III ZOOM Journal Club 2013

NH Hotel Bologna

21 Febbraio 2014

PBI: quali modalità di trattamento? In quali pazienti?

Rapporteur: **M. GATTI**

CANDIOLO Fondazione del Piemonte per l'Oncologia

QUAL E' IL RAZIONALE DELLA IRRADIAZIONE PARZIALE DELLA MAMMELLA

?

RAZIONALE I

- La filosofia attuale del trattamento locale del carcinoma della mammella prevede il trattamento dell'intera ghiandola facendo ricorso alla mastectomia totale o associando alla chirurgia conservativa la radioterapia sulla mammella residua.

- Studi istopatologici recenti suggeriscono che nelle pazienti candidate ad una chirurgia conservativa secondo le linee guida attuali sia improbabile l'estensione microscopica di malattia oltre 1 cm dai margini di resezione chirurgica

RAZIONALE II

- **Un altro dato a sostegno della irradiazione parziale della mammella deriva dal fatto che la maggior parte delle recidive locali si verificano nel quadrante mammario dove era localizzata la neoplasia primitiva**

- **La recidiva omolaterale al di fuori del quadrante interessato è da considerarsi un secondo tumore, in quanto l'intervallo libero da malattia è in genere superiore a 5 anni**

- **La RT non diminuisce il tasso di recidiva al di fuori del quadrante interessato**

- **Alla luce delle nuove acquisizioni si è suggerita una revisione dello standard terapeutico del trattamento radioterapico del carcinoma della mammella**

- **Studio di nuove metodiche di irradiazione finalizzate a diminuire la tossicità mediante l'utilizzo di tecniche sofisticate: la radioterapia conformazionale tridimensionale (3D-CRT), la radioterapia a modulazione di intensità (IMRT), la Tomoterapia, la brachiterapia e infine la radioterapia intraoperatoria (IORT)**

- **Accelerare il trattamento somministrando dosi più alte per frazione consentite dalla diminuzione dei volumi d'irradiazione (irradiazione parziale della mammella)**

PBI MODALITY

- **Tecniche -perioperatorie: the prescribed dose is delivered with electron-beam collimated on tumor bed using dedicated accelerator or traditional accelerator or with brachiterapy implant LDR, HDR or pulsed**

- **Tecniche post-operatorie: the prescribed dose is delivered on tumor bed only with mammosite® implant or with external radiotherapy 3D-CRT IMRT and TOMO**

ACCELERATED PARTIAL BREAST IRRADIATION USING 3D CONFORMAL RADIATION THERAPY (3D-CRT)

KATHY L. BAGLAN, M.D., MICHAEL B. SHARPE, PH.D., DAVID JAFFRAY, PH.D., ROBERT C. FRAZIER, M.D., JULIE FAYAD, M.S., LARRY L. KESTIN, M.D., VINCENT REMOUCHAMPS, M.D., ALVARO A. MARTINEZ, M.D., F.A.C.R., JOHN WONG, PH.D., AND FRANK A. VICINI, M.D.

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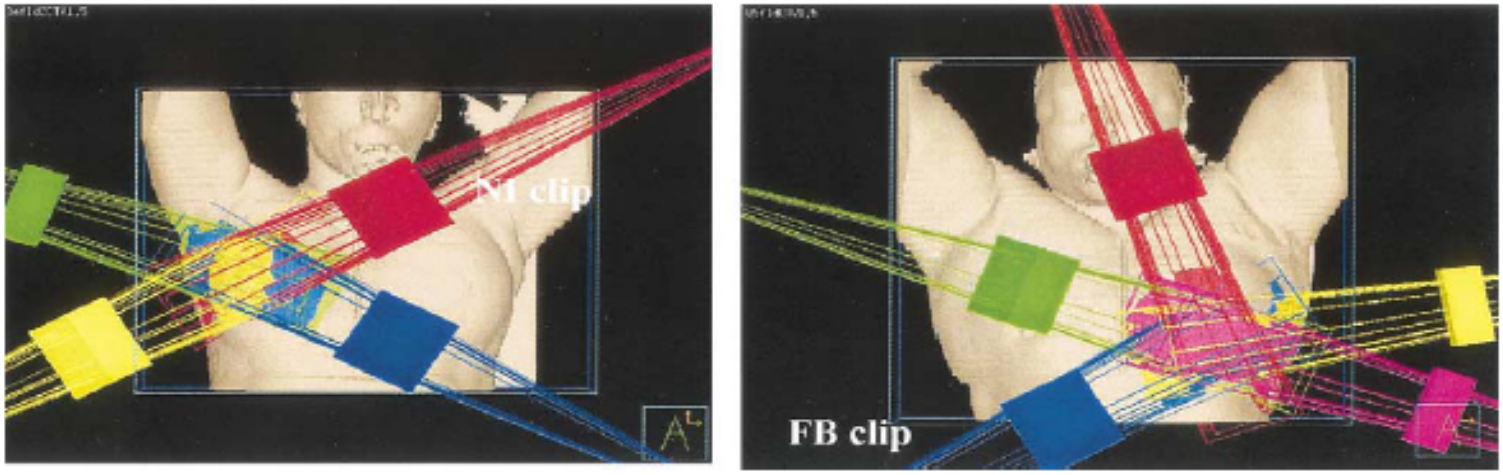

Fig. 1. Typical 4-field arrangement for right-sided lesions and 5-field arrangement for left-sided lesions.

ACCELERATED PARTIAL BREAST IRRADIATION CONSENSUS STATEMENT FROM THE AMERICAN SOCIETY FOR RADIATION ONCOLOGY (ASTRO)

Table 2. Patients "suitable" for APBI if all criteria are present

Factor	Criterion
Patient factors	
Age	≥60 y
BRCA1/2 mutation	Not present
Pathologic factors	
Tumor size	≤2 cm*
T stage	T1
Margins	Negative by at least 2 mm
Grade	Any
LVSI	No†
ER status	Positive
Multicentricity	Unicentric only
Multifocality	Clinically unifocal with total size ≤2.0 cm‡
Histology	Invasive ductal or other favorable subtypes§
Pure DCIS	Not allowed
EIC	Not allowed
Associated LCIS	Allowed
Nodal factors	
N stage	pN0 (i^-, i^+)
Nodal surgery	SN Bx or ALND‖
Treatment factors	
Neoadjuvant therapy	Not allowed

Table 3. "Cautionary" group: Any of these criteria should invoke caution and concern when considering APBI

Factor	Criterion
Patient factors	
Age	50–59 y
Pathologic factors	
Tumor size	2.1–3.0 cm*
T stage	T0 or T2
Margins	Close (<2 mm)
LVSI	Limited/focal
ER status	Negative†
Multifocality	Clinically unifocal with total size 2.1–3.0 cm‡
Histology	Invasive lobular
Pure DCIS	≤3 cm
EIC	≤3 cm

ACCELERATED PARTIAL BREAST IRRADIATION CONSENSUS STATEMENT FROM THE AMERICAN SOCIETY FOR RADIATION ONCOLOGY (ASTRO)

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Table 4. Patients "unsuitable" for APBI outside of a clinical trial if any of these criteria are present

Factor	Criterion
Patient factors	
Age	<50 y
BRCA1/2 mutation	Present
Pathologic factors	
Tumor size*	>3 cm
T stage	T3-4
Margins	Positive
LVSI	Extensive
Multicentricity	Present
Multifocality	If microscopically multifocal >3 cm in total size or if clinically multifocal
Pure DCIS	If >3 cm in size
EIC	If >3 cm in size
Nodal factors	
N stage	pN1, pN2, pN3
Nodal surgery	None performed
Treatment factors	
Neoadjuvant therapy	If used

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GEC-ESTRO Recommendations

Patient selection for accelerated partial-breast irradiation (APBI) after breast-conserving surgery: Recommendations of the Groupe Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) breast cancer working group based on clinical evidence (2009)

GEC-ESTRO recommendations on patient selection for accelerated partial-breast irradiation.

Characteristic	A/low-risk group – good candidates for APBI	B/intermediate-risk group – possible candidates for APBI	C/high-risk group – contraindication for APBI
Patient age	>50 years	>40–50 years	⩽40 years
Histology	IDC, mucinous, tubular, medullary, and colloid cc.	IDC, ILC, mucinous, tubular, medullary, and colloid cc	–
ILC	Not allowed	Allowed	–
Associated LCIS	Allowed	Allowed	–
DCIS	Not allowed	Allowed	–
HG	Any	Any	–
Tumour size	pT1–2 (⩽30 mm)	pT1–2 (⩽30 mm)	pT2 (>30 mm), pT3, pT4
Surgical margins	Negative (⩾2 mm)	Negative, but close (<2 mm)	Positive
Multicentricity	Unicentric	Unicentric	Multicentric
Multifocality	Unifocal	Multifocal (limited within 2 cm of the index lesion)	Multifocal (>2 cm from the index lesion)
EIC	Not allowed	Not allowed	Present
LVI	Not allowed	Not allowed	Present
ER, PR status	Any	Any	–
Nodal status	pN0 (by SLNB or ALND[a])	pN1mi, pN1a (by ALND[a])	pNx; ⩾pN2a (4 or more positive nodes)
Neoadjuvant chemotherapy	Not allowed	Not allowed	If used

Radiotherapy and Oncology 108 (2013) 209–214

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Phase II trial

Phase II trial of proton beam accelerated partial breast irradiation in breast cancer

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Background and purpose: Here, we report the results of our phase II, prospective study of proton beam accelerated partial breast irradiation (PB-APBI) in patients with breast cancer after breast conserving surgery (BCS).

Materials and methods: Thirty patients diagnosed with breast cancer were treated with PB-APBI using a single-field proton beam or two fields after BCS. The treatment dose was 30 cobalt gray equivalent (CGE) in six CGE fractions delivered once daily over five consecutive working days.

Results: All patients completed PB-APBI. The median follow-up time was 59 months (range: 43–70 months). Of the 30 patients, none had ipsilateral breast recurrence or regional or distant metastasis, and all were alive at the last follow-up. Physician-evaluated toxicities were mild to moderate, except in one patient who had severe wet desquamation at 2 months that was not observed beyond 6 months. Qualitative physician cosmetic assessments of good or excellent were noted in 83% and 80% of the patients at the end of PB-APBI and at 2 months, respectively, and decreased to 69% at 3 years. A good or excellent cosmetic outcome was noted in all patients treated with a two-field proton beam at any follow-up time point except for one. For all patients, the mean percentage breast retraction assessment (pBRA) value increased significantly during the follow-up period ($p = 0.02$); however, it did not increase in patients treated with two-field PB-APBI ($p = 0.3$).

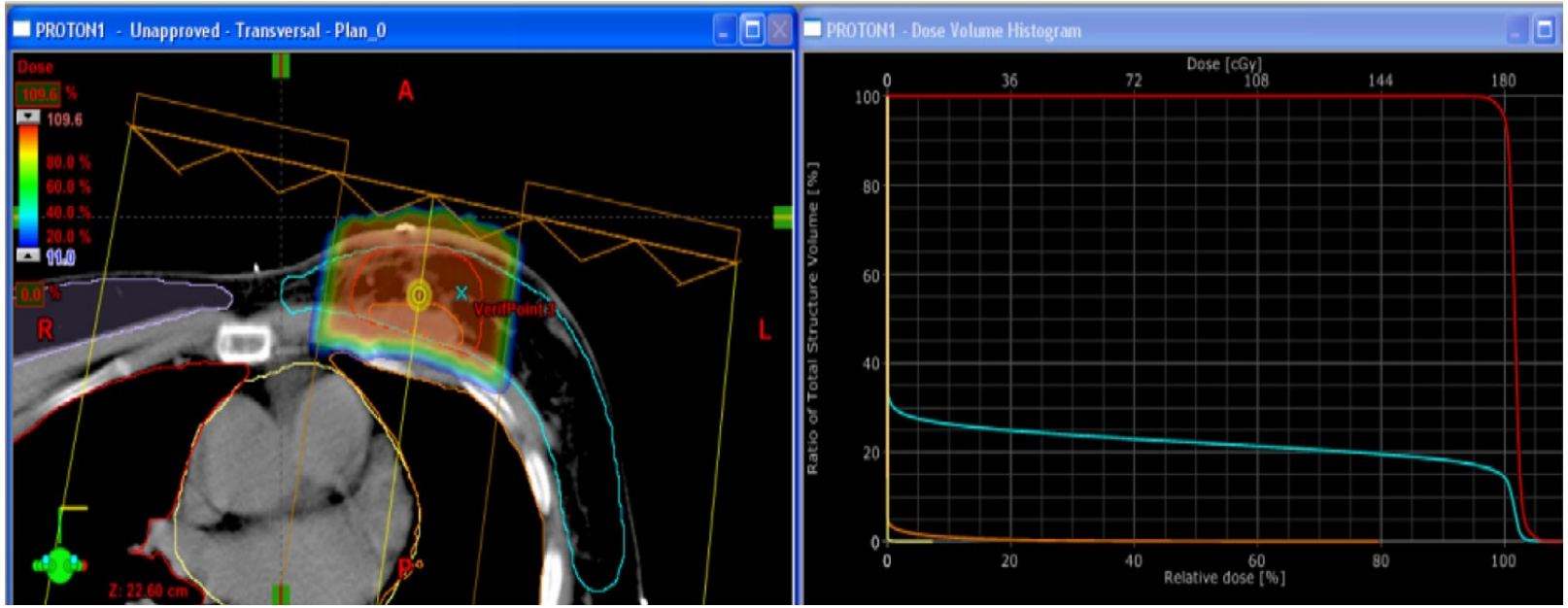
Conclusions: PB-APBI consisting of 30 CGE in six CGE fractions once daily for five consecutive days can be delivered with excellent disease control and tolerable skin toxicity to properly selected patients with early-stage breast cancer. Multiple-field PB-APBI may achieve a high rate of good-to-excellent cosmetic outcomes. Additional clinical trials with larger patient groups are needed.

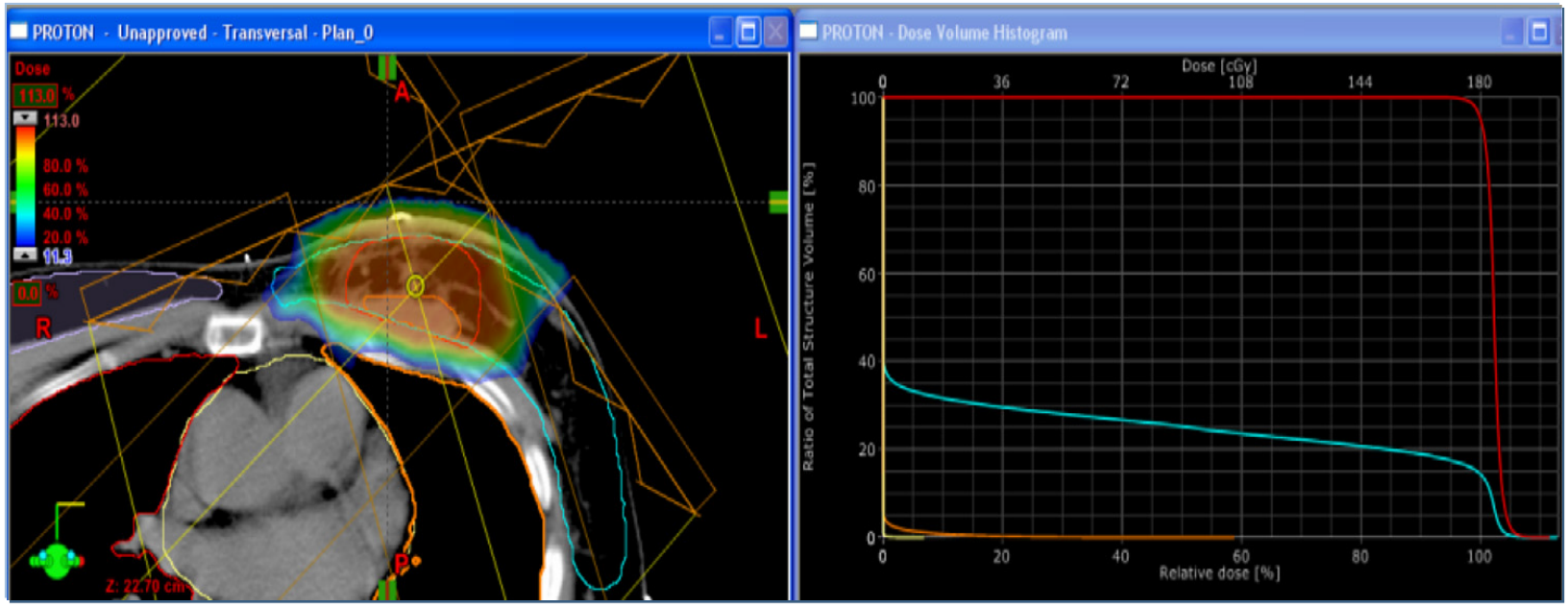
Treatment-related toxicities.

Toxicity	Incidence, % of patients																	
	At RT end			At 2 months				At 6 months			At 1 year			At 2 years			At 3 years		
	G0	G1	G2	G0	G1	G2	G3	G0	G1	G2	G0	G1	G2	G0	G1	G2	G0	G1	G2
Breast pain	22(73)	8(27)	0	19(63)	11(37)	0	0	27(90)	3(10)	0	29(97)	1(3)	0	26(96)	1(4)	0	22(96)	1(4)	0
Breast edema	28(93)	2(7)	0	23(77)	6(20)	1(3)	0	25(83)	4(13)	1(3)	28(93)	2(7)	0	27(100)	0	0	23(100)	0	0
Erythema / Hyperpigmentation	4(13)	26(87)	0	0	21(70)	9(30)	0	2(7)	24(80)	4(13)	6(20)	20(67)	4(15)	13(48)	12(44)	2(7)	9(39)	12(52)	2(9)
Wet desquamation	30(100)	0	0	24(80)	4(13)	1(3)	1(3)	29(97)	1(3)	0	30(100)	0	0	27(100)	0	0	23(100)	0	0
Induration	30(100)	0	0	0	0	0	0	25(83)	4(13)	1(3)	21(70)	7(23)	2(7)	19(70)	7(26)	1(4)	16(70)	6(26)	1(4)

Qualitative cosmetic outcome.

Physician Assessment	Number of patients (%)						
	Beam field	At pre-RT/RT end ($n = 30$)	At 2 months ($n = 30$)	At 6 months ($n = 30$)	At 1 year ($n = 30$)	At 2 years ($n = 27$)	At 3 years ($n = 23$)
Excellent	Single field	1 (3)	1 (3)	1 (3)	1 (3)	1 (4)	1 (4)
	Two fields	4 (14)	4 (14)	4 (14)	4 (14)	4 (15)	3 (13)
Good	Single field	10 (33)	9 (30)	7 (23)	7 (23)	7 (26)	7 (30)
	Two fields	10 (33)	10 (33)	11 (37)	11 (37)	8 (30)	5 (22)
Fair	Single field	4 (14)	4 (14)	5 (17)	6 (20)	6 (22)	5 (22)
	Two fields	1 (3)	1 (3)	1 (3)	1 (3)	1 (4)	1 (4)
Poor	Single field	0	1 (3)	1 (3)	0	0	1 (4)
	Two fields	0	0	0	0	0	0


PROTON1 - Unapproved - Transversal - Plan_0
Dose
109.6 %
109.6
80.0 %
60.0 %
40.0 %
20.0 %
11.0
0.0 %
A
R
L
P
VerifPoint 1
Z: 22.60 cm
PROTON1 - Dose Volume Histogram
Dose [cGy]
0
36
72
108
144
180
Ratio of Total Structure Volume [%]
100
80
60
40
20
0
0
20
40
60
80
100
Relative dose [%]


PROTON - Unapproved - Transversal - Plan_0
Dose
113.0 %
113.0
80.0 %
60.0 %
40.0 %
20.0 %
11.3
0.0 %
A
R
L
P
Z: 22.70 cm
PROTON - Dose Volume Histogram
Dose [cGy]
0
36
72
108
144
180
Ratio of Total Structure Volume [%]
100
80
60
40
20
0
0
20
40
60
80
100
Relative dose [%]

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Phase I/II trial

A phase I/II study piloting accelerated partial breast irradiation using CT-guided intensity modulated radiation therapy in the prone position ☆

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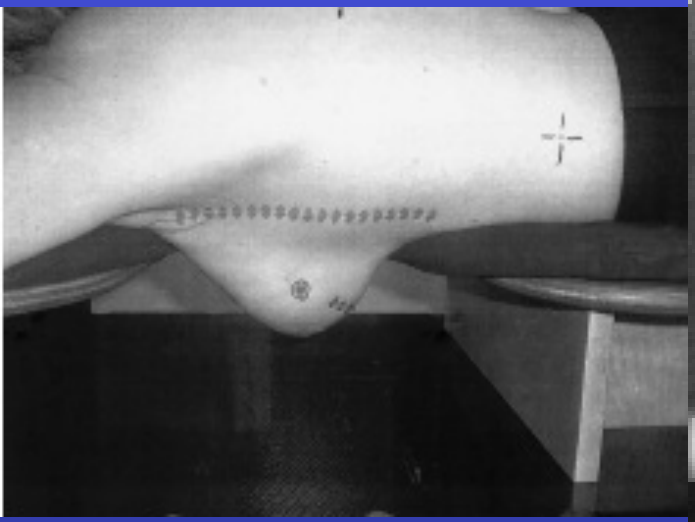
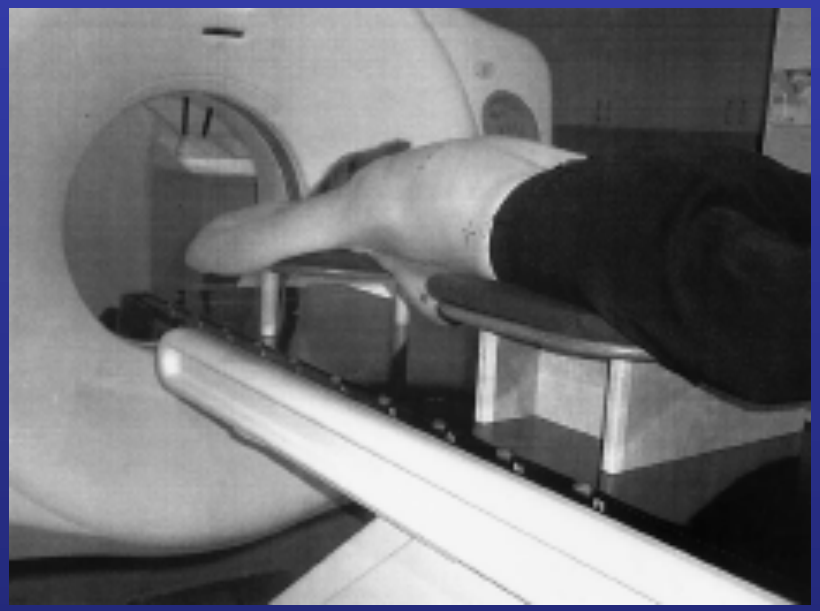
- Con questa tecnica gli autori enfatizzano la possibilità di diminuire l'espansione da CTV a PTV a 0.5 cm in virtù della minore escursione della parete toracica durante il respiro.
- …oltre ai noti vantaggi della posizione supina in termini esposizione della dose al cuore, al polmone e alla parete toracica, ma…intra-fraction reproducibility > inter-fraction reproducibility

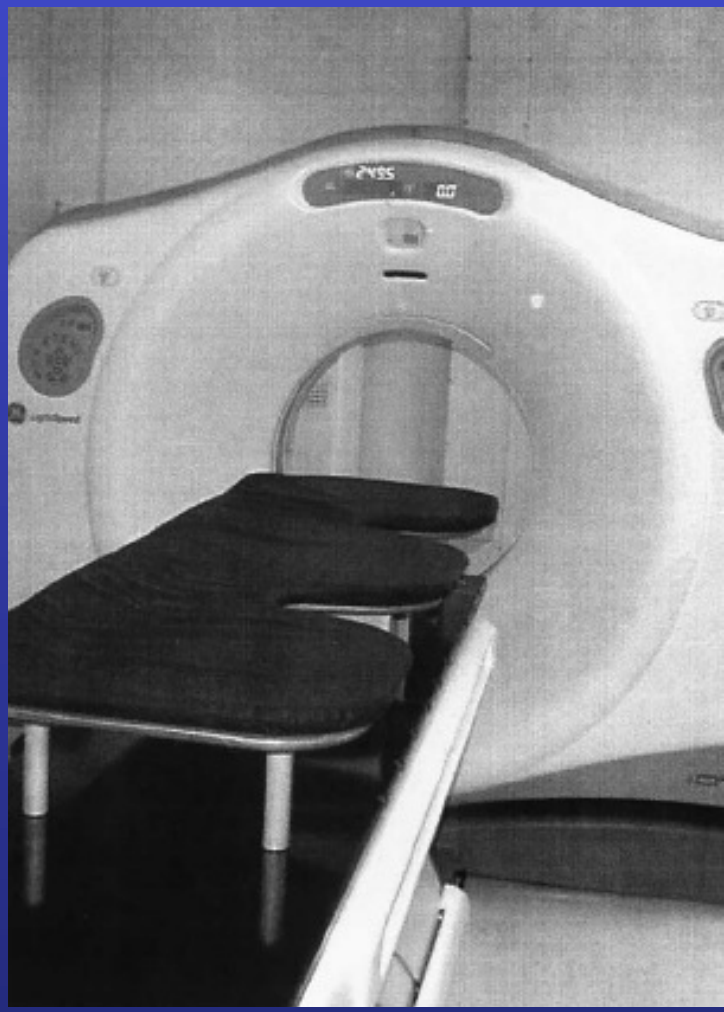
NYU 00-23: Prone accelerated breast irradiation (PABI)*

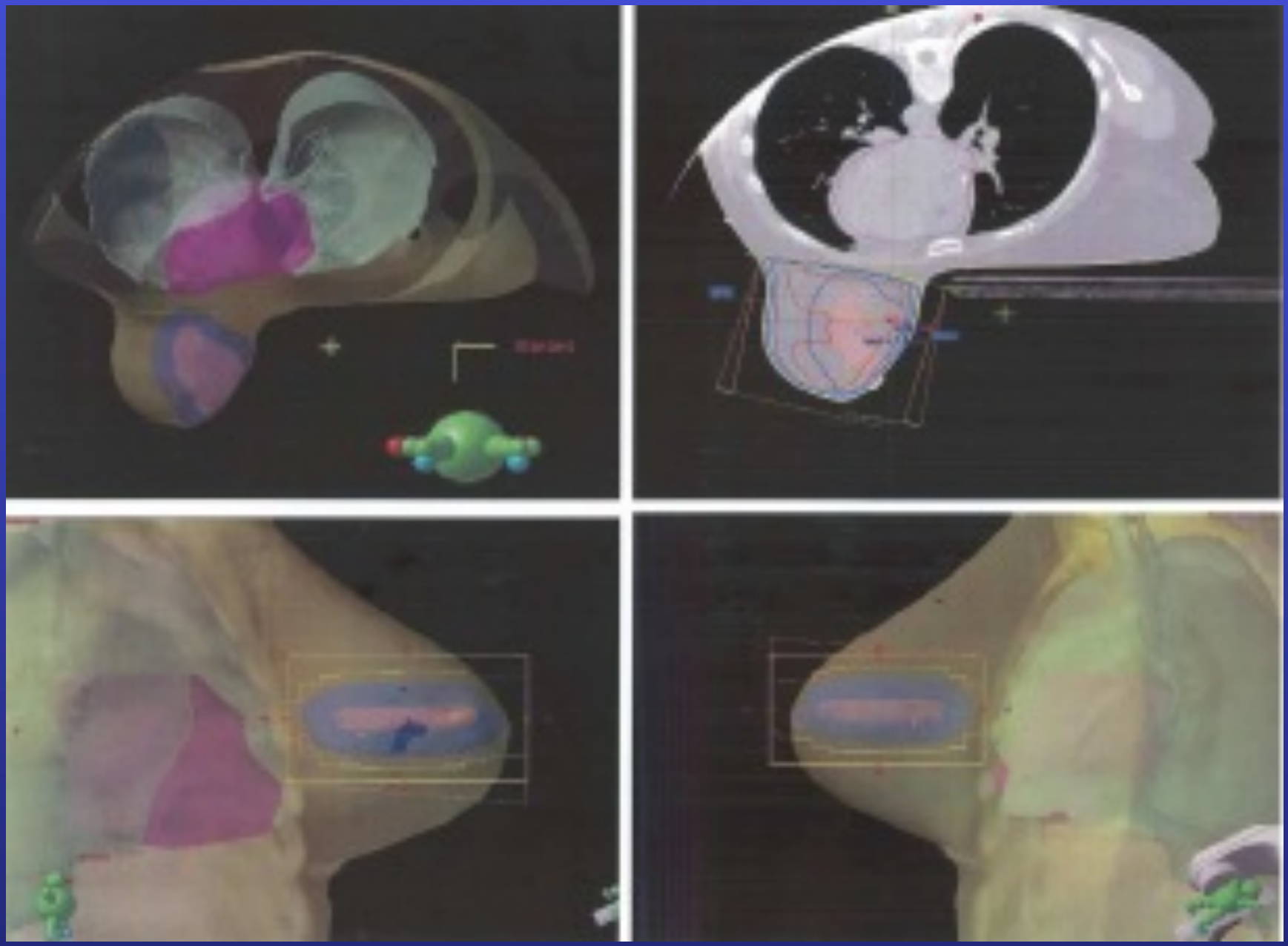
- **Eligible: post-menopausal breast cancer patients with non palpable, pT1 N0 M0, no EIC and negative margins (at least 5 mm), ER/PR positive**
- **RT dose/schedule: 600 cGy X 5, over 10 days.**
- **PTV: tumor bed with 1.5-2cm margins, imaged at CT in prone position on a dedicated table.**
- **Technique: parallel opposed mini-tangents---3fld photons or photons/electron—-4-5 non coplanar beams**

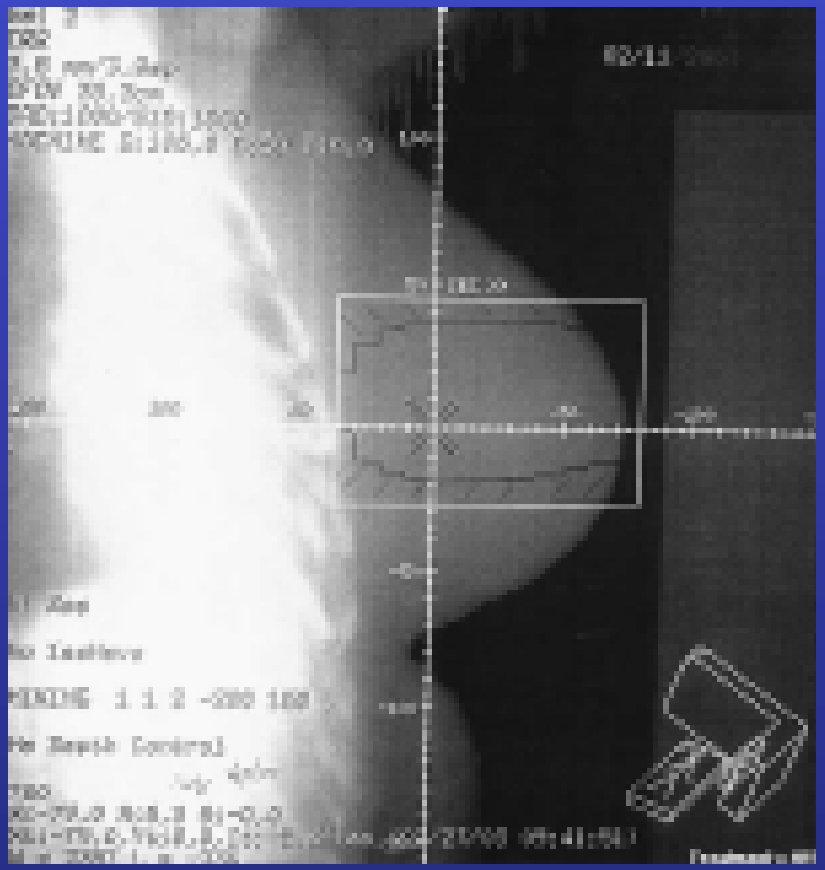
Silvia C.Formenti et al, Semin Radiat Oncol 15:92-99,2005

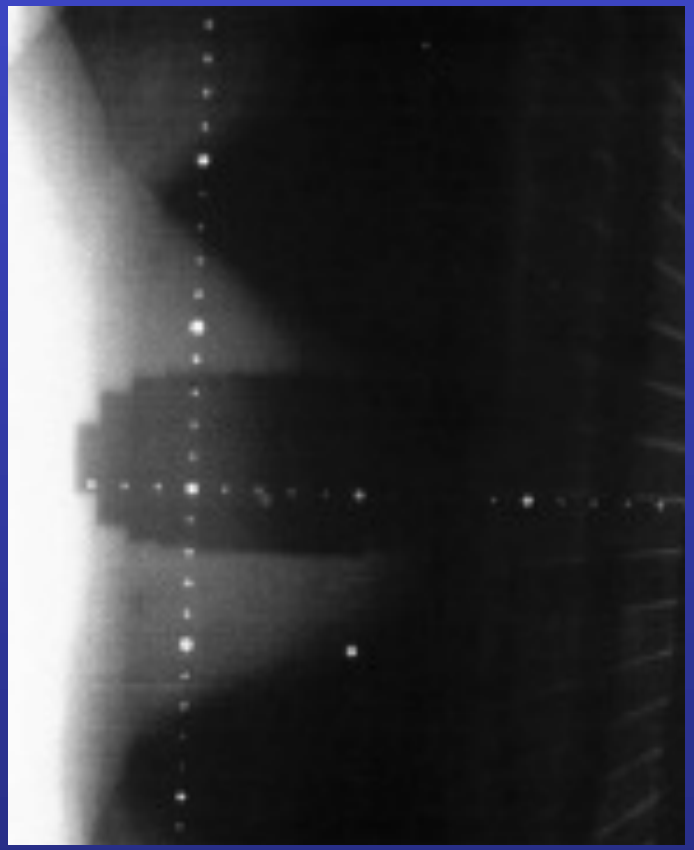












- **Preliminary data in the first 78 patients suggest that this approach is feasible and well tolerated.**
- **DVH heterogeneity reflects PTV/IBV as well as the size/ position of the surgical cavity within the breast.**
- **Lung and heart are optimally spared**
- **Longer follow up is required to assess efficacy, late morbidity**
- **95 % of patients had good to excellent cosmesis**

Silvia C.Formenti et al, Semin Radiat Oncol 15:92-99,2005

The Seven Advantages of the NYU Prone Technique

1. Reduction of respiratory motion in the prone position
2. Optimal normal tissue sparing
3. Adequate “conformality” with just opposed tangents
4. Immediate feasibility after minimal training
5. Equipment available at most radiation oncology facilities
6. Only 5 visit: more convenience to the patients
7. Economically, the most convenient form of APBI

Silvia C.Formenti et al, Semin Radiat Oncol 15:92-99,2005

Is IMRT better? Prone or Supine?

- Three to five beam approach
- Beam directon to avoid lungs and heart

- Beam directions and couch rotations limited by possible collisions of the treatment head with the couch and/or the patient

Silvia C.Formenti et al, Semin Radiat Oncol 15:92-99,2005

Comparison of prone vs supine PBI IMRT

- 10 patients CT planned prone and supine.
- Structures contoured by the same operator
- Individually optimized plans created for both positions, using the same criteria .

Parameters:

- Conformality index: Prescription isodose volume/PTV volume
- BRV 50%: percentage of the non-involved breast volume receiving 50% of the prescription dose
- LV 10 (cc): Lung volume receiving 10% of the prescription

Silvia C.Formenti et al, Semin Radiat Oncol 15:92-99,2005

Conclusion

Partial Breast IMRT is feasible in either position:

- **Depending on the location of the tumor bed, a specific set-up might be preferable, e.g.: PTVs separated from the chest wall are better treated prone, outer quadrant lesions tend to be better treated supine.**

- **Since the IMRT constraints were met with either positions, non-dosimetrical considerations should influence the choice of positioning, such as reproducibility, intra-fraction motion, patient confort.**

Silvia C.Formenti et al, Semin Radiat Oncol 15:92-99,2005

Conclusion

- **PBI by IMRT is more costly, more time consuming and possibly associated with a higher risk of second malignancies (0,09 Sv total body exposure compared to 0,03 Sv of CRT)**

- **Prone 3D-conformal PBI remains our choice to deliver external beam**

Silvia C.Formenti et al, Semin Radiat Oncol 15:92-99,2005

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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*

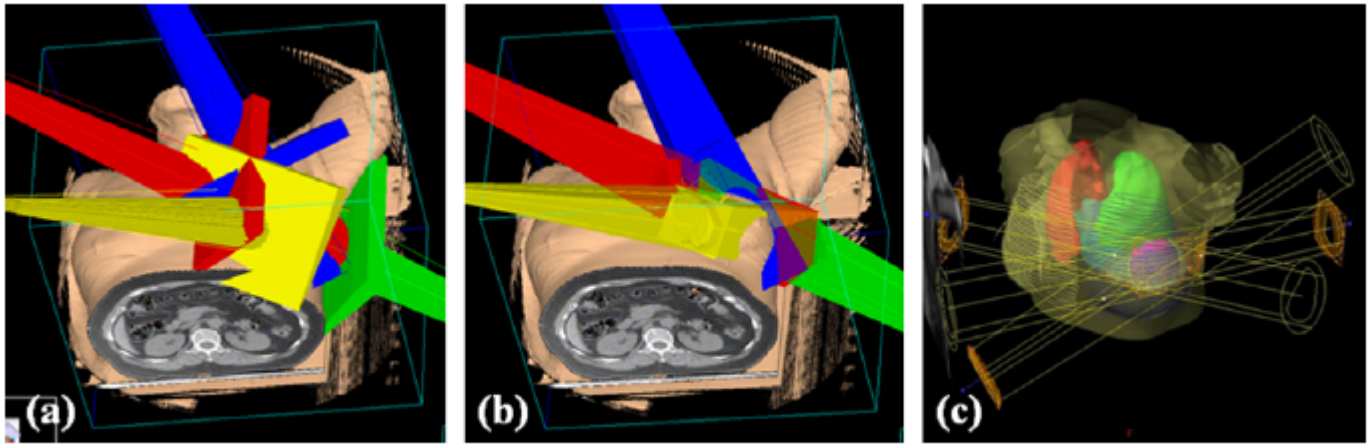

Fig. 1. Beam arrangements for (a) three-dimensional conformal radiotherapy, (b) intensity-modulated radiotherapy, and (c) proton beam therapy.

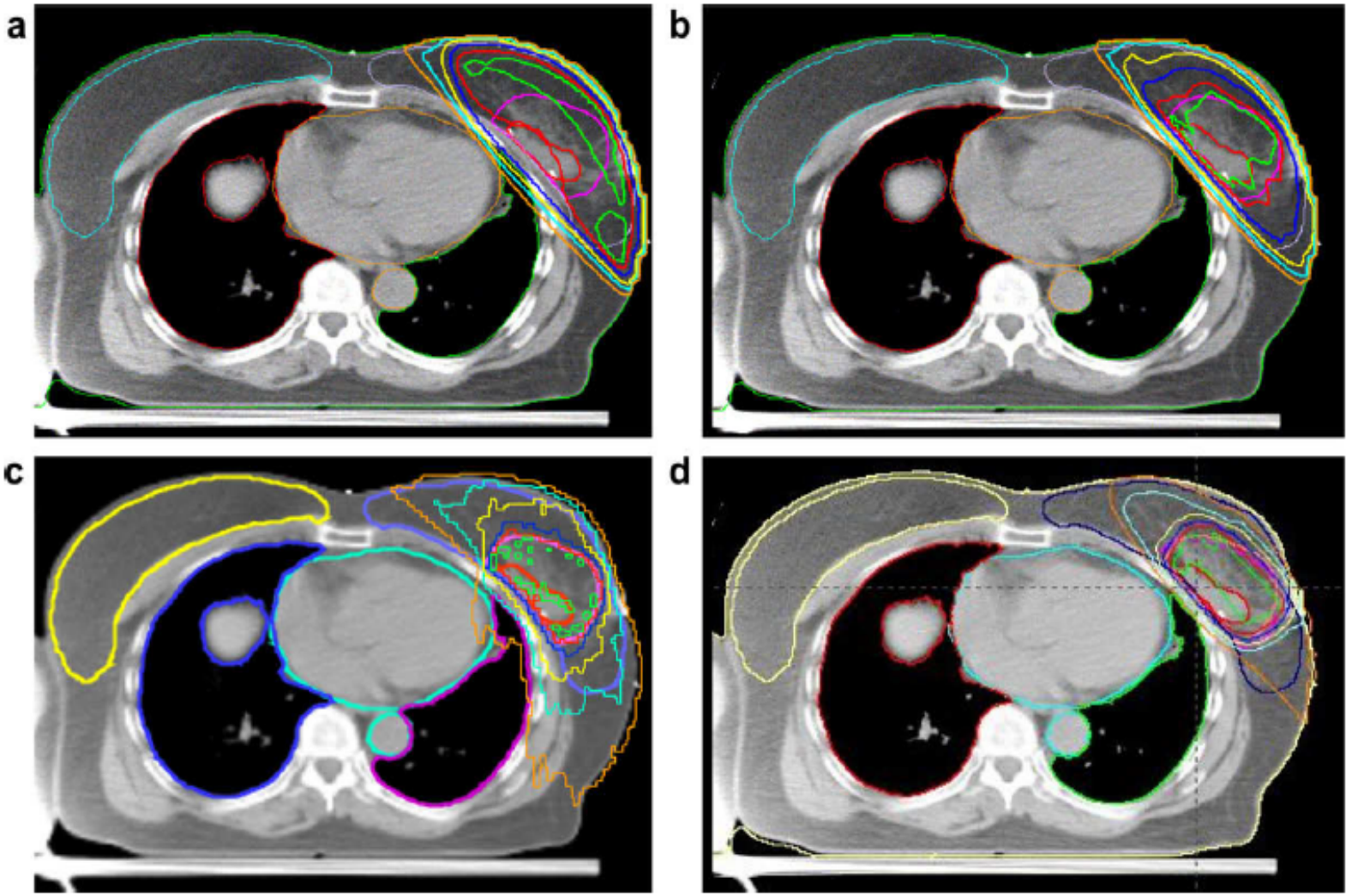

Fig. 2. Dose distribution of (a) three-dimensional conformal radiotherapy, (b) intensity-modulated radiotherapy, (c) helical tomotherapy, and (d) proton beam therapy in the axial plane. Lumpectomy cavity (red), PTV (pink), and isodose lines of 103% (green), 100% (red), 90% (blue), 70% (yellow), 50% (cyan), and 30% (orange) are depicted.

Parametri di confronto tra le diverse tecniche

- **HI: Homogeneity index (dose covering 2% and 98% of the PTV)**
- **CI: Conformity index (degree of isodose conformity to the PTV)**
- **CovI: Coverage index (% of PTV receiving the PD)**

Homogeneity index	$[(D_{2\_PTV} - D_{98\_PTV})/D_{prescription\_PTV}] \times 100$
Conformity index	$1 + (V_{100\_NORM}/V_{100\_PTV})$
Coverage index	V_{100_PTV}/V_{PTV}
D_{2_PTV} (Gy)	Dose covering 2% volume of PTV
D_{98_PTV} (Gy)	Dose covering 98% volume of PTV
$D_{prescription\_PTV}$ (Gy)	Prescribed dose to PTV
V_{100_NORM} (mL)	Volume of normal tissue receiving at least 100% of prescribed dose
V_{100_PTV} (mL)	PTV receiving at least 100% of prescribed dose
V_{PTV} (mL)	Actual volume of PTV

Comparison of homogeneity index (HI), conformity index (CI), and coverage index (CovI) for three-dimensional radiotherapy (3D-CRT), intensity-modulated radiotherapy (IMRT), helical tomotherapy (TOMO), and proton beam therapy (PBT).

	Range (mean)				p^a
	3D-CRT	IMRT	TOMO	PBT	
HI	4.7–13.1 (8.10)	1.80–13.50 (5.48)	6.81–10.9 (8.34)	5.0–12.1 (7.37)	TOMO vs. 3D-CRT (1.000), 3D-CRT vs. PBT (1.000), PBT vs. IMRT (0.005)
CI	1.9–8.9 (3.04)	1.42–2.85 (1.99)	1.10–1.44 (1.21)	1.66–2.20 (1.95)	3D-CRT vs. IMRT (<0.001), IMRT vs. PBT (1.000), PBT vs. TOMO (<0.001)
CovI	0.87–0.99 (0.95)	0.94–1.00 (0.97)	0.95–0.96 (0.95)	0.95–0.98 (0.96)	3D-CRT vs. TOMO (1.000), TOMO vs. PBT (0.331), PBT vs. IMRT (0.165)

[a] By Bonferroni post hoc analysis with statistical significance defined as $p < 0.008$.

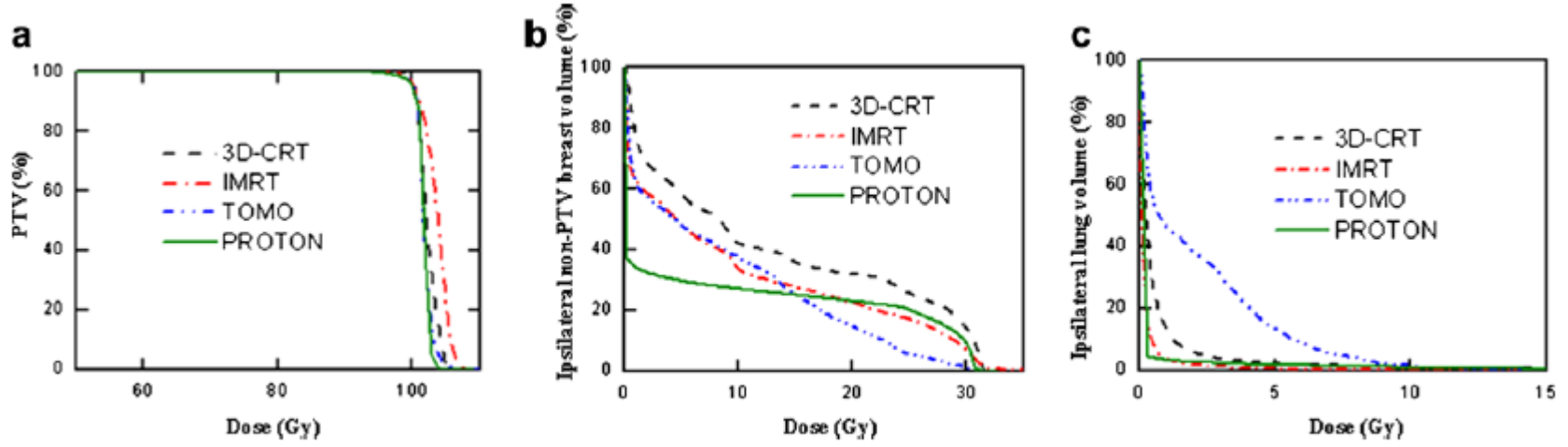

Fig. 3. Dose–volume histogram (DVH) data for PTV (a), the ipsilateral non-PTV breast volume (b) and the ipsilateral lung volume (c).

Comparison of PTV and breast dosimetry for three-dimensional conformal radiotherapy (3D-CRT), intensity-modulated radiotherapy (IMRT), helical tomotherapy (TOMO), and proton beam therapy (PBT).

	Range (mean)				p^a
	3D-CRT	IMRT	TOMO	PBT	
PTV coverage (%)					
V_{100_PTV}	87.3–98.8 (94.8)	94.4–99.9 (97.1)	94.5–95.8 (95.2)	95.0–97.9 (96.1)	3D-CRT vs. TOMO (1.000), TOMO vs. PBT (0.331), PBT vs. IMRT (0.165)
V_{95_PTV}	99.3–100 (99.9)	97.3–100 (99.4)	98.8–99.9 (99.2)	98.6–100 (99.8)	TOMO vs. IMRT (0.731), IMRT vs. PBT(0.003), PBT vs. 3D-CRT (1.000)
V_{90_PTV}	100 (100)	98.7–100 (99.8)	99.7–99.9 (99.8)	99.5–100 (100)	IMRT vs. TOMO (1.000), TOMO vs. PBT (0.010), PBT vs. 3D-CRT (1.000)
Ipsilateral breast (%)					
V_{100_IB}	18.1–55.9 (32.8)	15.1–44.9 (27.2)	10.0–31.8 (18.7)	9.9–29.0 (18.2)	3D-CRT vs. IMRT (0.016), IMRT vs. TOMO (<0.001), TOMO vs. PBT (1.000)
V_{75_IB}	33.2–69.8 (48.9)	27.3–56.4 (41.4)	17.8–42.9 (27.4)	16.2–41.5 (26.8)	3D-CRT vs. IMRT (0.002), IMRT vs. TOMO (<0.001), TOMO vs. PBT (1.000)
V_{50_IB}	42.2–82.2 (57.6)	35.5–66.3 (50.3)	23.1–62.2 (39.8)	21.0–50.1 (33.0)	3D-CRT vs. IMRT (0.009), IMRT vs. TOMO (<0.001), TOMO vs. PBT (0.018)
V_{25_IB}	54.6–92.4 (67.3)	47.8–85.1 (60.5)	34.9–81.3 (62.9)	25.4–55.2 (38.0)	3D-CRT vs. TOMO (0.503), TOMO vs. IMRT (1.000), IMRT vs. PBT (<0.001)
Non-PTV breast (%)					
$V_{50\_IB-NPTV}$	25.0–64.7 (40.9)	22.1–48.7 (33.3)	10.6–32.4 (22.8)	10.3–23.2 (16.5)	3D-CRT vs. IMRT (<0.001), IMRT vs. TOMO (<0.001), TOMO vs. PBT (0.002)

Comparison of lung and heart dosimetry for three-dimensional conformal radiotherapy (3D-CRT), intensity-modulated radiotherapy (IMRT), helical tomotherapy (TOMO), and proton beam therapy (PBT).

	Range (mean)				p^a
	3D-CRT	IMRT	TOMO	PBT	
Ipsilateral lung (%)					
V_{20_IL}	1.8–18.9 (6.0)	0–14.3(2.3)	3.9–29.1 (14.2)	0–1.7 (0.4)	TOMO vs.3D-CRT (<0.001), 3D-CRT vs. IMRT (0.003), IMRT vs. PBT (0.398)
V_{10_IL}	3.7–23.1 (9.6)	0–18.1 (4.7)	13.2–57.7 (37.6)	0–2.6 (0.8)	TOMO vs.3D-CRT (<0.001), 3D-CRT vs. IMRT (0.025), IMRT vs. PBT (0.118)
V_{5_IL}	7.4–29.8 (15.9)	0–28.1 (8.2)	23.1–78.3 (53.9)	0–3.6 (1.2)	TOMO vs.3D-CRT (<0.001), 3D-CRT vs. IMRT (<0.001), IMRT vs. PBT (0.002)
$D_{20\%\_IL}$	1.5–16.2 (4.0)	0–7.5 (1.8)	6.8–24.5 (16.2)	0	TOMO vs.3D-CRT (<0.001), 3D-CRT vs. IMRT (0.014), IMRT vs. PBT (0.055)
$D_{10\%\_IL}$	3.6–55.1 (11.2)	0–35.0 (4.8)	11.3–34.8 (23.0)	0	TOMO vs.3D-CRT (<0.001), 3D-CRT vs. IMRT (0.001), IMRT vs. PBT (0.024)
$D_{5\%\_IL}$	9.8–79.9 (26.1)	0–54.5(10.5)	16.4–46.3 (30.0)	0–1.0 (0.3)	TOMO vs.3D-CRT (0.840), 3D-CRT vs. IMRT (<0.001), IMRT vs. PBT (0.001)
Heart (%) (N = 19, left-sided)					
V_{20_H}	0–9.0 (1.5)	0–7.9 (1.2)	0–33.5 (8.0)	0–0.2 (0)	TOMO vs. 3D-CRT (<0.001), 3D-CRT vs. IMRT (1.000), IMRT vs. PBT (1.000)
V_{10_H}	0–13.3 (3.1)	0–40.2 (4.0)	0–53.3 (19.4)	0–0.3 (0)	TOMO vs. IMRT (<0.001), IMRT vs. 3D-CRT (1.000), 3D-CRT vs. PBT (1.000)
V_{5_H}	0–22.5 (6.7)	0–50.4 (5.4)	0.10–64.5 (25.7)	0–0.5 (0)	TOMO vs. 3D-CRT (<0.001), 3D-CRT vs. IMRT (1.000), IMRT vs. PBT (0.911)
$D_{20\%\_H}$	0.7–5.5 (2.3)	0–15.3(1.6)	0.8–27.9 (8.8)	0	TOMO vs. 3D-CRT (<0.001), 3D-CRT vs. IMRT (1.000), IMRT vs. PBT (1.000)
$D_{10\%\_H}$	1.1–24.0 (4.9)	0–52.0 (7.1)	0.9–37.6 (14.6)	0	TOMO vs. IMRT (<0.001), IMRT vs. 3D-CRT (1.000), 3D-CRT vs. PBT (0.068)
Contralateral lung (%)					
$D_{5\%\_CL}$	0–2.4 (0.1)	0	0	0	3D-CRT vs. IMRT (0.960), IMRT vs. TOMO (1.000), TOMO vs. PBT (1.000)
Contralateral breast (%)					
$D_{2.5\%\_CB}$	0–7.3 (0.7)	0–5.9 (0.2)	0–0.02 (0)	0	3D-CRT vs. IMRT (0.458), IMRT vs. TOMO (1.000), TOMO vs. PBT (1.000)

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Accelerated partial breast irradiation

Defining an optimal role for breast magnetic resonance imaging when evaluating patients otherwise eligible for accelerated partial breast irradiation

Kathleen C. Horst [a,*], Katherine E. Fero [a], Debra M. Ikeda [b], Bruce L. Daniel [b], Frederick M. Dirbas [c]

[a] Department of Radiation Oncology; [b] Department of Radiology; [c] Department of Surgery, Stanford University School of Medicine, Stanford Cancer Institute, United States

- La RM è stata in grado di identificare una malattia multifocale/multicentrica risp. nel 10.5 e nell' 1,6% dei 181 pazienti dello studio inizialmente candidati alla PBI con la stadiazione convenzionale
- L'età pre-menopausale e i tumori >2 cm sono i fattori di rischio maggiori

Contents lists available at SciVerse ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

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

Felix Sedlmayer[a,*], Franz Zehentmayr[b], Gerd Fastner[a]

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

Primary treatment and time to IBTR

Study	N (pts.)	Primary treatment		Time to IBTR (months)	
		EQD_2 (max. to the tumour bed)	Technique	Minimum	Median
Chadha 2008	15	Not reported	Not reported	28	94
Hannoun-Levi 2004	69	50 Gy + boost (not specified)	EBRT	Not reported	70
Trombetta 2009	26	60.4 Gy physical dose	EBRT	4.8	96
Guix 2010	36	50 Gy + boost (not specified)	EBRT + boost (HDR)	12	38
Hannoun-Levi 2011	42	66 Gy	EBRT	12	132
Polgar 2012	15	Not reported	Not reported	Not reported	79.7
Kauer-Dorner 2012	39	62.5 Gy – 75.9 Gy	EBRT + boost (LDR or HDR)	12	131
Resch 2002	17	50 + boost (not specified)	HDR	11	50
Deutsch 2002	39	50 Gy + boost (not specified)	EBRT	16	63
Kraus-Tiefenbacher 2007	17	62 Gy	EBRT	36	120
Total	**315**				

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Original article

Accelerated partial breast irradiation using 3D conformal radiotherapy: Toxicity and cosmetic outcome

M. Gatti [a,*], R. Ponzone [c], S. Bresciani [b], R. Panaia [a], F. Kubatzki [c], F. Maggiorotto [c], M.R. Di Virgilio [d], A. Salatino [a], B. Baiotto [b], F. Montemurro [e,f], M. Stasi [b], P. Gabriele [a]

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[e] Unit of Medical Oncology, Fondazione del Piemonte per l'Oncologia/Institute for Cancer Research and Treatment of Candiolo (IRCCS), Italy
[f] Unit of Investigative Clinical Oncology, Fondazione del Piemonte per l'Oncologia/Institute for Cancer Research and Treatment of Candiolo (IRCCS), Italy

Baseline patient characteristics ($n = 84$).

Variable	Number (%)
Age (years)	
Median	66
Range	51–87
Follow-up (months)	
Median	36.5
Range	13–83
Breast side	
Left	37 (44)
Right	46 (55)
Bilateral	1 (1)
pT Stage	
pT1mi	4 (4.8)
pT1a	9 (11)
pT1b	32 (38.1)
pT1c	38 (45.2)
pT2	1 (1.2)
Histology	
Ductal N.O.S.[a]	72 (85.7)
Mucinous	7 (8.3)
Tubular	3 (3.6)
Intracystic papillary	2 (2.4)
Grading	
1	30 (35.7)
2	34 (40.5)
3	18 (21.4)
n.e.[b]	2 (2.4)
Tumor estrogen receptor status	
Negative[c]	0
Positive[c]	84 (100)
Radiation dose	
34 Gy	60 (71.4)
38.5 Gy	24 (28.6)
Endocrine therapy[d]	83(98.8)
Chemotherapy	0

APBI CON 3D-CRT

- **Viene somministrata una dose di 34 Gy in 10 frazioni/ sett., 2 frazioni/die a distanza di almeno 6 ore per un totale di 5 gg di trattamento**

- **Il volume bersaglio è costituito dal letto tumorale (clips) detto "*gross tumor volume*" (GTV), più un margine di di 15 mm detto "*clinical tumor volume*" (CTV) che tiene conto della presenza di eventuali foci microscopici di malattia**

- **Il "*planning tumor volume*" (PTV) è costituito da un ulteriore margine di 10 mm in modo da tener conto delle escursioni respiratorie e del**

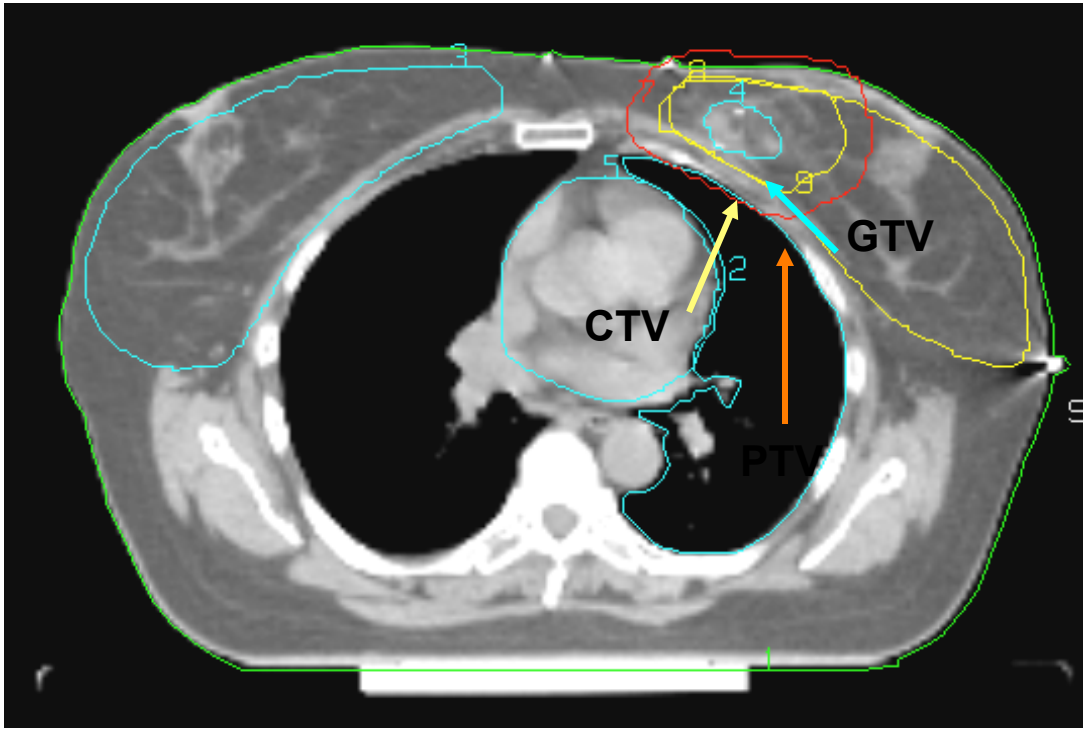
Baglan K.L. et al, *Accelerated PBI using 3DCRT*,
Int J Radiat Oncol Biol Phys, 55,2,302-311, 2003

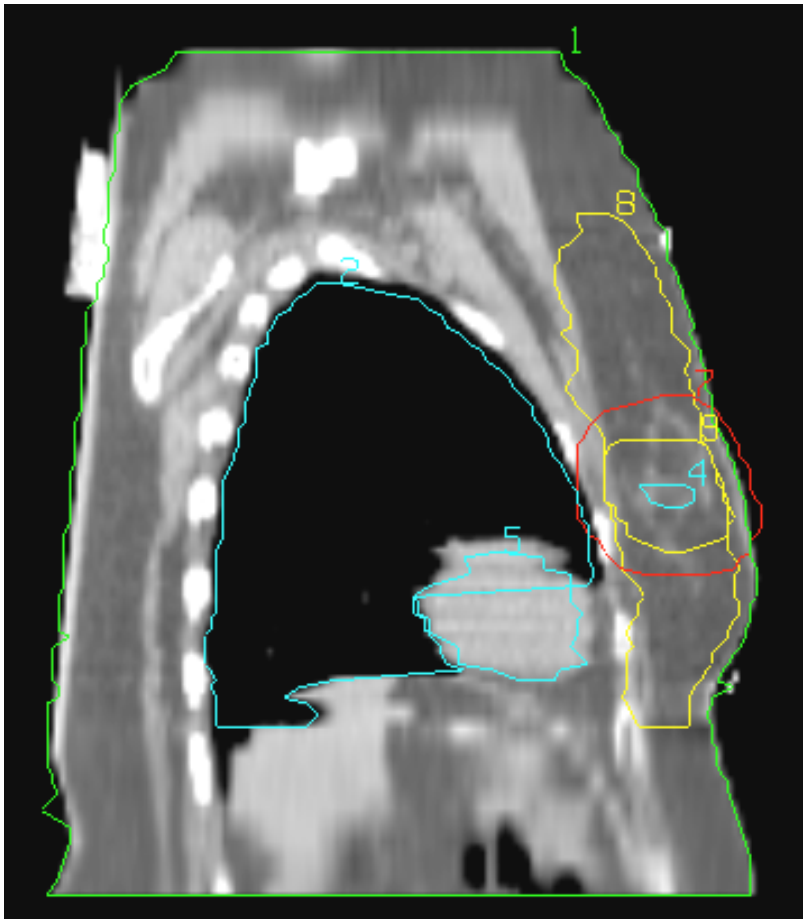
Volumi, dosi, DVH

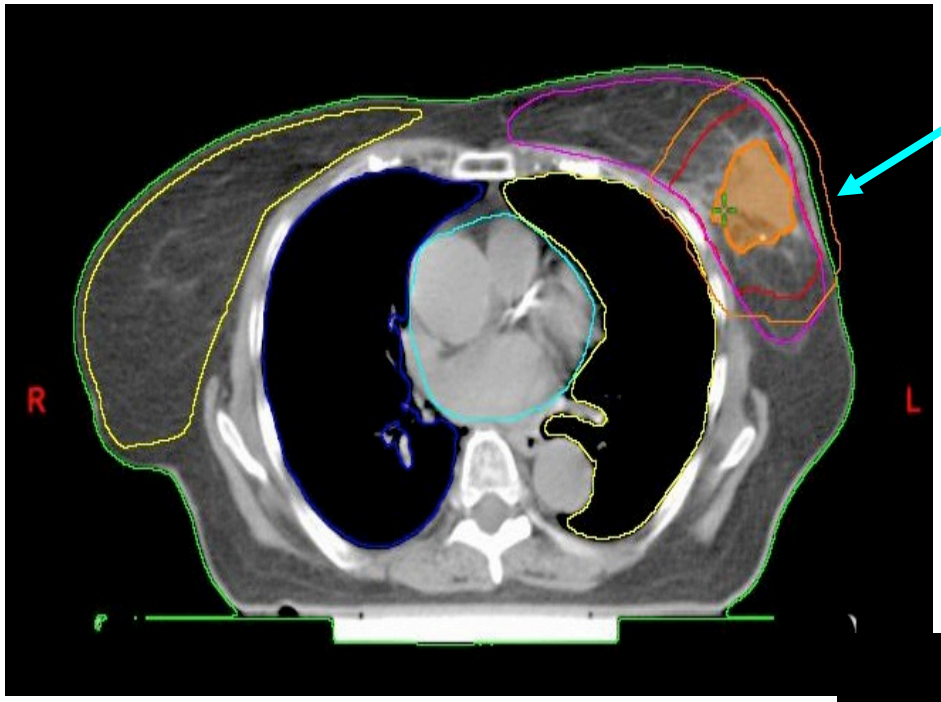
- Gross Tumor Volume (GTV): clips chirurgiche
- Clinical Target Volume (CTV): GTV+1.5 cm (-cute, -parete torax)
- Planning Target Volume (PTV): setup+organ motion ⇒ CTV+0.5+0.5 cm
- PTV Eval: PTV modificato a 5 mm da cute per valutazione DVH

- DFT: 34 Gy, 3.4 Gy/fraz, 2 fraz/die (distanza di >6h)
- Istogrammi Dose/Volume (DVH):
  - Mammella omolaterale: 50%vol<50% DFT, 25%vol<100% DFT
  - Mammella controlaterale: ogni punto ≤3% DFT (scatter)
  - Polmone omolaterale: 15%vol<30% DFT
  - Cuore: ogni punto ≤ 5% DFT (scatter) se lesioni dx, DVH < del trattamento con campi tangenti standard se lesioni sin

Contornazione del target sulle slices TC

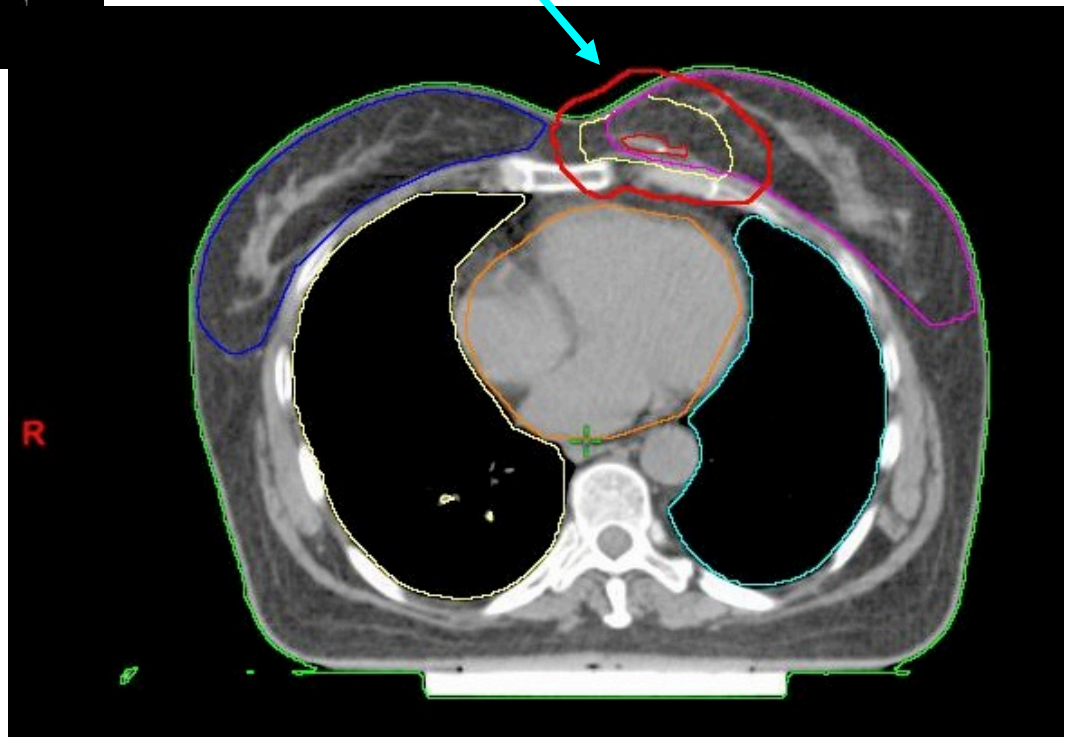






favorevole

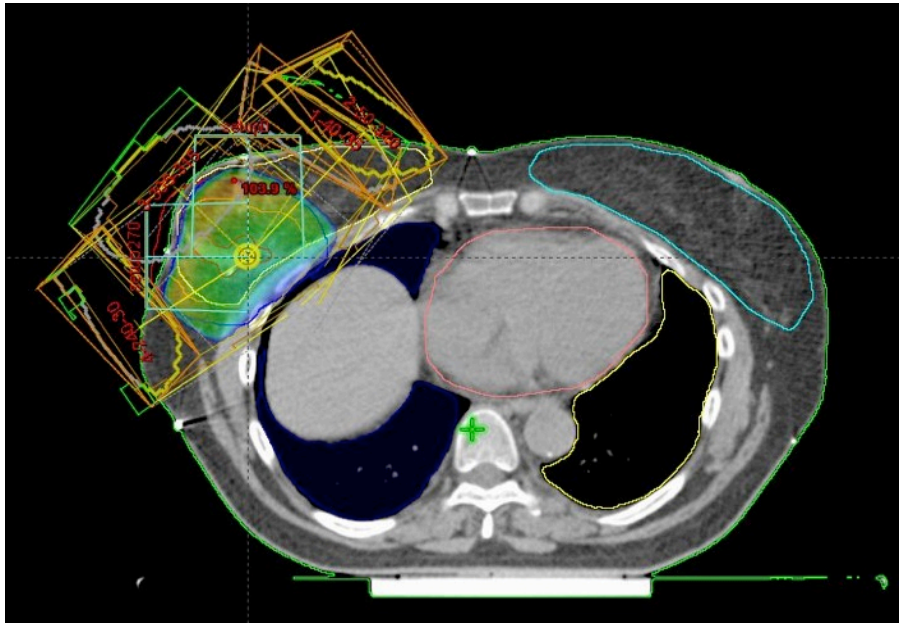
sfavorevole

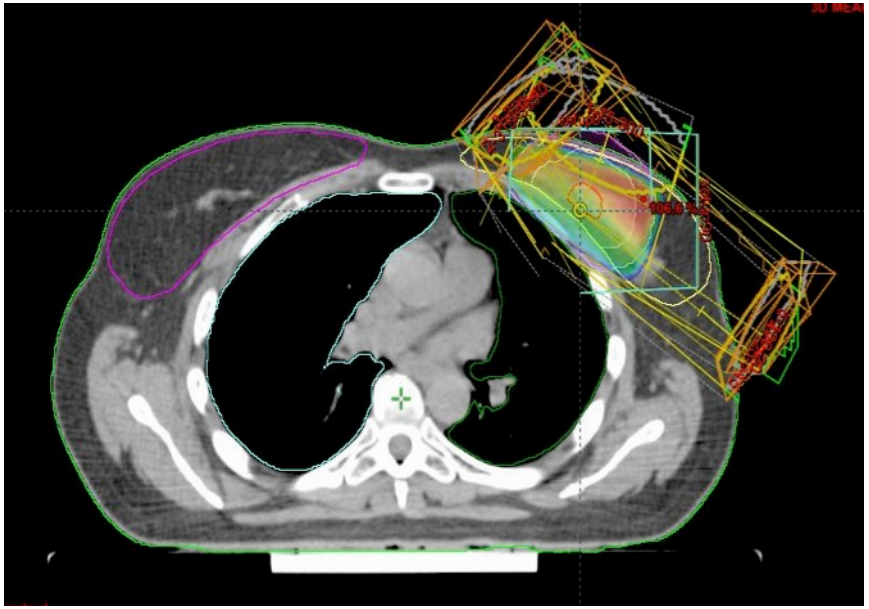


Es. di posizioni del letto tumorale

Piani di cura

- **Mammella sin: 4 campi n.c.**
- **Mammella dx: 5 campi n.c.**





Baglan K.L. et al, *Accelerated PBI using 3DCRT*,

Int J Radiat Oncol Biol Phys, 55,2,302-311, 2003

Fattori limitanti della tecnica di irradiazione

CLINICAL INVESTIGATION **Breast**

ONGOING CLINICAL EXPERIENCE UTILIZING 3D CONFORMAL EXTERNAL BEAM RADIOTHERAPY TO DELIVER PARTIAL-BREAST IRRADIATION IN PATIENTS WITH EARLY-STAGE BREAST CANCER TREATED WITH BREAST-CONSERVING THERAPY

Frank A. Vicini, M.D.,* Vincent Remouchamps, M.D.,* Michelle Wallace, R.N.,* Michael Sharpe, Ph.D.,* Julie Fayad, M.S.,* Laura Tyburski,* Nicola Letts, B.Sc.,* Larry Kestin, M.D., Gregory Edmundson, M.Sc.,* Jane Pettinga, M.D.,† Neal S. Goldstein, M.D.,‡ and John Wong, Ph.D.*

Departments of *Radiation Oncology, †Surgery, and ‡Anatomic Pathology, William Beaumont Hospital, Royal Oak, Michigan

- **Valutazione dei volumi di irradiazione: GTV, CTV, PTV, Breast Volume (BV), CTV/BV, PTV/BV**
- **PTV/BV: parametro di fattibilità**

PTV/BV >0.2: potrebbe non soddisfare i constraints di dose adottati

(PTV grande, mammella piccola!)

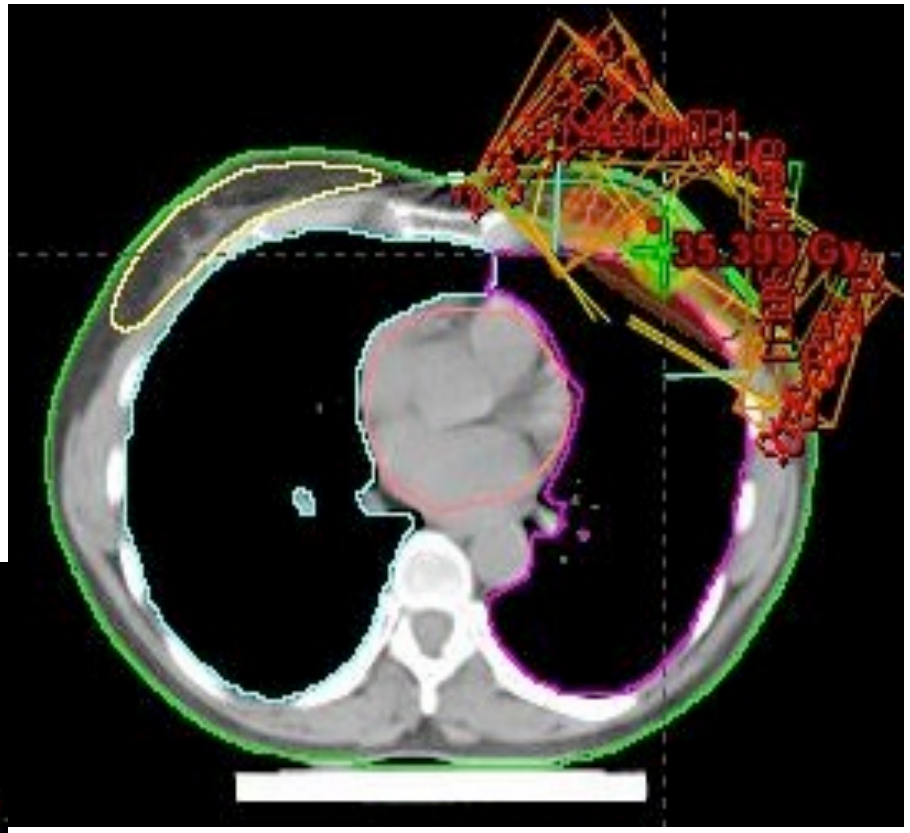
Volumi di trattamento

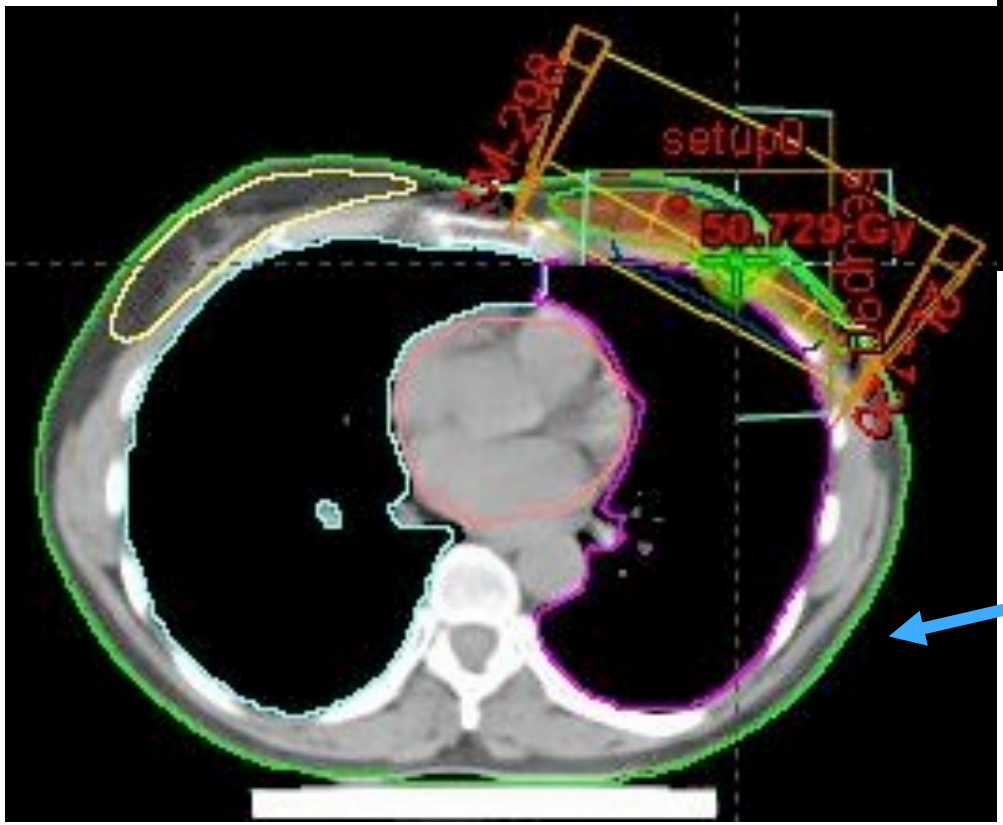
cc	GTV	CTV (-paroi thorac.-peau) a1.5 cm	PTV à 1 cm	PTV eval	CTV/sein homolat	PTVeval/sein homolat
moyenne	**15.8**	118.9	308.9	269.1	**0.16**	**0.38**
dev std	13	50	89.7	89	0.06	0.14
median	12.4	103.3	284.9	250.1	0.15	0.37
min	4.8	51.7	167.8	117.7	0.06	0.16
max	68.9	264.6	573.6	476.6	0.31	0.83

PTV/BV > 0.2: potrebbero non soddisfare i constraints di Franck Vicini

CTV/BV > 0.3: esclusione dal protocollo IRMA

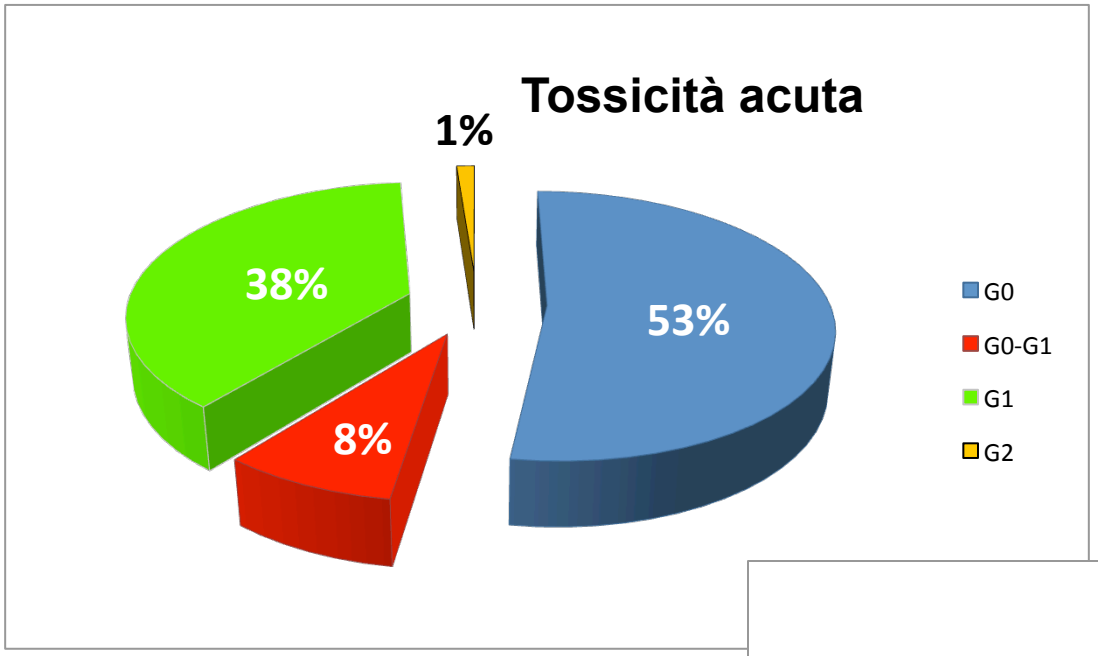
- **PTVeval/mammella omolat.= 0.83**
- **CTV/mammella omolaterale= 0.31**

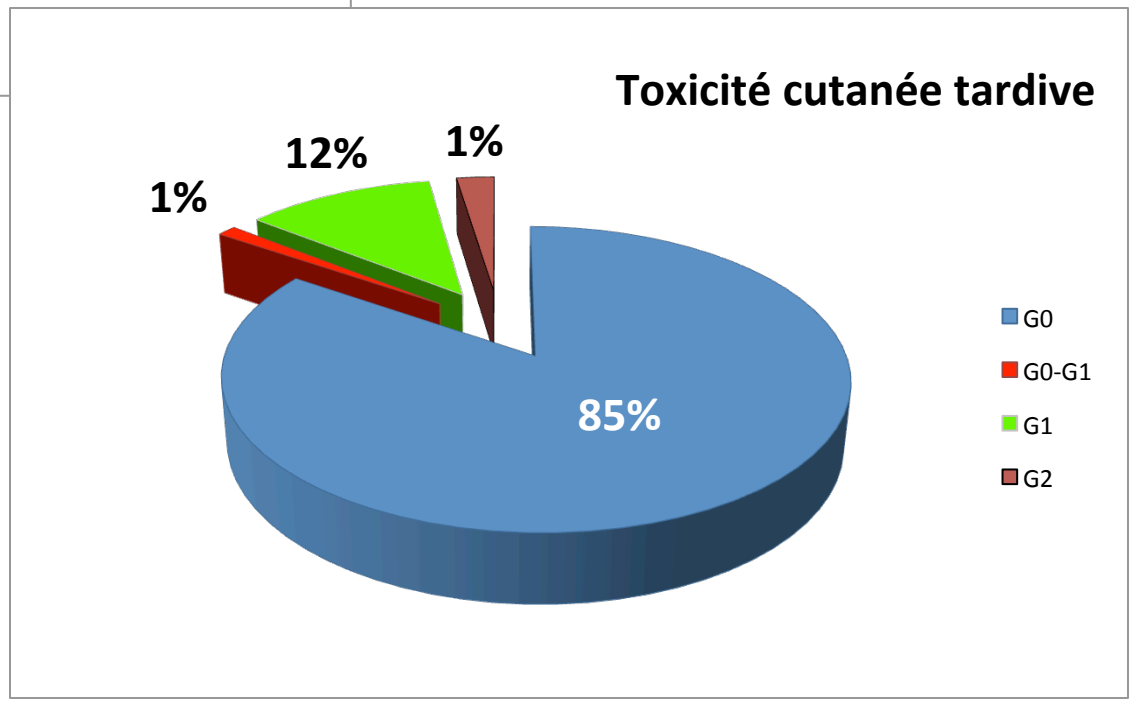




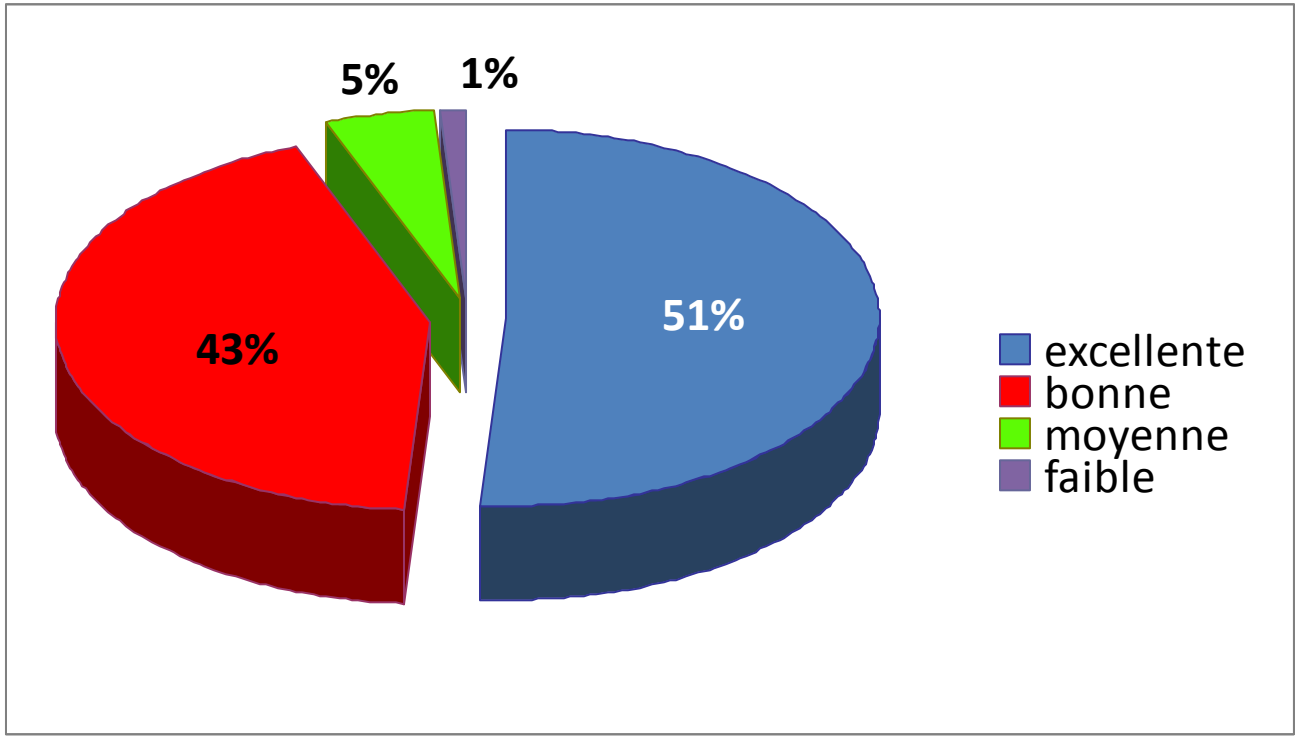
Trattamento effettuato con tecnica a campi tangenti e fraz. standard

Tossicità cutanea acuta e tardiva





Risultati cosmetici



Acute and late toxicity.

Variable	Grade	Number (%)
Acute		
Erythema	G1	39 (46.4)
Late		
Erythema	G1	13 (16.7)
Fibrosis	G2	4 (4.8)
Hyperpigmentation	G1	10 (11.9)
Telangiectasia	G3	3 (3.6)

Patients' assessment of cosmetic outcome of the treated vs the untreated breast.

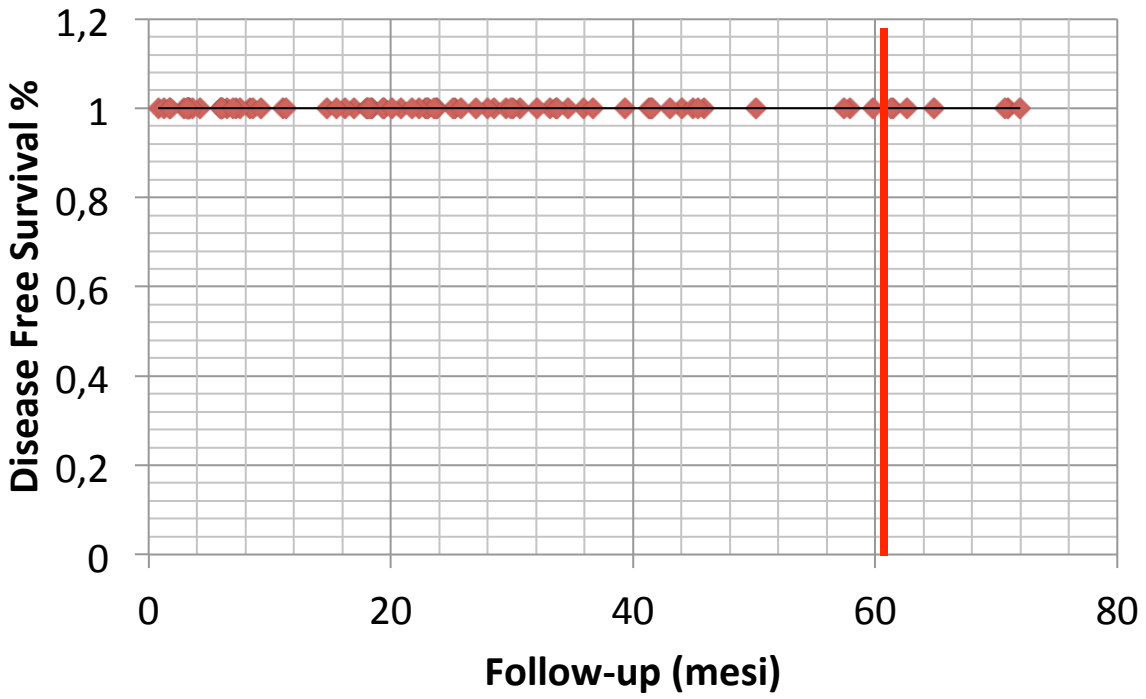
Parameter	No difference or excellent *n* (%)	Small difference or good *n* (%)	Moderate difference or fair *n* (%)	Large difference or poor *n* (%)
Breast size	42 (50%)	36 (42.8%)	6 (7.2%)	0 (0%)
Breast shape	44 (52.3%)	35 (41.6%)	5 (6.1%)	0 (0%)
Location and shape of areola/nipple	65 (77.4%)	15 (17.8%)	3 (3.6%)	1 (1.2%)
Skin color	62 (73.8%)	20 (23.8%)	2 (2.4%)	0 (0%)
Breast edema	75 (89.3%)	8 (9.5%)	1 (1.2%)	0 (0%)
Appearance of surgical scar	64 (76.2%)	16 (19%)	2 (2.4%)	2 (2.4%)
Teleangectasia	79 (94%)	2 (2.4%)	2 (2.4%)	1 (1.2%)
Global cosmetic assessment	37 (44%)	38 (45.2%)	8 (9.6%)	1 (1.2%)

Nessuna correlazione tra la dimensione del PTV/WB e l'impatto sulla tossicità acuta e tardiva (p=0.45)

+

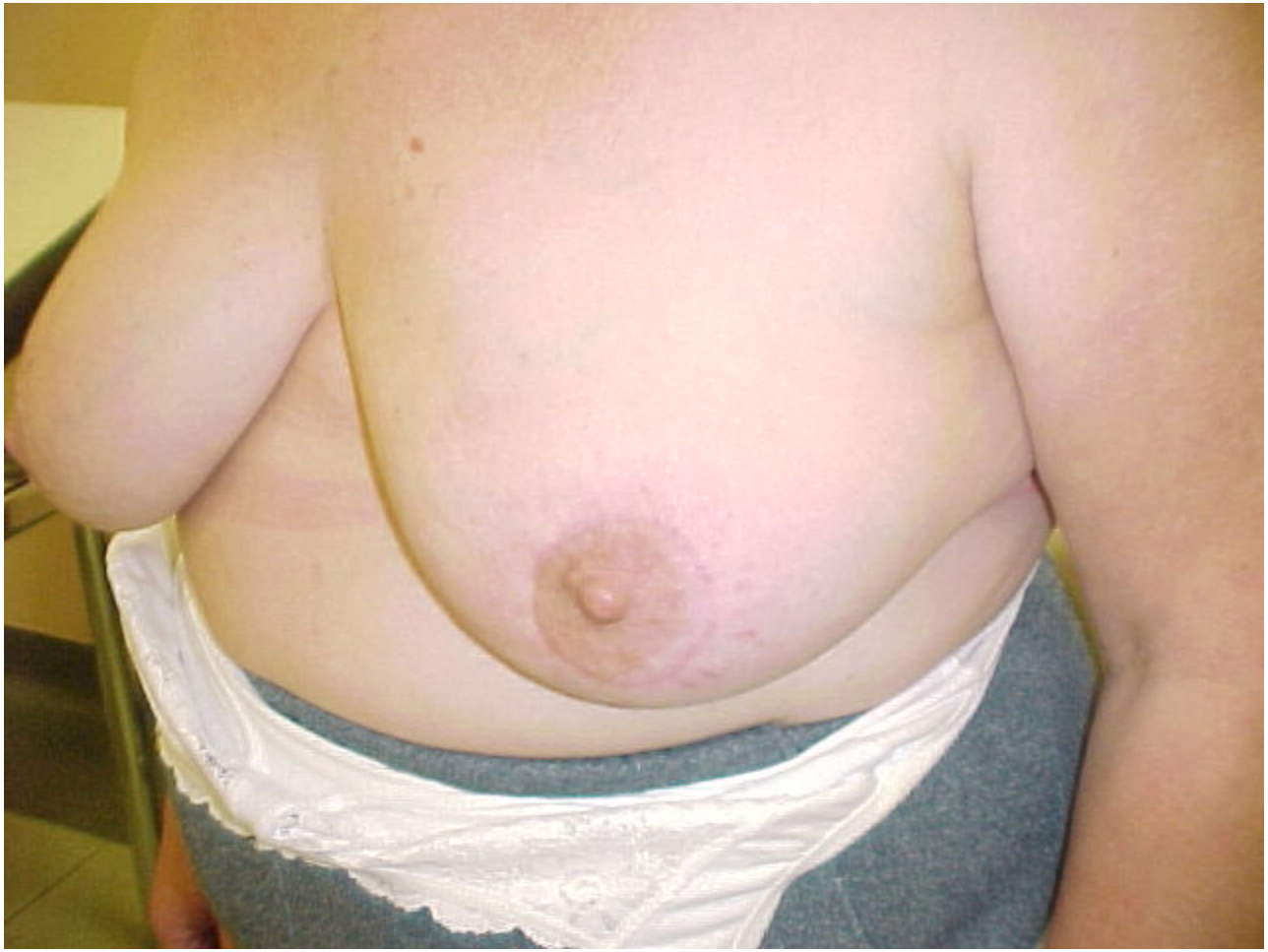
Nessuna correlazione tra le differenti dosi adottate (34 e 38.5) e la tossicità acuta e tardiva (p=0.33)

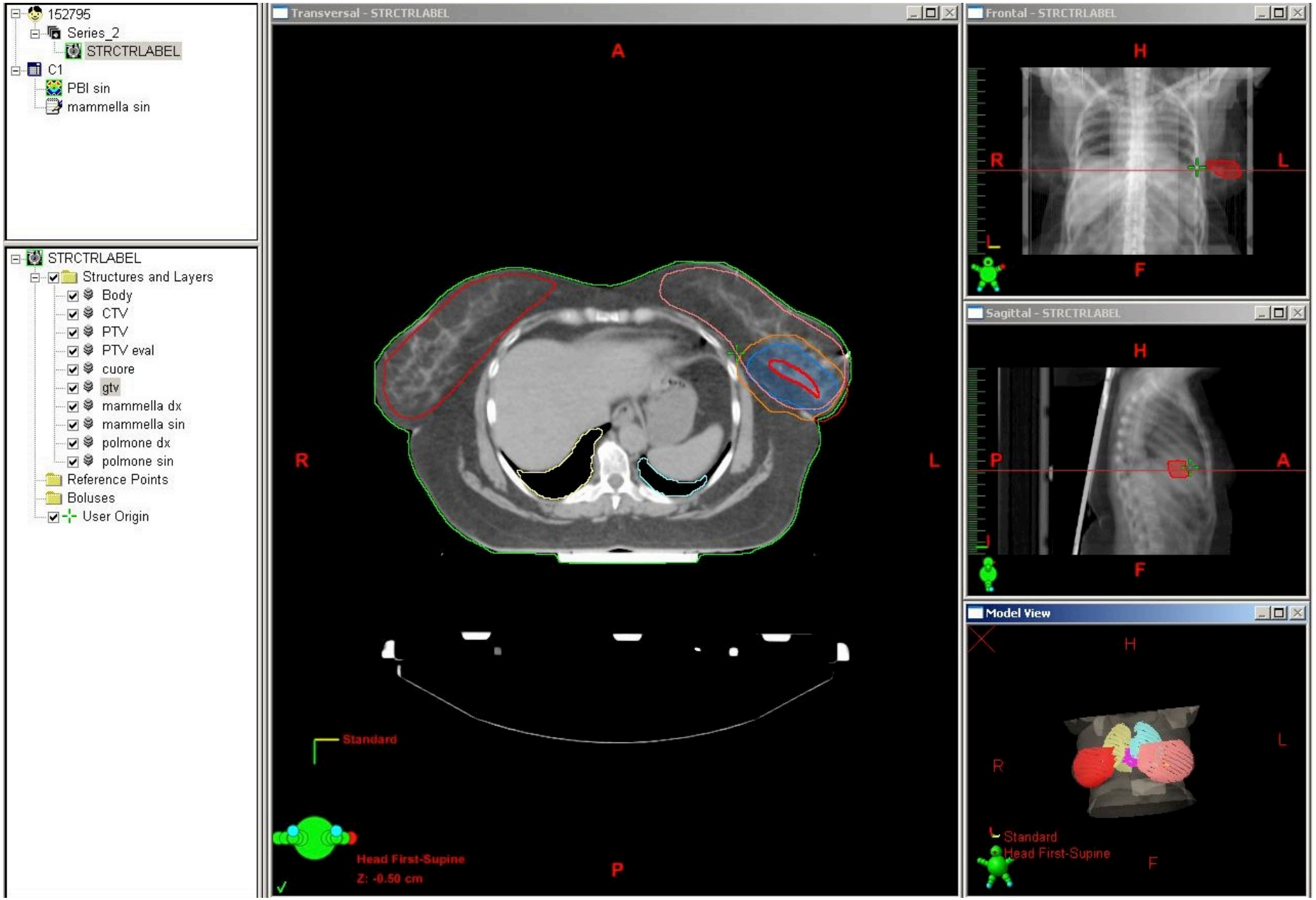
Sopravvivenza libera da malattia



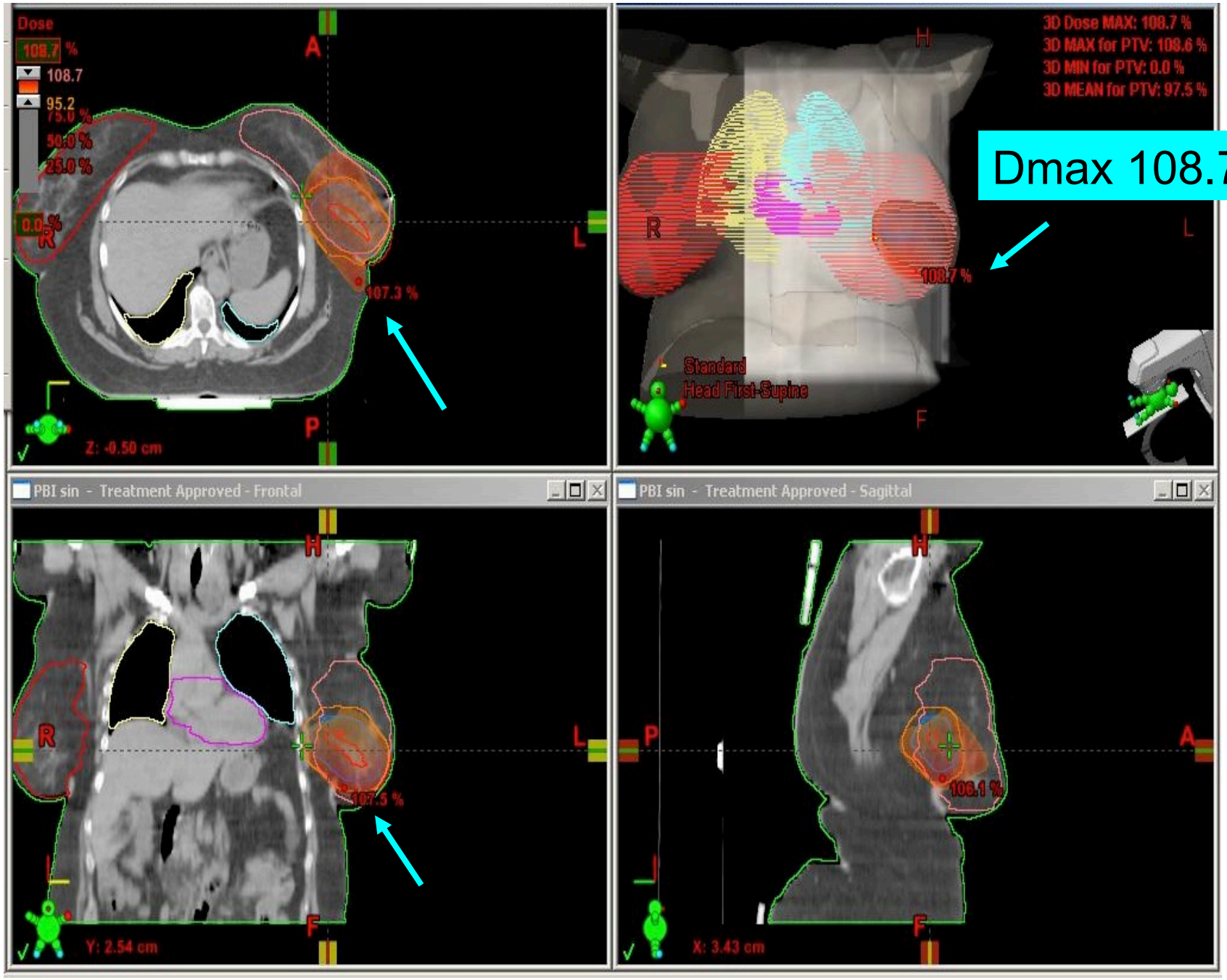
8% dei pazienti con controllo > 5 anni

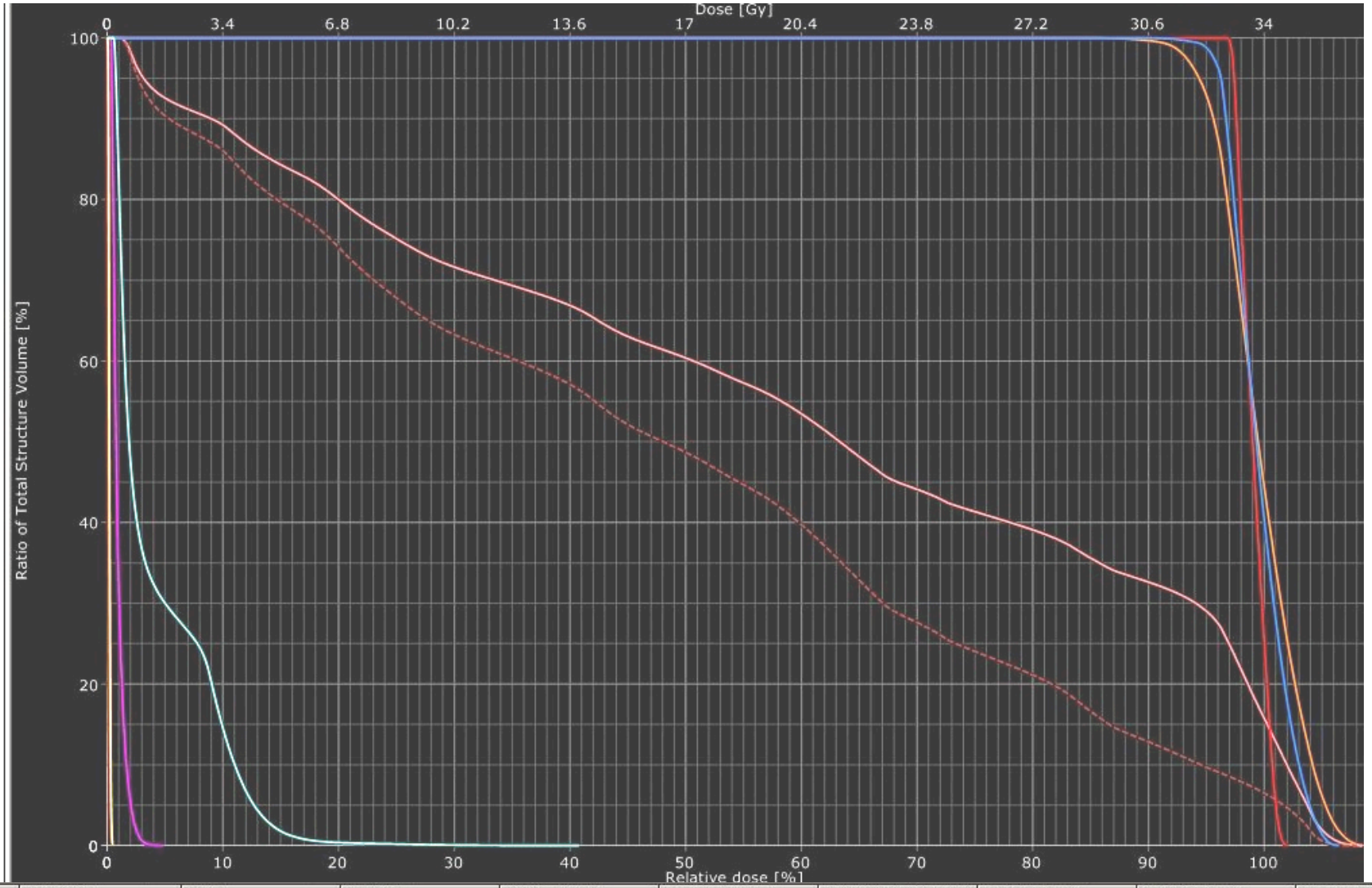
RESULTATS COSMETIQUES APRES 7 ANS





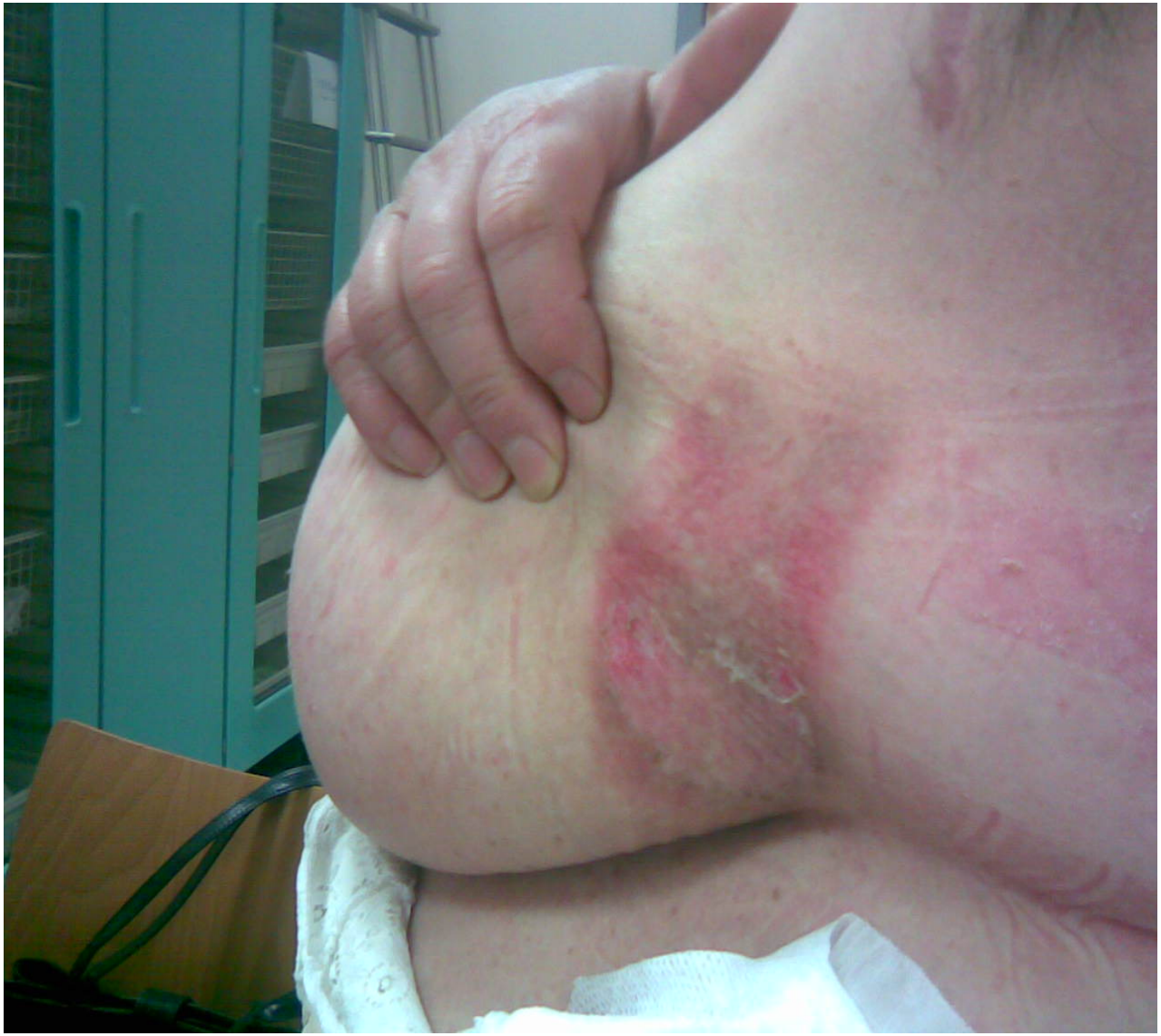
Paziente che ha sviluppato una tossicità acuta G2, Q3, GTV 24.2 cc, mammella di 1769.5 cc


Dose
108.7 %
108.7
95.2
75.0 %
50.0 %
25.0 %
0.0 %
A
R
L
P
107.3 %
Z: -0.50 cm
3D Dose MAX: 108.7 %
3D MAX for PTV: 108.6 %
3D MIN for PTV: 0.0 %
3D MEAN for PTV: 97.5 %
Dmax 108.7%
H
R
L
108.7 %
Standard
Head First-Supine
F
PBI sin - Treatment Approved - Frontal
H
R
L
107.5 %
F
Y: 2.54 cm
PBI sin - Treatment Approved - Sagittal
H
P
A
108.1 %
F
X: 3.43 cm

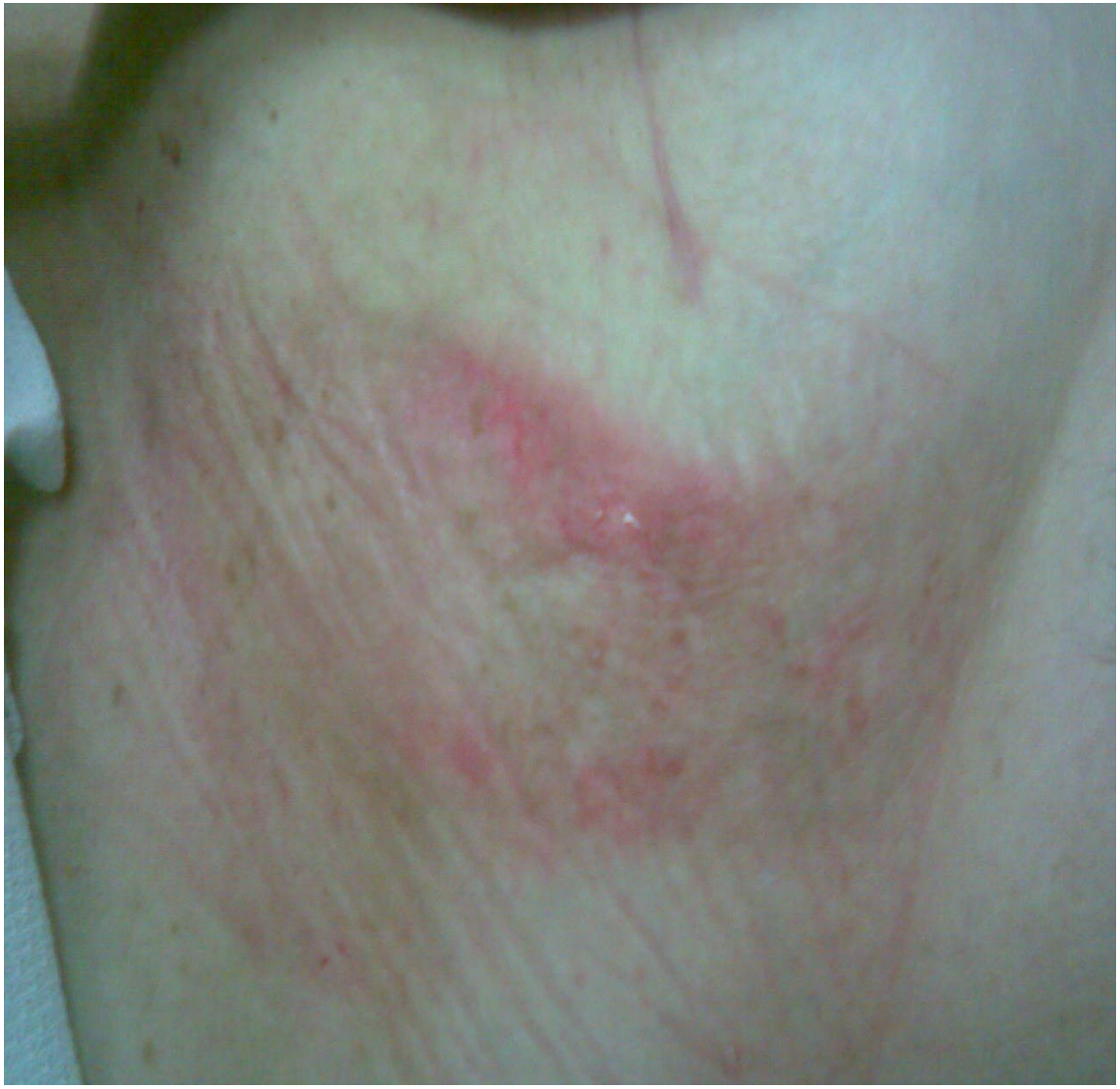


DVH Line	Structure	Plan	Course	Volume [cm³]	Dose Cover.[%]	Sampling Cover.[%]	Min Dose [%]	Max Dose [%]	Mean Dose [%]
	CTV	PBI sin	C1	227.4	100.0	100.0	88.6	106.5	99.6
	PTV	PBI sin	C1	494.8	100.0	100.0	0.0	108.7	97.5
	PTV eval	PBI sin	C1	465.4	100.0	100.0	83.0	108.7	99.6
	cuore	PBI sin	C1	488.7	100.0	100.0	0.3	4.9	0.9
	gtv	PBI sin	C1	24.2	100.0	100.0	96.8	102.1	99.1
	mammella dx	PBI sin	C1	1502.5	100.0	100.0	0.0	0.5	0.1
	mammella sin	PBI sin	C1	1769.5	100.0	100.0	1.0	108.6	60.0
	polmone dx	PBI sin	C1	1597.6	100.0	100.0	0.0	0.6	0.2

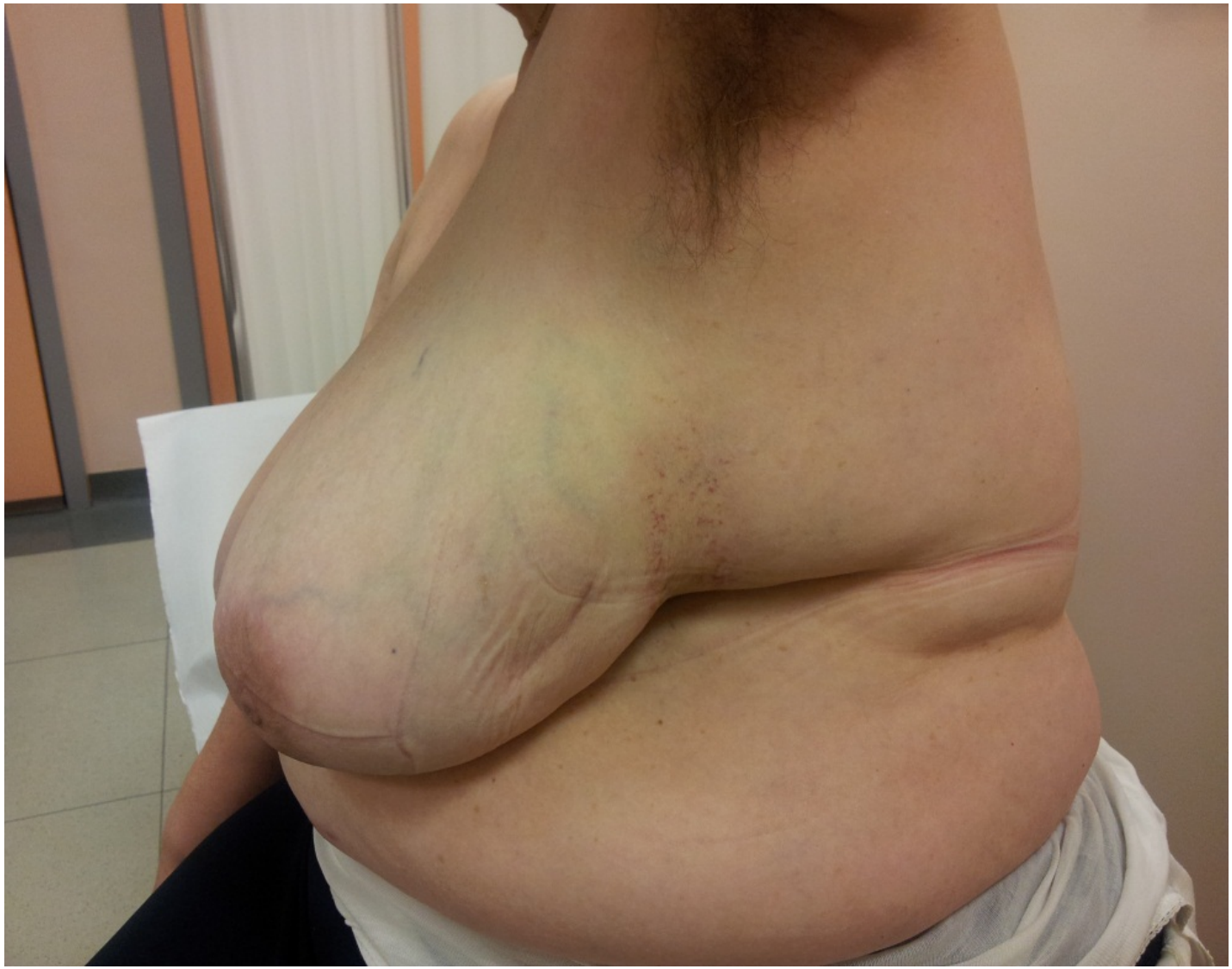
Tossicità acuta a 8 gg dal termine della RT



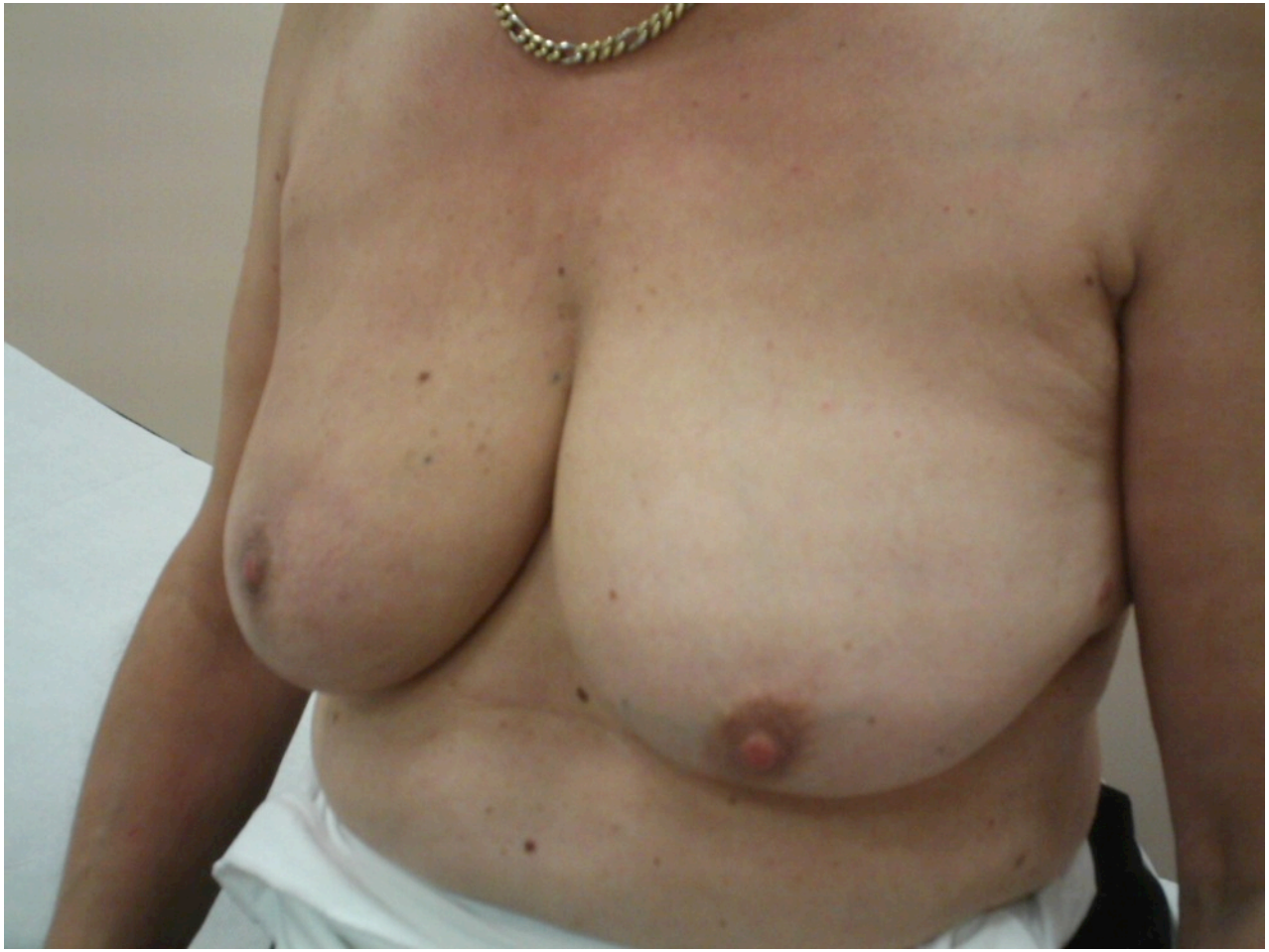
Tossicità acuta a 16 giorni dalla fine della RT



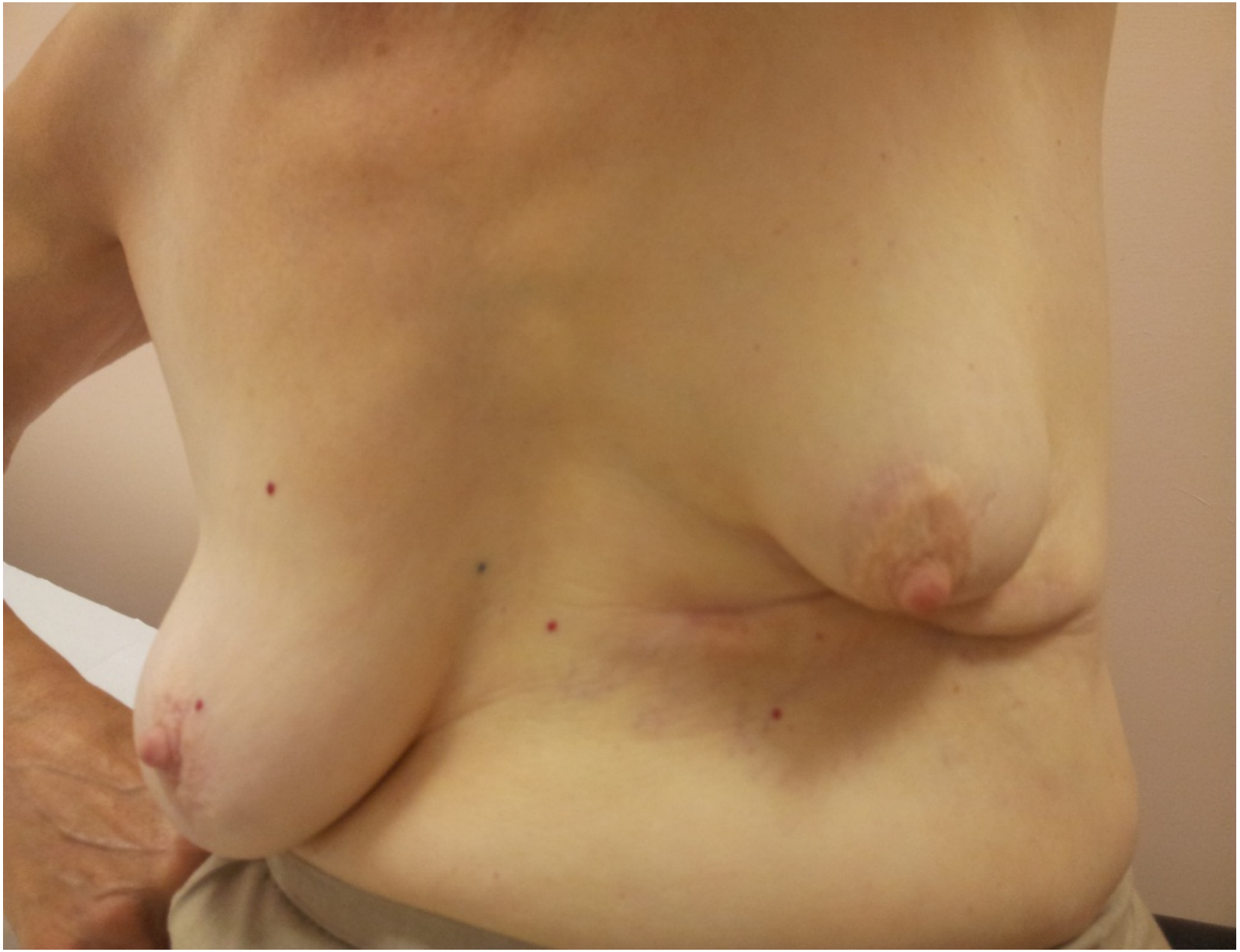
Tossicità a sei mesi dalla fine della RT



Caso di RT parziale a sin e standard a dx



C. N. 25/12/34



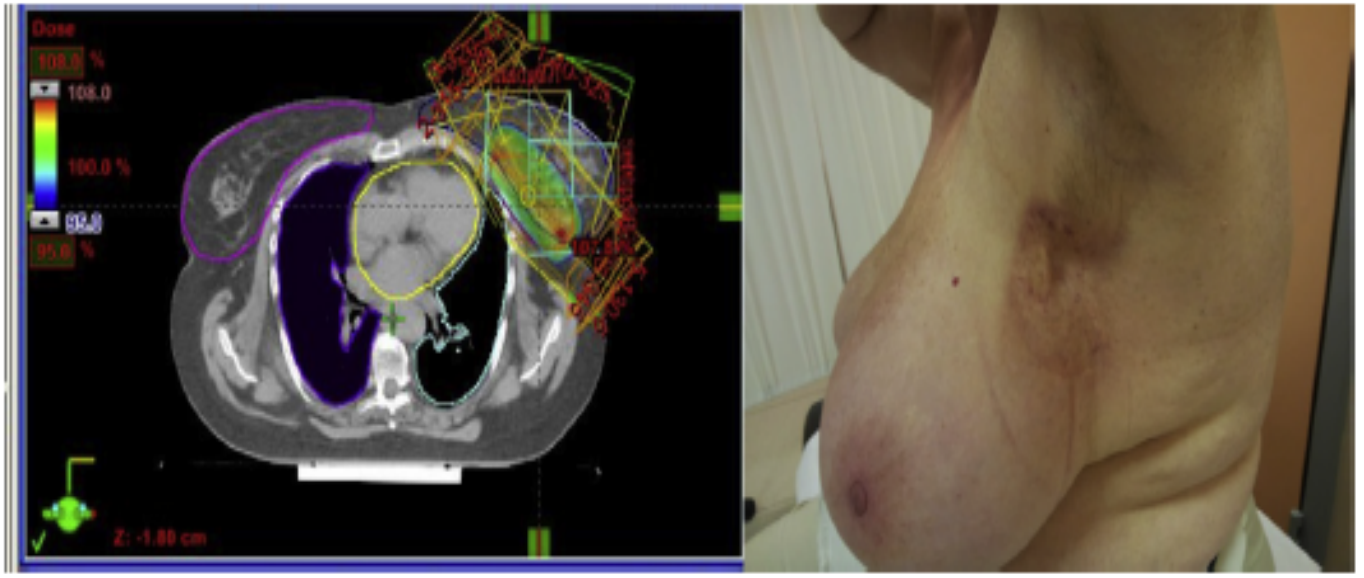


Fig. 1. Treatment plan with axial dose distribution and follow-up picture of the patient with important telangiectasia.

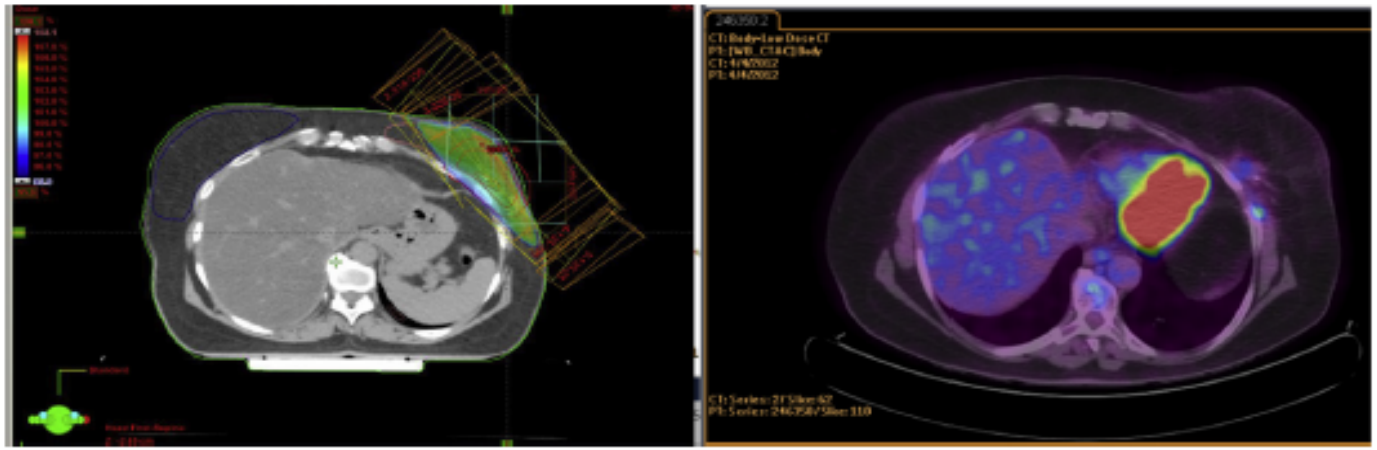


Fig. 2. Treatment plan with dose distribution of the patient with rib fracture. The fractured rib is covered by 100% of isodose.

CONCLUSIONI

- Tecnica complessa ma non invasiva
- Non necessita di personale addestrato ad hoc
- Il coinvolgimento del chirurgo nella fase di contouring “sarebbe” importante.
- Test anti-collisione obbligatorio prima dell’inizio della RT
- Positionamento del paziente ben tollerato, sul piano inclinato standard e posizione supina
- Il tempo di trattamento è di 20/25 min per seduta

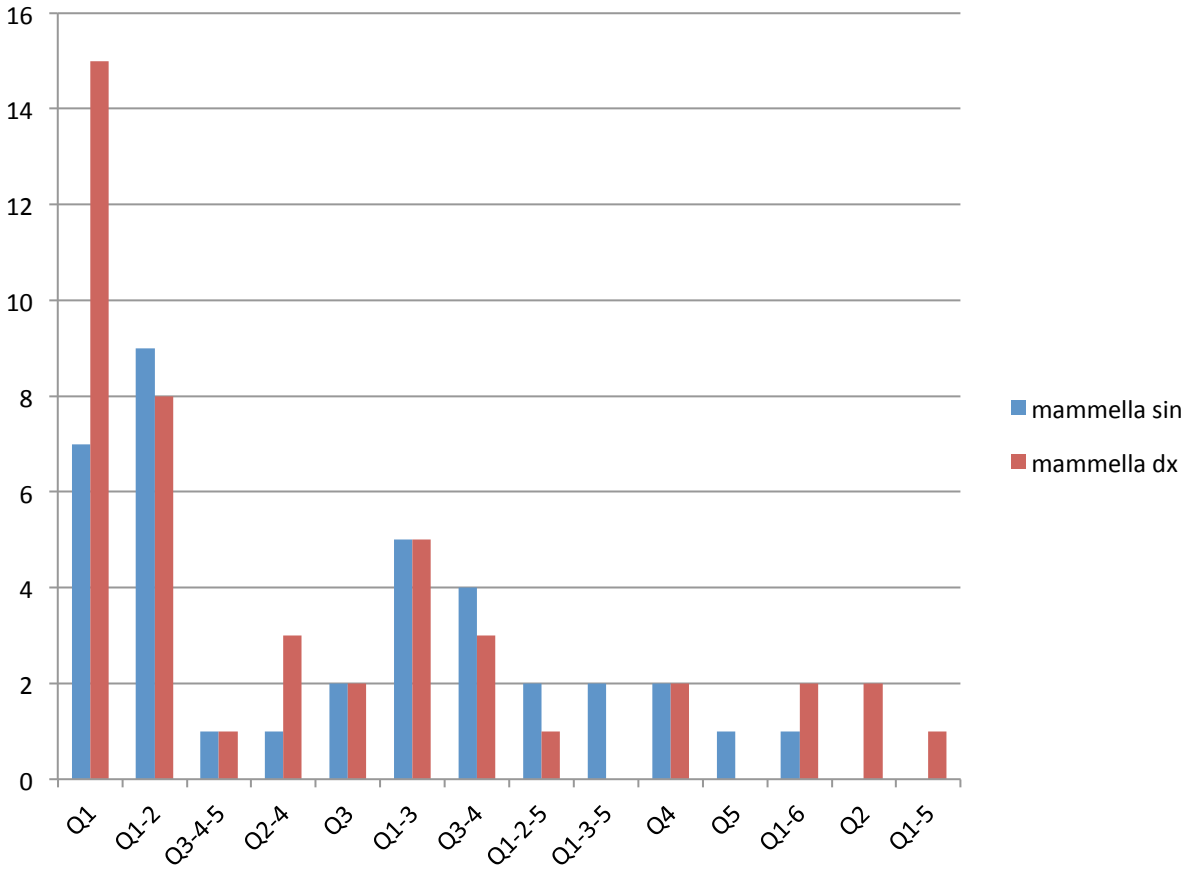
…ma bisogna attendere un follow-up più lungo…

Numero dei pazienti: 84

Mammella dx: 46 casi

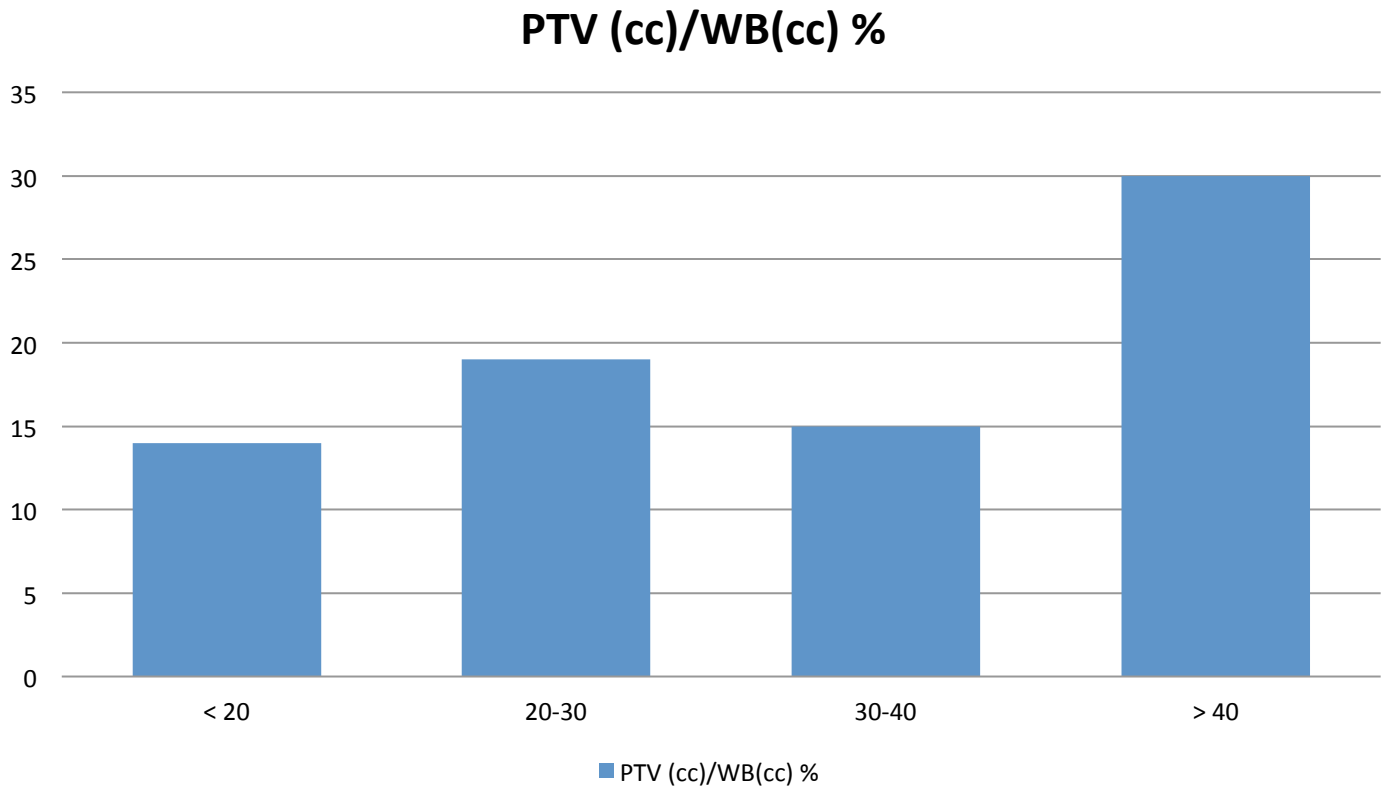
1 caso bilaterale

Mammella sin: 37 casi



Caratteristiche dei pazienti

Età mediana (anni)	69 (intervallo da 53 a 88)
Follow-up mediano	23 (1-72)
Stadio	
pT1a pT1b pT1c pT1mic pT2	9 (11%) 32 (38.1%) 38 (45.2%) 1 (1.2%) 4 (4.8%)
Recettori ormonali espressi	100%
Dose 34 Gy 38.5 Gy	 60 (71.4%) 24 (28.6%)


PTV (cc)/WB(cc) %
35
30
25
20
15
10
5
0
< 20
20-30
30-40
> 40
PTV (cc)/WB(cc) %

OBIETTIVI PRIMARI DELLO STUDIO

- **Determinare la fattibilità e la riproducibilità della 3D-CRT parziale e accelerata nelle a basso rischio di recidiva locale sottoposte a chirurgia conservativa della mammella e a biopsia del linf sentinella e/o dissezione dei linf ascellari**

- **Determinare l'esito cosmetico nelle pazienti trattate con la metodica**

- **Determinare il tasso di complicazioni nelle pazienti trattate con la metodica**

OBIETTIVO SECONDARIO DELLO STUDIO

- **Determinare il tasso di controllo locale della malattia nelle pazienti trattate con 3D-CRT parziale e accelerata della mammella.**

CRITERI DI ELIGIBILITA' I

- **Carcinoma della mammella invasivo confermato istologicamente:**

- pT 1-2 (< 3 cm di diametro) pN0 M0 secondo la classificazione TNM
- Malattia unifocale (confermata radiologicamente e istologicamente)
- Istotipi eleggibili: Duttale invasivo, Midollare, Papillare, Colloide (mucinoso), Tubulare

CRITERI DI ELIGIBILITA' II

- **Pazienti sottoposte a chirurgia mammaria conservativa per neoplasie di diametro < 3 cm ed a biopsia del linf sentinella o a dissezione ascellare:**

- Margini della resezione mammaria istologicamente negativi (≥ 2 mm) al primo intervento o dopo successivo ampliamento
- Conferma radiologica del pezzo operatorio dell'inclusione delle lesioni occulte e/o delle microcalcificazioni se presenti nella mammografia pre-intervento
- Posizionamento di 6 clip in titanio per delineare la cavità bioptica (letto tumorale)

CRITERI DI ELIGIBILITA III

- **Devono essere trascorse almeno due settimane dalla fine della chemioterapia qualora questa venga somministrata prima della radioterapia**

- **Non deve essere eseguita alcuna chemioterapia durante e per almeno due settimane dopo il completamento della radioterapia**

- **Ammessa terapia con tamoxifene o inibitori dell'aromatasi concomitante**
- **Età ≥ 50 anni**
- **Sesso: femminile**

CRITERI DI INELIGIBILITÀ I

- **Carcinoma lobulare invasivo o carcinoma lobulare in situ (CLIS) o carcinoma duttale in situ puro (CDIS)**
- **Neoplasie mammarie non epiteliali (sarcoma, linfoma etc.)**
- **Micro/macrometastasi nei linfonodi ascellari e/o mammari interni e/o sovra e sottoclaveari**
- **Carcinomi multicentrici.**
- **Linfonodi palpabili o radiologicamente sospetti in sede: ascellare controlaterale, sopra e infraclavicolare, e mammaria interna**

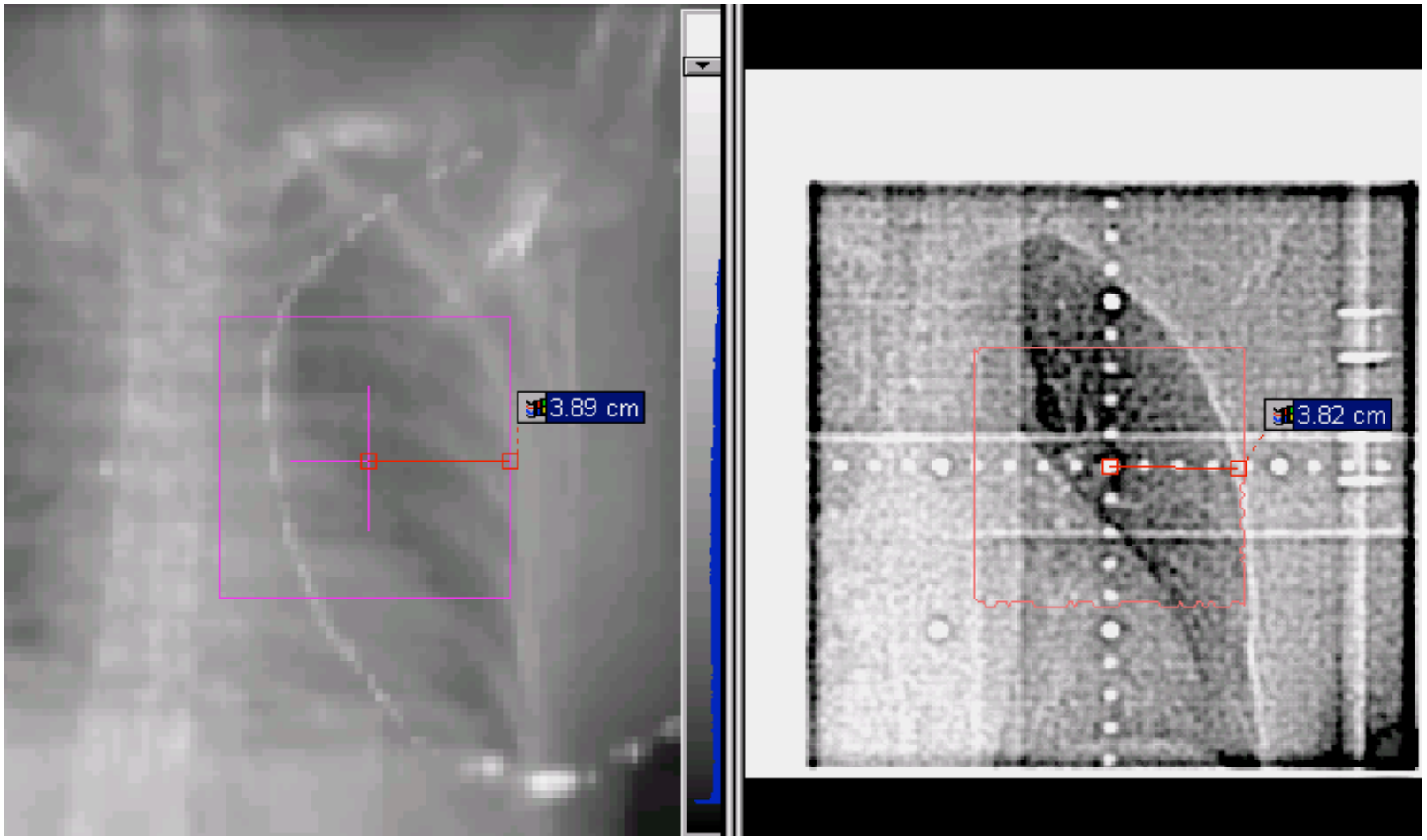
CRITERI DI INELIGIBILITA II

seguenti criteri (definizione di Harvard):

a. Più del 25 % della neoplasia invasive costituita da CDIS e/o presenza di CDIS nel tessuto mammario adiacente alla neoplasia invasiva
b. CDIS con microinvasione

- **Trattamenti per precedenti carcinomi mammari controlaterali o ipsilaterali**
- **Malattia di Paget del capezzolo**
- **Coinvolgimento cutaneo di malattia, indipendentemente dal diametro tumorale**
- **Metastasi a distanza**
- **Pregressi trattamenti radianti sulla regione toracica**
- **Malattie del collageno (lupus eritematoso sistemico, sclerodermia, dermatomiosite)**

DRR vs. DPI a 0°: tolleranza 5 mm



DRR vs. DPI a 90°: tolleranza 5 mm