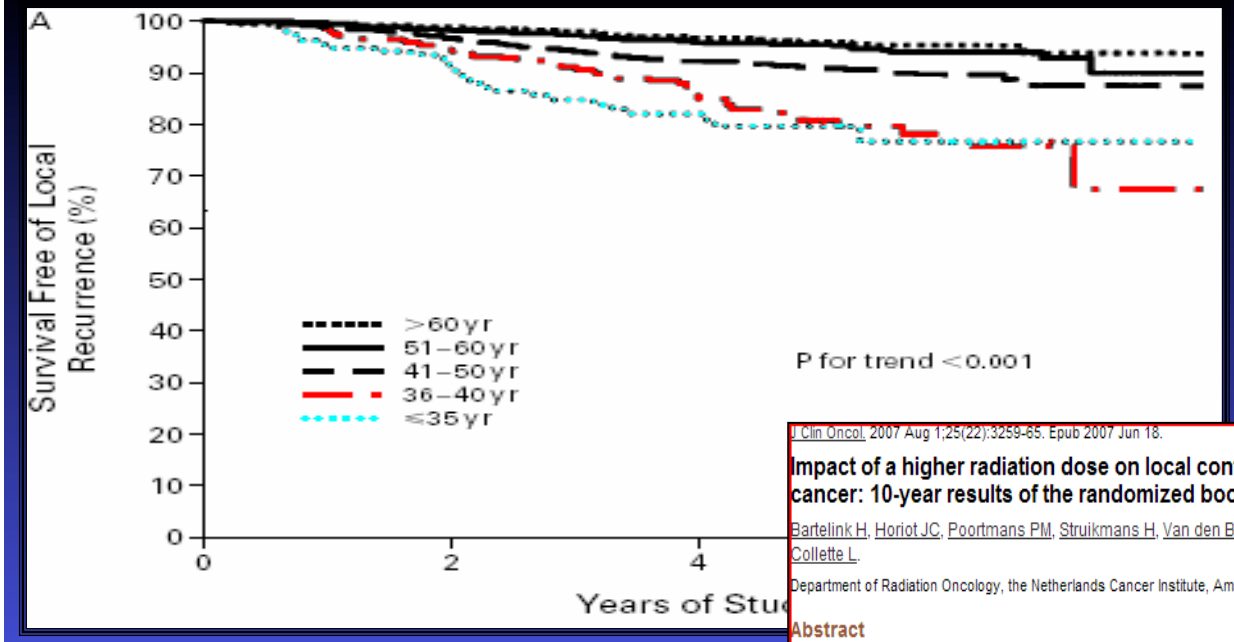
# L'impatto sulla tossicità cronica del trattamento adiuvante radio-chemioterapico del carcinoma della mammella dopo intervento chirurgico conservativo nelle pazienti trattate con ELIOT sul letto operatorio come boost e schema ipofrazionato sulla mammella in toto


J Clin Oncol. 2007 Aug 1;25(22):3259-65. Epub 2007 Jun 18.

**Impact of a higher radiation dose on local control and survival in breast-conserving therapy of early breast cancer: 10-year results of the randomized boost versus no boost EORTC 22881-10882 trial.**

Bartelink H, Horiot JC, Poortmans PM, Struikmans H, Van den Bogaert W, Fourquet A, Jager JJ, Hoogenraad WJ, Oei SB, Wárlám-Rodenhuis CC, Pierart M, Collette L.

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**Abstract**

**PURPOSE:** To investigate the long-term impact of a boost radiation dose of 16 Gy on local control, fibrosis, and overall survival for patients with stage I and II breast cancer who underwent breast-conserving therapy.

**PATIENTS AND METHODS:** A total of 5,318 patients with microscopically complete excision followed by whole-breast irradiation of 50 Gy were randomly assigned to receive either a boost dose of 16 Gy (2,661 patients) or no boost dose (2,657 patients), with a median follow-up of 10.8 years.

**RESULTS:** The median age was 55 years. Local recurrence was reported as the first treatment failure in 278 patients with no boost versus 165 patients with boost; at 10 years, the cumulative incidence of local recurrence was 10.2% versus 6.2% for the no boost and the boost group, respectively (P < .0001). The hazard ratio of local recurrence was 0.59 (0.46 to 0.76) in favor of the boost, with no statistically significant interaction per age group. The absolute risk reduction at 10 years per age group was the largest in patients <or= 40 years of age: 23.9% to 13.5% (P = .0014). As a result, the number of salvage mastectomies has been reduced by 41%. Severe fibrosis was statistically significantly increased (P < .0001) in the boost group, with a 10-year rate of 4.4% versus 1.6% in the no boost group (P < .0001). Survival at 10 years was 82% in both arms.

**CONCLUSION:** After a median follow-up period of 10.8 years, a boost dose of 16 Gy led to improved local control in all age groups, but no difference in survival.

| | Bartelink | Ipofrazionamenti |
|---|---|---|
| Ys>50 | 0.7% | 0,4 % (START A) |
| Ys 41-50 | 1,2% | 0,72% (Whelan) |
| Ys 35-40 | 2% | 0,72% (Whelan) |

# Tasso annuale di recidiva locale

-Ys>50: 0.7% (Bartelink)

0.4 % (START B ipofrazionamento)

-Ys 41-50: 1.2% (Bartelink)

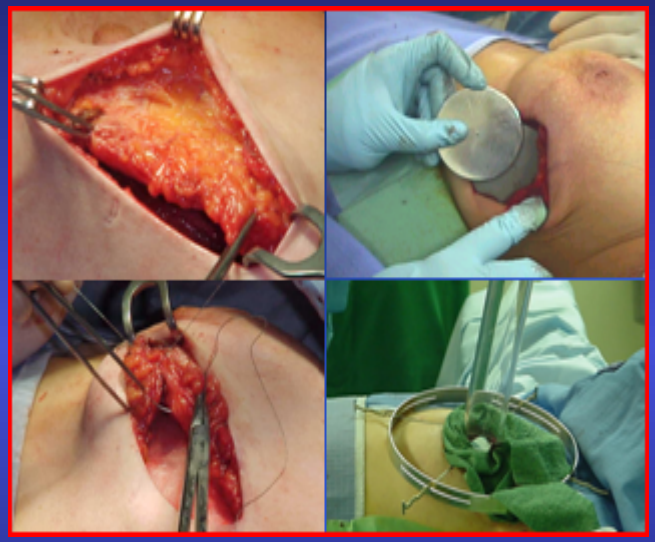
0.72 % (Whelan ipofrazionamento)

-Ys 35-40: 2% (Bartelink)

0.72 % (Whelan ipofrazionamento)

# ELIOT BOOST

pazienti premenopausa



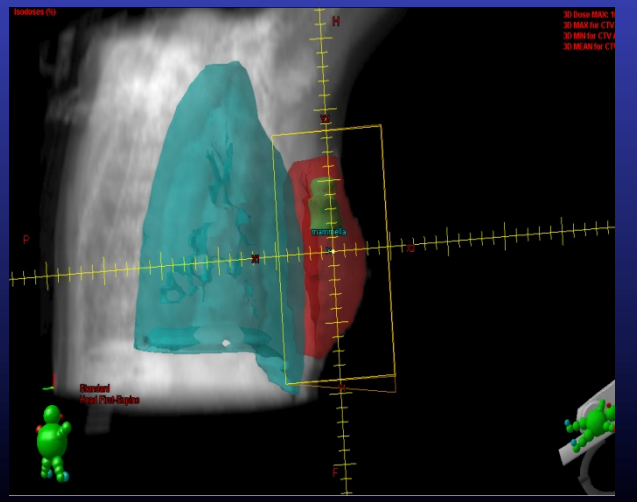
**CHIRURGIA**

**+**

**ELIOT BOOST (12 Gy)**

**RTE IPOFRAZIONATA 3D**

**(2.85 Gy/FR x 13 fr)**



Radiother Oncol. 2013 Aug;108(2):279-86. doi: 10.1016/j.radonc.2013.05.031. Epub 2013 Jul 2.

# IORT with electrons as boost strategy during breast conserving therapy in limited stage breast cancer: Long term results of an ISIORT pooled analysis.

Fastner G, Sedlmayer F, Merz F, Deutschmann H, Reitsamer R, Menzel C, Stierle C, Farmini A, Fischer T, Ciabattoni A, Mirri A, Hager E, Reinartz G, Lemanski C, Orecchia R, Valentini V.

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## Abstract

**PURPOSE:** Linac-based intraoperative radiotherapy with electrons (IOERT) was implemented to prevent local recurrences after breast conserving therapy (BCT) and was delivered as an intraoperative boost to the tumor bed prior to whole breast radiotherapy (WBI). A collaborative analysis has been performed by European ISIORT member institutions for long term evaluation of this strategy.

**MATERIAL AND METHODS:** Until 10/2005, 1109 unselected patients of any risk group have been identified among seven centers using identical methods, sequencing and dosage for intra- and postoperative radiotherapy. A median IOERT dose of 10Gy was applied (90% reference isodose), preceding WBI with 50-54Gy (single doses 1.7-2Gy).

**RESULTS:** At a median follow up of 72.4months (0.8-239), only 16 in-breast recurrences were observed, yielding a local tumor control rate of 99.2%. Relapses occurred 12.5-151months after primary treatment. In multivariate analysis only grade 3 reached significance (p=0.031) to be predictive for local recurrence development. Taking into account patient age, annual in-breast recurrence rates amounted 0.64%, 0.34%, 0.21% and 0.16% in patients <40years; 40-49years; 50-59years and □60years, respectively.

**CONCLUSION:** In all risk subgroups, a 10Gy IOERT boost prior to WBI provided outstanding local control rates, comparing favourably to all trials with similar length of follow up.



**KEYWORDS:** Boost, Breast cancer, Electrons, IOERT, Intraoperative radiotherapy

$$EQD2 = D \frac{d + (\alpha/\beta)}{2 + (\alpha/\beta)} \Rightarrow EQD2 = 37.05 \frac{2.85 + 4}{2+4} = 42.3 \text{ Gy}$$

- $EQD_{2,T} = EQD_{2,t} - (T-t) \times D_{prolif} \Rightarrow EQD_{2,17} = 42.3 - (17-33) \times 0.7 = 53.5$ Gy

( tenendo conto dell'effetto tempo, la dose di 37.05 Gy in 2.85 Gy /die in 17 giorni corrisponde radiobiologicamente alla dose di 53.5 Gy erogata in 2 Gy/frazione, utilizzando un valore di $\alpha/\beta$ pari a 4;

- Utilizzando ancora il modello lineare-quadratico, la cui validità sembra confermata fino a 18 Gy in singola somministrazione (29), utilizzando un valore di $\alpha/\beta$ pari a 4, 12 Gy erogati in singola frazione equivalgono a 32 Gy somministrati con schema convenzionale di 2 Gy/frazione

## Preliminary results of electron intraoperative therapy boost and hypofractionated external beam radiotherapy after breast-conserving surgery in premenopausal women.

Ivaldi GB, Leonardi MC, Orecchia R, Zerini D, Morra A, Galimberti V, Gatti G, Luini A, Veronesi P, Ciocca M, Sangalli C, Fodor C, Veronesi U.

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### Abstract

**PURPOSE:** To report the acute and preliminary data on late toxicity of a pilot study of boost with electron intraoperative therapy followed by hypofractionated external beam radiotherapy (HEBRT) of the whole breast.

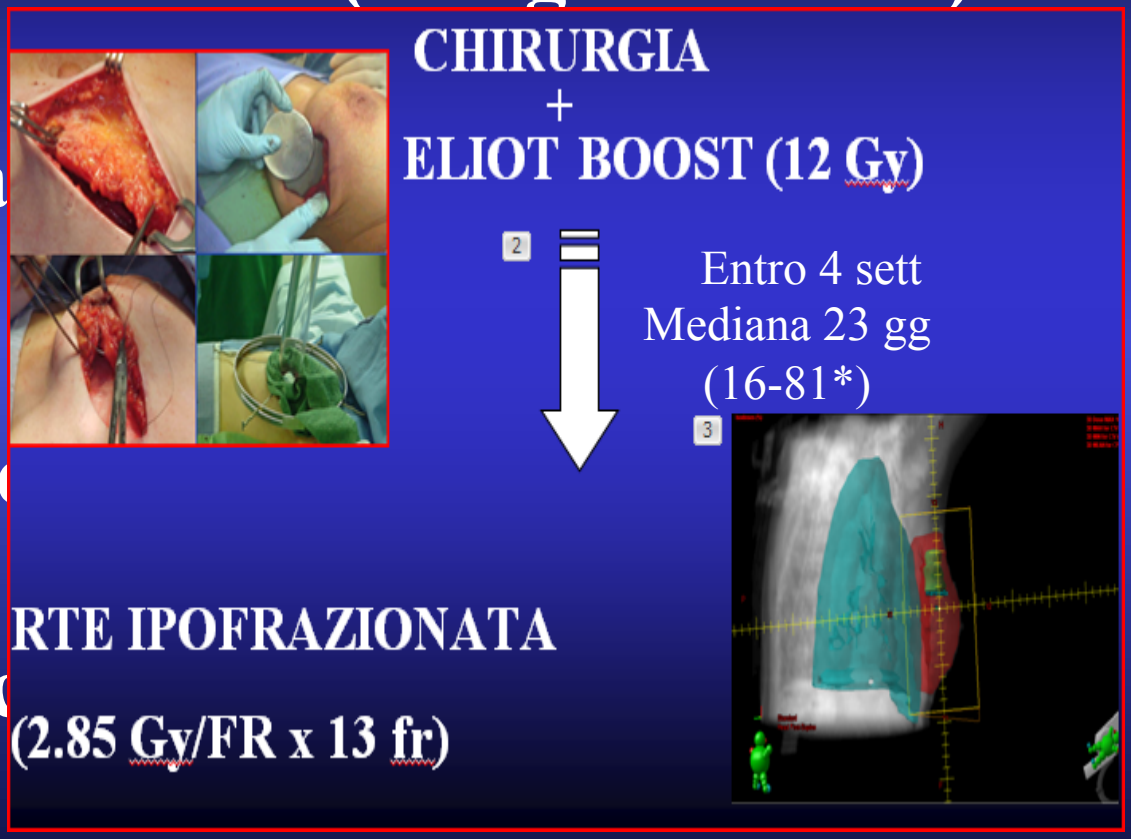
**METHODS AND MATERIALS:** Between June 2004 and March 2007, 211 women with a diagnosis of early-stage breast cancer were treated with breast-conserving surgery. During surgery, an electron intraoperative therapy boost of 12 Gy was administered to the tumor bed. Adjuvant local treatment was completed with HEBRT, consisting of a course of 13 daily fractions of 2.85 Gy to the whole breast to a total dose of 37.05 Gy. Acute toxicity of the breast was evaluated at the end of HEBRT and at 1 month of follow-up. Late toxicity was recorded at 6 and 12 months of follow-up.

**RESULTS:** We report the data from 204 patients. The maximal acute skin toxicity was observed at the end of HEBRT (182 patients evaluable) with 7 (3.8%) Grade 3, 52 (28.6%) Grade 2, 123 (67.6%) Grade 1, and no Grade 0 or Grade 4 cases. A total of 108 patients were evaluated for late toxicity. The recorded late skin toxicity was Grade 4 in 1 patient (0.9%), Grade 3 in 1 patient, and Grade 2 or less in 106 patients (98.2%).

**CONCLUSIONS:** The results of this study have shown that electron intraoperative therapy followed by HEBRT allows for the delivery of a high dose to the tumor bed and an adequate dose to the whole breast. This treatment is feasible, compliance is high, and the rate of acute toxicity and the preliminary data on chronic toxicity seem acceptable.

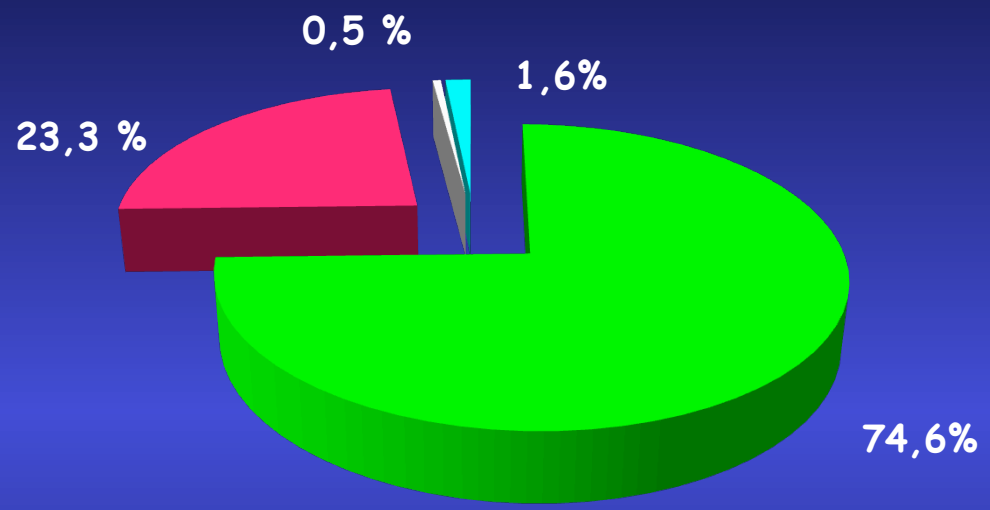
# Materiali e metodi (1)

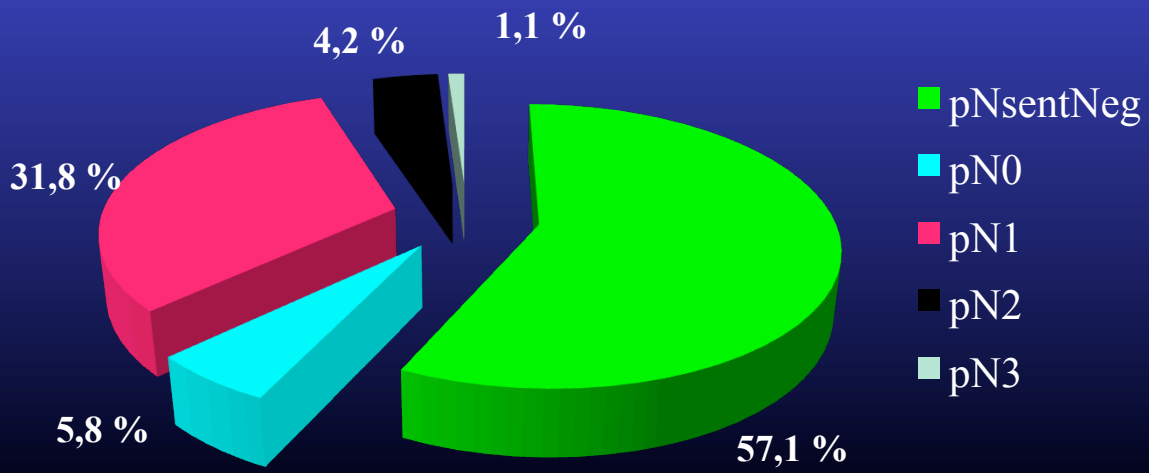
- **189 pazienti con F.U. minimo di 24 mesi**
  **Mediana 64.3 mesi (Range 24 - 94.7)**
- **Tutte le pz ha**
  **radioterapia**
- **Età all'interv**
- **cT1-T3, cN0-**
- **Chirurgia conservativa (in 64 casi + DA)**



# Materiali e metodi (2)

## 189 pazienti



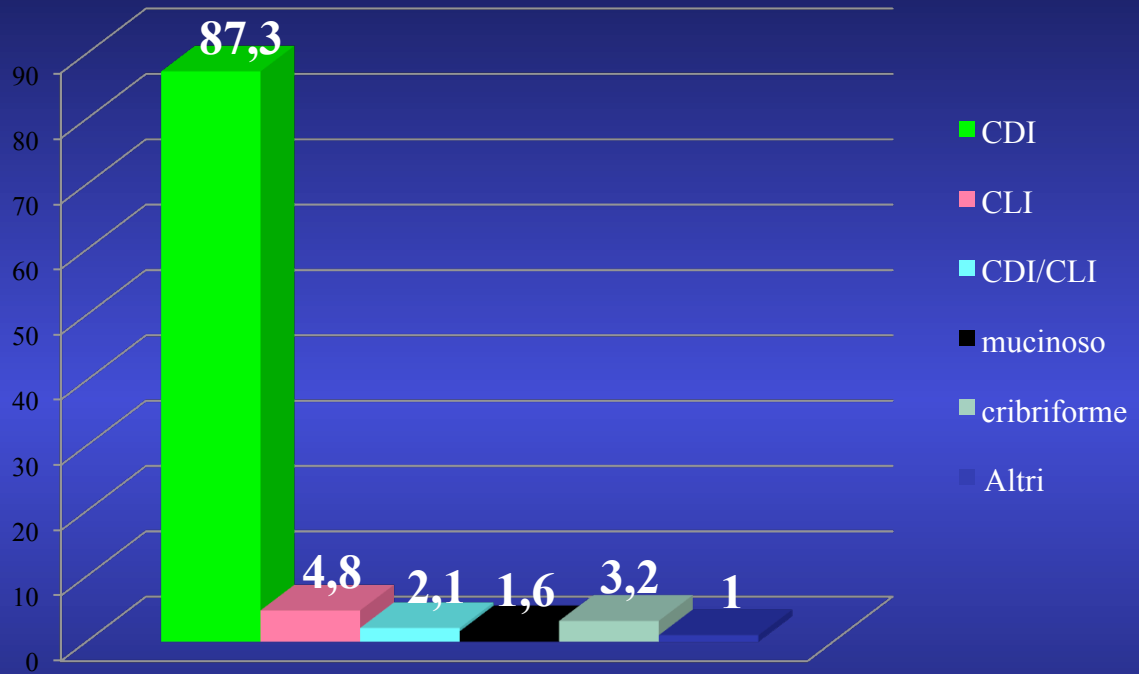



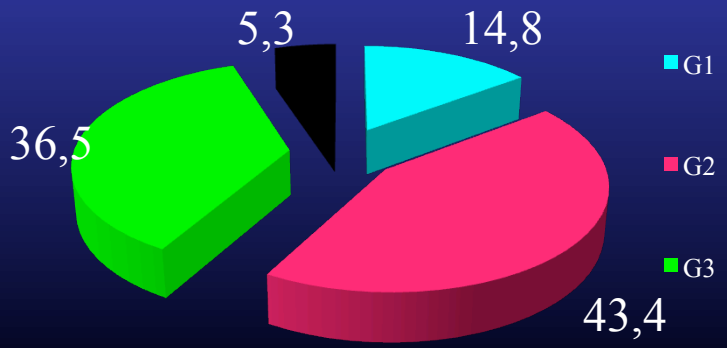

| Stadio | N pazienti (189) |
|---|---|
| 0 | 2 |
| I | 92 |
| IIA | 69 |
| IIB | 15 |
| IIIA | 8 |
| IIIC | 3 |

# Materiali e metodi (3)

189 pazienti

ISTOLOGIA %




GRADING %

# Trattamento sistemico

- 76 p
  in
  34
  26
  16
- 109
- 4 p

## TIMING OF CHEMOTHERAPY AFTER MAMMOSITE RADIATION THERAPY SYSTEM BREAST BRACHYTHERAPY: ANALYSIS OF THE AMERICAN SOCIETY OF BREAST SURGEONS MAMMOSITE BREAST BRACHYTHERAPY REGISTRY TRIAL


Bruce G. Haffty, M.D.,[*] Frank A. Vicini, M.D.,[†] Peter Beitsch, M.D.,[‡] Coral Quiet, M.D.,[§] Angela Keleher, M.D.,[‖] Delia Garcia, M.D.,[¶] Howard Snider, M.D.,[#] Mark Gittleman, M.D.,[**] Victor Zannis, M.D.,[††] Henry Kuerer, M.D.,[‡‡] Eric Whitacre, M.D.,[§§] Pat Whitworth, M.D.,[‖‖] Richard Fine, M.D.,[¶¶] and Martin Keisch, M.D.[##]

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**Purpose:** To evaluate cosmetic outcome and radiation recall in the American Society of Breast Surgeons registry trial, as a function of the interval between accelerated partial breast irradiation (APBI) and initiation of chemotherapy (CTX).

**Methods and Materials:** A total of 1440 patients at 97 institutions participated in this trial. After lumpectomy for early-stage breast cancer, patients received APBI (34 Gy in 10 fractions) with MammoSite RTS brachytherapy. A total of 148 patients received CTX within 90 days of APBI. Cosmetic outcome was evaluated at each follow-up visit and dichotomized as excellent/good or fair/poor.

**Results:** Chemotherapy was initiated at a mean of 3.9 weeks after the final MammoSite procedure and was administered ≤3 weeks after APBI in 54 patients (36%) and >3 weeks after APBI in 94 patients (64%). The early and delayed groups were well balanced with respect to multiple factors that may impact on cosmetic outcome. There was a superior cosmetic outcome in those receiving chemotherapy >3 weeks after APBI (excellent/good in 72.2% at ≤3 weeks vs. excellent/good in 93.8% at >3 weeks; $p = 0.01$). Radiation recall in those receiving CTX at ≤3 weeks was 9 of 50 (18%), compared with 6 of 81(7.4%) in those receiving chemotherapy at >3 weeks ($p = 0.09$).

**Conclusion:** The majority of patients receiving CTX after APBI have excellent/good cosmetic outcomes, with a low rate of radiation recall. Chemotherapy initiated >3 weeks after the final MammoSite procedure seems to be associated with a better cosmetic outcome and lower rate of radiation recall. An excellent/good cosmetic outcome in patients receiving CTX after 3 weeks was similar to the cosmetic outcome of the overall patient population who did not receive CTX.

- For the purpose of the study, patients were categorized into two groups; endocrine therapy alone and chemotherapy ( with or without endocrine therapy). The CT group was further stratified according to the time interval between the RT completion and the CT initiation: subgroup 1 within 7 days , subgroup 2 from day to day 15, subgroup 3 from day 16 and on. In the context of late toxicity, the first analysis is addressed to detect any difference between HT and CT groups, and within CT groups, any influence of timing of initiation. Subsequent analysis investigate the impact of different CT schedules on late side effects and cosmesis.

# Tossicità Cronica

F.U. mediano: 64.3 mesi

- **SCALA SOMA LENT**
- **Tossicità complessiva** (valore massimo riscontrato tra mammella/letto chirurgico alla data dell'ultimo contatto) : dolore e fibrosi
- Tossicità globale (189 pz)
- Confronto CT vs HT
- Influenza timing CT (gruppo 1 vs 2 vs 3)

# Risultati (1)

- Tossicità globale (189 pz)

**Dolore**

| Grado | N (%) |
|---|---|
| 0 | 138 (73,1) |
| 1 | 42 (22,2) |
| 2 | 9 (4,7) |
| 3 | 0 |

26.9%

**Fibrosi**

| | |
|---|---|
| 2 | 42 (22,2) |
| 3 | 3* (1,6) |

*letto chirurgico

**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.

**Intraoperative radiotherapy as a boost during breast-conserving surgery using low-kilovoltage X-rays: the first 5 years of experience with a novel approach.**

Wenz F, Welzel G, Blank E, Hermann B, Steil V, Sütterlin M, Kraus-Tiefenbacher U.

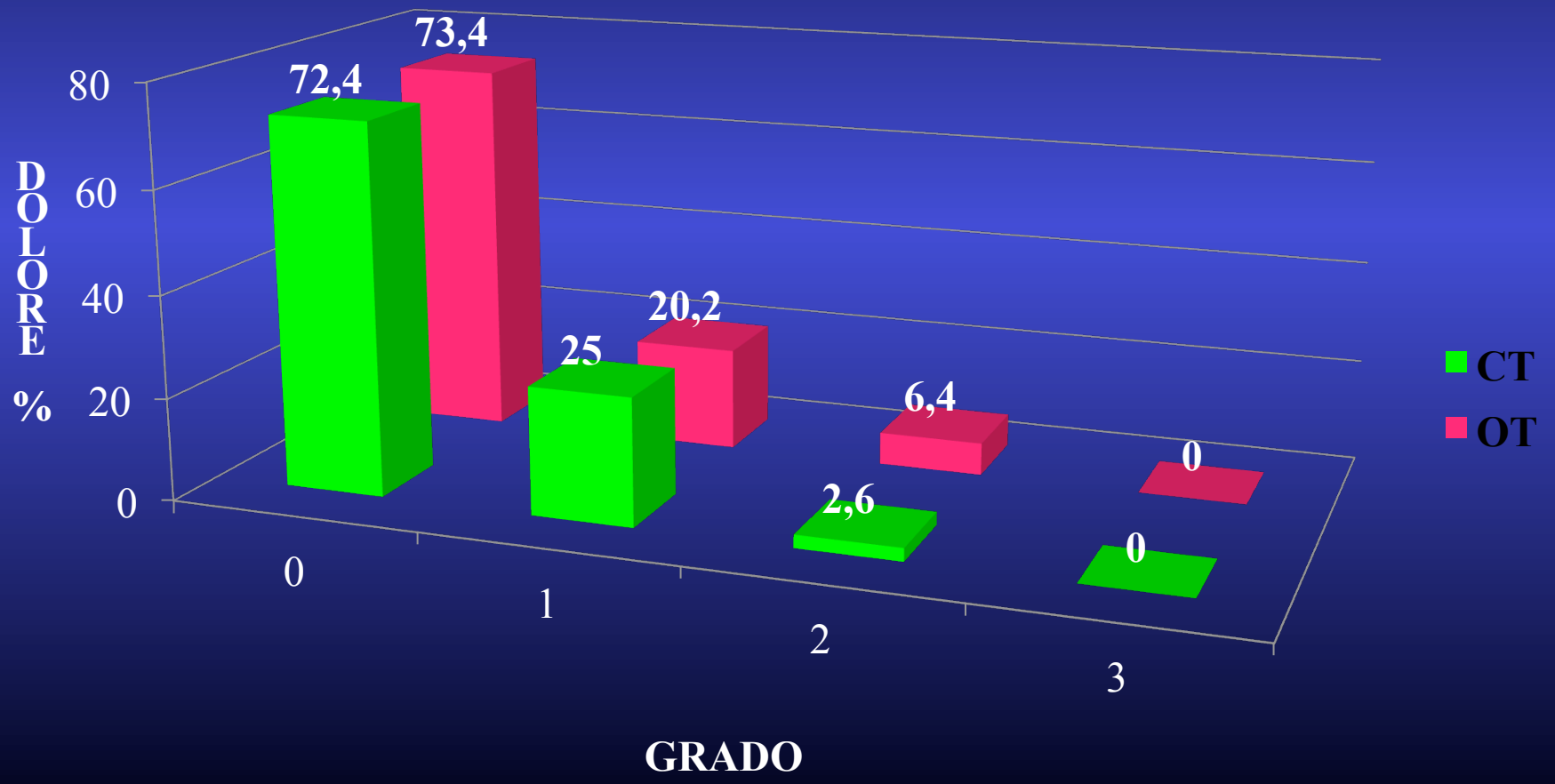
Department of Radiation Oncology, University Medical Center Mannheim, University of Heidelberg, Mannheim, Germany. frederik.wenz@medma.uni-heidelberg.de

| FIBROSI | | DOLORE G2 (9/189 PZ) |
|---|---|---|
| G0 | P: 0,03 | 2,5 % |
| G1 | | 5,6% |
| G2-3 | | 6,7% |

# Risultati (2)

solo per pz che fanno tp sistemica (185)

- Confronto CT (76 pz) vs HT (109): DOLORE



# Risultati (3)

- Confronto CT (76 pz) vs HT (109): FIBROSI

**Factors associated with optimal cosmetic results at 36 months in patients treated with accelerated partial breast irradiation (APBI) on the American Society of Breast Surgeons (ASBrS) MammoSite Breast Brachytherapy Registry Trial.**

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Department of Radiation Oncology, The Cancer Institute of New Jersey, New Brunswick, NJ, USA. goyalsh@umdnj.edu

**Abstract**

**PURPOSE:** To evaluate factors associated with optimal cosmetic results at 36 months for early-stage breast cancer patients enrolled on the American Society of Breast Surgeons (ASBrS) MammoSite Breast Brachytherapy registry trial.

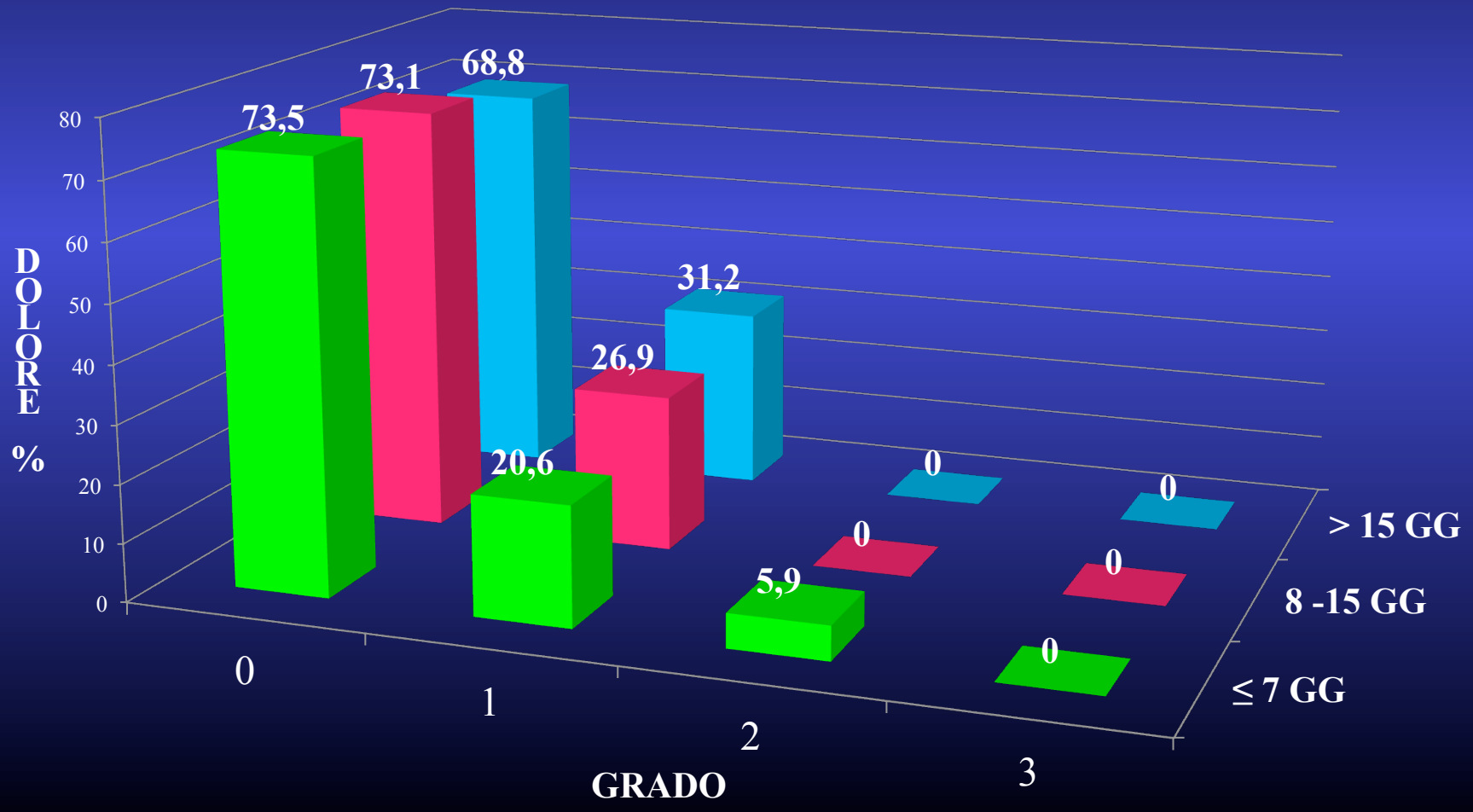
**MATERIALS AND METHODS:** 1,440 patients (1,449 cases) with early-stage breast cancer undergoing breast-conserving therapy were treated with the MammoSite radiation therapy system (RTS) brachytherapy catheter to deliver adjuvant accelerated partial breast irradiation (APBI) (34 Gy in 3.4-Gy fractions). Cosmetic outcome was evaluated at each follow-up visit and dichotomized as excellent/good or fair/poor. Median follow-up for surviving patients was 43.0 months (range 0-73.0 months).

**RESULTS:** The percentage of patients with good/excellent cosmetic results at 12, 24, 36, and 48 months were as follows: 94.5% (n = 950/1,005), 93.8% (n = 781/833), 93.1% (n = 683/734), and 90.4% (n = 520/575), respectively. Three-year absolute rates of good/excellent cosmesis were as follows: breast-related wound infection (BWI) (83.3%) versus no BWI (94%), <7 mm skin spacing (87.5%) versus >or=7 mm skin spacing (93.6%). Using multiple regression analysis, factors predictive of worse cosmetic outcome at 36 months included smaller skin spacing [odds ratio (OR) 1.06, confidence interval (CI) 1.01-1.12] and BWI (OR 0.33, CI 0.16-0.70). A predictive model developed showed that presence of a BWI, use of chemotherapy, and skin spacing had the most effect on cosmetic outcomes. However, in patients that did not develop a breast infection, skin spacing and use of chemotherapy had the most effect on cosmesis.

**CONCLUSION:** APBI delivered by MammoSite brachytherapy lead to good/excellent cosmesis in 93% of patients with 3-year follow-up. Breast wound infection, use of chemotherapy, and skin spacing were found to be the three most important predictors of cosmesis at 36 months in our cohort of

# Risultati (4)

- Confronto gruppi CT (pz: 34 vs 26 vs 16):DOLORE



# Risultati (5)

- Confronto gruppi CT (pz: 34 vs 26 vs 16): FIBROSI (G1+G2+G3)
  - →1: 78,8% (G2+G3: 45,4%)
  - →2: 53,8 % (G2+G3: 19,2%) P: 0.03
  - →3: 56,2% (G2+G3: 18.7%)

Int J Radiat Oncol Biol Phys. 2006 Feb 1;64(2):489-95. Epub 2005 Oct 24.

**Accelerated partial breast irradiation: an analysis of variables associated with late toxicity and long-term cosmetic outcome after high-dose-rate interstitial brachytherapy.**

Wazer DE, Kaufman S, Cuttino L, DiPetrillo T, Arthur DW.

Department of Radiation Oncology, Tufts-New England Medical Center, Tufts University School of Medicine, Boston, MA 02111, and Department of Radiation Oncology, Rhode Island Hospital, Providence, RI, USA. dwazer@tufts-nemc.org

# Conclusioni (1)

- *Vantaggi IORT e schemi ipofrazionati*
- *Tempistica accettabile per inizio CT*
- *Tossicità globale in linea con i dati di letteratura*
- *OT vs CT → Dolore = ; Fibrosi G2-G3 < OT*
- *Timing CT→Dolore = ; inizio > 8 gg dal termine RTP associato a fibrosi G2-G3 minore*

# Conclusioni (2)

- *Risultati incoraggianti*
- *Necessari altri studi*

*… Grazie per l'attenzione…*