Automated Functional Imaging (AFI)

Leading the way in strain imaging from research to clinical routine

White Paper

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Introduction

One of the most common reasons for echocardiographic examinations is the assessment of left ventricular (LV) function but this is time-consuming and often rather subjective, especially when the endocardium cannot be clearly visualized.

Global and segmental quantification of heart function by speckle tracking technology (STE), tries to address these challenges, and has gained a lot of momentum for the past 15 years, not only for research, but also for clinical routine applications.

Starting in the late 90´s GE Healthcare (GEHC) pioneered development in this field with the introduction of tissue doppler based technology. However, these techniques are angle dependent and require substantial training to be used in the clinical setting. 2D Strain, the first in industry speckle tracking tool for ultrasound images, overcomes these limitations, and was introduced to the market in 2004. Following the introduction of 2D Strain GEHC has provided clinicians with clinically valuable tools based on speckle tracking: Automated Function Imaging (AFI), 4D strain, AFI stress, Myocardial work. Recently GEHC extended the well-established strain- based functional assessment to the left atrium and right ventricle.

At present in 2021, 60% of publications and research studies in the context of Myocardial Strain Imaging use GE Healthcare's speckle tracking technology, second most cited at 12%.

2004 2D Strain

Introduced in 2004 as the first in industry speckle tracking tool for ultrasound images, 2D strain became available as a workstation based advanced research tool designed for left ventricular quantification, though its versatility enabled usage on the other chambers as well. 2D strain is still available today in our EchoPAC™ software offering.

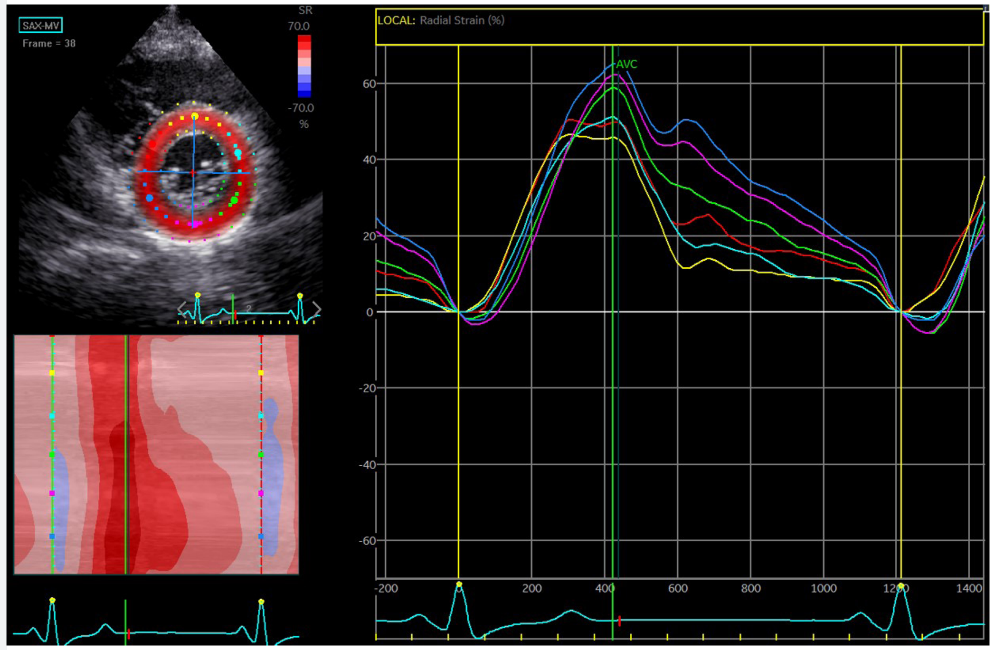


Fig. 1: Assessing radial strain on a LV short axis view with the help of 2D Strain

2006 Automated Function Imaging (AFI)

Following the introduction of 2D Strain extensive research showed that global and regional longitudinal strain seemed to be promising parameters for the quantitative evaluation of LV function that should be considered for implementation into daily clinical routine.

In 2006, GEHC introduced Automated Function Imaging (AFI), a clinical STE tool, focused on streamlining the workflow and assessing only left ventricular longitudinal global and segmental strain. AFI was made available on the GE Vivid™ scanners in addition to on EchoPAC™.

AFI allows objective quantitative analysis of the complete longitudinal myocardial deformation of the left ventricle throughout the heart cycle. AFI has proven a valuable clinical tool helping in the assessment of a variety of cardiac diseases, such as HCM, MI, HFpEF, Amyloidosis[1] and in the management of chemotherapy[2].

One of the results of the AFI analysis is a parametric left ventricular bullseye displaying the segmental values, with easily recognizable colorization of the different LV segments according to their strain values. The whole ventricle is covered by combining the strain results from the three standardized apical 2D views.

Additionally, available are a Post Systolic Index (PSI) map indicating shortening of the myocardium after Aortic Valve closure, and a Time to Peak (TTP) strain map providing peak strain dispersion, a measure of dyssynchrony. Furthermore, segmental traces for more detailed analysis are displayed.

To further automate the workflow of the AFI, the AI-based View Recognition algorithm was introduced in 2018. The algorithm combines the view information with the heart rate and frame rate to automatically select a trio of apical images suitable for AFI LV analysis.

Clinical evaluation of AFI was performed by an external company based on literature review concluding that:

- AFI is a more sensitive method for assessment of LV function than the EF and WM (standard echo parameters)
- AFI provides both a global and regional quantitative assessment of the contractile function of the heart
- AFI is less operator dependent than EF and WM assessments
- AFI is fast < 3 min
- AFI works up to heart rates of ~120 beats/min
- AFI has the potential to reduce costs by replacing procedures with a higher Medicare cost

The average Medicare cost of an AFI assessment is 50% lower than SPECT[3]

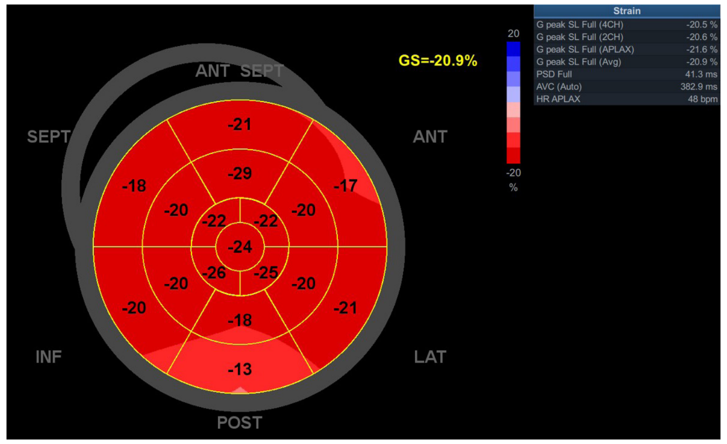


Fig. 2: AFI bull's-eye view of a normal left ventricle.

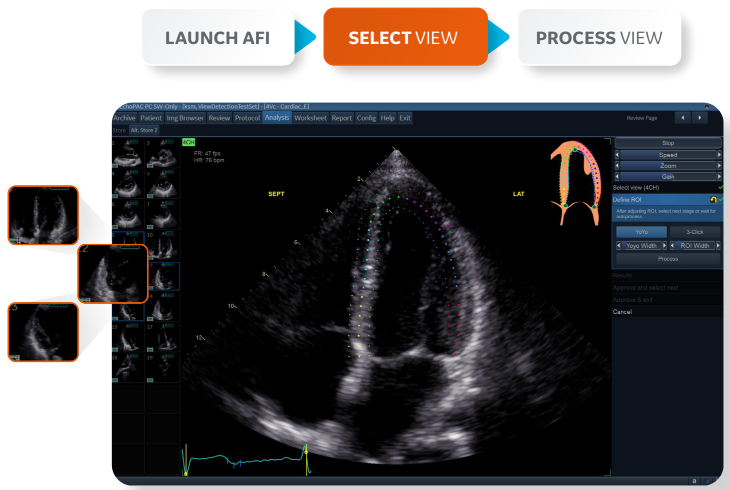


Fig. 3: AI-enabled AFI LV: images have been pre-selected and labelled ready for processing.

2010

4D Strain

Speckle tracking applied to two-dimensional images is limited because regions of the myocardium represented by speckle patterns in reality move through three-dimensional space, rather than being limited by the two-dimensional sector. This might imply that three-dimensional speckle tracking echocardiography could be an attractive new method, not only for the assessment of left ventricular volumes, however for the assessment of left ventricular function as well.

In 2010, GEHC introduced four-dimensional (4D) Strain which is an analysis method designed for left ventricular (LV) myocardial deformation analysis based on 4D LV data sets. 4D Strain integrates speckle-tracking with three-dimensional echocardiography, enabling the computation of all LV Strain components from a single apical data set. In comparison with two-dimensional (2D) speckle-tracking, 4D Strain has the potential to capture the complex LV deformation addressing the issues related to the “out-of-plane” motion of speckles.

In the clinical setting, 4D area strain correlated best with common LV systolic function parameters[4] Furthermore, 4D strain parameters are considered useful indices of early-stage heart dysfunction caused by Aortic Valve Diseases[5].

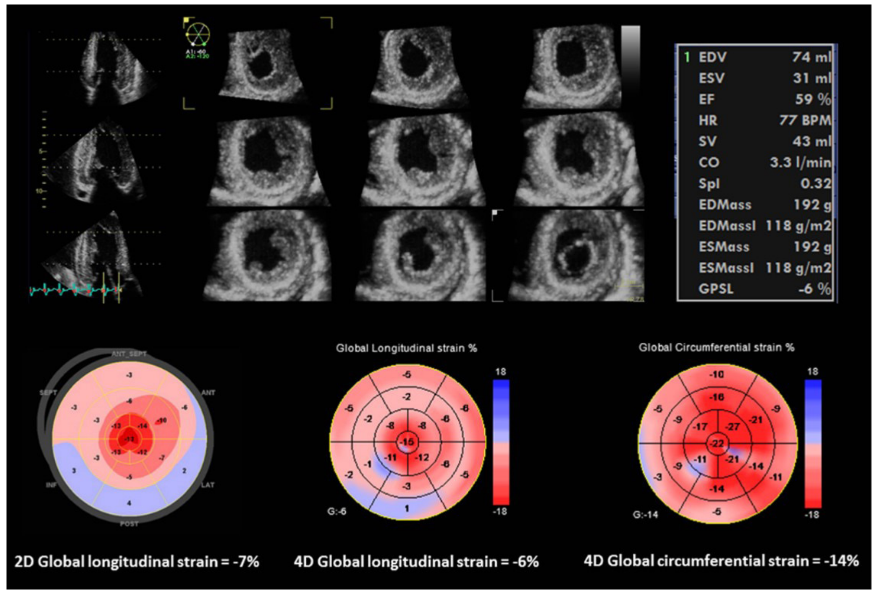


Fig. 4:
Comprehensive assessment of left ventricular function by 4D strain in a patient with restrictive cardiomyopathy (amyloidosis).

2014

AFI Stress

Assessing myocardial function during stress echocardiography adds valuable insights when the clinician is diagnosing patients with ischemic conditions[6], helping clinicians in assessing response to CRT[7] and stratifying the risk of patients with heart failure and preserved ejection fraction (HFPEF)[8].

In 2014, GEHC incorporated AFI into dedicated stress echo protocols thus enabling quantitative analysis of myocardial function for all levels of exercise and pharmacologic stress echocardiography.

To support convenient interpretation of the results, parametric left ventricular bullseyes for different stress levels are displayed side by side.

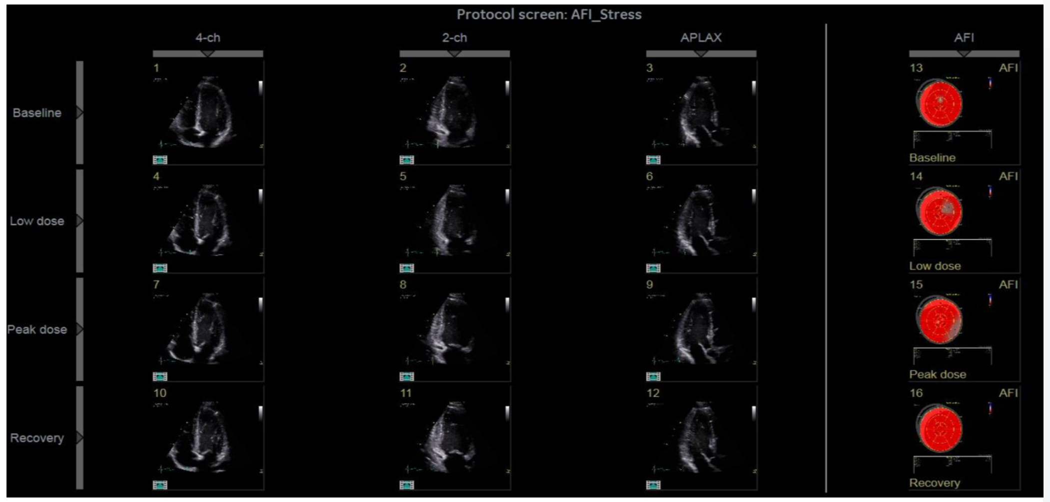


Fig. 5:
AFI stress protocol screen with LV GLS bull´s-eye plots for each stress level

2017

Myocardial work

Global longitudinal strain (GLS), derived from STE, emerged as an accurate, highly sensitive, and reproducible parameter in the detection of LV dysfunction. One limitation of GLS, however, is its dependency on loading conditions, making it difficult to distinguish between abnormal GLS due to intrinsic reduced LV contractility and increased LV afterload.

In 2017 GEHC extended AFI by introducing dynamic LV pressure into the functional analysis. LV pressure adds an important dimension to the assessment of LV function and facilitates interpretation of strain traces in relation to LV pressure dynamics. This industry´s unique tool in echocardiography calculates a set of myocardial work parameters that are less load dependent than strain alone. This might particularly be valuable in follow-up of patients.

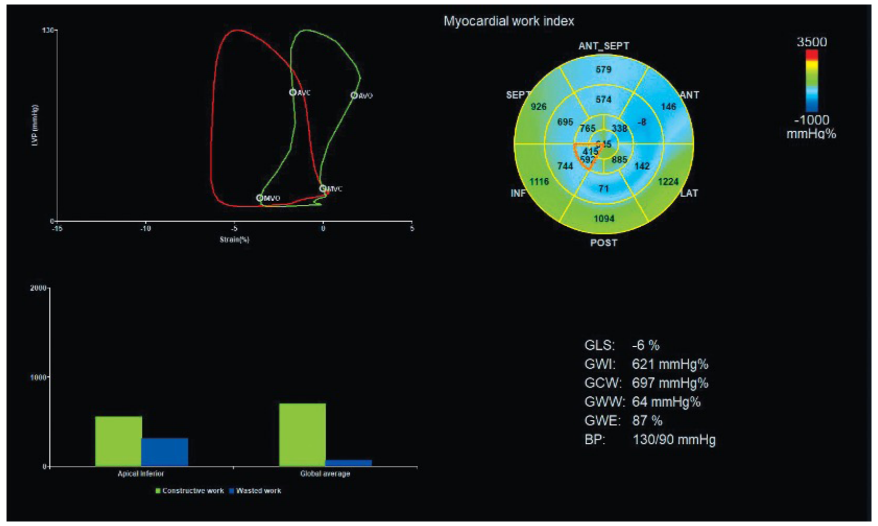


Fig. 6:
Myocardial Work parameters are based upon the results obtained with AFI by accounting for the systolic blood pressure

The estimation of myocardial performance with the help of myocardial work provides further insights into the mechanisms of dyssynchrony[9], in the early diagnosis of CAD[10], showed distinct patterns in postinfarct and HFrEF patients[11] and helped determining the severity of aortic stenosis[12].

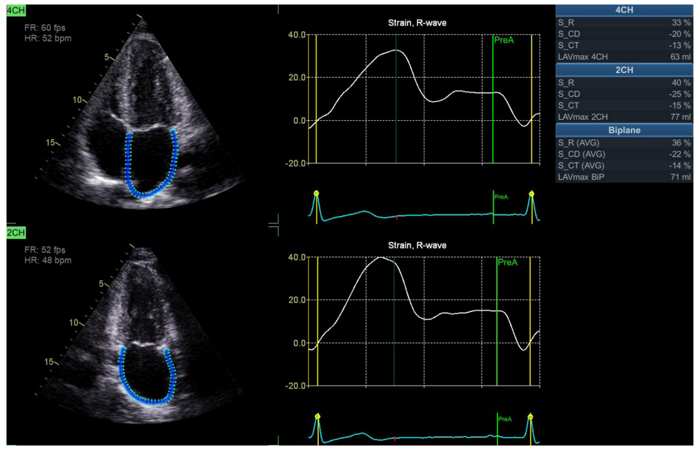
AFI LA

The utilization of a chamber specific dedicated software to evaluate LA Function using speckle tracking echocardiography providing both, single plane as well as biplane measurements for left atrial strains and volumes is recommended by the Standardization Task Force (2018)[13]. In 2020, GEHC extended its proven AFI technology to quantitatively assess the function of the left atrium.

Quantifying the LA function may help identifying changes in LA dynamics and defects influencing filling pattern, volumes and emptying fraction. These are relevant in e.g. patients with heart failure with preserved ejection fraction, heart valve diseases, LV diastolic dysfunction, and atrial fibrillation[14].

The ability of AFI to provide highly feasible and highly reproducible measurements of LAVmax has also been demonstrated[15].

Fig. 7:
AFI LA helps quantifying LA Function which is an important biomarker for several cardiovascular diseases and a strong predictor of clinical outcomes

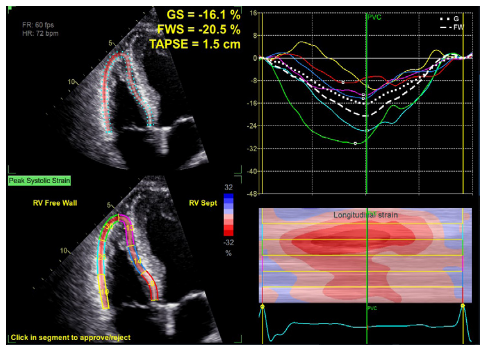


AFI RV

In 2020 GEHC also extended AFI with the possibility to quantify the function of the right ventricle. As recommended by the Standardization Task Force (2018)[13] regional and global strain values as well as right ventricular free wall results are provided. Alongside with the recommended parameters, speckle tracking based TAPSE is presented.

Assessing the RV function may be useful to support the prognosis and address management in patients with e.g. pulmonary hypertension, pulmonary embolism, acute coronary syndromes, left ventricular failure, arrhythmogenic cardiomyopathy, and congenital heart diseases[16,17].

Fig. 8:
AFI RV helps evaluating of RV Function which is directly related to clinical outcomes in several cardiovascular diseases



AFI on Dicom

Since 2020, AFI can also be used for processing of pure Dicom files, without raw data. This allows users performing left ventricle strain analysis on data from other ultrasound vendors utilizing the same robust tracking algorithm and intuitive workflows of the AFI tools.

Collaboration with the ASE/EACVI Standardization Task Force:

One of the main challenges for the wide clinical use of Speckle Tracking has been the inter-vendor variability of the results. Thus in 2010 the ASE and EAE (now EACVI) invited technical representatives from all interested vendors to participate in a concerted effort to reduce inter-vendor variability of strain measurement. GEHC substantially contributed to the technical document which was the basis for the following studies by providing definitions, names, abbreviations, formulas, and procedures for calculation of physical quantities derived from speckle tracking echocardiography and thus creating a common standard that was also published17.

Based on the standard all participating vendors agreed to test their algorithms on computer generated, synthetic ultrasound data representing a variety of clinical models (normal, dilatation, hypertrophy, exercise) with synthetic noise injected to determine accuracy and intra-vendor reproducibility.[18]

Whether these results could be extrapolated to the clinical setting had to be determined next. For this purpose, the Standardization Task Force created a database of 62 patients and volunteers with a wide range of LV function and studied the absolute values of global longitudinal strain (GLS) as well as the inter-/intra-observer variabilities. All subjects were tested on 7 different ultrasound machines and 2 stand-alone software packages, demonstrating gratifying convergence in the strain values from different vendors[19].

Speckle tracking echocardiography has also been considered a promising tool for the quantitative assessment of regional myocardial function. In order to compare the accuracy of vendor-specific and independent strain analysis tools to detect regional myocardial function abnormality in a clinical setting, sixty-three subjects (5 healthy volunteers and 58 patients) were examined, again with 7 different ultrasound machines and 2 software packages. All patients had experienced a previous myocardial infarction with MRI documentation of scar. Analysis demonstrated some remaining vendor differences in scar detection, possibly related to varying degrees of spatial smoothing. Philips Healthcare withdrew during the study for technical reasons[20].

Some vendors base their speckle tracking algorithm on analyzing the endocardial border only, while others in addition provide analysis of the full myocardium. To study a potential impact the Standardization Task Force used the idealized database created in 2015 and compared 5 vendors capable of layer-specific analysis. The results didn't reveal a preference of the layer used to measure GLS on this database of patients acquired using standardized views[21].

However, foreshortening of apical views is a common problem in routine two-dimensional echocardiography. In 2019 the Standardization Task Force published a study comparing endocardial versus full wall tracking to assess GLS on foreshortened views. The conclusion states "Our data suggest that measuring mid-wall strain might therefore be the more robust approach for clinical routine use."[22]

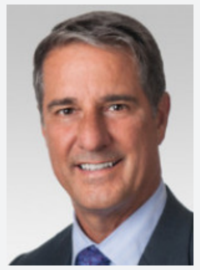
All studies published by the EACVI-ASE Strain Standardization Task Force show that GEHC´s speckle tracking algorithm has excellent sensitivity and reproducibility, especially when assessing foreshortened views.

The strain standardization task force has been co-chaired by James D. Thomas, MD, FASE, who was president of ASE at the time of its formation. Said Dr. Thomas of the effort, "The collaboration between EACVI, ASE, and our industry partners to harmonize strain measurements between vendors has been a significant achievement in the history of echocardiography. The ability to use different vendors to follow patients being monitored with strain may have even helped in the establishment of a specific CPT code for strain imaging, 93356. With reimbursement now available for strain imaging, we are seeing increased utilization in important clinical arenas, such as cardio-oncology, valvular heart disease, cardiomyopathies, heart failure (particularly with preserved ejection fraction) and right heart dysfunction."

Clinical importance of Myocardial Strain Imaging

Quantification of myocardial mechanics using speckle tracking has been included in several guidelines, expert consensus papers and recommendations. It has proven its clinical value in the context of e.g. Heart Failure, Oncology and beyond. This is also reflected by the fact that from January 1, 2020 it has accomplished a specific reimbursement code in the U.S. (CPT code 93356). This is an important milestone, and the first new echocardiography service to achieve CPT category I status in decades.

(Specific in U.S.A.: It is intended to report myocardial strain imaging in conjunction with various transthoracic echocardiography procedures 93303, 93304, 93306 and 93308 in addition to stress echocardiography services 93350 and 93351)



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Summary

First and foremost, clinical evaluation performed by an external company based on literature review demonstrated that GE Healthcare's strain algorithm, AFI is fast (< 3 min), cost efficient, and robust, reproducible for assessment of LV function than the EF and WM.[1]

At present in 2021, 60% of publications and research studies in the context of Myocardial Strain Imaging use GE Healthcare's speckle tracking technology. Second most cited is 12%.

The reason for this is in part because our algorithms have been extensively tested and GE Healthcare takes extra steps in the processing of strain to optimize accuracy.

GEHC was the first company to provide speckle-based strain technology to help clinicians diagnose with higher confidence and to drive standardization of the technology across the industry. GEHC continuously extends its portfolio of speckle-based strain tools to help solve clinical problems.

Please visit **https://gevividultraedition.com** for details.

References:

1- Zito et.al. Ten Years of 2D Longitudinal Strain for Early Myocardial Dysfunction Detection: A Clinical Overview. BioMed Research International, Volume 2018, Article ID 8979407

2- Plana 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. J Am Soc Echocardiogr. 2014 Sep;27(9):911-39

3- Oxford Analytica; Automated Function Imaging Healthymagination Validation Summary. Oxford Analytica 2012

4- Reant et.al, Evaluation of Global Left Ventricular Systolic Function Using Three-Dimensional Echocardiography Speckle-Tracking Strain Parameters. J Am Soc Echocardiogr. 2012 Jan;25(1):68-79.

5- Li et.al. Value of Three-Dimensional Speckle-Tracking in Detecting Left Ventricular Dysfunction in Patients with Aortic Valvular Diseases. J Am Soc Echocardiogr. 2013 Nov;26(11):1245-52.

6- Uusitalo et al, Two-Dimensional Speckle-Tracking during Dobutamine Stress Echocardiography in the Detection of Myocardial Ischemia in Patients with Suspected Coronary Artery Disease. J Am Soc Echocardiogr 2016;29:470-9.

7- Brunet-Bernard et.al. Defining patients at-risk of non-response to cardiac resynchronization therapy. Value of rest and exercise echocardiography. International Journal of Cardiology, doi: 10.1016/j.ijcard.2013.11.085

8- Wang et al, Left Ventricular Long-Axis Performance during Exercise is An Important Prognosticator in Patients with Heart Failure and Preserved Ejection Fraction. Int J Cardiol 2015 Jan 15;178:131-5.

9- Galli et al, Value of Myocardial Work Estimation in the Prediction of Response to Cardiac Resynchronization Therapy. J Am Soc Echocardiogr. 2018 Feb;31(2):220-230.

10- Edwards et al, Global Myocardial Work Is Superior to Global Longitudinal Strain to Predict Significant Coronary Artery Disease in Patients With Normal Left Ventricular Function and Wall Motion. J Am Soc Echocardiogr. 2019 Aug;32(8):947-957.

11- El Mahdiui et al, Global Left Ventricular Myocardial Work Efficiency in Healthy Individuals and Patients with Cardiovascular Disease. J Am Soc Echocardiogr. 2019 Sep;32(9):1120-1127.

12- Prihadi et al, Determinants and prognostic implications of left ventricular mechanical dispersion in aortic stenosis. European Heart Journal - Cardiovascular Imaging 2019 Jul 1;20(7):740-748.

13- Badano et al, Standardization of left atrial, right ventricular, and right atrial deformation imaging using two-dimensional speckle tracking echocardiography: a consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging Eur Heart J -Cardiovasc Imaging 2018;19, 591–600

14- Thomas et al, Left Atrial Structure and Function, and Left Ventricular Diastolic Dysfunction. J Am Coll Cardiol 2019;73:1961–77;

15- Florescu et al, Automated left atrial volume measurement by two-dimensional speckle-tracking echocardiography: feasibility, accuracy, and reproducibility. European Heart Journal - Cardiovascular Imaging 2021; 00, 1–10

16- Sanz et al, Anatomy, Function, and Dysfunction of the Right Ventricle. Journal of the American College of Cardiology, Volume 73, Issue 12, 2 April 2019, Pages 1463-1482

17- Jones et al., Echocardiographic Assessment of the Right Ventricle–State of the Art. Heart, Lung and Circulation, Volume 28, Issue 9, 1339 – 1350

18- Voigt et al, Definitions for a Common Standard for 2D Speckle Tracking Echocardiography: Consensus Document of the EACVI/ASE/Industry Task Force to Standardize Deformation Imaging. J Am Soc Echocardiogr 2015;28:183-93

19- D´Hooge et al, Two-dimensional speckle tracking echocardiography: standardization efforts based on synthetic ultrasound data. Eur Heart J Cardiovasc Imaging 2016 Jun;17(6):693-701

20- Farsalinos et al., Head-to-Head Comparison of Global Longitudinal Strain Measurements among Nine Different Vendors The EACVI/ASE Inter-Vendor Comparison Study J Am Soc Echocardiogr 2015;28:1171-81

21- Mirea et al, Intervendor Differences in the Accuracy of Detecting Regional Functional Abnormalities. Eur Heart J Cardiovasc Imaging 2016 Jun;17(6):693-701.

22- Ünlü et al, Comparison of Feasibility, Accuracy, and Reproducibility of Layer-Specific Global Longitudinal Strain Measurements Among Five Different Vendors: A Report from the EACVI-ASE Strain Standardization Task Force. J Am Soc Echocardiogr 2019;32:624-32

23- Ünlü et al, Impact of apical foreshortening on deformation measurements: a report from the EACVI-ASE Strain Standardization Task Force European Heart Journal -Cardiovascular Imaging 2019; 0, 1–7