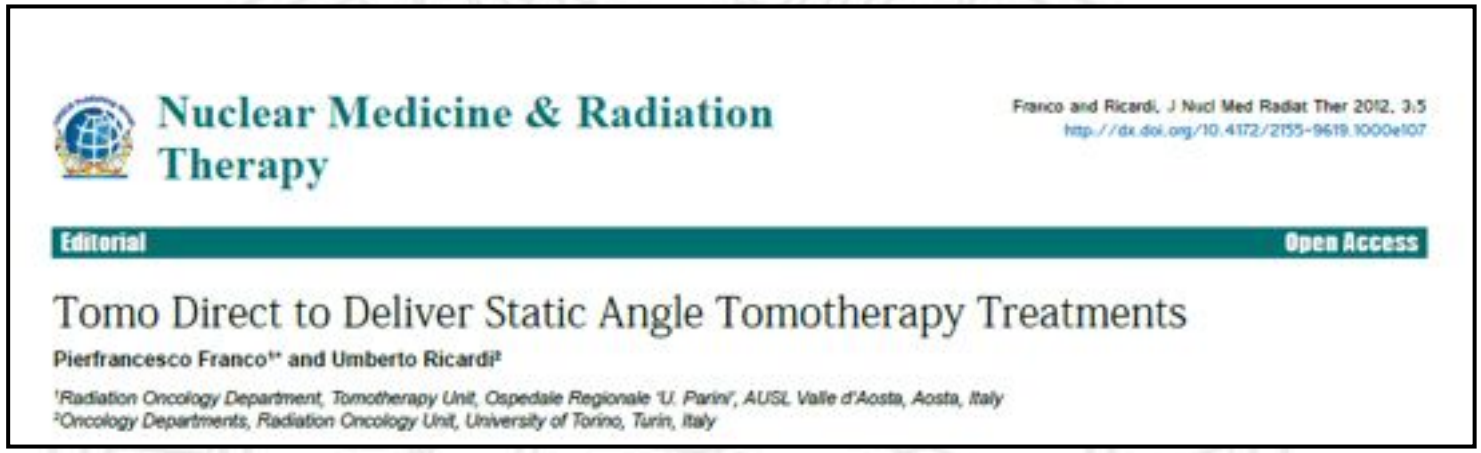
**XXIV Congresso Nazionale AIRO**
**Padova 8-11 Novembre 2014**

# TomoDirect™ IMRT for Hypofractionated Whole Breast Irradiation with a Simultaneous Integrated Boost


Pierfrancesco Franco, MD
Radiation Oncology
Department of Oncology
University of Torino

# What is TomoDirect?



Nuclear Medicine & Radiation Therapy

Franco and Ricardi, J Nucl Med Radiat Ther 2012, 3:5
http://dx.doi.org/10.4172/2155-9619.1000e107

Editorial Open Access

Tomo Direct to Deliver Static Angle Tomotherapy Treatments

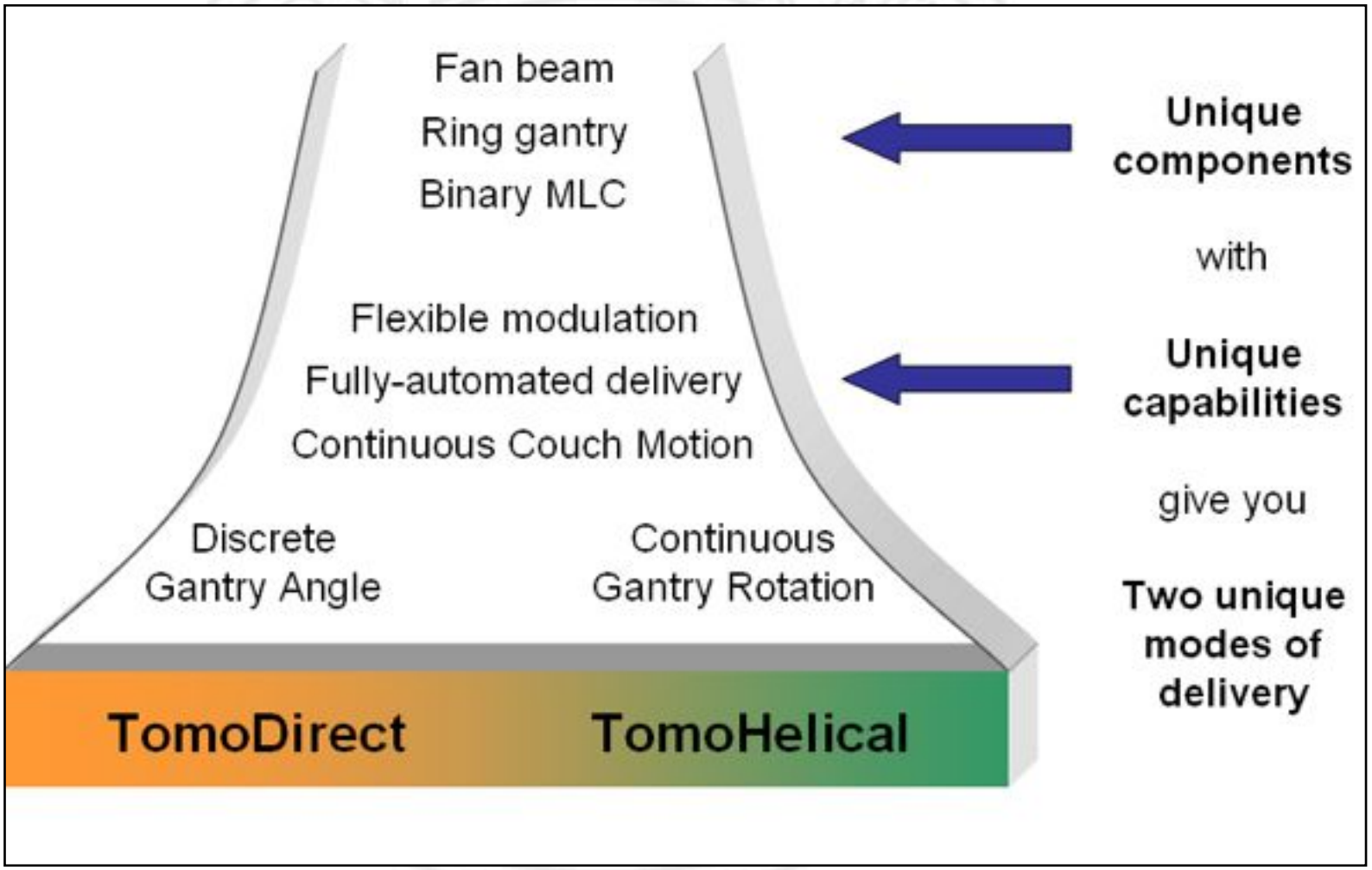
Pierfrancesco Franco[1*] and Umberto Ricardi[2]

[1]Radiation Oncology Department, Tomotherapy Unit, Ospedale Regionale 'U. Parini', AUSL Valle d'Aosta, Aosta, Italy
[2]Oncology Departments, Radiation Oncology Unit, University of Torino, Turin, Italy

- **Upgrade of the Tomotherapy plaftorm**
- **It allows for the delivery of radiation at discrete angles with a fixed gantry**
- **Suitable for clinical situations where beam arrangement is constrained to a limited number of pre-established directions**

**Franco P and Ricardi U - JNMRT 2012**

# TomoDirect


Fan beam
Ring gantry
Binary MLC
Flexible modulation
Fully-automated delivery
Continuous Couch Motion
Discrete
Gantry Angle
Continuous
Gantry Rotation
TomoDirect
TomoHelical
Unique components
with
Unique capabilities
give you
Two unique modes of delivery

# How does it work?

**Fixed gantry but moving couch to deliver highly modulated multiple-fields plans**

**Static gantry positions are combined with concomitant couch translation and multileaf collimator modulation**

- **Patient translated along CC-axis past the fixed fan-beam during each field delivery**
- **Beam intensity is modulated by the binary MLC while the pitch regulates the degree modulation in the sup-inf direction**
- **After delivery from 1 gantry angle, the gantry is rotated to a different beam direction and the patient is passed through the bore again for the subsequent field**

# First clinical experience

Tumori, 97: 498-502, 2011

## TomoDirect: an efficient means to deliver radiation at static angles with tomotherapy

Pierfrancesco Franco[1], Paola Catuzzo[2], Domenico Cante[1,6], Maria Rosa La Porta[1,6], Piera Sciacero[1,6], Giuseppe Girelli[1,6], Valeria Casanova Borca[2,7], Massimo Pasquino[2,7], Gianmauro Numico[3], Santi Tofani[2,7], Teodoro Meloni[4], Umberto Ricardi[5], and Franca Ozzello[1,6]

- ✓ **Adjuvant whole breast radiation**
- ✓ **Segmental bone pain palliation**
- ✓ **Whole brain radiotherapy**

**Franco et al, Tumori 2011**

# Convetionally fractionated WBRT and sequential boost (HT)

J Cancer Res Clin Oncol
DOI 10.1007/s00432-013-1515-0

ORIGINAL PAPER

**Intensity-modulated adjuvant whole breast radiation delivered with static angle tomotherapy (TomoDirect): a prospective case series**

Pierfrancesco Franco · Michele Zeverino · Fernanda Migliaccio · Piera Sciacero · Domenico Cante · Valeria Casanova Borca · Paolo Torielli · Cecilia Arrichiello · Giuseppe Girelli · Gianmauro Numico · Maria Rosa La Porta · Santi Tofani · Umberto Ricardi

**WBRT: 50 Gy/25 fr (2 Gy daily) over 5 weeks delivered with TomoDirect**

**Sequential boost of 10 Gy/5 fr (2 Gy daily) for R0 resection or 16 Gy/8 fr (2 Gy daily) for R1 resection delivered with Helical Tomotherapy**

**Total OTT 6-7 weeks**

**120 patients**

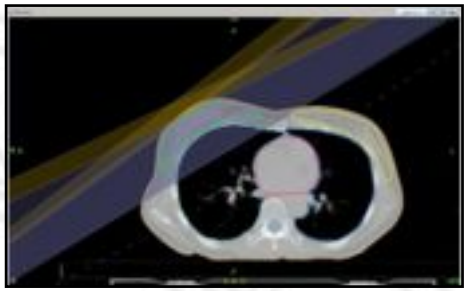
**RT delivered < 3 months from surgery or after adjuvant CT if high-risk features were present**

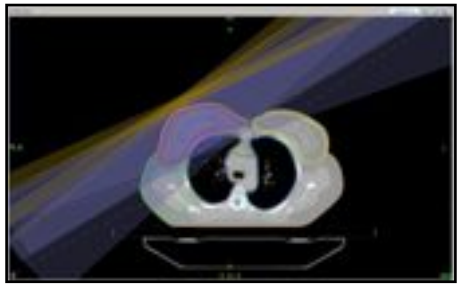
**Franco et al, JCRCO 2013**

# Planning and dose distribution

- ✓ 2-5 tangents fields arrangement to cover pt anatomy
- ✓ Dose prescription: $D_{median}$ (homogeneity)
- ✓ Target coverage
  - 95% PTV receiving at least 95% of the prescribed dose
  - 99% PTV receiving at least 90% of the prescribed dose
  - $D_{max}$ to PTV < 105% of the prescribed dose

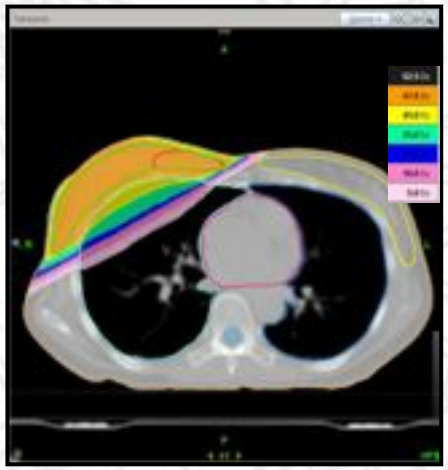
- ✓ OARS
  - ✓ Ipsilateral lung: $V_{20}$<10%; $V_{10}$<20%, $V_5$<40%
  - ✓ Contralateral lung: $V_5$< 5%
  - ✓ Contralateral breast: $D_{max}$< 5 Gy
  - ✓ Heart: $V_{25}$<10%
  - ✓ Excess irradiation ($D_{2cc}$): % of the prescription dose delivered to a volume of 2 cc of the normal tissues external to PTV

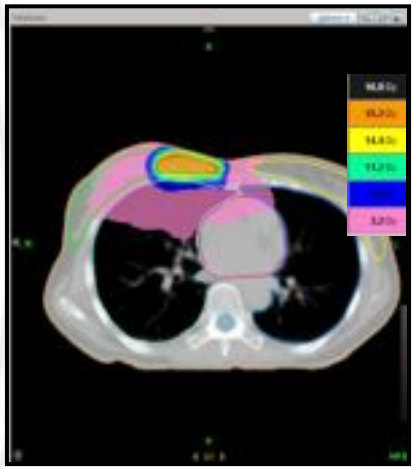


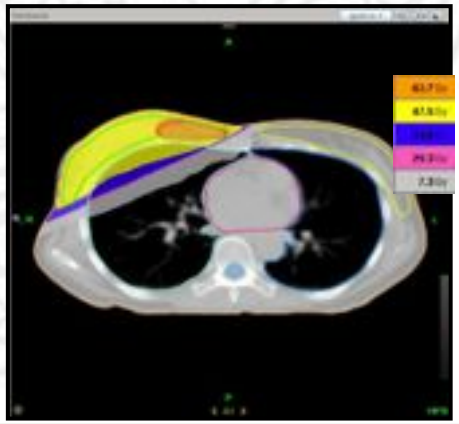


2 fields

4 fields







# Dosimetric results

| | Boost dose | | | |
|---|---|---|---|---|
| | 10 Gy | | 16 Gy | |
| | Mean | SD | Mean | SD |
| PTV | | | | |
| WB | | | | |
| $D_{98}$ (Gy) | 47.2 | 3.1 | 48.6 | 2.7 |
| $D_2$ (Gy) | 59.9 | 0.5 | 66.8 | 2.1 |
| $V_{95}$ (%) | 95.6 | 15.2 | 99.9 | 5.1 |
| $V_{105}$ (%) | 38.8 | 12.6 | 54.0 | 10.4 |
| Boost | | | | |
| $D_{98}$ (Gy) | 58.6 | 0.7 | 65.0 | 2.6 |
| $D_2$ (Gy) | 59.5 | 7.6 | 67.6 | 2.0 |
| $V_{95}$ (%) | 99.7 | 1.1 | 101.0 | 4.8 |
| $V_{105}$ (%) | 0.0 | 0.0 | 0.0 | 0.0 |
| WB (excluding boost) | | | | |
| Receiving 52.5 Gy (%) | 32.6 | 9.9 | 46.0 | 9.0 |
| Receiving 55 Gy (%) | 19.9 | 10.1 | 35.2 | 11.6 |
| Receiving 57.5 Gy (%) | 11.5 | 6.1 | 22.7 | 8.3 |
| OARs | | | | |
| Ipsilateral lung | | | | |
| $V_5$ (%) | 20.2 | 4.4 | 22.4 | 6.5 |
| $V_{10}$ (%) | 14.1 | 3.7 | 15.4 | 4.5 |
| $V_{20}$ (%) | 9.7 | 2.9 | 10.8 | 3.1 |
| $D_{max}$ (Gy) | 53.8 | 2.3 | 57.6 | 4.2 |
| MLD (Gy) | 6.0 | 1.3 | 6.5 | 1.3 |
| Contralateral lung | | | | |
| $D_{max}$ (Gy) | 1.9 | 0.9 | 2.3 | 1.4 |
| Heart left-sided tumors | | | | |
| $V_5$ (%) | 11.7 | 9.6 | 12.3 | 4.5 |
| $V_{10}$ (%) | 5.6 | 3.9 | 6.6 | 1.3 |
| $V_{20}$ (%) | 3.5 | 2.8 | 4.2 | 8.6 |
| $V_{25}$ (%) | 2.9 | 2.5 | 2.4 | 8.5 |
| MHD (Gy) | 1.5 | 1.5 | 1.8 | 2.5 |
| $D_{max}$ (Gy) | 29.6 | 23.7 | 19.1 | 23.8 |
| Contralateral breast | | | | |
| $D_{max}$ (Gy) | 2.6 | 1.1 | 3.0 | 1.2 |

**Very robust results but:**

- **1/3 breast volume outside TB gets 105%**
- **1/5 pts gets 110%**
- **1/10 gets 115%**

Franco et al, JCRCO 2013

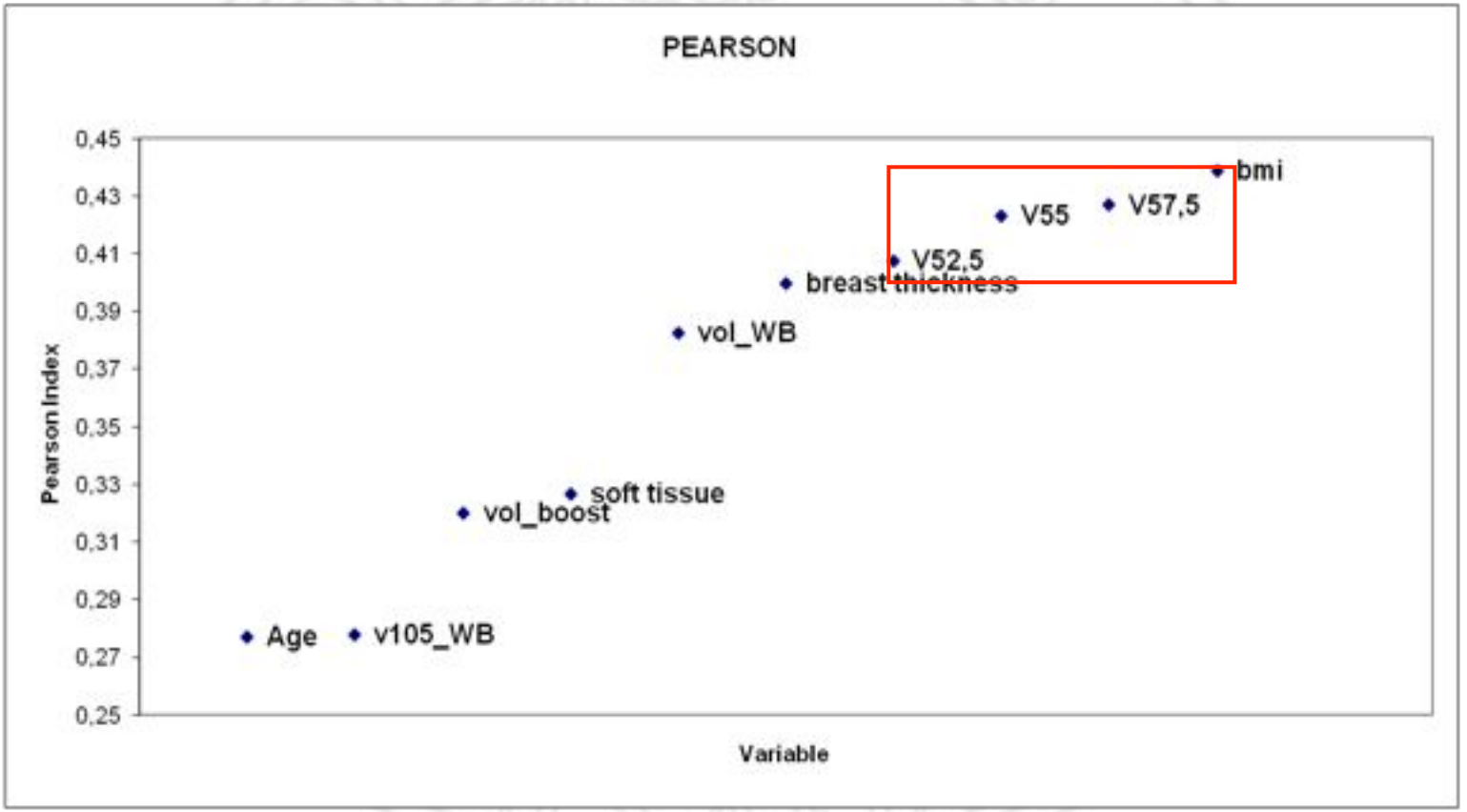
# Skin toxicity and cosmesis

| Skin toxicity | Grade | Patients | % |
|---|---|---|---|
| No change over baseline | 0 | 26 | 22 |
| Follicular, faint or dull erythema/epilation/dry desquamation/decreased sweating | 1 | 75 | 63 |
| Tender or bright erythema, patchy moist desquamation/moderate edema | 2 | 15 | 12 |
| Confluent, moist desquamation other than skin folds, pitting edema | 3 | 4 | 3 |
| Ulceration, hemorrhage, necrosis | 4 | 0 | 0 |

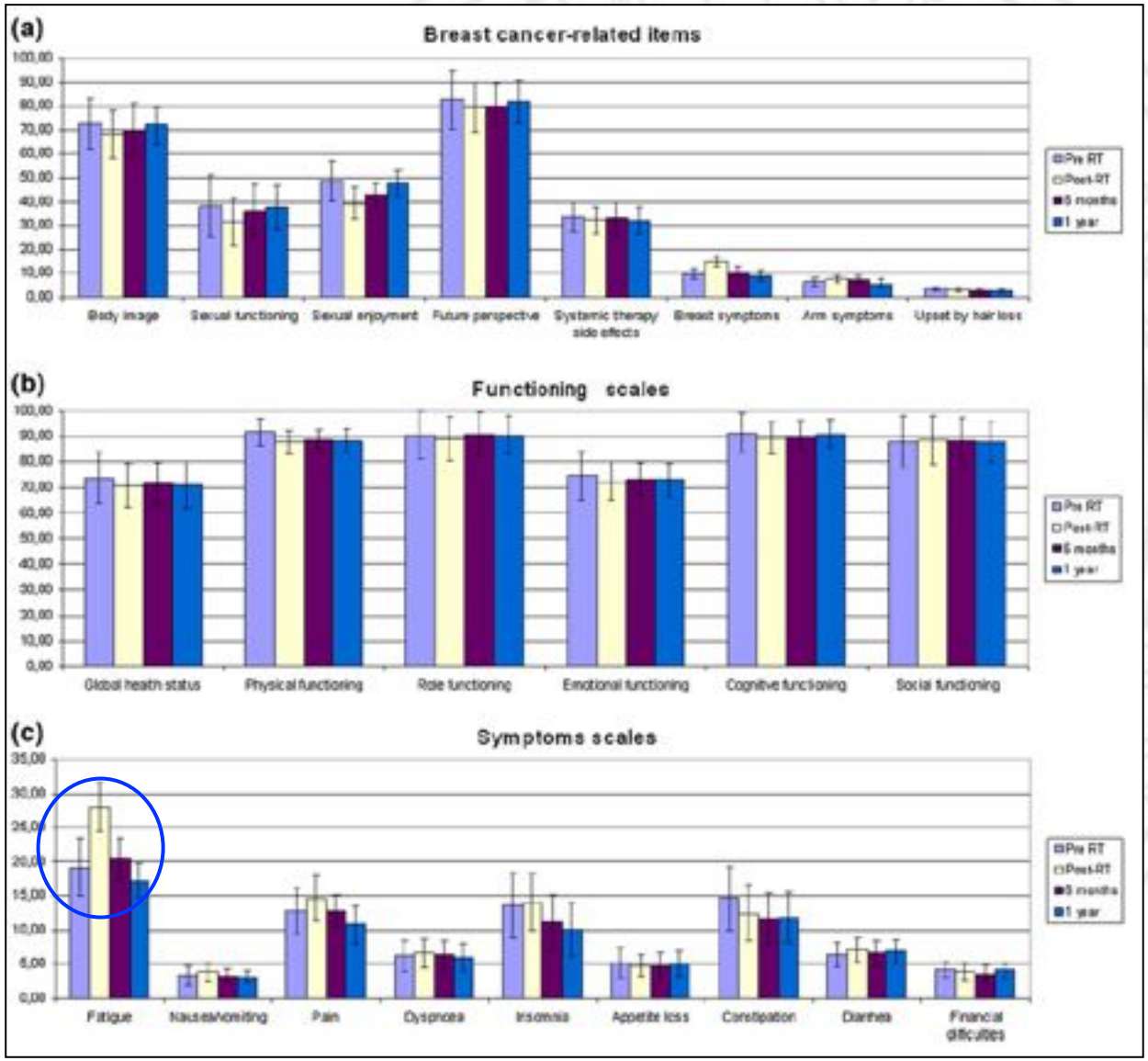
| Parameter | Grade (%) | | | |
|---|---|---|---|---|
| | *G1* | *G2* | *G3* | *G4* |
| Induration-Fibrosis | 3 (2.5) | 2 (1.7) | 0 | – |
| Atrophy | 2 (1.6) | 0 | – | – |
| Telangiectasia | 1 (0.8) | 0 | 0 | – |
| Hyperpigmentation | 24 (20) | 6 (5) | – | – |
| Striae | 3 (2.5) | 0 | – | – |
| Ulceration | – | 0 | 0 | 0 |
| Cosmesis | | | | |
| Definition | Poor | Fair | Good | Excellent |
| | 3 (2.5) | 7 (5.8) | 28 (23.4) | 82 (68.3) |

Franco et al, JCRCO 2013

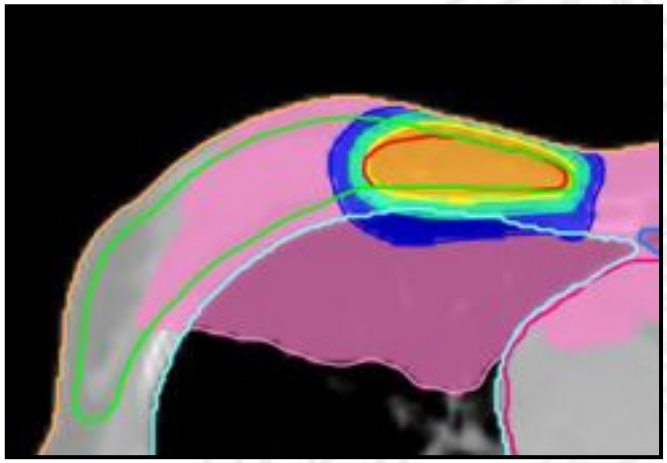
# Acute toxicity predictors

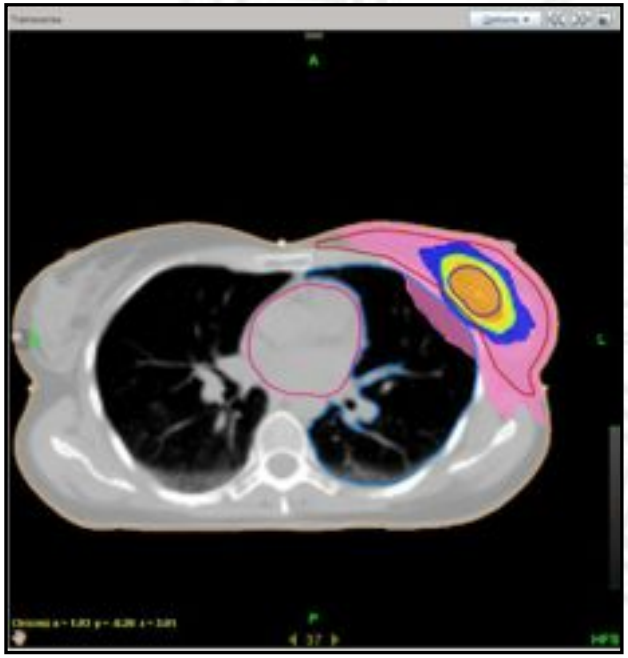


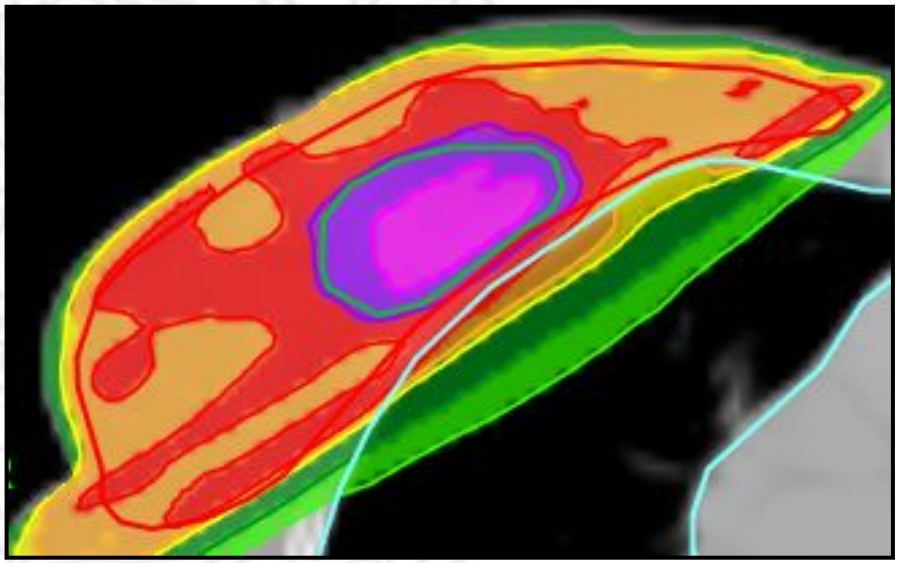
# QoL – EORTC QLQ-C30 and BR-23



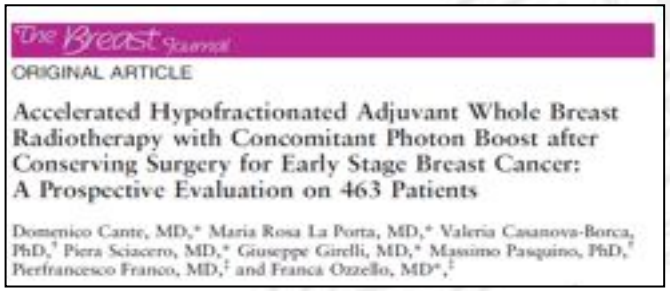
# Reducing unintended dose outside tumor bed with SIB





# LINAC-based concomitant boost to the tumor bed



The Breast Journal

ORIGINAL ARTICLE

Accelerated Hypofractionated Adjuvant Whole Breast Radiotherapy with Concomitant Photon Boost after Conserving Surgery for Early Stage Breast Cancer: A Prospective Evaluation on 463 Patients

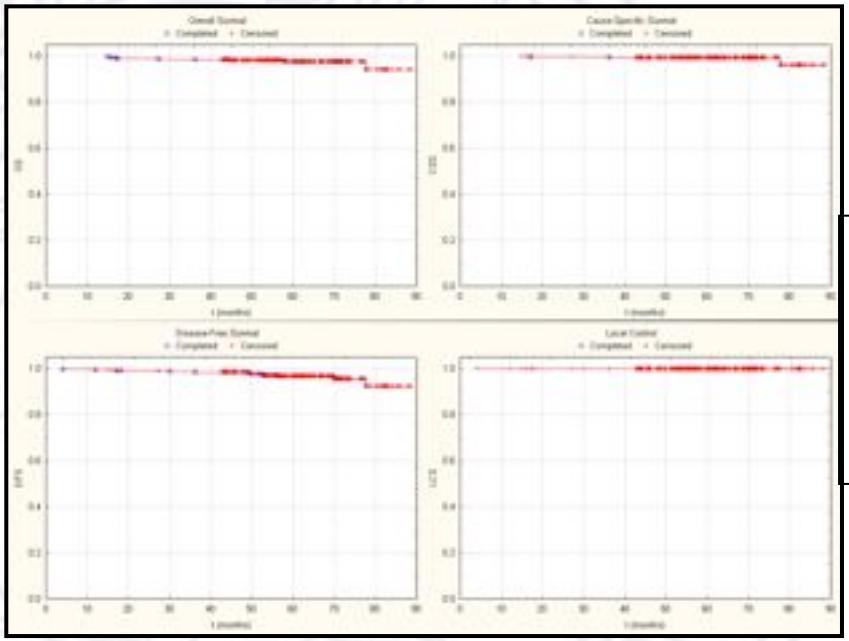
Domenico Cante, MD,* Maria Rosa La Porta, MD,* Valeria Casanova-Borca, PhD,† Piera Sciacero, MD,* Giuseppe Girelli, MD,* Massimo Pasquino, PhD,† Pierfrancesco Franco, MD,‡ and Franca Ozzello, MD*,‡

ORIGINAL PAPER

Five-year results of a prospective case series of accelerated hypofractionated whole breast radiation with concomitant boost to the surgical bed after conserving surgery for early breast cancer

ORIGINAL PAPER

Hypofractionation and concomitant boost to deliver adjuvant whole-breast radiation in ductal carcinoma in situ (DCIS): a subgroup analysis of a prospective case series



- 5yr-OS: 97.6%
- 5yr-CSS: 99.4
- 5yr-DFS: 96.6%
- 5yr-LC: 100%

**Over 1.000 pts treated; long-term results on 375 pts**

- 45 Gy/20 fr 2.25 Gy/daily - WBRT
- 50 Gy/20 fr 2.5 Gy/daily – Tumor bed (Direct Photon Field and then FIF)

Cante et al, Breast J 2011; Med Oncol 2013 and 2014

# SIB WBRT delivered with TomoDirect:

# A prospective phase II trial

J Cancer Res Clin Oncol
DOI 10.1007/s00432-013-1560-8

ORIGINAL PAPER

**Intensity-modulated and hypofractionated simultaneous integrated boost adjuvant breast radiation employing statics ports of tomotherapy (TomoDirect): a prospective phase II trial**

Pierfrancesco Franco · Michele Zeverino · Fernanda Migliaccio · Domenico Cante · Piera Sciacero · Valeria Casanova Borca · Paolo Torielli · Cecilia Arrichiello · Giuseppe Girelli · Maria Rosa La Porta · Santi Tofani · Gianmauro Numico · Umberto Ricardi

- ❑ 45 Gy/20 fr over 4 weeks (2.25 Gy daily) as WBRT
- ❑ Simultaneous 0.25 Gy to the surgical bed
- ❑ 5 adjunctive Gy to the surgical bed
- ❑ 50 Gy/20 fr over 5 weeks

Franco et al, JCRCO 2014

# Trial design

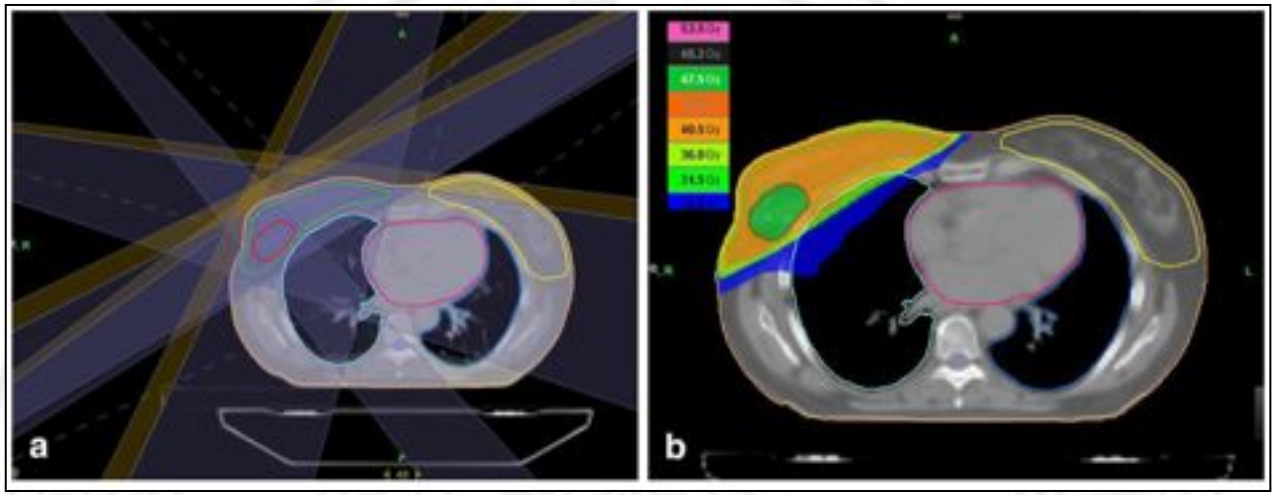
- One-armed optimal two-stage Simon's design
- Historical data of success (p0): 85% G0-G1 acute sking toxicity (G2-G3: 15%) with TD + HT
- Threshold for successful trial (p1): set to 94% of G1-G2 acute sking toxicity (G2-G3: 6%)
- α error (one-sided type I error): 5%
- β error (type II error; power 80%): 20%
- $H_0$: no difference in acute skin toxicity

  - First stage: 18/21 (86%) pts should have scored as G0-G1 acute skin toxicity
  - Second stage: another 61 pts accrued; at least 74/82 (90.2%) is the threshold for H0 rejection and definition of SIB-TD as 'promising'

Franco et al, JCRCO 2014



# Technical issues




- 4 beams conformed to the WB-PTV: 2 canonical tangential beams, 1 anterior-posterior (AP) and 1 latero-lateral (LL) with a ± 15° gantry angle range
- 1 or 2 small beams conformed to the TB-PTV to improve homogeneity and confomality; oblique incidence to reduce dose spread around TB-PTV
- 3 MLC leaves (19 mm to isocenter plane) opened on anterior edge of each beam
- FW: 2.5 cm; Pitch: 0.25 cm/projection; MF: 2-2.5
- A 10 mm ring was used around WB-PTV and TB-PTV to reduce overdosage (skin and breast tissue)
- Helping structures around WB-PTV used to avoid hotspots
- OARs as avoidance structures

Franco et al, JCRCO 2014

| | Mean | SD |
|---|---|---|
| *PTV* | | |
| WB | | |
| $D_{98}$ (Gy) | 42.8 | 2.1 |
| $D_2$ (Gy) | 47.3 | 1.2 |
| $V_{95}$ (%) | 98.1 | 11.3 |
| $V_{105}$ (%) | 1.9 | 0.9 |
| Boost | | |
| $D_{98}$ (Gy) | 48.1 | 1.9 |
| $D_2$ (Gy) | 50.9 | 5.6 |
| $V_{95}$ (%) | 99.5 | 1.1 |
| $V_{105}$ (%) | 0 | 0 |
| WB (excluding boost) | | |
| $V_{105}$ (%) | 2.4 | 0.9 |
| $V_{110}$ (%) | 0.01 | 0 |
| *OARs* | | |
| Ipsilateral lung | | |
| $V_5$ (%) | 26.2 | 4.5 |
| $V_{10}$ (%) | 15.6 | 3.4 |
| $V_{20}$ (%) | 9.6 | 3.1 |
| $D_{max}$ (Gy) | 45 | 2.9 |
| MLD (Gy) | 6.4 | 1.5 |
| Contralateral lung | | |
| $D_{max}$ (Gy) | 2.1 | 1.1 |
| Heart (left-sided tumors) | | |
| $V_5$ (%) | 12.8 | 8.6 |
| $V_{10}$ (%) | 2.7 | 1.1 |
| $V_{20}$ (%) | 1.3 | 0.5 |
| $V_{35}$ (%) | 1.1 | 0.3 |
| MHD (Gy) | 2.1 | 1.2 |
| $D_{max}$ (Gy) | 25.1 | 19.1 |
| Contralateral breast | | |
| $D_{max}$ (Gy) | 2.9 | 1.3 |

# Dosimetric results (82 pts)

**Still very robust results and interestingly:**

- **2.5% breast volume outside TB gets 105%**
- **No volume gets 110%-115%**

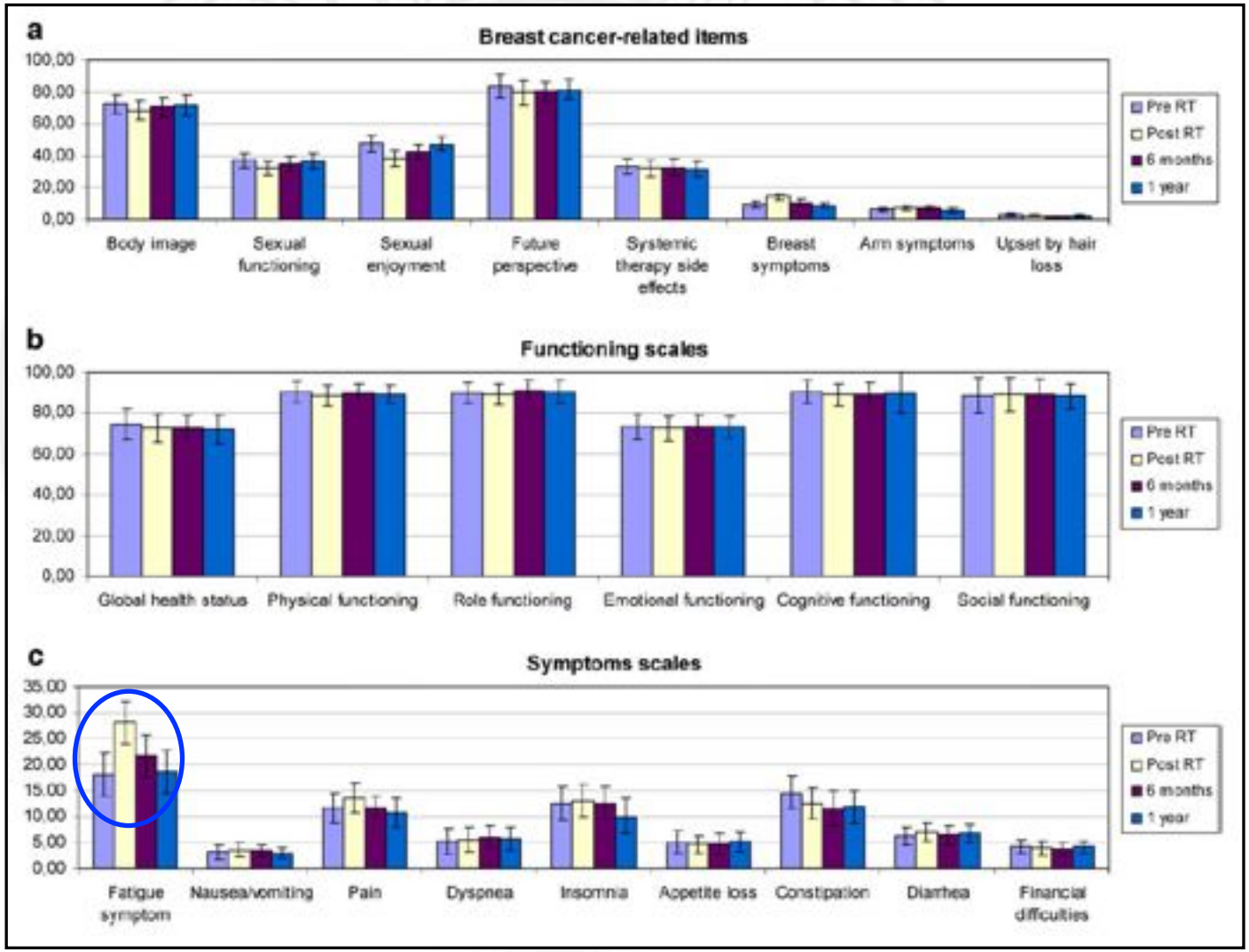
# Skin toxicity and cosmesis (82 pts)

| Skin toxicity | Grade | Patients | % |
|---|---|---|---|
| No change over baseline | 0 | 33 | 41 |
| Follicular, faint or dull erythema/epilation/dry desquamation/decreased sweating | 1 | 43 | 53 |
| Tender or bright erythema, patchy moist desquamation/moderate edema | 2 | 5 | 6 |
| Confluent, moist desquamation other than skin folds, pitting edema | 3 | 1 | <1 |
| Ulceration, hemorrhage, necrosis | 4 | 0 | 0 |

| Parameters | Grade (%) | | | |
|---|---|---|---|---|
| | G1 | G2 | G3 | G4 |
| Induration–fibrosis | 4 (5) | 1 (1) | 0 | – |
| Atrophy | 3 (4) | 0 | – | – |
| Telangiectasia | 1 (1) | 0 | 0 | – |
| Hyperpigmentation | 10 (12) | 2 (2) | – | – |
| Striae | 2 (2) | 0 | – | – |
| Ulceration | – | 0 | 0 | 0 |
| Cosmesis | | | | |
| Definition | Poor | Fair | Good | Excellent |
| | 3 (4) | 4 (5) | 18 (22) | 57 (69) |

Franco et al, JCRCO 2014

# QoL – EORTC QLQ-C30 and BR-23



# To avoid hotspots

- Plan dose prescription: mean dose (50%of WB-PTV)

Higher prescription dose → higher hotspots

- Planned MF up to 2.5
- 2 dummy volumes for planning: medial (sternal region) and lateral (axillary region)
- Smaller penalities values than with HT ( < 100 both for PTVs and OARs)
- 1-2 small fields reduce spillage outiside TB

# Conclusions

**TomoDirect is:**
- **Feasible**
- **Reliable**
- **Dosimetrically consistent**
- **Clinically effective**

**An option to deliver radiation for breast cancer employing hypofractionation and SIB**

**TomoDirect provides**

**Versatility**

**to the Tomotherapy platform**

**XXIV Congresso Nazionale AIRO**
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**Pierfrancesco Franco, MD**

**Thank you for your attention**


**Mario Schifano – Indicazione - 1963**

**Padova, 9 Novembre 2014**