HUMANITAS
CANCER CENTER

IBDC
International Breast Disease Centers

4th International Congress of Breast Disease Centers 2014

Single Institution experience with hypofractionated simultaneous integrated boost using volumetric modulated arc therapy and extending its indications for DCIS

FIORENZA DE ROSE MD

RADIATION ONCOLOGY

Humanitas Research Hospital, Rozzano (Milan)

BACKGROUND

- Breast-conserving surgery and radiation is a standard alternative to mastectomy for most patients with early stage breast cancer (stage I-II)

- Conventional radiation fractionation of 1,8-2 Gy per day is delivered in 6-7 weeks of treatment

Hypofractionated WBI: Why?

THE RADIOBIOLOGIC ISSUE

- Breast cancer has an alpha/beta ratio for tumor control of 4,6 (larger fraction sizes maximize local control in tumor tissue)
- Radiobiologic models show that increasing fraction size with a large reduction of the total radiation dose can keep late toxicity comparable to that seen with conventional fractionation
- Moreover, the reduction of treatment time (3/4 weeks) reduces the possibility of tumor cells to repair the radiation injury

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

Hypofractionated WBI: When?

LITERATURE DATA

ELSEVIER

International Journal of Radiation Oncology*Biology*Physics

Volume 81, Issue 1, 1 September 2011, Pages 59–68

Clinical Investigation

Fractionation for Whole Breast Irradiation: An American Society for Radiation Oncology (ASTRO) Evidence-Based Guideline

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

[4]Bent: hypofra

[5]Bent: hypofra

[6]Owe local tu

cer after

[7]Whel 2010;36

Hypofractionated WBI: Which?

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

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

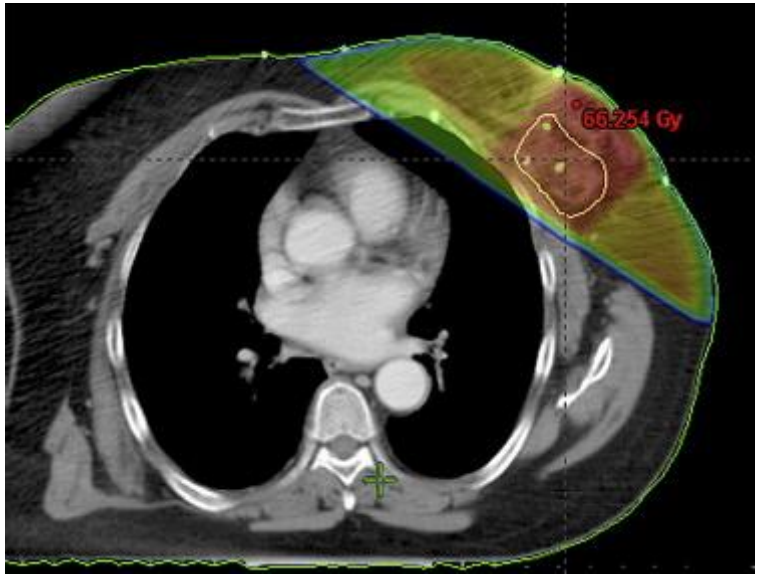
... Whole-breast dose of 40 Gy delivered in 15 fractions is gentler on normal tissues than conventional regimen without evidence of inferior local tumor control …

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

Hypofractionated WBI: OPEN ISSUES
Tumor bed boost

- The use of tumor bed boost reduced the risk of local recurrence even in patients with negative resection margins

- Few data to define the indications for and toxicity of tumor bed boost in patients treated with hypofractionated WBI



Bartelink H. et al. Impact of higher radiation dose on local control and survival in breast-conserving therapy of early breast cancer: 10-year results of the randomized boostversus no boost. EORTC trial . Am J Clin Onc 2007;25:3259-65

Smith BD. Et al . Fractionation for whole breast irradiation: an American Society for Radiation Oncology (ASTRO) evidence-based guideline. Int J Radiat Oncol Biol Phys 2011; 81: 59-68

Hypofractionated WBI: OPEN ISSUES
Tumor bed boost

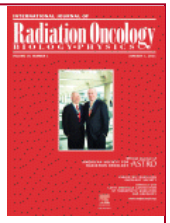
Phase I/II trials of whole-breast hypofractionation and concurrent boost reporting in-breast recurrence rates in early stage breast cancer.

Trial	Accrued	Median F/U (yr.)	Fractionation		In-breast recurrence
			Whole breast fractionation	Lumpectomy volume Fractionation	
Formenti [40]	91	1	2.7 Gy × 15 = 40.5 Gy	3.2 Gy × 15 = 48 Gy	0
Teh [47]	15	1	2.65 Gy × 16 = 42.2 Gy	3.28 Gy × 16 = 52.48 Gy	0
Cante [44]	463	2.3	2.25 Gy × 20 = 45 Gy	2.75 Gy × 20 = 55 Gy	0
Morganti [48]	201	2.6	2.5 Gy × 16 = 40 Gy 2 Gy × 25 = 50 Gy	2.75 Gy × 16 = 44 Gy 2.4 Gy × 25 = 60 Gy	0
Corvo [45]	377	3	2.3 Gy × 20 = 46 Gy	3.5 Gy × 5 = 52 Gy	0
Ciervide [41]	145	5	2.8 Gy × 15 = 42 Gy2.7 Gy × 15 = 40.5 Gy	3.3 Gy × 15 = 49.5 Gy3.2 Gy × 15 = 48 Gy	4.1%
Freedman [43]	75	5.8	2.25 Gy × 20 = 45 Gy	2.8 Gy × 20 = 56 Gy	2.7%

Hypofractionated WBI: OPEN ISSUES
Ductal Carcinoma in situ

- There are few published data evaluating the effectiveness of hypofractionated RT in DCIS
- The role of additional RT to the surgical bed in patients with DCIS has not been studied in phase III trials

Clinical Investigation



Hypofractionated Radiation Therapy for Breast Ductal Carcinoma In Situ

Lara Hathout, MD,* Tarek Hijal, MD,† Valérie Théberge, MD,‡,§ Bernard Fortin, MD,* Horia Vulpe, MD,† Jean-Charles Hogue, MD,§,|| Christine Lambert, MD,† Houda Bahig, MD,* Louise Provencher, MD,§,|| Peter Vavassis, MD,* and Michael Yassa, MD*

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

RADIATION ONCOLOGY

STUDY PROTOCOL Open Access

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

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

Characteristics of the STUDY

- This is a **phase I-II prospective non-randomized trial** of adjuvant radiotherapy with simultaneous integrated boost (SIB) delivered with RapidArc technology.

- The study was approved by the **internal ethical committee** and patient consent was obtained.

- The study will include 450 patients with a total period of 10 years of follow-up.

Characteristics of the study: OBJECTIVES

- **Primary endpoint** of the study is to evaluate the feasibility of VMAT and hypofractionation with simultaneous integrated boost in breast cancer patients at early stage and undergoing conservative surgery.

- **Secondary endpoint** of the study is the evaluation of toxicity in terms of acute and late side effects.

- It will also be assessed the local control, even if it is not an explicit objective of the study.

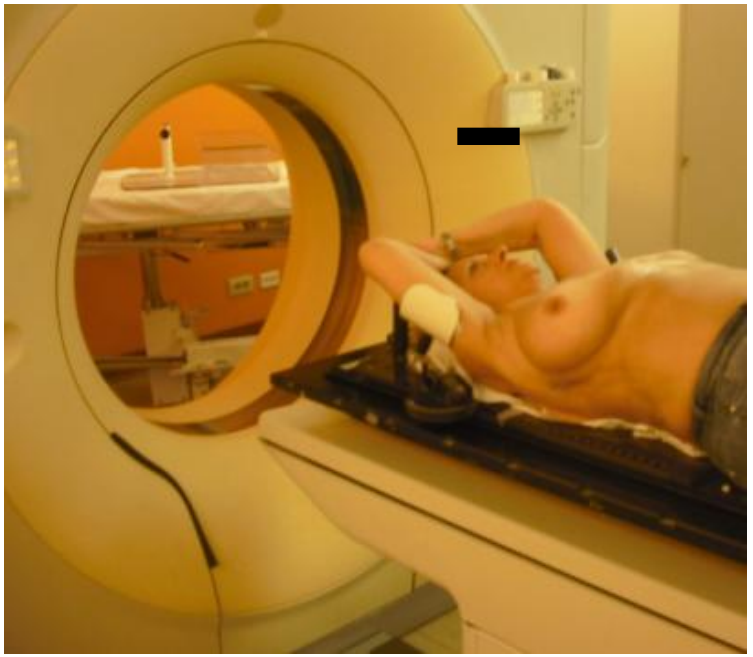
Characteristics of the study: PATIENTS SELECTION

•The study is still recruiting patients: here we present the preliminary data of toxicity and clinical assessment of the first 252 patients

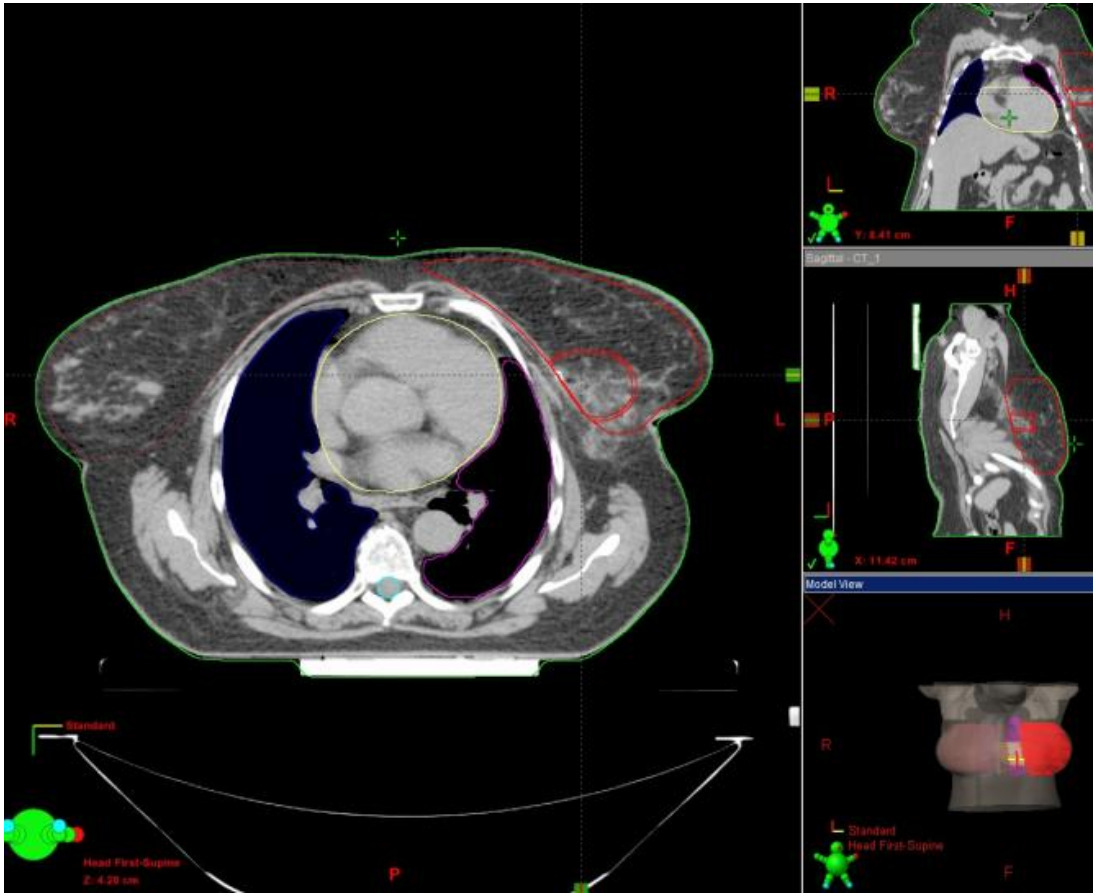
•Eligibility criteria were:
- age >18 years
- invasive cancer or DCIS
- American Joint Committee on Cancer AJCC Stage I to II
- breast-conserving surgery
- any systemic therapy

Characteristics of the study: PLANNING DETAILS

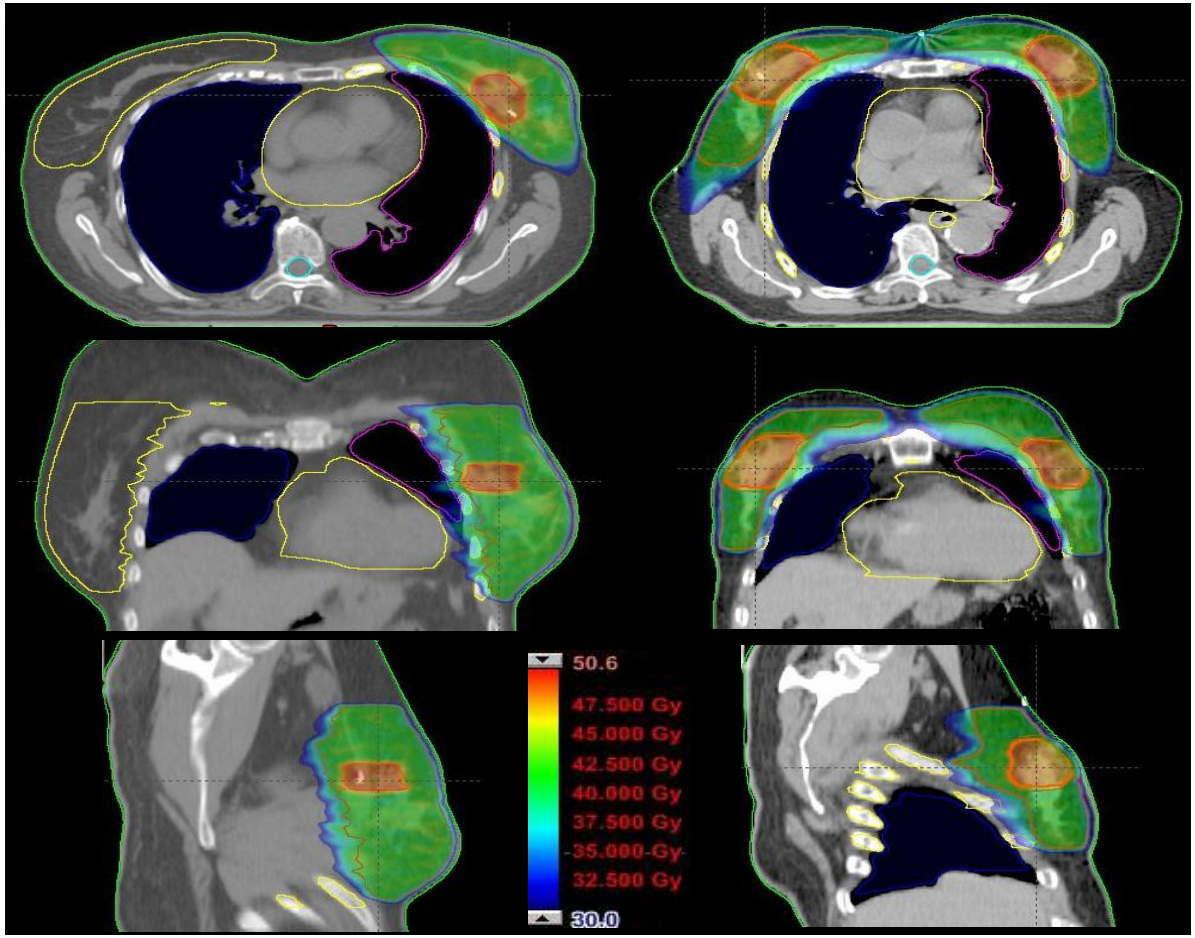
- Patients were in supine position, with both arms above the head
- CT dataset was acquired with 3 mm thick adjacent slices
- No respiratory gating was adopted



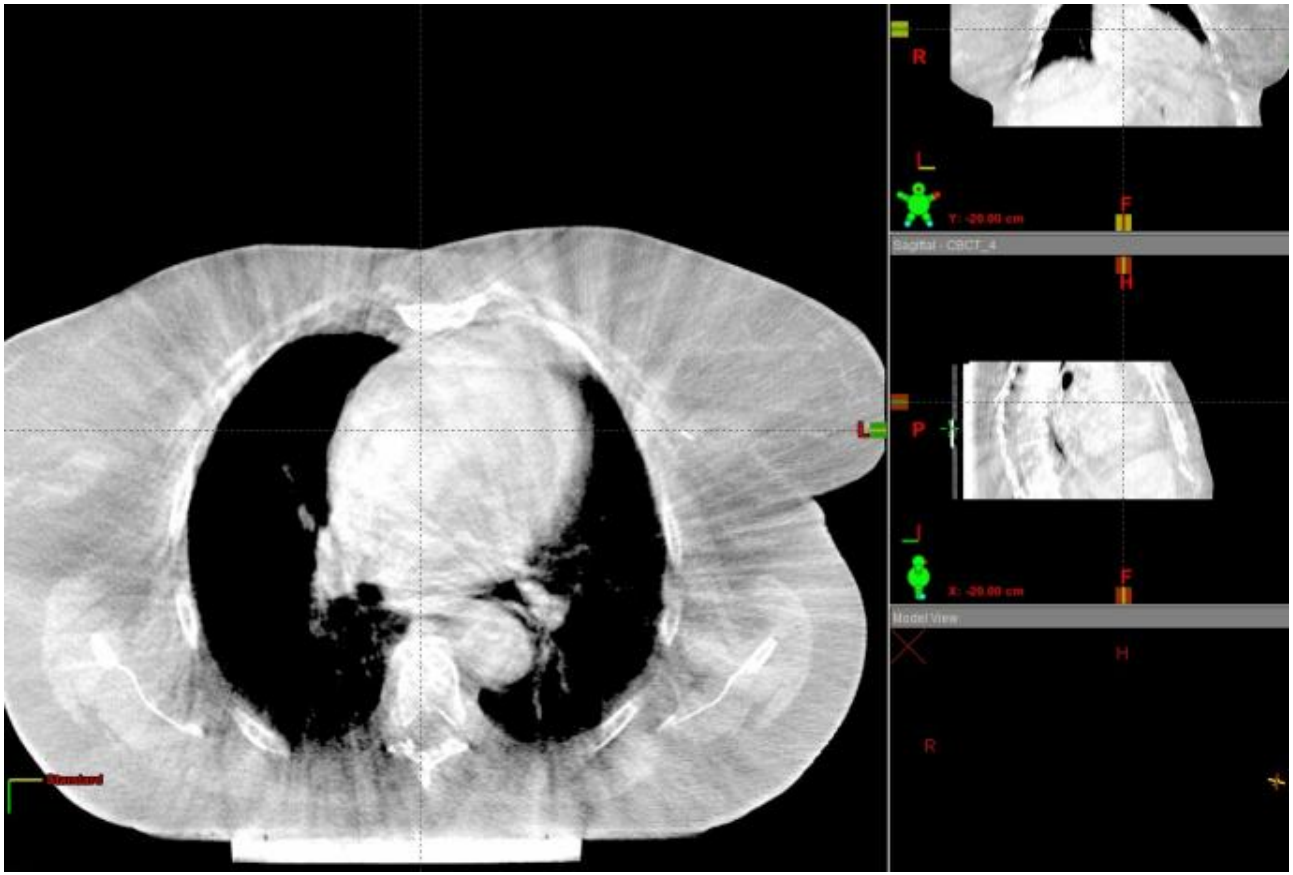
Characteristics of the study: PLANNING DETAILS



Characteristics of the study: PLANNING DETAILS



Characteristics of the study: PLANNING DETAILS

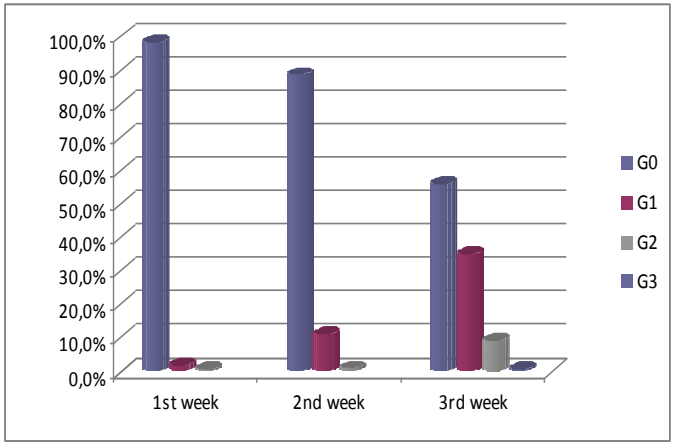


Characteristics of the study: CLINICAL ASSESSMENT

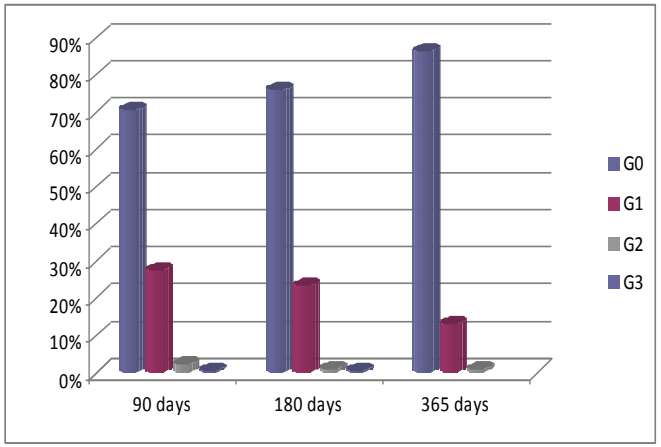
- Skin toxicity was visually assessed by objective clinical exam and pictures of irradiated breast during each visit (during treatment and during follow-up)
- Acute skin toxicities were recorded according to RTOG scoring criteria
- Late skin toxicities were recorded according to CTCAE v4.0
- Cosmetic outcomes were assessed as excellent/good or fair/poor

Characteristics of the study: CLINICAL RESULTS

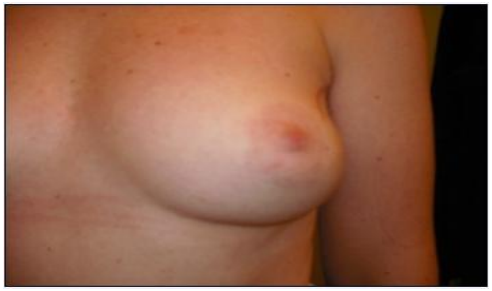
- Median follow up of 22 months
- All patients were scored as excellent/good (252/252) compared with baseline
- 3 cases of recurrences, all of them out of RT fields



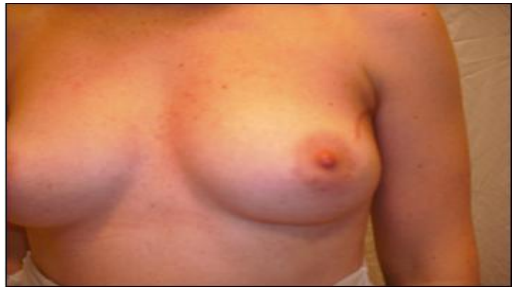
Skin Toxicity during treatment



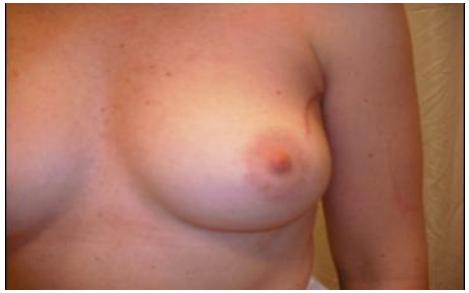
Skin Toxicity after treatment



Pre RT



End of RT



Follow up @ 90 days

Skin clinical results: comparison with literature

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

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

CONCLUSIONS

- The 3-week course of postoperative radiation using VMAT with SIB showed to be well tolerated in acute and early late setting and was associated with optimal local control.

- Long-term follow-up data are needed to assess late toxicity and clinical outcomes.

THANKS FOR YOUR ATTENTION