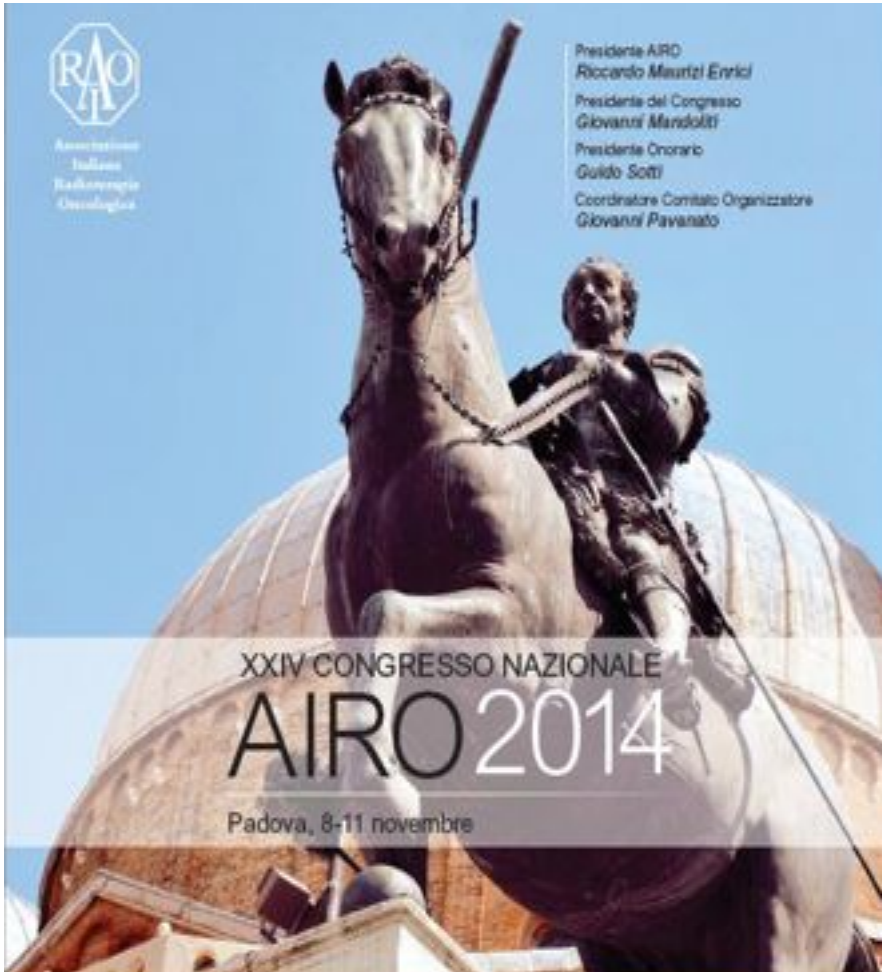


TOSSICITÀ E SICUREZZA DELL'IRRADIAZIONE PARZIALE ACCELERATA DELLA MAMMELLA CON TECNICA AD INTENSITÀ MODULATA (IMRT) VERSUS TECNICA CONVENZIONALE:

RISULTATI A CINQUE ANNI DI UNO STUDIO RANDOMIZZATO DI FASE 3 CONDOTTO PRESSO L'UNIVERSITÀ DI FIRENZE

V. Di Cataldo[1]***, C. Ciabatti***[2]***, A. Turkaj***[2]***, I. Desideri***[2]***, C. De Luca Cardillo***[2]***, V. Scotti***[2]***, G. Zei***[2]***, S. Cassani***[2]***, I. Giacomelli***[2]***, F. Meacci***[2]***, J. Topulli***[2]***, C. Muntoni***[2]***, I. Meattini***[2]***, L. Livi***[2]***.***

[1]Centro Cyberknife Firenze, Istituto Fiorentino di Cura ed Assistenza (IFCA), Università di Firenze;
[2]Radioterapia Oncologica, Azienda Ospedaliero Universitaria Careggi (AOUC), Università di Firenze

PHASE III TRIAL DESIGN

ACCELERATED IMRT TO TREAT THE INDEX QUADRANT

30 Gy in 5 fractions (6 Gy/fr in 2 weeks)

versus

STANDARD WHOLE BREAST RADIOTHERAPY

50 Gy + boost 10 Gy in 30 fractions (2 Gy/fr in 6 weeks)

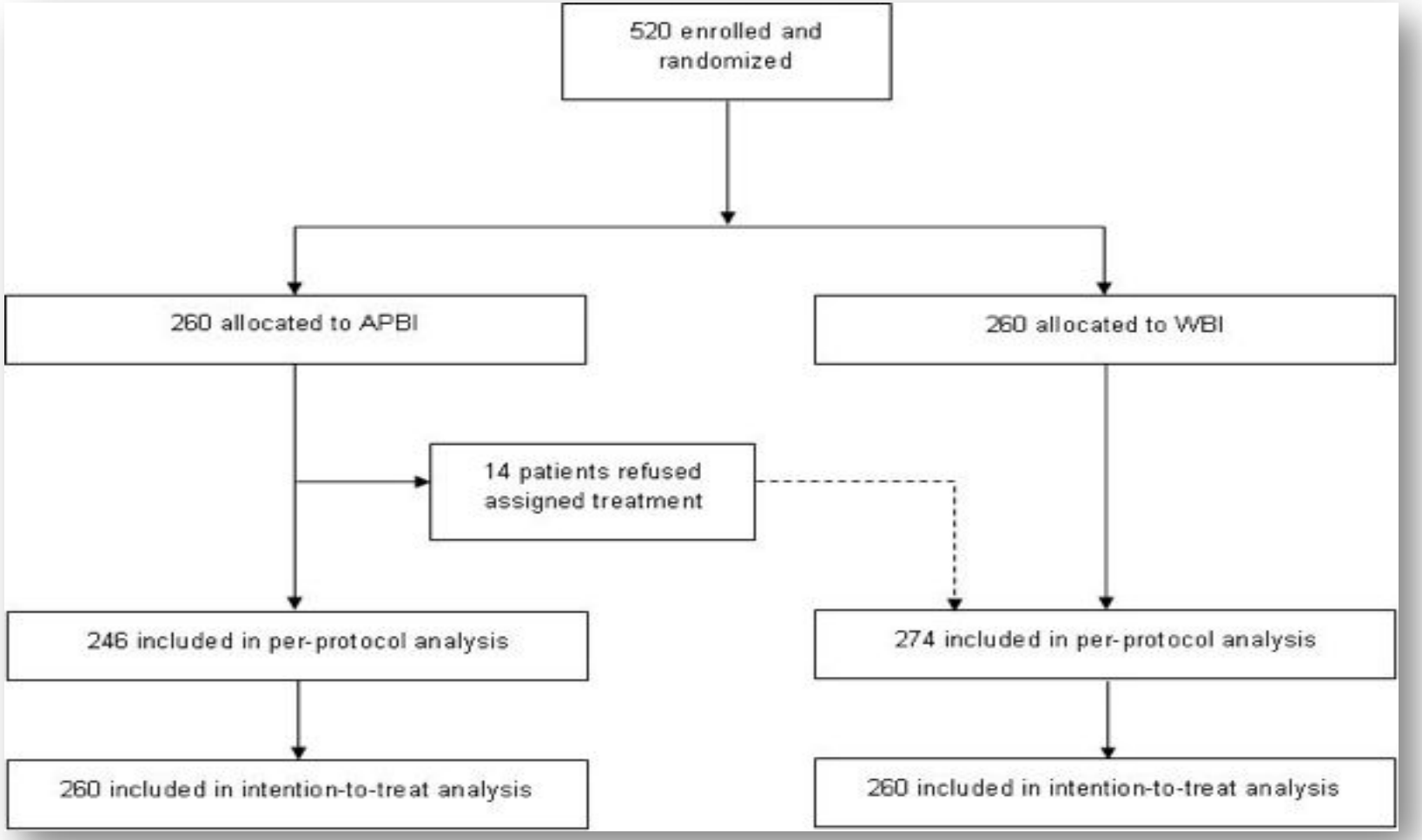
*AFTER CONSERVING SURGERY IN HIGHLY **SELECTED** EARLY BREAST CANCER **PATIENTS***

pT < 25 mm
surgical margins > 5 mm
aged > 40 year

Livi et al, IJROBP, 2010

Meattini et al, ESTRO 2014

PHASE III TRIAL DESIGN



2005-2013 (recruitment closed). *ClinicalTrials.gov Identifier: NCT02104895*

TARGET IDENTIFICATION

Surgical Clips

(mandatory)

to CTV identification

⇩

CTV

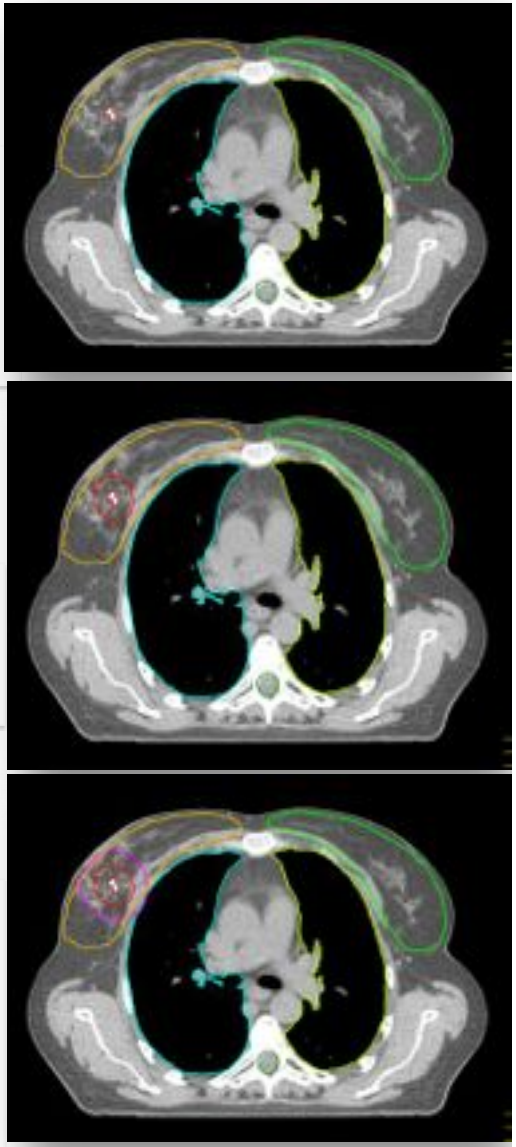
Surgical Clips + 1 cm 3D expansion

⇩

PTV

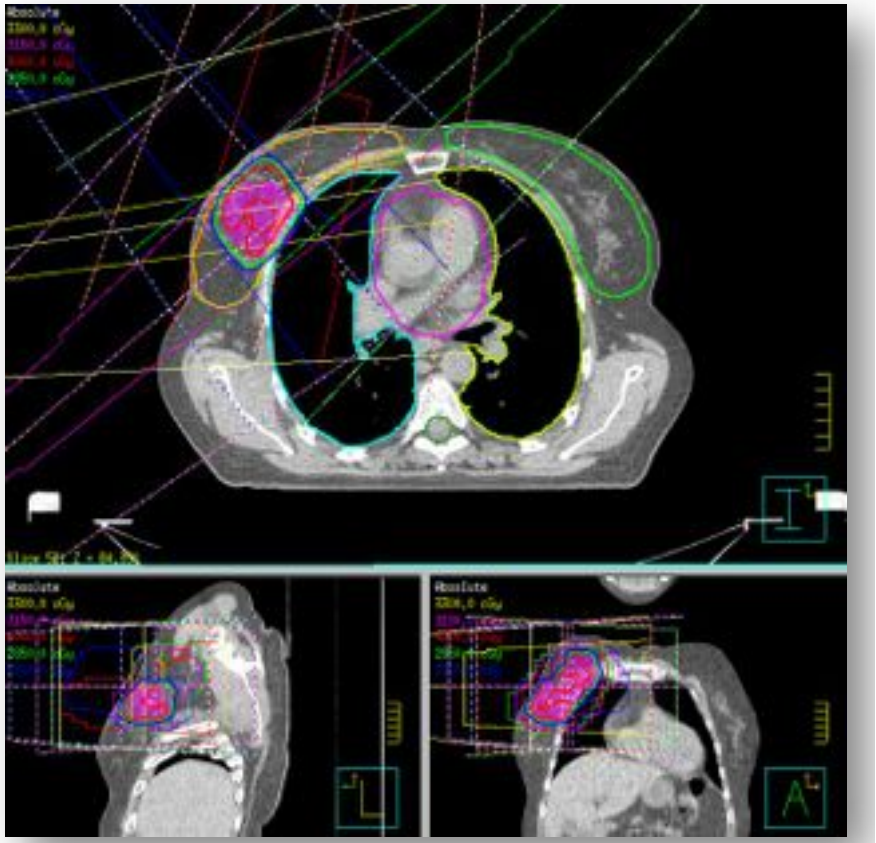
CTV + 1 cm 3D expansion

(limiting to 3 mm from skin and to 4 mm intrusion in homolateral lung)



APBI USING S&S IMRT TECHNIQUE

OARs	Constraints
Contralateral Lung	V5 < 10%
Homolateral Lung	V10 < 20%
Heart	V3 < 10%
Homolateral breast (uninvolved tissue)	V15 < 50%
Contralateral Breast	Max 1 Gy in each point



DVH analysis of PTV and CTV coverage

	Mean CTV dose (Gy)	Mean PTV dose (Gy)	Minimum PTV dose (Gy; 2% of PTV)	Maximum PTV dose (Gy)	CTV ≥95% of prescribed dose (28,5 Gy) (%)	PTV ≥95% of prescribed dose (28,5 Gy) (%)
Mean	30.4	30.1	28.3	32.2	98.9	96.6
Standard deviation	1.1	0.3	0.7	0.9	2.3	2.8
Median	30.3	30.0	28.4	32.1	100	97
Range	29.4-40.0	29.4-30.8	26.2-29.7	30.0-34.8	90-100	88-100

Abbreviations: DVH= dose-volume histogram; PTV=planning target volume; CTV= clinical target volume.

The planning constraints were fully satisfied in most patients.

Quality assurance procedures were performed according to our internal quality assurance protocol, with excellent results.

DVH analysis of OAR doses

	Heart volume ≥3Gy (%)	Dose to 10% of heart volume (Gy)	Uninvolved breast volume ≥15Gy (%)	Contralateral breast volume ≥ 1Gy (%)	Ipsilateral lung volume ≥10Gy (%)	Contralateral lung volume ≥5Gy (%)
Mean	7.4	2.5	32.3	1.1	10.3	0.9
Standard deviation	5.6	1.3	11.4	4.1	4.9	3.0
Median	8.0	2.8	31.0	0.0	11.0	0.0
Range	0.0-24.0*	0.0-6.4*	8.0-62.0*	0.0-36.0*	0.0-22.0*	0.0-19.0*

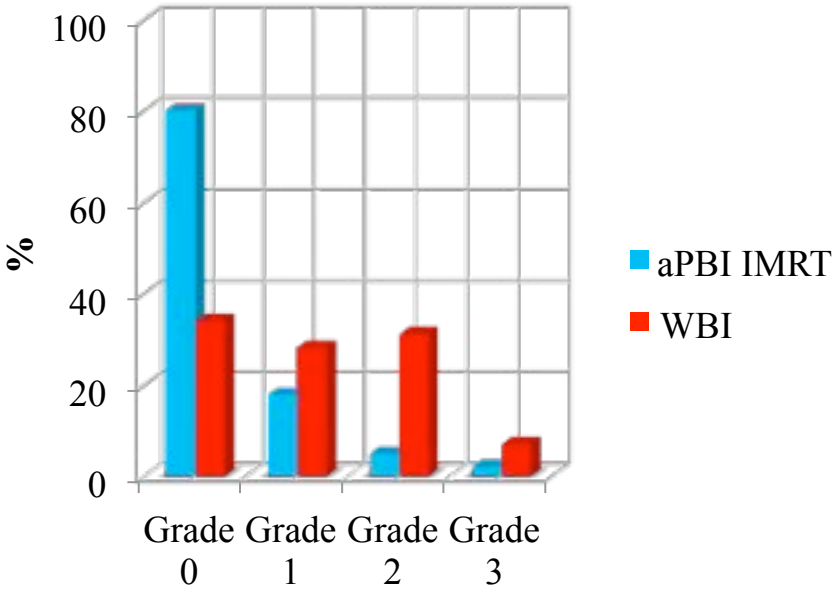
Abbreviations: DVH= dose volume histogram; OAR=organ at risk.

The planning constraints were fully satisfied in most patients.

Quality assurance procedures were performed according to our internal quality assurance protocol, with excellent results.

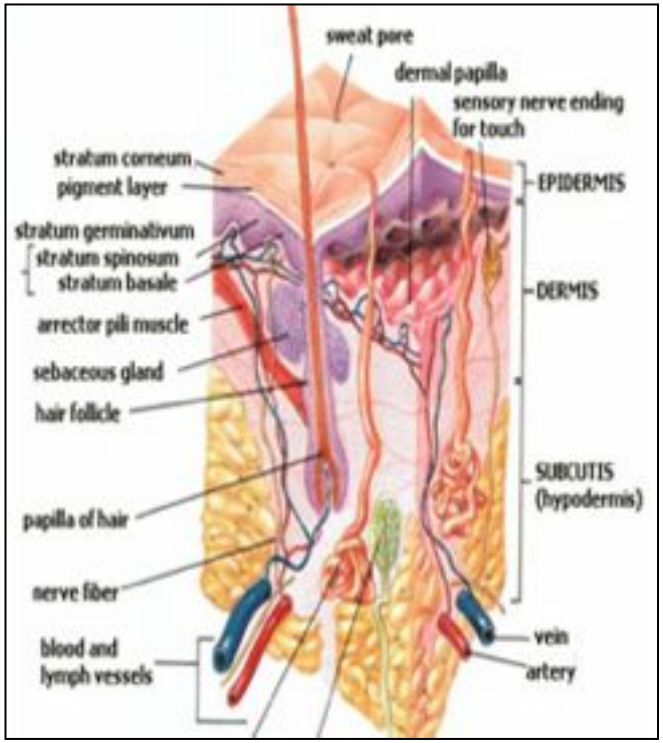
ACUTE SKIN TOXICITY

	WBI (n:274) N	%	APBI (n:246) N	%	p-value
Any skin toxicity					
None	93	33.9	197	80.1	
Yes, any Grade	181	66.1	49	19.9	**0.0001**
None	93	33.9	197	80.1	
Grade 1	77	28.1	44	17.9	
Grade 2	85	31.1	5	2.0	
Grade 3	19	6.9	0	0	
Grade 4	0	0	0	0	**0.0001**
Grade 0-1	170	62.0	241	98.0	
Grade ≥2	104	38.0	5	2.0	**0.0001**
Erythema					
None	93	33.9	197	80.1	
Grade 1-2	162	59.2	49	19.9	
Grade 3-4	19	6.9	0	0	
Breast edema					
None	225	82.1	246	100	
Grade 1-2	44	16.1	0	0	
Grade 3-4	5	1.8	0	0	
Pain					
None	244	89.1	246	100	
Grade 1-2	25	9.1	0	0	
Grade 3-4	5	1.8	0	0	



Acute toxicity was assessed using the Radiation Therapy Oncology Group (RTOG) acute radiation morbidity scoring criteria

ACUTE SKIN TOXICITY



Significantly higher acute toxicity in WBI arm

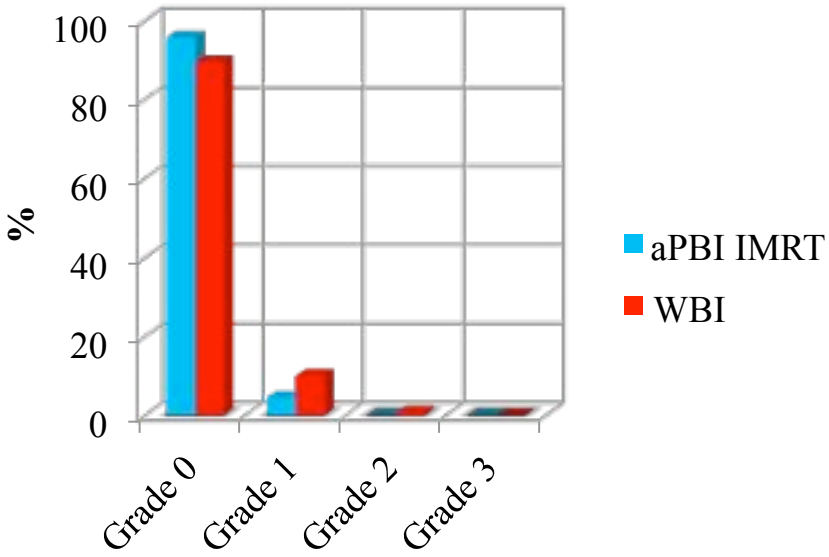
- Any grade *(p=0.0001)*
- ≥ Grade 2 *(p=0.0001)*

Most represented skin adverse event

- Grade 1-2 erythema **59.2% (WBI) *vs* 19.9% (APBI)**
- **No Grade 3** toxicity recorded in APBI arm

LATE SKIN TOXICITY

	WBI (n:274) N	%	APBI (n:246) N	%	p-value
Any skin toxicity					
None	245	89.4	235	95.5	
Yes, any Grade	29	10.6	11	4.5	**0.013**
None	245	89.4	235	95.5	
Grade 1	27	9.9	11	4.5	
Grade 2	2	0.7	0	0	
Grade 3	0	0	0	0	
Grade 4	0	0	0	0	**0.024**
Grade 0-1	272	99.3	246	100.0	
Grade ≥2	2	0.7	0	0	0.50
Fibrosis					
None	245	89.4	235	95.5	
Grade 1-2	29	10.6	11	4.5	
Grade 3-4	0	0	0	0	
Hyperpigmentation					
None	264	96.4	241	98.0	
Grade 1-2	10	3.6	5	2.0	
Grade 3-4	0	0	0	0	
Telangiectasia					
None	267	97.4	244	99.2	
Grade 1-2	7	2.6	2	0.8	
Grade 3-4	0	0	0	0	

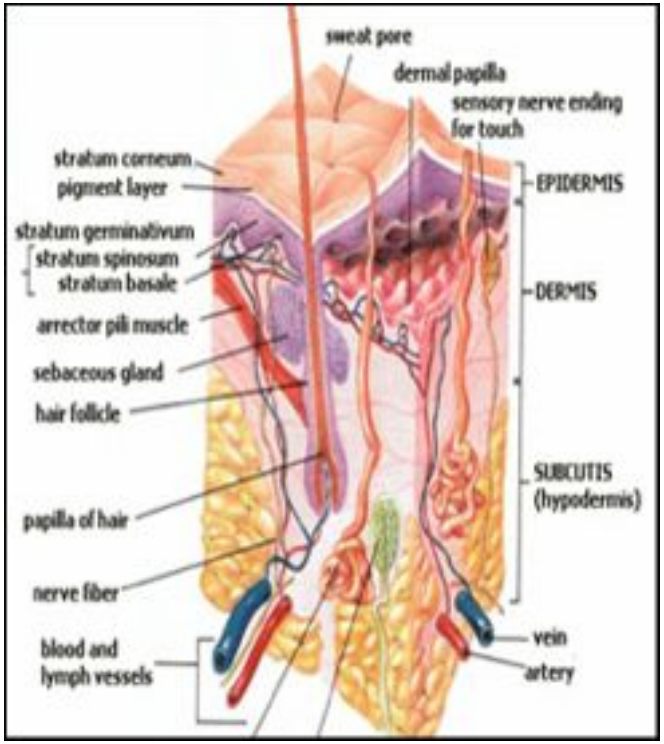


Late toxicity was assessed using the RTOG/EORTC late radiation morbidity scoring schema

LATE SKIN TOXICITY

Significantly higher late toxicity in WBI arm

- Any grade *(p=0.013)*
- Any single Grade *(p=0.024)*



Most represented skin adverse event

- Grade 1-2 fibrosis **10.6% (WBI) *vs* 4.5% (APBI)**
- No Grade 3 toxicity recorded in both arms

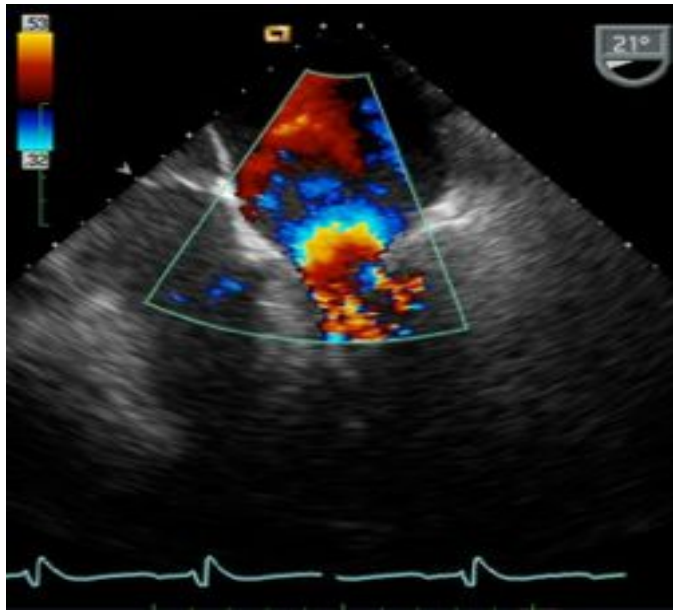
EARLY LATE TOXICITY

- Annual ecographic measurement of left ventricular ejection fraction (LVEF)

→ LVEF dysfunction ≥ Grade 2: None observed

- Basal and annual measurement of forced expiratory volume in 1 sec (FEV_1)
- →FEV_1 significant decrease: None

- No rib fractures or fat necrosis observed



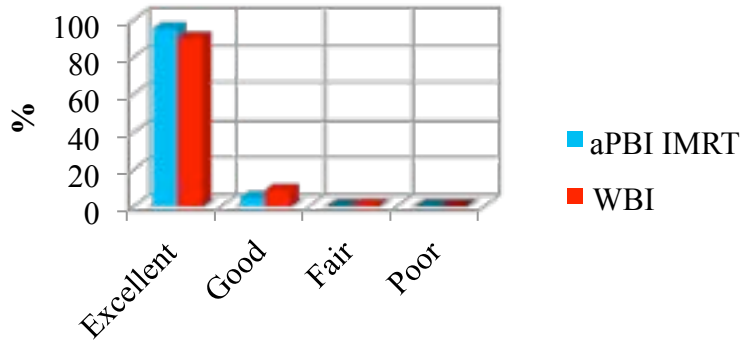
COSMESIS

	All patients n=520		>12 months follow-up n=487		>24 months follow-up n=457		>36 months follow-up n=407		>48 months follow-up n=337	
Cosmetic result	*APBI n=246*	*WBI n=274*	*APBI n=221*	*WBI n=266*	*APBI n=198*	*WBI n=259*	*APBI n=182*	*WBI n=225*	*APBI n=154*	*WBI n=183*
Excellent	234 (95.1)	247 (90.1)	209 (94.6)	239 (89.8)	186 (93.9)	232 (89.6)	172 (94.5)	200 (88.9)	144 (93.5)	162 (88.5)
Good	12 (4.9)	25 (9.1)	12 (5.4)	25 (9.4)	12 (6.1)	25 (9.7)	10 (5.5)	23 (10.2)	10 (6.5)	19 (10.4)
Fair	0	2 (0.8)	0	2 (0.8)	0	2 (0.8)	0	2 (0.9)	0	2 (1.1)
Poor	0	0	0	0	0	0	0	0	0	0

-337 patients **(64.8%)** had a cosmetic evaluation with a **minimum follow-up of 48 months.**

-In both treatment groups the cosmetic result was rated as **excellent/good** for more than **90%** of patients.

-Overall, APBI arm showed **comparable outcome** to WBI arm (p=0.066).



CONCLUSIONS

- Overall rates of **acute toxicity** and ≥ Grade 2 acute toxicity were significantly higher among WBI patients;
- Overall rates of **late toxicity** were significantly higher among WBI patients
- **No Grade 3 late toxicity** was recorded in APBI arm
- Breast retraction, pulmonary and cardiac symptoms, and rib fracture were **not** observed
- The **planning constraints** were fully satisfied in most patients
- **Cosmesis and safety** were excellent at 5-year median follow up
- **APBI** can be safely administered using **IMRT**

GRAZIE PER L'ATTENZIONE