Gruppo di Studio per la Patologia Mammaria

FATTORI DECISIONALI PER L'IRRADIAZIONE LINFONODALE (1-3 N+)

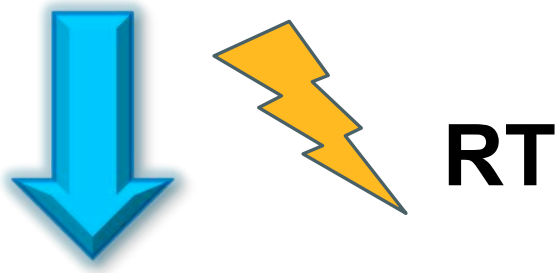
Lorenza Marino

Alfio Di Grazia

ZOOM JOURNAL CLUB 2012

Roma 25 Gennaio 2013

Il tasso di fallimento locoregionale a 15 anni è del 27% negli 1-3 N+ e del 51% negli ≥ 4 N+.



1-3 N+ 23%
≥ 4 N+ 41%

International Journal of Radiation Oncology biology • physics

Yates et al , IJROBP: 2012; 82 (5): 2093-2103

LE DUE IPOTESI

- **Halsted**

- **Fisher**

Linee Guida AIRO

2.3.3 Radioterapia delle stazioni linfonodali

L'irradiazione delle stazioni linfonodali dovrebbe tenere in considerazione le seguenti raccomandazioni:

- Linfonodi ascellari: la RT sulle stazioni linfonodali ascellari non è indicata nelle pazienti sottoposte ad adeguata dissezione indipendentemente dal numero dei linfonodi coinvolti e/o dalla presenza di estensione extra-capsulare, a meno che non ci sia un fondato sospetto o la presenza accertata di malattia residua (20)
- Linfonodi infra-sopraclaveari: è indicata l'irradiazione nelle pazienti con interessamento dei linfonodi stessi, nei T3-4 indipendentemente dallo stato linfonodale e nei T1-2 con quattro o più linfonodi ascellari positivi (12,13,22-27)
- Linfonodi della catena mammaria interna: l'indicazione al trattamento precauzionale rappresenta uno degli argomenti più controversi nella terapia del tumore della mammella (52-56). Attualmente, in attesa dei risultati dello studio EORTC 22922, chiuso a gennaio 2004, non se ne può raccomandare o sconsigliare l'irradiazione.

Tabella 2. **Sedi oggetto di irradiazione**

• mammella dopo chirurgia conservativa
• parete toracica*
• linfonodi infra-sopraclaveari*
• linfonodi ascellari, solo in presenza di malattia residua
• linfonodi mammari interni: non vi è sufficiente evidenza per raccomandarne o sconsigliarne l'irradiazione

* Qualora esistano le condizioni indicate nella Tabella 1 e ai punti 2.2.2 e 2.2.3

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Discussion

LOCOREGIONAL TREATMENT OF CLINICAL STAGE I, IIA, OR IIB DISEASE OR T3, N1, M0

Lumpectomy with surgical axillary staging (category 1)[i,j,k]

or

- ≥ 4 positive[n] axillary nodes → Radiation therapy to whole breast with or without boost[o] (by photons, brachytherapy, or electron beam) to tumor bed (category 1), infraclavicular region and supraclavicular area. Strongly consider radiation therapy to internal mammary nodes[p] (category 2B). Radiation therapy should follow chemotherapy when chemotherapy indicated.
- 1-3 positive axillary nodes → Radiation therapy to whole breast with or without boost[o] (by photons, brachytherapy, or electron beam) to tumor bed (category 1) following chemotherapy when chemotherapy indicated. Strongly consider radiation therapy to infraclavicular region and supraclavicular area (category 2B). Strongly consider radiation therapy to internal mammary nodes[p] (category 2B). Radiation therapy should follow chemotherapy when chemotherapy indicated.
- Negative axillary nodes → Radiation therapy to whole breast with or without boost[o] (by photons, brachytherapy, or electron beam) to tumor bed or consideration of partial breast irradiation (PBI) in selected patients.[o,q] Radiation therapy should follow chemotherapy when chemotherapy indicated.[r]

See BINV-4

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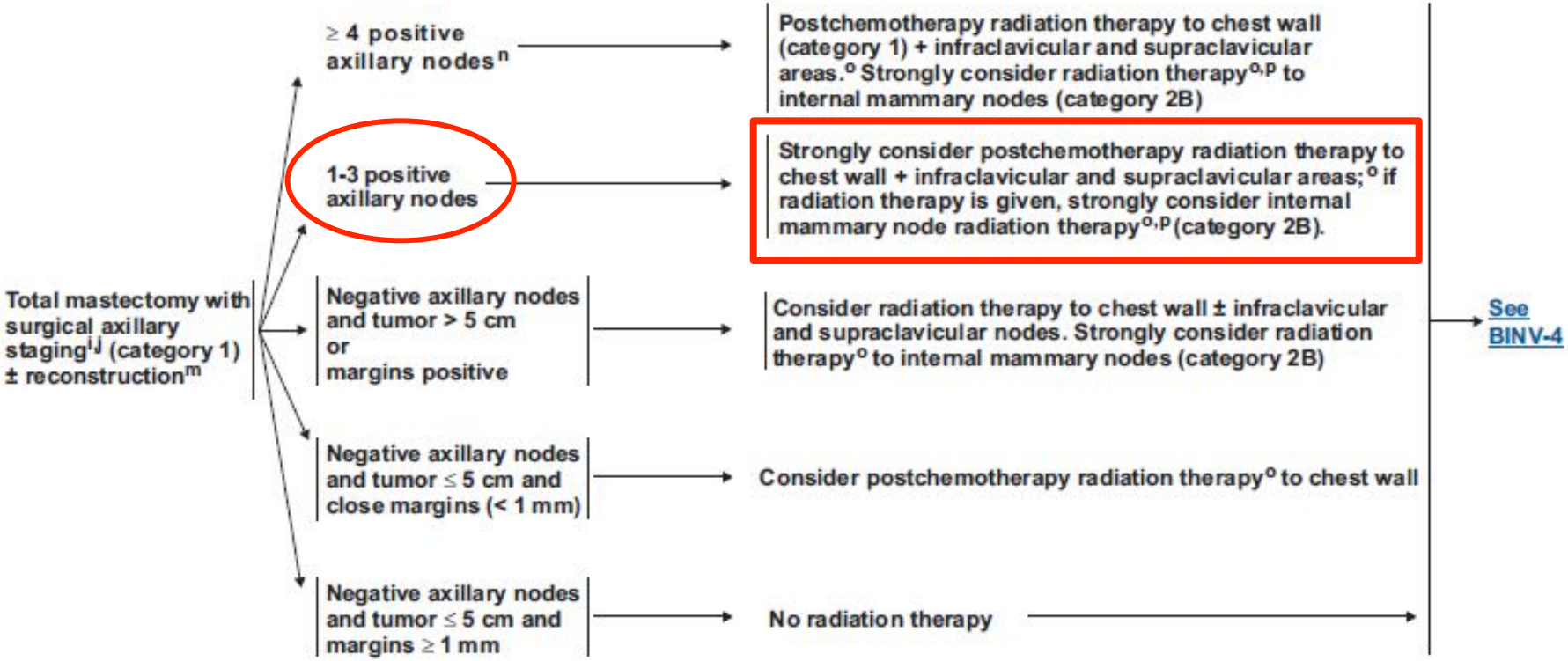
LOCOREGIONAL TREATMENT OF CLINICAL STAGE I, IIA, OR IIB DISEASE OR T3, N1, M0



RT profilattica 1-3 N+

Fattori di rischio per recidiva locoregionale

RT dopo NAC

CLINICAL INVESTIGATION

RISK FACTORS FOR REGIONAL NODAL RELAPSE IN BREAST CANCER PATIENTS WITH ONE TO THREE POSITIVE AXILLARY NODES

LUCY YATES, M.B.B.S.,* ANNA KIRBY, PH.D.,*† SIOBHAN CRICHTON, M.SC.,‡ CHERYL GILLETT, PH.D.,§ PAUL CANE, PH.D.,¶ IAN FENTIMAN, M.D.,* AND ELINOR SAWYER, PH.D.*

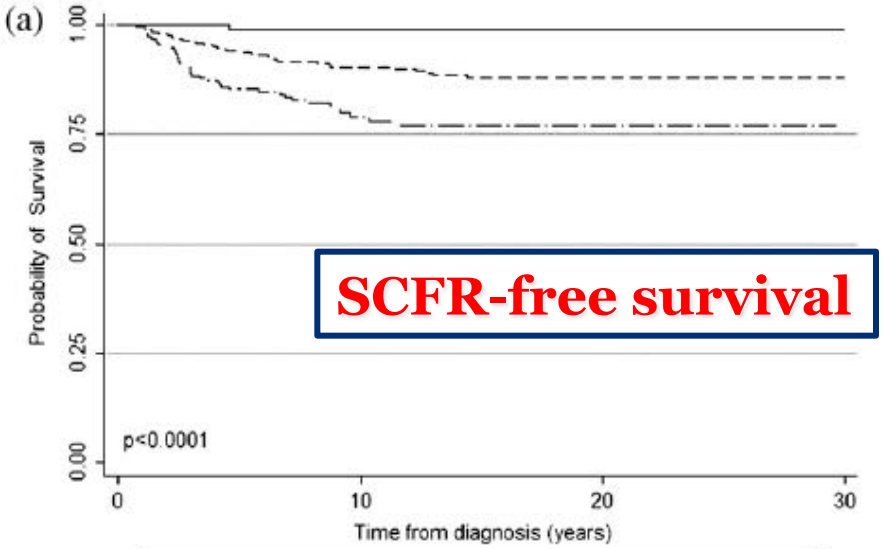
		Grade		
No. LNs		1	2	3
1	5 y	1.4	4.9	6.5
	10 y	1.4	8.9	8.9
2	5 y	0	7.6	12.1
	10 y	0	11.8	19.4
3	5 y	0	10.9	21.1
	10 y	0	14.8	29.6

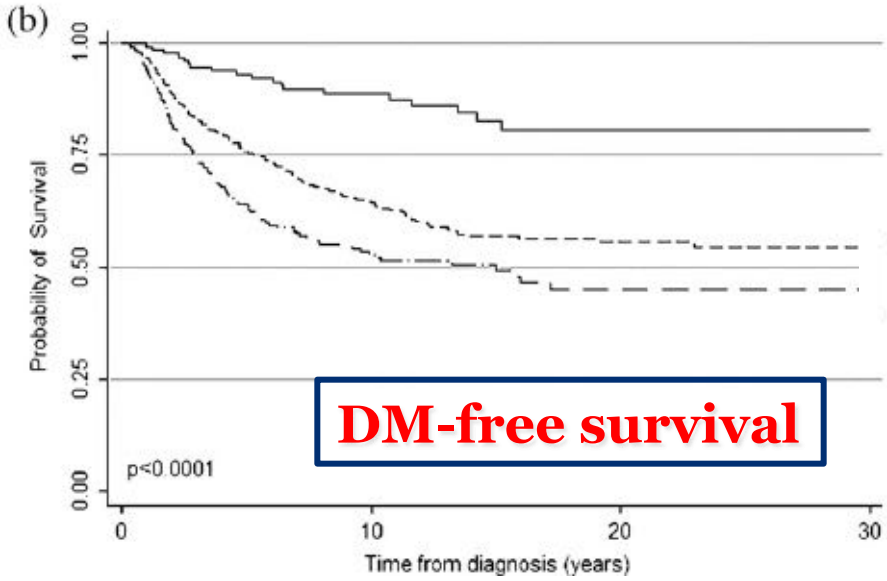
	G1	G2	G3
1 N	Low	Int	Int
2 N	Low	Int	High
3 N	Low	High	High

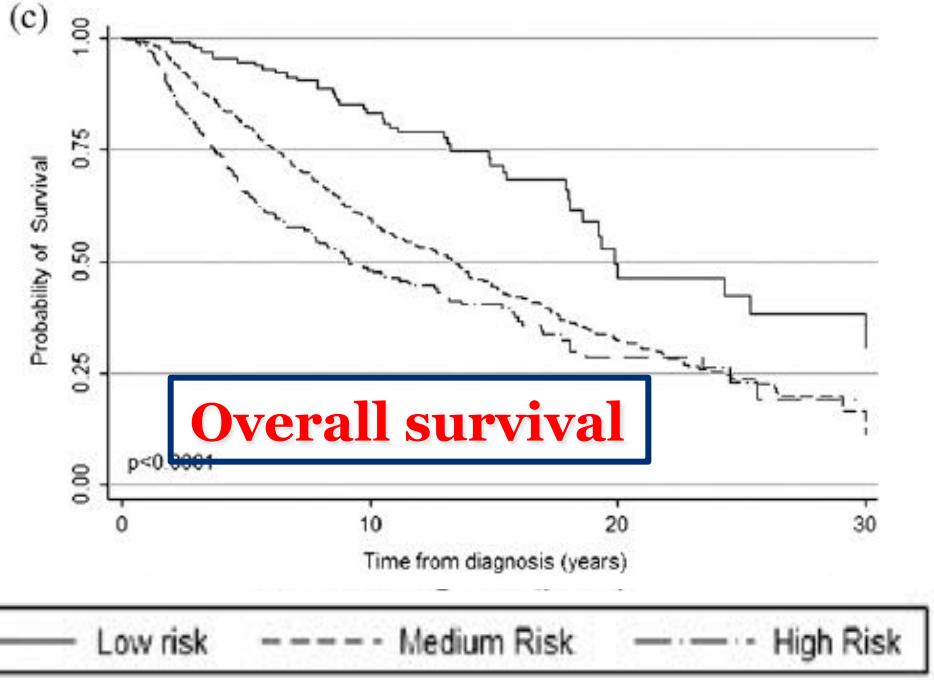
Table 4b. 5- and 10-year SCFR rate and hazard ratios according to the three risk* groups

Risk Group	Number (%)	5-y SCFR (%)	10-y SCFR (%)	HR (95% CI)	*p* Value
Low	131 (14)	0.8	0.8	1.0	<0.001
Intermediate	580 (60)	6.0	9.6	13.5 (1.9–97.9)	
High	252 (26)	14.6	21.0	30.3 (4.2–220.3)	

Yates et al , IJROBP: 2012; 82 (5): 2093-2103







Yates et al , IJROBP: 2012; 82 (5): 2093-2103

In conclusion, our results indicate that a subgroup of patients with 1-3LN+ are at high risk of SCFR. The absolute number of positive LNs and tumor grade are the most powerful predictors of SCFR. High- and possibly intermediate-risk patients should be offered SCFRT because it is likely to reduce regional relapse rates. Whether an improvement in regional control will translates into a survival benefit remains to be clarified by randomized trials.

Yates et al , IJROBP: 2012; 82 (5): 2093-2103

Original article

Strahlenther Onkol 2012 · 188:417–423
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[2] Department of Thoracic Surgery, Dr.Horst-Schmidt-Clinic Wiesbaden, Wiesbaden

Postoperative periclavicular radiotherapy in breast cancer patients with 1–3 positive axillary lymph nodes

Outcome and morbidity

Tab. 2 Sites of failure for patients with (*PCLNI*) or without periclavicular lymph node irradiation (*noPCLNI*)

Site of relapse	noPCLNI (n = 168) (n, %)	PCLNI (n = 67) (n, %)	p value
Local	15 (8.9)	7 (10.4)	0.718
Contralateral	8 (4.8)	1 (1.5)	0.238
Axillary	6 (3.6)	3 (4.5)	0.744
Periclavicular	2 (1.2)	2 (3.0)	0.337
Distant	29 (17.3)	12 (17.9)	0.906

Biancosino et al , Strahlenther Oncol: 2012; 188: 417-423

Tab. 3 Univariate (*univar.*) and multivariate (*multivar.*) analyses for locoregional recurrence free survival (*LRRFS*), disease free survival (*DFS*), and overall survival (*OS*)

Parameter	LRRFS Univar.	LRRFS multivar.	DFS Univar.	DFS multivar.	OS Univar.	OS multivar.
Tumor size						
T1 vs. T2	0.05	0.55	0.03	0.03	0.02	0.01
Lymph nodes						
1 vs. 2+3	0.01	0.02	0.01	0.01	0.28	0.34
ECS						
Yes vs.No	0.45	0.41	0.08	0.77	0.17	0.29
Age						
≤ 50 vs. > 50	0.71	0.55	0.74	0.52	0.65	0.18
HT						
Yes vs. No	0.01	0.87	0.00	0.01	0.00	0.01
ER						
+ vs. –	0.00	0.01	0.01	0.08	0.01	0.2
PR						
+ vs. –	0.02	0.07	0.32	0.14	0.06	0.61
PCLNI						
Yes vs. No	0.3	0.32	0.4	0.55	0.3	0.37

ER estrogen receptor, **ECS** extracapsular spread, **HT** hormonal therapy, **PR** progesterone receptor, **PCLNI** peri-clavicular lymph node irradiation.

Biancosino et al , Strahlenther Oncol: 2012; 188: 417-423

There was no increase in patients' assessed late toxicity with the addition of PCLNI in terms of pain, fibrosis, plexopathy, or teleangiectasia.

Biancosino et al , Strahlenther Oncol: 2012; 188: 417-423

Curr Oncol, Vol. 19, pp. e319-328; doi: http://dx.doi.org/10.3747/co.19.1038

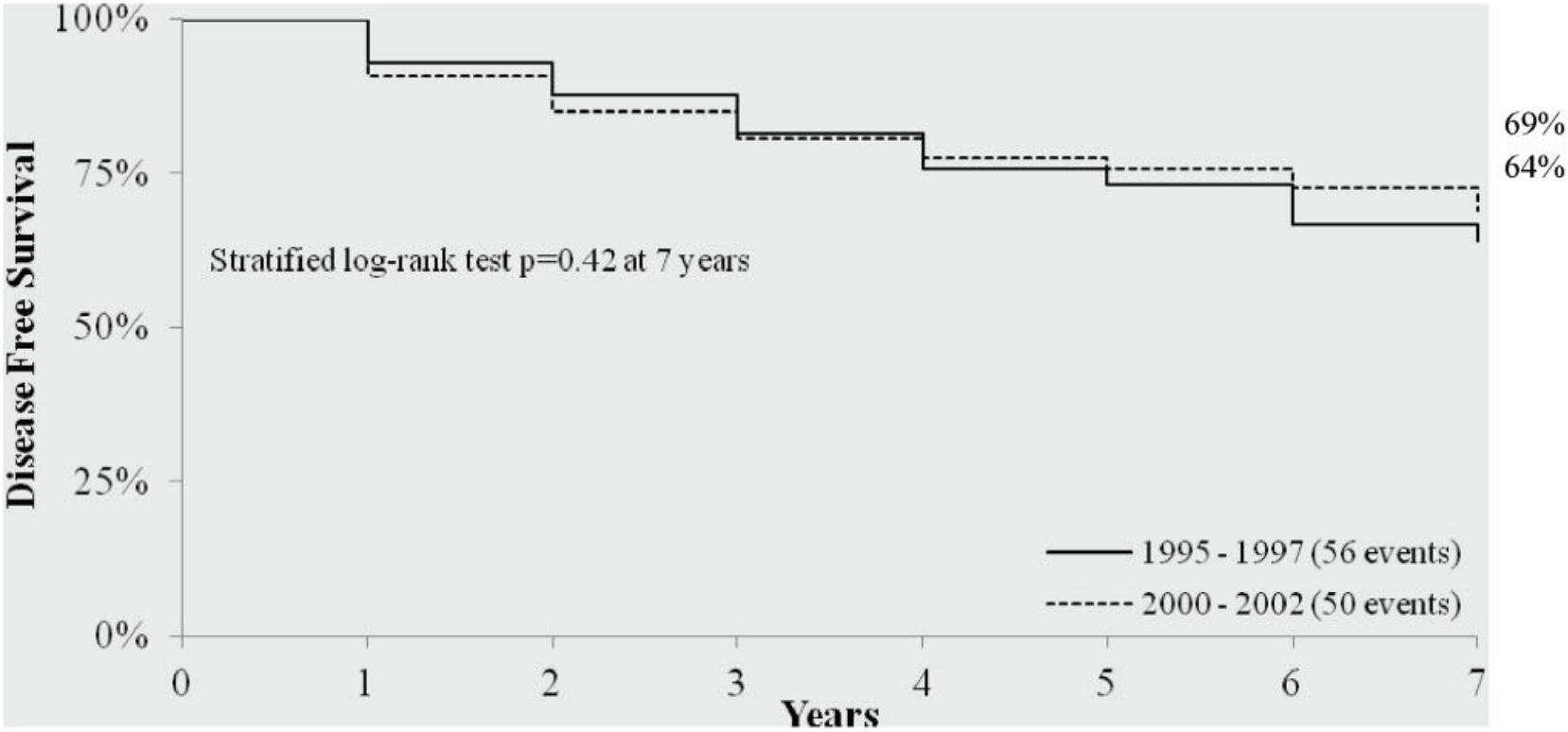
ORIGINAL ARTICLE

Evaluating the efficacy of current clinical practice of adjuvant chemotherapy in postmenopausal women with early-stage, estrogen or progesterone receptor–positive, one-to-three positive axillary lymph node, breast cancer

M.B. Hannouf, M. Brackstone MD,†‡ B. Xie PhD,*§ and G.S. Zaric PhD*||*

	95-97	00-02	03-05		
Breast surgery[b] [*n* (%)]	151(97)	153 (95)	161 (94.1)	0.42	0.72
Breast-conserving surgery	55(36.5)	76(49.7)	82 (51)	0.02	0.36
Mastectomy	96(63.5)	77(50.3)	77 (47.8)		
Unknown	0	0	2 (1.2)		
Radiotherapy[b] [*n* (%)]	57 (36.5)	96 (59.6)	102 (59.6)	<0.0001	0.99
Endocrine therapy[b] [*n* (%)]	125 (80)	143 (88.9)	147 (86)	0.03	0.43
Tamoxifen	107 (85.6)	81 (56.6)	64 (43.5)	<0.0001	<0.0001
AIS + tamoxifen	9 (7.2)	51 (35.7)	25 (17)		
AIS	9 (7.2)	11 (7.7)	58 (39.5)		
Adjuvant chemotherapy[b] [*n* (%)]	44 (28.2)	103 (64)	111 (64.9)	<0.0001	0.85
Non-anthracycline-based	32 (72.7)	30 (29.1)	24 (21.6)	<.0001	<.0001
Anthracycline-based	8 (18.2)	66 (64.1)	51 (46)		
Combination taxane–anthracycline	2 (4.5)	4 (3.9)	32 (28.8)		
Unknown	2 (4.5)	3 (2.9)	4 (3.6)		

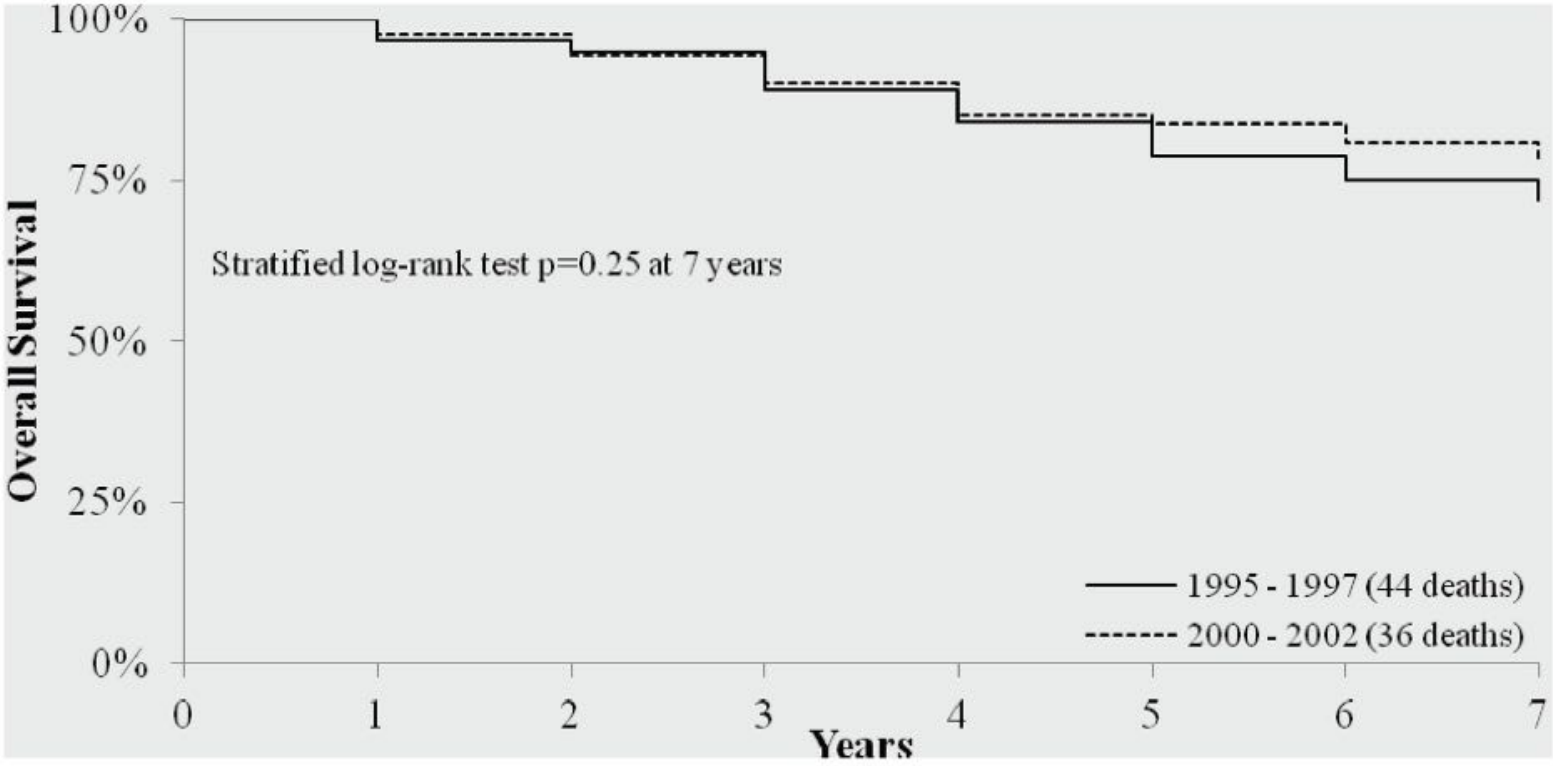
(A)



Number at risk								
1995-1997	156	145	137	127	118	114	104	100
2000-2002	161	146	137	130	125	122	117	111

Hannouf et al , Curr Oncol: 2012; 19: 319-328

(B)



Number at risk								
1995-1997	156	151	148	139	131	123	117	112
2000-2002	161	157	152	145	137	135	130	125

Hannouf et al , Curr Oncol: 2012; 19: 319-328

Conclusions

The treatment standard of adjuvant chemotherapy in addition to endocrine therapy may not be effective for all women with ER/PR+ 1–3 LN+ ESBC. There could be a subgroup of those women who do not benefit from adjuvant chemotherapy as expected and who are therefore being overtreated. Further studies with a larger sample size are warranted to confirm our results.

Hannouf et al , Curr Oncol: 2012; 19: 319-328

RT profilattica 1-3 N+

Fattori di rischio per recidiva locoregionale

RT dopo NAC

Post mastectomy radiotherapy in one to three lymph node positive breast cancer

ANUSHEEL MUNSHI[1], ARUNA PRABHU[2] & IAN KUNKLER[3]

[1]*Department of Radiation Oncology, Tata Memorial Hospital, Parel, Mumbai, India,* [2]*Department of Surgical Oncology, Tata Memorial Hospital, Parel, Mumbai, India,* [3]*Department of Clinical Oncology, Edinburgh Cancer Centre, University of Edinburgh*

Do any risk factors predict benefit from local radiotherapy in patients with one to three nodes?

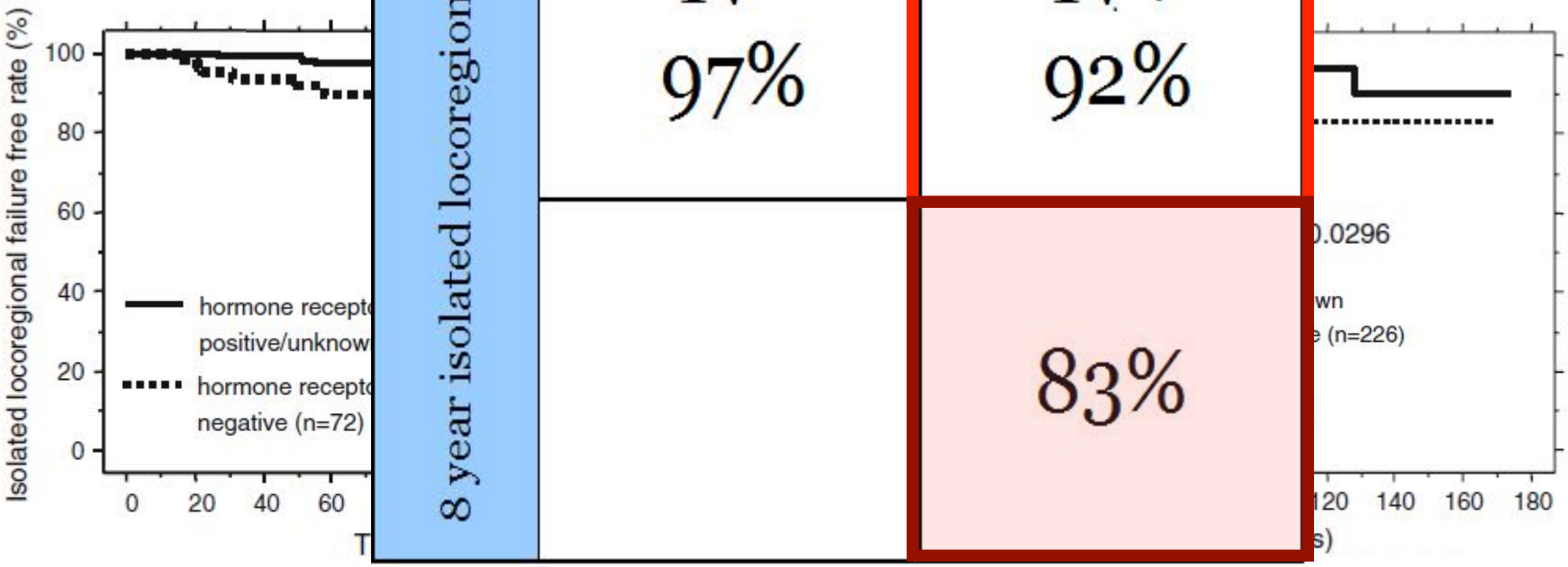
Autori	Fattori di rischio
Ragaz, JNCI 2005.	Age, >25 % N+, ER-.
Shang, IJROBP 2010.	G, ER-, LVI, No RT.
Truong, IJROBP 2007.	NR>0.2,
Kyndi, RO 2009.	N+, T, G, ER-

Breast Cancer
DOI 10.1007/s12282-012-0369-7

ORIGINAL ARTICLE

Are there high-ris
in patients who ha
lymph nodes and

Yasushi Hamamoto · Shozo
Kenjiro Aogi · Syuichi Shino
Masaaki Kataoka · Shigemit



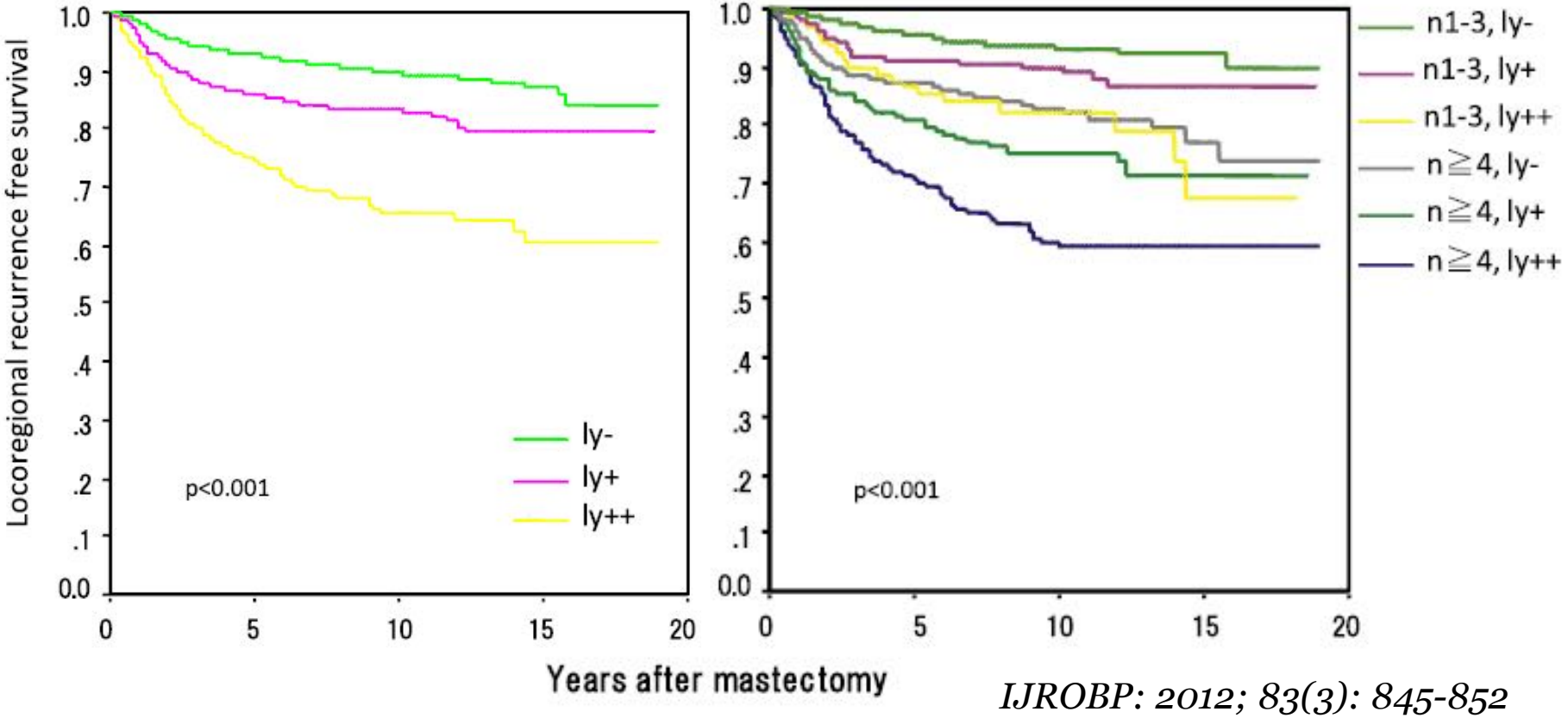
8 year isolated locoregional failure-free rates (%)

ER+ 98%	ER- 90%
IV- 97%	IV+ 92%
	83%

Clinical Investigation: Breast Cancer

Influence of Lymphatic Invasion on Locoregional Recurrence Following Mastectomy: Indication for Postmastectomy Radiotherapy for Breast Cancer Patients With One to Three Positive Nodes

Ryoichi Matsunuma, M.D.

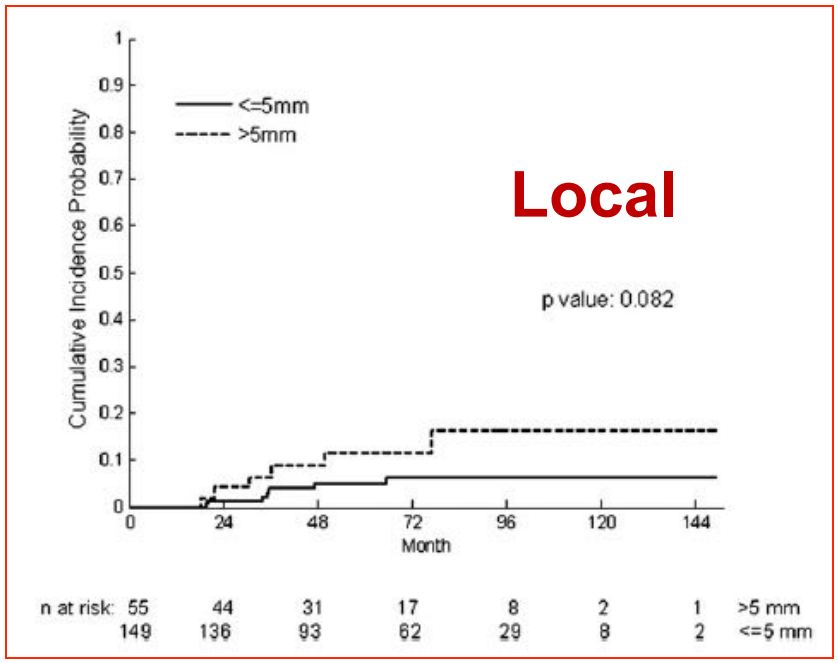


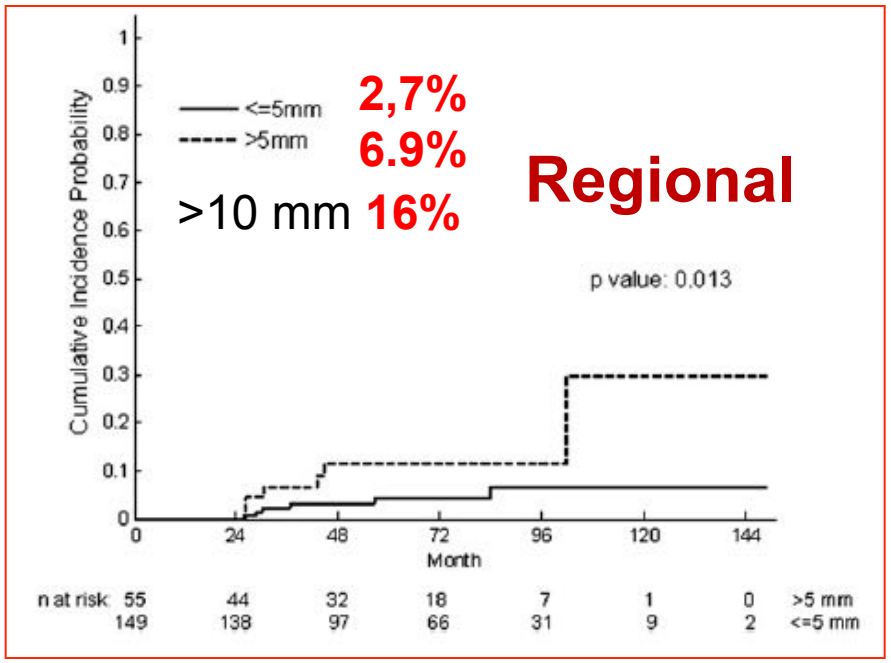
IJROBP: 2012; 83(3): 845-852

Clinical Investigation

The Impact of the Size of Nodal Metastases on Recurrence Risk in Breast Cancer Patients With 1-3 Positive Axillary Nodes After Mastectomy

Eleanor E.R. Harris, MD,* Jessica Freilich, MD,* Hui-Yi Lin, PhD,† Michael Chuong, MD,* and Geza Acs, MD, PhD‡





IJROBP: 2012; (in press)

Impact of Postmastectomy Radiation on Locoregional Recurrence in Breast Cancer Patients With 1-3 Positive Lymph Nodes Treated With Modern Systemic Therapy

Rahul D. Tendulkar, MD,* Sana Rehman, BS,* Monica E. Shukla, MD,* Chandana A. Reddy, MS,* Halle Moore, MD,† G. Thomas Budd, MD,† Jill Dietz, MD,‡ Joseph P. Crowe, MD,‡ and Roger Macklis, MD*

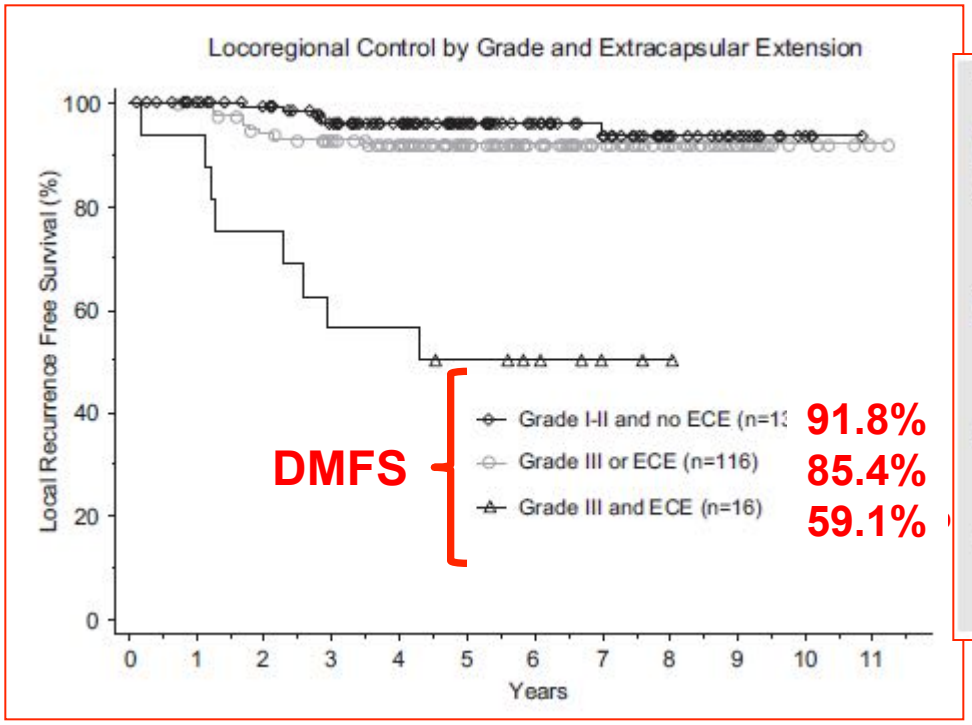


Table 3 Multivariate analysis for risk factors for locoregional recurrences in patients who did not receive radiation therapy (n = 271)

Variable	Hazard ratio (95% CI)	P value
Extracapsular extension		
Present (gross or microscopic)	4.31 (1.88-9.90)	**.0006**
Absent		
Bloom-Richardson grade		
3	3.61 (1.52-8.57)	**.0036**
1-2		

Abbreviation: CI = confidence interval.
Values in bold are statistically significant.

IJROBP: 2012; 83(5):e577-e581

Table 2 Univariate Cox proportional hazard regression analysis for locoregional recurrences in patients who did not receive radiation therapy ($n = 271$)

Variable	Hazard ratio (95% CI)	*P* value
Age (y)		
<50	0.80 (0.33-1.94)	.62
≥50		
ER/PR status		
Both negative	2.60 (1.10-6.12)	**.03**
Either positive		
Lymphovascular invasion		
Present	2.36 (1.033-5.37)	**.04**
Absent		
Number of positive lymph nodes		
2-3	2.59 (1.12-5.99)	**.03**
1		
Extracapsular extension		
Present	3.72 (1.63-8.48)	**.002**
Absent		
Microscopic vs absent	4.21 (1.60-11.09)	**.004**
Gross vs absent	3.16 (1.03-9.70)	**.04**
Tumor size (cm)		
>2	1.92 (0.83-4.44)	.13
≤2		
Bloom-Richardson grade		
3	3.14 (1.33-7.41)	**.009**
1-2		
Surgical margin		
Negative	1.08 (0.25-4.62)	.92
Positive/close		
Menopause		
Pre/peri	1.05 (0.45-2.46)	.91
Post		
Percent of positive lymph nodes		
>25%	2.73 (1.16-6.46)	**.02**
≤25%		

Abbreviations: CI = confidence interval; ER = estrogen receptor; PR = progesterone receptor.
Values in bold are statistically significant.

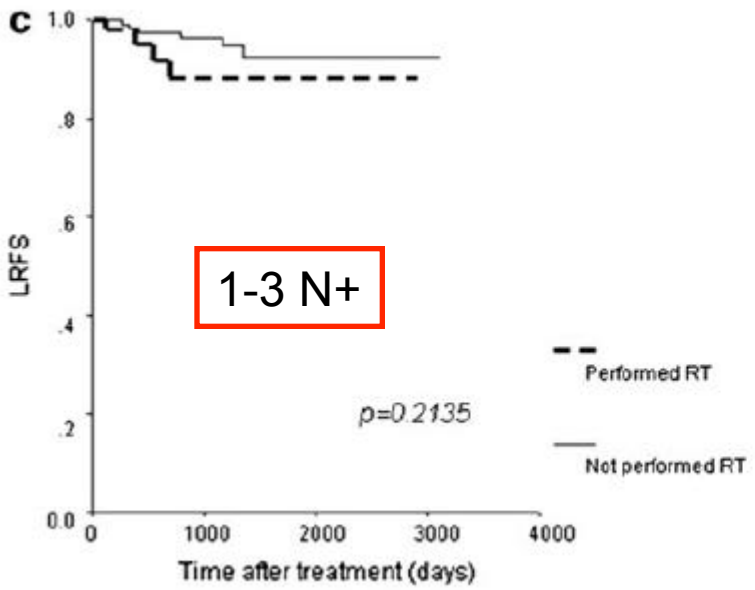
0-1 risk factor → LRR 3.4%
≥ 2 risk factors → LRR 14.6%

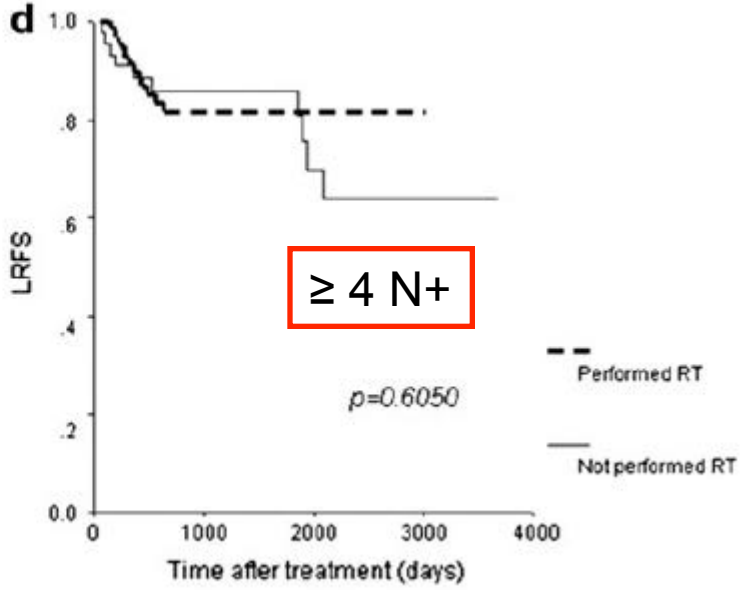
IJROBP: 2012; 83(5):e577-e581

Breast Cancer
DOI 10.1007/s12282-012-0391-9

Locoregional recurrence risk factors and the impact of postmastectomy radiotherapy on patients with tumors 5 cm or larger

Tomoya Nagao · Takayuki Kinoshita · Nobuko Tamura · Takashi Hojo · Madoka Morota · Yoshikazu Kagami





	1–3 positive nodes			≥4 positive nodes		
	HR	95 % CI	*p*	HR	95 % CI	*p*
Histological stage						0.291
G1/2				1		
G3				1.86	0.58–5.92	
Nuclear grade			0.108			0.656
G1/2	1			1		
G3	3.71	0.75–18.33		1.38	0.34–5.66	
Lymphatic invasion						0.014
Absent/1+/2+				1		
3+				3.62	1.30–10.06	
Pectoral invasion			<0.001			
Absent	1					
Present	174.71	15.62–1953.73				
Estrogen receptor						0.031
Negative				1		
Positive				0.36	0.14–0.91	
Progesterone receptor						0.118
Negative				1		
Positive				0.47	0.18–1.22	
NR						0.044
<50 %				1		
≥50 %				2.59	1.02–6.53	

Breast Cancer: 2012;

In conclusion, for patients with tumors larger than 5 cm, PMRT was effective for the patients with lymph node metastasis, but the role and efficacy were limited under adequate axillary lymph node dissection. Due to the low incidence of LRR, PMRT is not necessary for patients without metastasis. The role of PMRT in patients with 1–3 metastatic nodes is still unclear, and detection of the high-risk group is necessary.

Breast Cancer: 2012;

RT profilattica 1-3 N+

Fattori di rischio per recidiva locoregionale

RT dopo NAC

Should radiotherapy after primary systemic therapy be administered with the same recommendations made for operable breast cancer patients who receive surgery as first treatment? A critical review

Simona Allis[1], Alessia Reali[1], Gianluca Mortellaro[1], Francesca Arcadipane[2], Sara Bartoncini[2], and Maria Grazia Ruo Redda[1]

[1]*Department of Clinical and Biological Sciences, Radiation Oncology Unit, University of Turin, S. Luigi Hospital, Orbassano;*
[2]*Department of Medical and Surgical Sciences, Radiation Oncology Unit, University of Turin, S Giovanni Battista Hospital, Turin, Italy*

tumori
a Journal of Experimental and Clinical Oncology

Radiation oncology considerations corcening regional lymph node therapy

Irradiation of supraclavicular fossa should be performed in cases of 4 or more positive lymph nodes,whereas in patients with 1-3 positive lymph nodes radiotherapy should be considered on evaluation of nodal ratio. In patients with pN0 status after PST, radiotherapy is not necessary because irradiation does not influence LRR, as suggested by the examined literature data. However, considering the variability of data on this issue, an appropriate approach can be still to tailor treatment decision to the individual clinical case.

Tumori 98: 543-549, 2012

Journal of Breast Cancer

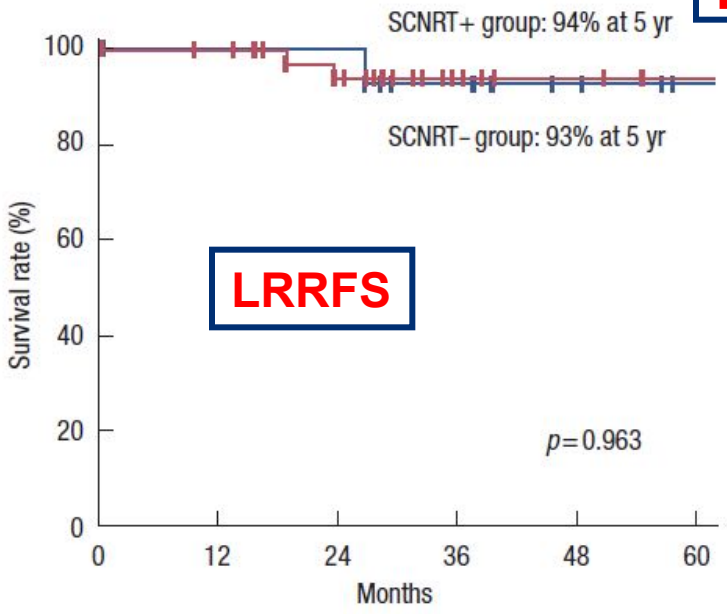
J Breast Cancer 2012 September; 15(3): 329-336 http://dx.doi.org/10.4048/jbc.2012.15.3.329

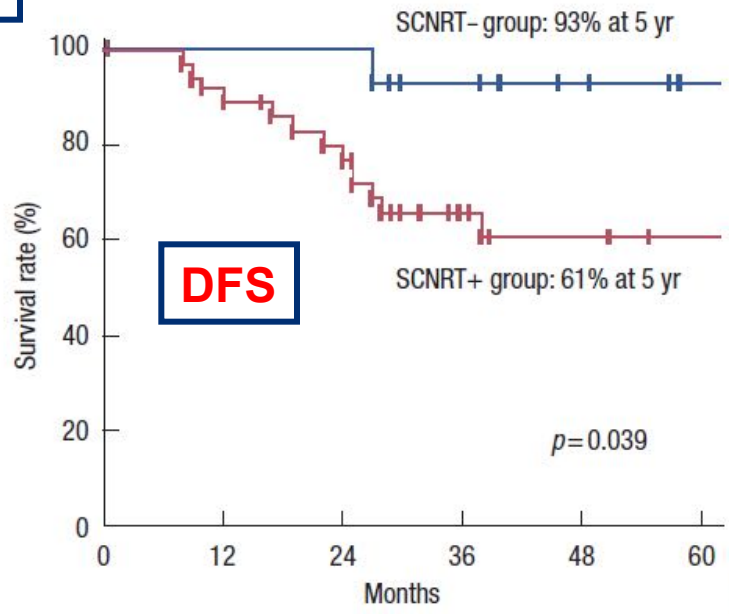
ORIGINAL ARTICLE

Radiation Treatment in Pathologic N0-N1 Patients Treated with Neoadjuvant Chemotherapy Followed by Surgery for Locally Advanced Breast Cancer

Sun Hyun Bae, Won Park[1], Seung Jae Huh[1], Doo Ho Choi[1], Seok Jin Nam[2], Young-Hyuck Im[3], Jin Seok Ahn[3]

pN1



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Physica Medica (2012) 28, 281–287

Available online at www.sciencedirect.com

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journal homepage: http://intl.elsevierhealth.com/journals/ejmp

ORIGINAL PAPER

A new isocentric technique for exact geometric matching in the radiotherapy of the breast and ipsilateral supraclavicular fossa using dual asymmetric jaws

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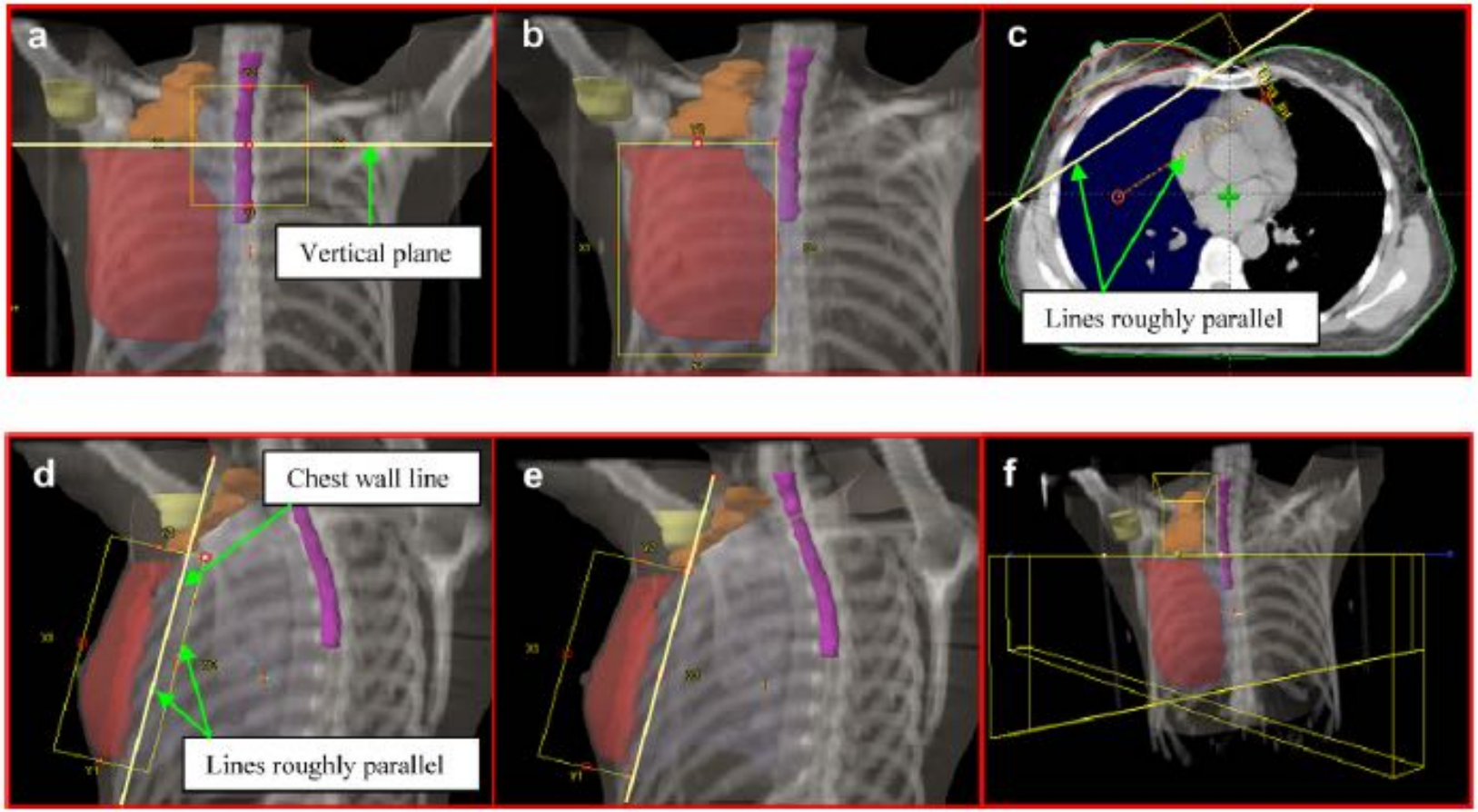

The standard fields for the treatment of the breast and supraclavicular fossa are arranged to achieve a perfect match at the match plane; the technique is simple to carry out with modern equipment and gives advantages due to the use of dual independent and asymmetric jaws.

$$\cos(\theta_{G-Ant}) = \frac{\cos(\theta_{C-Int})}{\sqrt{\cos^2(\theta_{C-Int}) + \sin^2(\theta_{C-Int})\sin^2(\theta_{G-Int})}}$$

$$\sin(\theta_{C-Ant}) = \sin(\theta_{C-Int})\cos(\theta_{G-Int})$$

$$\theta_{T-Ant} = 90^{\circ}$$

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Meglio soli….

che male accompagnati!