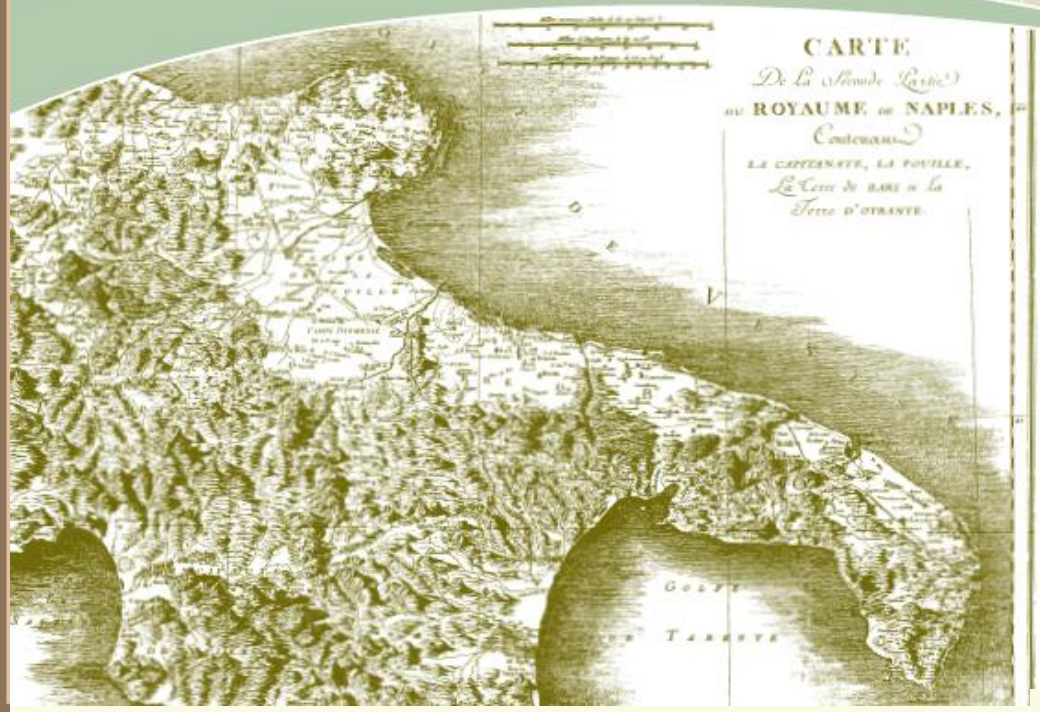



Gruppo Regionale
AIRO APPULO-LUCANO

**La Radioterapia nel cancro della mammella: indicazioni e tecnica**

I Convegno
del Gruppo Regionale AIRO APPULO-LUCANO

**Taranto, 19 giugno 2010**
Auditorium Ospedale SS. Annunziata
Padiglione Vinci

# La irradiazione parziale della mammella: EBRT,BCT,IORT

Dott. Marco Lioce
U.O.C. di Radioterapia Oncologica
IRCCS ISTITUTO TUMORI
"Giovanni Paolo II " – BARI

# Partial breast irradiation

## DEFINIZIONE

"Irradiazione del letto tumorale con margine di sicurezza di 1-2 cm, sede a piu' elevato rischio di ricaduta"

# Pbi Razionale

L' 80-85% delle recidive si manifesta su sede iniziale di malattia

Clark *JNCI* 84:683, 1992
Liljegren *JCO* 17:2326, 1999
Veronesi *Ann Oncol* 12:997, 2001

In pazienti sottoposte o meno a RT, uguale incidenza di recidiva al di fuori della sede iniziale e nella mammella controlaterale

Fisher, *Cancer* 57:1717, 1986
Veronesi *NEJM* 328:1587, 1993
Liljegren *JNCI* 86:717, 1994
Clark *JNCI* 88:1659, 1996

L'irradiazione della mammella in toto potrebbe essere superflua in un'elevata percentuale di pazienti

# Vantaggi della PBI rispetto al trattamento convenzionale:

- Riduzione intervallo con chirurgia
- Riduzione della durata totale del trattamento (overall time 1-5 gg)
- Riduzione disagi logistici / costi (possibile miglioramento della Q. of L. delle pazienti)
- Riduzione delle liste d'attesa nei Centri di Radioterapia
- Maggior numero di pazienti sottoposto a trattamento conservativo
- Eliminazione interferenze con la chemioterapia (timing)
- Ipotizzabile più bassa incidenza di recidiva rispetto ad un frazionamento convenzionale, per una riduzione del processo di ripopolazione cellulare
- Riduzione degli effetti collaterali rispetto al trattamento standard, evidenti prevalentemente in pazienti con mammelle voluminose

CONSENSUS STATEMENT

## Accelerated Partial Breast Irradiation Consensus Statement from the American Society for Radiation Oncology (ASTRO)

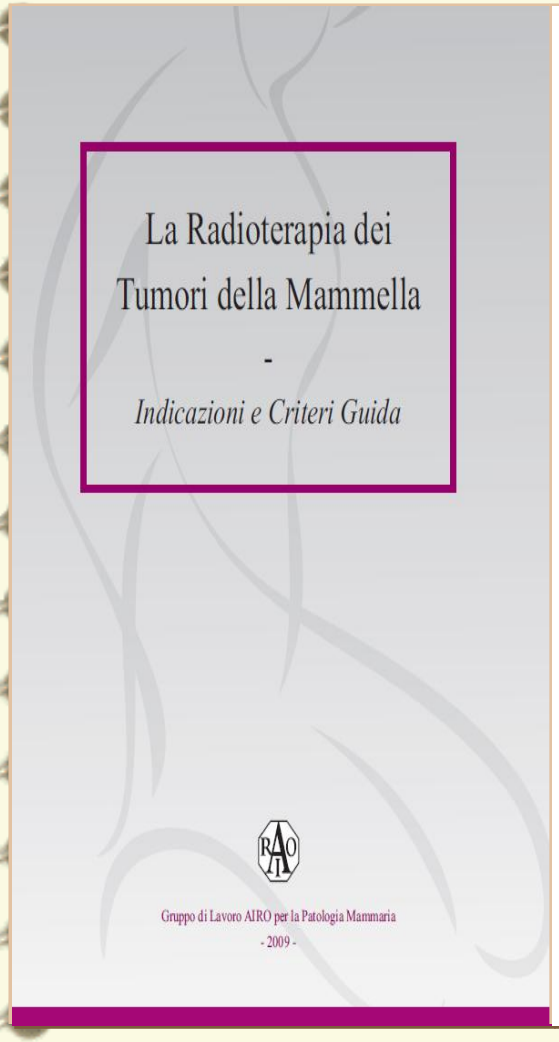
Benjamin D Smith, MD, Douglas W Arthur, MD, Thomas A Buchholz, MD, Bruce G Haffty, MD, Carol A Hahn, MD, Patricia H Hardenbergh, MD, Thomas B Julian, MD, Lawrence B Marks, MD, Dorin A Todor, PhD, Frank A Vicini, MD, Timothy J Whelan, MD, Julia White, MD, Jennifer Y Wo, MD, Jay R Harris, MD

# Patient Selection Criteria

| | ASTRO guidelines strict | ASTRO "with caution" | ASTRO on trial |
|---|---|---|---|
| **Age** | ≥ 60 | 50-59 | < 50 |
| **Diagnosis** | Invasive ductal, mucinous, tubular, or colloid, no EIC or LVI, ER (+) | Invasive lobular, EIC < 3 cm, limited or focal LVI, ER (-), DCIS < 3cm | Extensive LVI, pure DCIS > 3 cm, neoadjuvant chemo |
| **Tumor size** | cUnifocal, < 2 cm | 2.1 - 3 cm | > 3cm, T3, T4 or cmultifocal, multicentric |
| **Surgical margins** | ≥ 2 mm | < 2 mm | (+) |
| **Nodal status** | N0 or IHC (+) only | | N(+) or undissected |

Vol. 209, No. 2, August 2009

# PBI: criteri di inclusione (restrittivi )

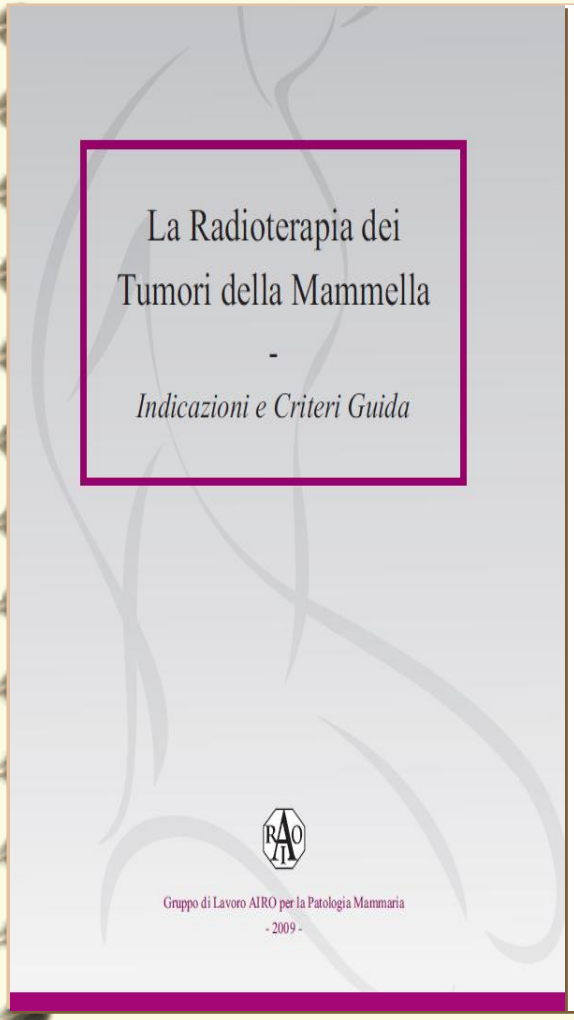



Recentemente è stato pubblicato un Consensus Statement dell'ASTRO (American Society for Radiation Oncology) che ha stabilito i criteri di inclusione per la PBI, da seguire al di fuori dei trials clinici (7).

Sono considerate idonee alla PBI le pazienti che presentino tutte le seguenti caratteristiche:

- tipo istologico: carcinoma duttale invasivo (o altri tipi istologici favorevoli, che comprendono il mucinoso, il tubulare ed il colloide)
- qualsiasi grading
- stadio T1, pN0 (i-, i+) documentato su linfonodo sentinella o dissezione linfonodale ascellare
- stato recettoriale: ER +
- unicentrico e clinicamente unifocale, con dimensioni complessive ≤ 2 cm (la multifocalità microscopica è consentita)
- margini di resezione negativi (≥ 2 mm)
- assenza di estesa componente in situ (≥ 25%) e di invasione linfo-vascolare
- assenza di chemioterapia neoadiuvante
- età: ≥ 60 anni
- assenza di mutazione BRCA 1-2

# PBI: criteri di inclusione (meno restrittivi)




Sono considerati criteri di inclusione meno restrittivi, da valutare in modo cautelativo al di fuori dei trials clinici, tenuto conto del numero limitato di dati riportati in letteratura, i seguenti:

- tipo istologico: carcinoma lobulare invasivo, DCIS puro (≤ 3 cm)
- stadioT0 e T2 (≤ 3 cm)
- stato recettoriale: ER –
- clinicamente unifocale, con dimensioni complessive comprese tra 2,1 e 3 cm (la multifocalità microscopica è consentita)
- margini "close" (< 2 mm)
- presenza di estesa componente in situ di dimensioni ≤ 3 cm
- invasione linfo-vascolare limitata o focale
- età: 50-59 anni

Gli Autori sottolineano che tali criteri non sono applicabili alle pazienti sottoposte a IORT, in quanto il quadro patologico definitivo non può essere stabilito prima del trattamento

# Partial breast irradiation : risultati disponibili

Studi fase II con corretta selezione pazienti : controllo locale equivalente a RT standard, buon risultato estetico

## Partial Breast Irradiation as Primary Treatment ≥ 2 Yr Median Follow-Up

| Site / Study | # Patients | Follow-up (mos.) | Local recurrence rate |
|---|---|---|---|
| William Beaumont | 199 | 65 | 1.2% |
| Ochsner Clinic | 163 | 65 | 2.0% |
| Virginia Commonwealth | 44 | 42 | 0.0% |
| NIO– (Hungary: Phase I/II) | 45 | 60 | 4.4% |
| NIO – (Hungary: Phase III) | 181 | 30 | 1.1% |
| Tuft's/New England Medical Ctr. | 32 | 33 | 4.0% |
| Keisch et al. (multi-institution) | 43 | 30 | 0.0% |
| RTOG 95 - 17 | 99 | 44 | 3.0% |
| University of Kansas | 24 | 37 | 0.0% |
| Cionini (Florence, Italy) | 90 | 27 | 4.4% |
| **Total** | **920** | | |

# FIVE-YEAR ANALYSIS OF TREATMENT EFFICACY AND COSMESIS BY THE AMERICAN SOCIETY OF BREAST SURGEONS MAMMOSITE BREAST BRACHYTHERAPY REGISTRY TRIAL IN PATIENTS TREATED WITH ACCELERATED PARTIAL BREAST IRRADIATION

FRANK VICINI, M.D.,* PETER BEITSCH, M.D.,† CORAL QUIET, M.D.,‡ MARK GITTLEMAN, M. D.,§ VIC ZANNIS, M.D.,‖ RICKY FINE, M.D.,¶ PAT WHITWORTH, M.D.,# HENRY KUERER, M.D.,** BRUCE HAFFTY, M.D.,†† MARTIN KEISCH, M.D.,‡‡ AND MAUREEN LYDEN, M.S.§§

*Department of Radiation Oncology, William Beaumont Hospital, Royal Oak, MI; †Department of Surgery, Dallas Breast Center, Dallas, TX; ‡Arizona Breast Cancer Specialists, Scottsdale, AZ; §Department of Surgery, Sacred Heart Hospital, Allentown, PA; ‖Department of Surgery, Breast Care Center of the Southwest, Phoenix, AZ; ¶The Breast Center, Marietta, GA; #Nashville Breast Center, Nashville, TN; **Department of Surgery, M.D. Anderson Cancer Center, Houston, TX; ††Robert Wood Johnson University Hospital/ Cancer Institute of New Jersey, New Brunswick, NJ; ‡‡Cancer HealthCare Associates, University of Miami Hospital, Miami, FL; and §§BioStat International, Tampa, FL

**Purpose:** To present 5-year data on treatment efficacy, cosmetic results, and toxicities for patients enrolled on the American Society of Breast Surgeons MammoSite breast brachytherapy registry trial.

**Methods and Materials:** A total of 1440 patients (1449 cases) with early-stage breast cancer receiving breast-conserving therapy were treated with the MammoSite device to deliver accelerated partial-breast irradiation (APBI) (34 Gy in 3.4-Gy fractions). Of 1449 cases, 1255 (87%) had invasive breast cancer (IBC) (median size, 10 mm) and 194 (13%) had ductal carcinoma *in situ* (DCIS) (median size, 8 mm). Median follow-up was 54 months.

**Results:** Thirty-seven cases (2.6%) developed an ipsilateral breast tumor recurrence (IBTR), for a 5-year actuarial rate of 3.80% (3.86% for IBC and 3.39% for DCIS). Negative estrogen receptor status ($p = 0.0011$) was the only clinical, pathologic, or treatment-related variable associated with IBTR for patients with IBC and young age (<50 years; $p = 0.0096$) and positive margin status ($p = 0.0126$) in those with DCIS. The percentage of breasts with good/excellent cosmetic results at 60 months ($n = 371$) was 90.6%. Symptomatic breast seromas were reported in 13.0% of cases, and 2.3% developed fat necrosis. A subset analysis of the first 400 consecutive cases enrolled was performed (352 with IBC, 48 DCIS). With a median follow-up of 60.5 months, the 5-year actuarial rate of IBTR was 3.04%.

**Conclusion:** Treatment efficacy, cosmesis, and toxicity 5 years after treatment with APBI using the MammoSite device are good and similar to those reported with other forms of APBI with similar follow-up. 

Breast-conserving therapy, Brachytherapy, Radiation, Partial-breast irradiation, MammoSite, Breast cancer.

Table 8. Contemporary Phase III trials of accelerated partial-breast irradiation

| Phase III Trial | *N* | Control arm | Investigational arm |
|---|---|---|---|
| NSABP B39/RTOG 0413 (US) | 4300 | 50–50.4 Gy WB ± 10–16 Gy boost | (*1*) Interstitial brachytherapy, or<br>(*2*) MammoSite, or<br>(*3*) 3D conformal EBRT |
| Medical Research Council (UK), IMPORT LOW | 1935 | WB 2.67 Gy × 15 | (*1*) WB 2.4 Gy × 15; PB 2.67 Gy × 15<br>(*2*) PB only 2.67 Gy × 15 |
| European Institute of Oncology (Milan), ELIOT | 1200* | 50 Gy WB + 10 Gy boost | Intraoperative<br>Single fraction EBRT<br>21 Gy × 1 |
| University College of London (UK), TARGIT | 1600 | WB radiotherapy (per center) + boost | Intraoperative<br>Single fraction EBRT<br>5 Gy × 1 |
| Canadian Trial, RAPID | 2128 | WB 42.5 Gy in 16 fractions or<br>50 Gy in 25 fractions ± 10 Gy boost | 3D-CRT only<br>38.5 Gy in 10 fractions |
| National Institute of Oncology (Budapest) | 258* | 50 Gy WB | (*1*) Interstitial brachytherapy<br>(5.2 Gy × 7) or<br>(*2*) Electrons (50 Gy) |
| European Brachytherapy Breast Cancer GEC-ESTRO Working Group | 1170* | 50–50.4 Gy WB + 10 Gy Boost | Brachytherapy only<br>32.0 Gy 8 fractions HDR<br>30.3 Gy 7 fractions HDR<br>50 Gy PDR |

*Abbreviations:* NSABP = National Surgical Adjuvant Breast and Bowel Project; RTOG = Radiation Therapy Oncology Group; US = United States; WB = whole breast; 3D = three-dimensional; EBRT = external-beam radiptherapy; UK = United Kingdom; IMPORT LOW = intensity-modulated and partial organ radiotherapy, low risk; PB = partial breast; ELIOT = intraoperative radiotherapy with electrons; TARGIT = targeted intraoperative radiotherapy; RAPID = randomized trial of accelerated partial breast irradiation; 3D-CRT = 3D conformal radiotherapy; GEC-ESTRO = Groupe Europeen de Curietherapie European Society for Therapeutic Radiology and Oncology; HDR = high dose rate; PDR = pulsed dose rate.

* Closed to accrual

| PBI : TRIAL in corso | TARGIT | ELIOT | IMPORT | RAPID | NSABP /RTOG | GEC/ ESTRO | IRMA |
|---|---|---|---|---|---|---|---|
| N pz | 2232 | 2000 | 2100 | 2128 | 3000 | 1170 | 3302 |
| Età | >40 | >48 | >50 | >40 | >18 | >40 | >49 |
| T Ø | <30 | < 25 | <20 | <30 | < 30 | < 30 | < 30 |
| N | N- | N- | N- | N- | N- N+(3) | N- $N_{MIC}$ | N-N+ (3) |
| Margini | Neg. | >10 | >2 | Neg | Neg | Neg | >2 |
| Tecnica | Peri X 50Kv | Peri $e^-$ | IMRT /3DRT | 3DRT | 3DRT / BT (I/M) | BT HDR e PDR | 3DRT |
| Dose/fr | 20 Gy/1 | 21Gy/1 | - | 38.5 Gy/10 | RT 38.5 Gy/10 BT 34 Gy/10 | HDR 34/10 PDR 50 Gy | 38.5 Gy/10 |

# Hungarian Trial
# Polgar C, et al IJROBP 69;694, 2007

INTERNATIONAL JOURNAL OF Radiation Oncology BIOLOGY• PHYSICS
Official Journal of the American Society for Radiation Oncology ASTRO

Volume 69, Issue 3, Pages 694-702 (1 November 2007)

previ

## Breast-Conserving Treatment With Partial or Whole Breast Irradiation for Low-Risk Invasive Breast Carcinoma—5-Year Results of a Randomized Trial

Csaba Polgár, M.D., Ph.D.*, János Fodor, M.D., Ph.D., D.Sc.*, Tibor Major, M.Sc., Ph.D.*, György Németh, M.D., Ph.D., D.Sc.*, Katalin Lövey, M.D.*, Zsolt Orosz, M.D., Ph.D.†, Zoltán Sulyok, M.D.‡, Zoltán Takácsi-Nagy, M.D., Ph.D.*, Miklós Kásler, M.D., Ph.D.*

Received 30 November 2006; received in revised form 9 April 2007; accepted 10 April 2007. published online 24 May 2007.

**Purpose**

To report the 5-year results of a randomized study comparing the survival and cosmetic results of breast-conserving treatment with partial breast irradiation (PBI) or conventional whole breast irradiation (WBI).

**Methods and Materials**

Between 1998 and 2004, 258 selected patients with T1 N0–1mi, Grade 1–2, nonlobular breast cancer without presence of extensive intraductal component and resected with negative margins were randomized after breast-conserving surgery to receive 50 Gy/25 fractions WBI ($n$ = 130) or PBI ($n$ = 128). The latter consisted of either 7 × 5.2 Gy high-dose-rate (HDR) multicatheter brachytherapy (BT; $n$ = 88) or 50 Gy/25 fractions electron beam (EB) irradiation ($n$ = 40).

INTERNATIONAL JOURNAL OF
Radiation Oncology
BIOLOGY·PHYSICS
Official Journal of the American Society for Radiation Oncology
ASTRO

*Hungarian Trial*
*Polgar C, et al IJROBP 69;694, 2007*

**Results**

At a median follow-up of 66 months, the 5-year actuarial rate of local recurrence was 4.7% and 3.4% in the PBI and WBI arms, respectively ($p = 0.50$). There was no significant difference in the 5-year probability of overall survival (94.6% vs. 91.8%), cancer-specific survival (98.3% vs. 96.0%), and disease-free survival (88.3% vs. 90.3%). The rate of excellent to good cosmetic result was 77.6% in the PBI group (81.2% after HDR BT; 70.0% after EB) and 62.9% in the control group (52.2% after telecobalt; 65.6% after 6–9-MV photons; $p_{WBI/PBI} = 0.009$).

**Conclusions**

Partial breast irradiation using interstitial HDR implants or EB to deliver radiation to the tumor bed alone for a selected group of early-stage breast cancer patients produces 5-year results similar to those achieved with conventional WBI. Significantly better cosmetic outcome can be achieved with carefully designed HDR multicatheter implants compared with the outcome after WBI.

Il trattamento deve essere considerato ancora sperimentale e condotto nell'ambito di studi clinici, approvati da Comitati Etici, dopo aver ottenuto il consenso informato della Paziente

# APBI – Accelerated Partial breast irradiation

## modalità tecniche

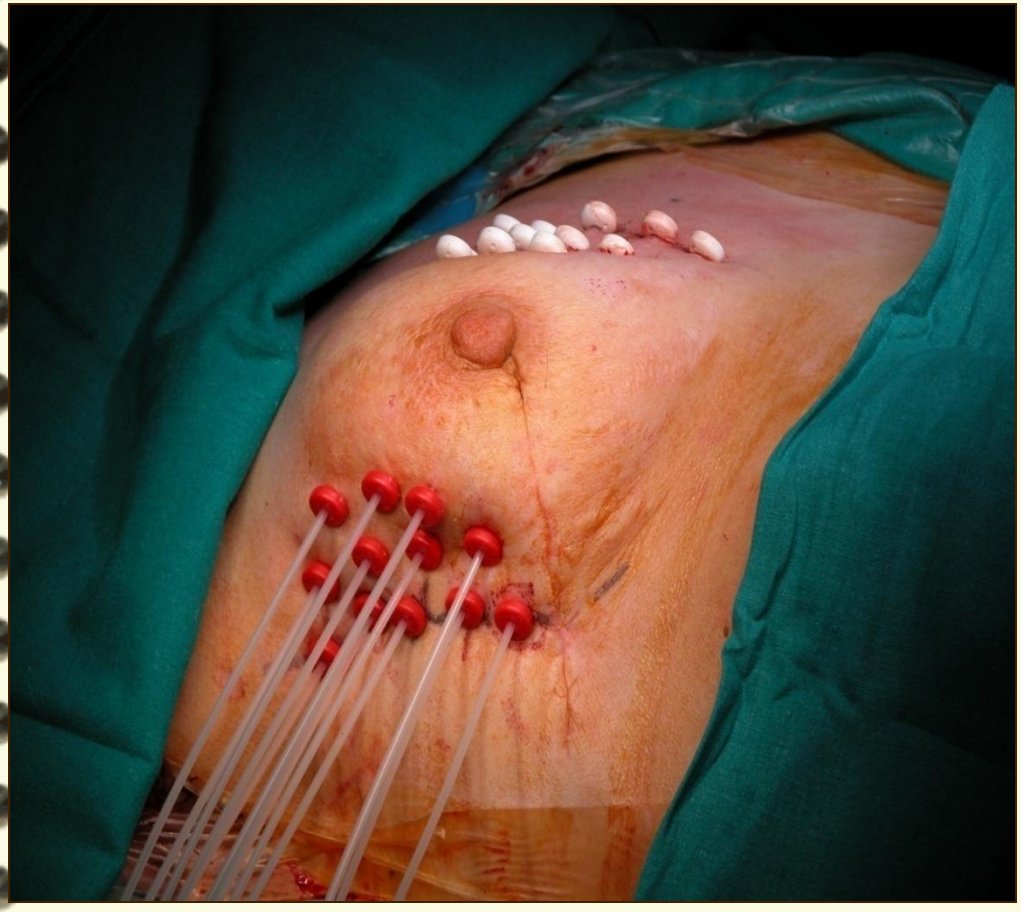
- BCT
  - interstiziale (vario dose rate , imp. permanenti,
  - Mammosite
- Fasci esterni
  - tecnica 3DCRT o IMRT
  - Protoni
- IORT
  - con elettroni (Acc. Lin., macchina dedicata)
  - con fotoni RX bassa energia (PSR)

**Considerevole diversità:**

- della quantità di tessuto mammario irradiato
- della distribuzione di dose

# Partial breast irradiation

# Brachiterapia interstiziale



Inserzione cateteri intraop. o postop. entro 8-12 settimane dalla Chirurgia

Caricamento dopo esame an. patol. del pezzo operatorio

Copertura del quadrante a tutto spessore

Calcolo della dose alla periferia dell'impianto

# SISTEMI DI IMPIANTO DELLE SORGENTI BRACHITERAPICHE

Obbiettivi principali dei piani di trattamento:

a.ottenere una distribuzione di dose ottimale attraverso adeguati posizionamenti e tipi di sorgenti

b.fornire una distribuzione di dose completa nel volume irradiato

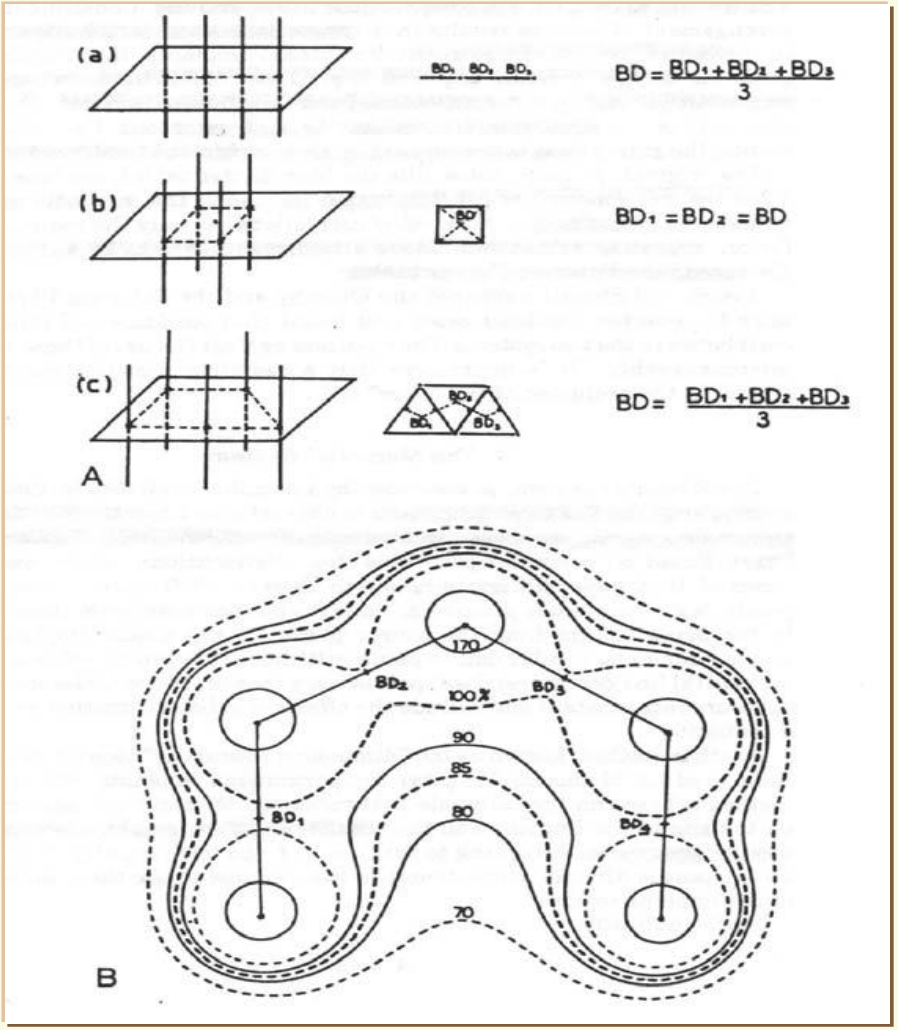
Sistemi di trattamento più usati:

1.SISTEMA DI MANCHESTER

2. SISTEMA DI QUIMBY

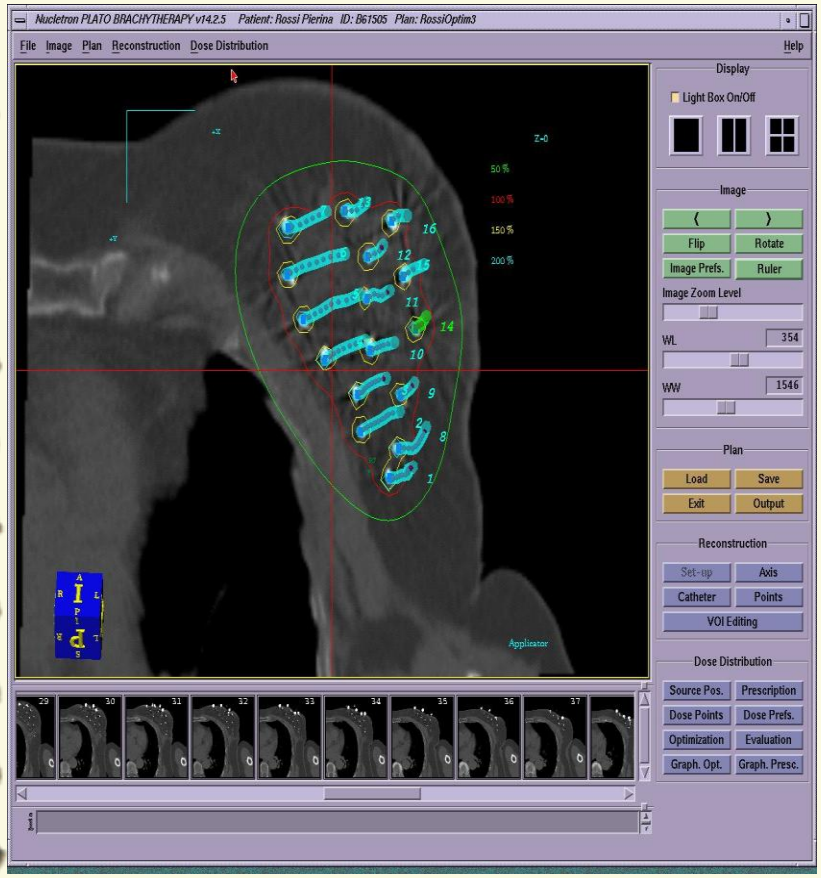
3. SISTEMA DI PARIGI

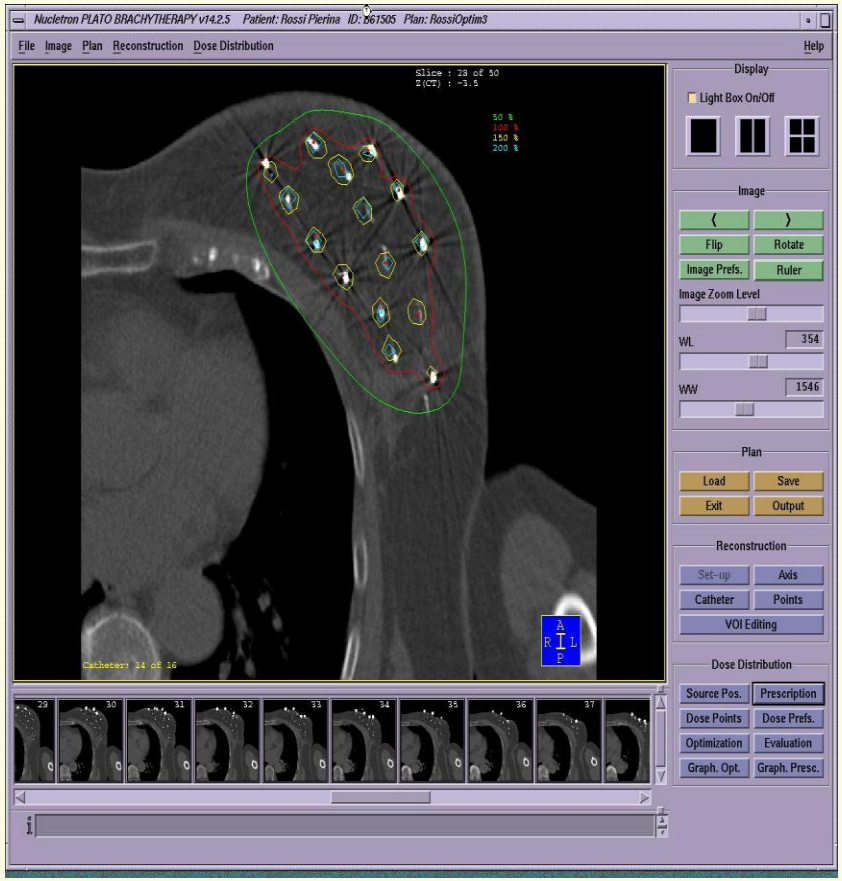
# SISTEMA DI PARIGI



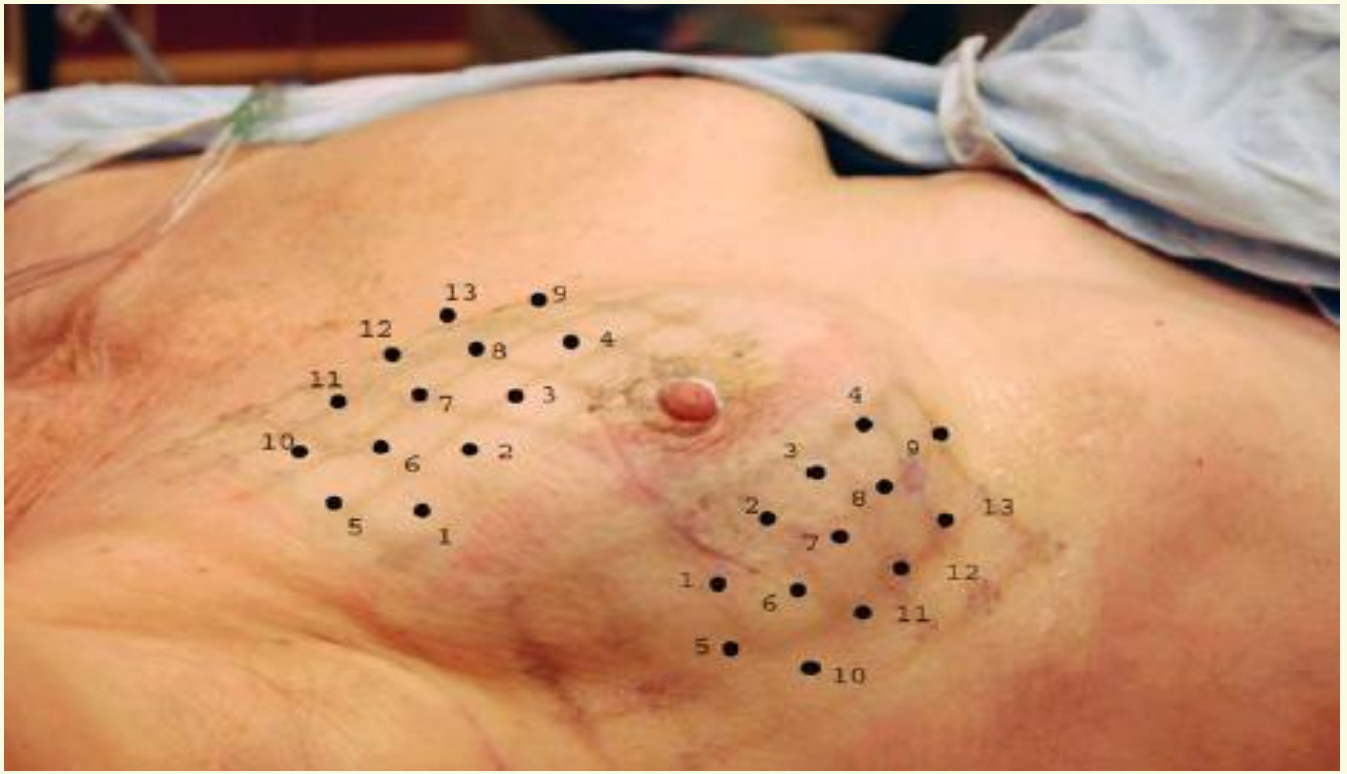
# Interstizial BT HDR

## Dose distribution



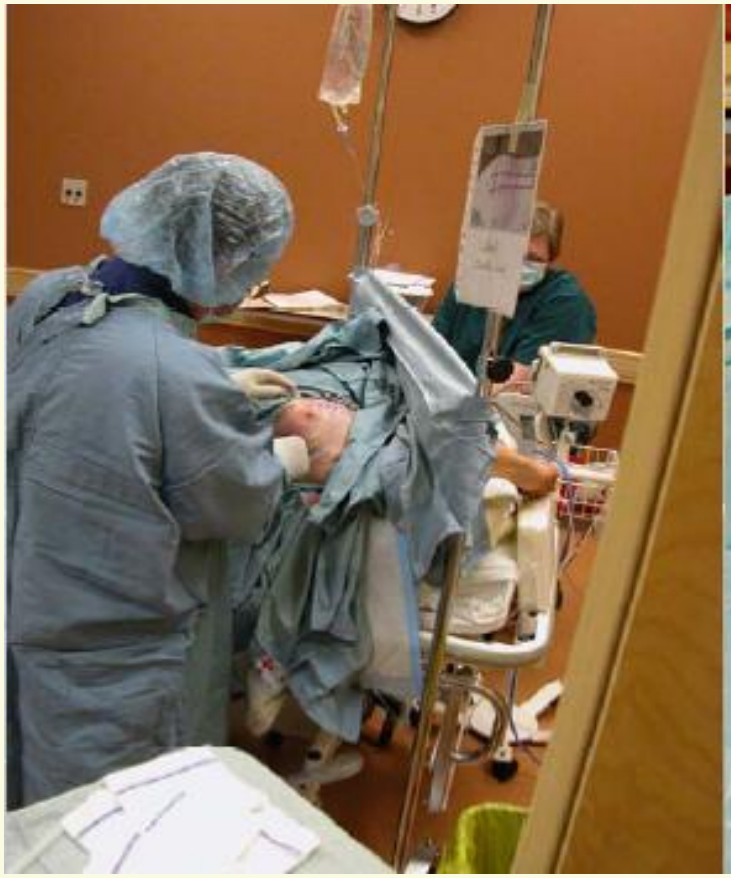



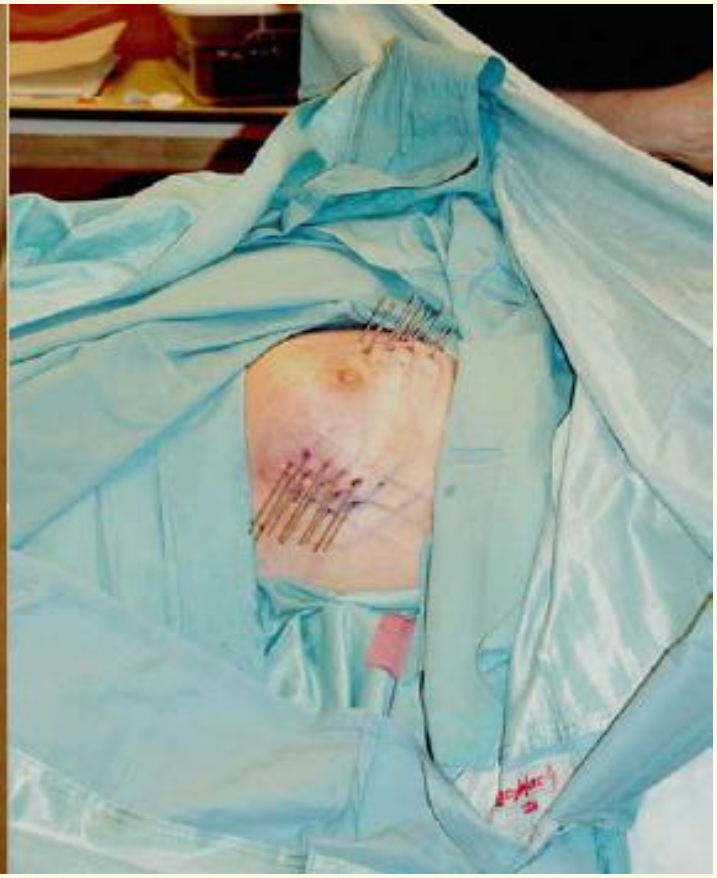
# Insertion Procedure



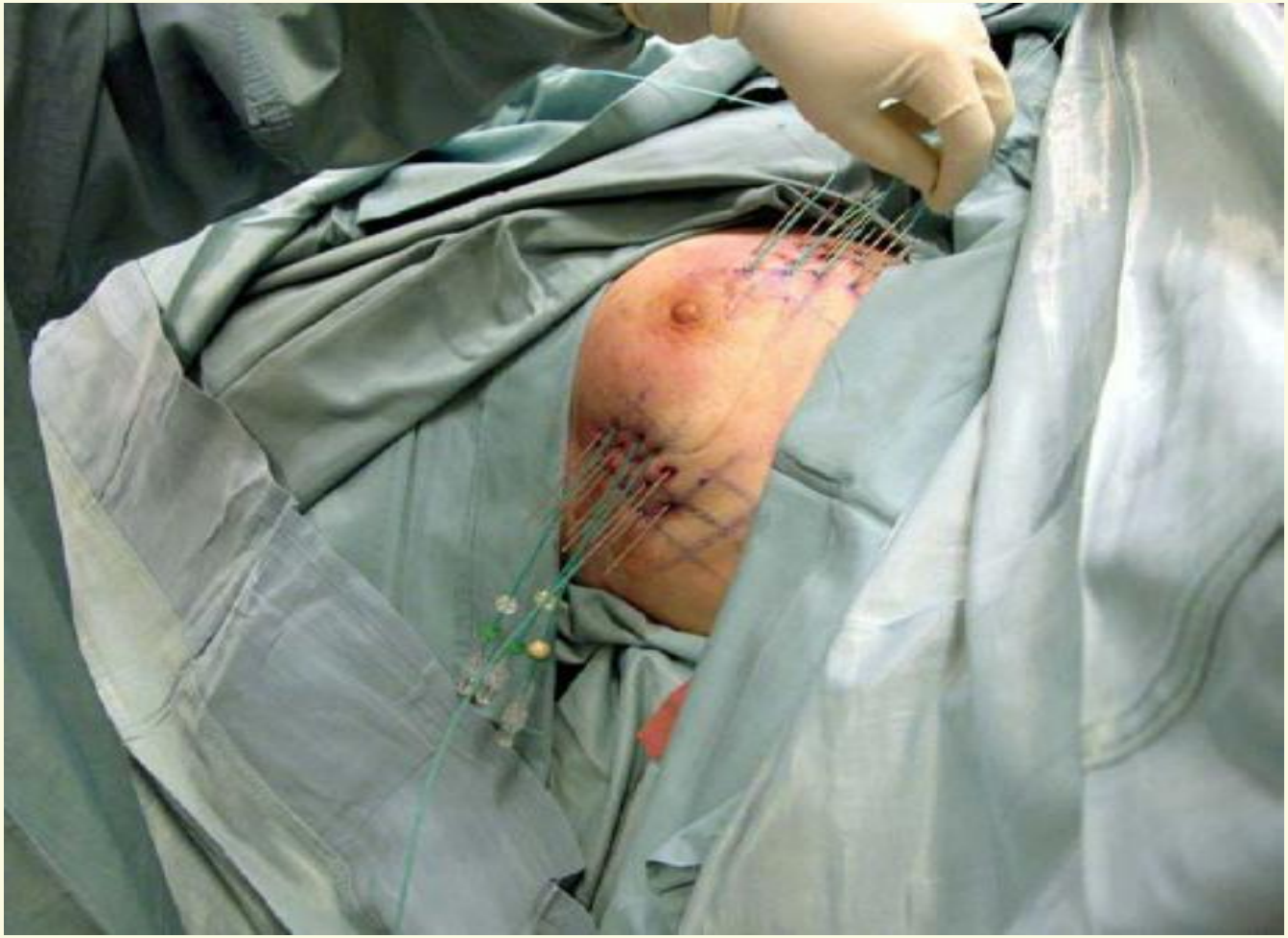

Entrance and exit points are drawn on skin relative to the grid

# Insertion of needles

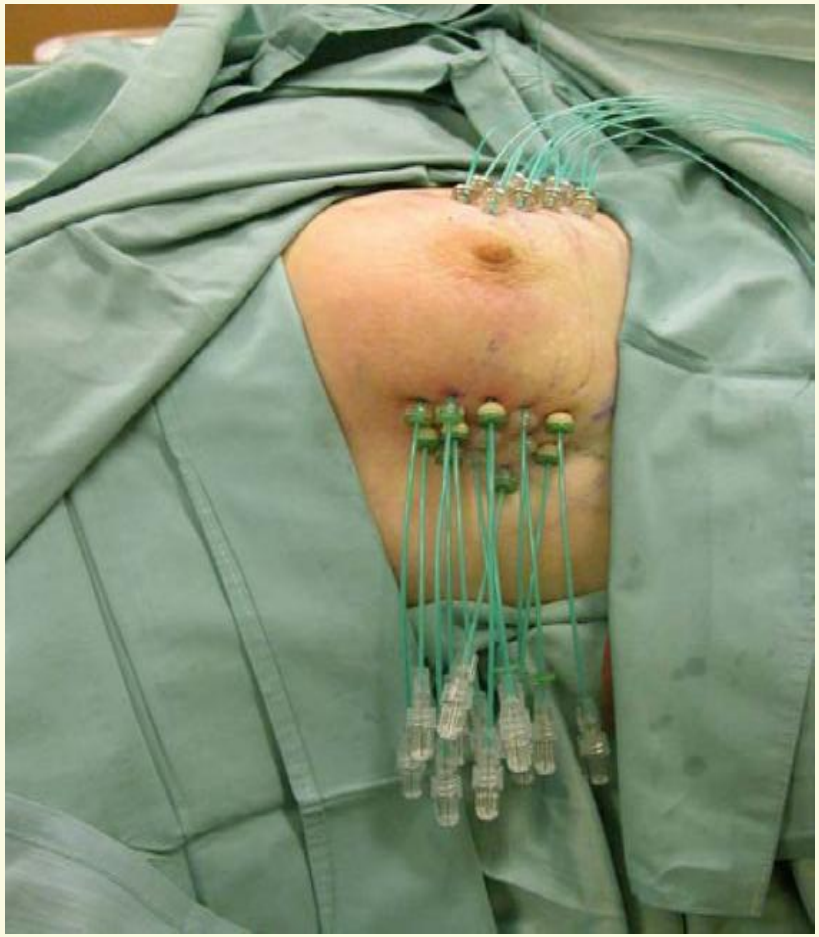


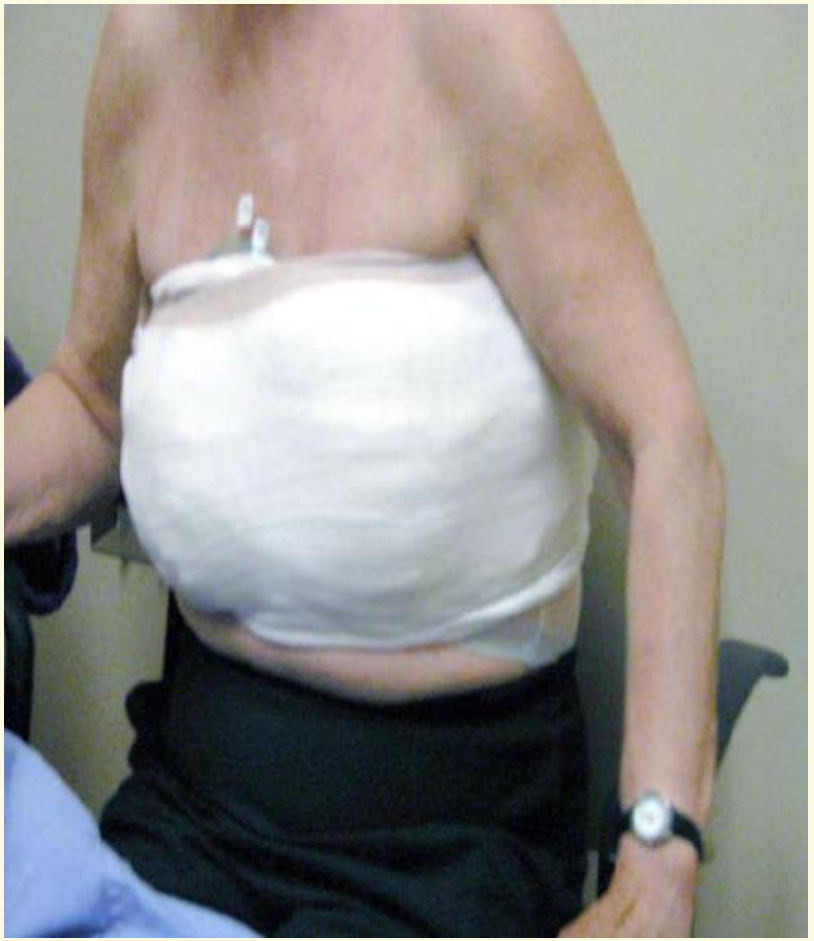


# Catheters Replacing Needles

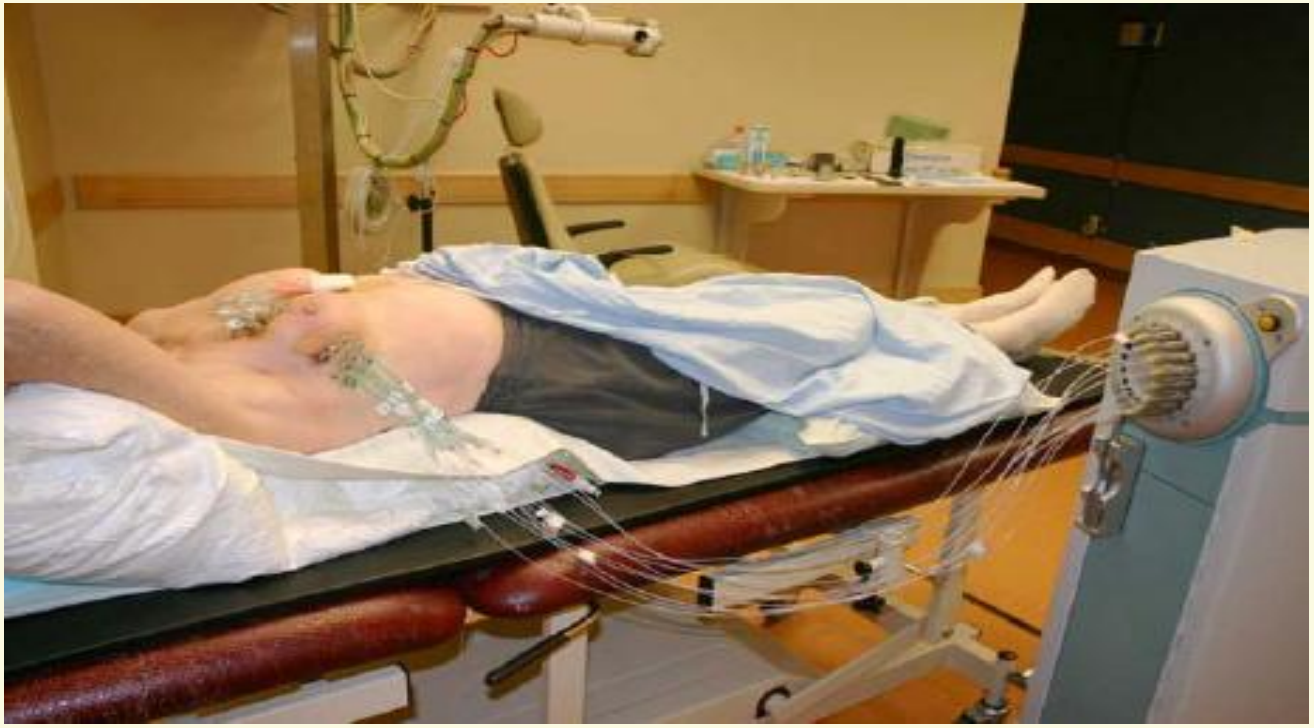


# Catheters Inserted





# Treatment



Prescribed Dose: 3.6Gy x 9 fractions 2 X daily
Catheters inserted on Monday morning
1 fraction given in the afternoon, there after 2 x daily

# Risultati BT interstiziale

| Auteurs, références | Nombre | Suivi (mois) | Type de RT | Nombre de fractions et débit (cGy/h) | Dose totale (Gy) | Pourcentage de rechute locale | Résultats esthétiques bon–excellents |
|---|---|---|---|---|---|---|---|
| Curiethérapie interstitielle | | | | | | | |
| Fentinman et al. [19] | 27 | 72 | BDD | 40 | 55 | 37 | 83 |
| Cionini et. [11] | 90 | 27 | BDD | – | 50–60 | 4,4 | – |
| King et al. [31] | 26 | 75 | BDD | > 40 | 45 | 2[a] | 75[b] |
| Vicini et al. [58] | 120 | 82 | BDD | 52 | 50 | 1 | 91 |
| Krishnan et al. [32] | 25 | 47 | BDD | – | 20–25 | 0 | 100 |
| Clarke et al. [12] | 45 | 18 | HDD | Hétérogène[c] | 20–36 | 8,8 | 95 |
| Perera et al. [40] | 39 | 20 | HDD | 3,72 Gy × 10 | 37,2 | 2,6[a] | – |
| Vicini et al. [58] | 79 | 52 | HDD | 4 Gy × 8 | 32 | 1 | 100 |
| Polgar et al. [42] | 45 | 81 | HDD | 5,2 Gy × 7 | 36,4 | 6,7 | 84 |
| | | | | 4,33 Gy × 7 | 30,3 | | |
| Ott et al. [39] | 69[e] | 24 | HDD | 4 Gy × 8 | 32 | 0 | 92 |
| | | | ou BDP | 60 | 49,8 | | |
| Wazer et al. [59] | 75 | 73 | HDD | 3,4 Gy × 10 | 34 | 3 | 91 |
| Kuske et al. [33] | 99 | 36[d] | HDD | 3,4 Gy × 10 | 34 | | – |
| | | | ou BDD | > 40 | 45 | 0 | |
| Chen et al. [10] | 199 | 77 | HDD | 4 × 8 or 3,4 × 10 | 32–34 | | 95–97 |
| | | | ou BDD | 52 | 50 | – | |

HDD : haut débit de dose; BDD : bas débit de dose ; BDP : bas débit pulsé.

[a] BDD/HDD série combinée.

[b] Irradiation large associée.

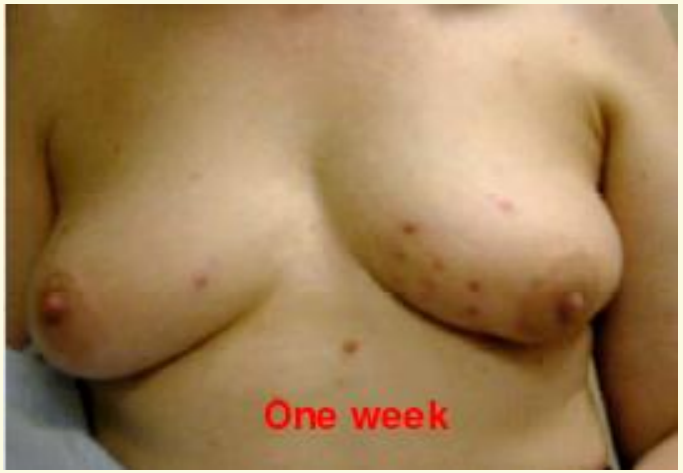
[c] Fractionnement utilisé : 10 Gy × 2, 7 Gy × 4, 6 Gy × 6 fractions ; Patientes traitées avec un HDD ou un BDP.

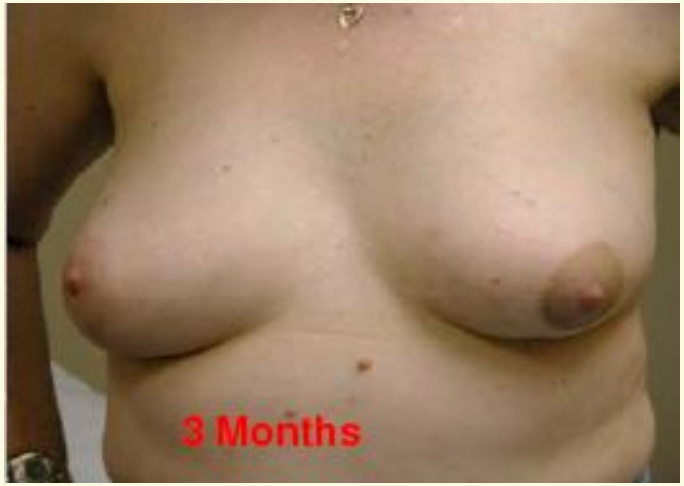
[d] Suivis pour le BDD ($n = 33$) et le HDD ($n = 66$) patients.

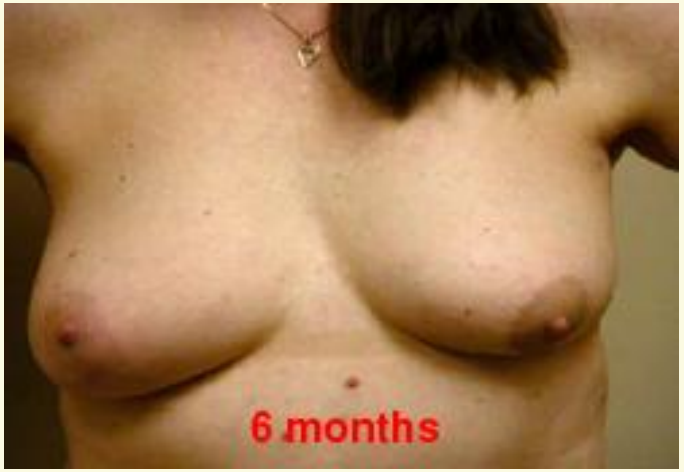
[e] Deux patientes ont développé des métastases cérébrales.

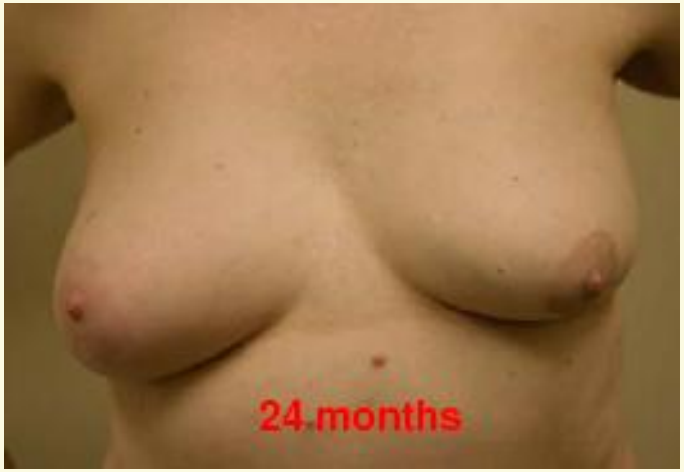
BelKacémi Y, Cancer Radiothérapie, 11: 287-295, 2007

# Results



# Brachiterapia Interstiziale

## VANTAGGI

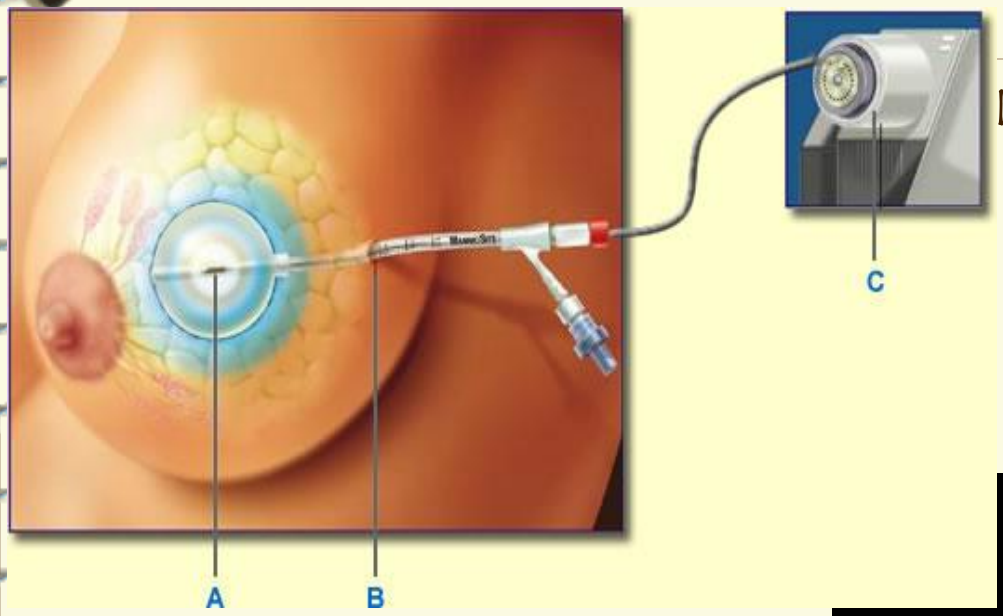
- Ottima conformazione della distribuzione di dose (anche per volumi bersaglio irregolari)
- Procedura riproducibile

## SVANTAGGI

- Procedura abbastanza invasiva (può richiedere anestesia totale)
- Procedura operatore – dipendente (necessità di formazione del personale), time-consuming, complessa

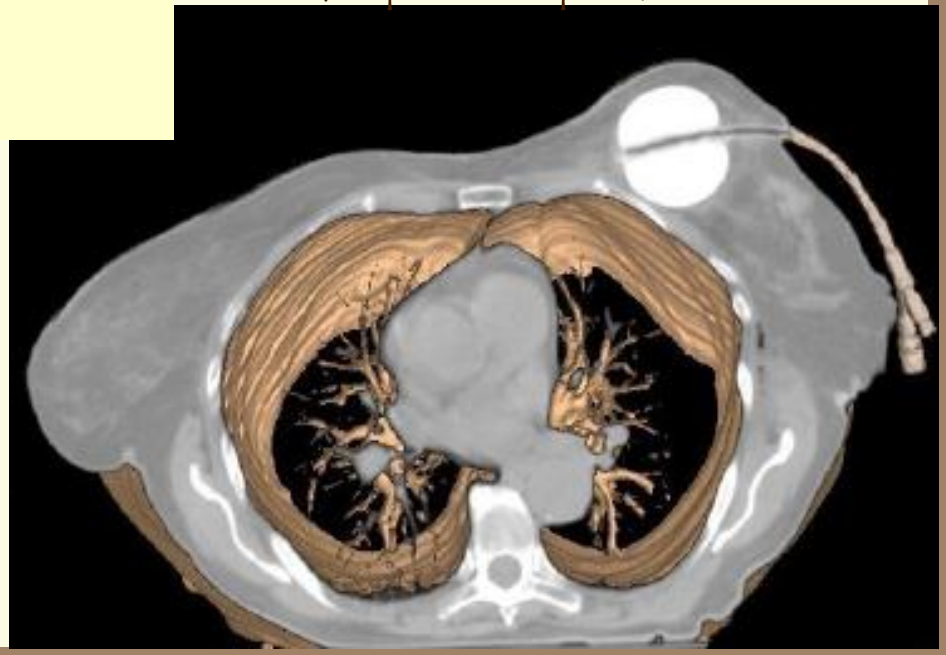
# Partial breast irradiation

# mammosite




Inserzione intra/postoperatoria del palloncino nella cavità escissionale

Distensione e caricamento differiti dopo esame An. Patol. del pezzo operatorio

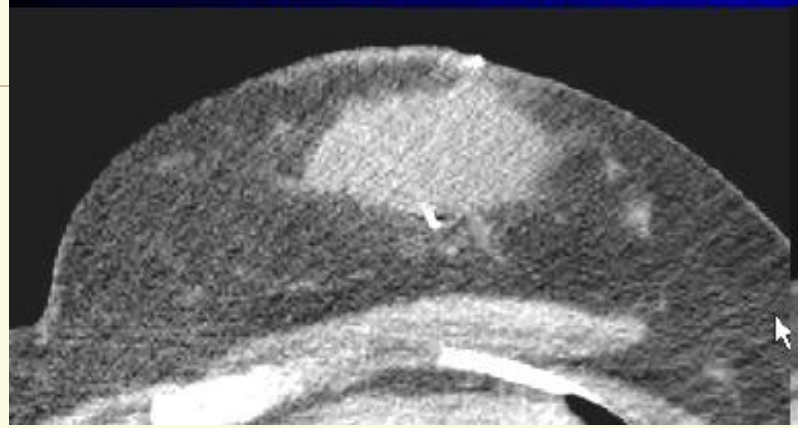


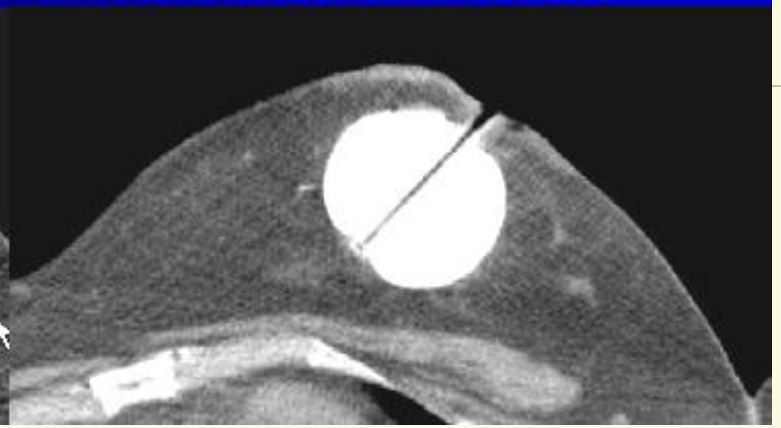
Irradiazione di tutta la cavità chirurgica a 360°

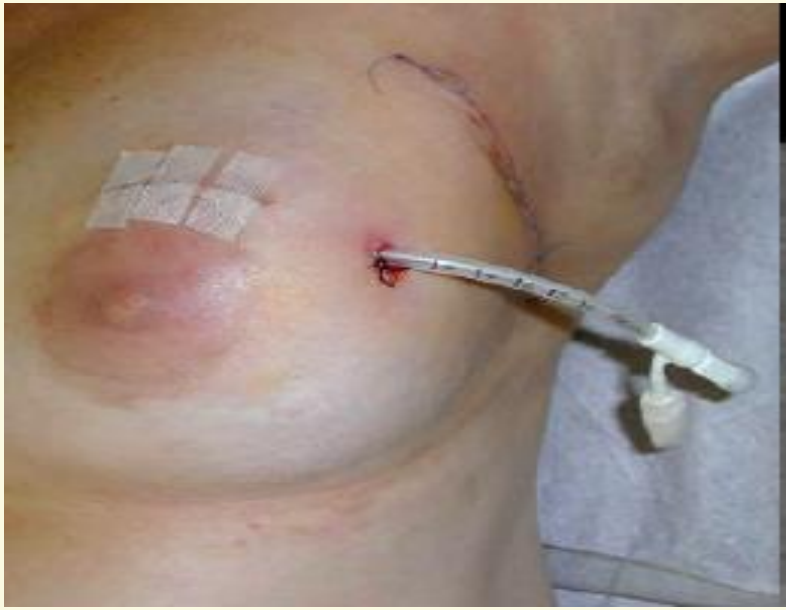
Calcolo della dose a 0.5 cm dalla superficie del palloncino

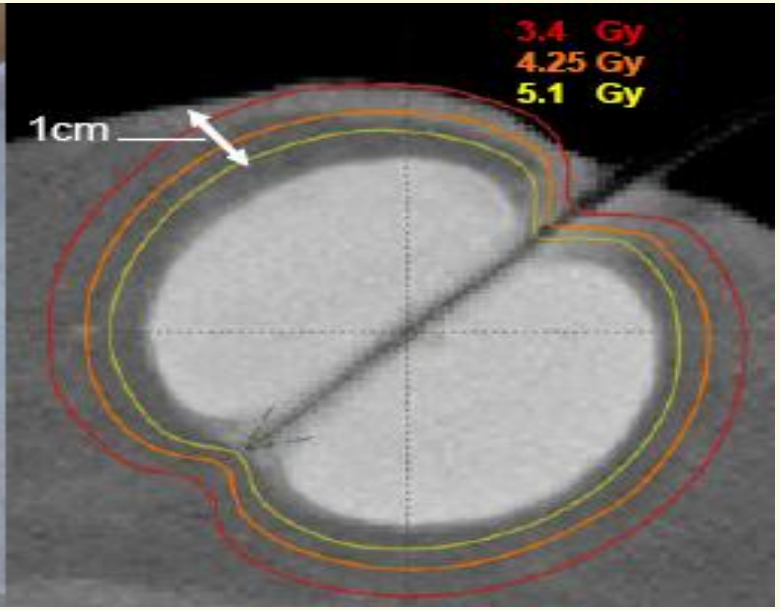
Caduta di dose progressiva nella zona circostante

# Ideal Case for MammoSite





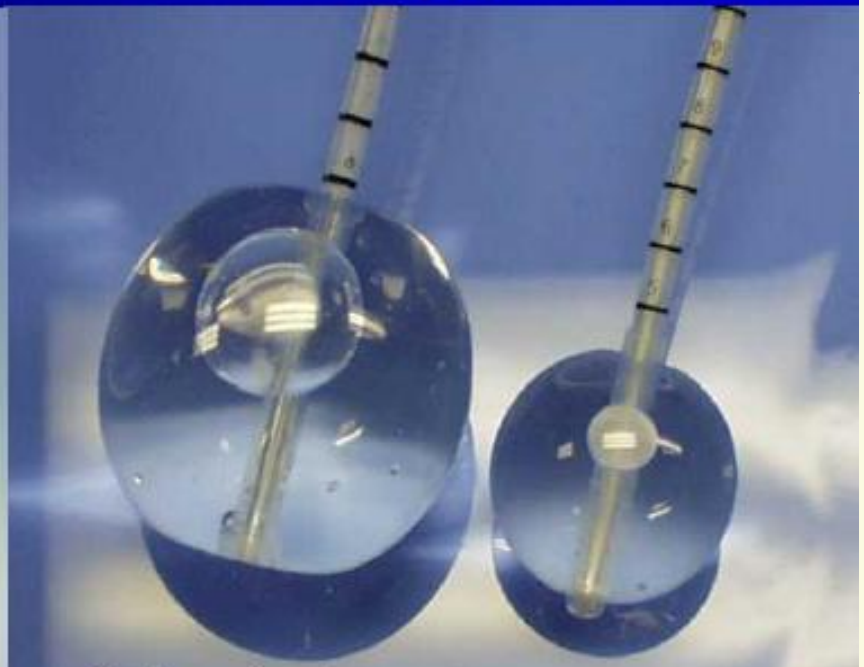




# MammoSite Radiation Therapy System

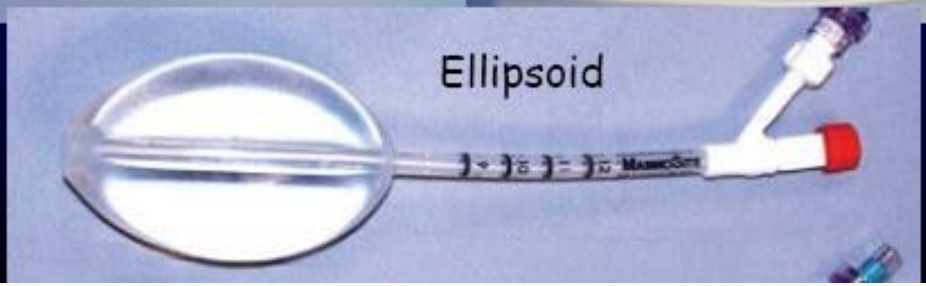
15cm length

6mm diameter



Spherical

4 to 5 cm (35 - 70 cc)



Ellipsoid

# Prescribed dose:

- Standard:8 Fx of 4Gy (32Gy)
- Younger patients or less robust:10fx of 3.4Gy (34 Gy)

# Mammosite ® Rts

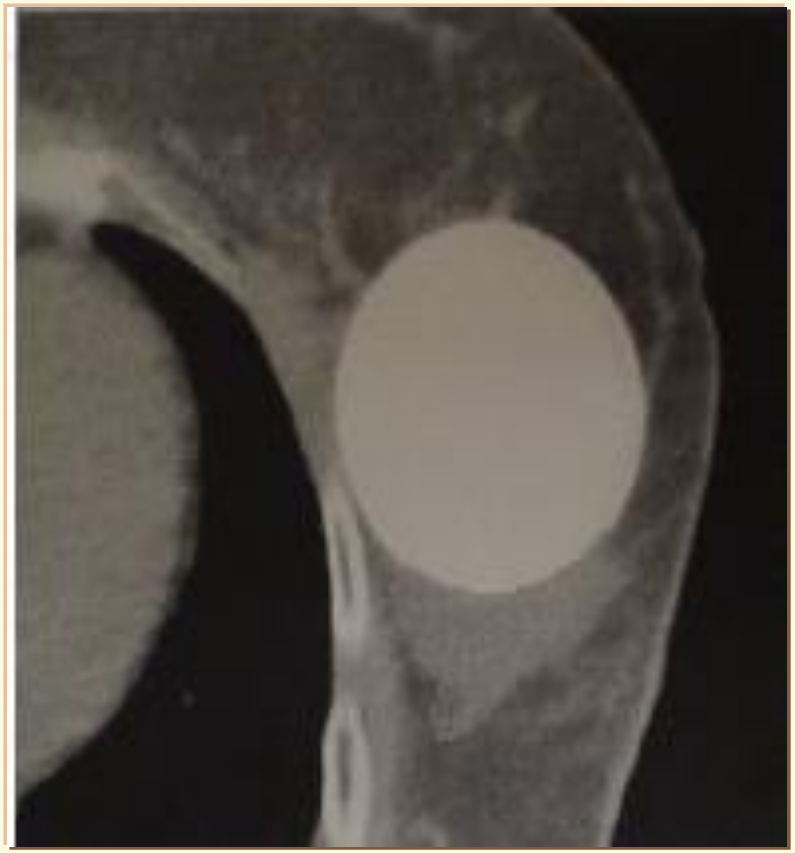
## VANTAGGI

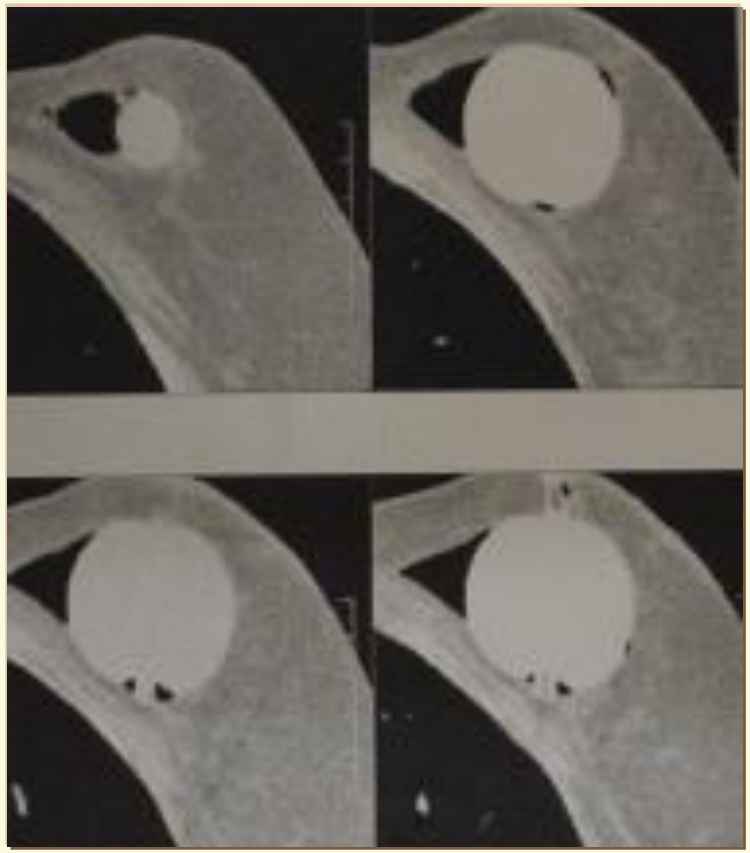
- Tecnica semplice, riproducibile e poco invasiva
- Piano di trattamento semplice

## SVANTAGGI

- Difficile una buona conformazione della dose per volumi bersaglio non sferici (cavità chirurgiche irregolari)
- Rottura da contatto con clips
- Volume di irradiazione limitato (1 cm)
- Infezioni (16%)

# NON- CONFORMANCE
## Seroma – Air

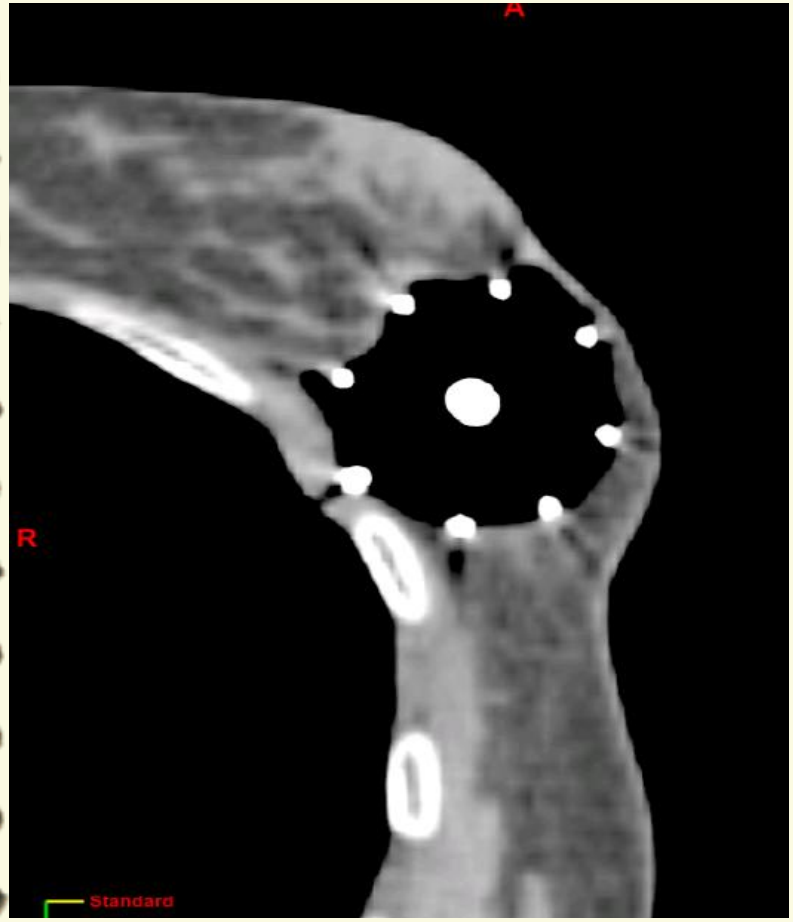


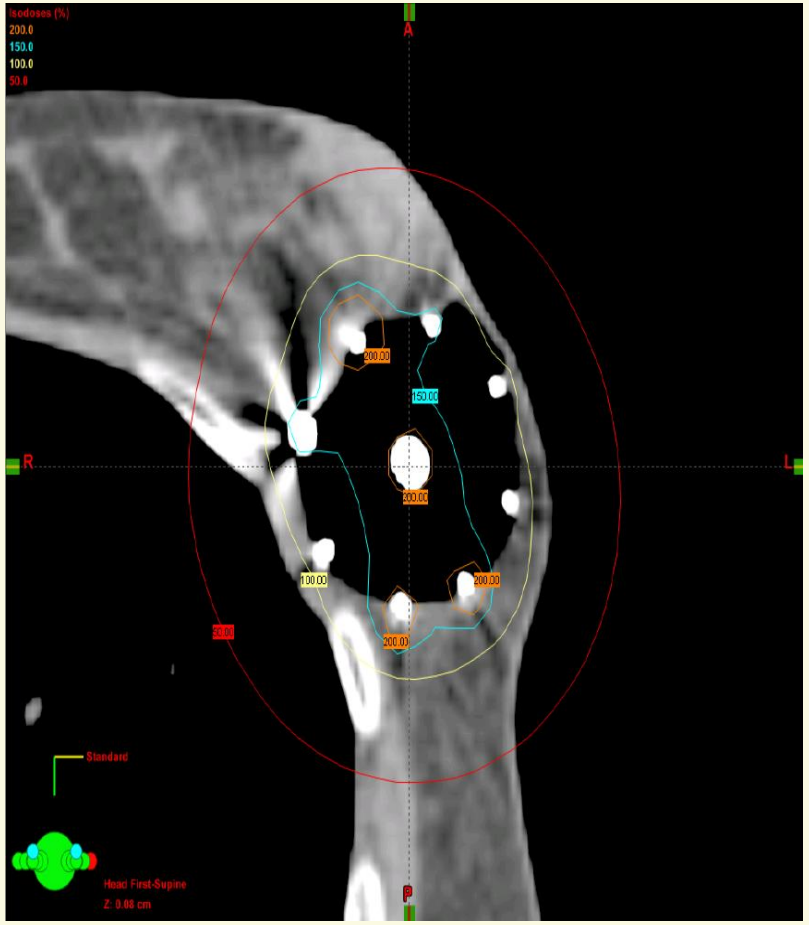


# SAVI
## *(Strut Adjusted Volume Implant)*

Collapsed for insertion

# SAVI

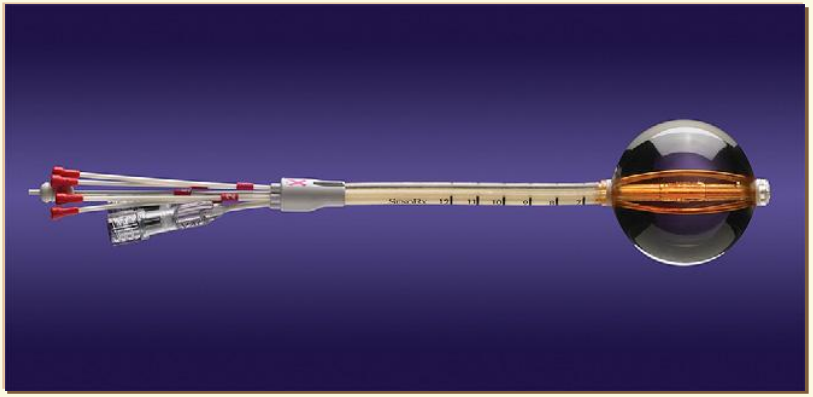

A
R
Standard


Isodoses (%)
200.0
150.0
100.0
50.0
A
R
L
P
Standard
Head First-Supine

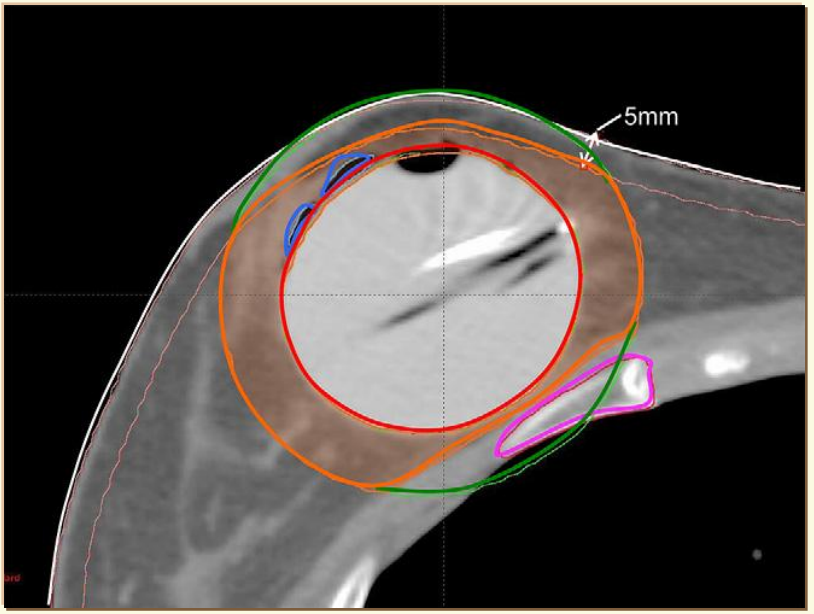
# IMPROVEMENTS IN CRITICAL DOSIMETRIC ENDPOINTS USING THE CONTURA MULTILUMEN BALLOON BREAST BRACHYTHERAPY CATHETER TO DELIVER ACCELERATED PARTIAL BREAST IRRADIATION: PRELIMINARY DOSIMETRIC FINDINGS OF A PHASE IV TRIAL

DOUGLAS W. ARTHUR, M.D.,* FRANK A. VICINI, M.D.,† DORIN A. TODOR, PH.D.,*
THOMAS B. JULIAN, M.D.,‡ AND MAUREEN R. LYDEN, M.S.§

*Department of Radiation Oncology, Virginia Commonwealth University, Richmond, VA, †Department of Radiation Oncology, William Beaumont Hospital, Royal Oak, MI, ‡Department of Human Oncology, Allegheny General Hospital, Pittsburgh, PA, and §BioStat International, Inc., Tampa, FL

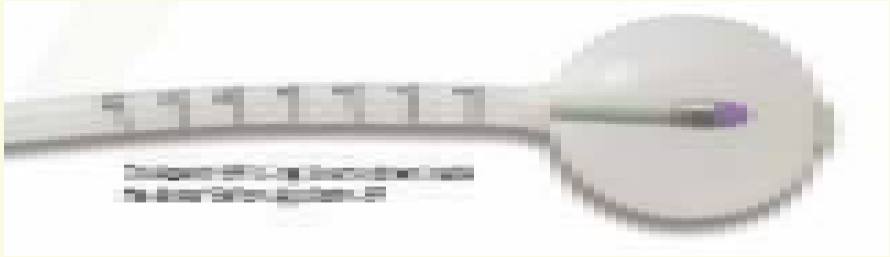


**Contura Multi-Lumen Balloon (MLB) Catheter.**




**Contouring for Dosimetric Planning. Contura balloon surface – red contour, 1 cm expansion – green line, planning target •volume for evaluation (PTV_EVAL) – orange contour, skin surface– white contour, closest rib – pink contour, •air/fluid outside balloon– blue contour**

# Xoft



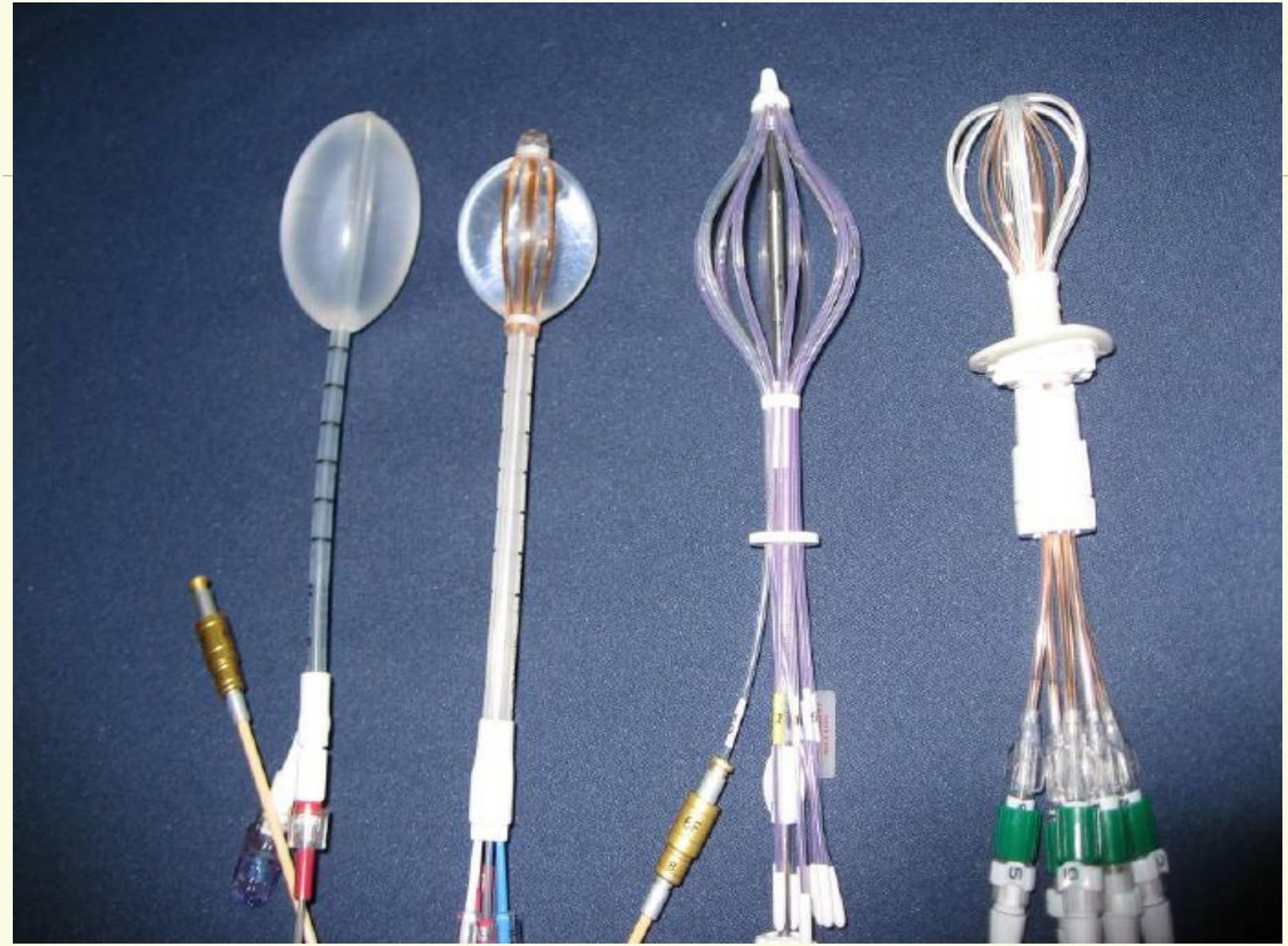
A tiny 50 kV source

Advantages:

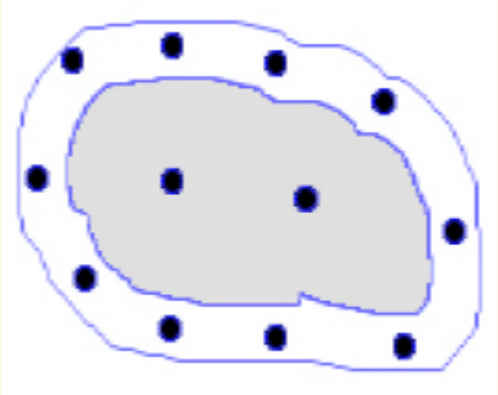
- Can be plugged into the wall
- Less shielding issues

Uses a balloon "electronic" brachytherapy

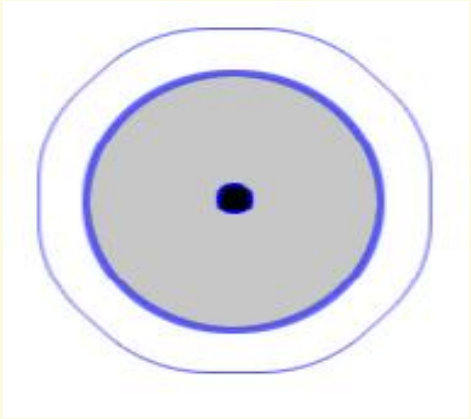
Dosimetry of source makes higher dose at balloon with more rapid falloff - ?better



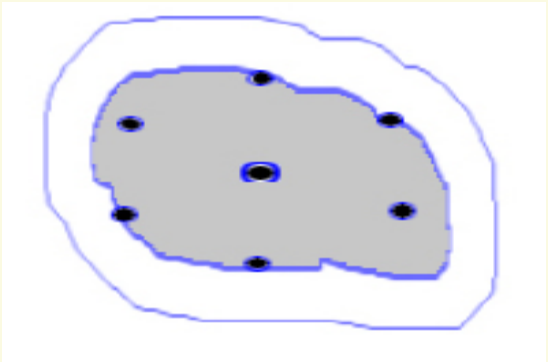
# Spectrum of Approaches



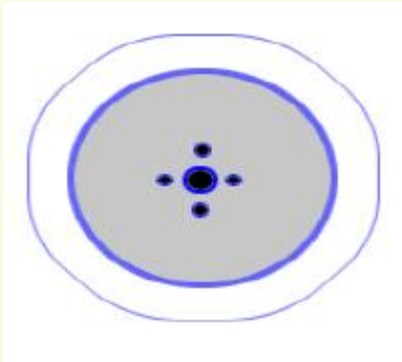
Interstitial



MammoSite



SAVI



SenoRx

Figures courtesy of Greg Edmundson

# Risultati BT Mammosite

| Auteurs, références | Nombre | Suivi (mois) | Type de RT | Nombre de fractions et débit (cGy/h) | Dose totale (Gy) | Pourcentage de rechute locale | Résultats esthétiques bon–excellents |
|---|---|---|---|---|---|---|---|
| Curiethérapie par MammoSite® | | | | | | | |
| | | | HDD | 3,4 Gy × 10 | 34 | 0 | 88/80[a] |
| Keisch et al. [29] | 43 | 30/48 | HDD | 3,4 Gy × 10 | 34 | 0 | 90 |
| Gittleman et al. [26] | 92 | 19 | HDD | 3,4 Gy × 10 | 34 | 0 | 93 |
| Shah et al. [48] | 28 | 11 | HDD | 3,4 Gy × 10 | 34 | 0 | 86 |
| Richards et al. [46] | 32 | – | HDD | 3,4 Gy × 10 | 34 | 0 | 80 |
| Dowlatshahi et al. [16] | 112 | 13 | HDD | 3,4 Gy × 10 | 34 | | 93 |
| Dickler et al. [15] | 30 | – | HDD | 3,4 Gy × 10 | 34 | 0 | 90 |
| Stolier et al. [49] | 19 | 12 | HDD | 3,4 Gy × 10 | 34 | 0 | 93 |
| Agarwal et al. [1] | 100 | 16 | HDD | 3,4 Gy × 10 | 34 | 0 | 97 |
| Tsai et al. [51] | 51 | 12 | HDD | 3,4 Gy × 10 | 34 | 0,1 | 92–96 |
| Zannis et al. [61] | 1403 | 17 | HDD | 3,4 Gy × 10 | 34 | 0 | 61–83[b] |
| Evans et al. [18] | 38 | 20 (mean) | HDD | 2,5 Gy × 3 to 5 | 7,5–15 | 0 | 67 |
| Niehoff et al. [37] | 23 | 14 | HDD | 3,4 Gy × 10 | 34 | 0.8 | 93,5 |
| Vicini et al. [56] | 1449 | 12 | HDD | 3, 4 × 10 | 30,6–34 | 0 | 94 |
| Amendola et al. [2] | 58 | | HDD | 3,75– 4 × 10 | 33,7–40 | 0 | 89 |

HDD : haut débit de dose.

[a] Résultats mis à jour à 48 mois : 80 % de scores bons à excellents.

[b] Selon la présence d'un *seroma*.

BelKacémi Y, Cancer Radiothérapie, 11: 287-295, 2007

The American Journal of Surgery (2009) 198, 83-91

The American Journal of Surgery

Clinical Surgery-American

# Four-year clinical update from the American Society of Breast Surgeons MammoSite brachytherapy trial

**Jonathan C. Nelson, M.D.[a], Peter D. Beitsch, M.D.[b], Frank A. Vicini, M.D.[c], Coral A. Quiet, M.D.[d], Delia Garcia, M.D.[e], Howard C. Snider, M.D.[f], Mark A. Gittleman, M.D.[g], Victor J. Zannis, M.D.[h], Pat W. Whitworth, M.D.[i], Richard E. Fine, M.D.[j], Angela J. Keleher, M.D.[k], Henry M. Kuerer, M.D., Ph.D.[a,*]**

*[a]Department of Surgical Oncology, The University of Texas M. D. Anderson, Cancer Center, 1515 Holcombe Blvd., Unit 444, Houston, TX 77030, USA; [b]Department of Surgery, Dallas Breast Center, Dallas, TX, USA; [c]Department of Radiation Oncology, William Beaumont Hospital, Royal Oak, MI, USA; [d]Foundation for Cancer Research and Education, Arizona Oncology Services, Scottsdale, AZ, USA; [e]Department of Radiation Oncology, St. Louis Cancer & Breast Center, St. Louis, MO, USA; [f]Department of Surgery, Alabama Breast Center, Montgomery, AL, USA; [g]Department of Surgery, Sacred Heart Hospital, Allentown, PA, USA; [h]Department of Surgery, Breast Care Center of the Southwest, Phoenix, AZ, USA; [i]Nashville Breast Center, Nashville, TN, USA; [j]Advanced Breast Care, Marietta, GA, USA; [k]Department of Surgery, Vassar Brothers Medical Center, Poughkeepsie, NY, USA*

## Abstract

**BACKGROUND:** We present a 4-year update on the efficacy, cosmetic results, and complications of MammoSite breast brachytherapy in patients enrolled in the American Society of Breast Surgeons registry trial.

**METHODS:** A total of 1,449 breasts in 1,440 patients with early stage breast cancer undergoing breast-conserving therapy were treated with adjuvant, accelerated partial breast irradiation (APBI) (34 Gy in 3.4-Gy fractions) delivered with the MammoSite device. The median follow-up period for the entire group was 36.1 months.

**RESULTS:** The 3-year actuarial rate of ipsilateral breast tumor recurrence was 2.15%. The 3-year actuarial rate of axillary recurrence was .36%. Complication rates were as follows: infection, 9.5%; seroma, 26.8% (symptomatic seroma, 12.7%); and fat necrosis, 2.0%. The percentages of breasts with good or excellent cosmetic results were as follows: 12 months, 95%; 24 months, 94%; 36 months, 94%; and 48 months, 91%.

**CONCLUSIONS:** Locoregional control, complications, and cosmetic outcomes from MammoSite APBI at the 4-year update are acceptable and similar to results seen with other forms of APBI.

# Bt Con Palladio o Iodio

Int. J. Radiation Oncology Biol. Phys., Vol. 64, No. 1, pp. 176–181, 2006

0360-3016/06/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2005.06.031

**CLINICAL INVESTIGATION** **Breast**

## FIRST REPORT OF A PERMANENT BREAST $^{103}$PD SEED IMPLANT AS ADJUVANT RADIATION TREATMENT FOR EARLY-STAGE BREAST CANCER

JEAN-PHILIPPE PIGNOL, M.D., PH.D., BRIAN KELLER, M.SC., EILEEN RAKOVITCH, M.D., M.SC., RAXA SANKREACHA, M.SC., HARRY EASTON, B.SC., AND WILLIAM QUE, PH.D.

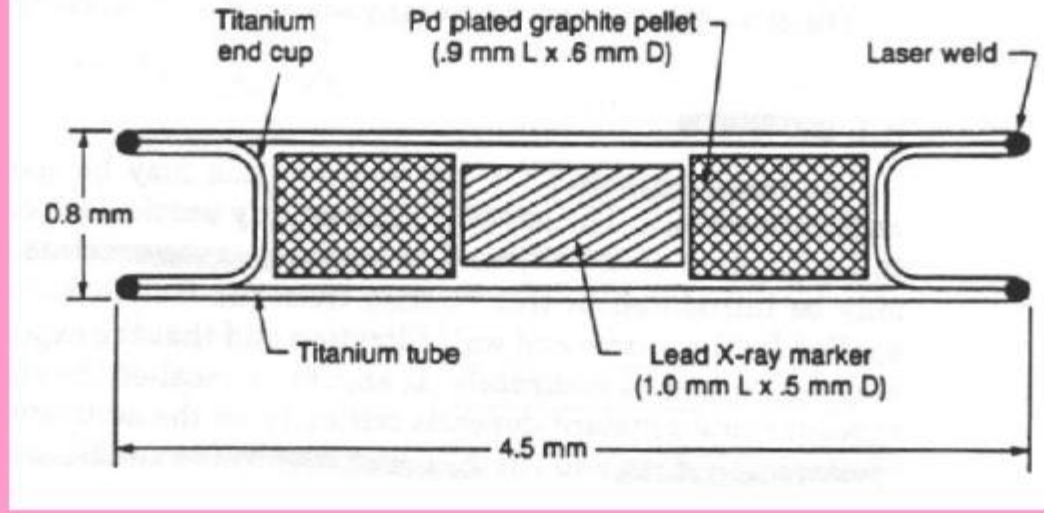
Department of Radiation Oncology, Sunnybrook and Women's Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada

**Purpose:** A new technique of adjuvant partial breast irradiation using $^{103}$Pd permanent breast seed implants (PBSI) is presented. The procedure is performed in a single 1-hour session under local anesthesia.
**Methods and Materials:** Patients referred to a single institution for adjuvant radiotherapy after lumpectomy for an infiltrating ductal carcinoma ≤3 cm in diameter, surgical margin ≥2 mm, no extensive *in situ* carcinoma, no lymphovascular invasion, and minimal or negative lymph node involvement were offered a PBSI.
**Results:** Between May and December 2004, 31 eligible patients underwent CT scan and ultrasound simulations assessing PBSI feasibility. Fifteen were excluded because of feasibility issues, and 16 received PBSI. A minimal peripheral dose of 90 Gy was prescribed to the planning target volume corresponding to the clinical target volume identified on the CT scan plus a margin of 1 cm. The procedure was well tolerated; 56% of the patients reported no pain during the procedure, and 46% of the patients developed National Cancer Institute Common Toxicity Criteria Grade 1 acute reaction. None experienced toxicity Grade 2 or 3.
**Conclusions:** Permanent breast seed implantation seems feasible and well tolerated on these preliminary clinical data and represents an ultimate step in the reduction of treatment fraction for partial breast irradiation.

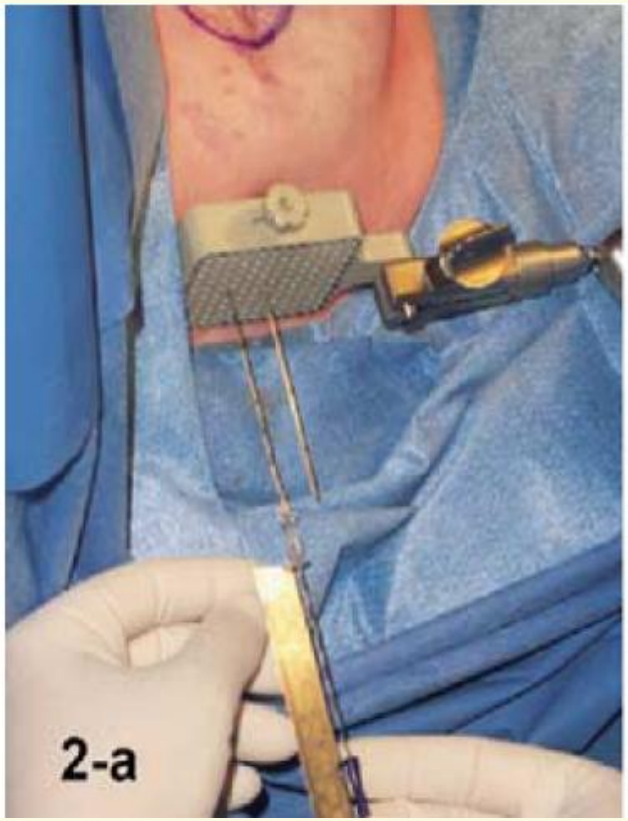

**Breast cancer, Radiation treatment, $^{103}$PD seed implant, Adjuvant radiotherapy.**

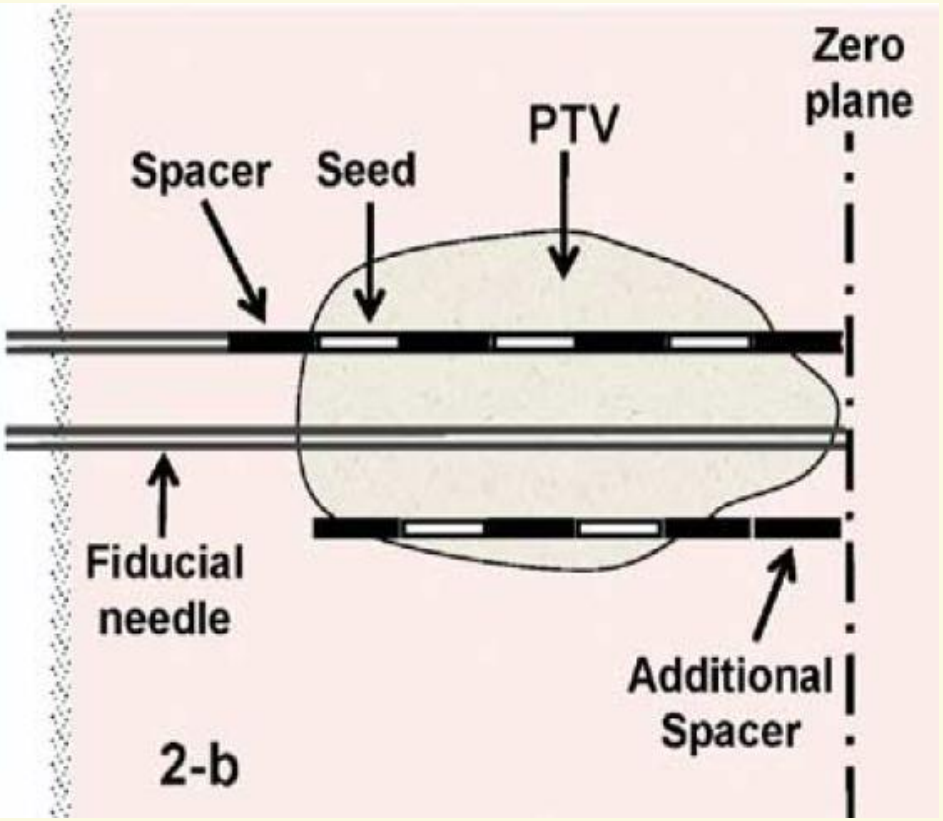
# $^{103}Pd$

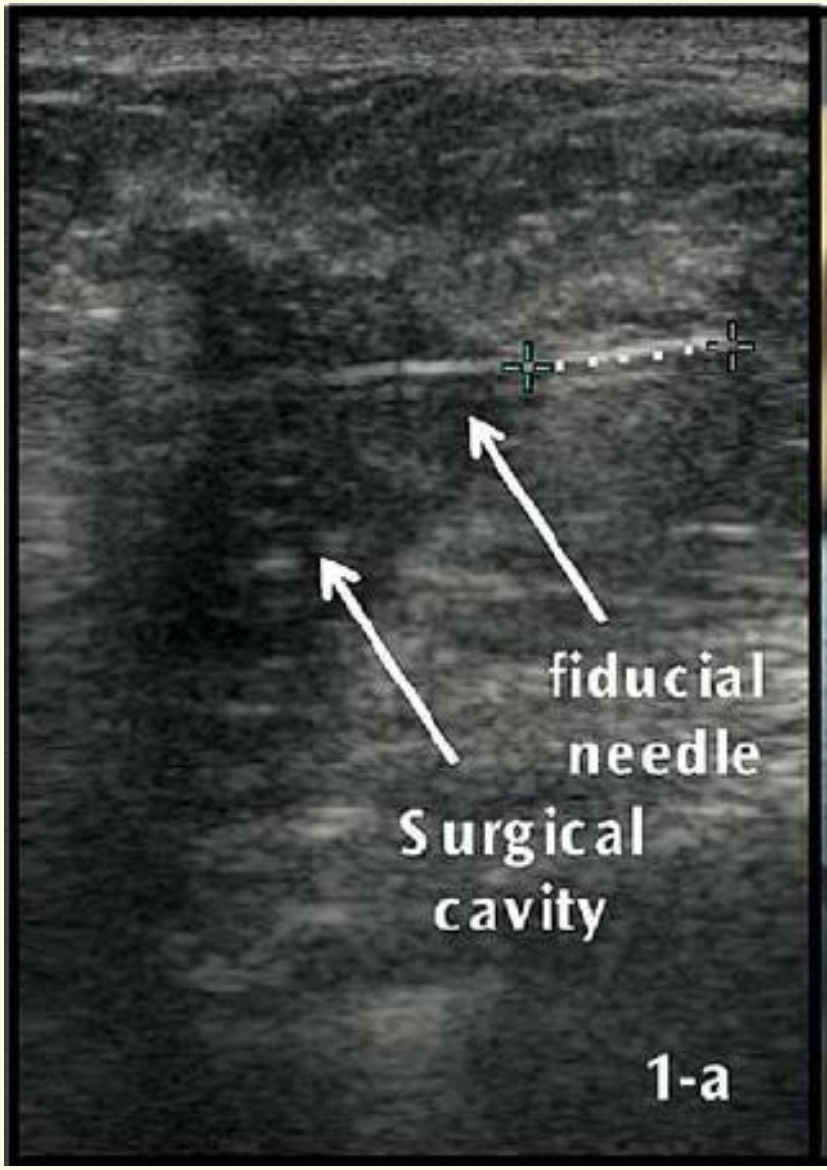
- Struttura della sorgente: tubo di titanio saldato a laser contenente due palline di grafite placcate di Pd-103; un marker di Pb visibile radiograficamente è presente tra le due palline

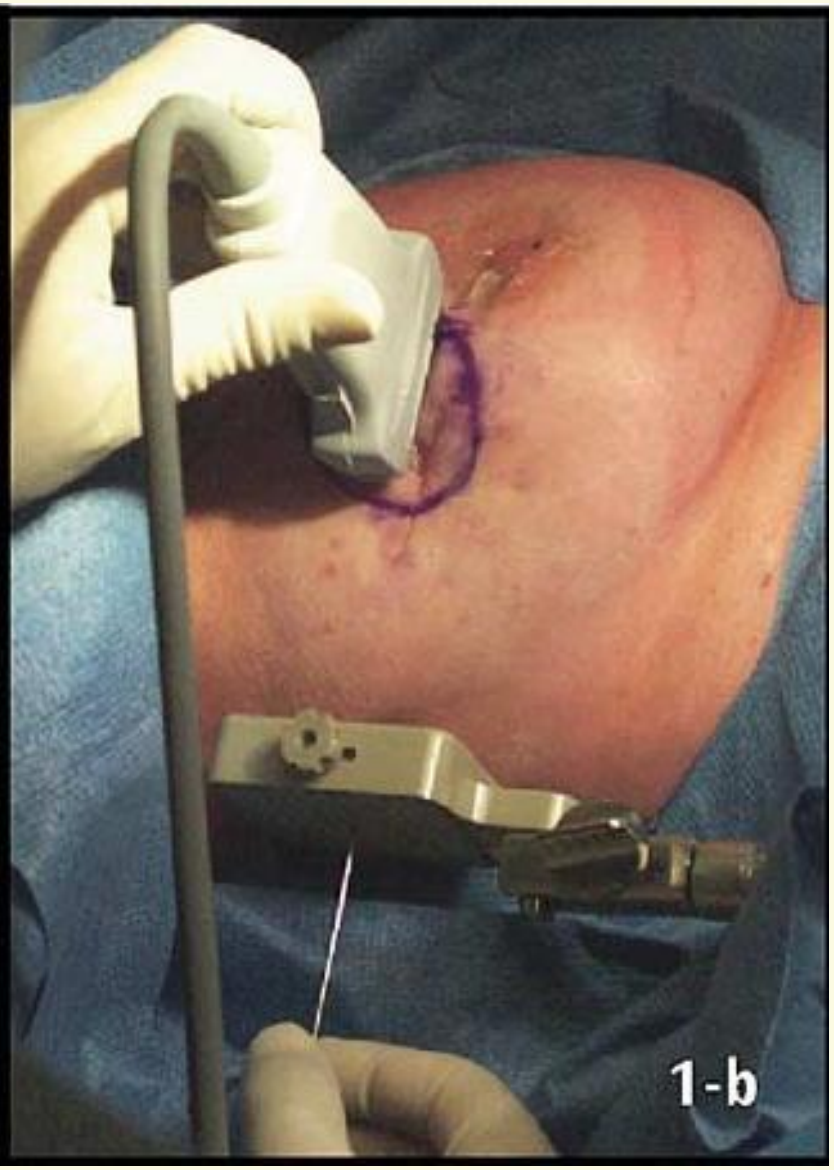


# Impianti permanenti



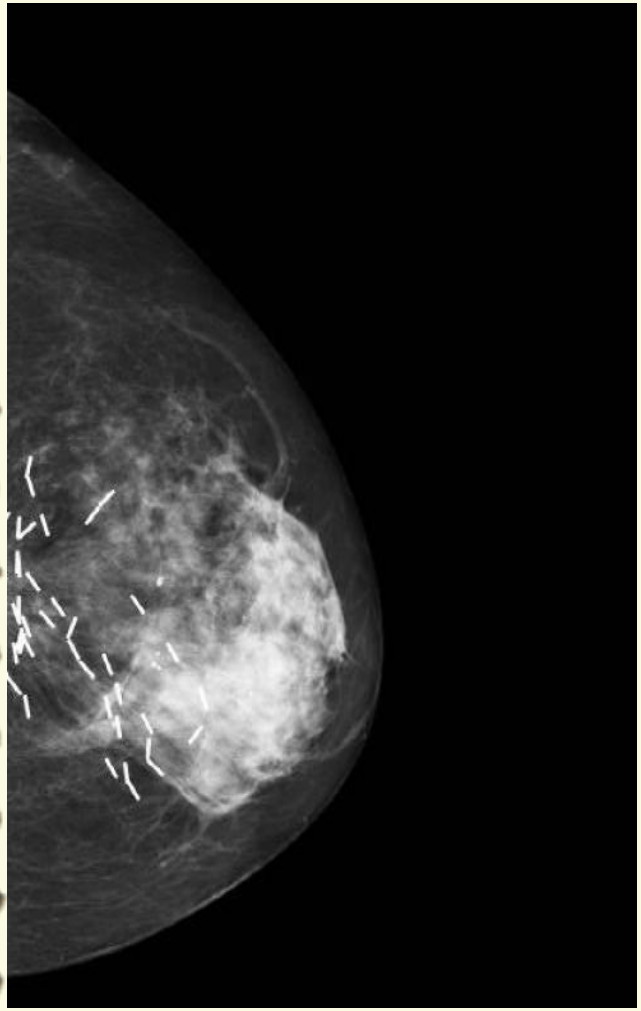



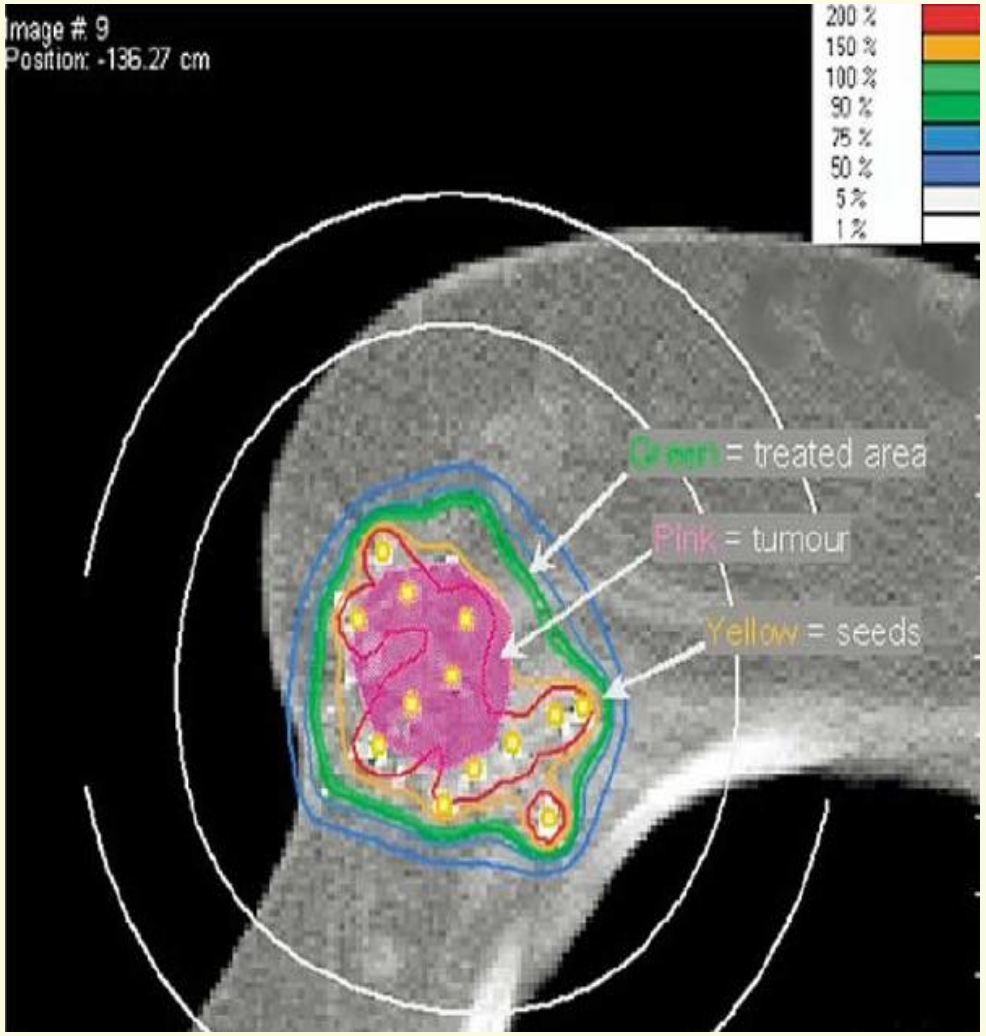

fiducial needle
Surgical cavity
1-a


1-b

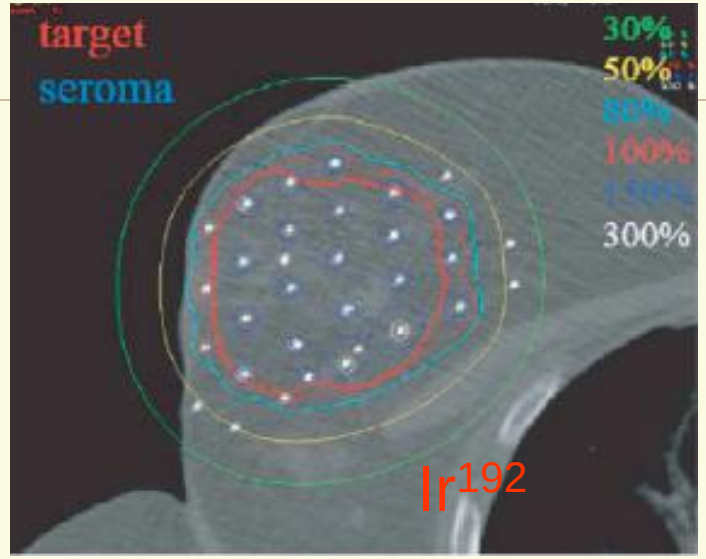
# Distribuzione della dose

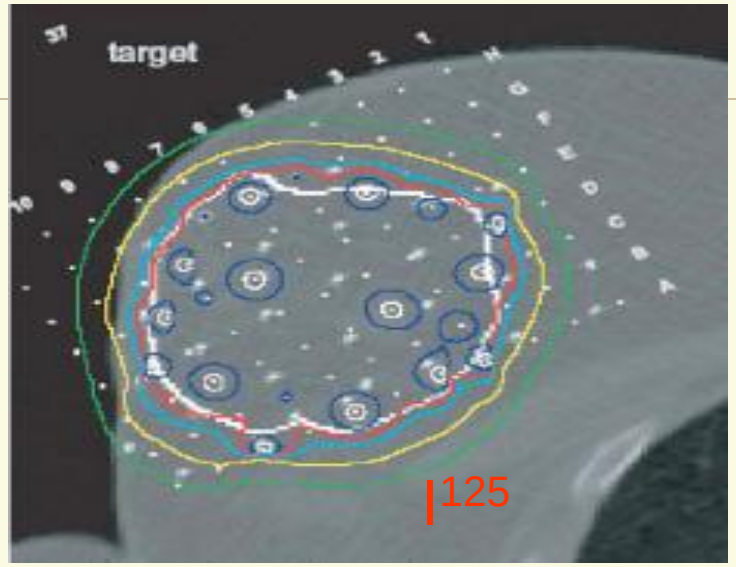
## Impianti permanenti





# $I^{125}$ PBSI




- Distribuzione della dose al target sovrapponibile alla tecnica interstiziale
- V50 ridotto
- Migliore distribuzione in T vicini alla cute o alla parete toracica e/o nelle mammelle piccole

Lin L. Medical Physics, 35(1): 240-247, 2008

# PBSI(Partial Breast Seed Implant)

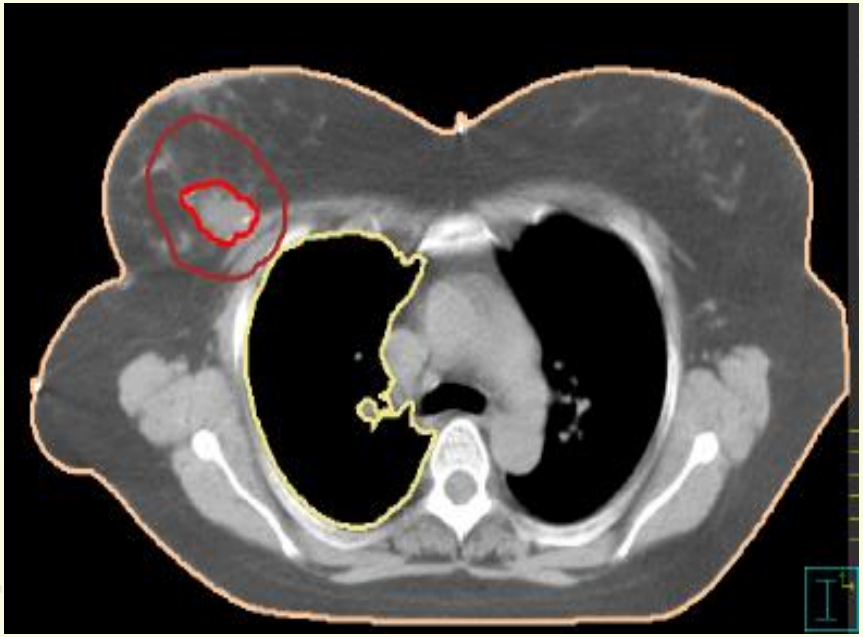
## VANTAGGI

- ✓ Procedura post-operat.
- ✓ Impianto ecoguidato
- ✓ L'utilizzo di un'ago guida all'interno della cavità garantisce l'accuratezza 3D

## SVANTAGGI

- ✓Tecnica operatore dipendente
- ✓Learning curve lunga
- ✓Presenza di sieroma
- ✓PTV> 70cc : problemi radioprotezionistici

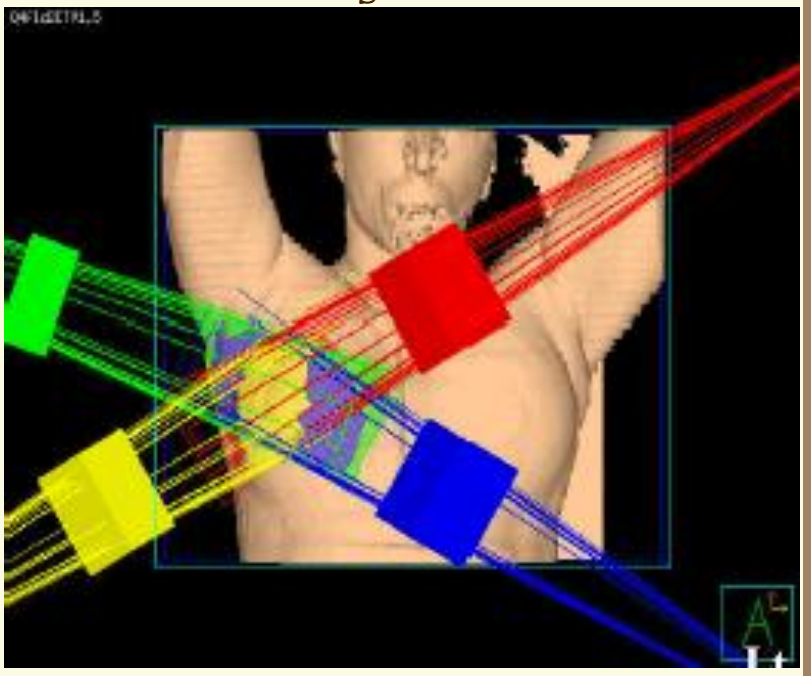
# Partial breast irradiation
## Fasci esterni 3DCRT



Trattamento postoperatorio

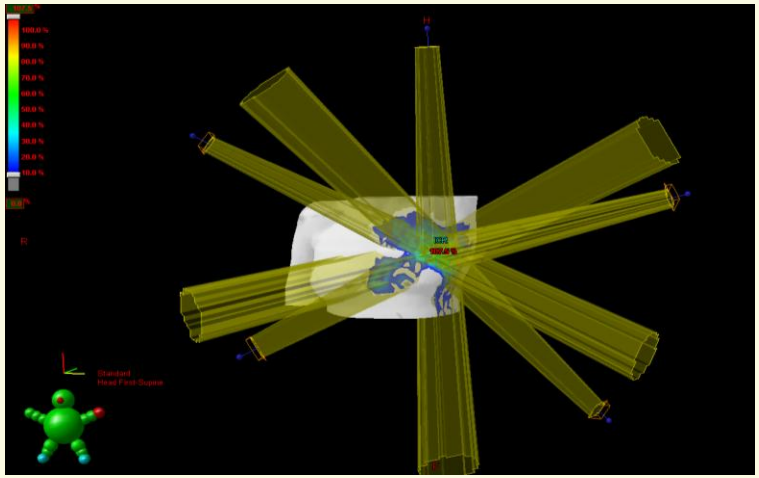
Identificazione cicatrice sulle sezioni TAC

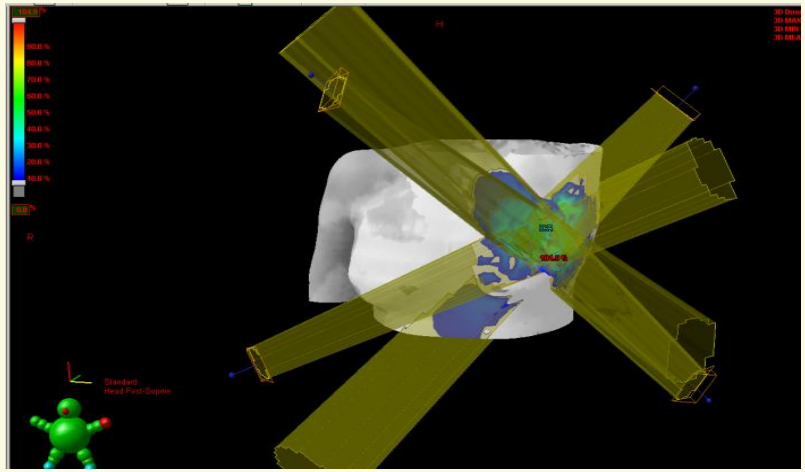
Disegno CTV

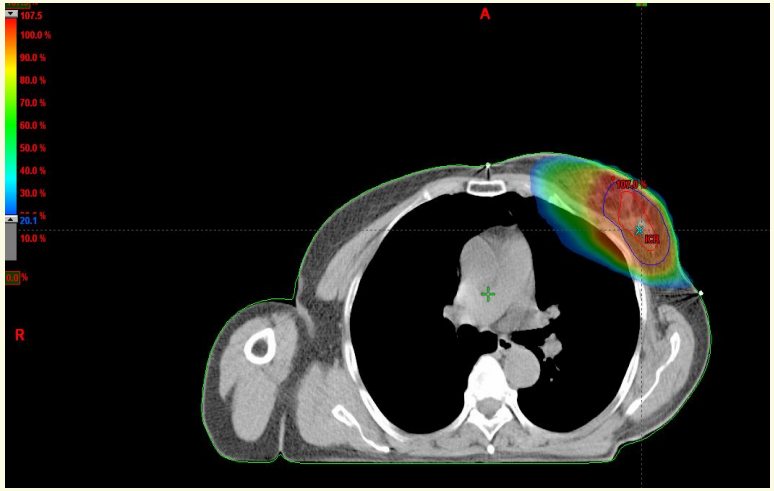


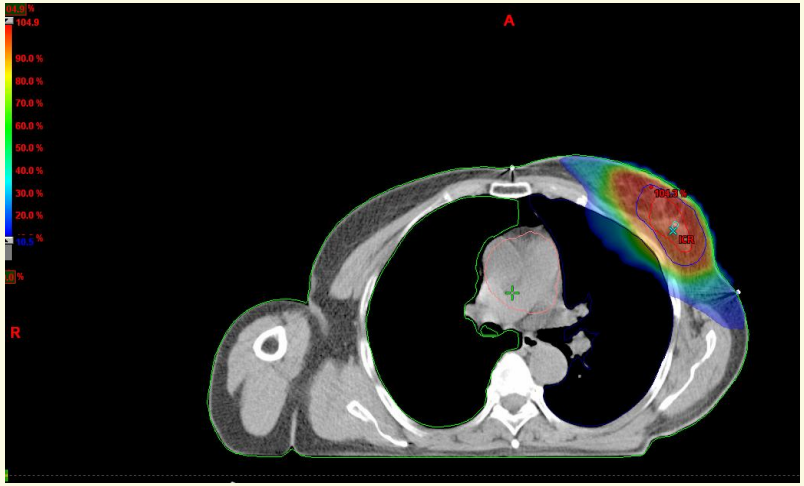
Somministrazione dose omogenea ad una ampia porzione della mammella con tecnica a campi multipli

# RT 3D CRT







Int. J. Radiation Oncology Biol. Phys., Vol. 60, No. 2, pp. 493–504, 2004

0360-3016/04/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2004.04.036

**CLINICAL INVESTIGATION** **Breast**

# PRONE ACCELERATED PARTIAL BREAST IRRADIATION AFTER BREAST-CONSERVING SURGERY: PRELIMINARY CLINICAL RESULTS AND DOSE–VOLUME HISTOGRAM ANALYSIS

SILVIA C. FORMENTI, M.D.,* MINH TAM TRUONG, M.B.B.S.,* JUDITH D. GOLDBERG, SC.D.,†
VANDANA MUKHI, M.A.,† BARRY ROSENSTEIN, PH.D.,* DANIEL ROSES, M.D.,‡
RICHARD SHAPIRO, M.D.,‡ AMBER GUTH, M.D.,‡ AND J. KEITH DEWYNGAERT, PH.D.*

*Departments of Radiation Oncology and ‡Surgery, New York University School of Medicine, New York, NY; †Division of Biostatistics, New York University School of Medicine and Biostatistics Shared Resource, New York University Cancer Institute, New York, NY

**Purpose:** To report the clinical and dose–volume histogram results of the first 47 patients accrued to a protocol of accelerated partial breast irradiation. Patients were treated in the prone position with three-dimensional conformal radiotherapy after breast-conserving surgery.

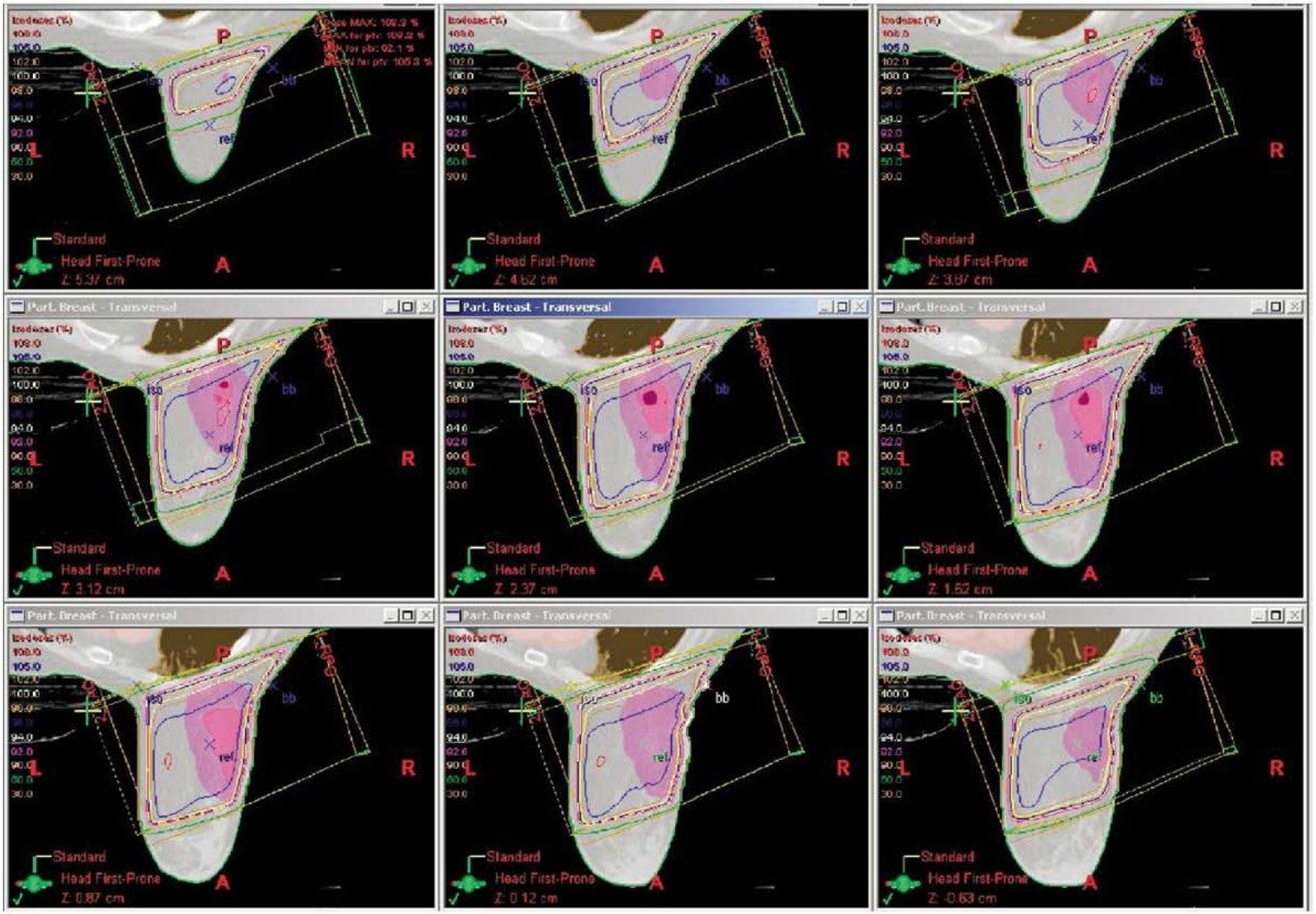
**Methods and Materials:** Postmenopausal women with Stage T1N0 breast cancer were eligible only after they had first refused to undergo 6 weeks of standard radiotherapy. Planning CT in the prone position was performed on a dedicated table. The postoperative cavity was defined as the clinical target volume, with a 1.5-cm margin added to determine the planning target volume. A total dose of 30 Gy at 6 Gy/fraction was delivered in five fractions within 10 days.

**Results:** The median age of the patients was 67.5 years (range, 51–88 years). The median tumor diameter was 9 mm (range, 1.3–19 mm). In all patients, the prescribed dose encompassed the planning target volume. The mean volume of the ipsilateral breast receiving 100% of the prescription dose was 26% (range, 10–45%), and the mean volume contained within the 50% isodose surface was 47% (range, 23–75%). The lung and heart were spared by treating in the prone position. Acute toxicity was modest, limited mainly to Grade 1–2 erythema. With a median follow-up of 18 months, only Grade 1 late toxicity occurred, and no patient developed local recurrence.

**Conclusion:** These data suggest that this approach is well tolerated, with only mild acute side effects and sparing of the heart and lung. © 2004 Elsevier Inc.

**Hypofractionation, Prone, Partial breast irradiation, Early-stage breast cancer.**

# RTE 3D-CRT


Part. Breast - Transversal
Standard
Head First-Prone
iso
bb
ref
P
A
R
L

# RTE 3D-CRT

## VANTAGGI

- ✓ Tecnica non invasiva, ben accettata dalle pazienti
- ✓ Ottima distribuzione di dose

## SVANTAGGI

- ✓ Piano di trattamento elaborato
- ✓ Tempi di trattamento lunghi (18-47 minuti)
- ✓ Imprecisione dovuta ai movimenti respiratori

Int. J. Radiation Oncology Biol. Phys., Vol. ■, No. ■, pp. 1–9, 2010

0360-3016/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2009.10.036

**PHYSICS CONTRIBUTION**

# IMPACT OF VOLUMETRIC MODULATED ARC THERAPY TECHNIQUE ON TREATMENT WITH PARTIAL BREAST IRRADIATION

JIAN-JIAN QIU, B.S.,*† ZHENG CHANG, PH.D.,* Q. JACKIE WU, PH.D.,* SUA YOO, PH.D.,* JANET HORTON, M.D.,* AND FANG-FANG YIN, PH.D.*

*Department of Radiation Oncology, Duke University Medical Center, Durham, North Carolina, and †Department of Radiation Therapy, Fudan University Cancer Hospital, Shanghai, China

**Purpose:** To investigate the technical feasibility of volumetric modulated arc therapy (V-MAT) in the delivery of partial breast irradiation (PBI).

**Methods and Materials:** V-MAT and the standard, three-dimensional conformal radiotherapy (3D-CRT), were compared retrospectively in 8 patients previously treated with PBI. These patients' plans were replanned with a single partial arc using V-MAT that included partial blocking to minimize normal tissue dose. Dosimetric parameters were calculated to evaluate plan quality. Quality assurance studies included verifying both the point and the multiple planar doses. Total monitor units and delivery time were also evaluated, and collision clearance was analyzed.

**Results:** Volumes of ipsilateral lung irradiated to 10 Gy (V10) and 20 Gy (V20) by V-MAT were significantly less than those of 3D-CRT ($p = 0.03$ for V10 and $p = 0.025$ for V20). The volume of ipsilateral breast irradiated to 5 Gy was significantly less by using V-MAT than with 3D-CRT ($p = 0.02$), with a ratio of integrated dose of <1.00. The total mean monitor units (489 ± 38) for V-MAT were significantly less than those for 3D-CRT (634 ± 123) ($p = 0.017$), with a 23% reduction. The average machine delivery time was 1.21 ± 0.10 min for the V-MAT plans and 6.28 ± 1.40 min for the 3D-CRT plans, resulting in a reduction factor of 80.1%. The conformity indexes were 1.3 in the V-MAT plans and 1.5 in the 3D-CRT plans ($p = 0.102$).

**Conclusions:** V-MAT technology is feasible for PBI patients. Compared to a conventional 3D-CRT technique, it is more efficient, offers equivalent or better dose conformity, delivers lower doses to the ipsilateral lung and breast, and may potentially reduce intrafractional motion. © 2010 Elsevier Inc.

Volumetric modulated arc therapy (V-MAT), Intensity-modulated arc therapy (IMRT), Partial breast irradiation (PBI).

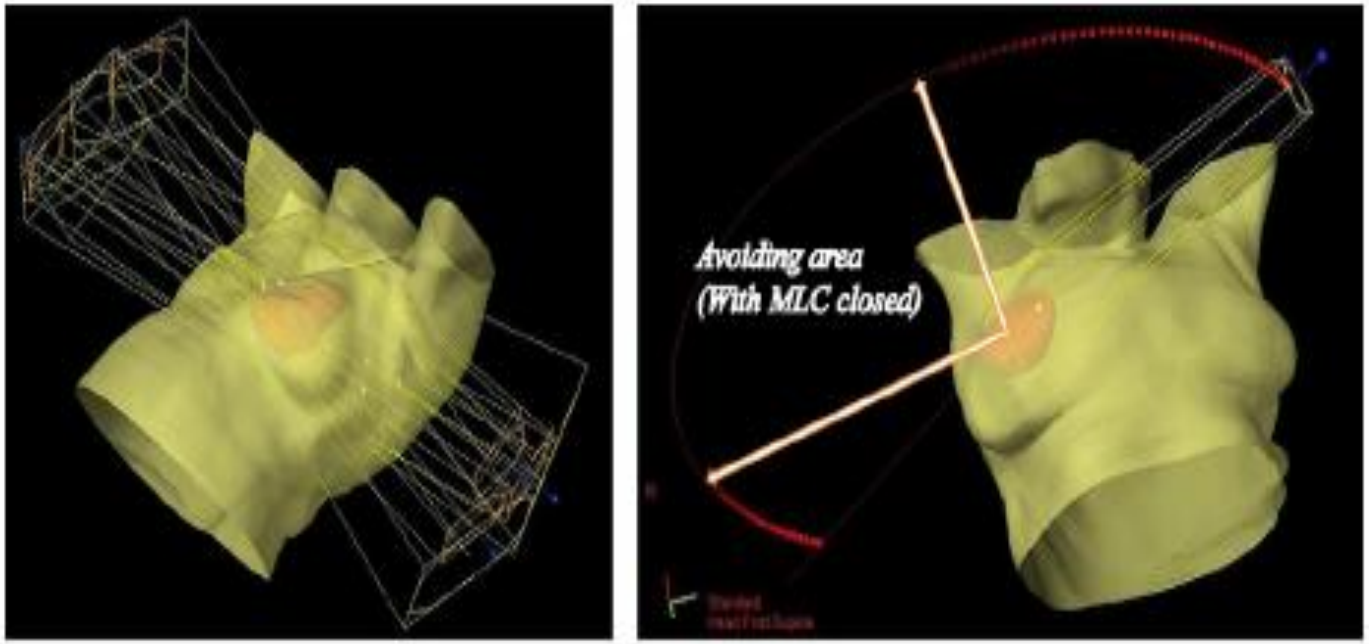



Fig. 1. Examples of (a) noncoplanar 3D-CRT with five beams and five wedges and (b) RapidArc plan (V-MAT) with a partial arc in which MLC is closed for a portion of the arc. Orange colored regions indicate PTVs.

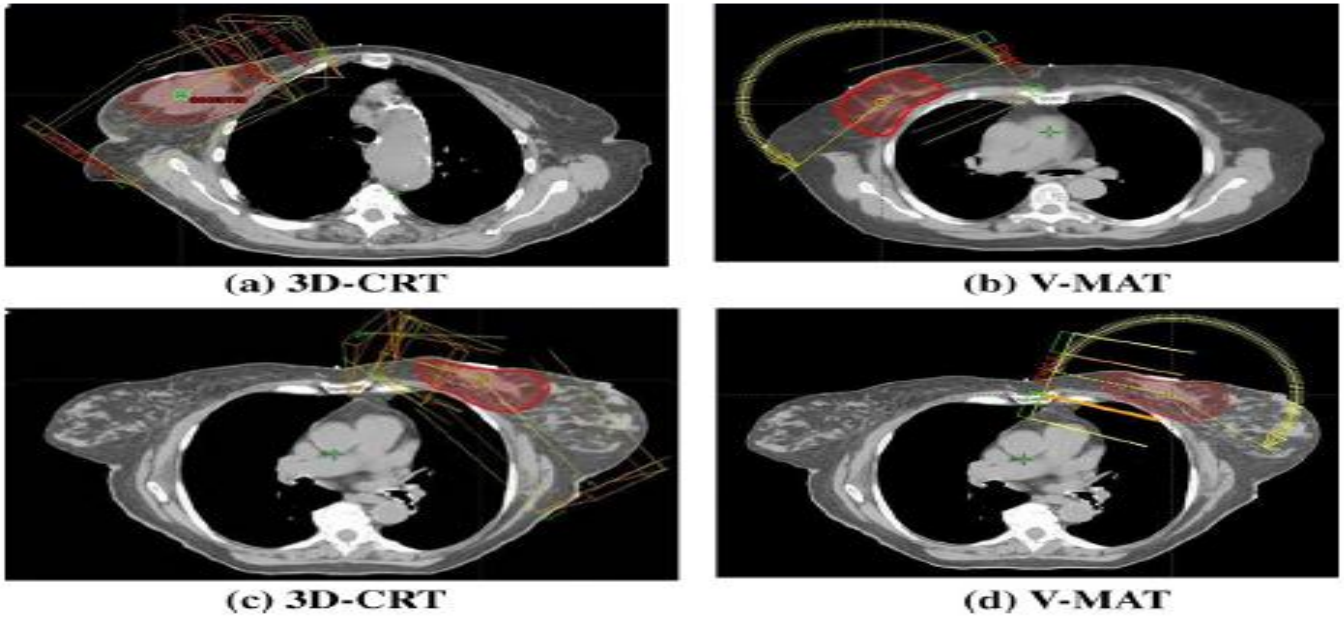



Fig. 2. Axial view of right (a, c) and left (b, d) breast radiation with both 3D-CRT and V-MAT beam arrangements

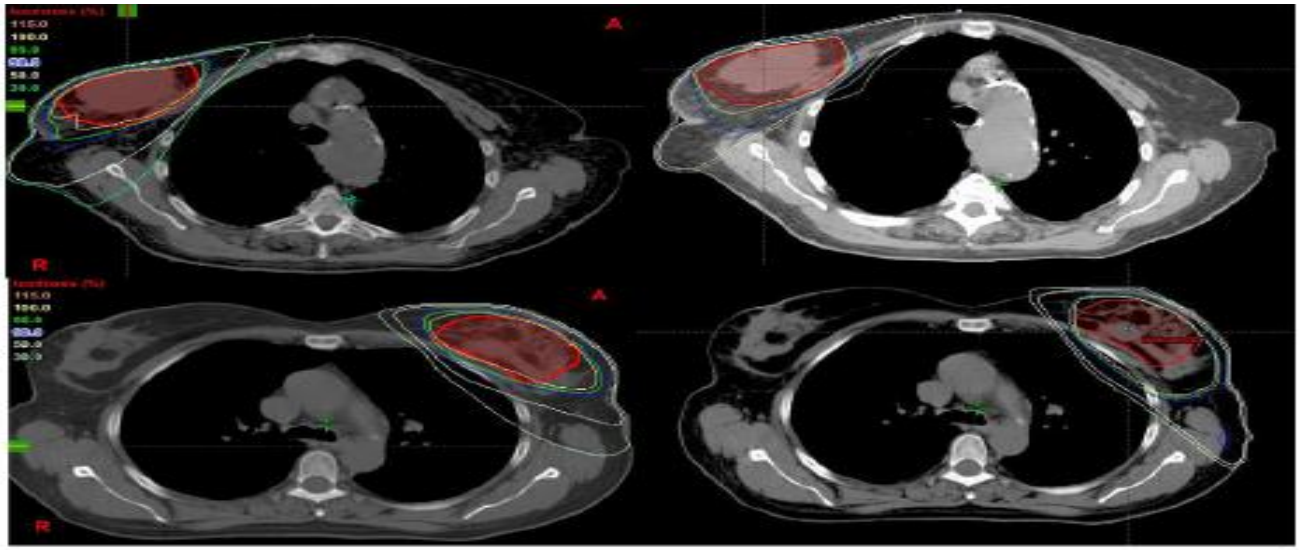



Fig. 4. Isodose distributions in transverse planes of two PBI cases: RapidArc (V-MAT) (a) and 3D-CRT (b) plans for lesions in both the left and the right breasts (red colored regions indicate PTVs).

# PBI E PROTONI

Int. J. Radiation Oncology Biol. Phys., Vol. 65, No. 5, pp. 1404–1410, 2006

0360-3016/06/$–see front matter

doi:10.1016/j.ijrobp.2006.03.017

**CLINICAL INVESTIGATION** **Breast**

## ACCELERATED PARTIAL BREAST IRRADIATION USING PROTON BEAMS: INITIAL DOSIMETRIC EXPERIENCE

ALPHONSE G. TAGHIAN, M.D., PH.D., KEVIN R. KOZAK, M.D., PH.D., ANGELA KATZ, M.D., JUDITH ADAMS, C.M.D., HSIAO-MING LU, PH.D., SIMON N. POWELL, M.D., PH.D., AND THOMAS F. DELANEY, M.D.

Department of Radiation Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, MA

**Purpose:** The unique dosimetric features of proton radiotherapy make it an attractive modality for normal tissue sparing. We present our initial experience with protons for three-dimensional, conformal, external-beam accelerated partial breast irradiation (3D-CPBI).

**Methods and Materials:** From March 2004 to June 2005, 25 patients with tumors ≤2 cm and negative axillary nodes were treated with proton 3D-CPBI. The prescribed dose was 32 Cobalt Gray Equivalents (CGE) in 4 CGE fractions given twice daily. One to three fields were used to provide adequate planning target volume (PTV) coverage and dose homogeneity.

**Results:** Excellent PTV coverage and dose homogeneity were obtained in all patients with one to three proton beams. The median PTV receiving 95% of the prescribed dose was 100%. Dose inhomogeneity exceeded 10% in only 1 patient (4%). The median volume of nontarget breast tissue receiving 50% of the prescribed dose was 23%. Median volumes of ipsilateral lung receiving 20 CGE, 10 CGE, and 5 CGE were 0%, 1%, and 2%, respectively. The contralateral lung and heart received essentially no radiation dose. Cost analysis suggests that proton 3D-CPBI is only modestly more expensive (25%) than traditional whole-breast irradiation (WBI).

**Conclusion:** Proton 3D-CPBI is technically feasible, providing both excellent PTV coverage and normal tissue sparing. It markedly reduces the volume of nontarget breast tissue irradiated compared with photon-based 3D-CPBI, addressing a principle disadvantage of external-beam approaches to PBI. As proton therapy becomes more widely available, it may prove an attractive tool for 3D-CPBI. © 2006 Elsevier Inc.

Breast cancer, Partial breast irradiation, 3D-conformal, Proton beams, Cost analysis.

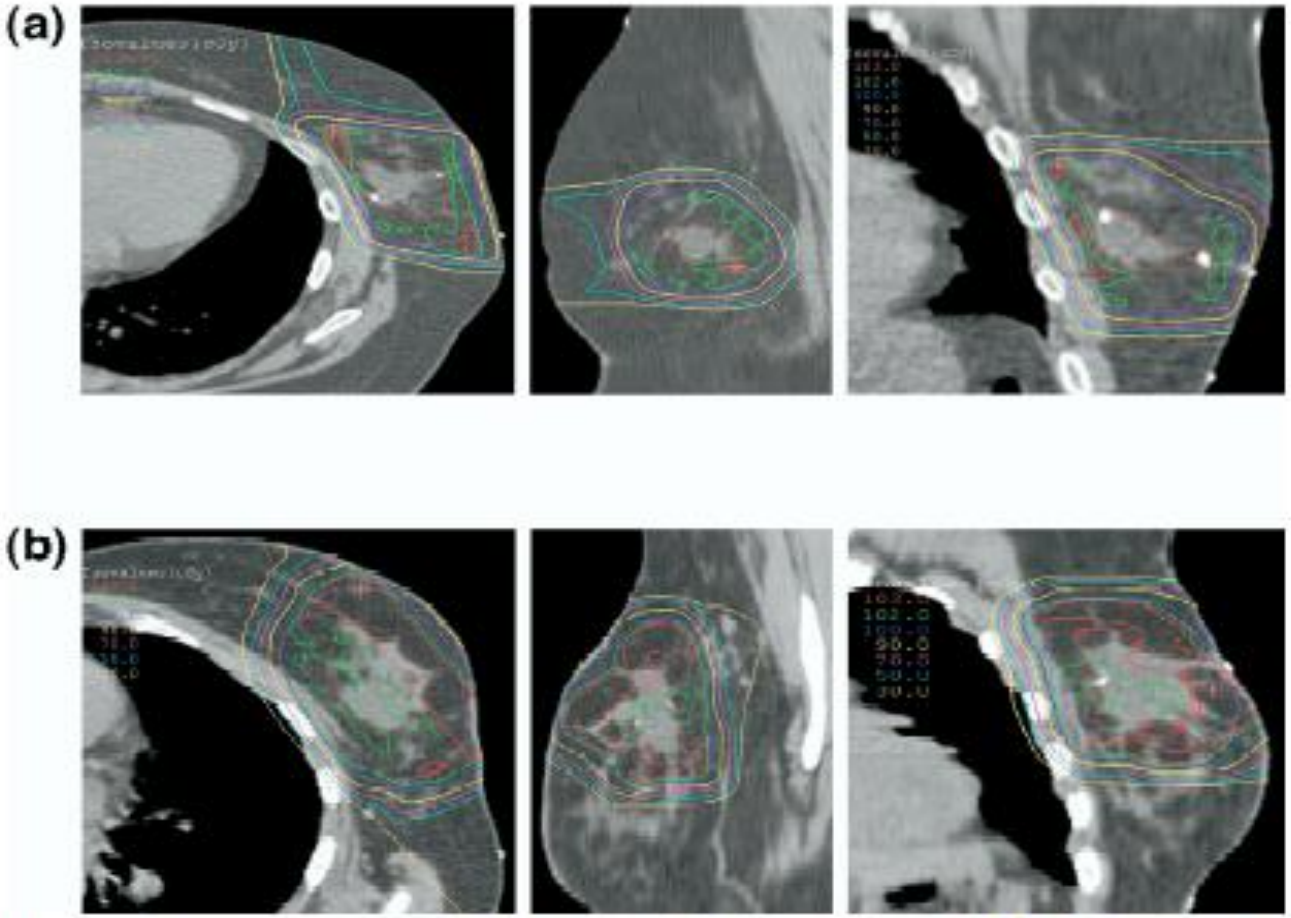



Fig. 1. (a) Representative dosimetry for a two-field, proton beam, partial breast irradiation treatment plan with axial, sagittal and coronal views. The surgical cavity (thin red), planning target volume (PTV) (thin purple) and 103% (thick red), 102% (green), 100% (dark blue), 90% (yellow), 70% (thick purple), 50% (light blue) and 30% (orange) isodose lines are depicted. (b) Representative dosimetry for a three-field, proton beam, partial breast irradiation treatment plan with axial, sagittal and coronal views. The surgical cavity (thin red), PTV (thin purple) and 103% (thick red), 102% (green), 100% (dark blue), 90% (yellow), 70% (thick purple), 50% (light blue) and 30% (orange) isodose lines are depicted.

Radiotherapy and Oncology 90 (2009) 66–73

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Partial breast irradiation

# Dosimetric comparison of four different external beam partial breast irradiation techniques: Three-dimensional conformal radiotherapy, intensity-modulated radiotherapy, helical tomotherapy, and proton beam therapy

Sung Ho Moon [a], Kyung Hwan Shin [a,b,*], Tae Hyun Kim [a], Myonggeun Yoon [a], Soah Park [a], Doo-Hyun Lee [a], Jong Won Kim [a], Dae Woong Kim [a], Sung Yong Park [a], Kwan Ho Cho [a]

[a] *Proton Therapy Center, National Cancer Center, Gyeonggi-do, Republic of Korea*
[b] *Center for Breast Cancer, National Cancer Center, Gyeonggi-do, Republic of Korea*

ARTICLE INFO

*Article history:*
Received 29 May 2008
Received in revised form 11 September 2008
Accepted 13 September 2008
Available online 5 November 2008

*Keywords:*
Breast cancer
Accelerated partial breast irradiation
Protons
Helical tomotherapy
Intensity-modulated radiotherapy
3D-conformal
Comparison

ABSTRACT

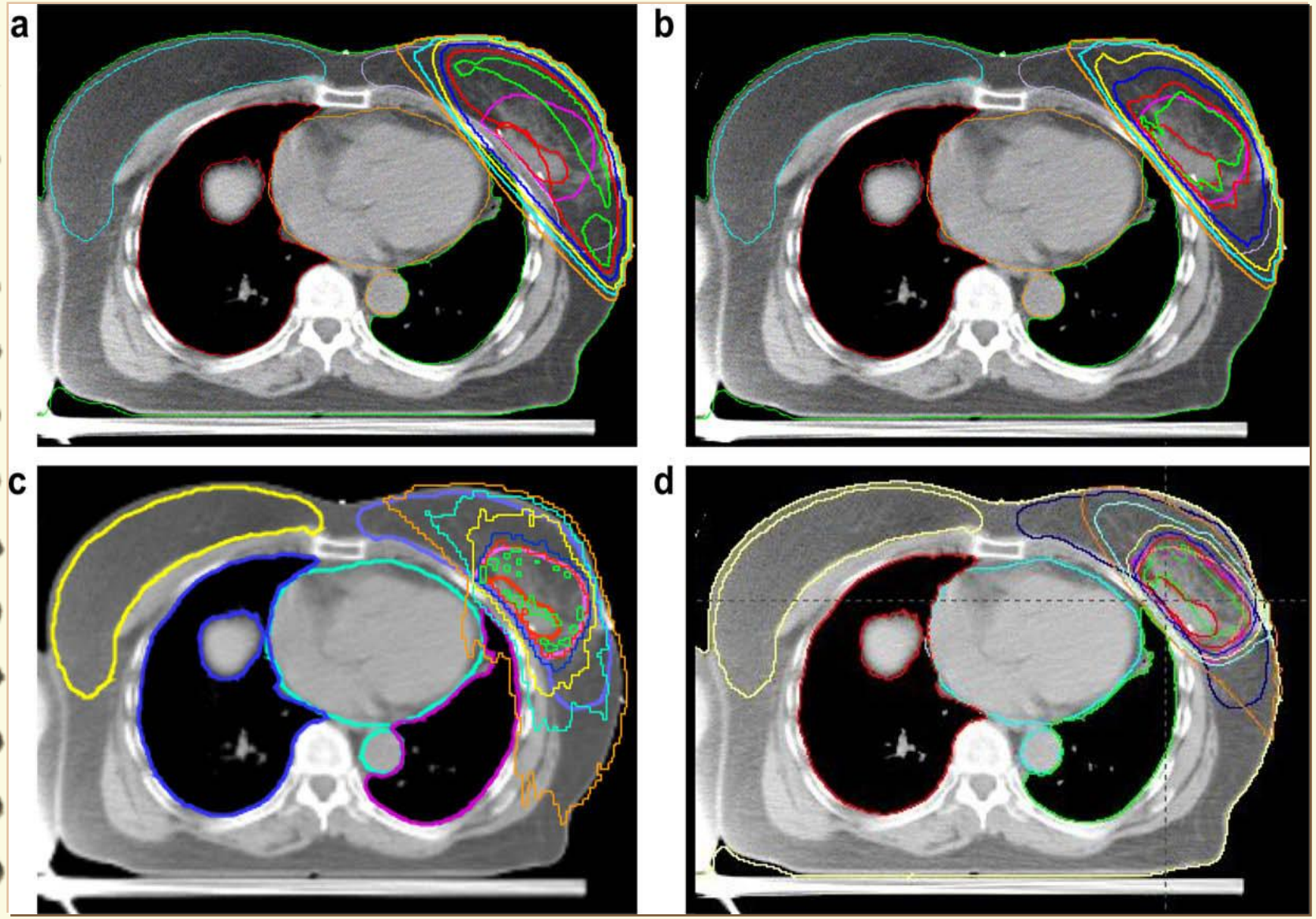
*Background and purpose:* As an alternative to whole breast irradiation in early breast cancer, a variety of accelerated partial breast irradiation (APBI) techniques have been investigated. The purpose of our study is to compare the dosimetry of four different external beam APBI (EB-APBI) plans: three-dimensional conformal radiation therapy (3D-CRT), intensity-modulated radiation therapy (IMRT), helical tomotherapy (TOMO), and proton beam therapy (PBT).

*Methods and materials:* Thirty patients were included in the study, and plans for four techniques were developed for each patient. A total dose of 30 Gy in 6 Gy fractions once daily was prescribed in all treatment plans.

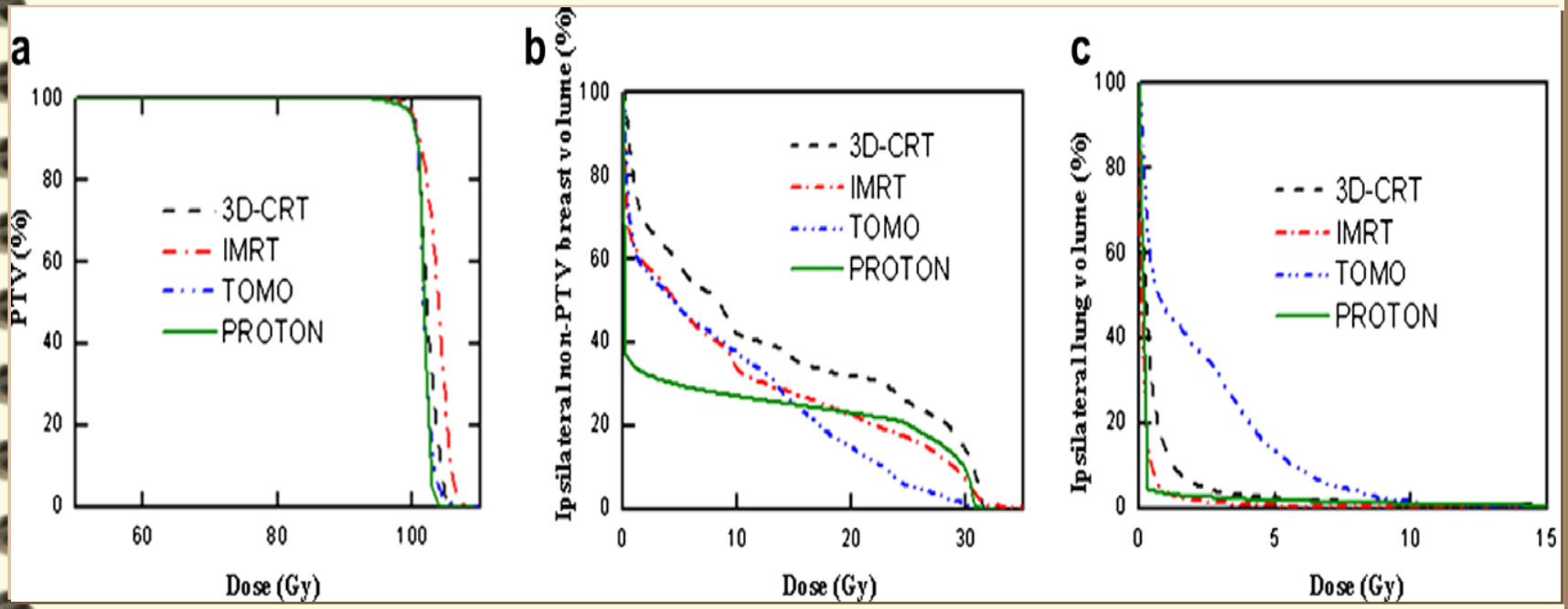
*Results:* In the analysis of the non-PTV breast volume that was delivered 50% of the prescribed dose (PD), PBT (mean: 16.5%) was superior to TOMO (mean: 22.8%), IMRT (mean: 33.3%), and 3D-CRT (mean: 40.9%) ($p < 0.001$). The average ipsilateral lung volume percentage receiving 20% of the PD was significantly lower in PBT (0.4%) and IMRT (2.3%) compared with 3D-CRT (6.0%) and TOMO (14.2%) ($p < 0.001$). The average heart volume percentage receiving 20% and 10% of the PD in left-sided breast cancer ($N = 19$) was significantly larger with TOMO (8.0%, 19.4%) compared to 3D-CRT (1.5%, 3.1%), IMRT (1.2%, 4.0%), and PBT (0%, 0%) ($p < 0.001$).

*Conclusions:* All four EB-APBI techniques showed acceptable coverage of the PTV. However, effective non-PTV breast sparing was achieved at the cost of considerable dose exposure to the lung and heart in TOMO.




Dose distribution of (a) three-dimensional conformal radiotherapy, (b) intensity-modulated radiotherapy, (c) helical tomotherapy, and (d) proton beam therapy in the axial plane. Lumpectomy cavity (red), PTV (pink), and isodose lines of 103% (green), 100% (red), 90% (blue), 70% (yellow), 50% (cyan), and 30% (orange) are depicted




Dose-volume histogram (DVH) data for PTV (a), the ipsilateral non-PTV breast volume (b) and the ipsilateral lung volume (c).

# IORT:radioterapia intraoperatoria: definizione

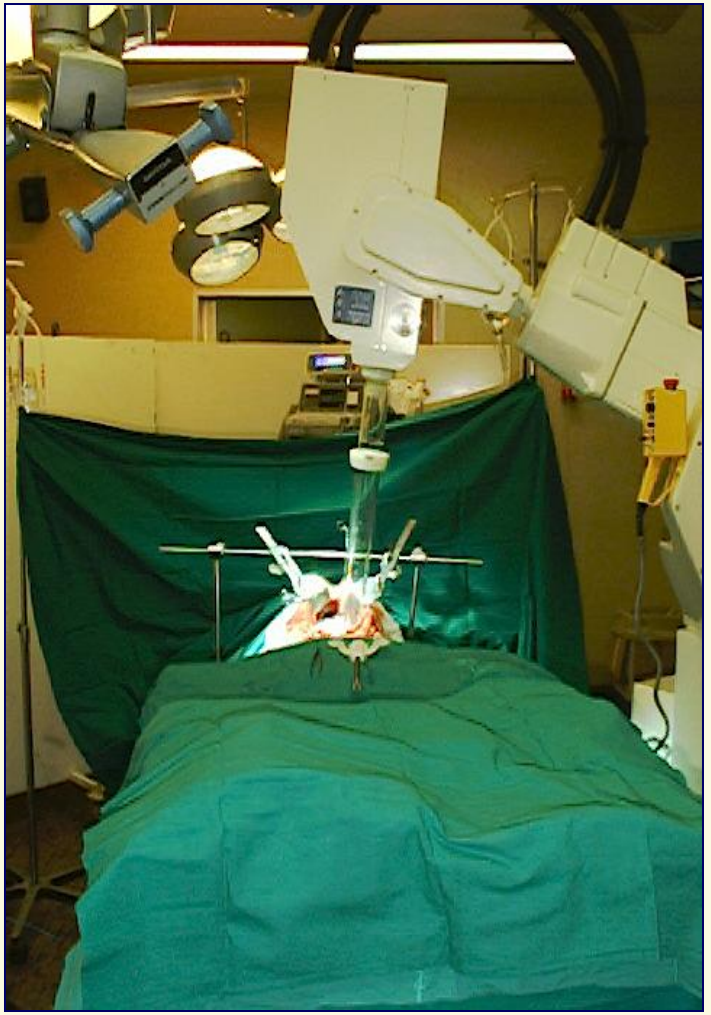
Si identifica con il termine di "radioterapia intraoperatoria" un'irradiazione effettuata durante un intervento chirurgico, dopo la exeresi di una massa neoplastica, utilizzando la breccia operatoria per far arrivare il fascio di radiazioni direttamente sul letto tumorale, possibile sede di malattia subclinica o sede di residuo macroscopico nel caso di resezione non radicale.

ISSN 1123-3117
Rapporti ISTISAN 03/1 IT

# IORT: Radioterapia Intraoperatoria

Unica frazione seguita da Rte, come:

- ✓ Sovradosaggio (boost)
- ✓ Trattamento esclusivo in neoplasie di piccolo volume o non resecabili a scopo palliativo



ISSN 1123-3117
Rapporti ISTISAN 03/1 IT

ISTITUTO SUPERIORE DI SANITÀ

# Linee guida per la garanzia di qualità nella radioterapia intraoperatoria

A cura di
Antonella Rosi e Vincenza Viti
*Laboratorio di Fisica*

ISSN 1123-3117
**Rapporti ISTISAN**
**03/1 IT**

# Gruppo di Studio Nazionale Radioterapia Intraoperatoria

*Coordinatore: Prof. Vincenzo Valentini*

## Scopi generali:

- confronto di esperienze
- procedure di trattamento
- programmi di QA
- studi cooperativi
- monitoraggio e sviluppo di attività IORT

**Associazione Italiana di Radioterapia Oncologica**
***Gruppo di Studio***
***Sulla Radioterapia Intraoperatoria* (IORT)**

# INDICAZIONI ALL'USO DELLA IORT

# SECONDO

# LA MEDICINA BASATA SULLE EVIDENZE

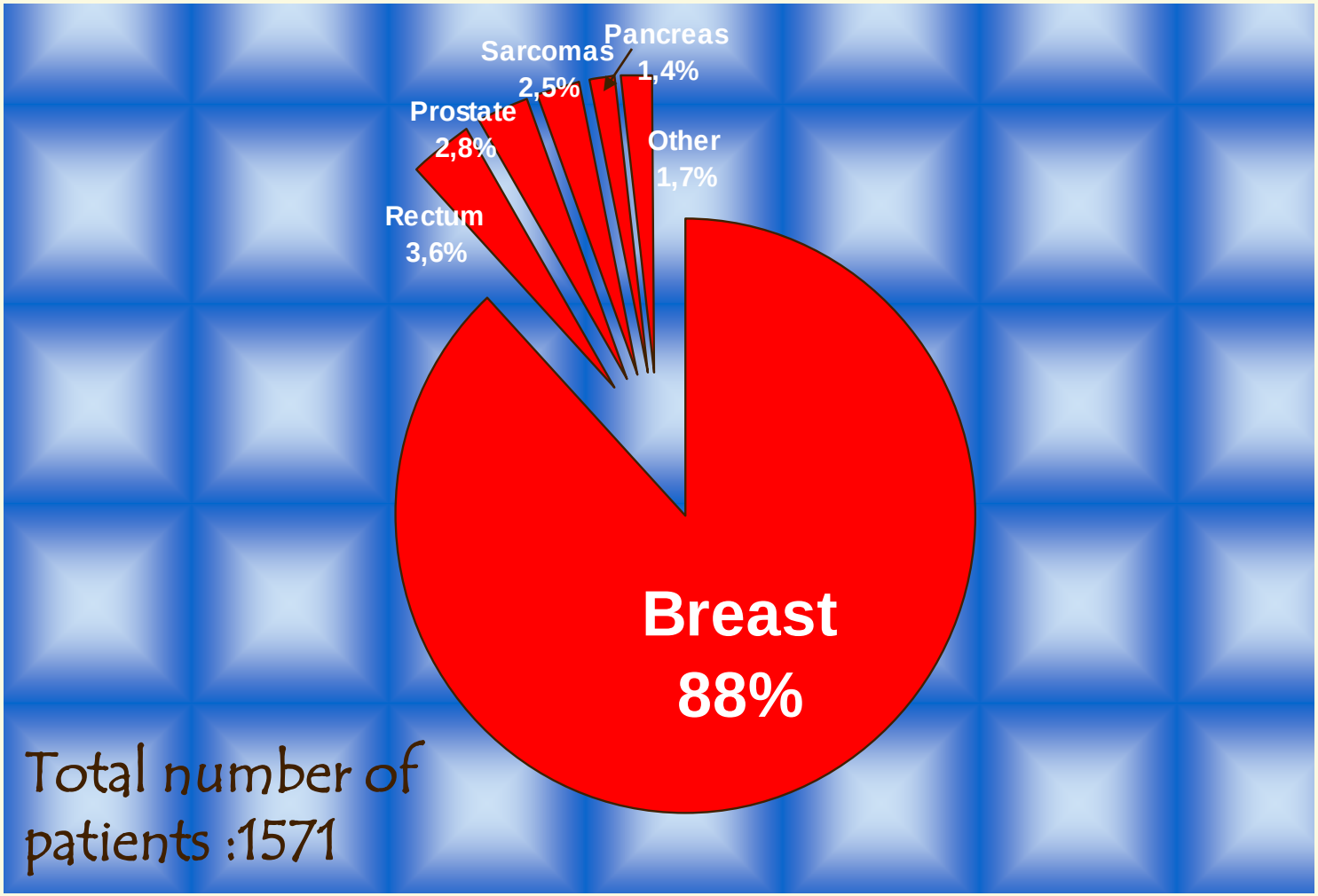
**Report 04/01 ( approvato dal C. D. A.I.R.O. in data 03/12/04)**

# IORT centres in Italy - 2007


| Area | IORT centres | Before 1999 | After 1999 |
|---|---|---|---|
| Piemonte/ Valle d'Aosta | 3 | 0 | 3 |
| Lombardia | 3 | 1 | 2 |
| Trentino AA | 1 | 1 | |
| Friuli VG | 2 | 1 | 1 |
| Veneto | 3 | 0 | 3 |
| Emilia Romagna | 0 | | |
| Liguria | 0 | | |
| Toscana | 3 | 0 | 3 |
| Umbria | 1 | 0 | 1 |
| Marche | 1 | 0 | 1 |
| Lazio | 5 | 2 | 3 |
| Abruzzo | 0 | | |
| Molise | 0 | | |
| Campania | 0 | | |
| Puglia | 1 | 0 | 1 |
| Basilicata | 0 | | |
| Calabria | 1 | 0 | 1 |
| Sicilia | 2 | 0 | 2 |
| Sardegna | 1 | 0 | 1 |
| Italia | 27 | 5 | 22 |

In early 2008: + 7

# Treatment sites (%) in 2007



# Iort Nelle Neoplasie Mammarie

## Indicazioni

- Neoplasia limitata T1-T2
- Nodulo unico o adiacenti (<0,5 cm)
- Non documentata multicentricità e/o estesa multifocalità della lesione
- Non carcinoma duttale o lobulare in situ, non Paget, non EIC
- Non tumore in stretta prossimità della cute o sul prolungamento ascellare

# Iort Nelle Neoplasie Mammarie

## *VANTAGGI*

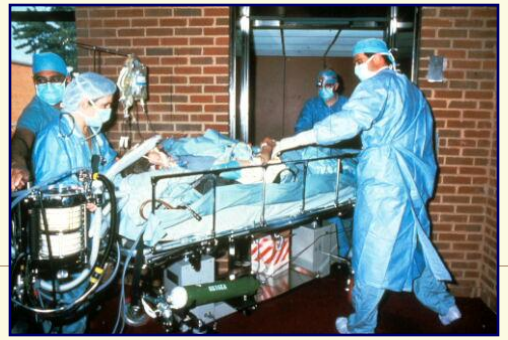
- ✓ Eliminazione di *geographic missing*
- ✓ Risparmio tessuti sani
- ✓ Omogeneità di dose
- ✓ Non interferenza con altre terapie (CT, RTE,…)
- ✓ Riduzione o annullamento dell'intervallo CHIR-RT

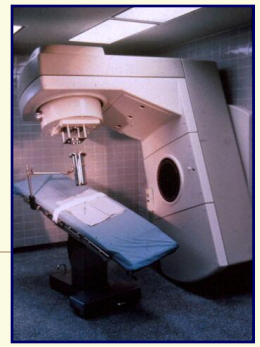
## *SVANTAGGI*

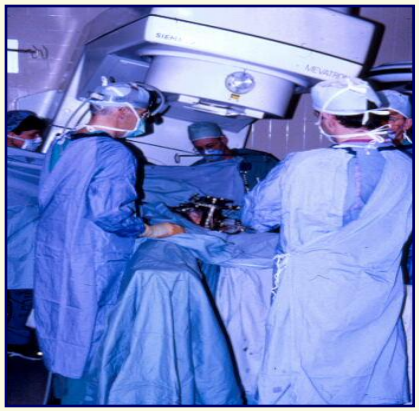
- ✓ Trattamento effettuato prima di conoscere l'esame istologico definitivo
- ✓ Rischio di tossicita' tardiva per l' impiego di una dose singola elevata

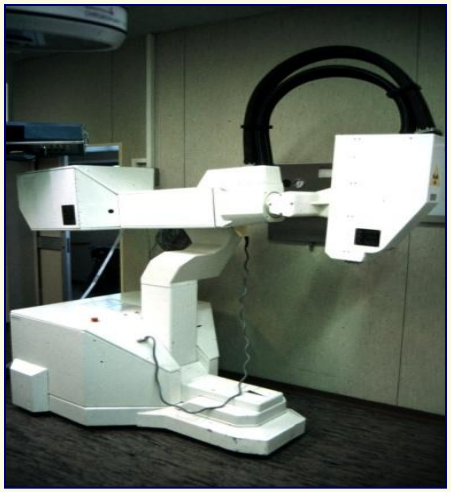
# IORT: Modalita'

- ACCELERATORE NON DEDICATO (BUNKER) E TRASPORTO PZ
- ACCELERATORE DEDICATO
- ACCELERATORE MOBILE







# Iort con Acceleratore Lineare Mobile

- ✓ riduce le difficoltà tecniche
- ✓ riduce il tempo aggiuntivo di anestesia
- ✓ elimina il trasporto e rischi di infezione

RENDE PIU' SEMPLICE IL TRATTAMENTO

# IORT

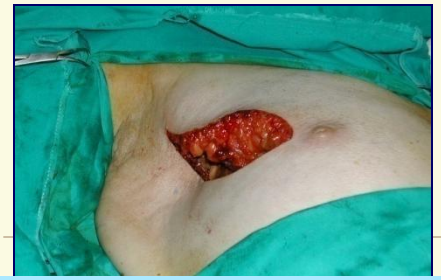
## GRUPPO OPERATIVO

<u>esegue il trattamento</u>

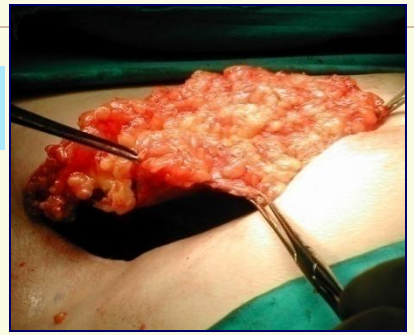
- Radioterapista
- Chirurgo
- Fisico medico
- Anestesista
- TSRM
- Infermiere professionale

Rapporto ISTISAN 03/1

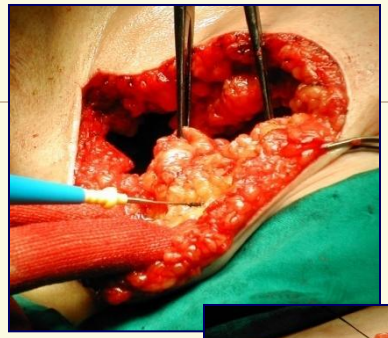
# Note Di Tecnica

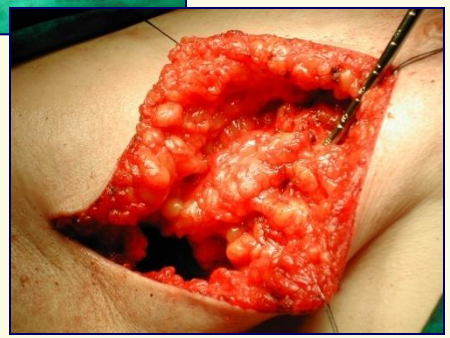


1. Campo post-resezione

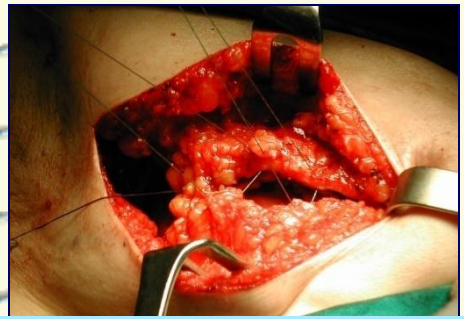


2. Scollamento cute

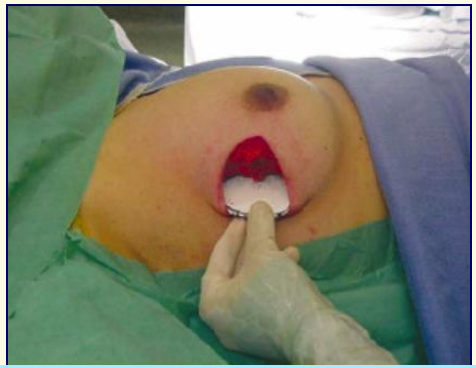




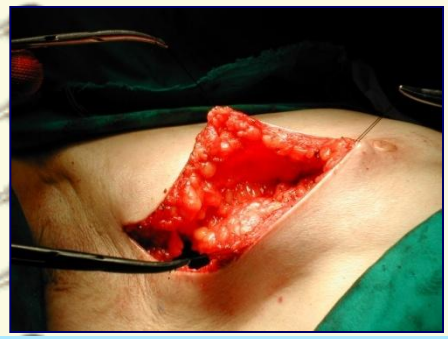
4. Misurazione spessore



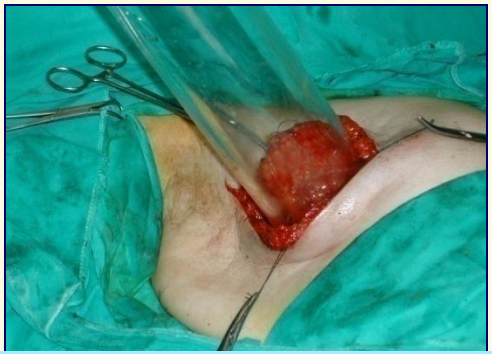
3. Accostamento ghiandola



6. Posizionamento disco



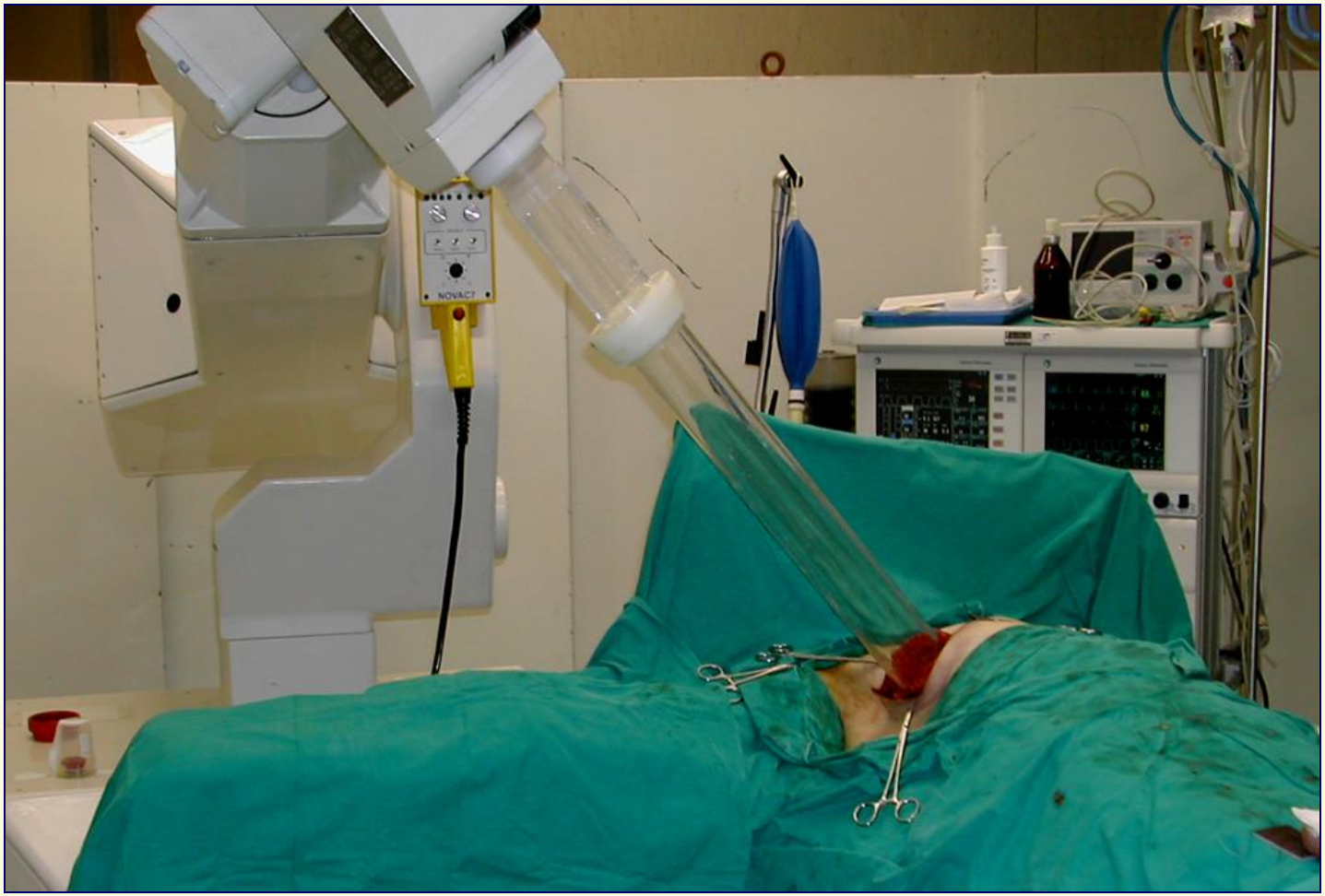
5. Allontanamento cute



7. Campo di irradiazione

# Note Di Tecnica

## Irradiazione



Int. J. Radiation Oncology Biol. Phys., Vol. ■, No. ■, pp. 1–8, 2010

0360-3016/10/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2009.10.032

**CLINICAL INVESTIGATION**

# COSMETIC OUTCOMES FOR ACCELERATED PARTIAL BREAST IRRADIATION BEFORE SURGICAL EXCISION OF EARLY-STAGE BREAST CANCER USING SINGLE-DOSE INTRAOPERATIVE RADIOTHERAPY

RANDALL J. KIMPLE, M.D., PH.D.,* NANCY KLAUBER-DEMORE, M.D.,†¶ CHERIE M. KUZMIAK, D.O.,‡¶ DAG PAVIC, M.D.,‡¶ JUN LIAN, PH.D.,* CHAD A. LIVASY, M.D.,§¶ LAURA ESLER, B.A.,* DOMINIC T. MOORE, M.P.H.,¶ CAROLYN I. SARTOR, M.D.,*¶ AND DAVID W. OLLILA, M.D.†¶

Departments of *Radiation Oncology, †Surgery, ‡Radiology, and §Pathology, and the ¶Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, NC

**Purpose:** Determine cosmetic outcome and toxicity profile of intraoperative radiation delivered before tumor excision for patients with early-stage breast cancer.

**Methods and Materials:** Patients age 48 or older with ultrasound-visible invasive ductal cancers <3 cm and clinically negative lymph nodes were eligible for treatment on this institutional review board—approved Phase II clinical trial. Treatment planning ultrasound was used to select an electron energy and cone size sufficient to cover the tumor plus a 1.5- to 2.0-cm circumferential margin laterally and a 1-cm-deep margin with the 90% isodose line. The dose was prescribed to a nominal 15 Gy and delivered using a Mobetron electron irradiator before tumor excision by segmental mastectomy. Physician- and patient-assessed cosmetic outcome and patient satisfaction were determined by questionnaire.

**Results:** From March 2003 to July 2007, 71 patients were treated with intraoperative radiation therapy. Of those, 56 patients were evaluable, with a median follow-up of 3.1 years (minimum 1 year). Physician and patient assessment of cosmesis was "good or excellent" (Radiation Therapy Oncology Group cosmesis scale) in 45/56 (80%) and 32/42 (76%) of all patients, respectively. Eleven patients who received additional whole breast radiation had similar rates of good or excellent cosmesis: 40/48 (83%) and 29/36 (81%), respectively). Grade 1 or 2 acute toxicities were seen in 4/71 (6%) patients. No Grade 3 or 4 toxicities or serious adverse events have been seen.

**Conclusion:** Intraoperative radiotherapy delivered to an *in situ* tumor is feasible with acceptable acute tolerance. Patient and physician assessment of the cosmetic outcome is good to excellent. © 2010 Elsevier Inc.

Breast cancer, Accelerated partial breast irradiation, Intraoperative radiation.

# Early Breast Cancer Boost

## STUDI RANDOMIZZATI

*Romestaing '97*
*Bartelink '01*
*Polgar '02*

BOOST vs no BOOST

EORTC 22881-10882 *Poortmans PM '08*

5.659 pz. T1-2, N0-1 '89-'96

% RECIDIVA a 10 aa.

6.2% vs 10.2%

p< 0.0001

# Iort In Breast Cancer as a Boost

## Iort-boost Ebm

- ✓ Crescente evidenza di fattibilità ed efficacia
- ✓ Incoraggianti risultati a lungo termine
- ✓ Metodica potenzialmente › al boost postop.

**DobelbowerRR ’89**
**Dubois JB ’97**
**Merrik HW ’97**
**Veronesi U ’01**
**Reitsamer R’04,‘06**
**Ciabattoni A ’05**
**Vaidya J ’06**
**Lemanski ’06**
**Sedelmayer F ’07**
**Ivaldi GB. ’08**
**ISIORT ’08**
**Wenz F ‘08**

Strahlenther Onkol. 2001 Jul;177(7):330-7.

# [Intraoperative radiotherapy (IORT) in treatment of breast carcinoma--a new therapeutic alternative within the scope of breast-saving therapy? Current status and future prospects. Report of experiences from the European Institute of Oncology (EIO), Mailand]

[Article in German]

Gatzemeier W, Orecchia R, Gatti G, Intra M, Veronesi U.

Division of Senology, European Institute of Oncology, Milan, Italy. wgatzemei@aol.com

## Abstract

BACKGROUND: External beam radiation therapy (EBRT) represents an integral component of breast-conserving treatment. In published series it has been demonstrated that the external boost can be replaced by intraoperative radiotherapy (IORT) where irradiation at a single dose from 10 up to 15 Gy was safely delivered directly to the tumor bed. PATIENTS AND METHODS: At the European Institute of Oncology, Milan, we initiated a dose escalation study to investigate the feasibility of applying single doses of IORT from 10 Gy up to 22 Gy. A portable IORT equipment with different electron energies was used. From July to December 1999, a total of 65 patients with T1-2 (max. 2.5 cm) No-1 breast cancer, median age 58 years (range 33-80 years) was treated. Ten patients received 10 Gy, eight patients were treated with an IORT of 15 Gy, eight received 17 Gy, six had 19 Gy, and 33 were treated with 21-22 Gy. Patients with 10 and 15 Gy received an additional EBRT of 44 and 40 Gy, respectively. In all other patients IORT was the sole radiation treatment. RESULTS: No acute side effects or intermediate untoward effects after a follow-up from three to nine months related to IORT were observed. CONCLUSIONS: Since the applicator can be safely placed under the control of the surgeon and radiotherapist IORT has the potential of accurately treating the tumor bed. Skin and subcutaneous tissue are not irradiated thus decreasing the potential risk of fibrosis and eventually obtaining a better cosmesis. With IORT single doses of 22 Gy being equivalent to a 60 Gy EBRT can safely be delivered. Even so the average time of operation was prolonged by around 20 minutes IORT application ultimately improves the quality of life of the patients in shortening overall treatment. Long-term follow-up is necessary to demonstrate whether large single doses of IORT might have the potential of sufficient local tumor control without major side effects. As a future perspective a randomized trial comparing EBRT with IORT as sole treatment will be performed.

# Iort in Breast Cancer as a Boost

Int J Cancer. 2006 Jun 1;118(11):2882-7.

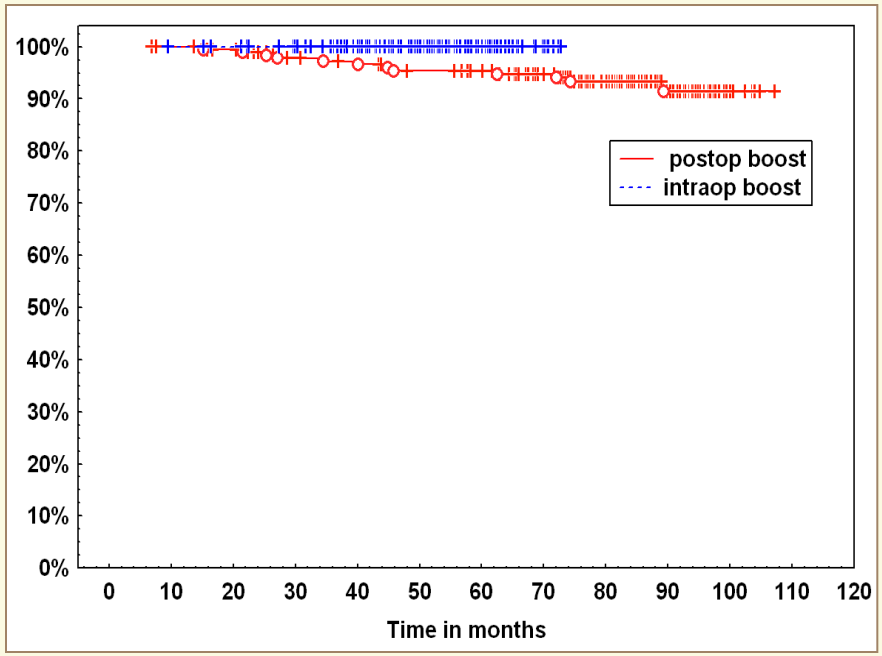
**The Salzburg concept of intraoperative radiotherapy for breast cancer: results and considerations.**

Reitsamer R, Sedlmayer F, Kopp M, Kametriser G, Menzel C, Deutschmann H, Nairz O, Hitzl W, Peintinger F.

Confronto sequenziale
378 pz.cr invasivo T1-2 N0-1

F. up mediano: 51 mesi

IORT-BOOST vs BOOST postop




RECIDIVA LOCALE a 5 aa.

0% vs 4.3%

p= 0.002

> LC con IORT-BOOST

Int J Cancer 2006

Int J Radiat Oncol Biol Phys. 2006 Apr 1;64(5):1410-5. Epub 2006 Jan 25.

# Intraoperative radiotherapy given as a boost for early breast cancer: long-term clinical and cosmetic results.

Lemanski C, Azria D, Thezenas S, Gutowski M, Saint-Aubert B, Rouanet P, Fenoglietto P, Ailleres N, Dubois JB.

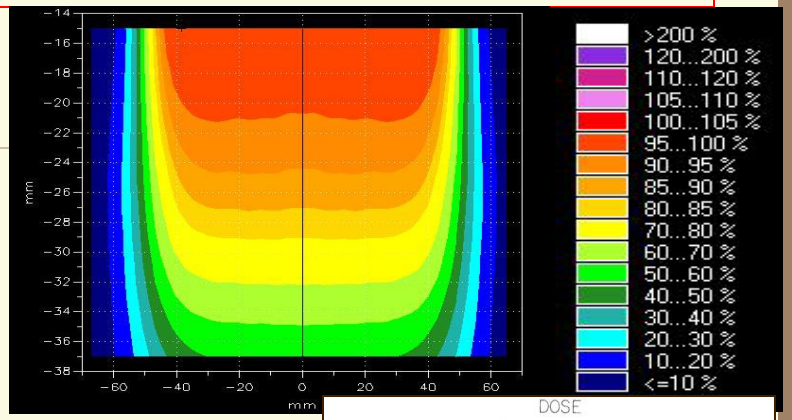
Department of Radiation Oncology, Val d'Aurelle Cancer Institute, Montpellier, France.

## Abstract

PURPOSE: The standard radiotherapy (RT) of breast cancer consists of 50 Gy external beam RT (EBRT) to the whole breast followed by an electron boost of 10-16 Gy to the tumor bed, but this has several cosmetic disadvantages. Intraoperative radiotherapy (IORT) could be an alternative to overcome these. METHODS AND MATERIALS: We evaluated 50 women with early breast cancer operated on in a dedicated IORT facility. Median dose of 10 Gy was delivered using 9-MeV electron beams. All patients received postoperative EBRT (50 Gy in 2 Gy fractions). Late toxicity and cosmetic results were assessed independently by two physicians according to the Common Terminology Criteria for Adverse Event v3.0 grading system and the European Organization for Research and Treatment of Cancer questionnaires. RESULTS: After a median follow-up of 9.1 years (range, 5-15 years), two local recurrences were observed within the primary tumor bed. At the time of analysis, 45 patients are alive with (n = 1) or without disease. Among the 42 disease-free remaining patients, 6 experienced Grade 2 late subcutaneous fibrosis within the boost area. Overall, the scores indicated a very good quality of life and cosmesis was good to excellent in the evaluated patients. CONCLUSION: Our results confirm that IORT given as a boost after breast-conserving surgery is a reliable alternative to conventional postoperative fractionated boost radiation.

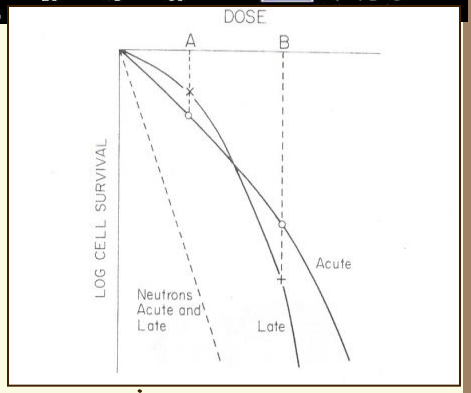
# Iort in Breast Cancer as a Boost

## VANTAGGI TECNICI




Esatta definizione del target
Dislocazione /schermatura degli OAR
Distribuzione omogenea della dose

## VANTAGGI RADIOBIOLOGICI




Stimato $\alpha/\beta \sim 4$ Gy nel carcinoma mammario
Effetto radiobiologico della dose singola elevata
Azione sul potenziale residuo tumorale micro-macroscopico
Annulla il ripopolamento cellulare accelerato post-chirurgico
Perdita della proliferazione, migrazione, invasione cellulare dopo IORT

*Whelan T '02, Shelley W '00, Yarnold J '05, Calvo F '06, Belletti B '08*

# Iort In Breast Cancer As Boost

## EFFETTO RADIOBIOLOGICO DELLA SINGOLA DOSE

Dose singola elevata = 2-3 volte la stessa dose impiegata con frazionamento convenzionale

WBRT 50Gy + IORT-BOOST

| BOOST | DOSE TOT |
|---|---|
| 10 Gy | ~70 Gy |

Calvo F JCO '06

Breast. 2008 Dec;17(6):617-22. Epub 2008 Jul 22.

**Early initiation of external beam radiotherapy (EBRT) may increase the risk of long-term toxicity in patients undergoing intraoperative radiotherapy (IORT) as a boost for breast cancer.**

Wenz F, Welzel G, Keller A, Blank E, Vorodi F, Herskind C, Tomé O, Sütterlin M, Kraus-Tiefenbacher U.

Department of Radiation Oncology, University of Heidelberg, University Medical Center Mannheim, Theodor-Kutzer Ufer 1-3, 68167 Mannheim, Germany. frederik.wenz@medma.uni-heidelberg.de

Abstract

BACKGROUND: Intraoperative radiotherapy (IORT) during breast-conserving surgery is increasingly used. We analyzed the influence of the interval between an IORT boost and external beam radiotherapy (EBRT) on late toxicity. METHODS: Forty-eight patients received 20 Gy IORT (50 kV X-rays (Intrabeam, Carl Zeiss, Oberkochen, Germany) followed by 46-50 Gy EBRT with a median interval of 36 days (14-197). Late toxicity was assessed with the modified LENT SOMA score after a median of 36 months. RESULTS: Twelve patients developed a higher grade fibrosis ( degrees II-III), three teleangiectases, one a breast edema grade degrees II, six retractions, four hyperpigmentations and five pain ( degrees II-III). The median interval between IORT and EBRT was significantly shorter in these patients (n=18) compared to the 30 patients without higher grade toxicity (29.5 days vs. 39.5 days, p=0.023, Mann-Whitney U-test). CONCLUSION: Starting EBRT about 5-6 weeks after IORT appears to be associated with a decreased risk of chronic late toxicity compared with a shorter interval. The impact on local recurrence of prolonged gaps between IORT and EBRT is not known.

L'intervallo di tempo IORT BOOST-WBRT può influenzare il controllo tumorale e la tossicità:

Effetto detrimentale in TCP correlato al dilazionamento e al tempo totale di trattamento RT

WBRT dopo 6 settimane dal boost IORT è associata a < tossicità

Nell' esperienza clinica l'intervallo è nel range 4-7 settimane

*Wenz F '08, Wyatt RM '08,*

# Partial breast irradiation

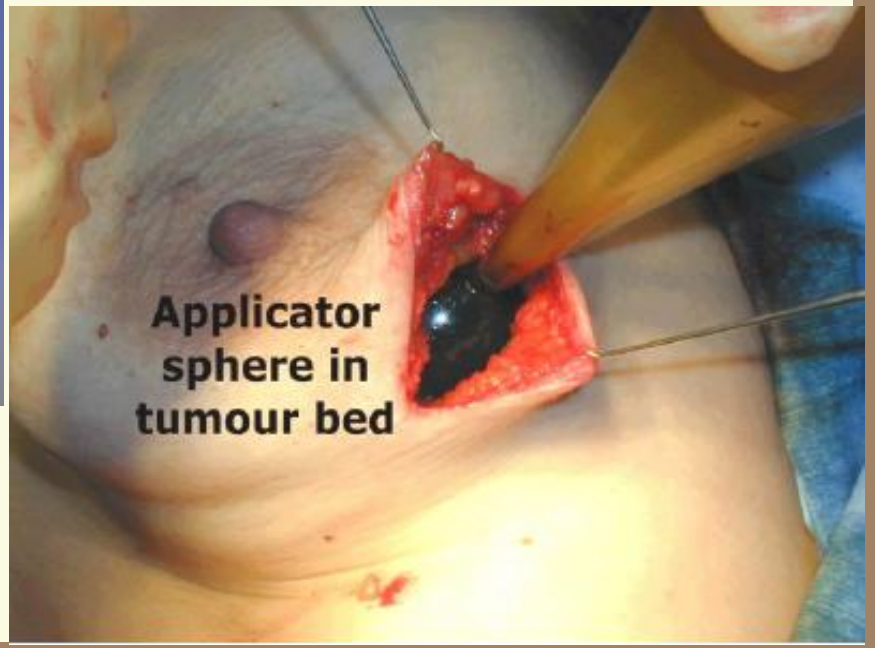
# Targit PRS 400 Intrabeam


Caduta estremamente rapida della dose

Trattamento intraoperatorio a ferita aperta dopo verifica margini

Irradiazione della cavità chirurgica a 360°

Calcolo della dose a 0.5 cm dalla superficie



ARTICLE IN PRESS

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. ■, No. ■, pp. 1–6, 2010

0360-3016/10/$–see front matter

doi:10.1016/j.ijrobp.2009.06.085

**CLINICAL INVESTIGATION**

# INTRAOPERATIVE RADIOTHERAPY AS A BOOST DURING BREAST-CONSERVING SURGERY USING LOW-KILOVOLTAGE X-RAYS: THE FIRST 5 YEARS OF EXPERIENCE WITH A NOVEL APPROACH

FREDERIK WENZ, M.D.,* GRIT WELZEL, M.SC.,* ELENA BLANK, M.S.,* BRIGITTE HERMANN, M.D.,* VOLKER STEIL, M.SC.,* MARC SÜTTERLIN, M.D.,† AND UTA KRAUS-TIEFENBACHER, M.D.*

Departments of *Radiation Oncology and †Obstetrics and Gynecology, University Medical Center Mannheim, University of Heidelberg, Mannheim, Germany

**Purpose:** Intraoperative radiotherapy (IORT) during breast-conserving surgery (BCS) has been recently introduced using different devices. We report the first 5 years of a single-center experience after introduction of a novel approach to deliver IORT as a tumor bed boost during BCS for breast cancer.

**Methods and Materials:** A total of 155 breast cancers in 154 women (median age, 63 years; range, 30–83 years; T1/T2 = 100/55; N0/N+ = 108/47) were treated between February 2002 and December 2007 at the University Medical Center Mannheim, in whom IORT as tumor bed boost was applied using 50-kV X-rays (20 Gy) followed by 46–50 Gy whole-breast external-beam radiotherapy (EBRT). Chemotherapy, if indicated, was given before EBRT. The median interval between BCS plus IORT and EBRT was 40 days. Median follow-up was 34 months (maximum 80 months, 1 patient lost to follow-up). Overall survival and local relapse-free survival were calculated at 5 years using the Kaplan-Meier method. Seventy-nine patients were evaluated at 3-year follow-up for late toxicity according to the Late Effects in Normal Tissues–Subjective, Objective, Management, and Analytic system.

**Results:** Ten patients died, 2 had in-breast relapse, and 8 developed distant metastases (5-year overall survival = 87.0%; 5-year local relapse-free survival = 98.5%). Grade 3 fibroses of the tumor bed were detected in 5% of the patients after 3 years. Skin toxicity was mild (telangiectases and hyperpigmentations in approximately 6% each).

**Conclusions:** Intraoperative radiotherapy as a tumor bed boost during BCS for breast cancer using low-kilovoltage X-rays followed by EBRT yields low recurrence and toxicity rates. © 2010 Elsevier Inc.

Breast cancer, Intraoperative radiotherapy, Boost, Local recurrence, Late toxicity.

# TARGIT: PRS 400 –INTRABEAM

## VANTAGGI

- ✓ Piccole dimensioni dello strumento
- ✓ Utilizzo di raggi x di energie modeste → pochi problemi radioprotezionistici

## SVANTAGGI

- ✓ Trattamento effettuato prima di conoscere l'esame istologico definitivo
- ✓ Difficile una buona conformazione della dose per volumi bersaglio non sferici
- ✓ Utilizzo di raggi x di energie modeste→ rapida attenuazione della dose in profondita
- ✓ (20 Gy → 5 Gy a 1 cm)

# PBI: CONCLUSION

APBI is a new technology that provides faster, more convenient treatment after breast-conserving surgery and that may ultimately demonstrate longterm effectiveness and safety comparable to WBI for selected patients with early breast cancer

CONSENSUS STATEMENT

**Accelerated Partial Breast Irradiation Consensus Statement from the American Society for Radiation Oncology (ASTRO)**

Vol. 209, No. 2, August 2009

# PBI :CONCLUSION

Interstitial brachytherapy is the technique with the longest followup reported; follow up data for other APBI techniques remain limited.

Currently,there are insufficient clinical and dosimetric data to determine the optimal technique for APBI delivery.

CONSENSUS STATEMENT

**Accelerated Partial Breast Irradiation Consensus Statement from the American Society for Radiation Oncology (ASTRO)**

Vol. 209, No. 2, August 2009

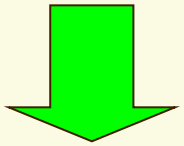
# PBI: CONCLUSIONI

- le diverse metodiche di partial breast irradiation non sono equivalenti
- notevoli diversità del volume irradiato
- necessità di linee guida specifiche
- nell'ambito di studi controllati

Workshop Bethesda 8-10/12/2002 - J Natl Cancer Inst 2004, 96: 175-84

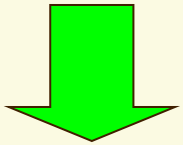
# PROBLEMATICHE APERTE

Programmi di screening



Diagnosi precoce, in fase preclinica

Qualità degli esami mammografici



Migliore valutazione multifocalità

# PROBLEMATICHE APERTE

- Imaging
- Criteri di selezione delle pazienti
- Tecniche di irradiazione
- Tipo di frazionamento
- Dose totale
- Associazione con CT e/o OT
- Incidenza di recidiva locale nel quadrante e al di fuori
- Sopravvivenza libera da malattia e globale
- Tossicità acuta e tardiva
- Cosmesi
- Qualità di vita

RISPONDERANNO GLI STUDI RANDOMIZZATI IN CORSO

# Grazie per l'attenzione

Marco Lioce

Raffaella Caponio