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Faire avancer la sûreté nucléaire

Use of myocardial strain imaging by echocardiography for the early detection of radiotherapy-induced cardiotoxicity in breast cancer patients (BACCARAT Study)

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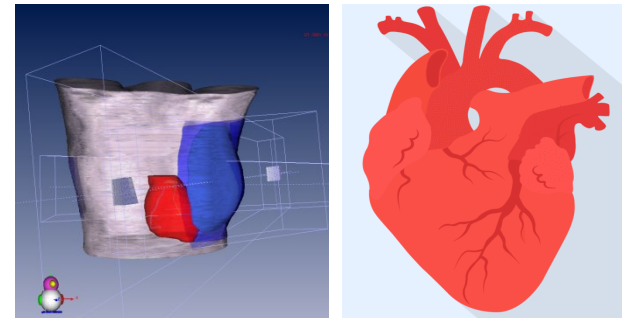
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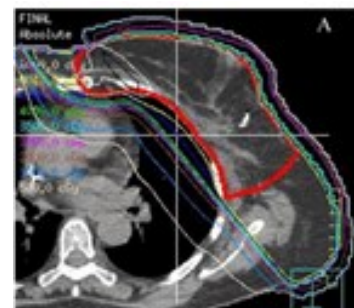
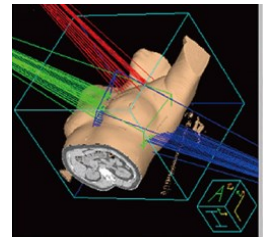


Conflicts of Interest:

None declared

Introduction

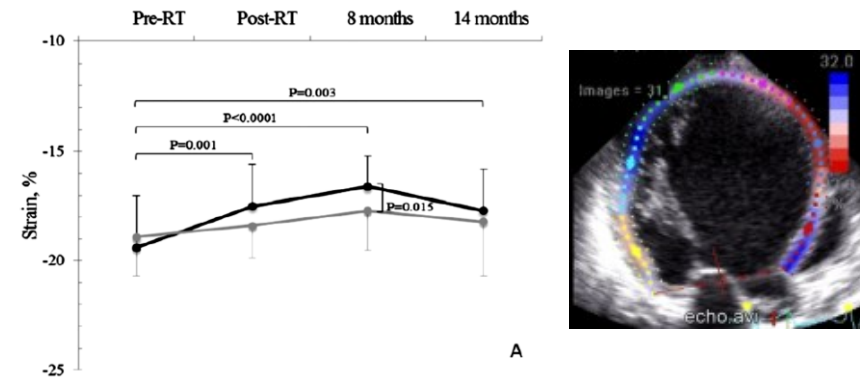
- ◆ **Breast cancer**: the most common cancer in women, with 50 000 new cases each year in France
 - ◆ Standard treatment for breast cancer is
 - **Surgery**: either breast-conserving surgery or mastectomy
 - Followed by **adjuvant therapies** : breast radiotherapy, chemotherapy, hormonal therapy, immunotherapy
 - ◆ Improved prognosis of breast cancer patients over the last decades : **5-year survival around 90%**, due partly to earlier diagnosis and greater use of adjuvant therapies
- ◆ Radiotherapy (RT) can lead to secondary effects due to the presence of neighboring **normal tissues within the irradiation** field, **heart** in particular
- ◆ **Breast cancer RT** irradiation of the heart has been shown to be associated with **long-term cardiac complications** such as heart failure, coronary artery disease, myocardial infarction, but also valvular heart diseases, and finally cardiovascular death **more than 10 years after RT** (*Darby et al., NEJM, 2013*).



Long before the onset of clinically significant late cardiac complications

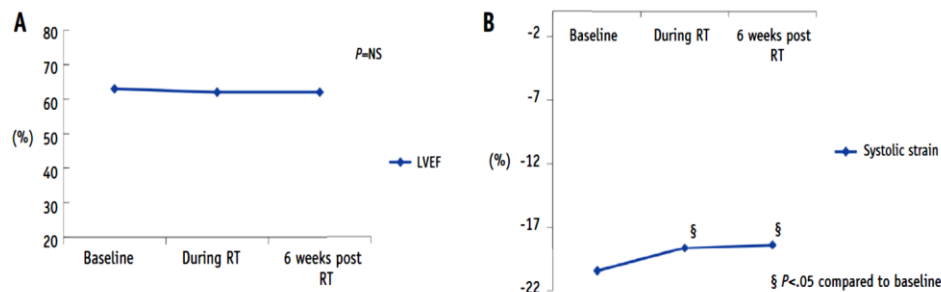
◆ Echocardiographic strain imaging for the detection of **subclinical myocardial dysfunction** (Left ventricular) arising **less than 2 years after breast cancer RT**.

- Erven et al, *Int J Radiation Oncol Biol Phys*, 2012: 51 left sided, 24 right sided patients (most of them with chemo)



- Lo et al, *Int J Radiation Oncol Biol Phys*, 2015 : 40 patients, without chemo, 6 weeks of follow-up

➤ No significant changes in LVEF but **significant increase in Global Longitudinal Strain**



◆ No information on heart dose...

- No association with heart dose: missing element for causality

A new study for early detection and prediction of cardiac changes after BC RT

◆ Objectives of the BACCARAT study

Based on a **2-year prospective cohort of patients** treated with RT for breast cancer, the BACCARAT study aims to :

- Quantify early **subclinical cardiac dysfunction and modifications** induced by breast cancer RT based **functional (ECHO) and anatomical (CCTA) repeated cardiac imaging**
- Investigate potential **biological mechanisms** involved in cardiac toxicity, based on repeated assessment of multiple **circulating biomarkers**
- Provide **accurate heart dosimetry** based on cardiac imaging (CCTA and RT CT scan)
- Provide materials (clinical, dosimetry, biology) for precise **modélisation** and to **predict cardiac toxicity**

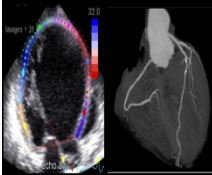
Fundings: Fédération Française de Cardiologie, Electricité de France, European MEDIRAD project (Euratom , grant agreement No 755523)

STUDY DESIGN

Cohort



Before RT (Baseline):

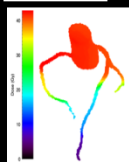


Cardiologic examination

- Echocardiography
- CCTA



Blood samples for biomarkers measures



Individual heart substructure dosimetry

At the end of RT:

Blood samples for biomarkers measures

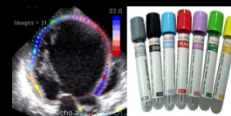


6 months after RT:

Cardiologic examination

- Echocardiography

Blood sample for biomarkers measures

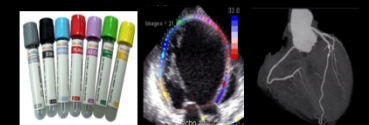


24 months after RT:

Cardiologic examination

- Echocardiography
- CCTA

Blood sample for biomarkers measures



Jacob S, Pathak A, Franck D, Latorzeff I, Jimenez G, Fondard O, Lapeyre M, Colombier D, Bruguiere E, Lairez O, Fontenel B, Milliat F, Tamarat R, Broggio D, Derreumaux S, Ducassou M, Ferrières J, Laurier D, Benderitter M, Bernier MO. [Early detection and prediction of cardiotoxicity after radiation therapy for breast cancer: the BACCARAT prospective cohort study](#). Radiat Oncol. 2016 Apr 7;11:54.

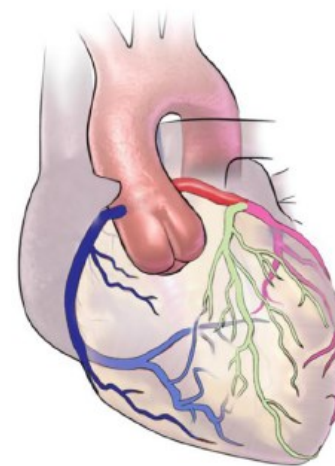
Material and Methods

◆ 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 cardiac disease
- ◆ Echocardiography 2D speckle tracking (**Siemens**) performed before RT and 6 months after RT
- ◆ LVEF > 45%

◆ Cardiac dosimetry (doses in Gy):

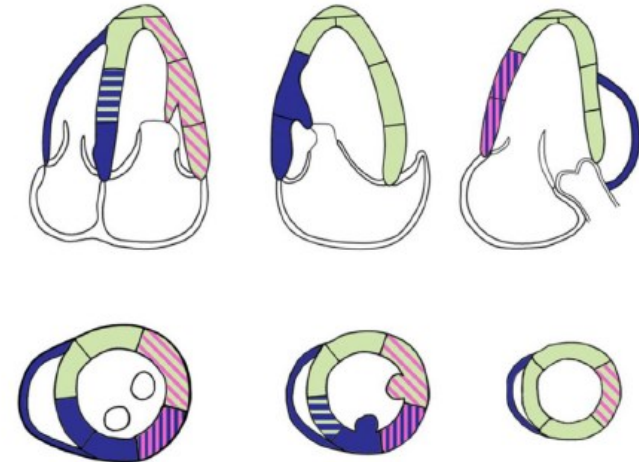
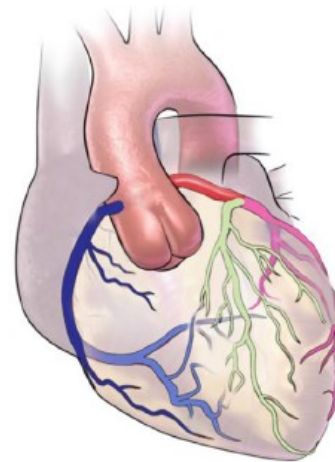
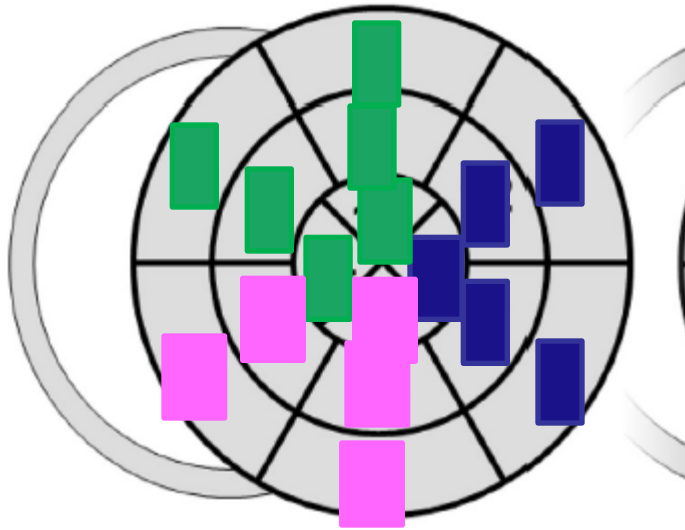
- ◆ Whole heart,
- ◆ Left ventricle (LV),
- ◆ Left anterior coronary artery (LAD),
- ◆ left circumflex coronary (LCX),
- ◆ right coronary artery (RCA)



◆ Global longitudinal strain (GLS) and strain rates based on segmental values

- ◆ Sub analysis by distribution of coronary arteries area

Schematic diagram of the different LV segmentation models: 16-segment model



■ RCA
■ LAD
■ CX
■ RCA or CX
■ LAD or CX
■ RCA or LAD

Roberto M. Lang, J Am Soc Echocardiogr 2015;28:1-39

all models

- | | |
|------------------------|-----------------------|
| 1. basal anterior | 7. mid anterior |
| 2. basal anteroseptal | 8. mid anteroseptal |
| 3. basal inferoseptal | 9. mid inferoseptal |
| 4. basal inferior | 10. mid inferior |
| 5. basal inferolateral | 11. mid inferolateral |
| 6. basal anterolateral | 12. mid anterolateral |

16 segment model

- 13. apical anterior
- 14. apical septal
- 15. apical inferior
- 16. apical lateral

GLS= mean of 16 segments

GLS_LAD= mean (s1, 2, 7, 8, 13, 14)

GLS_LCX=mean (s3, 3, 9, 10, 15)

GLS_RCA=mean (s5, 6, 11, 12, 16)

Results

◆ Baseline characteristics

| | All patients N=94 | Right-sided BC RT N=18 | Left-sided BC RT N=76 | p-val |
|----------------------------------|----------------------|---------------------------|--------------------------|----------|
| Age (y) | 58 ± 8 | 59 ± 7 | 58 ± 8 | 0.64 |
| BMI (kg/m ²) | 24.5 ± 4.1 | 24.4 ± 4.7 | 24.6 ± 4.0 | 0.66 |
| Systolic blood pressure (mm Hg) | 120 ± 15 | 124 ± 21 | 120 ± 14 | 0.21 |
| Diastolic blood pressure (mm Hg) | 75 ± 10 | 73 ± 14 | 76 ± 10 | 0.44 |
| Smoking | | | | 0.95 |
| | Current | 19 (20%) | 4 (22%) | |
| | Previous | 25 (27%) | 5 (28%) | 20 (26%) |
| Hypertension | 23 (25%) | 6 (33%) | 17 (22%) | 0.33 |
| Diabetes | 4 (4%) | 0 | 4 (5%) | - |
| Hypercholesterolemia | 22 (23%) | 4 (22%) | 18 (24%) | 0.89 |
| GFR (mL/min/1,73m ²) | 89 ± 14 | 87 ± 14 | 90 ± 15 | 0.26 |

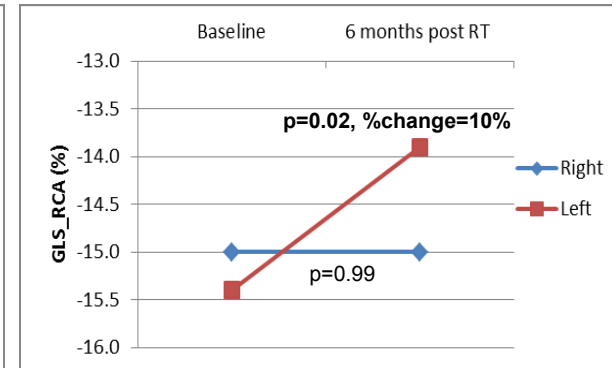
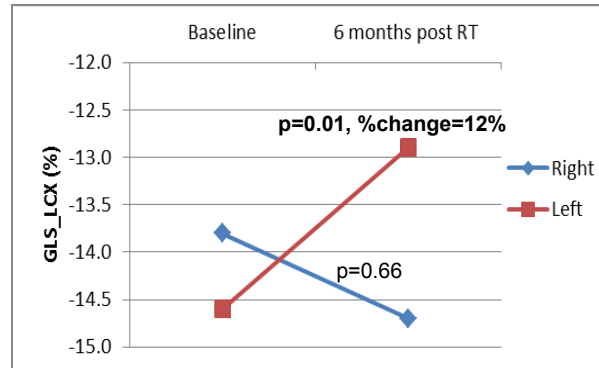
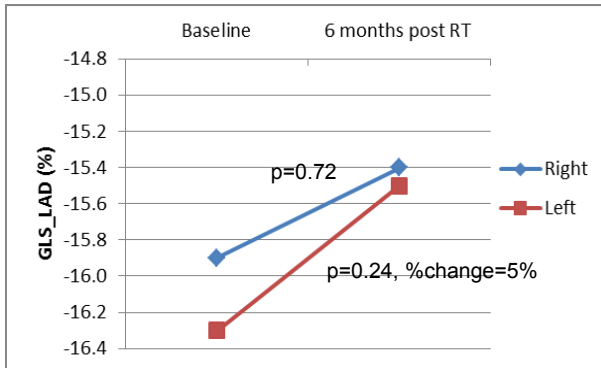
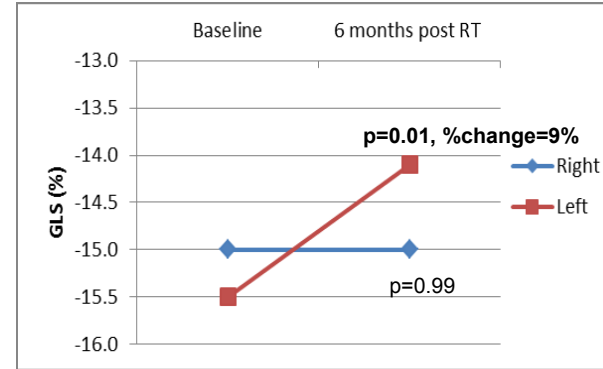
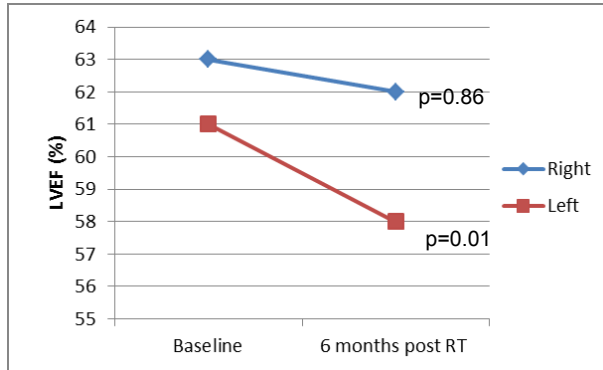
Results

◆ Heart absorbed dose due to RT: whole heart, LV and coronary arteries

| | All patients N=94 | Right-sided BC RT N=18 | Left-sided BC RT N=76 | p-val |
|---------------------------------------|-----------------------|---------------------------|------------------------------|-------|
| Heart dose (Gy) : median (min-max) | 2.34 (0.25 - 6.37) | 0.49 (0.25 - 2.17) | 3.10 (0.87 - 6.37) | <0.05 |
| LV dose (Gy) | 5.31 (0.04 - 19.66) | 0.09 (0.04 - 1.24) | 6.93 (1.16 - 19.66) | <0.05 |
| LAD dose (Gy) | 14.81 (0.01 - 37.61) | 0.11 (0.04 - 2.16) | 17.22 (1.68 - 37.61) | <0.05 |
| LCX dose (Gy) | 1.27 (0.04 - 4.34) | 0.13 (0.04 - 1.77) | 1.44 (0.53 - 4.34) | <0.05 |
| RCA dose (Gy) | 0.27 (0.14 - 4.01) | 1.29 (0.68 - 4.01) | 0.66 (0.14 - 2.50) | <0.05 |

Results

◆ Echographic parameters at baseline and 6 months after RT



No significant results with strain rate

Results

- ◆ Mean % of change in GLS measurements between V0 and V6 according to dose, for left sided BC patients

| | Heart dose | | LV dose | |
|---------|-------------|--------------|---------|--------------|
| | <3 Gy | > 3 Gy | <7 Gy | > 7 Gy |
| GLS | 4.5% | 12.3% | 4.3% | 13.5% |
| GLS_LAD | 0.0% | 8.0% | 2.0% | 7.5% |
| GLS_LCX | 10.1% | 11.8% | 7.4% | 14.6% |
| GLS_RCA | 4.8% | 16.7% | 4.4% | 18.9% |

In **bold** are significant decrease, in **red** are the most importance differences between low exposed and high exposed patients

Conclusion and Perspectives

- ◆ A significant decrease in GLS of 9% between baseline and 6 months after RT was observed only for left sided BC RT
- ◆ LV dose or even more LAD dose are better than heart dose to discriminate patients with low decrease and high decrease in GLS
- ◆ Further analysis should be performed to clarify the impact of cardiac dose in multivariate models

Thank you for your attention !