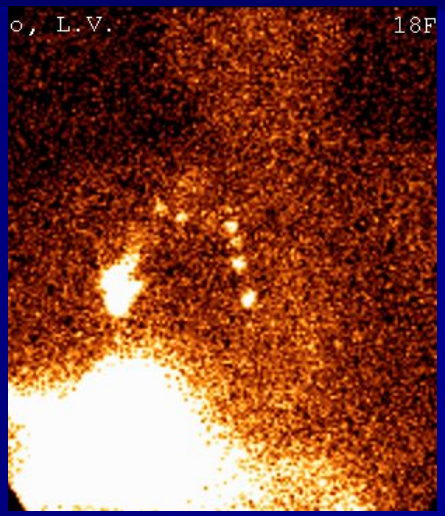
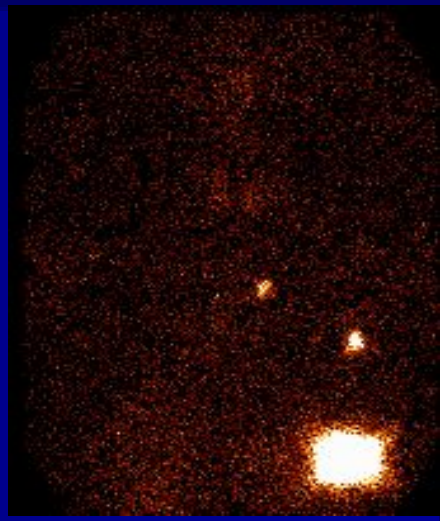
Визуализация сигнальных лимфоузлов - краеугольный камень в определении тактики лучевого лечения больных раком молочной железы

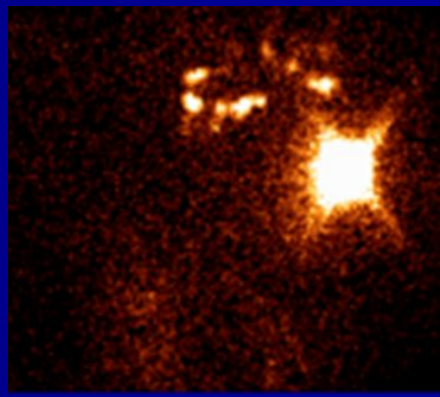
«НИИ онкологии им. Н.Н. Петрова»

Визуализация сигнальных лимфоузлов в парастернальной области

- 99mTc-наноколлоиды
- внутриопухолевое введение 75-100 МБк (0.2-0.3 мл)
- Планарное исследование через 2-3 часа







Облучение парастернальных ЛУ

За

- ↑ выживаемости (RTOG 22922, MA 20, Gustave-Roussy, Canadian & Dansih)
- МТС в ПС ЛУ – ↓ ОВ
- ОВ выше при латер. локализации РМЖ
- При визуализации ПС ЛУ (сигнальных) ОВ ↓

Против

- NSABP B-04, Manchester II, Milan I
- Частота регион. рец в ПС области <1%
- ↑ риск возникновения ССЗ и РМЖ в противо-положной железе

OC-0523

Lymph node RT improves survival in breast cancer: 10 years results of the EORTC ROG and BCG phase III trial 22922/10925.

P. Poortmans[1], H. Struikmans[2], S. Collette[3], C. Kirkove[4], V. Budach[5], P. Maingon[6], M.C. Valli[7], A. Fourquet[8], W. Van den Bogaert[9], H. Bartelink[10]

- 4004 б-ых (43 цетра); стадия I-III
- PN+ или pN- при центр., мед. локализации
- 2002 б-ых с облучение ПС ЛУ (50Гр)
- ЛТ ПСЛУ увеличивает 10 летнюю:

OS - 82.3% vs 80.7% (1.6%) p=0.056

DFS - 72.1% vs 69.1% (2%) p= 0.044

DMFS- 78% vs 75% (3%) p=0.02

EORTC trial 22922-10925 investigates the role of internal mammary and medial supraclavicular (IM-MS) LN RT (Clinical trials.gov NCT00002851)

Radiotherapy & Oncology | **Volume 111 Supplement 1 (2014)**

Does the Intent to Irradiate the Internal Mammary Nodes Impact Survival in Women With Breast Cancer? A Population-Based Analysis in British Columbia

Robert A. Olson, F.R.C.P.C.,*,† Ryan Woods, M.Sc.,‡
Caroline Speers, B.A.,‡ Jeffrey Lau, B.Sc.,† Andrea Lo, M.D.,*,†

Table 1 Patient, tumor, and treatment characteristics

	Intended to include IMN region in RT volume					
	Entire cohort			N1-3+ subgroup		
Characteristic	No (n = 1413)	Yes (n = 1000)	p value	No (n = 779)	Yes (n = 529)	p value
Mean age (y)	57	53	<0.001	56	52	<0.001
Ductal histology	91%	87%	0.01	93%	89%	0.02
Tumor location						
Central	7%	9%	<0.001	6%	7%	<0.001
Medial	11%	18%		43%	57%	
Lateral	58%	50%		65%	34%	
Multifocal	9%	10%		8%	10%	
Unknown	16%	14%		16%	16%	
Chemo-therapy						
None	21%	11%	<0.001	23% 14%		<0.001
Anthracycline	78%	88%		76% 85%		
Other	2%	1%		1% 1%		
[illegible]	[illegible]	[illegible]	0.57	[illegible]		0.12

Int J Radiation Oncol Biol Phys, Vol. 83, No. 1, pp. e35–e41, 2012

Does the Intent to Irradiate the Internal Mammary Nodes Impact Survival in Women With Breast Cancer? A Population-Based Analysis in British Columbia

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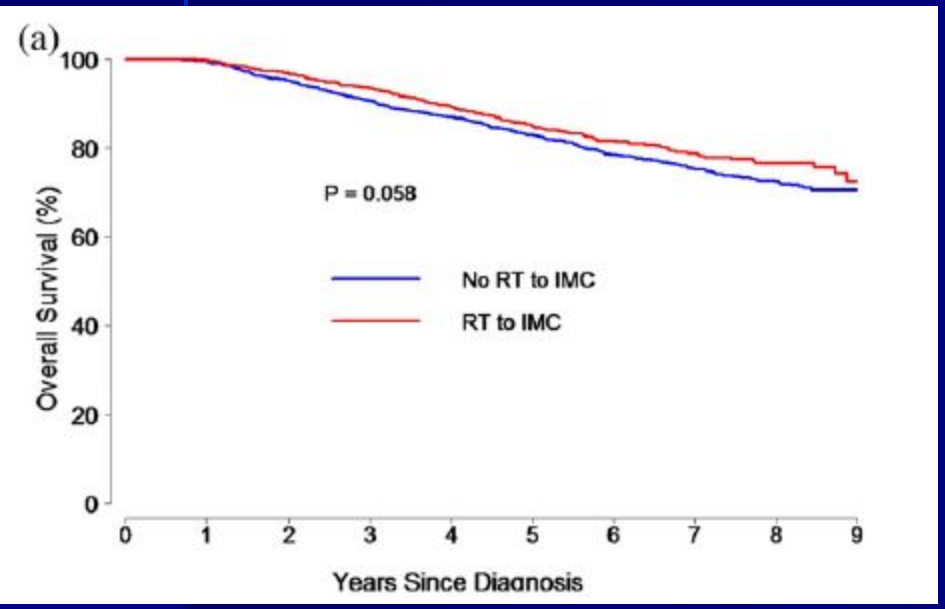

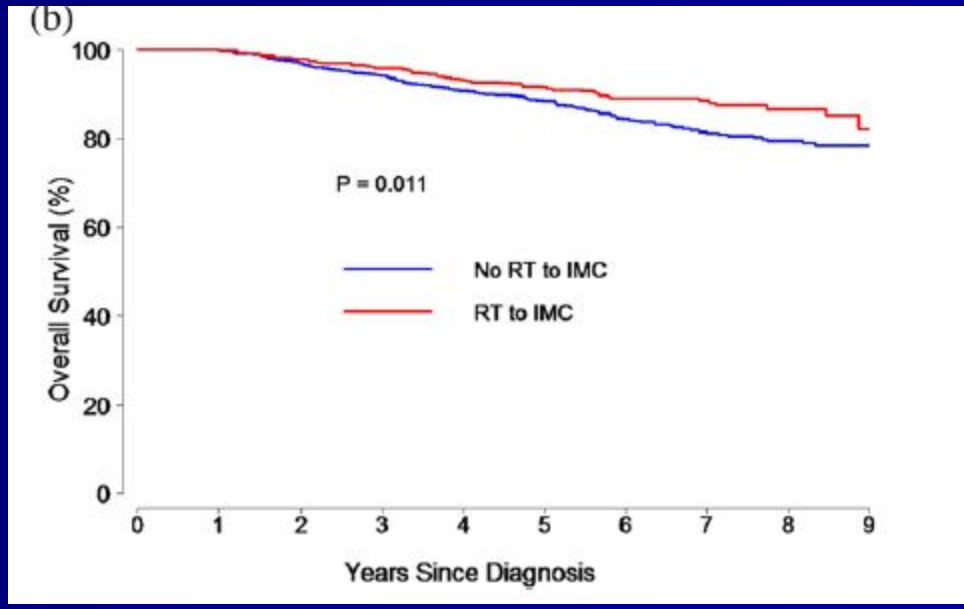

Fig. 3. (a) Univariate analysis of overall survival in entire study cohort. (b) Univariate analysis of overall survival in N1 subgroup. RT = radiation therapy; IMC = internal mammary nodes.

Int J Radiation Oncol Biol Phys, Vol. 83, No. 1, pp. e35–e41, 2012

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Table 2 5-year survival rates by inclusion or exclusion of internal mammary nodes in radiotherapy volume

Outcome	Inclusion of IMN region in RT volume		Inclusion of IMN region in RT volume: N1 subset	
	No	Yes	No	Yes
Breast cancer–specific survival	87% (85–89%)	87% (85–90%)	92% (90–94%)	94% (91–96%)
RFS	82% (80–84%)	81% (79–84%)	87% (85–90%)	89% (87–92%)
Local RFS	98% (97–99%)	97% (96–98%)	99% (98–100%)	98% (97–100%)
Locoregional RFS	97% (96–98%)	96% (95–97%)	98% (97–99%)	98% (97–99%)
Distant RFS	82% (80–84%)	82% (80–85%)	88% (86–90%)	90% (87–93%)
Overall survival	83% (81–85%)	85% (83–87%)	88% (86–91%)	91% (89–94%)

Abbreviations: IMN = internal mammary node; RT = radiotherapy; RFS = relapse-free survival.
Numbers in parens represent the confidence interval.

Int J Radiation Oncol Biol Phys, Vol. 83, No. 1, pp. e35–e41, 2012

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

Adel Courdi [a,*], Emmanuel Chamorey [b], Jean-Marc Ferrero [c], Jean-Michel Hannoun-Lévi [a]

Single center; from 1975 to 2008; N pos. 67%

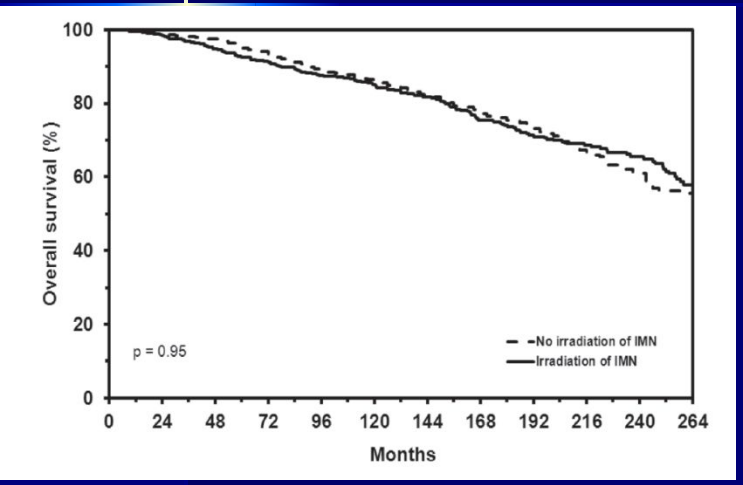
Tumour characteristics. For tumour size, mean values and 95% confidence intervals are shown. For other variables, the number of patients and the percentage in the corresponding group are mentioned.

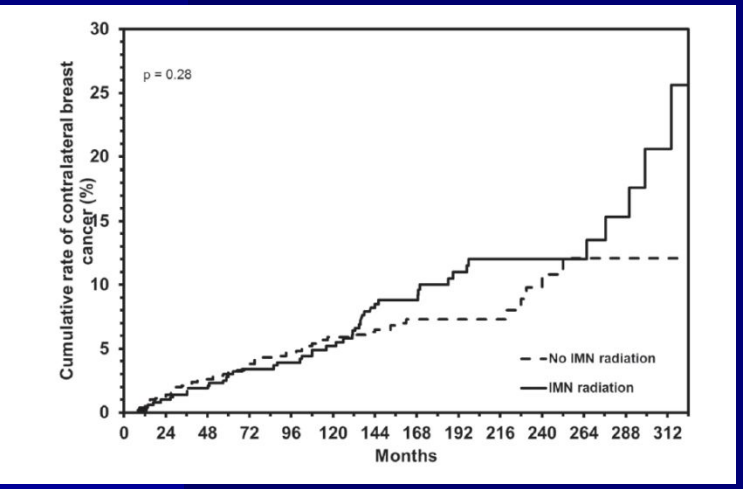
	IMN irradiated	IMN not irradiated	Statistical significance
Tumour location			
Inner or central	$n = 289$ (71.2%)	$n = 332$ (31.9%)	$P < 10^{-4}$
Outer	$n = 117$ (28.8%)	$n = 710$ (68.1%)	
Tumour size (mm)	15.3 ± 0.65	14.9 ± 0.46	$p = 0.36$
Tumour grade			
1	$n = 208$ (51.7%)	$n = 466$ (48.3%)	$p = 0.15$
2	$n = 146$ (36.3%)	$n = 346$ (35.9%)	
3	$n = 48$ (11.9%)	$n = 153$ (15.8%)	
Hormone receptors			
Positive	$n = 403$ (91.6%)	$n = 929$ (88.6%)	$p = 0.10$
Negative	$n = 37$ (8.4%)	$n = 120$ (11.4%)	

Radiotherapy and Oncology 108 (2013) 259–265

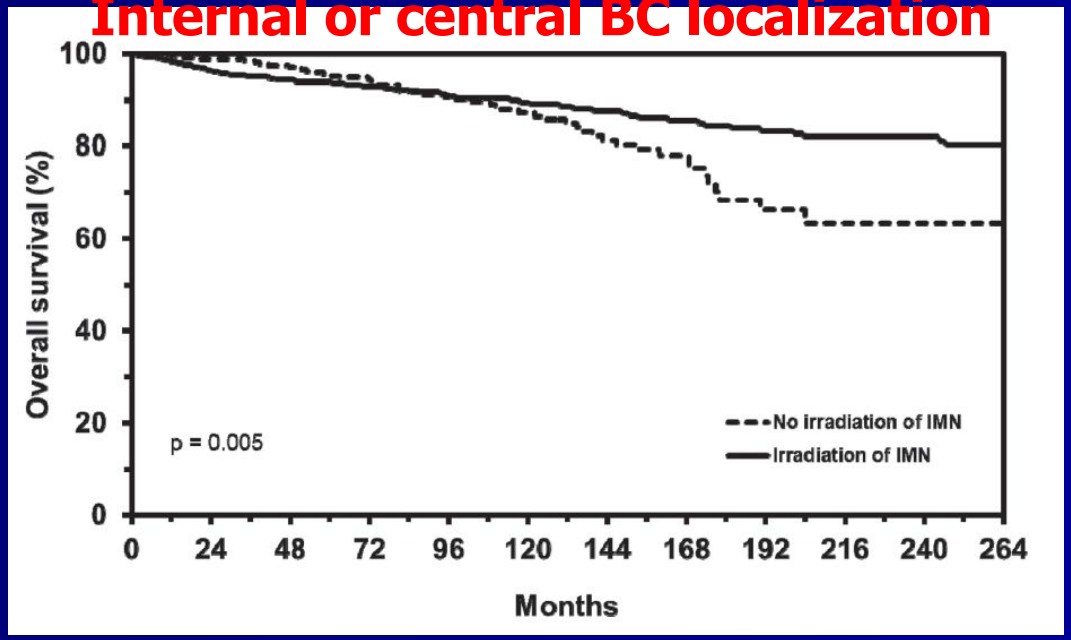
Influence of internal mammary node irradiation on long-term outcome and contralateral breast cancer incidence in node-negative breast cancer patients

Adel Courdi [a,*], Emmanuel Chamorey [b], Jean-Marc Ferrero [c], Jean-Michel Hannoun-Lévi [a]





Internal or central BC localization



The findings that IMN RT is associated with an improved outcome in patients with inner/central tumours and an increase in the incidence of CBC whatever the tumour location do not give a clear-cut answer about the usefulness of IMN RT. The possible in-

Radiotherapy and Oncology 108 (2013) 259–265

NCIC CTG MA.20: An intergroup trial of regional nodal irradiation in early breast cancer.

T. J. Whelan, I. Olivotto, I. Ackerman, J. W. Chapman, B. Chua, A. Nabid, K. A. Vallis, J. R. White, P. Rousseau, A. Fortin, L. J. Pierce, L. Manchul, P. Craighead, M. C. Nolan, J. Bowen, D. R. McCready, K. I. Pritchard, M. N. Levine and W. Parulekar

- 1,832 б-ых: WBI+RNI (916) или WBI (916).
- Медитана наблюдения - 62 мес.
- Подм. ЛУ отр., 10%; 1-3 метастат. ЛУ, 85%; > 4 метаст. ЛУ, 5%; адъювант. ПХТ, 91%;
- WBI+RNI против WBI (5 лет): LRFS 96.8% vs 94.5%; DMFS 92.4% vs 87.0%, DFS 89.7% vs 84.0%; OB 92.3% vs 90.7%

Journal of Clinical Oncology, 2011 ASCO Annual Meeting Abstracts Part 2. Vol 29, No 18_suppl (June 20 Supplement), 2011: LBA1003

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]

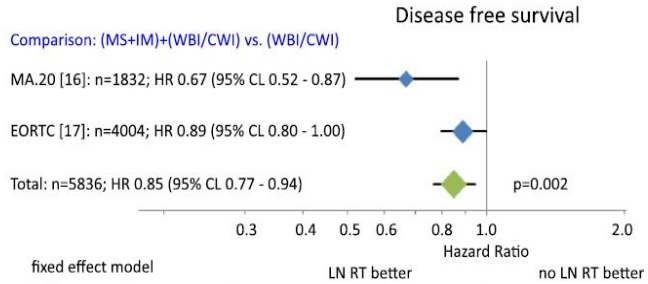


Figure 3 Disease free survival. The area of the symbols reflect the number of patients. MS + IM = medial supraclavicular and internal mammary lymph node irradiation, WBI/CWI = whole breast irradiation or chest wall irradiation.

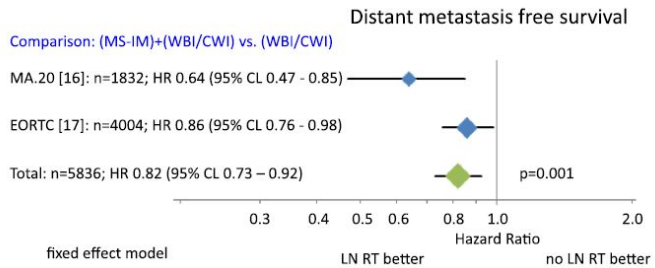


Figure 4 Distant metastasis free survival. The area of the symbols reflect the number of patients, MS + IM = medial supraclavicular and internal mammary lymph node irradiation, WBI/CWI = whole breast irradiation or chest wall irradiation.

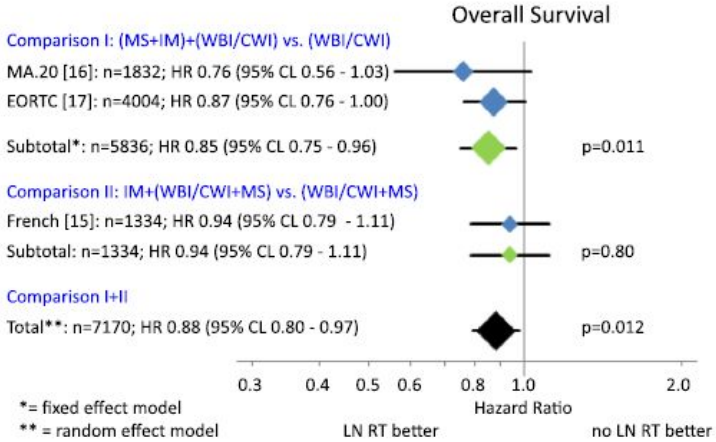


Figure 2 Overall survival. The area of the symbols reflect the number of patients, MS + IM = medial supraclavicular and internal mammary lymph node irradiation, WBI/CWI = whole breast irradiation or chest wall irradiation, MS = medial supraclavicular lymph node irradiation.

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

Lymphoscintigraphy Can Select Breast Cancer Patients for Internal Mammary Chain Radiotherapy

Elif Hindié, M.D., Ph.D.,*,¶ David Groheux, M.D.,* Christophe Hennequin, M.D., Ph.D.,† Paolo Zanotti-Fregonara, M.D., Ph.D.,* Laetitia Vercellino, M.D.,* Nathalie Berenger, M.D.,* Marie-Elisabeth Toubert, M.D.,* Claude Maylin, M.D.,† Jacques-Robert Vilcoq, M.D.,‡ and Marc Espié, M.D.§

Table Internal mammary visualization rate and biopsy result

Investigator (city)	Patients (*n*)/trial type	Tumor size	Injection technique*	Axilla positive	IM drainage	Successful IM biopsy	Positive IM biopsy	Axilla staged	IM positivity: Axilla negative	IM positivity: Axilla positive
Estourgie *et al.* (14) (Amsterdam)	691/ Prospective	Median 1.8 cm	Intratumoral ^{99m}Tc-Nanocoll	34% (222/659)	22% (n = 150)	130 (87%)	17% (n = 22)	88%† (114/130)	8.4% (9/107)‡	56% (13/23)‡
Paredes *et al.* (15) (Barcelona)	323/ Prospective	<3 cm	Intratumoral or peritumoral (n = 107) ^{99m}Tc-Nanocoll	NA	17% (n = 55)	32 (58%)	16% (n = 5)	100%	4.3% (1/23)	44% (4/9)
Leidenius *et al.* (16) (Helsinki)	984/ Prospective	T1-T2 (T1, 73%)	Intratumoral ^{99m}Tc-Nanocoll	41% (n = 400)	14% (n = 138)	121 (88%)	15% (n = 18)	100%	8.7% (8/92)‡	35% (10/29)‡
Madsen *et al.* (17) (Utrecht)	506/ Prospective	T1-T2 (T1, 63%)	Peritumoral ^{99m}Tc-Nanocoll	42% (n = 210) (1–3 in 174)	22% (n = 109)	85 (78%)	24% (n = 20)	100%	7% (4/57)‡	57% (16/28)‡
Heuts *et al.* (18) (Maastricht)	764/ Prospective	T1, 52%; T2, 42%; T3, 6%	Peritumoral ^{99m}Tc-Nanocoll	46% (n = 351)	22% (n = 166)	115 (69%)	24% (n = 28)	100%	13% (7/53)	34% (21/62)
Bourre *et al.* (19) (Grenoble)	608/ Prospective	T1 only (73% ≤1 cm)	Peri and subtumoral ^{99m}Tc-Nanocoll	25% (n = 150)	28% (n = 174)	161 (93%)	11% (n = 18)	100%	5.4% (7/129)‡	34% (11/32)‡
Total	3,876			~38% (1,333/3,521)	20.4% (792/3,876)	644 (81.3%)	17.2% (111/644)		7.8% (36/461)	41% (75/183)

Abbreviations: IM = internal mammary; ^{99m}Tc = technetium-99m.

* In case of nonpalpable lesions, sonographic or mammographic guidance was used; Heuts *et al.* (18) simply injected in corresponding quadrant; scintigraphy usually obtained 3–4 h after tracer injection; Heuts *et al.* (18) performed scintigraphy the next morning.

† Sixteen patients with failure to identify axillary SN did not receive routine axillary lymph node dissection and were considered axillary negative by the investigators.

‡ Investigators of these studies were contacted and kindly provided data on IM positivity according to axilla status; this information could not be easily extracted from the original report.

Int J Radiation Oncol Biol Phys, Vol. 83, No. 4, pp. 1081–1088, 2012

Lymphoscintigraphy Can Select Breast Cancer Patients for Internal Mammary Chain Radiotherapy

Elif Hindié, M.D., Ph.D.,*,¶ David Groheux, M.D.,* Christophe Hennequin, M.D., Ph.D.,†

Int J Radiation Oncol Biol Phys, Vol. 83, No. 4, pp. 1081–1088, 2012

Sentinel lymph node biopsy of the internal mammary chain in breast cancer

E. L. Postma · S. van Wieringen · M. G. Hobbelink · H. M. Verkooijen · H. J. G. D. van den Bongard · I. H. M. Borel Rinkes · A. J. Witkamp

Breast Cancer Res Treat (2012) 134:735–741

Comparison of two treatment strategies for irradiation of regional lymph nodes in patients with breast cancer: Lymph flow guided portals versus standard radiation fields

Sergey Nikolaevich Novikov[a,*], *Sergey Vasilevich Kanaev*[a], *Vladimir Fedorovich Semiglazov*[b], *Ludmila Alekseevna Jukova*[a], *Pavel Ivanovich Krzhivitckiy*[a]

REPORTS OF PRACTICAL ONCOLOGY AND RADIOTHERAPY 20 (2015) 27–31

Вероятность поражения парастернальных лимфоузлов у больных РМЖ

Вероятность визуал-ии ПС ЛУ в зависимости от лок-ции РМЖ:

- Латеральная - 16%
- Мед./Центр. - 35%

Вероятность поражения ПС ЛУ у больных с сигн. ПСЛУ:

- Подм. ЛУ без МТС - 7.8%
- Подм. ЛУ с МТС - 38.1%

- Латер. с МТС в подм. ЛУ – 5.6%
- Латер без МТС в подм. ЛУ – 1.3%
- Мед./Центр. с МТС в подм. ЛУ – 13.3%
- Мед./Центр. без МТС в подм. ЛУ – 2.7%

Название исследования	MA.20	French study	EORTC 22922/ 10925	British-Columbia	Danish BCCG
Количество больных (с облучением ПС ЛУ***)	1832 (916)	1334 (404)	4004 (2002)	2413 (989)	3072 (1586)
Количество больных с поражением ПМ ЛУ** (%)	1557 (85%)	1000 (75%)	2242 (56%)	375 (37.9%)	1586 (100%)
С внутренней и центральной локализацией РМЖ (с облучением ПС ЛУ***)	-	621	-	-	564º -
Число больных с поражением ПС ЛУ*** (на 100 чел)	70.8 (7.7)	38 (9.3)	92 (4.6-6.1)	34.8-50º† (9.3-13.3 º)	131.4 (8.8)
Увеличение ОВ (КБ*)	1.6%† (4.8)	3.3%†† (2.8)	1.6%†† (2.1)	3% º † (3.3-4.3)	3%††† (2.9)
Увеличение безрецидивной выживаемости (КБ*)	5.7% † (1.35)	3.9%†† (2.4)	3.0%†† (1.5)	2% º † (4.6-6.5)	
Увеличение DMFS (КБ*)	5.4% † (1.4)	-	3.0%†† (1.5)	2% º † (4.6-6.5)	
Отсутствие лимфооттока в ПС ЛУ (отказ от их облучения) (%)	703 (76.8%)	120 (70.5%)	1515 (75.6%)	285 (76%)	1242 (76.8%)

OC-0523

Lymph node RT improves survival in breast cancer: 10 years results of the EORTC ROG and BCG phase III trial 22922/10925.

P. Poortmans[1], H. Struikmans[2], S. Collette[3], C. Kirkove[4], V. Budach[5], P. Maingon[6], M.C. Valli[7], A. Fourquet[8], W. Van den Bogaert[9], H. Bartelink[10]

- 2002 (4004) б-ых с облученными ПС ЛУ
- Расчетное число б-ых с МТС в ПС ЛУ – 92 (4.6-6.1%)
- ЛТ на ПС ЛУ увеличивает 10л. ОВ на 1.6% и 10л. DFS на 3.9%
- У пациентов с лимфооттоком в ПС ЛУ расчетные показатели увел. 10л OS - 6.6% и DFS- 12.3%
- Облучение ПС ЛУ у 2.1 б-ых с ПС ЛУ+ спасает 1 жизнь; 1.5 б-ых – предотвращает 1 рецидив

EORTC trial 22922- 10925 investigates the role of internal mammary and medial supraclavicular (IM-MS) LN RT (Clinical trials.gov NCT00002851)

Radiotherapy & Oncology | **Volume 111 Supplement 1 (2014)**

NCIC CTG MA.20: An intergroup trial of regional nodal irradiation in early breast cancer.

T. J. Whelan, I. Olivotto, I. Ackerman, J. W. Chapman, B. Chua, A. Nabid, K. A. Vallis, J. R. White, P. Rousseau, A. Fortin, L. J. Pierce, L. Manchul, P. Craighead, M. C. Nolan, J. Bowen, D. R. McCready, K. I. Pritchard, M. N. Levine and W. Parulekar

- 916 (1823) б-ых с облученными ПС ЛУ
- Расчетное число б-ых с МТС в ПС ЛУ -70.8 (7.7%)
- Облучение ПС ЛУ увеличивает 5л. OS на 1.6%
- У пациентов с лимфооттоком в ПС ЛУ расчет-ные показатели увел. 5л OS - 6.9% и DFS – 24.4%
- Облучение ПС ЛУ у 4.8 жен. с ПС ЛУ+ спасает 1 жизнь в первые 5 лет;
- Облучение ПС ЛУ у 1.35 жен. С ПС ЛУ+ предотвращает 1 рецидив РМЖ

Journal of Clinical Oncology, 2011 ASCO Annual Meeting Abstracts Part 2. Vol 29, No 18_suppl (June 20 Supplement), 2011: LBA1003

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

Adel Courdi [a,*], Emmanuel Chamorey [b], Jean-Marc Ferrero [c], Jean-Michel Hannoun-Lévi [a]

- 404 (1334) б-ых с облученными ПС ЛУ
- Расчетное число б-ых с МТС в ПС ЛУ 38 (9.3%)
- Обл. ПСЛУ увел.10л.OS на 3.3% и 10лDFS на 3.9%
- У пациентов с лимфооттоком в ПС ЛУ расчетные показатели увел. 10л OS -11.2% и DFS- 13.2%
- Облучение ПС ЛУ у 2.8 жен. с ПС ЛУ+ спасает 1 жизнь; 2.4 жен. – предотвращает 1 рецидив РМЖ

Radiotherapy and Oncology 108 (2013) 259–265

Does the Intent to Irradiate the Internal Mammary Nodes Impact Survival in Women With Breast Cancer? A Population-Based Analysis in British Columbia

Robert A. Olson, F.R.C.P.C.,*,† Ryan Woods, M.Sc.,‡
Caroline Speers, B.A.,‡ Jeffrey Lau, B.Sc.,† Andrea Lo, M.D.,*,†

- 2413 pts б-ых с облученными ПС ЛУ
- У 375 больных с Акс. ЛУ+ расчетное число жен. с МТС в ПС ЛУ составило 34.8-50 человек (9.3%-13.3%)
- Облучение ПС ЛУ увеличило OS на 3%
- У пациентов с лимфооттоком в ПС ЛУ расчетные показатели увел. OS 8%-12.5%
- Облучение 3.1-4.3 жен. с ПС ЛУ+ спасет 1 жизнь

Int J Radiation Oncol Biol Phys, Vol. 83, No. 1, pp. e35–e41, 2012

Заключение

- Визуализация путей лимфооттока от РМЖ может существенно повлиять на решение о целесообразности облучения ПС ЛУ
- У 70%-75% женщин из группы “высокого риска” можно отказаться от облучения ПС ЛУ
- У больных с лимфооттоком в ПС ЛУ их облучение может привести к 6.9% и 11.2%-12.5% увеличению показателей 5 и 10 летней общей выживаемости

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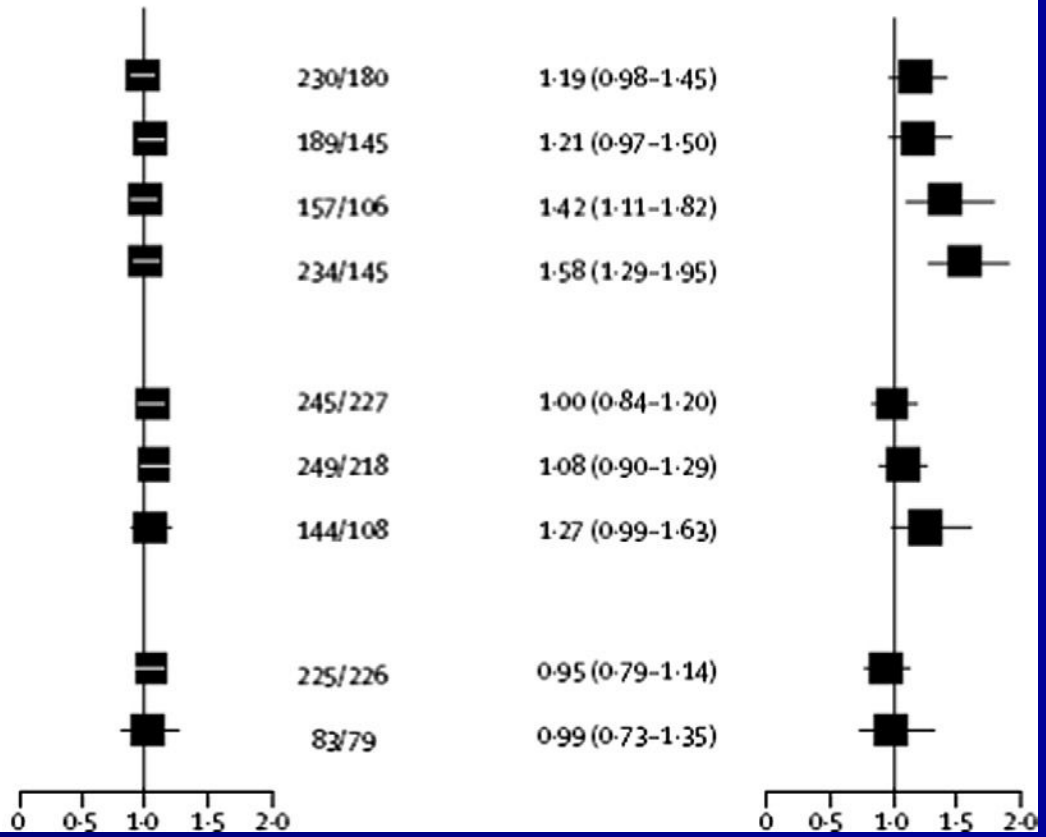
Cardiac deaths after IM LN RT

Years from breast cancer diagnosis to cardiac death	No radiotherapy		Radiotherapy	
	Cardiac deaths left/right	Cardiac mortality ratio, left-sided vs right-sided (95% CI)	Cardiac deaths left/right	Cardiac mortality ratio, left-sided vs right-sided (95% CI)
Diagnosed 1973–82				
<5 years	717/679	0·98 (0·89–1·09)	230/180	1·19 (0·98–1·45)
5–9	673/614	1·04 (0·93–1·15)	189/145	1·21 (0·97–1·50)
10–14	469/441	1·00 (0·87–1·13)	157/106	1·42 (1·11–1·82)
≥15	515/480	1·01 (0·89–1·15)	234/145	1·58 (1·29–1·95)
Diagnosed 1983–92				
<5 years	880/785	1·06 (0·96–1·16)	245/227	1·00 (0·84–1·20)
5–9	815/729	1·07 (0·97–1·18)	249/218	1·08 (0·90–1·29)
≥10	390/361	1·04 (0·90–1·20)	144/108	1·27 (0·99–1·63)
Diagnosed 1993–2001				
<5 years	567/508	1·05 (0·93–1·18)	225/226	0·95 (0·79–1·14)
5–9	144/136	1·02 (0·81–1·29)	83/79	0·99 (0·73–1·35)



Sardaro A et al. Radiother Oncol (2012)

Влияние облучения парастернальных ЛУ на выживаемость больных РМЖ

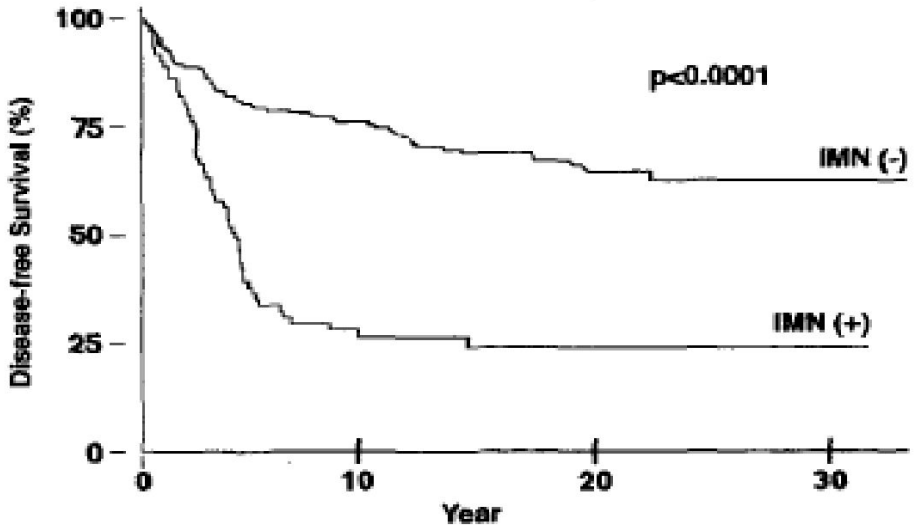


FIG. 1. Disease-free survival in 286 patients according to internal mammary node status. Curves are labeled IMN (+) = internal mammary node metastases, IMN (-) = no internal mammary node metastases.

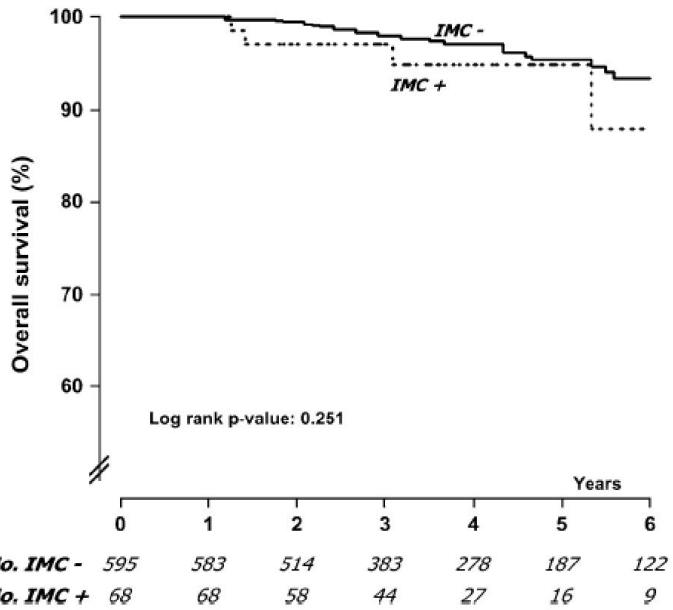


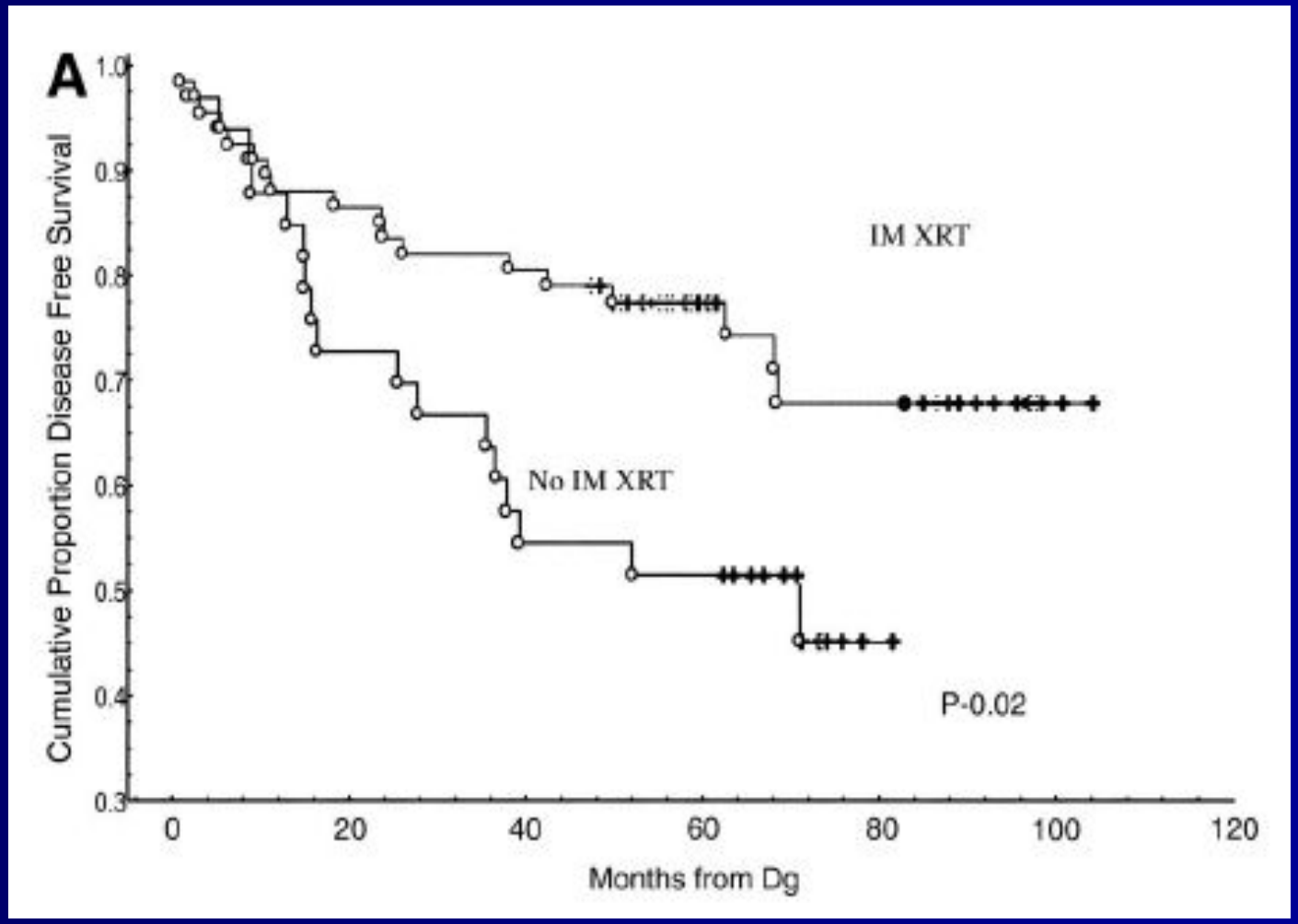
Figure 1. Overall survival stratified according to internal mammary chain (IMC) status.

Should Internal Mammary Nodes Be Sampled in the Sentinel Lymph Node Era?

Sonia L. Sugg, MD, Donald J. Ferguson, MD, Mitchell C. Posner, MD, and Ruth Heimann, MD, PhD

Veronesi et al. *Annals of Oncology* 19: 1553–1560, 2008

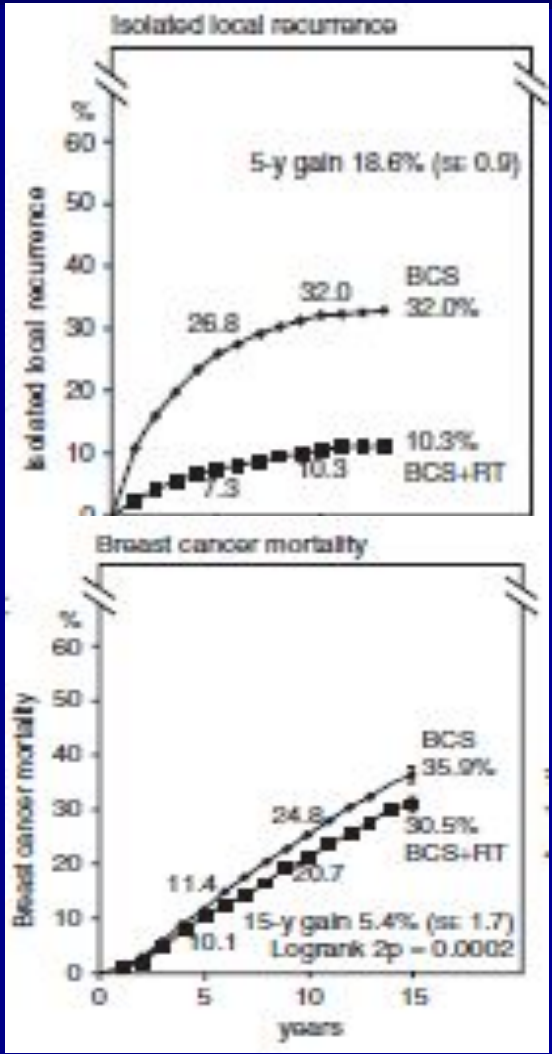
Влияние облучения парастернальных ЛУ на выживаемость больных РМЖ



Лучевая терапия раннего рака молочной железы

Частота локальных рецидивов

Исследование	ОП+ЛТ	Только ОП
NSABP B-06	14.3%	39%
JCRT (T1N0)	-	34%
Finsih (T1N0)	7.7%	18.1%
NSABP (tamox)	2.3%	16.6%



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]

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.

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

Лучевая терапия распространенного РМЖ

Table 3. Randomized Trials Comparing Mastectomy With Axillary Dissection Followed by Systemic Therapy to Mastectomy With Axillary Dissection Followed by Systemic Therapy and Radiotherapy

Series	No. of Patients	Follow-Up (months)	LRF		RFS		OS	
			ST (%)	RT (%)	ST (%)	RT (%)	ST (%)	RT (%)
DBCG 82b[9]	1,708	114	32	9*	34	48*	45	54*
DBCG 82c[29]	1,375	123	35	8*	24	36*	36	45*
S. Sweden-TAM[28]	483	96	18	6*	61	69	?	?
British Columbia[10]	318	150	33	13*	33	50*	46	54
ECOG stage III[48]	312	109	24	15	44	40	47	46
SECSG[38]	295	120	23	13*	38	51*	44	55
S. Sweden-cyclophosphamide[28]	287	96	17	6*	63	65	?	?
Glasgow[37]	219	63	25	11*	43	51*	57	61
Mayo[168,250]	217	48 (min)	30	10*	48	53	66	68
German BCG[122]†	199	96	—	0.35*	—	0.82	—	0.93
DFCI-AC[39]	123	45	20	6*	53	49	63	59
Israel[251]†	112	?	24	4	?	?	71	61
Coimbra, Portugal[252]	112	?	?	?	42	54	35	33
M.D. Anderson 7730B†	97	?	?	?	?	?	56	35
Helsinki[184]	97	90	24	7	56	56	69	65
DFCI-CMF/MF[39]	83	53	5	2	75	79	85	77
Piedmont-CMF[221]	83	132 (min)	16	8	50	45	46	53
Helsinki stage III[47]	79	?	60	13	30	67	69	94
Piedmont-LPAM[221]	76	132 (min)	35	18	41	58	48	61
Köln, Germany[253]	71	36 (ave)	?	?	68	84	84	96

RECHT ET AL J Clin Oncol 19:1539-1569. © 2001

Показатели выживаемости в зависимости от локализации РМЖ

Axillary Nodal Status	No. of Patients	Disease-Free Survival: 10-Year Disease-Free Survival %	SE	Hazards Ratio*	95% CI	P	Overall Survival: 10-Year Overall Survival %	SE	Hazards Ratio*	95% CI	P
Tumor size											
N− (≤ 2 cm)											
Medial	372	69	3	1.19	0.95 to 1.50	.31	80	3	1.20	0.90 to 1.61	.21
Lateral/central/other	1,127	72	2				83	1			
N− (> 2 cm)											
Medial	321	51	3	1.49	1.24 to 1.80	.0001	66	3	1.56	1.25 to 1.96	.0001
Lateral/central/other	1,058	62	2				76	2			
N+ (≤ 2 cm)											
Medial	377	50	3	1.03	0.88 to 1.19	.73	64	3	1.03	0.87 to 1.22	.74
Lateral/central/other	1,676	50	1				64	1			
N+ (> 2 cm)											
Medial	536	27	2	1.25	1.13 to 1.40	.0001	41	2	1.24	1.10 to 1.39	.0001
Lateral/central/other	2,858	35	1				48	1			

Marco Colleoni, David Zahrieh, Richard D. Gelber, J Clin Oncol 23:1390-1400. © 2005

Relationship Between Tumor Location and Relapse in 6,781 Women With Early Invasive Breast Cancer

By Caroline Lohrisch, Jeremy Jackson, Amanda Jones, Donna Mates, and Ivo A. Olivotto

Table 5. Actuarial 5-Year Systemic DFS and Disease-Specific Survival for Medial and Lateral Tumors According to Systemic Therapy Received and Risk Group

	Low Risk			High Risk		
	Medial	Lateral	*P*	Medial	Lateral	*P*
Systemic therapy						
No. of patients	128	300		683	1985	
Systemic DFS, %	89.3	85.3	.604	66.3	74.2	.003
Disease-specific survival, %	93.1	90.6	.691	75.7	80.8	.028
No systemic therapy						
No. of patients	562	1,201		133	350	
Systemic DFS, %	90.9	93.7	.187	75.8	76.3	.434
Disease-specific survival, %	96.4	96.8	.869	87.5	85.6	.662

Table 4. Multivariate Analysis of Prognostic Factors and Treatment for Disease-Specific Survival

No Systemic Therapy		Systemic Therapy	
Variable*	*P*	Variable*	*P*
Tumor size	< .0001	Axillary node status	< .0001
Tumor grade	.0016	Tumor grade	< .0001
Local treatment	.0028	Tumor size	< .0001
LVN invasion	.0039		
Axillary node status	.0210		
Medial versus lateral	.7887	Medial versus lateral	.0026

*Variables are listed according to their order of entry into the model.

Table 3. Multivariate Analysis of Prognostic Factors and Treatment for Systemic DFS

No Systemic Therapy		Systemic Therapy	
Variable*	*P*	Variable*	*P*
Local treatment	< .0001	Axillary node status	< .0001
Tumor size	< .0001	Tumor size	< .0001
LVN invasion	< .0001	LVN invasion	.0001
Tumor grade	.0015	Tumor grade	.0003
Axillary node status	.0054		
Medial versus lateral	.1608	Medial versus lateral	.0001

*Variables are listed according to their order of entry into the model.

Impact of Internal Mammary Lymph Node Drainage Identified by Preoperative Lymphoscintigraphy on Outcomes in Patients With Stage I to III Breast Cancer

- 1772 pts (1996-2005)
- IM drainage: 334 pts (18.8%)
- Distal rec. rates (IM+/IM-): 6.9%/4.7% (p=0.1)
- DDFS sign. On multivariate analysys (HR 0.9)

Cancer 2012;118:6287-96.

Impact of Internal Mammary Lymph Node Drainage Identified by Preoperative Lymphoscintigraphy on Outcomes in Patients With Stage I to III Breast Cancer

Table 7. Incidence of IM Drainage and Pathologically Confirmed IM Nodal Metastases in Published Series of Breast Cancer Patients

First Author	Year	IM Drainage on LSG	IMN+	IMN+/ALN–
Johnson[20]	2000	12.5% (10/80)	30% (3/10)	0%
Noguchi[21]	2000	12.2% (5/41)	10.5% (2/19)	N/A
Dupont[22]	2001	N/A	16.7% (5/30)	10% (3/30)
van der Ent[23]	2001	25.4% (65/256)	26.8% (11/41)	7.3% (3/41)
Uren[9]	2001	44.5% (65/146)[a,b]		
Galimberti[11]	2002	N/A	8.8% (14/160)[c]	2.5% (4/160)
Tanis[12]	2002	19.1% (105/549)[d]	18.9% (17/90)	8.9% (8/90)
Estourgie[13]	2003	21.7% (150/691)	16.9% (22/130)	6.9% (9/130)
Farrus[24]	2004	13.8% (31/225)	14.3% (2/14)	0%
Mansel[25]	2004	8.8% (62/707)	12.9% (4/31)	6.5% (2/31)
Paredes[26]	2005	14.1% (55/391)	12.5% (4/32)	0%
Carcoforo[27]	2006	12.8% (95/741)	15.4% (10/65)	4.6% (3/65)
Madsen[4]	2007	21.7% (109/502)	23.5% (20/85)	4.7% (4/85)
Veronesi[28]	2008	40.8% (254/623)[e]	10.3% (68/663)	2.6% (17/663)
Avisar[29]	2008	N/A	25.0% (7/28)	7.1% (2/28)
Coombs[30]	2009	18.0% (88/490)[b]	22.2% (20/90)	13.3% (12/90)
Heuts[31]	2009	19.4% (196/1008)	22% (31/139)	29% (9/31)
Domenech-Vilardell[32]	2009	9.0% (82/914)	13.6% (6/44)	9.1% (4/44)
Van Esser[33]	2011	19.0% (426/2203)	25.0% (4/16)[f]	6.2% (1/16)

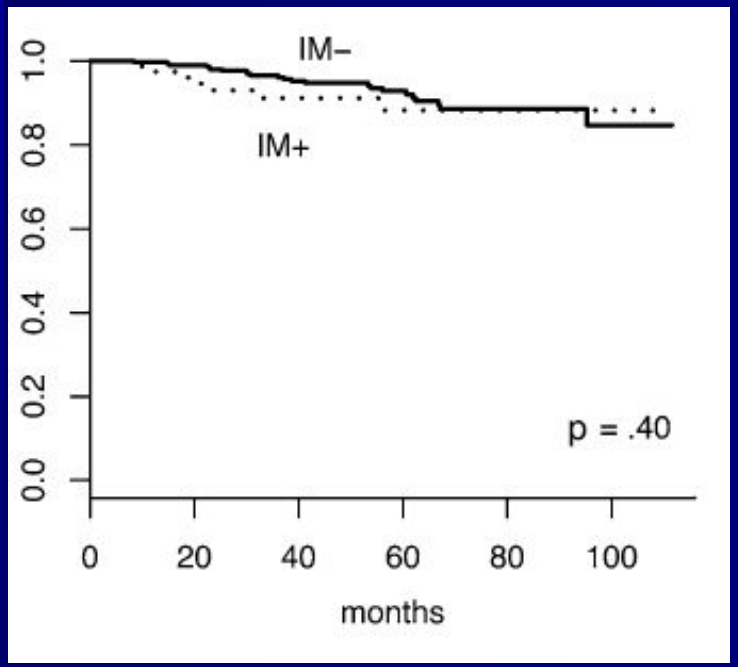
IM indicates internal mammary; LSG, lymphoscintigraphy; IMN, internal mammary lymph node; IMN+, positive for metastasis; ALN, axillary lymph node; ALN–, negative for metastasis; N/A, not available.
[a] IM node biopsy was not performed in this series.
[b] Series used antimony-labeled sulfur colloid, rest of series used nanocolloid or sulfur colloid.
[c] IM sentinel lymph node biopsy was performed only in patients with medial tumor or who demonstrated IM drainage on LSG.
[d] One patient had drainage to the contralateral IM chain.
[e] Patients has mostly inner quadrant tumors (520/663).
[f] IM sentinel lymph node biopsy was performed only in patients who demonstrated IM chain drainage only (25/2203) and was successful in 16.

Cancer 2012;118:6287-96.

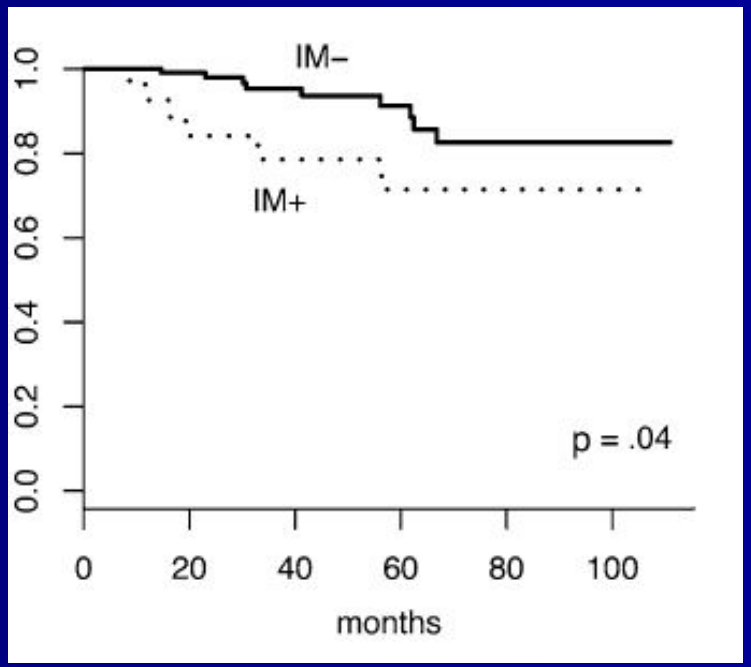
Internal Mammary Nodal Chain Drainage Is a Prognostic Indicator in Axillary Node-Positive Breast Cancer

Michelle S. Yao,[1] Brenda F. Kurland,[2] Anne H. Smith,[3] Erin K. Schubert,[4] Lisa K. Dunnwald,[4] David R. Byrd,[5] and David A. Mankoff, MD, PhD[3,4]

Overall survival in entire study population



axillary node-positive population



Ann. Surg. Oncol. Vol. 14, No. 10, 2007

Internal Mammary Nodal Chain Drainage Is a Prognostic Indicator in Axillary Node-Positive Breast Cancer

Michelle S. Yao,[1] Brenda F. Kurland,[2] Anne H. Smith,[3] Erin K. Schubert,[4] Lisa K. Dunnwald,[4] David R. Byrd,[5] and David A. Mankoff, MD, PhD[3,4]

TABLE 2. *Univariate Cox proportional hazards models predicting overall survival in the entire study cohort and in axillary node-positive populations*

	All patients (n = 604) [a]			Node+ patients (n = 186) [b]		
	HR	95% CI	P value	HR	95% CI	P value
IM drainage	1.43	0.62–3.33	.40	2.89	1.03–8.12	.04
Axillary node positive	2.24	1.11–4.54	.02			
1–3 axillary nodes (vs 0)	1.42	0.58–3.44	.006			
4–9 nodes (vs 0)	4.59	1.80–11.74				
10+ nodes (vs 0)	4.53	1.03–19.91				
4+ axillary nodes (vs 1–3)				3.20	1.16–8.84	.02
Upper-outer quadrant	0.59	0.29–1.22	.15	0.54	0.18–1.57	.25
Medial (vs lateral)	1.62	0.76–3.44	.21	1.89	0.65–5.54	.24
T2 (vs T1)	4.00	1.87–8.56	.001	3.16	0.99–10.09	.14
T3 (vs T1)	3.38	0.94–12.15		1.40	0.16–12.59	
Intermediate grade (vs low)	1.24	0.47–3.27	.11	1.81	0.36–8.99	.49
High grade (vs low)	2.40	0.97–5.96		2.55	0.53–12.26	
ER negative	2.75	1.30–5.82	.008	3.38	1.17–9.76	.02
PR negative	2.24	1.06–4.72	.03	1.57	0.53–4.72	.42
HER2/neu overexpressing	1.09	0.46–2.60	.84	0.72	0.20–2.62	.62
Ki-67 (high vs low/int)	3.46	1.47–8.17	.005	6.84	1.49–31.27	.01
p53 overexpressing	2.43	1.05–5.61	.04	2.24	0.72–6.96	.16
Menopausal	1.07	0.51–2.25	.85	1.32	0.44–3.96	.62
Radiation	0.47	0.20–1.09	.08	0.58	0.12–2.70	.49

HR, hazard ratio; CI, confidence interval; IM, internal mammary; ER, estrogen receptor; PR, progesterone receptor; int, intermediate.

[a] Except for tumor stage (N = 603), nuclear grade (N = 601), ER (N = 564), PR (N = 563), HER2/neu (N = 550), Ki-67 (N = 448), P53 (N = 427), menopausal (N = 600, 4 males excluded), and radiation (N = 477).

[b] Except for nuclear grade (N = 185), ER and PR (N = 182), HER2/neu (N = 177), Ki-67 (N = 141), P53 (N = 137), menopausal (N = 183, 3 males excluded), and radiation (N = 138).

Ann. Surg. Oncol. Vol. 14, No. 10, 2007

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]

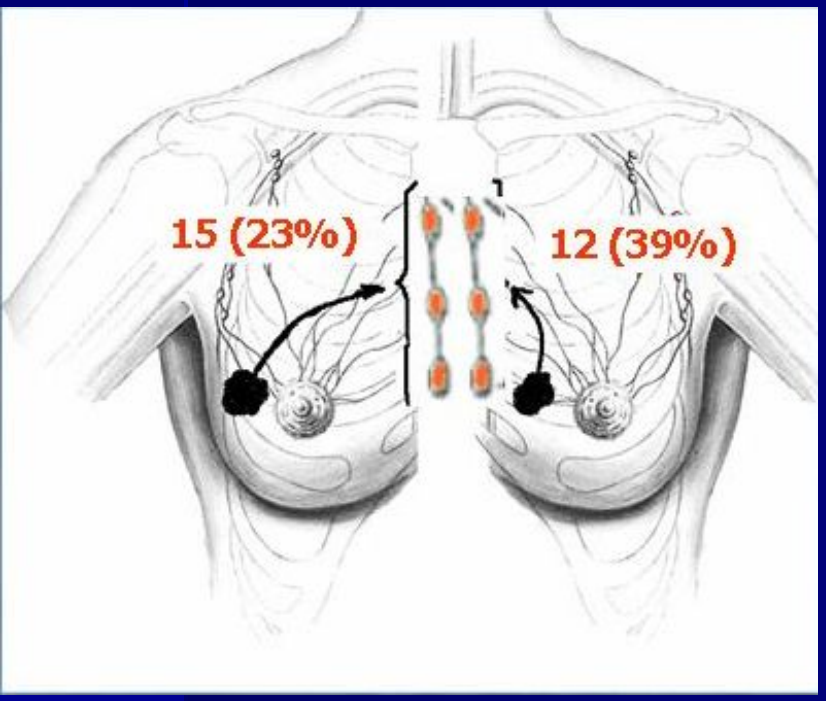
Table 1 Patient characteristic

	MA.20 [16]	EORTC [17]	French [15]
Recruitment years	2000-2007	1996-2004	1991-1997
Number of patients	1832	4004	1334
Median age	54	54	57
Node positive	85%	56%	75%
Breast surgery	100% breast conserving	75% breast conserving	100% mastectomy
CHX	91%	85%	61%
ER/PR negative	25%	16%	7%
Unknown ER/PR status	n.a.	6%	40%
Main inclusion criteria	N + or high risk* N0 any location	N + or medial/central tumor	N + or medial/central tumor
Breast/chest wall	Both arms: 50 Gy / 25 fx	Both arms 50 Gy / 25 fx	Both arms according to practice of the center
Medial supraclavicular nodes	Experimental arm: 45 Gy / 25 fx	50 Gy / 25 fx	All patients: dose and fractionation according to practice of the center
Internal mammary nodes	Experimental arm: 45 Gy / 25 fx	Experimental arm: 50 Gy / 25 fx	Experimental arm: 45 Gy / 20 fx

*= > = 5 cm tumor, > = 2 cm tumor, and <10 axillary nodes removed with ER-, G3, or lymph vacular invation; n.a. = not available; fx = fractions; ER = estrogene receptor; PR = progesterone receptor.

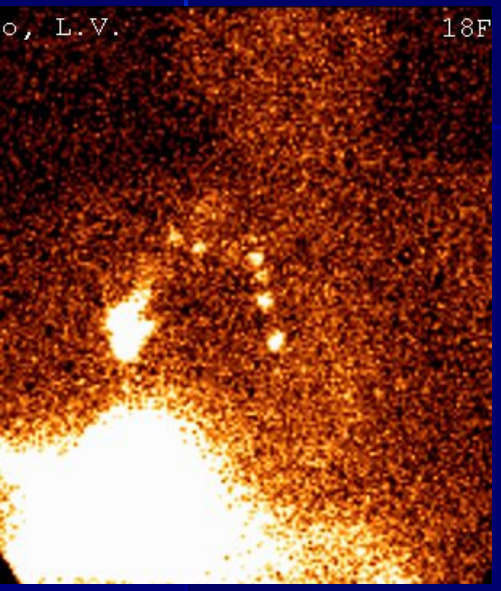
Budach *et al. Radiation Oncology* 2013, **8**:267
http://www.ro-journal.com/content/8/1/267

Парастернальные ЛУ



- Лимфоотток в ПСТ ЛУ обнаружен у 27 из 84 (32.1%) больных:
- 15 больных - РМЖ в наружных квадрантах (23%)
- 12 – во внутренних квадрантах (39%)

Топография парастернальных полей облучения

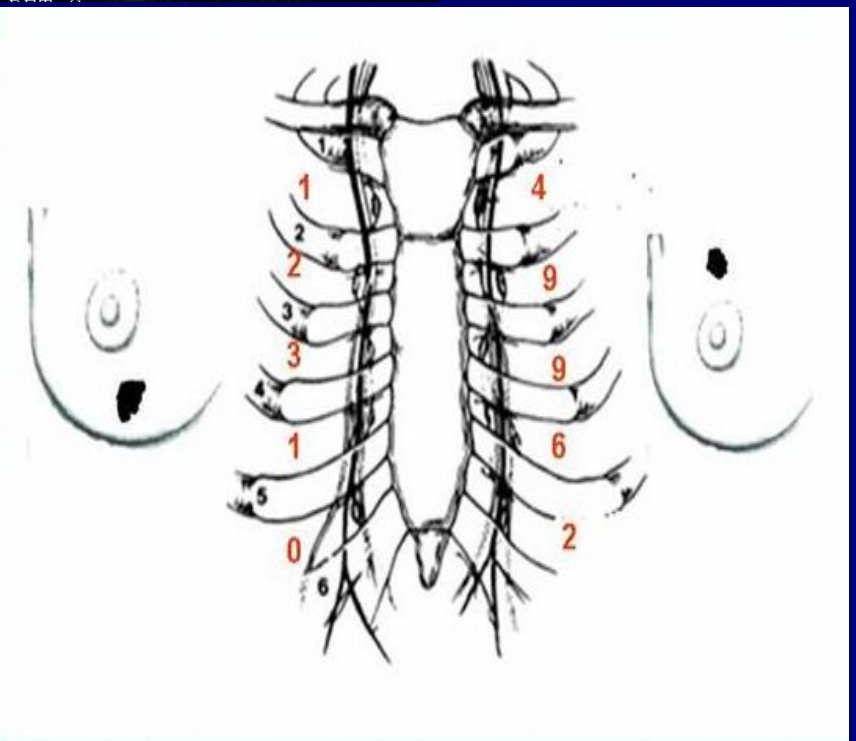


Традиционный подход к определению локализации парастернальных ЛУ:

нижние квадранты – лимфоотток в III-IV межреберья

верхние квадранты – лимфоотток в I-II межреберья

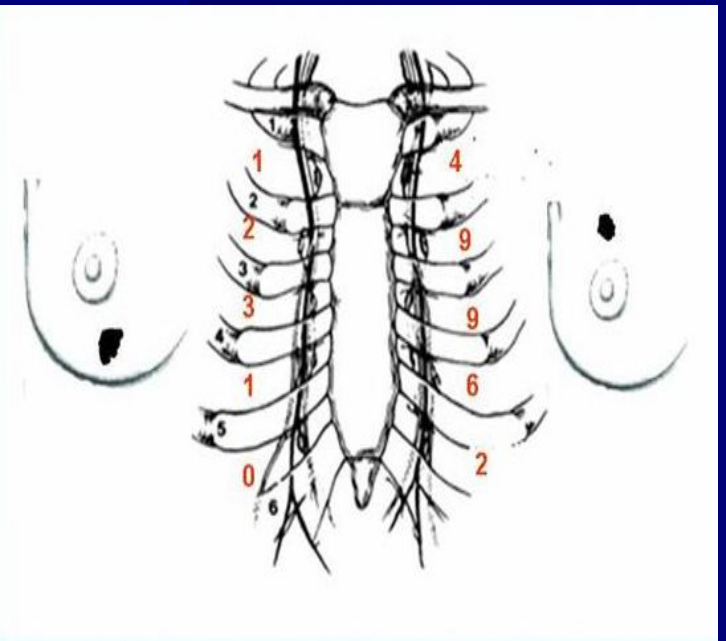
Топография парастернальных полей облучения



Локализация СЛУ в парастернальной области при РМЖ нижних квадрантов:

- I межреберье – 1,
- II межреберье -2,
- III межреберье – 3,
- IV межреберье – 1,
- V межреберье – 0

Топография парастернальных полей облучения



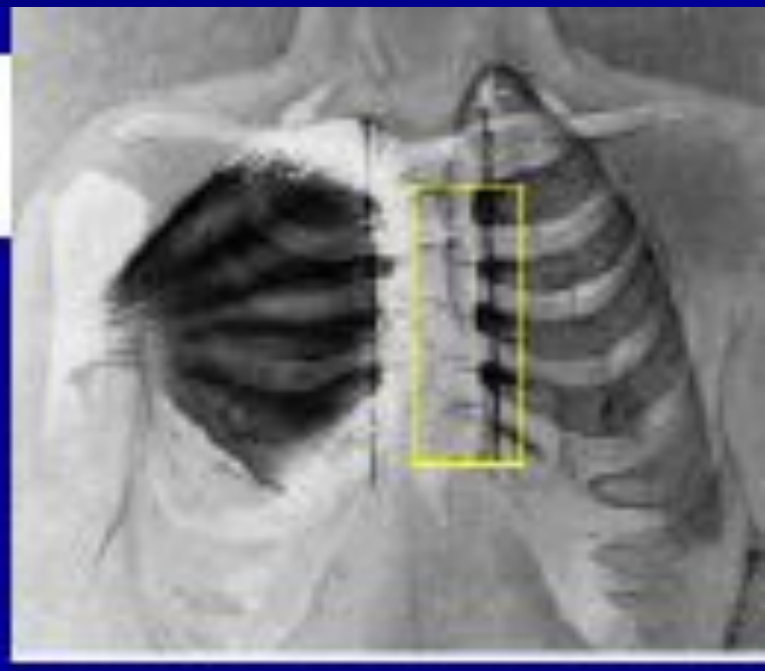
Локализация СЛУ при РМЖ верхних квадрантов:

- I межреберье – 4,
- II межреберье – 9,
- III межреберье – 9,
- IV межреберье – 6,
- V межреберье – 2 .

у 10 из 22 больных (45%) с РМЖ верхних квадрантов ПСТ СЛУ локализовались в III-V межреберьях

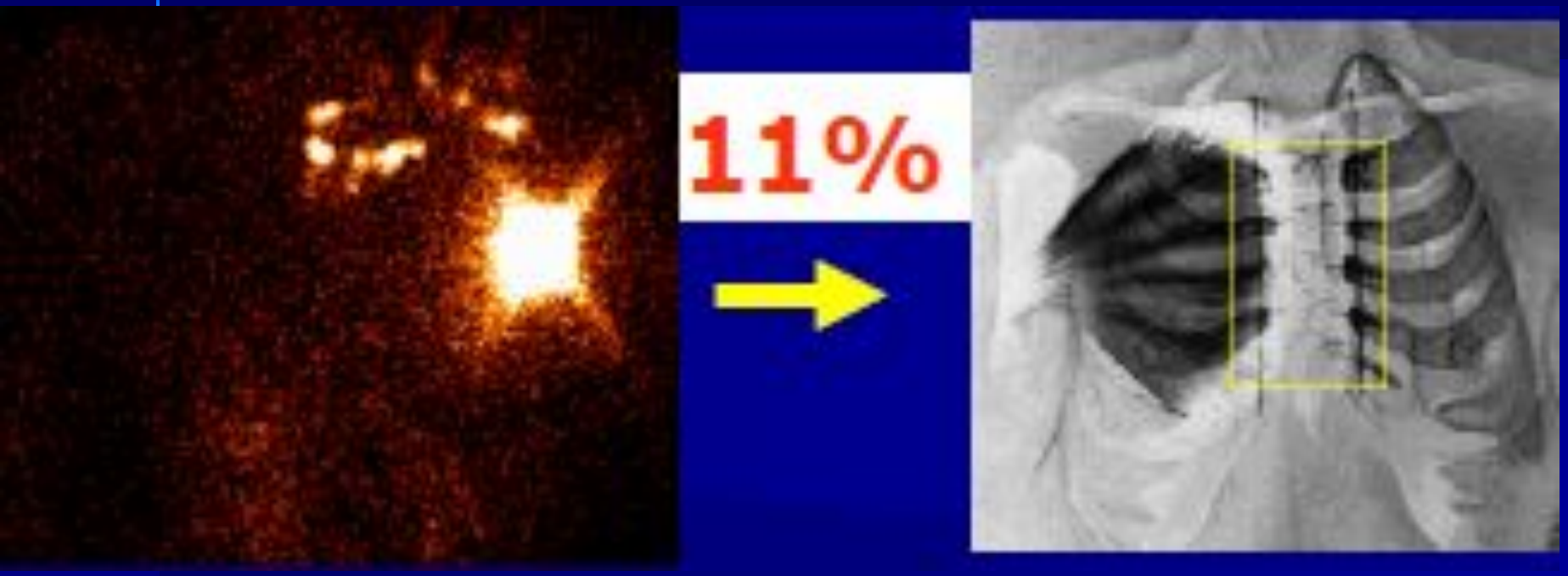
Топография парастернальных полей облучения

89%



В 24 из 27 (89%) случаев парастернальные ЛУ были расположены только с одной стороны грудины.

Топография парастернальных полей облучения



У 3 больных (11%) парастернальные ЛУ визуализировались по обе стороны от грудины и облучались с помощью широких радиационных полей

Риск поражения ЛУ II-III уровня

При поражении акс. ЛУ I уровня

Tumor size	Risk
T1	28.4%
T2	51.3%
T3	67.9%
All cases	41.1%

Риск “skip” Mts

Level	No. (%)
I	314 (58.2)
I + II	117 (21.7)
I + II + III	88 (16.3)
Total no. of cases with regular distribution	519 (96.2)
II	6 (1.2)
III	2 (0.4)
I + III	12 (2.2)
II + III	0
Total no. of cases with “skip” distribution	20 (100)

	Levels involved				
Tumor size	I	I + II	I + II + III	“Skip” distribution	Total
T1	179 (69.9%)	34 (13.2%)	29 (11.3%)	14 (5.6%)	256 (100%)
T2	113 (48.5%)	70 (30.0%)	47 (20.2%)	3 (1.3%)	233 (100%)
T3	9 (32.1%)	8 (28.6%)	9 (32.1%)	2 (7.2%)	28 (100%)
Total	301	112	85	19	517*

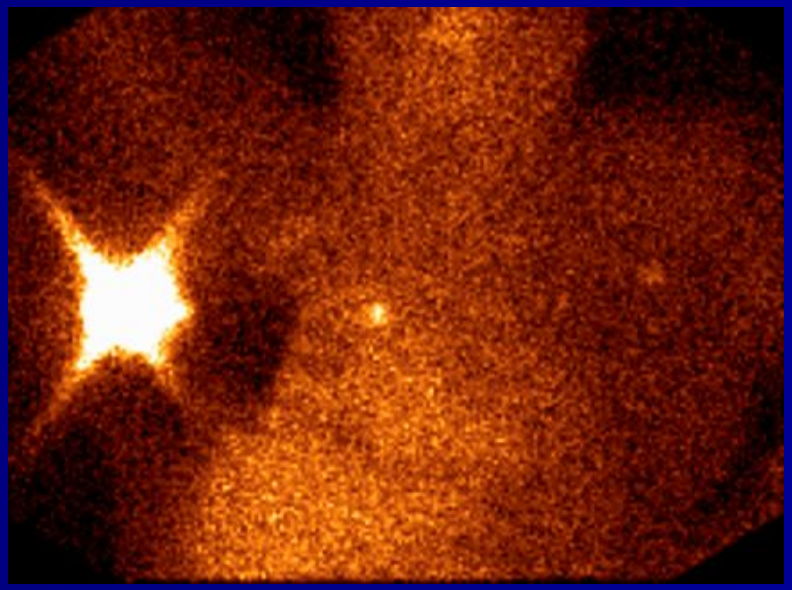
VERONESI, *Cancer* 59:682–687, 1987.

Риск поражения парастернальных ЛУ

Размер опухоли

- T1-T2 15%-18%
- T3 28%-48%

Кол-во пор-ых подм. ЛУ

- 0 5%
- 1-3 19%
- >3 52%

Локализация опухоли