

# An Overview of Three-Dimensional Speckle Tracking Echocardiography

Islam Ghanem Ahmed Ghanem, Ahmed Shafie Ammar, Abdel-Rahman Osama Abdel-Kareem\*, Ahmed Shaker Mousa

Cardiology Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt

\*Corresponding author: Abdel-Rahman Osama Abdel-Kareem

Email: ao.khattaby@gmail.com,

## Abstract:

Speckle-tracking echocardiography (STE) is an advanced echocardiographic technique that allows a novel approach to the assessment of cardiac physiology through the study of myocardial mechanics. In its three-dimensional (3D) modality, it overcomes the drawbacks inherent to other echocardiographic techniques, namely two-dimensional echocardiography and tissue Doppler imaging. Several research studies and software improvements have led 3D-STE to become a promising tool for accurate evaluation of global and regional cardiac function. This article addresses the image acquisition, analytical methods, and parameters of myocardial mechanics that could be derived from 3D-STE. This systematic guidance may help to establish its usefulness in the global and regional evaluation of cardiac function, and to facilitate its clinical application.

**Keywords:** evaluation, facilitate, assessment, promising

*Tob Regul Sci.*<sup>TM</sup> 2023 ;9(1): 7209 - 7228

DOI: [doi.org/10.18001/TRS.9.1.510](https://doi.org/10.18001/TRS.9.1.510)

## Introduction:

Echocardiographic myocardial deformation imaging, is a technological advancement that has been developed as a means to objectively quantify regional myocardial function (1).

Myocardial deformation imaging was first introduced as a post-processing feature of tissue Doppler imaging (TDI) with velocity data converted to strain and strain rate (2).

Strain represents a measure that evaluates the degree of deformation of the analyzed segment in relation to its initial dimensions. It is expressed as a percentage. The strain equation ( $\epsilon$ ) is as follows: ( $\epsilon = L - L_0 / L_0$ ), where L is the length of the object after deformation and L<sub>0</sub> is the basal length of the object (3).

Strain rate represents the speed at which strain occurs. The unit of strain rate is S<sup>-1</sup>, therefore, the less the time tissue takes to reach a certain strain the higher the strain rate value (4).

A more recent feasible and reproducible method to measure strain and strain rate is STE (5).

STE is a method based on tracking of characteristic speckle patterns created by interference of ultrasound beams in the myocardium (6). These acoustic markers are fairly equally distributed throughout the myocardium and about 20-40 pixels in size. STE analyses motion by tracking these natural acoustic markers from frame to frame. The geometric shift of each speckle represents local tissue movement and when the frame rate is known, the change in speckle position allows determination of its velocity. The motion pattern of myocardial tissue is reflected by the motion pattern of speckles and by tracking these speckles, strain and strain rate can be calculated. One advantage of this method is that tracking occurs in two dimensions, along the direction of the wall and not along the ultrasound beam, therefore, unlike TDI, STE is angle independent (7). This allows angle independent quantification of LV strain and strain rate in all three orthogonal axes (circumferential, radial, and longitudinal) (8).

The amount of strain is dimensionless and expressed in per cent. Negative strain values describe shortening and positive values describe thickening of a given myocardial segment related to the original length (7).

The results produced from speckle tracking echocardiography have been confirmed against sonomicrometry and tagged cardiac magnetic resonance, demonstrating good feasibility and repeatability (8).

### **Fundamentals of myocardial mechanics**

Knowledge of the anatomical structure and 3D mechanics of the LV myocardium is key to understand and interpret strain in clinical practice. In brief, LV myocardial fibers are oriented in the subendocardium in a right-handed longitudinal helix and in the subepicardium in a left-handed oblique helix, with circumferential fibers lying in between (9). This complex anatomical structure of the myocardium explains the various patterns of myocardial deformation (**Figure 1**).

Accordingly, during systole the LV shortens (longitudinal and circumferential dimension) and twists along its long axis, while its wall thickens (radial dimension) (10). Longitudinal contraction depends on the subendocardial layer and transmural myocardial injury leads to a reduction in LV circumferential and torsional deformation and results in a decreased ejection fraction. Therefore, the combination of multiple deformation indices provides insight into the pathophysiologic mechanics of LV dysfunction (11).

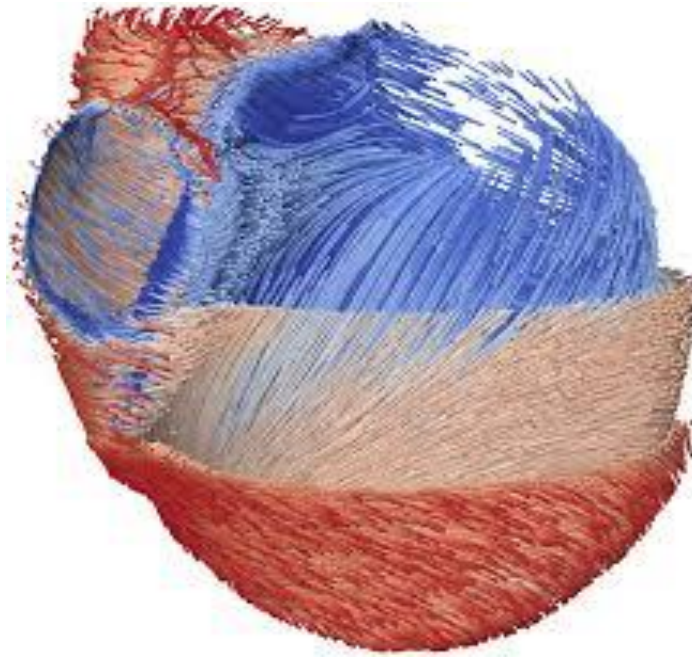


Figure 1: A model showing myocardial fiber direction in different myocardial layers. Subendocardial layer (Upper blue), Mid wall (Middle pink) and Subepicardial layer (Lower red) (12)

Furthermore, the LV is characterized also by twist mechanics. Since mechanical activation occurs first in the right-handed helix, the base and apex rotate first in an anticlockwise direction during isovolumic contraction (13), followed by further anti-clockwise movement of the apex during ejection phase and clockwise rotation of the base due to the activation of the subepicardial left-handed helix (14). During isovolumic relaxation, the cardiac apex untwists by a clockwise rotation, generating active intraventricular suction forces that promote LV rapid filling (15).

By understanding different myocardial mechanics, strain components could be divided as follows:

1- **Longitudinal strain:**

Longitudinal strain represents myocardial deformation directed from the base to the apex. During systole, ventricular myocardial fibers shorten with a translational movement from the base to the apex, this leads to shortening the distance between kernels and is represented by negative values and negative curves (*Figure 2a*). Global longitudinal strain has been validated as a quantitative index for global LV function (8).

2- **Circumferential strain:**

Circumferential strain represents myocardial deformation throughout the circular perimeter of LV. During systole LV fibers shorten circumferentially this leads to shortening the distance between kernels and is represented by negative values and negative curves (*Figure 2b*) (16).

3- **Radial strain:**

Radial strain represents myocardial deformation along LV radius towards LV cavity center. During systole, inward thickening of myocardium occurs. Radial strain is presented by positive values and

positive curves (*Figure 2c*) (8). Among basic strain components, radial strain is the least reproducible and the least correlated with sonomicrometry and tagged CMR (10).

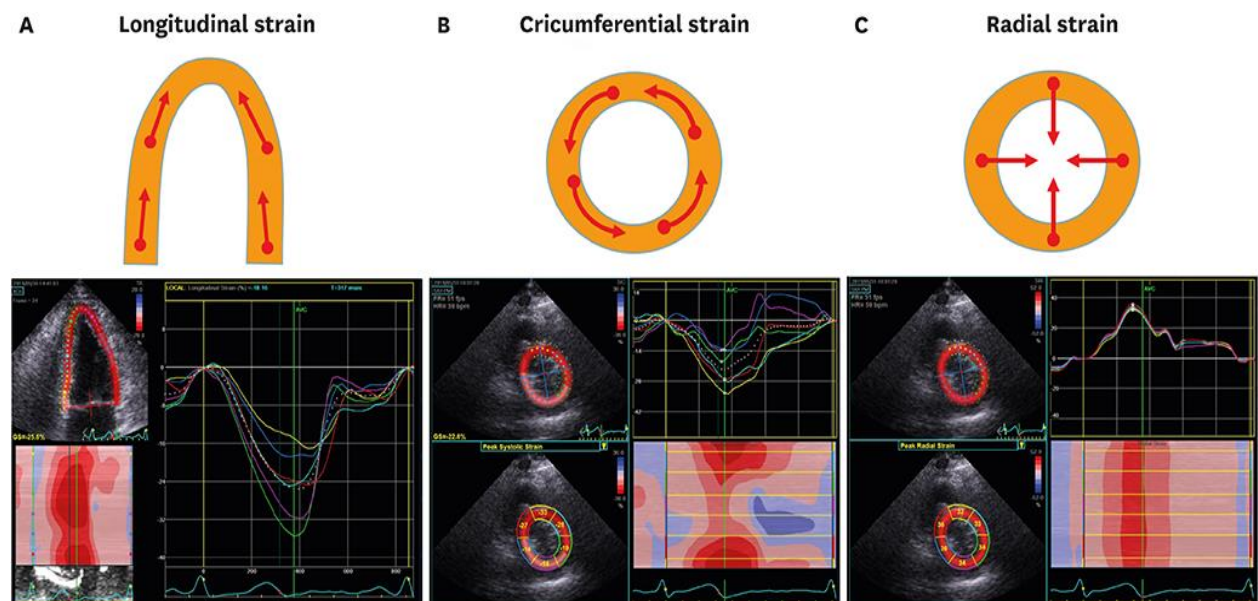


Figure 2: Representing different patterns of myocardial strain. Red arrows represent the direction of myocardial deformation (17)

#### 4- Area strain:

A novel deformation parameter that can only be measured by 3D STE. Area strain reflects the relative area change that combines the effect of both longitudinal and circumferential shortening (10). Area strain is calculated by measuring the segmental area at end diastole ( $A_{ed}$ ) and at end systole ( $A_{es}$ ) using the formula  $A_{es}-A_{ed}/A_{ed} \times 100$  and thus normally has negative values. Since it results from the combination of longitudinal and circumferential strain, it can be regarded as an integrative parameter of deformation making it attractive to study LV subclinical dysfunction (18).

As area strain combines longitudinal strain that is measured from apical views and circumferential strain that is measured from short axis (SAX) views, it can only be measured by 3D STE which can acquire these data simultaneously (10).

Area strain was validated in animal models sonomicrometry experimental studies and against CMR tagging (18), and its measurement by 3DSTE was found to strongly correlate with that by sonomicrometry ( $r=0.87$ ). Accordingly, Area strain appears to have the best reproducibility among all 3D strain parameters (19).

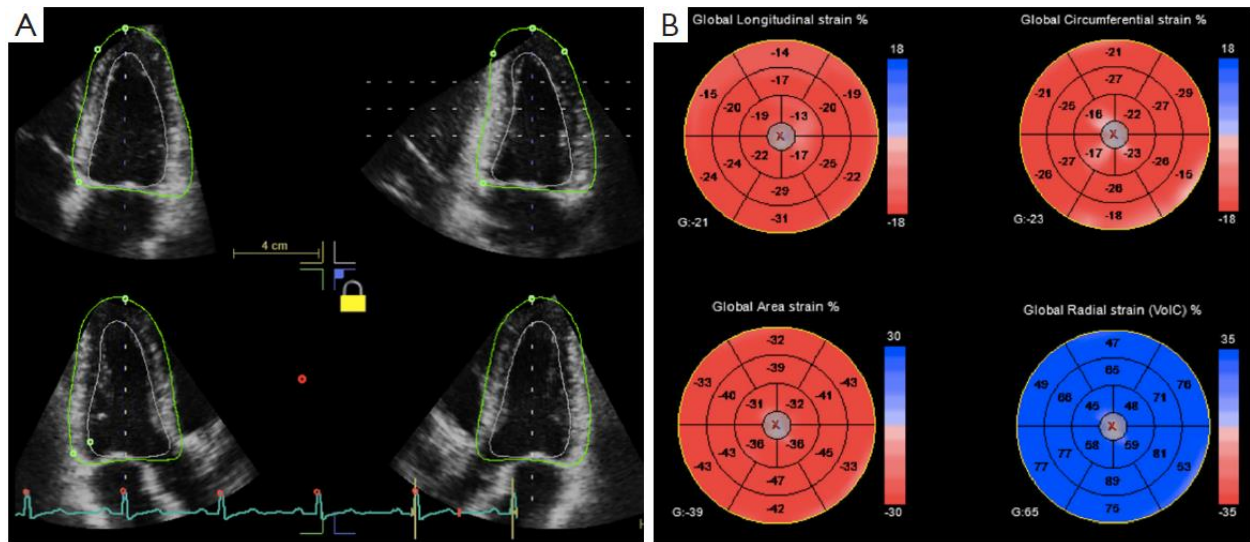


Figure 3: Simultaneous calculation of longitudinal, circumferential, area and radial strains from a single 3D acquisition of apical views in a healthy adult. Bull's eye charts represent regional strain in each myocardial segment with global strain calculated at bottom left corner of each parameter (10).

#### 5- Rotation, Twist and torsion:

Rotation, twist and torsion are parameters used to study the LV twist mechanics.

**Rotation** refers to the angle of deformation measured on a short-axis LV plane and is expressed in degrees. Positive values represent anticlockwise rotation (as viewed from the apex), while negative values are used for clockwise rotation.

**Twist** refers to the absolute difference of rotation between base and apex.

**Torsion** is calculated by dividing LV twist by the length of the LV to allow comparability of LV twist in ventricles of different sizes (10).

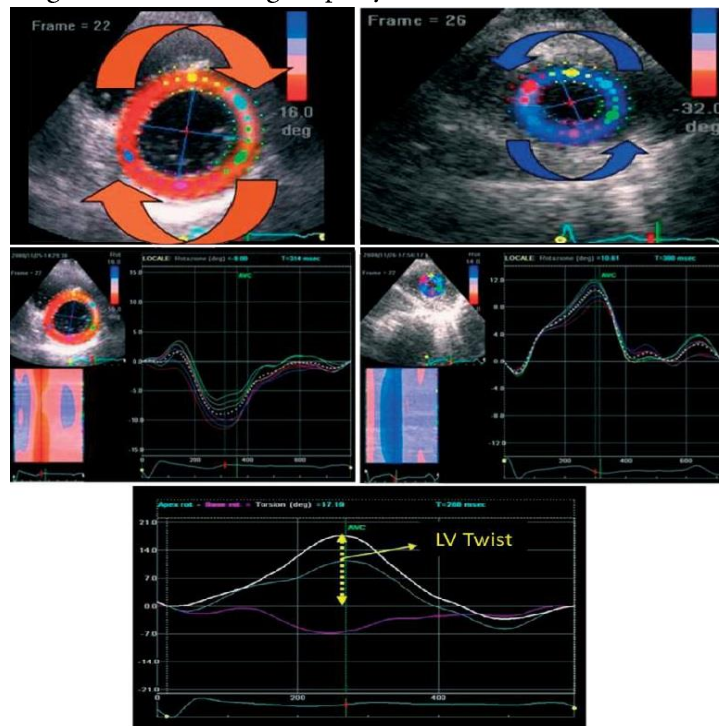
#### 6- Untwisting:

Untwisting's significance in diastolic LV filling mechanics has recently gotten a lot of attention. Untwisting velocity is regarded to be a vital first expression of active relaxation, making it useful for studying diastole and, in particular, isovolumic relaxation, because it appears to be less load-dependent than other diastolic measures (20).

#### Advent of three-dimensional STE

To obtain all strain components using two-dimensional (2D) STE, at least six acquisitions of different parasternal and apical LV views are required to obtain all strain components in all LV segments. This can be an issue in certain experimental and clinical situations, particularly when

heart rate or LV loading conditions change rapidly due to non-simultaneous data acquisition



(21).

**Figure 4:** Graphic representation of LV rotational dynamics. Rotation of cardiac base (left) and apex (right). The lower panel represents a diagram of LV twisting measurement as the net difference between mean apical and basal rotation (8).

Furthermore, 2D STE relies on the assumption that speckles are moving within the scan plane of the 2D image in the consecutive frames of the cardiac cycle. However, since LV deformation involves a combination of apex-to-base shortening and thickening with simultaneous twisting, speckles have a complex motion in the 3D space and the whole heart moves through the 2D plane of interest. Therefore, the 2D plane of interest may disappear through a cardiac cycle, this is caused by the fact that longitudinal motion is not detected in parasternal short axis (PSAX) view and circumferential motion is not detected in apical views, which is well known as the 'out of plane motion' (10).

With developments in ultrasound transducer technology and both hardware and software computing, systems capable of acquiring 3D images with reasonable spatial and temporal resolution are now widely available. The ability to estimate true 3D myocardial motion and deformation using 3D STE approach may provide cardiologists with a better view of regional myocardial mechanics, which may be important for diagnosis, prognosis, and therapy (22).

As 3DE does not rely on geometric assumptions about LV shape and allows assessment of LV volumes, LV ejection fraction, and all strain components within a single data set acquisition, it has overcome most of the 2D echocardiographic limitations (23). Accuracy of 3DE is similar to that of CMR (24). Compared with conventional 2D echocardiography, 3DE has better intra-observer, inter-observer reproducibility and test–retest variability. Accordingly, the recent guidelines on chamber quantification from American society of echocardiography (ASE) and European association of cardiovascular imaging (EACVI) recommend assessing and monitoring LV volumes

and function with 3D echocardiography when feasible depending on image quality and the experience of the laboratory (25) particularly in cancer patients (26).

### Advantages of 3D STE

#### Time saving

3D approaches can measure all strain components in all LV segments from a single acquisition. A 3D volume acquisition with the probe on cardiac apex can generate all apical and short axis views simultaneously (27).

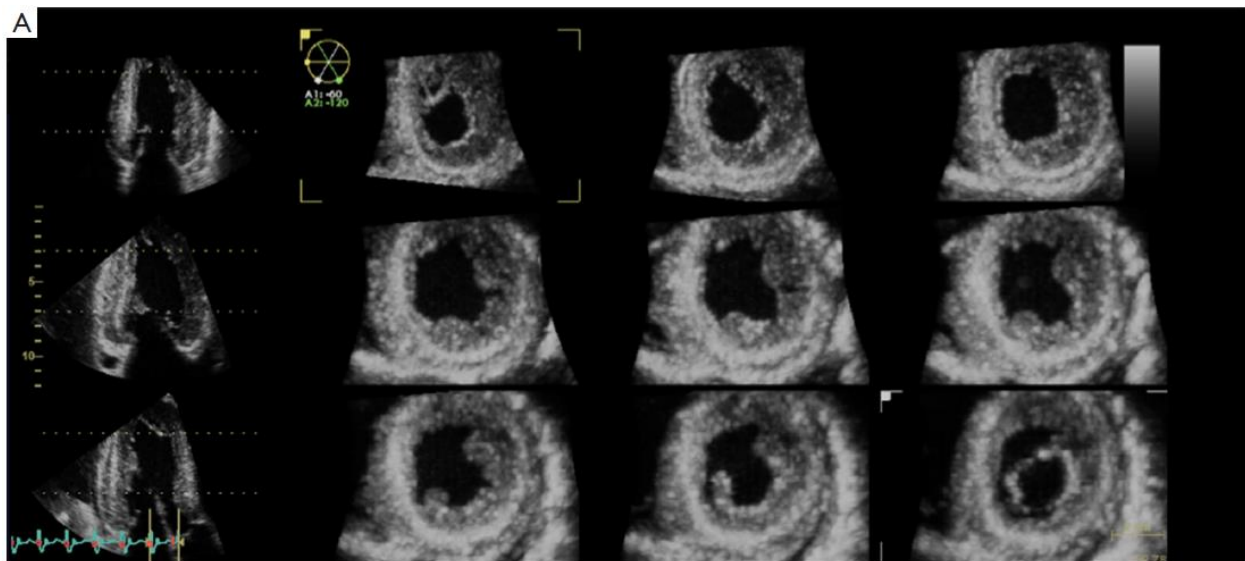


Figure 5: 3D image acquisition with the transducer on apex showing simultaneous acquisition of apical four, two and three chamber views and nine cuts of parasternal short axis view (10).

#### Imaging plane independent

2D STE is angle independent, however, it's still limited by out of plane motion. On the other hand, 3D STE is imaging plane independent and still follows myocardial segments even if they move out of the 2D plane due to its ability of generating 3D volumes, therefore, 3D STE does not suffer from strain estimation errors associated with out-of-plane motion, and may in theory allow more precise calculations of LV strains (21).

#### Performance at lower frame rate

3D STE allows quantification of strain parameters at a relatively lower frame rate compared to 2D STE. This may be attributed to the ability of 3D imaging to acquire complex ventricular systolic mechanics without the limitations imposed by out-of-plane motion (28).

#### Calculation of novel parameters

As area strain combines longitudinal strain that is measured from apical views and circumferential strain that is measured from SAX views, it can only be measured by 3D STE which can acquire these data simultaneously (10). Area strain is more sensitive to changes in regional deformation

compared with circumferential and longitudinal strains. The sensitivity of area strain may be created by combining the deformation data in 2 orthogonal directions, thus, it can reduce the tracking error because of higher signal-noise ratio compared with that of circumferential and longitudinal strain, subsequently, area strain may be a more reliable parameter of myocardial deformation (18).

Furthermore, more accurate LV torsion values can be calculated through the simultaneous measurement of rotations in each short-axis plane and the distance between the planes. Therefore, the novel parameter of regional torsion is measurable and represents the spatial distribution of torsion values (29).

### Reproducibility

Intra- or inter-observer variability occurs to some extent in strain measurements. The intra- and interobserver variabilities of 3D STE are better than that of 2D STE, despite the complex computations of 3D STE. This may be related to the full-volume data acquisitions and automatic or semi-automatic measurement (23).

The variability is greater for radial strain values than for other parameters (30). In clinical studies also, reproducibility of radial strain is lower than for longitudinal, circumferential, and area strains. The absolute differences of radial strain between 2 repeated measurements were greater than 10%. In contrast, intra-observer variabilities of longitudinal, circumferential, and area strains were less than 10%, and inter-observer variabilities were approximately 10%. Among them, the best reproducibility was revealed for area strain measurements. All studies reported that both intra- and interobserver variabilities were  $\leq 8\%$  (11).

### Reference ranges for normal left ventricular function and strain by 3D echocardiography

To date, the largest study of normal LV function by 3D echocardiography is the NORRE study (Normal Reference Ranges for Echocardiography) by EACVI where a total of 440 healthy participant (mean age:  $45 \pm 13$  years) were enrolled at 22 collaborating institutions to study LV function by 3D echocardiography analyzed with a vendor-independent software package (4D LV Function, TomTec Imaging Systems version 2.0, Unterschleissheim, Germany) allowing homogeneous measurements regardless of the echocardiographic machine used to acquire the data sets (23). Normal reference ranges for 3D LV volumes, 3D ejection fraction, and 3D global longitudinal, circumferential, area and radial strains are shown in table 1.

Table 1 Normal reference ranges for 3D LV volumes, 3D ejection fraction, and 3D global longitudinal, circumferential, area and radial strains adopted from the NORRE study by EACVI (23)

Parameters	Total, Mean $\pm$ SD	Interquartile range (25%–75%)	Male, mean $\pm$ SD	Interquartile range (25%–75%)	Female, mean $\pm$ SD	Interquartile range (25%–75%)	P value*
LV end-diastolic volume, mL	115.6 $\pm$ 29.6	93.1–132.3	133.3 $\pm$ 30.5	114.2–150.2	102.5 $\pm$ 20.8	87.4–114.2	<0.001
LV end-systolic volume, mL	47.1 $\pm$ 13.7	36.6–55.3	55.4 $\pm$ 13.9	45.4–63.0	41.0 $\pm$ 9.9	33.6–48.5	<0.001
LV ejection fraction, %	59.4 $\pm$ 4.6	55.9–62.5	58.5 $\pm$ 4.3	54.9–61.6	60.1 $\pm$ 4.6	56.7–63.2	<0.001
Normalized to BSA							
LV end-diastolic volume, mL/m <sup>2</sup>	63.9 $\pm$ 12.9	54.8–72.0	68.7 $\pm$ 14.0	58.6–77.2	60.4 $\pm$ 10.8	52.7–67.1	<0.001
LV end-systolic volume, mL/m <sup>2</sup>	26.0 $\pm$ 6.2	21.3–29.7	28.5 $\pm$ 6.5	24.4–32.6	24.1 $\pm$ 5.3	20.4–27.5	<0.001
Longitudinal strain, %	-21.0 $\pm$ 2.6	-19.0 to 22.7	-20.4 $\pm$ 2.7	-18.6 to 22	-21.4 $\pm$ 2.4	-19.5 to 22.9	<0.001
Circumferential strain, %	-30.3 $\pm$ 4.0	-27.4 to 33.0	-29.7 $\pm$ 3.9	-27.0 to 32.5	-30.7 $\pm$ 4.1	-27.6 to 33.3	0.012
Area strain, %	-36.5 $\pm$ 3.9	-33.8 to 39.2	-36.0 $\pm$ 3.9	-33.2 to 38.9	-37.0 $\pm$ 3.8	-34.4 to 39.4	0.008
Radial strain, %	43.2 $\pm$ 4.5	40.0 to 46.2	42.1 $\pm$ 4.6	38.8 to 45.2	43.9 $\pm$ 4.3	40.7–46.7	<0.001

BSA; body surface area, LV; left ventricle, SD; standard deviation \*P value is for difference between males and females.

The study noted that Upper limits of LV end-diastolic and end-systolic volumes were larger in men (97 and 42 mL/m<sup>2</sup>) than in women (82 and 35 mL/m<sup>2</sup>; P<0.0001). Conversely, lower limits of LV ejection fraction were higher in women than in men (51% vs. 50%; P<0.01). Similarly, all strain components were higher in women than in men. Lower range was -18.6% in men and -19.5% in women for 3D longitudinal strain, -27.0% and -27.6% for 3D circumferential strain, -33.2% and -34.4% for 3D Area strain and 38.8% and 40.7% for 3D radial strain, respectively. LV volumes decreased with age in both genders (P<0.0001), whereas LV ejection fraction increased with age only in men. Among 3DE LV strain components, the only one, which did not change with age was longitudinal strain (23).

Additionally, other studies evaluating normal ranges of left ventricular strain parameters by 3D STE among healthy individuals are shown in table 2 (31) (32) (33) and (34). These studies used different scanners and software algorithms to compute 3D strain. This aspect confirms the suboptimal intervendor agreement for strain measurement and the resulting need of development of specific reference values of the strain components for each ultrasound system (35).

Table 2: Different studies of normal ranges of left ventricular strain parameters by 3D STE among healthy individuals.

Author	Number population (age range)	Ultrasound system	3DSTE software	3D global longitudinal strain	3D global circumferential strain	3D global radial strain	3D area strain (or 3D principal tangential strain <sup>^</sup> )
Kleijn <i>et al.</i> [2015] (41)	303 [18–82]	Artida 4D (Toshiba Medical Systems)	Toshiba Medical Systems	-15.9 $\pm$ 2.4	-30.6 $\pm$ 2.6	35.6 $\pm$ 10.3	-42.0 $\pm$ 2.4
Muraru <i>et al.</i> [2014] (18)	265 [18–76]	Vivid E9 scanner (GE Vingmed Ultrasound)	4D AutoLVQ (EchoPac BT12 and 13, GE Vingmed Ultrasound)	-19 [-21, -17]*	-18 [-20, -17]*	52 [47–59]*	-33 [-36, -31]*
Muraru <i>et al.</i> [2014] (18)	265 [18–76]	Vivid E9 scanner (GE Vingmed Ultrasound)	4D LV Analysis (TomTec Imaging Systems)	-20 [-23, -18]*	-28 [-31, -25]*	41 [36–44]*	-32 [-35, -29]*
Kaku <i>et al.</i> [2014] (40)	313 [1–88]	Sonos 7500 or iE33 scanner (Philips Medical Systems)	4D LV Analysis (TomTec Imaging Systems)	-20.3 $\pm$ 3.2	-28.9 $\pm$ 4.6	-	-37.6 $\pm$ 4.8
Pérez de Isla <i>et al.</i> [2011] (43)	60 [23–53]	Artida 4D (Toshiba Medical Systems)	Toshiba Medical Systems	-	-	-	-38.8 $\pm$ 5.8

## Limitations of 3D STE

### B-Mode Image Quality

The accuracy of STE measurements strongly depends on the B-mode image quality. Because 3D datasets are acquired from the cardiac apex, image quality in the anterior and anterolateral regions are poorer than in other regions, which affects the reliability of the strain data. Accordingly, caution needs to be taken when interpreting strain data in a segment with poor B-mode image quality (36).

### Temporal resolution

3D-STE has a limitation of temporal resolution. The strain value may be underestimated in conditions of inappropriately lower frame rate because the tracking points to obtain accurate maximum and minimum myocardial lengths may be lost. However, compared with earlier systems the latest systems have a relatively higher frame rate of more than 50 volume/s, but a higher than necessary frame rate degrades the image quality, which causes tracking errors (37).

### Artifacts

Because full-volume LV datasets comprise multiple sectors, the artifact occurring around the border between sectors, primarily caused by breathing, may affect the reliability of speckle tracking (11).

### Beat to beat variations

The system is not suitable for use in patients with beat-to-beat variability, mainly atrial fibrillation. To overcome this limitation, recent advanced systems allow the entire 3D dataset to be obtained from a single beat (11).

### Vendor-dependent variability

Another important issue is the vendor-dependent variability of deformation data (35). As with 2D-STE, the high vendor dependence of 3D-STE data means that inter-vendor discordance of data must be taken into account when interpreting 3D deformation data (38).

## Clinical applications of 3D STE

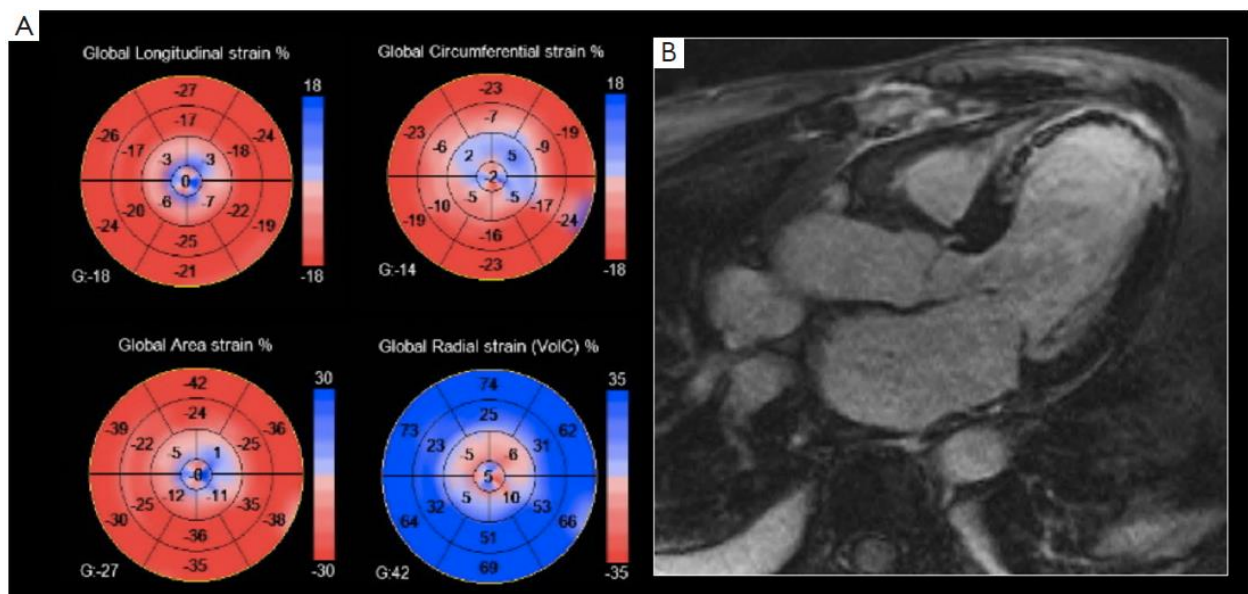
According to the most recent literature, 3D STE popularity is increasing and research studies continue to explore its clinical added value over conventional 2D STE. The following are among the various clinical applications of 3D STE.

### 1- Coronary artery disease

Assessment of regional wall motion continues to be an issue in the clinical setting, as a considerable amount of training is needed and interobserver differences continue to exist in spite of good image quality (39). Area strain derived by 3DSTE, as an objective measure of regional wall motion abnormalities (WMA), has been shown to be accurate and reproducible when compared with the visual wall motion assessment by experienced echocardiographers (40). However, despite a good agreement between area strain values and expert wall motion score evaluation to discriminate normal and akinetic segments, there was a substantially lower agreement for hypokinetic segments, as expected. This fact may be attributable to the subjectivity in wall motion score evaluation or to

the possibility that 3D area strain is a more sensitive index of regional ischemia than regional WMA (40). Because 3D area strain quantification is semi-automated, more objective and reproducible, and requires less training, it emerges as an attractive tool to identify regional WMA in patients with suspected or known coronary artery disease (10).

While LVEF is well known as an important prognostic factor in patients who survive a myocardial infarction (MI), myocardial strain, assessed by STE, has been found to further improve prognostic risk stratification (41). Recent data has shown that both 2DSTE and 3DSTE can be helpful in predicting LV remodeling and in stratifying risk after acute MI (42). The evaluation of 3D global longitudinal strain enabled to identify patients with massive MI size (>12% of the LV mass) compared to single photon emission computed tomography (SPECT) (43). This concept is further supported by comparisons with late gadolinium enhancement CMR, in which 3D global longitudinal strain and area strain have been found to closely correlate with infarct size (44).



**Figure 6: Correlation between 3D STE strain parameters (A) and CMR late gadolinium enhancement images (B) in a patient with previous anterior myocardial infarction, both techniques are showing involvement of apical segments and mid septum (10).**

3D area strain has been found to be independently associated with increased risk of death or heart failure after acute MI, suggesting that it can be a useful prognostic parameter in this setting (42). 3D area strain was also the most accurate among the various 3D strain parameters for predicting myocardial viability identified by SPECT and positron emission tomography (PET) imaging (45).

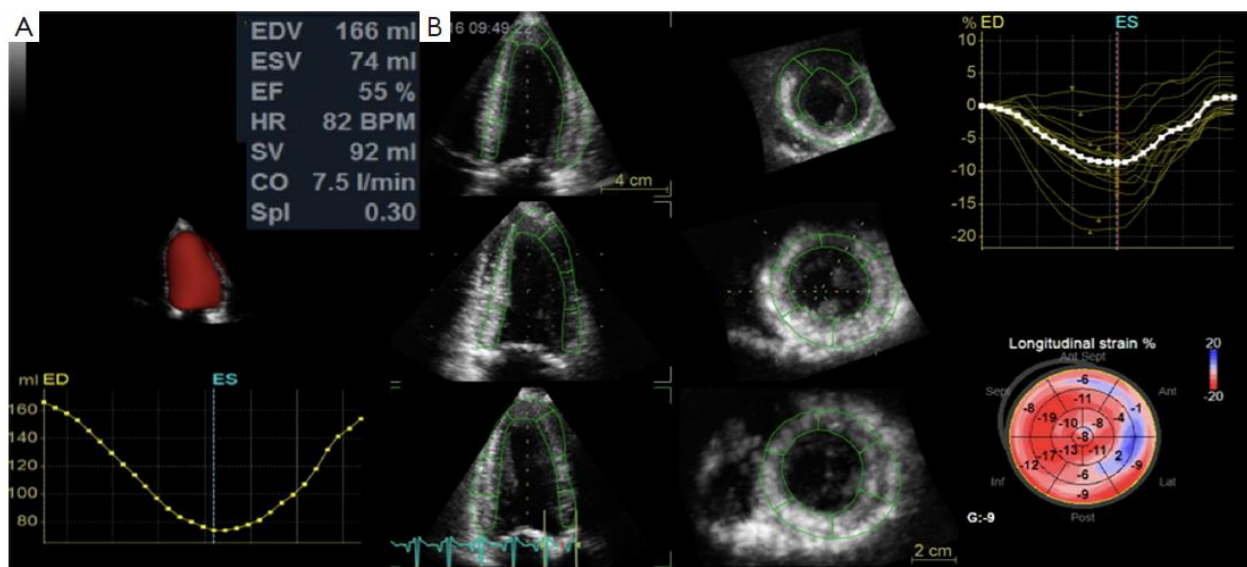
## 2- Valvular heart disease

3DSTE derived strain may be useful to refine the assessment of cardiac performance, which is of utmost importance in patients with valvular heart disease, as the detection of subclinical LV myocardial dysfunction may aid in deciding the timing of surgical or interventional treatment. However, only a few published studies limited to left-sided valve diseases have reported on the added value of 3DSTE.

In aortic stenosis (AS), survival drops significantly after symptom onset. Thus, 2D longitudinal strain has been proposed as an early marker of LV dysfunction in asymptomatic patients with severe AS, in order to optimize the timing of intervention in these patients. LV strain parameters measured by 3DSTE, particularly global longitudinal strain (46), were shown to be useful indices of early-stage LV myocardial dysfunction in patients with AS. In a study of 104 asymptomatic patients with severe AS and preserved LVEF, it was reported that LV global longitudinal strain using either 2D STE or 3D STE was associated with increased risk of adverse events. However, after correcting for mean gradient and LV mass index at multivariable analysis, 3D longitudinal strain was found to be the only independent predictor of future adverse events, with an optimal cut-off value of  $-14.5\%$  (47).

In asymptomatic patients with severe aortic regurgitation, it was found that 3D global circumferential strain compensates for the reduction in 3D longitudinal strain for preserving the LVEF (48).

Further supporting the clinical use of 3DSTE, 3D strain was reported to be an independent predictor of acute and long-term clinical outcomes after cardiac surgery (49). 3DSTE was feasible, reproducible and time saving for assessing LV systolic function in patients before and after transcatheter aortic valve implantation (50).



**Figure 7: 3D STE analysis in a patient with severe AS and preserved EF (LVEF=55%) (A), 3D GLS is markedly impaired (-9%) despite preserved LVEF (10).**

In severe chronic mitral regurgitation (MR), guidelines recommend intervening on symptomatic patients or when LVEF drops below 60% (51). However, in patients with severe MR and LVEF still within normal range, subclinical LV dysfunction may be unrecognized (52). It was demonstrated that 2DSTE-derived LV global longitudinal strain may be useful to identify a maladaptive preload-related change associated with the risk for a substantial reduction in LVEF immediately following mitral valve repair (53).

At present, few studies have looked at the role of 3DSTE in patients with MR. In patients with MR with preserved LVEF, 3D area strain was shown to be an independent predictor of early

symptoms or LV dysfunction (52). Preliminary results in patients with functional MR undergoing MitraClip procedure showed that 3DSTE could predict an unfavorable outcome and persistence of symptoms after the procedure (54).

### 3- Cardiac resynchronization therapy (CRT)

Despite the discouraging results of the PROSPECT trial (Predictors of Response to Cardiac Resynchronization Therapy trial) (55), interest has built in the use of advanced echocardiographic imaging to select patients that would benefit from CRT. The systolic dyssynchrony index (SDI) derived from segmental 3D volume curves of all 16/17 segments of the LV was shown to be useful for this purpose (56).

3DSTE offers the advantage to directly assess and quantify myocardial deformation in individual LV segments, rather than the segmental volume changes provided by 3D echocardiography. By building 3DSTE time-strain curves of the 16/17 LV segments, quantitative information on both the timing and the magnitude of peak segmental strain can be obtained, which may improve prediction of response to CRT (57). The sites of latest mechanical activation of LV can also be identified, suggesting that 3DSTE might be useful to guide lead positioning in CRT patients (58).

### 4- Hypertrophic cardiomyopathy (HCM)

3DSTE has provided insights into LV mechanics, showing evidence of increased twist, preserved circumferential and decreased longitudinal strain in the setting of hypertrophic cardiomyopathy (59). Due to its ability to estimate separately LV 3D strain in different directions in a practical and clinically-feasible manner, 3DSTE could allow the early detection of myocardial function impairment, before a reduction in LVEF occurs. 3D STE could help to differentiate between early hypertrophic cardiomyopathy and adaptative changes due to athletic training (10).

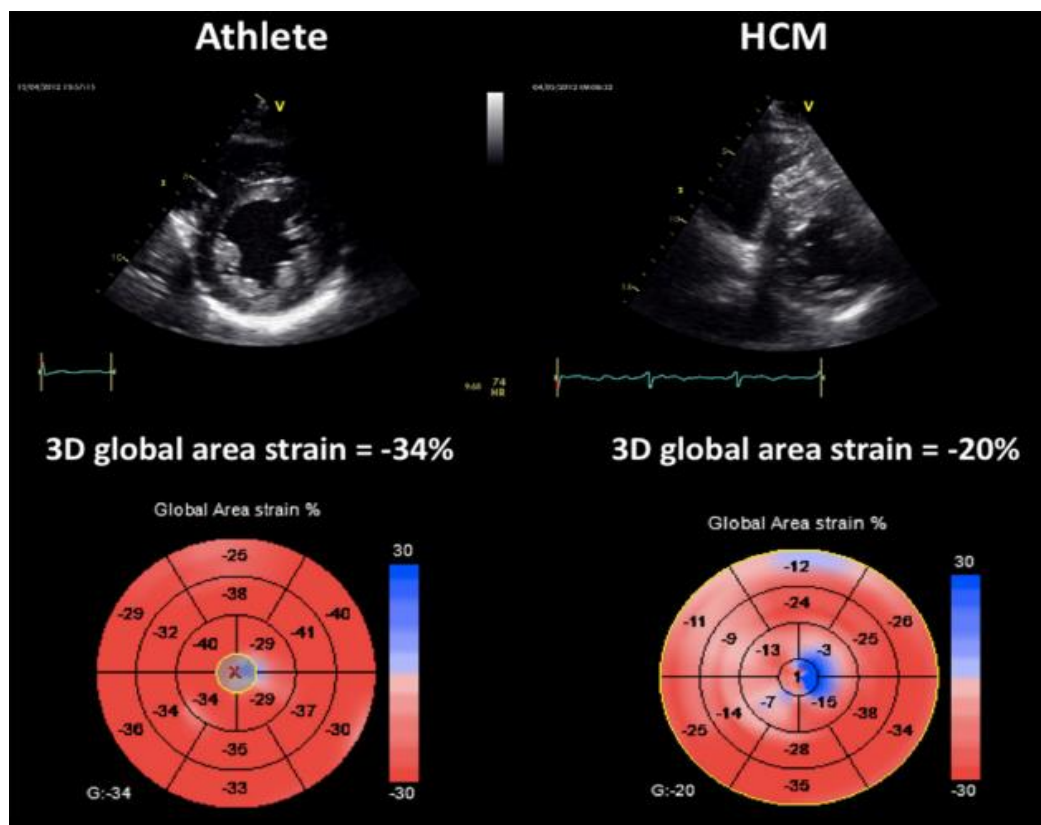


Figure 8: 3D area strain in an athlete having normal area strain values (left) and HCM patient with marked reduction in global area strain due to impaired deformation of hypertrophied septal and apical segments (right) (10).

Furthermore, as both hypertrophic cardiomyopathy and amyloidosis may present with increased LV wall thickness by conventional echocardiography, 3D strain might be used to identify characteristic strain patterns to support in the differential diagnosis (60).

Since 3D echocardiography allows to avoid foreshortening of LV apex, 3D strain can also be useful to confirm the apical form of hypertrophic cardiomyopathy, by showing a decreased magnitude of myocardial deformation in the apical segments (10).

## References

1. D'hooge J, Heimdal A, Jamal F, Kukulski T, Bijnens B, Rademakers F, et al. Regional strain and strain rate measurements by cardiac ultrasound: principles, implementation and limitations. *European Journal of Echocardiography*. 2000;1(3):154-70.
2. Amundsen BH, Helle-Valle T, Edvardsen T, Torp H, Crosby J, Lyseggen E, et al. Noninvasive myocardial strain measurement by speckle tracking echocardiography: validation against sonomicrometry and tagged magnetic resonance imaging. *Journal of the American College of Cardiology*. 2006;47(4):789-93.
3. Støylen A. Strain rate imaging of the left ventricle by ultrasound: Feasibility, clinical validation and physiological aspects. 2001.

4. Pislaru C, Abraham TP, Belohlavek M. Strain and strain rate echocardiography. *Current opinion in cardiology*. 2002;17(5):443-54.
5. Gorcsan J, Tanaka H. Echocardiographic assessment of myocardial strain. *Journal of the American College of Cardiology*. 2011;58(14):1401-13.
6. Marwick TH. Measurement of strain and strain rate by echocardiography: ready for prime time? *Journal of the American College of cardiology*. 2006;47(7):1313-27.
7. Geyer H, Caracciolo G, Abe H, Wilansky S, Carerj S, Gentile F, et al. Assessment of myocardial mechanics using speckle tracking echocardiography: fundamentals and clinical applications. *Journal of the American Society of Echocardiography*. 2010;23(4):351-69.
8. Mondillo S, Galderisi M, Mele D, Cameli M, Lomoriello VS, Zacà V, et al. Speckle-tracking echocardiography: a new technique for assessing myocardial function. *Journal of Ultrasound in Medicine*. 2011;30(1):71-83.
9. Sengupta PP, Korinek J, Belohlavek M, Narula J, Vannan MA, Jahangir A, et al. Left ventricular structure and function: basic science for cardiac imaging. *Journal of the American College of Cardiology*. 2006;48(10):1988-2001.
10. Muraru D, Niero A, Rodriguez-Zanella H, Cherata D, Badano L. Three-dimensional speckle-tracking echocardiography: benefits and limitations of integrating myocardial mechanics with three-dimensional imaging. *Cardiovascular diagnosis and therapy*. 2018;8(1):101.
11. Seo Y, Ishizu T, Atsumi A, Kawamura R, Aonuma K. Three-Dimensional Speckle Tracking Echocardiography—A Promising Tool for Cardiac Functional Analysis—. *Circulation Journal*. 2014;78(6):1290-301.
12. Crozier A, Augustin C, Neic A, Prassl A, Holler M, Fastl T, et al. Image-based personalization of cardiac anatomy for coupled electromechanical modeling. *Annals of biomedical engineering*. 2016;44:58-70.
13. Lorenz CH, Pastorek JS, Bundy JM. Function: delineation of normal human left ventricular twist throughout systole by tagged cine magnetic resonance imaging. *Journal of Cardiovascular Magnetic Resonance*. 2000;2(2):97-108.
14. Buckberg G, Hoffman JI, Mahajan A, Saleh S, Coghlan C. Cardiac mechanics revisited: the relationship of cardiac architecture to ventricular function. *Circulation*. 2008;118(24):2571-87.
15. Burns AT, La Gerche A, Prior DL, MacIsaac AI. Left ventricular untwisting is an important determinant of early diastolic function. *JACC: Cardiovascular Imaging*. 2009;2(6):709-16.
16. Biswas M, Sudhakar S, Nanda NC, Buckberg G, Pradhan M, Roomi AU, et al. Two-and three-dimensional speckle tracking echocardiography: clinical applications and future directions. *Echocardiography*. 2013;30(1):88-105.

17. Park J-H. Two-dimensional Echocardiographic Assessment of Myocardial Strain: Important Echocardiographic Parameter Readily Useful in Clinical Field. *Korean Circ J.* 2019;49(10):908-31.
18. Seo Y, Ishizu T, Enomoto Y, Sugimori H, Aonuma K. Endocardial surface area tracking for assessment of regional LV wall deformation with 3D speckle tracking imaging. *JACC: Cardiovascular Imaging.* 2011;4(4):358-65.
19. Reant P, Barbot L, Touche C, Dijos M, Arsac F, Pillois X, et al. Evaluation of global left ventricular systolic function using three-dimensional echocardiography speckle-tracking strain parameters. *Journal of the American Society of Echocardiography.* 2012;25(1):68-79.
20. Shibata S, Hirabuki K, Hata N, Suzuki R, Suda T, Uechi T, et al. Pivotal role of heart for orthostasis: left ventricular untwisting mechanics and physical fitness. *Exercise and Sport Sciences Reviews.* 2021;49(2):88-98.
21. Jasaityte R, Heyde B, D'hooge J. Current state of three-dimensional myocardial strain estimation using echocardiography. *Journal of the American Society of Echocardiography.* 2013;26(1):15-28.
22. Crosby J, Amundsen BH, Hergum T, Remme EW, Langeland S, Torp H. 3-D speckle tracking for assessment of regional left ventricular function. *Ultrasound in medicine & biology.* 2009;35(3):458-71.
23. Bernard A, Addetia K, Dulgheru R, Caballero L, Sugimoto T, Akhaladze N, et al. 3D echocardiographic reference ranges for normal left ventricular volumes and strain: results from the EACVI NORRE study. *European Heart Journal–Cardiovascular Imaging.* 2017;18(4):475-83.
24. Dorosz JL, Lezotte DC, Weitzenkamp DA, Allen LA, Salcedo EE. Performance of 3-dimensional echocardiography in measuring left ventricular volumes and ejection fraction: a systematic review and meta-analysis. *Journal of the American College of Cardiology.* 2012;59(20):1799-808.
25. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *European Heart Journal-Cardiovascular Imaging.* 2015;16(3):233-71.
26. Plana JC, Galderisi M, Barac A, Ewer MS, Ky B, Scherrer-Crosbie M, et al. Expert consensus for multimodality imaging evaluation of adult patients during and after cancer therapy: a report from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *European Heart Journal–Cardiovascular Imaging.* 2014;15(10):1063-93.

27. Elen A, Choi HF, Loeckx D, Gao H, Claus P, Suetens P, et al. Three-dimensional cardiac strain estimation using spatio-temporal elastic registration of ultrasound images: A feasibility study. *IEEE transactions on medical imaging*. 2008;27(11):1580-91.
28. Yodwut C, Weinert L, Klas B, Lang RM, Mor-Avi V. Effects of frame rate on three-dimensional speckle-tracking-based measurements of myocardial deformation. *Journal of the American Society of Echocardiography*. 2012;25(9):978-85.
29. Evangelista A, Nardinocchi P, Puddu P, Teresi L, Torromeo C, Varano V. Torsion of the human left ventricle: experimental analysis and computational modeling. *Progress in biophysics and molecular biology*. 2011;107(1):112-21.
30. Seo Y, Ishizu T, Enomoto Y, Sugimori H, Yamamoto M, Machino T, et al. Validation of 3-dimensional speckle tracking imaging to quantify regional myocardial deformation. *Circulation: Cardiovascular Imaging*. 2009;2(6):451-9.
31. Kleijn SA, Pandian NG, Thomas JD, Perez de Isla L, Kamp O, Zuber M, et al. Normal reference values of left ventricular strain using three-dimensional speckle tracking echocardiography: results from a multicentre study. *European Heart Journal-Cardiovascular Imaging*. 2015;16(4):410-6.
32. Muraru D, Cucchini U, Mihăilă S, Miglioranza MH, Aruta P, Cavalli G, et al. Left ventricular myocardial strain by three-dimensional speckle-tracking echocardiography in healthy subjects: reference values and analysis of their physiologic and technical determinants. *Journal of the American Society of Echocardiography*. 2014;27(8):858-71. e1.
33. Kaku K, Takeuchi M, Tsang W, Takigiku K, Yasukochi S, Patel AR, et al. Age-related normal range of left ventricular strain and torsion using three-dimensional speckle-tracking echocardiography. *Journal of the American Society of Echocardiography*. 2014;27(1):55-64.
34. de Isla LP, Millán M, Lennie V, Quezada M, Guinea J, Macaya C, et al. Area strain: normal values for a new parameter in healthy people. *Revista Española de Cardiología (English Edition)*. 2011;64(12):1194-7.
35. Badano LP, Cucchini U, Muraru D, Al Nono O, Sarais C, Iliceto S. Use of three-dimensional speckle tracking to assess left ventricular myocardial mechanics: inter-vendor consistency and reproducibility of strain measurements. *European Heart Journal-Cardiovascular Imaging*. 2013;14(3):285-93.
36. Kawamura R, Seo Y, Ishizu T, Atsumi A, Yamamoto M, Machino-Ohtsuka T, et al. Feasibility of left ventricular volume measurements by three-dimensional speckle tracking echocardiography depends on image quality and degree of left ventricular enlargement: validation study with cardiac magnetic resonance imaging. *Journal of cardiology*. 2014;63(3):230-8.
37. Negishi K, Negishi T, Agler DA, Plana JC, Marwick TH. Role of temporal resolution in selection of the appropriate strain technique for evaluation of subclinical myocardial dysfunction. *Echocardiography*. 2012;29(3):334-9.

38. Gayat E, Ahmad H, Weinert L, Lang RM, Mor-Avi V. Reproducibility and inter-vendor variability of left ventricular deformation measurements by three-dimensional speckle-tracking echocardiography. *Journal of the American Society of Echocardiography*. 2011;24(8):878-85.
39. Hoffmann R, von Bardeleben S, Kasprzak JD, Borges AC, ten Cate F, Firschke C, et al. Analysis of regional left ventricular function by cineventriculography, cardiac magnetic resonance imaging, and unenhanced and contrast-enhanced echocardiography: a multicenter comparison of methods. *Journal of the American College of Cardiology*. 2006;47(1):121-8.
40. Ternacle J, Gallet R, Champagne S, Teiger E, Gellen B, Randé J-LD, et al. Changes in three-dimensional speckle-tracking-derived myocardial strain during percutaneous coronary intervention. *Journal of the American Society of Echocardiography*. 2013;26(12):1444-9.
41. Ersbøll M, Valeur N, Mogensen UM, Andersen MJ, Møller JE, Velazquez EJ, et al. Prediction of all-cause mortality and heart failure admissions from global left ventricular longitudinal strain in patients with acute myocardial infarction and preserved left ventricular ejection fraction. *Journal of the American College of Cardiology*. 2013;61(23):2365-73.
42. Shin SH, Suh YJ, Baek YS, Lee MJ, Park SD, Kwon SW, et al. Impact of area strain by 3D speckle tracking on clinical outcome in patients after acute myocardial infarction. *Echocardiography*. 2016;33(12):1854-9.
43. Wang Q, Zhang C, Huang D, Zhang L, Yang F, An X, et al. Evaluation of myocardial infarction size with three-dimensional speckle tracking echocardiography: a comparison with single photon emission computed tomography. *The International Journal of Cardiovascular Imaging*. 2015;31:1571-81.
44. Hayat D, Kloeckner M, Nahum J, Ecochard-Dugelay E, Dubois-Randé J-L, Jean-François D, et al. Comparison of real-time three-dimensional speckle tracking to magnetic resonance imaging in patients with coronary heart disease. *The American journal of cardiology*. 2012;109(2):180-6.
45. Ran H, Zhang P-Y, Zhang Y-X, Zhang J-X, Wu W-F, Dong J, et al. Assessment of Left Ventricular Myocardial Viability by 3-Dimensional Speckle-Tracking Echocardiography in Patients With Myocardial Infarction. *Journal of Ultrasound in Medicine*. 2016;35(8):1631-8.
46. Li C-m, Li C, Bai W-j, Zhang X-l, Tang H, Qing Z, et al. Value of three-dimensional speckle-tracking in detecting left ventricular dysfunction in patients with aortic valvular diseases. *Journal of the American Society of Echocardiography*. 2013;26(11):1245-52.
47. Nagata Y, Takeuchi M, Wu VC-C, Izumo M, Suzuki K, Sato K, et al. Prognostic value of LV deformation parameters using 2D and 3D speckle-tracking echocardiography in asymptomatic patients with severe aortic stenosis and preserved LV ejection fraction. *Cardiovascular Imaging*. 2015;8(3):235-45.

48. Broch K, de Marchi SF, Massey R, Hisdal J, Aakhus S, Gullestad L, et al. Left ventricular contraction pattern in chronic aortic regurgitation and preserved ejection fraction: simultaneous stress-strain analysis by three-dimensional echocardiography. *Journal of the American Society of Echocardiography*. 2017;30(4):422-30. e2.
49. Howard-Quijano K, Salem A, Barkulis C, Mazor E, Scovotti JC, Ho JK, et al. Preoperative three-dimensional strain imaging identifies reduction in left ventricular function and predicts outcomes after cardiac surgery. *Anesthesia & Analgesia*. 2017;124(2):419-28.
50. Schueler R, Sinning J-M, Momcilovic D, Weber M, Ghanem A, Werner N, et al. Three-dimensional speckle-tracking analysis of left ventricular function after transcatheter aortic valve implantation. *Journal of the American Society of Echocardiography*. 2012;25(8):827-34. e1.
51. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease: developed by the Task Force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *European heart journal*. 2022;43(7):561-632.
52. Casas-Rojo E, Fernández-Golfín C, Moya-Mur JL, González-Gómez A, García-Martín A, Morán-Fernández L, et al. Area strain from 3D speckle-tracking echocardiography as an independent predictor of early symptoms or ventricular dysfunction in asymptomatic severe mitral regurgitation with preserved ejection fraction. *The international journal of cardiovascular imaging*. 2016;32:1189-98.
53. Pandis D, Sengupta PP, Castillo JG, Caracciolo G, Fischer GW, Narula J, et al. Assessment of longitudinal myocardial mechanics in patients with degenerative mitral valve regurgitation predicts postoperative worsening of left ventricular systolic function. *Journal of the American Society of Echocardiography*. 2014;27(6):627-38.
54. Vitarelli A, Mangieri E, Capotosto L, Tanzilli G, D'Angeli I, Viceconte N, et al. Assessment of biventricular function by three-dimensional speckle-tracking echocardiography in secondary mitral regurgitation after repair with the MitraClip system. *Journal of the American Society of Echocardiography*. 2015;28(9):1070-82.
55. Bax JJ, Gorcsan J. Echocardiography and noninvasive imaging in cardiac resynchronization therapy: results of the PROSPECT (Predictors of Response to Cardiac Resynchronization Therapy) study in perspective. *Journal of the American College of Cardiology*. 2009;53(21):1933-43.
56. Kleijn SA, Aly MF, Knol DL, Terwee CB, Jansma EP, Abd El-Hady YA, et al. A meta-analysis of left ventricular dyssynchrony assessment and prediction of response to cardiac resynchronization therapy by three-dimensional echocardiography. *European Heart Journal—Cardiovascular Imaging*. 2012;13(9):763-75.

57. Tatsumi K, Tanaka H, Tsuji T, Kaneko A, Ryo K, Yamawaki K, et al. Strain dyssynchrony index determined by three-dimensional speckle area tracking can predict response to cardiac resynchronization therapy. *Cardiovascular Ultrasound*. 2011;9:1-9.
58. Tanaka H, Hara H, Saba S, Gorcsan III J. Usefulness of three-dimensional speckle tracking strain to quantify dyssynchrony and the site of latest mechanical activation. *The American journal of cardiology*. 2010;105(2):235-42.
59. Voilliot D, Huttin O, Hammache N, Filippetti L, Vaugrenard T, Aliot E, et al. Impact of global and segmental hypertrophy on two-dimensional strain derived from three-dimensional echocardiography in hypertrophic cardiomyopathy: comparison with healthy subjects. *Journal of the American Society of Echocardiography*. 2015;28(9):1093-102.
60. Baccouche H, Maunz M, Beck T, Gaa E, Banzhaf M, Knayer U, et al. Differentiating cardiac amyloidosis and hypertrophic cardiomyopathy by use of three-dimensional speckle tracking echocardiography. *Echocardiography*. 2012;29(6):668-77.