



Early subclinical left ventricular dysfunction post radiotherapy in breast cancer: speckle-tracking echocardiography detects dose-related longitudinal strain changes after irradiation (BACCARAT study)

Sophie Jacob, Valentin Walker, Olivier Fondard, Atul Pathak, Baptiste Pinel, Gaëlle Jimenez, Jeremy Camilleri, David Broggio, Sylvie Derreumaux, Marie Odile Bernier, et al.

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**Early subclinical left ventricular dysfunction
post radiotherapy in breast cancer:
Speckle-tracking echocardiography detects dose-related
longitudinal strain changes after irradiation
(BACCARAT study)**

Sophie Jacob, Valentin Walker, Olivier Fondard, Atul Pathak, Baptiste Pinel, Christian Chevelle, Gaëlle Jimenez, Jérémy Camilleri, David Broggio, Sylvie Derreumeaux, Marie-Odile Bernier, Dominique Laurier, Jean Ferrières, Olivier Lairez

I currently have, or have had over the last two years, an affiliation or financial interests or interests of any order with a company or I receive compensation or fees or research grants with a commercial company :

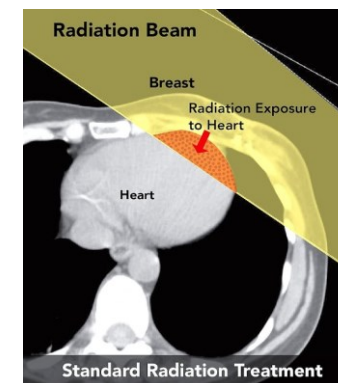
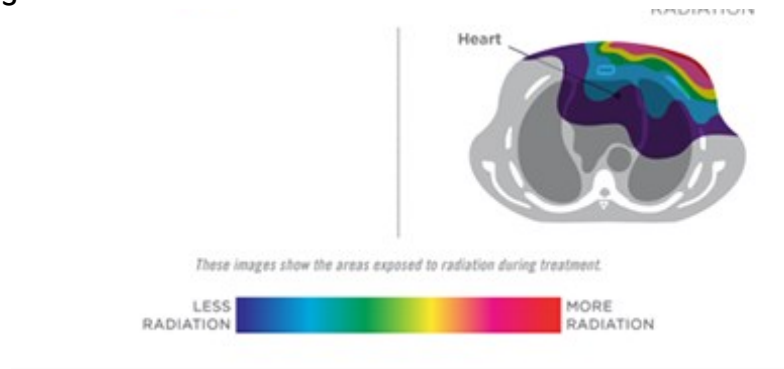
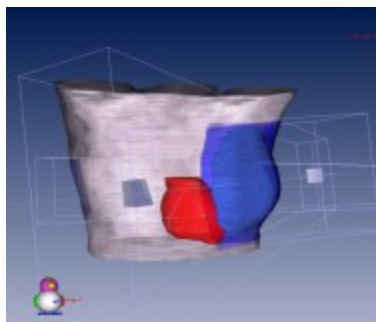
Speaker's name : Sophie Jacob, Fontenay Aux Roses Cedex

☒ I do not have any potential conflict of interest

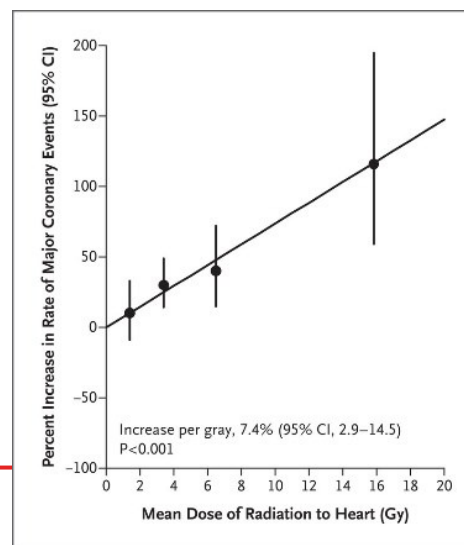


➤ Breast cancer RT: exposure of the heart to ionizing radiation

- Mean heart doses: 2-4 Gy for left sided breast cancer
- Heterogeneity of doses



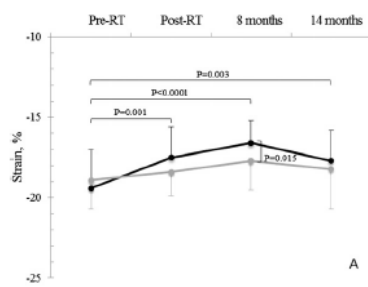
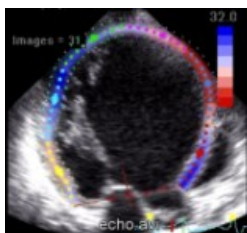
➤ Association between breast RT and long term cardiac complications



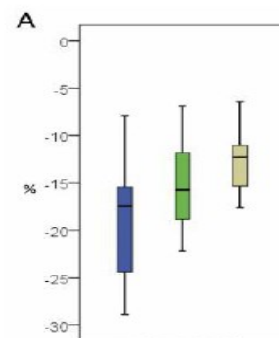
Darby et al NEJM 2013



- Subclinical left ventricular dysfunction can be detected early **after BC RT with longitudinal strain (LS)** measurement based on 2D speckle tracking



Erven et al 2013
Black: 51 left sided BC, Grey: 24 Right sided BC



Tuohinen et al 2019
64 left sided BC

But no measurable alteration of LVEF

- Higher sensitivity and prognostic value of the global longitudinal strain (GLS), compared with left ventricular ejection fraction (LVEF), for early detection of left ventricular dysfunction
 - **Patients with a relative drop in GLS > 10% - 15%** : this threshold is considered to define subclinical left ventricular dysfunction and has been reported to be **predictive of subsequent cardiotoxicity** (Thavendiranathan P et al. J Am Coll Cardiol. 2014;63:2751–68)
 - Chemotherapy-induced cardiotoxicity : drop > 10% of LVEF to a value < 53%



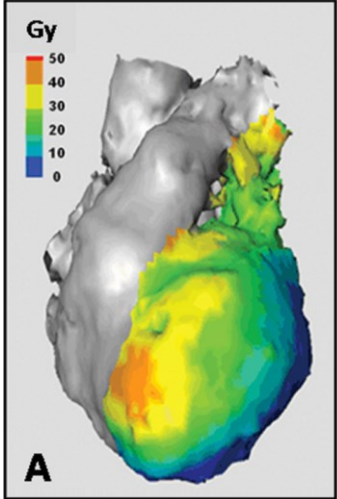
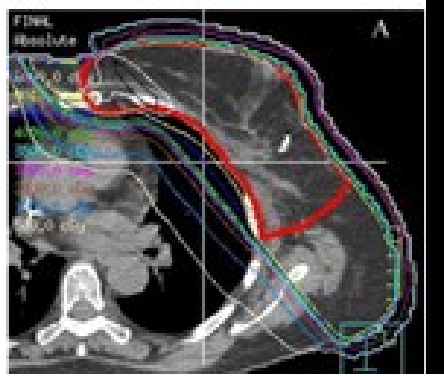
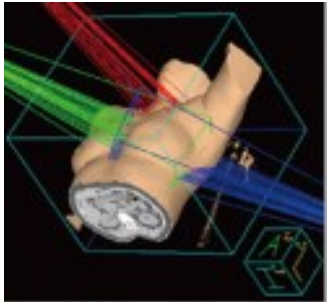
- Based on a prospective cohort of BC patients treated with 3D-CRT
To analyze the associations between radiation exposure to the whole heart and the left ventricle (LV) and the evolution of GLS from baseline to 6 months after RT, in particular for subclinical left ventricular dysfunction defined as GLS decrease $> 10\%$.



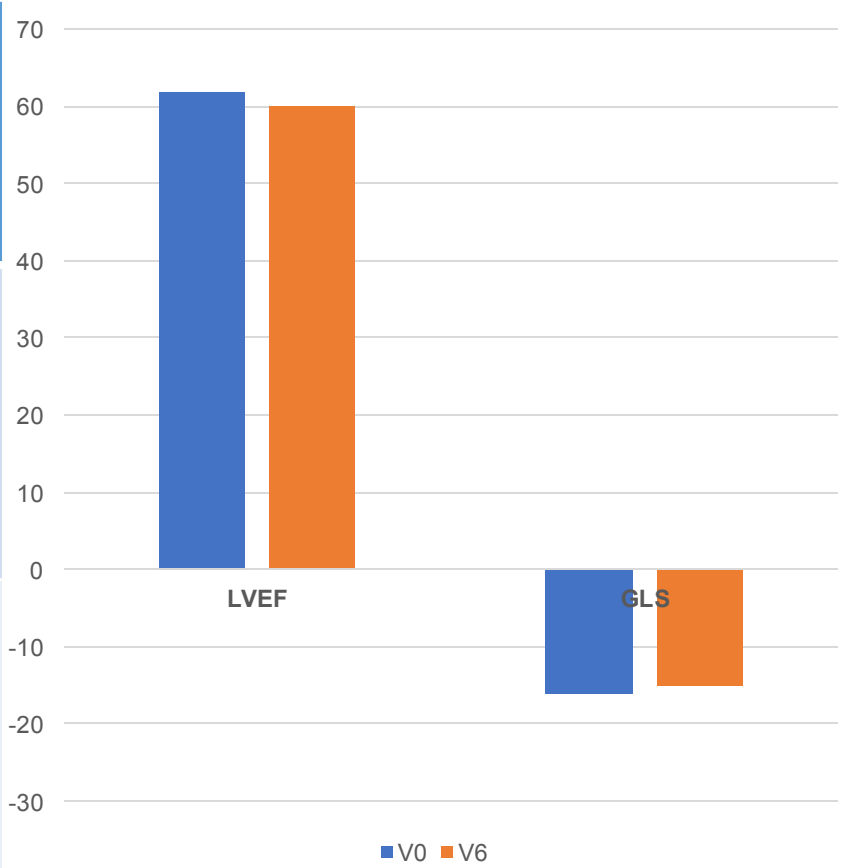
- Prospective cohort study
- BC patients of the BACCARAT study
 - RT between October 2015 and December 2017 in Clinique Pasteur Toulouse
 - Aged 40-75 years
 - No chemotherapy
 - No history of major cardiac disease
 - LVEF > 45%
 - Echocardiography 2D speckle tracking (Siemens) performed before **RT and 6 months after RT**
- **Global longitudinal strain (GLS)** at baseline and RT+6months
- Cardiac dosimetry (doses in Gy)

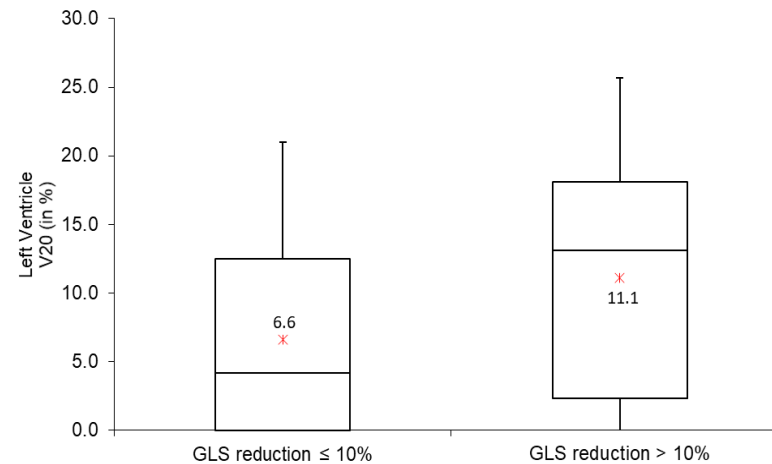
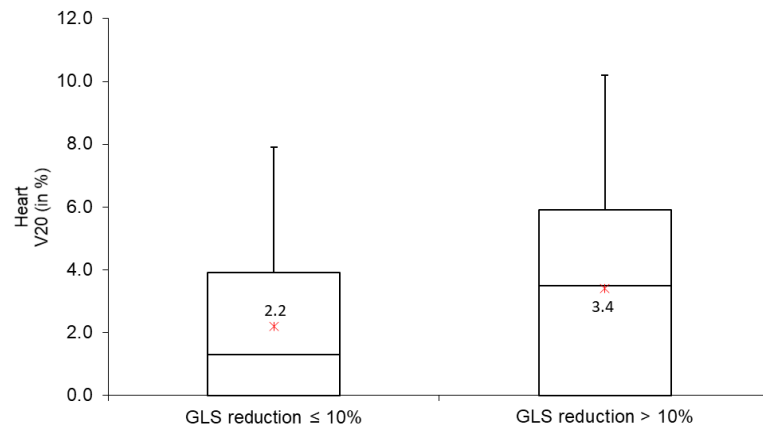
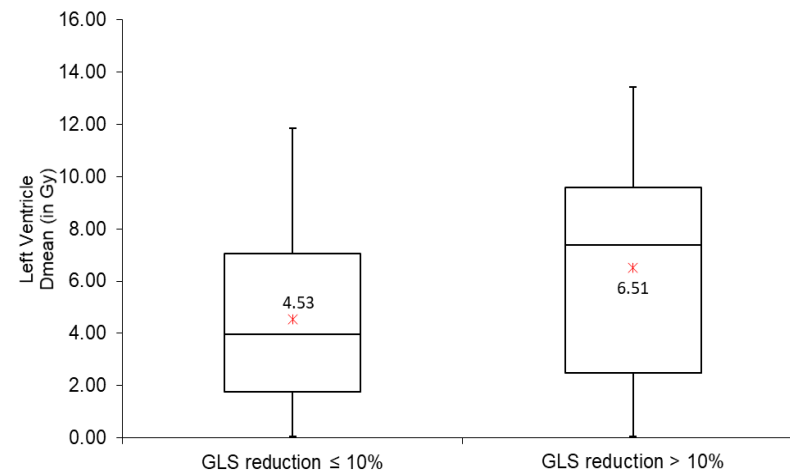
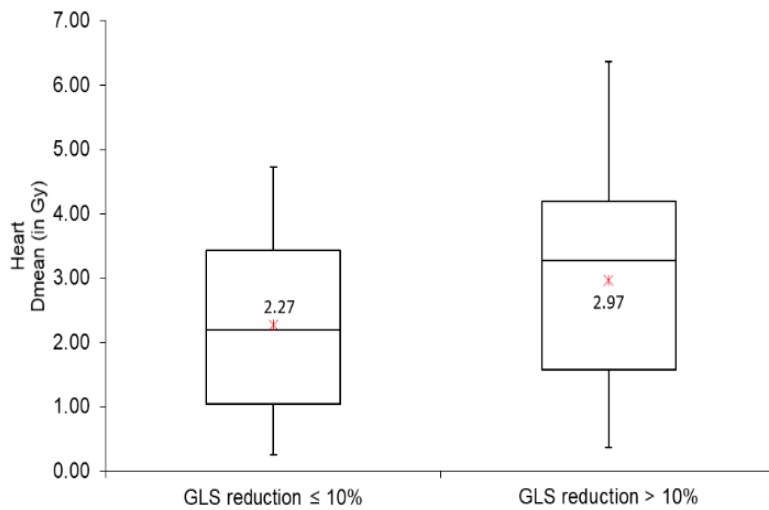
	All patients N = 79
Age in years, mean ± SD	58 ± 9
Left-sided BC patients	64 (81%)
Hormonotherapy	60 (76%)
Anti-aromatase	34
Tamoxifen	26
Body mass index in kg/m², mean ± SD	24.4 ± 4.1
Smoking, n (%)	
Never-smokers	42 (53%)
Former smokers	23 (29%)
Current smokers	14 (18%)
Hypertension, n (%)	19 (24%)
Diabetes, n (%)	5 (6%)
Hypercholesterolemia, n (%)	24 (30%)

	Left-sided BC patients N = 64		Right-sided BC patients N = 15	
	Mean ± SD Median (Q1-Q3)	Range	Mean ± SD Median (Q1-Q3)	Range
Heart				
Dmean (Gy)	3.05 ± 1.31	0.87 – 6.37	0.65 ± 0.49	0.25 – 2.17
V20 (%)	3 (1 – 6)	0 - 10	0	0
Left Ventricle				
Dmean (Gy)	6.68 ± 3.36	1.16 – 13.42	0.09 (0.08 – 0.12)	0.06 – 1.24
V20 (%)	11 (4 – 18)	0 - 26	0	0




	All BC patients N = 79	Left-sided BC patients N = 64	Right-sided BC patients N = 15	
LVEF (in %)	Before RT	62 ± 7	61 ± 7	64 ± 8
	RT+6months	60 ± 9	60 ± 9	63 ± 8
	p-value	0.07	0.09	0.51
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
	Patients with GLS reduction >10% after RT	37 (47%)	31 (48%)	6 (40%)






Event: GLS reduction 6 months post RT > 10%

	OR (95% CI)	p-value
Age (in years)	0.98 (0.93 – 1.04)	0.52
BMI (in Kg.m ⁻²)	1.15 (1.02 – 1.30)	0.02^a
Smoking	Former vs. No	0.59 (0.20 – 1.68)
	Current vs No	1.98 (0.57 – 6.91)
Hypertension	1.03 (0.37 – 2.89)	0.95
Diabetes	1.76 (0.28 – 11.19)	0.55
Hypercholesterolemia	1.95 (0.74 – 5.15)	0.18^a
Endocrine therapy		3.20 (1.02 – 10.10)
	Anti-aromatase	0.04^a
	Tamoxifen	0.02
	2.05 (0.57 – 7.41)	0.27



Association between doses and GLS reduction >10%



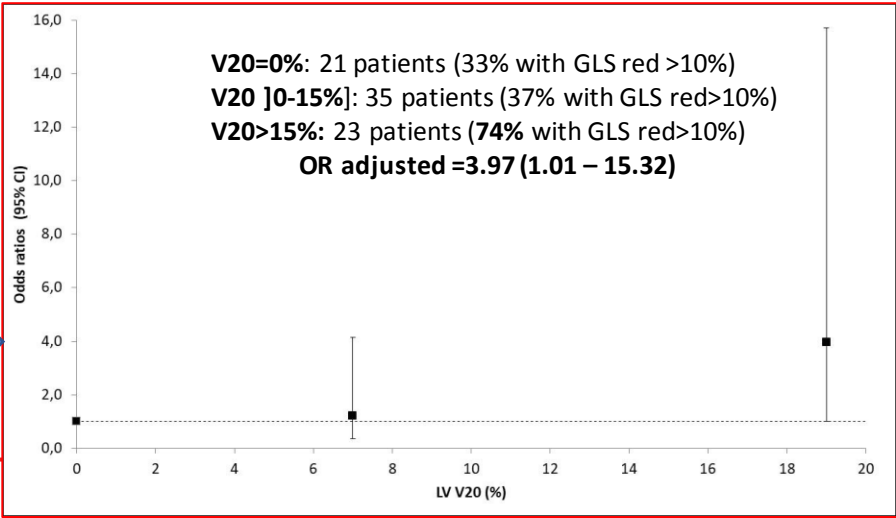
Associations between cardiac radiation doses and subclinical LV dysfunction (GLS reduction >10%) after RT.

Univariate analysis		
	OR (95% CI)	
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
V20 (%)	1.20 (1.01 – 1.43)	0.04
Left Ventricle		
Dmean (Gy)	1.14 (1.01 – 1.28)	0.03
V20 (%)	1.08 (1.01 – 1.14)	0.02

* Adjusted for BMI, hypercholesterolemia, hormonotherapy

Increase of 1 Gy in mean heart dose
-> 37% increased risk of GLS red > 10%

Increase of 1 Gy in mean LV dose
-> 14% increased risk of GLS red > 10%





- **Subclinical LV dysfunction defined as a GLS decrease >10%** is associated with cardiac doses: dose-response relationship
- Non-radiation factors such as **hormonal treatment** : mandatory to evaluate the impact of radiation independently of other risk factors
- **Dosimetry of the LV (V20)** : may be promising to identify high risk subpopulations

Walker et al. Radiation Oncology 2019, 14 (1), 204.

- **Perspectives:**
 - Multilayer and territorial analysis according to coronary arteries
 - Evolution of GLS 24 months after RT



THANK YOU FOR YOUR ATTENTION