Congresso Nazionale AIRO-AIRB-AIRO Giovani

Associazione Italiana Radioterapia Oncologica

Società Italiana di Radiobiologia

CARDIOTOSSICITÀ NEI DIFFERENTI IPOFRAZIONAMENTI RADIOTERAPICI ASSOCIATI A TERAPIA CON TRASTUZUMAB NEL TUMORE DELLA MAMMELLA

Dott.ssa BONZANO ELISABETTA

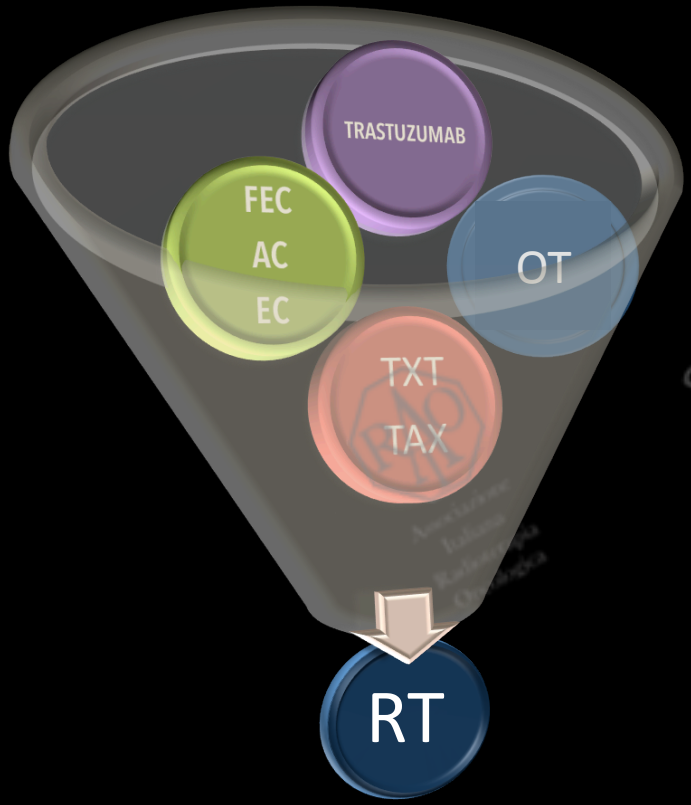
DICHIARAZIONE

Relatore: ELISABETTA BONZANO

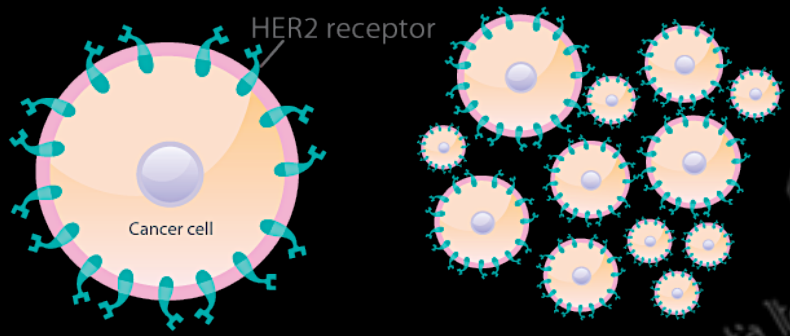
Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero Della Salute è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario

Dichiaro di non trovarmi in situazioni di incompatibilità né in condizioni di conflitto di interessi anche potenziali

TERAPIE SISTEMICHE



TRASTUZUMAB



CONTROLLO LOCALE

SOPRAVVIVENZA GLOBALE

CARDIOTOSSICITÀ

The HEART of the MATTER

Cardiac Surveillance Guidelines for Trastuzumab-Containing Therapy in Early-Stage Breast Cancer: Getting to the Heart of the Matter

Chau T. Dang, Anthony F. Yu, Lee W. Jones, Jennifer Liu, Richard M. Steingart, Daniel F. Argolo, Larry Norton and Clifford A. Hudis

Author Affiliations

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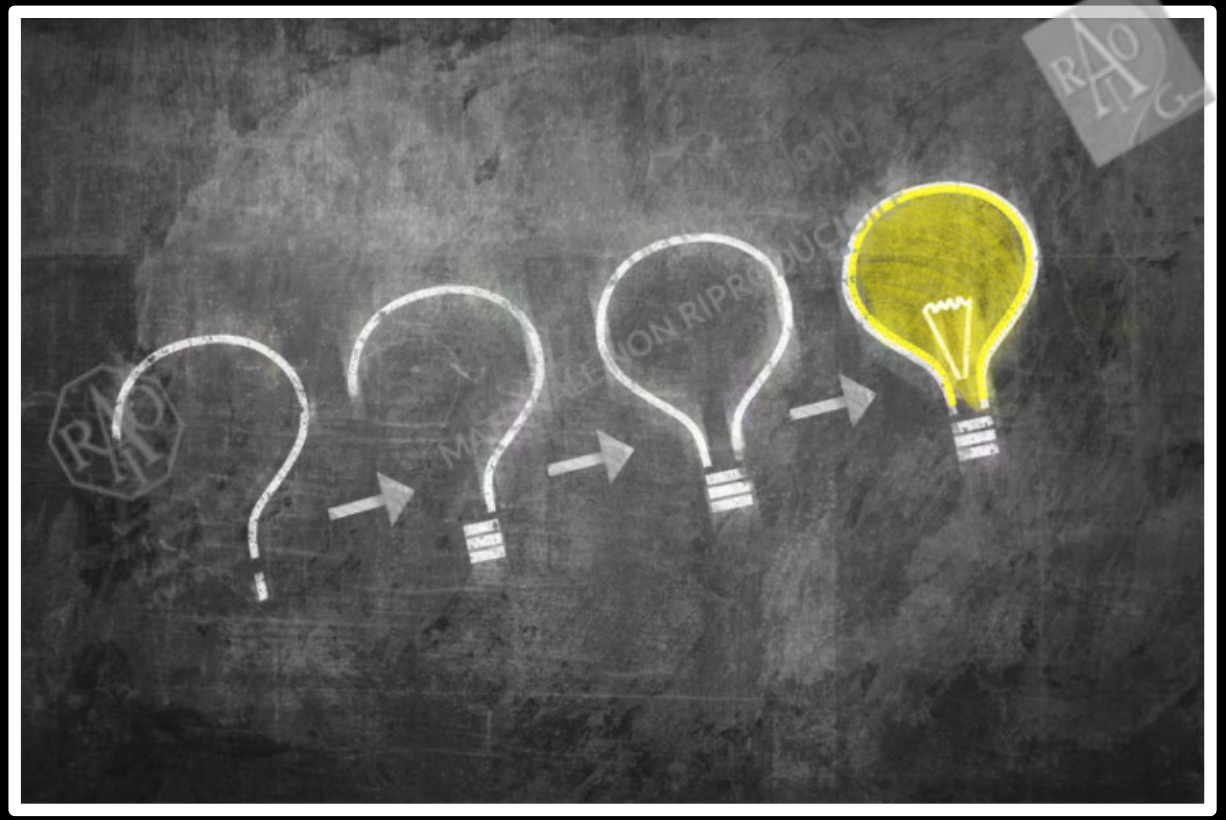
Trastuzumab-containing regimens for breast cancer have significantly improved survival both in the early-stage and metastatic settings.[1-8] Nevertheless, given the early signals of cardiotoxicity, a prevailing concern exists regarding the risk of cardiotoxicity, defined as a decline in left ventricular ejection fraction (LVEF) both asymptomatic and symptomatic. This concern that LVEF decline would be an early and actionable surrogate for subsequent development of congestive heart failure (CHF) led to the design and implementation of specific eligibility criteria and LVEF surveillance guidelines for the pivotal randomized adjuvant trials. These guidelines were subsequently adopted as the standard of care. However, it is increasingly unclear whether these specific recommendations are justified for all patients. Resolution of this matter is critical for our community because adherence to these guidelines was recently proposed as a quality metric.[9] This issue raises the general question of the level of evidence needed to accept a toxicity screening schedule as a quality indicator. If following these guidelines is not associated with improved outcomes, then adherence to them as a quality metric should be challenged. Cardiotoxicity screening can serve to illuminate this issue. Here, we review the historical events that led to the development of the current guidelines and highlight critical knowledge gaps with regard to the benefits of screening and intervention.

RADIOTERAPIA + TRASTUZUMAB



LITERATURE

Ann Oncol. 2008 Jun;19(6):1110-6. doi: 10.1093/annonc/mdn029. Epub 2008 Mar 15.

Concurrent trastuzumab with adjuvant radiotherapy in HER2-positive breast cancer patients: acute toxicity analyses from the French multicentric study.

Belkacémi Y[1], Gligorov J, Ozsahin M, Marsiglia H, De Lafontan B, Laharie-Mineur H, Aimard L, Antoine EC, Cutuli B, Namer M, Azria D.

Author information

[1]Department of Radiation Oncology, CLCC Oscar Lambret Anti-Cancer Center, University of Lille II, Lille, France. y-belkacemi@o-lambret.fr

Abstract

BACKGROUND: Trastuzumab (T) combined with chemotherapy has been recently shown to improve outcome in HER2-positive breast cancer (BC). The aim of this study was to evaluate the toxic effects of concurrent radiation therapy (RT) and T admi

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Breast Cancer Res Treat. 2014 Nov;148(2):345-53. doi: 10.1007/s10549-014-3166-5. Epub 2014 Oct 16.

Concurrent administration of trastuzumab with locoregional breast radiotherapy: long-term results of a prospective study.

Med Oncol. 2014 Apr;31(4):891. doi: 10.1007/s12032-014-0891-x. Epub 2014 Feb 18.

Cutaneous and cardiac toxicity of concurrent trastuzumab and adjuvant breast radiotherapy: a single inst

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Oncotarget. 2016 Jan 5;7(1):1042-54. doi: 10.18632/oncotarget.6053.

Early cardiac toxicity following adjuvant radiotherapy of left-sided breast cancer with or without concurrent trastuzumab.

Cao L[1,2,3], Cai G[1,2,3], Chang C[4,3], Yang ZZ[1,3], Feng Y[1,3], Yu XL[1,3], Ma JL[1,3], Wu J[5,3], Guo XM[1,3], Chen JY[1,2,3].

⊕ **Author Information**

Abstract

PURPOSE: To evaluate the influence of concurrent trastuzumab on the cardiotoxicity in patients receiving left-sided adjuvant radiotherapy.

MATERIALS AND METHODS: Medical records of stage I-III left-sided breast cancer patients, including 64 receiving concurrent trastuzumab with radiotherapy and 73 receiving radiotherapy alone were retrospectively reviewed. All of the patients had normal LVEF after adjuvant chemotherapy. Information of doses volume to cardiac structures was collected. Cardiac events were assessed according to CTC 2.0.

RESULTS: Median follow-up of LVEF and clinical assessment of cardiac function from the initiation of radiotherapy was 6.7 months (range 3-60.9) and 26 months (range 6.4-60.9), respectively. Grade 1 LVEF dysfunction occurred in 5 (7.8%) and 3 (4.1%) patients of the concurrent-trastuzumab and radiotherapy alone cohort, respectively. Trastuzumab was the only significant factor influencing absolute LVEF decrease in univariate analysis. In multivariate analysis of concurrent-trastuzumab cohort, IMC radiotherapy and start trastuzumab during radiotherapy were independent risk factors. For concurrent cohort, mean heart dose, as well as D10-D30, D50-D55, V5-V20 of the heart and D30-D45, D65-D75, V6-V15 of the LV were significantly higher in patients developing LVEF dysfunction.

CONCLUSIONS: Concurrent trastuzumab and left-sided radiotherapy is well tolerated in terms of cardiotoxicity in patients with normal baseline cardiac function after adjuvant chemotherapy. However, increases in mean dose and low-dose volume of cardiac structures are associated with a higher risk of acute LVEF dysfunction.

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CONCLUSION: I

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and the skin toxicity were deemed acceptable. Further follow-up is needed.

IL NOSTRO STUDIO

FEBBRAIO 2008-GIUGNO 2016

52 PZ SOTTOPOSTE A CT seguita da TRASTUZUMAB + RT IPOFRAZIONATA

RT

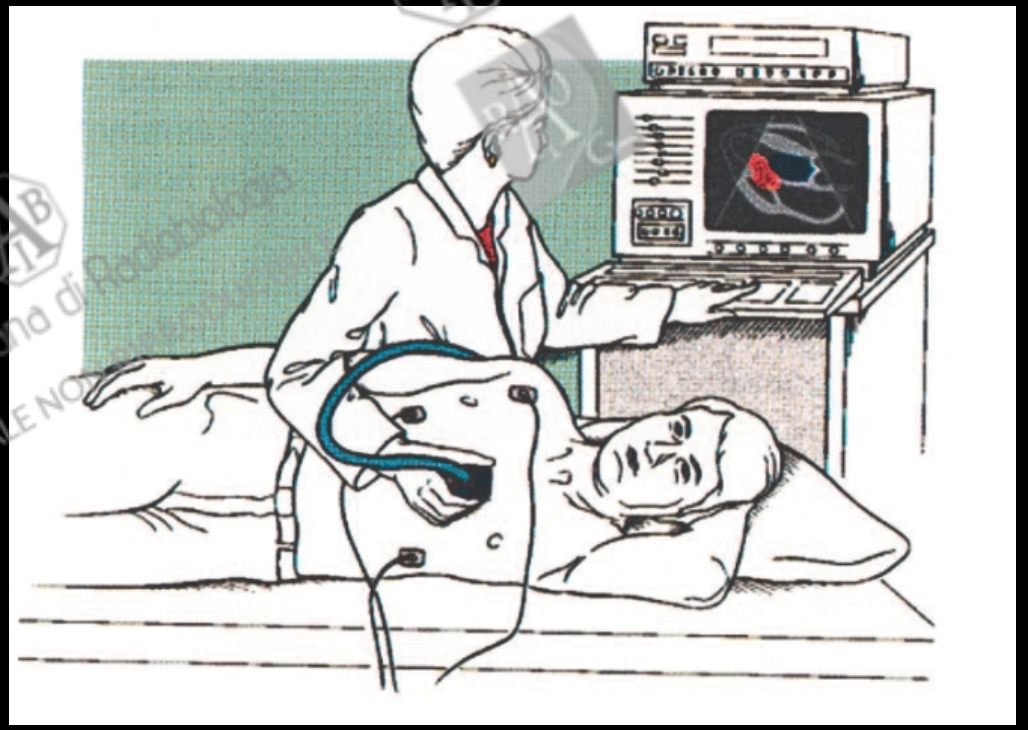
COMMON TERMINOLOGY CRITERIA FOR ADVERSE EVENTS (CTCAE-V3)

CARDIAC GENERAL					
	Grade				
Short Name	1	2	3	4	5
Hypotension	Changes, intervention not indicated	Brief (<24 hrs) fluid replacement or other therapy; no physiologic consequences	Sustained (≥24 hrs) therapy, resolves without persisting physiologic consequences	Shock (e.g., acidemia; impairment of vital organ function)	Death
fainting).					
Left ventricular diastolic dysfunction	Asymptomatic diagnostic finding; intervention not indicated	Asymptomatic, intervention indicated	Symptomatic CHF responsive to intervention	Refractory CHF, poorly controlled; intervention such as ventricular assist device or heart transplant indicated	Death
Left ventricular systolic dysfunction	Asymptomatic, resting ejection fraction (EF) <60 – 50%; shortening fraction (SF) <30 – 24% <60-50%	Asymptomatic, resting EF <50 – 40%; SF <24 – 15% <50%-40%	Symptomatic CHF responsive to intervention; EF <40 – 20% SF <15% <40-20%	Refractory CHF or poorly controlled; EF <20%; intervention such as ventricular assist device, ventricular reduction surgery, or heart transplant indicated	Death

ECOCARDIOGRAMMA

RIDUZIONE FRAZIONE DI EIEZIONE

ECO PRIMA E DOPO



IL NOSTRO STUDIO

≤ pT 2 ≤ pN1a

età 34 aa – 87 aa

27 (52%) pz OT

FATTORI DI RISCHIO CV.

3 IPOFRAZIONAMENTI

LATERALITÀ

FATTORI DI RISCHIO CARDIOVASCOLARI

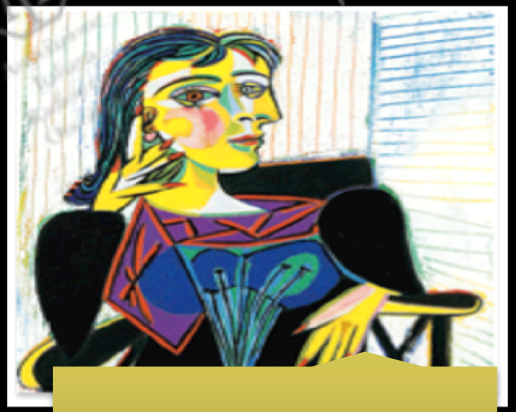
6 PZ(12%)

FUMO

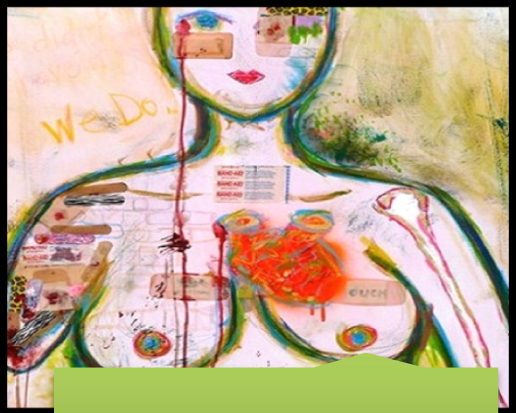
IPERCOLESTEROLEMIA

2 PZ(4%)

10 PZ(19%)



IPERTENSIONE



FIBRILLAZIONE ATRIALE

1 PZ(2%)

DIVERSI IPOFRAZIONAMENTI

Pz < 40 anni

46 Gy in 20 fx (4 fx a settimana) — 15 pz

Pz tra 40-46 anni

39 Gy in 13 fx (4 fx a settimana) — 16 pz

Pz > 46 anni

35 Gy in 10 fx (4 fx a settimana) — 21 pz

IN BASE ALL'ETÀ DELLE PAZIENTI

LATERALITÀ

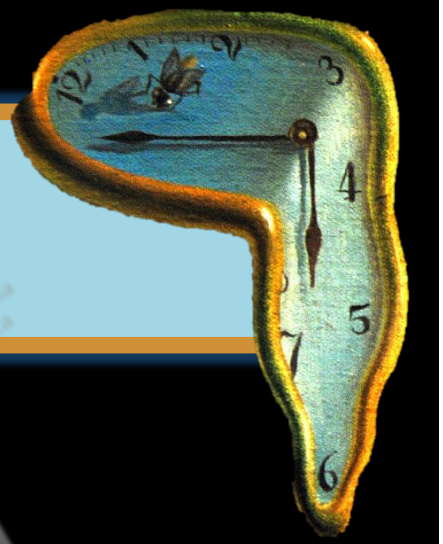
29 PZ
MAMMELLA
SINISTRA

1/29 pz (3%) => G2
9/29 pz (31%) => G1
19/29 pz (66%) => G0

23 PZ
MAMMELLA
DESTRA

2/23 pz (8%) => G2
4/23 pz (18%) => G1
17/23 pz (74%) => G0

FOLLOW UP MEDIANO



5 AA

RANGE: 6-96 MESI

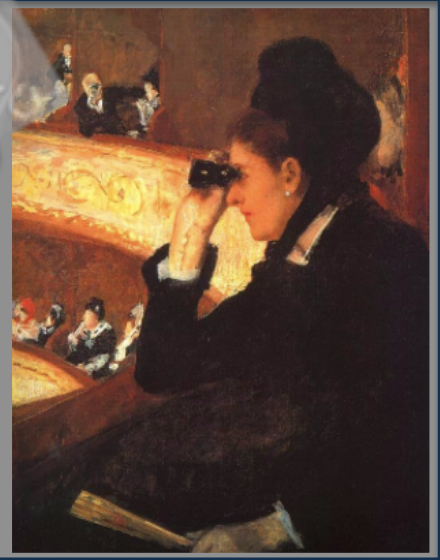
94% (49 PAZIENTI) : VIVE e LIBERE DA MALATTIA

2% (1 PAZIENTE) : RECIDIVA LOCOREGIONALE

4% (2 PAZIENTI) : METASTASI A DISTANZA

UNO SGUARDO AI RISULTATI

	46 Gy/20 fx		39 Gy/13 fx		35 Gy/10 fx	
	pts	%	pts	%	pts	%
Grade 2 *LVEF 50%-40%*	2/15	13%	0/16	0%	1/21	5%
Grade 1 *LVEF 60%50%*	3/15	20%	5/16	31%	5/21	24%
Grade 0 *LVEF >60%*	10/15	67%	11/16	69%	15/21	71%



No G3
G1-2 sovrapponibili alla letteratura

ELSEVIER

European Journal of Surgical Oncology (EJSO)

Volume 42, Issue 4, April 2016, Pages 437–440

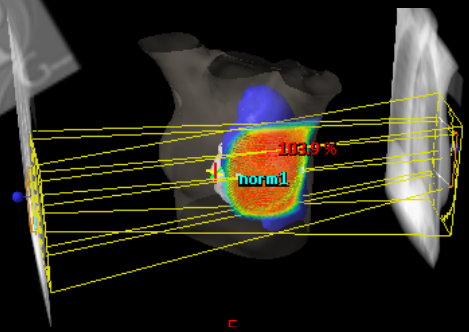
Review

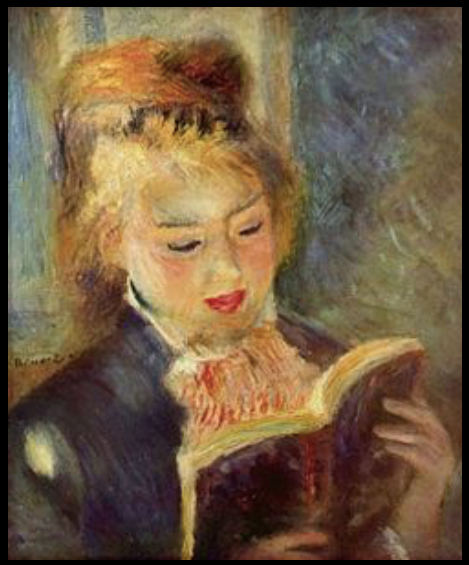
Radiation therapy (RT) after breast-conserving surgery (BCS) in 2015 – The year of radiation therapy advances

Y.M. Kirova

Association between radiation therapy and new targeted treatments

Interestingly, 2015 also saw more information regarding the association between radiation therapy in early-stage breast cancer and new targeted treatments such as trastuzumab and bevacuzumab.[18, 19 and 20] A single-center prospective study at the Institut Curie, Paris – recruiting 308 patients who were followed up for a median of 50.2 months (13.0–126.0) and 227 patients (73.7%) who underwent IMNI – reported a locoregional control rate of 95% (95%CI 92; 98), and an overall survival of 98% (95%CI 96; 100). Univariate analysis showed how neither the treated breast side (p = 0.655) nor IMNI (p = 0.213) exposes patients to left ventricular ejection fraction (LVEF) alteration. Multivariate analysis demonstrated that clinical lymph-node involvement is associated with an increased risk of locoregional and distant recurrence (p = 0.016 and p = 0.007, respectively). In this prospective study, the toxicities of concurrent trastuzumab with locoregional breast RT were acceptable and the outcomes were favorable. nch multicenter prospective and descriptive study was conducted to determine late toxicities and outcomes among patients with non-metastatic breast cancer receiving concurrent bevacizumab (BV) and RT.[19 and 20] Early and late toxicities were assessed in 63 patients at 12 months. With this experience the authors concluded that the concurrent BV with locoregional RT provides acceptable toxicities, although longer follow-up is needed to confirm these early findings.[19 and 20]



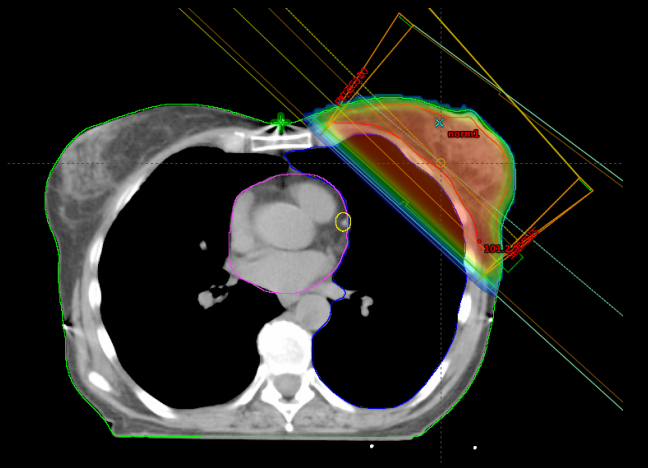


CONCLUSIONI

LA LVEF NON SEMBRA VARIARE
NEI DIVERSI IPOFRAZIONAMENTI

SEMPRE MAGGIORE IMPORTANZA
CONTORNAMENTO DI CUORE E
ARTERIA CORONARIA DISCENDENTE
ANTERIORE

NECESSARIO CONTINUARE
IL FOLLOW UP



GRAZIE PER L'ATTENZIONE