

## My Approach to 3-Dimensional Left Ventricular Strain

Rafael Bonafim Piveta,<sup>1,2</sup> Miguel Osman Dias Aguiar,<sup>1,2</sup> Liria Lima Maria da Silva,<sup>1,2,3</sup> Marcelo Luiz Campos Vieira<sup>1,4</sup>

Hospital Israelita Albert Einstein,<sup>1</sup> São Paulo, SP – Brazil

Hospital Beneficência Portuguesa,<sup>2</sup> São Paulo, SP – Brazil

Hospital Dante Pazzanese de Cardiologia,<sup>3</sup> São Paulo, SP – Brazil

Universidade de São Paulo, Instituto do Coração, Ecocardiografia Adultos,<sup>4</sup> São Paulo, SP – Brazil

### Abstract

The role of strain analysis using 2-dimensional speckle tracking (2DST) has been well documented, and it represents an important complementary tool in the assessment of cardiac mechanics, adding value in the identification of incipient and subclinical myocardial injury in different clinical scenarios. A significant advance related to echocardiography was the development of 3-dimensional speckle tracking (3DST), which has the potential to overcome many limitations intrinsic to 2-dimensional technology, offering additional parameters of myocardial deformation (such as area strain) and a more comprehensive quantification of the geometry and function of the left ventricular myocardium, based on a single image acquisition. Among its main limitations, the low temporal and spatial resolution stands out, in addition to the dependence on high-quality images and a well-trained operator. Although it is a relatively recent technique that is still under development, several experimental studies and some clinical investigations have already demonstrated the reproducibility and potential applicability of 3DST. The objective of this article is to add information about adequate analysis of 3-dimensional left ventricular strain and explore its main points of vulnerability, discussing important variables to increase the accuracy and reproducibility of this technology.

### Introduction

Echocardiographic analysis of myocardial deformation (strain) is a robust tool that adds important information regarding conventional parameters in relation to prognosis, specific parametric patterns of different cardiomyopathies, and detection of subclinical or incipient injury in different clinical scenarios.

Strain reflects myocardial deformation, which represents the percentage of shortening or lengthening of a determined myocardial segment in relation to its initial measurement, in systole or diastole. Currently, echocardiographic assessment of

strain is mainly performed using the speckle tracking technique in the ventricular myocardium. The bright white dots that are visible on grayscale images are natural acoustic markers that represent specific tissue patterns in the myocardium, characterizing that segment's "fingerprint." The software identifies these speckles and tracks their movements in all directions. Strain is then evaluated based on frame-by-frame comparison of the patterns of these speckles during the cardiac cycle.<sup>1</sup>

The role of strain analysis using 2-dimensional speckle tracking (2DST) has been well documented; it is a sensitive and reproducible marker for analyzing cardiac mechanics, validated in both *in vitro* and *in vivo* models.<sup>2</sup> Its value in the subclinical detection of ventricular dysfunction and its prognostic role have been demonstrated in different clinical scenarios; the main parameter involved is global longitudinal strain calculated by 2DST.

Strain can also be assessed using the 3-dimensional speckle tracking (3DST) technique, which, in theory, has greater anatomical correspondence and minimizes many limitations related to the 2-dimensional technique.<sup>3</sup> 3DST does not depend on geometric assumptions, as 2-dimensional imaging does, and speckle tracking is conducted by means of a homogeneous spatial distribution of each component of the myocardial displacement vector, minimizing errors related to tracking, which often occur with the 2-dimensional technique, in which the analysis of real cardiac mechanics is technically limited.<sup>4</sup> Furthermore, 3DST analysis is less time-consuming (one third shorter than 2DST), and it calculates all components of myocardial deformation in the same cardiac cycle, under the same hemodynamic condition.<sup>5</sup> The 3-dimensional technique allows for assessment of all parameters related to ventricular mechanics only by obtaining an image in the apical 4-chamber plane, at the same moment of the cardiac cycle, unlike images obtained with the 2-dimensional technique, which requires multiple image acquisitions, at different moments. As left ventricular myocardial fibers have a complex spatial orientation and they contract simultaneously in different directions, ventricular mechanics are by nature a 3-dimensional phenomenon; therefore, this assessment requires a 3D imaging method.<sup>6</sup> 3DST analysis was compared to 2DST in relation to reference parameters of cardiac magnetic resonance imaging, and it was shown to be more accurate and reproducible in patients with different left ventricular morphologies (different sizes, normal and abnormal systolic function).<sup>7</sup> 3DST is, therefore, potentially more accurate and efficient than 2DST for analyzing ventricular mechanics.<sup>8</sup>

Important limitations related to the 3-dimensional technique include its low spatial and temporal resolution, lower availability, higher cost, dependence on high-quality images, and the fact that it requires examiners who are well

### Keywords

Echocardiography; Three-Dimensional Imaging; Heart Ventricles

**Mailing Address:** Rafael Bonafim Piveta •

Hospital Israelita Albert Einstein. Av. Albert Einstein, 627/701. Postal code: 05652-900. Morumbi, São Paulo, SP – Brazil

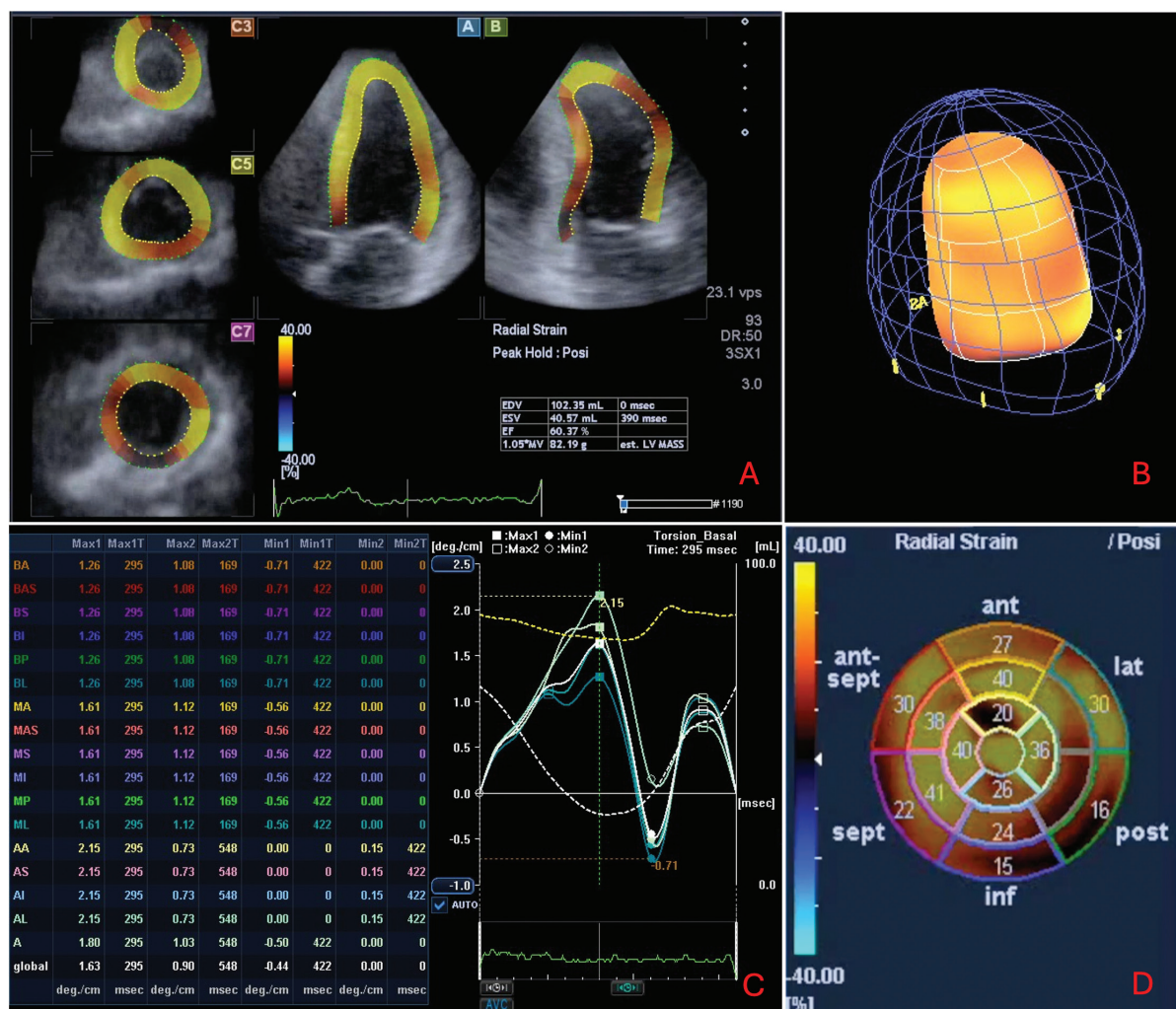
E-mail: rbpiveta@hotmail.com

Manuscript received April 6, 2024; revised April 8, 2024; accepted April 9, 2024.

Editor responsible for the review: Marcelo Dantas Tavares de Mell

**DOI:** <https://doi.org/10.36660/abcimg.20240028i>

## Central Illustration: My Approach to 3-Dimensional Left Ventricular Strain



Arq Bras Cardiol: Imagem cardiovasc. 2024;37(2):e20240028

Example of sequence in left ventricular strain analysis using three-dimensional speckle tracking technique. A: Multiplanar image post three-dimensional acquisition, demonstrating tracking in the left ventricular myocardium. B: Illustrative image demonstrating evaluation of the full left ventricular volume. C: Curves and table with 3D strain values of all myocardial segments, in this case, an example of basal left ventricular twist calculation. D: Bull's Eye with 3D strain values of all myocardial segments, in this case, an example of left ventricular radial deformation.

trained in the technique. Additionally, accurate acquisition is not always feasible in multiple cycles, as required, for example, in the presence of arrhythmia.

Analysis of left ventricular mechanics through 3DST allows the calculation of longitudinal strain, radial strain, circumferential strain, apical or basal rotation, twist, torsion, untwist, and area strain. Area strain is a more recent index that has been shown to be promising in several scenarios, reflecting the calculation of relative change in the endocardial surface area of a determined segment in relation to its original area (integrating analysis of myocardial fibers in the longitudinal and circumferential direction).<sup>9</sup>

The objective of this article is to provide step-by-step guidance for adequate analysis of 3-dimensional left ventricular strain and to explore the main points of vulnerability involved with this technique, discussing tools that should be considered to increase the accuracy and reproducibility of this technology.

### Calculation of 3-dimensional left ventricular strain

#### Apical 4-chamber plane image acquisition

Strain calculated by ST3D is analyzed based on the 3-dimensional full volume technique. Regardless of

the software used, the first and main step towards an accurate assessment is the adequate acquisition of the echocardiographic image in apical 4-chamber view (for at least 3 cardiac cycles). The patient should be under satisfactory electrocardiographic monitoring; if possible, expiratory apnea should be attempted, avoiding translational movements of the heart with respiration. Regarding device adjustments, focus, depth, sector angle width, and gain should be adjusted in order to adequately include the left ventricle within the pyramidal volume. Adjustments should be made with the aim of obtaining adequate temporal resolution (at least 20 to 30 volumes per second).

Some special precautions should be taken, especially during acquisition. Foreshortening of the left ventricular cavity should be avoided as much as possible, as this may lead to an overestimated calculation of longitudinal strain. Care is required to include the entire endocardial border of the anterolateral wall, which is often acquired inadequately, leading to underestimation of strain values due to tracking error. Artifacts, reverberations, and especially limited visualization of the myocardium can cause speckles to be tracked inadequately, generating incorrect results. Images should be acquired using harmonics, in order to optimize their quality as much as possible.

### Tracing – Defining the region of interest (ROI)

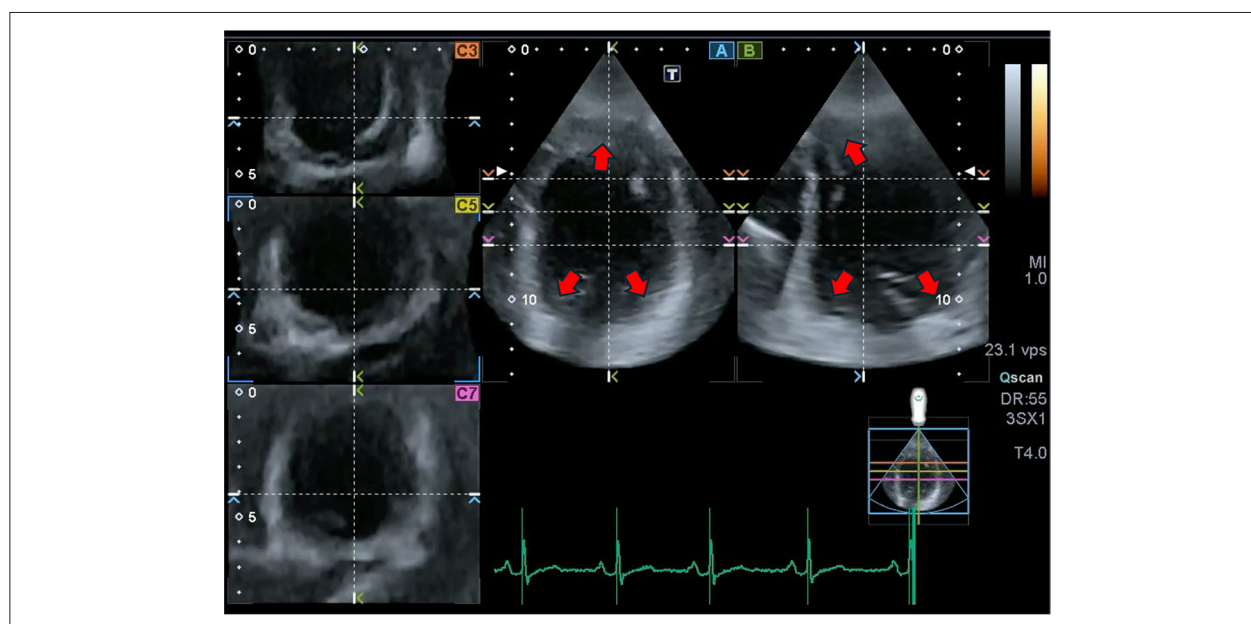
After acquiring the image in the apical 4-chamber plane, views are displayed in 5 planes in a standard axis, with 2 orthogonal longitudinal and 3 transverse views. The ROI, which is the left ventricular myocardium, will then be defined for full volume and strain analysis. This definition begins

by marking 3 points on the left ventricular myocardium in both orthogonal views, namely, 2 points at the edges of the mitral valve annulus and 1 point at the left ventricular apex (Figure 1). Depending on the software used for analysis, this display format may vary.

Subsequently, left ventricular endocardial tracing, in this case, the ROI, is semi-automatically generated by Wall Motion Tracking software. At this point, if necessary, manual adjustments can be made to incorporate the entire thickness of the wall under analysis, leaving its shape and width as close as possible to the myocardial anatomy. Angulation of the ROI should be avoided; likewise, the pericardium, mitral annulus (especially when calcified), and extracardiac spaces should not be included, as these variables may underestimate the strain value. The left ventricle segmentation model may vary between software, which may include 16, 17, or 18 segments; the 17-segment model is generally more used in echocardiography and other diagnostic modalities, as it reflects myocardial perfusion territory. Currently, most devices automatically identify moments in the cardiac cycle. Current software commonly uses the peak of the QRS complex to define end diastole, marking it automatically, without interference from the examiner. However, it is possible to use event markers to manually define the beginning (end diastole) and end (end systole) of myocardial contraction in the cardiac cycle.

### Assessing the tracking quality

After properly defining the ROI, the software automatically generates calculations of volumes, 3-dimensional ejection



**Figure 1** – Echocardiographic image after 3-dimensional acquisition, for technical adjustments and 3DST analysis. Five planes are shown, 3 transverse and 2 longitudinal. At this point, adjustments such as alignment, gain, and choice of cardiac cycle can be made. The ROI is defined by marking 3 points on the left ventricular myocardium, 2 points at the edges of the mitral valve annulus and 1 point at the left ventricular apex (indicated by arrows).

fraction, and strain with all left ventricular mechanical indices (Figures 2 and 3).

At this moment, speckle tracking should be carefully analyzed in order to define its accuracy. This analysis is essentially subjective, and adequate training and learning curve are important for the reproducibility of results. If, based on a subjective analysis, tracking errors are identified, the analysis should be corrected, restarted, or not used. Segments that do not read properly after an initial adjustment should be discarded. The greater the number of discarded segments, the less reliable the result. In general, when more than 2 myocardial segments are not well visualized, especially if they are contiguous, the analysis should not be used.

Depending on the software used, the ROI can encompass the entire myocardial wall or be divided into endocardial, mesocardial, and epicardial layers, with each contour selected automatically or manually. Usually, when no specific layer is selected, the results correspond to the entire wall thickness.

### Interpretation of the results

Analysis of left ventricular myocardial strain using the 3-dimensional technique makes it possible to calculate the following mechanical indices:

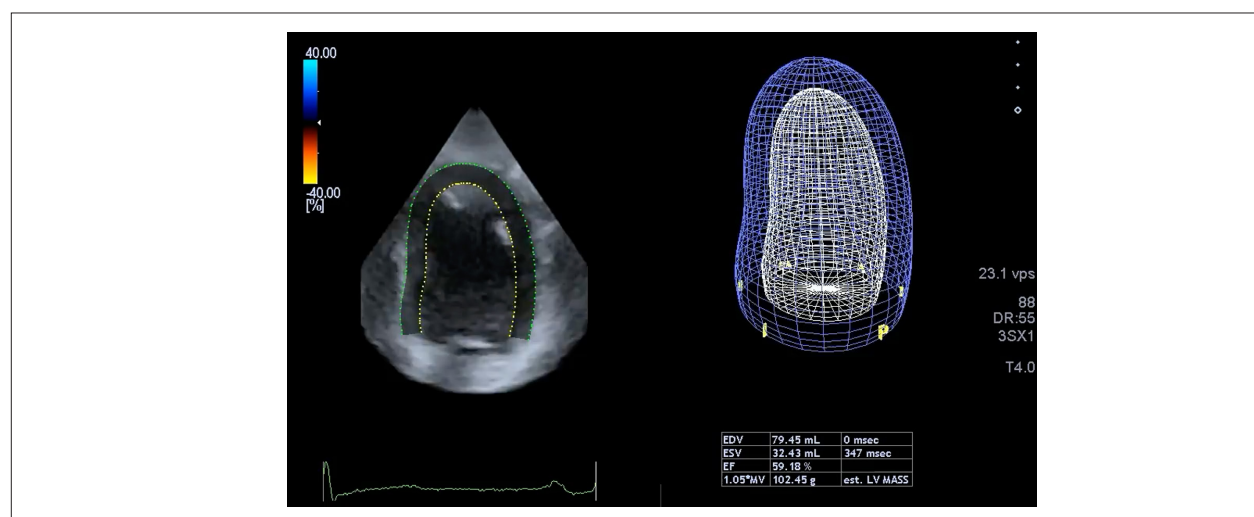
- Global longitudinal strain: represents systolic myocardial fiber shortening in the longitudinal direction, with negative values, expressed as a percentage.
- Global radial strain: represents systolic myocardial fiber thickening in the radial direction, with positive values, expressed as a percentage.
- Global circumferential strain: represents systolic myocardial fiber shortening in the circumferential direction, with negative values, expressed as a percentage.
- Rotation: represents the calculation of apical or basal rotation, with values expressed in degrees.
- Twist: represents the difference between apical and basal rotations, during systole, expressed in degrees.

- Torsion: represents the difference between apical and basal rotations, indexed by the longitudinal length of the left ventricle, expressed in degrees per centimeter.
- Untwist: represents the difference between apical and basal reverse rotations, during diastole (elastic recoil), with a value expressed in degrees.
- Global area strain: represents the calculation of the relative change in the endocardial surface area of a given segment in relation to its original area.

It is important to highlight that, although many mechanical indices are expressed in negative values, some authors prefer to use absolute values in order to avoid interpretation errors.

The results of strain analysis are displayed in curves for each segment evaluated; depending on the software, they are also displayed in a table with the strain values for each segment, as well as the global strain value. All mechanical indices can be calculated based on a single acquisition in apical 4-chamber view (Figure 4). Furthermore, the calculations are displayed on a polar map (better known as bull's eye), which is a graphic representation of the strain values of each segment, also allowing subjective parametric analysis of the myocardial deformation pattern, which is often peculiar and corresponds to certain cardiomyopathies (Figure 5).

It is extremely important to understand and properly interpret the morphology and values of strain curves, also taking into consideration the moment when they occur in the cardiac cycle. In this context, multiple parameters can be analyzed, especially considering indices related to systolic function, such as end-systolic strain, which represents the deformation at the time of aortic valve closure. This is the standard parameter to describe the systolic strain value. Peak systolic strain represents the largest value of negative strain during systole. Positive peak systolic strain, which occurs at the end of diastole, represents significant myocardial stretching or possibly a relevant change in situations of regional dysfunction. Post-systolic strain (or post-systolic shortening), which is the maximum value of deformation that



**Figure 2** – Example of a 3-dimensional echocardiographic study presenting full volume analysis, with estimated left ventricular volumes and ejection fraction.



**Figure 3** – Three-dimensional speckle tracking for strain analysis. Example of the 3-dimensional area strain calculation, with a table displaying the values found in each myocardial segment, in addition to the average representing the global value (red circle:  $-40.86\%$ ) and curves referring to each myocardial segment assessed.

can arise after aortic valve closure, reflects the deformation of segments that contract after aortic valve closure and do not contribute to ventricular ejection, which is often associated with ischemic myocardial disease.<sup>10</sup>

As is the case with 2DST, an important limitation related to 3DST is the variability of strain measurements obtained between different software and device manufacturers, with evidence of significant disagreements. Therefore, it is suggested that the examination report include which device/software the analysis was conducted on, in order to adapt management and interpretation in assessments of evolution. Furthermore, 3-dimensional strain values are also influenced by age, sex, and hemodynamic conditions such as heart rate, blood pressure, and situations associated with pre- and post-load changes.<sup>11</sup>

Strain is calculated for each ventricular segment, and the average of these values represents global strain, reflecting global left ventricular function. Several studies have demonstrated that the method has good reproducibility, and the normal ranges for the main mechanical indices derived from 3DST, considering the main software used, are well established for clinical use (Table 1).<sup>12</sup> It is worth highlighting the importance of interpreting the results of 3DST analysis considering the patient's clinical context, individualizing on a case-by-case basis.

The application of 3DST has been demonstrated in different clinical scenarios, such as chemotherapy-induced cardiotoxicity; ischemic cardiomyopathy; hypertensive heart disease; heart failure with preserved ejection fraction; prognosis and identification of acute rejection in transplant patients; hypertrophic, dilated, and infiltrative cardiomyopathies; valvular heart disease; and after procedures such as percutaneous implantation of an aortic valve prosthesis and percutaneous correction of mitral insufficiency with MitraClip®.<sup>13–19</sup>

The analysis of left ventricular mechanics using 3DST makes it possible to calculate 3-dimensional area strain. This index represents a semi-automatic and relatively new parameter, which has shown to be very promising in different clinical conditions, in addition to presenting excellent reproducibility, therefore making it consistent and reliable.<sup>12</sup> Conceptually, it represents the fractional change in myocardial surface area during systole and integrates the assessment of circumferential and longitudinal fibers in the endocardial and subendocardial layers.<sup>9</sup> In different clinical contexts, especially those involving cellular oxidative stress as one of the mechanisms of myocardial injury, such as chemotherapy-induced cardiotoxicity, studies suggest that altered 3-dimensional area strain is a more sensitive marker of ventricular dysfunction and that it may represent very early damage to cardiomyocytes, with a potential prognostic impact in these scenarios.<sup>19</sup>

Although numerous studies have demonstrated the potential impact of 3-dimensional technology for analysis of ventricular mechanics, larger, more robust studies with greater scientific potential are necessary to establish the routine use of 3DST in echocardiography laboratories. Furthermore, technological advances with improved spatial and temporal resolution and a standardized methodology to obtain manufacturer-independent 3-dimensional strain measurements are expected in the future for a broad application of 3DST not only in research environments, but also in specific clinical scenarios (Central Illustration).

## Author Contributions

Conception and design of the research and critical revision of the manuscript for intellectual content: Piveta RB; writing of the manuscript: Piveta RB, Aguiar MOD, Silva LLM, Vieira MLC.



Figure 4 – Example of twist calculated by 3DST demonstrated by the curves and table displaying the values found in each myocardial segment.

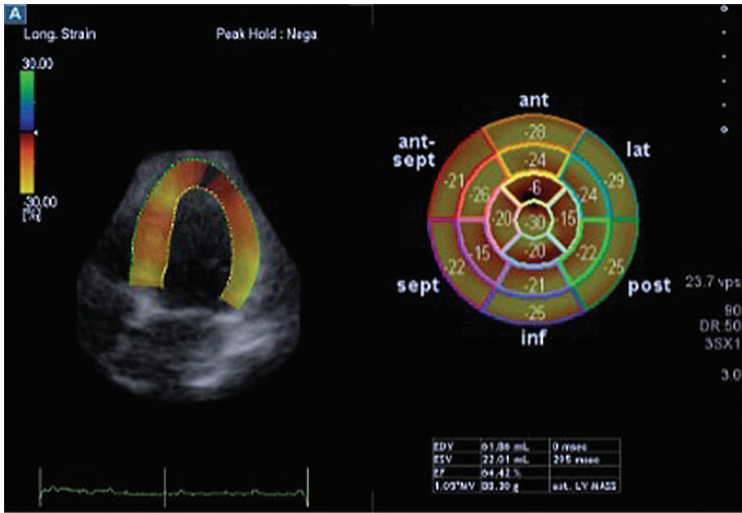


Figure 5 – Example of a polar map or bull's eye for left ventricular longitudinal strain calculated by 3DST.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

**Table 1 – Reference values (%) for left ventricular strain calculated by 3DST according to the leading manufacturers and software**

|                        | TomTec                      | EchoPAC                     | 3DWM<br>tracking software   | Philips                     | General Elettric            | Toshiba Medical<br>Systems  |
|------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| Longitudinal strain    | −19,84<br>(−21,21 a −18,48) | −19,40<br>(−20,06 a −18,74) | −17,04<br>(−17,91 a −16,17) | −19,67<br>(−21,27 a −18,08) | −19,40<br>(−20,06 a −18,74) | −17,04<br>(−17,91 a −16,17) |
| Circumferential strain | 23,30<br>(28,33 a 18,26)    | −19,47<br>(−20,49 a −18,45) | −28,79<br>(−32,90 a 24,78)  | −22,13<br>(−26,73 a −17,52) | −19,47<br>(−21,49 a −18,45) | −28,79<br>(−32,90 a 24,78)  |
| Radial strain          | 55,99<br>(44,73 a 67,25)    | 50,41<br>(47,96 a −52,87)   | 33,17<br>(24,38 a 41,97)    | 59,24<br>(41,91 a 76,56)    | 50,41<br>(47,96 a 52,87)    | 33,17<br>(−24,38 a 41,97)   |
| Area strain            | −34,14<br>(−37,21 a −31,07) | −32,50<br>(−33,87 a −31,14) | −42,07<br>(−46,28 a −39,86) | −33,54<br>(−37,29 a −29,79) | −32,50<br>(−33,87 a −31,14) | −43,07<br>(−46,28 a −39,86) |

95% confidence interval shown in parentheses. 3DWM: 3-dimensional wall motion.

## References

- Arias-Godínez JA, Guadalajara-Boo JF, Patel AR, Pandian NG. Function and Mechanics of the Left Ventricle: From Tissue Doppler Imaging to Three Dimensional Speckle Tracking. Arch Cardiol Mex. 2011;81(2):114-25.
- 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. J Am Coll Cardiol. 2006;47(4):789-93. doi: 10.1016/j.jacc.2005.10.040.
- Sorrentino R, Esposito R, Pezzullo E, Galderisi M. Real-time Three-dimensional Speckle Tracking Echocardiography: Technical Aspects and Clinical Applications. Res Reports Clin Cardiol. 2016;7:147-58. doi: 10.2147/RRCC.S107374.
- Isla LP, Balcones DV, Zamorano J. Three-dimensional Speckle Tracking. Curr Cardiovasc Imaging Rep. 2008;1(1):25-9.
- Isla LP, Balcones DV, Fernández-Golfín C, Marcos-Alberca P, Almería C, Rodrigo JL, et al. Three-dimensional-wall Motion Tracking: A New and Faster Tool for Myocardial Strain Assessment: Comparison with Two-dimensional-wall Motion Tracking. J Am Soc Echocardiogr. 2009;22(4):325-30. doi: 10.1016/j.echo.2009.01.001.
- 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. Cardiovasc Diagn Ther. 2018;8(1):101-17. doi: 10.21037/cdt.2017.06.01.
- Nesser HJ, Mor-Avi V, Gorissen W, Weinert L, Steringer-Mascherbauer R, Niel J, et al. Quantification of Left Ventricular Volumes Using Three-dimensional Echocardiographic Speckle Tracking: Comparison with MRI. Eur Heart J. 2009;30(13):1565-73. doi: 10.1093/eurheartj/ehp187.
- Kleijn SA, Aly MF, Terwee CB, van Rossum AC, Kamp O. Reliability of Left Ventricular Volumes and Function Measurements Using Three-dimensional Speckle Tracking Echocardiography. Eur Heart J Cardiovasc Imaging. 2012;13(2):159-68. doi: 10.1093/ehjcard/ehj174.
- Kleijn SA, Aly MF, Terwee CB, van Rossum AC, Kamp O. Three-dimensional Speckle Tracking Echocardiography for Automatic Assessment of Global and Regional Left Ventricular Function Based on Area Strain. J Am Soc Echocardiogr. 2011;24(3):314-21. doi: 10.1016/j.echo.2011.01.014.
- Mor-Avi V, Lang RM, Badano LP, Belohlavek M, Cardim NM, Derumeaux G, et al. Current and Evolving Echocardiographic Techniques for the Quantitative Evaluation of Cardiac Mechanics: ASE/EAE Consensus Statement on Methodology and Indications Endorsed by the Japanese Society of Echocardiography. Eur J Echocardiogr. 2011;12(3):167-205. doi: 10.1093/ejehocardiogr/erj021.
- Kleijn SA, Pandian NG, Thomas JD, Isla LP, Kamp O, Zuber M, et al. Normal Reference Values of Left Ventricular Strain Using Three-dimensional Speckle Tracking Echocardiography: Results from a Multicentre Study. Eur Heart J Cardiovasc Imaging. 2015;16(4):410-6. doi: 10.1093/ehjci/jeu213.
- Truong VT, Phan HT, Pham KNP, Duong HNH, Ngo TNM, Palmer C, et al. Normal Ranges of Left Ventricular Strain by Three-Dimensional Speckle-Tracking Echocardiography in Adults: A Systematic Review and Meta-Analysis. J Am Soc Echocardiogr. 2019;32(12):1586-97. doi: 10.1016/j.echo.2019.07.012.
- Du GQ, Hsiung MC, Wu Y, Qu SH, Wei J, Yin WH, et al. Three-Dimensional Speckle-Tracking Echocardiographic Monitoring of Acute Rejection in Heart Transplant Recipients. J Ultrasound Med. 2016;35(6):1167-76. doi: 10.7863/ultra.15.07013.
- Matsumoto K, Tanaka H, Kaneko A, Ryo K, Fukuda Y, Tatsumi K, et al. Contractile Reserve Assessed by Three-dimensional Global Circumferential Strain as a Predictor of Cardiovascular Events in Patients with Idiopathic Dilated Cardiomyopathy. J Am Soc Echocardiogr. 2012;25(12):1299-308. doi: 10.1016/j.echo.2012.09.018.
- Li CM, Li C, Bai WJ, Zhang XL, Tang H, Qing Z, et al. Value of Three-dimensional Speckle-tracking in Detecting Left Ventricular Dysfunction in Patients with Aortic Valvular Diseases. J Am Soc Echocardiogr. 2013;26(11):1245-52. doi: 10.1016/j.echo.2013.07.018.
- Schueler R, Sinning JM, Momcilovic D, Weber M, Ghanem A, Werner N, et al. Three-dimensional Speckle-tracking Analysis of Left Ventricular Function After Transcatheter Aortic Valve Implantation. J Am Soc Echocardiogr. 2012;25(8):827-34. doi: 10.1016/j.echo.2012.04.023.
- Vitelli 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. J Am Soc Echocardiogr. 2015;28(9):1070-82. doi: 10.1016/j.echo.2015.04.005.
- Monte IP, Mangiafico S, Buccheri S, Bottari VE, Lavanco V, Arcidiacono AA, et al. Myocardial Deformational Adaptations to Different Forms of Training: A Real-time Three-dimensional Speckle Tracking Echocardiographic Study. Heart Vessels. 2015;30(3):386-95. doi: 10.1007/s00380-014-0520-9.
- Piveta RB, Rodrigues ACT, Vieira MLC, Fischer CH, Afonso TR, Daminello E, et al. Early Change in Area Strain Detected by 3D Speckle Tracking Is Associated With Subsequent Cardiotoxicity in Patients Treated With Low Doses of Anthracyclines. Front Cardiovasc Med. 2022;9:842532. doi: 10.3389/fcvm.2022.842532.



This is an open-access article distributed under the terms of the Creative Commons Attribution License