A Guide to the Use of Left Ventricular Analysis with 3D Echo in Dyssynchrony

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Abstract

Data from single-centre studies suggest that echocardiographic parameters of mechanical dyssynchrony may improve patient selection for cardiac resynchronisation therapy (CRT). To our knowledge, the only published multicentre trial that compared 12 echocardiographic methods, the Predictors of response to cardiac resynchronization therapy (PROSPECT) trial, stated that none of the echocardiographic measurements of ventricular dyssynchrony applied in the study were able to distinguish responders from non-responders. Realtime 3D echocardiography is able to measure left ventricular (LV) size, function and dyssynchrony to identify the presence and extension of scar tissue and to evaluate where the site of latest mechanical activation is. After CRT device implantation, it also allows physicians to detect where the first mechanical activation secondary to LV pacing is located. Indeed, it can be useful in interventricular (VV) delay optimisation of the device after the implantation and, in single-centre studies, it was able to predict response to CRT and to identify responders from non-responders. Care must be taken to optimise temporal resolution, but now volume rates of 70–80vps can be easily obtained in the majority of cases. VV optimisation using realtime 3D echocardiography is feasible and intuitive, but time-consuming compared with traditional methods based on Doppler or algorithms. In this article we illustrate our approach to LV analysis with realtime 3D echocardiography in the study of dyssynchrony.

Keywords

Volume echocardiography, realtime 3D echocardiography, left ventricular (LV) analysis, dyssynchrony, response to cardiac resynchronisation therapy (CRT), interventricular (VV) optimisation

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The presence of electrical dyssynchrony (which following an electrocardiogram can be visualised as a left bundle branch block [LBBB]) is an indication for biventricular pacing if it is associated with systolic dysfunction (ejection fraction [EF] <35%) and dyspnoea in New York Heart Association (NYHA) class II–IV. In the great majority of patients, biventricular pacing determines a significant improvement in ejection fraction and NYHA class, but there is still one-third of patients, named non-responders, who show no benefit after implantation of the device. Ventricular dyssynchrony has been evaluated by echocardiography with a great variety of methods, ranging from m-Mode to strain rate passing by pulsed wave Doppler and tissue Doppler imaging (TDI). All these methods in small and single-centre trials gave good results in predicting the response to cardiac resynchronisation therapy (CRT) and distinguishing responders from non-responders with a high degree of accuracy.[1–9] Nevertheless, in 2005, the first multicentre trial that compared the ability of 12 different echocardiographic methods to predict response to CRT – the Predictors of response to cardiac resynchronization therapy (PROSPECT) trial – stated that none of the echocardiographic measurements of ventricular dyssynchrony applied in the study were able to distinguish responders from non-responders to a degree that could affect clinical decision-making.[10] This lack of usefulness could be due to the fact that echocardiography is able to measure mechanical dyssynchrony that is different from electrical dyssynchrony, or to some limits of the trial itself.[10,11] After the publication of the PROSPECT trial results, many editorials and state-of-the-art papers criticised the usefulness of echocardiography in the evaluation of dyssynchrony. They stated that "echocardiographic parameters have no place in denying potentially life-saving treatment or in exposing patients to unnecessary risks and draining healthcare resources."[12] However, if we continue to use as selection criteria for CRT therapy, the presence LBBB, of EF<35% and of NYHA class II–IV, we will probably continue to have about 35% of non-responders. In the PROSPECT trial, about 16% of patients actually worsened, probably because CRT induced dyssynchrony where it did not exist before.[10] For this reason, other authors have stated that the attempt to identify methods that allow to select the patients who will not benefit from cardiac resynchronisation therapy, or who may clinically worsen, should continue.[13]

3D Echocardiography – Advantages and Limits

Even the authors of the PROSPECT trial stated that, among the echocardiographic methods under investigation, strain measurements, 3D imaging and scar location could be able to predict the response to CRT with more accuracy.[10] There are some points that must be taken into account: according to a review by JJ Bax and J Gorcsan, the likelihood of CRT response is low in the absence of dyssynchrony and in the presence of extensive scarring, scar tissue around the left ventricular (LV) lead and LV lead mismatch (versus site of late mechanical activation). Therefore, the echocardiographic method used to evaluate a patient scheduled for CRT, besides giving a reliable measure of ejection fraction, must be able to measure dyssynchrony, to identify the presence and extension of scar tissue, to evaluate where the site of latest mechanical activation is and, after the implantation of a CRT device, to detect where the first mechanical activation due to LV pacing is located. Realtime 3D echocardiography is able to comply with all of these needs: it can give an exact estimation of systolic function and EF; it provides optimal information on LV dyssynchrony throughout the entire LV and not only between septal and lateral wall; detects the presence of scar tissue and gives an idea of the position of LV lead by evaluation of contraction front mapping (CFM).

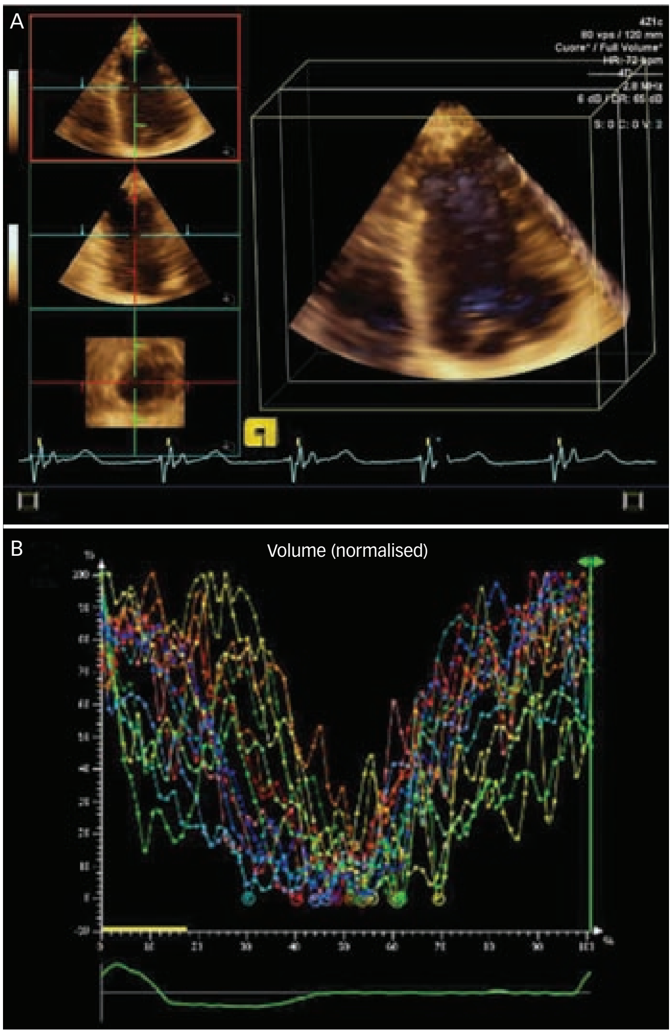
The advantages of realtime 3D echocardiography in this setting are clear and are confirmed also by the American Society of Echocardiography (ASE) Consensus Statement 14 by the assumption that LV dyssynchrony in reality is a 3D phenomenon. Nevertheless, disadvantages are pointed out that primarily include a lower spatial and temporal resolution, with frame rates for 3D wide-sector image acquisition at 20 to 30 frames/second with gated acquisition[15,16] and even lower in some studies with single-beat acquisition. In the study of dyssynchrony, the temporal resolution is critical, and Doppler methods work with frame rates of more than 100fps. Using a frame rate of 20 or 30fps could lead to an unreliable assessment of mechanical activation of the various segments. But even with this limit, Kapetanakis and colleagues[15] and Ajmone Marsan and colleagues[16] showed good results in the study of dyssynchrony with realtime 3D echocardiography.

The first paper about the use of realtime 3D echocardiography in quantification of global LV mechanical dyssynchrony was by Kapetanakis and colleagues. A new index named the Systolic Dyssynchrony Index (SDI) was devised: by calculating the time taken by any segment to reach minimum regional, SDI was defined as the standard deviation of all these intervals; it was expressed as a percentage of the duration of the cardiac cycle rather than in milliseconds in order to allow comparison between patients with different heart rates.[15]

Using SDI, Ajmone Marsan and colleagues[16] were able to predict responders from non-responders performing realtime 3D echocardiography before and 48 hours after CRT device implantation. Receiver operating characteristic (ROC) curve analysis revealed that a cut-off value for SDI of 5.6% yielded a sensitivity of 88% with a specificity of 86% to predict acute echocardiographic response to CRT. Moreover, identifying as responders patients with an acute reduction of >15% of LV end-systolic volume, reflecting acute improvement in LV systolic function, they found that basal SDI in the non-responders group was normal – acute non-responders to CRT did not have mechanical dyssynchrony.

More recently, Lau and colleagues[17] performed realtime 3D echocardiography before implantation of the CRT pacemaker, 24 hours after implantation and six to 12 months after implantation. Using the same cut-off in reduction of LV end-systolic volume to identify responders from non-responders, they found that all responders had baseline SDI values of >10, with a negative predictive value of 100% and in these patients a decrease in the SDI value of more than five at 24 hours identified responders with a positive predictive value of 83%. These papers show that, besides variability of SDI cut-off, realtime 3D echocardiography seems to have good sensitivity and specificity in the prediction of acute response to CRT.

Figure 1: Volumetric Image of the Left Ventricle and Time Volume Curves with a Frame Rate of 80vps

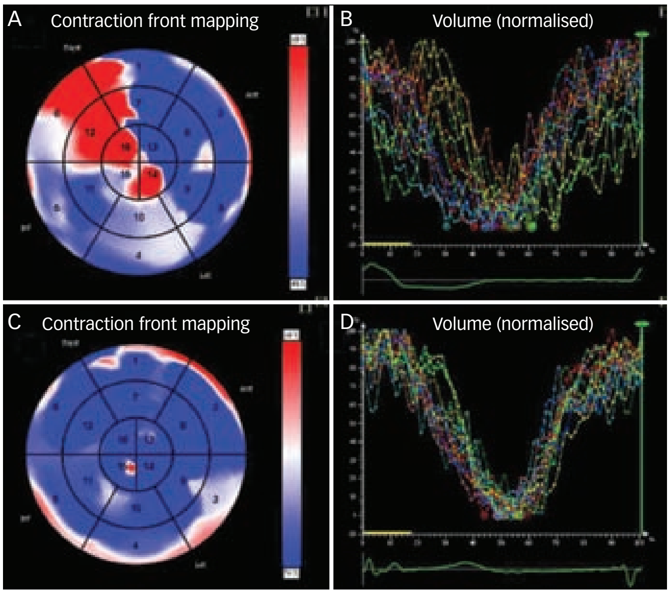


In the upper panel (A) a volumetric image of the LV is shown. Spatial resolution is not good because 'T2' preset and fundamental imaging have been chosen, but the endocardial border in 2D views on the left is well recognisable. With this setting, a reduced width of the window and depth just below the mitral valve a frame rate of 80vps is obtained, thus allowing a nice analysis of dyssynchrony, as curves in panel B show (focus on the multitude of points on a single-beat analysis). LV = left ventricle.

Realtime 3D Echocardiography in the Evaluation of Dyssynchrony – How to Perform the Exam

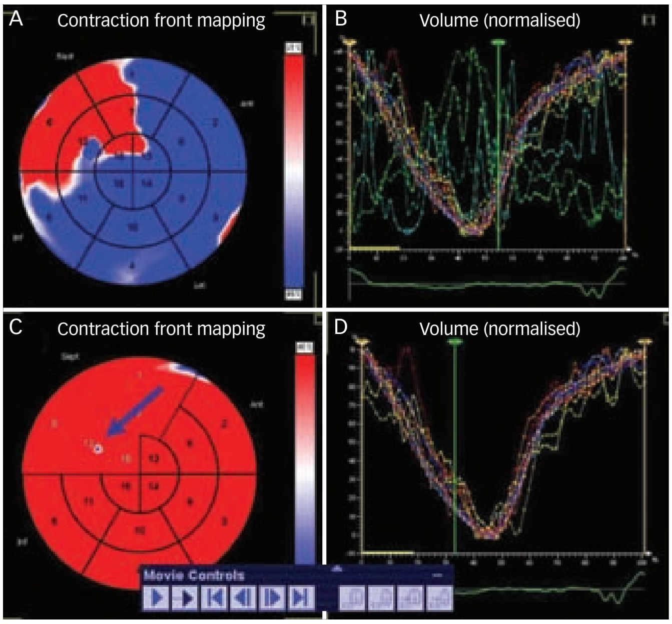
We suggest performing 3D echocardiography after a conventional 2D examination. It is necessary to use 2D echocardiography because spatial and time resolution are superior to realtime 3D echocardiography (RT3DE) in visualisation of dyskinetic areas and thickness of myocardial segments, and therefore in the evaluation of presence and extension of scar tissue.

Figure 2: Contraction Front Mapping and Time Volume Curves Before and After Cardiac Resynchronisation Therapy Device Implantation



A: contraction front mapping (CFM) before cardiac resynchronisation therapy (CRT) device implantation shows a delay in septal wall, which disappears after implantation of the device (C); basal curves in panel B show moderate dyssynchrony that is highly reduced with CRT (D).

Figure 3: An Example of Dyssynchrony Due to Scar Tissue



In panel A, delay is localised in the septal wall, where an extensive scar is present. In panel B, normalised curves show severe dyssynchrony that is due to the scar; in fact, it disappears if scar segments are excluded from the analysis (D). In panel C, the first point that reaches the minimum volume is shown by the blue arrow; this represents the position of left ventricular (LV) lead inside the scar.

When acquiring volume for LV analysis, great care must be taken to optimise time resolution. Some instruments allow you to choose between a good spatial and temporal resolution, for example the Siemens ACUSON SC2000™ ultrasound system allows you to choose between S2 (best spatial resolution), S1, T1 and T2 (best temporal resolution). Our suggestion is to look at 2D four- and two-chamber reconstruction more than the 3D volumetric image. If the endocardial border is clearly visualised in 2D images, LV analysis can even be performed in the presence of a suboptimal 3D image, as clearly shown in *Figure 1*. Time resolution can also be increased by working in fundamental imaging (without harmonic), reducing depth just below the mitral valve (visualisation of the left atrium is not necessary for LV analysis) and reducing the width of the volumetric data set. It must be ensured that all LV cavity is inside the volume; this can be easily provided looking at 2D reference planes extracted from the volume data set. These techniques can lead to a frame rate (or better, volume rate, dealing with a 3D image) of 70–80 volumes per second if the LV is not severely dilated (see *Figure 1*).

It is recommended to optimise brightness and contrast in order to improve the definition of the endocardial border and to check if the system has recognised the end diastolic frame and the end systolic frame properly. If a CRT device has been implanted, the system could recognise the spike as the end diastolic frame and you will have to correct it. The reliability of automated border detection is crucial. If the system does not properly recognise the endocardial border in four-, two- and three-chamber view and you have to correct it extensively, it will be unlikely to perform a nice LV analysis. Unfortunately, if the quality is low you cannot improve it with contrast, as automated border detection does not recognise contrast and is not able to recognise the endocardial border if the cavity is white and the muscle is dark. When LV analysis is complete, the system gives information about LV volumes and function (EF, stroke volume, sphericity index) and dyssynchrony (SDI with a 16-segments model and with a 17-segments model).

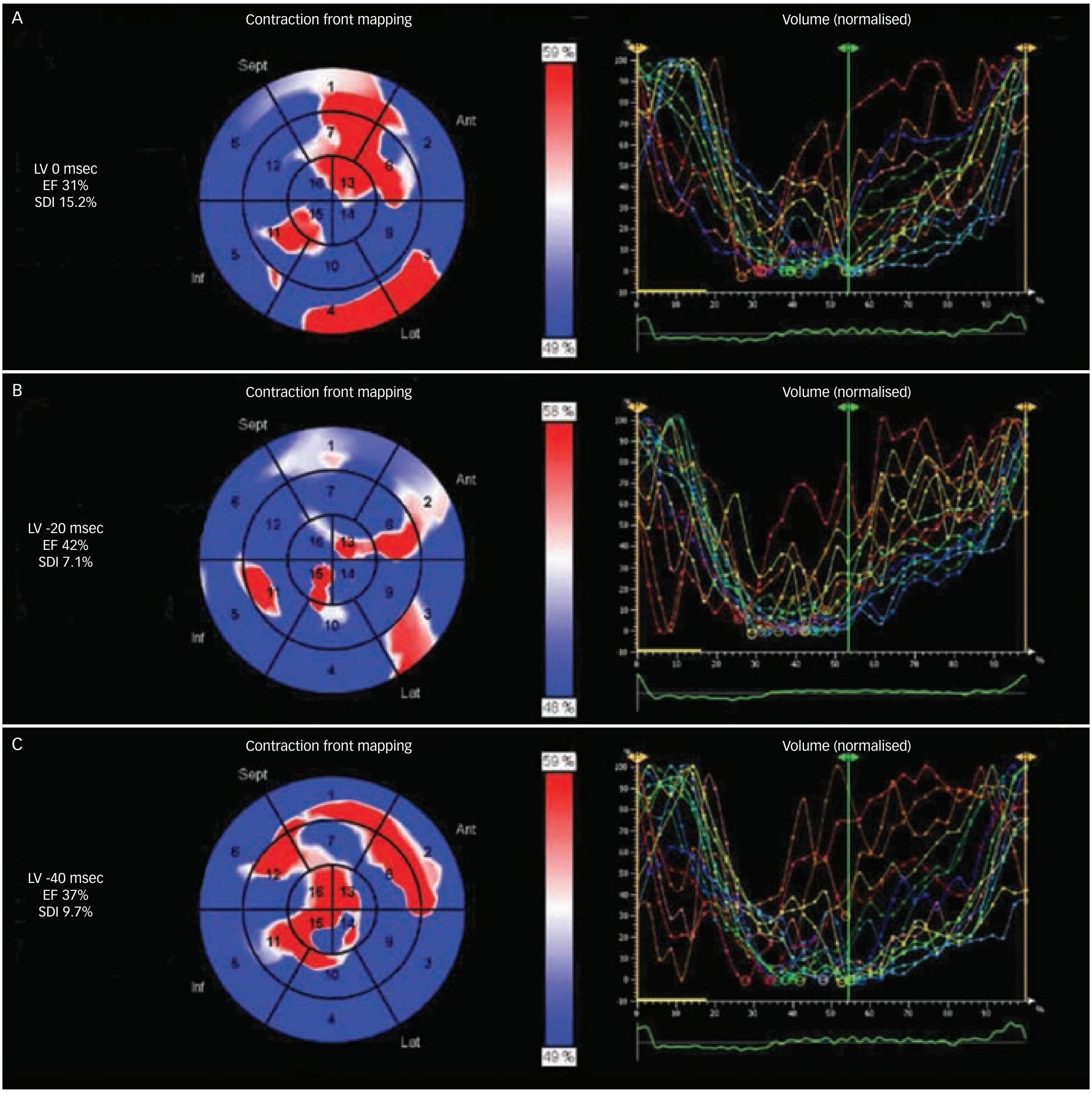
Time volume curves of all segments are visualised with absolute and normalised values. In the first modality you can have information about kinesis of each segment, eventually confirming the presence and the extension of a scar, while the second modality shows when each segment reaches the minimum volume – that gives an idea of dyssynchrony and detects which is the most delayed segment (see *Figure 1*).

Eventually, a bull's eye with contraction front mapping (CFM) can be shown visualising time to minimum volume (see *Figure 2*). This is a very intuitive way to show the contraction wavefront propagation and may suggest the best position to implant LV lead. In fact, the region of latest activation is not always in the posterolateral wall and positioning of the LV lead guided by the latest activated area may help in achieving CRT response, although conditioned by anatomical limitations. If the lead is positioned away from the region of latest activation it is likely that response to CRT would be poorer,[18] especially if the lead is placed in a segment with scar tissue.[11] CFM is a good and easy method also to identify, after implantation of the CRT device, where the first mechanical activation due to LV pacing is located and how the LV pacing modifies the contraction wavefront propagation map (see *Figure 3*).

The Use of Realtime 3D Echocardiography in Pacemaker Optimisation

After CRT device implantation, the pacemaker programming can be optimised in order to achieve the optimal resynchronisation and improve the outcome. Usefulness of optimisation of atrioventricular (AV) and interventricular (VV) delays is debated. Trials that compared various method of optimisation are controversial[19] and at this time routine use of optimisation techniques is not warranted.

Figure 4: Utility of Realtime 3D Echo in Interventricular Optimisation



Utility of realtime 3D echocardiography in interventricular (VV) optimisation. In upper panel (A) analysis with synchronous left ventricular (LV) and right ventricular (RV) leads is performed, showing a persistent delay in the anterolateral and posterolateral wall. By anticipating stimulus of LV lead of 20 milliseconds (B), delay is reduced and dyssynchrony (by Systolic Dyssynchrony Index [SDI]) and systolic function (by ejection fraction [EF]) improve, but still there is a little delay in anterolateral basal segment. Further anticipation of LV lead stimulus (C) leads to disappearance of lateral delay but an apical delay emerges and indexes of systolic function and dyssynchrony worsen.

Dyssynchrony can occur at three levels (AV, inter- and intraventricular), but a meta-analysis on 24 studies by J Bax and J Gorcsan[11] showed that intra-LV dyssynchrony is much more important than AV and VV dyssynchrony in evaluating the response to CRT. In AV optimisation, realtime 3D echocardiography is not useful and algorithms or methods based on mitral Doppler can be used. On the contrary, intra-LV dyssynchrony can be minimised by optimisation of VV delay using CFM as a guide. We suggest to start with a LV delay of zero milliseconds and perform an LV analysis and subsequently repeat it at LV +20 milliseconds and LV -20 milliseconds. LV systolic function, by means of EF and LV dyssynchrony, by means of SDI, can be analysed and compared between the three programs: so far we suggest to choose the best compromise between the best function and the least dyssynchrony. CFM, showing contraction wavefront propagation map and the region of maximum delay, will guide further steps in optimisation: if, for example, posterolateral segment is still delayed at LV -20 milliseconds, LV stimulus can be further anticipated at -40 milliseconds and LV analysis repeated to see how CFM, EF and SDI behave (see *Figure 4*). Obviously, this technique, requiring three or four LV volume analysis, is more time-consuming than the traditional methods in this setting.

Conclusion

Realtime 3D echocardiography allows accurate measurement of LV size, function and dyssynchrony to be performed; it measures all 16 myocardial segments in one single acquisition, allowing for a rapid assessment of the area of latest LV activation to guide optimal LV lead placement. It is a very promising technique, not only in predicting response to CRT but also in guiding VV optimisation. With single-beat acquisition, a nice analysis of left ventricle volumes, function and dyssynchrony can be performed, even in a condition of atrial fibrillation. Care must be taken to improve temporal resolution, but satisfactory volume rates can now be obtained by optimising the settings of the machine. ■

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