RAGMA 23

16ª Revisión Anual GEICAM de Avances en Cáncer de Mama

Realidades y esperanzas

Abordaje multidisciplinar del cáncer de mama

Avances en radioterapia en el cáncer de Mama

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Organizado por:
GEICAM investigación en cáncer de mama

1. BCS+RT y Mastectomía
2. RT DCIS
3. RT Ca. Infiltrante (C. Conservadora)
4. RT Ca. Infiltrante (Mastectomía)
5. RT axilar
6. RT tras TSP
7. Radiobiología y fraccionamientos
8. Volúmenes y secuencia
9. Ca mama metastásico
10. Avances técnicos

1. BCS+RT = Mastectomía (OS)…

- EORTC 10801 2000
- NSABP B06 2002
- Milan 2002

EORTC 10801. Van Dongen

Long-Term Results of a Randomized Trial Comparing Breast-Conserving Therapy With Mastectomy: European Organization for Research and Treatment of Cancer 10801 Trial

Joop A. van Dongen, Adri C. Voogd, Ian S. Fentiman, Catherine Legrand, Richard J. Sylvester, David Tong, Emmanuel van der Schueren, Peter A. Helle, Kobus van Zijl, Harry Bartelink

Journal of the National Cancer Institute, Vol. 92, No. 14, July 19, 2000

NSABP B06. Fisher B.

TOTAL MASTECTOMY VERSUS LUMPECTOMY

TWENTY-YEAR FOLLOW-UP OF A RANDOMIZED TRIAL COMPARING TOTAL MASTECTOMY, LUMPECTOMY, AND LUMPECTOMY PLUS IRRADIATION FOR THE TREATMENT OF INVASIVE BREAST CANCER

BERNARD FISHER, M.D., STEWART ANDERSON, PH.D., JOHN BRYANT, PH.D., RICHARD G. MARGOLESE, M.D., MELVIN DEUTSCH, M.D., EDWIN R. FISHER, M.D., JONG-HYEON JEONG, PH.D., AND NORMAN WOLMARK, M.D.

N Engl J Med, Vol. 347, No. 16 · October 17, 2002

MILAN. Veronesi U.

The New England Journal of Medicine

VOLUME 347 OCTOBER 17, 2002 NUMBER 16

TWENTY-YEAR FOLLOW-UP OF A RANDOMIZED STUDY COMPARING BREAST-CONSERVING SURGERY WITH RADICAL MASTECTOMY FOR EARLY BREAST CANCER

UMBERTO VERONESI, M.D., NATALE CASCINELLI, M.D., LUIGI MARIANI, M.D., MARCO GRECO, M.D., ROBERTO SACCOZZI, M.D., ALBERTO LUINI, M.D., MARISEL AGUILAR, M.D., AND ETTORE MARUBINI, PH.D.

1. … BCS+RT (↑OS) > Mastectomía

Further Comparison of Published Series, including RCT's, Comparing Outcomes in Women treated for breast cancer by either Breast Conserving Surgery or Mastectomy

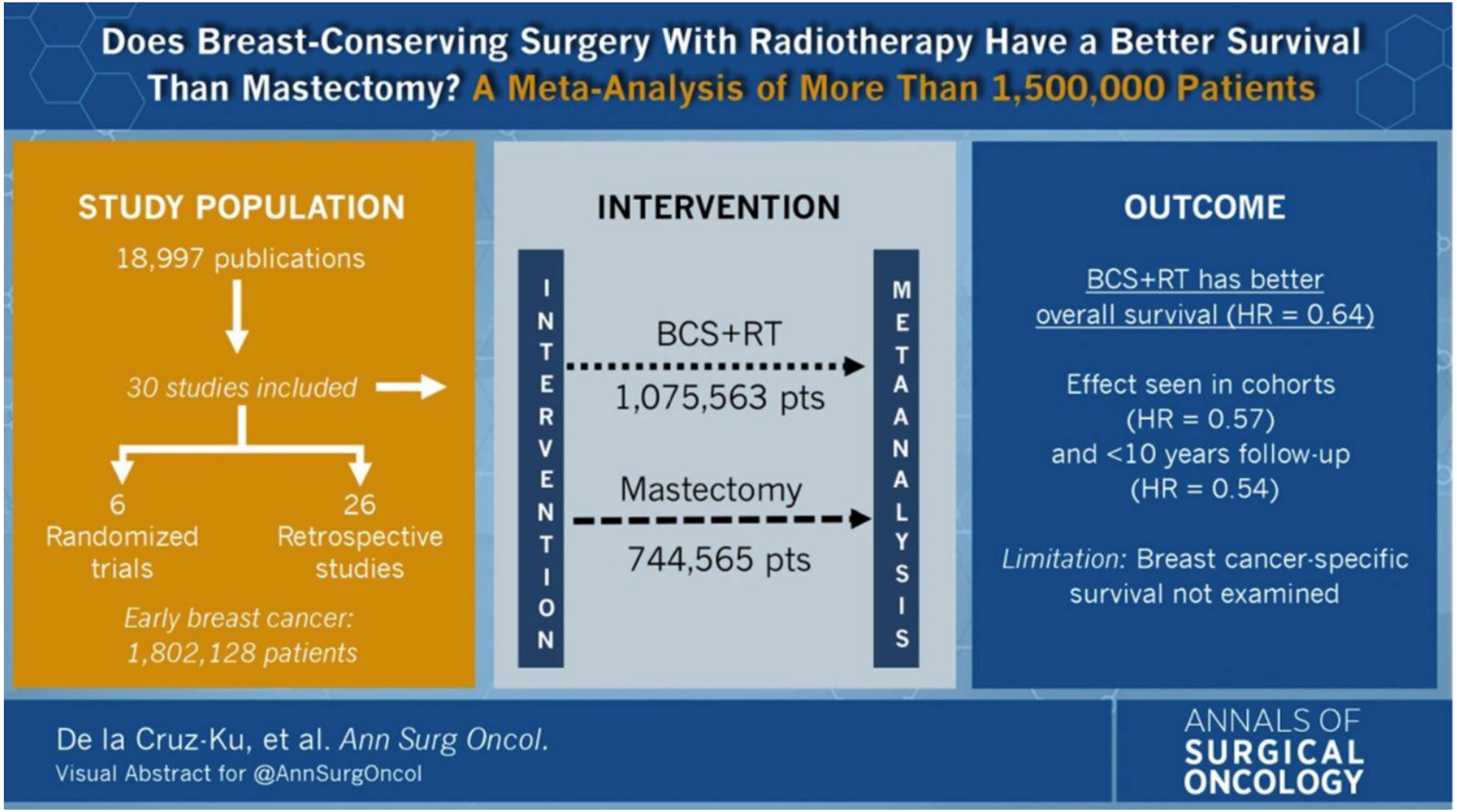
Reference	Data source/year	Number of patients	Follow-up	Hazard ratio (<1 favours better overall survival with breast-conserving surgery)	95% confidence interval
Hwang et al [27]	USA California Cancer Registry 1990–2004	112,154	110 months (median)	0.81	0.80–0.83
Saadatmand et al [33]	Netherlands Cancer Registry 1999–2012	173,797	47 months (median)	0.87	0.81–0.93
van Maaren et al [34,35]	Netherlands Cancer Registry 2000–2004	37,207	120 months overall survival	0.81	0.73–0.90
Hartmann-Johnsen et al [31]	Norwegian Cancer Registry 1998–2008	13,015	88 months (median)	0.61	0.53–0.70
Grover et al [66]	USA SEER 1995–2009	150,171	61 months (median)	0.73	0.71–0.76
Chen et al [39]	USA SEER 2010–2013	11,514 (triple-negative breast cancer)	22 months (median)	0.58	0.49–0.69
Lagendijk et al [37]	Netherlands Cancer Registry 1999–2012	129,692	144 months (median)	0.74	0.71–0.76
Almahariq et al [43]	USA National Cancer Database 2006–2014	231,642	84 months	0.66	0.64–0.69

Further Comparison of Published Series, including RCT's, Comparing Outcomes in Women treated for breast cancer by either Breast Conserving Surgery or Mastectomy

Reference	Data source/year	Number of patients	Follow-up	Hazard ratio (>1 favours worse overall survival with mastectomy)	95% confidence interval
Agarwal et al [28]	USA SEER 1998–2008	132,149	120 months breast cancer-specific survival	1.32	1.25–1.39
Onitilo et al [29]	USA Community Hospital 1994–2012	5335	67 months (median)	1.60	1.36–1.89
Hofvind et al [40]	Norwegian Breast Screening Cancer Registry 2005–2011	9547	60 months breast cancer-specific survival	1.7	1.3–2.4
Fisher et al [30]	Alberta Cancer Registry Canada 2002–2010	14,633	50 months (median)	1.36 (stage II), 1.74 (stage III)	1.13–1.48, 1.24–2.45
Christiansen et al [36]	Danish Breast Cancer Co-operative Group 1995–2012	58,331	138 months (median)	1.23	1.18–1.28
Hartmann-Johnsen et al [32]	Norwegian Breast Screening Cancer Registry 1998–2009	6387 (node positive only)	72 months (median)	1.39	1.02–1.89
de Boniface et al [44]	Swedish Multicentre Cohort Study 2000–2004	2767	156 months	1.69	1.22–2.33
Wang et al [48]	USA SEER 1995–2009	13,263	71 months (median)	1.18	1.09–1.28
Corradini et al [41]	Munich Cancer Registry (Germany) 1998–2014	7565	95 months (median)	1.268	1.055–1.525
Wang et al [48]	USA SEER 1973–2014	6342 (triple-negative breast cancer)	60 months	1.742	1.387–2.188

✓ Murphy J, Gandhi A. Does Mastectomy Reduce Overall Survival in Early Stage Breast Cancer? Clin Oncol (R Coll Radiol). 2021

1. … BCS+RT (↑OS) > Mastectomía



✓ A De la Cruz-Ku G et al . ASO Visual Abstract: Does Breast-Conserving Surgery with Radiotherapy Have a Better Survival Than Mastectomy? A Meta-Analysis of More Than 1,500,000 Patients. Ann Surg Oncol. 2022

2. DCIS: RT tras CC ↓ LF 50 % ….

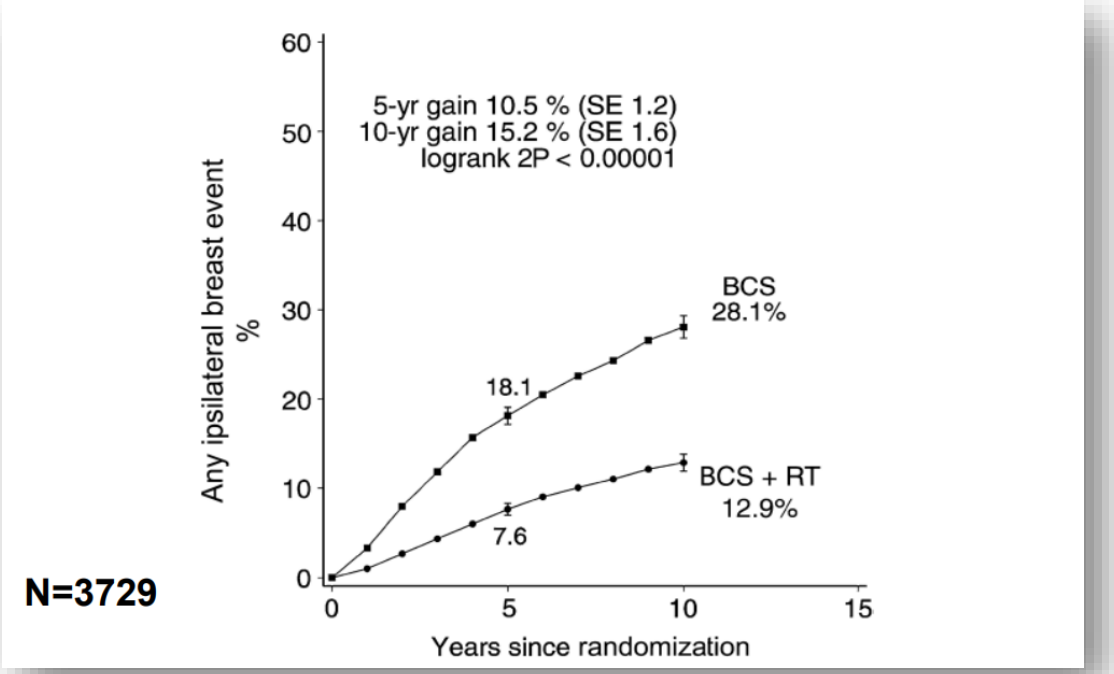
5 estudios aleatorizados

	n	MFU (years)	Treatment	New breast events	Invasive events	In situ events	HR (95% CI) for ipsilateral new breast events
NSABP B17 (2011)	813	17y	BCS BCS+WBRT	35% 20% p<0.001	20% 11% p<0.001	15% 9% p<0.001	0.48 (0.33-0.69)
UK/ANZ DCIS (2011)	1030* *(446 BCS±WBRT)	12.7Y	BCS BCS+WBRT	23% 8% p<0.0001	12.4% 5.5% p<0.001	13.4% 5.9% p<0.01	0.32 (0.22-0.47)
EORTC 10853 (2013)	1010	15y	BCS BCS+WBRT	31% 18% p<0.001	16% 10% p<0.001	16% 8% p=0.003	0.53 (0.40-0.70)
SweDCIS (2014)	1046	20y	BCS BCS+WBRT	32% 20% p<0.05	7% 12%	5% 15%	0.40 (0.30-0.54)
RTOG 9804 (2018)	629	12.4y	BCS BCS+WBRT	11.4% 2.8% p=0.0001	5.8% 1.5% p=0.016	NR	0.25 (0.12-0.53)

BCS: breast conserving surgery; WBRT: whole breast radiotherapy; HR: hazard ratio; MFU: median follow-up; NR: not reported

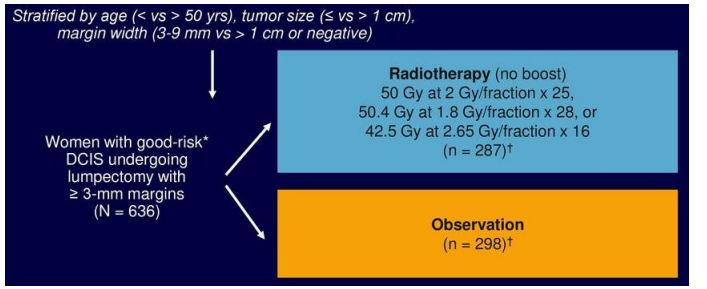
2. … ese beneficio ↑ conforme ↑ Fup incluso en DCIS de bajo riesgo

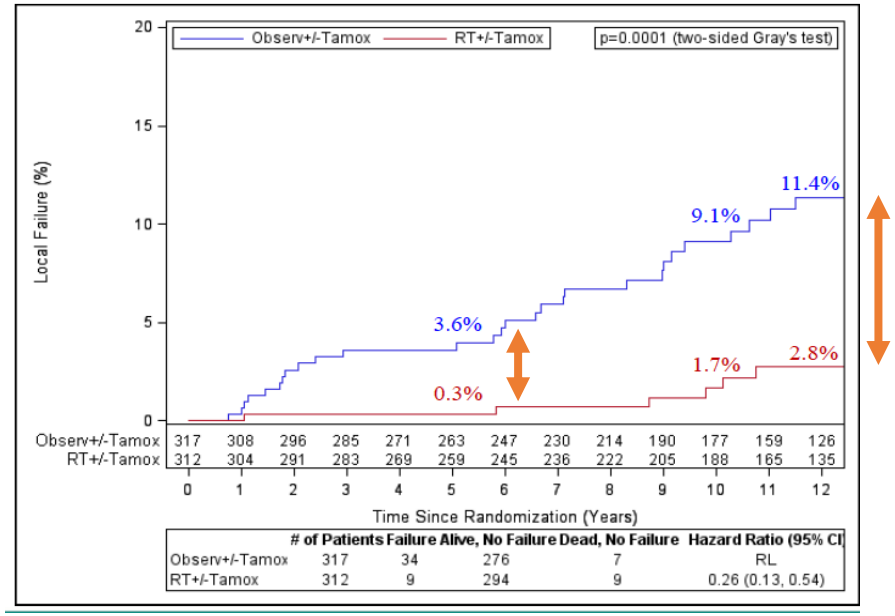
EBCTCG Meta-análisis: DCIS



Correa et al. JNCI Monogr 41: 162-177. 2010

NRG/RTOG 9804





B. Mc Cormick. MSKCC. San Antonio Breast Cancer Symposium 2018

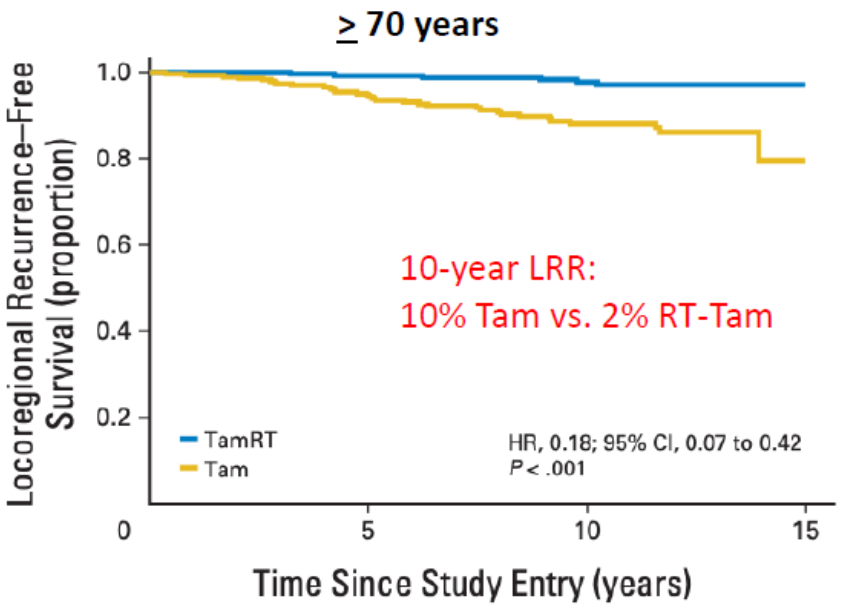
3. Ca. INFILTRANTE (C.Conservadora): RT tras CC↑ LC un 50 % ...

6 RCT

Study	Surgery	Radiotherapy	No.of pts	Loc.recc(%)	OS(%)	FU(yrs)
Fisher et al	Lumpectomy	50 Gy/25#/5wks.	567	**10**	64	12
(NSABP)		None	570	35	61	
Lilegren	Sector resec.	54 Gy/27#/5.5 wk	184	**8**	78	9
et al(Uppsala)		None	197	24	78	
Clark et al	Lumpectomy	40 Gy/16#3 wk + 12.5 Gy boost	416	**11**	79	7.6
		None	421	35	76	
Veronesi	Quadrentec.	50 Gy/25#/5 wk	294	**6**	82	9
(Milan)		10 Gy boost				
		None	273	24	77	
Forrest	Lumpectomy	50 Gy/25#/5 wk	291	**6**	83	5.7
(Scotland)		boost 10 Gy				
		None	294	25	83	
Holli	Lumpectomy	50 Gy/25#/5 wk	80	**8**	97	6.7
(Finland)		None	72	18	99	

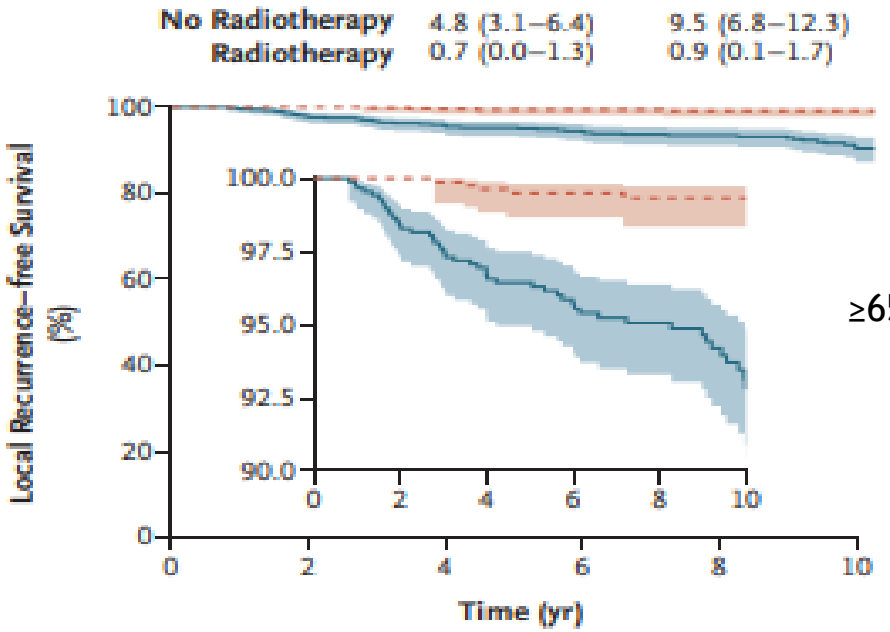
3. … incluso en C. Infiltrante de muy bajo riesgo

CALGB 9343



✓ Hughes et al. JCO 2013

PRIME II (Fup 10 años)



≥65 años

RT↑ control local, especialmente en fenotipos HR negativos

	Incidence of Local Recurrence (95% CI)	
	5 yr	10 yr
	percent	
ER-high, Radiotherapy	0.7 (0.0–1.5)	1.0 (0.1–1.9)
ER-high, No Radiotherapy	3.9 (2.3–5.6)	8.6 (5.7–11.4)
ER-low, Radiotherapy	0.0	0.0
ER-low, No Radiotherapy	12.7 (4.3–21.2)	19.1 (8.2–29.9)

✓ Kunkler I. et al. NEJM 2023

3. C. INFILTRANTE (C.Conservadora): RT tras CC ↑ LC y ↑ OS

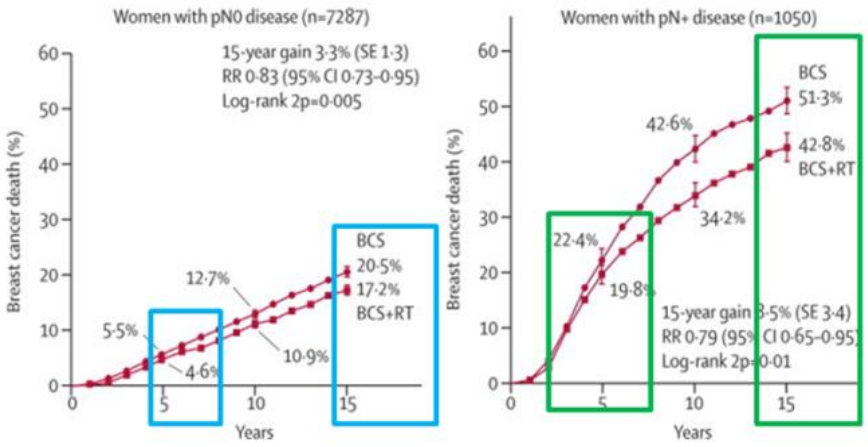
CONTROL LOCAL

SUPERVIVENCIA

(conservadora) EBCTCG 2011

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

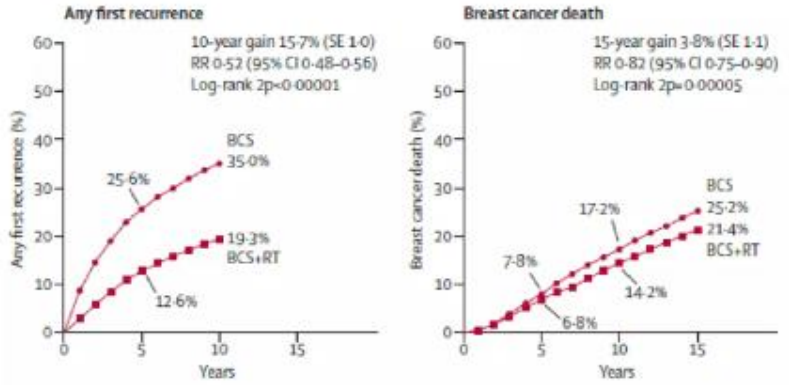
*Early Breast Cancer Trialists' Collaborative Group (EBCTCG)**



On average, in all the women in these trials, about one breast cancer death was avoided by year 15 for every four recurrences avoided by year 10

1/4

		No RT	RT	Absolute benefit
10 y LF	Overall	35%	19.3%	15.7
	pN0	31%	15.6%	15.4
	pN+	63.7%	42.5%	21.2
15y Mortality	Overall	25.2%	21.4%	3.8
	pN0	20.5%	17.2%	3.3
	pN+	51.3%	42.8%	8.5



RT tras CC ↓ LF a 10y y ↓mortalidad por ca. mama a 15 años (tanto N0 como N+)

✓ EBCTCG. Lancet 2011

3...además, el BOOST (C.Conservadora) también↑ LC, sobre todo ≤ 40 años

EORTC 22881-10882

Bartelink et al, 2001; updt 2007, 2015

- 5,318 patients with BCS followed by whole-breast RT (50 Gy).
  - 2661 patients (16 Gy) vs 2657 patients (no boost).
  - With a median follow-up of 17.2 years
    - 20 year OS: 59.7% (Boost) vs 61.1% (No boost)
    - 20 year IBTR: 12% (Boost) vs 16.4% (No boost)
    - 20 year Severe fibrosis: 5.2% (Boost) vs 1.8% (No boost)
  - Local recurrence was 10.2% vs 6.2% for the no boost and the boost group, respectively ($p = 0.0001$).

age	Boost	No Boost	Absolute benefit
≤ 40	13.5%	24%	10.5%
41-50	9%	12.5%	4%
51-60	5%	8%	3%
>60	4%	7%	3%

✓ Bartelink et al. 2001, 2007, 2015

4. C. Infiltrante (Mastectomía): RT tras mastect ↑ LC y ↑ OS

- Danish 82b
- Danish 82c
- British Columbia
- EBCTCG Meta-analysis (2014)

(mastectomía) EBCTCG 2014 (1-3 nodes)

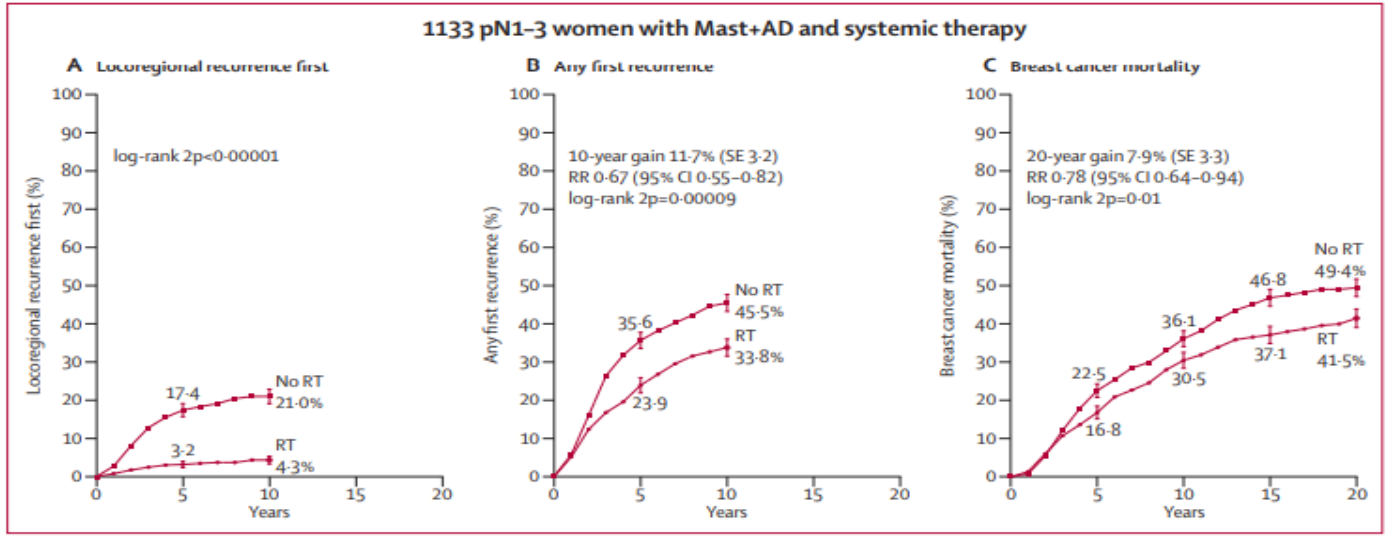
CONTROL LOCAL

SUPERVIVENCIA

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)*

- The finding comes from an IPD analysis of 8135 patients with an average follow up of 11 years.
- Included 22 trials in patients with EBC where patients underwent MRM ± locoregional RT.



after breast-conserving surgery and, for these women, about one breast cancer death was avoided in the 20 years after radiotherapy for every 1·5 recurrences of any type (ie, either locoregional or distant) avoided during the first 10 years after radiotherapy.

2/3

Interpretation After mastectomy and axillary dissection, radiotherapy reduced both recurrence and breast cancer mortality in the women with one to three positive lymph nodes in these trials even when systemic therapy was given.

4. C. Infiltrante (Mastectomía): RT tras mastectomía ↑ LC y ↑ OS

National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2023
Invasive Breast Cancer

NCCN Guidelines Index
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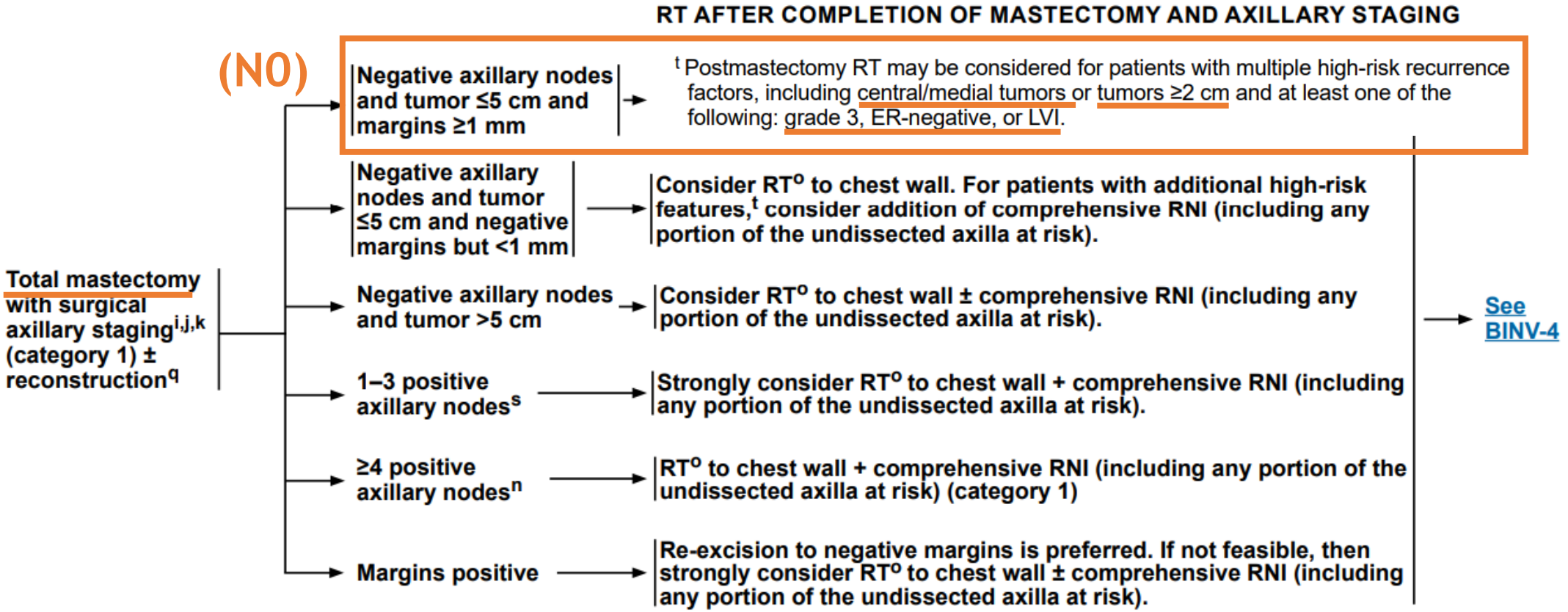
Discussion

LOCOREGIONAL TREATMENT OF cT1–3, cN0 or cN+, M0 DISEASE:[a,r]
MASTECTOMY FOLLOWED BY RT



5. Radioterapia AXILAR

Vaciamiento axilar vs observación

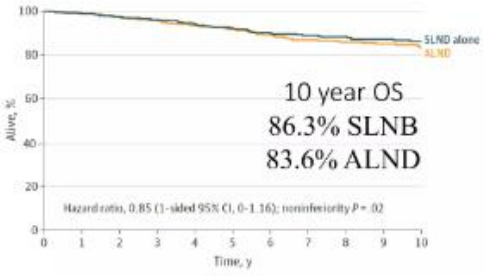
- ACOSOG Z0011 (2011)
- IBCSG 23-01 (2013)

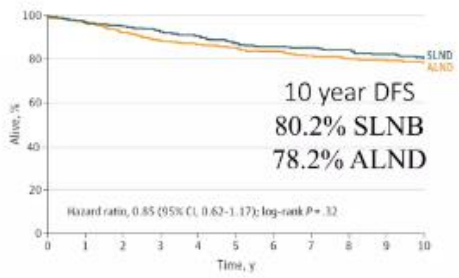
ACOSOG Z0011

Guiliano et al, 2011 (updated 2017)

- Upto T_2N_0 (target sample size: 1900)
- SLNB followed by randomization to ALND (445) or no ALND (446).
- Eligibility: ≤ 2 nodes +ve on SLNB
- ALND: Level I+II, ≥ 10 nodes

Primary end point
Overall survival

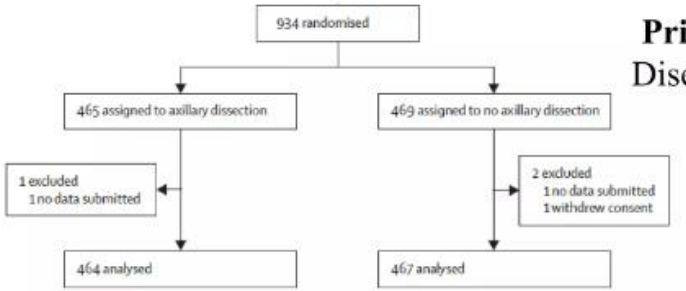




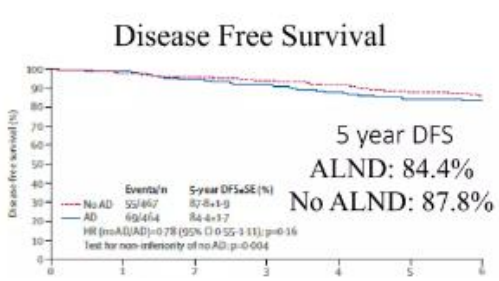
IBCSG 23-01

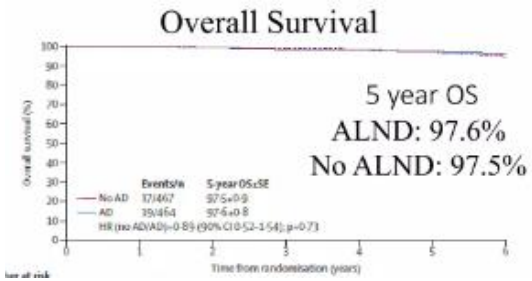
Galimberti et al, 2013.

- cT_2N_0 patients ≥1 micrometastatic (≤ 2mm) deposits on SLNB.



Primary end point:
Disease Free Survival





SLNB+ (≤ 2+ nodes): Omitir VA no impacta en Supervivencia : =DFS, = OS

5. Radioterapia AXILAR — Vaciamiento axilar vs RT axilar

- AMAROS (2014)
- OTOASOR (2017)

AMAROS - EORTC 10981-22023

Donker et al 2015. Bartels et al. JCO 2023

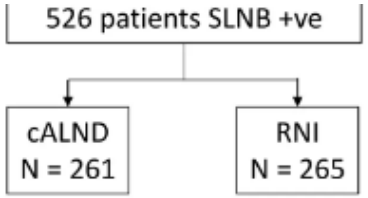
- N = 4823, upto T2N0; 1425 with +ve SLNB
- Median follow up (SLNB+): 10 years

- OS: 81.4% with RT vs 84.6% with ALND (NS)
- DFS also similar.
- Lymphedema significantly more in ALND arm, but not to extent defined in protocol (10% increase in circumference). Shoulder mobility, QoL were also similar. <at median F/U 6.1 yrs>

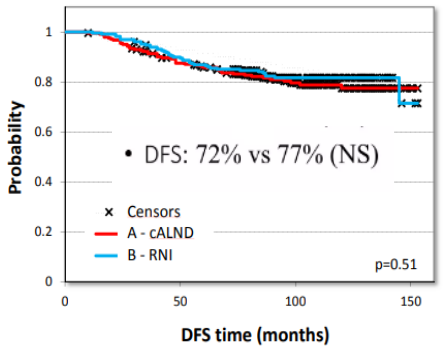
OTOASOR

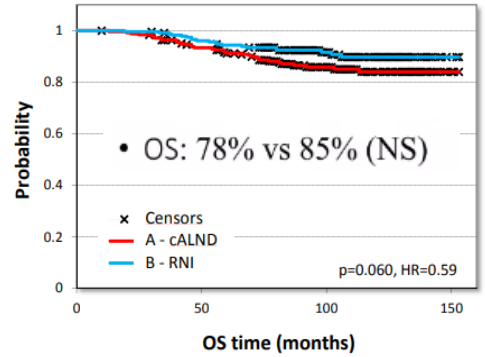
Savolt et al. Eur J Surg Oncol 2017

- N = 526; T ≤ 3cm, cN0 (Triple test)
- RT: WB + Axilla (1-3) + SCF; 50Gy/25#



- Mean F/U: 97 months (Range 54 – 134)





SLNB + (≤ 2 + nodes): Vaciamiento axilar = RT axilar := DFS =OS

5. Radioterapia AXILAR — RT axilar intencional vs RT axilar incidental

OPTIMAL I

SLN+: 250-15000 copias (OSNA)

Radiotherapy and Oncology 176 (2022) 76–82

Contents lists available at ScienceDirect

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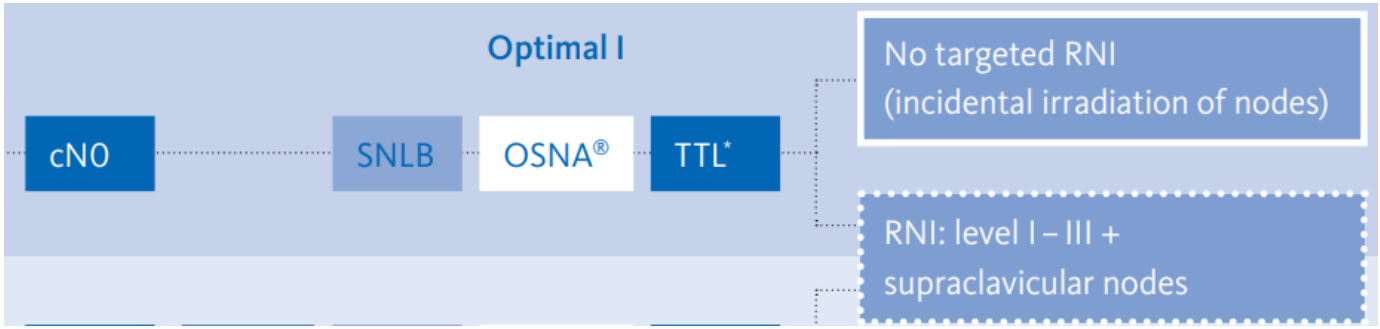
journal homepage: www.thegreenjournal.com

Original Article

OPTimizing Irradiation through Molecular Assessment of Lymph node (OPTIMAL): a randomized clinical trial

Manuel Algara [a,*], Elvira Rodríguez [b], Francisco José Martínez-Arcelus [c], Juan Salinas [d], Xavier Sanz [a], Inmaculada Beato [e], Aurea Manso [f], Ana Soler [g], José Reyes Rodríguez [h], Andere Frías [i], Ana Calín [j], Germán Juan [k], Pedro Meireles [l], Amanda Flaquer [m], on behalf of the OPTIMAL investigators

Trial	Type of study	Accrual time	Principal investigator, country	Cohort	Number of patients required	Main objective	Primary endpoint
Optimal I GIC-RAD-2014-0111	International, multicentre, prospective	April 2015 to December 2021	Manuel Ignacio Algara López, Spain	Early-stage BC, SLN assessed by OSNA® (250–15,000 copies/µL), no ALND	1,400	To demonstrate non-inferiority of incidental irradiation versus intentional irradiation to level I-III and supraclavicular nodes	5-year DFS



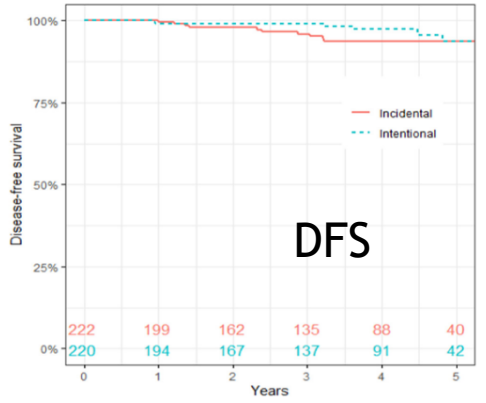


Fig. 1. Disease-free survival Kaplan-Meier estimates by irradiation modality. Numbers are patients at risk.

SLNB + (bajo nº copias OSNA): RT nodal intencional= incidental:= DFS

✓ Algara M et al. OPTIMAL investigators. OPTimizing Irradiation through Molecular Assessment of Lymph node (OPTIMAL): a randomized clinical trial. Radiother Oncol. 2022

5. Radioterapia AXILAR

VA→ RT axilar vs observación

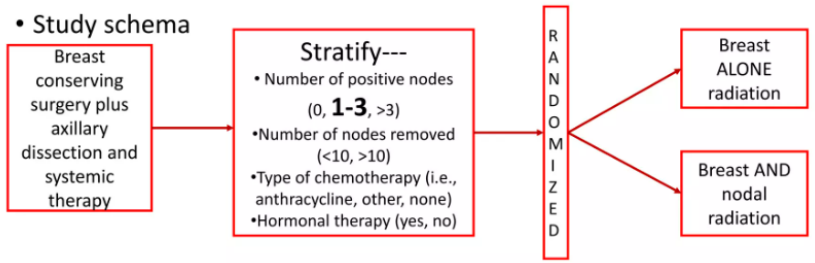
- NCIC-MA.20 (2015)
- EORTC Trial 22922/10925

NCIC-MA.20

Whelan T. et al. NEJM 2015

- **Node positive**
- **High risk node negative**

• Study schema



Ten-year Results (n=1832)

10-Yr	No Nodal RT	Nodal RT	HR	P-value
LRR*	6.8%	4.3%	0.59	.009
DFS	77.0%	82.0%	0.76	.01
OS	81.8%	82.8%	0.91	.38

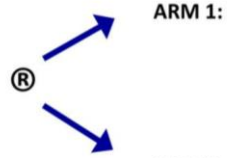
EORTC 22922/10925

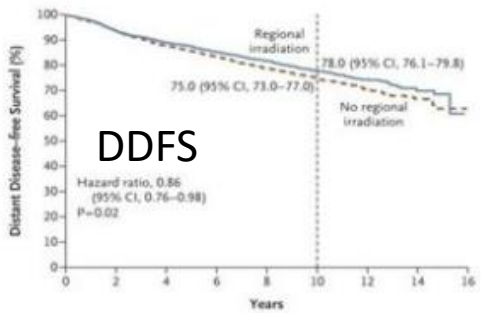
Poortmans P. et al. NEJM 2015

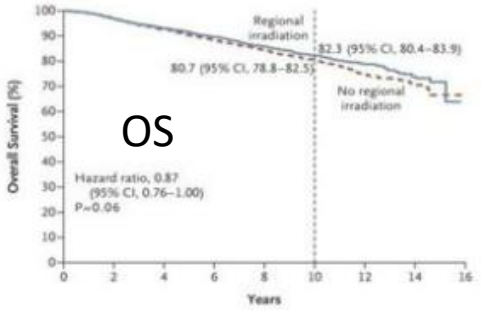
Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer

n= 4004

Stage I-III, pN+ or pN- w/ central/medial







VA: pN+ o pN0 de alto riesgo (<10 ggl VA, t. mediales..): RT nodal (RNI) : ↑DFS, ↑DDFS, ↓mortalidad

6. RT tras TSP

¿ Cómo evaluar la axila tras TSP?

Table 2. Trials assessing the use of SLN biopsy following NAST for clinically node-positive breast cancer

Study	ACOSOG Z1071 [39••]	SENTINA [38••]	SN FNAC [40••]
# of patients	637	592	135
Identification rate	92.7%	80.1%	87.6%
Overall FNR	12.6%†	14.2%	8.4%*
≥ 3 SLNs removed$^{\delta}$	9.1%	9.6%	4.9%*
Dual dye used	10.8%	8.6%	5.2%*
≥ 2 SLNs removed and removal of clipped node	6.8%	NA	NA
Study methodology	Multicenter, prospective	Multicenter, prospective	Multicenter, prospective

†With ≥ 2 SLN removed
*Considered IHC disease and ITC's to be positive
$^{\delta}$≥ 2 SLNs removed for SN FNAC

BSGC post TSP → ↑↑↑↑↑ Falsos negativos…

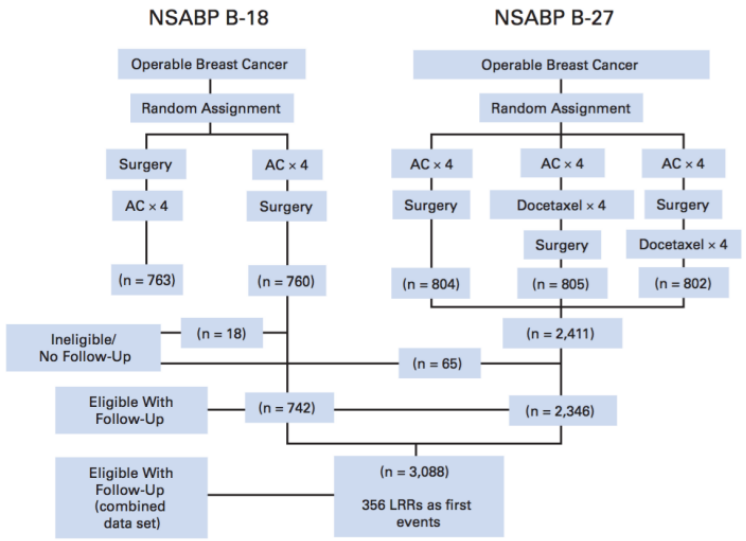
Recomendaciones internacionales FN < 10%

doble marcaje

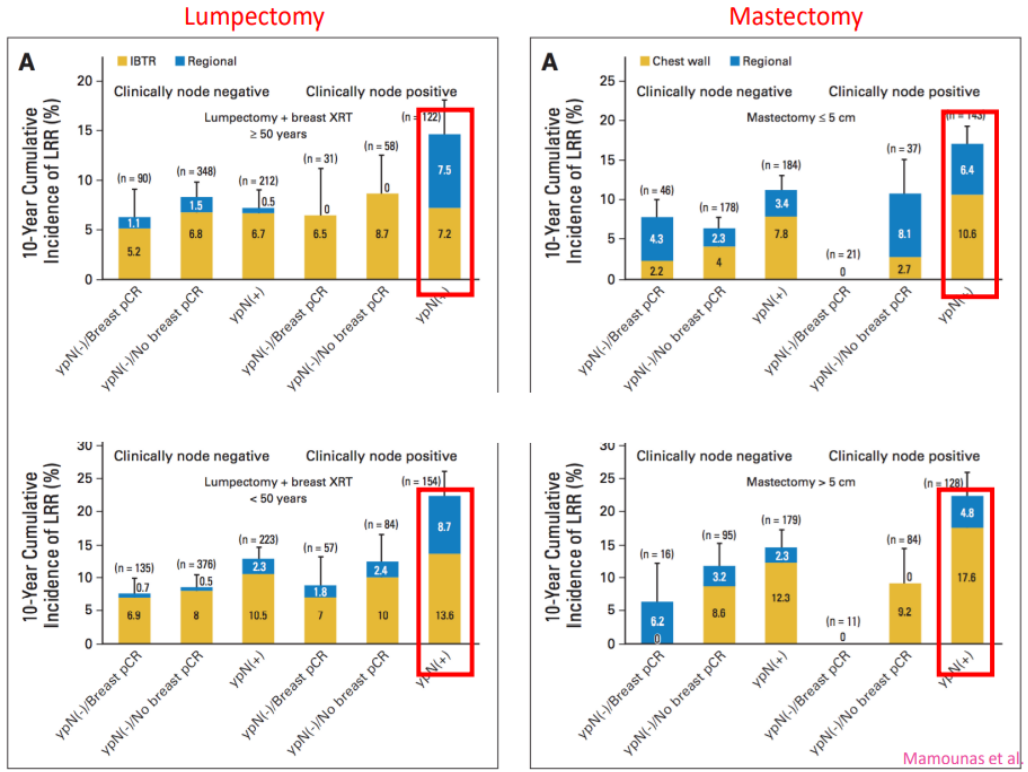
extraer >3 ganglios

National/International:	Staging Recommendation for cN+ → ycN0 Patients	Level of Evidence/Grade of Recommendation
European Society for Medical Oncology (ESMO) [10]	Sentinel lymph node biopsy (SLNB) can be an option, as long as additional recommendations are followed (e.g., dual tracer, clipping/marking of positive nodes, minimum of three sentinel nodes removed)	III, B
National Comprehensive Cancer Network (NCCN) [9]	Consider SLNB. Relatively high false-negative rate (FNR) (>10%) can be improved by marking biopsied lymph nodes to document their removal, using dual tracer, and by removing more than 2 sentinel nodes	2B
American Society of Breast Surgeons [13]	If SLNB after neoadjuvant therapy is attempted, dual tracer should be used. If a SLN and/or the clipped node (if clipped) is not identified, an Axillary lymph node dissection (ALND) is recommended	Not provided

6. RT tras TSP : cN+→ ypN+



- Full axillary lymph node dissection
- No regional nodal irradiation
- No postmastectomy radiation



NSABP B18 y B27:LR (sin RT) : 14-22%

✓Mamounas et al JCO 2012

6. RT tras TSP : cN+→ ypN+

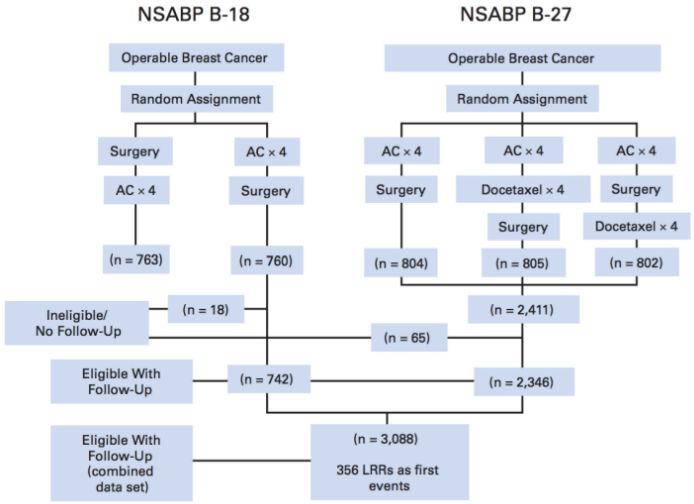
En marcha:

RT axilar vs ALND ALLIANCE 11202; ADARNAT; TAXIS

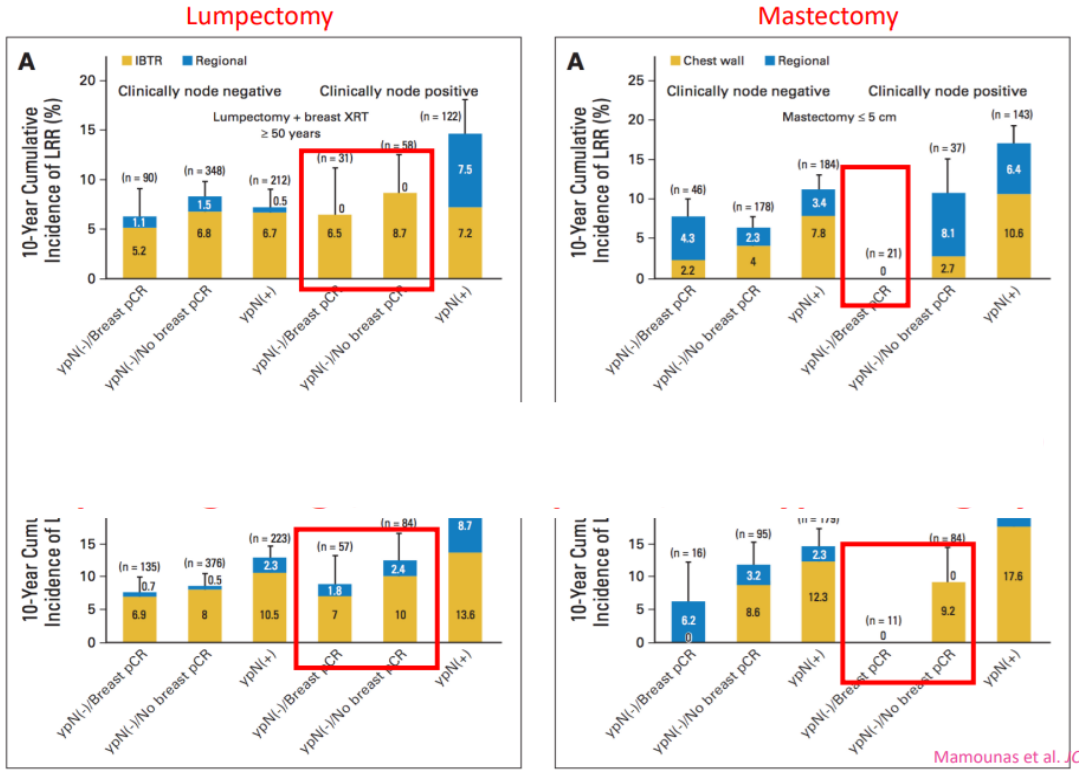
Table 2
Ongoing RCTs on de-escalating axillary treatment in patients with ypN1 disease. SLNB: Sentinel Lymph Node Biopsy; ALND: Axillary Lymph Node Dissection; (A)RT: (Axillary) Radiation Therapy, i.e. level 1 and 2; DFS: Disease-Free- Survival.

	Inclusion criteria	Randomization arms	Inclusion period and number of patients to include	Primary endpoint
ALLIANCE 11202 NCT 01901094	cT1-3N1, ypN1(SLNB)	ART vs ALND All patients receive RT to level 3 and 4 and IMN	2014–2024 N = 2918	5-year DFS
ADARNAT NCT04889924	cT1-T4bN0-1, ycN1 (<4 involved nodes); ypN1 (SLNB with ≤2 macrometastases)	ART vs ALND All patients receive RT to level 3 and 4 and IMN	2021–2026 N = 1666	5-year DFS
TAXIS NCT 03513614	cN1-2, ypN+ and removal of all clinically suspicious nodes	ALND and locoregional RT excluding the dissected axilla vs. Locoregional RT *including the axilla*	2018–2029 N = 1500	20-year DFS

6. RT tras TSP : cN+→ ypN0



- Full axillary lymph node dissection
- No regional nodal irradiation
- No postmastectomy radiation



NSABP B18 y B27: 10 y LR (sin RT) : 0-12% (recidivas sobre todo en mama o pared)

✓Mamounas et al JCO 2012

6. RT tras TSP : cN+→ ypN0

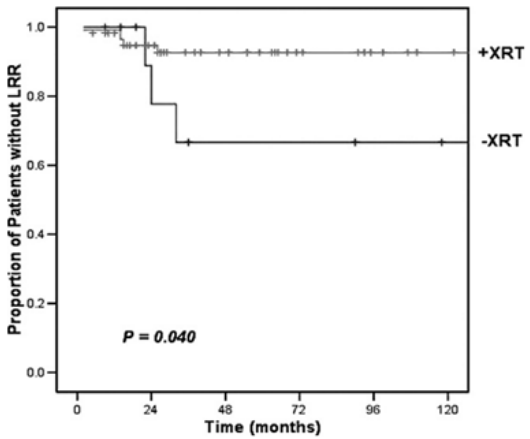
incluso en pCR: RT ↑LC y ↑Supervivencia

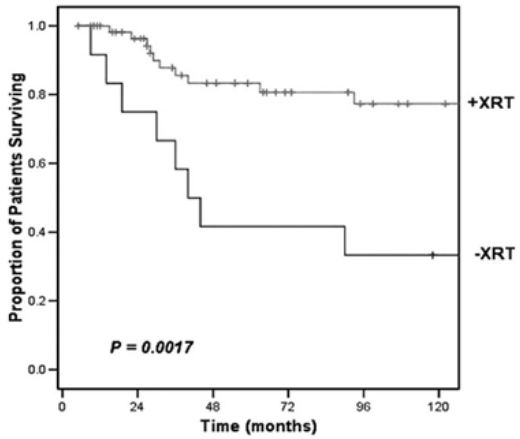
POSTMASTECTOMY RADIATION IMPROVES THE OUTCOME OF PATIENTS WITH LOCALLY ADVANCED BREAST CANCER WHO ACHIEVE A PATHOLOGIC COMPLETE RESPONSE TO NEOADJUVANT CHEMOTHERAPY

SEAN E. MCGUIRE, M.D., PH.D.,* ANA M. GONZALEZ-ANGULO, M.D.,† EUGENE H. HUANG, M.D.,*
SUSAN L. TUCKER, PH.D.,‡ SHU-WAN C. KAU, PH.D.,† TSE-KUAN YU, M.D., PH.D.,*
ERIC A. STROM, M.D.,* JULIA L. OH, M.D.,* WENDY A. WOODWARD, M.D., PH.D.,*
WELELA TEREFFE, M.D.,* KELLY K. HUNT, M.D.,§ HENRY M. KUERER, M.D., PH.D.,§
AYSEGUL A. SAHIN, M.D.,‖ GABRIEL N. HORTOBAGYI, M.D.,† AND THOMAS A. BUCHHOLZ, M.D.*

Análisis retrospectivo

226 pts cN+→ TSP→ pCR





RT ↑ 10y LRFS y OS

✓ Mc Guire et al. Int J Radiat Oncol Biol Phys. 2007

Pooled analysis of RCT GEPAR TRIALS

(GeparTrio, GeparQuattro, GeparQuinto) 3481 pts

RT ↑ 5y LFS (81,5% a 90%) y ↑ 5y DFS (67,4% a 75,4%)

tanto pCR como no pCR

✓Krug ASCO 2015

6. RT tras TSP : cN+→ ypN0

Cancer Treatment Reviews 101 (2021) 102297

Contents lists available at ScienceDirect

Cancer Treatment Reviews

journal homepage: www.elsevier.com/locate/ctrv

De-escalation of axillary irradiation for early breast cancer – Has the time come?

Elżbieta Senkus [a,*], Maria Joao Cardoso [b,c], Orit Kaidar-Person [d,e,f], Aleksandra Łacko [g,h], Icro Meattini [i,j], Philip Poortmans [k,l]

Table 4
Effect of radiation therapy in cN+ patients converting to ypN0 after primary systemic therapy.

	Type of breast surgery	Patient number	Effect of postoperative RT (RNI for BCS patients)
NCDB (2003–2011) [59]	mastectomy	3040	↑ OS
NCDB (1998–2009) [60]		1560	OS NS ↑ OS in clinical stage IIIB/ IIIC, T3/T4, no pCR (breast)
NCDB (2010–2015) [61]		7499	OS NS
NCDB (2004–2008) [62]		1937	OS NS ↑ OS in HR- patients
Gepar Trials [63]		158	borderline ↓ LRR
ACOSOG Z1071		157	LRR, DFS, BCSS, OS NS

…sin embargo, hay multitud de estudios retro y prospectivos que sugieren hay un grupos de bajo riesgo donde se podría valorar omitir RT tras TSP y pCR….

Table 4
Effect of radiation therapy in cN+ patients converting to ypN0 after primary systemic therapy.

	Type of breast surgery	Patient number	Effect of postoperative RT (RNI for BCS patients)
Chinese [64]		185	↓ LRR, ↓ DM, ↑ DFS, OS NS
KROG 12–05 [65]		151	LRR, DFS, OS NS
Institut Curie [66]		92	LRR, DFS, OS NS
MD Anderson [67]		106	Stage I and II LRR – NS, Stage III ↓ LRR
NCDB (2003–2011) [59]	breast conserving surgery	2070	OS NS
ACOSOG Z1071 [35]		125	LRR, DFS, BCSS, OS NS
NCDB (2010–2015) [61]		4842	OS NS
Centre René Huguenin [68]		84	DFS, OS NS
KROG 12–05 [65]		251	LRR, DFS, OS NS

…incluso revisiones de estudios que analizan el impacto de la RT locorregional …

6. RT tras TSP : cN+→ ypN0

Risk group definition:

- Low Risk: ≤2 cN+ before PST AND complete response in the breast AND age >40
- High Risk: >2 cN+ before PST AND/OR TNBC AND/OR incomplete response in the breast AND/OR age <40.

Table 5
Recommendations for axillary lymph node dissection and irradiation of axillary nodal volumes in relation to pathological nodal status in cN+ patients converting to ycN0 after primary systemic therapy and sentinel lymph node biopsy /targeted axillary dissection.

	Risk group	ypN0	ypN0(i+), ypN1mi	ypN1 ≤2	ypN1 >3
PST (ChT or ET)	Low	Axillary RT: level I and II; consider RNI omission if WBI or chest wall RT	Axillary RT: level I and II	ALND, if not: axillary RT: level I and II	ALND + axillary RT: non-resected part up to level IV
	High	Axillary RT: level I-IV	Axillary RT: level I-IV	ALND + axillary RT: non-resected part up to level IV	ALND + axillary RT: non-resected part up to level IV

Extreme caution should be taken, however, when deciding about omission of particular therapeutic components. We encourage strongly to conduct this de-escalation process in a stepwise manner, carefully monitoring for increased LRR rates. This should be accompanied by collecting relevant patient-, tumor- and treatment-related data to allow for fully informed evaluation of treatment de-escalation outcomes. For

…y emiten recomendaciones, aunque OJO!! advirtiendo de la limitación de las mismas.

✓ Senkus et al. Cancer treatment reviews. 2021

6. RT tras TSP : cN+→ ypN0 En marcha:

RT/ALND vs observación

NSABP-51, ATNEC

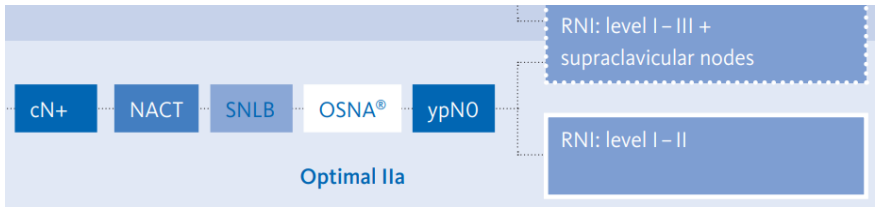
Table 1
Ongoing RCTs on de-escalating axillary treatment in patients with ypN0 disease. SLNB: Sentinel Lymph Node Biopsy; ALND: Axillary Lymph Node Dissection; (A)RT: (Axillary) Radiation Therapy, i.e. level 1 and 2; DFS: Disease-Free- Survival.

	Inclusion criteria	Randomization arms	Inclusion period and number of patients to include	Primary endpoint
NSABP-51/RTOG 1304 NCT01972975	cT1-3N1, ycN0, undergoing breast surgery and ypN0 (SLNB or ALND)	No additional RT (only breast RT in case of breast conservation) vs Regional Nodal RT, i.e. Level 1–4 and IMN	2013–2023 N = 1636	10-year DFS
ATNEC NCT 0410979	cT1-3N1, ycN0, undergoing breast surgery and ypN0(TAD)	No axillary treatment (No ART, and no ALND) vs Axillary treatment (ART or ALND)	2021–2030 N = 1900	5-year DFS, and 5 year Lymph-oedema of the arm

RT incidental vs intencional

OPTIMAL IIa

International, multicentre, prospective	January 2017 to January 2020	Manuel Ignacio Algara López, Spain	Early-stage BC, cN+ before NACT and ypN0 after NACT (SLN assessed by OSNA®), no ALND	1,212	To demonstrate non-inferiority of irradiation to level I-II nodes versus irradiation to level I-III and supraclavicular nodes	5-year DFS



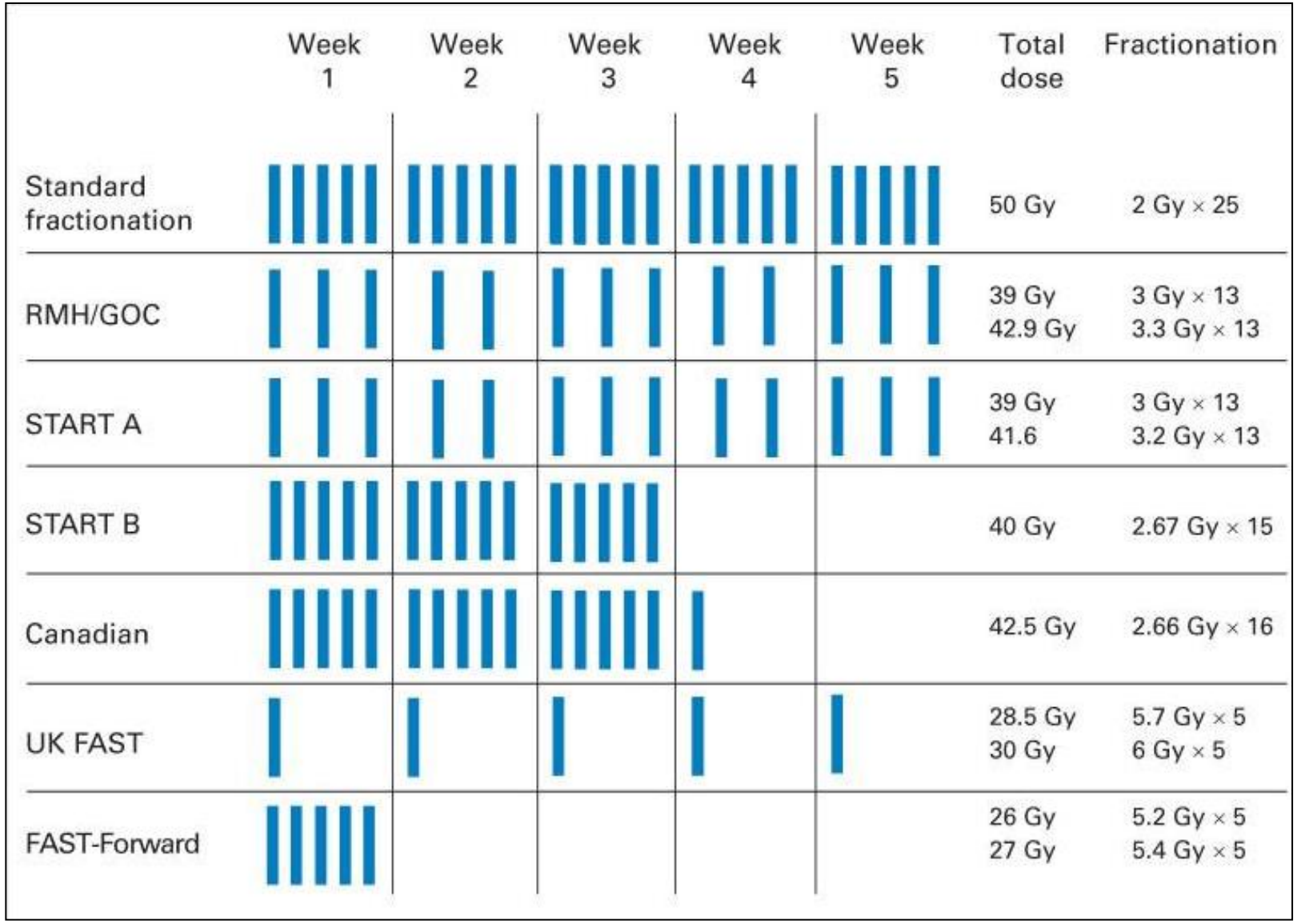
Guías: Estadio pre TSP más desfavorable

7. Radiobiología y Fraccionamientos

25-30 fx

15-16 fx

5fx fx



	Week 1	Week 2	Week 3	Week 4	Week 5	Total dose	Fractionation
Standard fractionation	▮▮▮▮▮	▮▮▮▮▮	▮▮▮▮▮	▮▮▮▮▮	▮▮▮▮▮	50 Gy	2 Gy × 25
RMH/GOC	▮ ▮ ▮	▮ ▮	▮ ▮ ▮	▮ ▮	▮ ▮ ▮	39 Gy 42.9 Gy	3 Gy × 13 3.3 Gy × 13
START A	▮ ▮ ▮	▮ ▮	▮ ▮ ▮	▮ ▮	▮ ▮ ▮	39 Gy 41.6	3 Gy × 13 3.2 Gy × 13
START B	▮▮▮▮▮	▮▮▮▮▮	▮▮▮▮▮			40 Gy	2.67 Gy × 15
Canadian	▮▮▮▮▮	▮▮▮▮▮	▮▮▮▮▮	▮		42.5 Gy	2.66 Gy × 16
UK FAST	▮	▮	▮	▮	▮	28.5 Gy 30 Gy	5.7 Gy × 5 6 Gy × 5
FAST-Forward	▮▮▮▮▮					26 Gy 27 Gy	5.2 Gy × 5 5.4 Gy × 5

Contents lists available at ScienceDirect

Journal of Geriatric Oncology

Letter to the Editor

Accelerating adjuvant breast irradiation in women over 65 years: Matched case analysis comparing a 5-fractions schedule with 15 fractions in early and locally advanced breast cancer

Hans Van Hulle [a], Dieter Naudts [a], Ellen Deschepper [b], Vincent Vakaet [a,c], Leen Paelinck [c], Giselle Post [a], Annick Van Greveling [c], Bruno Speleers [a], Pieter Deseyne [a,c], Yolande Lievens [a,c], Wilfried De Neve [a,c], Liv Veldeman [a,c], Chris Monten [a,c,*]

Van Hulle et al. Pilot and Feasibility Studies (2020) 6:154
https://doi.org/10.1186/s40814-020-00693-z

Pilot and Feasibility Studies

STUDY PROTOCOL Open Access

Feasibility study on pre or postoperative accelerated radiotherapy (POP-ART) in breast cancer patients

Hans Van Hulle[1*], Vincent Vakaet[1,2], Giselle Post[1], Annick Van Greveling[2], Chris Monten[1,2], An Hendrix[1], Koen Van de Vijver[3], Jo Van Dorpe[3], Pieter De Visschere[4], Geert Braems[1,5], Katrien Vandecasteele[1,2], Hannelore Denys[6,7], Wilfried De Neve[1,2] and Liv Veldeman[1,2]

The Breast 55 (2021) 105–111

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Original article

Acute toxicity and health-related quality of life after accelerated whole breast irradiation in 5 fractions with simultaneous integrated boost

Hans Van Hulle [a,*], Vincent Vakaet [a,b], Chris Monten [a,b], Pieter Deseyne [a,b], Max Schoepen [a,c], Cato Colman [a], Leen Paelinck [b], Annick Van Greveling [b], Giselle Post [a], Bruno Speleers [a], Katrien Vandecasteele [a,b], Marc Mareel [a], Wilfried De Neve [a,b], Liv Veldeman [a,b]

Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial

Adrian Murray Brunt*, Joanne S Haviland*, Duncan A Wheatley, Mark A Sydenham, Abdulla Alhasso, David J Bloomfield, Charlie Chan, Mark Churn, Susan Cleator, Charlotte E Coles, Andrew Goodman, Adrian Harnett, Penelope Hopwood, Anna M Kirby, Cliona C Kirwan, Carolyn Morris, Zohal Nabi, Elinor Sawyer, Navita Somaiah, Liba Stones, Isabel Syndikus, Judith M Bliss†, John R Yarnold†, on behalf of the FAST-Forward Trial Management Group

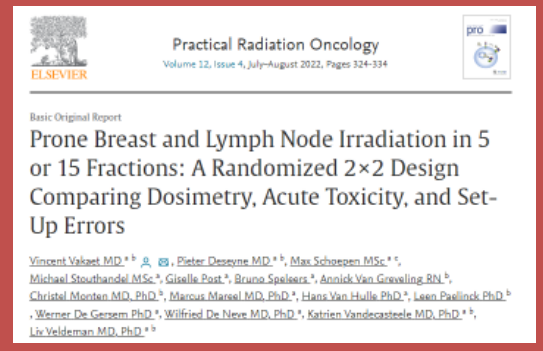
Journal Pre-proofs

Original Article

Health-related quality of life after accelerated breast irradiation in five fractions: a comparison with fifteen fractions

Hans Van Hulle, Vincent Vakaet, Renée Bultijnck, Pieter Deseyne, Max Schoepen, Annick Van Greveling, Giselle Post, Wilfried De Neve, Chris Monten, Yolande Lievens, Liv Veldeman

PII: S0167-8140(20)30400-X
DOI: https://doi.org/10.1016/j.radonc.2020.07.007
Reference: RADION 8421



Practical Radiation Oncology
Volume 12, Issue 4, July–August 2022, Pages 324–334

Basic Original Report

Prone Breast and Lymph Node Irradiation in 5 or 15 Fractions: A Randomized 2×2 Design Comparing Dosimetry, Acute Toxicity, and Set-Up Errors

Vincent Vakaet MD,* [b], Pieter Deseyne MD,* [b], Max Schoepen MSc,* [c], Michael Stouthandel MSc [a], Giselle Post [a], Bruno Speleers [a], Annick Van Greveling RN [b], Christel Monten MD, PhD [a], Marcus Mareel MD, PhD [a], Hans Van Hulle PhD [a], Leen Paelinck PhD [b], Werner De Gersem PhD [a], Wilfried De Neve MD, PhD [a], Katrien Vandecasteele MD, PhD [a,b], Liv Veldeman MD, PhD [a,b]

Clinical Investigation

5-Year Outcomes of a Randomized Trial Comparing Prone and Supine Whole Breast Irradiation in Large-Breasted Women

Vincent Vakaet, MD,*,† Hans Van Hulle, MA,* Marie Vergotte, BS,* Max Schoepen, MSc,*,† Pieter Deseyne, MD,*,† Annick Van Greveling, RN,† Giselle Post, PBa,* Bruno Speleers, PBa,* Leen Paelinck, MSc, PhD,† Chris Monten, MD, PhD,*,† Wilfried De Neve, MD, PhD,*,† and Liv Veldeman, MD, PhD*,†

*Department of Human Structure and Repair, Ghent University, Ghent, Belgium; †Department of Radiation Oncology, Ghent University Hospital, Ghent, Belgium; and ‡Department of Industrial Systems Engineering and Product Design, Kortrijk, Belgium

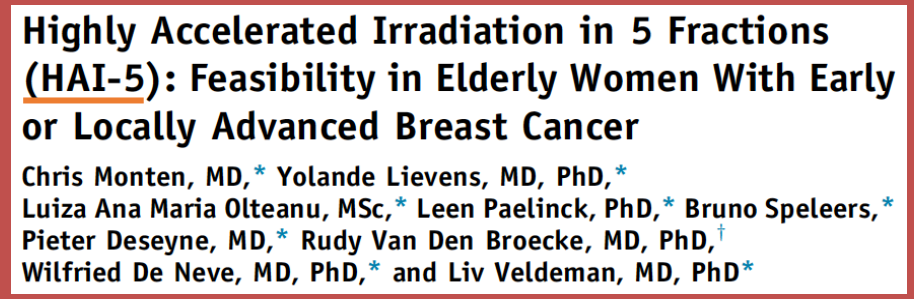
ACTA ONCOLOGICA
https://doi.org/10.1080/0284186X.2020.1747638

Taylor & Francis
Taylor & Francis Group

LETTER TO THE EDITOR

Two-year toxicity of hypofractionated breast cancer radiotherapy in five fractions

Hans Van Hulle[a], Vincent Vakaet[a,b], Kathleen Deckmyn[a], Chris Monten[a,b], Leen Paelinck[b], Annick Van Greveling[b], Giselle Post[a], Max Schoepen[a,c], Arthur Fonteyne[a], Bruno Speleers[a], Pieter Deseyne[a,b], Marc Mareel[a], Wilfried De Neve[a,b] and Liv Veldeman[a,b]

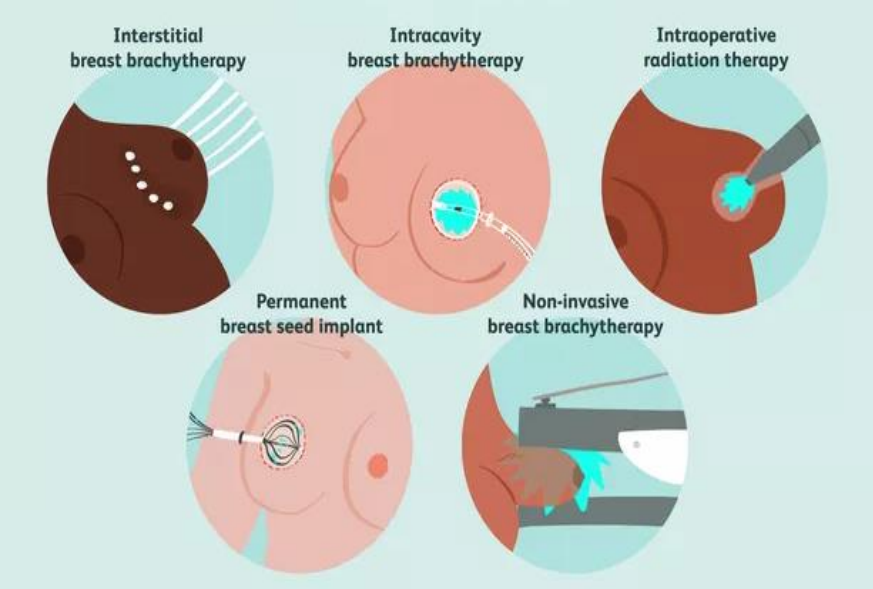


Highly Accelerated Irradiation in 5 Fractions (HAI-5): Feasibility in Elderly Women With Early or Locally Advanced Breast Cancer

Chris Monten, MD,* Yolande Lievens, MD, PhD,* Luiza Ana Maria Olteanu, MSc,* Leen Paelinck, PhD,* Bruno Speleers,* Pieter Deseyne, MD,* Rudy Van Den Broecke, MD, PhD,† Wilfried De Neve, MD, PhD,* and Liv Veldeman, MD, PhD*

Ultrahipofraccionamiento… y ya no sólo FAST FORWARD

8. Volúmenes y secuencia de irradiación: PBI y preop



APBI Patient and Tumor Characteristics

1. Majority of patients age ≥ 50 years
2. Tumor size < 2 or 3 cm
3. Node negative
4. Surgical margins > 2mm
5. Grade 1 or 2
6. ER+, Her2-
7. Excluded EIC, Invasive lobular carcinoma, LVSI

TABLE 2. Key Partial Breast Irradiation and IORT Trials

Partial Breast Irradiation

Trial	Years of Accrual	No. of Patients	F/U (years)	Radiation Dose/ Technique	Local Recurrence with WBI (%)	Local Recurrence with APBI (%)	Toxicity
National Institute of Oncology-Hungary	1998-2004	258	17	36.4 Gy/8 fx (interstitial) 50 Gy/25 fx (electrons)/ interstitial/electron	7.9	9.6	Improved cosmesis with APBI (81% *v* 63%)
GEC-ESTRO	2004-2009	1,184	6.6	32 Gy/8 fx 30.2 Gy/7 fx (HDR)/ 50 Gy (PDR)/ interstitial	0.9	1.4	Reduced late grade 2-3 skin toxicity with APBI
University of Florence	2005-2013	520	10.7	30 Gy/5 fx (every other day)/IMRT	2.5	3.7	Less acute and chronic toxicity with APBI
NSABP B39	2005-2013	4,216	10.2	38.5/10 fx 3D-CRT, 34 Gy/10 fx brachytherapy	3.9	4.6	Grade 3 toxicity: 10% APBI *v* 7% WBI
RAPID	2006-2011	2,135	8.6	38.5 Gy/10 fx/3D-CRT	2.8	3.0	Increased late toxicity with APBI (32% *v* 13%) and worse cosmesis with APBI
Barcelona	—	102	5.0	37.5 Gy/10 fx/3D-CRT	0	0	Lower rates of late toxicity with APBI and no difference in cosmesis
IMPORT LOW	2007-2010	2018	6.2	40 Gy/15 fx 36/15 fx (40/15 partial) 40/15 partial/3D-CRT	1.1 0.2	0.5	Similar photographic, patient, and clinical toxicity assessments, improved breast appearance, and firmness with partial breast

IORT

Trial	Years of Accrual	No. of Patients	F/U (years)	Radiation Dose (Gy)	Local Recurrence with WBI (%)	Local Recurrence with IORT (%)	Toxicity
ELIOT	2000-2007	1,305	12.4	21	2	11	Not collected
TARGIT-A	2000-2012	3,451 1,153 (postpathology) 2,298 (prepathology)		20	1.3 1.05 (5 year) 0.95 (5 year)	3.3 3.96 (5 year)-IORT inferior 2.11% (5 year)-noninferior Overall local recurrences (60 IORT *v* 24 WBI,	Wound complications similar

8. Volúmenes y secuencia de irradiación: PBI y preop

	ESTUDIO	N	PACIENTES	DISEÑO	TRATAMIENTO	OBJETIVO PRIMARIO
RT pre MAMA ± CADENAS	PRADA (RU)	25	Candidatas a mastectomía y reconstrucción con DIEP	Fase II	40Gy/15 ó 50Gy/25	Factibilidad de la reconstrucción tras RT preoperatoria
	PROBI (PB)	94	cT1-2N0	Fase I/II	46,2/21+boost	Complicaciones post-cirugía
	NeoRT (RU)	50	Luminal A	Fase II	40Gy/15+Letrozole	Respuesta
	RadioPARP (Francia)	24	T3-4N1-3M0-1 TNBC	Fase I	50Gy/25+Olaparib (PARPi)	MTD Olaparib
	POPI (EE.UU)	44	IIB-IV	Fase I	37,5Gy/16+Velaparib (PARPi)	MTD Velaparib
PBI pre	ARTEMIS (Canadá)	32	T1N0, >70años	Fase I	40Gy/5 SBRT	Factibilidad
	SIGNAL (EE.UU)	120	T1/T2aN0 ≥55años	Fase II	21Gy SBRT	Toxicidad RT
	Duke (EE.UU)	100	Tis/T1N0 >60años (>50 Oncotype 0-17)	Fase II	21 Gy SBRT	Cosmesis
	SPORT (Canadá)	10	T1N0 >60años	Fase I, escalado de dosis	15Gy, 18Gy, 20Gy	Toxicidad aguda RT
	ABLATIVE (PB)	25	T1-2N0(<3cm)	Fase II	20Gy	pCR

9. Ca mama metastásico: SBRT oligometástasis

CA MAMA PRECOZ

90 % se diagnostican precozmente
y tienen una SPV a 5a del **90%**

RECAÍDAS A DISTANCIA

20-30% desarrollaran metástasis a lo largo de su vida

ENFERMEDAD

METASTÁSICAS *DE NOVO*

6% metástasis al diagnóstico

El 90% de Pts con CMM mueren por el **cáncer**

Supervivencia media: 2-3 años

Supervivencia a 5 años: 26%

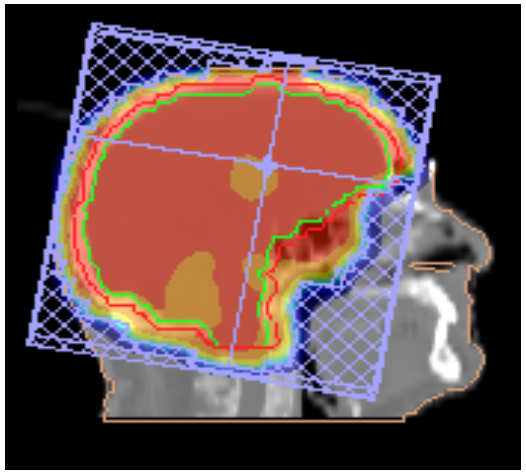
RETO → **Selección**

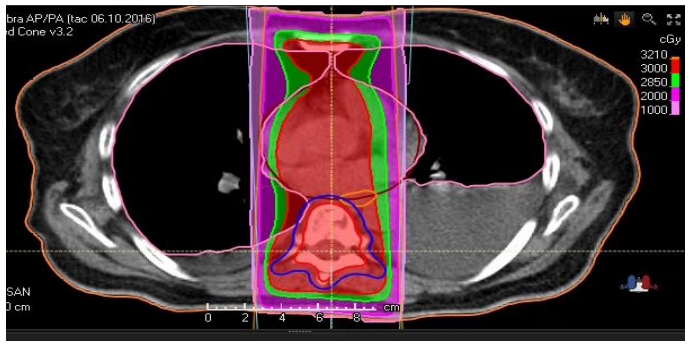
Existen pacientes capaces de vivir **más de 10 años**

✓ SEOM 2021

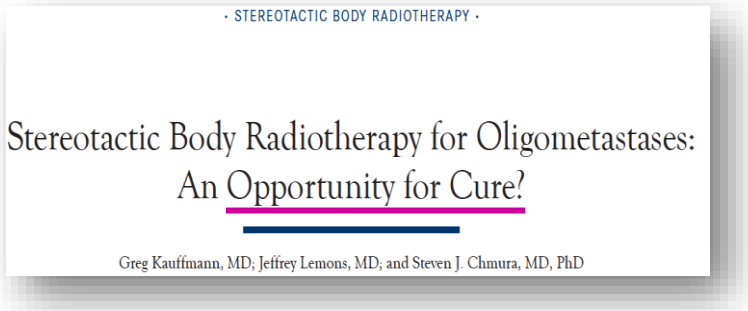
9. Ca mama metastásico: SBRT oligometástasis

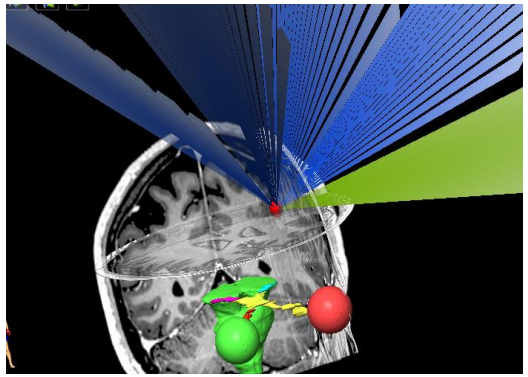
Paliativo

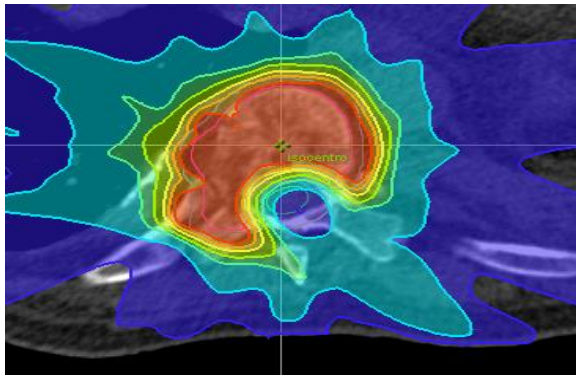




Radical: SBRT/SRS

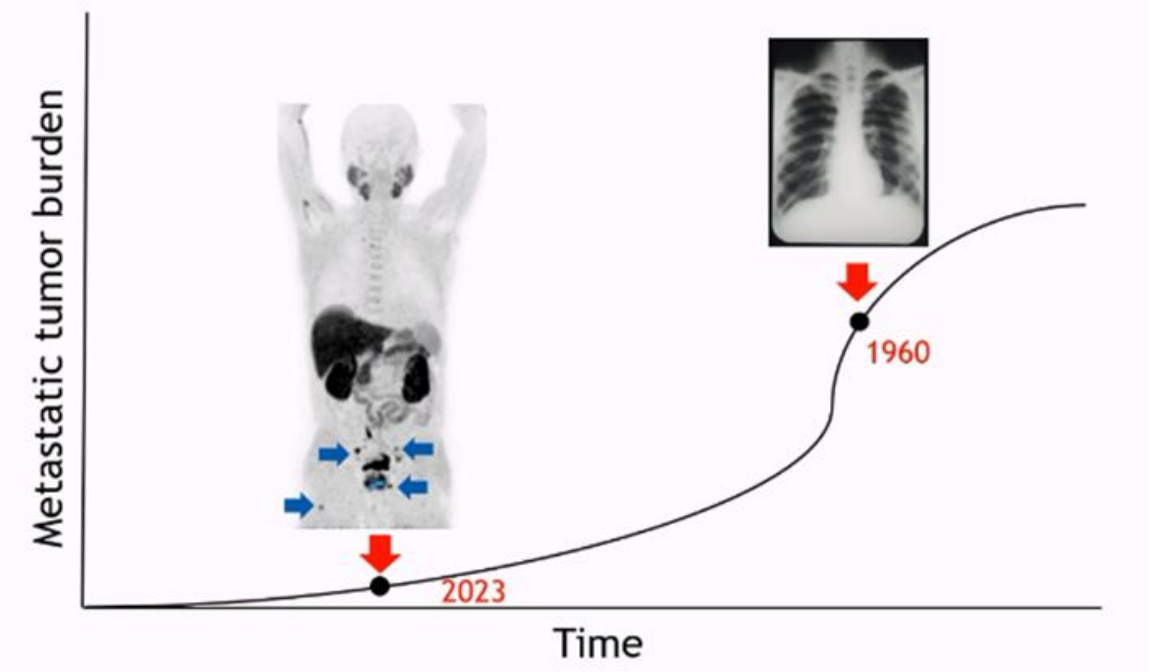






9. Ca mama metastásico: SBRT oligometástasis

Paciente OLIGOMETASTÁSICO



Enfermedad metastásica:

- ✓ Confinada a **uno** o a **un número limitado de órganos**
- ✓ Número limitado **(<5) de lesiones metástasicas**
- ✓ Periodos prolongados de **SLE** (↑spv libre enf)
- ✓ Oligo-recidivas metastásicas **potencialmente tratables**

✓ *Hellman S, Weichselbaum RR. Oligometastases. J Clin Oncol 1995;13:8-10.*
✓ *Niibe Y , Hayakawa K Jpn. J. Clin. Oncol. 2010;40:107-111 (2005)*

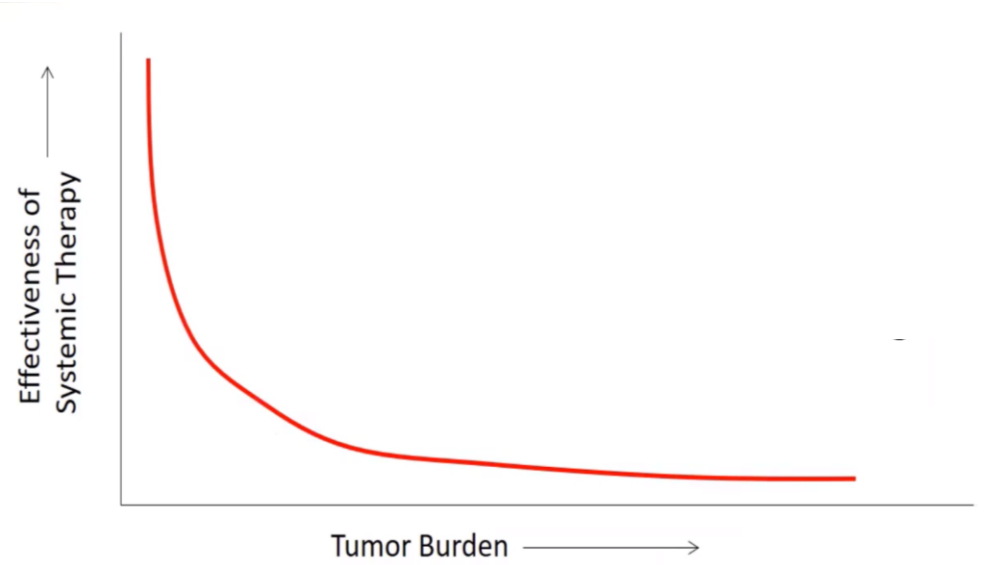
9. Ca mama metastásico: SBRT oligometástasis

1. Reducir siembra tumoral

✓ Correa and Palma, Cancer J, 2016

2.Efecto *Norton-Simon*:

Al ↓carga tumoral, ↑ efectividad de los ttos sistémicos



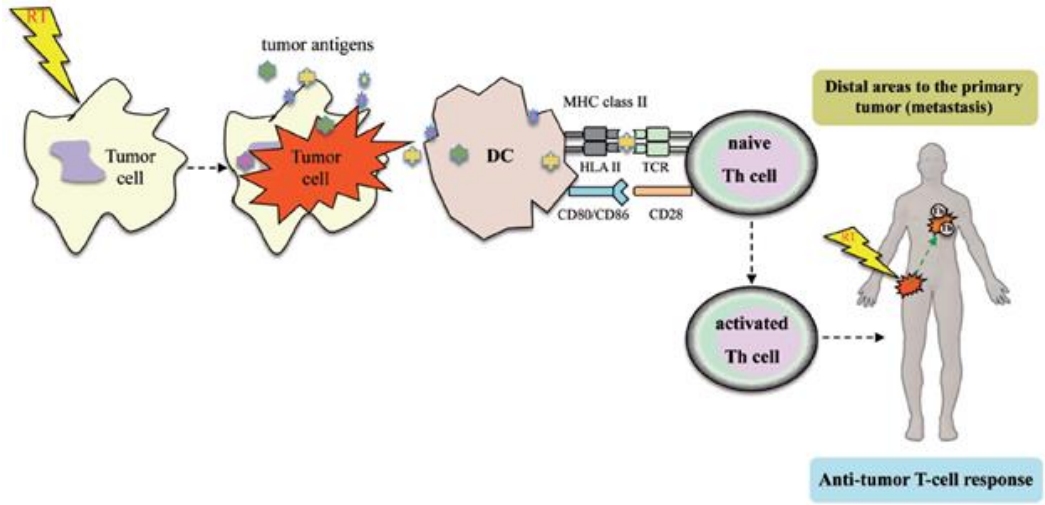
✓ Norton and Simon. Cancer Treat Rep 1977

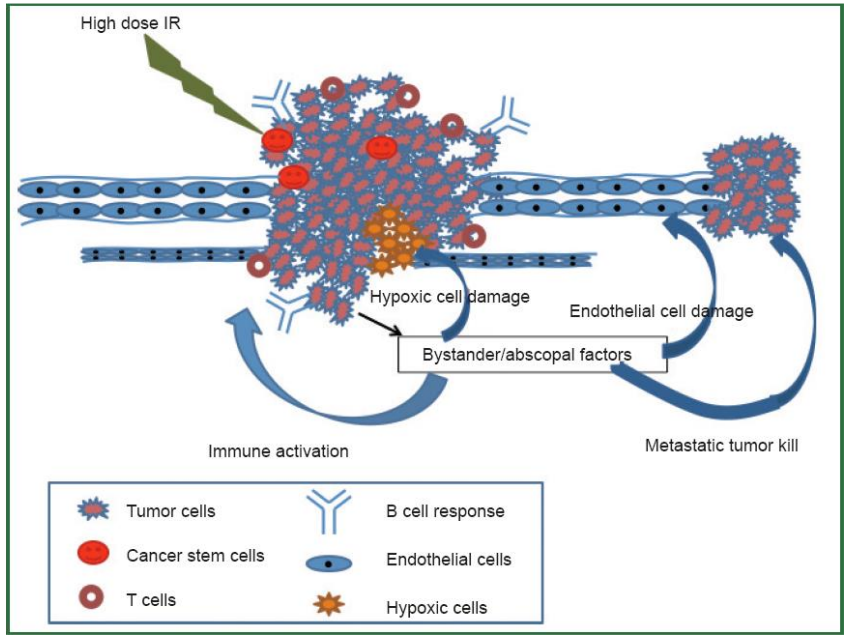
9. Ca mama metastásico: SBRT oligometástasis

3.Porque la RT potencia el ef. abscopal y modula áreas radioresistentes y microambiente

Reducción de la **inmunosupresión** inducida por el tumor

Aumento de la **respuesta inmune** inducida por la radioterapia





✓ Formenti, Demaria J Natl Cancer Inst 2013

9. Ca mama metastásico: SBRT oligometástasis

4. Porque la SBRT/SRS :

No es Invasiva

Alto control local

Bajo perfil toxicidad

Permite tratar varias lesiones /sitios simultáneamente

Puede combinarse con/ no interrumpe tto sistémico

9. Ca mama metastásico: SBRT oligometástasis

5. Porque parece efectiva: Estudios retrospectivos y prospectivos de SBRT oligomts CMM

Serie	Pat.	Treated lesions	Lesion sites	Design (characteristics)	Dose and fractionation	CTC toxicity	1y PFS	2y LC	2y DC	2y PFS	2y OS
Milano et al. [25]	40	85	17% bone 22% lung 39% liver 18% lymph node	Prospective pilot study ≤ 5met.	10 fx * 5 Gy	G3 ; n=1 (pleural/pericardial effusion)	n.a.	80%	50%	44%	76%
Yoo et al [26]	50	n.a.	100% bone	Retrospective ≤ 5met.	Median dose 30 Gy (range 20-60Gy)	G≥4; n=0	n.a.	70%	n.a.	n.a.	85%
Scorsetti et al. [27]	33	43	100% lung or liver	Observational ≤ 5met. (lung/liver)	3fx * 18-25Gy 4fx * 12Gy	G1-2; 18% G3-4; 0%	48%	90%	n.a.	27%	66%
Onal et al.[28]	22	29	100% liver	Retrospective ≤ 5met.	3fx * 18Gy		38%	88%	n.a.	8%	57%
Trovo et al. [29]	54	92	66% bone 25% lymph node 5% liver 4%lung	Prospective Multicenter Phase II PET ≤ 5met.	3fx * 10-15Gy	G3; n=2 (rib fracture, duodenal ulcer) G≥4; n=0	75%	97%	n.a.	53%	95%
David et al. [30]	15	19	100% bone	Prospective PET ≤ 3 met.	1fx * 20Gy	G1; n=67% G2; n=2% G≥3; n=0	80%	100%	n.a.	65%	100%
Weykamp et al [31]	46	58	bone 33% lung 33% liver 33% adrenal 1%	Retrospective ≤ 3met.	1fx * 24-30 Gy 3fx * 15-18Gy 8fx * 7.5Gy 10 fx * 5Gy	G1; 16% G2; 2% G≥3; 0 %	54%	89%	44%	17%	62%

Pat.: patients, n.a.: not available, CTC: common Terminology Criteria, LC: Local control; DC: distant control; PFS: Progression free survival; OS: overall survival

9. Ca mama metastásico: SBRT oligometástasis

5. Porque parece efectiva: Estudios fase II y III de SBRT en oligomts y oligoprogresión CMM

Table 1. Key clinical trials referred to in this review testing SBRT for oligometastases or oligoprogression in Stage IV breast cancer.

Trial	Phase	Number of Metastases	Number Patients	Number Breast Patients	Reference
SABR-COMET	IIR	1–5	99	18	
NRG-BR002	IIR	1–4	125	125	
CURB	III	1–5	106	47	

9. Ca mama metastásico: SBRT oligometástasis

5. Porque parece efectiva: 1er RCT donde SBRT en oligometástasis ↑↑ supervivencia

SABR-COMET

Signficativo ↑OS y ↑PFS

Fase II randomizado

Tumor primario controlado (al menos 3 m)

Pts oligometastásicos ≤ 5mts

N: 99 patients → 19 pts (20 % c. mama)

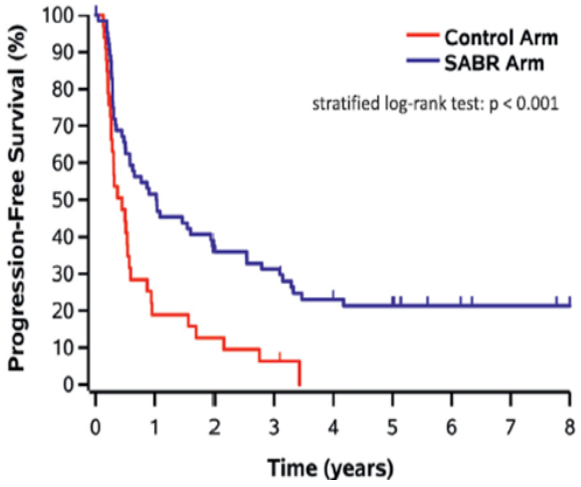
SOC (+ RT paliativa) vs SOC (+ RT-SBRT)

MFUp: **5,7 años**

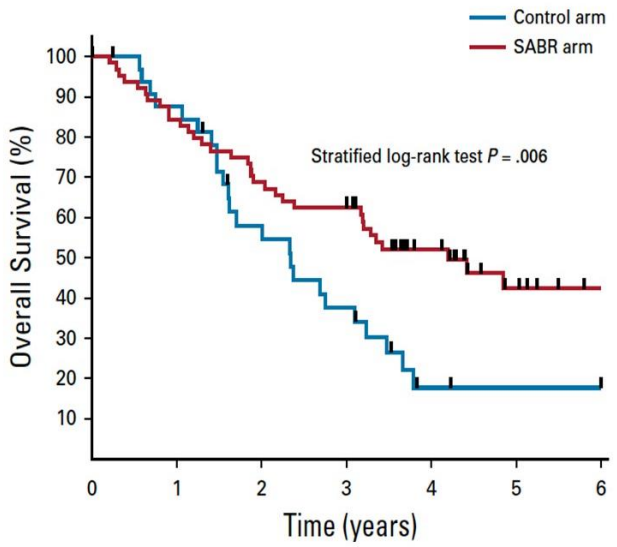
Pendientes resultados del fase III

(SABR-COMET-3 y SABR-COMET-10)

8y PFS 21% vs. 0% (p < 0.001)



8y OS : 27% vs. 14% (p = 0.008)



No tox G3-5

✓ Palma et al. JCO 2020; Harrow et al 2022

9. Ca mama metastásico: SBRT oligometástasis

5. Porque parece efectiva: Metanálisis estudios SBRT oligomts CMM

Contents lists available at ScienceDirect
Radiotherapy and Oncology
journal homepage: www.thegreenjournal.com

Systematic Review

Stereotactic body radiotherapy to treat breast cancer oligometastases: A systematic review with meta-analysis

Gustavo A. Viani [a,b,*], Andre G. Gouveia [b,c], Alexander V. Louie [d], Martin Korzeniowski [e], Juliana F. Pavoni [f], Ana Carolina Hamamura [a], Fabio Y. Moraes [b,e]

N = 467 ; retrospectivos: 7;prospectivos: 3

Author	Milano	Scorsetti	Trovo	Onal	David	Milano 1	Milano 2	Weykamp	Li	Tan	Weitjunga
Design	R	R	P	R	P	P	P	R	R	R	R
Patients	40	33	54	22	15	36	12	46	10	120	79
Lesions	85	43	92	29	19	83	21	58	10	193	103
Age (median)	55	57	57	55	61	60	44	55	54	55	56
Number of mets (median)	≤5	≤5	≤5	≤3	≤3	≤5	≤5	≤3	≤5	≤5	≤5
Site of mets	Mixed	Mixed	Mixed	Mixed	Bone only	Mixed	Bone only	Mixed	Bone only	Mixed	Mixed
KPS (median)	>70	>70	>70	>70	>70	>70	>70	>70	>70	>70	>70
Number of sites (median)	2	2	2	1	1	1	1	1	2	1	1
ER/PR%	63	70	80	77	73	56	92	76	80	83	84
Her-2 (+) %	NR	48	20	32	20	NR	NR	20	20	17	10
RT technique	VMAT	VMAT	IMRT	IMRT	IMRT	NR	NR	IMRT	3DRT	3DRT/IMRT	IMRT
SBRT total dose Gy/fractions (median)	NR	75/3fx	36/3fx	54/3 fx	20/1fx	50/10fx	50/10fx	28/3fx	20/1fx	NR	BED >60 Gy4
Follow-up (median) months	56	24	30	18	24	52	52	21	32	50	50

Outcomes	Number of studies Patients	% (CI95%) Heterogeneity
Any grade 2 toxicity	6	4% (1.4–6%)
	180 patients	$I^2 = 0\%$ $p = 0.230$
Any grade 3toxicity	7	0.7 (0.3–1%)
	300 patients	$I^2 = 0\%$ $p = 0.230$
Any grade 4 or 5 toxicity	3	
	300 patients	0

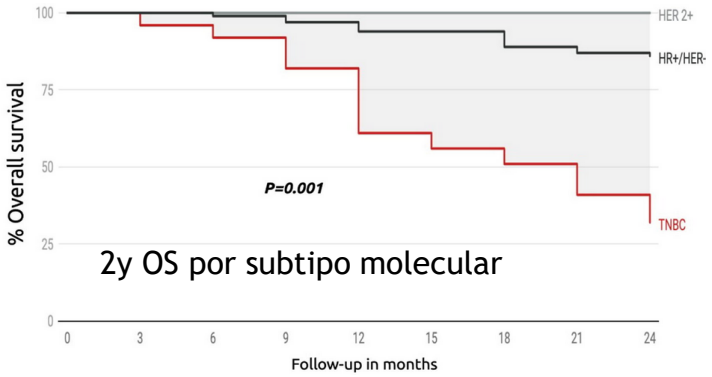
OS a 1 año: 93%

OS a 2 años: 81%

LC a 1 año: 97%

LC a 2 años: 90%

Variable	B	P
Overall Survival at 2 years		
Bone only	0.20	0.01
Prospective design	0.18	0.001
%ER/PR	0.005	0.230
%HER-2 (+)	−0.007	0.105
≤ 3 sites	0.08	0.491
BEDGy10	−0.002	0.212
Local Control at 2 years		
Bone only	0.05	0.297
Prospective design	0.009	0.210
%ER/PR	0.05	0.001
%HER-2 (+)	0.001	0.978
≤ 3 sites	−0.009	0.858
BEDGy10	−0.001	0.802



2y OS por subtipo molecular

✓ Viani et al. Radiotherapy and Oncology 164 (2021) 245–250

9. Ca mama metastásico: SBRT oligometástasis

5. Porque parece efectiva: Metanálisis estudios SBRT oligomts CMM

Highlights

- SABR in oligometastatic breast cancer is safe and correlated with high rates of local control.
- In the meta-regression analysis prospective design ($p = 0.001$) and bone-only metastases ($p = 0.01$) were significantly associated with better OS.
- Hormone receptor status was associated with improved local control ($p = 0.01$) on meta-regression analysis.
- Longer follow-up of existing data and ongoing prospective trials will help further define the role of this management strategy.

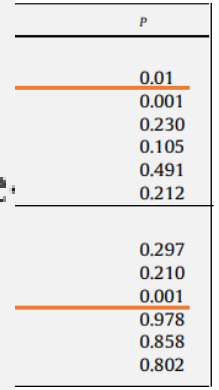
año: 97%

años: 90%

N = 467

Author	Mi
Design	R
Patients	40
Lesions	85
Age (median)	55
Number of mets (median)	≤5
Site of mets	Mi
KPS (median)	>7
Number of sites (median)	2
ER/PR%	63
Her-2 (+) %	NR
RT technique	VM
SBRT total dose Gy/fractions (median)	NR
Follow-up (median) months	56

Any grade 2 toxicity	6 180 patients	4% (1.4–6%) $I^2 = 0\%$ $p = 0.230$
Any grade 3toxicity	7 300 patients	0.7 (0.3–1%) $I^2 = 0\%$ $p = 0.230$
Any grade 4 or 5 toxicity	3 300 patients	0



✓ Viani et al. Radiotherapy and Oncology 164 (2021) 245–250

9. Ca mama metastásico: SBRT oligometástasis

5. …aunque tb hay estudios que no encuentran diferencias…

NRG-BR002 phase IIR/III trial of standard of care systemic therapy with or without stereotactic body radiotherapy (SBRT) and/or surgical resection (SR) for newly oligometastatic breast cancer

OLIGOMETASTATIC BREAST CANCER
Controlled Locoregional Disease and ≤ 4 Metastases (***standard imaging***)
≤ 12 months systemic therapy without progression

STRATIFICATION
- Metastases (1 vs. >1)
- Hormone receptor status (ER+ and/or PR+ vs. ER- and PR-)
- HER2 status (Positive vs. Negative)
- Chemotherapy for MBC (Yes vs. No)

RANDOMIZATION 1:1 N=125 patients

ARM 1
Symptom directed palliative therapy as needed

Standard ***systemic*** therapy

ARM 2
Total **ablation** of all metastases

Standard ***systemic*** therapy

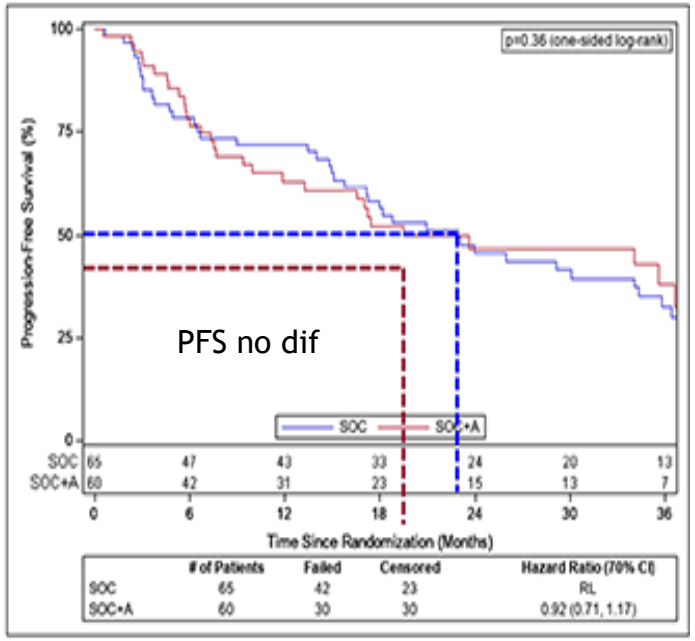
N: 125 pts

Sistemico (N: 65) vs Sistemico + Local(N: 60)

Tto Local (93% SBRT, 2% surgery 5% no protocol)

Metástasis: 78% metacrónicas, 22% sincrónicas

Mfup: **3 years**



NRG-BR002: Se permitía repetir SBRT, pero no se ofrecía de rutina

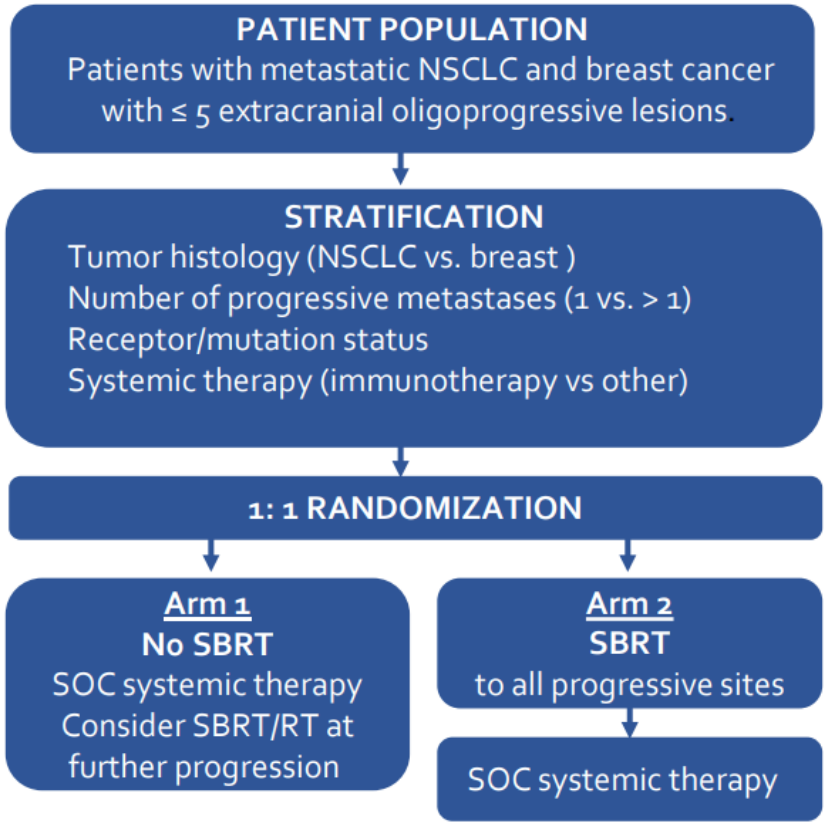
SABRT-COMET: Se ofrecía repetir SBRT si factible

PRESENTED BY:
Gaorav Gupta, MD PhD
University of North Carolina at Chapel Hill

9. Ca mama metastásico: SBRT oligometástasis

5. ….aunque tb hay estudios que no encuentran diferencias …

CURB



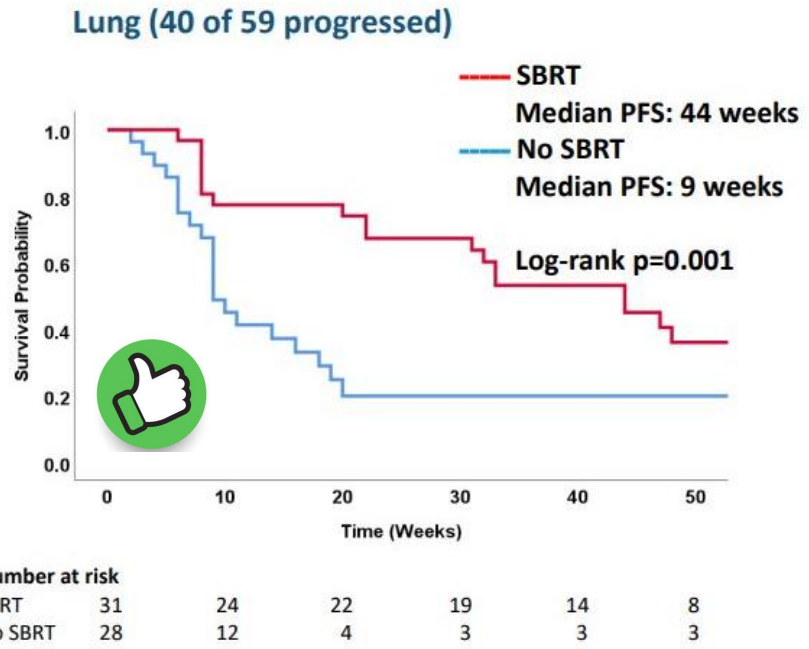
- Metastatic NSCLC or breast cancer
- ≤5 oligoprogressive lesions after ≥1 line of systemic therapy.
- Randomized 1:1 to standard of care (SOC) with or without SBRT to all progressive sites
- N: **106 patients** were randomized: 59 NSCLC, **47 BC**
- Most (75%) had >1 site of oligoprogression and 47% had >5 total lesions
- 86% of NSCLCs (had no actionable driver mutation) and **66%** of BC were **triple-negative**
- Median PFS was 3.2 months in SOC arm vs. 7.2 months in SBRT arm (p=0.002).

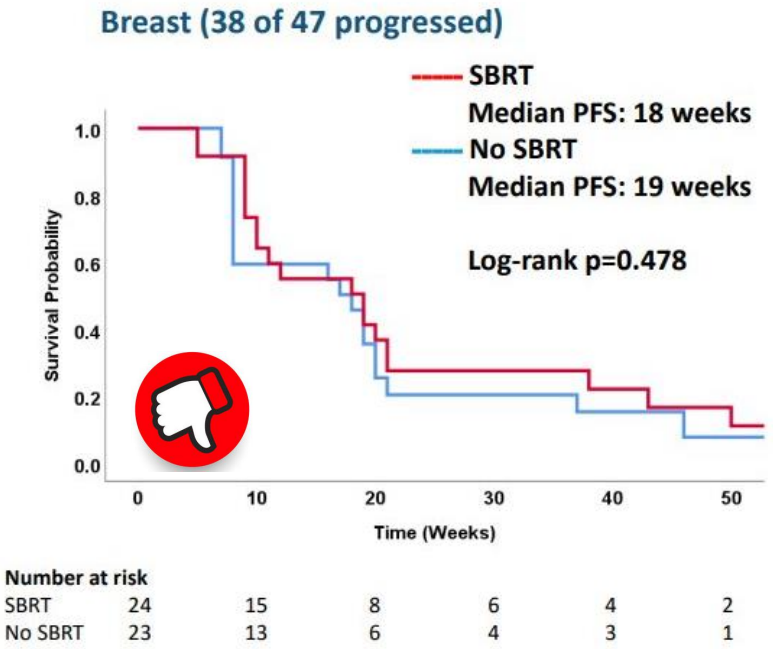
✓ ASTRO 2021, Tsai J. et al from MSKCC

9. Ca mama metastásico: SBRT oligometástasis

5. ….aunque tb hay estudios que no encuentran diferencias …

CURB





PATIE
Patients with meta
with ≤ 5 extracra

ST
Tumor histology (
Number of progre
Receptor/mutatio
Systemic therapy

1: 1 R

Arm 1
No SBRT
SOC systemic thera
Consider SBRT/RT
further progressio..

SOC systemic therapy

ıpy.

t SBRT to all

ɔ total lesions

6% of BC were

SBRT arm

AMERICAN SOCIETY FOR RADIATION ONCOLOGY (ASTRO) 2021 ANNUAL MEETING

✓ ASTRO 2021, Tsai J. et al from MSKCC

9. Ca mama metastásico: SBRT oligometástasis

6.Porque es costo-efectiva

Is SABR Cost-Effective in Oligometastatic Cancer? An Economic Analysis of SABR-Comet

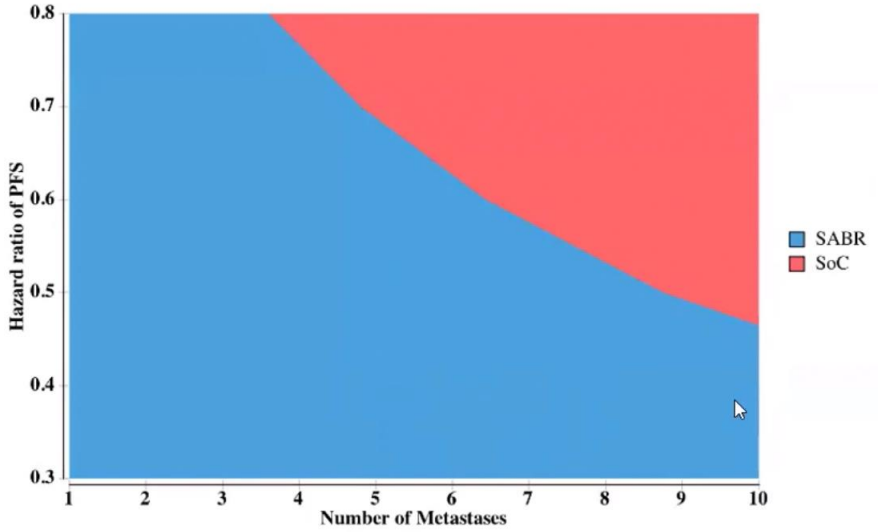
M.X. Qu • Y. Chen • G. Zaric • S. Senan • R.A. Olson • S. Harrow • A. John-Baptiste • S. Gaede • L. Mulroy • D. Schellenberg • S. Senthi • A. Swaminath • N. Kopek • M. Liu • A. Warner • G. Rodrigues • D.A. Palma • A.V. Louie • Show less

SABR is cost-effective at ICER of $37,157/QALY (CAD)

Cost-effectiveness Analysis of Stereotactic Ablative Radiotherapy in Patients with Oligometastatic Cancer

Abhishek Kumar, MD MAS • Christopher Straka, MD • Patrick T. Courtney, BA • Lucas Vitzthum, MD MAS • Paul Riviere, MD • James D. Murphy, MD MS

SABR is cost-effective at ICER of $28,906/QALY (USD)



9. Ca mama metastásico: SBRT oligometástasis

¿Hacia dónde?

Ongoing randomized phase II/III trials of local ablative therapy + systemic therapy in BC.

Identifier	Phase	Patients	End of Study	Primary Endpoint(s)	Local treatment	Number and site of metastases allowed	Tumour biology	Brain mts	Settings	Sponsor
NCT04413409 (OMIT)	Phase III randomized	172	2025	OS	Surgery	≤3 metastatic lesions, involving 1–2 organs, single lesion ≤ 5 cm	Any			Fudan Shangai cancer center
NCT04495309 (OLIGOMA)	Phase III randomized	564	2025	PFS HRQoL	SBRT	Up to 5 clinically manifest metastases (maximum 3 CNS lesions)	Any	allowed	Any line, any tumor biology	Schelswig-Holstein hosp.
NCT04698252 (LARA)	Phase II randomized	74	2031	PFS	SBRT, surgery, RFA	1–4 bone lesions; 1–4 lung and/ or liver lesions	HR+/HER2-			Inst cancer Sao Paulo
NCT04424732 JORDANIA	Phase II single arm	50	2026	PFS	SBRT	1–3 bone metastases	Any			King Hussein Cancer center
NCT03750396 (CLEAR)	Phase II single arm	110	2025	PFS	Palliative RT, SBRT, surgery, RFA	≤2 lesions in single organ or site (lung, bone, liver, adrenal glands, nodal)	HR+/HER2-			Gangnam Severance Hosp.
NCT02089100 (STEREO-SEIN)	Phase III randomized	280	2023	PFS	SBRT	≤5 metastatic lesions	HR+ (HER2+/-)	Not allowed	First line mts, ER+	Gustave Roussy
NCT05301881 (COSMO)	Phase II single arm	118	2040	PFS	SBRT, surgery, RFA	Oligoprogression defined as 1–2 metastatic lesions, limited to one organ, or the primary tumour or regional nodes	Any			Netherlands cancer institute
NCT05377047 (TAORMINA)	Phase III randomized	345	2027	OS	SBRT	1–5 lesions in 1–2 organs	Any			Sahlgrenska hosp. Sweden
ACTRN1262 0001212943 (AVATAR)	Phase II	32	-	Time to change systemic therapy	SBRT (with endocrine therapy and CDK 4/6 inhibitor)	limited to 5 lesions	ER-positive HER2-negative			Peter McCallum Cancer Center

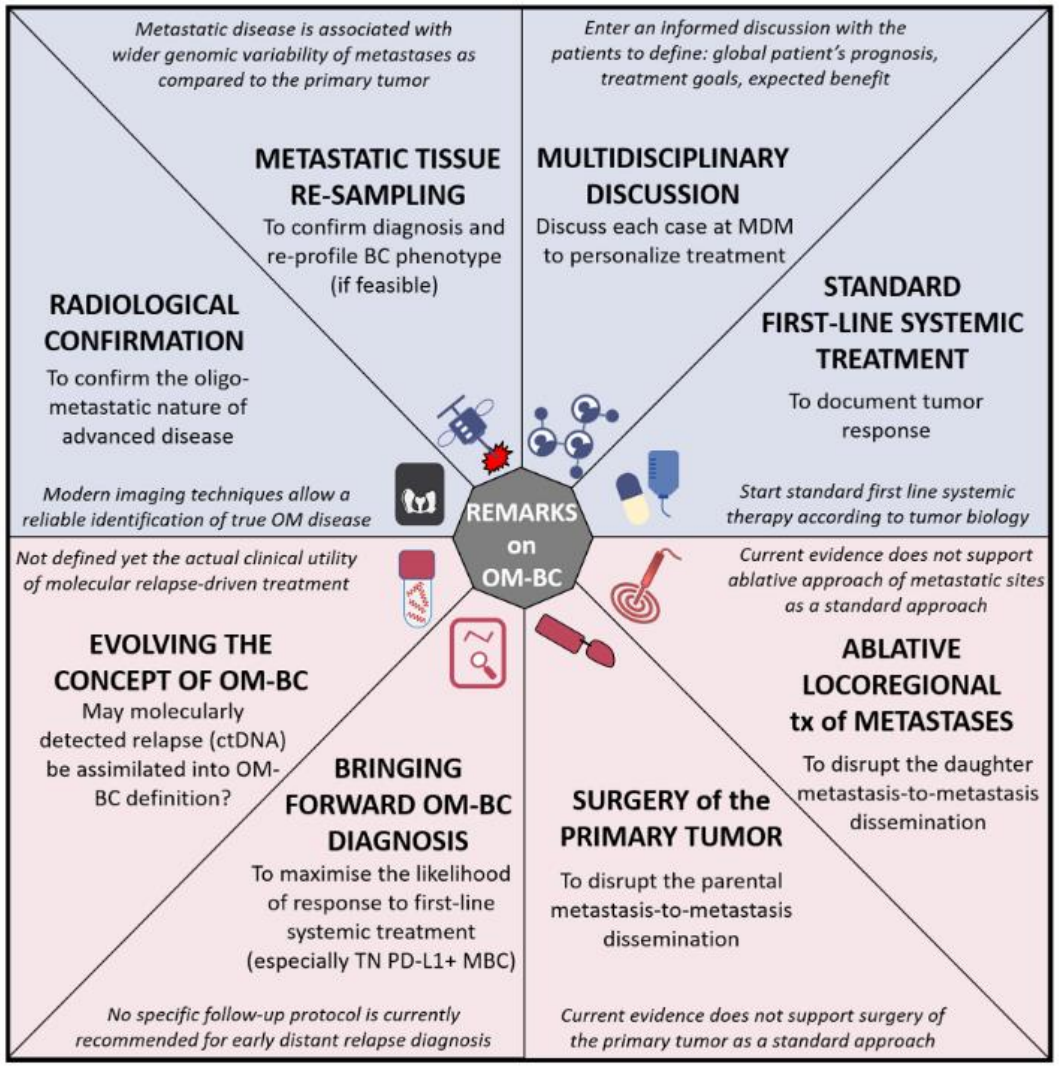
9. Ca mama metastásico: SBRT oligometástasis

¿¿Hacia dónde??

- **Feasibility** of conducting rigorous trials evaluating this approach
- Importance of **defining optimal contexts** where metastasis ablation may be beneficial (using biomarkers and examining failure patterns)

Systemic Therapy

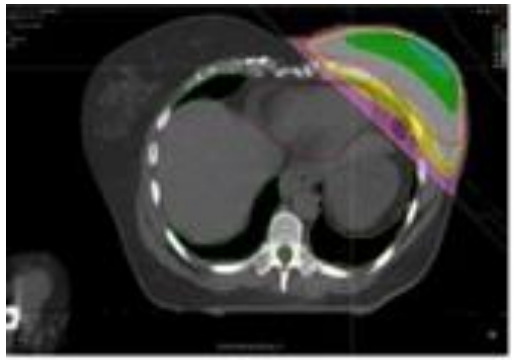
Local Therapy



✓ Miglietta et al. Cancer treatment reviews 2022

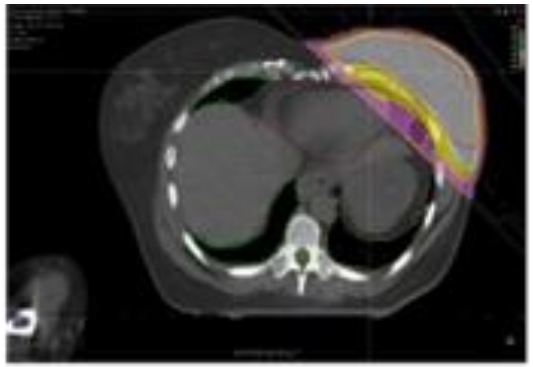
10. Avances Técnicos:

Mayor conformación, mejor distribución de dosis: 3D → IMRT, VMAT

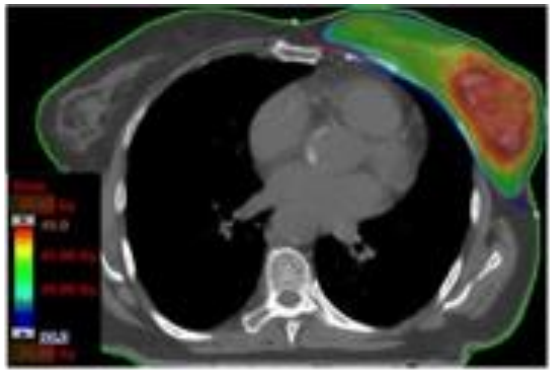


3D-Sólo Tangenciales.

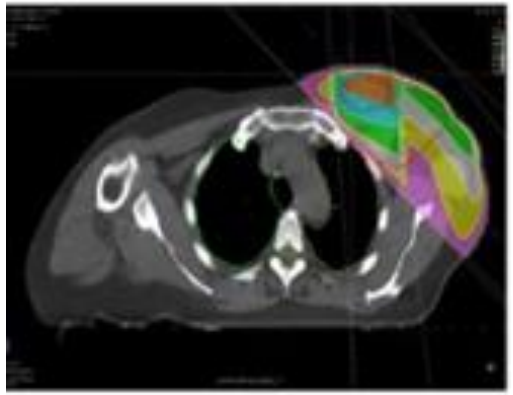
3D-Con cuñas.



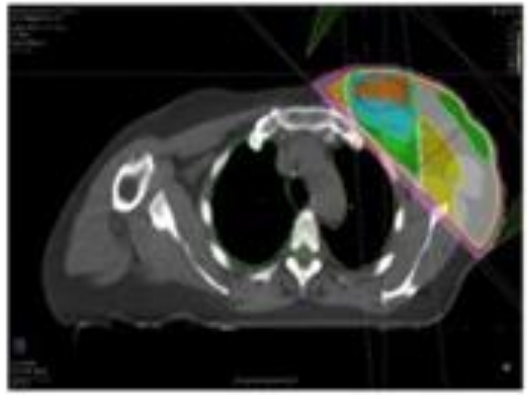
3D-Con Segmentos.



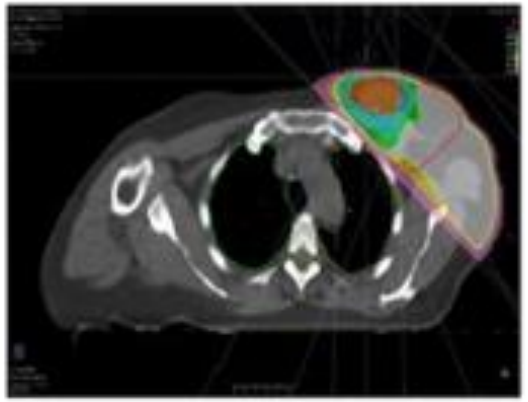
VMAT



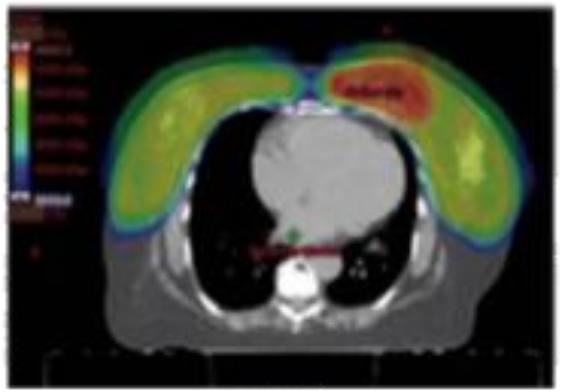
3D-Sólo Tangenciales.



3D-Con cuñas.



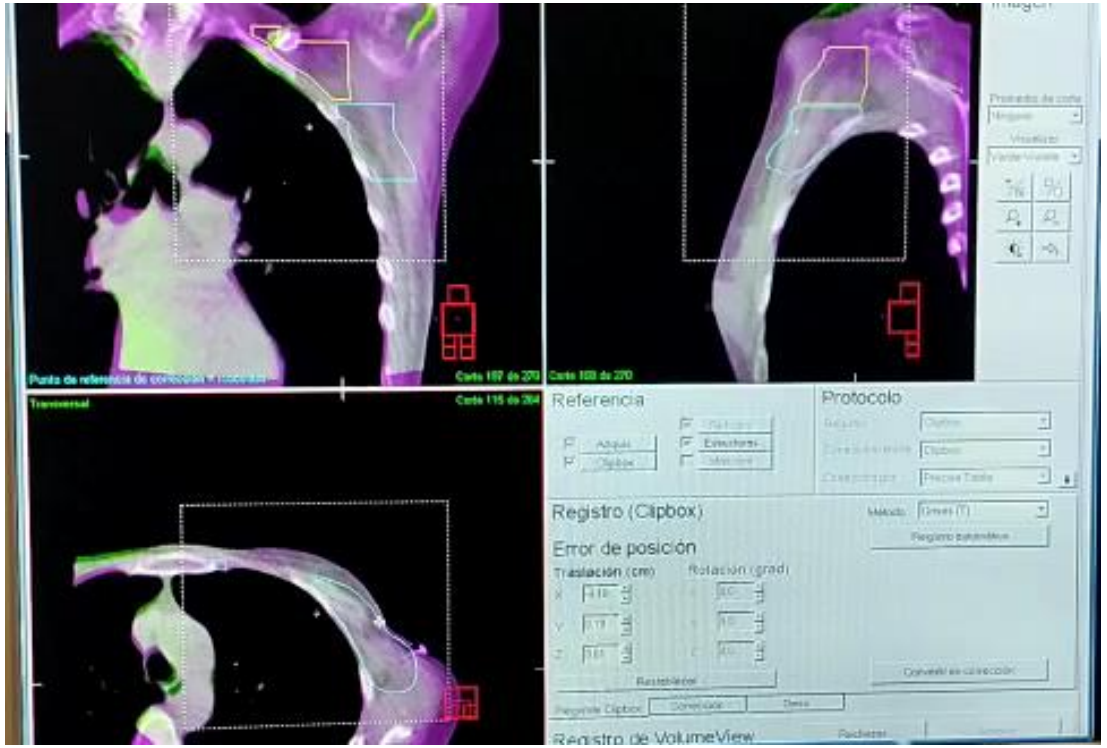
3D-Con Segmentos.



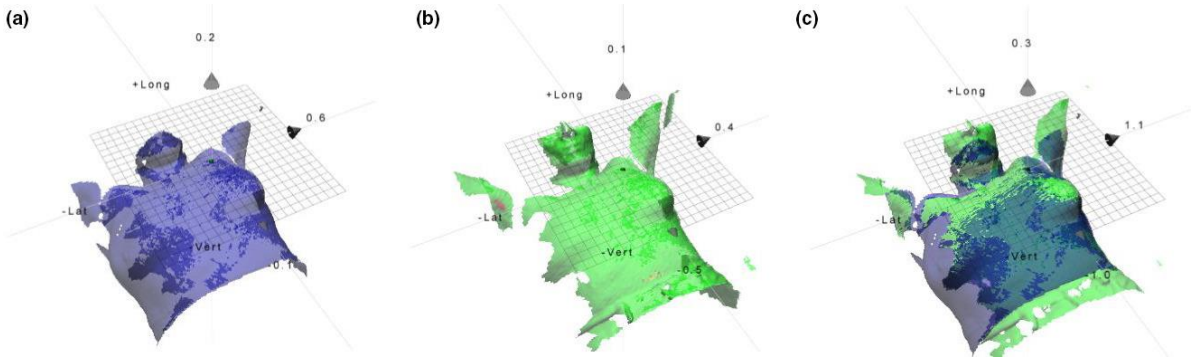
IMPT

10. Avances Técnicos:

RT guiada por imagen: IGRT



RT guiada por superficie: SGRT

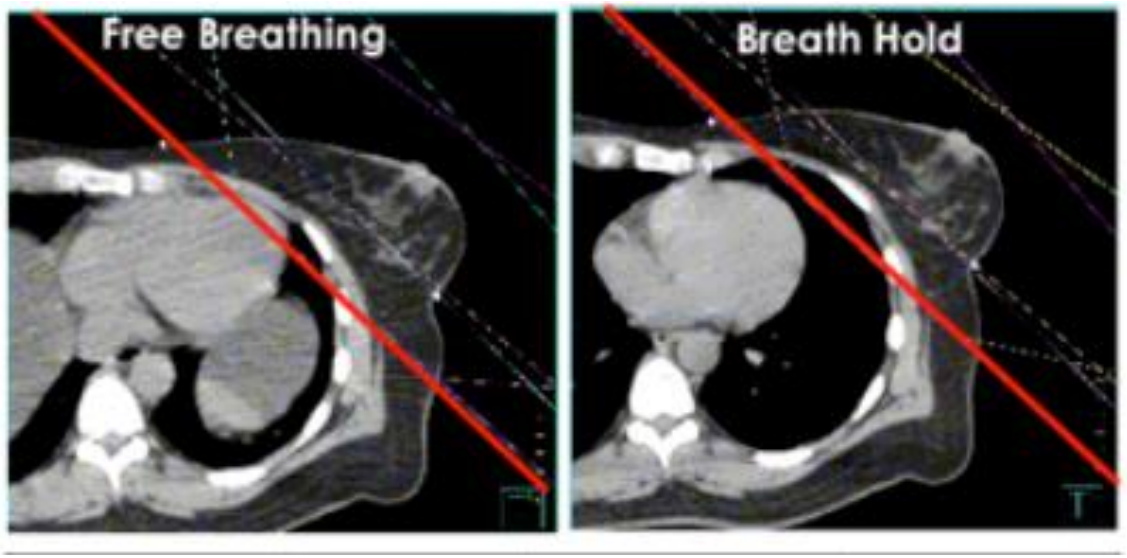


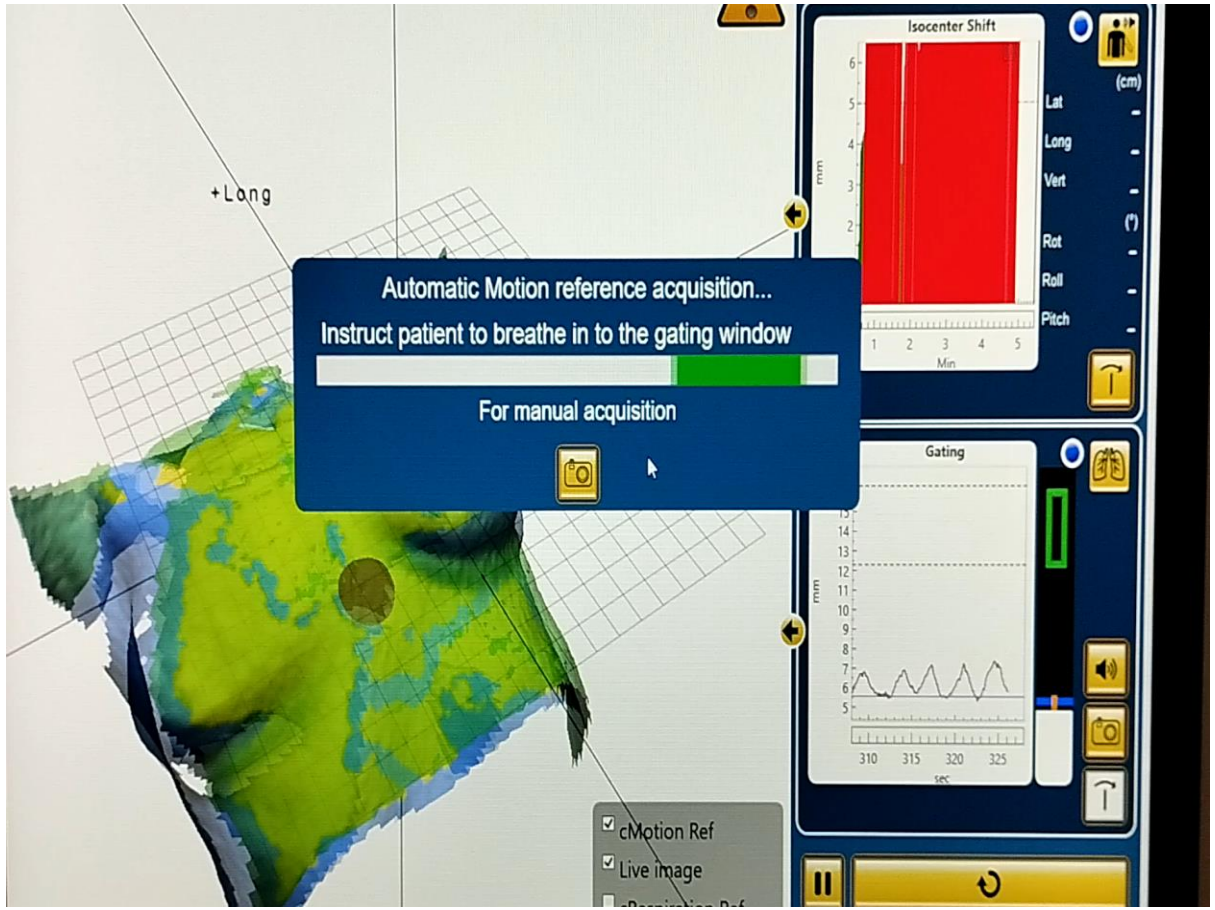
Evitando tatuajes

10. Avances Técnicos:

Monitorizar el Movimiento Respiratorio: Gating, DIBH, ABC…

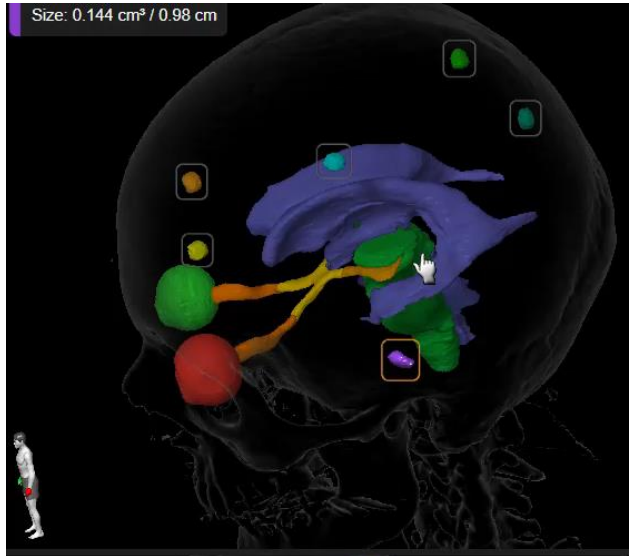
permitiendo↓dosis en órganos sanos

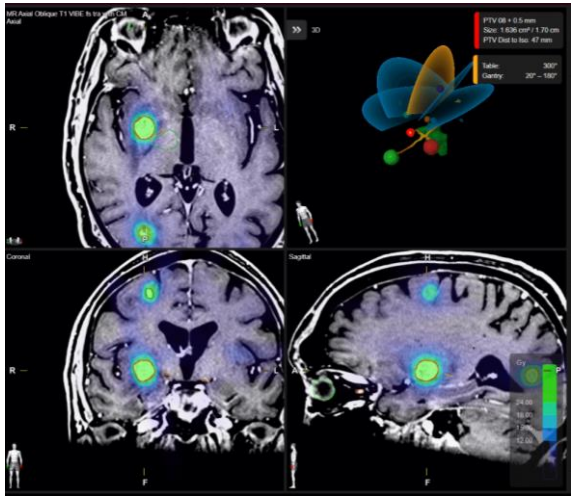


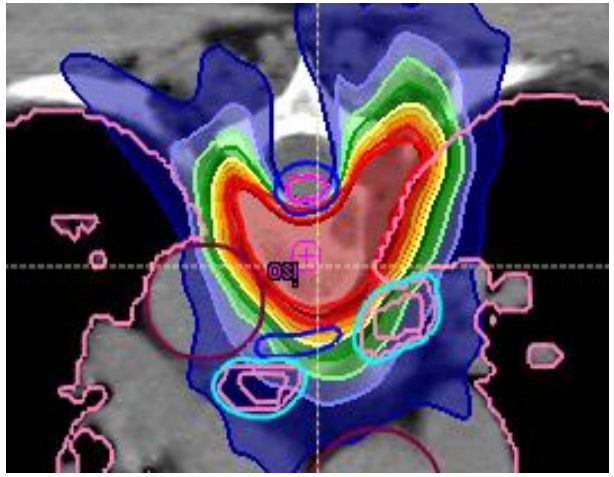


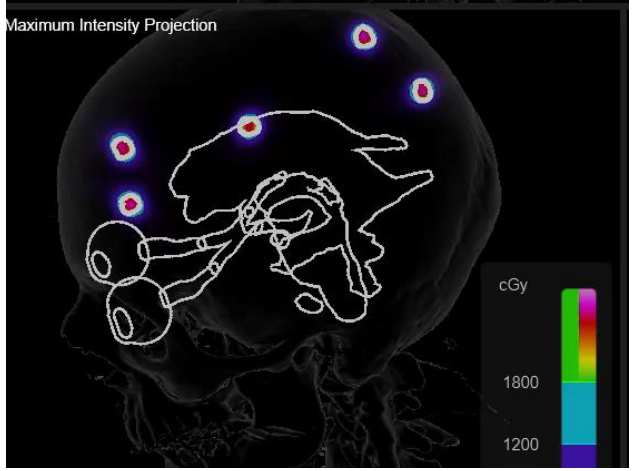
10. Avances Técnicos:

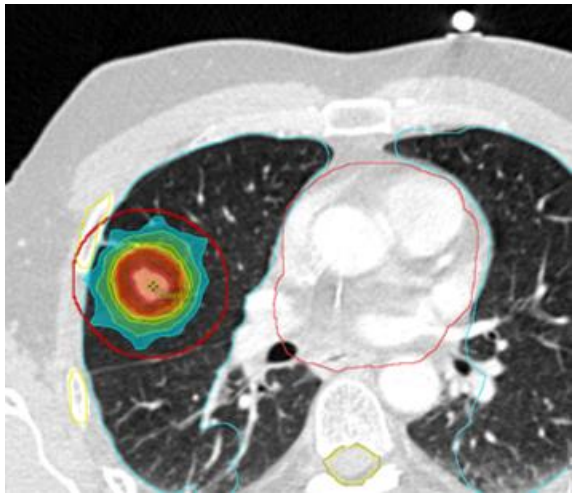
RC craneal y SBRT extracraneal

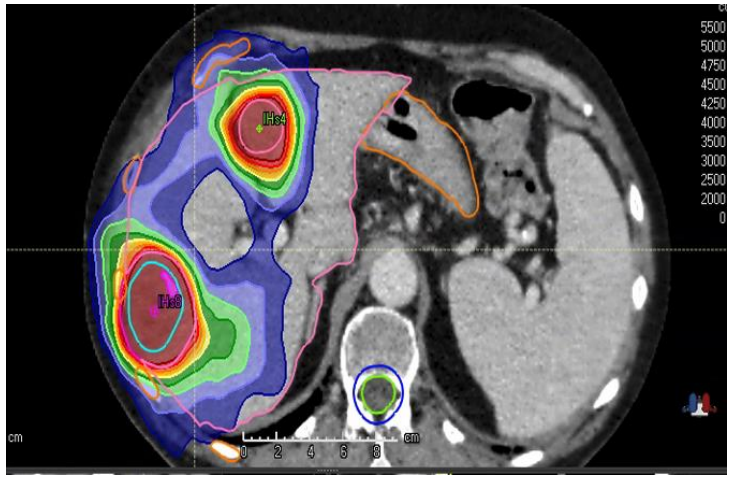












1. BCS+RT (↑OS) > Mastectomía

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2. RT DCIS: RT tras CC ↑ LC 50 % (beneficio ↑ si ↑Fup, incluso en bajo riesgo)

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4. RT Ca. Infiltrante (mastectomía): ↑ LC y ↑ OS (2/3)

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5. RT axilar: Indicada en todos los ptes N+. Si SLNB+ ≤ 2+ nodes: ALND (DFS,OS) = RT axilar

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7. Avances en radiobiología y fraccionamientos: Ultrahipofraccionamiento

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8. Avances en volúmenes y secuencia: PBI, RT preoperatoria

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8. Avances en volúmenes y secuencia: PBI, RT preoperatoria
9. Avances en ca mama metastásico: SBRT en oligometástasis

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10. Avances técnicos: DIBH, IGRT, SGRT, IMRT, RC craneal, SBRT extracraneal…

RAGMA 23

16ª Revisión Anual GEICAM de Avances en Cáncer de Mama

Realidades y esperanzas

GRACIAS

Raquel Ciérvide

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Organizado por:

GEICAM investigación en cáncer de mama