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# AIRO2023

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PALAZZO DEI CONGRESSI

Radioterapia Oncologica: l'evoluzione al servizio dei pazienti

## **MARCATORI DI DANNO CARDIACO RADIOINDOTTO IN PAZIENTI CON MALATTIA DELLA MAMMELLA IN STADIO INIZIALE TRATTATE CON RADIOTERAPIA ADIUVANTE: UN TRIAL PROSPETTICO**

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## RADIATION-INDUCED HEART DISEASE

### Lessons from the past in the era of “modern” radiation therapy

#### The NEW ENGLAND JOURNAL of MEDICINE

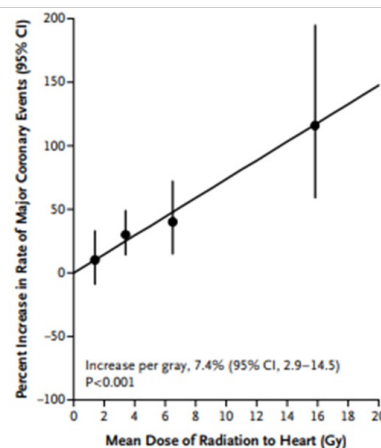
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#### Risk of Ischemic Heart Disease in Women after Radiotherapy for Breast Cancer

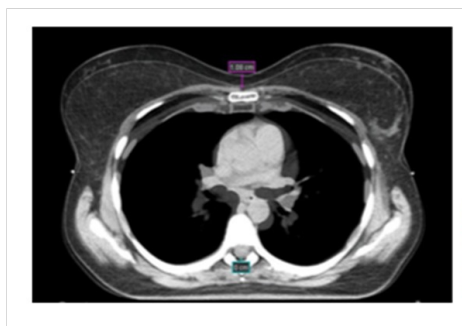
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#### Figure 1. Rate of Major Coronary Events According to Mean Radiation Dose to the Heart, as Compared with the Estimated Rate with No Radiation Exposure to the Heart.

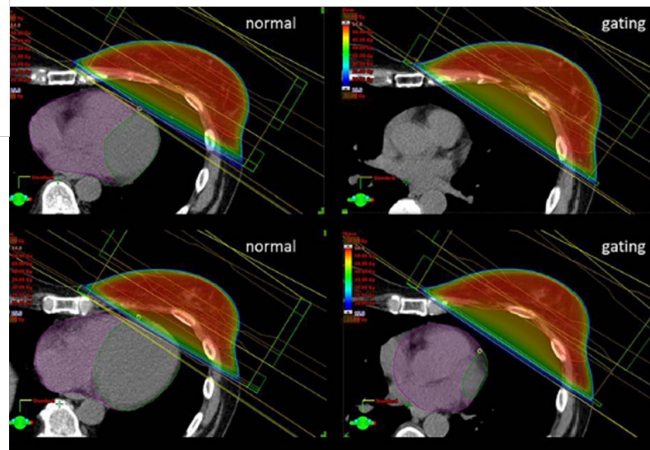
Major coronary events included myocardial infarction, coronary revascularization, and death from ischemic heart disease. The values for the solid line were calculated with the use of dose estimates for individual women. The circles show values for groups of women, classified according to dose categories; the associated vertical lines represent 95% confidence intervals. All estimates were calculated after stratification for country and for age at breast-cancer diagnosis, year of breast-cancer diagnosis, interval between breast-cancer diagnosis and first major coronary event for case patients or index date for controls (all in 5-year categories), and presence or absence of a cardiac risk factor. The radiation categories were less than 2, 2 to 4, 5 to 9, and 10 Gy or more, and the overall averages of the mean doses to the heart of women in these categories were 1.4, 3.4, 6.5, and 15.8 Gy, respectively.



## RADIATION-INDUCED HEART DISEASE Lessons from the past in the era of “modern” radiation therapy



TC-SIM Breath-Hold  
↑ > 1 cm  
TC-SIM Free-Breathing





## STUDY Design

Pilot study, non-profit, prospective single-center (Ethical Committee approval 06/2019)

## STUDY Objectives

To assess any alterations in cardiac function before and after radiotherapy (end of radiation treatment, at 6 and 12 months) by means of

- Biochemical parameters (**high sensitivity myocardial troponin I and N-terminal pro-BNP**)
- Instrumental parameters (**echo-cardiogram with evaluation of ejection fraction and GLS-global longitudinal strand or longitudinal deformation**)

## Population of study

### *Inclusion criteria*

- Age  $\geq 18$  years
- **Breast cancer subtypes Luminal A or Luminal B** not candidates for chemotherapy and/or target therapy
- Conservative surgery with negative or close margins
- **Stage pT1-2 pN0-N1** Absence of distant metastases (M0)
- Karnofsky status  $> 70$
- Signature of specific informed consent

### *Exclusion criteria*

- Pregnancy
- **Positive history of cardiovascular diseases** (previous acute myocardial infarction, coronary syndrome, congenital or acquired cardiomyopathy, rhythm disorders)

## Methods

- ❑ **Sample size:** 60 pts (30 left side and 30 right side)
- ❑ **RT details:** whole breast with SIB (SIB for age > 60y) IMRT 3/4-fields conventional fractionation
- ❑ **Statistical analysis:** Correlation between heart d-mean and left anterior descending (LAD) coronary artery d-mean with:
  1. Troponin I high sensitivity
  2. N-terminal pro-BNP
  3. LVEF-left ventricular ejection fraction
  4. GLS-global longitudinal strand

## Results (1)

- ✓ Median age was 54 years old (range, 35-77) for entire sample size
- ✓ 33 patients affected by **left side** BC (30 pT1pN0; 4 pT2pN0, Luminal A)
- ✓ 30 patients affected by **right side** BC were analyzed (26 pT1pN0; 5 pT2pN0, Luminal A)

Baseline dosimetric parameters	LEFT SIDE BC	RIGHT SIDE BC	P-value
Heart mean dose	1.8Gy (range, 0.1-8Gy)	0.69Gy (range, 0.05-3.9 Gy)	0.007
LAD mean dose	2.5Gy (range, 0-17Gy)	0.14Gy (range, 0-21Gy)	0.003

Patients were stratified at the 75<sup>th</sup> percentile for dosimetric variables  
Heart mean dose < or > 1.9 Gy *and* LAD mean dose < or > 3.9 Gy

## Results (2): Troponin I

Patients were stratified at the 75th percentile for dosimetric variables  
Heart mean dose  $<$  or  $>$  1.9 Gy and LAD mean dose  $<$  or  $>$  3.9 Gy

At baseline non statistically significance of Troponin I levels according to stratification (p-value 0.17 and 0.37, respectively)

There was an increase of troponin I high sensitivity values at the end of RT ( $\Delta$  pre- and post-RT 1.16 ng/L) with a subsequent recovery at 6 and 12 months post-RT for patients with heart d-mean  $>$  1.9Gy (p-value  $<$  0.5)



## Results (3): N-terminal Pro-BNP

Patients were stratified at the 75th percentile for dosimetric variables  
Heart mean dose  $<$  or  $>$  1.9 Gy and LAD mean dose  $<$  or  $>$  3.9 Gy

At baseline non statistically significance of N-terminal Pro-BNP levels according to stratification (p-value 0.19 and 0.23, respectively)

There was a statistically significant increase of N-terminal Pro-BNP lately, at 6 AND 12 months, post-RT (p-value  $<$  0.07 and 0.00, respectively) for dmean LAD  $>$  3.9Gy

## Results (4): ecocardiographic parameters

Patients were stratified at the 75th percentile for dosimetric variables  
Heart mean dose  $<$  or  $>$  1.9 Gy and LAD mean dose  $<$  or  $>$  3.9 Gy

At baseline non statistically significance regarding LVEF-left ventricular ejection fraction and GLS-global longitudinal strand according to dosimetric stratification criteria

Regarding the ecocardiographic parameters here analyzed, there was a 2% LVEF reduction at the end of RT for LAD d-mean  $>$  3.9Gy (p-value 0.008; range, +8%/-10%) with a subsequent recovery over the time of follow up

No statistically significance regarding GLS-variable variation over time

## CONCLUSION

- ❑ In the case of **heart d-mean > 1.9Gy** it was observed an acute cardiac damage documented by increased levels of Troponin I
- ❑ In the case of **LAD d-mean > 3.9Gy** it was observed a ventricular dysfunction documented by increased levels of pro-BNP (lately) and 2% LVEF reduction at the end of RT
- ❑ Long-term results are awaited to understand the clinical risk of cardiac events