Cardio-Oncology
An integrative Approach

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Disclosures

- **Bracco Imaging: research grant, honoraria for presentations on Bracco sponsored workshops**
- **Siemens Healthineers: research grant**
- **Philips Imaging: funding for regional rounds**
- **Ultromics: consulting, research grant**
- **Springer publisher, Oxford University press: book royalties**

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Overview

- Need for a cardio-oncology service
- Case studies on management of patients with concordant and discordant findings of EF and GLS
- Need for accurate quantification of EF and GLS (Recommendations of the EACVI/ASE)
- Updated quality criteria for optimal echocardiographic recordings and accurate measurements of EF

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Cancer and Cardiovascular Disease

- High risk of heart failure following treatment with trastuzumab and anthracycline in patients with breast cancer
- Increasing number of cancer survivors who will die from cardiovascular disease
- The younger the patient the higher risk of death due to heart disease
- Pts <55 yrs have a tenfold risk of dying from heart disease compared to the general population Sturgeon K et al. European Heart Journal 2019

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In a study of the University of Ottawa hospital 80% of patients referred to a cardio-oncology clinic could complete the cancer therapy

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Cardio-Oncology Service in Edmonton/Alberta (capital region)

oncology clinic
Dr Mackey and colleagues

cardio-oncology clinic –Tuesday am
E Pituskin PhD NP, I Paterson MD

echo lab – available Monday - Friday
reports same day on EMR
sonographer B Foster (back up: A Durand)
J Choy MD, H Becher MD)

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Key steps and milestones towards a successful cardio-oncology service

access to echocardiography

- echocardiography scanner
- skilled sonographer in GLS imaging
- cover for annual/sick leave

cardiologist (ideally echocardiographer)

- to assess patients in clinic
- to provide timely consultations
- cover for annual/sick leave

oncologist

- to communicate the referral criteria
- to support and educate staff and patients

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Alberta Heart Institute echo protocol

Patients referred before chemotherapy with cardiotoxic drugs

- Comprehensive echocardiogram according ASE recommendations
- 2D Contrast Echocardiography
  for measurement of EF (4CV, 2CV)
- GLS measurement (3 apical views) on non contrast images, if adequate image quality

Objective: to provide reliable advice for oncologists on

- Which patients cannot undo chemotherapy with cardiotoxic drugs
- Which patients need cardiology consultation before chemotherapy
- In which patients chemotherapy has to be paused or stopped

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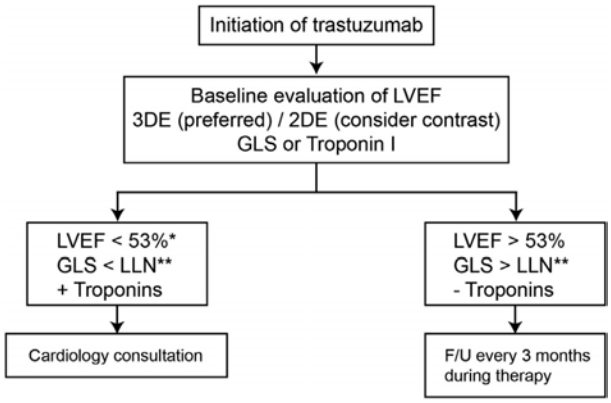
ASE/ EACVI Expert Consensus for Multimodality Imaging Evaluation of Adult Patients during and after Cancer Therapy



* Consider confirmation with CMR.
** LLN = Lower limit of normal. Please refer to Table 5 for normal GLS values based on vendor, gender and age.

Plana JC et al. J Am Soc Echocardiogr 2014;27:911-39

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Quality check

Do you feel comfortable to perform quantitative assessment of EF and GLS

1. **Yes**
2. **Only EF, not GLS**
3. **Only GLS, not EF**
4. **No**

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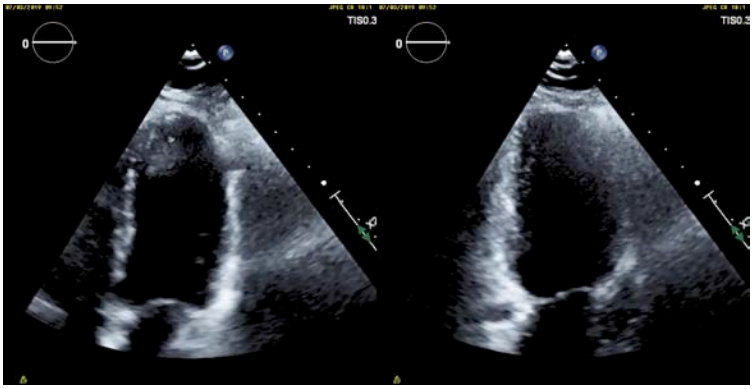

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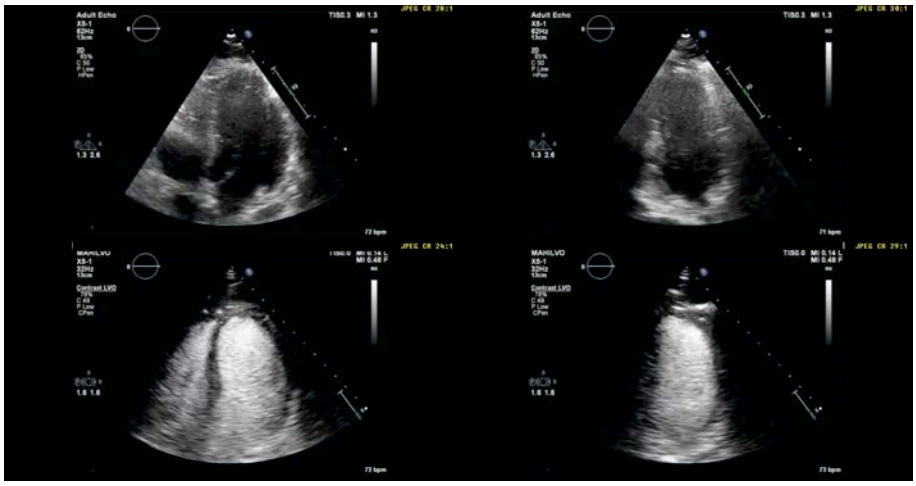

When 2D image quality is not optimal for assessment of EF
it is also not optimal for assessment of GLS

At present we do not report GLS when non contrast image quality is suboptimal

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Echocardiographic measurements of EF in patients undergoing chemotherapy

3D echocardiography	2D contrast echocardiography
Good agreement with MRI	Good agreement with MRI
No geometrical assumptions	Geometrical assumptions adequate for for most cardio-oncology patients
Foreshortening can be avoided	Foreshortening can be avoided
Depends on image quality	**Accurate in patients with poor quality of non-contrast images**
Up to 50% patients need to be excluded	**hardly any patient has to excluded**
	high volume of clinical studies demonstrating the accuracy and reproducibility in clinical practice

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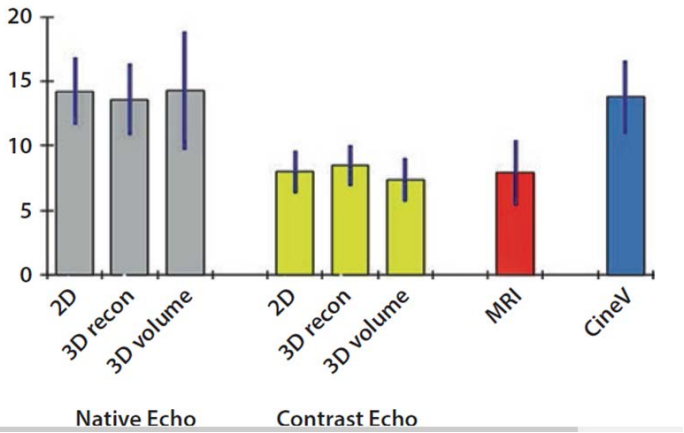
Echocardiographic measurements of EF in patients undergoing chemotherapy



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Hoffmann R et al. JASE 2014

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Diagnostic tools for the detection of cardiotoxicity

- **Nuclear cardiac imaging** – (RNV, MUGA) EF — **8-12 mSv (400 chest Xray or 80 chest CT)**
- **Echocardiography** – Ejection fraction (EF), Global longitudinal strain (GLS)
- **Cardiac MRI** – EF, GLS — **$$$, limited availability**
- **Cardiac biomarkers** – Troponin I or high-sensitivity Troponin I – BNP or NT-proBNP — **poor predictors of LV dysfunction**

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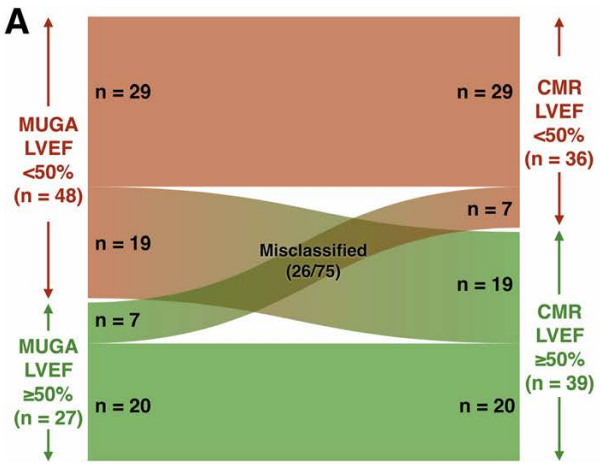
MUGA EF vs MRI EF



MUGA clinical LVEFs are only modestly accurate when compared with CMR reference

Huang et al. Journal of Cardiovascular Magnetic Resonance (2017) 19:34

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Clinical applications of ultrasonic enhancing agents (UEA) in echocardiography: 2018 American Society of Echocardiography Guidelines Update

	COR	LOE
For routine resting echocardiographic studies, UEAs should be used when two or more LV segments cannot be visualized adequately for the assessment of LV function (LVEF and RWM assessment) and/or in settings in which the study indication requires accurate analysis of RWM (COR I, LOE A).	I	A
Ultrasound enhancement should be used in all patients in whom quantitative assessment of LVEF is important to prognosis or management of the clinical condition. VLMI and low-MI harmonic imaging techniques should be used to provide optimal LVO (COR I, LOE B-R).	I	B-R

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Optimize recordings for assessment of EF

- **Very low MI contrast specific imaging**
  - **Recommended by ASE**
- Adequate dosage
  - small dosage!
  - all approved agents suitable
  - slow bolus injection
- Complete LV opacification without artifacts

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Lumason®	Optison®	Definity®
0.5 ml undiluted suspension	0.3 ml undiluted suspension	1 ml diluted suspension (dilute 0.5 ml suspension in 10 ml saline)

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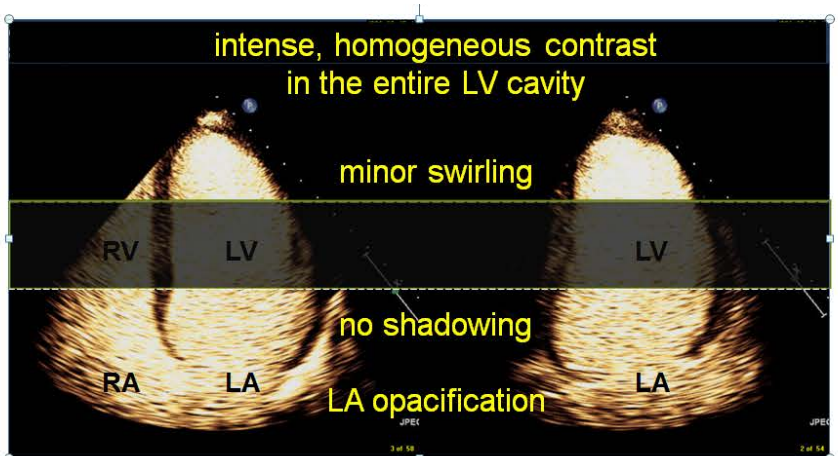
Contrast Echocardiography – Adequate LV opacification



Becher H, Helfen A. Contrast echocardiography – Compendium for Clinical Practice. 2019 Springer

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Optimize scan planes for assessment of EF II

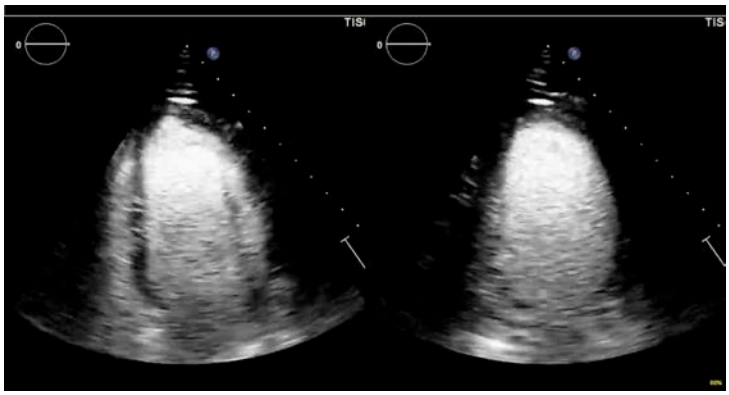
Shape of the apex (systole)

Thickness of the apex

Movement of the apex

Avoid papillary muscles in 2CV

Avoid rib shaddow



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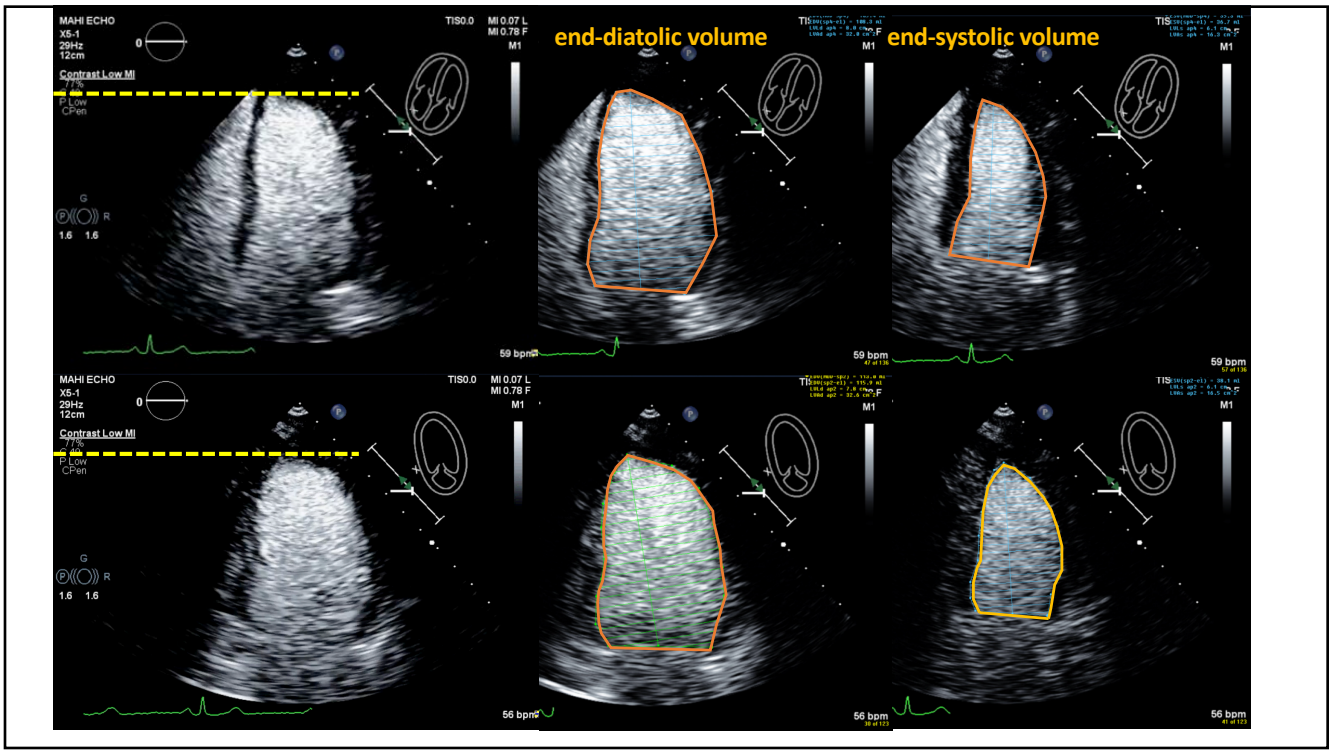

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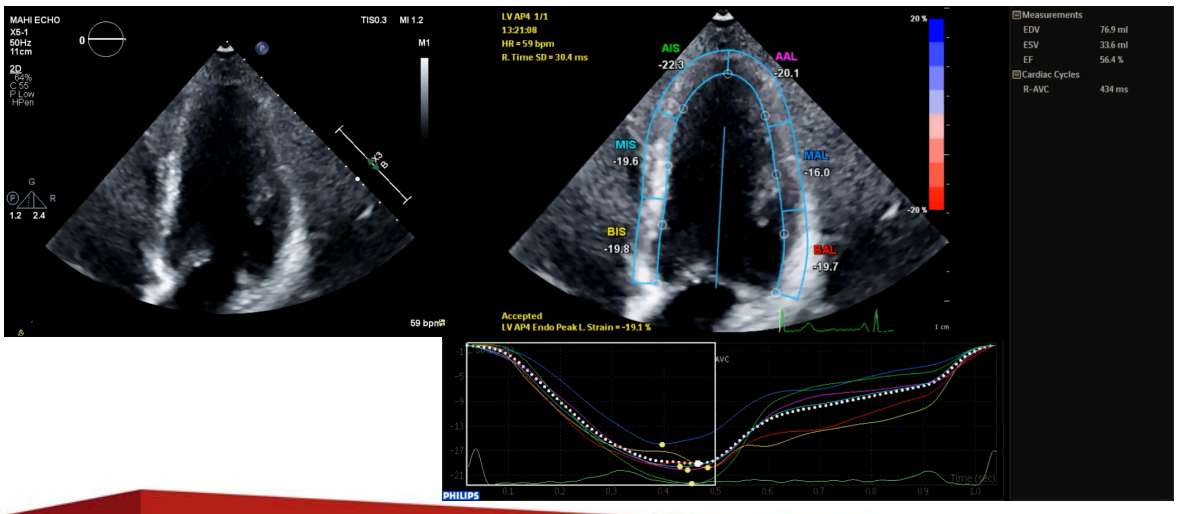
Adjustment of the ROI for GLS measurement

ASE American Society of Echocardiography

- the inner contour should be aligned along the interface between the compact and trabeculated myocardium -



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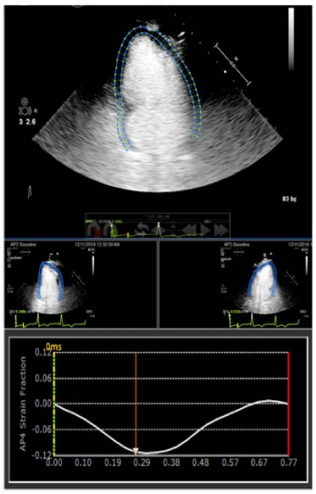
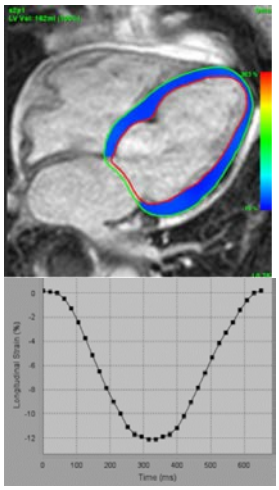
Contrast-enhanced echocardiographic measurement of GLS: accuracy and its relationship with image quality





25 patients

12/25 patients suboptimal 2D echo GLS difficult

IE33 or EPIQ systems,
Philips Healthcare Optison bolus

Off-line GLS measurement
EchoInsight, Epsilon Imaging,

CMRI feature tracking

Karagodin I et al. 2019, International Journal of Cardiovascular Imaging

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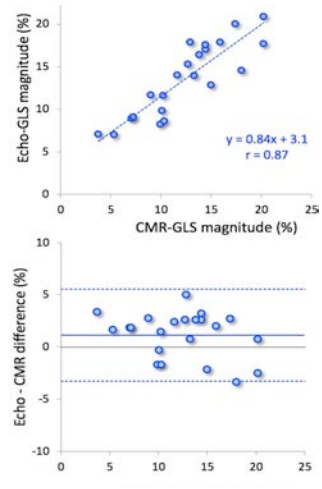

	Randomly selected sub-group of patients (N = 15)		Patients with suboptimal acoustic windows (N = 12)	
	Contrast-enhanced GLS	Non-enhanced GLS	Contrast-enhanced GLS	Non-enhanced GLS
Inter-observer variability (ICC)	0.88	0.82	0.83	0.76
Intra-observer variability (ICC)	0.91	0.88	0.88	0.82

Karagodin I et al. 2019, International Journal of Cardiovascular Imaging

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Contrast-enhanced echocardiographic measurement of GLS: accuracy and its relationship with image quality

Conclusion:

GLS measured from contrast-enhanced TTE was more accurate and reproducible than GLS obtained from non-enhanced images even in those patients with suboptimal acoustic windows.

These results suggest that the routine use Of UEA should be considered when measuring GLS in patients with limited echocardiographic windows, who may otherwise be diagnostically disadvantaged.

Karagodin I et al. 2019, International Journal of Cardiovascular Imaging

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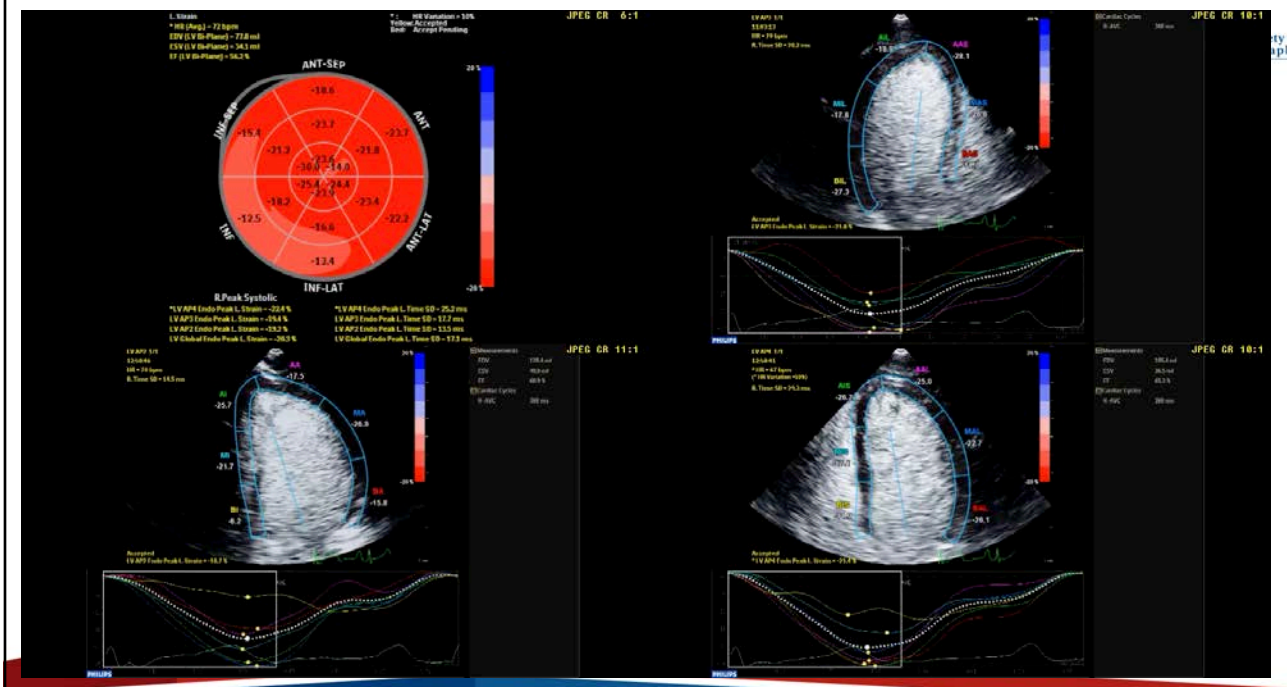

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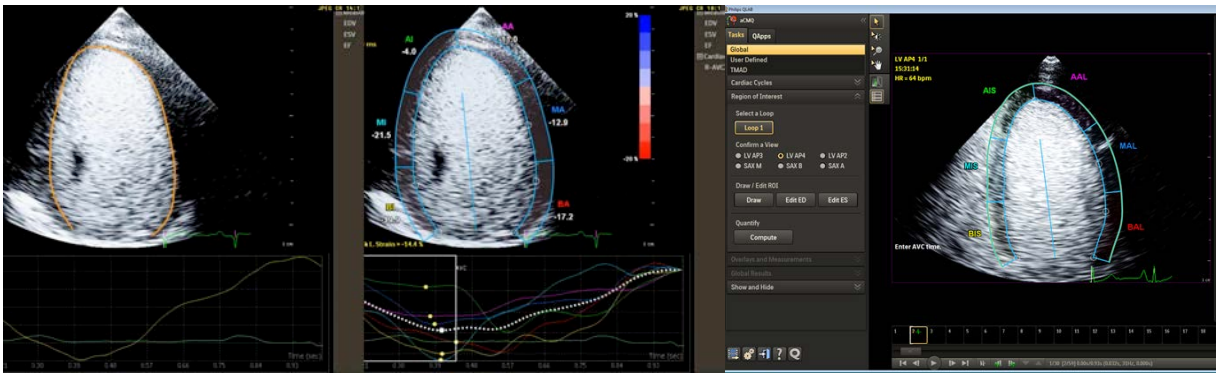
Contrast-enhanced measurement of GLS

using the program available for non contrast recordings



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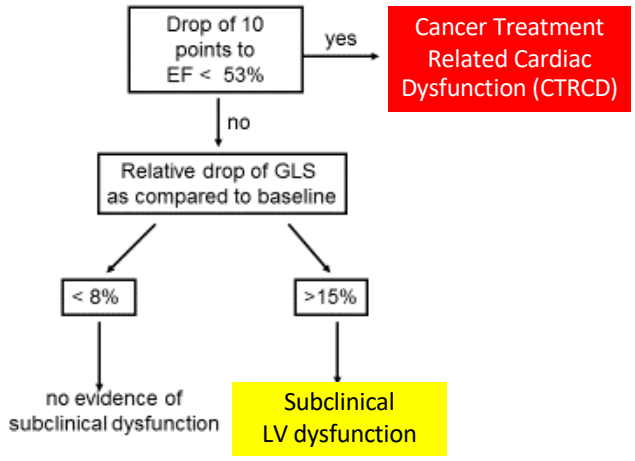
Follow-up Measurements of LV function

every 3 months for 1 year in pts treated with Trastuzumab



Plana JC et al. J Am Soc Echocardiogr 2014;27:911-39

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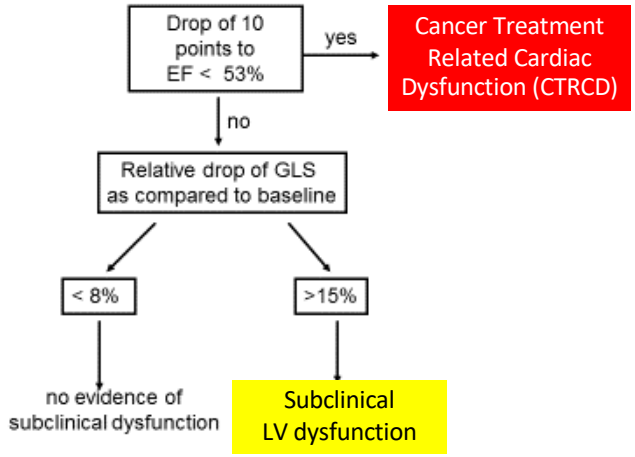

Pause chemotherapy
Reduce dosage
Start on ACE/ARBs + betablocker
Rescan after 3-4 weeks

Plana JC et al. J Am Soc Echocardiogr 2014;27:911-39

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Incidence of left ventricular dysfunction associated with chemotherapy drugs

Chemotherapy agents	Incidence (%)
Anthracyclines (dose dependent)	
Doxorubicin (Adriamycin) 400 mg/m² 550 mg/m² 700 mg/m²	 3–5 7–26 18–48
Idarubicin (>90 mg/m²)	5–18
Epirubicin (>900 mg/m²)	0.9–11.4
Mitoxanthone >120 mg/m²	2.6
Liposomal anthracyclines (>900 mg/m²)	2
Alkylating agents	
Cyclophosphamide	7–28
Ifosfamide <10 g/m² 12.5–16 g/m²	 0.5 17
Antimetabolites	
Clofarabine	27

Trastuzumab 1.7 -20.1%

2016 ESC Position Paper
on cancer treatments
and cardiovascular toxicity

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Follow-up Measurements of LV function
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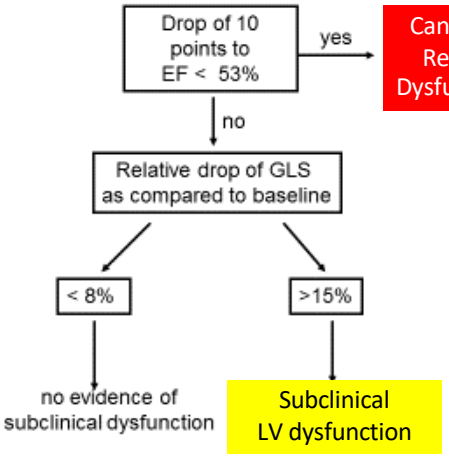

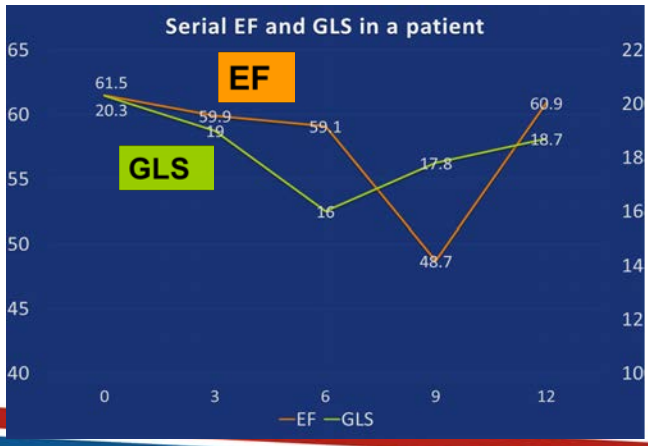

Plana JC et al. J Am Soc Echocardiogr 2014;27:911-39

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How EF and GLS measurements affect management

Echo Measurements	Action
EF decreases >10% but not below 50%	repeat EF measurement shortly after and during the duration of cancer treatment
EF decreases <10%, remains >50% GLS decreases > 15%	**No change in chemotherapy!** **?preventive medical treatment**
EF decreases >10% to EF <50% with heart failure	**ACE inhibitors (or ARBs)+beta-blockers**

2016 ESC Position paper on cancer treatments and cardiovascular toxicity

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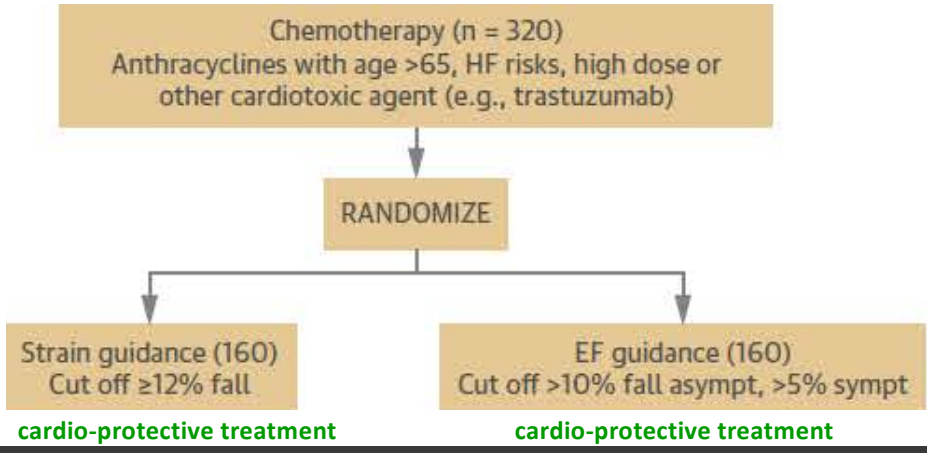
Rationale and Design of the Strain Surveillance of Chemotherapy for Improving Cardiovascular Outcomes
The SUCCOUR Trial



3 year follow-up endpoint: change in EF

Negishi T et al. JACC cardiovascular Imaging 2018

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Conclusions

1. **State-of the art oncology needs a cardio-oncology service**
2. **A crucial component is timely access to echocardiographic imaging**
3. **Ideally the cardiologist reading the echocardiograms is also providing consultations**
4. **Management of the patients is still mainly dependent on an accurate measurement of EF**
5. **Communication: eg whom to refer for echo or cardiology consult, educate staff and patients**

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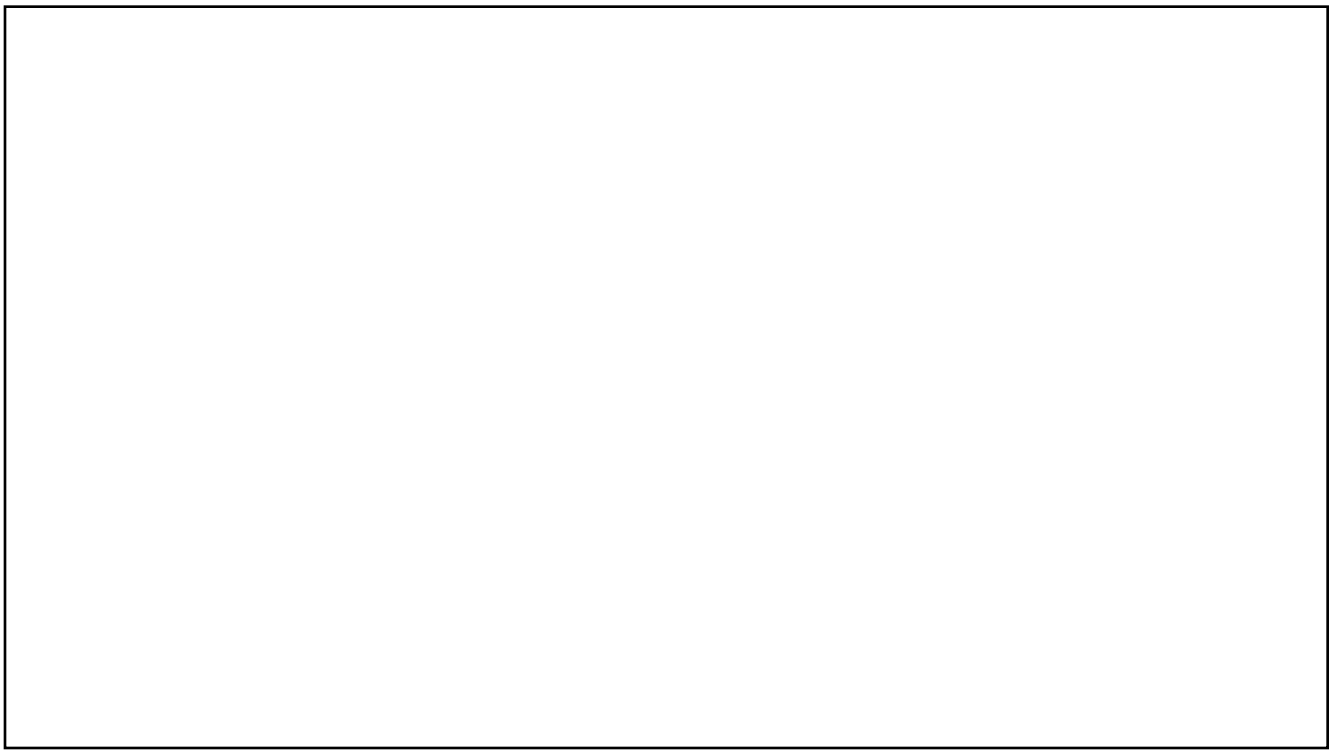

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