Ruolo della Radioterapia post-operatoria.

Filippo Alongi

Direttore U.O.C. RADIOTERAPIA ONCOLOGICA

Ospedale Sacro Cuore Don Calabria

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RAZIONALE RT DOPO CHIRUGIA CONSERVATIVA

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Tumore della mammella: cronistoria

Anni ’60 : massimo trattamento tollerabile

Razionale:

- Difficoltà a controllare la malattia
- Incertezze sulla sua biologia
- Diagnosi spesso tardive

Trattamenti molto aggressivi:

mastectomia radicale

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Tumore della mammella: cronistoria

Anni ’60 : massimo trattamento tollerabile

Conseguenze della mastectomia radicale:

- Pazienti lungo sopravviventi.
- Trauma psicologico (no chirurgia ricostruttiva).
- Rifiuto dell’intervento demolitivo e quindi della malattia.

Impatto drammatico sulla qualità della vita.

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Tumore della mammella: cronistoria

Anni ‘70 : minimo trattamento efficace

Razionale:

- Le migliori conoscenze biologiche
- La maggior precocità diagnostica
- L’introduzione della multidisciplinarietà

Terapie conservative:

quadrantectomia + radioterapia

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Tumore della mammella: cronistoria

Conseguenze della **quadrantectomia + radioterapia**:

- Uguale percentuale di sopravvivenza.
- Maggior accettazione della cura e quindi della malattia.
- Miglior risultato estetico e quindi migliore qualità della vita.

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Tumore della mammella: cronistoria

Trattamenti locali:
"dal massimo trattamento tollerabile al minimo efficace"

- U. Veronesi. New England Journal Medicine 1981:"**Trial Milano I**" studio prospettico randomizzato con 701 pts, due bracci:

Comparazione tra mastectomia radicale secondo Halsted e QUART

OS E DFS sovrapponibili nei due bracci. Recidiva locale con QUART del 4,8 %

- B.Fisher. New England Journal Medicine 1985 e 89. "**Studio NSABP** "con 1843 pts, 3 bracci:

Comparazione tra mastectomia radicale, tumorectomia + RT, tumorectomia senza RT

OS e DFS comparabili nei primi due bracci (uguale tasso di recidive del 12%).
Tasso di recidive alto per la sola tumorectomia (quasi del 50%).

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Tumore della mammella: cronistoria

Trattamenti locali:
"dal massimo trattamento tollerabile al minimo efficace"

- U. Veronesi. New England Journal Medicine 1981:"**Trial Milano I**" studio prospettico randomizzato con 701 pts, due bracci:

Comparazione tra mastectomia radicale secondo Halsted e QUART

DATI CONFERMATI A 20 ANNI

- B.Fisher. New England Journal Medicine 1985 e 89. "**Studio NSABP** "con 1843 pts, 3 bracci:

Comparazione tra mastectomia radicale, tumorectomia + RT, tumorectomia senza RT

DATI CONFERMATI A 20 ANNI

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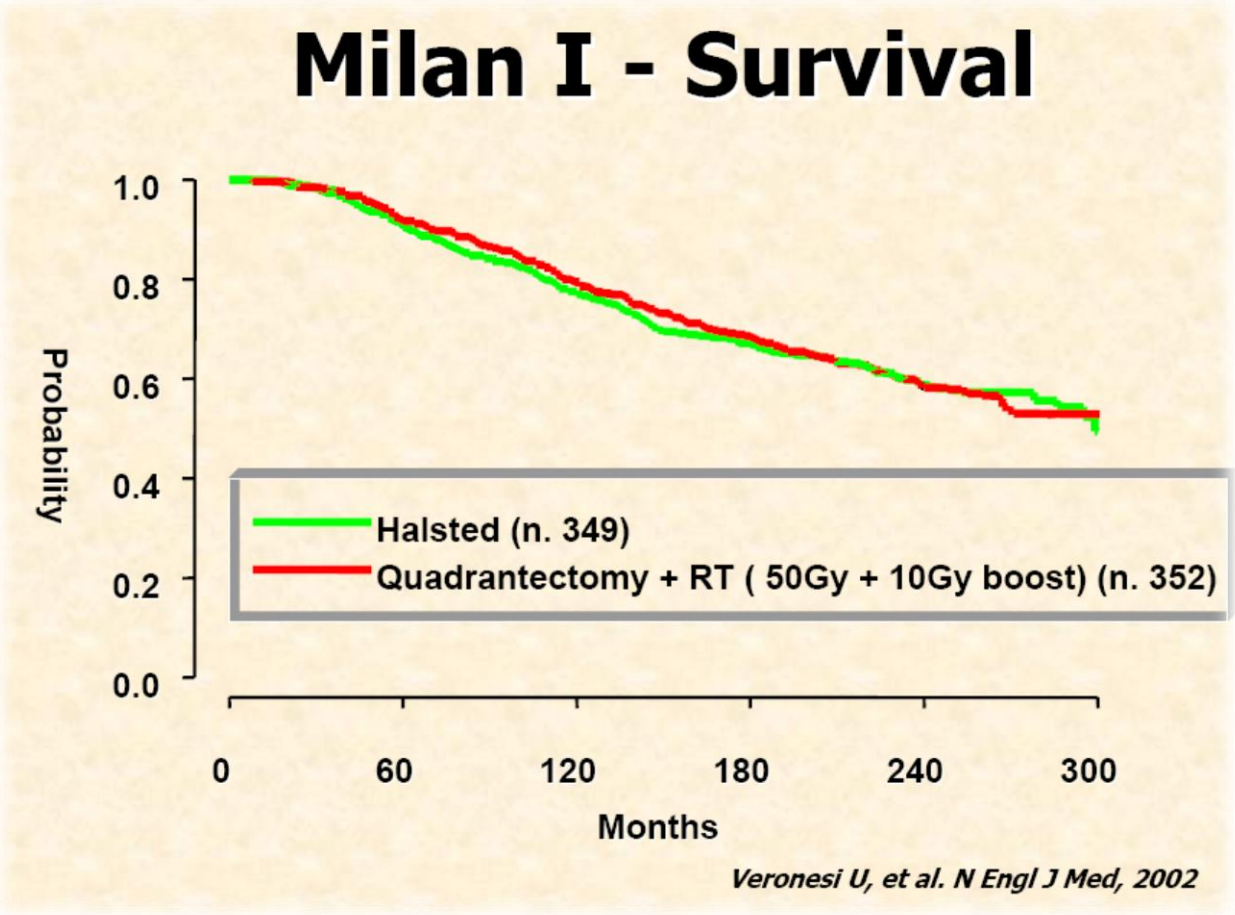
Tumore della mammella: cronistoria

Trattamenti locali:
"dal massimo trattamento tollerabile al minimo efficace"



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Tumore della mammella: cronistoria

Trattamenti locali:
“dal massimo trattamento tollerabile al minimo efficace”

….. SENZA RT?

SOLO CHIRUGIA CONSERVATIVA?

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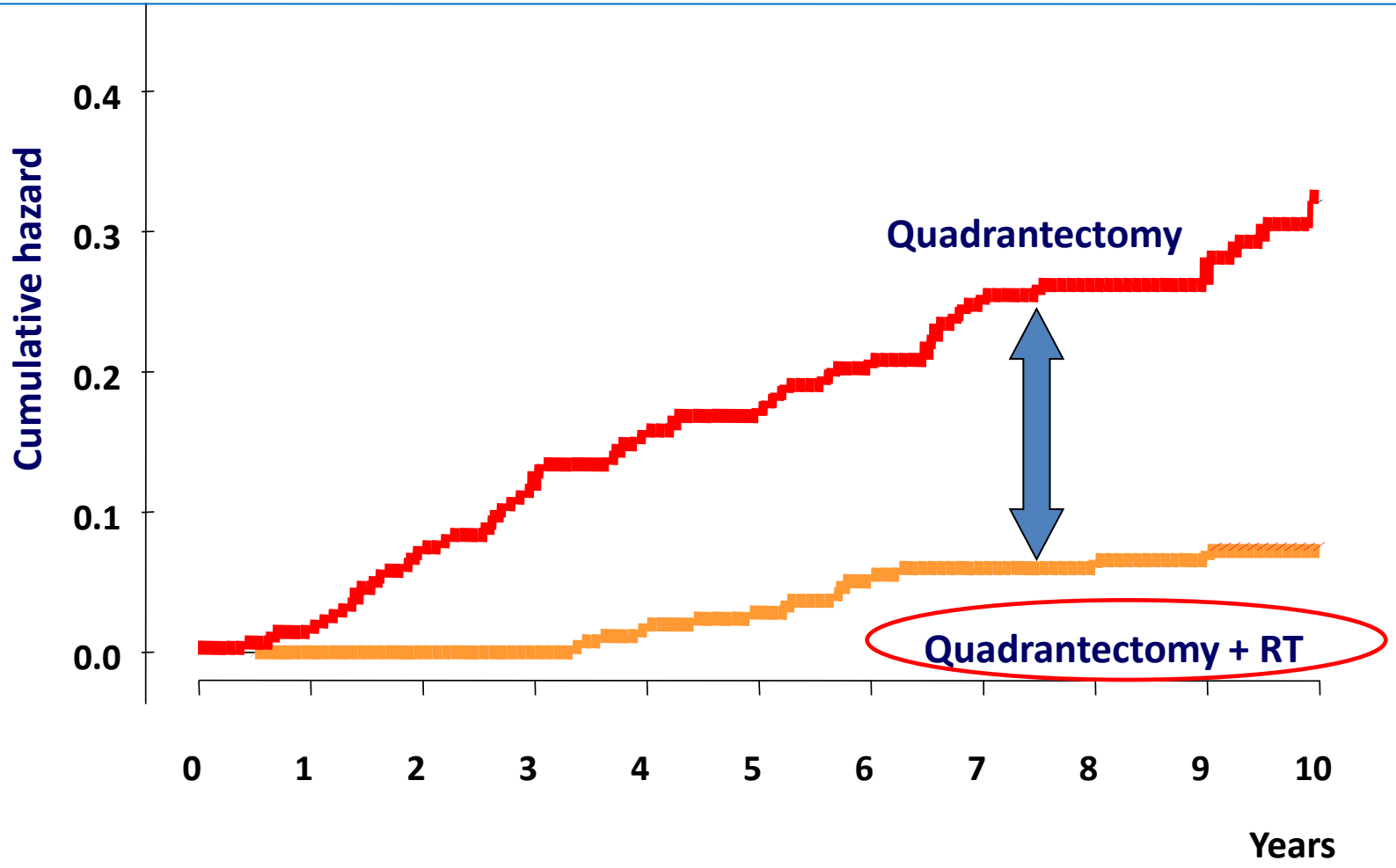
Tumore della mammella: cronistoria



Milan 3 Trial: Recidive locali

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RAZIONALE RT DOPO MASTECTOMIA

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Tumore della mammella: cronistoria

RT POST-MASTECTOMIA: QUANDO?

2.2.2 Radioterapia dopo mastectomia totale

L'irradiazione della parete toracica e delle stazioni di drenaggio linfonodale è indicata nei seguenti casi:

a) Nei T3N+ e nei T4 qualsiasi N (15-17,25-34) **(categoria di evidenza 1** del NCCN). **Nei T3N0, in base ai fattori di rischio, il trattamento potrebbe essere somministrato sulla sola parete toracica o non essere seffettuato**

b) **Tumore di qualsiasi dimensione con estensione alla parete toracica, al muscolo pettorale, alla cute, indipendentemente dallo stato linfonodale** (34)

c) **Tumore di dimensioni fino a 5 cm (T1-2) con metastasi ai linfonodi ascellari in numero uguale o superiore a 4 (15,16,29-34) (categoria di evidenza 2A** del NCCN)

d) **Presenza di margini positivi, soprattutto in presenza di altri fattori di rischio (15,35), anche se i dati della letteratura non sono conclusivi.**

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Tumore della mammella: cronistoria

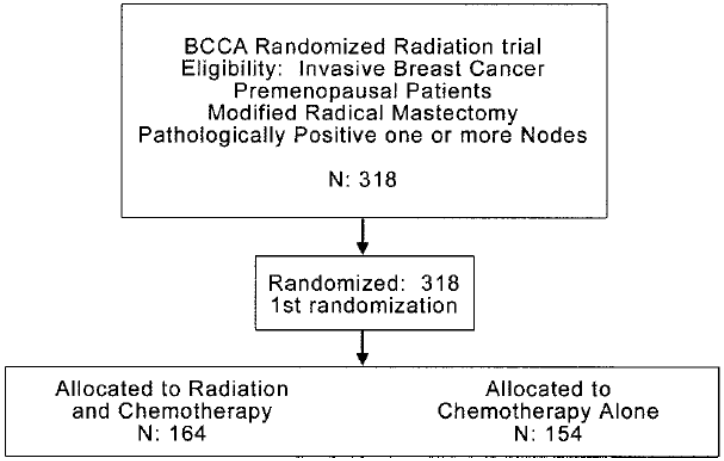
RT POST-MASTECTOMIA: PERCHE'?

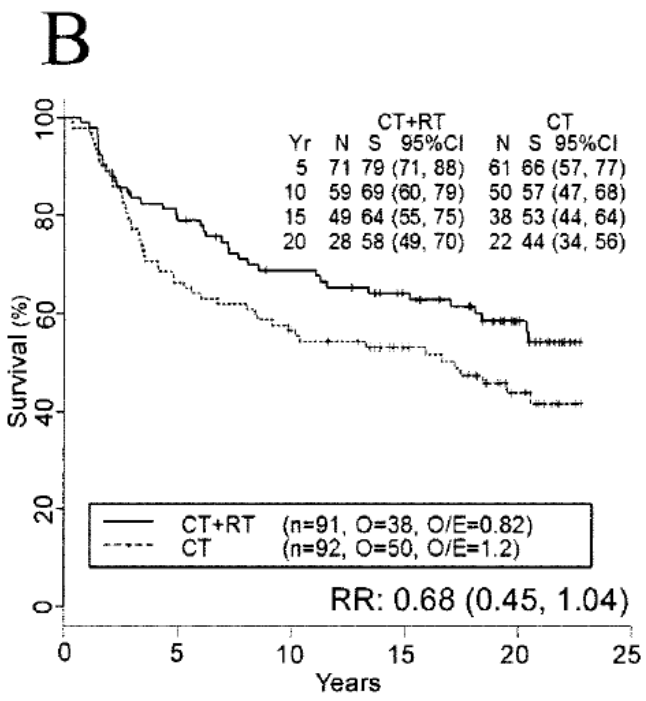
ARTICLES

Locoregional Radiation Therapy in Patients With High-Risk Breast Cancer Receiving Adjuvant Chemotherapy: 20-Year Results of the British Columbia Randomized Trial

Joseph Ragaz, Ivo A. Olivotto, John J. Spinelli, Norman Phillips, Stewart M. Jackson, Kenneth. S. Wilson, Margaret A. Knowling, Christopher M. L. Coppin, Lorna Weir, Karen Gelmon, Nhu Le, Ralph Durand, Andrew J. Coldman, Mohamed Manji

J Natl Cancer Inst. 2005 Jan 19;97(2):116-26.





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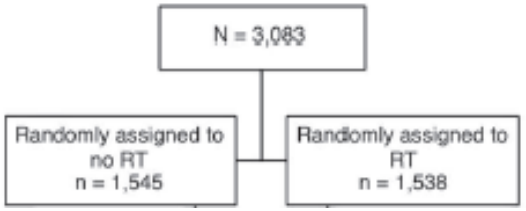
Tumore della mammella: cronistoria

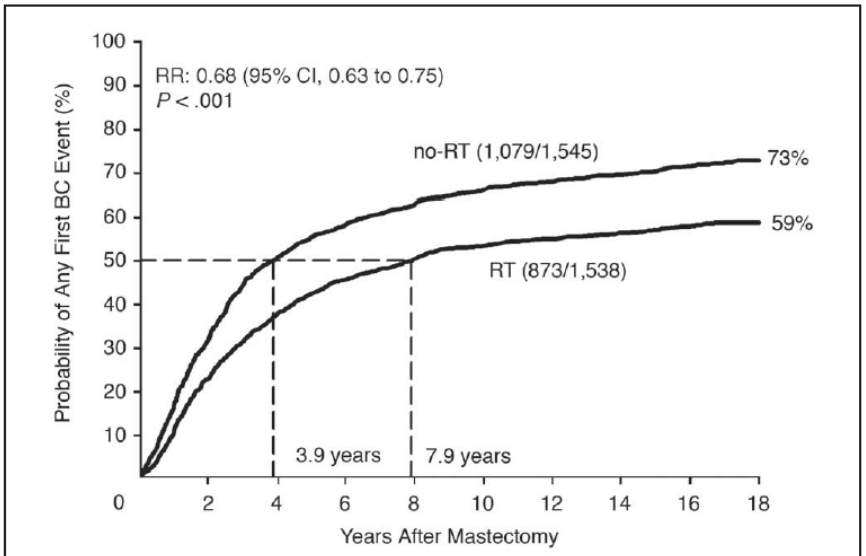
RT POST-MASTECTOMIA: PERCHE'?

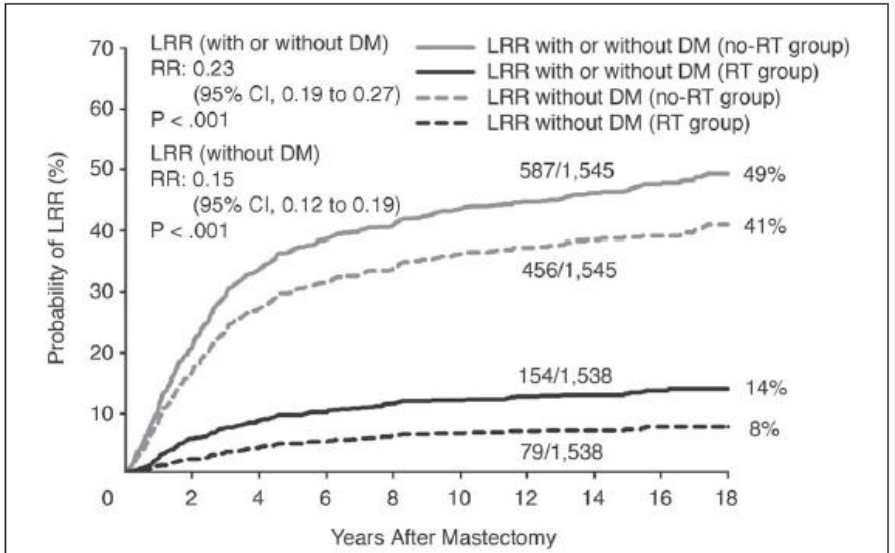
VOLUME 24 · NUMBER 15 · MAY 20 2006
JOURNAL OF CLINICAL ONCOLOGY
ORIGINAL REPORT

Danish Breast Cancer Cooperative Group

Study of Failure Pattern Among High-Risk Breast Cancer Patients With or Without Postmastectomy Radiotherapy in Addition to Adjuvant Systemic Therapy: Long-Term Results From the Danish Breast Cancer Cooperative Group DBCG 82 b and c Randomized Studies







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Tumore della mammella: cronistoria

RT STAZIONI LINFONODALI

- **Sopra/sottoclaveare**
- **Ascella**
  - III° livello (in continuità con sopclav)
  - I° - II° livello (spesso incluso nei campi tangenti)
  - tutta la ascella
- **Catene mammarie interne**

Breast lymph nodes

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Tumore della mammella: cronistoria

RT STAZIONI LINFONODALI

-***1. Linfonodi ascellari:*** la **RT non è indicata nelle pazienti sottoposte ad adeguata dissezione** indipendentemente dal numero dei linfonodi coinvolti e/o dalla presenza di estensione extra-capsulare, **a meno che non ci sia un fondato sospetto o la presenza accertata di malattia residua**. **Kurtz J , Eur J Cancer 38:1961-1974, 2002.**

-***2. Linfonodi infra-sopraclaveari:*** è indicata nelle pazienti **con interessamento dei linfonodi stessi, nei T3-4** indipendentemente dallo stato linfonodale e nei **T1-2 con quattro o più linfonodi ascellari positivi . Recht A, J Clin Oncol 2001- Pierce LJ. , J Natl Cancer Inst Monogr 2001. Recht A, J Clin Oncol 1999- Katz A, J Clin Oncol 2000. - Harris JR Int J Radiat Oncol Biol Phys, 1999. - Goldhirsch A, J Clin Oncol 2001. - Truong PT, CMAJ 2004.**

-***3. Linfonodi della catena mammaria interna:*** l'indicazione al trattamento precauzionale rappresenta uno degli **argomenti più controversi** nella terapia del tumore della mammella . Attualmente, in attesa dei risultati dello studio EORTC 22922, chiuso a gennaio 2004, e quello SWONG e della National Cancer Institute, non se ne può raccomandare o sconsigliare l'irradiazione. **Lacour J, Cancer , 1983 - Veronesi U, Eur J Cancer 35:1320-1325, 1999.**

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Tumore della mammella: cronistoria

RAZIONALE DEL TRATTAMENTO RADIANTE CONVENZIONALE

- Eliminare possibili aree di carcinoma occulto multifocale (RT whole breast ± Linfonodi)

- Distruggere eventuali microfocolai di cellule tumorali al letto operatorio (boost)

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Tumore della mammella: cronistoria

TRATTAMENTO RADIANTE STANDARD

Gruppo di Lavoro AIRO per la Patologia Mammaria

2.4 FRAZIONAMENTI E DOSI

Dopo chirurgia conservativa il trattamento standard prevede la somministrazione di 50,0-50,4 Gy in regime di frazionamento convenzionale (1,8-2 Gy/die, in 5 frazioni settimanali).
Poiché la maggior parte delle recidive locali è documentata in corrispondenza o nelle immediate vicinanze del letto tumorale, al fine di ridurne l'incidenza, l'erogazione di un sovradosaggio al letto operatorio (boost) è pratica routinaria presso la maggior parte dei centri di radioterapia (46,47). Di norma sono previste dosi totali al letto operatorio (irradiazione del corpo mammario e sovradosaggio) di 60,0 Gy in caso di margini di resezione istologicamente negativi. In presenza di margini non negativi è indicata la somministrazione di una dose più elevata, come indicato

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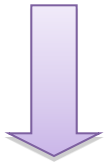
Tumore della mammella: OGGI

RADIOTERAPIA IPOFRAZIONATA

- Dopo chirurgia conservativa: stadi iniziali
  - Intero volume mammario
- Sovradose sul letto operatorio concomitante (SIB)
  - Utilizzo di frazionamenti alterati della dose



Riduzione del tempo globale di trattamento

(3-4 settimane *versus* 6 settimane)

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Tumore della mammella: OGGI

RADIOTERAPIA IPOFRAZIONATA: RAZIONALE

….”LA QUESTIONE RADIOBIOLOGICA”

Se riduciamo il tempo di trattamento da 6 a 3 settimane, riduciamo il potere di recupero del danno delle cellule tumorali, aumentando il controllo locale

[3] Qi XS, White J, Li XA. Is α/β for breast cancer really low? Radiother Oncol. 2011;100:282-288.

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…" I DATI PUBBLICATI"

Negli ultimi 20 anni, 7ooo donne sono state sottoposte a trattamento ipofrazionato all'interno di studi randomizzati:: START-A trial [4], START-B trial [5], RMH/GOC trial [6], ONTARIO trial [7].

E' stato ampiamente confermato che regimi di frazionamento in 13-16 frazioni sono sicuri ed efficaci come 50 in 25 sedute.

[4]Bentzen SM, Agrawal RK, Aird EG, et al. The UK Standardisation of Breast Radiotherapy (START) Trial A of radiotherapy hypofractionation for treatment of early breast cancer: A randomised trial. Lancet Oncol 2008;9:331–341.

[5]Bentzen SM, Agrawal RK, Aird EG, et al. The UK Standardisation of Breast Radiotherapy (START) Trial B of radiotherapy hypofractionation for treatment of early breast cancer: A randomised trial. Lancet 2008;371:1098–1107.

[6]Owen JR, Ashton A, Bliss JM, et al. Effect of radiotherapy fraction size on tumour control in patients with early-stage breast cancer after local tumour excision: long-term results of a randomised trial. Lancet Oncol 2006;7:467–471.

[7]Whelan TJ, Pignol JP, Levine MN, et al. Long-term results of hypofractionated radiation therapy for breast cancer. N Engl J Med 2010;362:513–520.

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Noi abbiamo scelto l'ipofrazionamento

Ma quale?

Table 1 Four prospective phase 3 randomized trials of hypofractionated WBI versus conventional fractionation in early-stage breast cancer

Trial	Years conducted	*n*	Fractionation Gy/*n* of fractions	Local recurrence,%	Good/excellent cosmesis,%	Time point
RMH/GOC	1986–1998	470	50/25	12.1	71	10 years
[7, 8]		466	42.9/13	9.6	74	
		474	39/13	14.8	58	
START A	1998–2002	749	50/25	3.6	60[a]	5 Years
[9]		750	41.6/13	3.5	58[a]	
		737	39/13	5.2	66[a]	
START B	1999–2001	1105	50/25	3.3	61[a]	5 Years
[10•]		1110	40/15	2.2	66[a]	
OCOG	1993–1996	612	50/25	6.7	71	10 Years
[11•]		622	42.5/16	6.2	70	

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Tumore della mammella: OGGI

- ***….” 40 Gy in 15 frazioni è ben tollerato e sicuro sui tessuti sani come 50 Gy in 25 frazioni, senza evidenza di inferiore controllo locale.***

Yarnold J et al. Hypofractionated whole-breast radiotherapy for women with early breast cancer: myths and realities. Int J Radiat Oncol Biol Phys. 2011 Jan 1;79(1):1-9.

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Tumore della mammella: OGGI

..e per il sovradosaggio sulla sede più a rischio del letto tumorale ?

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Tumore della mammella: OGGI

CRITICAL REVIEW

HYPOFRACTIONATED WHOLE-BREAST RADIOTHERAPY FOR WOMEN WITH EARLY BREAST CANCER: MYTHS AND REALITIES

JOHN YARNOLD, F.R.C.R.,* SØREN M. BENTZEN, D.SC.,† CHARLOTTE COLES, PH.D.,‡ AND JOANNE HAVILAND, M.SC.¶

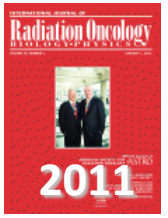

Table 1. Randomized clinical trials testing fraction size in adjuvant external beam radiotherapy

Trial year range	Test schedule (total dose/fraction no./treatment time (weeks) (fraction size))	No. of patients	% of patients undergoing breast-conserving surgery	% of patients prescribed a boost dose	Median follow up (months)
RMH/GOC 1986–1998	39.0/13/5.0 (3.0) 42.9/13/5.0 (3.3)	1,410	100	74.5	116
Ontario 1993–1996	42.5/16/3.2 (2.66)	1,234	100	0	> 132
START A 1999–2002	39.0/13/5.0 (3.0) 41.6/13/5.0 (3.2)	2,236	85	60.6*	61
START B 1999–2001	40.0/15/3.0 (2.67)	2,215	92	42.6*	72

Data compare designs of randomized clinical trials testing fraction size in adjuvant external beam radiotherapy to whole breast after local excision of early breast cancer. All trials used a control arm delivering 50 Gy in 25 fractions over 5 weeks.

* Breast conservation patients only.

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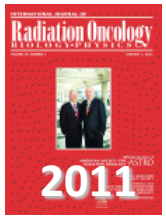
Tumore della mammella: OGGI



CLINICAL INVESTIGATION **Breast**

FRACTIONATION FOR WHOLE BREAST IRRADIATION: AN AMERICAN SOCIETY FOR RADIATION ONCOLOGY (ASTRO) EVIDENCE-BASED GUIDELINE

Benjamin D. Smith, M.D.,* Soren M. Bentzen, Ph.D., D.Sc.,† Candace R. Correa, M.D.,‡ Carol A. Hahn, M.D.,§ Patricia H. Hardenbergh, M.D.,¶ Geoffrey S. Ibbott, Ph.D.,‖ Beryl McCormick, M.D., FACR.,# Julie R. McQueen, CHES., RHEd.,** Lori J. Pierce, M.D.,†† Simon N. Powell, M.D., Ph.D.,# Abram Recht, M.D.,§§ Alphonse G. Taghian, M.D., Ph.D.,¶¶ Frank A. Vicini, M.D., FACR.,‖‖ Julia R. White, M.D.,## and Bruce G. Haffty, M.D.***

- Infatti dagli studi randomizzati sull'ipofrazionamento non sono emersi dati univoci sulle modalità e sulla dose del boost in caso di ipofrazionamento.

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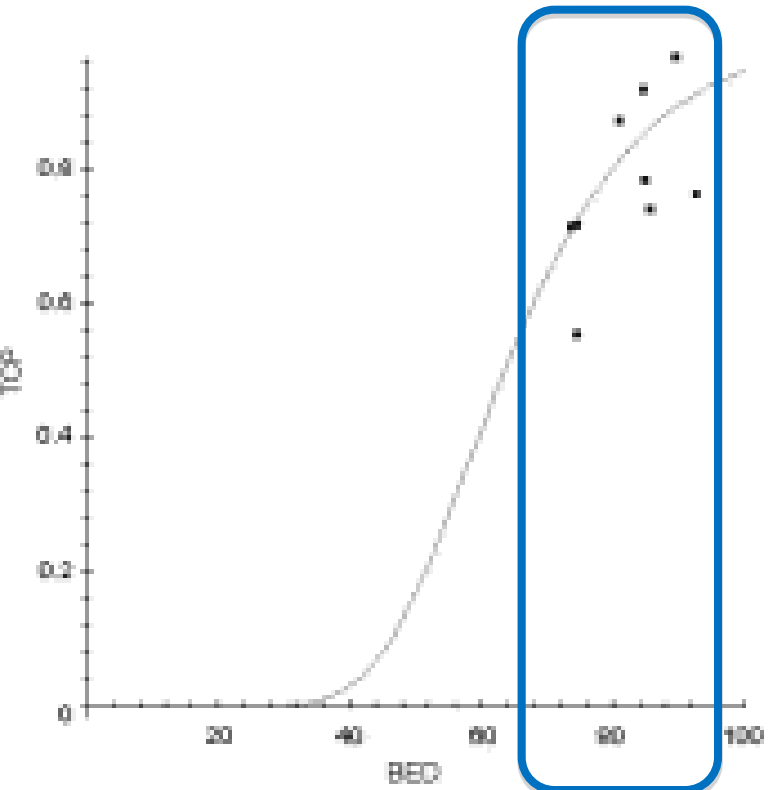
Tumore della mammella: OGGI

Noi abbiamo scelto il boost simultaneo..

Perche?



BIOLOGY CONTRIBUTION

BIOLOGICALLY EFFECTIVE DOSE–RESPONSE RELATIONSHIP FOR BREAST CANCER TREATED BY CONSERVATIVE SURGERY AND POSTOPERATIVE RADIOTHERAPY

GEORGE A. PLATANIOTIS, M.D., PH.D.,* AND ROGER G. DALE, PH.D., FIPEM., FRCR (HON).†

*Department of Oncology, Aberdeen Royal Infirmary, Aberdeen, United Kingdom; and †Imperial College Healthcare NHS Trust, London, United Kingdom

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Tumore della mammella: OGGI

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Phase I-II Trial of Prone Accelerated Intensity Modulated Radiation Therapy to the Breast to Optimally Spare Normal Tissue

Silvia C. Formenti, Daniela Gidea-Addeo, Judith D. Goldberg, Daniel F. Roses, Amber Guth, Barry S. Rosenstein, and Keith J. DeWyngaert

A B S T R A C T

Purpose
To report the clinical feasibility of a trial of accelerated whole-breast intensity modulated radiotherapy, with the patient in prone position, optimally to spare the heart and lung.

Patients and Methods
Patients with stages I or II breast cancer, excised by breast conserving surgery with negative margins, were eligible for this institutional review board–approved prospective trial. Computed tomography simulation was performed with the patient prone on a dedicated breast board, in the exact position used for treatment. A dose of 40.5 Gy, delivered at 2.7 Gy in 15 fractions, was prescribed to the index breast with an additional concomitant boost of 0.5 Gy delivered to the tumor bed, for a total dose of 48 Gy to the lumpectomy site. Physics constraints consisted of limiting ≤ 5% of the heart volume to receive ≥ 18 Gy and ≤ 10% of the ipsilateral lung volume to receive ≥ 20 Gy.

Results
Between September 2003 and August 2005, 91 patients were enrolled on the study. Median length of follow-up was 12 months (range, 1 to 28 months). In all patients the technique was feasible and heart and lung sparing was achieved as prescribed by the protocol. Acute toxicities consisting mostly of reversible grades 1-2 skin dermatitis (67%) and fatigue (18%) occurred in 75 patients. One patient sustained a regional recurrence rapidly followed by distant metastases.

Conclusion
Accelerated whole breast intensity modulated radiotherapy in the prone position is feasible and it permits a drastic reduction in the volume of lung and heart tissue exposed to significant radiation.

J Clin Oncol 25:2236-2242. © 2007 by American Society of Clinical Oncology

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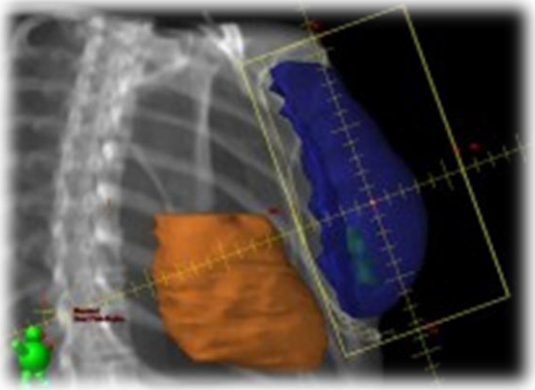
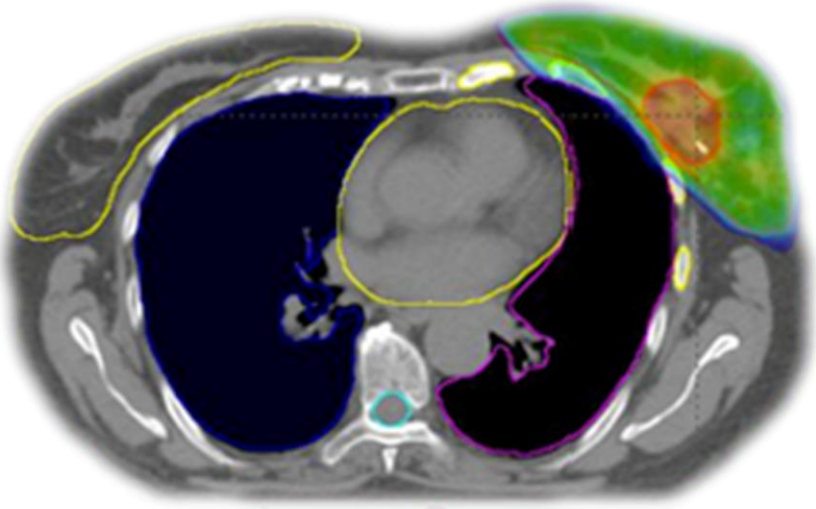
Tumore della mammella: OGGI



..perchè la tecnica ad archi modulati (RapidArc) ?



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Tumore della mammella: OGGI

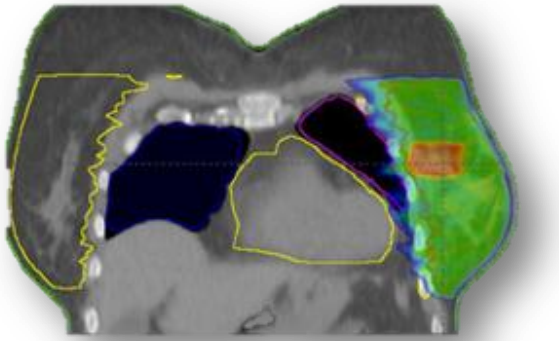
Scorsetti *et al. Radiation Oncology* 2012, 7:145
http://www.ro-journal.com/content/7/1/145

RADIATION ONCOLOGY

STUDY PROTOCOL **Open Access**

Phase I-II study of hypofractionated simultaneous integrated boost using volumetric modulated arc therapy for adjuvant radiation therapy in breast cancer patients: a report of feasibility and early toxicity results in the first 50 treatments

Marta Scorsetti[1], Filippo Alongi[1*], Antonella Fogliata[2], Sara Pentimalli[1], Pierina Navarria[1], Francesca Lobefalo[1], Carlos Garcia-Etienne[3], Alessandro Clivio[2], Luca Cozzi[2], Pietro Mancosu[1], Giorgia Nicolini[2], Eugenio Vanetti[2], Marco Eboli[3], Carlo Rossetti[3], Arianna Rubino[3], Andrea Sagona[3], Stefano Arcangeli[1], Wolfgang Gatzemeier[3], Giovanna Masci[4], Rosalba Torrisi[4], Alberto Testori[5], Marco Alloisio[5], Armando Santoro[4] and Corrado Tinterri[3]



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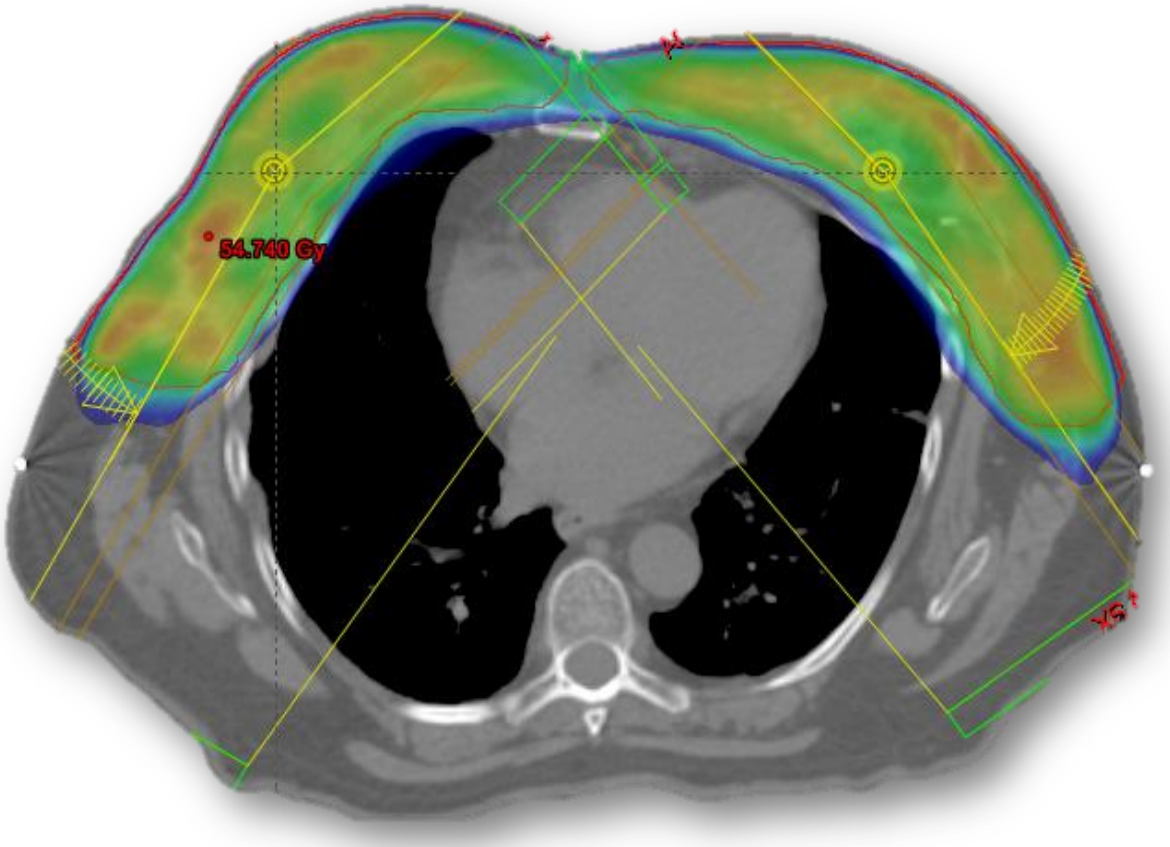
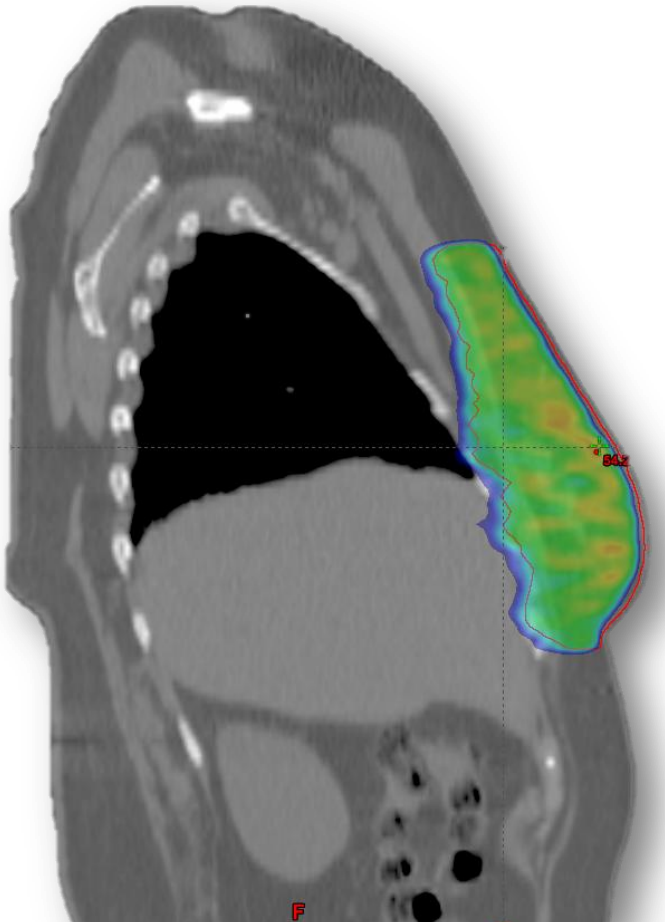


TECHNICAL REASONS.



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CLINICAL REASONS..

- There were no significant differences in cosmetic scores on baseline assessment vs. 3 months and 6 months after the treatment: all patients were scored as excellent/good (50/50) compared with baseline.

- No fair/poor judgment was recorded. No other toxicities or local failures were recorded during follow-up

Pre RT

End of RT

Follow up @ 90 days

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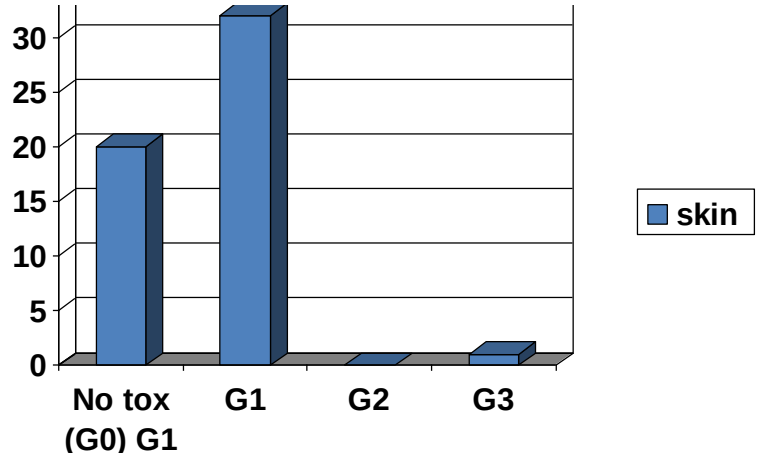
CLINICAL RESULTS:

Description of acute skin toxicity in the population of study, stratified for each grade, according to RTOG scale and clinical results

Grade	Skin toxicity description	Number of cases	% of cases
Grade 0	No change over baseline	20/50	40%
Grade 1	Follicular, faint or dull erythema/ epilation/dry desquamation/ decreased sweating	32/50	64%
Grade 2	Tender or bright erythema, patchy moist desquamation/ moderate edema	0/50	0%
Grade 3	Confluent, moist desquamatiom other than skin folds, pitting edema	1/50	2%
Grade 4	Ulceration, hemorrhage, necrosis	0/50	0%



- All Grade 1 toxicities had resolved by 3 weeks.

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SKIN CLINICAL RESULTS: COMPARISON WITH LITERATURE(IMRT)

	Dose Gy	n. fr	G1	G2	G3	G4
Scorsetti et al.2012	*40.5/48*	*15*	*64%*	*0*	*2%**	*0%*
Formenti et al.2006	*40.5/48*	15	58%	8%	1%	0%
Freedman et al.2007	45/56	20	65%	23%	0%	0%
Chada et al. 2012	*40.5/45*	15	96% (G0+G1)	4%	0%	0%

***1 case of G3= bilateral irradiation**

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Cancer/Radiothérapie xxx (2015) xxx–xxx

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Original article

Intensity modulated radiation therapy with simultaneous integrated boost in early breast cancer irradiation. Report of feasibility and preliminary toxicity

Radiothérapie conformationnelle avec modulation d'intensité avec boost *simultané dans le cancer du sein de stade T1-2, N0-1, M0. Faisabilité et toxicité*

A. Fiorentino[a], R. Mazzola[a,b,*], F. Ricchetti[a], N. Giaj Levra[a], S. Fersino[a], S. Naccarato[a], G. Sicignano[a], R. Ruggieri[a], G. Di Paola[c], A. Massocco[d], S. Gori[e], F. Alongi[a]

Please cite this article in press as: Fiorentino A, et al. Intensity modulated radiation therapy with simultaneous integrated boost in early breast cancer irradiation. Report of feasibility and preliminary toxicity. Cancer Radiother (2015), http://dx.doi.org/10.1016/j.canrad.2015.02.013

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Open Issue

Hypofractionated RT under age 50

Curr. Treat. Options in Oncol. (2015) 16:16
DOI 10.1007/s11864-015-0334-8

Breast Cancer (P Neven, Section Editor)

Breast Cancer Under Age 40: a Different Approach

D. Ribnikar, MD[1]

Age as biomarker (prognostic and predictive)

carried a worse prognosis than in older women. Age <40 predicted inferior survivals within the luminal subgroup. One must acknowledge that an important limitation of the study is the lack of further subtyping within the luminal group. It is possible that the inferior outcomes are driven by luminal B cancer in this group. In the HERceptin Adjuvant (HERA) trial (HER-2 positive BC), age <40 years was not prognostic for DFS or overall survival (OS) in the CT plus trastuzumab arm [29]. Such data supports the concept that age <40 years as a prognostic factor differs by biologic subtype.

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Breast Cancer (P Neven, Section Editor)

Breast Cancer Under Age 40: a Different Approach

D. Ribnikar, MD[1]

RT after BCS reduces local recurrence from 19.5 to 10.2 % in BC patients 40 years and younger (P=0.002) [48]. The 10-year results of the EORTC 22991/10883 trial (boost vs no boost trial) demonstrated that additional radiation had the largest absolute benefit on local control in younger patients and reported that close margin was associated with higher local recurrence rate only in younger patients (less than 45 years old), suggesting the importance of strict surgical local control for this patient population [67, 68].

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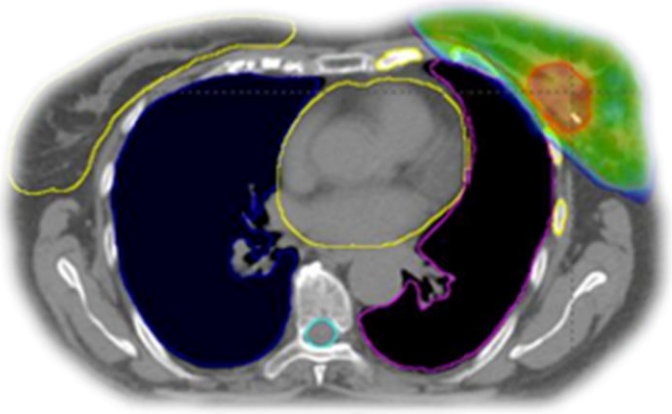
Open Issue

Hypofractionated RT under age 50

CLINICAL INVESTIGATION Int. J. Radiation Oncology Biol. Phys., Vol. 81, No. 1, pp. 59–68, 2011 **Breast**

FRACTIONATION FOR WHOLE BREAST IRRADIATION: AN AMERICAN SOCIETY FOR RADIATION ONCOLOGY (ASTRO) EVIDENCE-BASED GUIDELINE

Benjamin D. Smith, M.D.,* Soren M. Bentzen, Ph.D., D.Sc.,† Candace R. Correa, M.D.,‡ Carol A. Hahn, M.D.,§ Patricia H. Hardenbergh, M.D.,¶ Geoffrey S. Ibbott, Ph.D.,‖ Beryl McCormick, M.D., FACR.,# Julie R. McQueen, CHES., RHEd.,** Lori J. Pierce, M.D.,†† Simon N. Powell, M.D., Ph.D.,# Abram Recht, M.D.,§§ Alphonse G. Taghian, M.D., Ph.D.,¶¶ Frank A. Vicini, M.D., FACR.,‖‖ Julia R. White, M.D.,## and Bruce G. Haffty, M.D.***



ness of HF-WBI. The vast majority (approximately 70%–79%) of patients enrolled in clinical trials comparing HF-WBI with CF-WBI were aged 50 years or older at diagnosis (Table 4) (10, 16–21). The effect of age on outcome has only been reported for the Canadian trial, which stratified entry by age (younger than 50 years vs. 50 years or older) (18, 21). A preplanned analysis found that HF-WBI was equivalent to CF-WBI in both groups (18, 19, 21). However, the Canadian trial included only 305 women under 50, and no further division of results by age was performed within this group (*e.g.*, age 40 years or younger vs. age 41–49 years). Thus, the task force unanimously agreed that the available data supported the equivalence of HF-WBI with CF-WBI for patients aged 50 years or older at diagnosis. Although the available data did appear to support the equivalence of CF- and HF-WBI for patients under 50, a minority of the

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Tumore della mammella: OGGI
Open Issue

RT and neoadjuvant Chemotherapy

Tumori, 100: e212-e213, 2014

Postoperative breast radiotherapy after neoadjuvant chemotherapy: which uncertainties still remain?

Filippo Alongi[1], Francesco Ricchetti[1], Alba Fiorentino[1], and Stefania Gori[2]

However, there are still many concerns regarding the neoadjuvant chemotherapy approach. The first is the lack of upfront pathological staging, also considering that current imaging is not a reliable surrogate and that the risk of under- or overestimation may not be negligible. The second relevant issue regards the surgical procedure: obtaining a "real" conservative approach without the clear identification of the site and extent of disease at the time of resection without clip placement prior to chemotherapy could be challenging. Margin status can also change in significance after chemotherapy because tumor shrinkage may be anisotropic. Last but not least, the determination of radiation volumes and prescription doses after neoadjuvant chemotherapy remains unclear, especially after a complete pathological response. The absence of upfront pathological evidence should be taken into account in any decisions regarding locoregional radiotherapy. Unanswered questions for radiation oncologists are: a) when to include regional nodes in the treatment volume, and b) whether a radiation boost to the surgical bed is really useful and when[4]. Definitive data on the actual outcome of radiation therapy in this setting are still lacking[1].

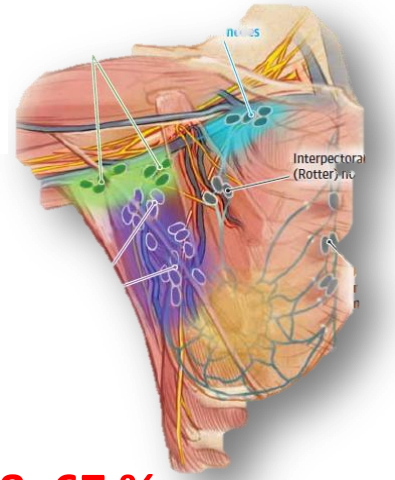
Tumore della mammella: OGGI
Open Issue

RT and lymph nodes micro-macrometastases without LA

REVIEW ARTICLE

Breast Cancer (2013) 20:41–46

The changing role of axillary lymph node dissection for breast cancer



It has been shown that **SLN is the only positive lymph node in 38–67 %** of patients when ALND followed.

This finding not only provides strong support for the SLN concept, but also **suggests that unnecessary ALND** can be avoided in such patients, because removal of negative lymph nodes does not provide any significant benefit as mentioned above.

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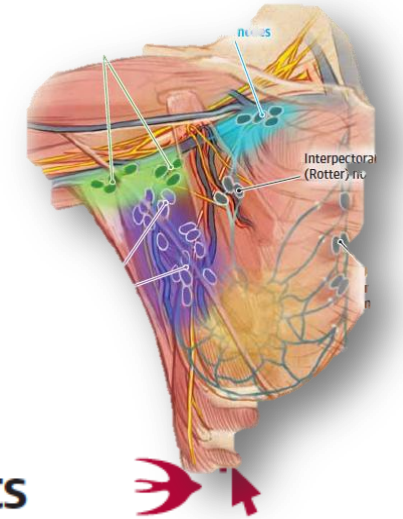
RT and lymph nodes **micrometastases** without LA

It has been shown that **85–90 % of patients with SLN micrometastases do not have disease in other non-SLNs**



Breast Cancer (2013) 20:41–46

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

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

Lancet Oncol 2013; 14: 297–305

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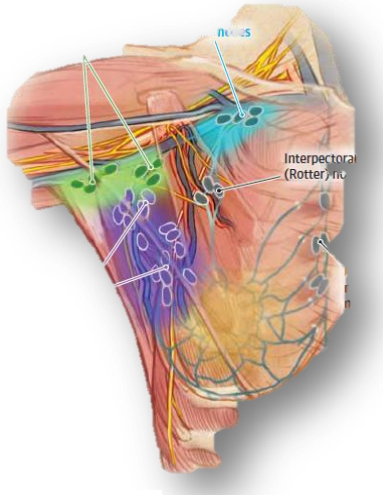
RT and lymph nodes **macrometastases** without LA

Whereas **48–87 % of patients with macrometastases** in SLN have disease in other non-SLNs.



Breast Cancer (2013) 20:41–46

ORIGINAL CONTRIBUTION

Axillary Dissection vs No Axillary Dissection in Women With Invasive Breast Cancer and Sentinel Node Metastasis

A Randomized Clinical Trial

JAMA. 2011;305(6):569-575

Armando E. Giuliano, MD

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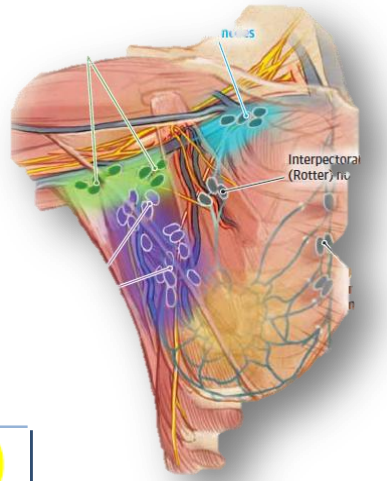
RT and lymph nodes **macrometastases** without LA

Axillary dissection versus no axillary dissection in women with invasive breast cancer and sentinel node metastasis

J can chir, Vol. Vol. 55, N° 1, février 2012

Steve Latosinsky, MD



study results, problems with the methodology, including what noninferiority margin the study can exclude in clinically understandable terms, trial accrual, the inclusion of a number of node-negative patients and loss of follow-up of a large number of patients, lead to difficulties with analysis, interpretation and confidence in the results.

Should the results of Z0011 change practice? Owing to its methodologic limitations, if we had to depend on Z0011 alone the standard of care following a positive sentinel node "may" still be an ALND. However, in light of the new

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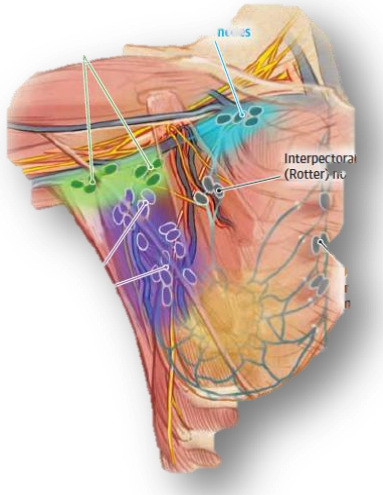
Open Issue

RT and lymph nodes **macrometastases** without LA

Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial

Lancet Oncol 2014; 15: 1303–10

Mila Donker, Geertjan van Tienhoven, Marieke E Straver, Philip Meijnen, Cornelis J H van de Velde, Robert E Mansel, Luigi Cataliotti, A Helen Westenberg, Jean H G Klinkenbijl, Lorenzo Orzalesi, Willem H Bouma, Huub C J van der Mijle, Grard A P Nieuwenhuijzen, Sanne C Veltkamp, Leen Slaets, Nicole J Duez, Peter W de Graaf, Thijs van Dalen, Andreas Marinelli, Herman Rijna, Marko Snoj, Nigel J Bundred, Jos W S Merkus, Yazid Belkacemi, Patrick Petignat, Dominic A X Schinagl, Corneel Coens, Carlo G M Messina, Jan Bogaerts, Emiel J T Rutgers



Interpretation Axillary lymph node dissection and axillary radiotherapy after a positive sentinel node provide excellent and comparable axillary control for patients with T1–2 primary breast cancer and no palpable lymphadenopathy. Axillary radiotherapy results in significantly less morbidity.

planned non-inferiority test was underpowered because of the low number of events.

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CONCLUSIONI:

La radioterapia rimane una parte cruciale del trattamento del tumore della mammella

La radioterapia moderna può essere più breve ed ugualmente efficace e ben tollerata