



Associazione Italiana Radioterapia Oncologica
Gruppo di Studio per la Patologia Mammaria



III Zoom Journal Club 2013

Bologna
21 Febbraio 2014
NH Hotel De La Gare

CASO CLINICO

IV Sessione- PBI: quali modalità di trattamento?
in quali pazienti?

A. Fozza





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Sig.ra C.A. 49 anni

Anamnesi patologica remota

-Aprile 1996: **Linfoma di Hodgkin SN a prevalenza linfocitaria** trattato con **RT esclusiva** (mantellina 36 Gy/20 frazioni + boost LC sx 3,6 Gy/2 frazioni). In RC.

-Dal 1996 ipotiroidismo post-attinico in terapia sostitutiva

-Allergia: acido acetilsalicilico, FANS, tetracicline

-Perimenopausa

-No familiarità per neoplasia mammaria



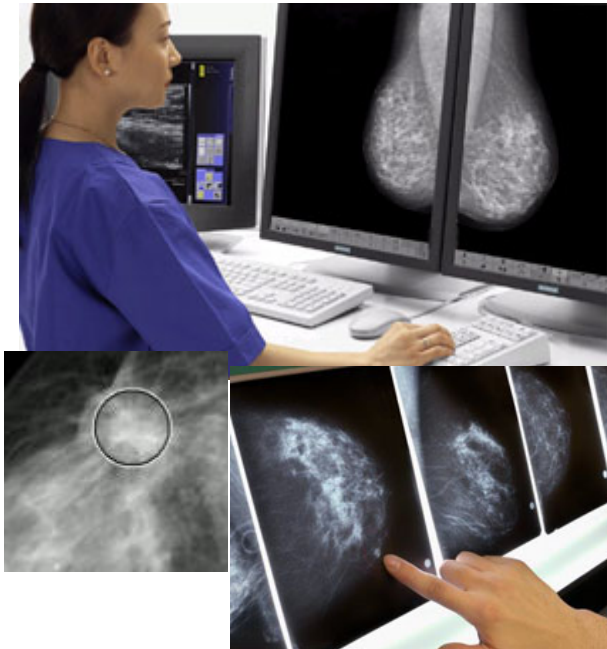


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Anamnesi oncologica:

-Febbraio 2012 Mammografia ed ETG mammaria:
neoformazione mammaria dx QSE (15mm), R5 U5.
Agobiopsia: **B5b, CDI G2.** NO fattori biologici

-Indicazione chirurgica: mastectomia → rifiutata!





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Aprile 2012 intervento chirurgico:
ampia resezione QQ esterni mammella dx + DLsn

**CDI pT1c (18mm) pN0sn (0/1) G2 + CDIS <25%, margini indenni,
LVI assente.**

ER 85%, PgR 90%, Ki-67 10% c-erb B2 1+ (luminal A)





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Maggio 2012 OT (Tamoxifene)



Giugno 2012 visita RT: che fare???





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Opzioni terapeutiche:

- 1. Mastectomia**
- 2. BCS + RT adiuvante**
- 3. BCS senza RT**





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Opzioni terapeutiche:

1. Mastectomia

Salvage mastectomy → standard therapy with **LC 90%**

OS at 5 and 10 years 70% and 65%

[J Clin Oncol](#). 2009 May 20;27(15):2466-73. doi: 10.1200/JCO.2008.19.8424. Epub 2009 Apr 6.

Prognosis after ipsilateral breast tumor recurrence and locoregional recurrences in patients treated by breast-conserving therapy in five National Surgical Adjuvant Breast and Bowel Project protocols of node-negative breast cancer.

[Anderson SJ](#), [Wapnir I](#), [Dignam JJ](#), [Fisher B](#), [Mamounas EP](#), [Jeong JH](#), [Geyer CE Jr](#), [Wickerham DL](#), [Costantino JP](#), [Wolmark N](#).

Department of Biostatistics, University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA 15261, USA. sja@pitt.edu

[Int J Radiat Oncol Biol Phys](#). 1990 Oct;19(4):833-42.

Breast recurrence following conservative surgery and radiation: patterns of failure, prognosis, and pathologic findings from mastectomy specimens with implications for treatment.

[Fowble B](#), [Solin LJ](#), [Schultz DJ](#), [Rubenstein J](#), [Goodman RL](#).

Department of Radiation Oncology, University of Pennsylvania, School of Medicine, Philadelphia.

...ma progresso LH!!!





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2. BCS + RT adiuvante

Additional **re-irradiation** → **prevent** subsequent **second relapses** with further deterioration of prognosis

Strahlenther Onkol. 2012 Jun;188(6):461-3. doi: 10.1007/s00066-012-0092-5.

One life saved by four prevented recurrences? Update of the Early Breast Cancer Trialists confirms: postoperative radiotherapy improves survival after breast conserving surgery.

Sautter-Bihl ML, Sedlmayer F, Budach W, Dunst J, Feyer P, Fietkau R, Haase W, Harms W, Rödel C, Souchon R, Wenz F, Sauer R.





2. BCS + RT adiuvante

WBRT vs PBI

- No dati certi estraibili dal precedente trattamento RT per LH
- Risparmiare i QQ int già irradiati
- Dati letteratura:

It seems feasible to apply dose of **50 Gy EQD2** to a PB volume of **80-100 ccm** with brachytherapy, EBRT or IORT



Partial breast re-irradiation for local recurrence of breast carcinoma: Benefit and long term side effects



Felix Sedlmayer^{a,*}, Franz Zehentmayr^b, Gerd Fastner^a

^a Department of Radiotherapy and Radio-Oncology, Landeskrankenhaus Salzburg, Paracelsus Medical University, Mülner Hauptstraße 48, A-5020 Salzburg, Austria

^b Institute on Research and Development of Advanced Radiation Technology (radART), Paracelsus Medical University, Mülner Hauptstraße 48, A-5020 Salzburg, Austria





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2. BCS + RT adiuvante

PBI

- **Tecnica**
- **Dose totale e frazionamento**
- **Constraints**
- **Tossicità**





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The Breast 22 (2013) 5141–5146



Contents lists available at SciVerse ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst



PBI

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Biologically effective dose and outcome.

| Study | EQD ₂ with $\alpha/\beta = 3$ | EQD ₂ with $\alpha/\beta = 4$ | Med FU (mo) | Tumor related results (y) | Late reactions/cosmetic outcome |
|-------------------------|--|--|---------------|---|---|
| Chadha 2008 | 45 Gy | 45 Gy | 36 (28–211) | 3a MFS (=LC) 89% OS 100% | "Good to excellent"; preexist. Asymmetry |
| Hannoun-Levi 2004 | Not calculable | Not calculable | 50.2 (2–139) | 5a LC 77.4% DFS 68.9% (50 Gy > 30–45 Gy) | Higher doses/volumes: à G2/3 reactions |
| Trombetta 2009 | 52 Gy or 65.8 Gy | 51.7 Gy or 60.5 Gy | 38 (6–75) | 3.2 a LC 96% DFS 88.5% OS 88.5% | Excellent: 22 good: 6 fair: 2 |
| Guix 2010 | 53.3 Gy | 49.4 Gy | 89 (15–169) | 10 a LC 89.4% DFS 64.4% OS 96.7% | 94% Excellent/good 6% poor 16 Pat. Fibrosis G1-2 (44%) |
| Hannoun-Levi 2011 | 66.6 Gy | 61.2 Gy | 21 (6–50) | 1.8a LC 97% | 60% Complications (fibrosis) VAS score 7 |
| Polgar 2012 | 32.6 Gy | 30.8 Gy | 62 (11–127) | 5a LC 100% DFS 69% OS 85% | Grade 2 fibrosis 7%, skin toxicity 7% Asymptomatic fat necrosis 40% G 3-4: none Cosmesis: 7% excellent, 66% good, 13% fair, 7% poor |
| Kauer-Dorner 2012 | 63.4 Gy | 61 Gy | 57 (27–87) | 5a LC 93% DFS 77% OS 87% | LENT-SOMA (24 pat) 79% G1-2 (fibrosis, teleangiectasia, pain), 17% G3 Cosmesis: 12% excellent, 25% good, 38% fair, 25% poor/unacceptable |
| Resch 2002 | 39.6 Gy or 59 Gy | 40.1 Gy or 57.5 Gy | 59 (20–84) | 5a LC 76% | Cosmesis: 12% excellent, 18% good 47% moderate 23% acceptable |
| Deutsch 2002 | 50 Gy | 50 Gy | 51.5 (16–291) | 5a LC 77% DFS 68.5% OS 77.9% | 33% Excellent 42% good 25% fair/poor |
| Kraus-Tiefenbacher 2007 | 47.6 Gy – 92 Gy | 42 Gy – 80 Gy | 26 (1–60) | 2.2a: LC 100% DFS 82% OS 94% | Cosmesis: 41% excellent, 41% good 18% fair |

G1-G2 fibrosis, teleangiectasia and pain 44-79%

Severe late reactions (skin necrosis o ulceration) → ever stated

Cosmesis: up to 1/3 pts excellent, half good, up to quarter poor





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3. BCS senza RT adiuvante

Close FU → early stage IBTR → second breast conserving approach??!

BCS alone → high LRR 7- 50%

Br J Surg, 1999 Jan;86(1):64-7.

Reoperation for locally recurrent breast cancer in patients previously treated with conservative surgery.

Salvadori B, Marubini E, Miceli R, Conti AR, Cusumano F, Andreola S, Zucali R, Veronesi U.

Chirurgia Generale C, Istituto Nazionale per lo Studio e la Cura dei Tumori di Milano, Milan, Italy.

Int J Radiat Oncol Biol Phys, 2005 Nov 1;63(3):845-51.

Ipsilateral breast tumor recurrence after breast conservation therapy: outcomes of salvage mastectomy vs. salvage breast-conserving surgery and prognostic factors for salvage breast preservation.

Alpert TE, Kuerer HM, Arthur DW, Lannin DR, Haffty BG.

Department of Radiation Oncology, Upstate Medical University, Syracuse, NY, USA.





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3. BCS senza RT adiuvante

Age → predictor for IBTR

Annual in-breast recurrence rates following BCT:

0.4%-0.7% >50 years

0.72 -1.2% 41-50 years

0.72-2% for <40 years



Randomized Trial of Breast Irradiation Schedules After Lumpectomy for Women With Lymph Node-Negative Breast Cancer

Timothy Whelan, Robert MacKenzie, Jim Julian, Mark Levine, Wendy Shelley, Laval Grimard, Barbara Lada, Himu Lukka, Francisco Perera, Anthony Fyles, Ethan Laukkanen, Sunil Gulavita, Veronique Benk, Barbara Szechtman

The New England Journal of Medicine

RECURRENCE RATES AFTER TREATMENT OF BREAST CANCER WITH STANDARD RADIOTHERAPY WITH OR WITHOUT ADDITIONAL RADIATION

HARRY BARTELINK, M.D., PH.D., JEAN-CLAUDE HORIOT, M.D., PH.D., PHILIP POORTMANS, M.D., HENK STRUIKMANS, M.D., PH.D., WALTER VAN DEN BOGAERT, M.D., PH.D., ISABELLE BARILLOT, M.D., ALAIN FOURQUET, M.D., JACQUES BORGER, M.D., PH.D., JOS JAGER, M.D., PH.D., WILLEM HOOGENRAAD, M.D., LAURENCE COLLETTE, M.Sc., AND MARIANNE PIERART, M.Sc., FOR THE EUROPEAN ORGANIZATION FOR RESEARCH AND TREATMENT OF CANCER RADIOTHERAPY AND BREAST CANCER GROUPS



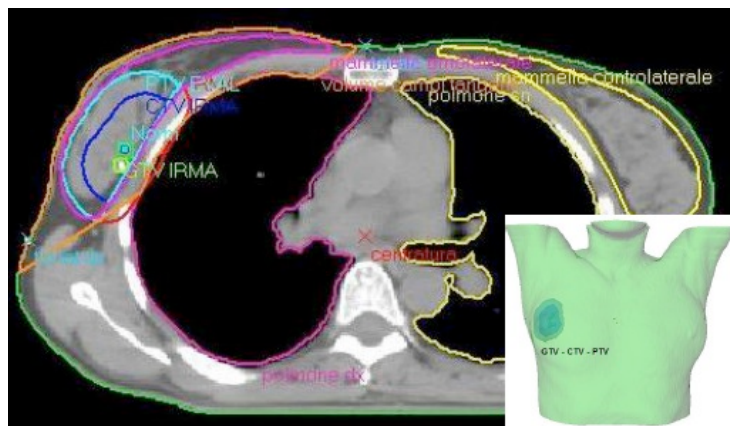


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SCELTA TERAPEUTICA:

RT adiuvante con **PBI con 3D-CRT**

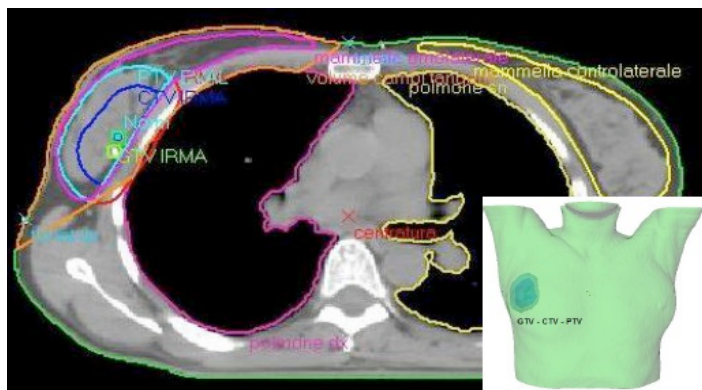
Giugno 2012 **38.5 Gy/10 fr** bi-giornaliere



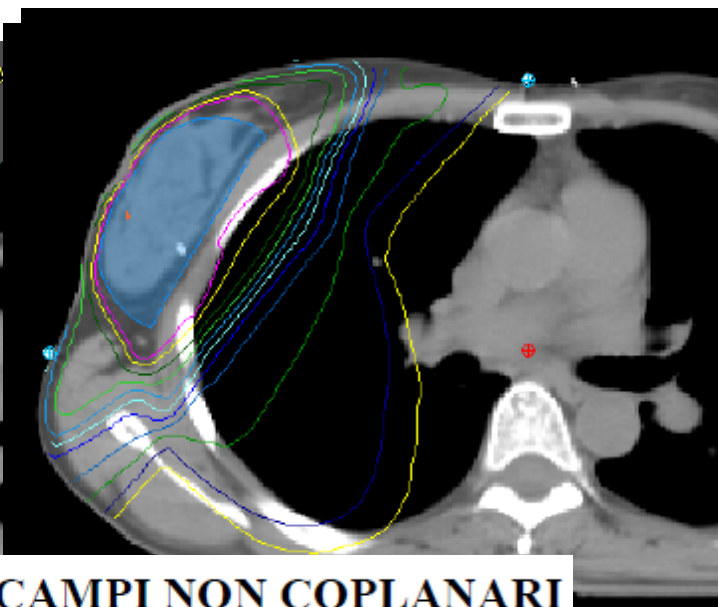
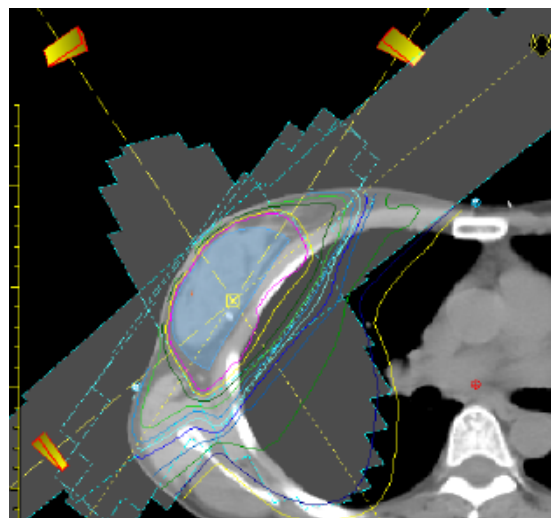


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| CAMPO: | GANTRY (°): | LETTINO (°): | COLLIMAT. (°): | CUNEO (°): | DOSE in cGy all'isocentro: | UM: |
|---------------|-------------|--------------|----------------|------------|----------------------------|---------------|
| Rt AISO: | 320 | 320 | 50 | 45 | 90 | 249,9 |
| Rt PSIO | 230 | 15 | 80 | 40 | 116 | 312,2 |
| Lt ASIO | 40 | 320 | 240 | 40 | 90 | 234,8 |
| Lt AISO | 40 | 40 | 300 | 40 | 90 | 264,8 |
| TOTALE | | | | | 385 | 1061,7 |



Isodosi relative:

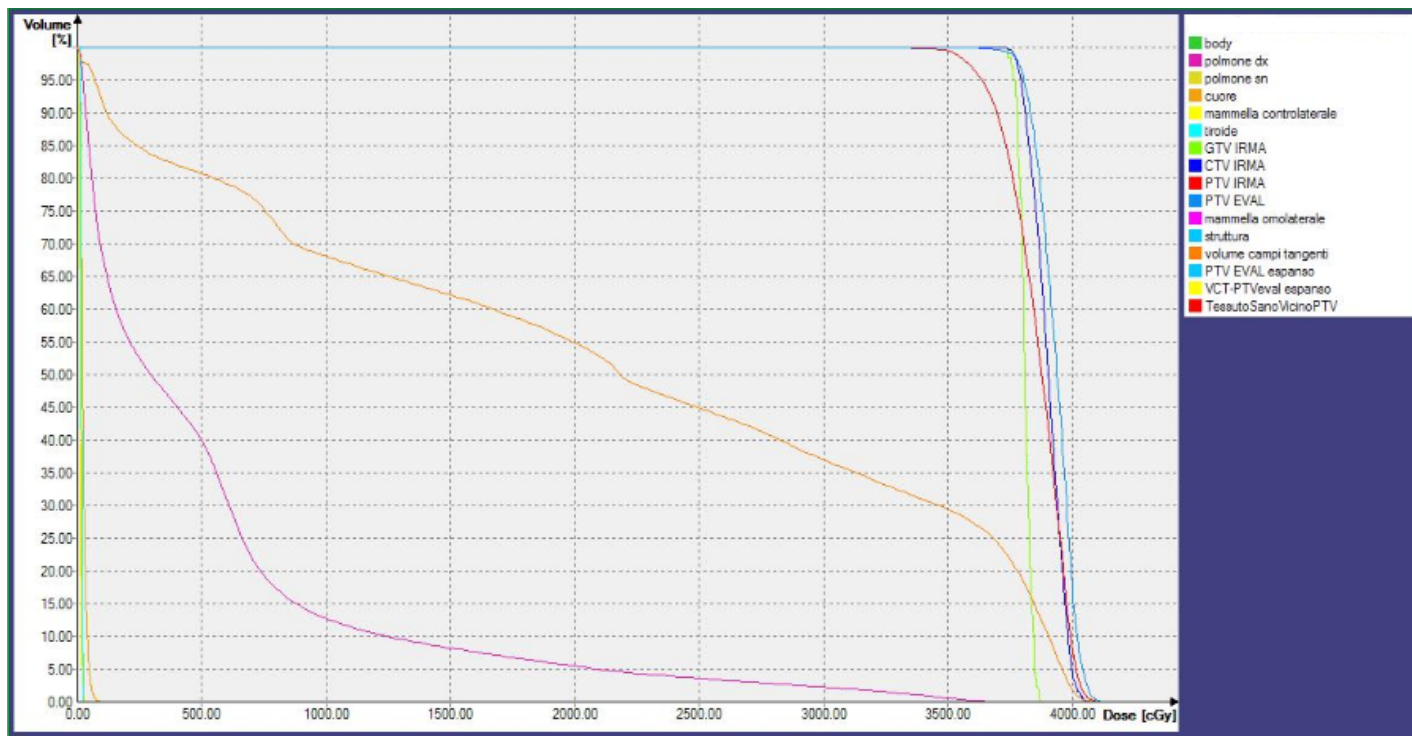
- 115%
- 112%
- 110%
- 105%
- 95%
- 90%
- 80%
- 70%
- 60%
- 50%
- 40%
- 30%
- 20%
- 10%
- 5%

TECNICA 3D-CRT A 4 CAMPI NON COPLANARI





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Summed Beams in IRMA MAMM DX OK

| ROI | Dose [%] | Dose [cGy] | Volume [%] | Volume [ccm] |
|-------------------------|----------|------------|------------|--------------|
| PTV EVAL | - | 3465.00 | 100.00 | 103.94 |
| PTV EVAL | - | 3850.00 | 85.51 | 88.88 |
| PTV EVAL | - | 4620.00 | - | - |
| cuore | - | 192.50 | - | - |
| mammella controlaterale | - | 115.00 | - | - |
| polmone dx | - | 1155.00 | 10.81 | 146.26 |
| polmone sn | - | 192.50 | - | - |
| tiroide | - | 192.50 | - | - |
| volume campi tangenti | - | 1925.00 | 56.13 | 377.09 |
| volume campi tangenti | - | 3850.00 | 14.60 | 98.06 |

Polmone dx: $V > 30\% < 15\%$

Cuore (mamm dx): $V > 5\% < 5\%$

Mammella omolat: $V > 50\% < 60\%$

$V_{100\%} < 35\%$

Mammella controlat $< 3\%$ della dose





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Follow up 18 MESI

Tossicità:

- tossicità acuta: G0
- tossicità tardiva: fibrosi ghiandolare G1-2

Risultato estetico: buono



Dicembre 2013 Mammografia ed ETG mammaria: negative per ripresa di malattia





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DISCUSSIONE

- 1) **Scelta terapeutica:** mastectomia vs BCS +/-RT
- 2) **Se RT:** WBRT vs PBI
- 3) **Se PBI:** tecnica, dose totale e frazionamento
- 4) **Constraints:** su che OAR e quali limiti





TOSSICITÀ e COSMESI

Biologically effective dose and outcome.

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EBRT



RTOG
RADIATION THERAPY
ONCOLOGY GROUP

RADIATION THERAPY ONCOLOGY GROUP

RTOG 1014

**A PHASE II STUDY OF REPEAT BREAST PRESERVING SURGERY AND
3D-CONFORMAL PARTIAL BREAST RE-IRRADIATION (PBRI) FOR LOCAL
RECURRENCE OF BREAST CARCINOMA**



This will be the **first series** where **precise dose-volume relationships** accounting for **PTV sizes, normal tissue doses and dose homogeneities** are assessed prospectively



Image Courtesy of Siemens

