

XXII CONGRESSO
AIRO
ROMA 2012
17-20 novembre
Ergife Palace Hotel



WORKSHOP

La radioterapia nelle forme avanzate e/o recidivate del carcinoma della mammella: quando e come

La Radioterapia dopo recidiva: è possibile un ritrattamento?



A black and white photograph of a very large, dense crowd of people. The crowd is filling the entire frame. Two individuals in the crowd are circled in red. One circle is located in the middle-left area, and the other is in the bottom-right area. Overlaid on the image are three red rectangular boxes containing text.

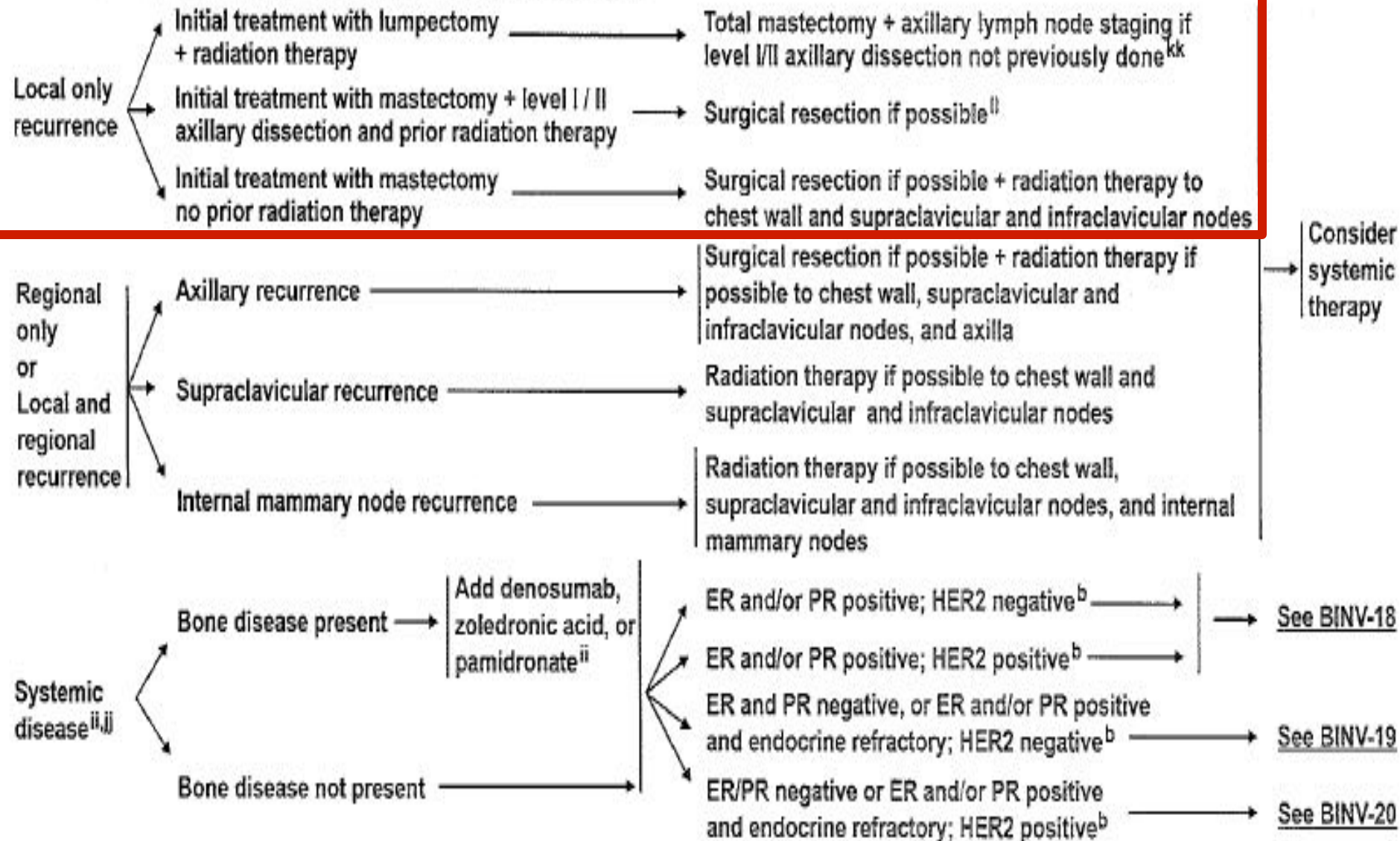
Recidiva operabile

>90%

Recidiva inoperabile

Category 2A recommendations

SYSTEMIC TREATMENT OF RECURRENT OR STAGE IV DISEASE





Locoregional recurrence after breast-conserving therapy remains an independent prognostic factor even after an event free interval of 10 years in early stage breast cancer

E. Tanis^a, C.J.H. van de Velde^b, H. Bartelink^c, M.J. van de Vijver^d, H. Putter^c, J.A. van der Hage^{a,*}

		Overall survival			Distant DFS		
	pts	HR	95%CI	p	HR	95%CI	p
>5 yrs							
LRR	363	3.98	3.08-5.14	<0.001	4.42	3.44-5.68	<0.001
>10yrs							
LRR	64	4.96	1.97-12.48	0.001	7.57	3.46-16.55	<0.001

Treatment Guidelines after Breast Conserving Therapy ACR Appropriateness Criteria

Recidiva locale dopo QUART

- **Mastectomia è raccomandata come trattamento di scelta quando la recidiva è operabile e confinata alla mammella**
- **Escissione +/- RT: solo in trials clinici**



2° LR dopo BCS di salvataggio è alta

Mastectomia di salvataggio non elimina il rischio



Mediocre cosmesi dopo 2° quadrantectomia

Dimensioni mammella/tumore

Preferenza della paziente

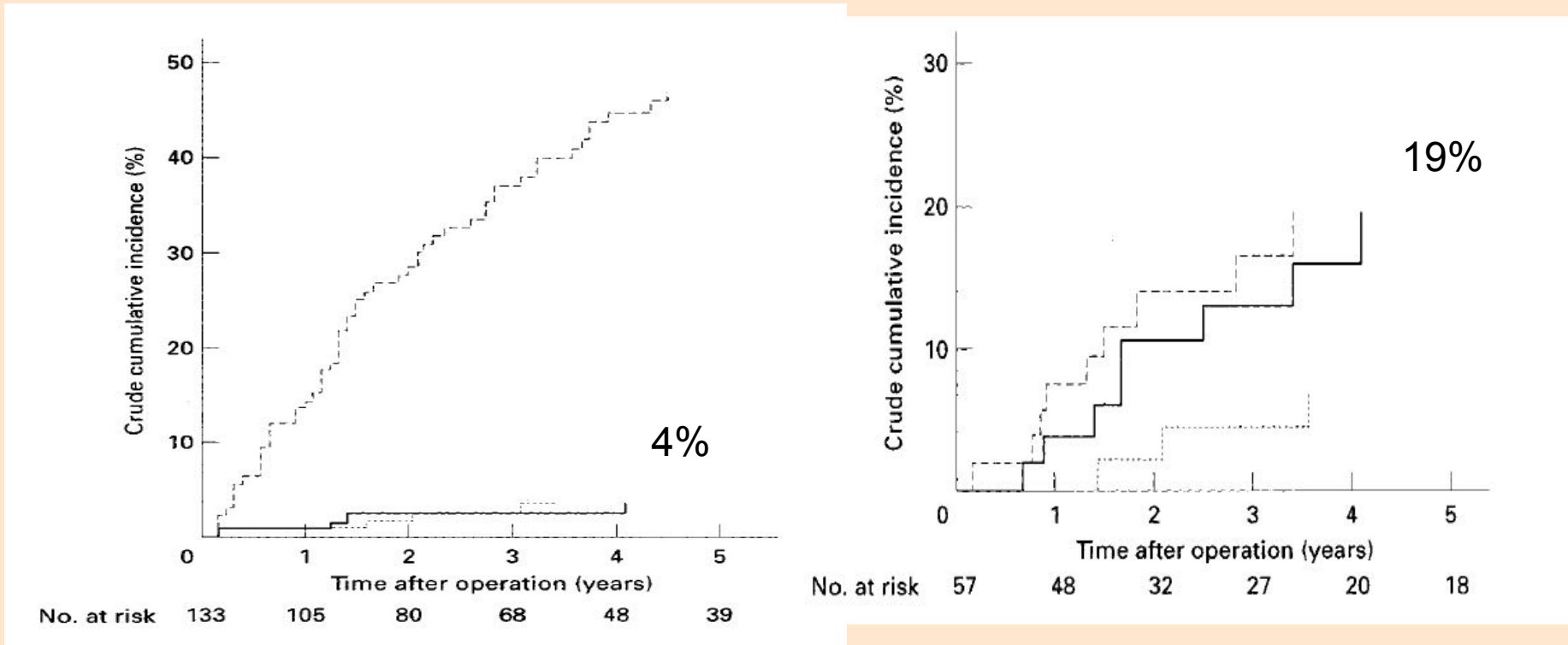


Danno tissutale della reirradiazione

Ruolo della PBI

Beneficio della mastectomia di salvataggio sulla recidiva locale, ma non sulla sopravvivenza (Salvadori 1999)

Incidence of first event following mastectomy and re-excision for IBTR



5- y Overall survival rate 70% mastectomy vs. 85% local excision

Table 3 Clinical Outcome After Salvage Mastectomy for IBTR After BCT

Series	No. Cases	Median Follow-Up, mo	Local Recurrence After Mastectomy, %	5-Y Survival After Mastectomy, %
Yale ⁴	116	166	6.9	65.7 (10-y data)
Sweden ⁶	65	156	12	—
Switzerland ⁷	43	53	12	—
NIH ⁸	18			—
Dutch ⁹	208			—
Milan ¹⁰	134	60	3	70
Japan ¹¹	51	53	11	57-100
Marseille ¹²	66	84	12.1	68
SEER ¹³	568	—	—	78

Range 2%-32%
Media 12%

Table 4 Clinical Outcome with Excision Alone for IBTR After BCT

Series	No. Cases	Median Follow-Up, mo	Local Recurrence After Excision, %	5-Y Survival After Excision, %
Yale ⁴	30	166	6.7	58 (10-y data)
Sweden ⁶	14	13	33	—
Switzerland ⁷	46			—
Dutch ⁹	16			—
Milan ¹⁰	57	60	14	85
Japan ¹¹	73	53	49	89-94
Marseille ¹²	52	84	23	79
SEER ¹³	179	—	—	67

Range 7-50%
Media: 32%

Nessuna differenza in sopravvivenza e recidive locoregionali a 5 anni dopo salvataggio con mastectomia o chirurgia conservativa

EORTC 10801- DBCG-82-TM pooled study

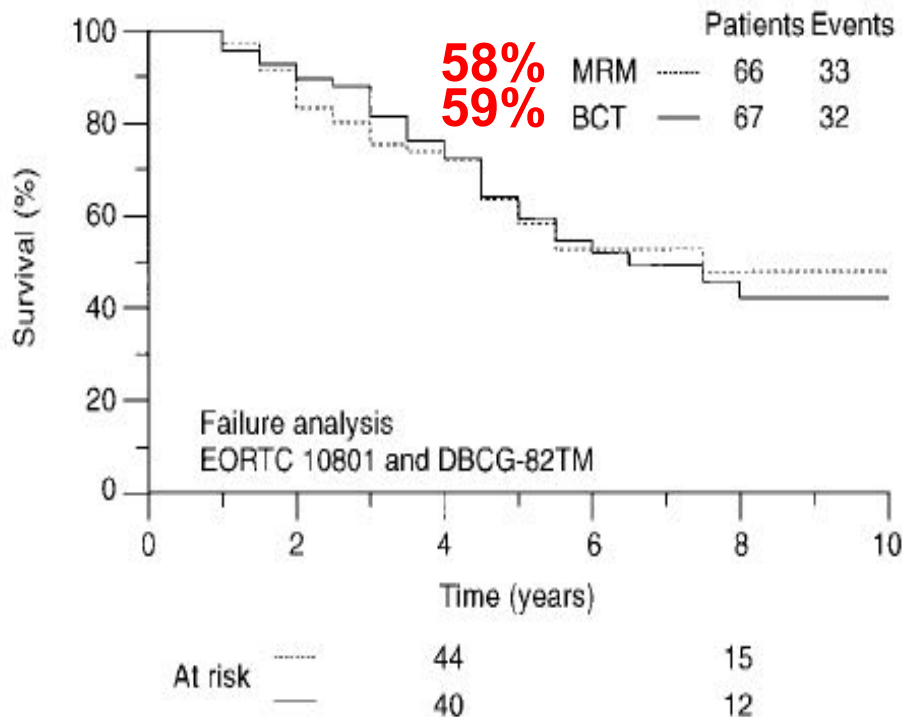


Figure 2. Actuarial overall survival from salvage treatment by original treatment group (MRM or BCT). Patients at risk at 4

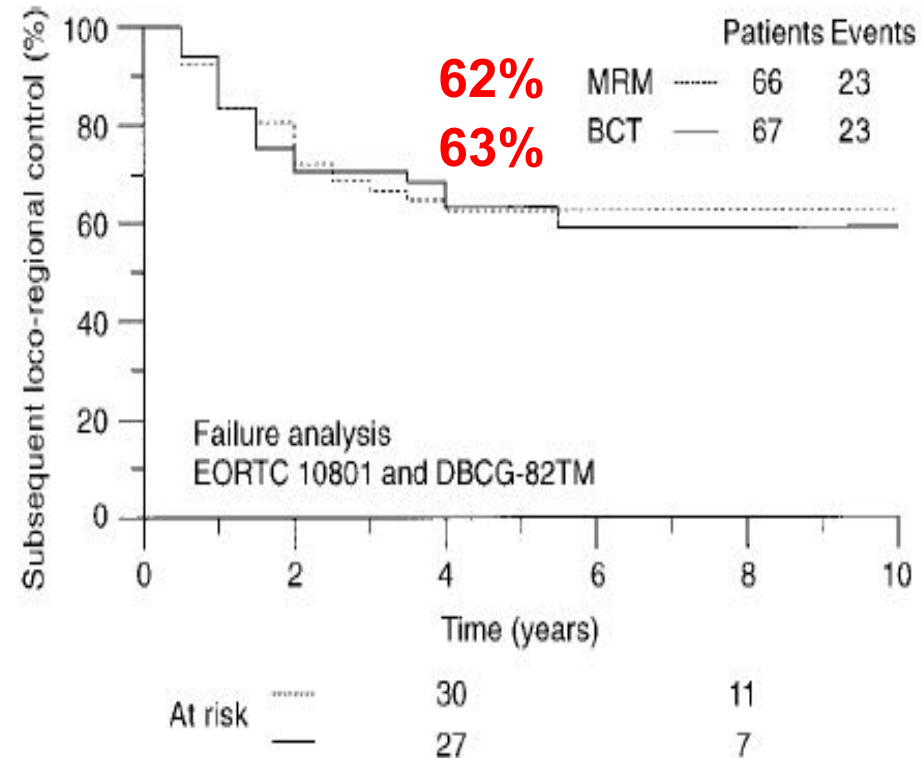


Figure 3. Actuarial time to subsequent LR from salvage treatment by original treatment group (MRM or BCT).

**Chirurgia conservativa da
sola
range :7-50%%
Media 33%**

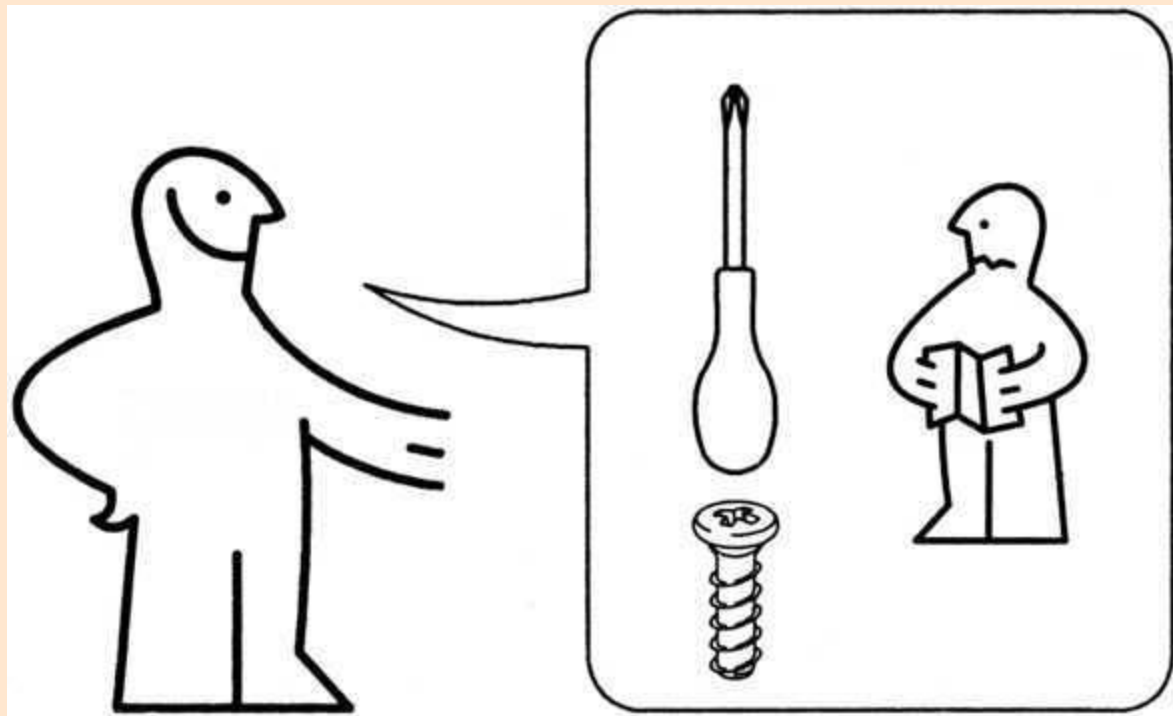


**Mastectomia
range :2-32%
Media 12%**



**Chirurgia
conservativa +
re RT
range :0-20%
media 10%**

Reirradiazione Come Istruzioni per l'uso

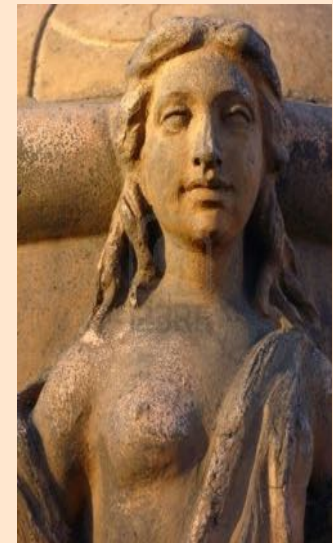


Reirradiazione con WBRT Resch 2002

12/17 TR dimensioni 1.5cm,
Dopo 50 mesi (med),
pregressa RT 50 Gy +/- boost



59 mesi

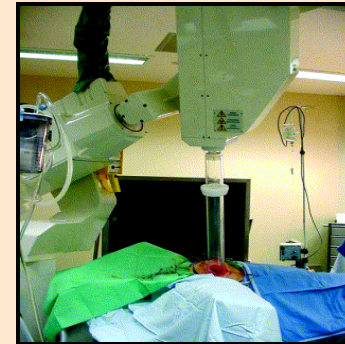
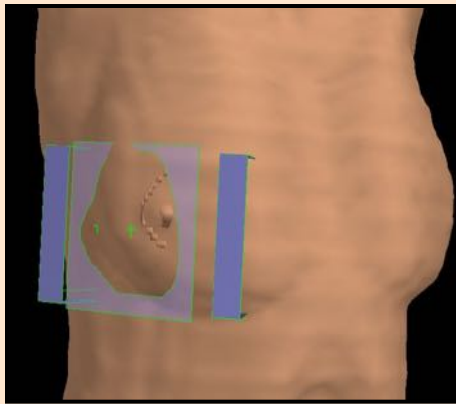
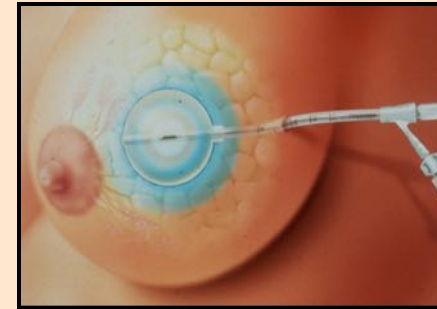
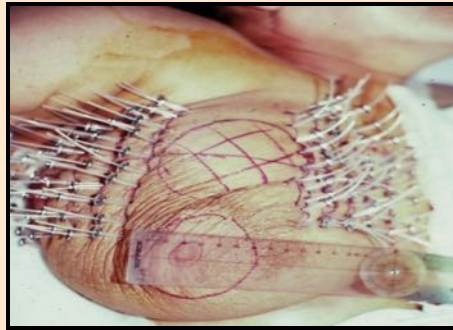
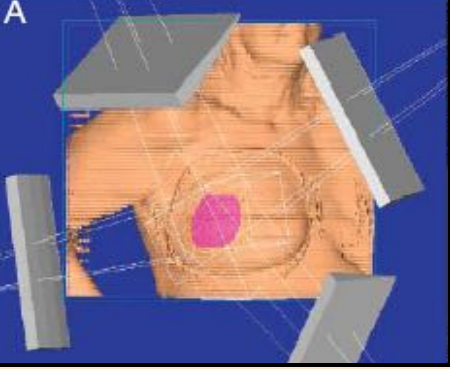


fibrosi G1-G2
3 iperpigmentazioni
2 minime telangiectasie
1/3 eccell-buona cosmesi

8 pts WBRT
(12-30 Gy)
+ PDR BRT boost
(12.5-28 Gy)

9 pts PDR BRT da sola
(40.2-50 Gy)

2° recidiva locale 24%
(WBRT+ PDR/BRT)
nella sede della 1° LR



**Esperienze limitate sull'utilizzo della
APBI nelle pazienti precedentemente
irradiate
reAPBI: teoricamente appropriata**

author	pts	BRT	dose	FU mo	2°LR
Voodg1999	15	BRT	30 Gy	48	26%
Chada 2008	15	LDR	First 6-30 Gy Last 9-45 Gy	36	6.7%
Hannoun-Levi 2004	69	LDR	24-30 Gy 45-45-50 Gy	50	16%
Hannoun-Levi 2011	42	HDR	34 Gy BID	21	5%
Trombetta 2011	26	21 LDR 5 HDR Mam.Site	45-50 Gy 34 Gy BID	40	3%
Niehoff 2005	32	15 HDR 17 PDR (4 +ERT)	Med. 28 Gy Mean 30 Gy (24-40 Gy e⁻)	19	37.5% (R0-2)
Guix 2010	36	HDR	30 Gy BID	89	2.7%
Kauer 1012	39	PDR	50 Gy	57	5.1%

autore	N° pts	tecnica	FU	2° LR
Mullen 1997	16 (pregressa RT 45-50 Gy)	Elettroni 50 Gy/25Fx(32 Gy/16 fx in 1)	62 mesi	20% 4/16 (25%) 3° IBTR)
Deutsch 2002	39(5 con marginii+) pregressa RT 45-50.4Gy	Electron 50 Gy/25fx (32 Gy in1)	60 mesi	20.5% (8/39, 1/8 marginii +) 2/8 (25%) 3° IBTR
Harkenri der 2011	8	Fotoni med. 46.7 Gy (+ BRT boost in 1 paz)	30 mesi	12.5% (1/8)

	pts	FU	dose	Recidiv a size	LR
IORT X- rays *	17	26 mesi	14.7-20 Gy	1-35 mm	0%
IORT** electron	81	53 mesi	16-21 Gy (85%)	≤1.5 cm 82%	9.9%

*Kraus-Tiefenbacher, BMC 2007

** IEO unpublished data

Effetti collaterali	BRT	Esterna	Intraoperatoria
Fibrosi G2 fibrosi G3	19%-50% 3%-10%	60% (G2-G3)	19%-35% 7.6%-8.3%
discromia	25%	23-37.5%	
teleangectasia	14%-21%	50%	
Frattura costale	2%	12.5%	
dolore	13%-28%	12.5%	17%
polmonite		2%	
liponecrosi	10%		4.9%

RADIATION THERAPY ONCOLOGY GROUP

RTOG 1014

A Phase II study of Repeat Breast Preserving Surgery and 3D-Conformal Partial Breast Re-Irradiation (PBri) for Local Recurrence of Breast Carcinoma

SCHEMA

R E G I S T E R	Partial Breast Re-Irradiation (PBri) 3D-Conformal External Beam 1.5 GY x 15 (BID) to 45 Gy Total
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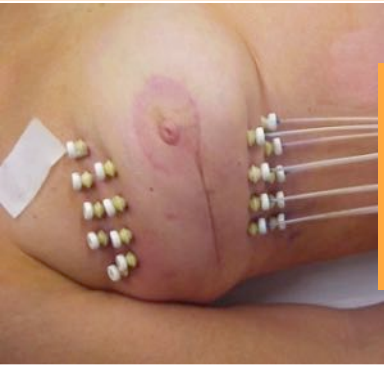
OBJECTIVES

2.1 Primary

To evaluate skin, breast, and chest wall adverse events occurring within 1 year from the completion of reirradiation.

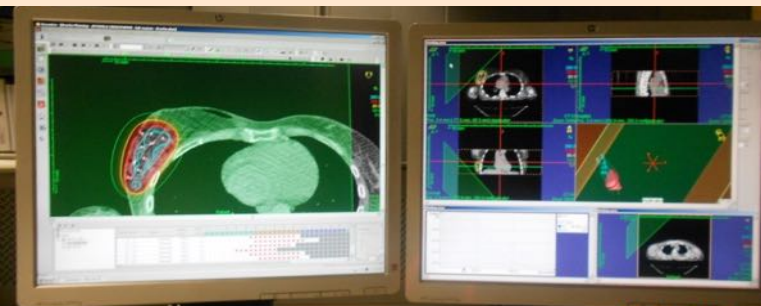
**precedente RT > 1 anno, ≤ 3 cm , invasivo o noninvasivo, margini negativi
ascella negativa o ≤ 3 N+**

La sopravvivenza libera da 2° recidiva a 5 anni aumenta con il n° totale di fili di Ir e piani (p significativo)



**97.7% \geq 5 fili Ir vs 56.2% $<$ 5 fili Ir
93.6% 2 piani vs. 62.6% 1 piano**

La sopravvivenza libera da 2° recidiva a 5 anni aumenta con la dose di re-RT (trenta)



**85.5% se BRT \geq 50 Gy
74.7% se BRT $<$ 50 Gy**

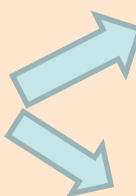


Controllo locale e tossicità

(Hannoun-Levi, 2004)

Effetti collaterali	dose	incidenza
G2-G3 secondo la dose BRT	≤ 45 Gy	14%
	≥ 46 Gy <i>(≤ 30 Gy)</i>	36% (p 0.007) <i>4%) (p 0.01)</i>
G2-G3 secondo la dose totale	≤ 100 Gy	4%
	> 100 Gy	30% (p 0.008)

2° LR dipende da BRT dose:

 **43.8% (30 Gy)**
5.3% (46 Gy)

Reirradiazione Quando Istruzioni per l'uso





Parametri istologici e biomolecolari

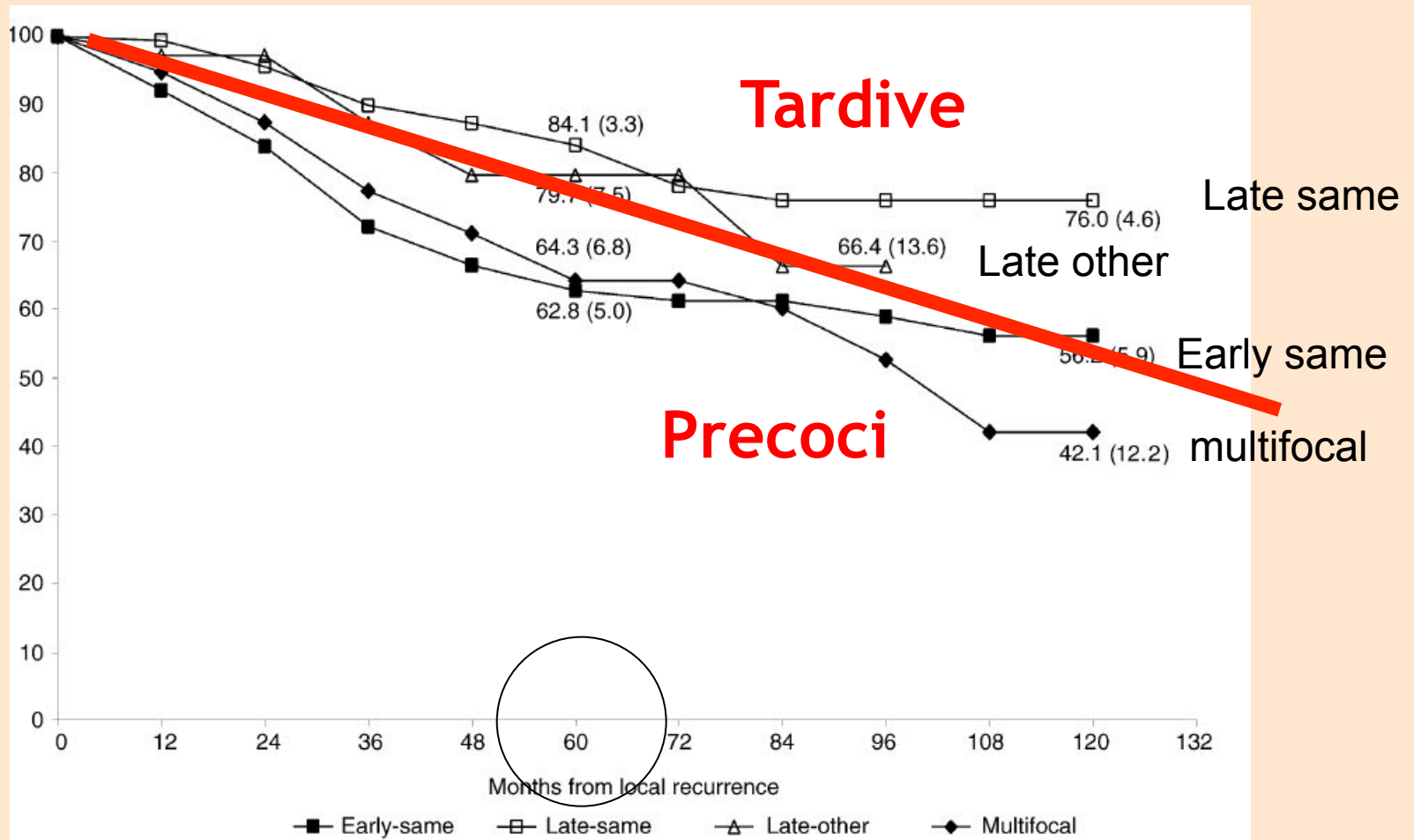
**Intervallo di tempo
T primario-recidiva**

**Status
linfonodale-
Iniziale e
alla
recidiva**

**Estensione,
sede,
età,
ER status,
LVI,
grado**



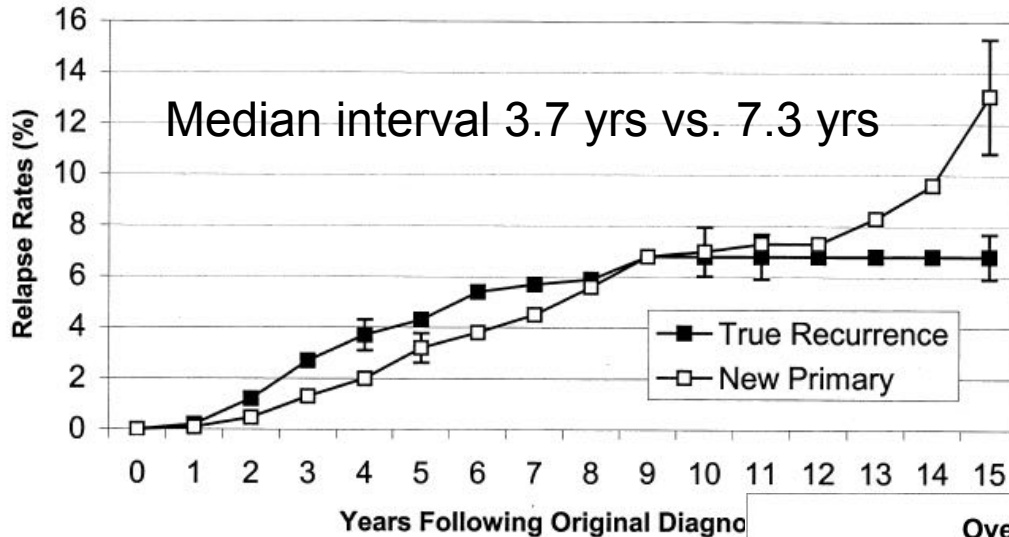
L'importanza dell'intervallo tra primitivo e recidiva



Life-table of BC-specific survival as measured from recurrence

True vs. elsewhere

Ipsilateral Breast Tumor Relapse Rates



Differente storia naturale

differente prognosi e implicazioni

Criteri di differenziazione

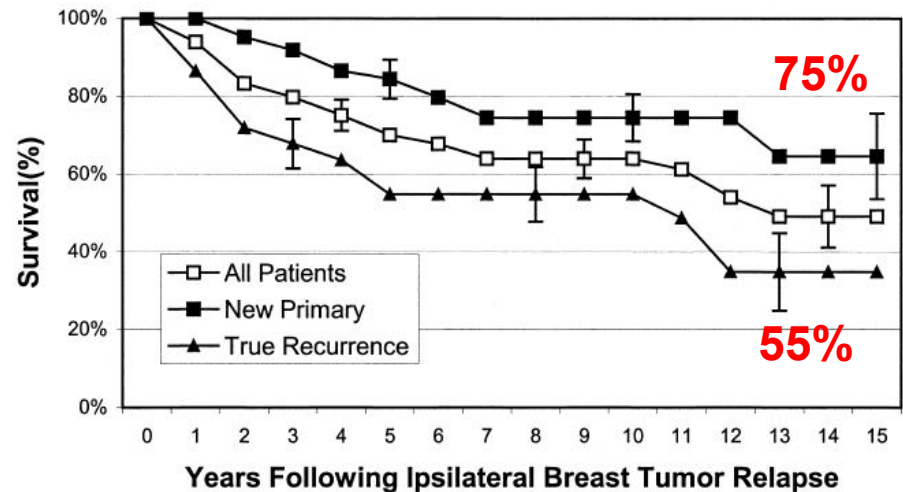
Sede

Istologia

Timing

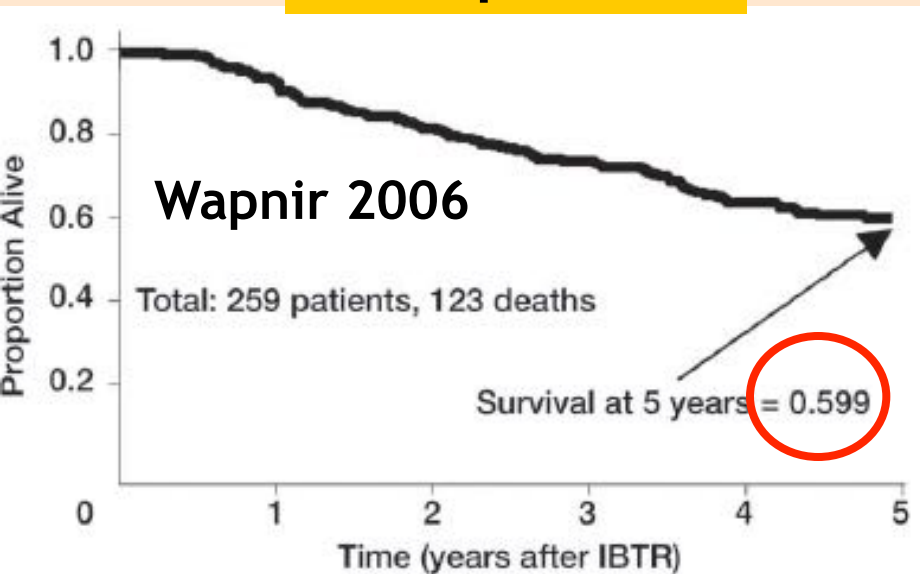
Clonalità

Overall Survival Following Ipsilateral Breast Tumor Relapse

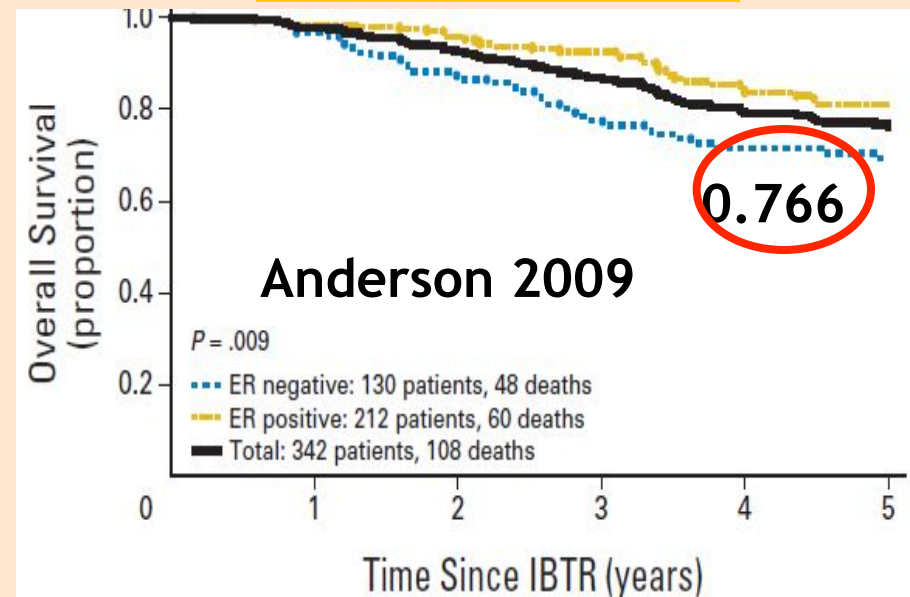


Lo stato linfonodale iniziale Impatto sulla sopravvivenza e sull'intervallo tra primitivo e recidiva

Node positive



Node negative



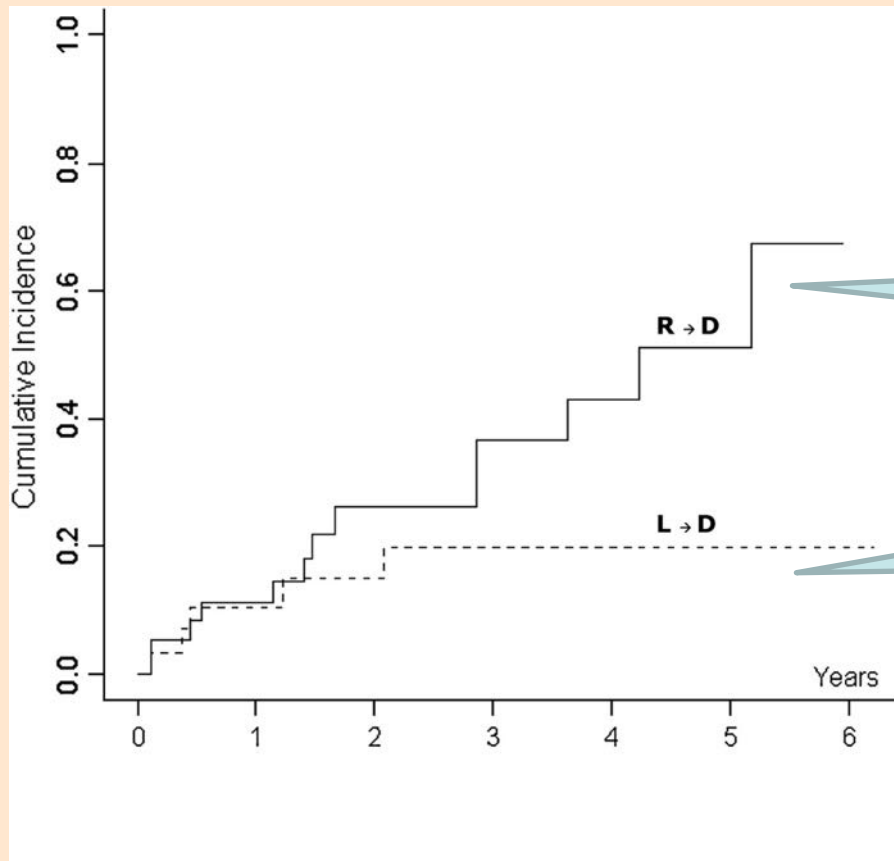
5 NSABP-B trials with BCS

N+: recidiva precoce

N-: recidiva tardiva

Lo stato linfonodale alla recidiva

Incidenza cumulativa di metastasi o morte



dopo eventi linfonodali

dopo eventi locali

Il potenziale metastatico



**Recidive precoci e N+:
elevato rischio di
ulteriori eventi e morte**



279 pts con LRR (1994-2005)
62% irradiate per il primario
Med FU 5.6 anni

Annals of Oncology

Annals of Oncology 23: 324–331, 2012

doi:10.1093/annonc/mdr129

Published online 27 April 2011

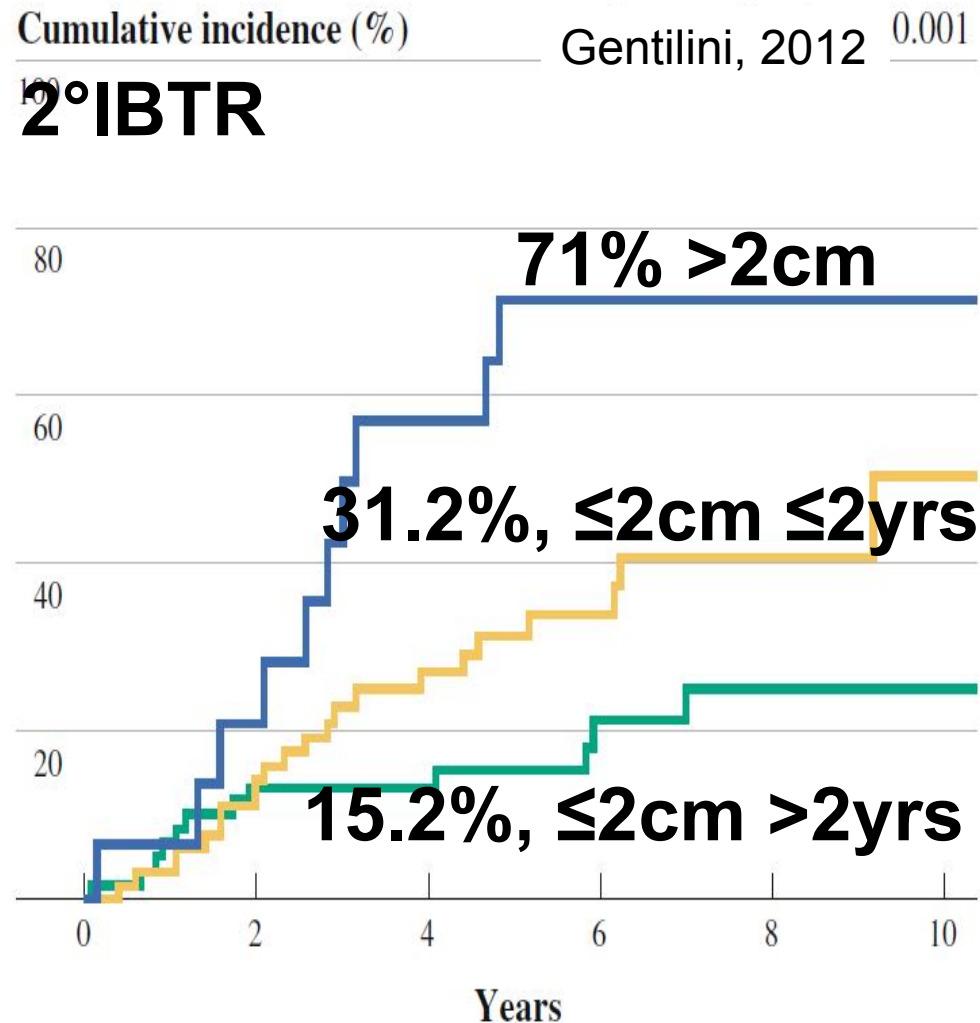
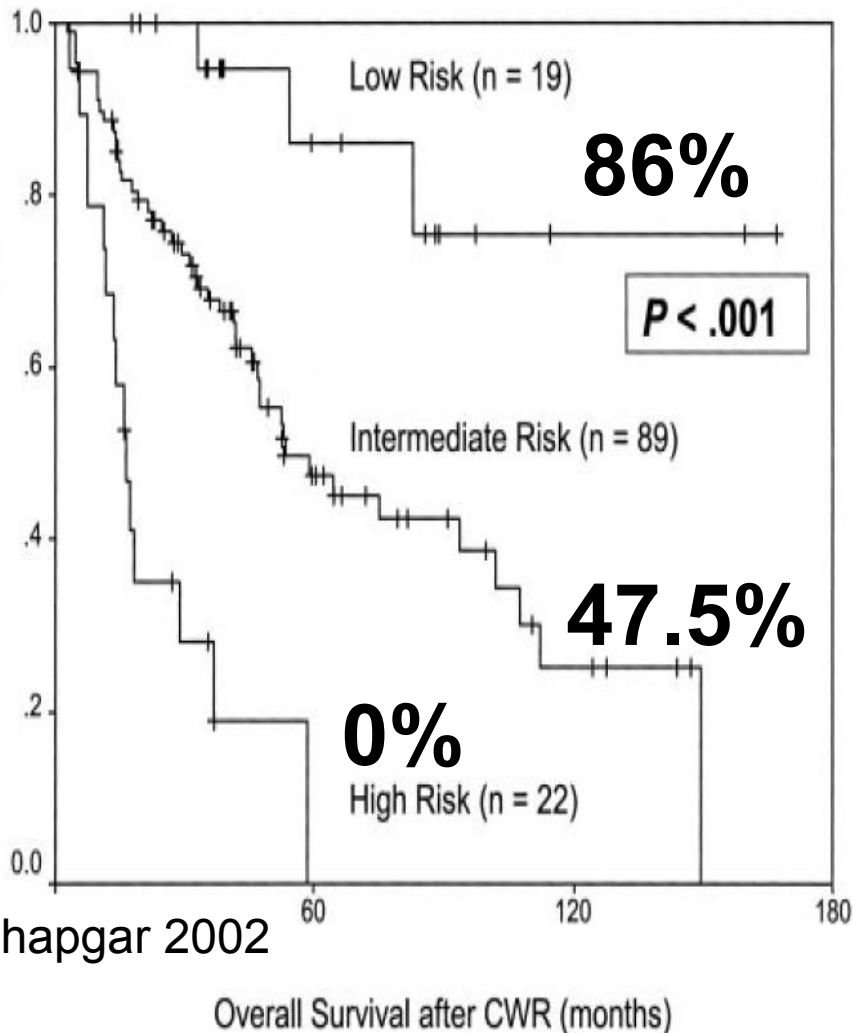
Breast cancer subtypes and outcome after local and regional relapse

E. Montagna^{1*}, V. Bagnardi^{2,3,4}, N. Rotmensz², G. Viale^{5,6}, G. Renne^{5,6}, G. Canello¹,
 A. Balduzzi¹, E. Scarano¹, P. Veronesi^{5,7}, A. Luini⁷, S. Zurrida^{5,7}, S. Monti⁷, M. G. Mastropasqua⁶,
 L. Bottiglieri⁶, A. Goldhirsch¹ & M. Colleoni¹

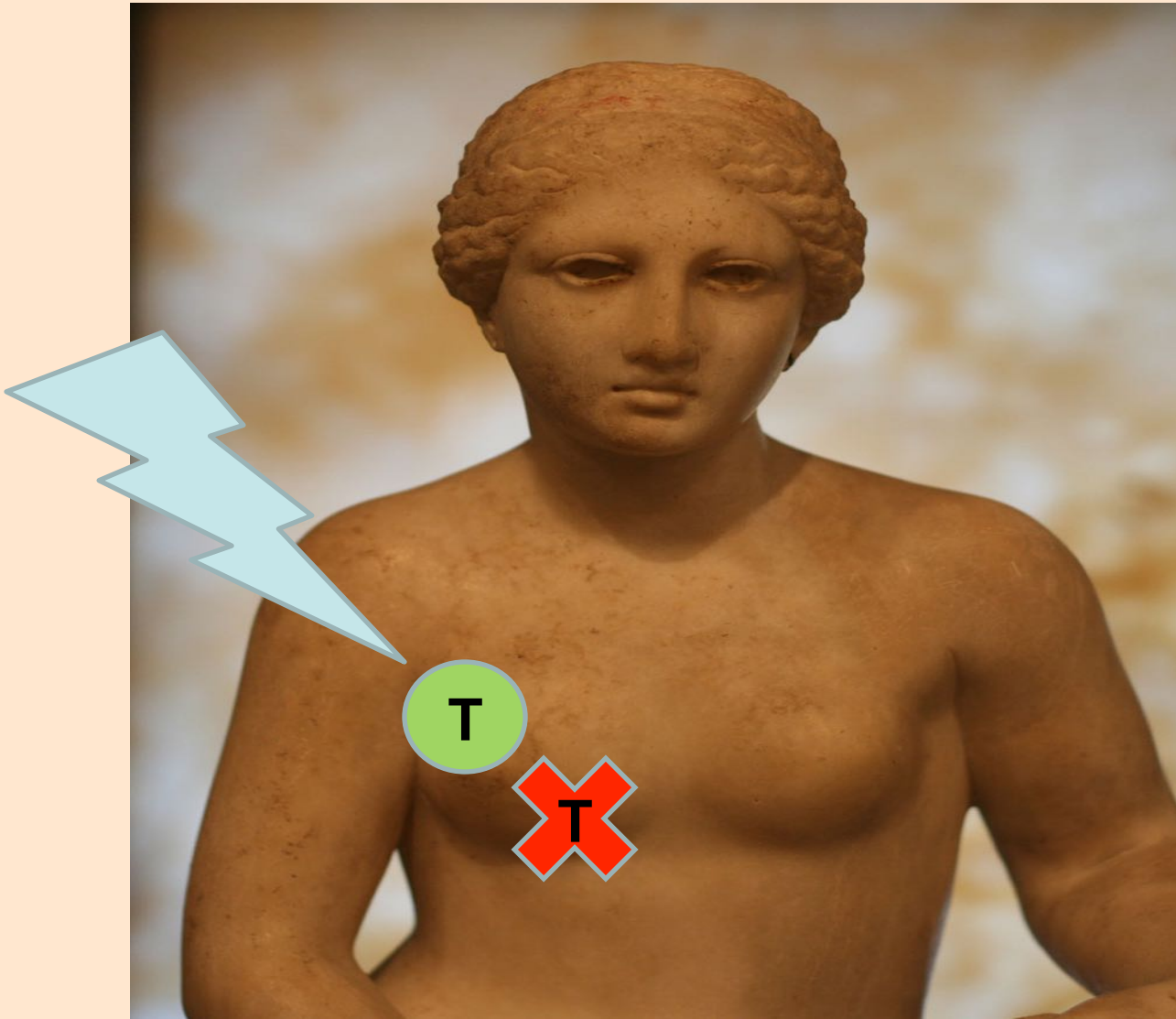
	PFS HR (95% CI)	OS HR (95% CI)	CSH-LR HR (95% CI)	CSH-D HR (95% CI)
Breast cancer subtype (at LRR) ^{a,b}				
Luminal A/B	Reference category			
HER2 positive	0.79 (0.38–1.66)	1.34 (0.78–2.30)	1.89 (0.83–4.31)	0.71 (0.30–1.64)
Triple negative	2.87 (1.67–4.91)	2.00 (1.25–3.19)	1.89 (0.87–4.13)	1.45 (0.74–2.83)

Reirradiazione: il quando

Basso rischio? Rischio intermedio?



Recidiva locale dopo APBI: Indicatore di metastasi o fonte di metastasi a distanza?



Outcome After Ipsilateral Breast Tumor
Recurrence in Patients With Early-Stage Breast
Cancer Treated With Accelerated Partial
Breast Irradiation

Clinical Breast Cancer Month 2012

Chirag Shah,¹ J. Ben Wilkinson,² Maha Jawad,² Jessica Wobb,² Sameer Berry,²
Christina Mitchell,² Michelle Wallace,² Frank Vicini³

**18 /534 pts con recidiva locale dopo
APBI (interstiziale, MammoSite e 3D)
(1993-2010)**

**Intervallo mediano di tempo alla recidiva
5.9 anni
4 true e 14 elsewhere**

**salvataggio: 14 mastectomie and 4
tumorectomie + reirradiazione con APBI**

Outcome After Ipsilateral Breast Tumor Recurrence in Patients With Early-Stage Breast Cancer Treated With Accelerated Partial Breast Irradiation

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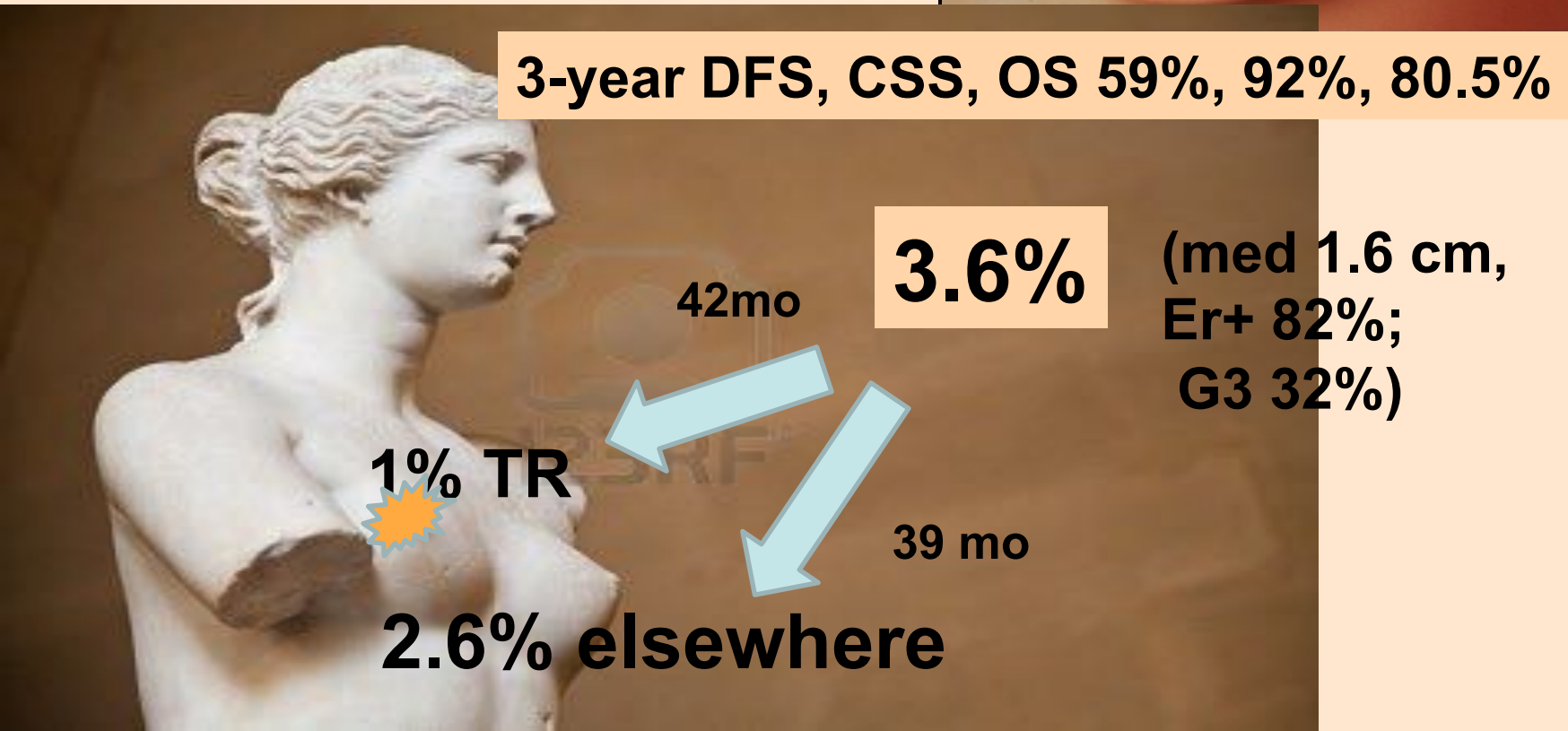
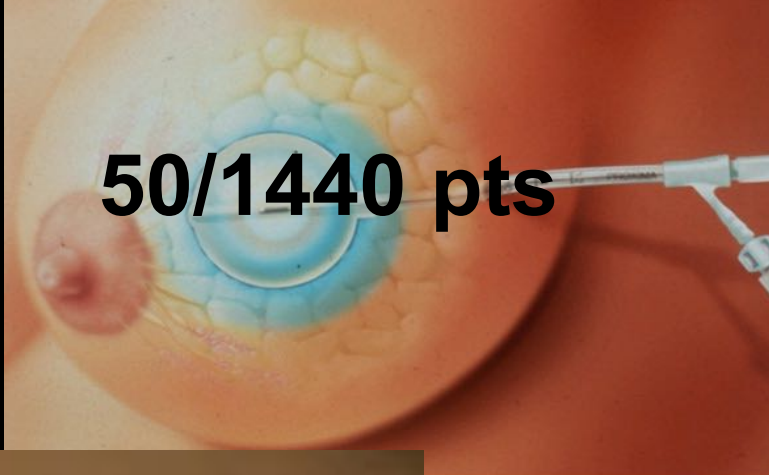
Table 2 Clinical Outcomes After Ipsilateral Breast Tumor Recurrence

Median FU 4.1 yrs	All (n = 18), %	True Recurrence and/or Marginal Miss (n = 4), %	Elsewhere (n = 14), %
Ipsilateral Breast Tumor Recurrence	6.7	0	9.1
Axillary Failure	12.3	0	16.4
Regional Recurrence	19.6	33.3	16.4
Distant Metastases	6.7	25	0
Disease-Free Survival	81	75	83.6
Cause-Specific Survival	100	100	100
Overall Survival	100	100	100

Nessuna 2° recidiva locale dopo tumorectomia +APBI

Prognosi dopo recidiva dopo APBI

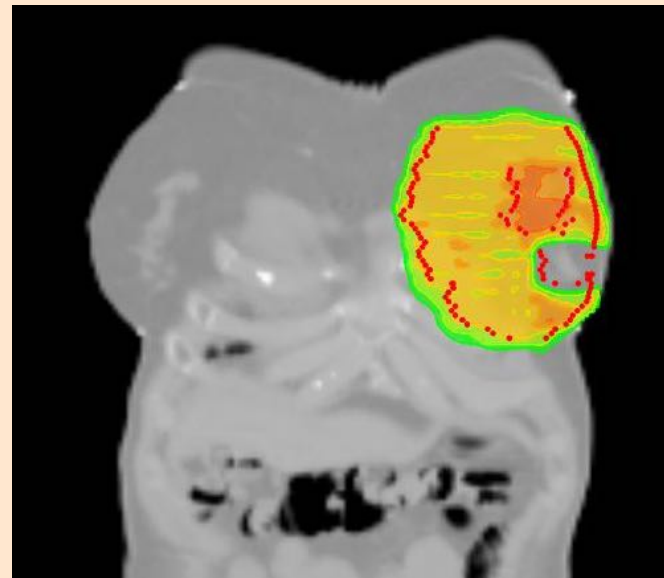
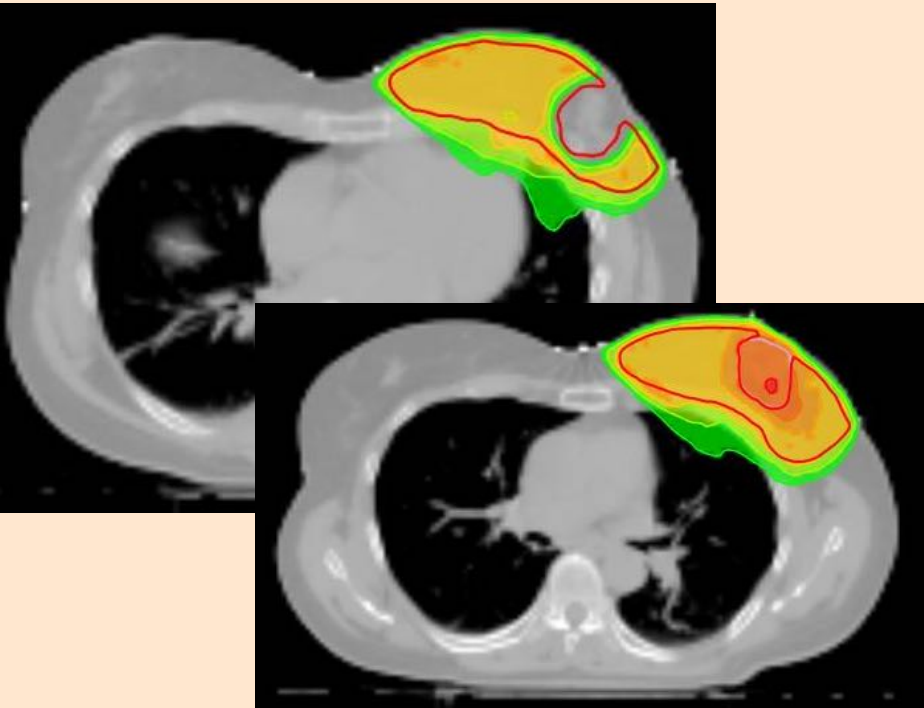
MammoSite Registry, Shah, Cancer 2012



Nessuna differenza tra mastectomia o 2° quadrantectomia di salvataggio (9 paz sottoposte a chirurgia conservativa)

Radioterapia Whole Breast dopo recidiva locale in pazienti trattate con APBI (ELIOT) studio *2.25 Gy * 20 fr over 4 weeks*

Boost Concomitante 2.50 Gy * 20 fr
(if different quadrant)

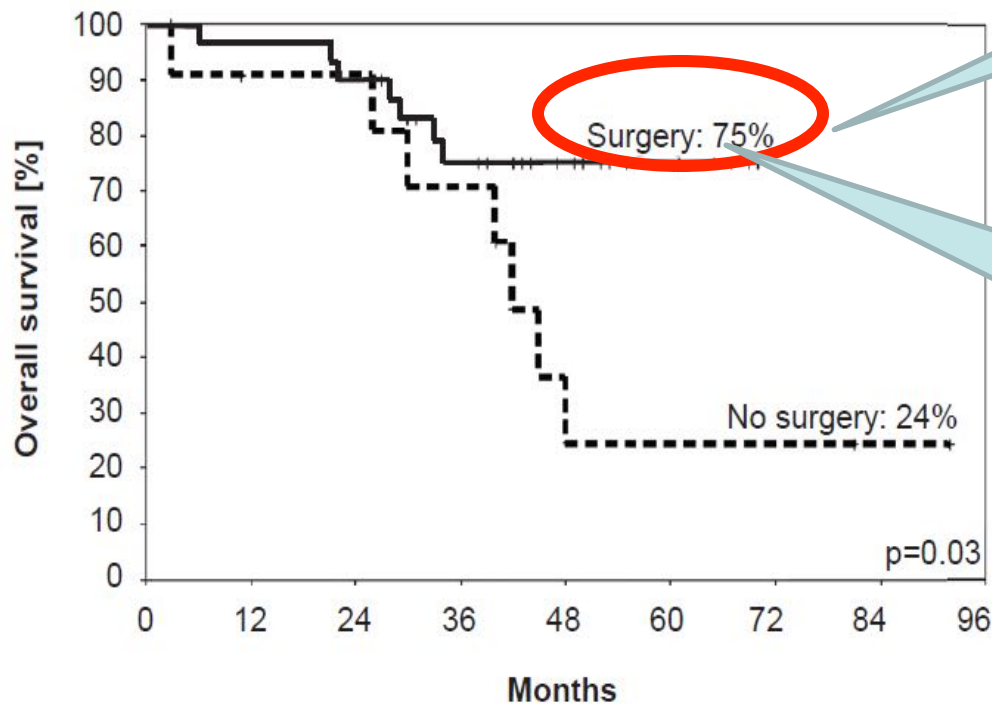


4 pts

A 1 mese dopo RT:
1 G1 edema
1 G1 eritema

Timing della reirradiazione

Overall survival and surgery



43% se non re-RT alla 1° LR (p 0.11)

34% se re-RT alla 2° LR (p 0.08)

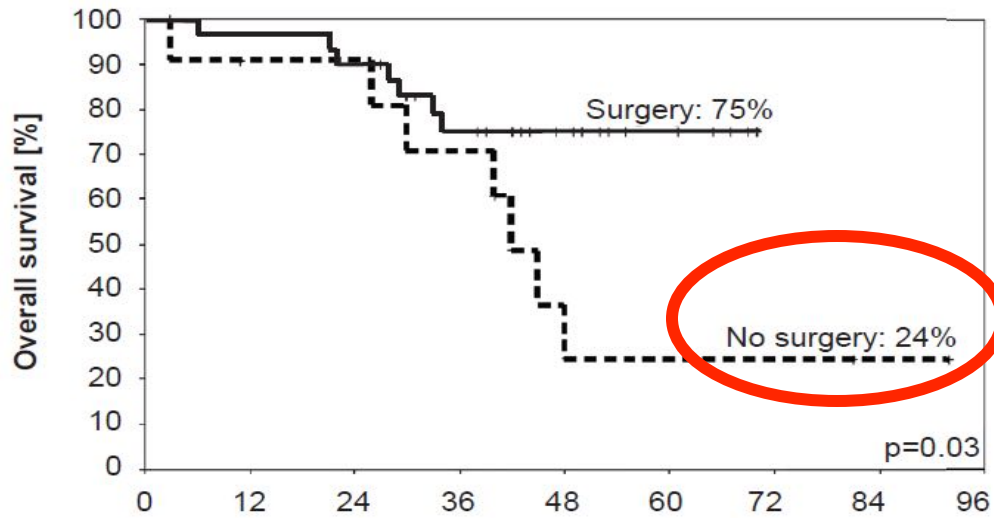


Recidiva inoperabile

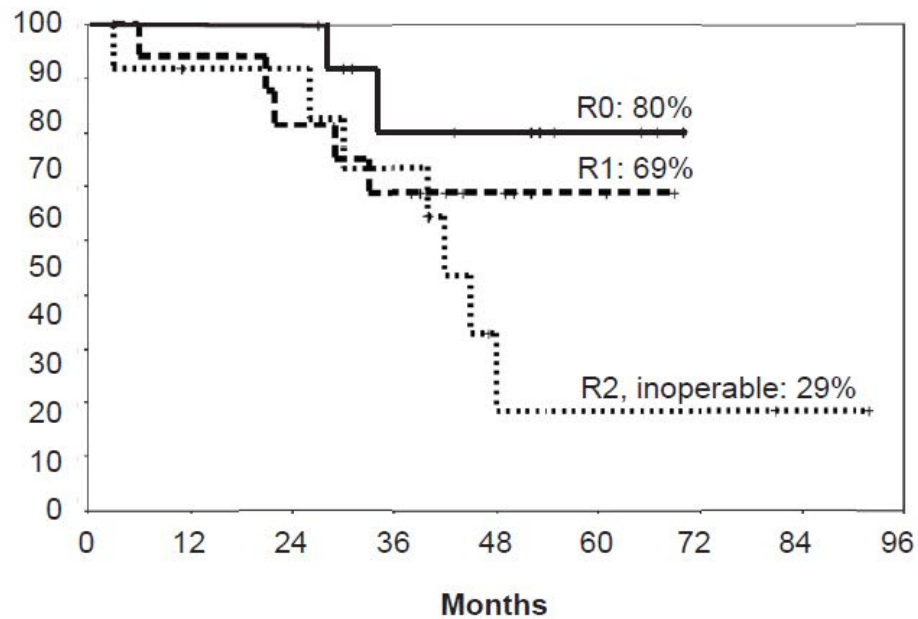


<10%

Overall survival and surgery



Overall survival and resection margin

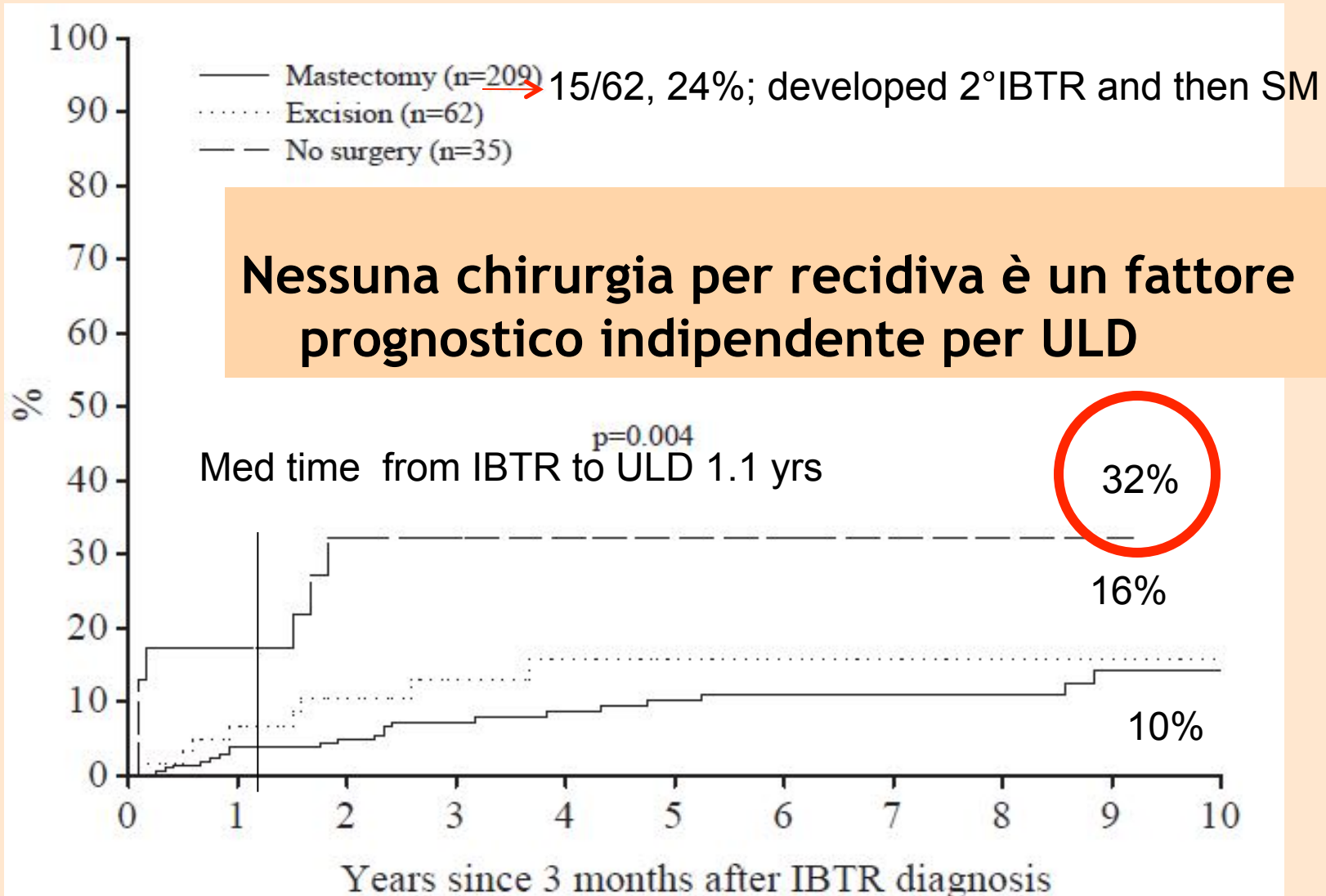


author	N°	1°RT	2°RT	Cum RT	CR	Local DFS
Laramore	13	40-50 Gy	30-50 Gy	70-100 Gy	62%	62% a 20 mo
Dragovic	30	50 Gy	32 Gy	82 Gy	57%	-
Phromratanapogse	44	59.7 Gy	29.4 Gy	89.1 Gy	41%	67% a 12 mo
Van der Zee	134	45 Gy	32 Gy	77 Gy	71%	-
Kouloulias	15	60 Gy	30.6 Gy	90.6 Gy	20%	-
Li	41	58 Gy	43 Gy	101 Gy	56%	-
Wagman	13	60.8 Gy	50.4 Gy	111.2 GY		85% a 24 mo
Jones	39	-	30-66 Gy	-	68%	-
Wahl	81	62 Gy	48 Gy	106 Gy (74.4-137.5 Gy)	57%	66% at 12 mo (86% in CR)

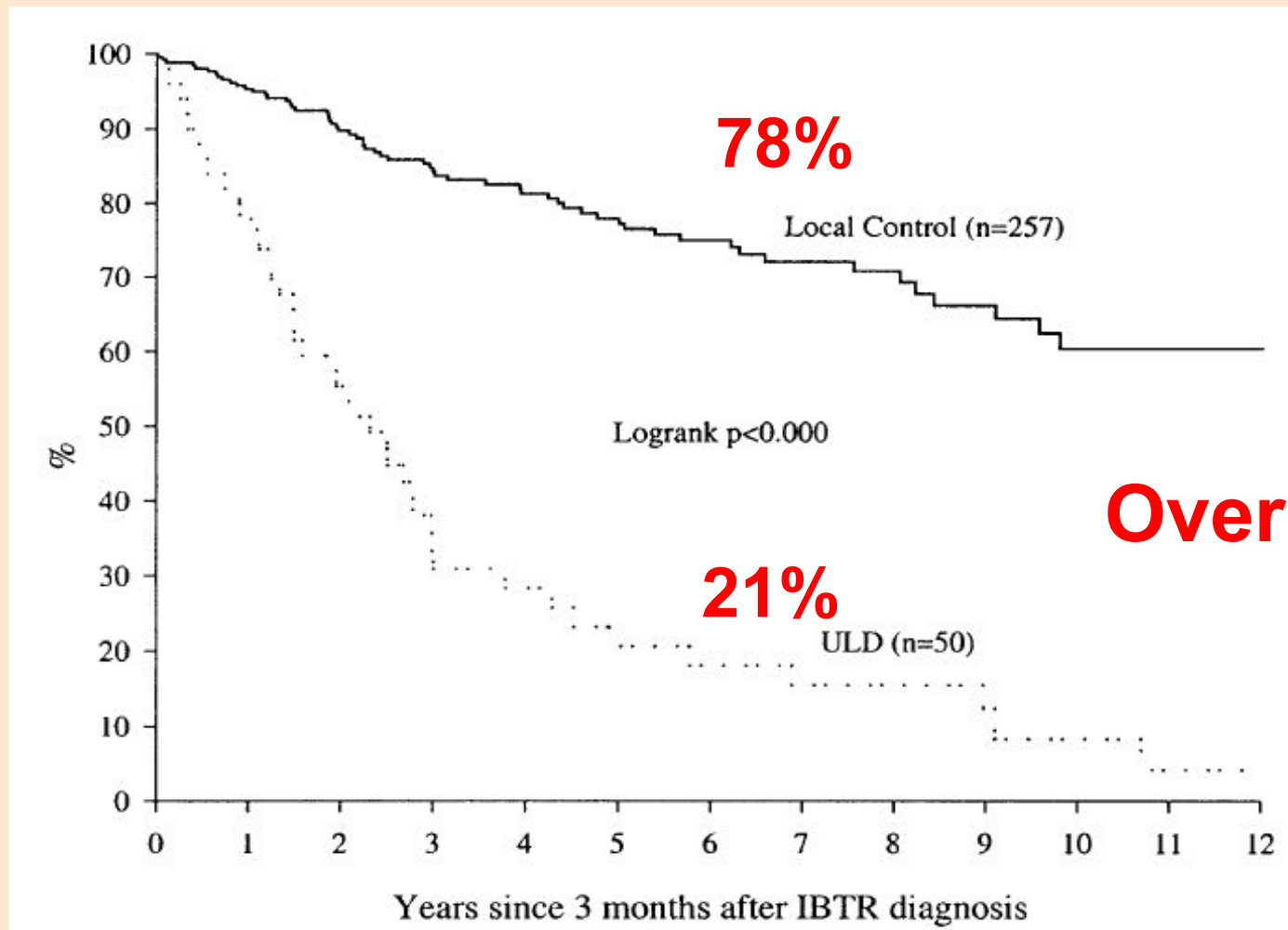
Variable	<i>n</i>	CR rate (<i>n</i>)	<i>n</i>	1-y Local DFS (%)
Total radiation dose (Gy)				
<100	18	9 (50)	22	63
100–110	17	10 (59)	22	64
>110	19	12 (63)	31	70
<i>p</i>		0.74		0.91
Second RT course dose (Gy)				
<45	28	14 (50)	30	53
≥45	26	17 (65)	45	75
<i>p</i>		0.28		0.035
Interval between RT courses (y)				
<3	28	13 (46)	33	48
≥3	23	16 (70)	39	82
<i>p</i>		0.16		0.0003
Modality				
Photons	7	3 (43)	10	70
Electrons	40	24 (60)	46	56
Both	7	4 (57)	19	89
<i>p</i>		0.75		0.09
Twice-daily RT				
Yes	10	4 (40)	15	48
No	38	22 (58)	54	70
<i>p</i>		0.48		0.40
Concurrent chemotherapy				
Yes	38	23 (61)	44	58
No	16	8 (50)	31	77
<i>p</i>		0.55		0.016
Concurrent hyperthermia				
Yes	36	24 (67)	36	58
No	18	7 (39)	18	44
<i>p</i>		0.08		0.32

tossicità tardiva G3-G4 (5%)
no tossicità maggiore in pts ≥120 Gy (med tot dose 106 Gy (74.4-137.5 Gy))

5-y incidenza cumulativa di malattia locale non controllata (ULD) dopo recidiva (Dalberg 2003)



Sopravvivenza globale a 5 anni dopo recidiva tra malattia locale controllata e non controllata (Dalberg 2003)



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Grazie!

