Gruppo di Studio per la Patologia Mammaria

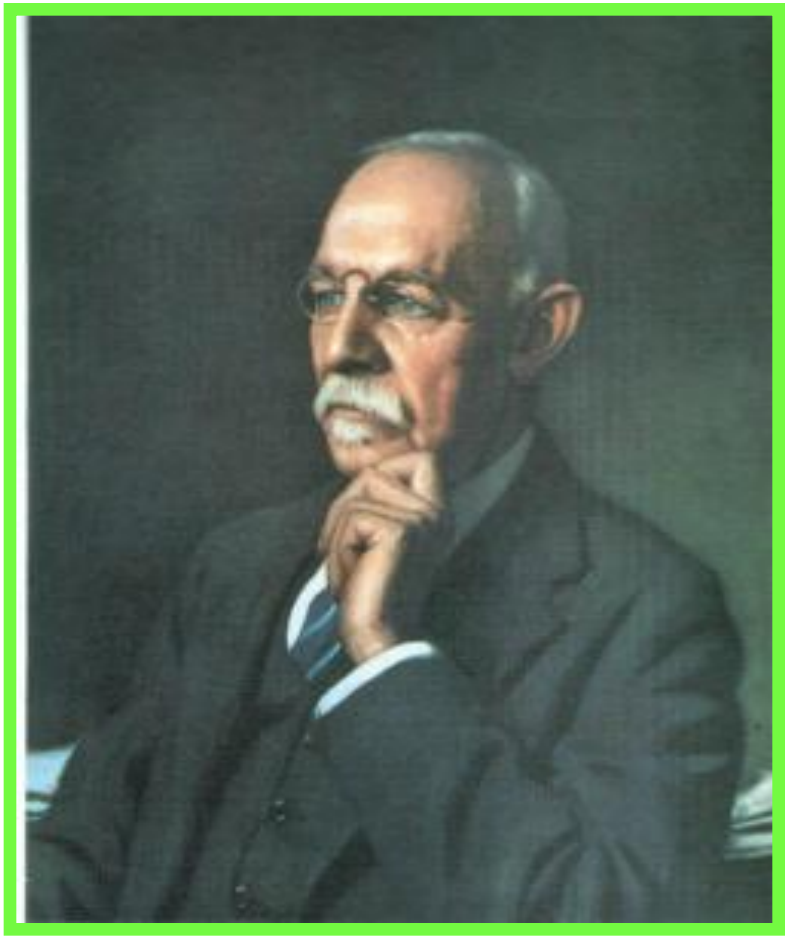
LINFONODO SENTINELLA POSITIVO: EVOLUZIONE NELL'APPROCCIO TERAPEUTICO

Alfio Di Grazia

Lorenza Marino

III ZOOM JOURNAL CLUB 2013

Bologna 21 Febbraio 2014



Halsted 1852 - 1922

Malattia loco-regionale
a diffusione centrifuga
che segue ben
determinate vie
anatomiche
(teoria di Halsted)

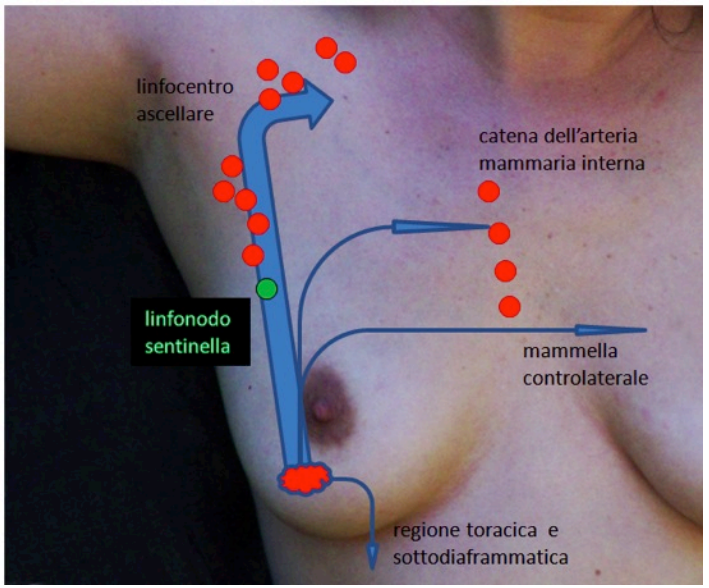
TABELLA 1 Cronologia dello sviluppo dei principali concetti che hanno influito sul trattamento del tumore della mammella

1750	1750 ca.	Ipotesi di una origine locale della malattia	Henri François Le Dran[11]
	1750 ca.	Mastectomia con escissione in blocco della mammella e dei linfonodi ascellari palpabili	Jean-Louis Petit[9]
	1838	Origine cellulare del cancro	Johannes Müller[6]
	1858	Effetto barriera dei linfonodi ascellari	Rudolph Virchow[5]
	1867	Diffusione locale della malattia in senso centrifugo	Charles H. Moore[13]
	1875	Inclusione della fascia del muscolo gran pettorale nella mastectomia	Richard von Volkmann[50]
1894	1894	Mastectomia radicale classica	William S. Halsted,[16] Willy Meyer[17]
	1896	Ovariectomia bilaterale nel trattamento del tumore metastatico	George Beatson[19]
	1922	Radioterapia come trattamento primario del tumore mammario	Geoffrey Keynes[22]
	1941	Mastectomia semplice seguita da radioterapia	Robert Mc Whirther[23]
	1943	Prima stadiazione ad ampia diffusione del tumore mammario	Cushman Haagensen e Arthur Purdy Stout[51]
1948	1948	Mastectomia radicale estesa ai linfonodi della catena mammaria interna	M. Margottini[24]
	1948	Mastectomia radicale modificata	David Howard Patey e W.H.T. Dyson[21]
	1950-1960	Tumorectomia semplice seguita da radioterapia loco-regionale	François Baclesse[42], Sakari Mustakallio[52]
1961	1961	Primo trial di chirurgia conservativa	H. Atkins e J.L. Hayward[53]
	1966	Trattamento delle pazienti con metastasi ascellari	Bernard Fisher[54]
1975	1975-1976	Primo trial di chemioterapia adjuvante	Gianni Bonadonna[54]
	1980	Formulazione della *teoria alternativa* alla teoria meccanicistica di Halsted sulla diffusione dei tumori mammari	Bernard Fisher, John Devitt e George Crile[29]
	1987	Formulazione della *teoria dello spettro* sulla diffusione dei tumori mammari	Samuel Hellman e Jay Harris[30]
1991	1991	Sviluppo della biopsia del linfonodo sentinella	Armando Giuliano[55]
	1994	Identificazione del gene BRCA1, seguita l'anno successivo dal BRCA2	Steven Narod[1]

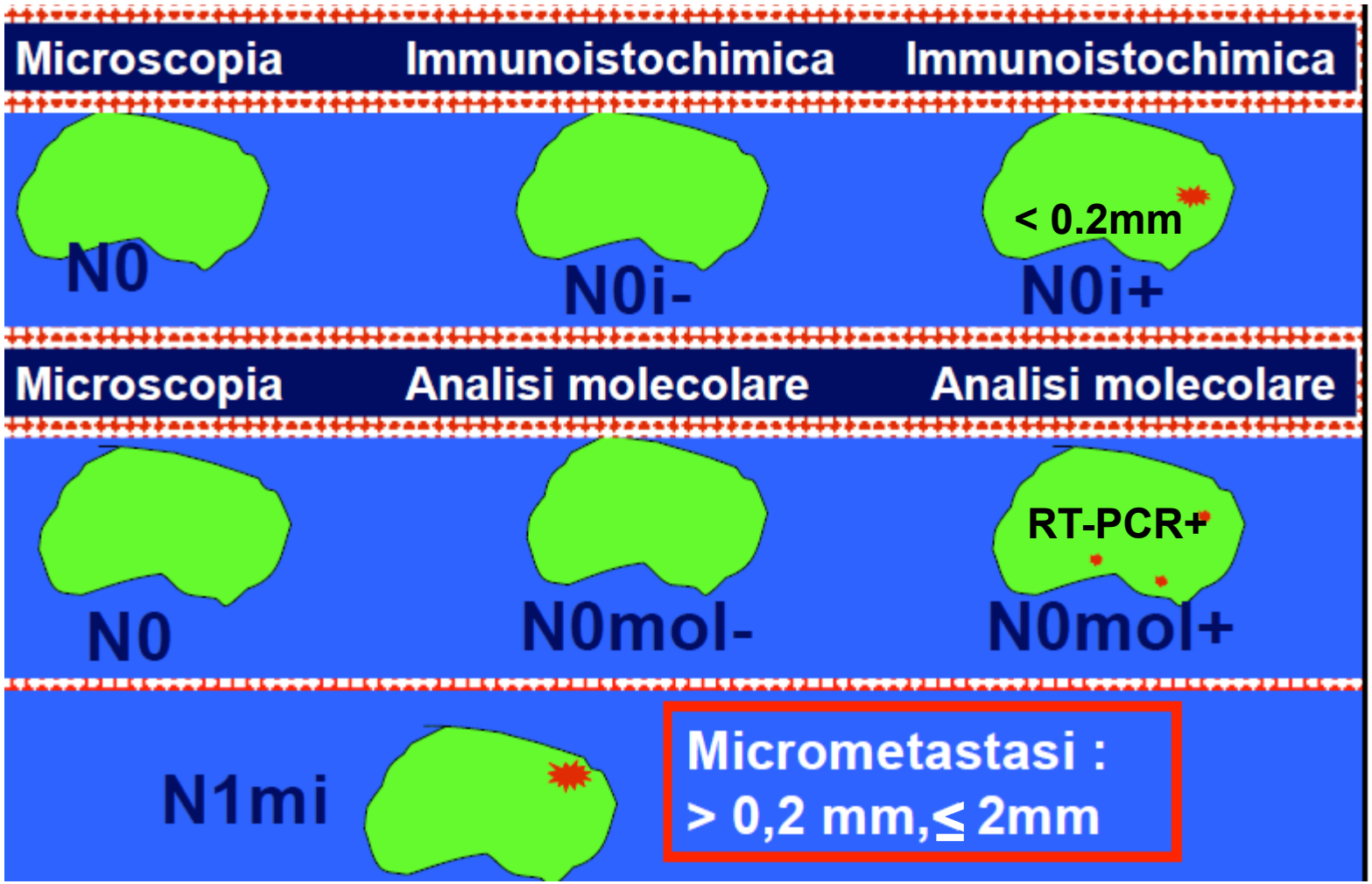
Il riscontro sempre più frequente di linfonodi negativi, associato alla dimostrazione che lo svuotamento ascellare non forniva un reale vantaggio sulla sopravvivenza , ha suggerito lo sviluppo di un metodo meno invasivo per la stadiazione dell'ascella……

IL LINFONODO SENTINELLA

Girolamo Induno: La sentinella garibaldina



Classificazione AJCC 2009 (settima edizione)



N+

7-12%

20-25%

pN1mac: >2mm

40-58%

La linfoadenectomia può essere omessa?

La RT su N può essere un ‘alternativa alla CH?

Ruolo dell’ Nsn in pz [illegible]oste a CT neoadiuvante

Clinical Review & Education

JAMA. 2013;310(13):1385-1394. doi:10.1001/jama.2013.277804

Review

Axillary Node Interventions in Breast Cancer
A Systematic Review

Roshni Rao. MD: David Euhus. MD: Helen G. Mavo. MLS: Charles Balch. MD

Table 1. Trials of Axillary Lymph Node Dissection vs No Directed Axillary Therapy (Level A Evidence)

Source	Study Period	Participant Age	Axillary Status	Tumor Size	Follow-up	Study Interventions	Sample Size	Recurrence, No. (%)	Survival, % (SE)[a]
Fisher et al,[4] 2002	1971-1974	Any age (70% >50 y)	Palpable, suspicious nodes on examination	Mean, 3.7 (SD, 2) cm	Mean, 20 y	Radical mastectomy	292	22 (8)[b]	11 (2)
						Total mastectomy + radiation	294	33 (11)[b]	10 (2)
Fisher et al,[4] 2002	1971-1974	Any age (70% ≥50 y)	No palpable, suspicious nodes on examination	Mean, 3.7 (SD, 2) cm	Mean, 20 y	Radical mastectomy	362	15 (4)	19 (2)
						Total mastectomy + radiation	352	15 (4)	13 (2)
						Total mastectomy	365	23 (6)[c]	19 (2)
Greco et al,[29] 2000	1986-1994	Any age (85% >50 y)	No palpable, suspicious nodes on examination	All tumors <3.0 cm on examination	Median, 5.1 y	Partial mastectomy or mastectomy with no axillary lymph node dissection + radiation if age <70 y	401	19 (5)	Not evaluated
Martelli et al,[30] 2010	1996-2000	Median, 76 y	No palpable, suspicious nodes on examination	Any tumor size (93% T1/T2)	Median, 15 y	BCT + axillary lymph node dissection	109	0	96
						BCT alone	110	2 (1.8)	94
Hughes et al,[31] 2004[d]	1994-1999	>70 y	No palpable, suspicious nodes on examination	All tumors <2.0 cm on examination	Median, 5 y	BCT + tamoxifen	200	0	87
						Partial mastectomy + tamoxifen	204	2 (1)	86
Rudenstam et al,[32] 2006	1993-2002	Median, 74 y	No palpable, suspicious nodes on examination	Any tumor size (56% <2 cm)	Median, 6.6 y	Mastectomy or BCT + axillary lymph node dissection	234	2 (1)	75
						Mastectomy or BCT with no axillary surgery	239	6 (3)	73

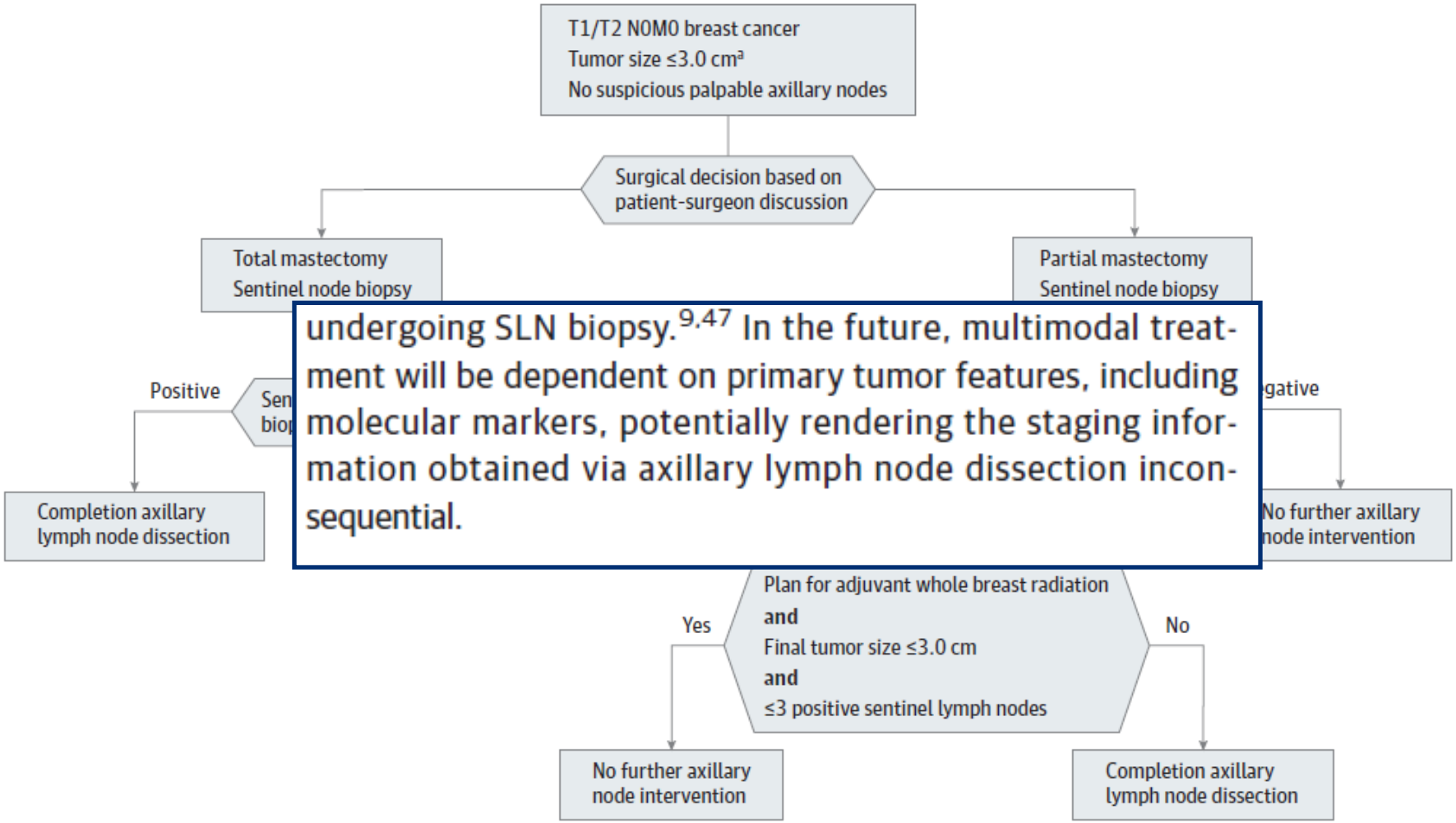
Table 4. Axillary Lymph Node Dissection or Not for Positive SLN Biopsy Result (Level B Evidence)

Source	Study Period	Participant Age	Axillary Status	Tumor Size	Follow-up	Study Interventions	Sample Size	Recurrence, No. (%)	Survival, %[a]
Giuliano et al,[19,33] 2011	1999-2004	Median, 56 y	No palpable, suspicious nodes on	Tumors ≤3.0 cm on examination	Median, 6.3 y	BCT + positive SLN biopsy result + completion axillary	388	2 (0.5)	88.8
								4 (0.9)	89.9
Straver et al,[41] 2010	2001-2005							NA[b]	NA[b]
								NA[b]	NA[b]
								NA[b]	NA[b]
Galimberti et al,[52] 2013	2001-2010	[illegible]	suspicious nodes on examination	cm on intraop-erative gross measurement	[illegible]	positive SLN biopsy result + completion axillary node dissection	[illegible]	1 (0.2)	87.8
						BCT or mastectomy + positive SLN biopsy result alone	467	4 (0.8)	84.4

Table 5. Long-term Rates of Adverse Outcomes Associated With Axillary Operations

Outcome	Axillary Lymph Node Dissection, %	Sentinel Node Biopsy Alone, %
Lymphedema	10-20[9,43,53,54]	5-7[9,43,53,54]
Quality-of-life reduction	35[9]	23[9]
Arm pain/numbness	31[9,42]	11[43,50]

Figure 2. Proposed Treatment Algorithm for Patients With Breast Cancer Who Present With No Palpable, Suspicious Axillary Nodes Based on the Results of the Systematic Review[a]



[a]If initial tumor size is >3.0 cm or patient is to undergo neoadjuvant chemotherapy, algorithm does not apply.

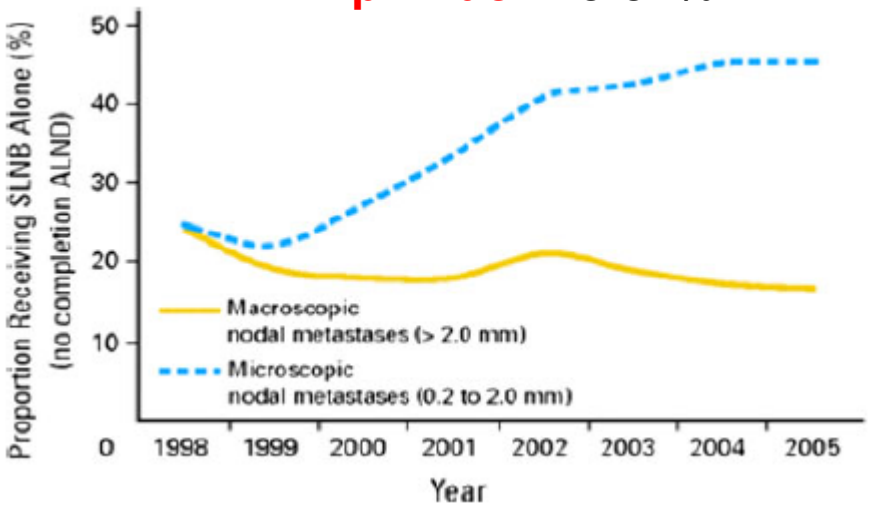
Breast Cancer (2013) 20:41–46
DOI 10.1007/s12282-012-0416-4

REVIEW ARTICLE

The changing role of axillary lymph node dissection for breast cancer

Masakuni Noguchi · Emi Morioka · Yukako Ohno · Miki Noguchi · Yasuharu Nakano · Takeo Kosaka

pNmic : 85-90% N0
pNmac: 48-87% N1



[28]. Therefore, ALND can be safely avoided in patients with SLN micrometastases if they undergo axillary or whole-breast irradiation and appropriate systemic therapy.

- ✓ size T
- ✓ size metastasi SLN
- ✓ num. di SLNs coinvolti
- ✓ ILV
- ✓ Estensione extranodale

However, the omission of ALND would be indicated in patients with a low axillary tumor burden. On the other hand, ALND remains a standard method of treating regional disease not only in patients with clinically positive nodes but also in other SLN-positive patients who do not meet the above criteria. Therefore, surgical treatment of the axilla can be individualized on the basis of the axillary nodal status.

Am Soc Clin Oncol Educ Book. 2013:61-5. doi: E10.1200/EdBook_AM.2013.33.61.

Which Patients with Sentinel Node–Positive Breast Cancer Can Avoid Axillary Dissection?

Author(s):
Alice Y. Ho, MD, MBA, and
Hiram S. Cody, MD

Article Summary:

Bilimoria et al.

	Axillary Local Recurrence (5 yr)	Relative Survival (5 yr)
SLN micrometastases (≤2 mm, pN0i+/N1mi)		
SLN only (n = 802)	0.4%	99%
SLN/ALND (n = 2,357)	0.2%	98%
SLN macrometastases (>2 mm, pN1)		
SLN only (n = 5,596)	1.0%	90%
SLN/ALND (n = 22,591)	1.1%	89%

ACOSOG Z0011

	SLN Biopsy/ALND n = 388	SLN Biopsy/No ALND n = 425
Loco-regional recurrence (6.3 yr)		
Local	3.6%	1.9%
Regional node	0.5%	0.9%
Local+Regional	4.1%	2.8% (*P* = NS)
Survival (6.3 yr)		
Disease-free survival	82%	84% (p = NS)
Overall survival	92%	93% (p = NS)

The principal implications of Z0011 are surgical, and over the last 2 years many institutions and surgeons in the United States (and to a lesser extent in Europe and worldwide) have found the results to be persuasive and practice-changing, incorporating into their treatment guidelines a policy of "no ALND" for SLN-positive patients who meet the Z0011 selection criteria. At our institution, we have done so since

What are the implications of Z0011 for the radiation oncologist?

	I liv	II liv	III liv
STANDARD Breast Tangents	66%	44%	31%
«HIGH» Breast Tangents	86%	71%	73%

It is quite possibile that *the "SNL biopsy of the future"* may be no SLN biopsy at all and that the *"ALND of the future"* will be limited to the salvage of locally persistent or recurrent disease

The Breast 22 (2013) 902–907

Contents lists available at SciVerse ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

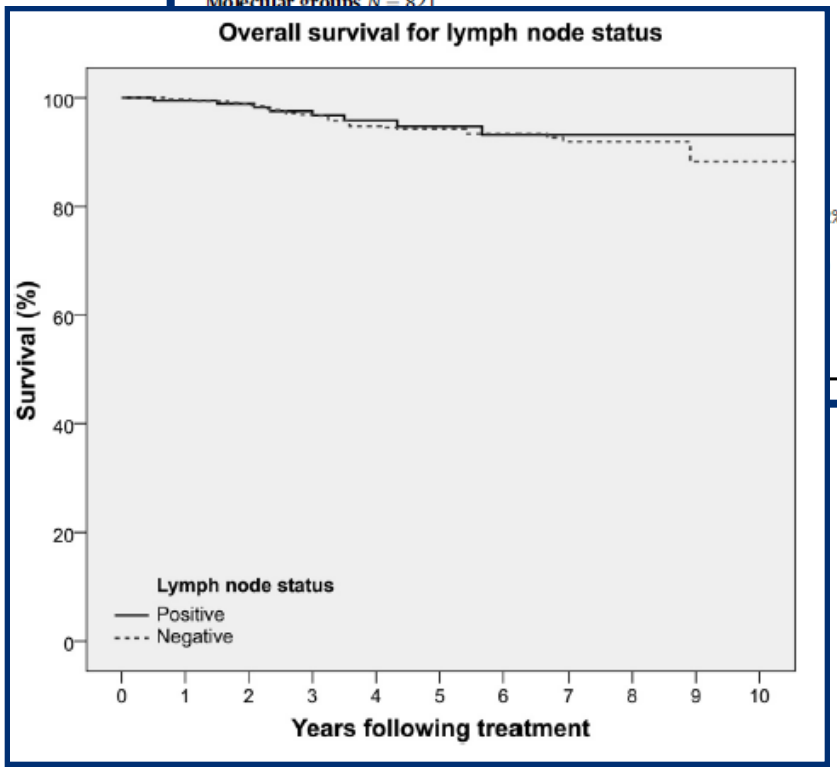
Original article

Positive versus negative sentinel nodes in early breast cancer patients: Axillary or loco-regional relapse and survival. A study spanning 2000–2012

Age	Size	Lymph node	IHQ subtypes	Disease free (months)	Metastases
61	10	Positive	Luminal A	92	No
48	10	Negative	Luminal A	21	Yes
51	20	Negative	Triple negative	11	Yes
49	28	Negative	Triple negative	24	No
66	30	Negative	Her2	38	Yes
59	30	Positive	Luminal A	39	No
45	45	Negative	Luminal B	42	No

Patient characteristic	Subject *n* (%)
Age *N* = 889	58 ± 13 (25–88)
<50	208 (23.4%)
50–69	506 (57.0%)
≥70	175 (19.6%)
Invasive tumour size (mm) *N* = 821	
≤10	220 (26.8%)
11 a 20	372 (45.3%)
21 a 30	170 (20.7%)
>30	59 (7.2%)
Invasive tumour size mean (mm)	17.2 (1–50)
DCIS size *N* = 87	
≤30 mm	57 (65.5%)
>30 mm	30 (34.5%)
Origin of the patients *N* = 889	
Diagnostic care	429 (48.3%)
Population screening	460 (51.7%)
Molecular groups *N* = 821	

	SN-	SN+
Axillary Recurrence	**0,8%**	**1.2%**
Distant recurrence	**3,3%**	**4.6%**
Overall and specific mortality	**4.9%-1.4%**	**4%-2.5%**



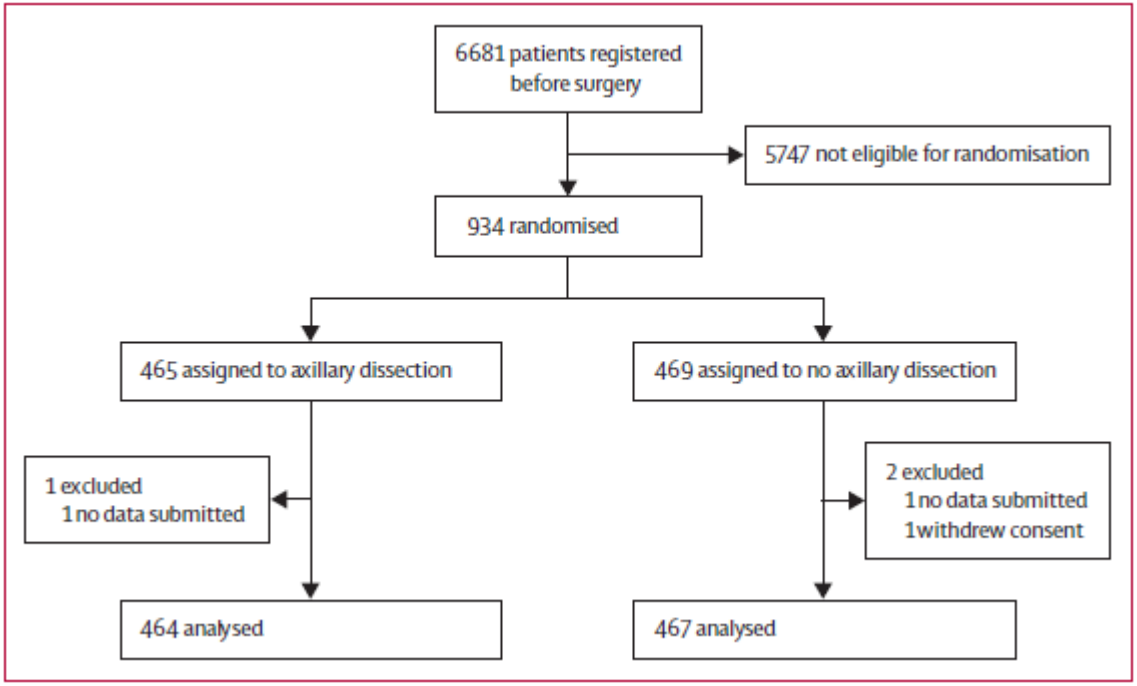
La linfoadenectomia può essere omessa?

MICROMETASTASI

Lancet Oncol 2013; 14: 297–305

Axillary dissection versus no axillary dissection in patients with sentinel-node micrometastases (IBCSG 23–01): a phase 3 randomised controlled trial

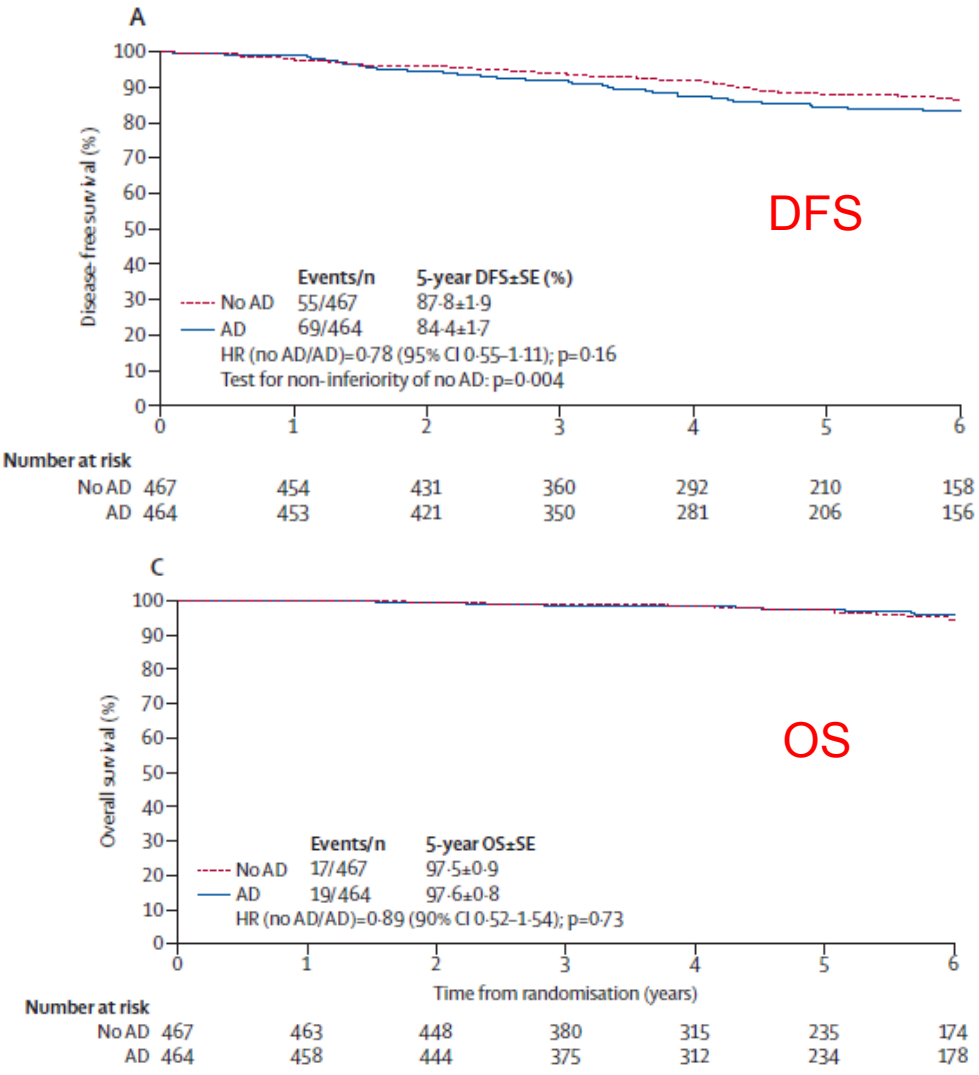
Viviana Galimberti, Bernard F Cole, Stefano Zurrida, Giuseppe Viale, Alberto Luini, Paolo Veronesi, Paola Baratella, Camelia Chifu, Manuela Sargenti, Mattia Intra, Oreste Gentilini, Mauro G Mastropasqua, Giovanni Mazzarol, Samuele Massarut, Jean-Rémi Garbay, Janez Zgajnar, Hanne Galatius, Angelo Recalcati, David Littlejohn, Monika Bamert, Marco Colleoni, Karen N Price, Meredith M Regan, Aron Goldhirsch, Alan S Coates, Richard D Gelber, Umberto Veronesi, for the International Breast Cancer Study Group Trial 23–01 investigators

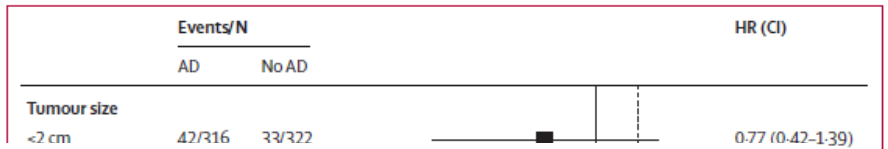


	Axillary dissection (n=464)	No axillary dissection (n=467)
Disease-free survival events*		
Total	69 (15%)	55 (12%)
Breast cancer events		
Local	10 (2%)	8 (2%)
Regional	1 (<1%)	5 (1%)
Distant	34 (7%)	25 (5%)
Contralateral breast	3 (<1%)	9 (2%)
Non-breast cancer events		
Second (non-breast) primary†	20 (4%)	6 (1%)
Death without cancer event	1 (<1%)	2 (<1%)
Deaths		
Total	19 (4%)	17 (4%)

*Includes all breast cancer events, all non-breast cancer events, and deaths with cause unknown. †Types (number) of second primaries in the group with axillary dissection were gastrointestinal (four), genitourinary (two), gynaecological (six), haematological (two), laryngeal (two), lung (one), and sarcoma (three). Types (number) in the group without axillary dissection were gastrointestinal (two), gynaecological (three), and melanoma (one).

Table 3: Disease-free survival events and deaths at 5·0 years median follow-up of intention-to-treat population





	Axillary dissection (n=447)	No axillary dissection (n=453)	p value†
Sensory neuropathy	82 (18%)	55 (12%)	0·012
Grade 1	60 (13%)	40 (9%)	
Grade 2	15 (3%)	6 (1%)	
Grade 3	1 (<1%)	0	
Grade 4	0	0	
Unknown grade	6 (1%)	9 (2%)	
Lymphoedema	59 (13%)	15 (3%)	<0·0001
Grade 1	33 (7%)	10 (2%)	
Grade 2	20 (4%)	3 (<1%)	
Grade 3	2 (<1%)	0	
Grade 4	1 (<1%)	0	
Unknown grade	3 (<1%)	2 (<1%)	
Motor neuropathy	37 (8%)	13 (3%)	0·0004
Grade 1	25 (6%)	11 (2%)	
Grade 2	9 (2%)	1 (<1%)	
Grade 3	3 (<1%)	1 (<1%)	
Grade 4	0	0	
Unknown grade	0	0	

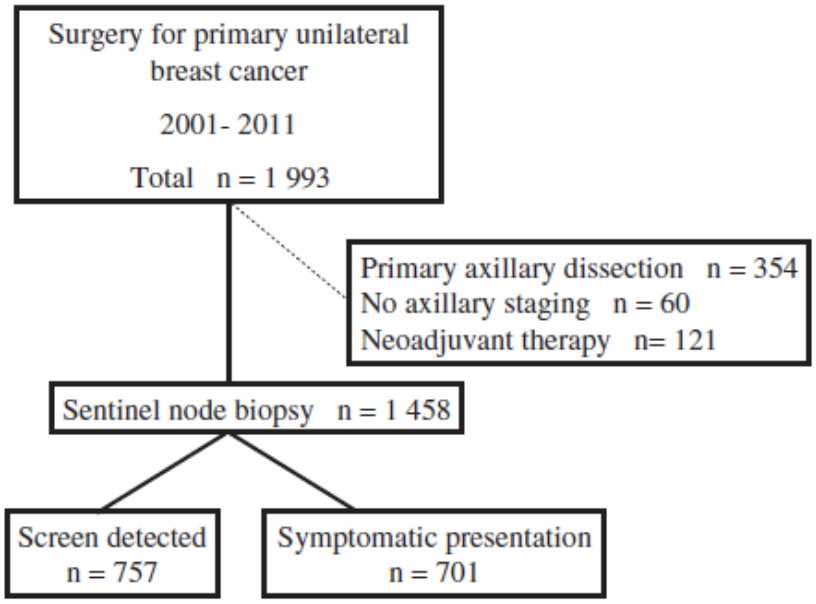
*Excludes 31 patients (17 in the axillary dissection group and 14 in the no-axillary-dissection group) who did not receive the randomly assigned treatment. †Based on Fisher's exact test comparison of the occurrence of any grade event across treatment groups.

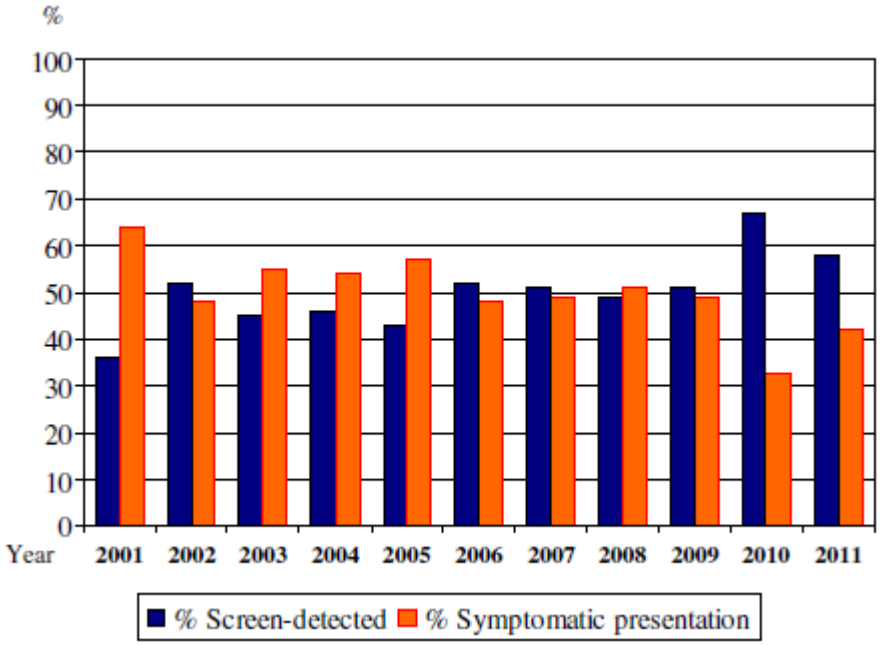
Table 2: **Long-term surgical events***

Available online at www.sciencedirect.com
SciVerse ScienceDirect
EJSO
the Journal of Cancer Surgery
ELSEVIER
EJSO 39 (2013) 601–607
www.ejso.com

Completion axillary dissection can safely be omitted in screen detected breast cancer patients with micrometastases. A decade's experience from a single institution

D. Grabau [a,b,*], L. Dihge [b,c], M. Fernö [d], C. Ingvar [b,c], L. Rydén [b,c]





	Screen-detected			Symptomatic presentation			*p* value
	n	*n* with ALND	*n* with positive ALND	n	*n* with ALND	*n* with positive ALND	
a, All patients with sentinel nodes							
SN with metastases >0.2/> 200 cells and ≤2.0 mm	62	61	3	81	79	18	0.01
Number of positive sentinel nodes							
1	50	49	2	68	67	16	0.01
2	10	10	0	11	10	2	
≥3	2	2	1	2	2	0	
SN with metastases >2.0 mm	164	164	73	195	193	110	0.03
Number of positive sentinel nodes							
1	97	97	31	115	114	57	0.02
2	47	47	29	53	52	31	
≥3	16	16	11	21	21	17	
b, Patients with micrometastases in sentinel nodes							
Tumour size							
1–10 mm	16	16	0	6	6	1	
11–20 mm	34	33	1	40	39	10	
21–30 mm	10	10	0	26	25	7	
>30 mm	2	2	2	9	9	0	

Conclusion: Despite the small number of patients with micrometastases in this large cohort of breast cancer patients, these results support the contention that completion ALND can safely be omitted in screen-detected breast cancer patients with micrometastases in the SNs.

Characteristic	Recurrent disease ($n = 4$)	Disease-free ($n = 223$)	p
Age (years)			
Mean (range)	48.5 (38.0–66.0)	54.5 (29.0–75.0)	0.250 (NS)
Missing	0	1	
Tumor palpability	3 (75.0 %)	84 (44.6 %)	0.234 (NS)[c]
Missing	1	32	
Diagnostic method			
Physical examination	2 (50.0 %)	61 (32.8 %)	0.060 (NS)[a,c]
Mammography	1 (25.0 %)	123 (66.1 %)	
Ultrasound	1 (25.0 %)	2 (1.1 %)	
Missing	0	24	
Tumor size (cm)			
Mean (range)	1.95 (1.00–2.50)	1.67 (0.10–3.50)	0.247 (NS)
Missing	0	0	
Tumor type			
Ductal	4 (100.0 %)	199 (90.5 %)	0.672 (NS)[b,c]
Lobular	0 (0 %)	10 (4.5 %)	
Other	0 (0 %)	11 (5.0 %)	
Missing	0	3	
Tumor grade II and III	4 (100.0 %)	152 (73.4 %)	0.296 (NS)[c]
Missing	0	16	
Lymphovascular invasion	0 (0 %)	50 (22.4 %)	0.367 (NS)[c]
Missing	0	0	
Presence of DCIS	2 (100.0 %)	84 (48.8 %)	0.243 (NS)[c]
Missing	2	51	
Expression of estrogen receptors	2 (50.0 %)	168 (84.8 %)	0.119 (NS)[c]
Missing	0	25	
Expression of progesterone receptors	2 (78.8 %)	150 (76.5 %)	0.244 (NS)[c]
Missing	0	27	
Sentinel node metastasis size (mm)			
Mean (range)	0.93	1.11	0.554 (NS)
Missing	1	54	

Annals of
SURGICAL ONCOLOGY
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ith Sentinel Node
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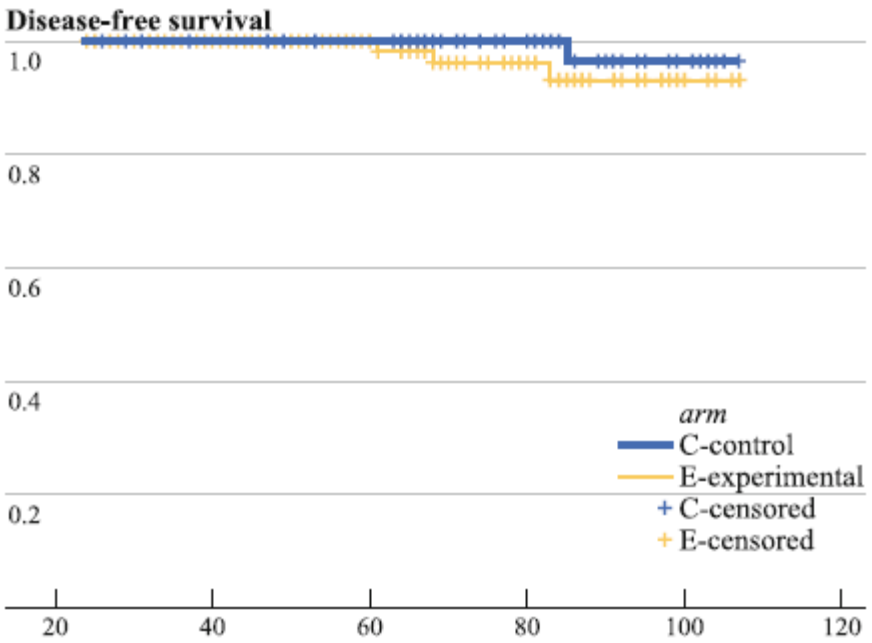
MD[1], Pilar Santesteban, MD[2], Manuel Ramos, MD[3],
MD[6], and Sergi Vidal, MD[7]



The American Journal of Surgery (2013) 205, 581-584

The American Journal of Surgery®

North Pacific Surgical Association

Routine completion axillary lymph node dissection for positive sentinel nodes in patients undergoing mastectomy is not associated with improved local control

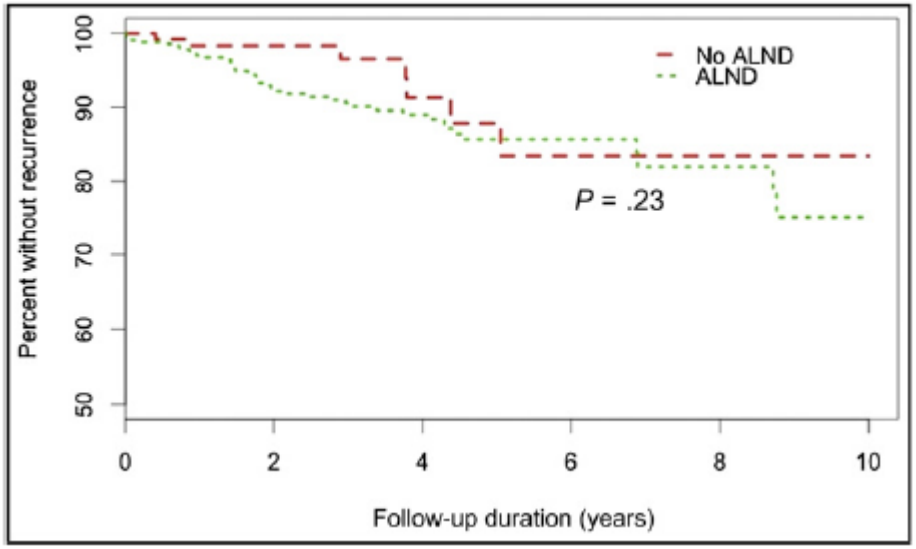
Jeffrey D. Crawford, M.D.[a], Mindy Ansteth, M.S.[b], Jim Barnett, M.S.[c], Margie Glissmeyer, P.A-C.[b], Nathalie G. Johnson, M.D.[b,*]

Characteristic	ALND (n = 426)	No ALND (n = 135)	*P* value
Age at diagnosis	55.7 (12.6)	58.8 (13.5)	.015
Primary tumor size (cm)	3.2 (2.6)	2.5 (1.7)	.003
Stage T1	21.8%	32.6%	.011
Stage T2	37.6%	34.8%	.406
State T3	13.1%	6.7%	.030
ER^+	83.5%	83.0%	.886
PR^+	76.4%	78.5%	.614
$HER2^+$	34.4%	21.8%	.007
No. nodes removed	14.0 (6.5)	6.6 (4.6)	<.001
No. positive nodes	3.8 (4.9)	1.7 (1.1)	<.001
Size of node metastasis (mm)	6.4 (6.3)	2.6 (1.9)	<.001
Micrometastases	15.5%	47.4%	<.001
Extranodal extension	36.0%	15.5%	<.001

Treatment	ALND (n = 426)	No ALND (n = 135)
Adjuvant radiation	18.1% (77)	13.3% (18)
Adjuvant chemotherapy	91.8% (391)	94.1% (127)
Neoadjuvant chemotherapy	3.05% (12)	1.5% (2)

Mean time to recurrence was *29.9 months*
Mean FUP for patients withouth recurrence was *40.3 months*

	ALND	No ALND
Recurrence	43 (10.1%)	7 (5.2%)
Distant recurrence	37 (8.7)%	6 (4.4)%
Locoregional recurrence	6 (14%)	1 (0.7%)



La linfoadenectomia può essere omessa?

MACROMETASTASI

Breast Cancer Res Treat (2013) 138:817–827
DOI 10.1007/s10549-013-2468-3

CLINICAL TRIAL

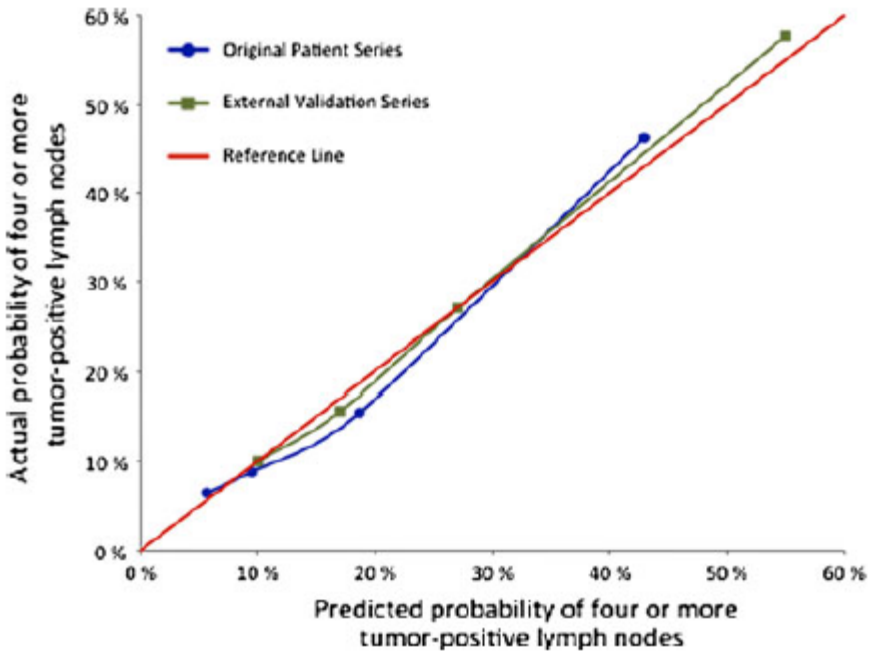
International multicenter tool to predict the risk of four or more tumor-positive axillary lymph nodes in breast cancer patients with sentinel node macrometastases

Tuomo J. Meretoja · R. A. Audisio · P. S. Heikkilä · R. Bori · I. Sejben · P. Regitnig · G. Luschin-Ebengreuth · J. Zgajnar · A. Perhavec · B. Gazic · G. Lázár · T. Takács · B. Kővári · Z. A. Saidan · R. M. Nadeem · I. Castellano · A. Sapino · S. Bianchi · V. Vezzosi · E. Barranger · R. Lousquy · R. Arisio · M. P. Foschini · S. Imoto · H. Kamma · T. F. Tvedskov · M.-B. Jensen · G. Cserni · M. H. K. Leidenius

	Coefficient	Standard error	Wald	*P*	Odds ratio	95 % CI for odds ratio	
						Lower	Upper
Prevalence of four or more tumor-positive nodes	0.049	0.019	6.637	0.010	1.050	1.012	1.090
Number of positive SNs	0.943	0.166	32.147	<0.0001	2.567	1.853	3.556
Number of negative SNs	−0.443	0.150	8.751	0.003	0.642	0.479	0.861
Histological tumor size (mm)	0.018	0.008	5.391	0.020	1.018	1.003	1.034
ECE of SN metastasis	1.036	0.218	22.539	<0.0001	2.818	1.837	4.321
Constant	−4.392	0.516	72.389	<0.0001	0.012		

$$\text{logit}(p) = -4.392 + 0.049 \times a + 0.943 \times b - 0.443 \times c + 0.018 \times d + 1.036 \times e.$$

a=prevalence di ≥ 4 N+
b= numero di SNs +
c= numero di SNs –
d= grandezza del T(mm)
e= ECE di SNs (0 se non presente, 1 se presente)



130 (19.1%) dei 675 pz aveva ≥ 4N+ (11.4-25%)

La linfoadenectomia può essere omessa?

La RT su N può essere un ‘alternativa alla CH?

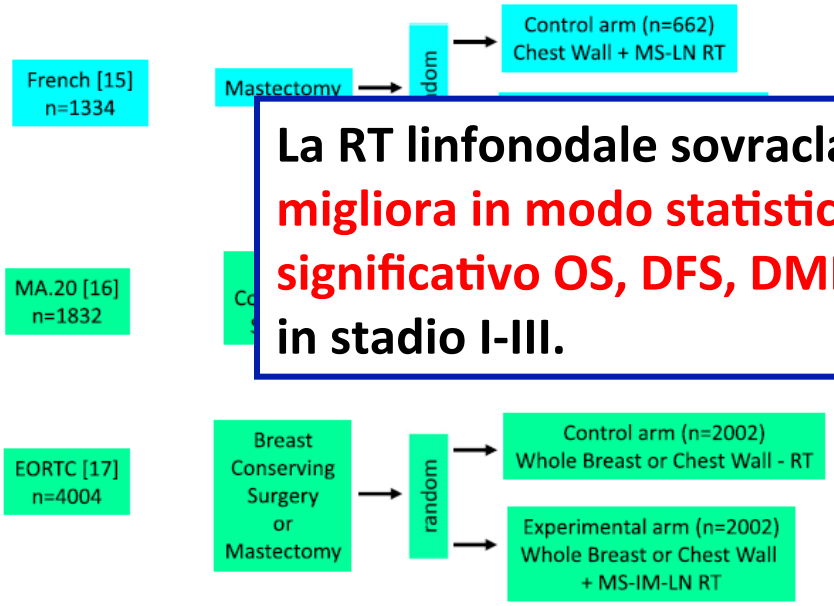
Budach *et al. Radiation Oncology* 2013, **8**:267
http://www.ro-journal.com/content/8/1/267

RADIATION ONCOLOGY

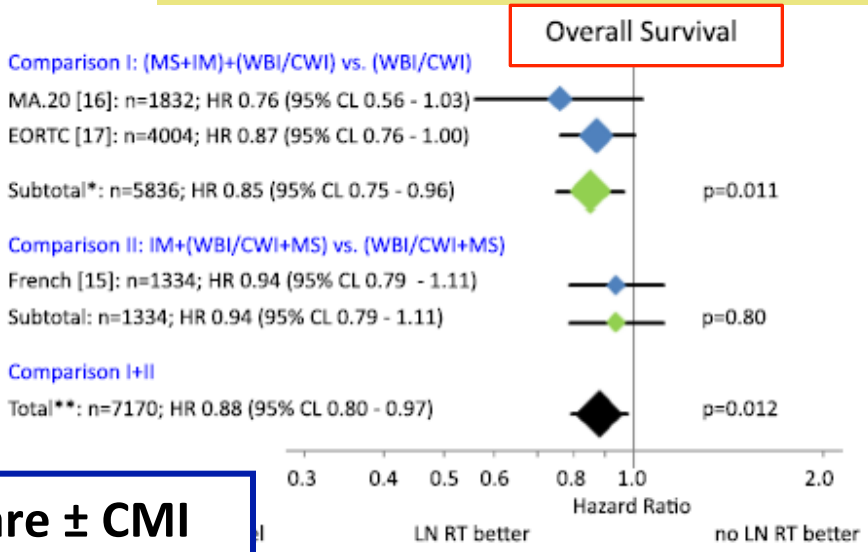
RESEARCH **Open Access**

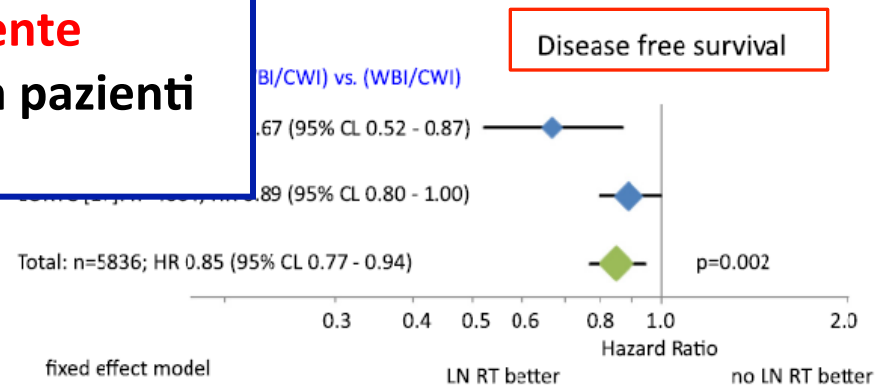
Adjuvant radiotherapy of regional lymph nodes in breast cancer - a meta-analysis of randomized trials

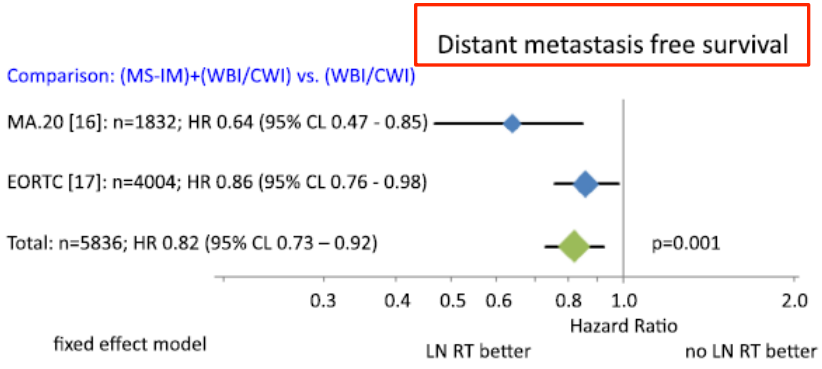
Wilfried Budach[1*], Kai Kammers[2], Edwin Boelke[1] and Christiane Matuschek[1]



La RT linfonodale sovraclaveare ± CMI migliora in modo statisticamente significativo OS, DFS, DMFS in pazienti in stadio I-III.







The Breast 22 (2013) S118–S128

Contents lists available at SciVerse ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Review

Is regional nodes radiotherapy an alternative to surgery?

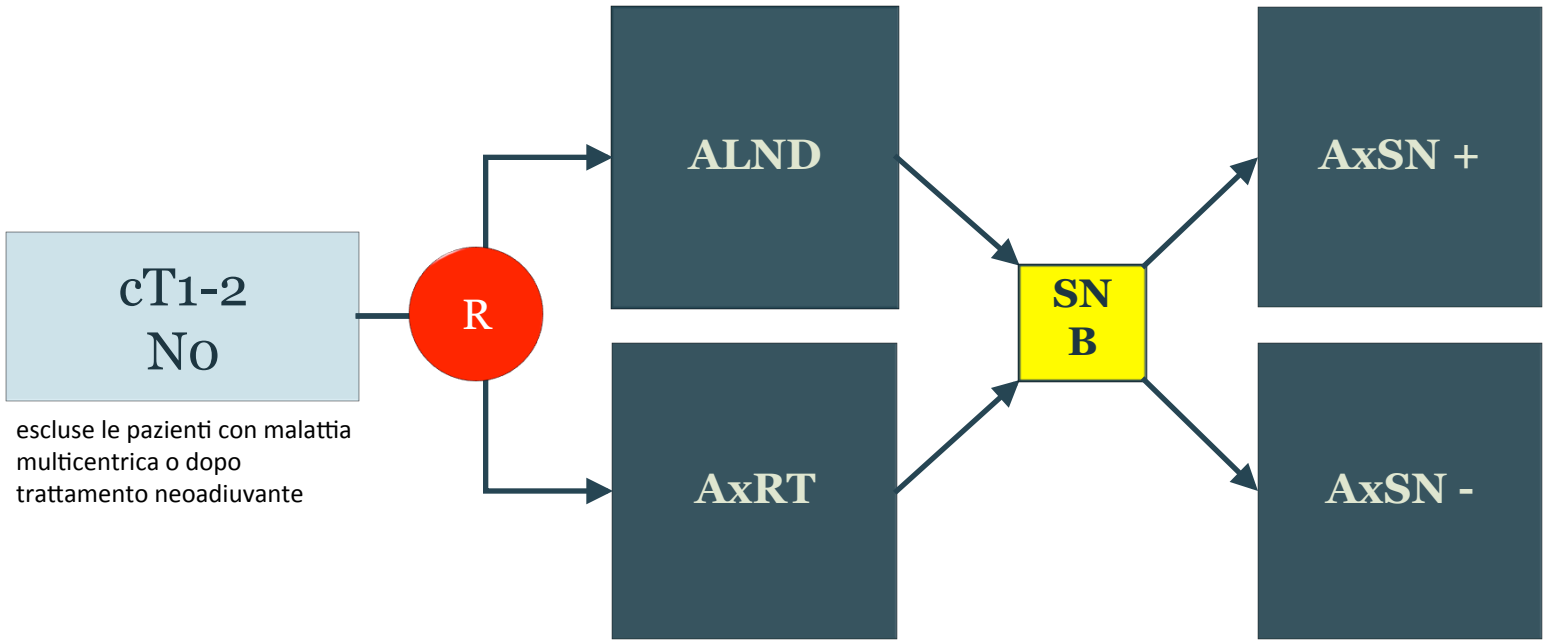
Birgitte Vrou Offersen [a,*], Hanne Melgaard Nielsen [a], Marie Overgaard [b], Jens Overgaard [b]

Regional RT → no regional recurrences at 5 years

An answer to the question if regional RT may be an alternative to dissection may be given with the results from the AMAROS trial later this year. Judged from the general results listed in Tables 1–4 and based on the fact that 74% of the tumours in the AMAROS trial were pT1, 71% were grades I/II and 61% were postmenopausal we may see that there will be only very few regional recurrences in the trial in total. We need more data on biological characteristics to identify relevant patients to be treated with nodal RT instead of cALND. Perhaps the 21-gene OncotypeDX recurrence score assay or other assays can be used to identify patients with a particularly high risk of regional recurrence [56,57]. Unfortunately, there is a lack of information in all the studies included in Tables 1–4 in this review regarding the regional recurrence risk in relation to biological classification, but hopefully more studies will report on this in the future. In 2010 A. Recht suggested that it could be acceptable to

EORTC-AMAROS Trial design

Presentazione ASCO 2013



Ipotesi : radioterapia ascellare offre le stesse probabilità di controllo locale e sopravvivenza – con meno effetti collaterali – rispetto alla dissezione ascellare.

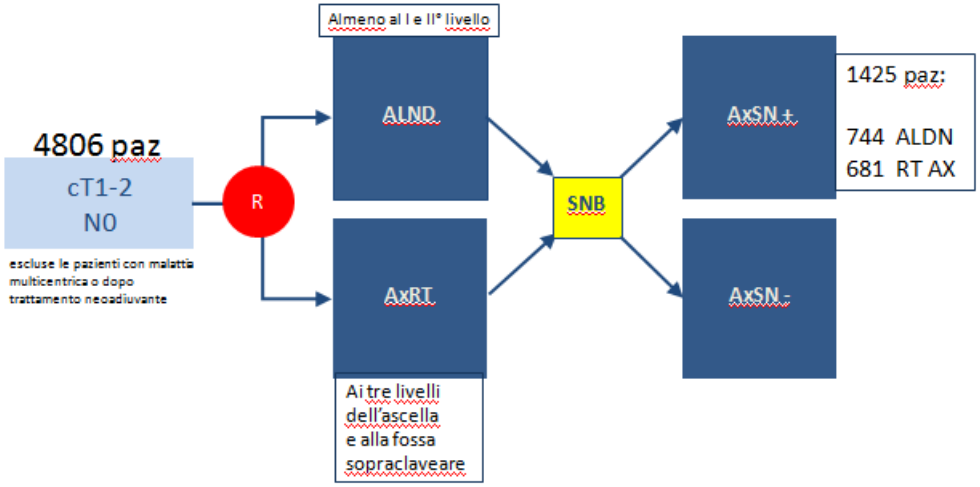
Obiettivo primario: dimostrare la «non-inferiorità» in termini di recidive ascellari (2% vs <4%)
Obiettivi secondari : confrontare OS e DFS; linfedema, funzionalità della spalla e QoL

Terapia sistemica a scelta delle singole Istituzioni

Mod. da: Rutgers EJ. ASCO 2013

	ALND (744 pts)	AxRT (681 pts)
Median age (Q1-Q3)	56 (48 - 64)	55 (48 - 63)
Menopausal stage		
pre-menopausal	38.1 %	42.5 %
post-menopausal	57.7 %	54.5 %
Median tumor size (Q1-Q3)	17 mm (13 - 22)	18 mm (13 - 23)
Grade		
1	24.1 %	22.6 %
2	47.8 %	45.7 %
3	25.8 %	29.4 %
Pre-operative ultrasound axilla	59.2 %	61.5 %
Breast surgery		
BCS	81.9 %	81.8 %
Mastectomy	17.1 %	17.8 %
Systemic treatment		
chemotherapy	60.9 %	61.3 %
hormonal therapy	78.6 %	77.1 %
immunotherapy	6.0 %	6.4 %
no systemic treatment	9.0 %	9.4 %
RT breast/chest wall	84.8 %	87.7 %
	(744 pts)	(681 pts)
Median number of SN removed (Q1-Q3)	2 (1-3)	2 (1-3)
Size of metastases in SN		
macrometastases	59.4 %	61.5 %
micrometastases	28.9 %	28.6 %
ITC	11.7 %	9.8 %

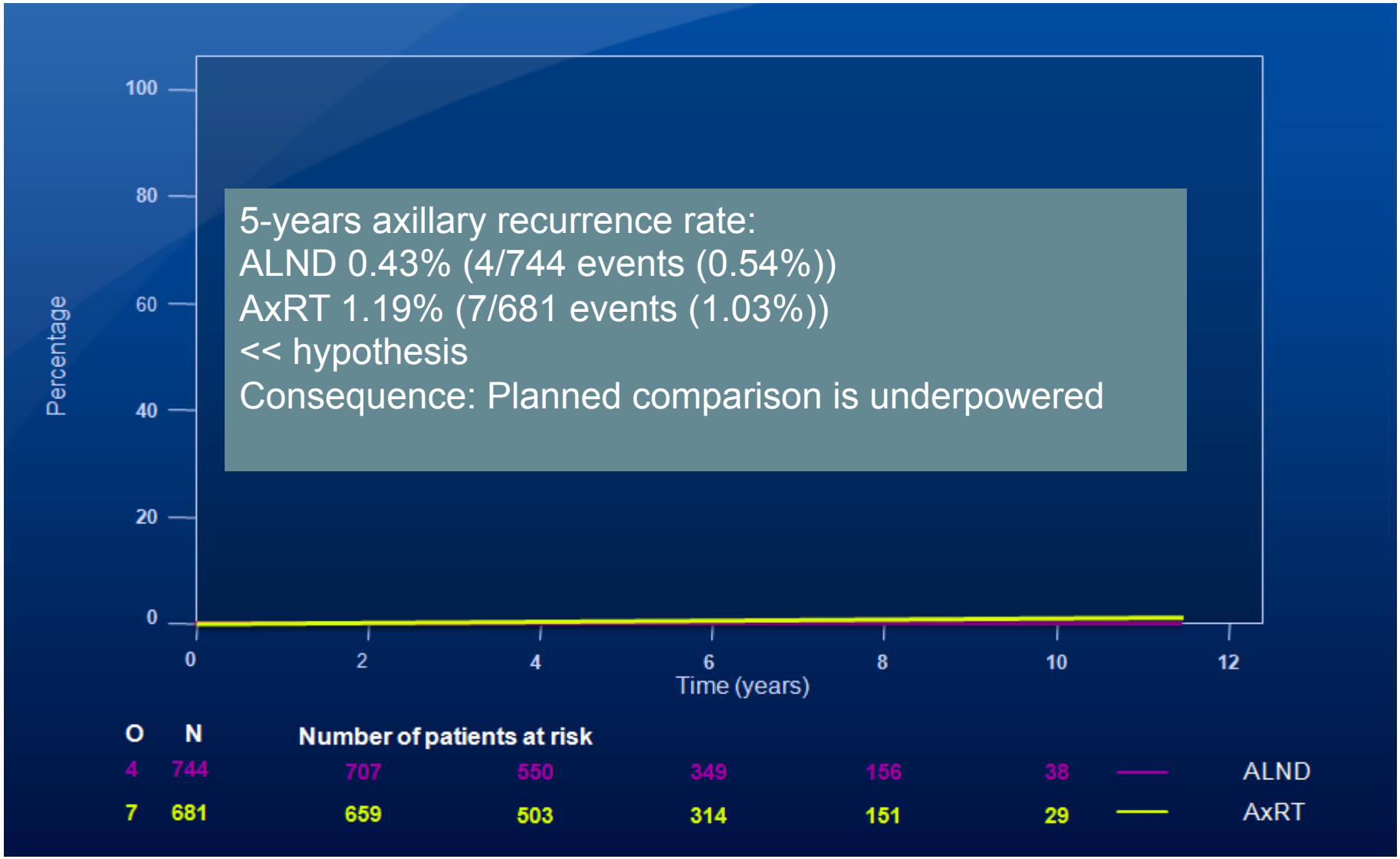
EORTC-AMAROS Trial design



>80% trattate con chirurgia conservativa
>60% ha ricevuto chemioterapia adiuvante
>77% ha ricevuto ormonoterapia adiuvante
≈ 60% presentava macrometastasi

Number of additional positive nodes (besides SN)	ALND
0	67.1 %
1-3	25.0 %
≥ 4	7.8 %

EORTC-AMAROS
Axillary recurrence rate

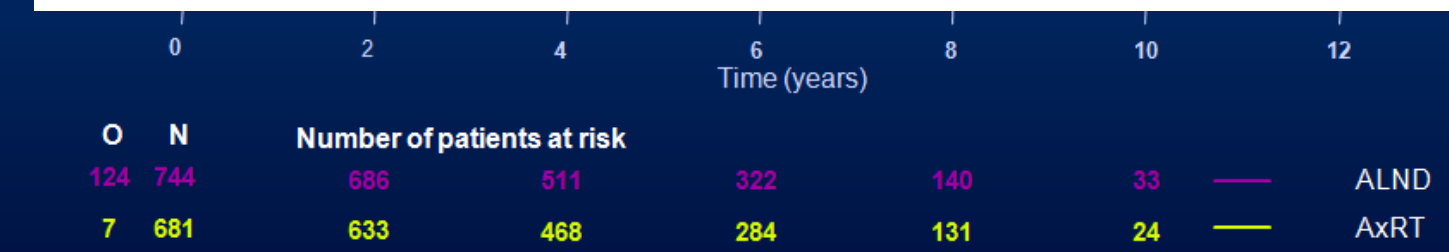


Mod. da: Rutgers EJ. ASCO 2013

EORTC-AMAROS
Disease-free survival

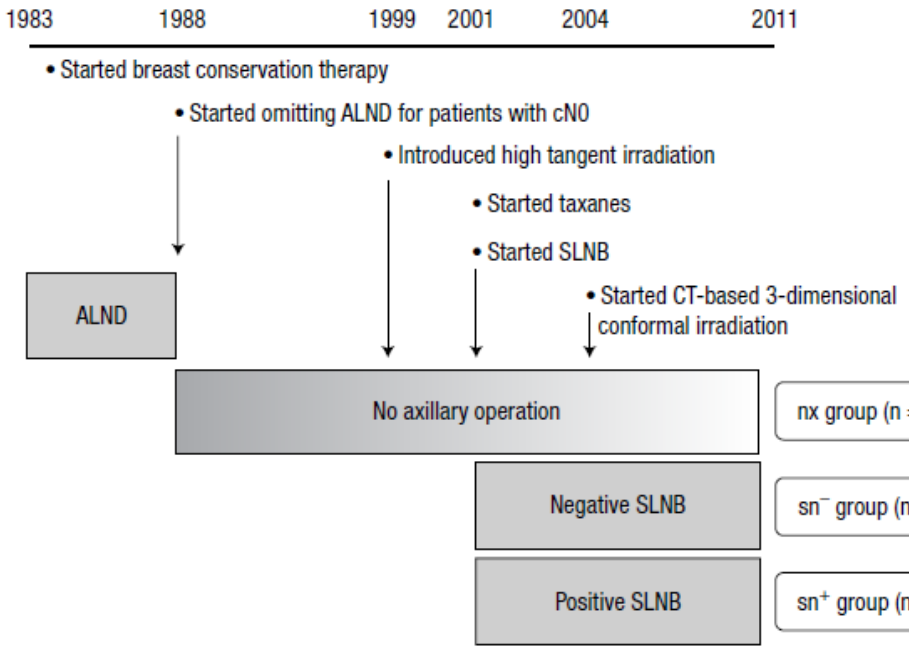
Conclusioni

Sia dissezione ascellare sia la radioterapia ascellare offrono un ottimo livello di controllo loco-regionale della malattia in queste pazienti



Outcomes of Clinically Node-Negative Breast Cancer Without Axillary Dissection: Can Preserved Axilla Be Safely Treated With Radiation After a Positive Sentinel Node Biopsy?

Naoko Sanuki,[1] Atsuya Takeda,[1,2] Atsushi Amemiya,[3] Toru Ofuchi,[3] Masashi Ono,[3] Haruki Ogata,[3] Ryo Yamagami,[3] Jun Hatayama,[3] Takahisa Eriguchi,[1] Etsuo Kunieda[2]



+ RT

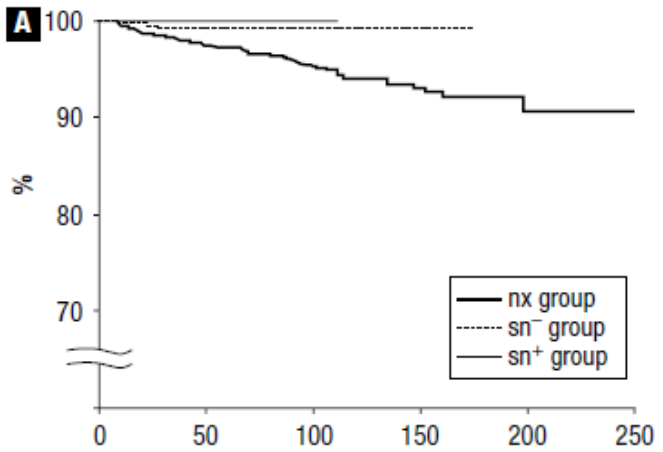
+ Tangents + supraclavicular field 83%

+ Tangents only

+ Tangents + supraclavicular field

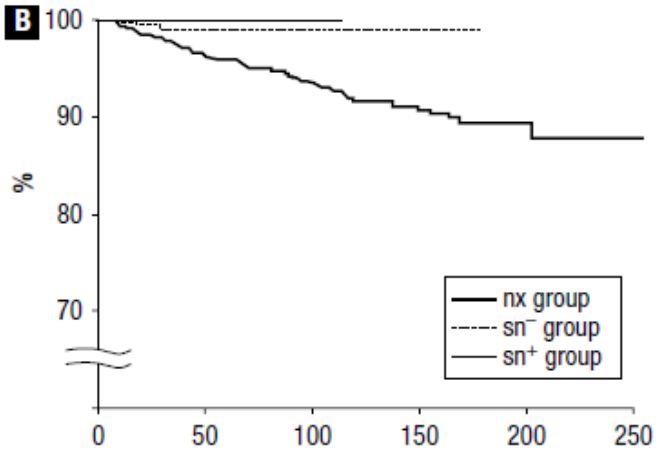
Clinical Breast Cancer February 2013

Axillary (A) and Regional (B) Nodal Control According to Axillary Intervention



(at risk)

nx	1548	1166	664	234	53	3
sn⁻	518	211	26	1	0	0
sn⁺	104	37	1	0	0	0



(at risk)

nx	1548	1155	664	232	53	3
sn⁻	518	211	26	1	0	0
sn⁺	104	39	1	0	0	0

	P[a]
	.0002
	.02
	.04
	.02
	.14
	.89
	.08
	.09
	.03

Conclusions: Treatment without axillary dissection showed excellent outcomes with negligible toxicity for patients with clinically node negative, including those with a positive SLNB. Regional nodal irradiation after a positive SLNB is a reasonable alternative to axillary dissection.

Annals of Oncology 24: 2023–2028, 2013
doi:10.1093/annonc/mdt151
Published online 24 April 2013

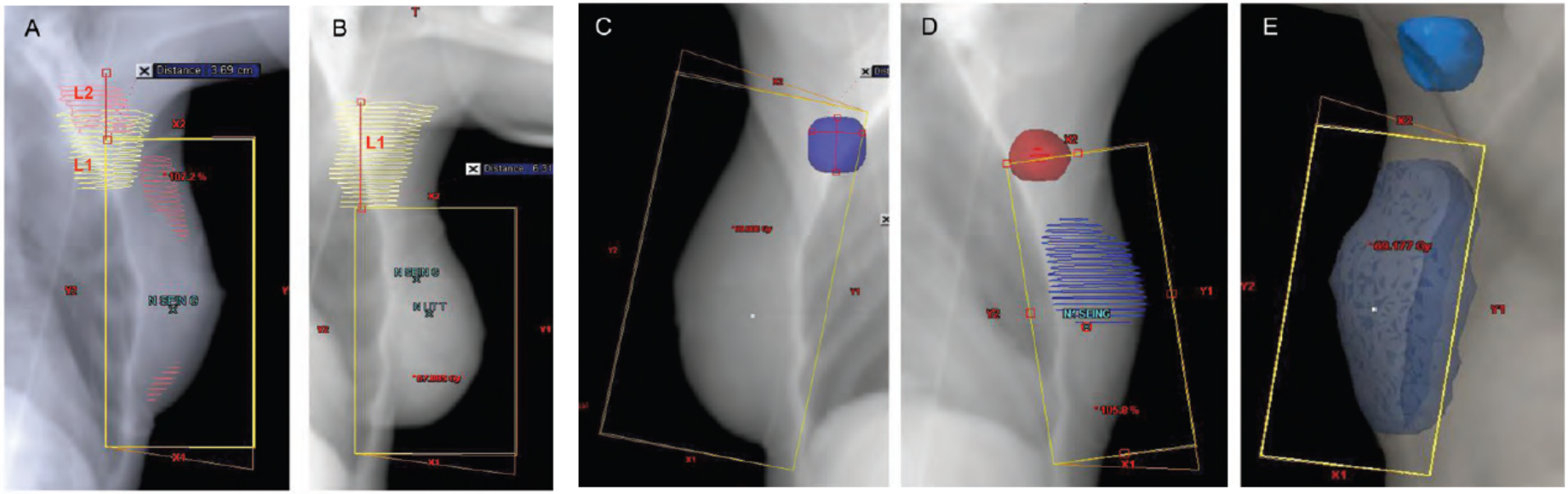
The standard tangential fields used for breast irradiation do not allow optimal coverage and dose distribution in axillary levels I–II and the sentinel node area

Y. Belkacemi[1,†*], Q. Allab-Pan[1], V. Bigorie[2], W. Khodari[1,†], P. Beaussart[3], J. -L. Totobenazara[4], J. -P. Mège[1], P. Caillet[5], F. Pigneur[3], T. -H. Dao[3], R. Salmon[6,†], E. Calitchi[1] & R. Bosc[2]

	Total ($n = 109$) Prescribed dose Mean (SD)	Group 1 ($n = 18$) (50 Gy) Mean (SD)	Group 2 ($n = 34$) (60 Gy) Mean (SD)	Group 3 ($n = 57$) (66 Gy) Mean (SD)	*P* value
(i) Dose distribution according to the total dose subgroups groups					
Level II					
D_{med} (Gy)[a]	22 (19)	23 (22)	25 (21)	21 (19)	0.005
V95 (%)	4 (11)	10 (20)	6 (17)	1 (4)	
V50 (%)	41 (30)	42 (36)	45 (30)	40 (29)	
Level II					
D_{med} (Gy)[a]	4 (9)	6 (14)	4 (7)	6 (11)	0.04
V95 (%)	0.3 (4)	3 (11)	0 (0)	0 (0)	
V50 (%)	7 (19)	11 (26)	5 (13)	9 (24)	

(ii) Dose distribution according to the tangential field size and initial tumor site

Axillary region	Mean dose (range)		D95 (range)			Median dose (UQ)			Median dose (LQ)	
	Level I (Gy)	Level II (Gy)	Level I (Gy)	Level II (Gy)	*N*	Level I (Gy)	Level II (Gy)	*N*	Level I (Gy)	Level II (Gy)
STgF	20 (1–57)	4 (0–46)	3 (0–53)	1 (0–8)	51 (47%)	21	5	21 (19%	17	1.6
HTgF	33 (7–53)	11 (4–42)	11 (0–46)	5 (0–42)	12 (11%)	35	12	7 (6%)	33	4.5
P value	<0.0001	0.002	<0.0001	<0.0001		0.001	0.03		0.04	0.003



Irradiazione con campi tangenti standard

Inadeguata copertura dell'area SNLB e del I e II livello

personalize radiation fields and select the patients for whom 'minimal axillary surgery' is acceptable.

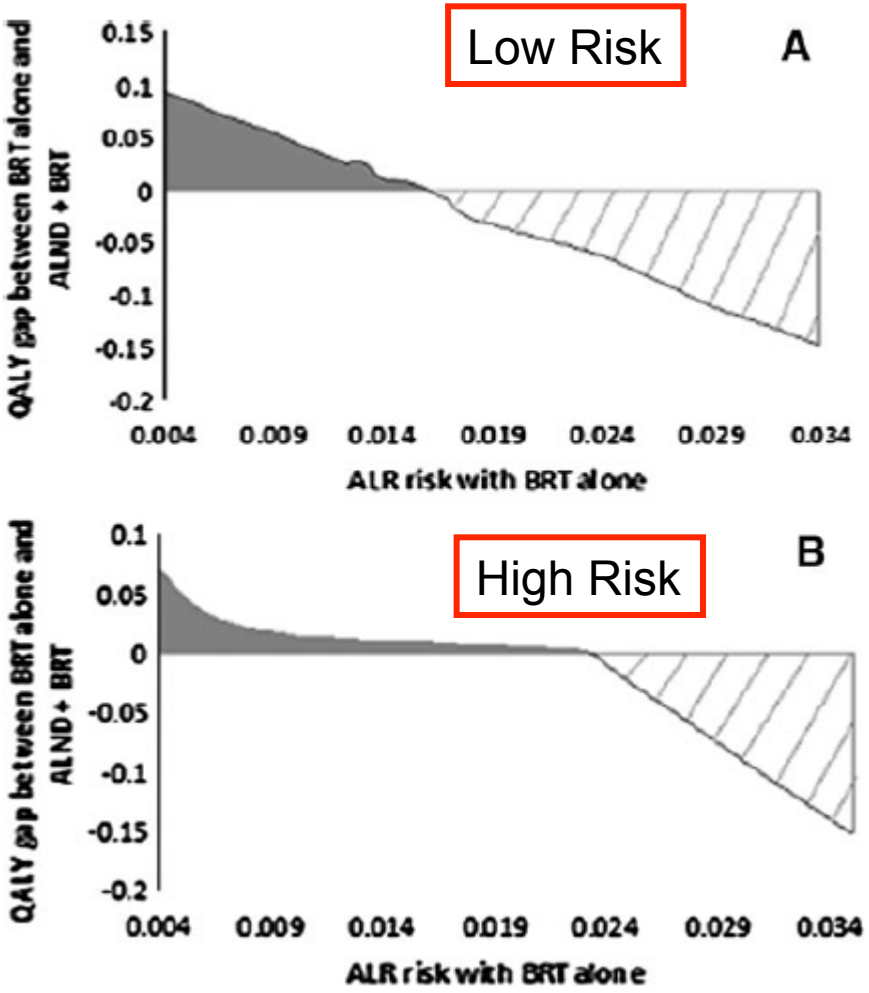
Breast Cancer Res Treat (2013) 138:205–213
DOI 10.1007/s10549-013-2418-0

EPIDEMIOLOGY

Trade-offs associated with axillary lymph node dissection with breast irradiation versus breast irradiation alone in patients with a positive sentinel node in relation to the risk of non-sentinel node involvement: implications of ACOSOG Z0011

Age/risk group	5 yr OS		5 yr DFS		20 yr OS		20 yr DFS		QALE	
	BRT alone (%)	ALND + BRT (%)	BRT alone (%)	ALND + BRT (%)	BRT alone (%)	ALND + BRT (%)	BRT alone (%)	ALND + BRT (%)	BRT alone	ALND + BRT
40										
Low risk[a]	90	90	76	76	56	56	56	56	**16.89**	16.83
High risk[b]	89	89	62	**73**	49	**54**	47	**53**	15.29	**16.30**
55										
Low risk[a]	88	88	75	75	47	47	47	47	**15.53**	15.46
High risk[b]	86	86	61	**72**	38	**42**	40	**44**	13.55	**14.36**
70										
Low risk[a]	82	82	69	69	19	19	19	19	**11.27**	11.24
High risk[b]	81	81	56	**57**	17	**18**	16	**18**	10.39	**10.95**

High risk (NSLN 51–60 %)	0.175	0.08–0.34
Lymphedema		
ALND + BRT [1, 2]	0.135 (3 yr)	0.09–0.20
BRT alone[b] [1, 2]	0.08 (3 yr)	0.04–0.10
Utilities		
NED [33]	0.97	Not varied
ALR [33, 35, 36	0.65	0.60–0.80
Distant metastases [33]	0.55	0.50–0.60
Severe lymphedema [33]	0.76	0.70–0.80
Mild lymphedema [34]	0.925	0.85–0.95


Low Risk
A
QALY gap between BRT alone and ALND + BRT
0.15
0.1
0.05
0
-0.05
-0.1
-0.15
-0.2
0.004
0.009
0.014
0.019
0.024
0.029
0.034
ALR risk with BRT alone
High Risk
B
QALY gap between BRT alone and ALND + BRT
0.1
0.05
0
-0.05
-0.1
-0.15
-0.2
0.004
0.009
0.014
0.019
0.024
0.029
0.034
ALR risk with BRT alone

Dai viaggi del mio capo….Tunisia 2013