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Review Article

Left Ventricular Myocardial Deformation Assessment by 4Dimensional XStrain Speckle Tracking Echocardiography: An Innovative Technology

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Abstract

Strain based imaging techniques, particularly speckle tracking echocardiography (STE) have been shown to have clinical utility in a variety of clinical settings. Currently, STE is being embraced and increasingly adopted in numerous echocardiographic laboratories worldwide. In context with contemporary non invasive cardiovascular procedures, 2Dimensional STE is most sought-after method to evaluate LV strain, rotation, twist and torsion. Two dimensional (2D), three dimensional (3D) and 4Dimensional (4D) deformation assessment by STE is inherently associated with certain limitations. For better appraisal of LV contractile properties recently introduced updated version of 4D XStrain STE has been employed to analyse the various complex multidimensional LV mechanics. This novel technology is a reliable, affordable and a simple tool for estimation of regional and global myocardial function. Furthermore, 4D XStrain STE can accurately quantify the 4D LV ejection-fraction, end-diastolic and end-systolic volumes and sphericity index (SI). However, this distinctive technology has not been widely adopted and its assessment is still limited to research applications. Hence we aimed to familiarize this innovative technology by comprehensively addressing its technique, advantages and limitations, with the intent that it may serve a more meaningful purpose in the current volatile scenario of cardio-vascular disease.

Keywords: *4Dimensional XStrain Echocardiography, LV strain, LV rotation, LVtwist, LV untwist, LV torsion.*

Introduction

Global longitudinal strain (GLS) is the most-studied two dimensional speckle tracking echocardiography (2D-STE) parameter worldwide[1]. American Society of echocardiography suggested a GLS value of ≥ -20 + 2% to be normal, after reviewing the enormous data on the subject[2]. STE by three dimensional techniques is advantageous and can expeditiously measure LV volumetric data, strain components, rotation, twist and torsion, in all the left ventricular (LV) segments by a single acquisition[3]. Even though temporal and spatial resolution of 3D imaging is inferior to 2D echocardiography, but 3D-STE remarkably overcomes the other constraints of 2D-STE1[4, 5]. The innovative technology of XStrain 4D merges Tomtec GMBH's 3D/4D rendering and Beutel™ computation capabilities[6] for LV border tracking, by fusing speckle tracking information obtained from standard apical 2CH, 3CH and 4CH views, thereby delivering a more complete picture of cardiac function (Figure 1). This tool, relying or high spatial and temporal resolution of 2D imaging, addresses the major limitations currently related to use of full volume 3D-STE [7-11].

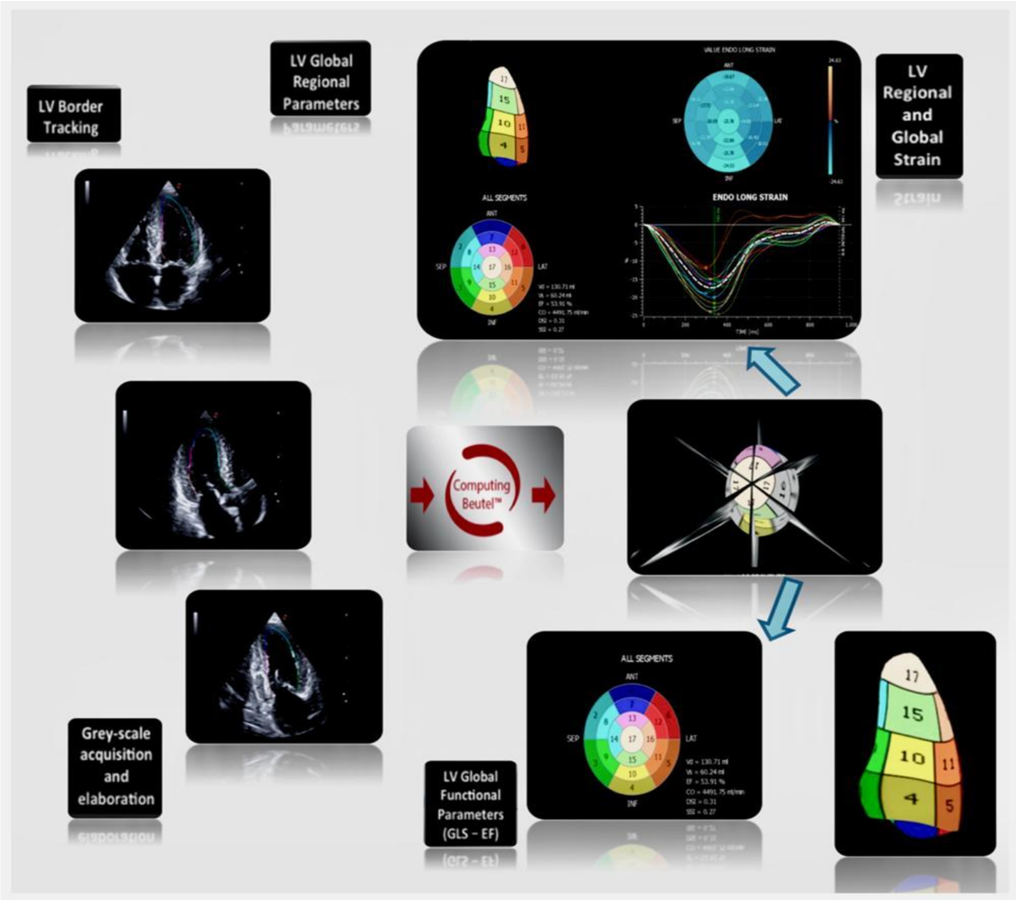

Figure 1: XStrain 4D global LV analysis. At the end of each scanning section, the three apical views are acquired. Then, after left ventricular (LV) endocardial border tracking, the software analyzes LV regional deformation parameters. Finally, the Beutel 3D reconstruction allows quantification of global LV function (global longitudinal strain (GLS)—ejection fraction)

Significant differences in strain measurements are to be expected when using either 2DSTE or 3DSTE (Figure 2).

Figure: 2 Comparison between 2D and 3D speckle-tracking analysis of LV myocardial strain by vendor-specific software (EchoPAC) [12]

Variable	2D strain	3D strain
Acquisition	Three parasternal and three apical 2D views	One apical 3D full volume
Temporal resolution	40-80 frames/sec	36.6 volumes/sec
Heart rate	Regular (consecutive 2D LV planes)	Regular (ECG** gated multibeat LV full volume)
Parameters	All strains (longitudinal, radial, circumferential)	All strains (longitudinal, radial, circumferential)
Two-directional strain	No	Yes
Bull's-eye map	Static	Dynamic
Calculation of global strain	Nonsimultaneous segmental peaks	Simultaneous segmental values
Radial strain	Measured	Calculated from area strain (by the law of volume conservation)
Positive peak rule	Yes	No
Drift compensation	Yes	No
Definition of end-systole	Time of aortic valve closure	Time of LV minimal volume

**ECG, Electrocardiography.

The Journal of American Society of Echocardiography (JASE) consensus statement document [13] reports that the much slower frame rates of 3D STE compared with 2D STE may limit analysis of rapid events such as isovolumic contraction and relaxation.

Another important aspect is the image quality of a single plane acquisition, obtained by the segmentation of the 4D volume echocardiography has lower quality resolution compared to native 2D imaging.

JASEs Expert Consensus Statement goes on to say "The major pitfall of 3D STE is its dependency on image quality. Random noise and relatively low temporal and spatial resolution affects its ability to define the endocardial and epicardial boundaries.

These issues likely affect the frame-to-frame correlation of local image features and contribute to sub-optimal myocardial tracking".

In view of this, 4D Xstrain STE concept is to combine high-quality and temporal resolution of 2D STE with 4D elaboration (namely XStrain™ 4D) providing the physician with a reliable, intuitive and easy-to-use tool for the quantification of regional myocardial function[6].

The present document provides basic understanding of myocardial deformation as relevant to the application of 4D XStrain STE and then describes the step-by-step approach to the technique, interpretation, clinical applications, advantages and limitations of this outstanding procedure.

4Dimensionsal XStrain Speckle Tracking Echocardiography

A breakthrough in cardiovascular imaging- the X-Strain™ 4D merges the X-Strain™ advanced technology with Tomtec GMBH's 3D/4D rendering Beutel™ computation capabilities[6]. Utilizing LV border tracking obtained with XStrain™ 2D on standard apical 4-chamber (AP 4CH)/ apical 2-chamber (AP 2CH) / and apical 3-chamber (AP 3CH) views, and then by fusing 2D speckle tracking information obtained from these views, XStrain™ 4D aims to make myocardial quantification imaging interpretation easier and faster. Ultimately this technology, now mostly reserved for clinical research, can be easily adopted for daily routines echocardiopgraphy and improve the quality of the diagnosis delivered to the patient.

According to current clinical literature on 2D STE technology, single plane acquisition must be performed with a temporal resolution ranging from 40-75 frames/sec. For instance, temporal resolution is very important in the evaluation of the diastolic contractility properties of the heart, characterized by faster and less intense movements compared to the systolic ones.[12]

Technique and Image Analysis

The echocardiographic evaluation is performed by acquiring the images using a harmonic variable (1-5 Mhz) electronic single crystal array transducer with the patient lying in the left lateral decubitus position. XStrain4D software package (Esaote, Itay) is employed for offline STE analysis.

At least three 2D clips, with duration of 1 cardiac cycle each, are acquired from each of the 3 following views: (1) left apical 4-chamber (4 CH) view demonstrating both atria and ventricles; (2) left apical 2-chamber (2 CH) view elucidating the left atrium (LA) and the LV; and (3) left apical 3-chamber (3 CH) view displaying LA, LV, and ascending aorta. A set of clips is composed of 3 cine-loops, 1 of each apical view. For each cine-loop, an end diastolic frame, in which endocardial and epicardial borders are clearly identified, chosen and processed by 2D-XStrain, which is a dedicated border tracking software. Left ventricular endocardial and epicardial borders are delineated by 13 equidistant tracking points (Figure 3) inserted manually under the guidance of a semiautomatic tool for border segmentation (AHS Aided Heart Segmentation, Esaote).

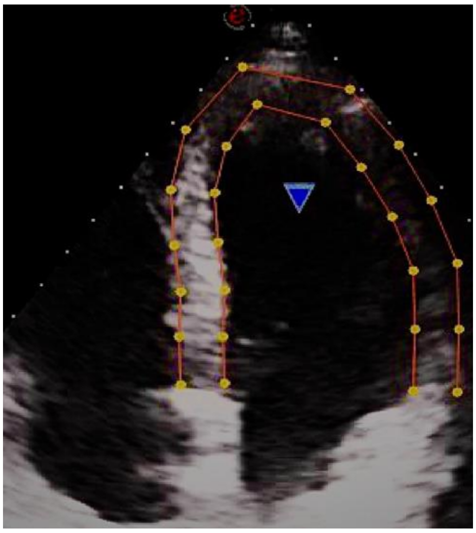

Figure 3: Apical 4CH View in which the LV endocardial and epicardial borders are clearly identified and delineated by 13 equidistant tracking points inserted manually under the guidance of semiautomatic tool for border segmentation (AHS- Aided Heart Segmentation, Esaote)

Then, 2D-XStrain software automatically divides the LV wall, of each apical view, in 6 segments and tracks them, frame-by-frame, throughout the entire cardiac cycle. The tracking quality is visually evaluated. It is considered adequate if the tracking point movements follow the endocardial and epicardial borders throughout the entire cardiac cycle. When necessary, manual adjustment of the tracking points is made. Only cardiac cycles with adequate tracking quality and with no signs of arrhythmia are included. The system used provides a quality control of the temporal resolution, it does not allow elaboration of clips having a frame rate (FR) < 40 Hz, which is adequate for HR < 100 beats per minute (bpm) [14]. In patients with HR 100 bpm, to ensure an adequate temporal resolution, the LV endocardial and epicardial borders are optimally visualized by adjustment of image depth, sector width, number of focal points, and line density. The XStrain-4D software, by combining the results of each set of clips analyzed by 2D-XStrain, generates the LV bull's eye representation according to the standard 17-segments model [14] (Figure 4).

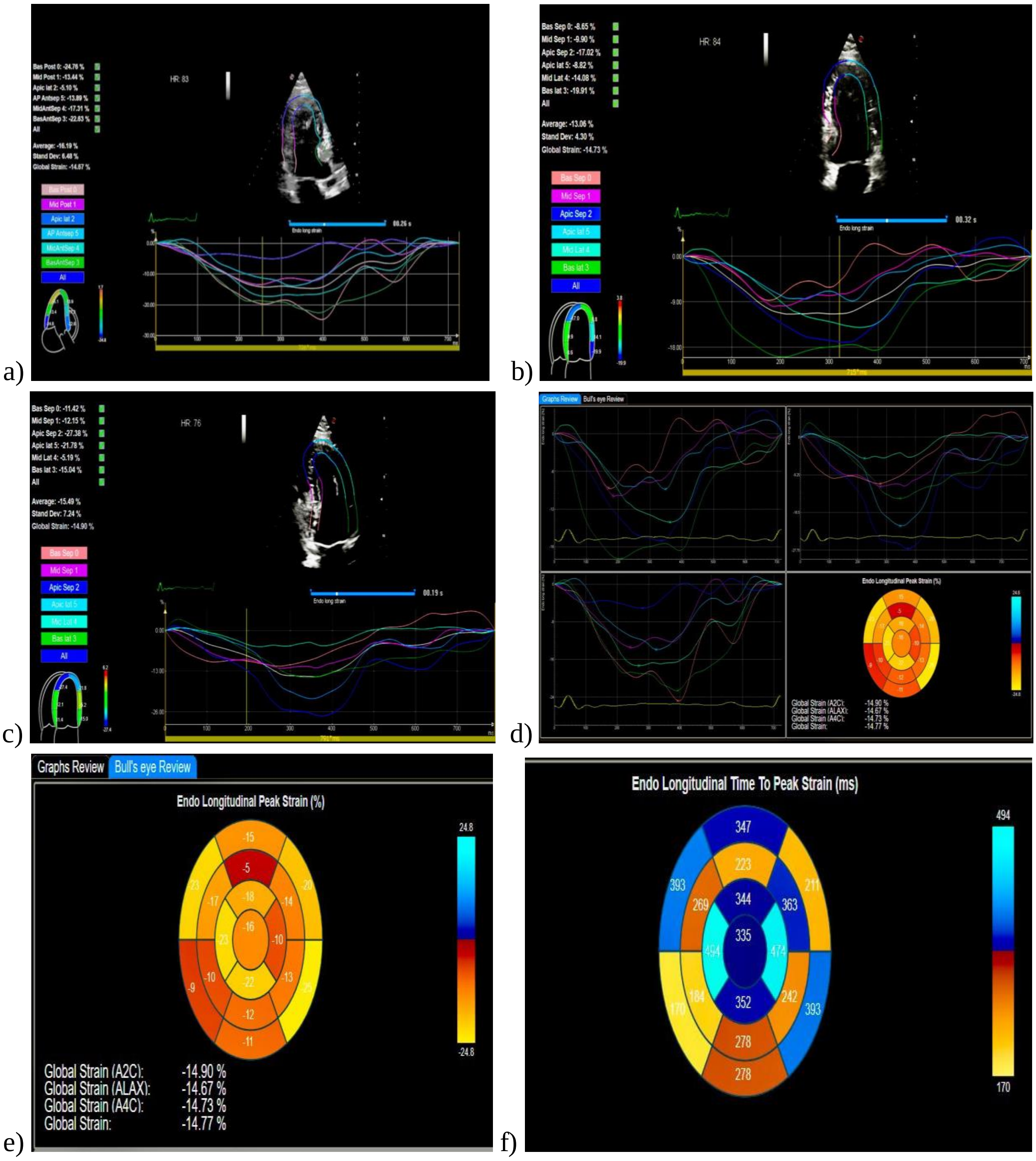

Figure 4: a) Apical 3CH Global Longitudinal View Strain Analysis, b) Apical 4CH Global Longitudinal Strain Analysis, c) Apical 2CH View Global Longitudinal Strain Analysis, d)Longitudinal Strain-Bulls Eye graph and plot, e) Longitudinal Strain- Bulls Eye, f) Longitudinal- Time to peak strain plot

The XStrain-4D software provides segmental, regional, and global peak systolic value of different strains of both endocardial and epicardial borders, from the apical views. The peak values of peak systolic strain and strain rate are calculated as the average of the 17 segmental peak values (Figure 5).

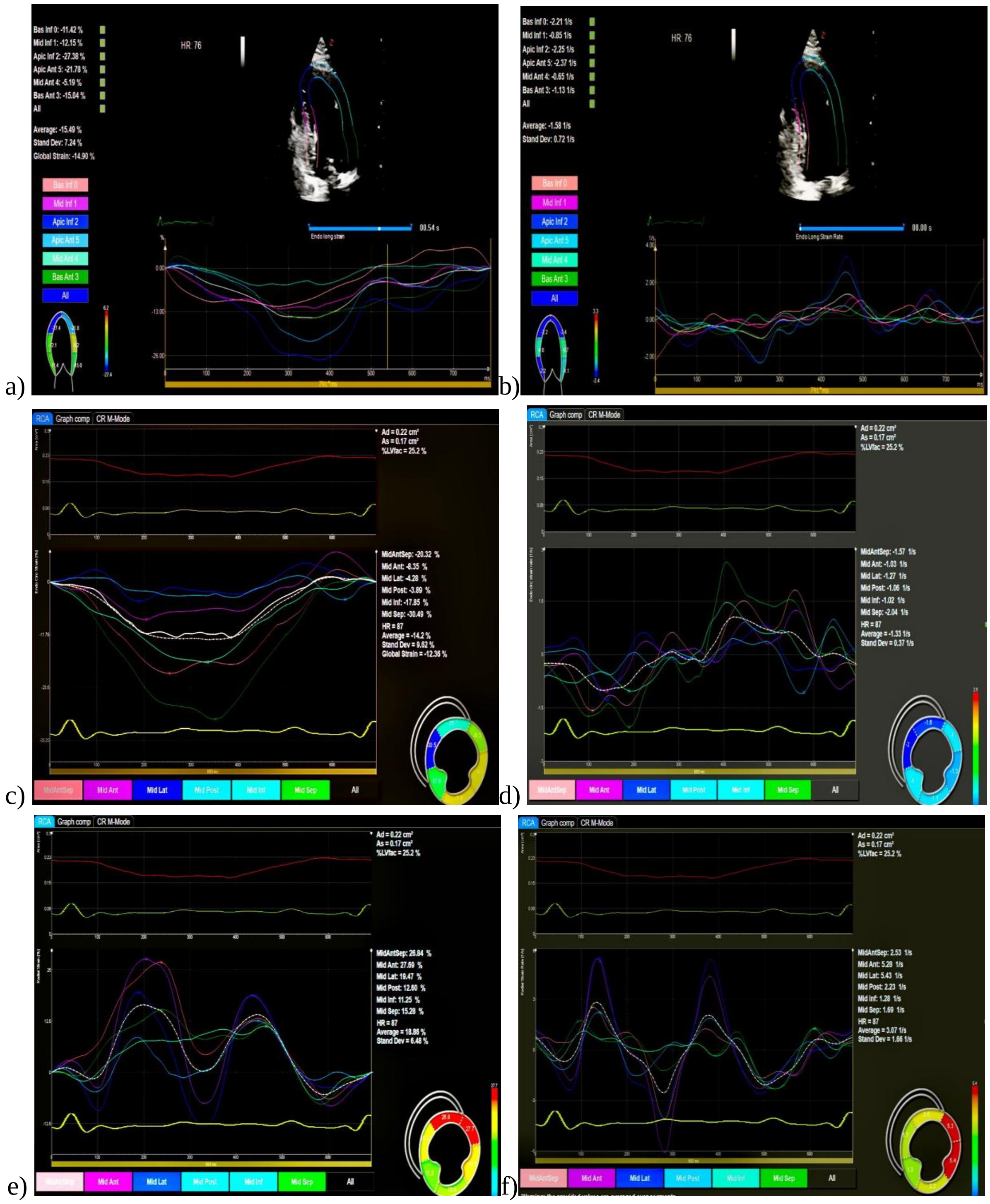

Figure 5 : a) LV Global Longitudinal Strain, b) LV Global Longitudinal Strain Rate, c) LV Circumferential Strain, d) LV Circumferential Strain Rate, e) LV Radial Strain, f) LV Radial Strain Rate

The XStrain-4D software, by providing temporal compensation for HR variation and spatial alignment of the 3 apical views, produces a LV 3-dimensional (3D) reconstruction and calculates LV volumes and EF[15] (X4D-EF) by the "Beutel model" method (Tomtec, Germany)[16] (Figure 6). Three sets of clips are analyzed for each patient and mean values are calculated.

a) b)

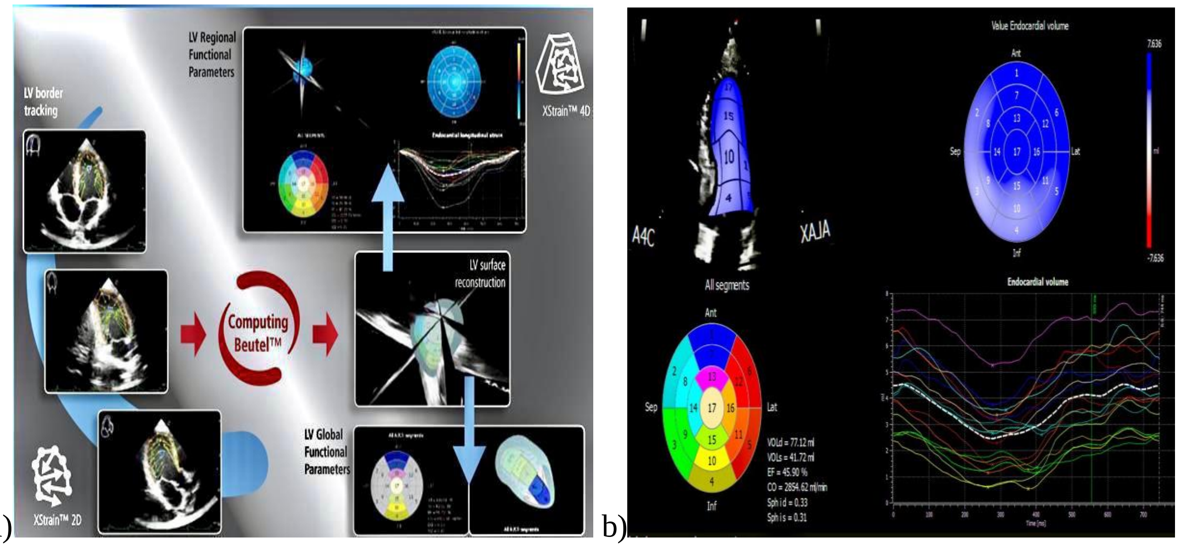

Figure 6: a) XStrain 4D software by providing temporal compensation for HR variation and spatial alignment of 3 apical Views, produces a LV 3-dimensional reconstruction,b) Determination of XStrain 4D Volumes, EF %, CO, Sphericity Index in diastole and systole

The software creates a LV model in 3D space, which ensures both smooth contours in the spatial domain and continuous motion in the temporal domain. The aim of this new tool is to provide an additional and intelligent solution to correlate and quantify several components of cardiac function in a 3D environment[6].

XStrain TM 4D, simplifies the interpretation of global longitudinal strain, and is a reliable solution that correlates with the most updated results coming from clinical research in this field. [17]

This approach simplifies the overall data interpretation, with no additional time or computations needed during exam data acquisition.

Special Precautions on performing 4Dimensional XStrain STE [18]

STE is a gray-scale based technique thus obtaining high quality gray-scale images is the most critical requirement for STE. The following points need to be adhered to during the image acquisition:

- Apical four-chamber, two-chamber and three-chamber views are required for acquiring decent images of LV, for the measurement of LV longitudinal strain whereas short-axis views at the mitral valve (MV) level, papillary muscle (PM) level and apical levels are necessary for the measurement of radial and circumferential strain. Short-axis images are also used for the measurement of LV rotation and torsion.
- Paramount attention should be paid to the quality of the images. The gain settings should be optimized. The depth should be reduced so that the LV occupies most of the image sector. In long-axis views, avoidance of foreshortening of LV is important. In short-axis views, the LV cavity should be as circular as possible to substantiate that the imaging plane is perpendicular to the long-axis of the LV.
- Imaging should be performed at frame rate of 40-75 frames/s. At lower frame rates, large displacement of the speckles between the successive frames precludes satisfactory tracking of the speckles, whereas at higher frame rates spatial resolution of the image gets compromised.
- High quality ECG gating is must. Effort must be made to obtain all the images at nearly uniform heart rates.

- Minimum three cardiac cycles should be acquired for each loop. This ensures that at least one complete cardiac cycle (the middle one), without any truncation, is always available for analysis.
- All the images should be acquired in breath-hold to avoid any breathing artifacts.
- After transferring the images, the speckle tracking analysis is executed judiciously.
- It is always desirable to analyze the apical long-axis image (i.e. three-chamber view) first. In this view, the movement of aortic valve leaflets assists in timing the aortic valve closure which is essential for the software to perform the deformation analysis.
- A region-of-interest (ROI) is generated by the software, to include the entire myocardial thickness. The width of the ROI can be manually adjusted as required. Care should be taken to avoid including bright, echogenic pericardium in the ROI.
- The software then tracks the myocardial speckles frame-by- frame and generates moving images displaying the tracking. Visual inspection of the moving image allows the operator to determine the adequacy of the tracking. If the tracking does not seem to be accurate, one can go back and readjust the ROI.
- The LV myocardium is divided into six segments by the software which display the segmental and global longitudinal strain, strain rate, velocity and displacement curves.
- From these curves, peak- systolic longitudinal strain and strain rate can be recorded for each of the myocardial segments. A color-coded parametric images furnishes quick, visual impression of the timing and the extent of segmental myocardial deformation.
- The same process is then repeated with the apical four- chamber and two-chamber images also. The strain values for all the segments are recorded and averaged to obtain the global longitudinal strain (GLS) and strain rate. Bull's eye display of the regional and global longitudinal stain is demonstrated.
- The short-axis images are also analyzed in the same manner to derive the segmental and global radial and circumferential strain and strain rate. It is important to recognize that during systole, the LV circumference usually shortens whereas the myocardial thickness increases. Hence, the normal circumferential strain is negative but the normal radial strain is positive.
- The rotation and rotation rate are automatically measured when the short-axis images are analyzed for strain measurement and no extra step is required. LV rotation has a unit of '°' and the rotation rate '°/s'. By convention, anticlockwise rotation is assigned a positive value whereas the opposite is true for the clockwise rotation. Thus, the normal apical rotation is positive and the basal rotation is negative.
- The LV twist is calculated by subtracting basal rotation from the apical rotation and torsion is calculated by dividing twist with the LV length (Figure 7).

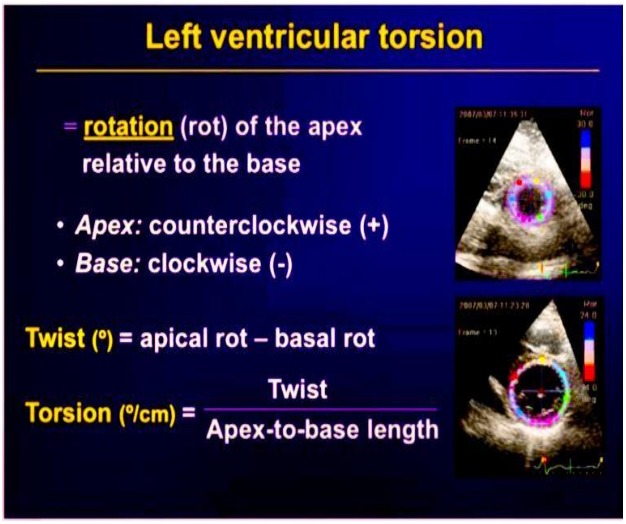

Figure 7: Calculation of LV twist and torsion

Parameters derived by 4Dimensional XStrain STEStrain Parameters

From the ingenious technology of 4DXstrain STE numerous strain parameters can be estimated and the commonly used ones are enumerated: global longitudinal strain (GLS), global longitudinal strain rate (GLSR), global circumferential strain (GCS), global circumferential strain rate (GCSR), global radial strain (GRS), global radial strain rate, transverse Strain, transverse strain rate, transverse velocity, longitudinal velocity, radial velocity, rotational velocity, shear and shear rate. Longitudinal and circumferential strains have negative values in systole and radial strain in characterized by positive values, strain, strain rate and velocity were delineated in %, 1/s, cm/sec and o/s where suitable.

Rotation and twist parameters

Peak apical rotation, time to peak apical rotation, peak twist, time to peak twist, twist rate, time to peak twist rate, untwist rate and time to peak untwist rate (Figures 8). The rotation, twist and untwist parameter indices are expressed in 0, ms, o/s where appropriate.

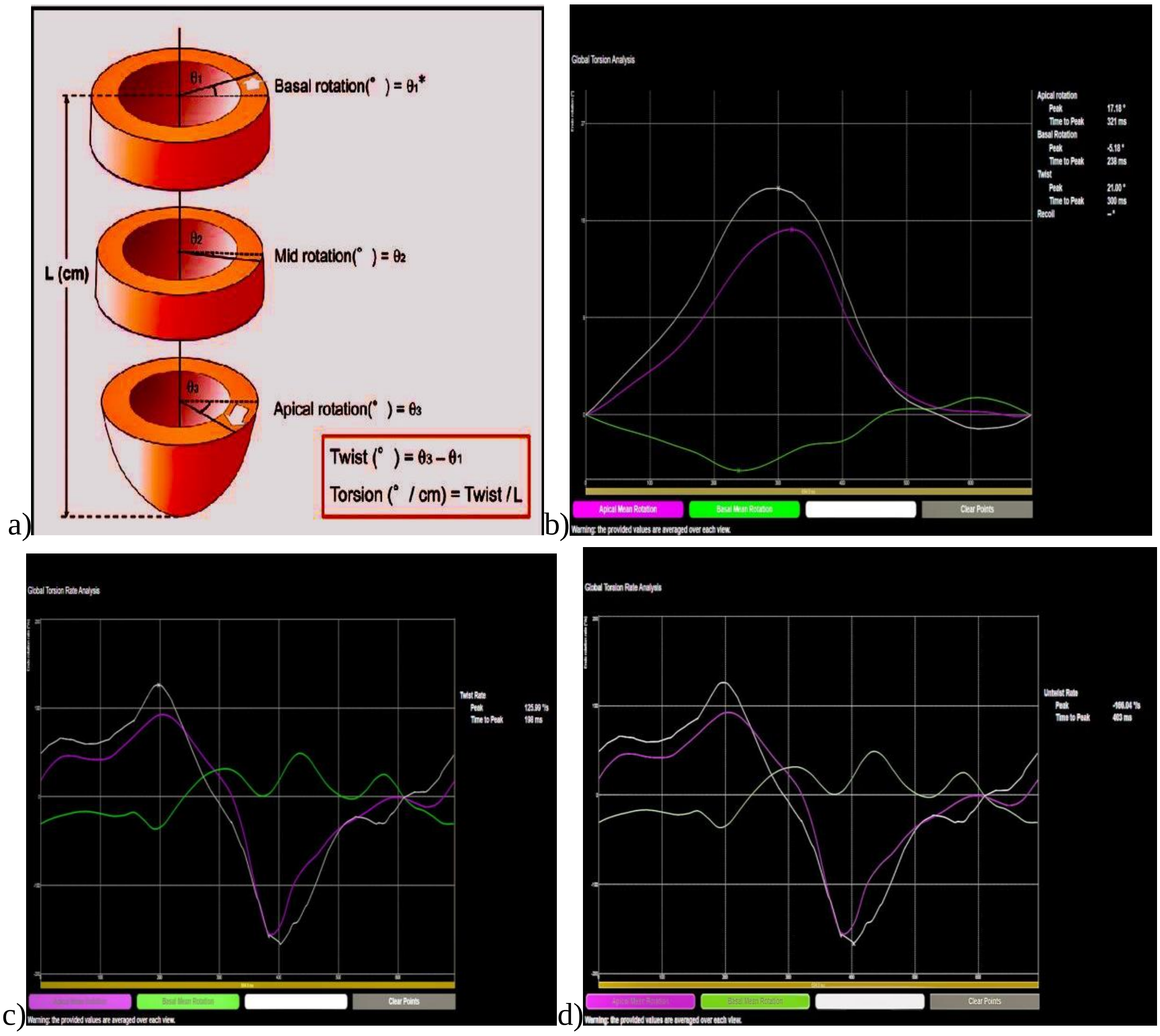

Figure 8: a) LV twisting mechanism. Basal segment rotatesin a counter clockwise direction and apex rotates in a clockwise direction. L, distance between base and apex, b) Rotation and Twist parameters analysis - Peak apicalrotation, Time to peak apical rotation, Peak basal rotation, Timeto peak basal rotation, Peak Twist, Time to peak twist, c) Twist rate and Time to peaktwist rate analysis, d) Untwist rateanalysis- Peak untwist rate, Time to peak untwist rate.

NB: The values of parameters are mentioned in lower right hand corner of Figure 8a and upper right hand corner of Figures 8b, 8c and 8d.

Volumetric Data

Sphericity index in diastole and systole left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), 4D-EF% and cardiac output (CO).

Clinical Application of XStrain Speckle Tracking Echocardiography

The assessment of LV deformation by STE has been shown to provide incremental information in many clinical settings. The fact that this technology offers the possibility of analyzing the different components of LV deformation means that it can provide important information about the transmural heterogeneity of myocardial contractile function that is extremely useful for detecting subclinical states that are likely to progress into either systolic or diastolic heart failure. According to the current clinical literature on XStrain 2D and XStrain 4D speckle tracking echocardiography the non-invasive assessment of myocardial deformation can be effectively used in healthy adults(12,13,17-22) and many common cardiovascular diseases affecting LV function which can provide important additional clinical information to the physicians. Among them we can mention:

- MYOCARDIAL INFARCTION: In patients with myocardial infarctions, longitudinal strains are significantly reduced proportionately within the area of infarction.[23-25]
- CORONARY ARTERY DISEASE: LV longitudinal mechanics at rest can be attenuated in patients with coronary artery disease, as the sub-endocardium of the left ventricle is most vulnerable to the effects of hypoperfusion and ischemia.[26, 27]
- VALVULAR DISEASE: STE can improve the results of a standard 2D echocardiography examination in valvular heart diseases, as it can provide insights into the pattern of adaptive remodeling and detect the presence of subclinical cardiac dysfunction (Figure 9). In fact, due to the LV adaptive remodeling, such patients can remain asymptomatic or minimally symptomatic for a long period of time even in the presence of severe valvular disease.[28, 29]

Figure 9: Speckle tracking for LV performance in young athletes with bicuspid aortic valve and mild aortic regurgitation.

GLS of LV was at lower extremes of normality and produced a marked gradient from basal to mid apical segments, which was not evident in healthy controls

- HYPERTROPHIC CARDIOMYOPATHY: STE has been reported to be used for detecting subclinical myocardial changes in LV hypertrophy (Figure 10), as well as for distinguishing the different causes of LV hypertrophy.[30-33]

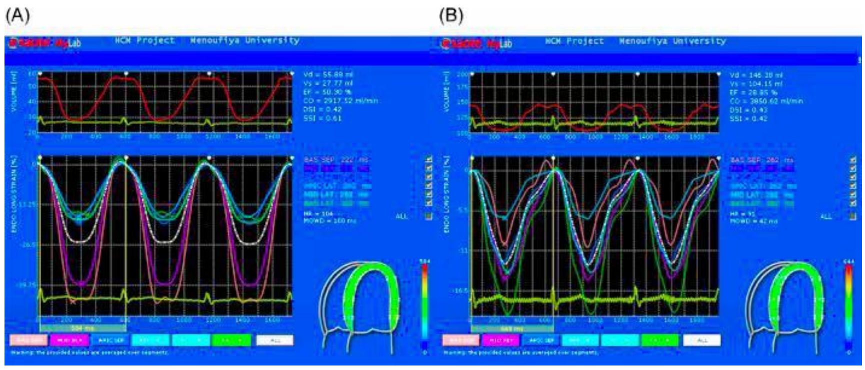

Figure 10: LV longitudinal strain curves in apical 3CH of Hypertrophic Cardiomyopathy (A) Latent obstruction showed lower strain values and increased electromechanical delay and (B) Non Obstructive demonstrated higher strain values and lower electromechanical delay

- DILATED CARDIOMYOPATHY: This pathology is associated with the reduction of strains in all 3 directions (Figure 11) and STE can therefore be widely used to detect and stage it.[34, 35]

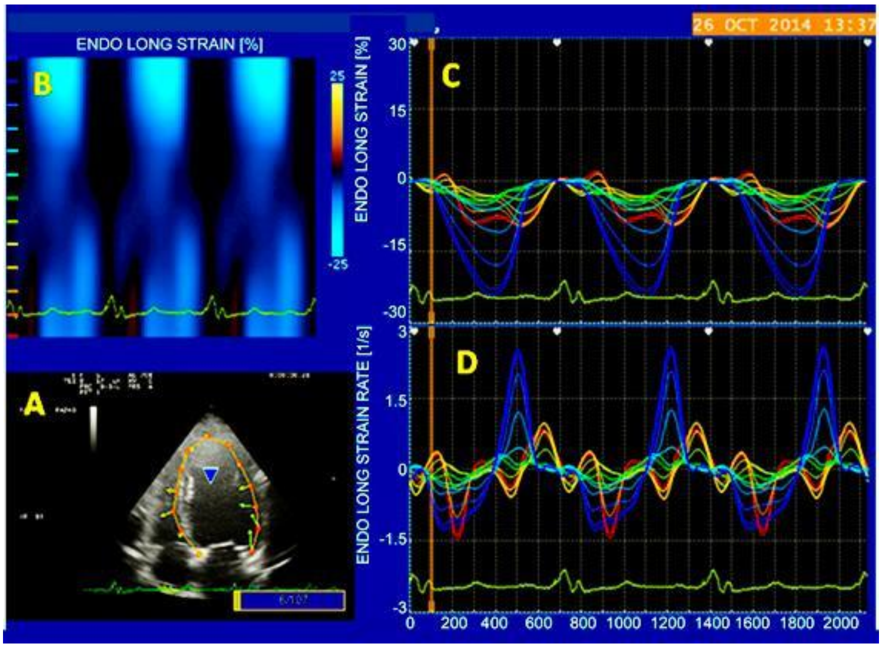

Figure 11: Strain and Strain rate in a patient of Idiopathic Dilated Cardiomyopathy with LBBB.LV Global Longitudinal Strain and Strain rate were significantly impaired compared to non LBBB group

- SUBCLINICAL CARDIAC INVOLVEMENT IN SYSTEMIC DISEASES: This technology proved to be extremely useful in the preclinical detection of cardiac involvement in systemic diseases such as Diabetes mellitus, Kawasaki disease, Rheumatoid arthritis, Lupus Nephritis, Psoriasis, Systemic Sclerosis, Thalassemia major Renal transplant recipients, Cardiac Amyloidosis, Cardiac toxicity on chemotherapy and Idiopathic pulmonary fibrosis (Figure 12-15).[36-45].

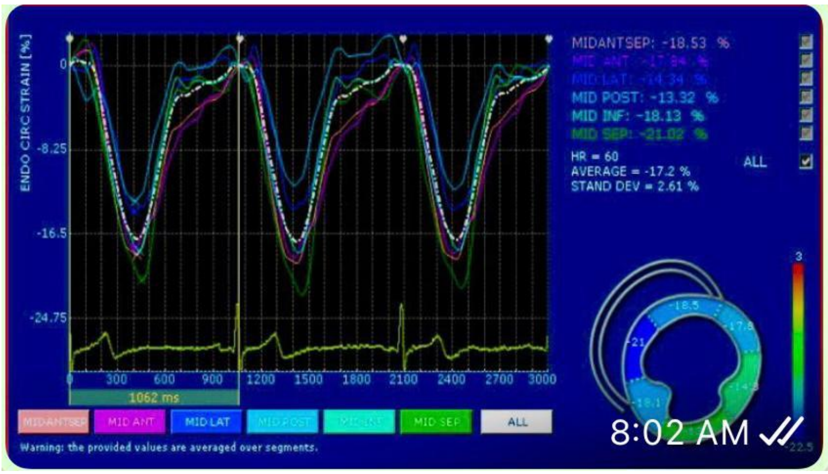

Figure 12: Xstrain Speckle Tracking Echocardiography in patients of Renal transplant recipients revealed significantly lower GLS compared to controls (P<0.001).

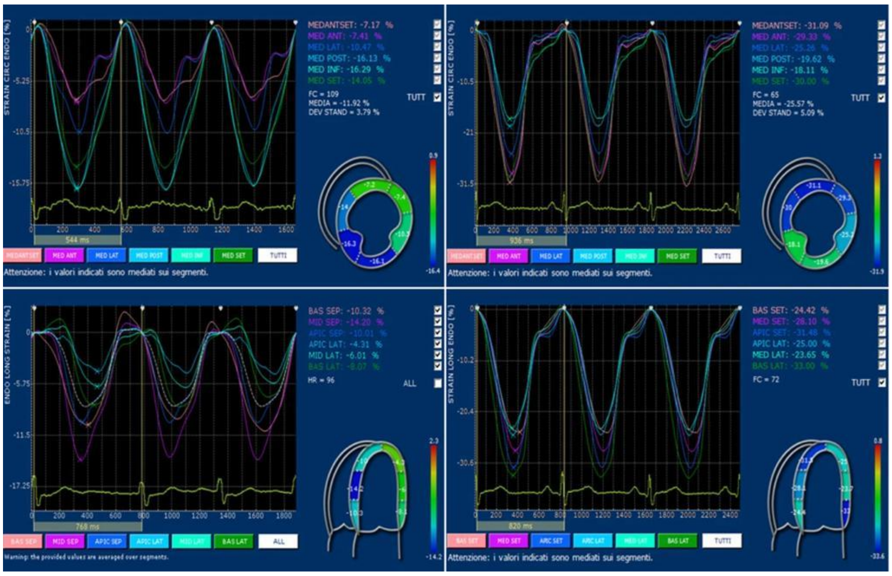

Figure 13: XStrain Speckle Tracking Echocardiography in patients of Systemic Sclerosis. Circumferential and Longitudinal Strain were significantly lower in patients in systemic sclerosis than in healthy healthy subjects (p= < 0.001).

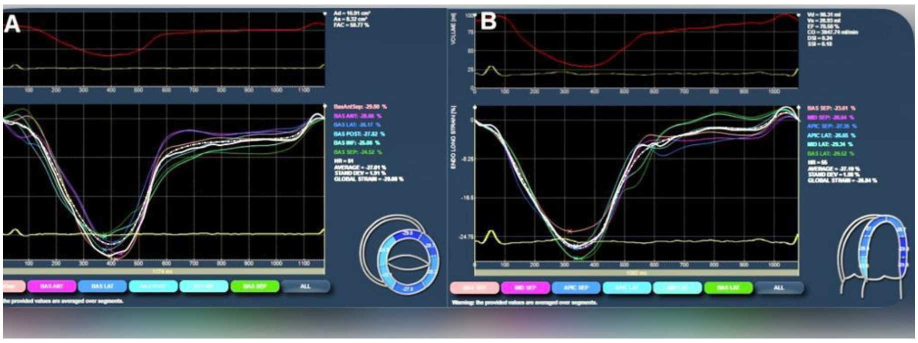

Figure 14: XStrain speckle tracking echocardiography in patients of Psoriasis. The GLS was significantly lower in the psoriasis group (B) than in controls (A).

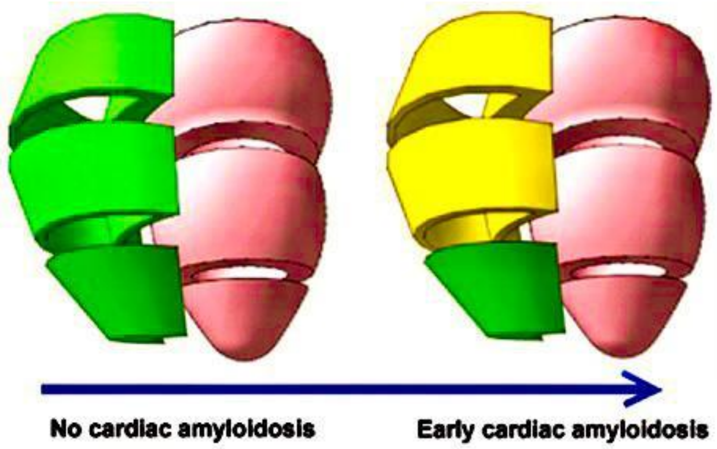

Figure 15: Right Ventricular (RV) Myocardial deformation in subjects with no Cardiac Amyloidosis (CA) and early phase of Cardiac Amyloidosis. Note the RV longitudinal dysfunction in mid and basal LV segment in early CA. Green, normal strain, Yellow, mild- moderate strain impairment.

- MISCELLANEOUS CONDITIONS: The impact of left anterior descending artery wrapping around the LV apex with normal coronary angiography on LV XStrainSTE was associated with better strain and rotational mechanics (Figure 16). Similarly, in the elite athletes improved apical LV twist was demonstrated in an Egyptian study [46, 47].

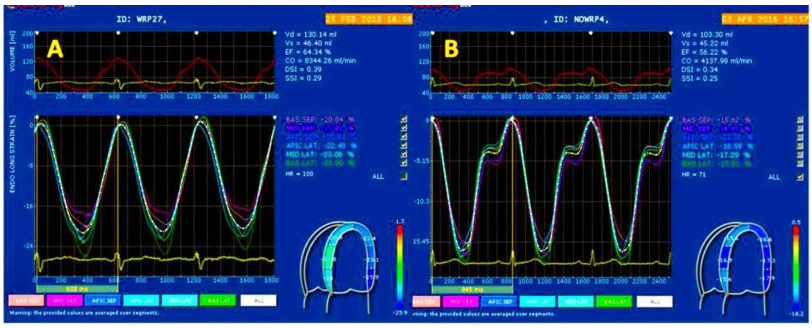

Figure 16: Impact of XStrain speckle trackingechocardiography in a patient with left anterior descending artery wrapping around the left ventricular apex on cardiac mechanics. The coronary angiography was normal.

Advantages

XStrain4D represents a further step forward in the interpretation of LV deformation mechanics.

Utilizing LV border tracking obtained with XStrain™ 2D on standard apical 4CH, 2CH, and 3CH views, XStrain4D delivers a more complete and intuitive picture of cardiac deformation behavior, providing temporal compensation for heart rate variations, spatial alignment of the 3 views in 3D space, and adaptation of a dynamic LV surface model [6].

This tool, relying on high spatial and temporal resolution 2D imaging acquisitions, addresses and resolves the major limitations and criticalities currently related to use of full-volume 3D STE solutions. These limitations are related to image quality (random noise), and low temporal (volume rate) and spatial resolution (voxel size) that affect the frame-to-frame correlation on local image features, thus contributing to suboptimal myocardial tracking [6].

One of the greatest advantages of 4DXStrainSTE is that, after the semi-automatic definition of the ROI, the software is capable to derive simultaneously all strain components together with accurate measurements of LV geometry [6, 17].

Moreover, 4DXStrainSTE will allow to clarify the clinical added value of assessing strain in multiple directions rather than rely mainly on LV longitudinal function, as currently done with 2D strain [6, 17].

Limitations

Despite being around for more than a decade, 4DXStrainSTE is still a research tool and not yet fully validated for clinical use. In addition, several limitations have not allowed its wide use in daily clinical practice.

A major disadvantage of 4DXStrainSTE is its reliance on good acoustic window and quality data sets, and on patient cooperation for breathholding, limiting its feasibility in a significant proportion of routine patients. The use of 4DXStrainSTE also requires an adequate temporal resolution to ensure the presence of recognizable natural acoustic markers. 4DXStainSTE requires the use of multi-beat 4DXStainSTE acquisition of the LV, limiting its use in patients with irregular rhythms.

Other limitations pertain to individual 4DXStrainSTE commercially available software and include: (I) no automatic validation of speckle-tracking quality; (II) no option to exclude the poorly tracked segments from the computation of global strain values by the operator; (III) no clear discrimination between poor tracking quality and poor function in abnormal segments etc.

Future research directions

The ultimate goal of implementing 4DXStrainSTE in large-scale clinical studies is to assess its incremental prognostic value for predicting morality and adverse events, and for arrhythmic risk stratification in comparison in with LVEF and 2D longitudinal strain.

Furthermore, it is mandatory that educational initiatives should include practical courses focusing on 4DXstrainSTE acquisition, analysis and interpretation, for a more uniform application of 4DXStrainSTE for clinical and research purposes.

Conclusions

4DXStrainSTE is an advanced imaging technique for estimating myocardial deformation that holds significant promise to improve the accuracy and the reproducibility of LV function analysis by echocardiography, as well as to reduce the subjectivity in the visual interpretation of regional wall motion. However, further clinical testing and robust evidence with this technique are needed in order to optimize its clinical use and to identify its benefits in comparison with the established methods.

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