

Cardiotoxicity after breast cancer radiotherapy: relationship between cardiac doses and early myocardial dysfunction (BACCARAT study)

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BACKGROUND

- **Radiotherapy (RT):** a major component of breast cancer treatment ¹
- **Breast cancer (BC) RT:** irradiation of the heart during the treatment ²
- **Heart irradiation:** associated with long term cardiac complication
- Long before the detection of cardiac complication, **early cardiovascular dysfunctions can appear** ³
- **2D speckle-tracking echocardiography (2DSTE):** Allows early detection of left ventricular dysfunction with longitudinal strain measurement ⁴

1. Clarke M. et al. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. Lancet Lond Engl 2005 Dec 17;366(9503):2087-2106. PMID:16360786

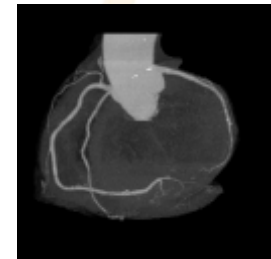
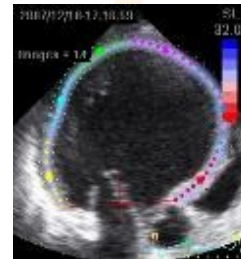
2. Jacob S, Ferrières J. Breast cancer radiotherapy: A case of double jeopardy. Arch Cardiovasc Dis 2016 Nov;109(11):587-590. PMID:27836785

3. Erven K. et al. Subclinical Cardiotoxicity Detected by Strain Rate Imaging up to 14 months After Breast Radiation Therapy. Int J Radiat Oncol. 2013;85:1172-8.

4. 15. Lo Q, Hee L, Batumalai V, Allman C, MacDonald P, Loneragan D, et al. Strain Imaging Detects Dose-Dependent Segmental Cardiac Dysfunction in the Acute Phase After Breast Irradiation. Int J Radiat Oncol. 2017;99:182-90.

RESEARCH QUESTION

- Early cardiotoxicity induced by current RT methods for the treatment of breast cancer ?
- Subclinical evolution ?



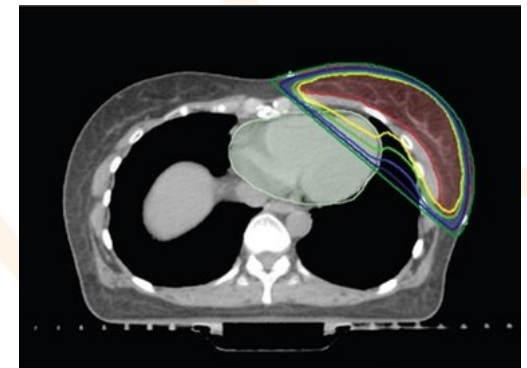
Objective

Use two-dimensional speckle tracking echocardiography to assess whether myocardial changes occurring after breast cancer RT are associated with doses absorbed by the heart and its substructures

PATIENTS AND METHODS (1/4)

■ The BACCARAT study⁵

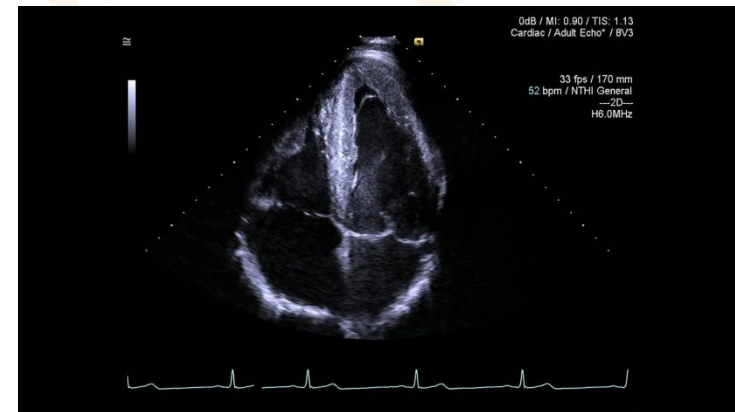
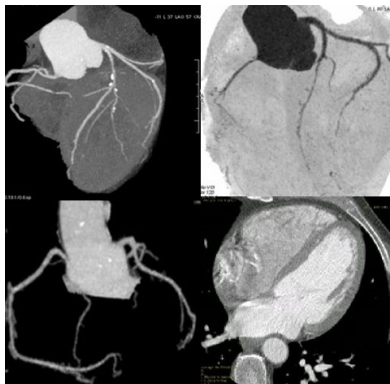
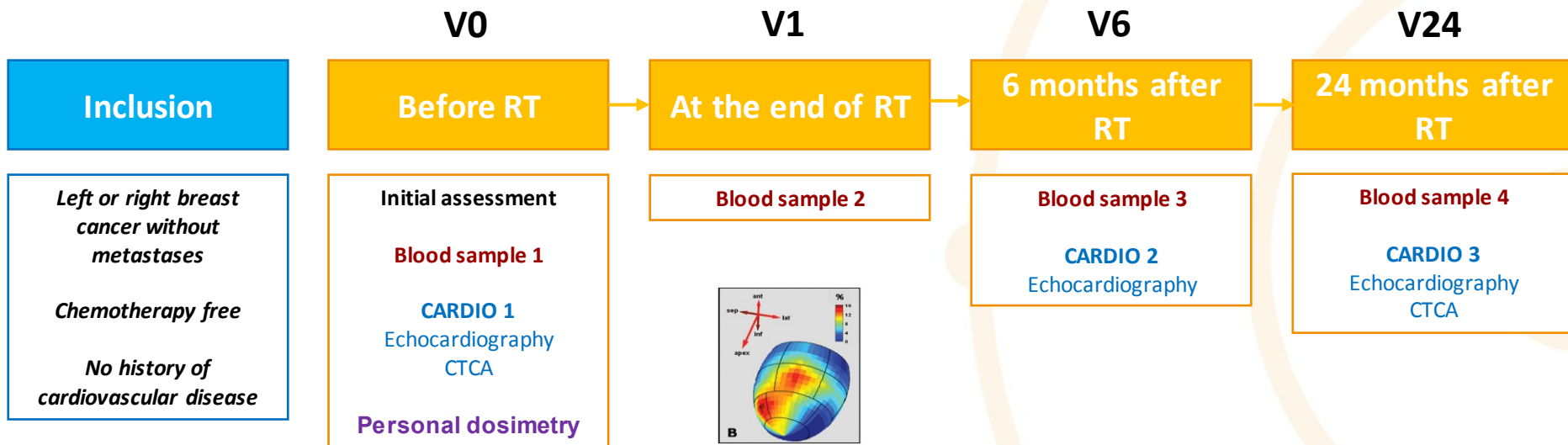
- Prospective monocentric cohort: inclusions at the Clinique Pasteur in Toulouse, France (2015-2017)
- **114 patients included with unilateral breast cancer**
 - No history of cardiovascular disease or cancer
 - Treated by RT (3D-CRT), without chemotherapy
 - Aged 40 to 75 years old
- End of follow-up early 2020



5. Jacob S et al. Early detection and prediction of cardiotoxicity after radiation therapy for breast cancer: the BACCARAT prospective cohort study. Radiat Oncol.

PATIENTS AND METHODS (2/4)

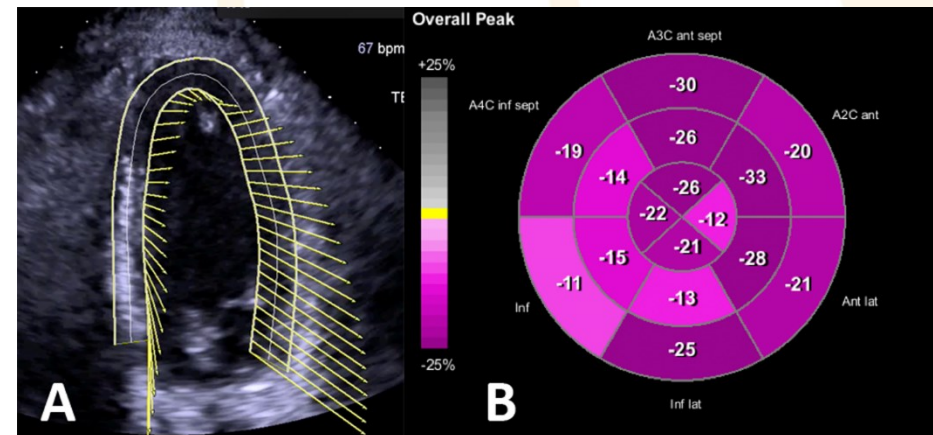
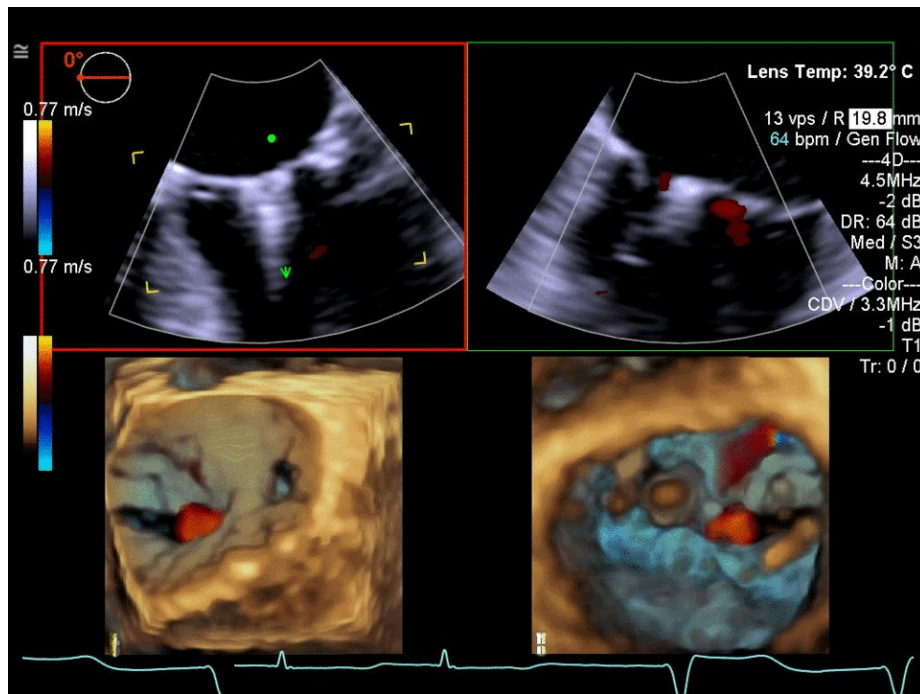
BACCARAT: from inclusion to 24-month follow-up



PATIENTS AND METHODS (3/4)

Concerning **myocardial strain**: available before RT and 6 months after RT

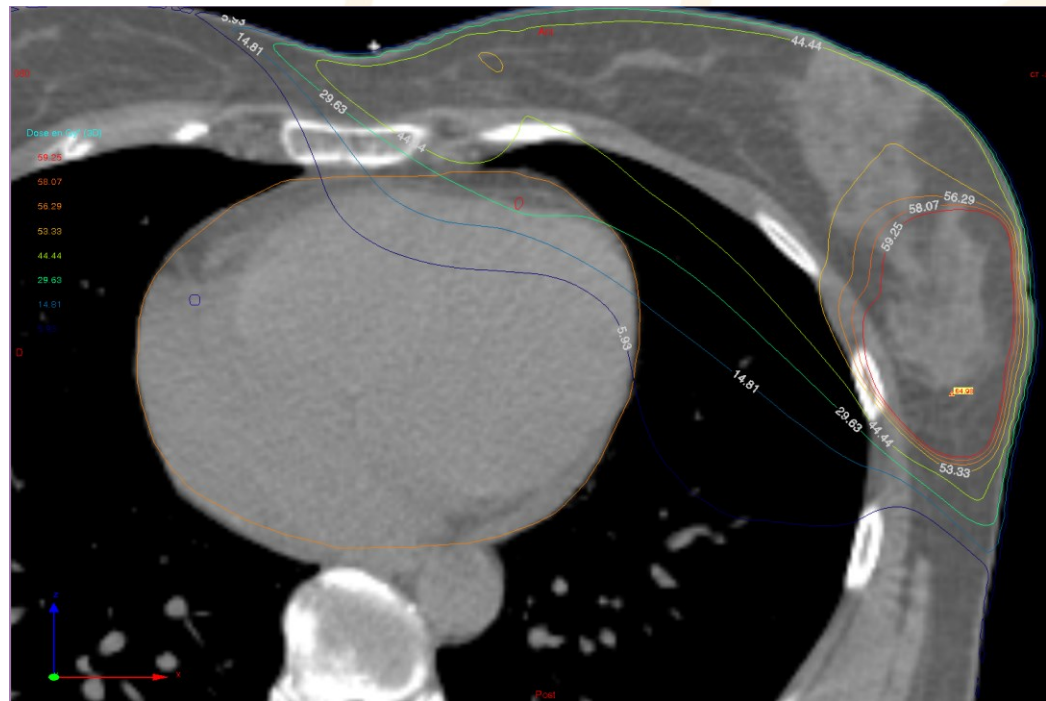
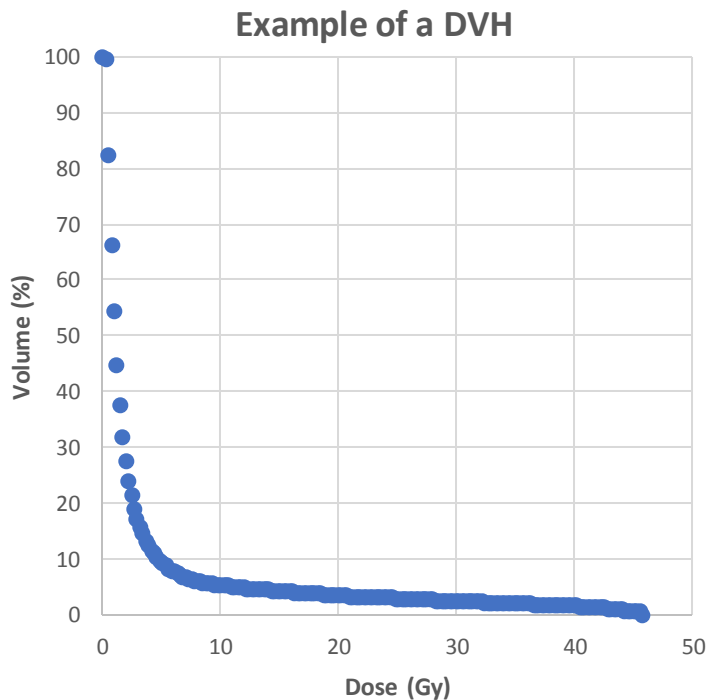
- Measured via **Two-dimensional speckle tracking echocardiography (2DSTE)**
- Allows the analysis of the **Global Longitudinal Strain (GLS)**



PATIENTS AND METHODS (4/4)

Cardiac dosimetry

- Work performed by D. Broggio and S. Derreumaux (IRSN)
- Several structures** (whole heart, left ventricle, the left anterior descending artery ...) with mean, D2, min-max dose... + Dose-Volume Histogram (DVH)



RESULTS (1/3)

- The study consisted of **79 females patients** with unilateral breast cancer
- **Mean age = 58 ± 9 years**
- Most patients underwent **breast conserving surgery (97%)**
- Most patient received **hormonal therapy (76%)**

Dosimetric data from patients in the BACCARAT study

	Left-sided BC patients N=64		Right-sided BC patients N=15	
	Mean \pm SD Median (Q1-Q3)	Range	Mean \pm SD Median (Q1-Q3)	Range
Heart				
Average dose (Gy)	3.05 ± 1.31	$0.87 - 6.37$	0.65 ± 0.48	$0.25 - 2.17$
V20 (%)	3 (1 – 6)	0 - 10	0	0
Left Ventricle				
Average dose (Gy)	6.72 ± 3.35	$1.16 - 13.42$	0.09 (0.08 – 0.12)	$0.04 - 1.24$
V20 (%)	11 (4 – 18)	0 - 26	0	0

RESULTS (2/3)

Echocardiographic measurements from patients in the BACCARAT study

	All BC patients N=79	Left-sided BC patients N=64	Right-sided BC patients N=15
GLS (in %)			
Before RT	-16.1 ± 2.7	-16.0 ± 2.6	-16.2 ± 2.8
RT+6months	-15.1 ± 3.2	-15.0 ± 3.0	-15.2 ± 4.0
p-value	0.01	0.02	0.26
GLS decrease > 10% after RT	37 (47%)	31 (48%)	6 (40%)

RESULTS (3/3)

Logistic regressions on a cardiotoxicity criterion

- **Subclinical cardiotoxicity event:** relative decrease in strain > 10% between 0 and 6 months

	Univariate analysis		Multivariate analysis*	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Laterality of BC (left vs. right)	1.41 (0.45 – 4.42)	0.55	-	-
Heart				
Dmean (Gy)	1.37 (1.01 – 1.86)	0.04	1.21 (0.87 – 1.71)	0.26
V20 (%)	1.20 (1.01 – 1.43)	0.04	1.13 (0.93 – 1.36)	0.23
Left Ventricle				
Dmean (Gy)	1.14 (1.01 – 1.28)	0.03	1.09 (0.96 – 1.25)	0.17
V20 (%)	1.08 (1.01 – 1.14)	0.02	1.05 (0.99 – 1.12)	0.12
LV V20 > 15% (%)	5.10 (1.73 – 15.00)	0.03	3.49 (1.12 – 10.91)	0.03

*Adjusted for BMI, hypercholesterolemia and Hormonotherapy.

DISCUSSION

- **A decrease in strain** as previously observed (Erven et al., Lo et al., etc.)
- **Relationship between heart dose and subclinical myocardial deformation**
- **Multivariate analysis:** no significant associations after adjustment for non-radiation factors
- **Results to be confirmed with longer follow-up:** need for information at V24
- Largest population at the moment but....
- ... Still relatively small (MEDIRAD EARLY HEART⁶ study)

6. Walker V et al. Early Detection of Cardiovascular Changes After Radiotherapy for Breast Cancer: Protocol for a European Multicenter Prospective Cohort Study (MEDIRAD EARLY HEART Study) JMIR Res Protoc 2018;7(10):e178

CONCLUSION / PERSPECTIVES

- First study to investigate the associations between BC RT-induced cardiac doses and subclinical LV dysfunction
- **LV exposure should be further investigated:**
 - Patients with V20 of the LV >15%
 - Important excess risk of subclinical LV dysfunction
- **Ongoing collection of 24-month 2DSTE data**

THANK YOU FOR YOUR ATTENTION

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Conflict of interest: none declared