RISULTATI DI CONTROLLO LOCALE E TOSSICITA', CON PARTICOLARE ATTENZIONE ALL'ASSOCIAZIONE CON TERAPIE SISTEMICHE, DEL TRATTAMENTO COMBINATO CON BOOST IORT E RADIOTERAPIA A FASCI ESTERNI SU TUTTA LA MAMMELLA

A. Ciabattoni §, A. Stefanelli °

§ UOC Radioterapia
Ospedale S. Filippo Neri, Roma

° UO C Radioterapia
Ospedale S. Anna, Ferrara

DICHIARAZIONE

Relatore: Antonella Ciabattoni

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Consulenza ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazione ad Advisory Board **(NIENTE DA DICHIARARE /)**
- Titolarietà di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**

Research

JAMA Oncology | Original Investigation

Prognostic Factors For Local Control in Breast Cancer After Long-term Follow-up in the EORTC Boost vs No Boost Trial
A Randomized Clinical Trial

Conny Vrieling, MD, PhD; Erik van Werkhoven, MSc; Philippe Maingon, MD, PhD; Philip Poortmans, MD, PhD; Caroline Weltens, MD, PhD; Alain Fourquet, MD, PhD; Dominic Schinagl, MD, PhD; Bing Oei, MD; Carla C. Rodenhuis, MD, PhD; Jean-Claude Horiot, MD, PhD; Henk Struikmans, MD, PhD; Erik Van Limbergen, MD, PhD; Youlia Kirova, MD; Paula Elkhuizen, MD, PhD; Rudolf Bongartz, MD; Raymond Miralbell, MD; David A. L. Morgan, MD; Jean-Bernard Dubois, MD; Vincent Remouchamps, MD, PhD; René-Olivier Mirimanoff, MD; Guus Hart, MSc; Sandra Collette, MSc; Laurence Collette, MSc, PhD; Harry Bartelink, MD, PhD; For the European Organisation for Research and Treatment of Cancer, Radiation Oncology and Breast Cancer Groups.

2016

Table 1. Cumulative Incidence of Ipsilateral Breast Tumor Recurrence as First Event at 20 Years of Follow-up (Univariate Effects)

Variable	Subjects	Events	Cumulative Local Recurrence Probability, % (95% CI)	P Value
Treatment				<.001
No boost	801	99	17 (13-20)	
16-Gy boost	815	61	12 (9-16)	
Age, y				<.001
27-40	183	49	34 (25-41)	
41-50	442	44	14 (10-18)	
>50	991	67	11 (8-15)	
Presence of DCIS				<.001
No	664	44	9 (6-12)	
Yes	914	110	18 (14-22)	
Histological grade of invasive tumor				.08
Low	784	70	12 (10-15)	
Intermediate	398	35	14 (9-18)	
High	363	42	16 (10-22)	

ASL ROMA 1 — REGIONE LAZIO

LANDESKRANKENHAUS SALZBURG
UNIVERSITÄTSKLINIKUM
DER PARACELSUS MEDIZINISCHEN PRIVATUNIVERSITÄT

Hypofractionated Whole-Breast Irradiation preceded by Intra-Operative Radiotherapy with Electrons as anticipated Boost

HIOB

A new Option in Breast-Conserving Treatment for Operated Breast Cancer Stages I and II

Prospective one-armed multi-center-trial
ISIORT 01

Principal Investigator: Univ. Prof. Dr. F. Sedlmayer
Co-Principal Investigator: Dr. G. Fastner

Study Site Salzburg : Co-Investigators
Radio-Oncology:
Dr. G. Kametriser
Dr. M. Kopp
Dr. A. Vaszi
Dr. K. Anderhuber
Dr. Karin Dagn
Special Gynegology
Univ.Prof. Dr. C. Menzel
Assoc. Prof Dr. R. Reitsamer
Dr. S. Glück
Dr. C. Wilhelm

Coordinator for Italy:
Dr. Antonella Ciabattoni, San Francisco Neri, Rome, Italy

Biostatistician:
PD Dr.W.Hitzl
Dr. P.Kopp
Dr. F. Merz

Study Coordinator: Protocol Office

Data management
DI Bernhard Mitterlechner

Sponsor
Intraop Medical, Krebshilfe Salzburg

2011

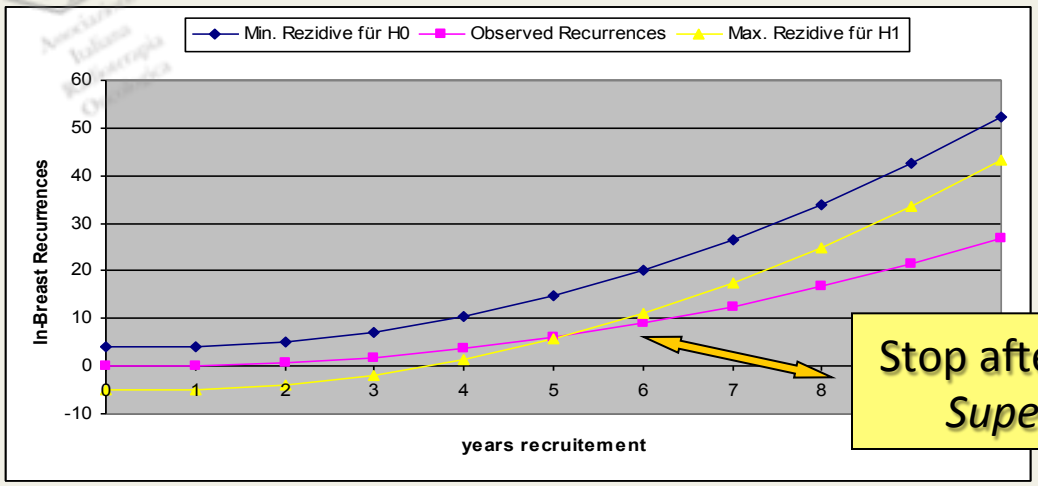
HIOB - WBI

- IORT anticipated boost (10 Gy)
- WBI only (no RNI)
- 2.7 Gy (ICRU) x 15 (5 Fx/week)

Statistics

Sequential Probability Ratio Test - SPRT

- Age > 50: 0.7% (Bartelink)
  0.4 % (START B)
- Age 41-50 : 1.2% (Bartelink) → Upper limit (tolerated)
  0.72% (Whelan) → Lower limit (best published)
- Age 35-40: 2% (Bartelink)
  0.72% (Whelan)



Stop after 5 years:
Superiority

Study Endpoints

Primary:
Proof of superiority of new treatment regimen

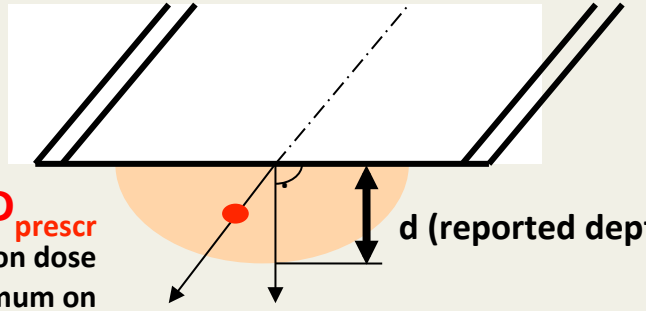
Secondary:
Disease free survival

Tertiary:
Assessment of acute toxicity (CTC)
Assessment of late toxicity (LENT-SOMA)
Assessment of cosmetic outcome (5-point-Scoring System)

Study Inclusion Criteria

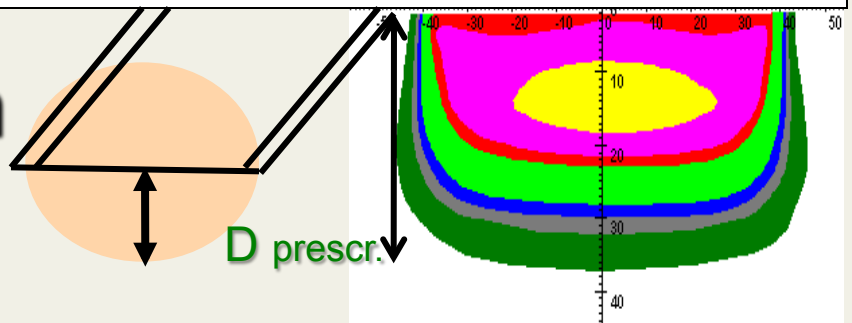
- Invasive breast cancer
- Age: ≥ 35 years
- Tumour stages T1-2
- Nodal status: N0-1
- R0 resection
- Multifocal disease within the same quadrant (< 5 cm)
- All grades and receptor status (G1-G3, any HR and Her-2)
- Adjuvant therapy : no limits (6 wks-9 mths)
- In case of conservative surgery after NAC

Dose Prescription



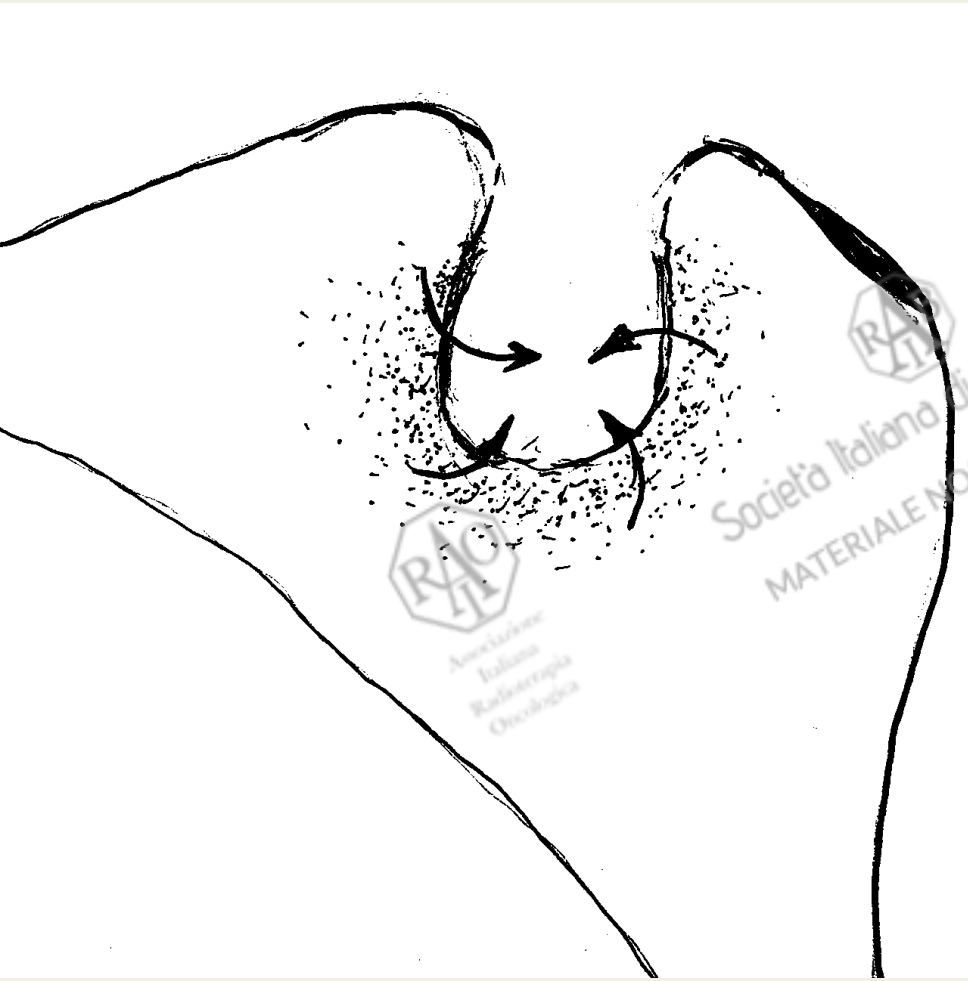
- mobile or fixed linacs , 4-12 MeV.
- **PTV is defined as a 3D volume of at least 2 cm beyond the former macroscopic tumor edge** (excluding skin, limit to anterior rib surface: 5 Gy)
- IOERT Dose (11.1 Gy) specified at the point of Dmax on the central axis
- The **PTV should be encompassed by 90%** of the prescribed dose (i.e. 10 Gy). Inhomogeneities of -10% within the target volume acceptable (up to 20% in small volumes of beam entrance region)

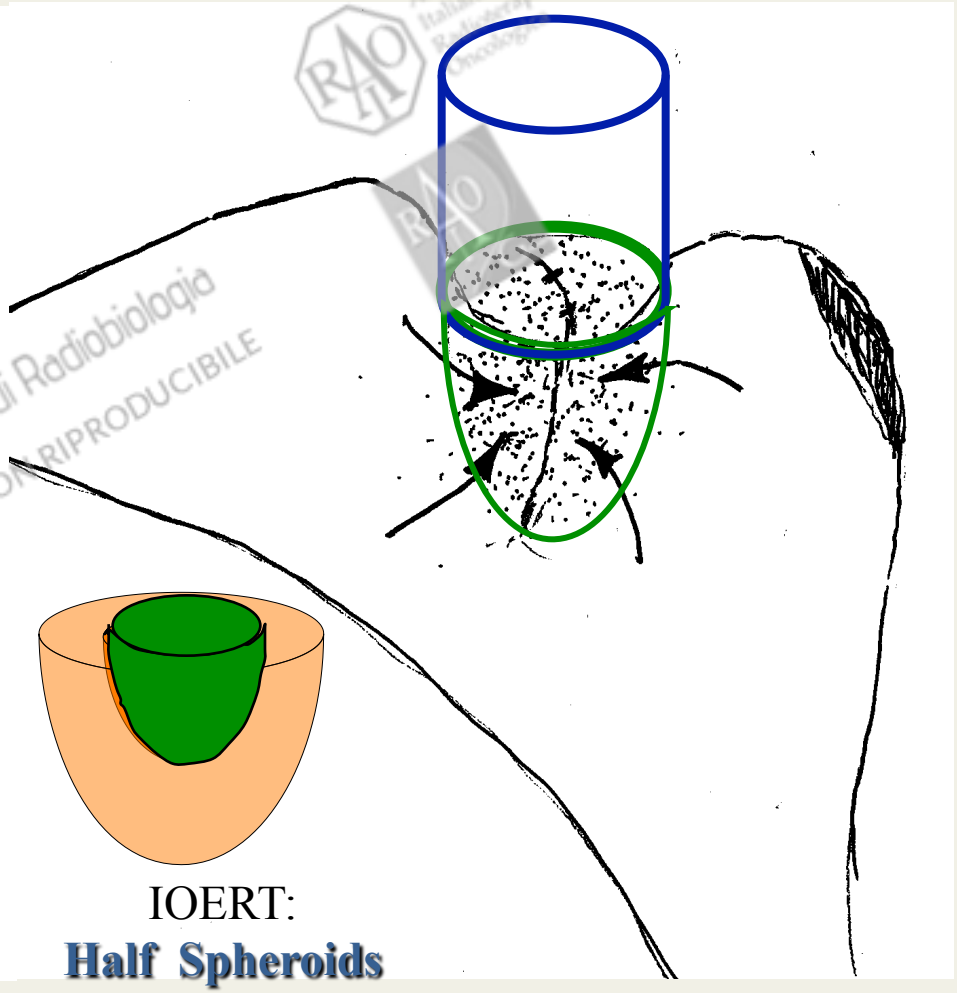
Dose Sum



90% ISODOSE

IOERT boost





By courtesy of F. Sedlmayer

Cosmetic Results

Qualitative 5-Point-Score Van Limbergen E 1989 & Harris JR 1979

E_0: Excellent

E_1: Good

E_2: Moderate

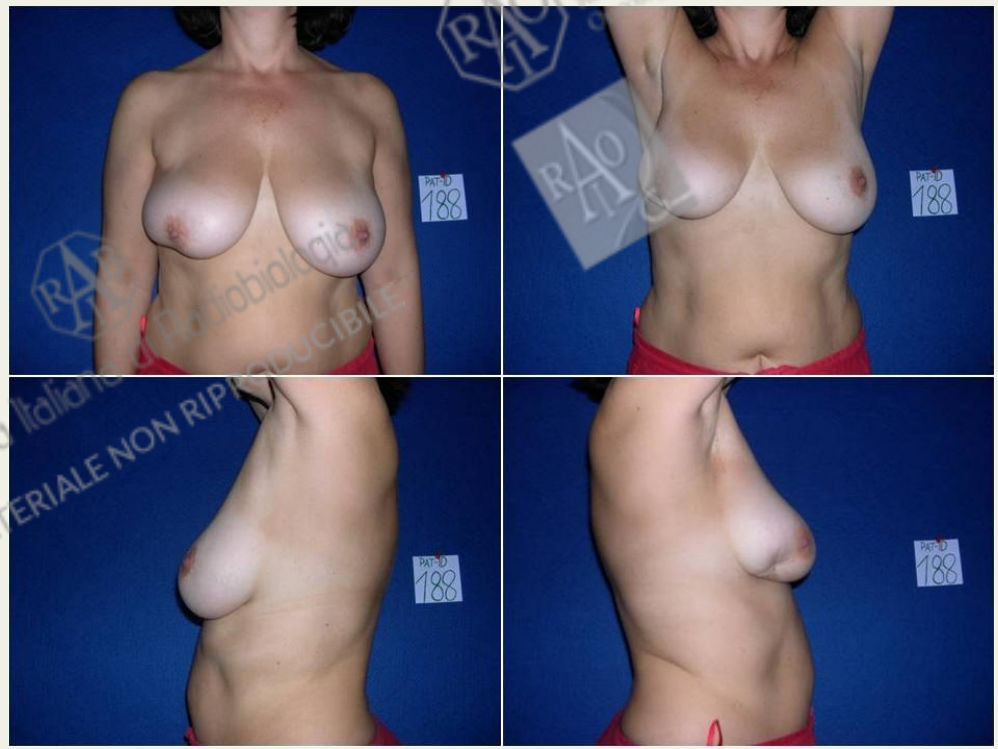
E_3: Bad

E_4: Complications

E_0-E_1: Satisfactory

E_0-E_2: Acceptable

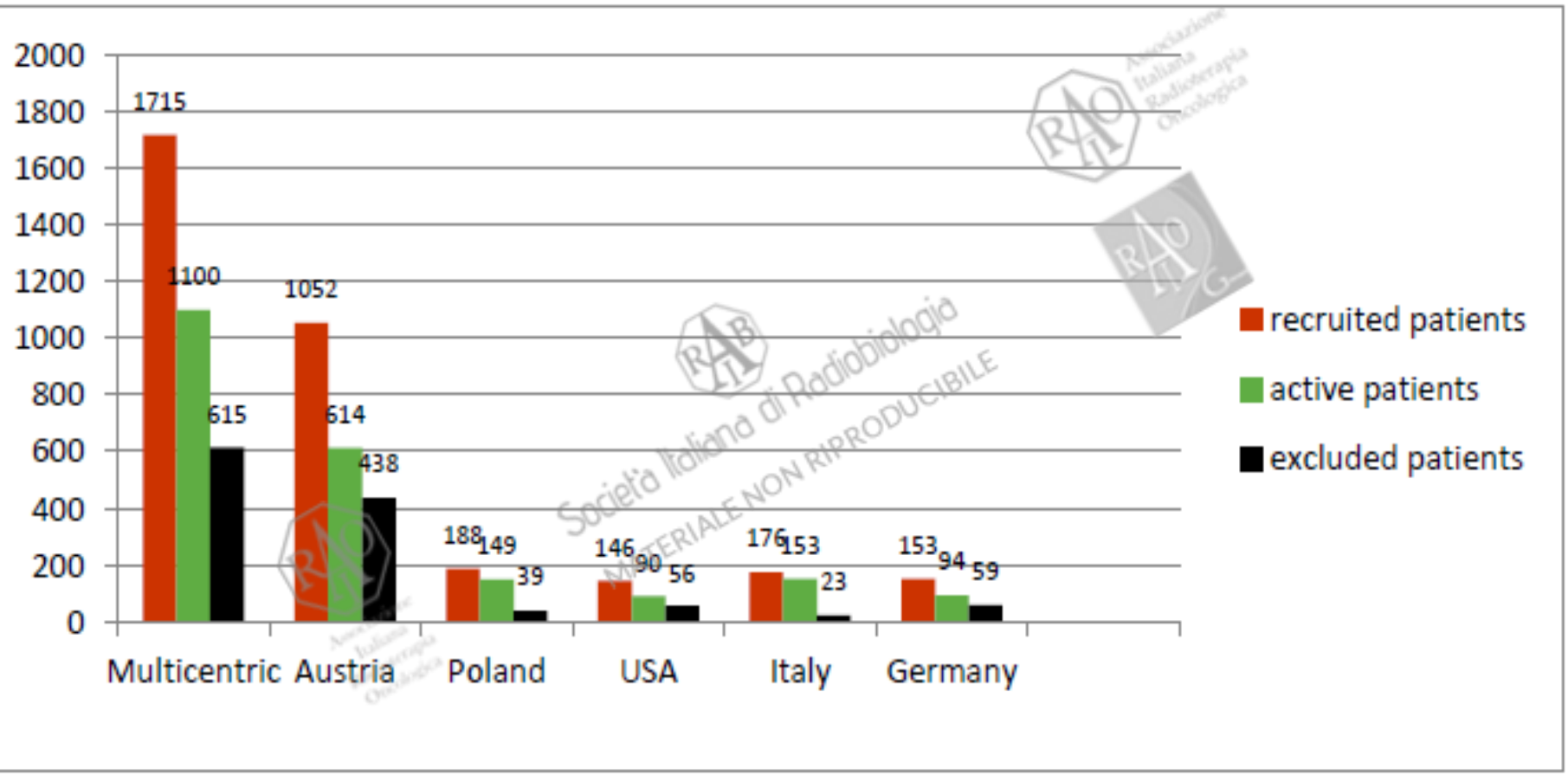
E_3-E_4: Unacceptable



- 24 Sites have access to the test surrounding
- 7 Countries
- 7 Sites access to real site, 19 recruiting

5-years Grant by Intraop Medical
Support for Investigators'Meeting by Sordina

HIOB-Interim Analysis 09/16



- **RECRUITMENT** for **PATIENTS AGE >50** is **CLOSED!**

By courtesy of F. Sedlmayer

HIOB (Italy) - Interim Analysis 09/16

- San Filippo Neri
- Bari
- Città di Castello
- Novara
- Pavia
- Rionero in Vulture
- Treviso
- Trieste
- Torino

- Ferrara

21/11/2011 al 1/10/2015
175 total patients
92 HIOB
83 excluded

Total 176 HIOB pts

Recruited patients 10/15

- Recruited active Patients: **799**
- Age groups: 35 - 40: 23 — **3 %**
  41 – 50: 162 — **20 %**
  > 50: 614 — **77 %** **CLOSED**
- Patients in FUP: **695**
- FUP (Months): Median 16 (0.13 – 51)

By courtesy of F. Sedlmayer

Patient age (y)	n
35-40	23
41-50	162
> 50	614
T-Stage	
1	687
2	111
x	1
N- Stage	
0	689
1	108
X	2
Resection-status	
R0	799
Margin	Med 5 mm (0.1-30)
Multifocality	
no	692
yes	107

Histology	n
IDC	612
ILC	77
mixed	66
mucinous	9
tubular	30
medullary	2
metaplastic	3
EIC-status	
negative	693
positive	106
Grade	
G1	210
G2	460
G3	129
HER2-status	
neg	701
pos	98
HR- status	
neg	58
pos	741

Patient age (y)	n
35-40	23
41-50	162
> 50	614
T-Stage	
1	687
2	111
x	1
N- Stage	
0	689
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12%

HIOB (Italy)
Chemotherapy ± Trastuzumab

20 Her2 + 11,5%

12 left breast (TxT, EC, TC + Herceptin)

RTE: 3D CRT 40,5/15 fr

SFN

D mean heart: 2 Gy

D mean lung: 3 Gy

Acute toxicity

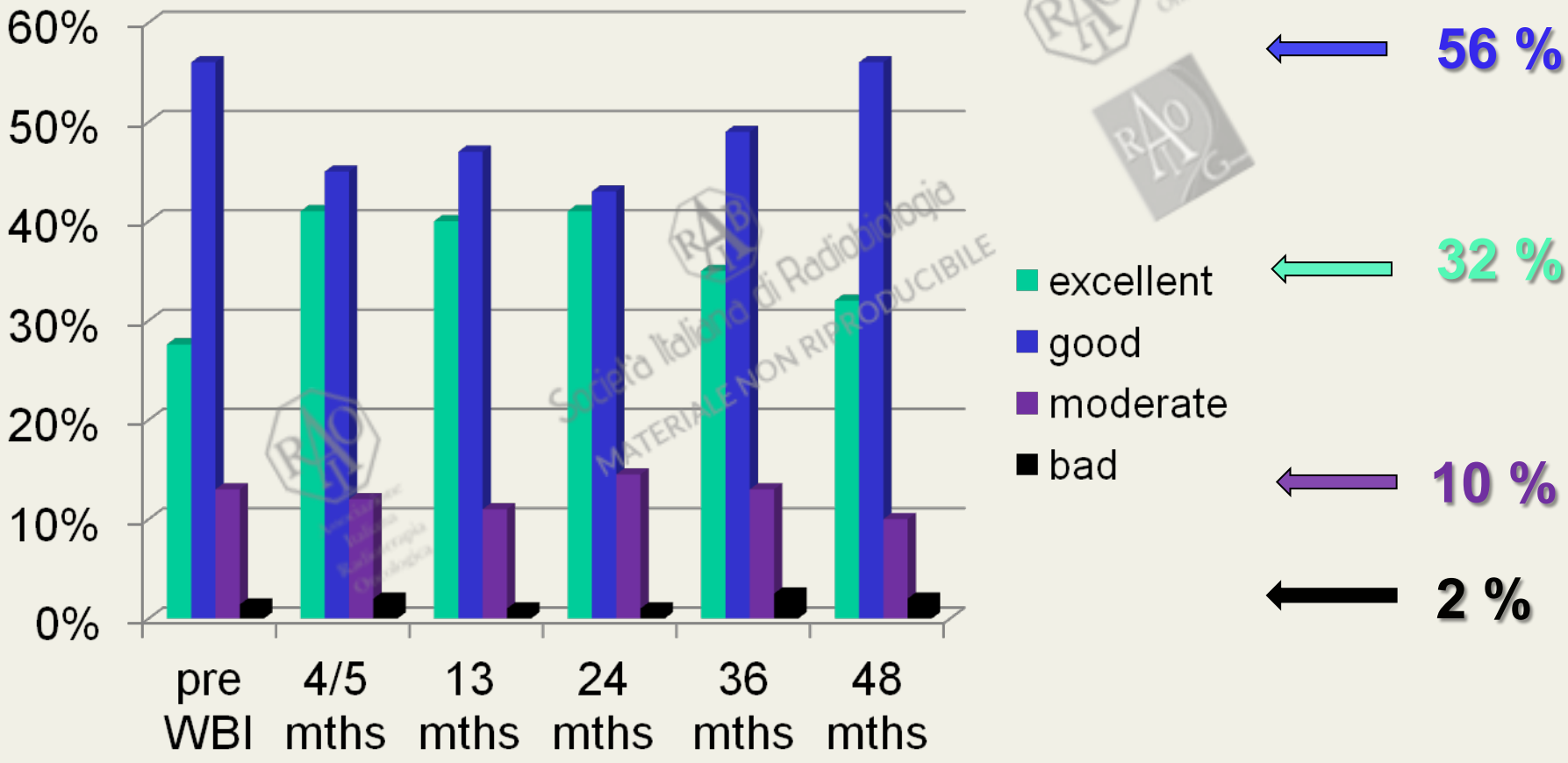
FUP (Months): : Med. 16 (0.13-51)

Evaluation:	*712*	*692*
CTC	*WBI – End*	*4 weeks post WBI*
CTC 0 (no reaction):	10.8 %	36.5%
CTC I (faint reaction):	80 %	56.3%
CTC II (moderate):	8.7 %	6.8%
CTC III(moist desquamation):	0.3 %	0.15%
ND	0.2 %	0.25%
∑ CTC 0/I	91%	93%

No cardiac or lung toxicity!!

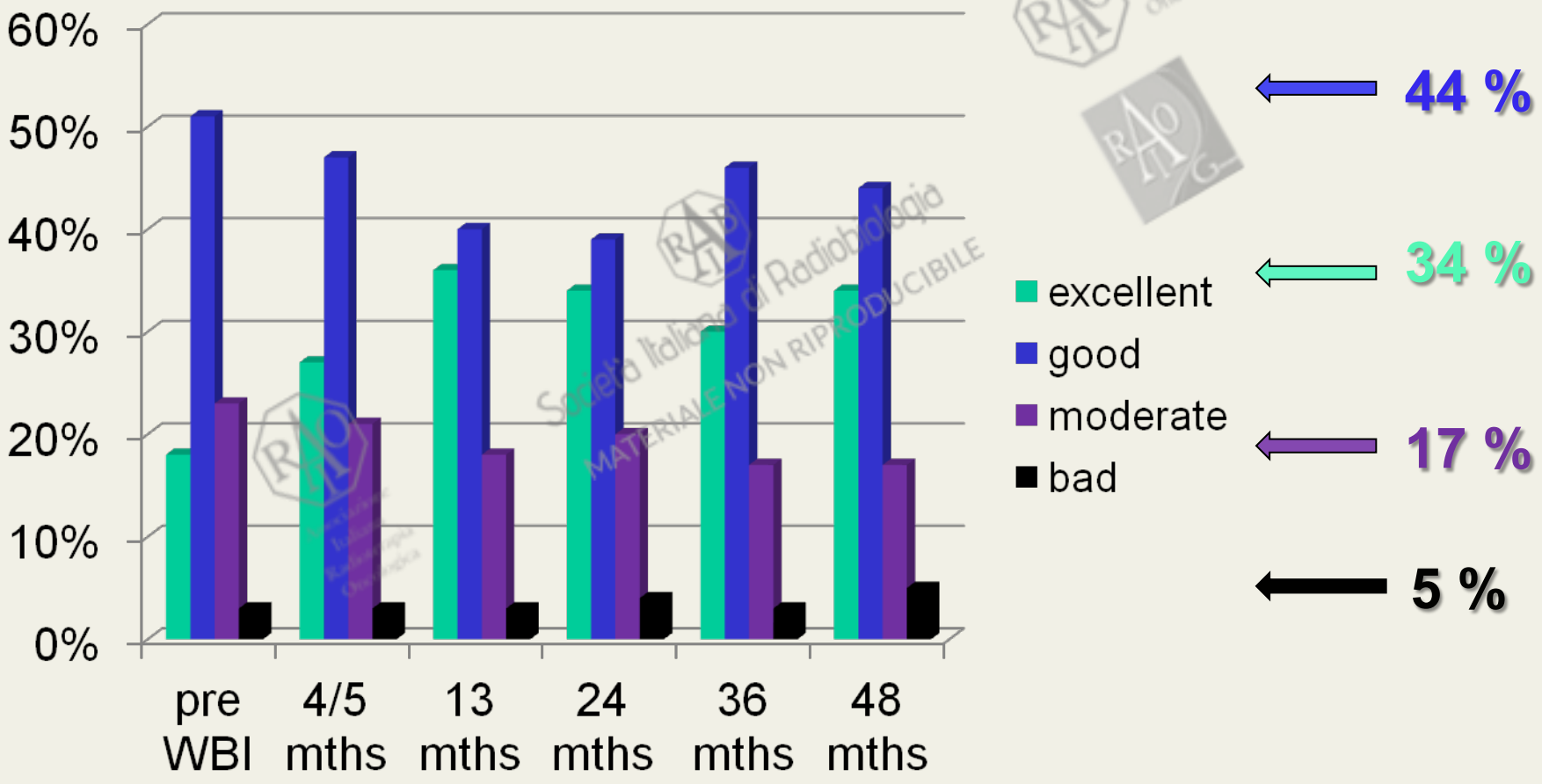
By courtesy of F. Sedlmayer

Subjective Cosmetic Outcome



By courtesy of F. Sedlmayer

Objective Cosmetic Outcome



By courtesy of F. Sedlmayer

Clinical Results

FUP (Months): : Med. 16 (0.13-51)

No regional or In Breast Recurrence

2 patients with metastases

2 deaths

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