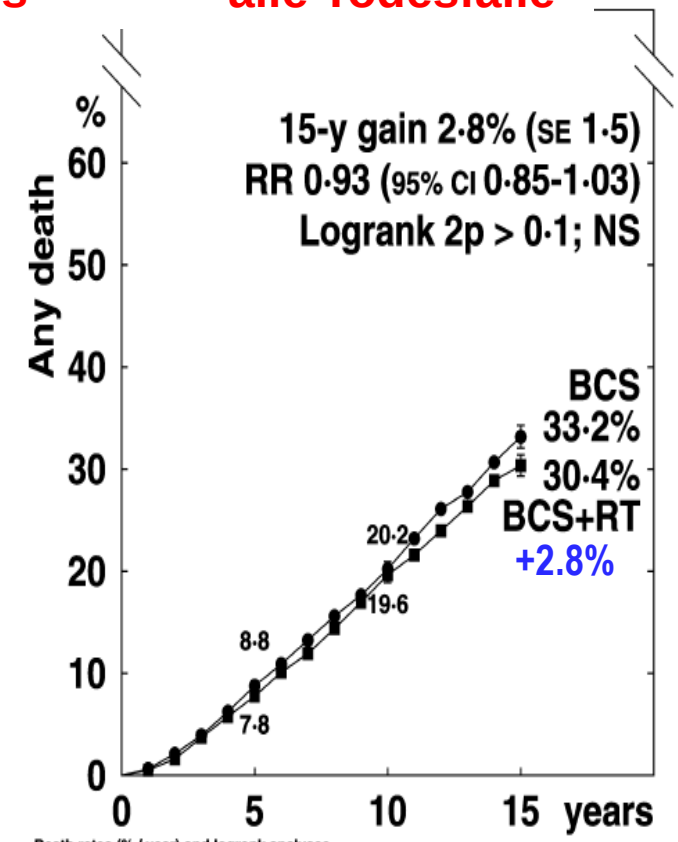
pN0: locoregionäre Rückfall



pN0: Tod durch Brustkrebs



alle Todesfälle



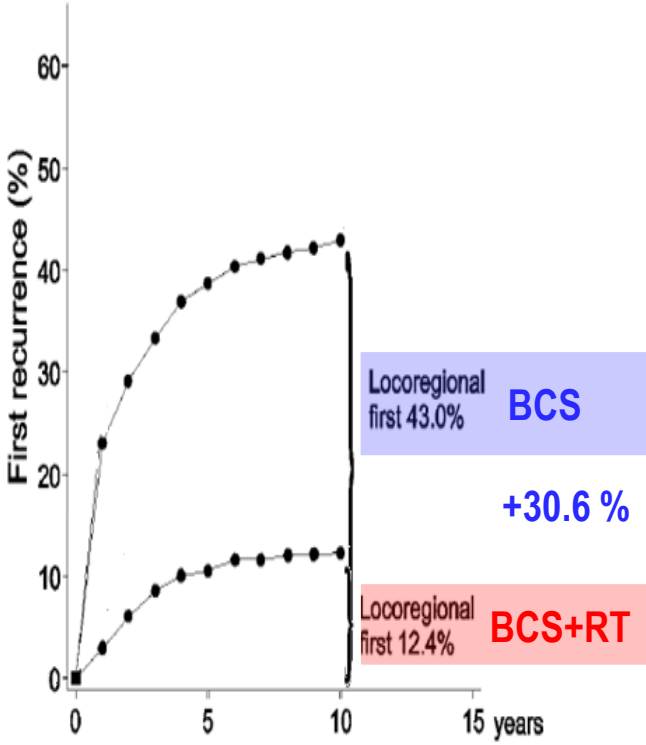
Death rates (% / year) and logrank analyses

	Years 0 - 4	Years 5 - 9	Years 10 - 14	Year 15+
BCS+RT	1·58 (271 / 17127)	2·70 (319 / 11816)	2·85 (164 / 5762)	4·75 (125 / 2630)
BCS	1·80 (303 / 16842)	2·66 (306 / 11499)	3·58 (200 / 5584)	4·61 (113 / 2449)
Rate ratio, from	0·88 SE 0·08	1·02 SE 0·08	0·80 SE 0·10	1·06 SE 0·14
(O-E) / V	-17·8 / 139·5	3·4 / 151·2	-19·0 / 87·3	3·4 / 54·5

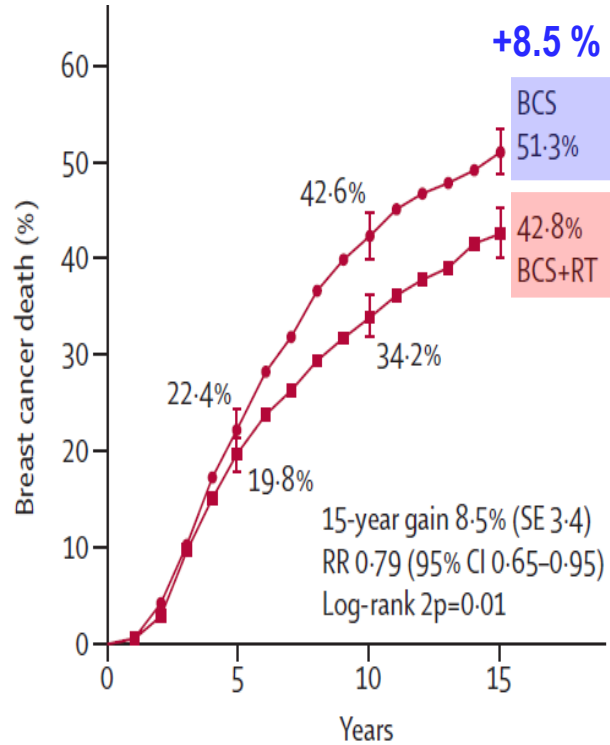
Radiotherapie nach brusterhaltender OP

(1050 women, Frauen, 10 Jahres-Ergebnisse) EBCTCG Lancet 2011

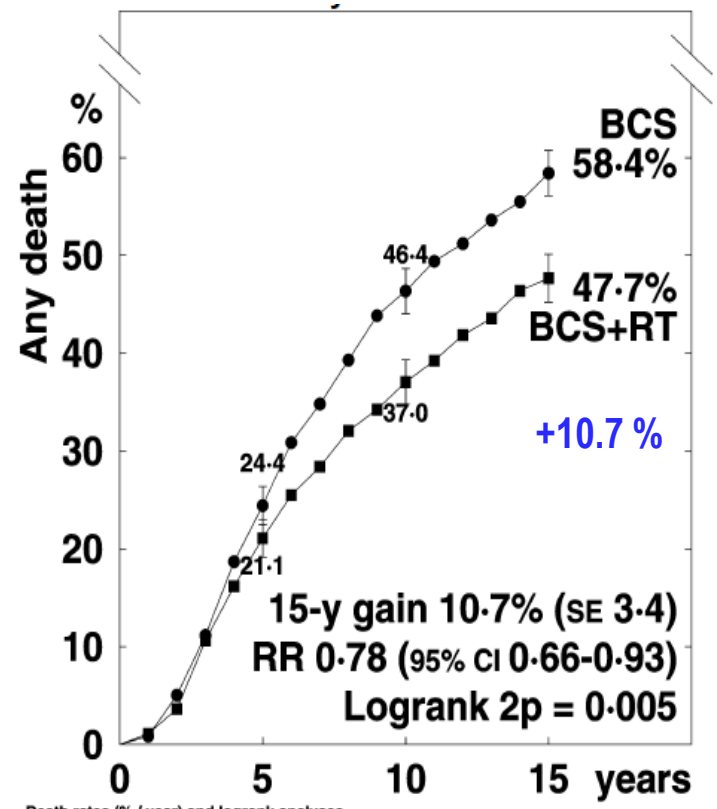
pN0: locoregionäre Rückfall



pN0: Tod durch Brustkrebs



alle Todesfälle

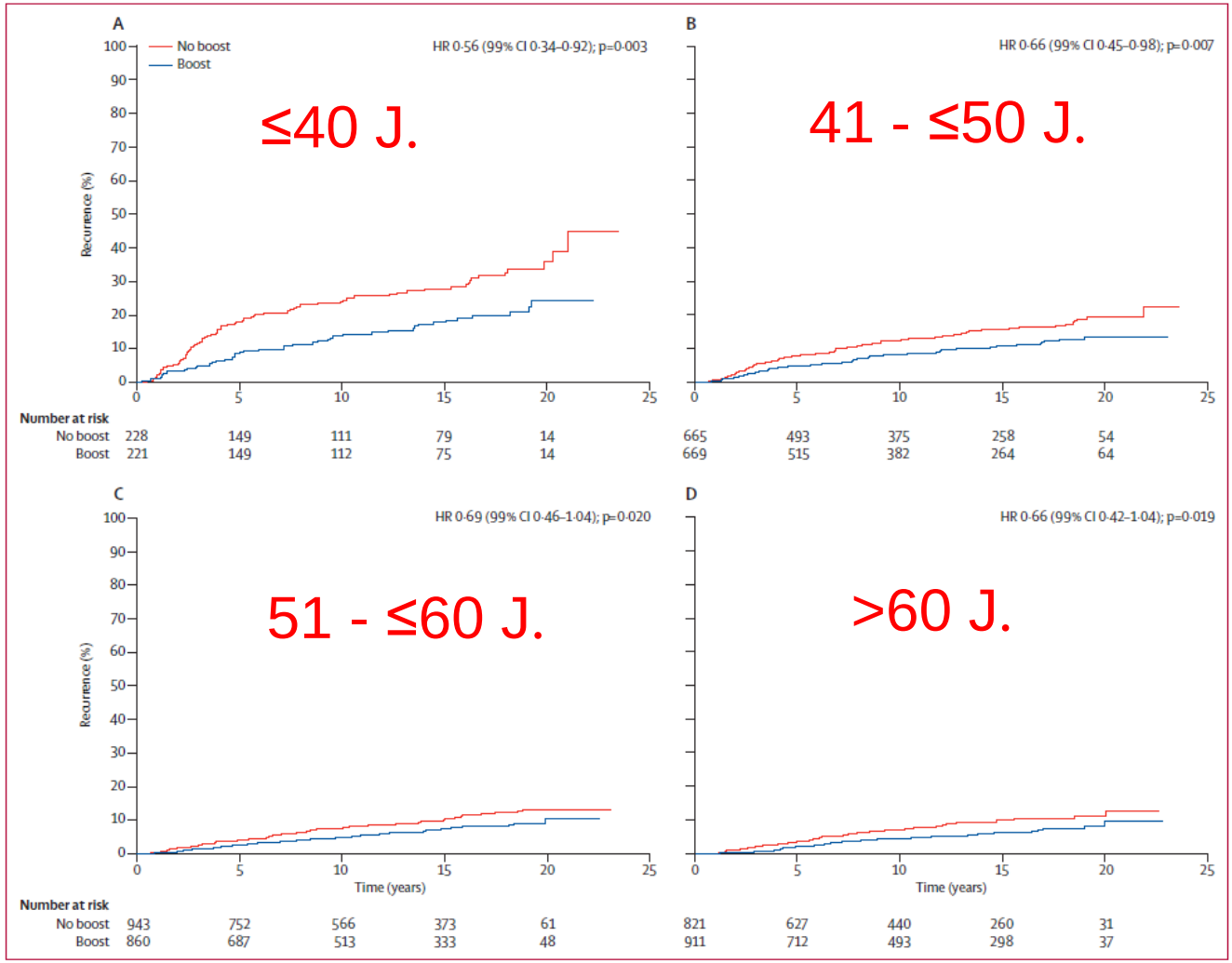


Death rates (% / year) and logrank analyses

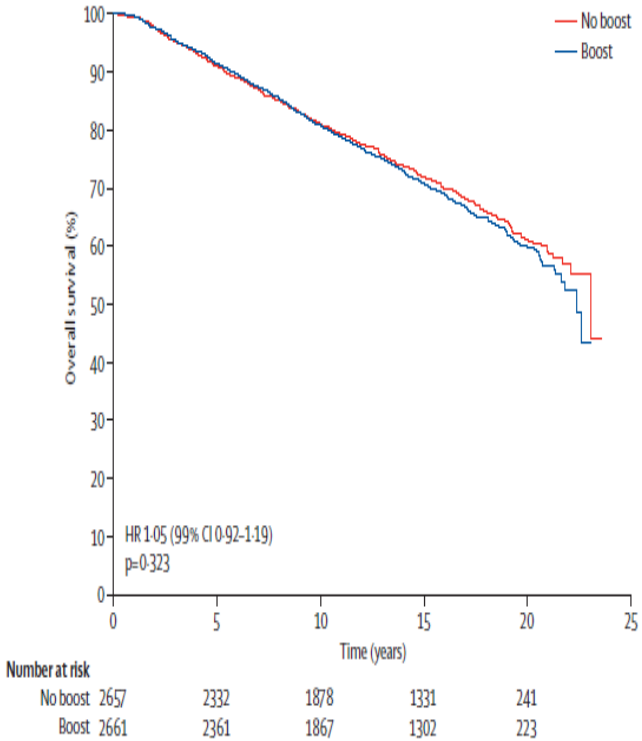
	Years 0 - 4	Years 5 - 9	Years 10 - 14	Year 15+
BCS+RT	4·72 (108 / 2289)	4·62 (78 / 1689)	4·02 (47 / 1168)	4·68 (42 / 898)
BCS	5·27 (120 / 2279)	6·98 (108 / 1547)	4·77 (50 / 1048)	4·02 (32 / 796)
Rate ratio, from	0·84 SE 0·13	0·65 SE 0·13	0·74 SE 0·19	1·06 SE 0·26
(O-E) / V	-8·4 / 49·4	-18·0 / 41·7	-6·5 / 21·7	0·9 / 16·2

Effekt eines 16 Gy „Boosts“ nach RT der Brust

Rückfälle in der betroffenen Brust



Überleben



EORTC trial 22881-10882, (update) Bartelink et al. Lancet Oncol 2014

Brustkrebs: adjuvante Strahlentherapie

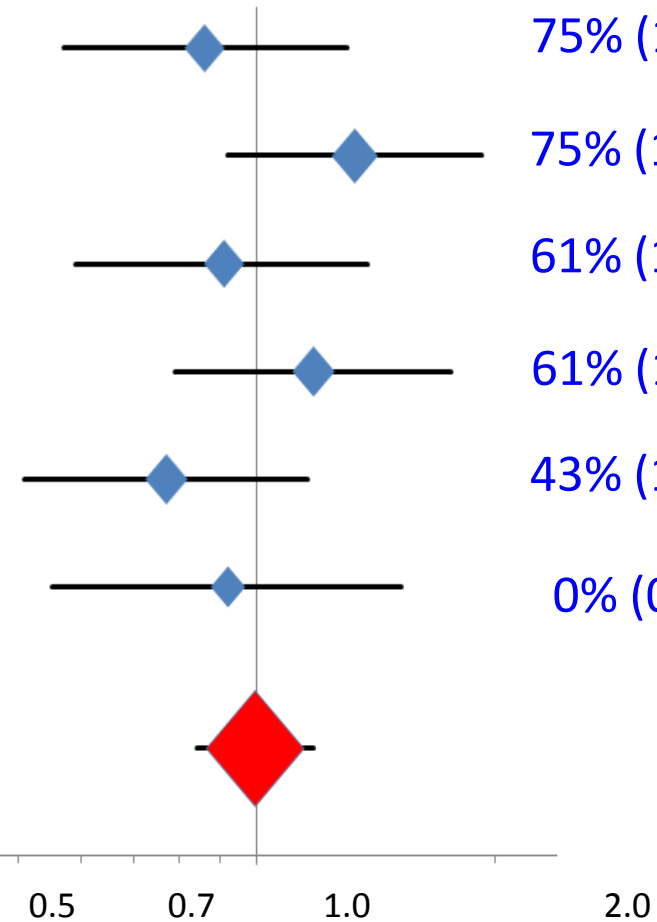
Studien zur hypofraktionierten Strahlentherapie

Study name	Total dose	Fractionation	Week 1	Week 2	Week 3	Week 4	Week 5
Conventional fraction	50 Gy	2 Gy × 25	●●●●●	●●●●●	●●●●●	●●●●●	●●●●●
UK RMH/GOC pilot	39 Gy	3 Gy × 13	● ● ●	● ●	● ● ●	● ●	● ● ●
	42.9 Gy	3.3 Gy × 13	● ● ●	● ●	● ● ●	● ●	● ● ●
START A	39 Gy	3 Gy × 13	● ● ●	● ●	● ● ●	● ●	● ● ●
	41.6 Gy	3.2 Gy × 13	● ● ●	● ●	● ● ●	● ●	● ● ●
START B	40 Gy	2.67 Gy × 15	●●●●●	●●●●●	●●●●●		
Canadian	42.5 Gy	2.66 Gy × 16	●●●●●	●●●●●	●●●●●	●	
UK FAST	28.5 Gy	5.7 Gy × 5	●	●	●	●	●
	30 Gy	6 Gy × 5	●	●	●	●	●

Zhou et al. Surg Oncol 2015

Metaanalyse Hypofraktionierte vs. konventionell fraktionierter RT: Lokale Rückfallrate nach 10 Jahren

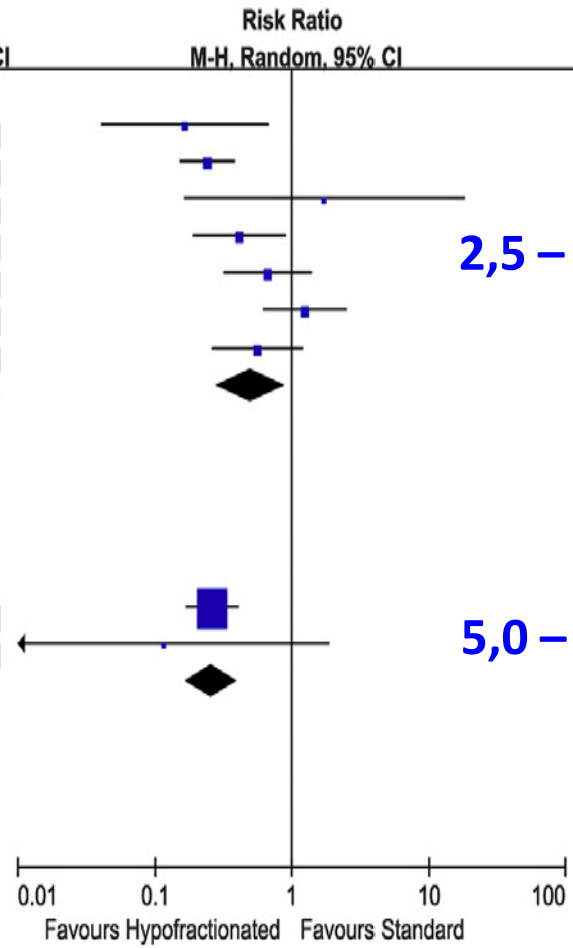
Trial	Dose	Weeks HFX	n (HFX vs CF)	HR	CL-	CL+	p	% Boost (dose)
START Pilot	42.9 Gy vs 50 Gy	5	466 vs. 470	0.86	0.57	1.30	0.47	75% (14Gy/2Gy)
START Pilot	39 Gy vs. 50 Gy	5	474 vs. 470	1.33	0.92	1.92	0.13	75% (14Gy/2Gy)
START A	41.6 Gy vs. 50 Gy	5	750 vs. 749	0.91	0.59	1.38	0.66	61% (10Gy/2Gy)
START A	39 Gy vs. 50 Gy	5	737 vs.749	1.18	0.79	1.76	0.42	61% (10Gy/2Gy)
START B	40 Gy vs. 50 Gy	3	1110 vs. 1105	0.77	0.51	1.16	0.21	43% (10Gy/2Gy)
Ontario	42.5 Gy vs. 50 Gy	3	622 vs. 612	0.92	0.55	1.52	0.75	0% (0 Gy)
Total			**7095**	**1.00**	**0.84**	**1.18**	**0.96**	



W. Budach et al. Breast Care 2015

Hypofraktionierungs-Studien: akute Grad 3/4 Hautreaktion

Study or Subgroup	Hypofractionated Events	Hypofractionated Total	Standard Events	Standard Total	Weight	Risk Ratio M-H, Random, 95% CI
1.7.1 2.5~3.0 Gy/F vs. 1.8~2.0 Gy/F						
Chadha 2012	2	50	18	74	9.6%	0.16 [0.04, 0.68]
Karasawa 2014	24	717	53	381	19.9%	0.24 [0.15, 0.38]
Karmacharya 2012	2	43	1	37	4.7%	1.72 [0.16, 18.22]
Osako 2008	6	66	83	377	16.0%	0.41 [0.19, 0.91]
Taher 2004	6	15	9	15	16.5%	0.67 [0.32, 1.40]
Van Parijs 2012(TomoBreast)	13	37	9	32	17.0%	1.25 [0.62, 2.53]
Wu 2003	10	177	15	149	16.2%	0.56 [0.26, 1.21]
Subtotal (95% CI)		**1105**		**1065**	**100.0%**	**0.50 [0.28, 0.89]**
Total events	63		188			
Heterogeneity: Tau² = 0.38; Chi² = 20.02, df = 6 (P = 0.003); I² = 70%						
Test for overall effect: Z = 2.36 (P = 0.02)						
1.7.2 5.0~6.5 Gy/F vs. 1.8~2.0 Gy/F						
Agrawal 2011(UK FAST)	27	613	51	302	97.5%	0.26 [0.17, 0.41]
Wu 2003	0	41	15	149	2.5%	0.12 [0.01, 1.89]
Subtotal (95% CI)		**654**		**451**	**100.0%**	**0.26 [0.16, 0.40]**
Total events	27		66			
Heterogeneity: Tau² = 0.00; Chi² = 0.34, df = 1 (P = 0.56); I² = 0%						
Test for overall effect: Z = 6.08 (P < 0.00001)						



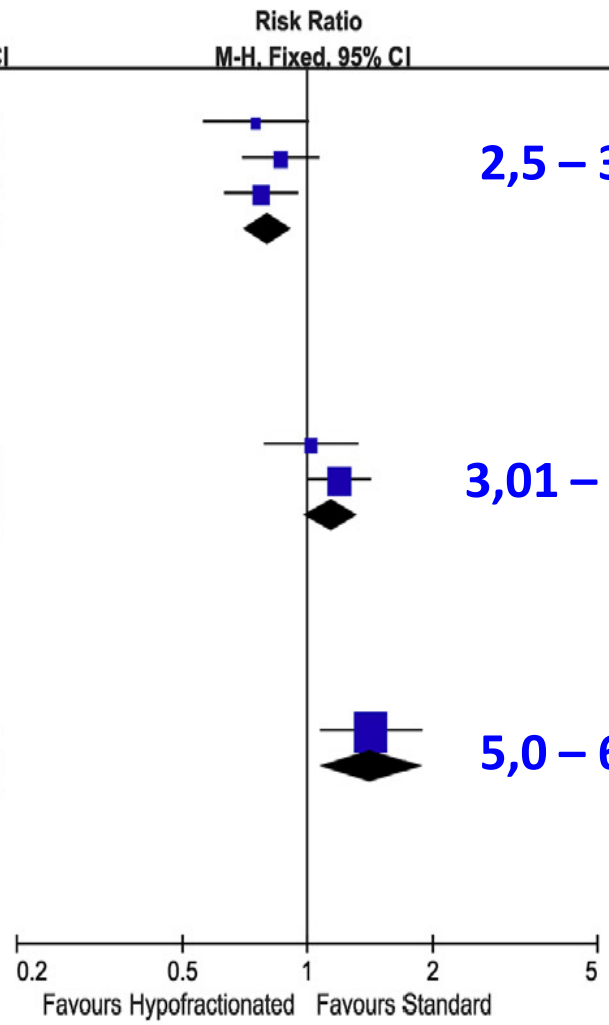
2,5 – 3,0 Gy pro Fraktion

5,0 – 6,5 Gy pro Fraktion

Zhou et al. Surg Oncol 2015

Hypofraktionierungs-Studien: deutliche Veränderung des Ausehens der Brust

Study or Subgroup	Hypofractionated Events	Hypofractionated Total	Standard Events	Standard Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.6.1 2.5~3.0 Gy/F vs. 1.8~2.0 Gy/F						
Bentzen 2008(START A)	51	158	61	142	20.4%	0.75 [0.56, 1.01]
Bentzen 2008(START B)	99	271	102	241	34.3%	0.86 [0.70, 1.07]
Owen 2006(RMH/GOC)	112	409	140	396	45.2%	0.77 [0.63, 0.95]
Subtotal (95% CI)		**838**		**779**	**100.0%**	**0.80 [0.70, 0.91]**
Total events	262		303			
Heterogeneity: Chi² = 0.75, df = 2 (P = 0.69); I² = 0%						
Test for overall effect: Z = 3.28 (P = 0.001)						
1.6.2 3.01~3.33 Gy/F vs. 1.8~2.0 Gy/F						
Bentzen 2008(START A)	65	148	61	142	30.8%	1.02 [0.79, 1.33]
Owen 2006(RMH/GOC)	168	397	140	396	69.2%	1.20 [1.00, 1.43]
Subtotal (95% CI)		**545**		**538**	**100.0%**	**1.14 [0.99, 1.32]**
Total events	233		201			
Heterogeneity: Chi² = 0.96, df = 1 (P = 0.33); I² = 0%						
Test for overall effect: Z = 1.80 (P = 0.07)						
1.6.3 5.0~6.5 Gy/F vs. 1.8~2.0 Gy/F						
Agrawal 2011(UK FAST)	146	490	50	239	100.0%	1.42 [1.07, 1.89]
Subtotal (95% CI)		**490**		**239**	**100.0%**	**1.42 [1.07, 1.89]**
Total events	146		50			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.46 (P = 0.01)						



2,5 – 3,0 Gy pro Fraktion

3,01 – 3,33 Gy pro Fraktion

5,0 – 6,5 Gy pro Fraktion

Zhou et al. Surg Oncol 2015

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Guidelines Breast
Version 2015.1D

Radiotherapie (RT) nach brusterhaltenden Operationen (BEO; invasive Karzinome): - Bestrahlung der Brust - (2016)

LoE 1b B AGO ++

< 50 Jahre	Hypofraktionierte RT mit sequentiellem Boost oder konventionelle RT (25-28 Fraktionen) mit integriertem oder sequentiellem Boost
≥ 50 Jahre	Niedriges Risiko*: hypofraktionierte RT ohne Boost (15-16 Fraktionen) Hohes Risiko: RT wie für <50 Jahre
Ältere Pat.	Individuelle Beratung einschließlich Verzicht auf RT je nach individuellem Risiko und geriatr. Einschätzung
Jedes Alter (Lymphabflusswege)	Bei zusätzlicher Bestrahlung der Lymphabflusswege konventionell fraktionierte RT (25-28 Fraktionen)

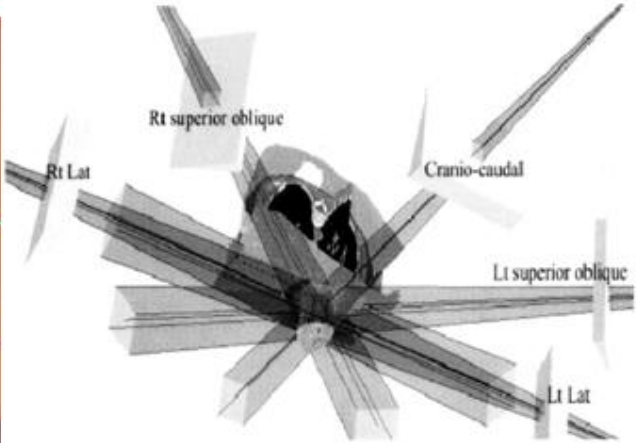
*wie Definition zur Boost-Bestrahlung

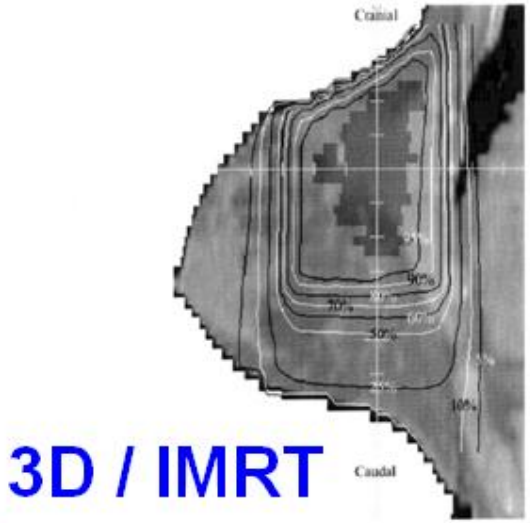
Studienteilnahme empfohlen

www.ago-online.de

FORSCHEN
LEHREN
HEILEN

Teilbrustbestrahlung

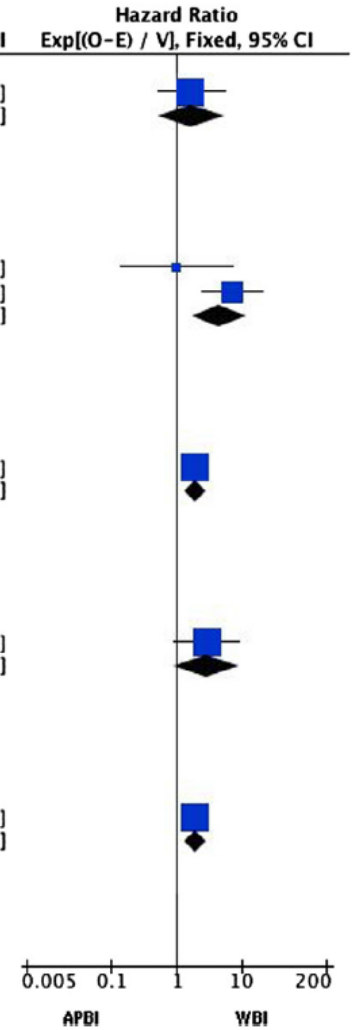




Partial breast irradiation (PBI) or whole breast radiotherapy (WBI) for early breast cancer: A meta-analysis of randomized controlled trials

Local recurrence: HR = 4.54, 95% CI: 1.78–11.61, p = 0.002 for PBI

Study or Subgroup	APBI Events	APBI Total	WBI Events	WBI Total	O-E	Variance	Weight	Hazard Ratio Exp[(O-E) / V], Fixed, 95% CI
1.1.1 Four years								
Vaidya 2010	6	1113	5	1119	1.365	2.727	100.0%	1.65 [0.50, 5.41]
Subtotal (95% CI)		**1113**		**1119**			**100.0%**	**1.65 [0.50, 5.41]**
Total events	6		5					
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.83 (P = 0.41)								
1.1.2 Five years								
Rodríguez 2013	0	51	0	51	0	1	22.9%	1.00 [0.14, 7.10]
Veronesi 2013	21	651	4	654	6.598	3.36	77.1%	7.13 [2.45, 20.76]
Subtotal (95% CI)		**702**		**705**			**100.0%**	**4.54 [1.78, 11.61]**
Total events	21		4					
Heterogeneity: Chi^2 = 2.97, df = 1 (P = 0.08); I^2 = 66%								
Test for overall effect: Z = 3.16 (P = 0.002)								
1.1.3 Seven years								
Ribeiro 1993	69	353	39	355	16.672	24.916	100.0%	1.95 [1.32, 2.89]
Subtotal (95% CI)		**353**		**355**			**100.0%**	**1.95 [1.32, 2.89]**
Total events	69		39					
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.34 (P = 0.0008)								
1.1.4 Eight years								
Dodwell 2005	10	84	4	90	3.03	2.857	100.0%	2.89 [0.91, 9.21]
Subtotal (95% CI)		**84**		**90**			**100.0%**	**2.89 [0.91, 9.21]**
Total events	10		4					
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.79 (P = 0.07)								
1.1.5 Ten years								
Polgar 2013	69	353	39	355	16.672	24.916	100.0%	1.95 [1.32, 2.89]
Subtotal (95% CI)		**353**		**355**			**100.0%**	**1.95 [1.32, 2.89]**
Total events	69		39					
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.34 (P = 0.0008)								



Marta et al. Radiotherapy and Oncology 2015

Partial breast RT using brachytherapy vs. WBI

	APBI group (n=633)	WBI group (n=551)
Age (years)		
Median (IQR)	62 (54–67)	62 (54–68)
>40–50	91 (14%)	91 (17%)
>50–60	192 (30%)	162 (29%)
>60–70	256 (40%)	202 (37%)
>70	94 (15%)	96 (17%)
Menopausal status		
Premenopausal	108 (17%)	92 (17%)
Postmenopausal	525 (83%)	459 (83%)
Tumour size and resection margins		
Tumour diameter (mm)	12 (9–17)	12 (9–17)
Surgical free margins (mm, range)	8 (2–40)	7 (2–25)
T stage		
pTis (DCIS)	36 (6%)	24 (4%)
pT1a	30 (5%)	21 (4%)
pT1b	187 (30%)	182 (33%)
pT1c	313 (49%)	262 (48%)
pT2 (≤3 cm)	67 (11%)	58 (11%)
N stage		
pN0	127 (20%)	118 (21%)
pN0 sn	470 (74%)	408 (74%)
pN1 mi	5 (1%)	5 (1%)
Grading		
1	248 (39%)	217 (39%)
2	319 (50%)	288 (52%)
3	57 (9%)	42 (8%)
Hormone receptor status		
ER+/PR+	510 (81%)	447 (81%)
Antihormonal treatment		
Yes	549 (87%)	482 (87%)
No	82 (13%)	69 (13%)
No data	2 (<1%)	0
Chemotherapy		
Yes	63 (10%)	65 (12%)
No	568 (90%)	486 (88%)
No data	2 (<1%)	0

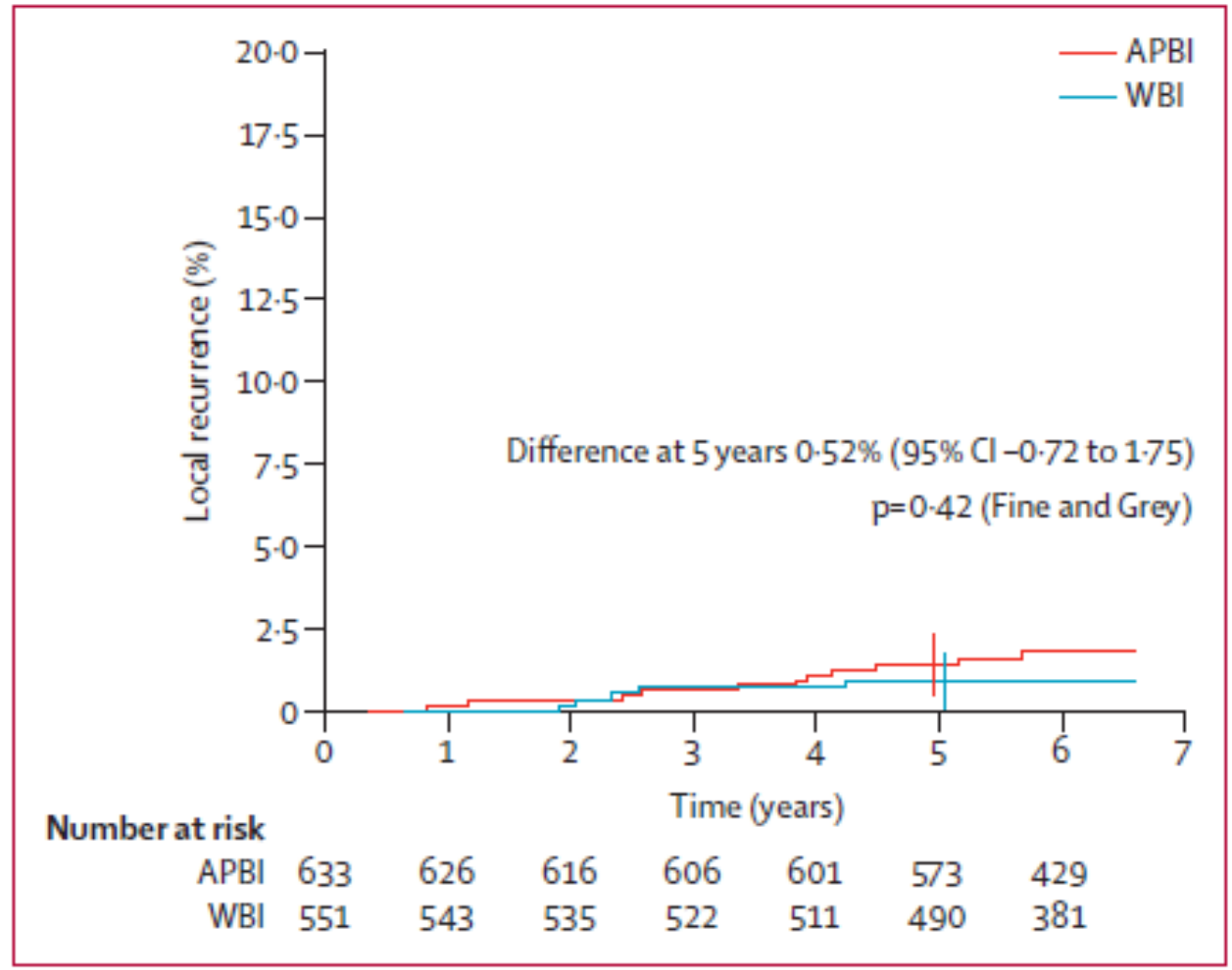


Figure 2: **Ipsilateral breast tumour recurrence**
APBI=accelerated partial breast irradiation. WBI=whole-breast irradiation.

Strnad et al. Lancet 2015

Boost und Teilbrustbestrahlung nach BEO beim invasiven Karzinom (2016)

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Guidelines Breast
Version 2015.1D

	Oxford / AGO LoE	GR	
➢ Boost-RT des Tumorbettes (verbesserte lokale Kontrolle, kein Überlebensbenefit)			
➢ < 40 Jahre	1b	B	++
➢ 40 - 60 Jahre	1b	B	+
➢ > 60 Jahre, G3 oder >pT1	2b	B	+/-
➢ Intraoperative Radiotherapie (intraop. APBI)			
➢ Als Boost-Bestrahlung vor Ganzbrust-RT	2a	B	+
➢ Als alleinige Radiotherapie-Maßnahme (IORT 50 kV, IOERT)**			
➢ >50 Jahre **	1b	B	+/-*
➢ >70 Jahre**	1b	B	+
➢ Postoperative Teilbrustbestrahlung als alleinige Radiotherapie-Maßnahme bei ausgewählten Pat. (APBI)			
➢ Interstitielle Brachytherapie	1b	B	+/-*
➢ >70 Jahre**	1b	B	+
➢ Intrakavitäre Ballontechnik	2b	B	-*
➢ IMRT***	2b	B	-*

*Studienteilnahme empfohlen; **nur bei pT1 pN0 R0 G1-2, HR+, nicht-lobulär, >50 J., kein extensives DCIS, IORT während des ersten Eingriffs; ***keine Langzeitdaten;

Die ältere Mammakarzinompatientin

Benötigt die ältere Patienten eine

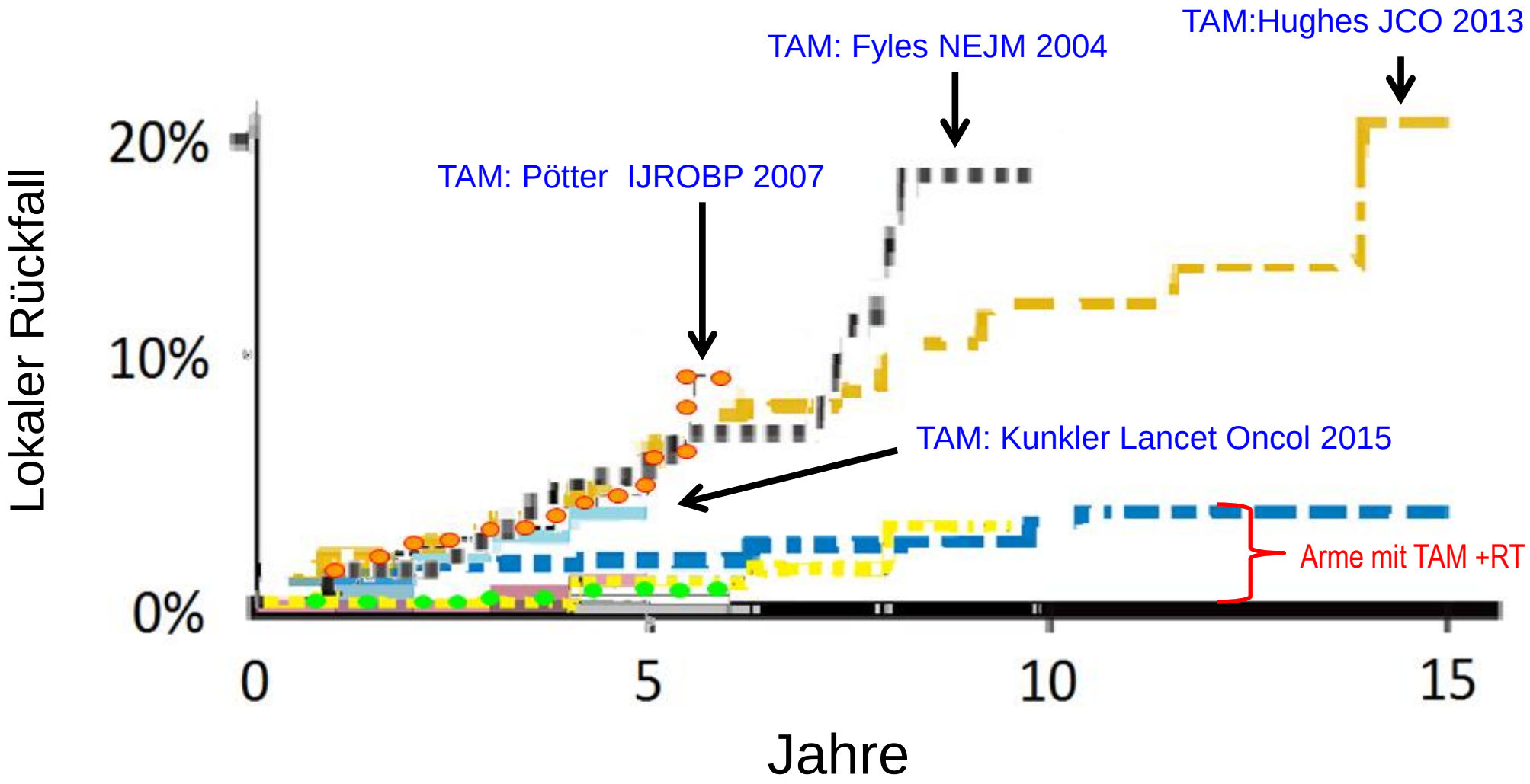
adjuvante Strahlentherapien

nach brusterhaltender Operation?

Summary of results: No RT vs. RT in low risk patients (T1-2 [<3 cm] N0, ER+)

Reference	n	local recurrence		p	OS
		Tam	Tam+RT		
Fyles et al. NEJM 2004	611	12.2% @8y.	3.6% @8y	<0.001	n.s
Hughes et al. JCO 2013	636	17.0% @10y.	7.0% @10y.	<0.001	n.s
Pötter et al. IJROBP 2007	831	9.5% @6y.	0.5% @6y.	<0.001	n.s
Blamey et al. EJC 2013	204	7.0% @10y.	0.0% @10y.	<0.05	n.s
Kunkler et al. Lancet Oncol 2015	1316	1.3% @5 y.	4.1% @5y.	0.0002	n.s.

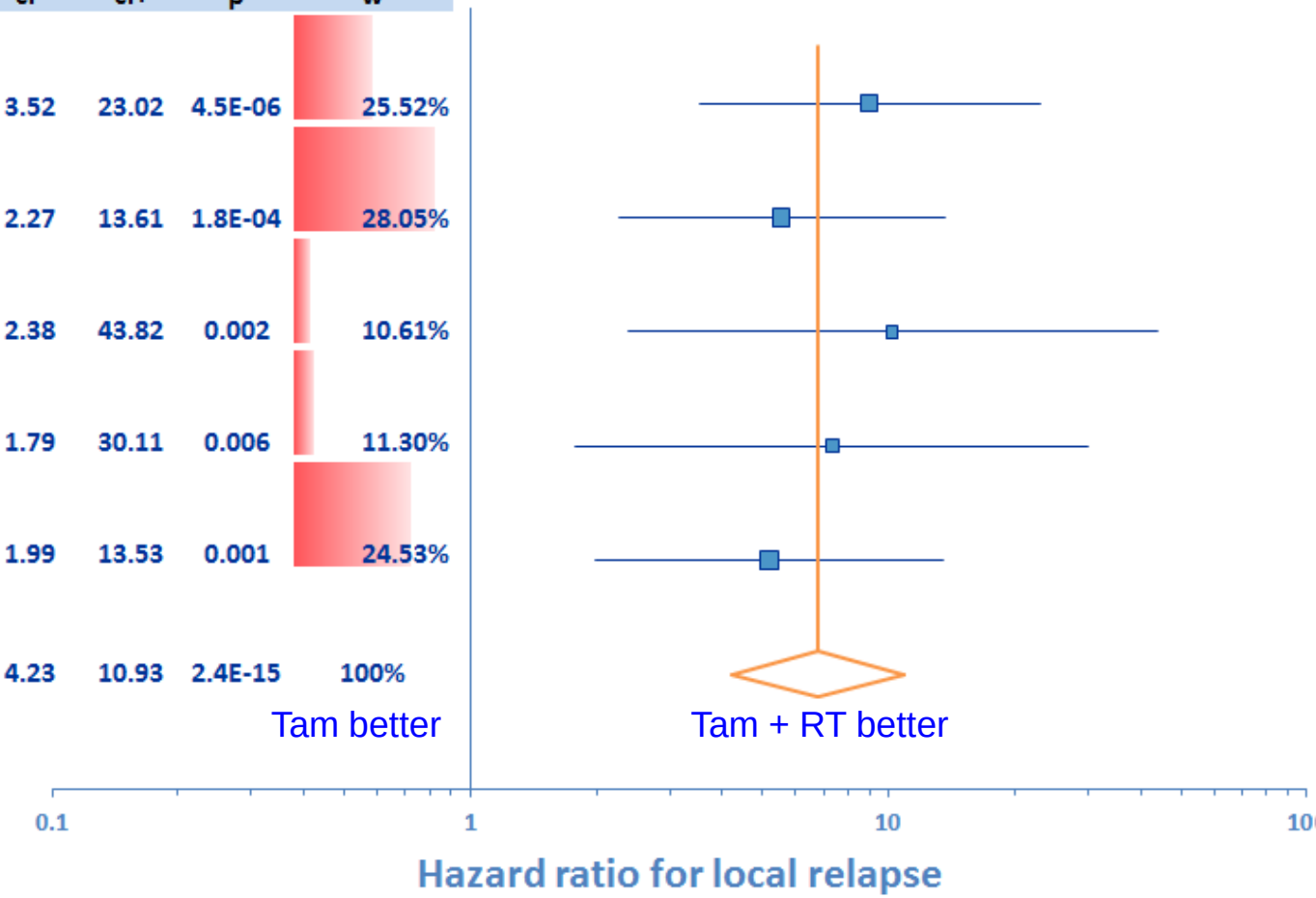
Keine RT vs. RT bei niedrigem Risiko (T1-T2<3cm,N0, HR+)



Meta-Analysis: Keine RT vs. RT bei niedrigem Risiko (T1-2 [<3 cm] N0, HR+)

Lokaler Rückfall

id	N	hr	ci-	ci+	p	w
Fyles et al 2004	769	9.00	3.52	23.02	4.5E-06	25.52%
Hughes et al. 2013	636	5.56	2.27	13.61	1.8E-04	28.05%
Pötter et al 2007	831	10.21	2.38	43.82	0.002	10.61%
Blamey et al. 2013	204	7.34	1.79	30.11	0.006	11.30%
Kunkler et al. Lancet Oncol 2015	1326	5.19	1.99	13.53	0.001	24.53%
Total	3766	6.80	4.23	10.93	2.4E-15	100%

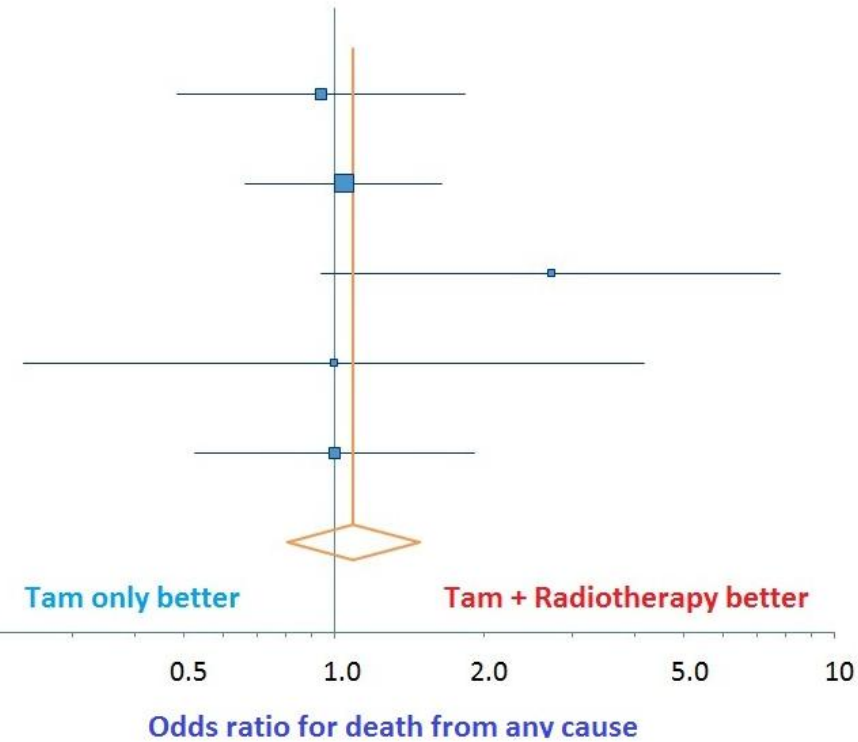


W. Budach et al. unpublished

Meta-Analysis: Keine RT vs. RT bei niedrigem Risiko (T1-2 [<3 cm] N0, HR+)

Gesamtüberleben

authors	N	years	OR	ci-	ci+	p	w
Fyles et al. 2004	769	5	0.94	0.48	1.82	0.86	0.21
Hughes et al. 2013	636	10	1.05	0.66	1.65	0.85	0.44
Pötter et al. 2007	831	5	2.71	0.94	7.82	0.06	0.08
Blamey et al. 2013	204	10	1.00	0.24	4.18	1.00	0.04
Kunkler et al. 2015	1326	5	1.00	0.53	1.90	1.00	0.22
Total	3766		1.09	0.81	1.48	0.57	1.00



W. Budach et al. unpublished

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Guidelines Breast
Version 2015.1

Radiotherapie bei der älteren Patientin Lebenserwartung <10 Jahre (2016)

Oxford / AGO
LoE / GR

- **Verzicht auf Radiotherapyie bei niedrigem Risiko, wenn adjuvante antihormonelle Therapie über 5 Jahre konsequent durchgeführt wird**

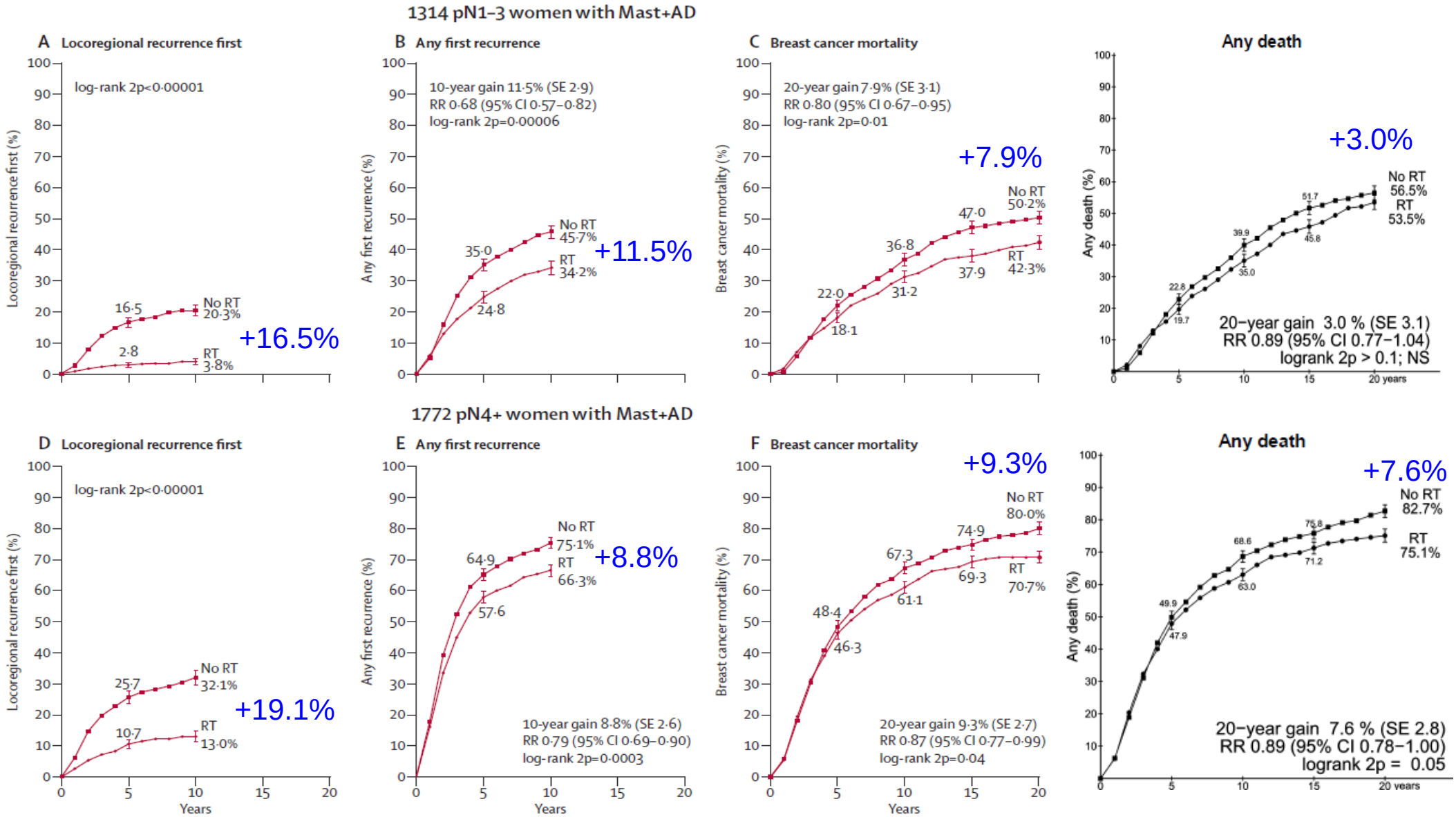
AGO[1]	**1b**	**B**	**+**
DEGRO[1]	**1b**	**C**	**+/-**

Increase in local recurrence,
no influence on OS, decrease in toxicity

- **Alter≥ 70 Jahre, pT1, pN0, HR positiv, G1-2, HER2-negativ, negative Resektionsränder (>1 mm)**

[1] **unterschiedliche Interpretation der Daten durch AGO und DEGRO**

Adjuvante RT nach Mastektomie – EBCTCG update 2014



Early Breast Cancer Trialists' Collaborative Group, Lancet 2014

Strahlentherapie der Brustwand nach Mastektomie (PMRT)**

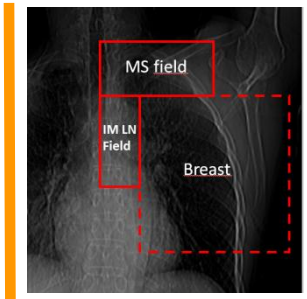
				Oxford / AGO LoE / GR
➢ > 3 befallene Lymphknoten (LK)		1a	A	++
➢ 1–3 befallene LK, hohes Risiko	AGO[1]	1a	A	+
➢ 1–3 befallene LK, niedriges Risiko *	AGO[1]	5	D	+/-
➢ 1-3 befallene LK (alle Risikogruppen)	DEGRO[1]	1a	A	+
➢ T3 / T4		1a	A	++
➢ pT3 pN0 R0 (ohne zusätzliche Risikfaktoren)		2b	B	+/-
➢ wenn R0 nicht möglich ist (invasive Tumoren)		1a	A	++
➢ Junge Patientinnen mit Risikofaktoren		2b	B	++
➢ Nach neoadjuvanter Chemotherapie (NACT) basierend auf dem Stadium vor NACT (cN+, cT3/4a-d)		2a	A	+
➢ Verzicht auf RT, wenn ypT0 ypN0 nach NACT**		2b	B	+/-
Die Indicationen für die PMRT und regionale RT sind unabhängig von der adjuvanten systemischen Therapie		1a	A	

[1] unterschiedliche Interpretation der Daten durch AGO und DEGRO

Randomisierte Studien zur Lymphabflussbestrahlung

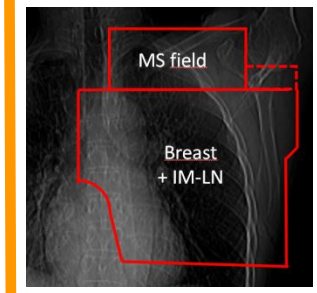
French [13]
n=1334

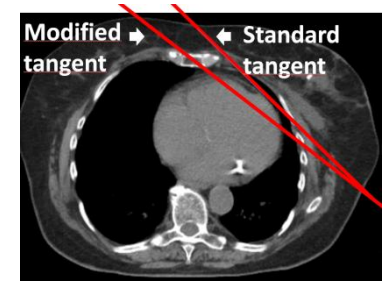
Mastectomy → random
- → Control arm (n=662) Chest Wall + MS-LN RT
- → Experimental arm (n=672) Chest Wall + MS-IM-LN RT



MA.20 [10]
n=1832

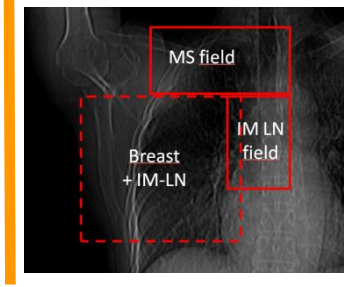
Breast Conserving Surgery → random
- → Control arm (n=916) Whole Breast - RT
- → Experimental arm (n=916) Whole Breast + MS-IM-LN RT

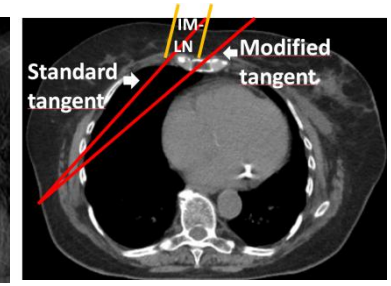




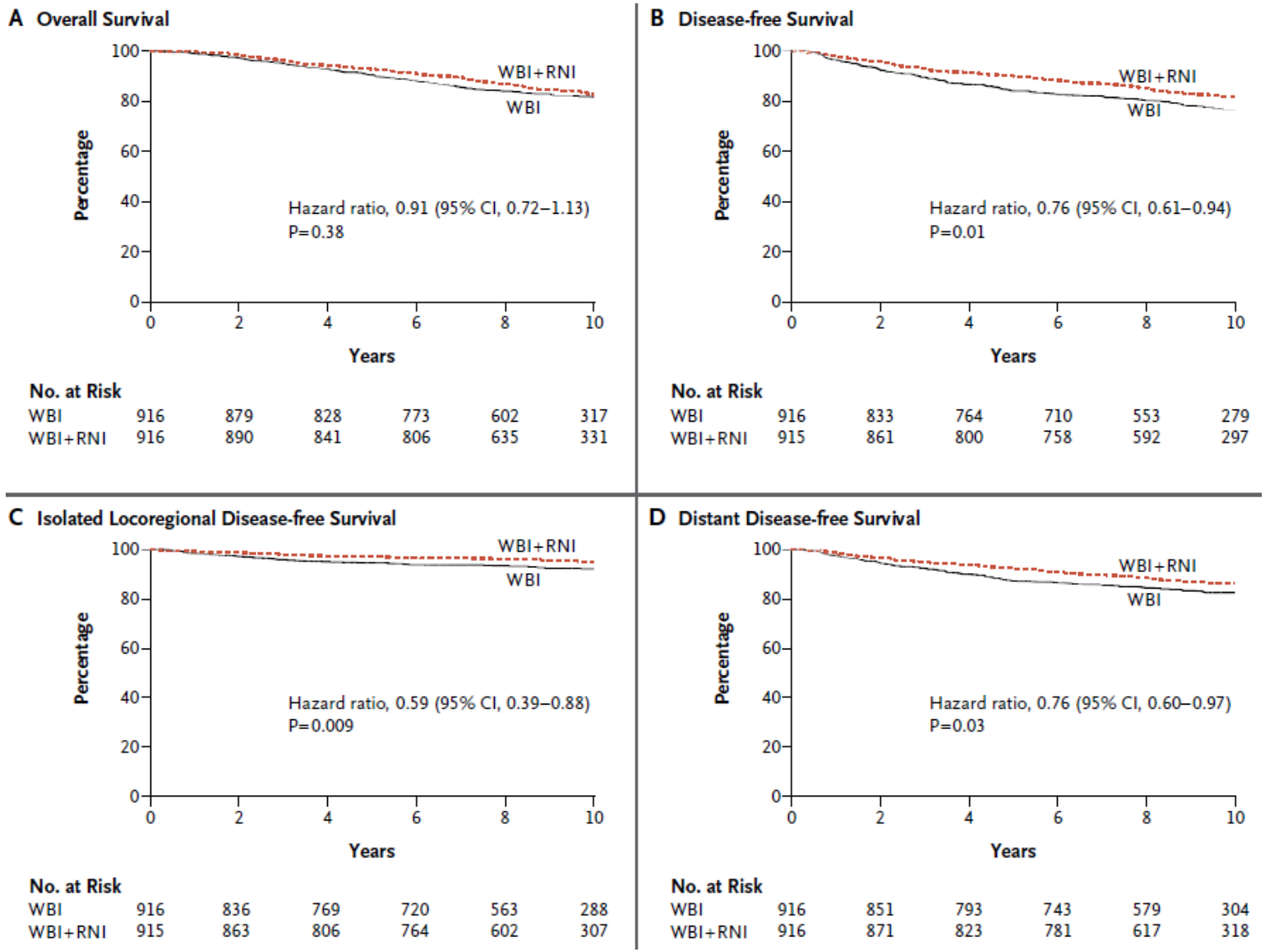
EORTC [12]
n=4004

Breast Conserving Surgery or Mastectomy → random
- → Control arm (n=2002) Whole Breast or Chest Wall - RT
- → Experimental arm (n=2002) Whole Breast or Chest Wall + MS-IM-LN RT



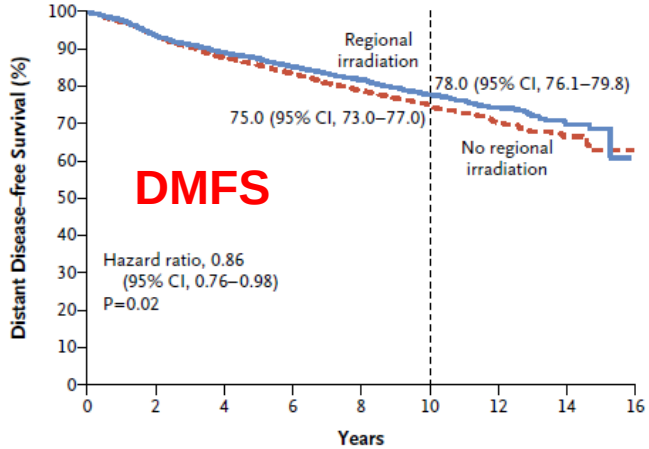


MA.20 trial: RT der Brust vs. RT der Brust + Lymphabfluss-RT

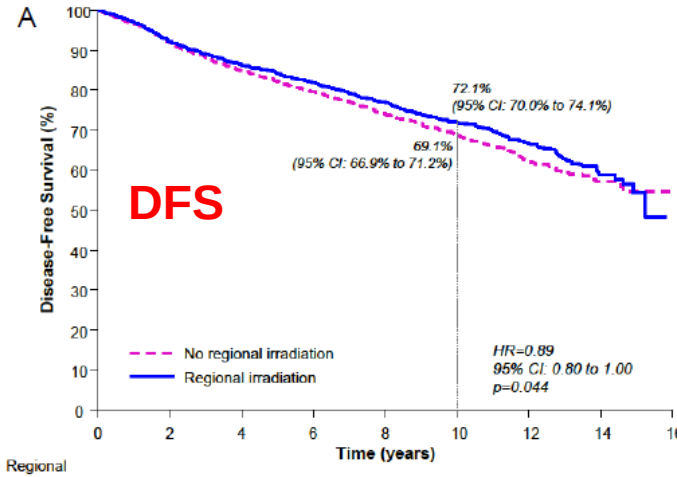


Whelan et al. NEJM 2015

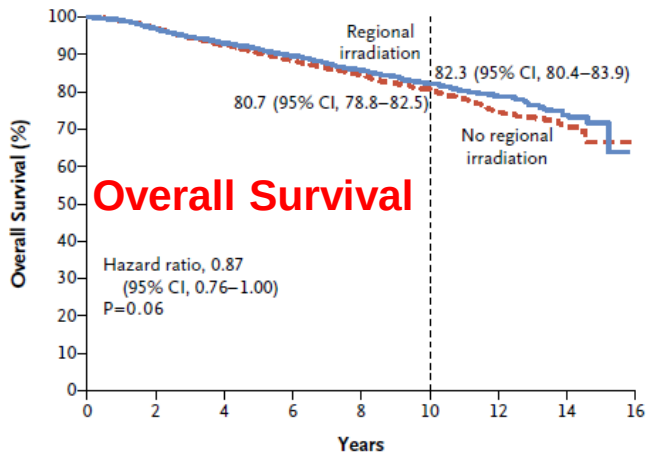
EORTC 22922/ trial: : RT der Brust vs. RT der Brust + Lymphabfluss-RT



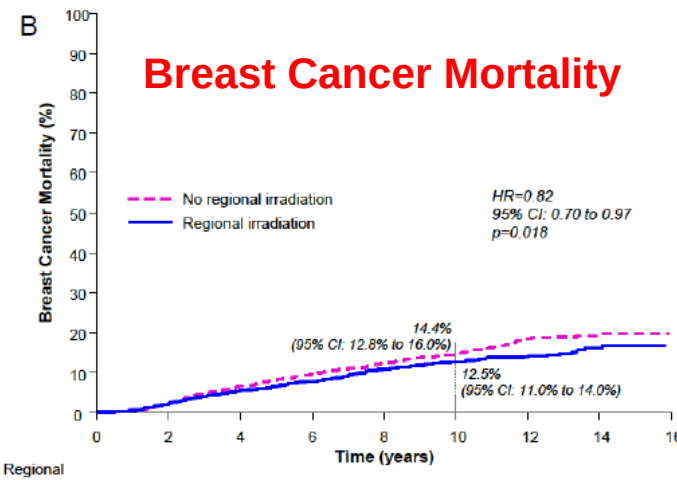
No. at Risk									No. of Events
No regional irradiation	2002	1862	1728	1606	1382	890	403	113	523
Regional irradiation	2002	1866	1764	1650	1464	939	437	117	462



Regional Irradiation	O	N	Number of patients at risk:						
No	655	2002	1831	1674	1535	1299	813	352	96
Yes	601	2002	1838	1710	1582	1368	858	395	101



No. at Risk									No. of Events
No regional irradiation	2002	1926	1819	1698	1475	969	434	119	429
Regional irradiation	2002	1931	1839	1732	1532	988	466	124	382



Regional Irradiation	O	N	Number of patients at risk:						
No	310	2002	1926	1819	1698	1476	970	434	120
Yes	259	2002	1931	1839	1732	1532	990	467	124

Poortmans et al. NEJM 2015

Update: Metaanalyse der Studien zur Lymphabfluss-RT beim Mamma-Ca.

Überleben

Vergleich I: (MS+IM)+(WBI/CWI) vs. (WBI/CWI)

MA.20 [16]: n=1832; HR 0.91 (95% CL 0.72 - 1.13)

EORTC [17]: n=4004; HR 0.87 (95% CL 0.76 - 1.00)

Subtotal*: n=5836; HR 0.88 (95% CL 0.78 - 0.99) — p=0,034

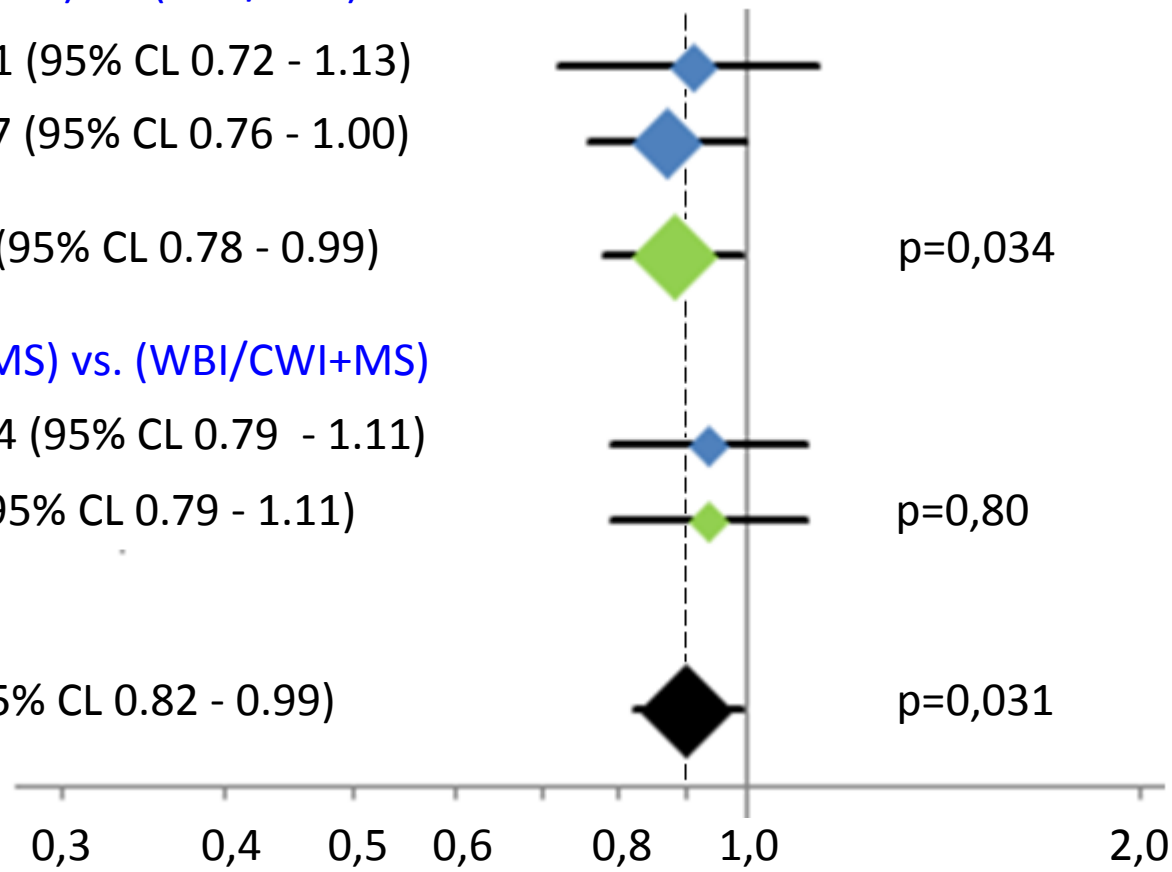
Vergleich II: IM+(WBI/CWI+MS) vs. (WBI/CWI+MS)

French [15]: n=1334; HR 0.94 (95% CL 0.79 - 1.11)

Subtotal: n=1334; HR 0.94 (95% CL 0.79 - 1.11) — p=0,80

Vergleiche I+II

Total**: n=7170; HR 0.90 (95% CL 0.82 - 0.99) — p=0,031



*= fixed effect model

** = random effect model

W. Budach et al. unpublished

Population based Danish breast cancer cohort trial: N+, <70 y.

Whole breast (WBI)/chest wall (CWI) RT + supra/infracalv. RT

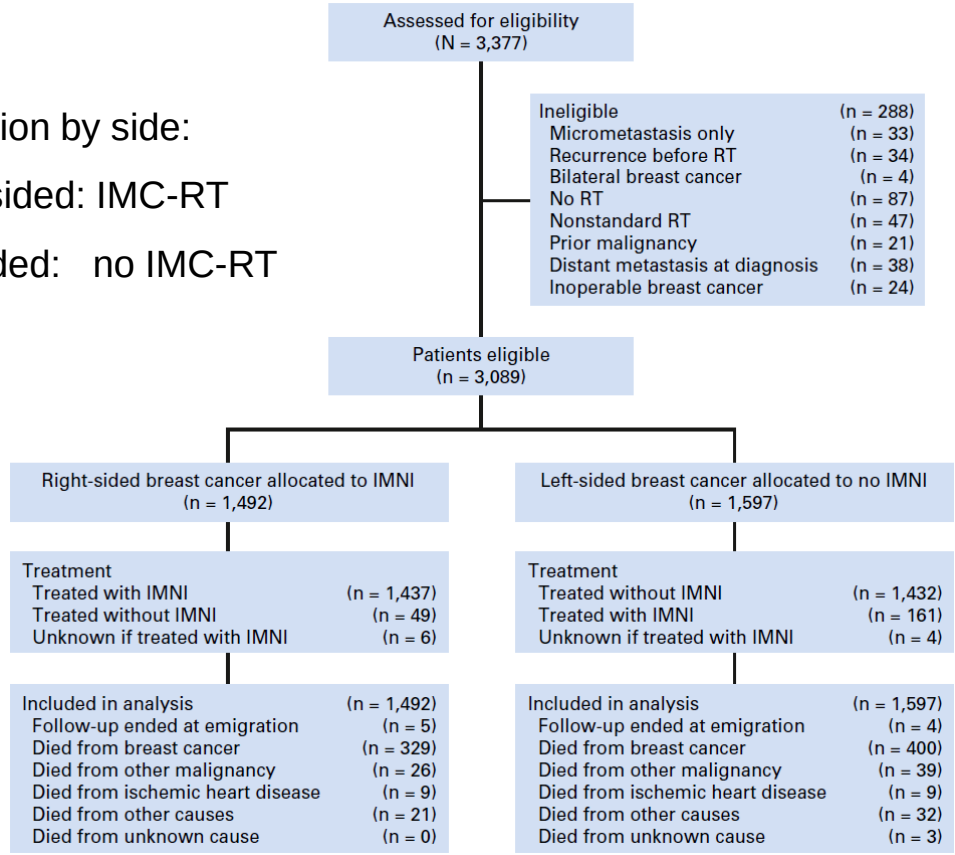
vs.

WBI/CWI + supra/infracalv. RT + internal mammary chain RT (IMC)

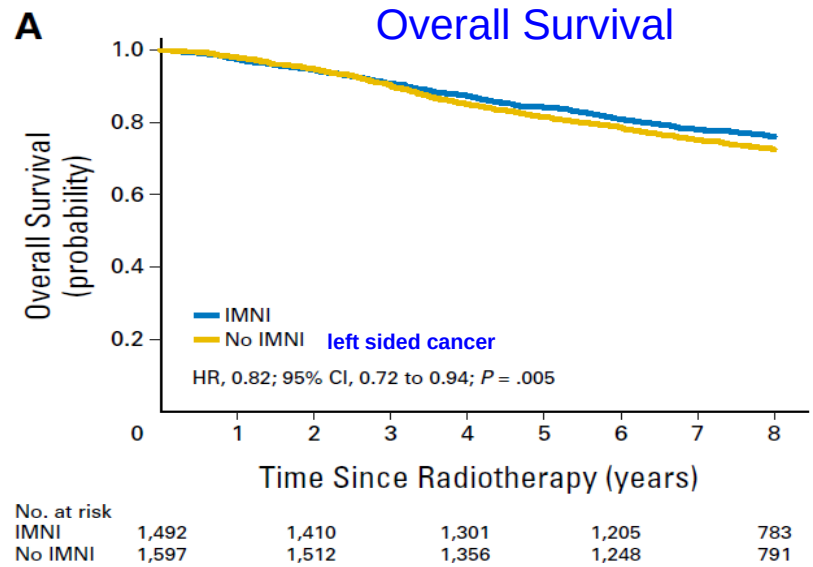
Allocation by side:

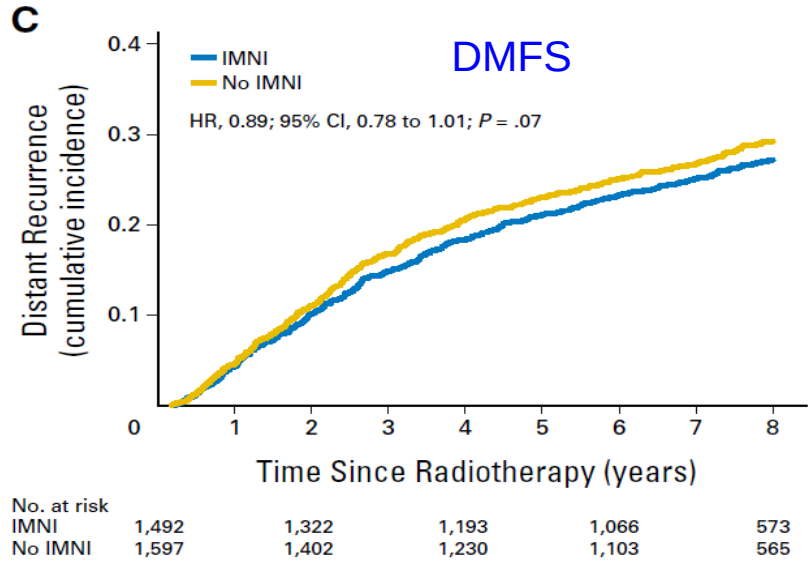
Right sided: IMC-RT

Left sided: no IMC-RT



Thorsen et al. JCO 2015





Meta-analysis: whole breast (WBI)/chest wall (CW) RT vs. WBI/CWI + regional lymph nodes

Table 2 Late toxicity in breast cancer trials on regional radiotherapy

Trial late toxicity	MA.20 [16]			EORTC [17]			French [15]		
	MS-IM-	IM-IM+	p	MS-IM-	IM-IM+	p	MS+	IM-IM+	p
Lung									
Grade 2	0.2%	1.3	0.01	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Grade >2	0%	0%	n.a.	n.s.					
Any grade n.a	n.a.	n.a.	n.a.	1.3%	4.3%	<0.0001	n.a.	n.a.	n.a.
Lymphedema									
Grade 2	3.7%	6.8%	0.004	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Grade >2	0.4%	0.4%	n.s.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Any grade (arm)	n.a.	n.a.	n.a.	3.6%	3.8%	n.s.	n.a.	n.a.	n.a.
Cardiac									
Any grade	n.a.	n.a.	n.a.	1.4%	1.6%	n.s.	1.7%	2.2%	n.s
Total late									
Any grade	n.a.	n.a.	n.a.	21.8%	25.5%	0.006	n.a.	n.a.	n.a.
Grade >2	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	2.3%	3.1%	n.s.

Late toxicitiy.
n.a. = not available; n.s. = not significant; MS-IM-: no radiotherapy of the medial supraclavicular and internal mammary lymph nodes; MS-IM+: radiotherapy of the medial supraclavicular and internal mammary lymph nodes; MS+: radiotherapy of the medial supraclavicular lymph nodes.

W. Budach et al. Radiat Oncol 2013

Radiotherapie (RT) anderer locoregionärer Lymphabflussregionen (SCG/ICG)

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Guidelines Breast
Version 2015.1D

	Oxford /AGO LoE	GR
RT der supra-/infraklavikulären Lymphregion		
➢ ≥pN2a oder Level III befallen	1b	A ++
➢ pN1a hohes Risiko*	2a	B +
*zentraler oder medialer Sitz und (G2-3 oder ER/PgR-negativ)		
* prämenopausal, lateraler Sitz und (G2-3 oder ER/PgR-negativ)		
➢ pN0 prämenopausal, hohes Risiko**	2a	B +/-
**zentraler oder medialer Sitz, und G2-3 und ER/PgR-negativ		
➢ Nach NACT/NAT (Indikationen as wie für eine PMRT)		
AGO[1]	2b	B +/-
➢ After NACT/NAT if cN+ (Indikationen gemäss PMRT)		
DEGRO[1]	2b	A +

[1] different interpretation of published data by AGO and DEGRO

Radiotherapie (RT) anderer lokoregionärer Lymphabflussregionen (IMC)

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Guidelines Breast
Version 2015.1D

Mammaria interna Lymphknotenregion (IMC)

		Oxford /AGO LoE	Oxford /AGO GR
➢ **pN0 prämenopausal, hohes Risiko*** ***zentraler oder medialer Sitz und G2-3 und ER/PgR-negativ		1b	B	+/-
➢ **pN1a hohes Risiko*** *zentraler oder medialer Sitz, und (G2-3 oder ER/PgR-negativ) *lateraler Sitz, prämenopausal und (G2-3 oder ER/PgR-negativ)		2a	B	+
➢ **pN2a hohes Risiko**** **G2-3 oder ER/PgR-negativ		2a	B	+
➢ **pN1b-c, pN2c, pN3b**		2a	B	+
➢ **IMC-RT, bei kardialem Risiko oder bei Gabe von Trastuzumab**		2b	A	-- Nach
NACT/NAT (indikation wie für PMRT)	AGO[1]	2b	B	+/-
➢ **Nach NACT/NAT bei cN+ (ind. acc. PMRT)**	DEGRO[1]	2b	A	+

[1] unterschiedliche Bewertung der publizierten Datendurch AGO und DEGRO

www.ago-online.de

FORSCHEN
LEHREN
HEILEN

Non Breast Cancer Mortality: EBCTCG update 2006 (unpublished)

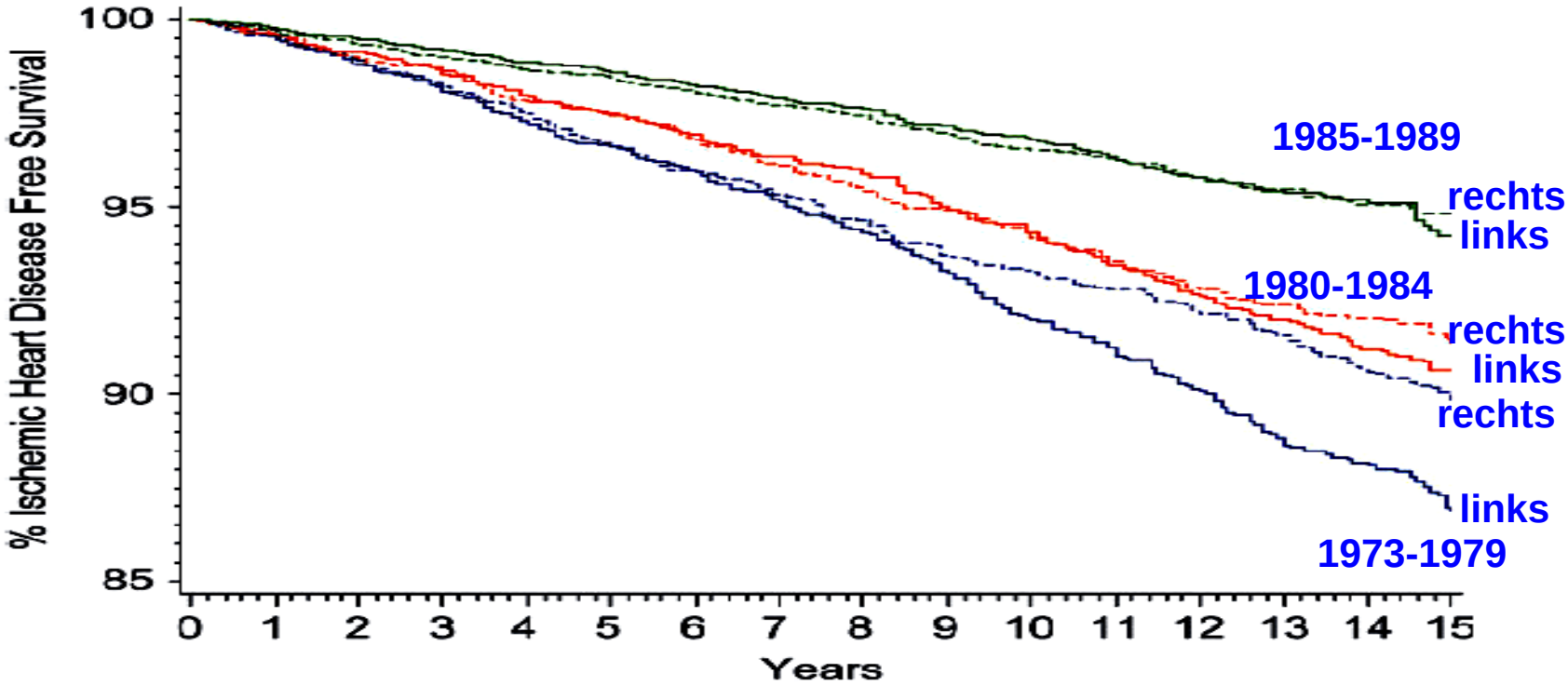
Cause of death	Total evets	Excess events	Ratio of rates (se)[a]	2p
Circulatory disease	1598	167	1.26 (0.06)	0.00001
Other causes	1615	43.4	1.06 (0.05)	NS
Respiratory disease	267	-1.4	0.99 (0.13)	NS
Other known causes	1122	-19.2	0.96 (0.06)	NS
Lung cancer	165	47.0	1.81 (0.22)	0.0002
Oesophagus cancer	23	11.8	2.89 (0.75)	0.01
Leukaemia	31	2.6	1.20 (0.41)	NS
Soft-tissue sarcoma	7	2.6	2.13 (1.14)	NS
Unspecified cause[b]	1610	103.8	1.16 (0.06)	0.005
Total	4823	314.2	1.16 (0.03)	<0.0001

[a] Ratio of annual event rates irradiated versus unirradiated

[b] Unspecified, but known not to be breast cancer

Technischen Weiterentwicklung der RT verbessert die Ergebnisse

Koronare Herzerkrankung nach RT in Abhängigkeit der bestrahlten Seite



No. of patients at risk		0 year	3 year	6 year	9 year	12 year	15 year
1973–1979	Right	4201	3113	2241	1761	1453	1214
	Left	4451	3305	2384	1885	1523	1272
1980–1984	Right	3131	2539	2044	1676	1425	1232
	Left	3364	2748	2159	1788	1512	1287
1985–1989	Right	5953	5266	4553	4014	2770	507
	Left	6183	5457	4780	4194	2868	533

Giordano et al. Lancet 2005

Schlussfolgerung

- Überstreblichkeit durch RT nach 10 Jahren 0,7% und nach 20 Jahren 2,2%, wenn alle Patienten berücksichtigt werden *(auch mit parasternaler RT und der vor 1975 bestrahlten)*

- Mit 3-D Technik und ohne parasternale RT wird das Risiko von RT-induzierten Tumoren halbiert und die kardiale Übersterblichkeit weitgehend vermieden

- Die Übersterblichkeit wird dadurch um ca. 2/3 reduziert, d.h. auf ca. 0,7% nach 20 Jahren

Die Risken der RT sind im Verhältnis zum Nutzen klein

© AGO e.V.
in der DGGG e.V.
sowie
in der DKG e.V.

Guidelines Breast
Version 2015.1D

Interaktion zwischen Strahlentherapie und Rauchen

	Oxford / AGO LoE	Oxford / AGO GR
➢ Nach einer Strahlentherapie wegen Brustkrebs ist das Risiko für ein Lungenkarzinom ist für Raucher erhöht	1a	A
➢ Patientinnen sollten über dieses Risiko informiert werden		++
➢ Das Rauchen sollte beendet werden.		++