PHILIPS

Ultrasound

Case study

Using advanced ultrasound tools to assess CTRCD

(cancer therapy-related cardiac dysfunction)

Teresa López-Fernández, MD
Cardiac Imaging Laboratory, Cardio-oncology unit, Hospital La Paz Institute for Health Research, Madrid, Spain

Overview

In recent decades, cancer survival rates have markedly improved as a result of advances in screening, early diagnosis and anticancer treatments.[1] At the same time, there is a growing awareness of the potentially negative effects of both traditional and novel cancer therapies on the cardiovascular (CV) system.[2,3] For that reason, multidisciplinary cardio-oncology care has been recommended to improve patient outcomes.[4]

Cardiotoxicity includes a wide spectrum of manifestations; currently the most prevalent is cancer therapy-related cardiac dysfunction (CTRCD).[3] This case study presents a practical approach to advanced ultrasound imaging for the prevention and monitoring of CTRCD.[5-7]

Surveillance and diagnosis of CTRCD

CTRCD is a continuous phenomenon starting with myocardial cell injury and followed by progressive left ventricular (LV) dysfunction that, if disregarded and left untreated, progressively leads to overt heart failure.[2,3] The surveillance and diagnosis of CTRCD is generally performed by echo-derived left ventricular ejection fraction (LVEF). The most common definition of CTRCD is a symptomatic or asymptomatic decrease of LVEF >10% to an LVEF below the normal value.[2,3]

Identifying true changes in ventricular function

Cardiac surveillance based exclusively on two-dimensional echocardiography (2DE) LVEF has a low sensitivity for the detection of small changes in myocardial function.[2,3] Because the development of CTRCD is associated with therapeutic decisions and poor clinical outcomes, serial evaluation of myocardial damage must be reliable enough to overcome the limitations of 2D LVEF and identify true changes in ventricular function.

A new approach based on the identification of the early injury markers that are predictive of CTRCD has been proposed to minimize cardiotoxicity and potential interruption to cancer treatment. Technologies such as three-dimensional echocardiography (3DE) and two-dimensional speckle tracking echocardiography (2DST) have enhanced the noninvasive assessment of myocardial function beyond conventional 2DE images. These technologies provide accurate and reproducible diagnostic and prognostic information throughout cancer treatment.[5-7] The use of Philips Anatomical Intelligence Ultrasound (AIUS) tools such as Philips Dynamic HeartModel[A.I.]* and TOMTEC AutoStrain simplifies the integration of advanced echocardiography in daily practice by shortening scanning and quantification times as well as the learning curve, to perform these assessments.[8,9]

*A.I. refers to Anatomical Intelligence.

Dynamic HeartModel[A.I.] and AutoStrain acquisition and analysis

Dynamic HeartModel[A.I.] detects the heart in a 3D volume data set, identifies global shape and heart orientation, and automatically displays LV and left atrial (LA) volumes, as well as LVEF without geometric assumptions and with a strong agreement with cardiac magnetic resonance imaging.[10,11]

AutoStrain LV is a robust and sensitive marker to detect preclinical myocardial damage, without additional time-consuming steps for image acquisition and with minimal time and steps for analysis.[5-7] **Figure 1** summarizes practical advice for Dynamic HeartModel[A.I.] and AutoStrain acquisition and analysis.

Figure 1 Practical advice for working with Philips AIUS tools Dynamic HeartModel[A.I.] and AutoStrain.

Dynamic HeartModel[A.I.]

Image optimization for acquisition

- Optimize ECG tracking
- Improve 2D image quality
- Adjust 3D sector width and depth to acquire an entire AP4 view

Detection of software analysis landmarks

- Segmentation of cardiac cycle
- Ensure appropriate apex and mitral annulus location
- Evaluate tracing quality of endocardial border

AutoStrain

Image optimization for acquisition

- Optimize ECG tracking
- Improve 2D image quality
- Frame rate > 50 Hz
- Acquire up to three LV-focused views (AP4, AP2 and AP3)

Detection of software analysis landmarks

- Segmentation of cardiac cycle
- Evaluate automatic tracing
- ROI adjustment:
  - Appropriate apex and mitral annulus location
  - Avoid inclusion of papillary muscles, left ventricular outflow tract and pericardium

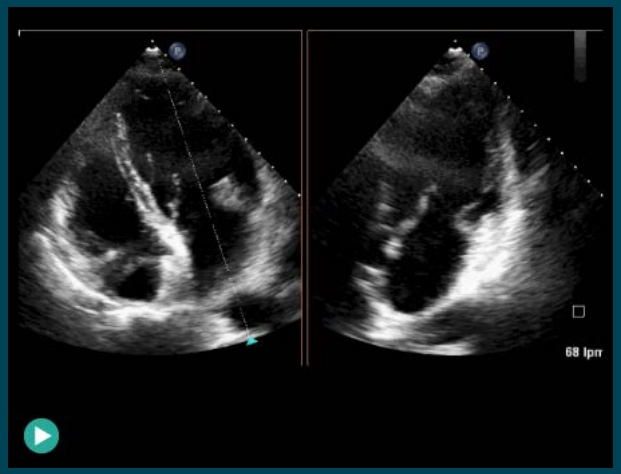
Dynamic HeartModel[A.I.] and AutoStrain in daily clinical practice

Case study

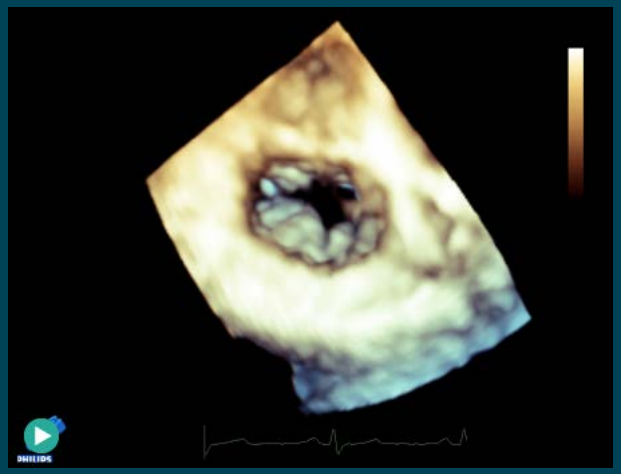
A 53-year-old woman was referred to our cardio-oncology clinic due to a recent diagnosis of invasive breast ductal carcinoma (T1cN0Mx RH+ and HER2+). An adjuvant treatment with anthracyclines, cyclophosphamide and paclitaxel, followed by trastuzumab, was planned.

The patient was asymptomatic, and in NYHA I class of heart failure. Looking over her previous medical records, we realized she had a diagnosis of untreated dislipidemia. Routine physicals showed normal vital signs and a mid-frequency holosystolic murmur suggestive of mitral regurgitation. Standard lab tests were unrevealing except for LDL cholesterol of 154 mg/dl. Her ECG showed sinus rhythm, with signs of left atrial dilation.

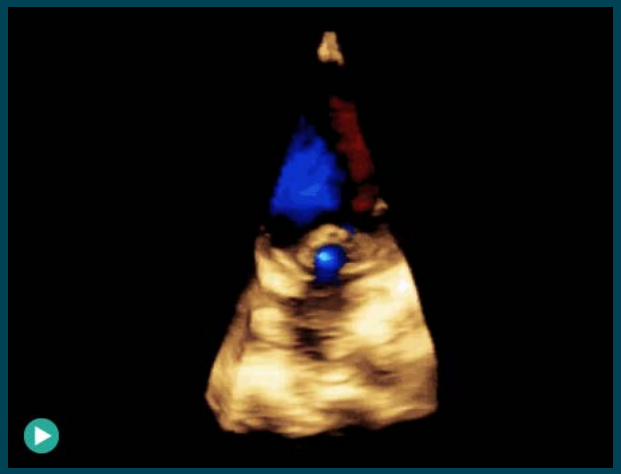
Baseline echocardiography revealed an unknown posterior mitral valve prolapse with severe mitral regurgitation and transthoracic 3D evaluation confirmed a P1P2 prolapse **(Videos 1-3)**.



Video 1 X-plane LV apical view showing posterior mitral valve prolapse, non-dilated LV, with preserved LVEF and moderate LA dilation.



Video 2 Transthoracic 3D evaluation of mitral valve from the atrial perspective, showing a P1P2 prolapse.



Video 3 Transthoracic 3D color Doppler evaluation of the excentric mitral regurgitation.

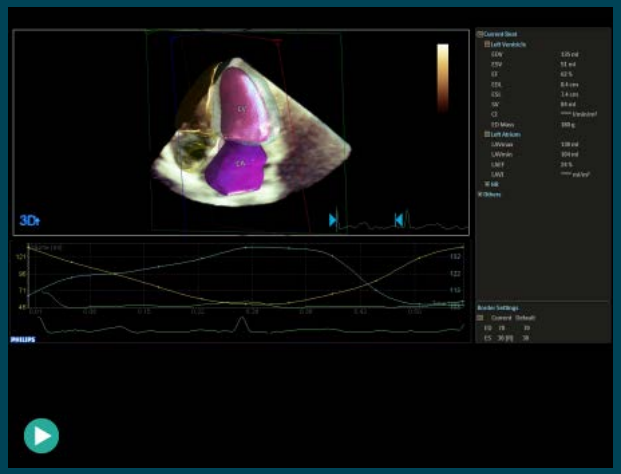
The importance of personalized baseline risk stratification

Left-ventricular volumes (LVV) and a 3D-LVEF were within the normal range, as well as automatic GLS measurements (end-diastolic LVV 71 ml/m^2; end-systolic LVV 27 ml/m^2, 3D-LVEF 62%, GLS -21%) **(Videos 4-5)**.

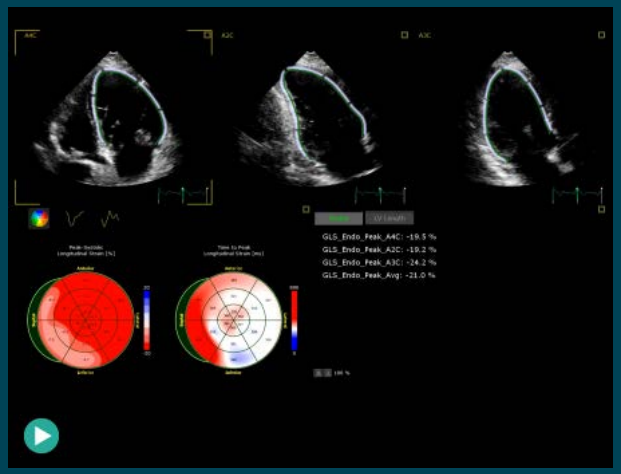
The left atrium was severely enlarged (3D indexed left atrial volume 72 ml/m^2). Right ventricular function was normal (free wall longitudinal strain -20.1%; S′ 11.2 cm/s; TAPSE 17 mm) and so was the estimated pulmonary artery pressure (PAP 36 mmHg).

Baseline CTRCD risk stratification is critical to personalize therapy for both cancer and the CV system. We know that cancer therapy increases the vulnerability of the CV system, particularly in patients with preexisting CV conditions such as significant valvular heart disease.[12] From an imaging point of view, baseline advanced echocardiography improves CTRCD risk stratification. Dynamic HeartModel[A.I.] provides lower temporal variability than 2DE for the longitudinal follow-up of patients undergoing chemotherapy and increases the ability to detect smaller changes in LVEF over 2DE.[13] The assessment of myocardial deformation further improves heart failure risk stratification. In fact, a baseline-reduced GLS was found to be associated with a six-fold increase in adverse CV events.[14]

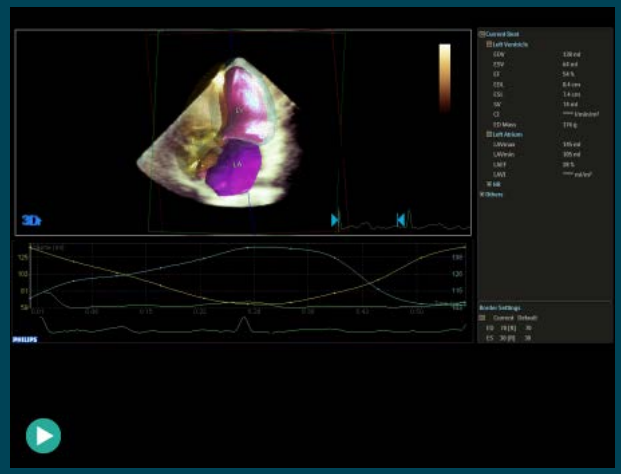
An active surveillance strategy was adopted and the patient started statin treatment. At a three-month follow-up, while the patient was free of cardiac symptoms, echocardiography showed a marked decline in GLS from -21% to -17.7%. 3D-LVEF was preserved, but lower than the basal measurement (3D-EF 54% with indexed end-systolic LVV of 33 ml/m^2) **(Videos 6-7)**.



Video 4 Quantification of 3D-LVEF and volumes using Dynamic HeartModel[A.I.] quantification.



Video 5 Baseline GLS quantification using AutoStrain.



Video 6 Three-month follow-up 3D-LVEF and volumes.

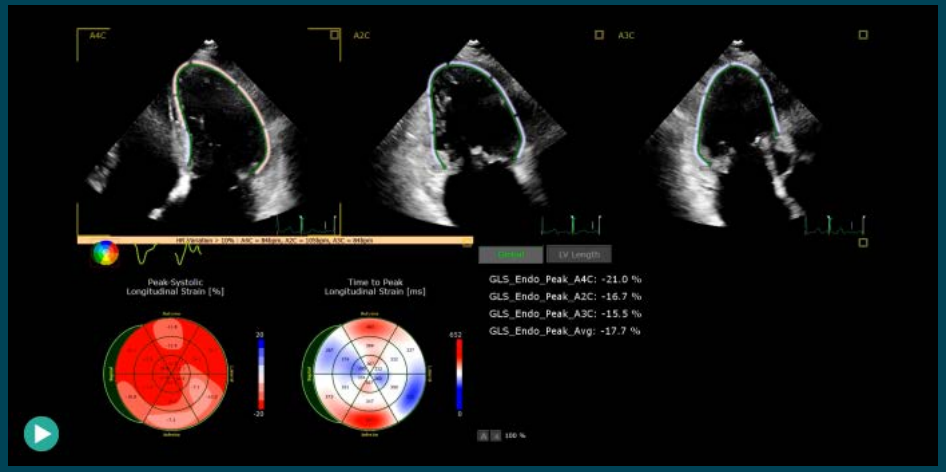
GLS monitoring to detect early myocardial damage

In patients at risk for CTRCD, GLS monitoring can be used to identify patients with early myocardial damage who may benefit from cardio-protective therapy to reduce chemotherapy interruptions. Several studies have demonstrated that the ideal strategy is to compare the GLS measurements obtained during chemotherapy with initial measurements obtained at baseline, allowing patients to serve as their own controls.

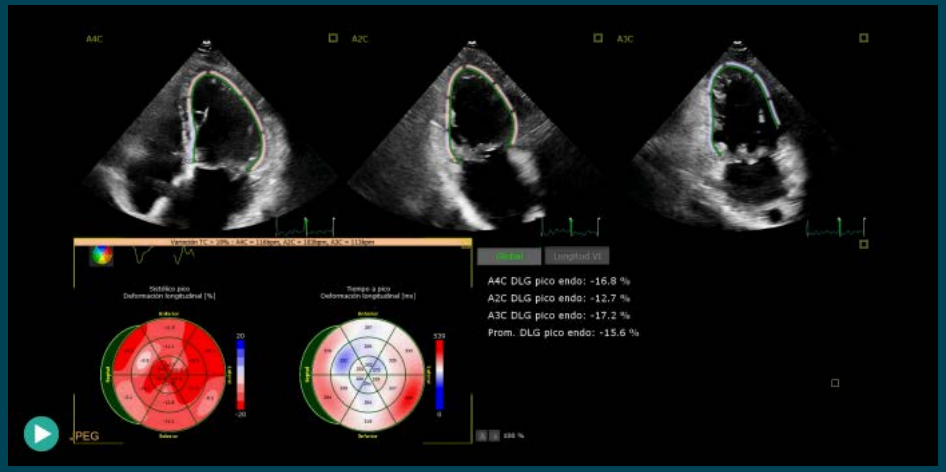
A relative drop in GLS >15% identifies asymptomatic structural heart disease (stage B heart failure) and favors the use of cardio-protective treatments to prevent adverse left ventricular remodeling.[2,3,15] Angiotensin-converting enzyme (ACE) inhibitors and beta-blockers were started, with good tolerance.

Over the following months, the patient was able to complete her cancer treatment and remains asymptomatic. Subsequent studies confirmed stable 3D-LVEF and GLS values **(Figure 2)**.

One year after cancer therapy, the patient was admitted to our hospital because of progressive dyspnea and palpitations over the preceding two weeks. On admission, ECG revealed uncontrolled atrial fibrillation. After the initial stabilization, transthoracic (TTE) and transesophageal echocardiography (TEE) were performed. TTE showed mild LV dysfunction **(Video 8, Figure 2)**, and TEE confirmed diagnosis of severe mitral regurgitation secondary to prolapse of the posterior mitral valve **(Video 9)**.



Video 7 Three-month follow-up GLS quantification.

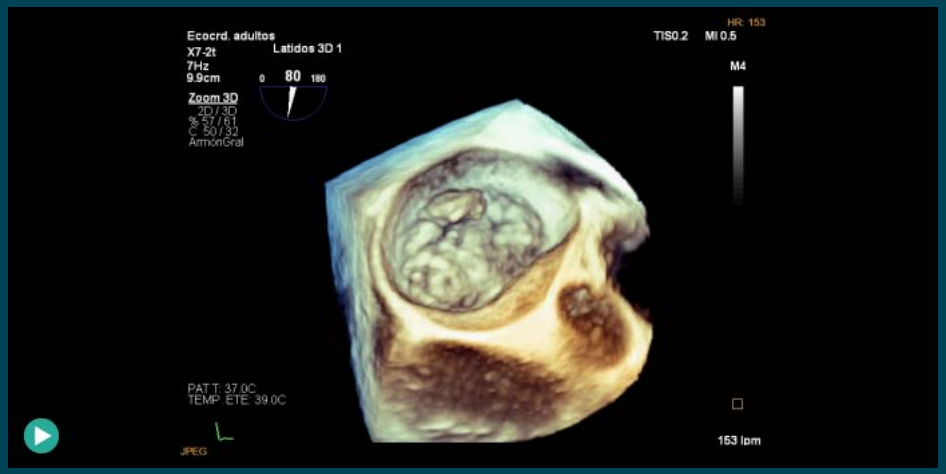


Video 8 Twelve-month follow-up GLS quantification.

Assessment	3D-EDLVV	3D-LVEF	GLS
Baseline	27 ml/m²	62%	-21%
3 months	33 ml/m²	↓54%	↓-17.7%
4 months	30 ml/m²	58%	-17.8%
6 months	29 ml/m²	57%	-17.7%
9 months	32 ml/m²	51%	-16.9%
12 months	38 ml/m²	53%	-15.6%

Figure 2 The evolution of this patient's LV systolic function parameters during cancer treatment monitoring.

Photorealistic 3D view of the mitral valve improves echocardiographic visualization of the anatomical details **(Figure 3)**. No evidence of early recurrence of breast cancer was found, and after reviewing the case with the oncologists and the valvular heart team, the patient was referred for mitral valve repair surgery.



Video 9 3D transesophageal echocardiography. 3D visualization of mitral valve from the atrial perspective.

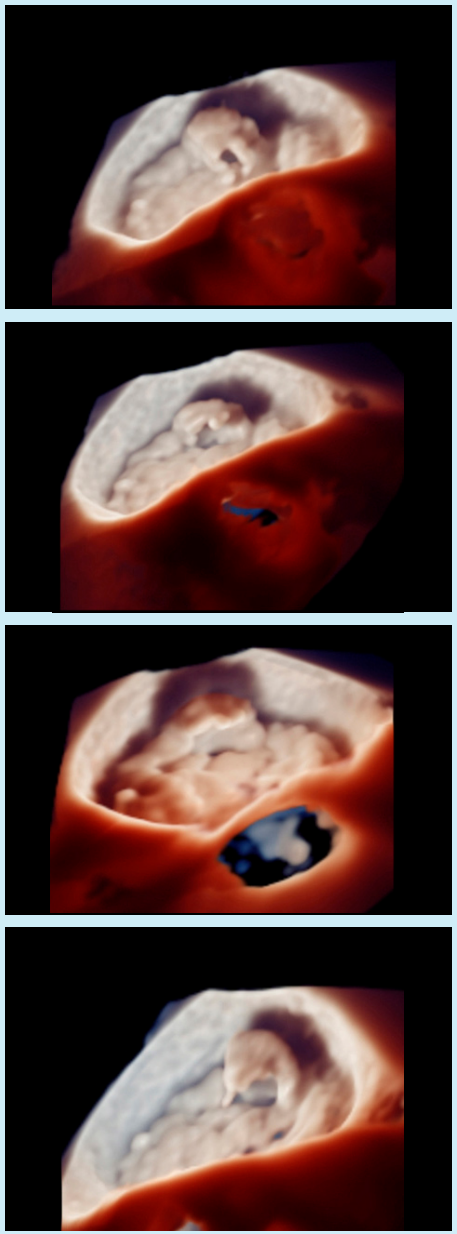


Figure 3 Photorealistic 3D view of the mitral valve from the atrial perspective.

Summary

Currently there is meaningful awareness of the detrimental impact of cardiac toxicity on the outcome of cancer patients. In this scenario, advanced echo imaging is a cornerstone of every cardio-oncology unit in order to facilitate cancer care. Nevertheless, the percentage of centers with an established echo monitoring protocol is far from optimal. One of the main reasons reported for this is that evaluation methods are time-consuming and clinical teams have a lack of experience with new echo techniques. Philips AIUS applied to cardiotoxicity prevention overcomes these limitations and allows for easy, fast and reproducible evaluation of myocardial function.

Clinical relevance

This case illustrates the usefulness of Dynamic HeartModel[A.I.] and AutoStrain to prevent adverse cardiac remodeling in patients with preexisting cardiac conditions who are treated with cardiotoxic drugs. A close collaboration between cancer specialists and cardiologists throughout the cancer treatment process is needed in order to minimize risk of CTRCD. A precise evaluation of myocardial function improves clinical decision-making to optimize CV preventive strategies and minimize cancer treatment interruptions. Long-term follow-up is also critical for the early diagnosis of cardiac events.

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