



## **Radioterapia Quando indicar?**

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# Conflitos de interesse

**Sou radio-oncologista**

# **Radioterapia**

**1) Mastectomia preservadora de pele e do CAP**

**2) Axila 1 a 3 linfonodos**

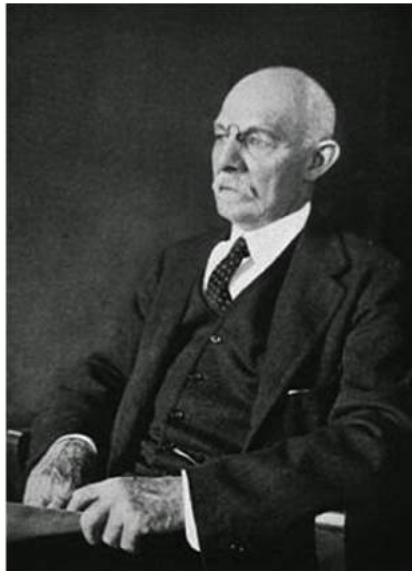
**3) RT após QT neoadjuvante**

# Mastectomia preservadora de pele e do CAP

*Skin-sparing mastectomy (SSM)*

*Nipple-sparing mastectomy (NSM)*

# Tratamento cirúrgico Câncer de mama



Halsted



Estudos clínicos  
Medicina baseada em evidência

Tratamento  
conservador  
da mama

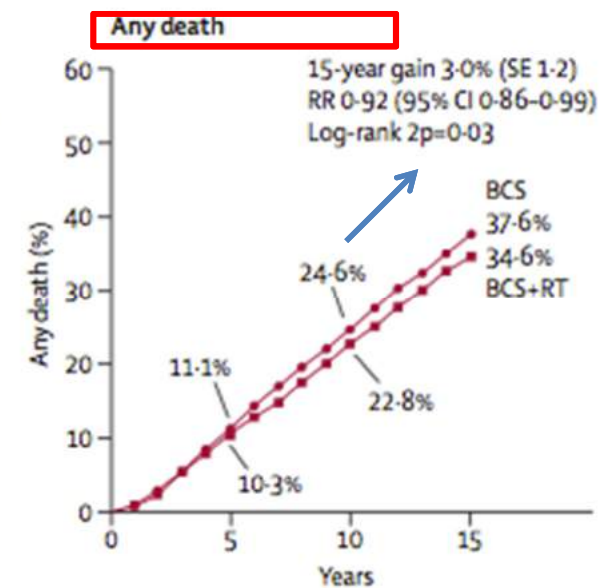
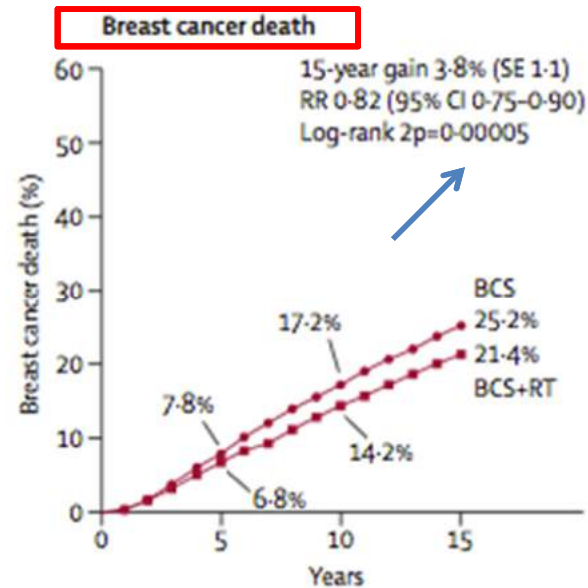
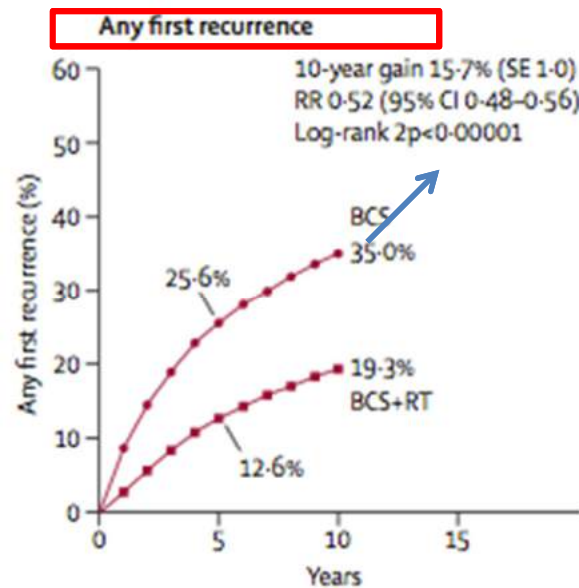
# Mastectomia versus Quadrantectomia + RT

Estudo	N	FU (a)	Falha local (%)		Recorrência à distância (%)		Sobrevida global (%)	
			MM	BCT	MM	BCT	MM	BCT
Francês	179	15	14	9	E	E	E	E
Milan I								42
NSABP - B								46
US NCI								53
EORTC 10801								55
Danish trial								32

**6 ECR : Ausência de vantagem em SG**  
**Sobrevida Global média:**  
**60,6% versus 59,99%**  
**Recidiva Global média:**  
**8,99% versus 11,8%**

## Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10 801 women in 17 randomised trials

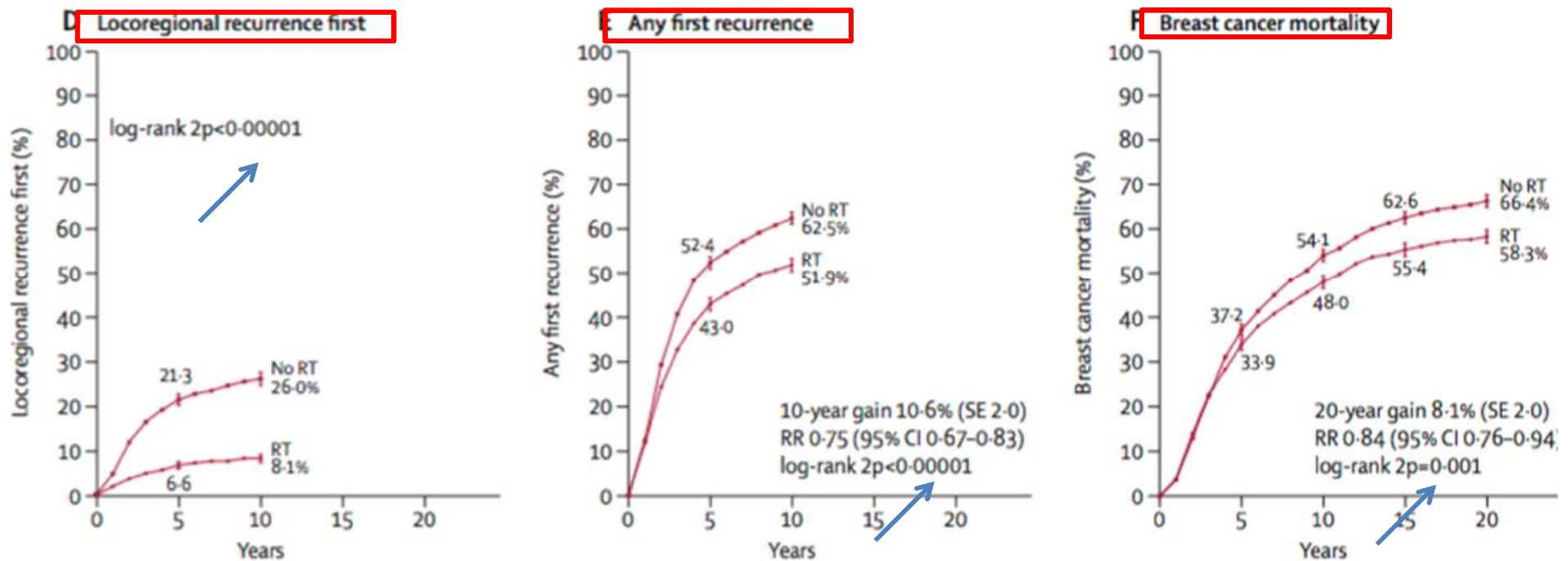
Early Breast Cancer Trialists' Collaborative Group (EBCTCG)\*



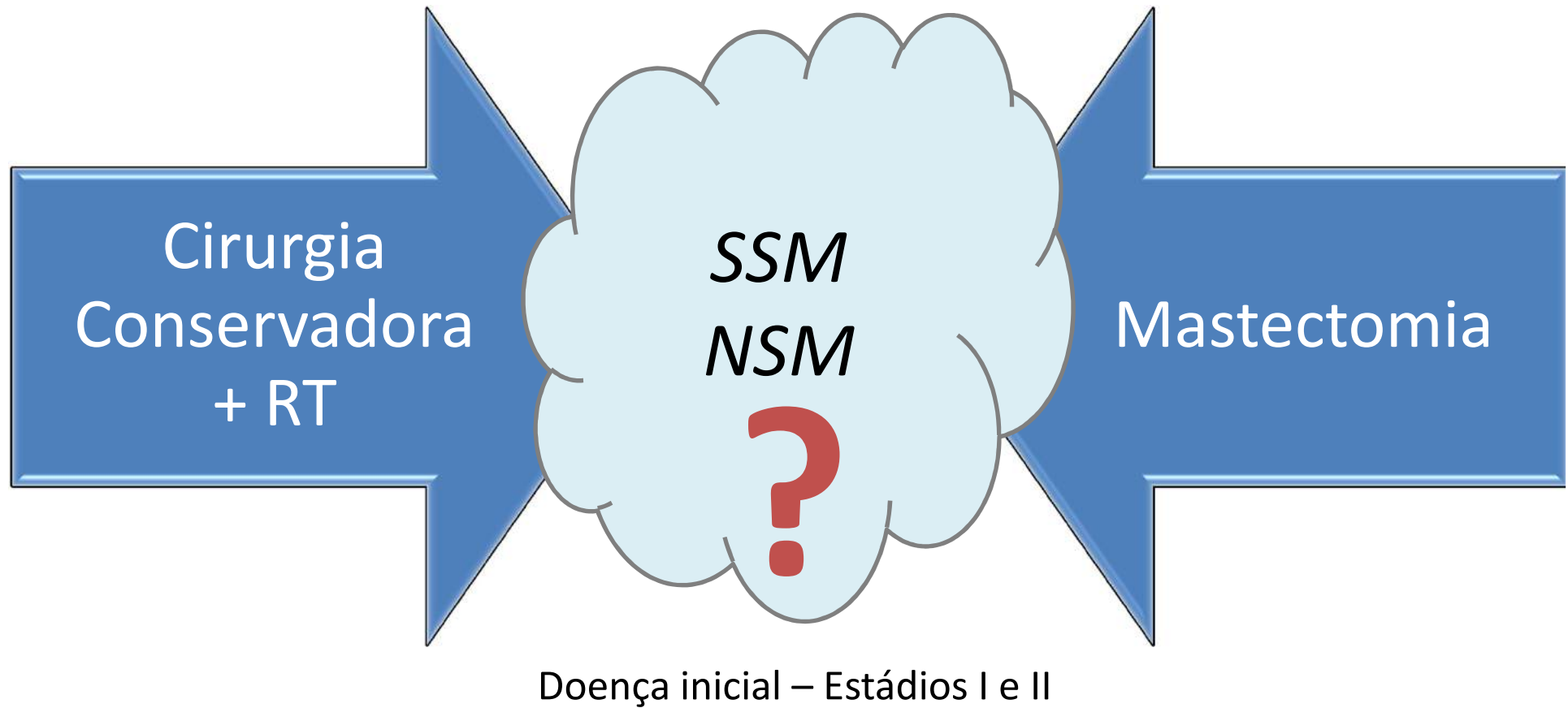


# Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials

EBCTCG (Early Breast Cancer Trialists' Collaborative Group)\*







## Local, Regional, and Systemic Recurrence Rates in Patients Undergoing Skin-Sparing Mastectomy Compared With Conventional Mastectomy

- Estudo prospectivo – 2000 a 2005
- Follow-up: 53 meses

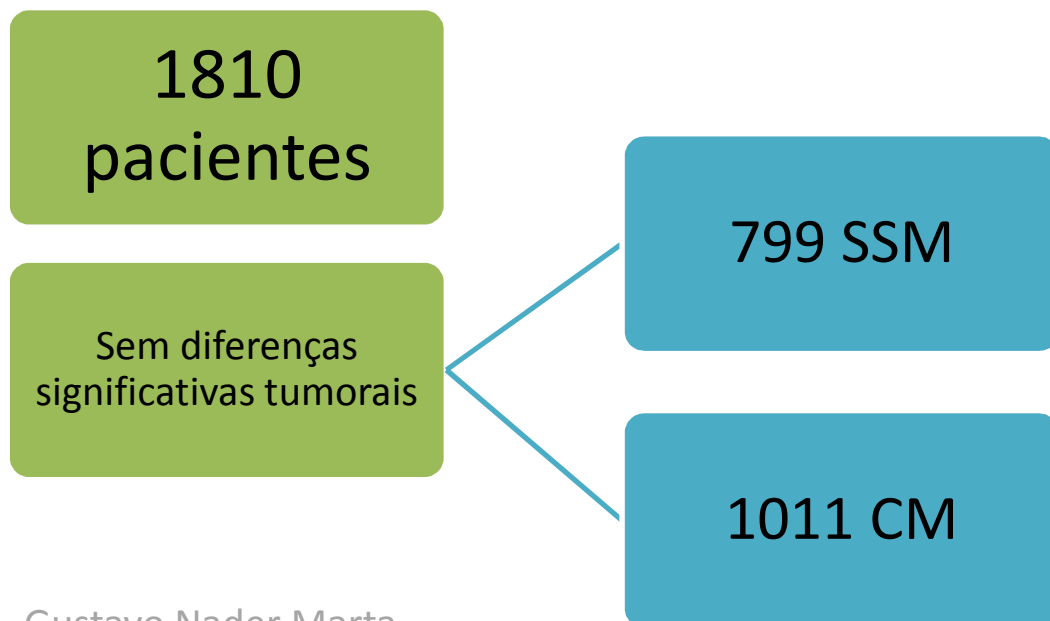


Table 4. Neoadjuvant and Adjuvant Therapy

Characteristic	CM n=1011 (%)	SSM n=799 (%)	P
<b>Neoadjuvant chemotherapy</b>			<.0001
No	712 (70.4)	635 (79.5)	
Yes	299 (29.6)	164 (20.5)	
<b>Adjuvant radiation therapy</b>			<.0001
Yes	254 (25.1)	93 (11.6)	
No	757 (74.9)	706 (88.4)	
<b>Adjuvant chemotherapy</b>			.73
Yes	373 (36.9)	301 (37.7)	
No	638 (63.1)	498 (62.3)	
<b>Adjuvant hormonal therapy</b>			.16
Yes	631 (62.4)	473 (59.2)	
No	380 (37.6)	326 (40.8)	

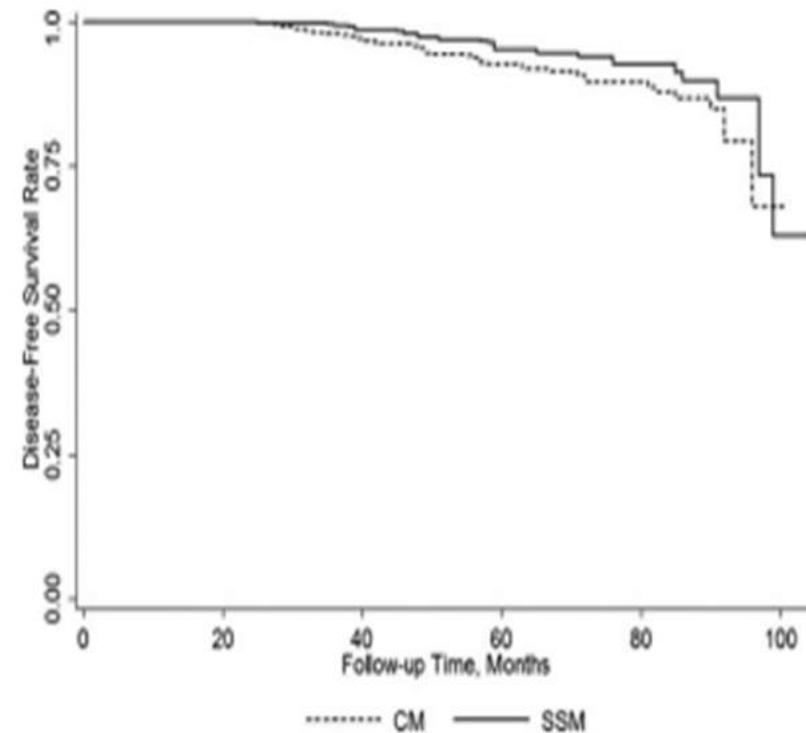
CM indicates conventional mastectomy; SSM, skin-sparing mastectomy.

**Table 5.** Recurrence Patterns

Characteristic	CM n=1011 (%)	SSM n=799 (%)	P
<b>Any recurrence</b>			.04
No	934 (92.4)	755 (94.5)	
Yes	77 (7.6)	42 (5.3)	
<b>Local recurrence</b>			.11
No	997 (98.6)	794 (99.4)	
Yes	14 (1.4)	5 (0.6)	
<b>Regional recurrence</b>			.70
No	998 (98.7)	787 (98.5)	
Yes	13 (1.3)	12 (1.5)	
<b>Systemic recurrence</b>			.05
No	941 (93.1)	761 (95.2)	
Yes	70 (6.9)	38 (4.8)	

CM, conventional mastectomy; SSM, skin-sparing mastectomy.

## Sobrevida livre de doença



**Figure 2.** Unadjusted disease-free survival rates in patients who underwent SSM vs CM.

## META-ANALYSIS

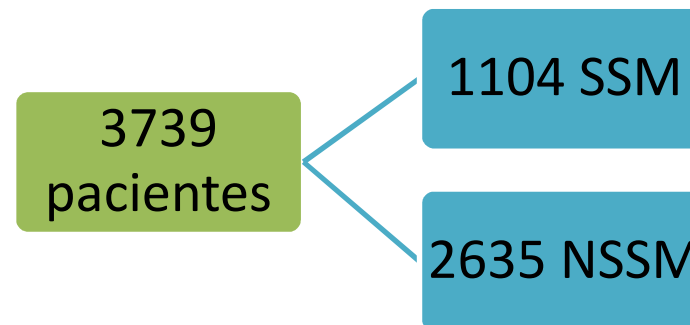
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# Comparison of Skin-Sparing Mastectomy Versus Non–Skin-Sparing Mastectomy for Breast Cancer

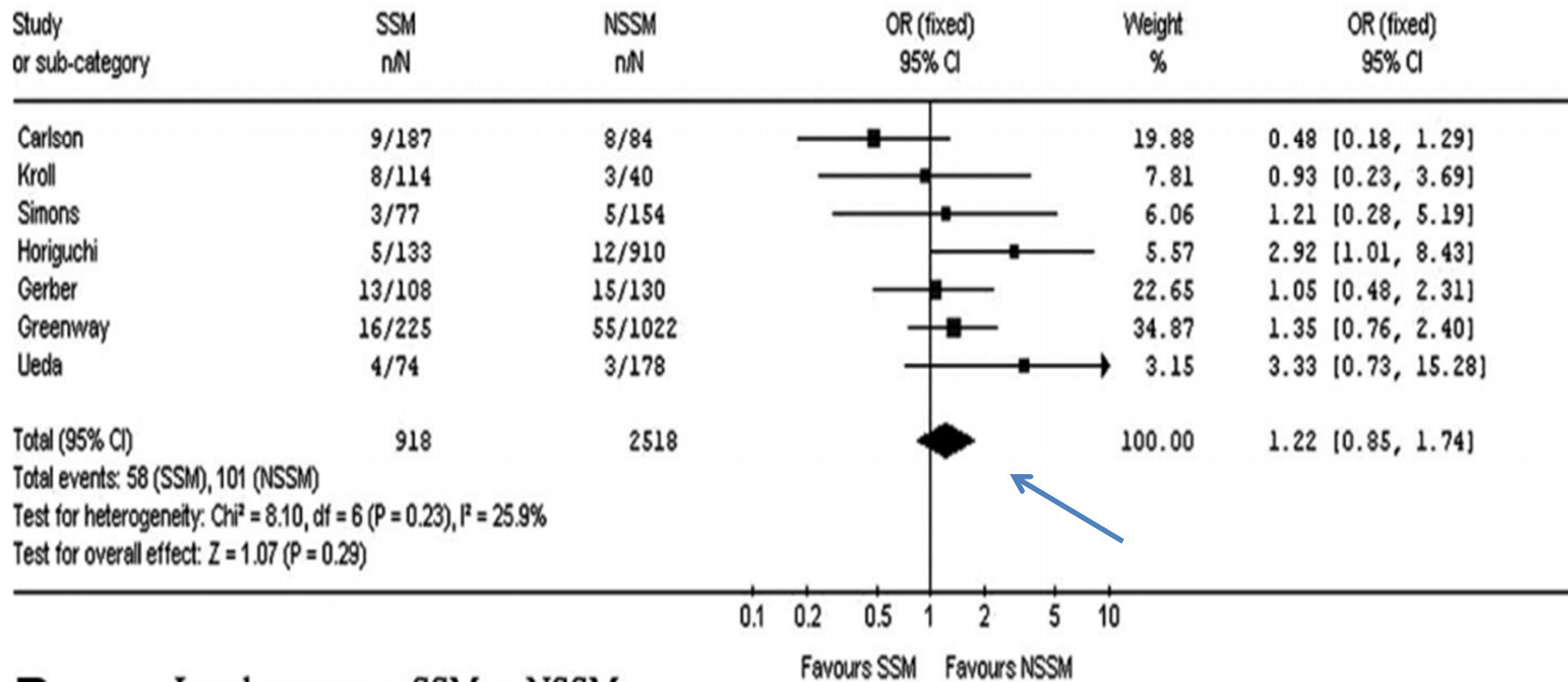
## *A Meta-Analysis of Observational Studies*

*Sophocles Lanitis, MD,\*† Paris P. Tekkis, MD, FRCS,‡ George Sgourakis, PhD,† Nikitas Dimopoulos, MD,\*  
Ragheed Al Mufti, MD, FRCS,\* and Dimitri J. Hadjiminias, MPhil, FRCS\**

- 9 estudos prospectivos não randomizados
- 1986 - 2005



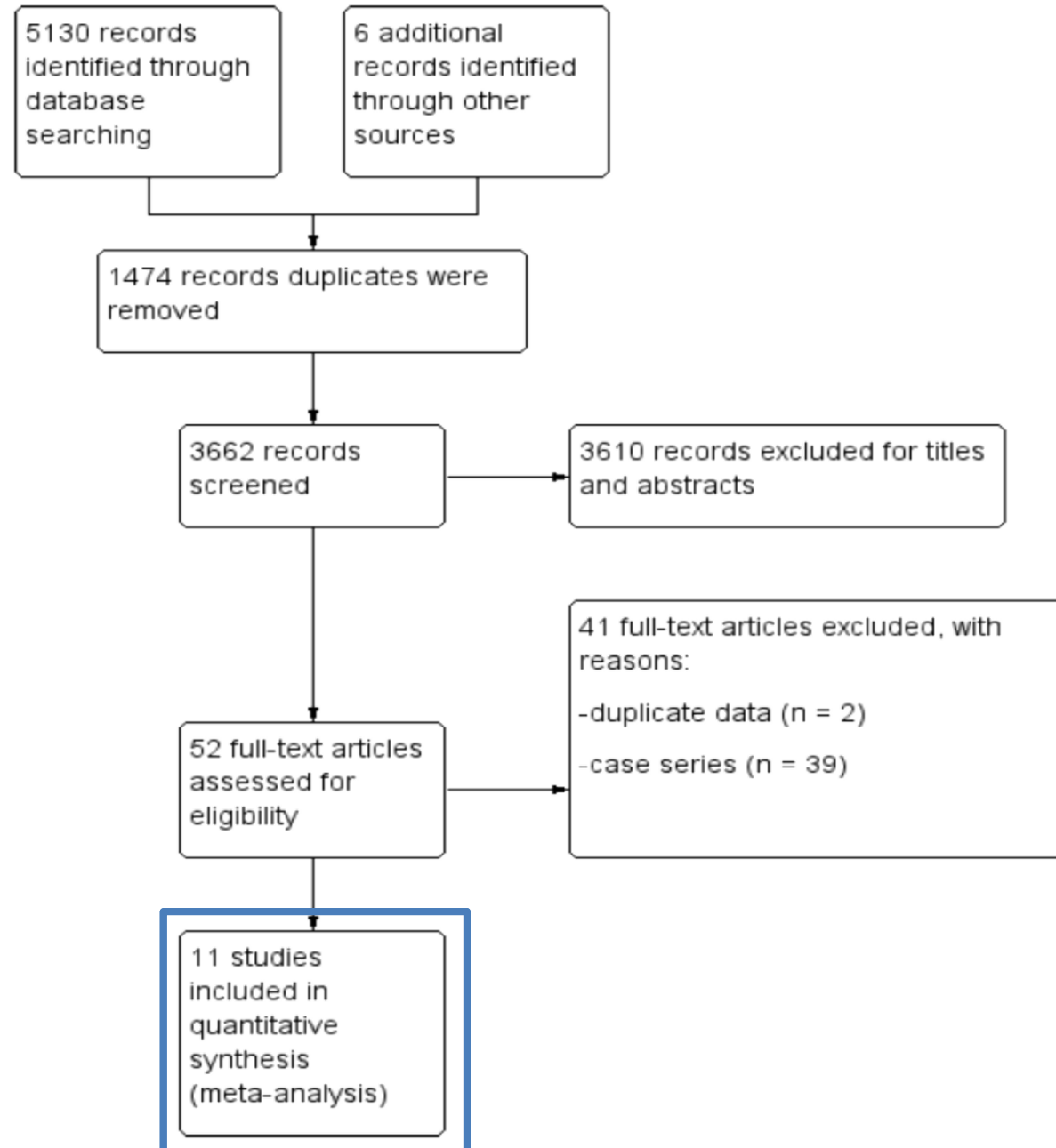
## A Local recurrence SSM vs NSSM





**Nipple- and areola-sparing mastectomy for the treatment of breast cancer (Review)**



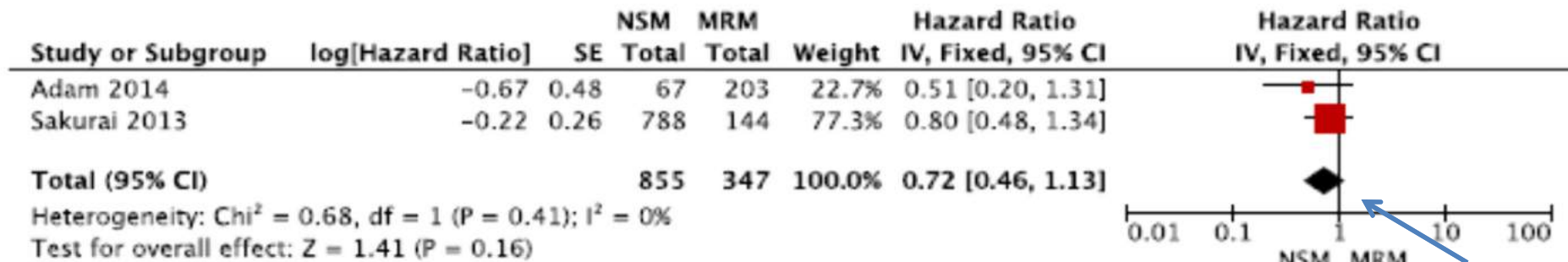


# Risco de viés

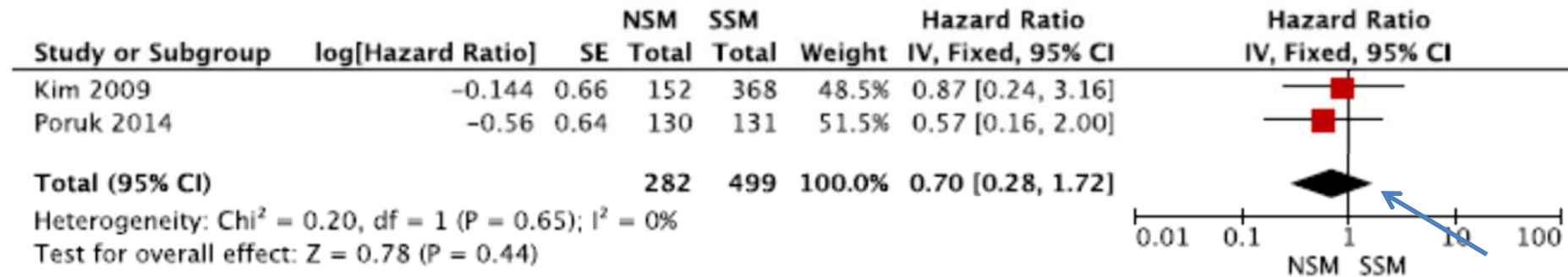
Author (Year)	Selection bias – was the allocation sequence adequately generated ?	Selection bias – was the allocation adequately concealed ?	Selection bias – were baseline characteristics different ?	Selection bias – was there adequate adjustment for confounding ?	Performance/detection bias – was interventions adequately prevented ?	Attrition bias – were incomplete outcome data adequately addressed ?	Reporting bias – were reports os the study free from selective outcome reporting ?	Reporting bias – were reports of the study free from selective analysis reporting ?
Adam 2014	-	-	?	-	-	?	+	+
Bonetti 2011	-	-	?	-	-	+	+	+
Burdge 2013	-	-	-	-	-	?	+	+
Gerber 2009	-	-	-	-	-	+	+	+
Horiguchi 2001	-	-	-	-	-	?	+	+
Kim 2010	-	-	-	-	-	?	+	+
Oura 1994	-	-	-	-	-	?	?	?
Poruk 2015	-	-	-	-	-	?	+	+
Sakurai 2013	-	-	-	-	-	?	+	+
Shi 2012	-	-	-	-	-	?	+	+
Staneć 2014	-	-	-	-	-	?	+	+

# Sobrevida Global

## *NSM versus MRM*

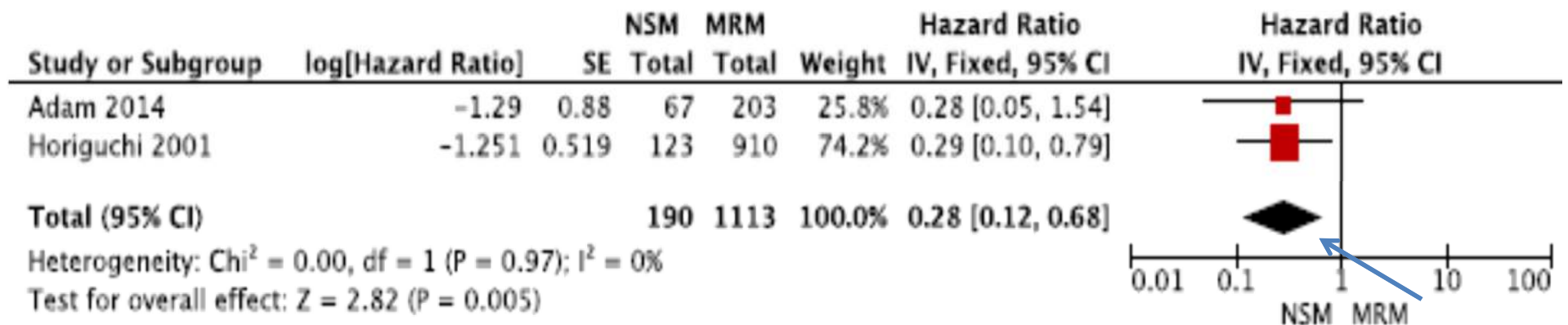


## *NSM versus SSM*



# Recidiva Local

## *NSM versus MRM*

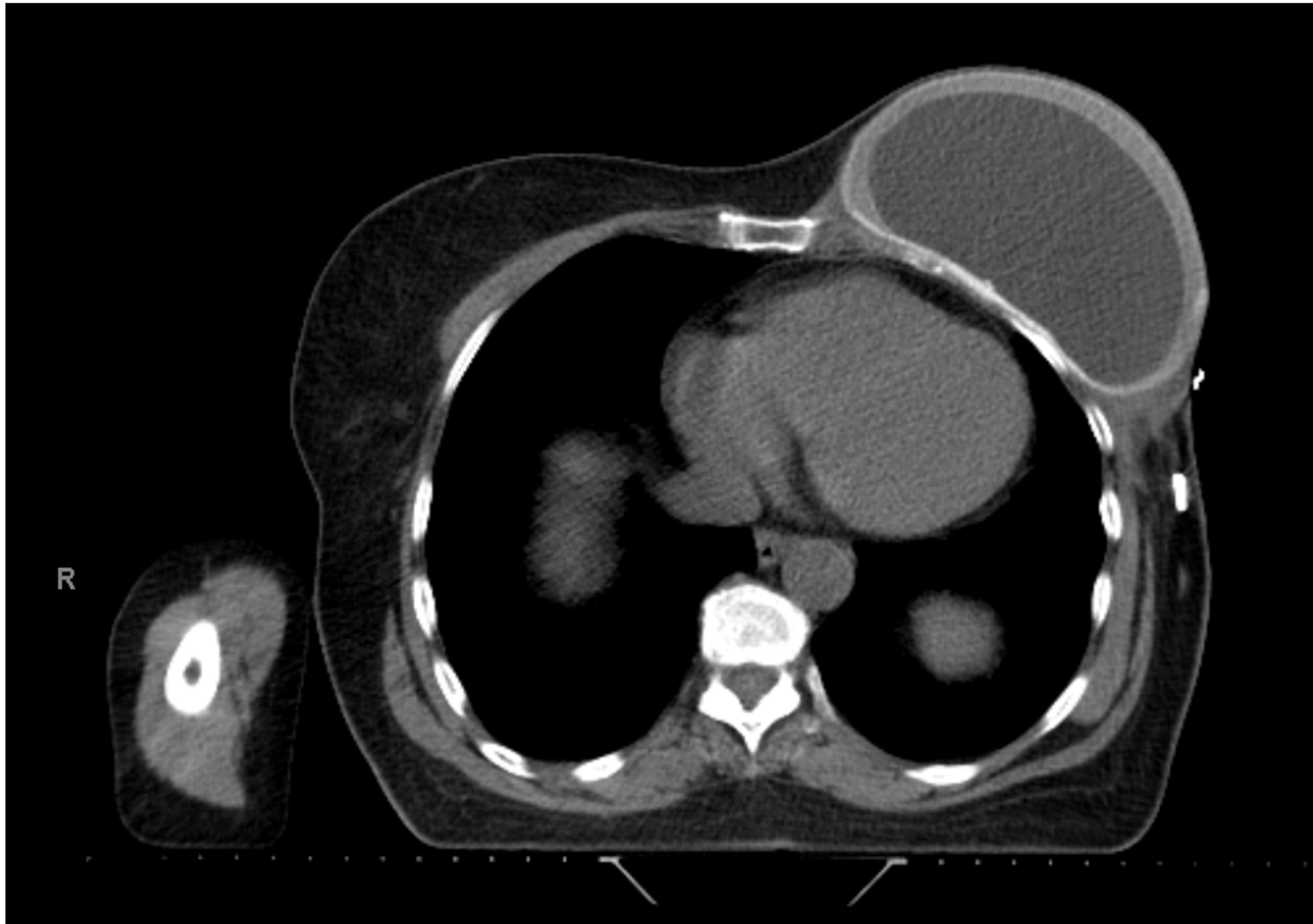


# Recidiva Local

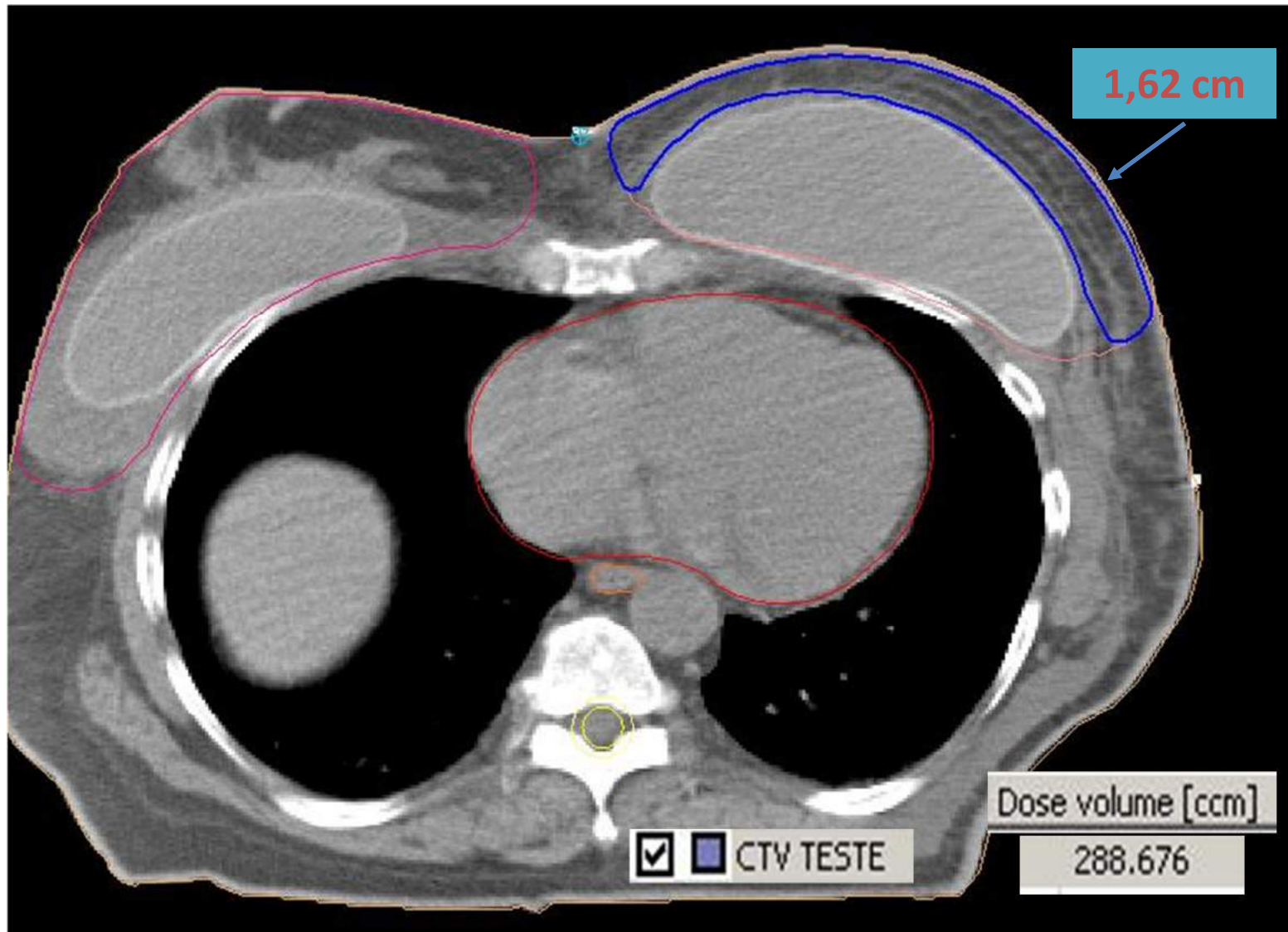
- Recidivas
  - seguimento mediano 42 (8-180) meses
- N = 144 recidivas em NSM
  - 32,2% no CAP
  - 67,8% no restante (retalho, parede, LN)

# Quanto de tecido residual é considerado seguro?





Gustavo Nader Marta



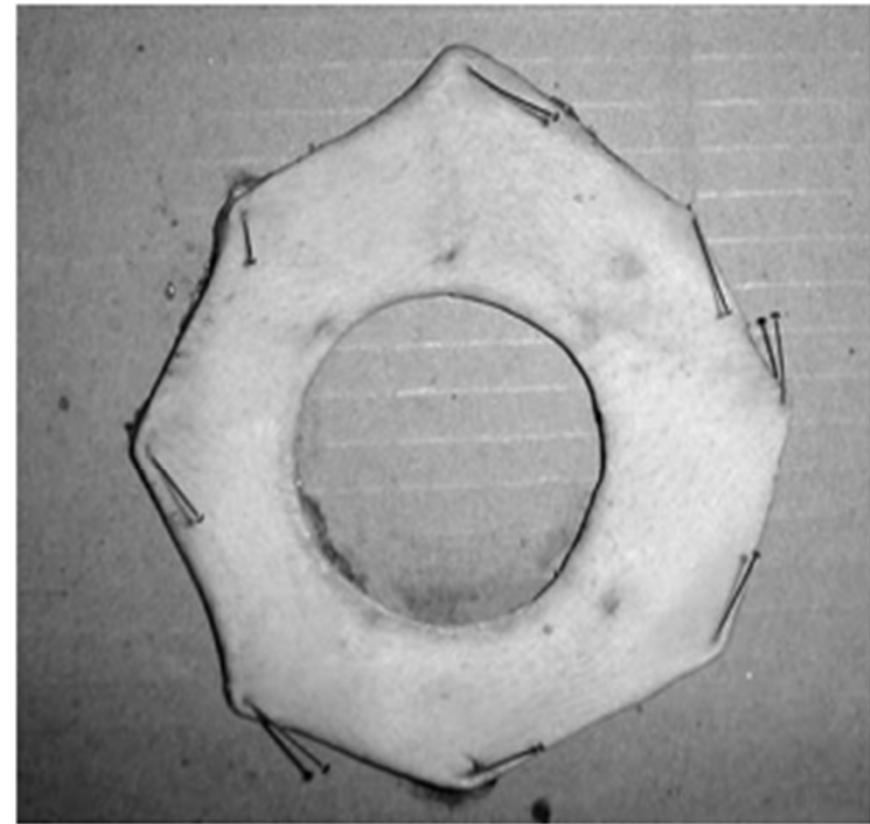
## Evaluation of Residual Glandular Tissue After Skin-Sparing Mastectomies

Renato Zocchio Torresan, PhD,<sup>1</sup> César Cabello dos Santos, PhD,<sup>1</sup> Hélio Okamura, PhD,<sup>2</sup>  
and Marcelo Alvarenga, PhD<sup>2</sup>

- Junho 2003 à Janeiro 2004
- 42 pacientes - Estádios I a IIIa
- Submetidas à SSM, onde foi demarcada margem pelo cirurgião com caneta
- Depois submetida à mastectomia, também demarcada margem pelo cirurgião



**FIG. 1.** Native breast skin with conventional mastectomy (dotted line) and skin-sparing mastectomy (continuous line) incisions.



**FIG. 2.** Skin flap after skin-sparing mastectomy stretched in a light cardboard.

- Unidades **ductais lobulares terminais** em **59,5%**, com associação significativa nos retalhos de pele mais espessos que 1 mm
- **Doença residual** encontrada em **9,5%** dos pacientes também com associação ao retalho de pele com mais de 5mm de espessura

## Analysis of skin flap thickness and residual breast tissue after mastectomy



- 501 casos
- Ressonância para avaliação de tecido residual após mastectomia, SSM e NSM



## Analysis of skin flap thickness and residual breast tissue after mastectomy

International Journal of  
**Radiation Oncology**  
biology • physics  
Official Journal of the American Society for Radiation Oncology

Table 1: Mean thickness (in mm) and frequency of RBT presence by point of measurement

	Point of measurement	N	Mean thickness (mm)	Presence of residual fibroglandular tissue (%)
Periphery	Inframammary fold	499	23.5	1.4
	Infraclavicular region	498	21.6	1.0
	Axillary tail	501	16.5	4.6
	Upper parasternal region	500	13.9	5.8
Central	Lower inner quadrant	501	10.4	12.6
	Upper inner quadrant	500	9.5	10.2
	Upper outer quadrant	501	9	6.8
	Intersection of inner quadrants	501	8	11.4
	Lower outer quadrant	501	7.4	6.8
	Areolar region	245	6.9	65.7
	Intersection of outer quadrants	501	6.6	6.4

## Analysis of skin flap thickness and residual breast tissue after mastectomy



Table 5: Multivariate analysis (binary logistic regression) for identification of independent predictors of presence of RBT

Residual breast tissue was identified in 29.9% of the cases: 21.3% of the therapeutic mastectomy cases and 51% of the NSM cases

Yes	0	1		
No	0.711	2.036	1.297 – 3.195	0.002
Constant	-3.561	0.028		0.089

TM, Total mastectomy; SSM, Skin-sparing mastectomy; NSM, Nipple-sparing mastectomy

# Quais são os critérios para RT adjuvante?

## Critérios

- Tumor > 5 cm
- > 3 LN positivos
- Invasão de parede torácica

*Boneti C, et al. J Am Coll Surg. 2011;212(4):686-93*

- Tumor > 4 cm
- > 3 LN positivos

*Romics L Jr, et al. Br J Surg. 2012;99(6):799-806*

- Tumor  $\geq$  5 cm
- LN positivo (s)

*Meretoja TJ, et al. Eur J Surg Oncol. 2007;33(10):1142-5*

## Sem critérios definidos

- 287 pacientes (T1=136; T2=96; T3=48; T4=7), 114 receberam RT

*Warren Peled, et al. Ann Surg Oncol. 2012;19(11):3402-9*

- 152 pacientes, 26 receberam RT

*Garwood ER, et al. Ann Surg. 2009;249(1):26-32*

- 60 pacientes (estádios I e II), 20 receberam RT

*Fersis N, et al. Breast. 2004;13(6):488-93*

- 799 pacientes (estádios I, II e III), 93 receberam RT

*Yi M, et al. Cancer. 2011;117(5):916-24*

*The Breast Journal*

ORIGINAL ARTICLE

## Postoperative Radiation Therapy after Nipple-Sparing or Skin-Sparing Mastectomy: A Survey of European, North American, and South American Practices

Gustavo Nader Marta, MD, PhD,<sup>\*</sup> Philip M. Poortmans, MD, PhD,<sup>†</sup>  
Thomas A. Buchholz, MD,<sup>‡</sup> and Tarek Hijal, MD<sup>§</sup>

*\*Hospital Sírio-Libanês and Instituto do Câncer do Estado de São Paulo (ICESP), Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil; <sup>†</sup>Radboud University Medical Center, Nijmegen, The Netherlands; <sup>‡</sup>University of Texas MD Anderson Cancer Center, Houston, Texas; <sup>§</sup>McGill University Health Centre, Montréal, Quebec, Canada*

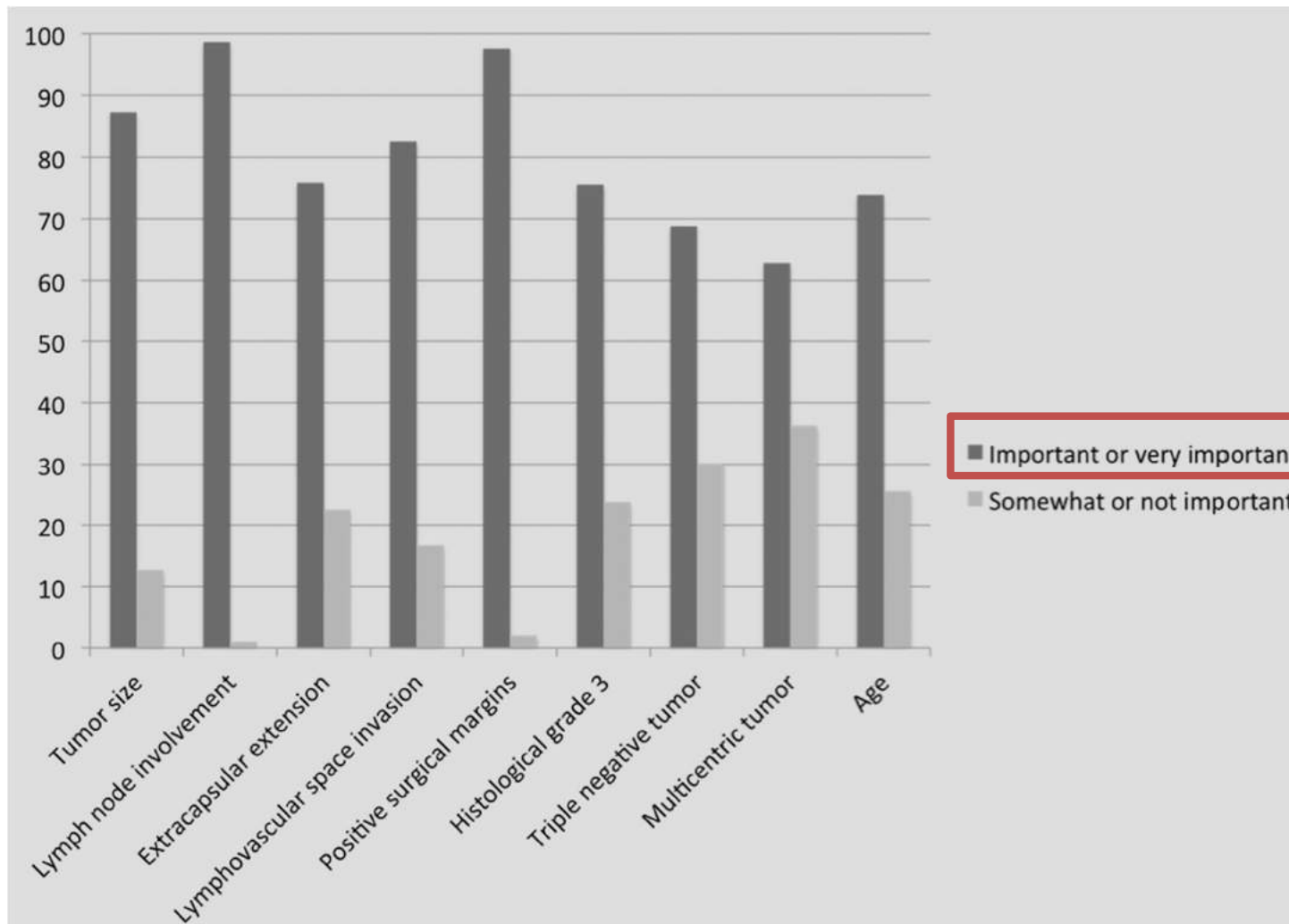


- 298 radio-oncologistas membros da ESTRO, ASTRO, CARO, ALATRO e SBRT foram convidados a participar do estudo entre Maio e Novembro de 2014.
- Um questionário com 22 perguntas foi criado para saber a opinião sobre a indicação de RTT após SSM e NSM.

## Demographic and practice characteristics of respondents (n= 298)

	RESPONDENTS			
	n	%		
<b>GENDER</b>				
Male	186	62.4		
Female	112	37.6		
<b>LOCATION</b>				
Asia	14	4.7		
Australia/New Zealand	2	0.7		
Europe	40	13.4		
North America	150	50.3		
South America	92	30.9		
<b>YEARS SINCE COMPLETING RESIDENCY</b>				
1 - 5 years	61	20.5		
5 - 10 years	58	19.5		
10 - 15 years	58	19.5		
> 15 years	121	40.6		
<b>SETTING OF PRIMARY PRACTICE</b>				
Large city (population > 500,000)	219	73.5		
Suburb or small city	75	25.2		
Rural	4	1.3		
			<b>NUMBER OF NEW BREAST CANCER CASES SEEN IN THE LAST 12 MONTHS</b>	
			1 to 5	4 1.3
			6 to 10	2 0.7
			11 to 20	7 2.3
			21 to 40	31 10.4
			42 to 60	35 11.7
			61 to 80	31 10.4
			81 to 100	33 11.1
			> 100	152 51.0
			None of the above	3 1.0
			<b>IS BREAST CANCER ONE OF YOUR SPECIALIZATIONS?</b>	
			Yes	271 90.9
			No	27 9.1
			<b>PERCENTAGE OF NEWLY DIAGNOSED BREAST CANCER PATIENTS DISCUSSED IN A MULTIDISCIPLINARY MEETING</b>	
			None	27 9.1
			Up to 10%	52 17.4
			11% - 25%	53 17.8
			26% - 50%	43 14.4
			51% - 90%	46 15.4
			> 90%	77 25.8

## Recurrence risk factors classified as major and minor elements



## Appropriate cut-off for recurrence risk factors (tumor size, lymph node involvement and age).

QUESTIONS	RESPONDENTS	
	n	%
<b>Considering tumor size as a recurrence risk factor, which size do you consider an appropriate cut-off?</b>		
2 cm	28	9.4
3 cm	42	14.1
5 cm	209	70.1
I don't know	0	2.7
Other	11	3.7
<b>Considering lymph node involvement as a recurrence risk factor, which extent of nodal involvement do you consider an appropriate cut-off?</b>		
1 - 3 lymph node (s)	193	64.8
> 3 lymph nodes	31	30.5
None of the above	12	4.0
I don't know	2	0.7
<b>Considering age as a recurrence risk factor, which age do you consider an appropriate cut-off?</b>		
35	40	13.4
40	105	35.2
50	89	29.9
60	13	4.4
70	9	3.0
None of the above	24	8.1
I don't know	13	4.4
Other	5	1.7

## Breast tissue evaluating

QUESTIONS	RESPONDENTS	
	n	%
After skin-sparing mastectomy / nipple-sparing mastectomy, residual breast tissue can be left behind. What amount of residual tissue do you consider as acceptable in the context of an oncologic surgery?		
<i>1 mm - 5 mm</i>	85	28.5
<i>6 mm - 10 mm</i>	32	10.7
<i>11 mm - 20 mm</i>	13	4.4
<i>&gt; 20 mm</i>	6	2.0
<i>None of the above</i>	56	18.8
<i>I don't know</i>	106	35.6
Do you consider it important to evaluate the residual breast tissue after skin-sparing mastectomy / nipple-sparing mastectomy through breast imaging?		
<i>Not important</i>	47	15.8
<i>Somewhat important</i>	73	24.5
<i>Important</i>	70	23.5
<i>Very important</i>	50	16.8
<i>I don't know</i>	58	19.5



## Breast tissue evaluating

QUESTIONS	RESPONDENTS	
	n	%
In your practice, how often do you request breast imaging to evaluate the residual breast tissue after skin-sparing mastectomy / nipple-sparing mastectomy (consider patients who underwent skin-sparing mastectomy / nipple-sparing mastectomy only)?		
<i>Never</i>	88	29.5
<i>Rarely</i>	104	34.9
<i>Sometimes</i>	58	19.5
<i>Often</i>	35	11.7
<i>Very often</i>	13	4.4
Which breast imaging modality do you consider more adequate to evaluate the residual breast tissue status after skin-sparing mastectomy / nipple-sparing mastectomy (select all that apply)?		
<i>Ultrasonography</i>	82	27.5
<i>Mammography</i>	55	18.5
<i>Magnetic resonance imaging</i>	206	69.1
<i>Computed tomography</i>	19	6.4
<i>None of the above</i>	36	12.1



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EJSO  
the Journal of Cancer Surgery

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Multidisciplinary international survey of post-operative  
radiation therapy practices after nipple-sparing or  
skin-sparing mastectomy

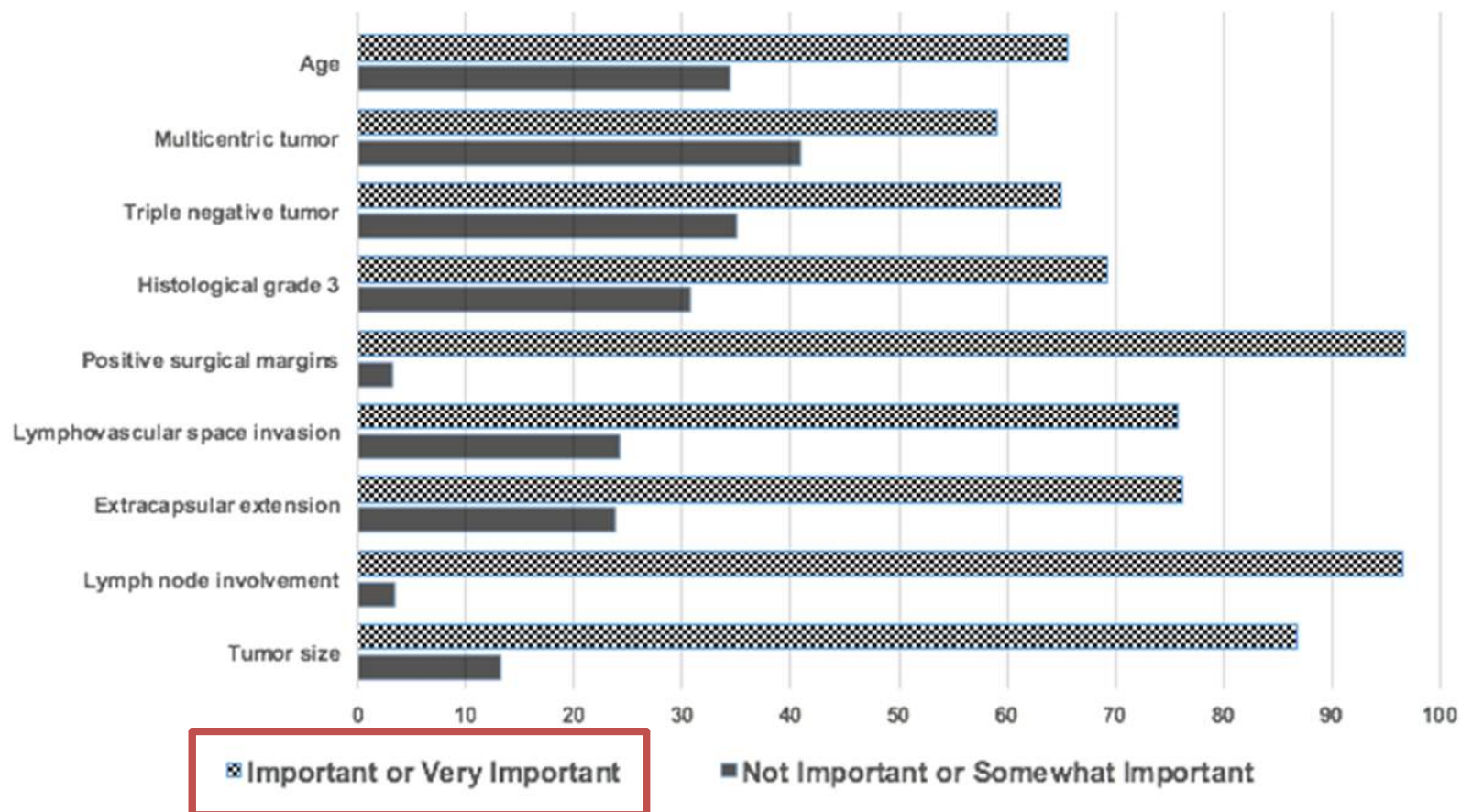
Gustavo Nader Marta <sup>a,\*</sup>, Philip Poortmans <sup>b</sup>, Alfredo C. de Barros <sup>c</sup>,  
José Roberto Filassi <sup>d</sup>, Ruffo Freitas Junior <sup>e</sup>, Riccardo A. Audisio <sup>f</sup>,  
Max Senna Mano <sup>g</sup>, Sarkis Meterissian <sup>h</sup>, Sarah M. DeSnyder <sup>i</sup>,  
Thomas A. Buchholz <sup>i</sup>, Tarek Hijal <sup>j</sup>

550 participantes

	RESPONDENTS	
	<i>n</i>	%
<b>MEDICAL SPECIALIZATION</b>		
<i>Radiation oncologist</i>	298	54.2
<i>Breast surgeon</i>	252	45.8



## Recurrence risk factors classified as major and minor elements (n=550)



## Recurrence risk factors after skin-sparing mastectomy and nipple-sparing mastectomy

Characteristic		Answer					P value
		Not important	Somewhat important	Important	Very important	I don't know	
		n (%)	n (%)	n (%)	n (%)	n (%)	
Tumor	RO	5 (1.5)	32 (10.7)	109 (36.6)	151 (50.7)	1 (0.3)	0.59
	BS	9 (3.6)	26 (10.3)	91 (36.1)	126 (50.0)	0 (0.0)	
Lymph node involvement	RO	2 (0.7)	1 (0.3)	26 (8.7)	268 (89.9)	1 (0.3)	<0.001
	BS	5 (1.2)	13 (5.2)	59 (23.4)	177 (70.2)	0 (0.0)	
Extracapsular extension	RO	16 (5.4)	51 (17.1)	89 (29.9)	137 (46.0)	5 (1.7)	0.80
	BS	18 (7.1)	44 (17.5)	76 (30.2)	112 (44.4)	2 (0.8)	
Lymphovascular space invasion	RO	3 (1.0)	47 (15.8)	142 (47.7)	104 (34.9)	2 (0.7)	<0.001
	BS	24 (9.5)	58 (23.0)	98 (38.9)	69 (27.4)	3 (1.2)	
Positive surgical margins	RO	0 (0.0)	6 (2.0)	35 (11.7)	256 (85.9)	1 (0.3)	0.147
	BS	4 (1.6)	8 (3.2)	29 (11.5)	211 (83.7)	0 (0.0)	
Histological grade 3	RO	11 (3.7)	60 (20.1)	160 (53.7)	65 (21.8)	2 (0.7)	<0.001
	BS	27 (10.7)	70 (27.8)	95 (37.7)	60 (23.8)	0 (0.0)	
Triple negative tumor	RO	19 (6.4)	71 (23.8)	134 (45.0)	71 (23.8)	3 (1.0)	<0.001
	BS	49 (19.4)	52 (20.6)	69 (27.4)	81 (32.1)	1 (0.4)	
Multicentric tumor	RO	40 (13.4)	68 (22.8)	101 (33.9)	86 (28.9)	3 (1.0)	0.16
	BS	46 (18.3)	70 (27.8)	57 (22.6)	79 (31.3)	0 (0.0)	
Age	RO	16 (5.4)	60 (20.1)	135 (45.3)	85 (28.5)	2 (0.0)	<0.001
	BS	40 (15.9)	72 (28.6)	97 (38.5)	43 (17.1)	0 (0.0)	

Note:

RO = Radiation oncologist; BS = Breast surgeon

n = number of patients; % = percentage

## Appropriate cut-off for recurrence risk factors (tumor size, lymph node involvement and age)

QUESTIONS	Radiation oncologist		Breast surgeon		P value
	n	%	n	%	
<b>Considering tumor size as a recurrence risk factor, which size do you consider an appropriate cut-off?</b>					0.244
1 cm	2	0.7	0	0.0	
2 cm	28	9.4	20	7.9	
3 cm	42	14.1	46	18.3	
4 cm	2	0.7	6	2.4	
<b>5 cm</b>	<b>209</b>	<b>70.1</b>	<b>172</b>	<b>68.3</b>	
None of the above	7	2.3	5	2.0	
I don't know	8	2.7	3	1.2	
<b>Considering lymph node involvement as a recurrence risk factor, which extent of nodal involvement do you consider an appropriate cut-off?</b>					<0.001
<b>1 - 3 lymph node (s)</b>	<b>193</b>	<b>64.8</b>	<b>81</b>	<b>32.1</b>	
<b>&gt; 3 lymph nodes</b>	<b>91</b>	<b>30.5</b>	<b>167</b>	<b>66.3</b>	
None of the above	12	4.0	3	1.2	
I don't know	2	0.7	1	0.4	
<b>Considering age as a recurrence risk factor, which age do you consider an appropriate cut-off?</b>					<0.001
35	40	13.4	40	15.9	
40	105	35.2	88	34.9	
50	89	29.9	40	15.9	
60	13	4.4	6	2.4	
70	9	3.0	8	3.2	
None of the above	29	9.7	56	22.2	
I don't know	13	4.4	14	5.6	

## Breast tissue evaluating

QUESTIONS	Radiation oncologist		Breast surgeon		P value
	n	%	n	%	
<b>After skin-sparing mastectomy / nipple-sparing mastectomy, residual breast tissue can be left behind. What amount of residual tissue do you consider as acceptable in the context of an oncologic surgery?</b>					<0,001
<b>1 mm - 5 mm</b>	85	28,5	138	54,8	
6 mm - 10 mm	32	10,7	53	21,0	
11 mm - 20 mm	13	4,4	5	2,0	
> 20 mm	6	2,0	0	0,0	
None of the above	56	18,8	51	20,2	
<b>I don't know</b>	106	35,6	5	2,0	
<b>Do you consider it important to evaluate the residual breast tissue after skin-sparing mastectomy / nipple-sparing</b>					<0.001
Not important	47	15,8	99	39,3	
Somewhat important	73	24,5	56	22,2	
Important	70	23,5	57	22,6	
Very important	50	16,8	30	11,9	
I don't know	58	19,5	10	4,0	





Contents lists available at [ScienceDirect](#)

## European Journal of Surgical Oncology

journal homepage: [www.ejso.com](http://www.ejso.com)



Correspondence

Reply to: Mastectomy skin flap thickness

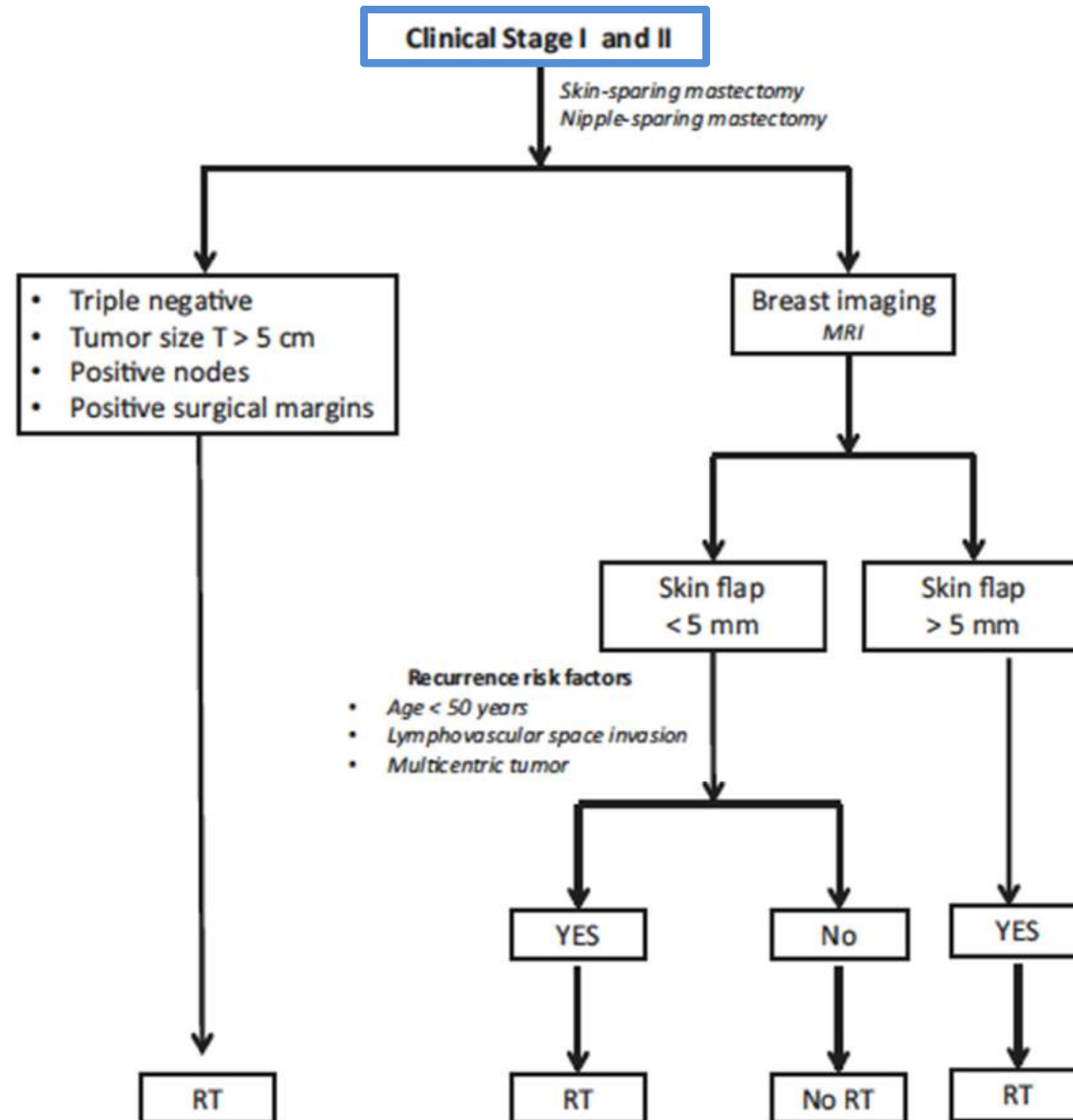


The optimal balance between oncologic outcome and necrosis of flaps is another important issue. Skin flap necrosis can occur after skin-sparing/nipple-sparing mastectomy and surgeons must resect therefore as much tissue as possible without compromising skin flap viability [6]. In this scenario, it is important to recognize that the more residual breast tissue is left after surgery, the higher the probability of requiring post-operative radiation therapy.

# Considerações finais

- **RT após SSM e NSM**
- Segurança oncológica (**SSM e NSM**): estudos retrospectivos e prospectivos de baixa qualidade
  - SSM e NSM = cirurgia conservadora ou mastectomia radical?
- Incertezas sobre as indicações da RT pós operatória (estádios I e II)
  - Considerar fatores de risco de recorrência
  - Avaliação formal do parênquima mamário residual
- Discussão multidisciplinar

# Considerações finais





# Radioterapia após mastectomia 1 a 3 LN positivos

- Estudo da Columbia Britânica
- N=318 (N+)
- Mastectomia + dissecação axilar + QT +/- RT
- Seguimento: 21 anos

<b>Sobrevida</b>	<b>Sem RT %</b>	<b>RT %</b>	<b>P</b>
Livre de eventos	25	35	0,009
Livre de metástase	31	48	0,004
Livre de falha loco-regional	74	90	0,002
Livre de câncer de mama	38	53	0,008
Global	37	47	0,03

- Estudos Dinamarqueses
- N=1460, estádios II e III (LN +, T>5cm, invasão de pele ou músculo)
- Mastectomia, seguida de CMF (TMX 30 mg, 1 ano) +/- RT
- Seguimento = 18 anos

<b>Desfecho</b>	<b>Sem RT %</b>	<b>Com RT %</b>	<b>P</b>
Falha locorregional	35 (32)	8 (9)	<0,001
SV livre de doença	34 (24)	48 (36)	<0,001
Global	45 (36)	54 (45)	<0,001

# Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials

*EBCTCG (Early Breast Cancer Trialists' Collaborative Group)\**

www.thelancet.com Published online March 19, 2014 [http://dx.doi.org/10.1016/S0140-6736\(14\)60488-8](http://dx.doi.org/10.1016/S0140-6736(14)60488-8)

Trials randomizados iniciados 1964-86

Pacientes

Trials randomizados iniciados 1964-86

Pacientes



Mastectomia

Trials randomizados iniciados 1964-86

Pacientes

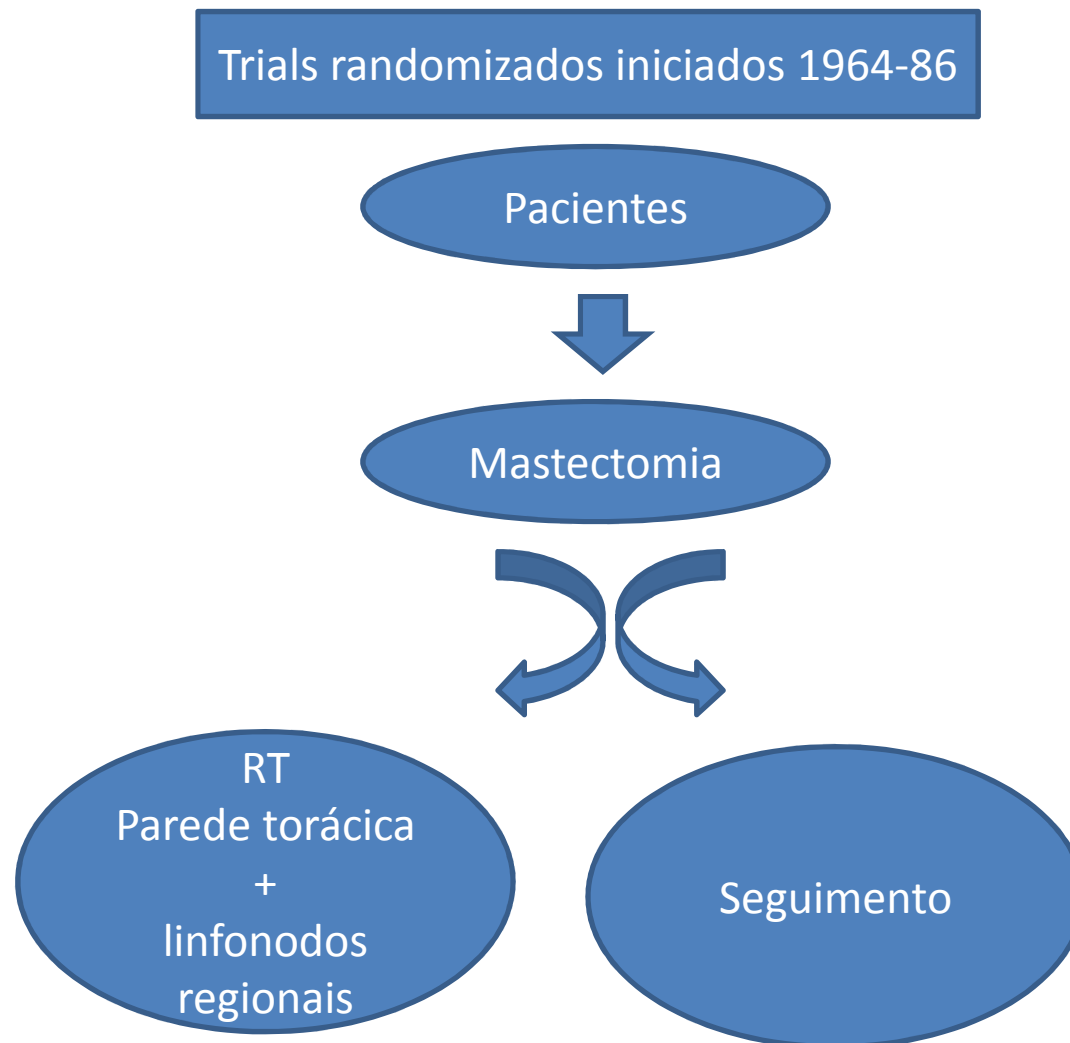


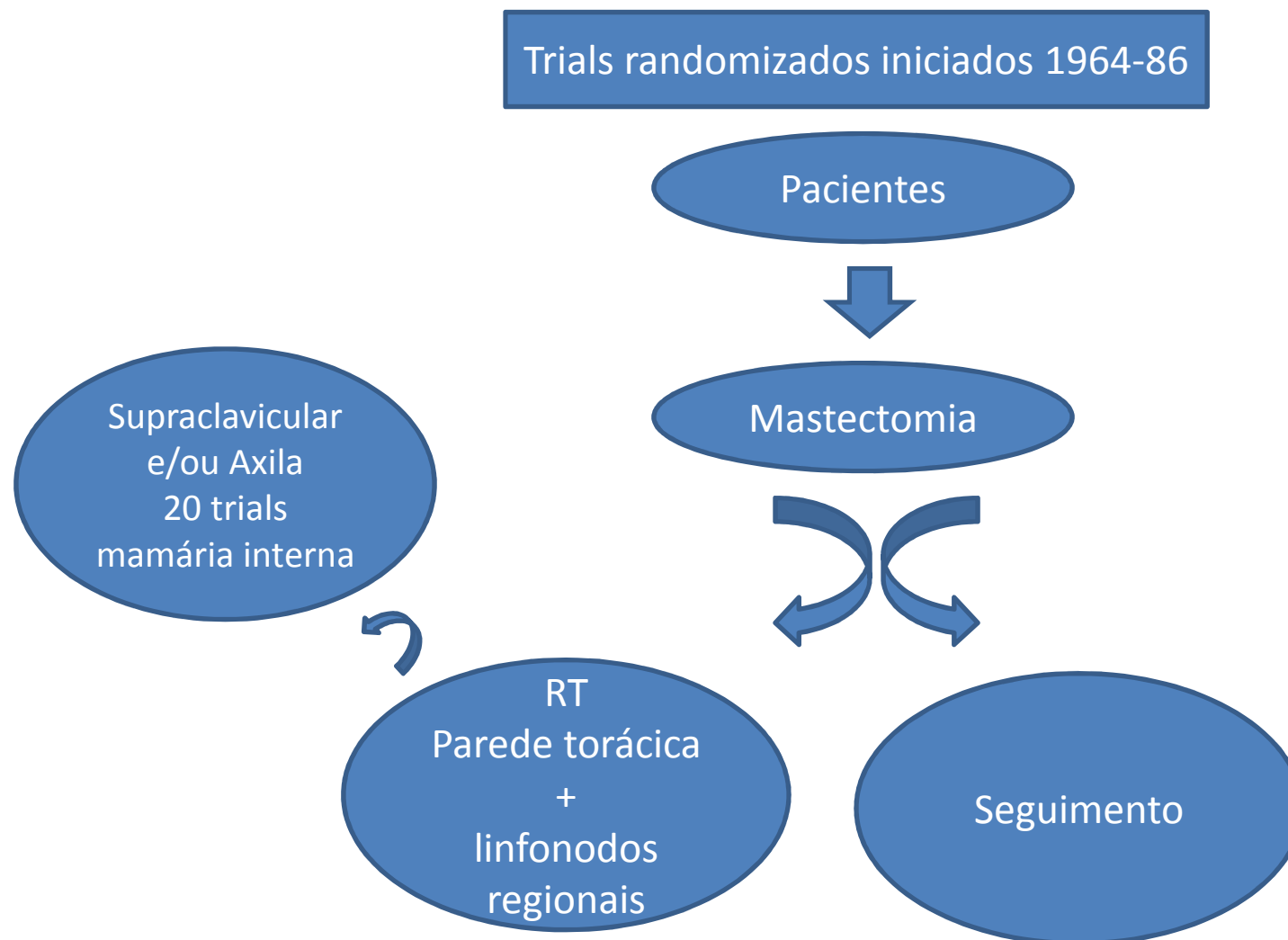
Mastectomia



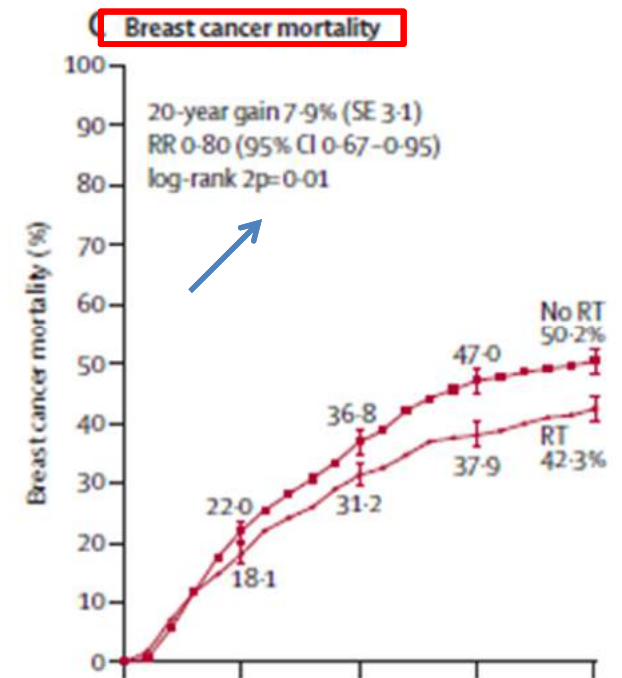
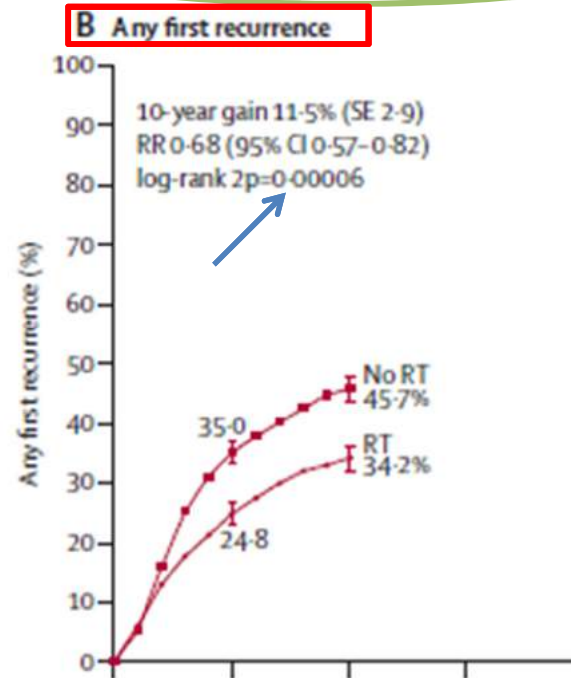
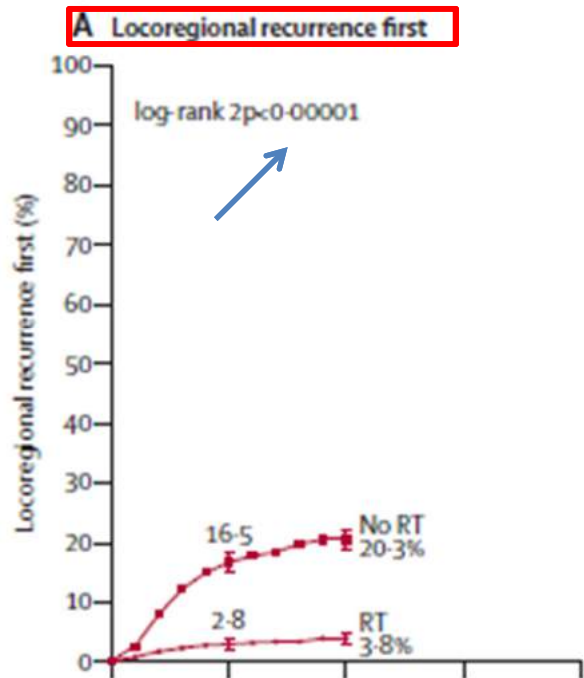
Seguimento



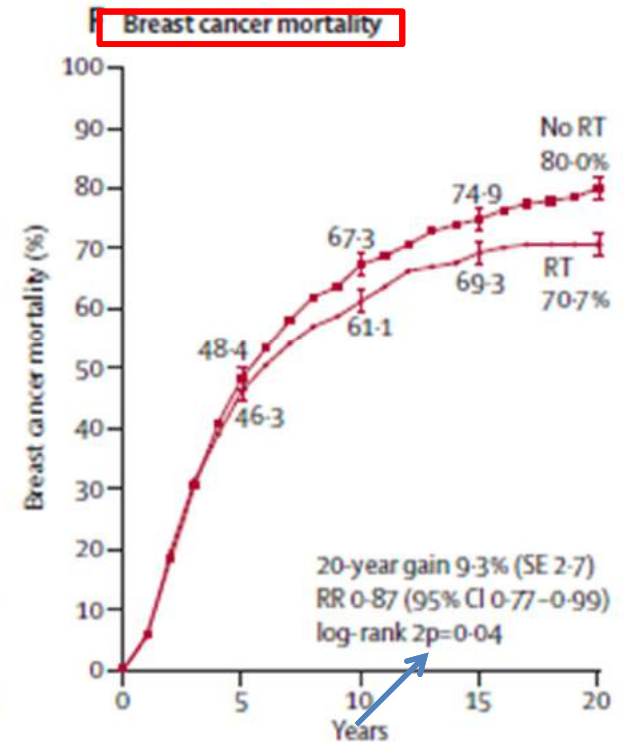
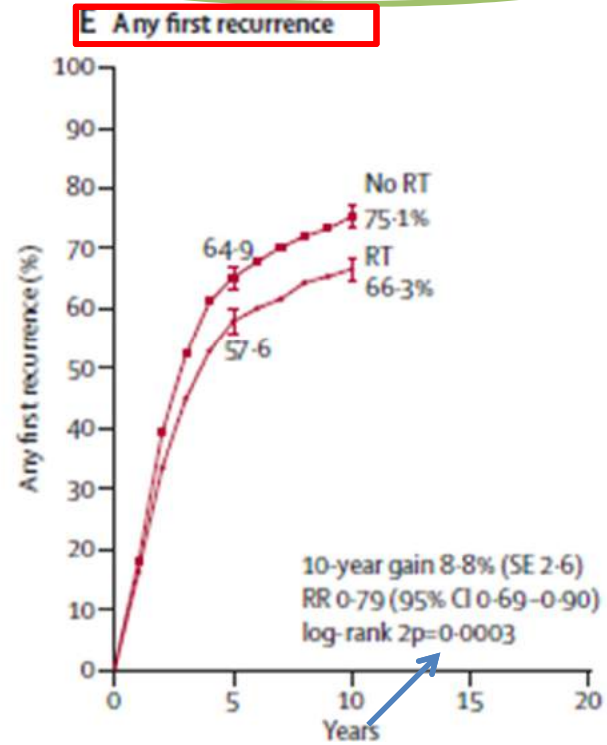
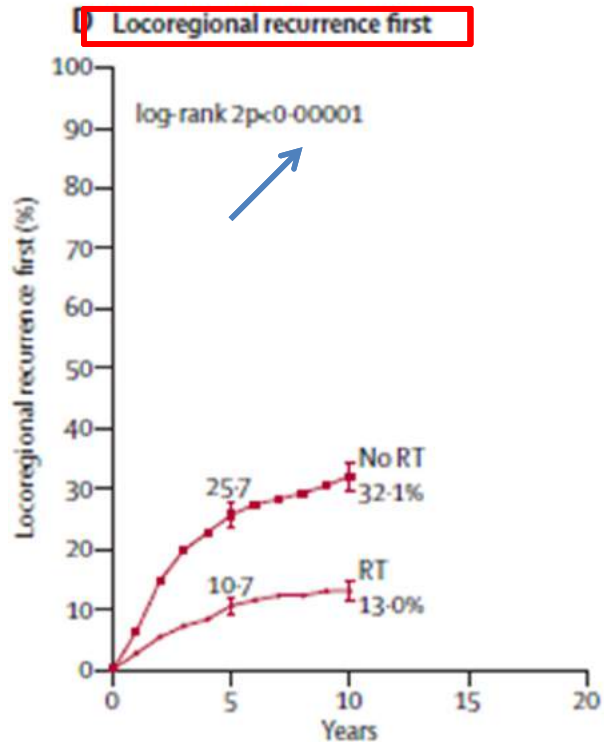


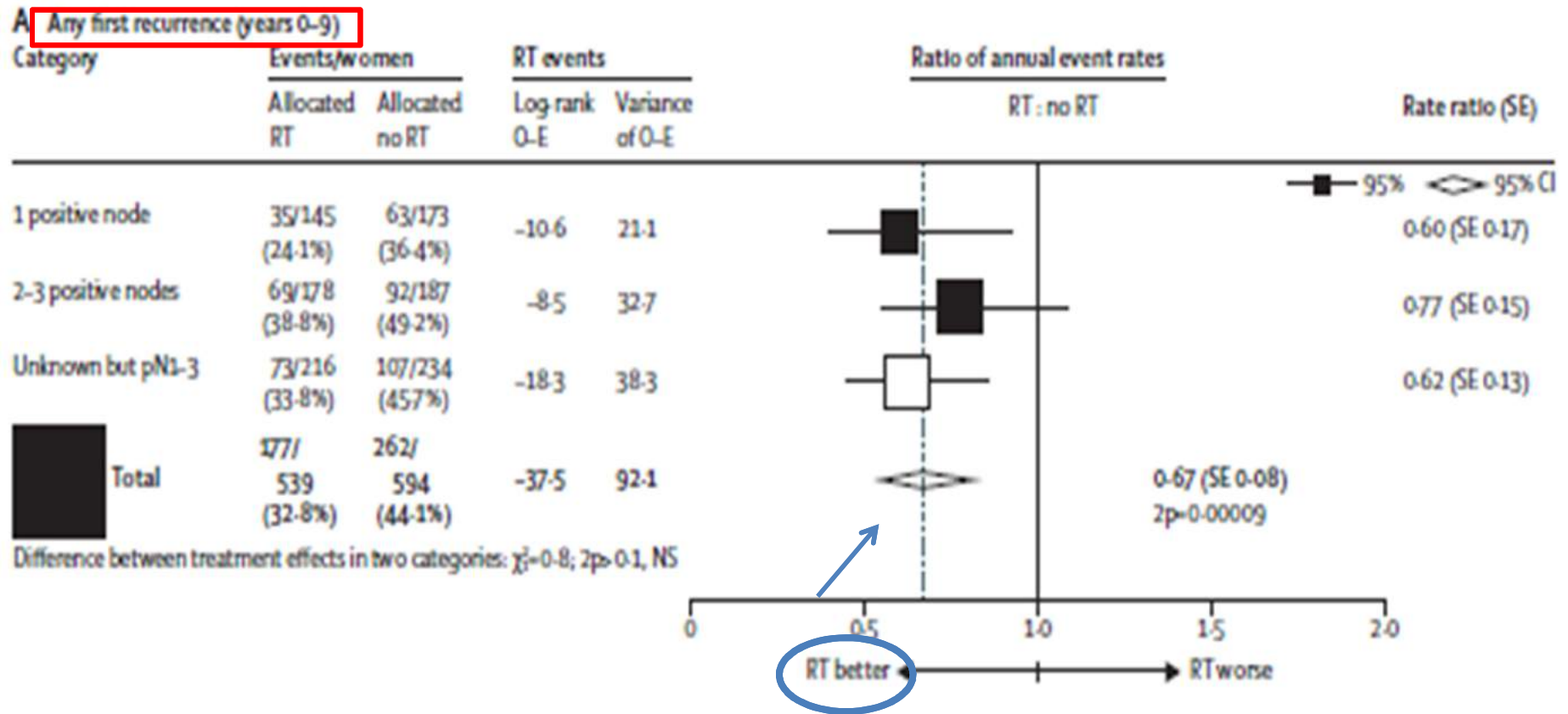


1314 pN1-3 women with Mast+AD

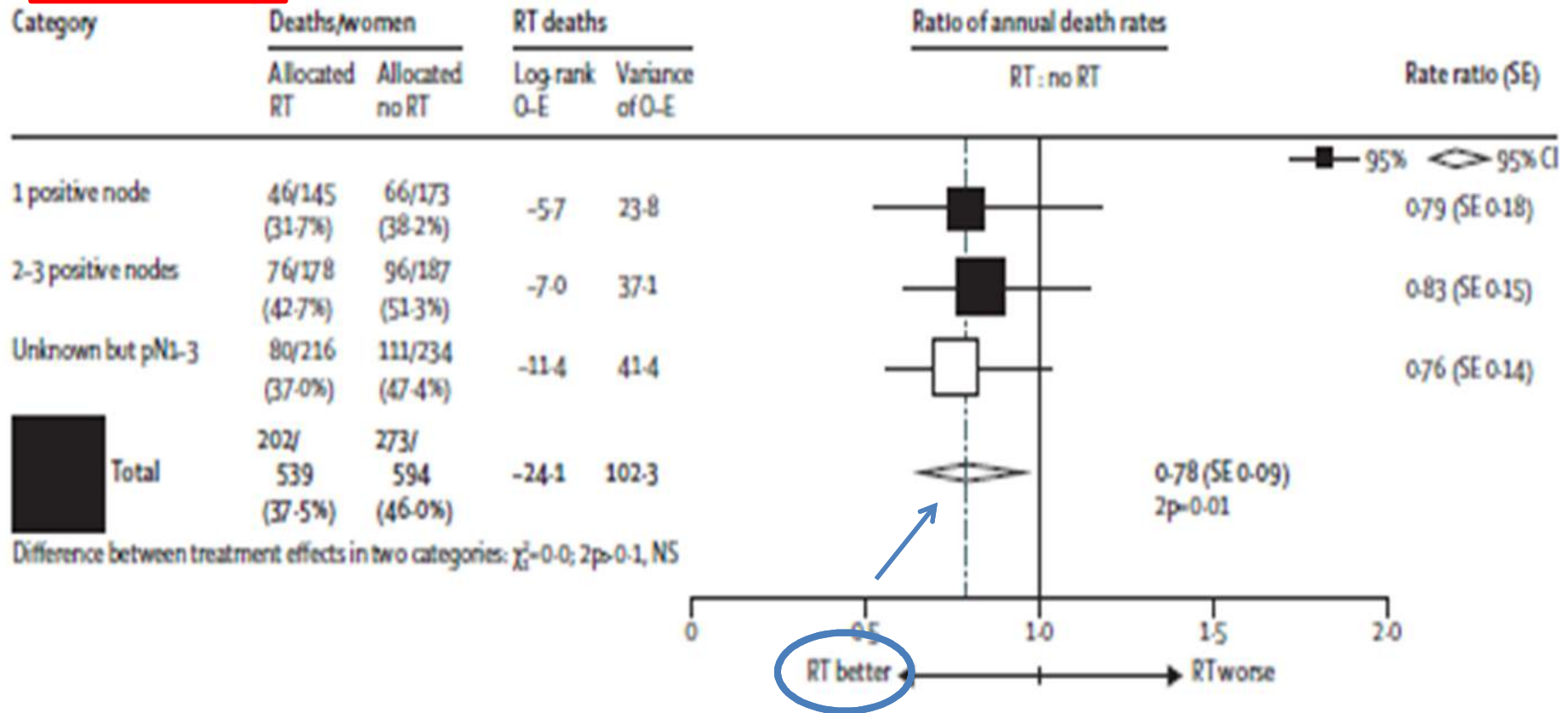


1772 pN4+ women with Mast+AD

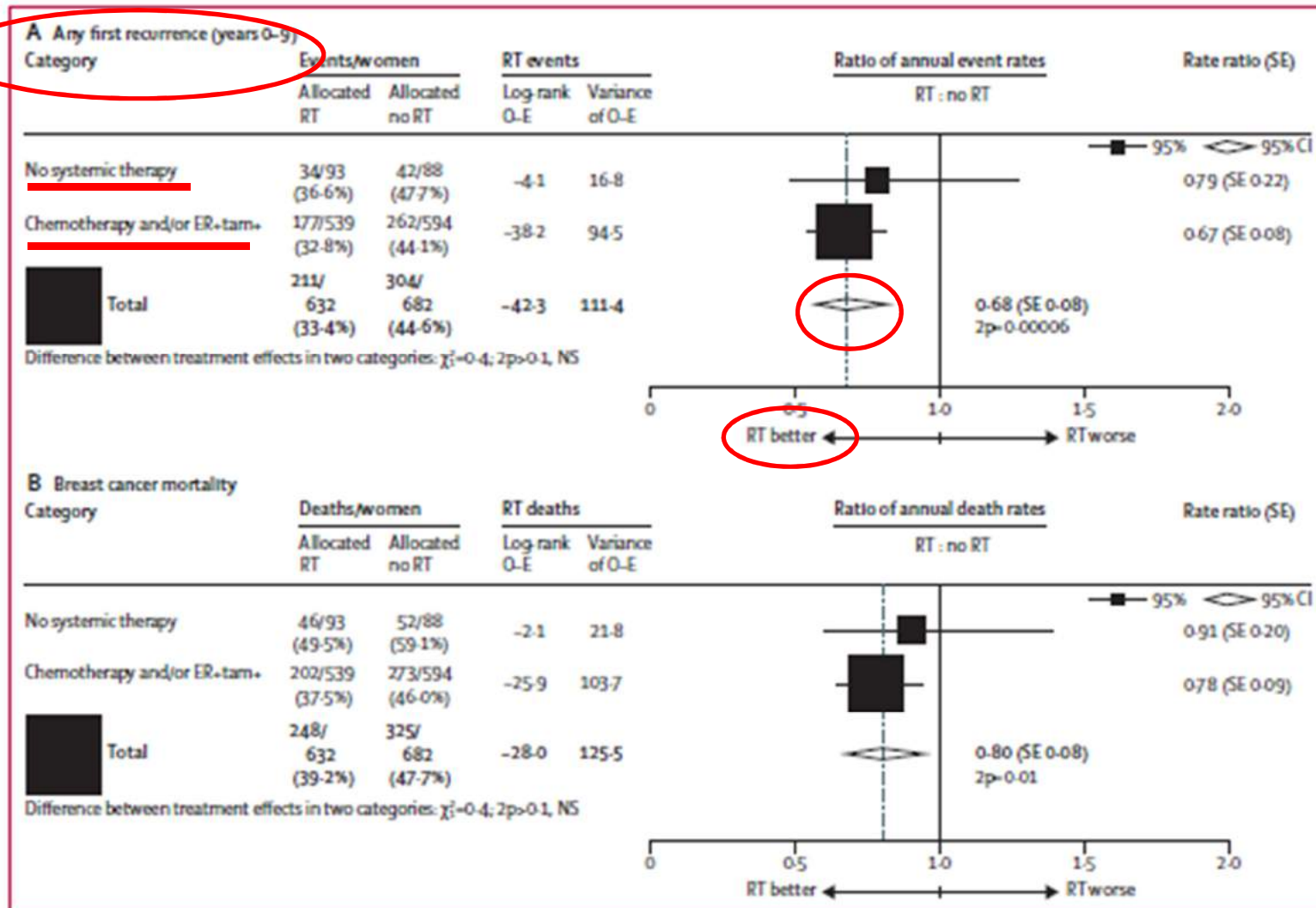




**B Breast cancer mortality**







**Figure 4: Effect of radiotherapy (RT) after mastectomy and axillary dissection on overall recurrence during years 0-9 and on breast cancer mortality for the entire follow-up in 1314 women with one to three pathologically positive nodes, according to whether or not they were in trials in which systemic therapy was given to both randomised treatment groups**

Chemotherapy was usually cyclophosphamide, methotrexate, and fluorouracil. ER-negative women in trials in which tamoxifen was given to both groups are included in the "no systemic" category. ER= oestrogen receptor. tam= tamoxifen. NS= not significant. SE= standard error.



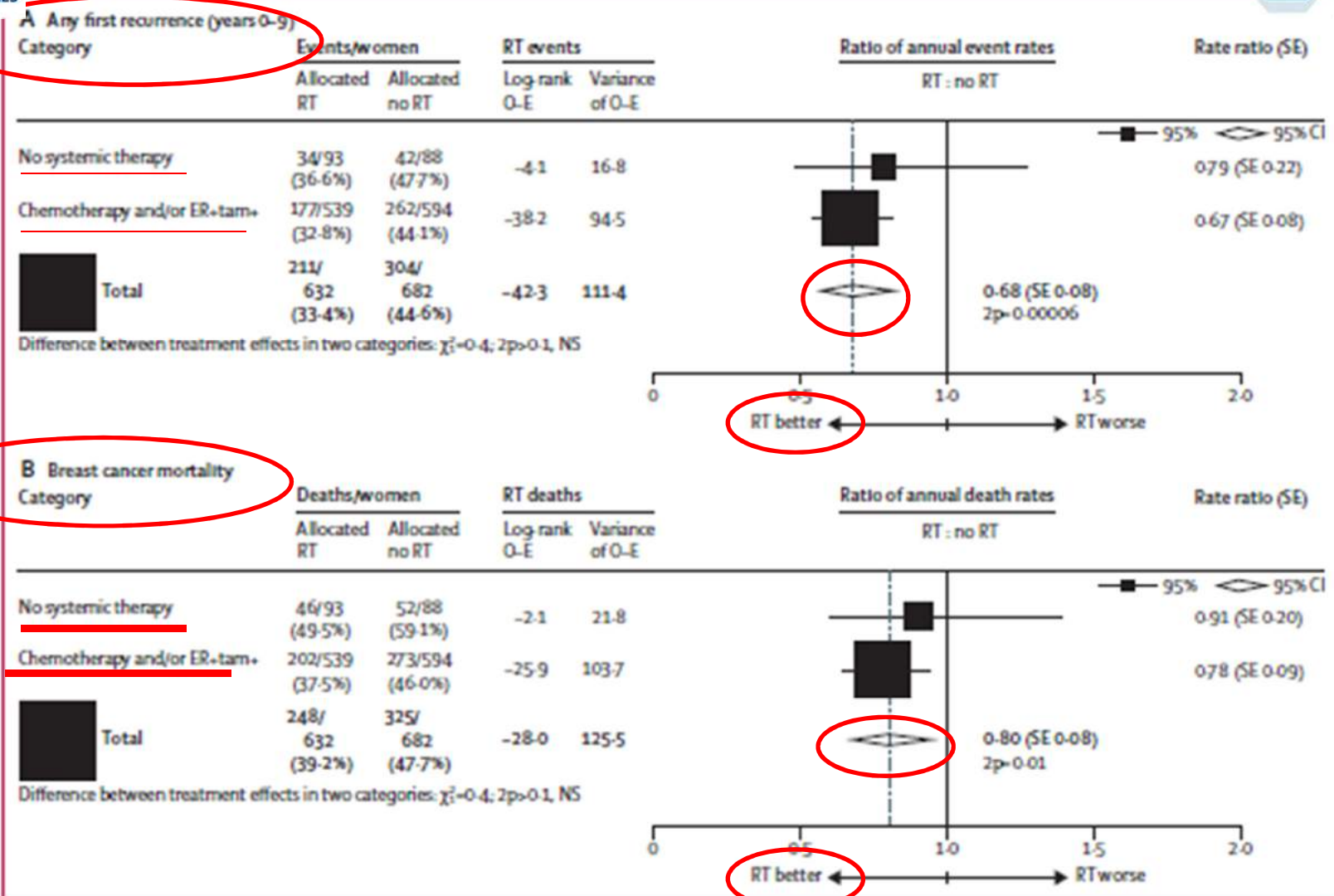
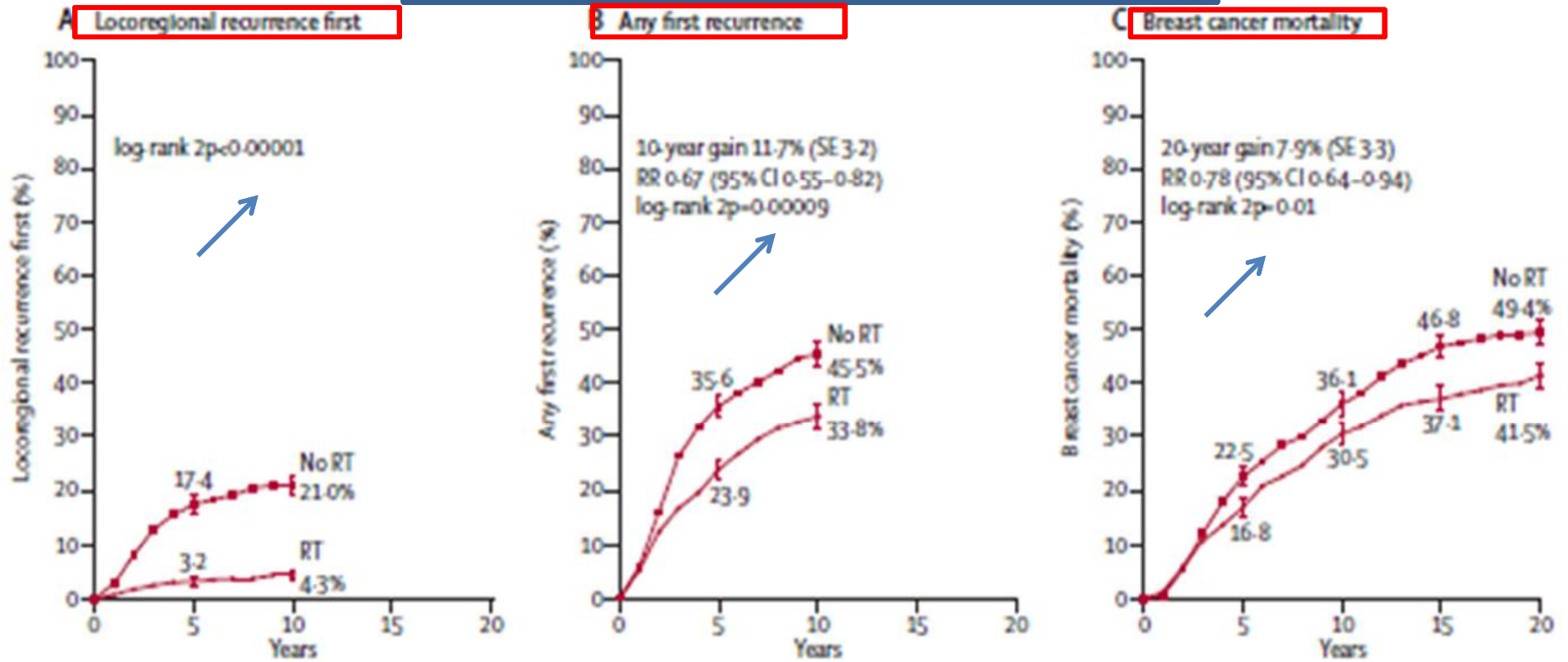


Figure 4: Effect of radiotherapy (RT) after mastectomy and axillary dissection on overall recurrence during years 0-9 and on breast cancer mortality for the entire follow-up in 1314 women with one to three pathologically positive nodes, according to whether or not they were in trials in which systemic therapy was given to both randomised treatment groups

Chemotherapy was usually cyclophosphamide, methotrexate, and fluorouracil. ER-negative women in trials in which tamoxifen was given to both groups are included in the "no systemic" category. ER= oestrogen receptor. tam= tamoxifen. NS= not significant. SE= standard error.

1133 pN1-3 women with Mast+AD and systemic therapy



# Reflexões

- Maioria dos estudos: QT = CMF (sem taxano)
- Sem terapia anti-Her
- Técnica antigas de RT

# THE LANCET

Volume 383, Issue 9935, 21–27 June 2014, Pages 2104-2106

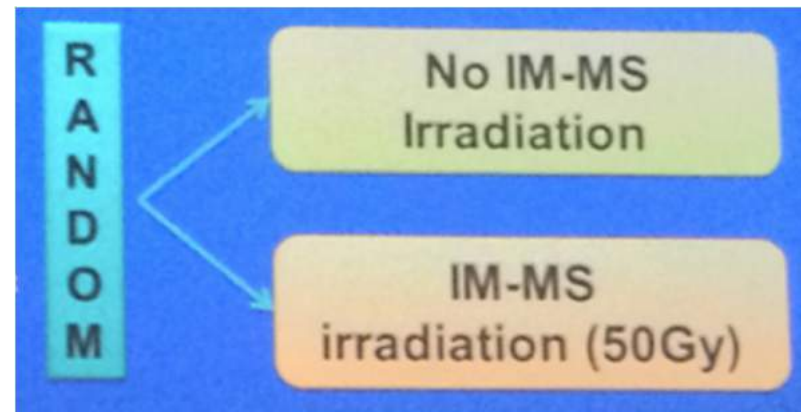


**Postmastectomy radiation in breast cancer with one to three involved lymph nodes: ending the debate**

*Prof. Philip Poortmans*

## Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer

- 4004 pacientes
- Estádio I, II ou III
- Tumor central ou medial (N0/N+) ou N +
- 23,9% mastectomia

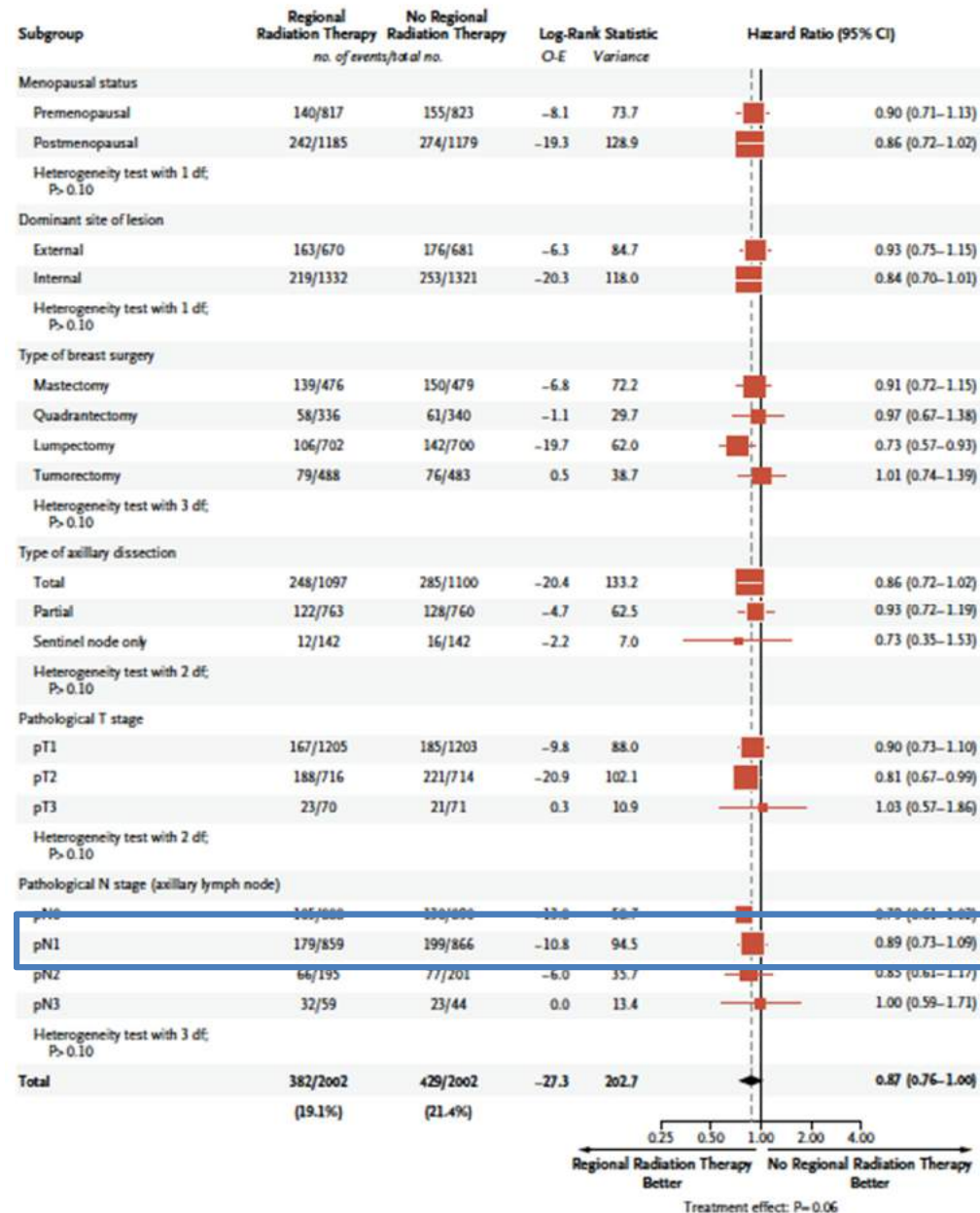


## Seguimento 10,9 anos

	COM RT	SEM RT	HR	p
Sobrevida global	82,3%	80,7%	0,87	0,056
Sobrevida livre de doença	72,1%	69,1%	0,89	<b>0,044</b>
Sobrevida livre de metástases	78%	75%	0,86	<b>0,02</b>
Toxicidade Pulmonar	4,3%	1,3%		<b>0,0001</b>
Cardíaca	0,4%	0,3%		NS

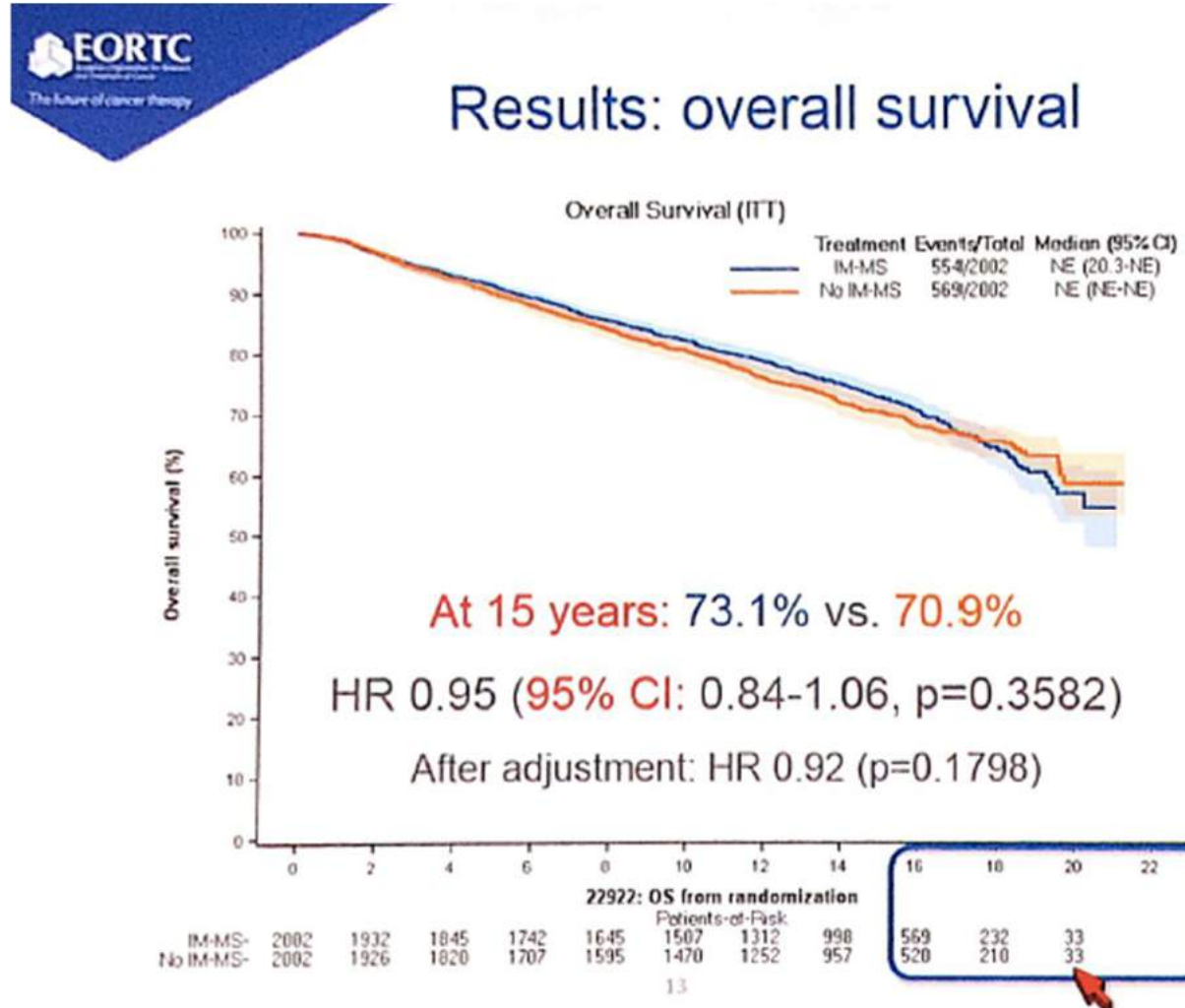


# Hazard Ratio for Death, According to Subgroups.





# EORTC – ATUALIZAÇÃO 15 anos

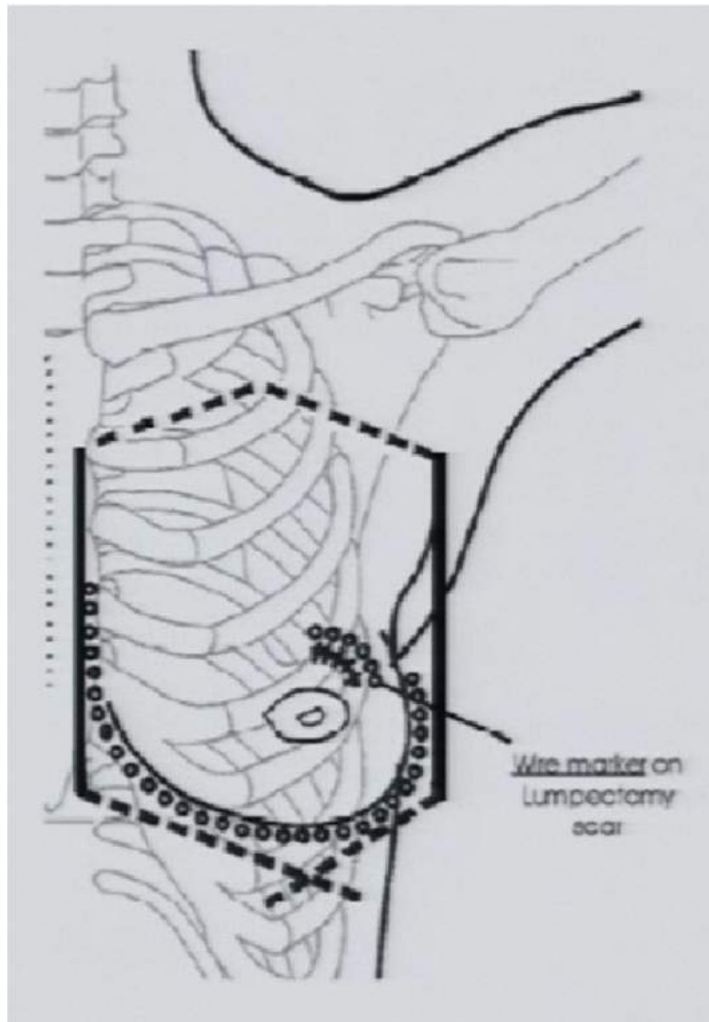


## Regional Nodal Irradiation in Early-Stage Breast Cancer

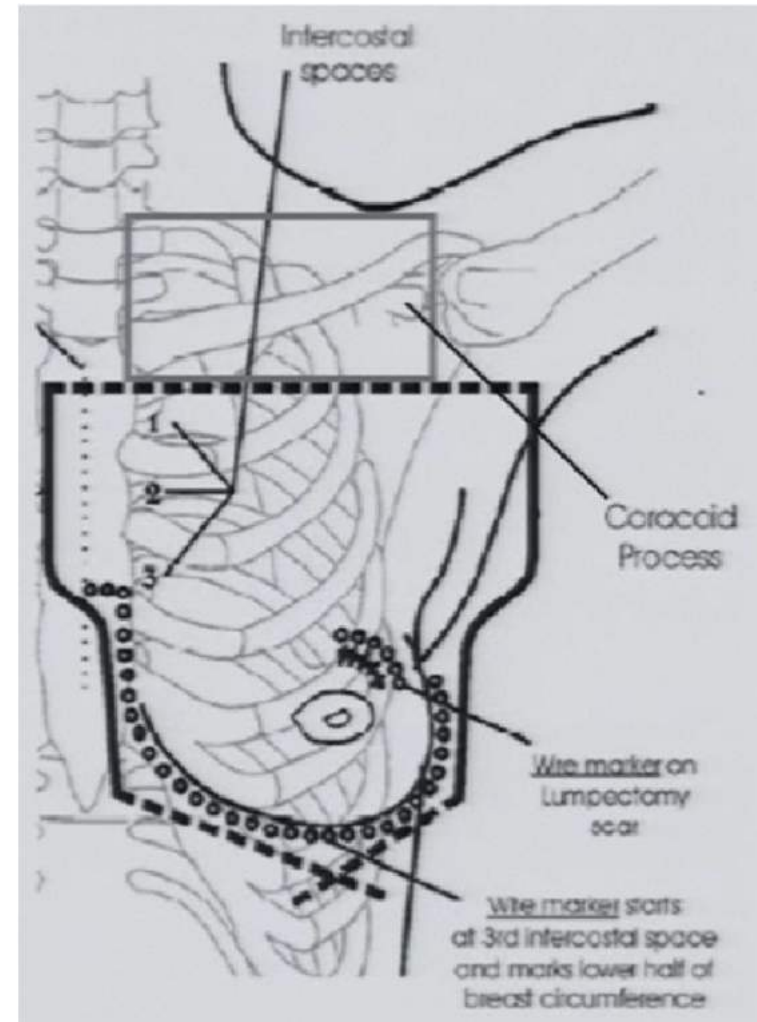
Timothy J. Whelan, B.M., B.Ch., Ivo A. Olivotto, M.D., Wendy R. Parulekar, M.D., Ida Ackerman, M.D., Boon H. Chua, M.B., B.S., Ph.D., Abdenour Nabid, M.D., Katherine A. Vallis, M.B., B.S., Ph.D., Julia R. White, M.D., Pierre Rousseau, M.D., Andre Fortin, M.D., Lori J. Pierce, M.D., Lee Manchul, M.D., Susan Chafe, M.D., Maureen C. Nolan, M.D., Peter Craighead, M.D., Julie Bowen, M.D., David R. McCready, M.D., Kathleen I. Pritchard, M.D., Karen Gelmon, M.D., Yvonne Murray, B.Sc., Judy-Anne W. Chapman, Ph.D., Bingshu E. Chen, Ph.D., and Mark N. Levine, M.D., for the MA.20 Study Investigators\*

- 1832 pacientes
- LN positivos
- LN negativos
  - Tumores > 5 cm
  - Tumores > 2 cm e < 10 LN removidos
    - Receptores hormonais negativos
    - Grau III
    - Invasão angiolinfática
- **Cirurgia conservadora**
  - BLS ou esvaziamento axilar

## MA.20 – Desenho do estudo

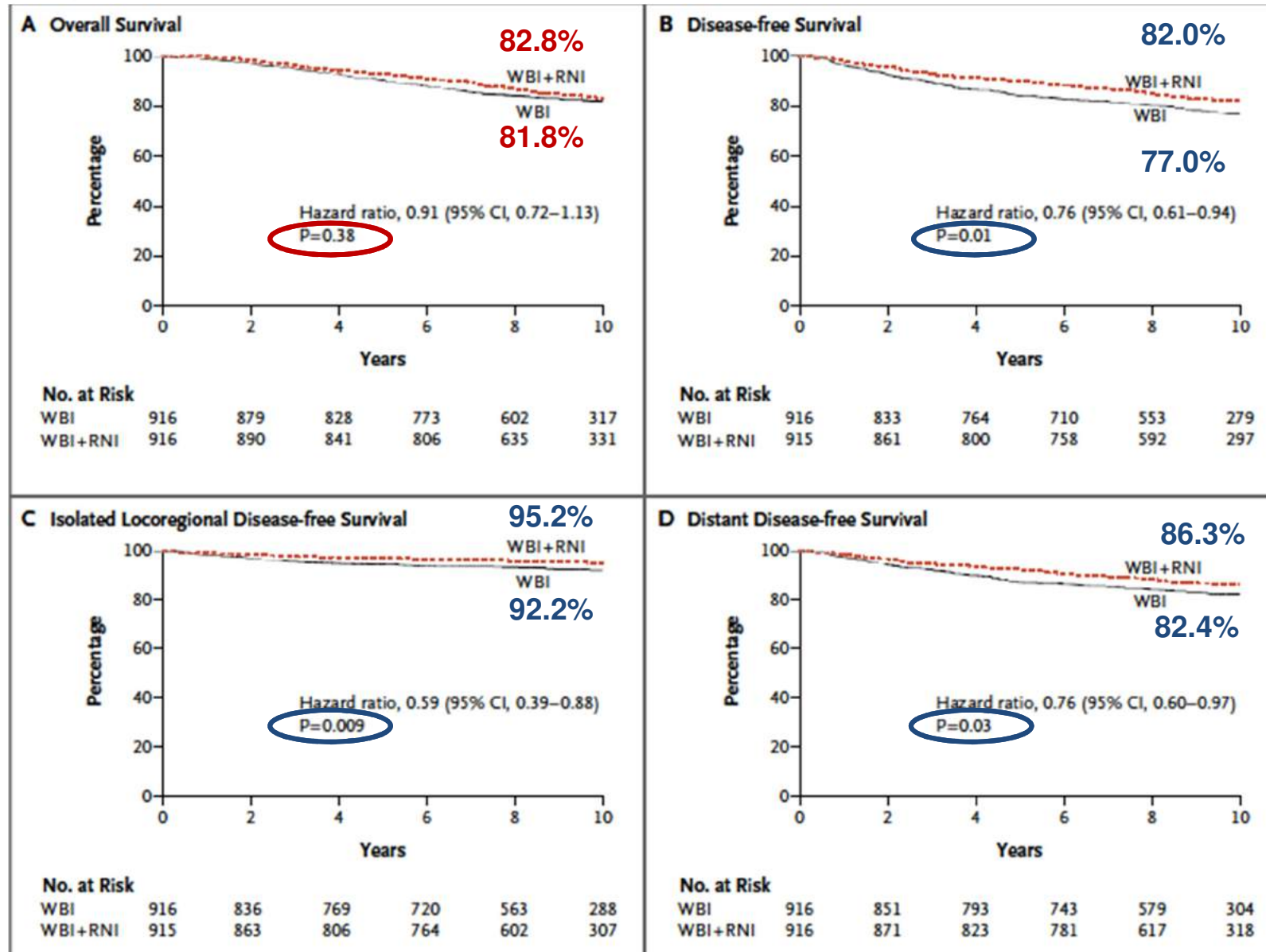


VS



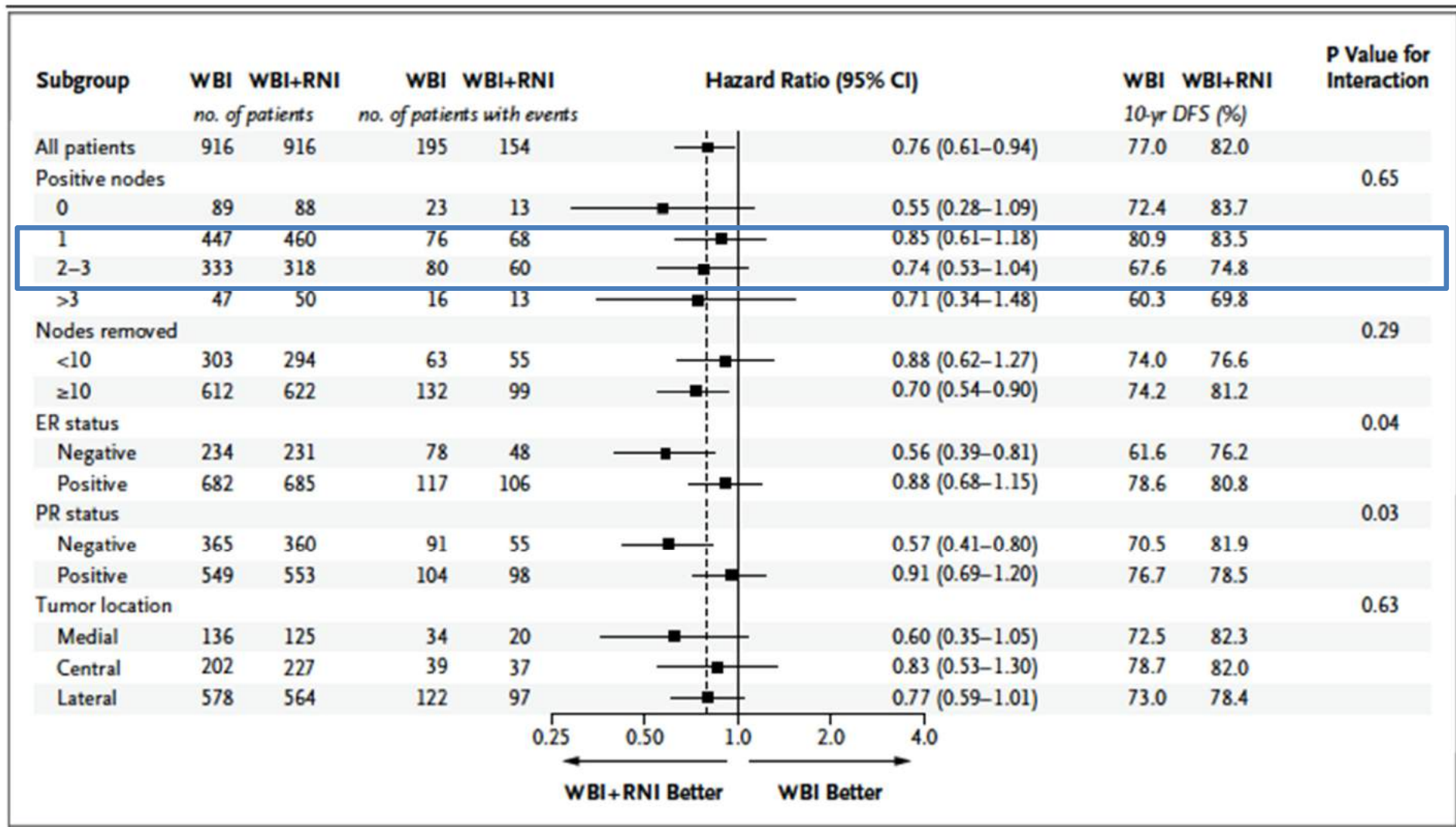
**Table 1. Characteristics of the Patients at Baseline.\***

Characteristic	WBI (N= 916)	WBI+RNI (N= 916)
Median age (range) — yr	53 (26–84)	54 (29–84)
Patients who underwent initial sentinel-lymph-node biopsy — no. (%)†	357 (39.0)	360 (39.3)
No. of axillary nodes removed		
Median (interquartile range)	12 (8–16)	12 (9–16)
1–9 — no. (%)	303 (33.1)	294 (32.1)
≥10 — no. (%)	612 (66.8)	622 (67.9)
No. of positive axillary nodes — no. (%)		
0	89 (9.7)	88 (9.6)
1	447 (48.8)	460 (50.2)
2	233 (25.4)	209 (22.8)
3	100 (10.9)	109 (11.9)
>3	85,1%	84,9%





## Disease-free Survival at 10 Years, According to Subgroup





## Expert Review of Anticancer Therapy

ISSN: 1473-7140 (Print) 1744-8328 (Online) Journal homepage: <http://www.tandfonline.com/loi/iery20>

# Postoperative nodal irradiation in breast cancer patients with 1 to 3 axillary lymph nodes involved: the debate continues...

Gustavo Nader Marta & Fabio Ynoe de Moraes



## Postmastectomy Radiotherapy: An American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology Focused Guideline Update

**Table 2.** LRF Rates Without RT After Modified Radical Mastectomy and Chemotherapy (with or without endocrine therapy) in Modern Series of Patients With pT1-2N1 Breast Cancer With Median Follow-Up of  $\geq$  5 Years

Institution	Accrual Dates	No. of Patients	Median Follow-Up (months)	Measure	Rate (%)
MDACC <sup>6</sup>	1975-1994	466	116	10-year actuarial	14
ECOG <sup>7</sup>	1978-1987	1,018	145	10-year actuarial	13
NSABP <sup>8</sup>	1984-1994	2,957	133	10-year actuarial	13
BCCA <sup>9</sup>	1989-1997	821	92	10-year actuarial	17
Ankara, Turkey <sup>10</sup>	1990-2004	326	70	Crude	4
MGH <sup>11</sup>	1990-2004	165	84	10-year actuarial	11
Shikoku, Japan <sup>12</sup>	1990-2002	248	82	8-year actuarial	5*
Kaohsiung, Taiwan <sup>13</sup>	1990-2008	155	102	10-year actuarial	11†
Seoul, Korea <sup>14</sup>	1992-2004	401	68	10-year actuarial	20†
CALGB 9344 <sup>15</sup>	1994-1997	254	67	Crude	8
MSKCC <sup>16</sup>	1995-2006	924	84	5-year actuarial	4†
Tampa, FL <sup>17</sup>	1996-2007	204	66	Crude	10
EIO <sup>18</sup>	1997-2001	262	120	10-year actuarial	10*
MDACC <sup>19</sup>	1997-2002	266	90	10-year actuarial	4
Cleveland Clinic <sup>20</sup>	2000-2007	271	62	5-year actuarial	9†
MDACC <sup>21</sup>	2000-2007	385	84	10-year actuarial	7
Tianjin, China <sup>22</sup>	2001-2005	368	86	8-year actuarial	11

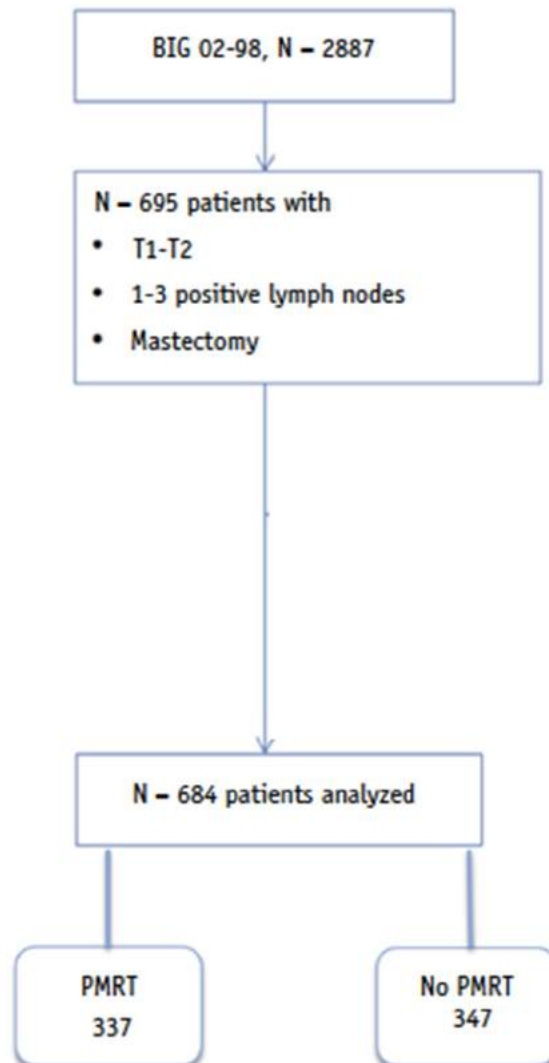
## Postmastectomy Radiotherapy: An American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology Focused Guideline Update

### Recommendations

The panel unanimously agreed that available evidence shows that PMRT reduces the risks of locoregional failure (LRF), any recurrence, and breast cancer mortality for patients with T1-2 breast cancer with one to three positive axillary nodes. However, some subsets of these patients are likely

to have such a low risk of LRF that the absolute benefit of PMRT is outweighed by its potential toxicities. In addition, the acceptable ratio of benefit to toxicity varies among patients and physicians.

## Postmastectomy Radiation Therapy in Women with T1-T2 Tumors and 1 to 3 Positive Lymph Nodes: Analysis of the Breast International Group 02-98 Trial



BIG 02-98 trial: ECR

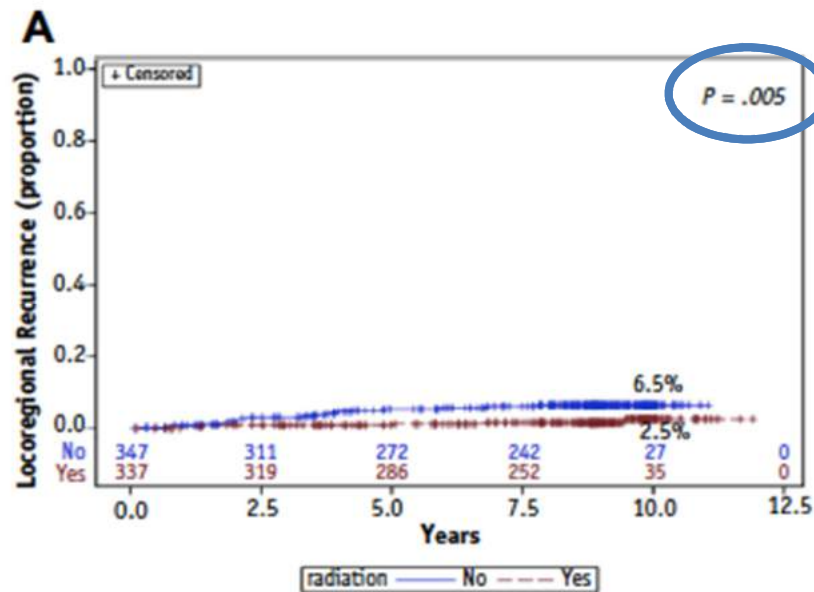
Antraciclina +/- taxano

PMRT: preferência institucional

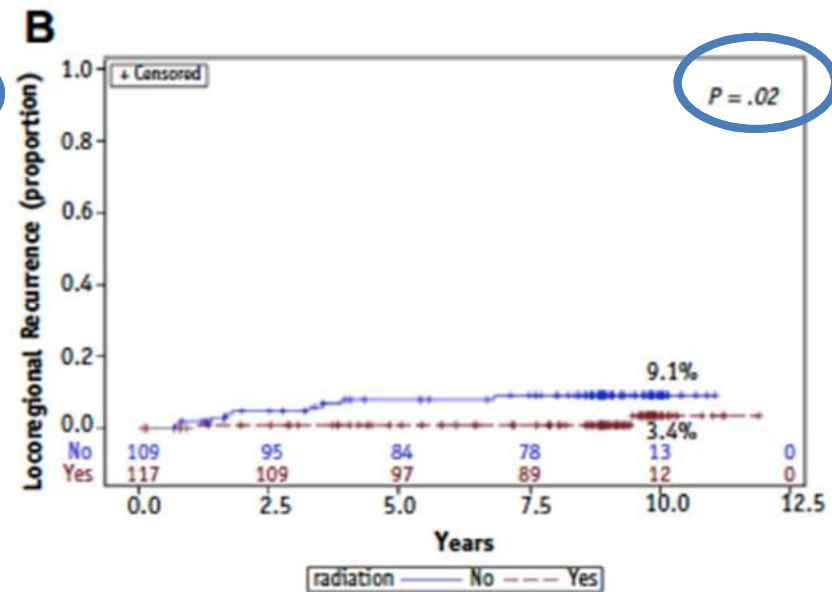


# Postmastectomy Radiation Therapy in Women with T1-T2 Tumors and 1 to 3 Positive Lymph Nodes: Analysis of the Breast International Group 02-98 Trial

Recorrência locorregional

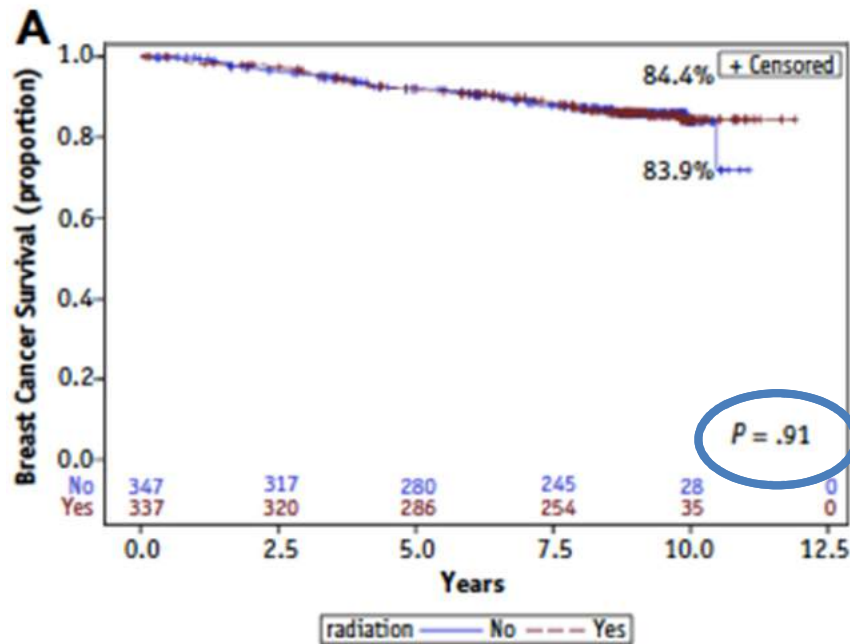


Recorrência locorregional – sem taxano

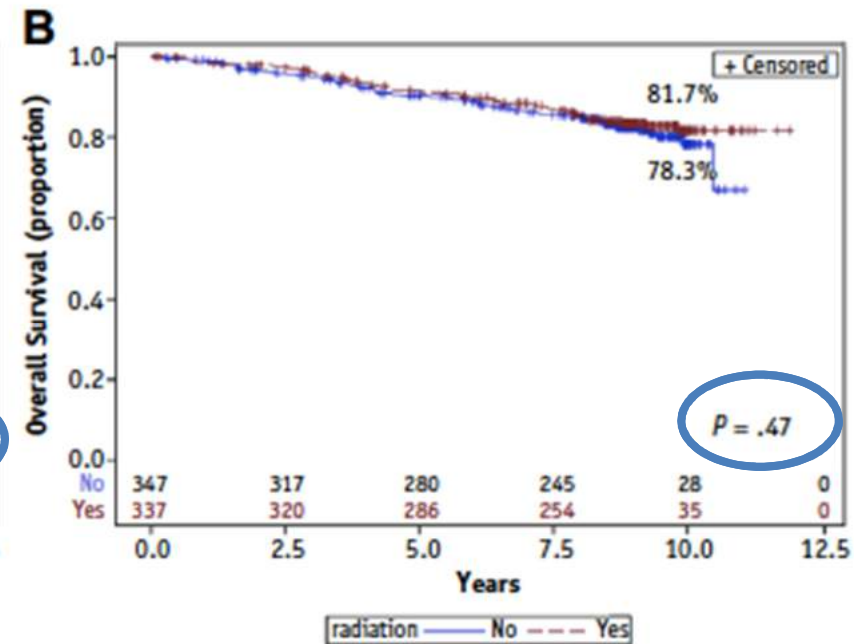


# Postmastectomy Radiation Therapy in Women with T1-T2 Tumors and 1 to 3 Positive Lymph Nodes: Analysis of the Breast International Group 02-98 Trial

Sobrevida por câncer de mama



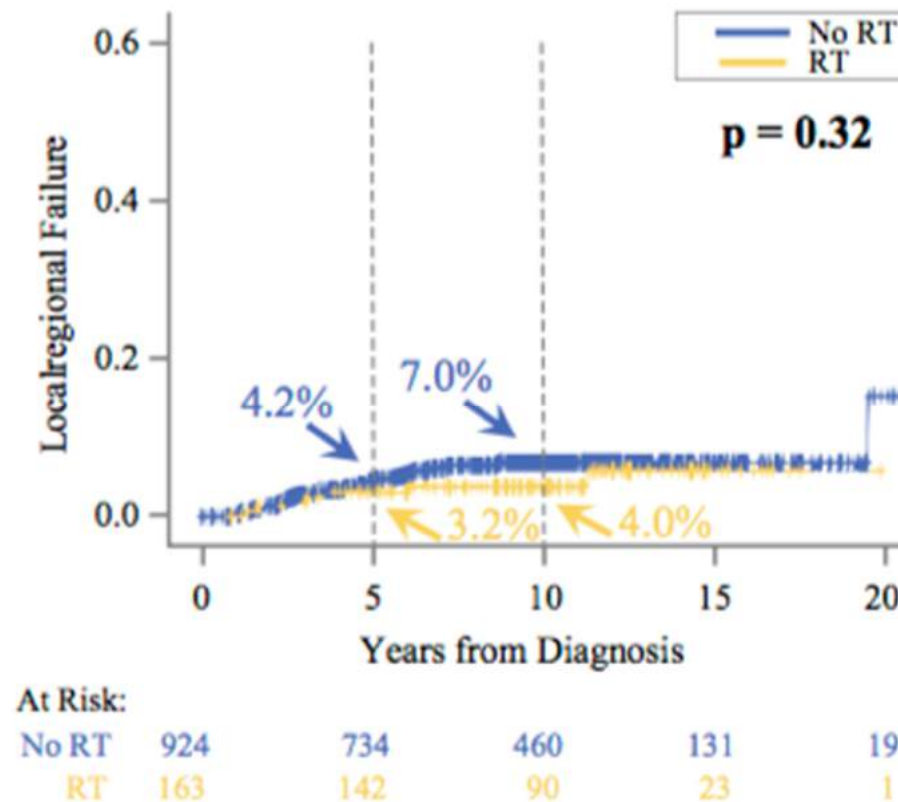
Sobrevida Global



## **Most Breast Cancer Patients with T1-2 Tumors and One to Three Positive Lymph Nodes Do Not Need Postmastectomy Radiotherapy**

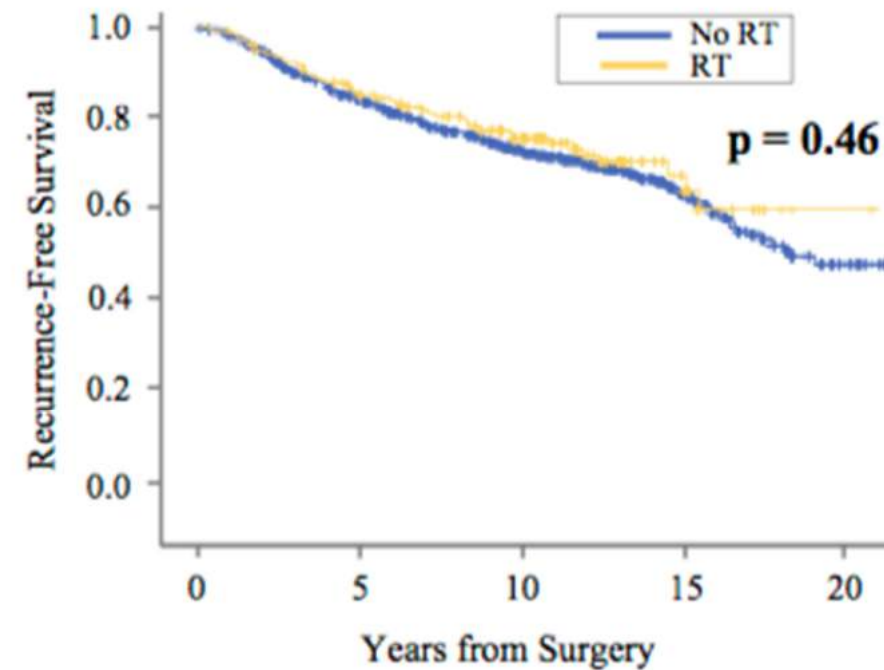
- MSKCC
- Retrospectivo
- T1-2 / 1 a 3 LN após mastectomia
- 924 sem PMRT
- 163 PMRT

## Most Breast Cancer Patients with T1-2 Tumors and One to Three Positive Lymph Nodes Do Not Need Postmastectomy Radiotherapy





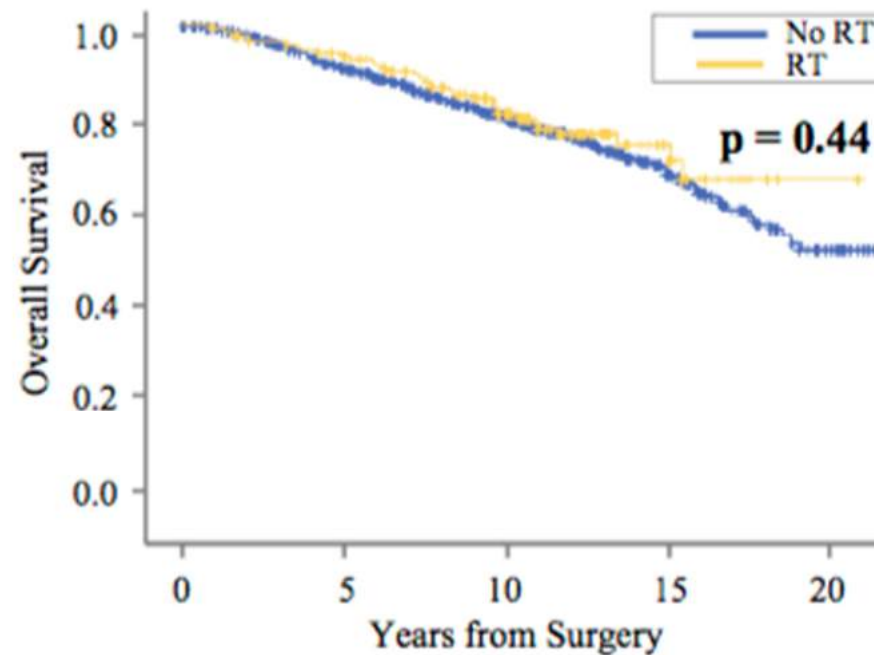
## Most Breast Cancer Patients with T1-2 Tumors and One to Three Positive Lymph Nodes Do Not Need Postmastectomy Radiotherapy



At Risk:

No RT	924	702	436	125	17
RT	163	132	85	21	1

## Most Breast Cancer Patients with T1-2 Tumors and One to Three Positive Lymph Nodes Do Not Need Postmastectomy Radiotherapy



At Risk:

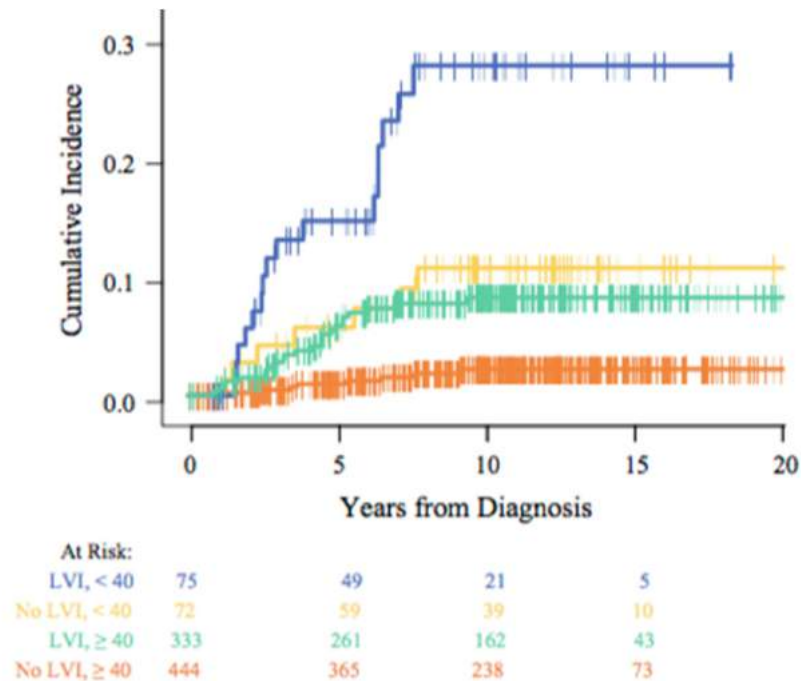
No RT	924	759	483	139	20
RT	163	145	91	23	1

## Most Breast Cancer Patients with T1-2 Tumors and One to Three Positive Lymph Nodes Do Not Need Postmastectomy Radiotherapy

Characteristic	No PMRT (n=924)	PMRT (n=163 15%)	p
Age		younger	0.019
Tumor size T2	39%	53%	0.0013
Histologic Grade		Higher grade	0.029
Nuclear Grade		Higher grade	0.044
LVI	44%	64%	<0.0001
Extracapsular extension	12%	33%	<0.0001
Number of positive nodes		More nodes	<0.0001
Size of met (macromets)	72%	88%	<0.0001
LR	7%	4%	

## Most Breast Cancer Patients with T1-2 Tumors and One to Three Positive Lymph Nodes Do Not Need Postmastectomy Radiotherapy

### Taxa de recorrência locorregional



5-year LRR	10-year LRR	
15%	28%	— < 40, LVI
6%	11%	— < 40, No LVI
6%	8%	— ≥ 40, LVI
1%	2%	— ≥ 40, No LVI

## Fatores prognósticos clássicos de recorrência

- Idade (jovens)
- Tamanho do tumor
- Invasão angiolinfática / perineural
- Alto grau
- Subtipos moleculares agressivos

## Subtipo: NCIC MA-20

10-yr Outcomes	WBI +RNI	WBI	Abs. Diff.	p	HR	95% CI
LRR-Free Survival	95.2%	92.2%	2.3%	.009	.59	.39-.88
Distant DFS	86.3%	82.4%	3.9%	.03	.76	.60-.97
DFS	82.0%	77.0%	5.0%	.01	.76	.61-.94
ER-negative DFS	76.2%	61.6%	14.6%	.04	.56	.39-.81
OS	82.8%	81.8%	1.0%	.38	.91	.72-1.13
ER-negative OS	81.3%	73.9%	7.4%	.05	.69	.47-1.0



# Axillary Surgery for Early-Stage, Node-Positive Mastectomy Patients and the Use of Postmastectomy Chest Wall Radiation Therapy

## Prática nos EUA

- *National Cancer Data Base (2012- 2014)*
- cT1/T2 N0 -> mastectomia com 1-3LN +
- N = 8089

Sentinela	2.482 (30,7%)
Dissecção axilar	1.339 (16,6%)
Sentinela -> Dissecção axilar	4.268 (52,7%)

## Axillary Surgery for Early-Stage, Node-Positive Mastectomy Patients and the Use of Postmastectomy Chest Wall Radiation Therapy

Characteristic	No RT N=4992 (61.7%)	CW RT N=824 (10.2%)	CW+RNI N=2193 (27.1%)	P value
Axillary surgery				0.014
SNB alone	62.8%	10.7%	26.5%	
ALND alone	64.7%	11.0%	24.3%	
SNB→ALND	61.3%	9.8%	28.8%	
Nodes positive				<0.001
1	69.9%	9.0%	21.0%	
2	51.5%	12.2%	36.3%	
3	39.3%	13.9%	46.8%	
Size of Met				<0.001
macro	57.7%	11.2%	31.0%	
micro	77.4%	7.1%	15.4%	
LVI				<0.001
absent	66.3%	9.1%	24.6%	
present	56.3%	11.8%	31.9%	

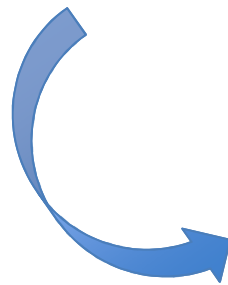
# **Axillary Surgery for Early-Stage, Node-Positive Mastectomy Patients and the Use of Postmastectomy Chest Wall Radiation Therapy**

## Preditores para RT

- Idade (jovens)
- Tamanho do tumor
- Número de LN positivos
- LN (micro versus macro)
- Tipo da abordagem axilar
  - Sentinela -> PMRT

# Considerações finais

- **T1-2 -> 1 a 3 LN após mastectomia**
- Considerar fortemente
  - ✓ Diminuição da recorrência
  - ✓ Diminuição da mortalidade por câncer de mama (metanálise)
  - ✓ Fatores de risco adicionais
    - Idade (jovens)
    - Subtipos moleculares agressivos
    - Invasão angiolinfática / perineural
    - Alto grau
    - Tipo de abordagem cirúrgica axilar



# Radioterapia após quimioterapia neoadjuvante

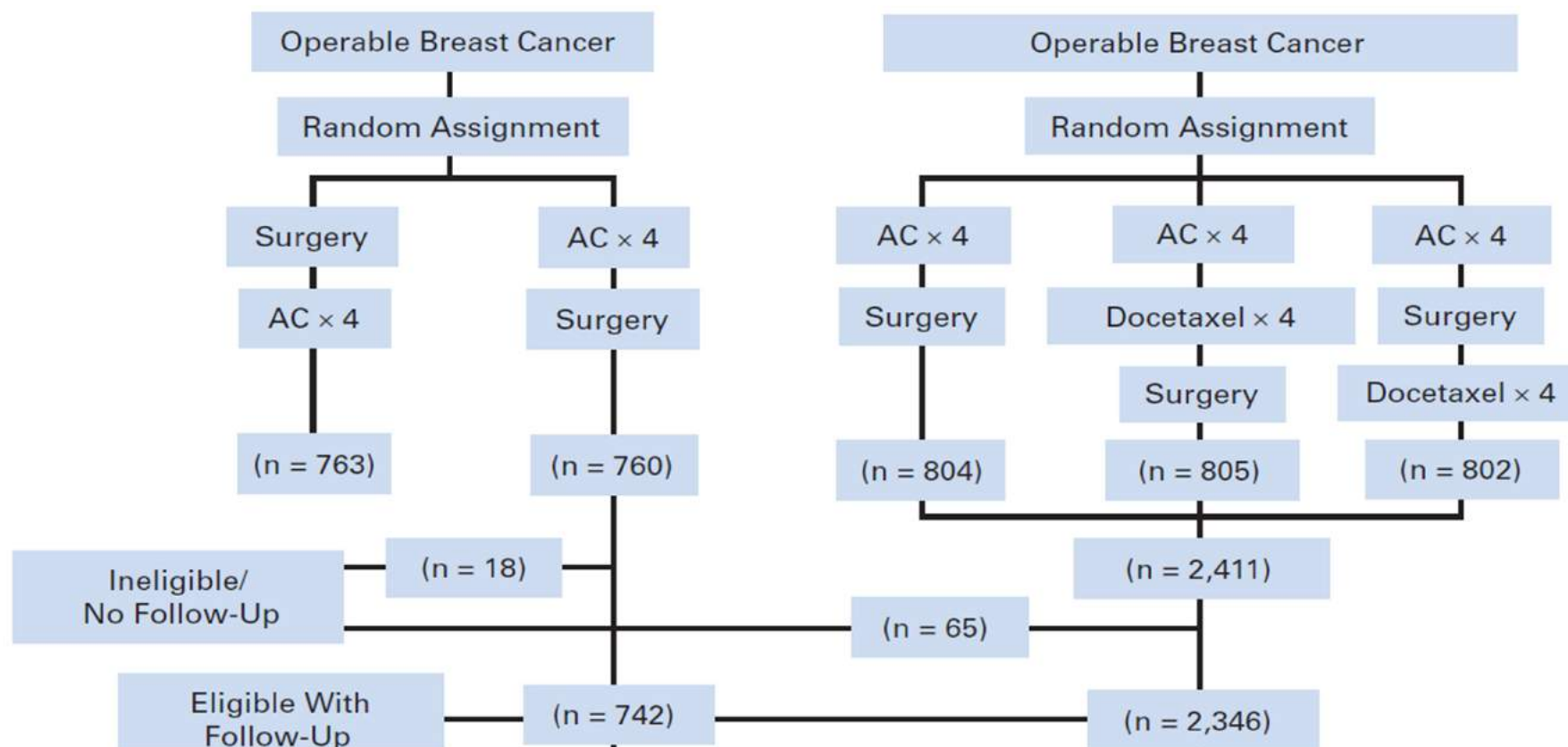
## QT neoadjuvante ou adjuvante?

Randomized phase III trials comparing neoadjuvant with adjuvant therapy using the same chemotherapy regimen

Study	<i>n</i> (stage and size)	Chemotherapy regimen	cRR (%)	pCR (%)	DFS benefit	OS benefit
Fisher et al. [3, 4], Wolmark et al. [5], NSABP B-18	1,523 (operable)	AC	80	13	No	No
Van der Hage et al. [6], EORTC 10902	698 (T1c-4bN0-1)	FEC	49	4	No	No
Gianni et al. [7, 8], ECTO	1,355	AT → CMF	78	23	No	No
Mauriac et al. [9]	272 (>3 cm)	EMV/MTV	81	NA	No	No
Scholl et al. [10], Broet et al. [11]	414 (T2-3N0-1)	FAC	85	NA	No	No
Makris et al. [12]	309 (operable)	MM(M)+Tam	84	10	No	No



## Análise combinada NSABP B18 e NSABP B27



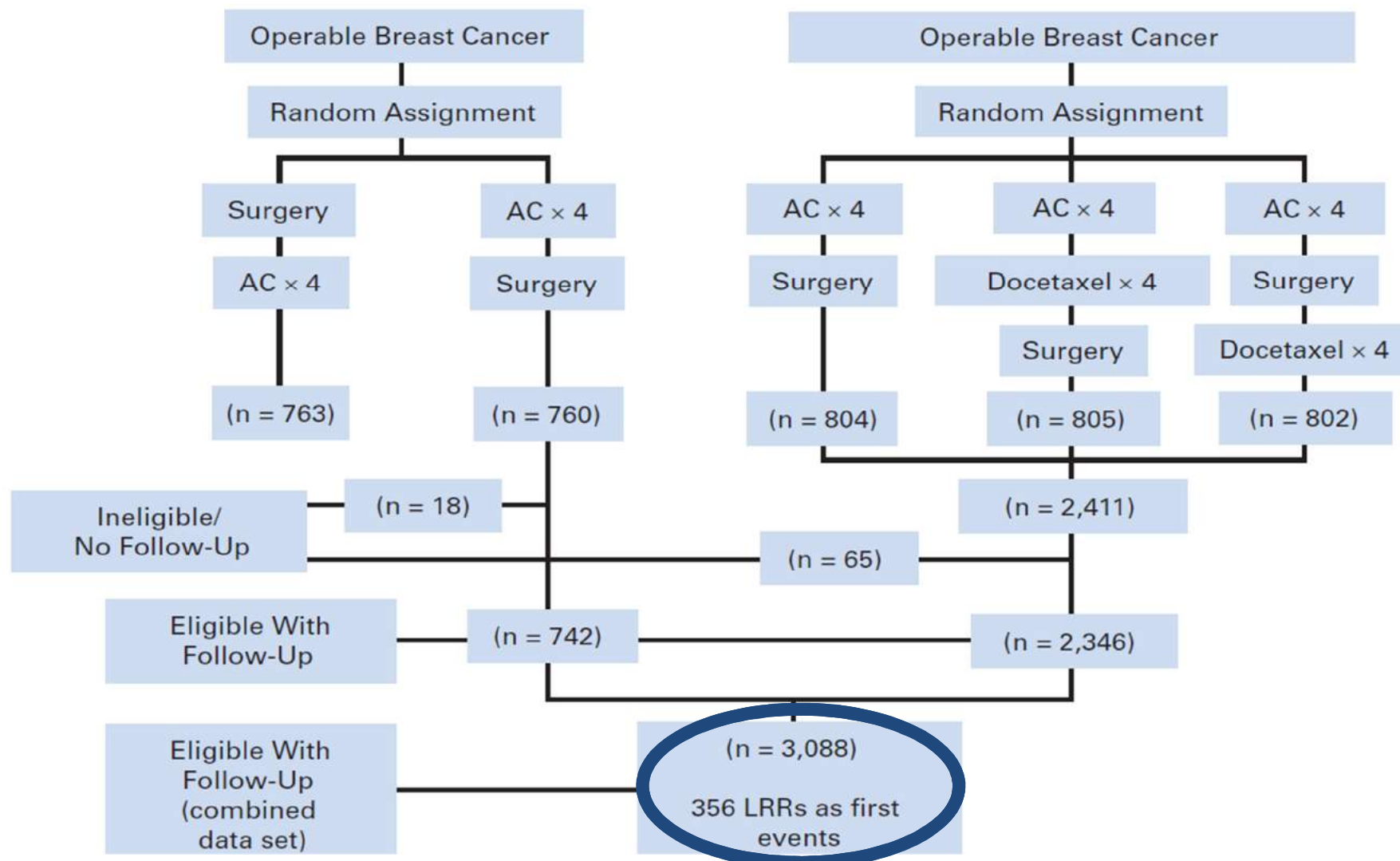
## Análise combinada NSABP B18 e NSABP B27

### Radioterapia nos estudos:

- Se cirurgia conservadora: mama apenas
- Mastectomia: sem RT
- Sem RT nas drenagens

# Evidências atuais

## Análise combinada NSABP B18 e NSABP B27



## Análise combinada NSABP B18 e NSABP B27

### 10 anos de seguimento:

- 356 recorrência locorregionais (RLR)

- Incidência de RLR em 10 anos:

12,3% (local 8,9%, regional 3,4%) para mastectomia

10,3% (local 8,1%, regional 2,2%) para cirurgia conservadora + RT

## Análise combinada NSABP B18 e NSABP B27

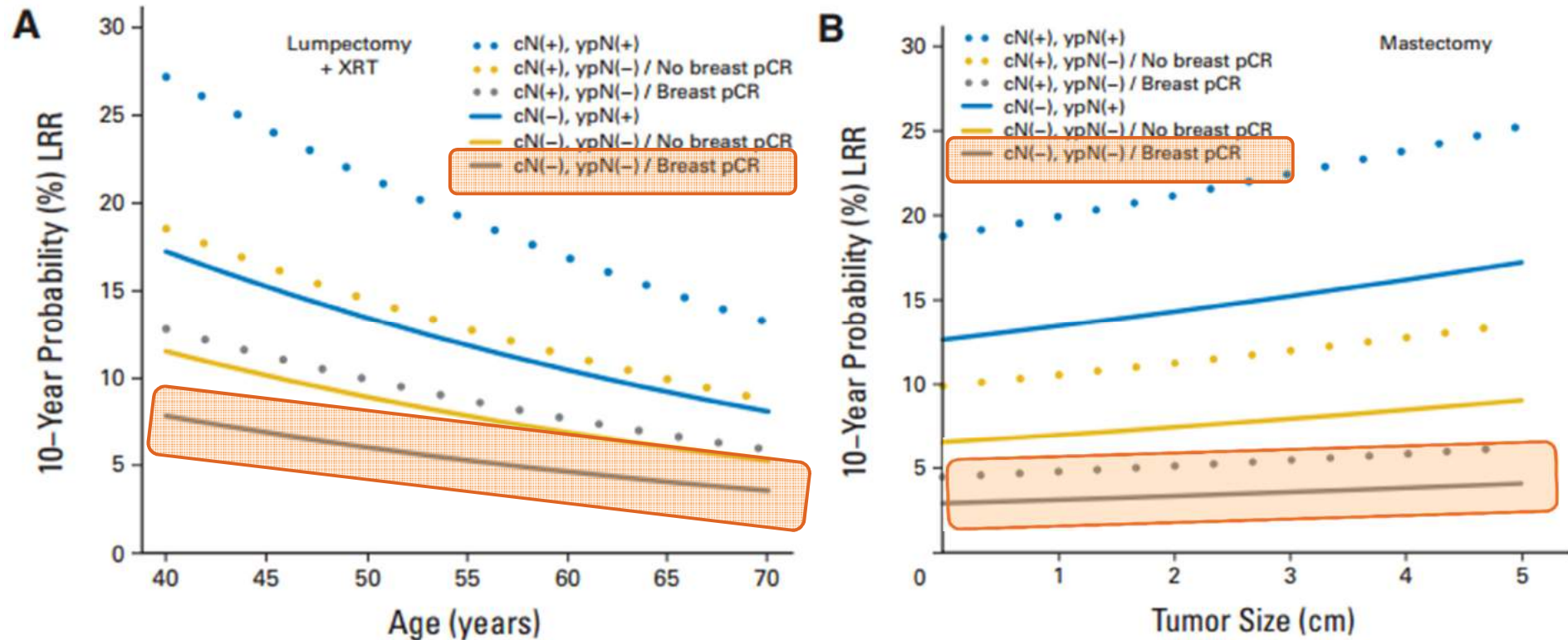
### *Preditores de RLR após QT neoadjuvante*

**Table 3.** Multivariate Analysis of Independent Predictors of 10-Year LRR According to Type of Surgery

Variable	No. of Patients	LRR Events	HR	95% CI	P	
<b>Patients treated with mastectomy*</b>						
Clinical tumor size > 5 v ≤ 5 cm†	1,071	131	1.58	1.12 to 2.23	.0095	
Clinical nodal status cN(+) v cN(-)†			1.53	1.08 to 2.18	.017	
Nodal/breast pathologic status						< .001
ypN(-)/no breast pCR v ypN(-)/breast pCR†			2.21	0.77 to 6.30		
ypN(+) v ypN(-)/breast pCR†			4.48	1.64 to 12.21		
<b>Patients treated with lumpectomy plus breast XRT*</b>						
Age ≥ 50 v < 50 years†	1,890	189	0.71	0.53 to 0.96	.025	
Clinical nodal status cN(+) v cN(-)†			1.70	1.26 to 2.31	< .001	
Nodal/breast pathologic status						< .001
ypN(-)/no breast pCR v ypN(-)/breast pCR†			1.44	0.90 to 2.33		
ypN(+) v ypN(-)/breast pCR†			2.25	1.41 to 3.59		

## Análise combinada NSABP B18 e NSABP B27

### Preditores de RLR após QT neoadjuvante





## Análise combinada NSABP B18 e NSABP B27

*Preditores de RLR após QT neoadjuvante*

### Resumo:

- Fatores preditores de recorrência:
  - idade
  - Estadiamento clínico avançado
  - Resposta patológica na mama e axila
- Impacto da idade e estadiamento clínico na taxa absoluta de recorrência locorregional foi baixa se pCR

## Análise combinada NSABP B18 e NSABP B27

### Limitações:

- T4 e N2 não foram elegíveis
- >85% pacientes diagnosticados com PAAF
- Desconhecido RE, RP, HER2 status
- Terapia sistêmica não contemporânea:
  - Tamoxifeno prescrito se >50 anos ( independente do RE)
  - Esquemas de QT(AC\*4 and AC\*4-D\*4)
  - Sem uso de trastuzumab

## Análise retrospectiva de 5 trials prospectivos

### QT neoadjuvante + mastectomia **sem RT**

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Table 2. Neoadjuvant Chemotherapy Treatment Details

Protocol	Years of Study	Neoadjuvant Chemotherapy	No. of Cycles	Included Patients/Total Study Population
Advanced Primary	1974-1985	FAC	3	40/191
85-01	1985-1989	VACP	3	23/200
89-007	1989-1991	FAC	4	15/203
91-015	1991-1994	FAC or dose-escalated FAC	4	60/202
94-002	1994-1998	FAC or paclitaxel	4	60/174
Total	1974-1998			150/970

*Estadiamento:*

<i>I</i>	-	<i>1%</i>
<i>II</i>	-	<i>43%</i>
<i>IIIA</i>	-	<i>23%</i>
<i>IIIB</i>	-	<i>25%</i>
<i>IV</i>	-	<i>7%</i>

# Evidências atuais

## *Fatores preditores de RLR*

### Fatores pré QT:

- ✓ Aumento do estágio T ( $p < 0,0001$ )
- ✓ Status nodal ( $p < 0,0001$ )

### Fatores pós-QT:

- ✓ Tamanho do tumor residual primário ( $p = 0,0048$ )
- ✓ Aumento do número de LN envolvidos ( $p < 0,0001$ )
- ✓ Sem tamoxifeno ( $p < 0,0013$ )

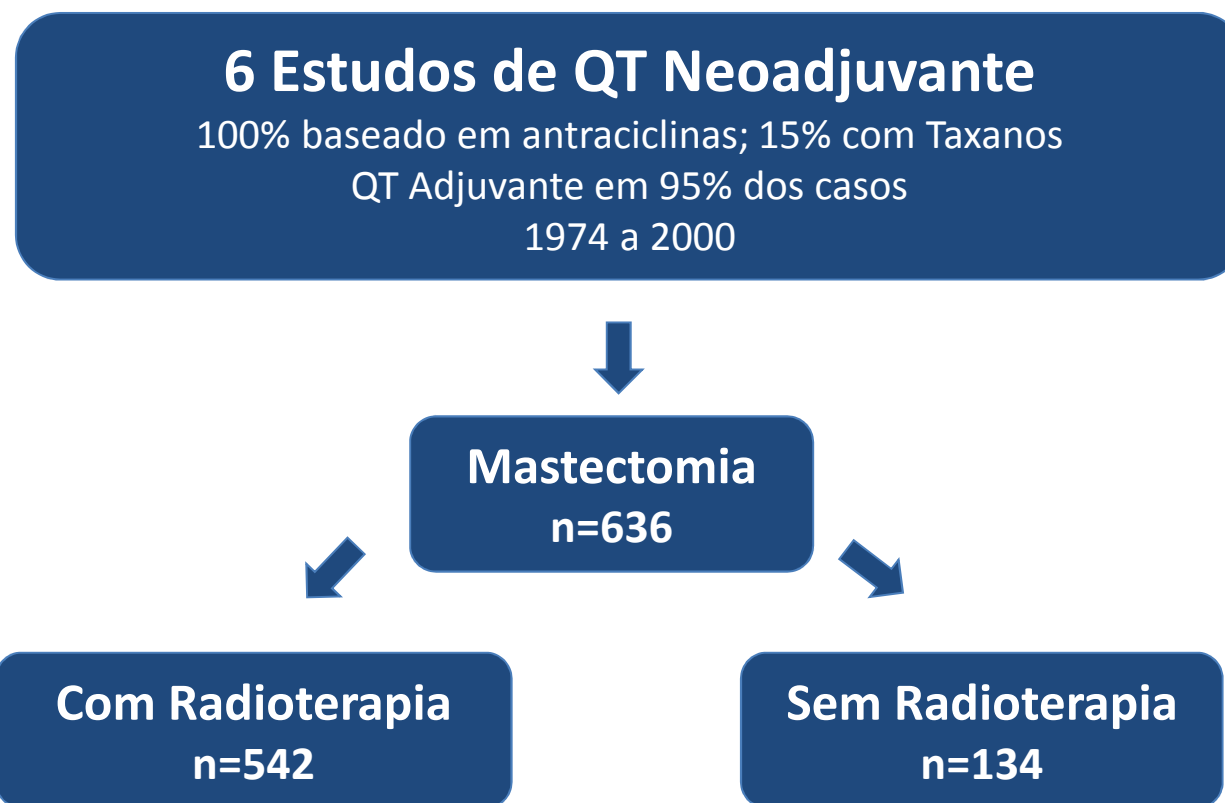
RLR após pCR ( $n = 18$ ) = 19%:

*→ A obtenção do pCR não exclui a necessidade de RT,  
se indicado pela fase inicial da doença*

# Evidências atuais

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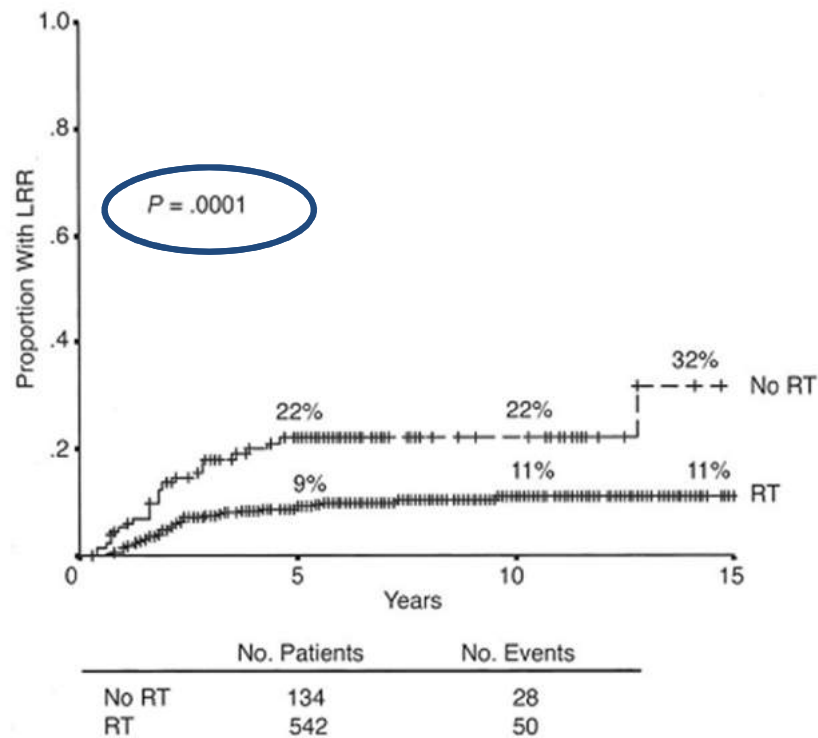
Postmastectomy Radiation Improves Local-Regional Control and Survival for Selected Patients With Locally Advanced Breast Cancer Treated With Neoadjuvant Chemotherapy and Mastectomy



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Postmastectomy Radiation Improves Local-Regional Control and Survival for Selected Patients With Locally Advanced Breast Cancer Treated With Neoadjuvant Chemotherapy and Mastectomy

## Recorrência locorregional



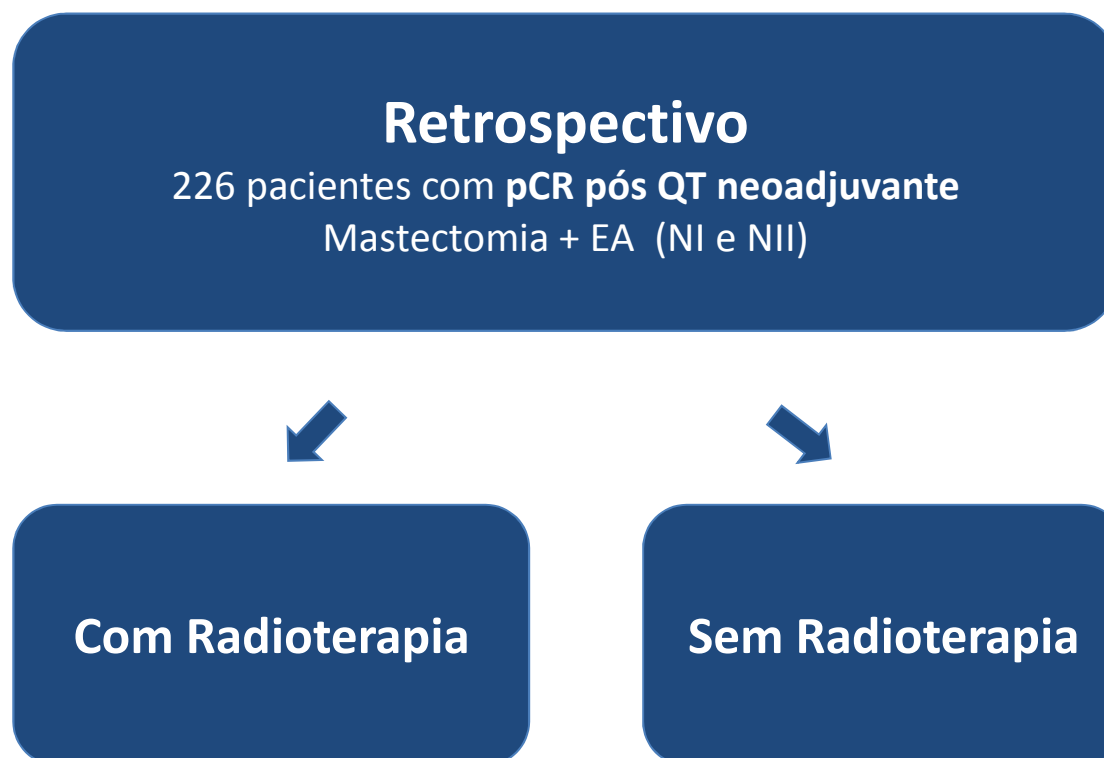
Factor	10-year LRR Rate		P
	No Radiation (%)	Radiation (%)	
<b>Clinical T-stage</b>			
T1	0	8	.535
T2	10	7	.408
T3	22	8	.002
T4	46	15	< .0001
<b>Clinical N-stage</b>			
N0	23	10	.014
N1	14	9	.062
N2-3	40	12	< .0001
<b>Pathological tumor size, cm</b>			
0-2	13	8	.051
2.1-5.0	31	14	.002
≥ 5.1	52	13	.001
<b>No. of positive nodes</b>			
0	11	4	.010
1-3	13	11	.636
≥ 4	59	16	< .0001



# Evidências atuais

**POSTMASTECTOMY RADIATION IMPROVES THE OUTCOME OF PATIENTS  
WITH LOCALLY ADVANCED BREAST CANCER WHO ACHIEVE A  
PATHOLOGIC COMPLETE RESPONSE TO NEOADJUVANT  
CHEMOTHERAPY**

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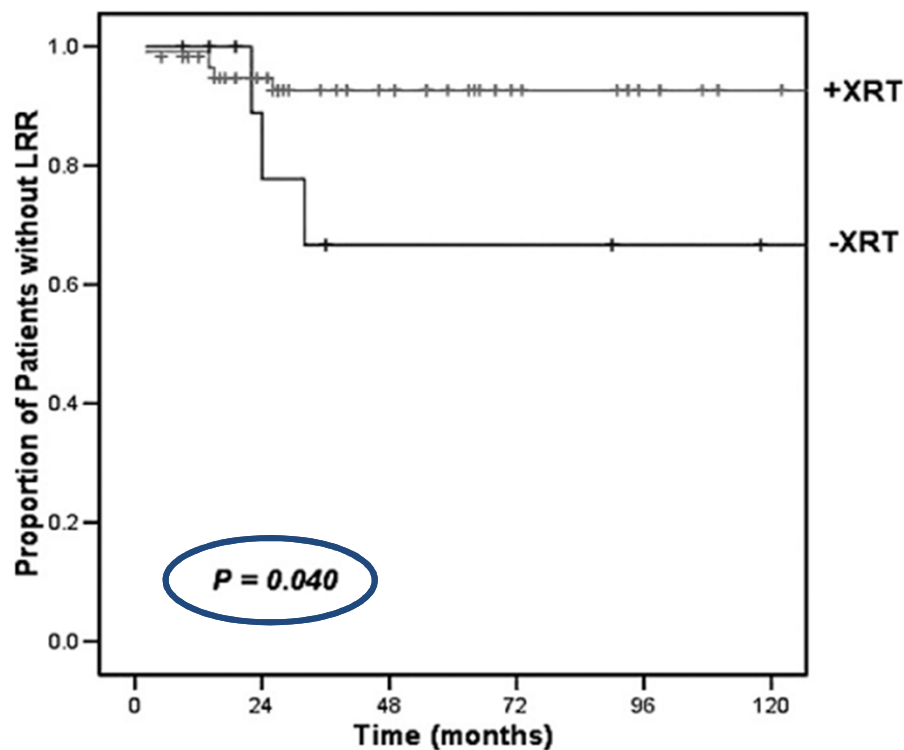


# Evidências atuais

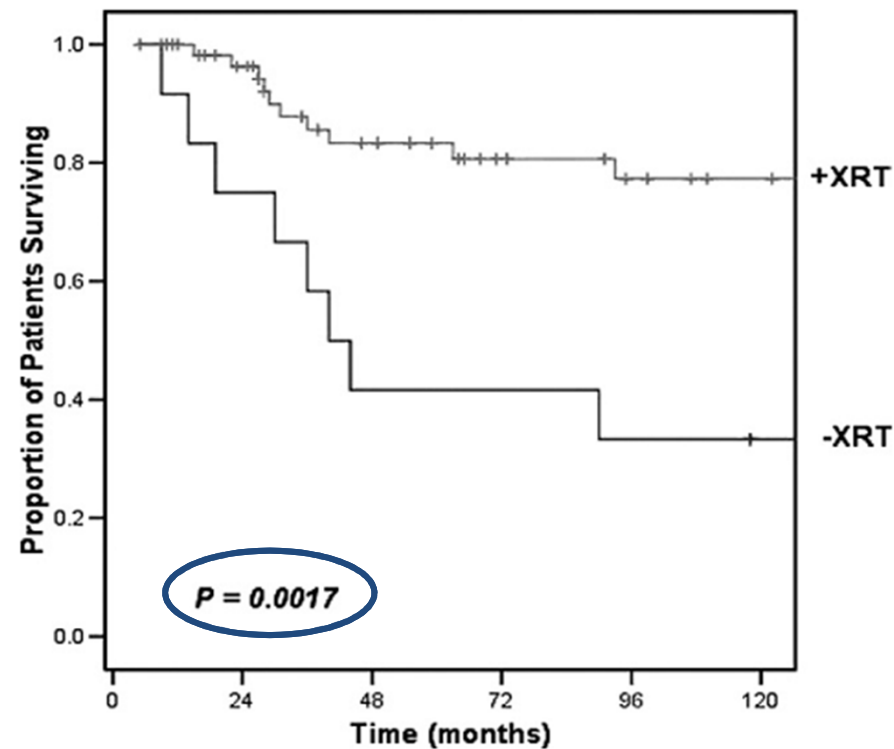
## POSTMASTECTOMY RADIATION IMPROVES THE OUTCOME OF PATIENTS WITH LOCALLY ADVANCED BREAST CANCER WHO ACHIEVE A PATHOLOGIC COMPLETE RESPONSE TO NEOADJUVANT CHEMOTHERAPY

MD Anderson  
~~Cancer Center~~

Recorrência locorregional



Sobrevida





# Evidências atuais



## Relationship of omission of adjuvant radiotherapy to outcomes of locoregional control and disease-free survival in patients with or without pCR after neoadjuvant chemotherapy for breast cancer: A meta-analysis on 3481 patients from the Gepar-trials.

David Krug, Bianca Lederer, Jürgen Debus, Jens Blohmer, Serban Costa, Holger Eidtmann, Claus Hanusch, Jörn Hilfrich, Jens Huober, Christian Jackisch, Sherko Kümmel, Stefan Paepke, Andreas Schneeweiss, Michael Untch, Gunter von Minckwitz, Sibylle Loibl  
for the GBG and AGO-B study groups

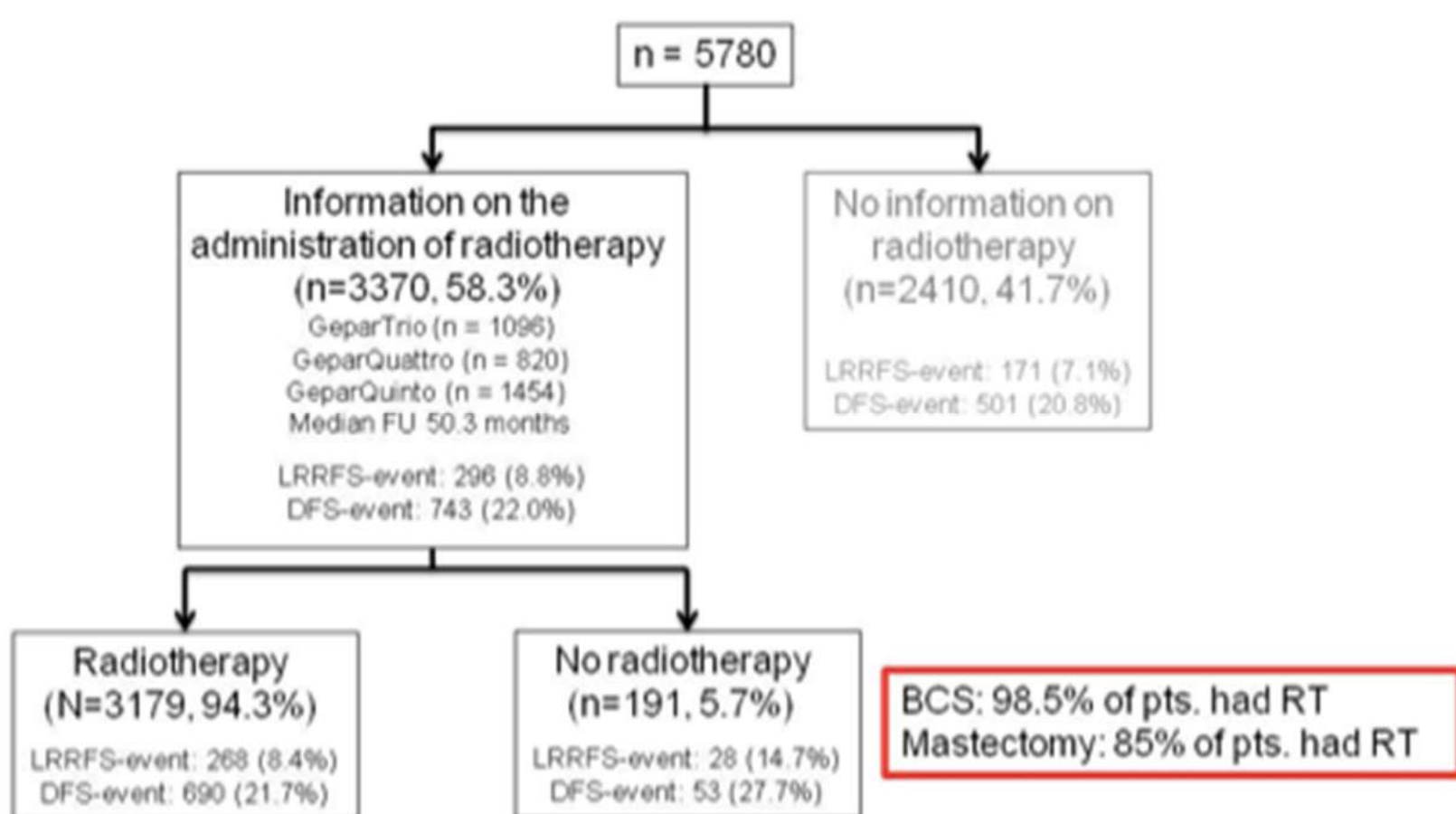


SLIDES ARE THE PROPERTY OF THE AUTHOR. PERMISSION REQUIRED FOR REUSE.

PRESENTED AT: ASCO Annual '15 Meeting

# Evidências atuais

## GBG Trials: GeparTrio, GeparQuatro, GeparQuinto



*Indicações da RT baseadas nos estadiamento inicial (cT3/4, cN+) ou ypN+*

## GBG Trials: GeparTrio, GeparQuatro, GeparQuinto

### Resultados (geral):

- SLRLR (5 anos): 90% vs 81.5%,  $p=0,001$  para  $\pm$  RT
- SLD (5 anos): 75% vs 67%,  $p=0,001$  para  $\pm$  RT

### Após pCR:

- SLRLR (5 anos): 96% vs 87%,  $p=0,049$  para  $\pm$  RT

### Sem pCR:

- SLRLR (5 anos): 89% vs 81%,  $p=0,001$  para  $\pm$  RT

*Na análise multivariada, ajustando as características basais e pCR, a RT foi confirmada como um fator prognóstico independente para SLRLR e SLD*

# Evidências atuais

Fatores para tomada de conduta baseado nas análises retrospectivas **NSABP-B18; NSABP- B27; séries do MDACC; GBG Trial metanálise**

- ✓ Estádio inicial
- ✓ Características biológicas
  - ✓ Doença residual
- ✓ Resposta à quimioterapia





National  
Comprehensive  
Cancer  
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## NCCN Guidelines Version 1.2018 Invasive Breast Cancer

### PREOPERATIVE SYSTEMIC THERAPY: ADJUVANT THERAPY

#### SURGICAL TREATMENT

Mastectomy and  
surgical axillary  
staging<sup>m</sup>  
+ reconstruction  
(optional)<sup>q</sup>

Lumpectomy with  
surgical axillary  
staging<sup>m</sup>

#### ADJUVANT TREATMENT

- Complete planned chemotherapy regimen course if not completed preoperatively.
- Consider adjuvant capecitabine in patients with triple-negative breast cancer and residual invasive cancer following standard neoadjuvant treatment with taxane-, alkylator-, and anthracycline-based chemotherapy.

Adjuvant radiation therapy<sup>s</sup> is based on maximal disease stage from prechemotherapy tumor characteristics at diagnosis and post-chemotherapy pathology results.

#### ► Post mastectomy:<sup>s</sup>

- ◊ Strongly consider radiation to the chest wall + infraclavicular region, supraclavicular area, internal mammary nodes, and any part of the axillary bed at risk for clinical N1, ypN0.
- ◊ For ANY positive axillary nodes after chemotherapy, radiation therapy as indicated to the chest wall + infraclavicular region, supraclavicular area, internal mammary nodes, and any part of the axillary bed at risk.

#### ► Post lumpectomy:<sup>s</sup>

- ◊ Adjuvant radiation post-lumpectomy is indicated to the whole breast.
- ◊ Strongly consider radiation to the whole breast + infraclavicular region, supraclavicular area, internal mammary nodes, and any part of the axillary bed at risk for clinical N1, ypN0.
- ◊ For ANY positive axillary nodes after chemotherapy, radiation therapy as indicated to the whole breast + infraclavicular region, supraclavicular area, internal mammary nodes, and any part of the axillary bed at risk.

and

- Adjuvant endocrine therapy<sup>bb</sup>, if ER-positive and/or PR-positive (category 1)

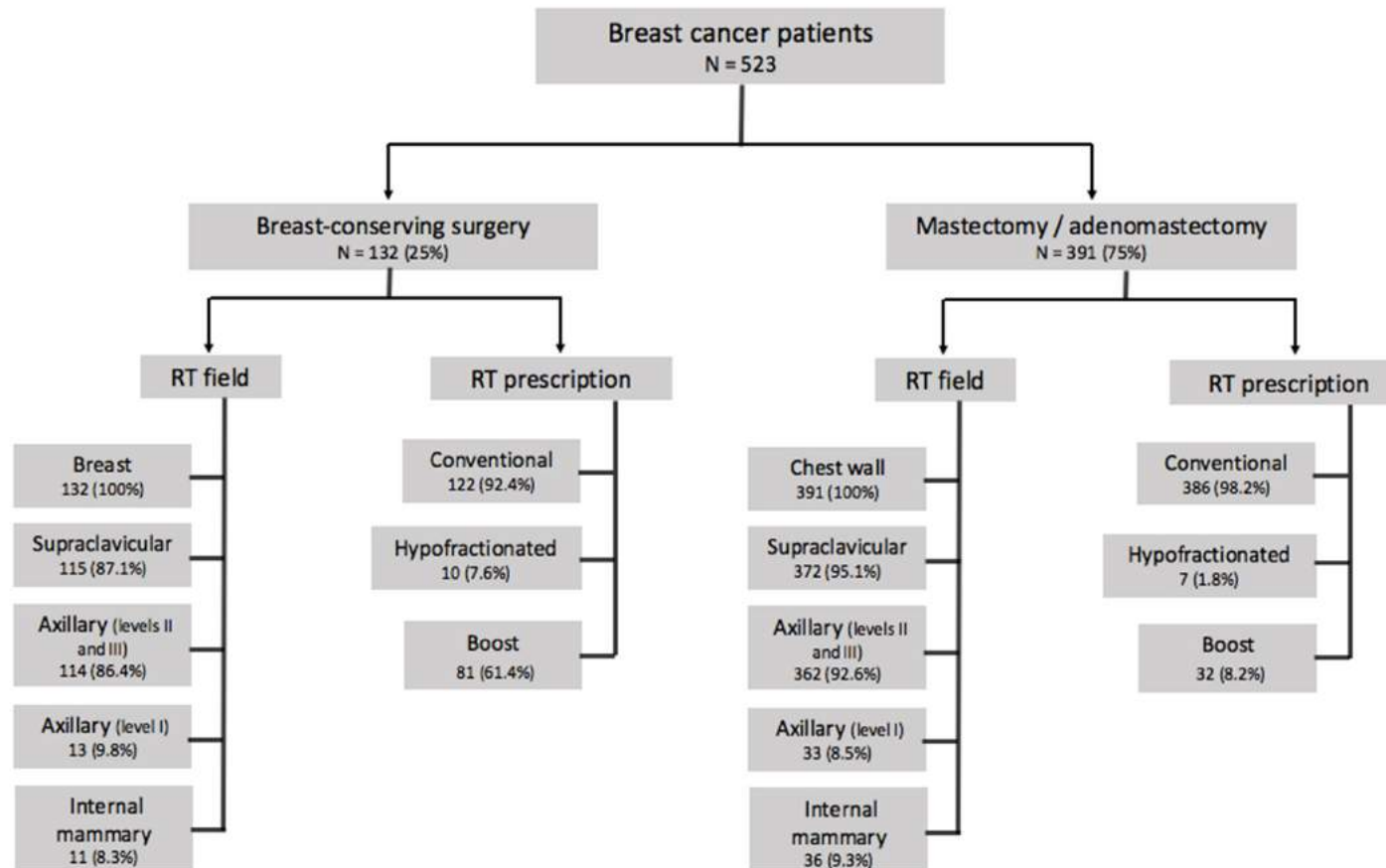
and

- If HER2-positive, complete up to one year of HER-2 targeted therapy with trastuzumab (category 1) ± pertuzumab. HER2-targeted therapy may be administered concurrently with radiation therapy and with endocrine therapy if indicated.<sup>ff</sup>

# Evidências atuais

## Patterns of post-operative irradiation in breast cancer patients submitted to neoadjuvant chemotherapy

Lima KMLB, Pereira AAL, de Freitas TB, Silva SB, Carvalho HA, Mano MS, Marta GN



# Evidências atuais

## Patterns of post-operative irradiation in breast cancer patients submitted to neoadjuvant chemotherapy

Lima KMLB, Pereira AAL, de Freitas TB, Silva SB, Carvalho HA, Mano MS, Marta GN

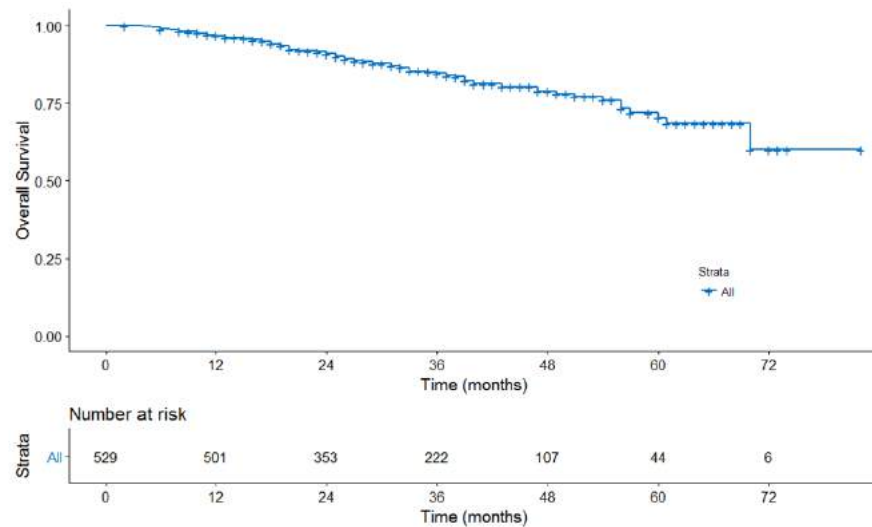
	TOTAL (N = 523)		Breast-conserving surgery (N = 132)		Mastectomy or nipple-sparing / skin-sparing mastectomy (N = 391)	
	N	%	N	%	N	%
<b>Clinical stage</b>						
I	2	0.4	2	1.6	0	0.0
IIA	37	7.1	19	14.4	18	4.6
IIB	97	18.5	38	28.8	59	15.1
IIIA	219	41.9	46	34.8	173	44.2
IIIB	124	23.7	16	12.1	108	27.6
IIIC	44	8.4	11	8.3	33	8.4
<b>"Molecular"</b>						
Luminal-like	232	44.4	51	38.6	181	46.3
Triple positive	75	14.3	19	14.4	56	14.3
HER-2 positive	66	12.6	23	17.4	43	11.0
Triple negative	150	28.7	39	29.5	111	28.4
<b>Neoadjuvant chemotherapy</b>						
Anthracycline-taxane	505	96.6	130	98.5	375	95.9
Others	18	3.4	2	1.5	26	4.1
<b>pCR</b>						
Yes	107	20.5	39	29.5	68	17.4
No	415	79.5	93	70.5	322	82.6



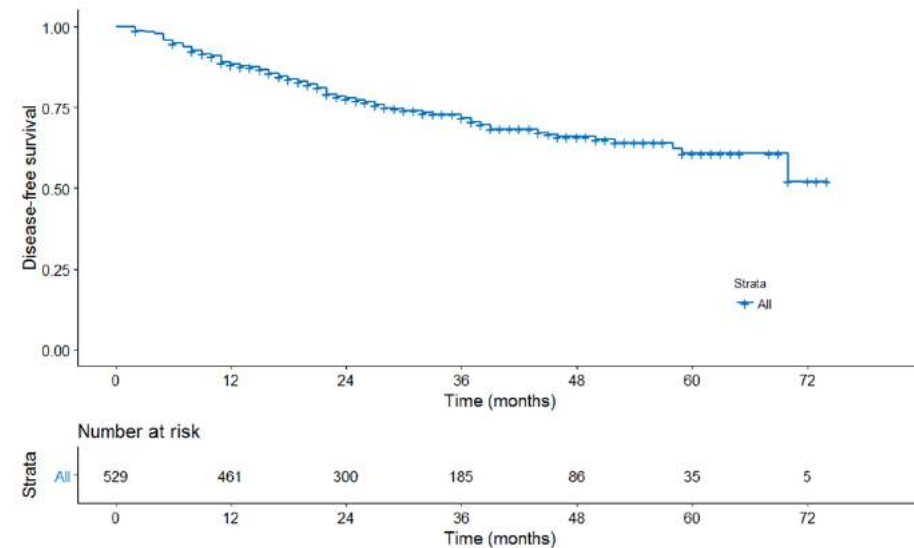
## Patterns of post-operative irradiation in breast cancer patients submitted to neoadjuvant chemotherapy

Lima KMLB, Pereira AAL, de Freitas TB, Silva SB, Carvalho HA, Mano MS, Marta GN

Sobrevida global



Sobrevida livre de recorrência

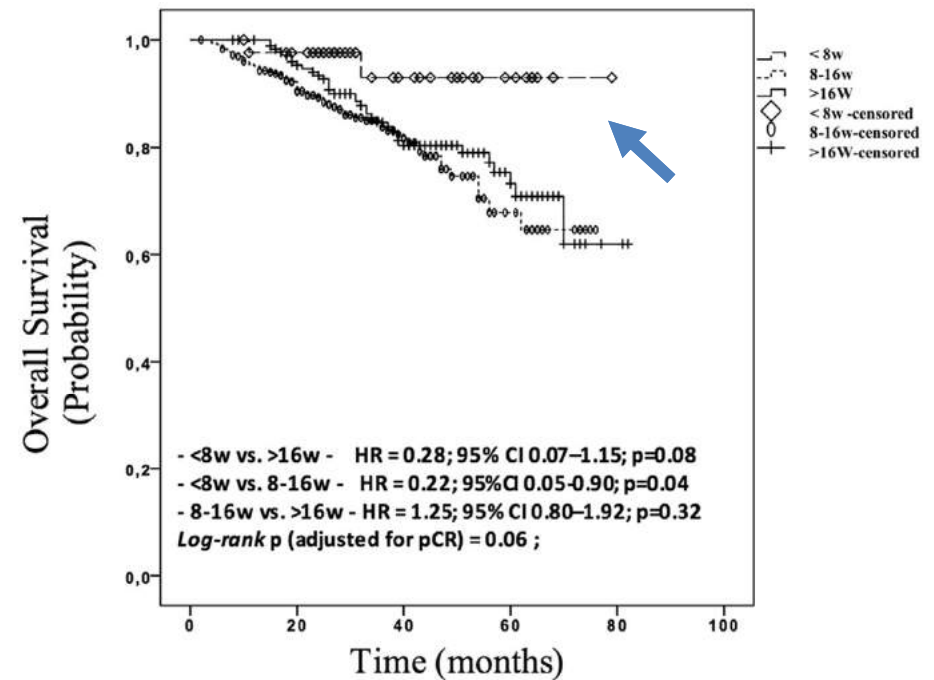
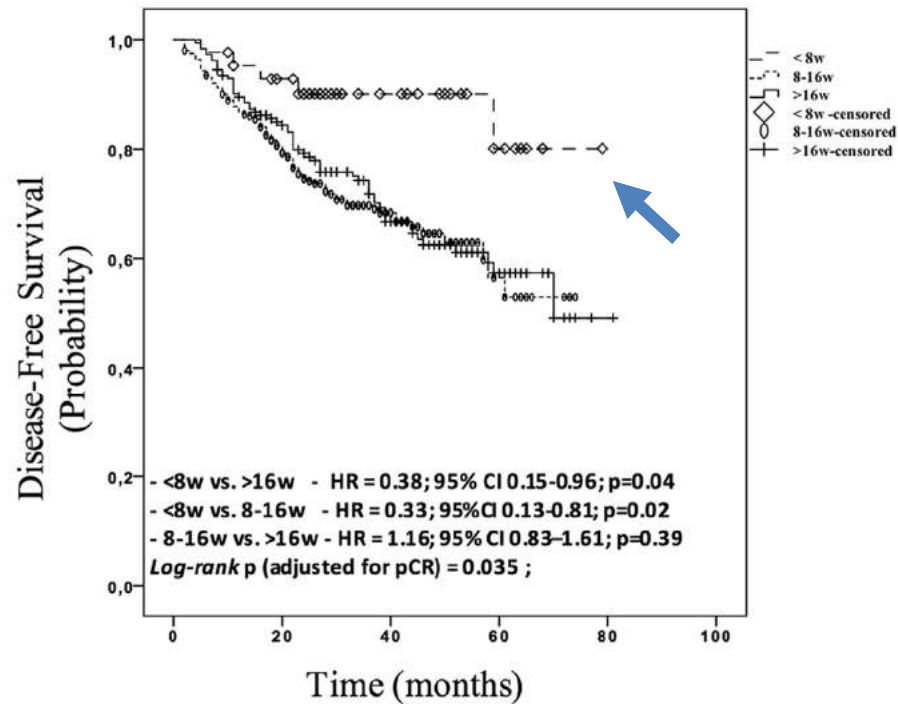


## Qual o timing da RT após QT neo?

**Clinical impact of adjuvant radiation therapy delay after neoadjuvant chemotherapy in locally advanced breast cancer.**

Silva SB<sup>1</sup>, Pereira AAL<sup>1</sup>, Marta GN<sup>2</sup>, de Barros Lima KML<sup>1</sup>, de Freitas TB<sup>1</sup>, Matutino ARB<sup>1</sup>, de Azevedo Souza MCL<sup>1</sup>, de Azevedo RGMV<sup>1</sup>, de Viveiros PAH<sup>1</sup>, da Silva Lima JM<sup>1</sup>, Filassi JR<sup>3</sup>, de Andrade Carvalho H<sup>1</sup>, Piato JRM<sup>3</sup>, Mano MS<sup>4</sup>.

581 pacientes



# Evidências atuais

## Qual o timing da RT após QT neo?

– Multivariate logistic regression adjusted for recurrence adjusted for PORT time for initiation, stage, molecular profile, pCR and histologic grade.

Variable	OR (Odds Ratio)	95%CI	p-value
<b>Time to Radiation therapy</b>			
<8 weeks	0.29	0.11–0.80	0.02
8-16 weeks	0.88	0.59–1.33	0.93
>16 weeks	(reference)	–	–
<b>Clinical Stage<sup>3</sup></b>			
EC I or II	0.49	0.30–0.81	0.006
ECIII	(reference)	–	–
<b>Molecular profile</b>			
Luminal	0.75	0.46–1.25	0.26
Triple Positive	0.81	0.42–1.53	0.51
HER-2 positive, ER negative	0.81	0.41–1.60	0.54
Triple Negative	(reference)	–	–
<b>Pathologic Complete Response</b>			
Yes	0.24	0.13–0.45	<0.001
No	(reference)	–	–
<b>Histologic Grade</b>			
1	0.74	0.32–1.70	0.48
2	0.78	0.51–1.19	0.24
3	(reference)	–	–
Age	1.00	0.99–1.02	0.58
<b>Surgery</b>			
Mastectomy	1.61	0.96–2.69	0.07
BCS	(reference)	–	–



# Evidências atuais

Qual o timing da RT após QT neo?

Validação com outros centros



# Evidências atuais

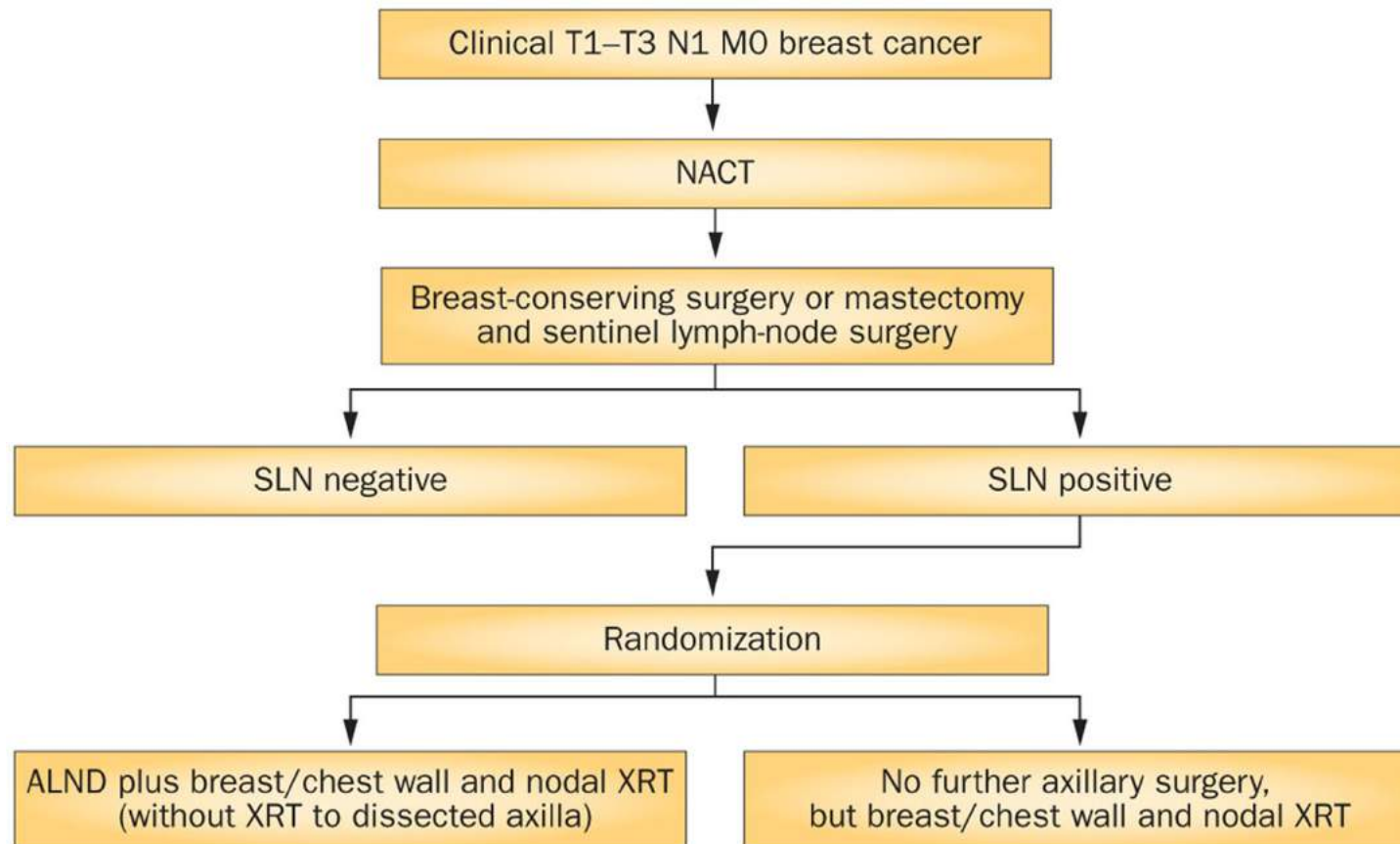
- Estudos realizados nos anos 80 e 90
- Desde então, a prática mudou:
  - ✓ Ferramentas de diagnóstico mais aprimoradas
  - ✓ Tratamentos sistêmicos mais eficazes
  - ✓ Melhor conhecimento sobre seleção de pacientes (subtipo molecular)

# Perspectivas futuras

- Estudos em andamento

# Perspectivas futuras

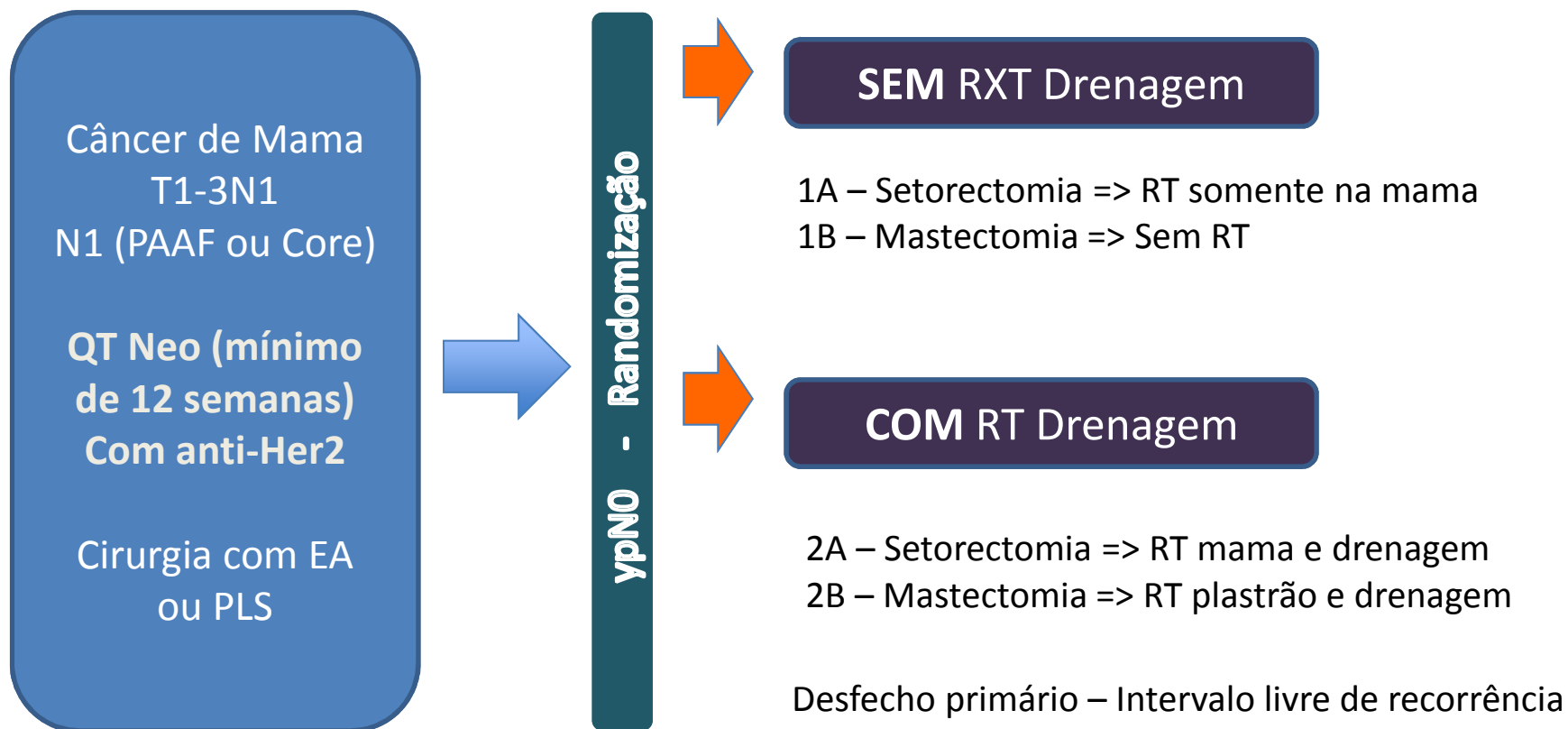
Alliance for Clinical Trials in Oncology A11202 trial schema



ALND = axillary lymph node dissection

# Perspectivas futuras

## NSABP B51 / RTOG 1304



### Estratificação

- Tipo de cirurgia (conservadora, mastectomia)
- Status hormonal (ER+ e/ou PR+; ER- e PR-)
- Her2 status (positivo vs negativo)
- QT adjuvante (sim/não)
- pCR na mama (sim/não)

# Perspectivas futuras

ACTO (Rússia)

cT0-T3 cN+ → QT neo → mastectomia

Se N-: ® RT vs. observação



# Perspectivas futuras

## BOOG 2010-03 RAPChem

cT1-T2 cN1 → QT neo

- Group I: ypT0-2N0
  - after MRM: no radiotherapy
  - after BCT: radiation treatment of the breast with boost
- Group II: ypT0-2N1:
  - after MRM: radiation treatment of the thoracic wall
  - after BCT: radiation treatment of the breast with boost
- Group III: ypT0-2N2-3, ypT3-4N0-1, and ypT3-4N0-3:
  - after MRM: radiation treatment of the thoracic wall and supraclavicular nodes
  - after BCT: radiation treatment of the breast with boost, and supraclavicular nodes

# Perspectivas futuras

**QT neo -> resposta completa  
Há necessidade de cirurgia?**

## *ClinicalTrials.gov*

A service of the U.S. National Institutes of Health

Trial record 31 of 115 for: breast cancer and radiotherapy and neoadjuvant chemotherapy

[Previous Study](#) | [Return to List](#) | [Next Study](#)

### Eliminating Breast Cancer Surgery in Exceptional Responders With Neoadjuvant Systemic Therapy

**This study is currently recruiting participants.** (see [Contacts and Locations](#))

Verified January 2017 by M.D. Anderson Cancer Center

**Sponsor:**

M.D. Anderson Cancer Center

**Information provided by (Responsible Party):**

M.D. Anderson Cancer Center

ClinicalTrials.gov Identifier:

NCT02945579

First received: October 24, 2016

Last updated: January 23, 2017

Last verified: January 2017

[History of Changes](#)

# Perspectivas futuras

**QT neo -> resposta completa**  
**Há necessidade de cirurgia?**

*ClinicalTrials.gov*

A service of the U.S. National Institutes of Health

## Neoadjuvant Chemotherapy Followed by Radiotherapy Alone in Patients With Breast Cancer

**This study is currently recruiting participants.**

See [▶ Contacts and Locations](#)

Verified July 2017 by **Gustavo Nader Marta**, Instituto do Cancer do Estado de São Paulo

**Sponsor:**

Instituto do Cancer do Estado de São Paulo

**Information provided by (Responsible Party):**

**Gustavo Nader Marta**, Instituto do Cancer do Estado de São Paulo

ClinicalTrials.gov Identifier:

NCT03213925

First received: July 8, 2017

Last updated: NA

Last verified: July 2017

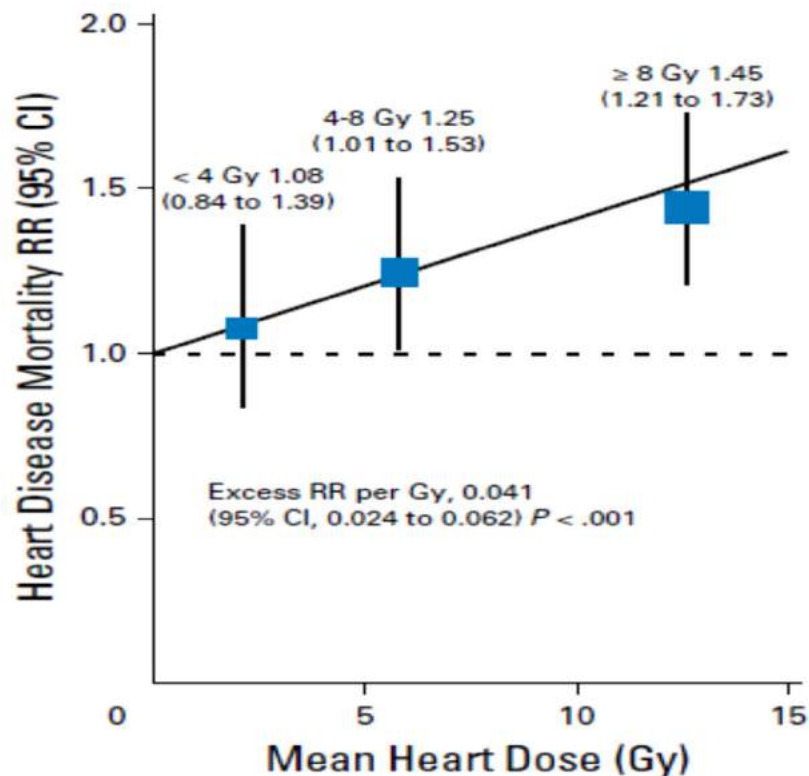
History: No changes posted

# Considerações finais

- **RT após quimioterapia neoadjuvante**
  - RT é indicada para a maioria das pacientes
  - Ausência de ECR fase 3
  - Indicações: baseadas nas características pré QT neo e resposta ao tratamento
  - Começar a RT em até 8 semanas
  - Aguardamos os resultados dos ECR

# Radioterapia moderna

Estimating the Risks of Breast Cancer Radiotherapy: Evidence From Modern Radiation Doses to the Lungs and Heart and From Previous Randomized Trials



## Doses em pulmão e coração

	Dose média nos trials	Dose típica em RT moderna	Doses atualmente atingidas*
<b>Pulmões</b>	10Gy	5Gy	3Gy
<b>Coração</b>	6Gy	4Gy	2Gy

(\*) revisão de literatura 2010 – 2015

## GUIDELINES IN FOCUS

### **Treatment with intensity-modulated radiation therapy (IMRT) for breast cancer**

**TRATAMENTO COM RADIOTERAPIA DE INTENSIDADE MODULADA (IMRT) PARA CÂNCER DE MAMA**

**Authorship:** Sociedade Brasileira de Radioterapia



# Radioterapia moderna

## Intensity-modulated versus conventional radiotherapy for breast cancer (Protocol)

Hanna SA, Marta GN, Riera R, da Silva JLF, de Andrade Carvalho H, De Barros ACSD



THE COCHRANE  
COLLABORATION®

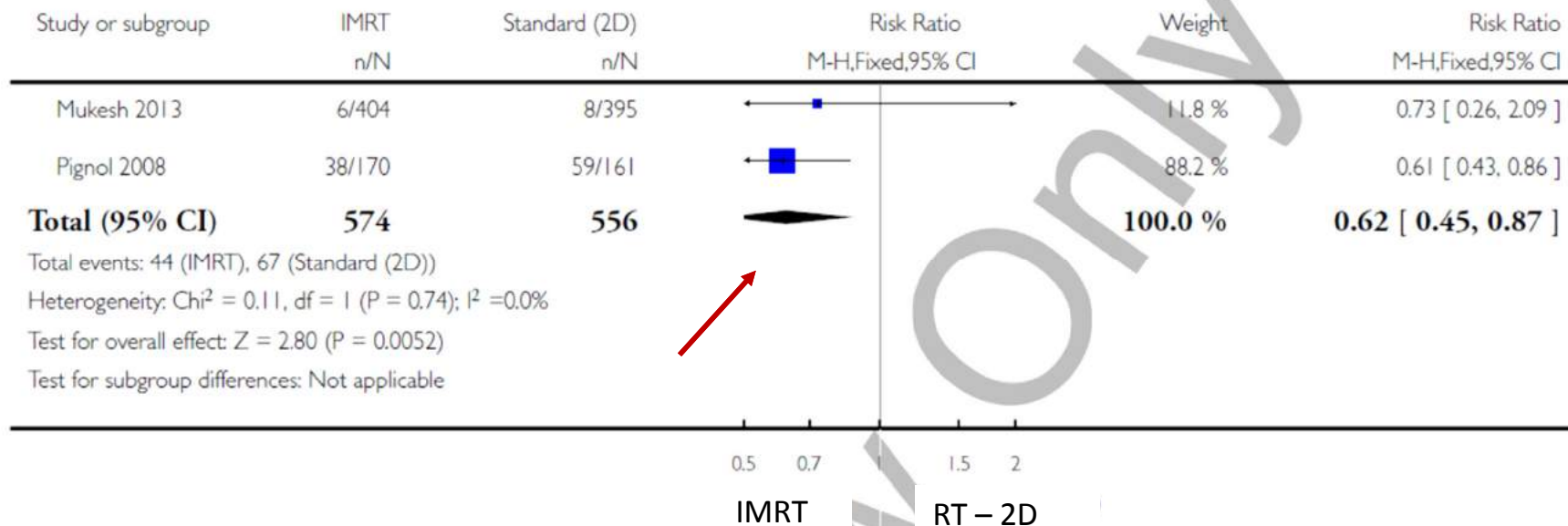
# Radioterapia moderna

## Analysis 1.4. Comparison 1 IMRT versus Standard (2D), Outcome 4 Acute Toxicity Grade 3 or 4.

Review: Intensity-modulated versus conventional radiotherapy for breast cancer

Comparison: 1 IMRT versus Standard (2D)

Outcome: 4 Acute Toxicity Grade 3 or 4





MEDICINA  
USP



# OBRIGADO

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