An Overview about Speckle-tracking imaging Values among asthmatic patients

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Abstract

Speckle-tracking imaging (STI) is a non-invasive ultrasound technique that allows an objective and quantitative evaluation of global and regional myocardial function, independently from the angle of insonation and partly from cardiac translational movements. Echocardiographic estimation of segmental left ventricular contractility is routinely accomplished through visual interpretation of endocardial motion and myocardial thickening. This method is subjective and requires a relatively experienced observer. Quantitative analysis based on tracing of the endocardial border may also be hampered by endocardial "dropout" and trabeculations. STI is based on bi-dimensional (2D) echocardiographic technology, not limited by Doppler analysis Segments of myocardial tissue show a pattern of gray values in the ultrasound. This pattern, resulting from the spatial distribution of gray values, is commonly referred to as speckle pattern, characterizes the underlying myocardial tissue acoustically and is unique for each myocardial segment. Speckle tracking allows the measure of all in-plane components of the velocity vector, in all pixels More recently, the addition of the third dimension (3D) has partly expanded the scope of this technology

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Introduction

Speckle-tracking imaging (STI) is a non-invasive ultrasound technique that allows an objective and quantitative evaluation of global and regional myocardial function, independently from the angle of insonation and partly from cardiac translational movements [1–4].

Echocardiographic estimation of segmental left ventricular contractility is routinely accomplished through visual interpretation of endocardial motion and myocardial thickening. This method is

subjective and requires a relatively experienced observer. Quantitative analysis based on tracing of the endocardial border may also be hampered by endocardial "dropout" and trabeculations.

Tissue Doppler imaging (TDI) has been previously used in deriving myocardial velocities and assessing fundamental parameters of myocardial deformation (strain and strain rate) [5]. Myocardial tissue velocities represent the net effect of the contractile and elastic properties of the area under investigation and the motion caused by traction and tethering from other regions. In contrast, strain is a dimensionless index reflecting the total deformation of the ventricular myocardium during a cardiac cycle, as a percentage of its initial length. Strain rate is the rate of deformation or stretch. Strain techniques are, in principle, the optimal modalities for the assessment of regional myocardial function. The major limitation of TDI has been its angle dependency [5], requiring alignment of the ultrasound beam parallel to the direction of tissue movement. Thus, deformation study was substantially limited to the analysis of the tissue moving toward or away from the probe.

STI is based on bi-dimensional (2D) echocardiographic technology, not limited by Doppler analysis [6–8]. Segments of myocardial tissue show a pattern of gray values in the ultrasound. This pattern, resulting from the spatial distribution of gray values, is commonly referred to as speckle pattern, characterizes the underlying myocardial tissue acoustically and is unique for each myocardial segment. Speckle tracking allows the measure of all in-plane components of the velocity vector, in all pixels [9]. More recently, the addition of the third dimension (3D) has partly expanded the scope of this technology.

Diagnostic values

Early detection of reduced myocardial function

Myocardial function in non-ischemic cardiomyopathy

Strain analysis increase sensitivity in detecting subclinical cardiac involvement in cardiomyopathies. Strain is frequently attenuated in cardiomyopathy and can be utilized for the evaluation of disease progression and the effect of therapeutic interventions.[2]

Hypertrophic cardiomyopathy

In hypertrophic cardiomyopathy, typically, longitudinal function is reduced, while circumferential and radial function is elevated. The specific pattern of reduced and delayed longitudinal shortening and paradoxical systolic lengthening has been proposed as being specific for hypertrophic cardiomyopathy. Regional heterogeneity, typically with basal or mid septal longitudinal strain being most affected, appears to be distinctive to hypertrophic cardiomyopathy. Similar changes are not typically seen in ventricular hypertrophy induced by longstanding hypertension. Diastolic dysfunction appears early in hypertrophic cardiomyopathy.

Dilated cardiomyopathy

Dilated cardiomyopathy is usually associated with reduced strain in all directions and reduced left ventricular twist. In addition, left ventricular dyssynchrony is often seen in patients with dilated cardiomyopathy (see below). Nevertheless, the measurement of choice remains ejection fraction in this group of patients.

Restrictive cardiomyopathy

In restrictive cardiomyopathies attenuated longitudinal strain, but normal circumferential strain and left ventricular torsion are typical. Interestingly, ejection fraction may remain within normal limits until disease progression impairs circumferential strain. Constrictive pericarditis, conversely, is characterized by reduced circumferential strain and twist but preserved longitudinal function.

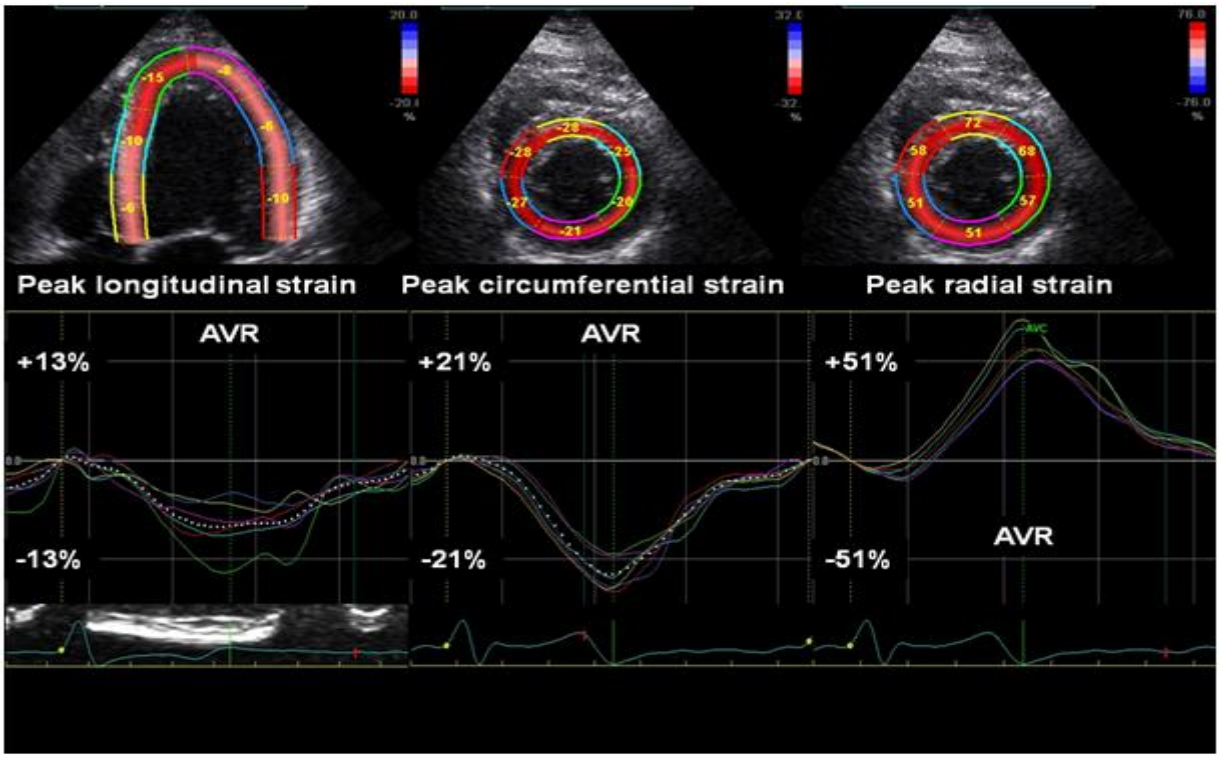

Figure 1: Left ventricular strain study in a patient with hypertrophic cardiomyopathy

Cancer therapy induced cardiomyopathy

Cancer patients receiving chemotherapy and/or radiation therapy may develop cardiomyopathy years or decades after ended theraphy[1]. This new cohort of patients has arised due to the advances in detection and therapy of cancer and is becoming a major public health issue. As a consequence of improved survival, these patients will live long enough to develop cardiac complications of the cancer therapy.

Chemotherapy-treated patients with normal ejection fraction may have significantly reduced myocardial function assessed by speckle tracking strain echocardiography compared to healthy

individuals[3]. Left ventricular dysfunction may progress until overt congestive heart failure, therefore early detection and treatment of cardiotoxicity is crucial in order to reduce the development of clinical manifestations.

Heart transplant recipients and cardiac function

Heart transplantation is the gold standard therapy for selected patients with end-stage heart failure, with 1-year survival approaching 90%. Graft dysfunction is a major cause of morbidity and mortality in heart transplant recipients. Importantly, not all cases of early cardiac allograft dysfunction can be explained by rejection. Early left ventricular function in heart transplant recipients is determined by immune response, and a variety of non-immune factors such as ischemia-reperfusion injury, post-surgical sympathetic denervation, reduction of pre-heart transplant pulmonary hypertension and left ventricular preload, advanced age, post-transplantation infections, and donor variables including age, ischemic time and left ventricular hypertrophy. The search for non-invasive techniques to assess cardiac allograft function is a high priority objective for heart transplant professionals. Sensitive assessment of myocardial function by speckle tracking strain in heart transplant recipients with normal left ventricular function by traditional echocardiographic measures is a non-invasive screening tool in the identification of patients with poor clinical prognosis[4].

Speckle tracking and left ventricular dyssynchrony

Strain assessment has contributed to improved understanding of left ventricular dyssynchrony. However, current guidelines still define the indications for cardiac resynchronization therapy exclusively on the basis of clinical findings (heart failure symptoms, New York Heart Association class II-IV), left ventricular function (ejection fraction ≤ 35%), and electrocardiographic findings (QRS ≥ 120msec). Nevertheless, only about 70% of patients treated with cardiac resynchronization therapy respond to this treatment with improvement in left ventricular function. This reflects the clinical need for better patient selection and methods of therapy optimization. Intraventricular dyssynchrony is commonly seen in patients with heart failure, and is believed to indicate more severe myocardial disease and poorer prognosis. One method to measure dyssynchrony is by assessing delay between anteroseptal radial strain and posterior (or inferior lateral) radial strain by speckle tracking echocardiography. Over 130 msec difference in time to peak radial strain between these two basal segments predicts response to cardiac resynchronization therapy. The standard deviation of time to peak longitudinal strains from 12 basal and mid segments may also be used to assess dyssynchrony. Values over 60 msec predict response to cardiac resynchronization therapy. Importantly, by combining radial and longitudinal dyssynchrony parameters a much higher accuracy is reached in predicting the response to cardiac resynchronization therapy[2].

Nevertheless, in spite of a significant number of various methods and dyssynchrony indices, there is still a lack of agreement on which indices should be utilized to predict cardiac resynchronization therapy response.

Speckle tracking in the detection of malignant arrhythmias

Patients with genetically diagnosed cardiomyopathy and relatives of patients with known heritable cardiac disease maybe mutation carriers without obvious myocardial dysfunction. These patients may eventually develop malignant arrhythmias even before myocardial changes can be shown with traditional imaging techniques. Accurate assessment of myocardial function is therefore particularly important in these patients[5]. A recently introduced application of deformation imaging that quantifies temporal nonuniformity of maximum myocardial contraction is mechanical dispersion. This variable is a promising marker of risk for ventricular arrhythmias and sudden death. Mechanical dispersion can be assessed by either myocardial velocities or strain imaging and is calculated as the standard deviation of the time from onset R in the ECG to maximum myocardial shortening in 16 left and 6 right ventricular segments. Increased right ventricular mechanical dispersion above 29 msec is associated with increased risk for malignant arrhythmias in patients with arrhythmogenic right ventricular cardiomyopathy Increased left ventricular mechanical dispersion is associated with malignant arrhythmias in long QT syndrome, dilated cardiomyopathy and in patients after myocardial infarctions.[5][6][7]

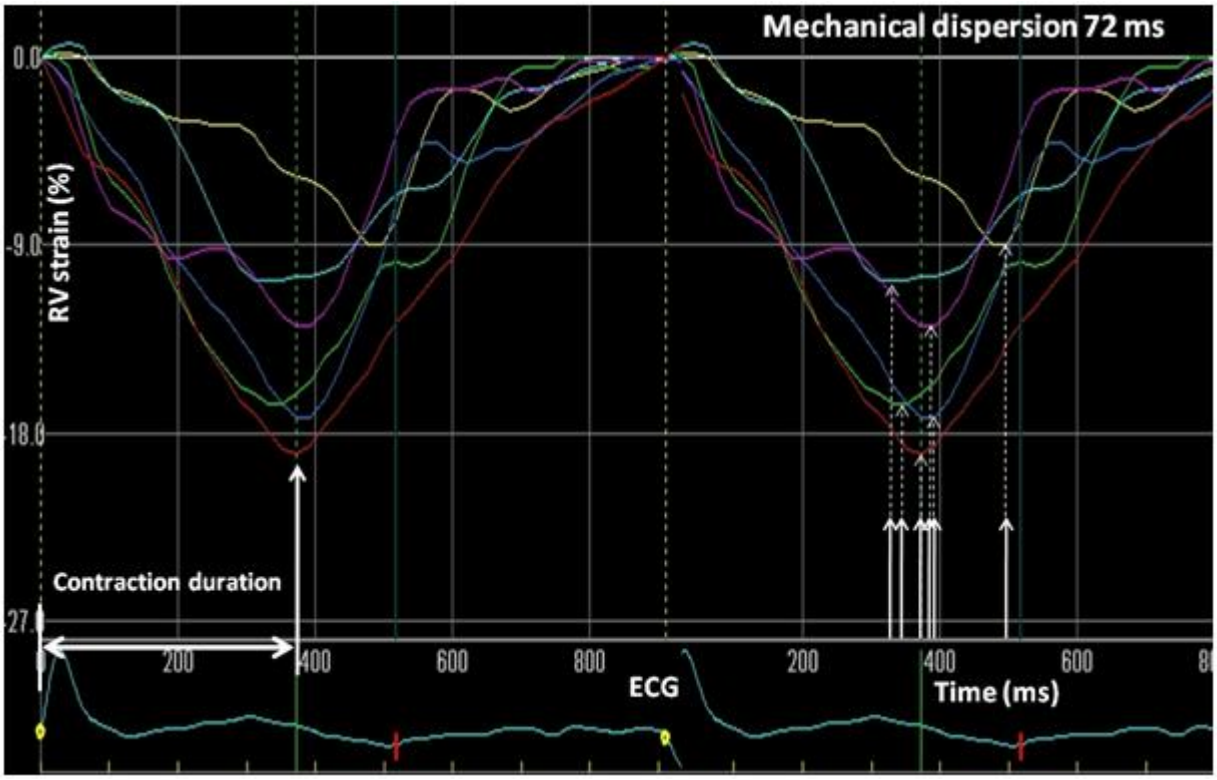

Figure 2: Definition of contraction duration and mechanical dispersion in the right ventricle

Speckle tracking in ischemic heart disease

Changes in strain facilitate recognition of ischemic myocardium at rest and during stress echocardiography and may provide prognostic information. It may also help defining the transmural extent of myocardial infarction and the presence of viable myocardium. The ischemic myocardium is characterized by reduced or lacking regional systolic longitudinal and circumferential shortening and radial thickening. Post systolic shortening after aortic valve closure is also a common finding in acute ischemia.

In patients with coronary artery disease infarct size might be assessed and the presence of coronary artery occlusions might be identified with speckle tracking echocardiography. [8] [9] The size of the myocardial infarction may give important prognostic information while the detection of coronary artery occlusions may have important clinical implications in patients with non ST-elevation acute coronary syndrome. Although, coronary artery occlusion is found in about 25% of patients with non-ST elevation acute coronary syndrome, ECG has limited sensitivity to detect the presence of occlusion. Even though these patients may develop extensive myocardial damage, criteria for acute reperfusion therapy may not be fulfilled. Correct identification of coronary occlusion in non ST-elevation acute coronary syndrome may prevent irreversible myocardial damage in these patients by urgent reperfusion therapy as practiced in patients with ST-elevation myocardial infarctions. The direct observation of a developing systolic dysfunction combined with a post systolic shortening indicates acute myocardial ischemia [2].

The place of strain echocardiography in the detection and assessment of fibrosis and myocardial viability is not yet settled. Currently, combination of strain with low- dose dobutamine stress pertains the strongest evidence for the evaluation of myocardial viability[2].

Finally, increased mechanical dispersion (described above) assessed by strain echocardiography has been associated with increased risk of arrhythmic events, independently of left ventricular function assessed by ejection fraction in patients with ischemic heart disease.[7] Since the majority of patients with ischemic heart disease and malignant arrhythmias have ejection fractions above 35%, there is a need for novel methods to identify risk in these patients.

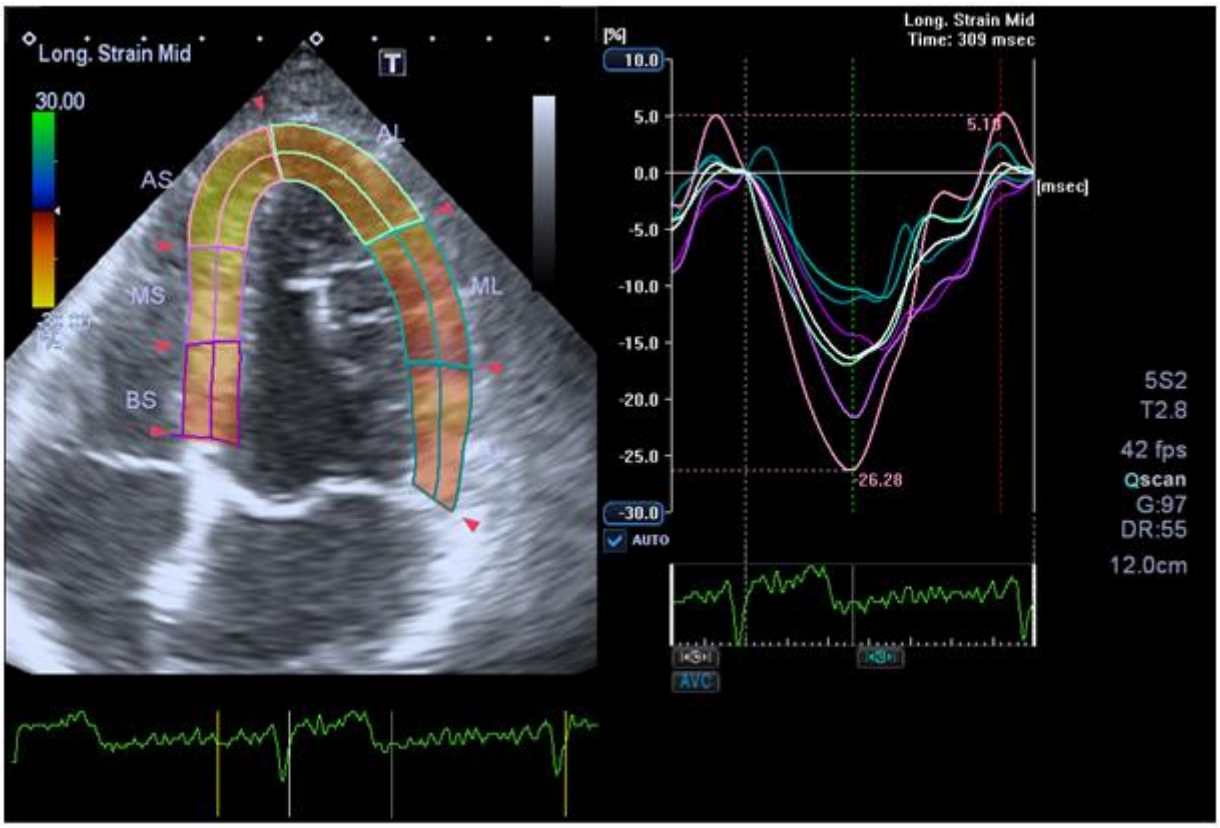

Figure 3: Left ventricular longitudinal strain study of a patient with coronary artery occlusion

Clinical applications of 3D speckle tracking

Three dimensional (3D) speckle tracking echocardiography is a novel and promising commercially available tool to characterize and quantify myocardial segmental and rotational mechanics. One possible application of the method is in the assessment of ventricular dyssyncrony. Assessment is done by measuring mechanical activation times derived from time-to-peak systolic strain of different segments, with the expectation that identification of the segments of latest mechanical activation could identify dyssynchrony and guide successful lead placement leading to optimal cardiac resynchronization therapy response. [10] However, there are only a few studies published so far using 3D speckle tracking in the clinical practice.

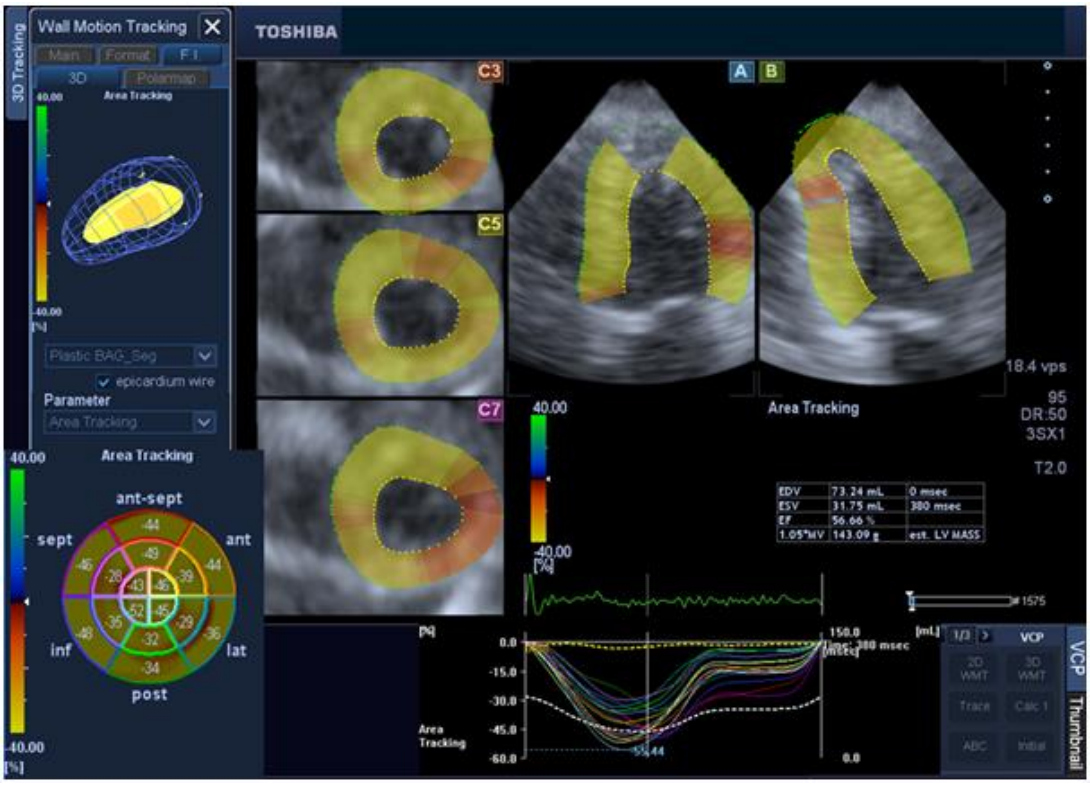

Figure 4: 3D speckle tracking area strain study in a healthy individual

Right ventricular function and speckle tracking echocardiography

Longitudinal shortening is the major contributor to overall right ventricular function with an equal contribution of the right ventricular free wall and the interventricular septum. Assessment of right ventricular function by conventional 2D echocardiography is, however, challenging due to the complex right ventricular geometry and the strongly trabeculated inner wall contour. Speckle tracking echocardiography is promising tool in assessing regional and global right ventricular deformation in different directions in terms of both amplitude and timing, with the advantage of being less affected than tissue Doppler imaging by overall heart motion. In healthy individuals, peak systolic longitudinal strain in the free right ventricular wall is approximately -28 ± 4%. In diseases with right ventricular involvement, longitudinal deformation decrease and the base-to-apex gradient tends to disappear. Arrhythmogenic right ventricular cardiomyopathy has typical involvement of the right ventricular free wall with early reduction of longitudinal deformation and increased mechanical dispersion [5]. These changes can be readily assessed by speckle tracking echocardiography. Furthermore, strain abnormalities of the right ventricle can also be detected in pulmonary hypertension, as well as in amyloidosis and congenital heart diseases [2]. In general, strain measurement is useful as an early indicator of right ventricular dysfunction.

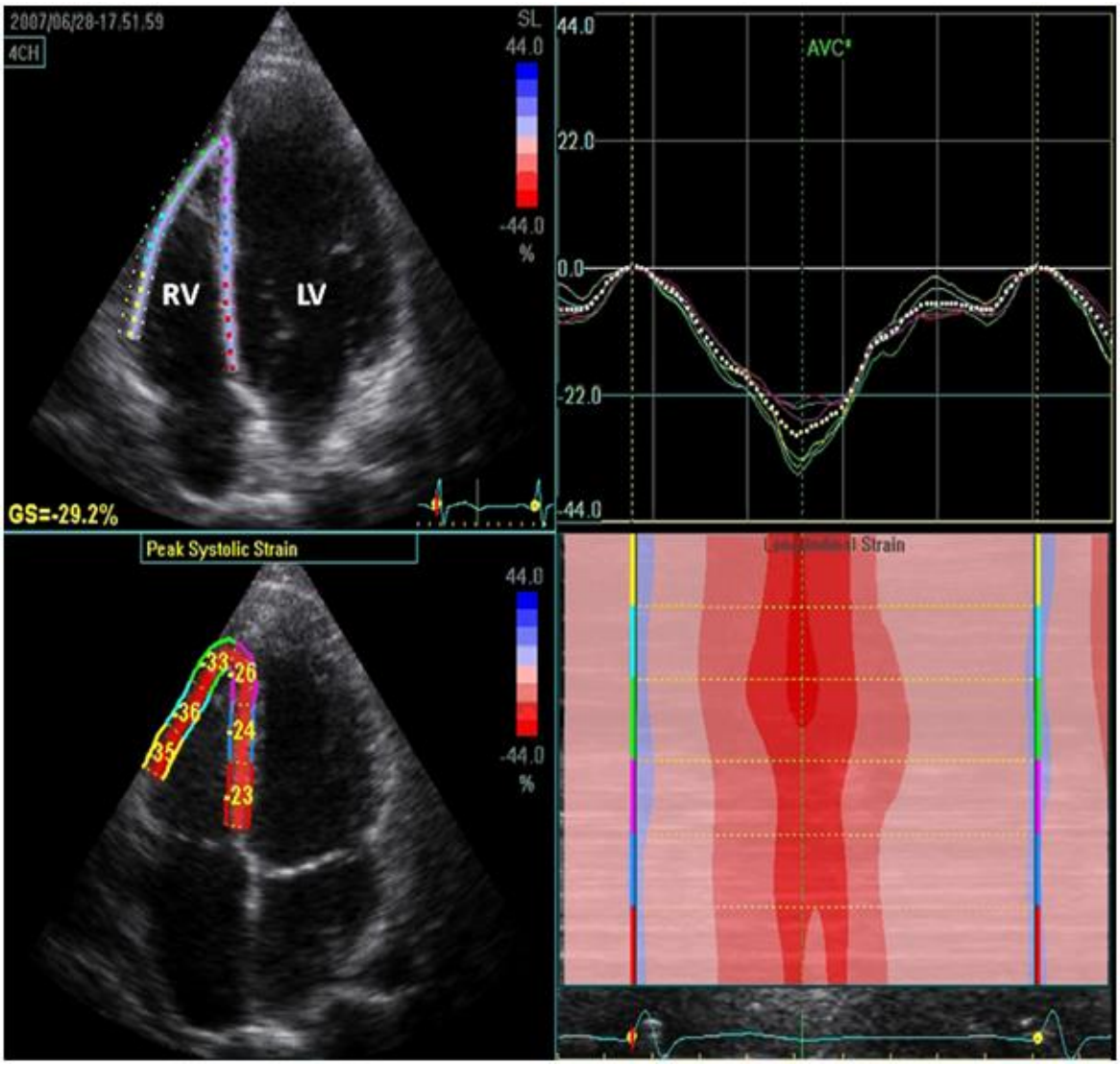

Figure 5: Right ventricular strain study in a healthy individual

Physics of Speckle-Tracking

"Speckles" are small groups of myocardial pixels created by the interaction of ultrasonic beams and the myocardium, with specific gray scale characteristics. A speckle is commonly defined as the spatial distribution of gray values in the ultrasound image. The result of a speckle-tracking procedure (followed by regularization process) is an estimate of the in-plane velocity vector in all pixels in each of the frames of the ultrasound data set (dynamic velocity vector field). The spatial distribution of the gray values within the ultrasound image is due to constructive and destructive interference of reflections from the individual scatterers within the myocardium. Reflections occur at transitions between different types of tissues or at specific sites, and are much smaller than the wavelength. Constructive interference generates a high-amplitude signal, destructive a low-amplitude one. The exact scatter positions determine the speckle characteristics. Speckle-tracking technology offers the ability to identify and track the same speckle throughout the cardiac cycle [4].

In the ultrasound image , the speckle pattern occurring at a position further away from the transducer. To correctly detect speckles, the motion of the tissue should be slower than the motion of the ultrasound beam (image lines). Sound waves propagate through tissues at an average velocity of 1530 m/s, while myocardial tissue moves at velocities in the order of centimeters per second: the basic condition is thus clearly met [16].

There are different algorithms used by different vendors in tracking these speckles. Some speckle-tracking methods are based on so-called block matching, where a region in the image is selected (the kernel) and is followed in the next image frame by subsequently trying out different positions and by determining the similarity between the kernel and the pattern observed in that position. The position where the similarity between the kernel ("fingerprint") and the observed pattern is maximal is assumed to be the new position of the speckle pattern [16]. Another common approach is based on conservation of gray value, that is, it is assumed that gray values do not change over time. Radio frequency (RF) speckle—used in block-matching method—is a high-frequency signal, so that small between-frame motion can be detected, whereas its corresponding gray-scale speckle—used in gray-scale tracking—is derived from lower-frequency signals, being less sensitive to small displacements. Importantly, speckle tracking of gray-scale images does not necessarily perform well on high frame-rate data [16]. Then, RF-based methods allow to obtain a higher spatial, temporal, and velocity resolution because they use a signal with a higher-frequency content; at the same time, these methods are more sensitive to decorrelation and noise, requiring more severe regularization, which in turn might limit their resolution. Because both RF and gray-scale approaches offer advantages, a hybrid method was recently proposed.

So far, it is possible to evaluate the direction of movement, the speed of movement, and the distance of such movement at any point in the myocardium, independently from the transducer, relative to adjacent segments. The semi-automated nature of speckle-tracking echocardiography guarantees good intra-observer and inter-observer reproducibility [4].

Given that the velocity vector field is known for all pixels within the image, the axes are known with minimal user interaction. The radial, longitudinal, or circumferential velocity profiles throughout the cardiac cycle can be reconstructed, independent of the angle between the ultrasound image line and the direction of motion as in the conventional Doppler imaging [16]. The process of correcting the initial velocity vector estimates by applying additional boundary conditions based on a priori knowledge about the characteristics of the velocity field is called regularization. Regularization can consist of median filtering, weighted smoothing, elastic model, and myocardial boundaries definition.

Velocity vector imaging is partly analogous to 2D STI as it too tracks the speckles using 2D echocardiography, but utilizes additional physiological information to more robustly track the speckle kernels [17]. Each vector is an expression of direction and the magnitude of the velocity. The qualitative evaluation of the velocity is determined by comparing vectors along the tracked

contour. Longitudinal strain is the percentage decrease in the length of the myocardium during systole (movement of the base toward the apex). It is expressed as a percent negative value (decrease in length in systole) [18]. Longitudinal strain may be calculated as an endocardial strain, midline strain, epicardial strain, or averaged over the entire cardiac wall. There is currently insufficient evidence to favor one way over another. Radial strain refers to the thickening of the myocardial wall during inward motion of the ventricle, measured in the short-axis views. The value is traditionally defined as percent positive (thickening in systole). Circumferential strain represents the change in the length along the circular perimeter, by definition percent negative in systole. Strain parameters can be individualized for each myocardial segment or can be expressed as global strain (averaging of all segments). Strain rate (evaluated globally or for each segment) represents rate of longitudinal, radial, or circumferential deformation in time. It has a marked systolic negative peak (S) with two positive peak in early (E) and late diastole (A).

Relevant strain values along strain curves are, but are not limited to:

- End-systolic strain: the value at end-systole
- Peak systolic strain: the peak value during systole
- Positive peak systolic strain

Peak strain: the peak value during the entire heart cycle. The peak strain may coincide with the systolic or end-systolic peak, or may appear after aortic valve closure (AVC) (it may be described as “post-systolic strain”) [19].

Modern software allows display of results in bull’s eye (polar map) similar to single-photon emission computed tomography (SPECT). This is more familiar to cardiologists as it depicts single myocardial segments with relative values of strain, strain rate, and time to peak strain/strain rate (synchronicity). A more unfamiliar method to display results in a monoplane view is the so-called curved anatomic M-mode (CAMM) which depicts timely variation of single parameters evaluated for a specific segment of interests from base to the apex and from septal to lateral wall. This offers a unique opportunity for timing and recognizing precise phases of a cardiac cycle (relaxation) and for the evaluation of AVC. End-systole coincides with AVC and can be visualized in the parasternal or apical long-axis view or by detecting the closure click on the spectral tracing of the pulsed-wave Doppler of aortic valve flow [19].

Rotation is the measure of the rotational movement of the myocardium in relation to an imaginary long-axis line from apex to base drawn through the middle of LV cavity 4]. Clockwise rotation is defined as negative, while counterclockwise rotation has a positive value. Twist is the algebraic difference in rotation between the apex and the base. Torsion is the twist normalized for the length of the LV cavity (degrees per centimeter). LV rotation or twisting motion has an important role in LV systolic and diastolic function. Normal values for LV rotation and twist angle have shown high variability (technique used, location of the region of interest, age, and loading hemodynamics of

the ventricle). The increase in LV twist angle with age observed in literature can be explained by less opposed apical rotation, resulting from a gradual decrease in subendocardial function with aging. Worsening of diastolic relaxation and reduced diastolic suction is, however, associated with an early reduced and delayed diastolic untwisting. [20-23].

Myocardial strain and Strain Rate (SR) are sensitive parameters for the quantification of diastolic function. Diastolic SR signals can be recorded during isovolumic relaxation, during early filling, and in late diastole. The hemodynamic determinants of protodiastolic strain rate include LV relaxation, regional diastolic stiffness, systolic function, end-systolic wall stress, and filling pressures. In addition, protodiastolic strain rate can assess interstitial fibrosis and can be used to identify viable myocardium after stunning and infarction. Measurement of diastolic strain and strain rate may be useful for research applications but is presently not recommended for routine clinical use. [20-23].

The detection of myocardial fibrosis and viability depends on the evaluation of myocardial characteristics and shape during the cardiac cycle. Fibrotic tissue may be focal (as occurs in patients with myocardial infarction [MI]) or diffuse (systemic or metabolic disturbances). Fibrosis is actually accurately identified using myocardial late enhancement or T-weighted mapping with cardiac magnetic resonance imaging (MRI), but speckle tracking (especially systolic and protodiastolic strain rate) has a good correlation with tissue fibrosis, evaluated via cardiac magnetic resonance or biopsy. [24-26]. All these parameters can be measured not only for the LV but also for the right ventricle (RV) and left and right atria (LA and RA, respectively), but have not been fully validated and, still together, commercial applications to process these chambers do not exist. Timing peak strain is pivotal in defining dyssynchrony as well as for the evaluation of ischemia (post-systolic thickening or shortening). [26].

Image acquisition

Gated images are obtained during end-expiratory breath holding with stable electrocardiographic traces, avoiding foreshortening of the ventricle and proper visualization of endocardial border. Images acquired should be of high quality. Optimal frame rate should be 60–110 frames per second (FPS). The operator should keep the sector width and depth minimal to focus on the structure of interest. Usually, three consecutive cardiac cycles are obtained and the values averaged for the final processing. Low FPS limits tracking efficacy, while higher FPS “smooths” speckle pattern and the final quality of the analysis. Apical four-chamber, two-chamber, and three-chamber views are necessary for estimation of LV strain and strain rates by 2D STI. This finally offers global longitudinal strain (GLS) value, that is, the average of longitudinal strain for all segments in all views. Parasternal short-axis views (basal, papillary muscles, and apex) are necessary for radial and circumferential strains (finally averaged in global radial and circumferential strain) and strain rates as well as for rotation, twist, and torsion analysis. The ways myocardial segments are divided widely vary among vendors, but in general, a 16–18-segment LV model is used. Myocardium is divided

into six segments: basal septal, mid septal, apical septal, apical lateral, mid lateral, and basal lateral. For the timing determination of cardiac events, mitral inflow and LV outflow velocities are recorded using pulsed-Doppler echocardiography and the aortic and mitral valve closure/opening (AVC/O and MVC/O, respectively) times are obtained, as well as visually (AVC in apical long-axis view) or semi-automatically (evaluation of CAMM). The recordings are analyzed offline using semi-automated computer software for estimation of strain and strain rate by 2D STI. A region of interest (ROI) has to be outlined manually, tracing the endocardium. The epicardium is automatically traced by the system, but the wall thickness can be manually adjusted. [27].

The ROI is defined at end-diastole by.:

- Endocardial border
- Epicardial border
- Myocardial midline.

Each of these contours can be user defined or generated automatically.

Topographic definitions of the myocardial ROI in apical views are:

- “Left/right base”
- “Midbase”
- “Apex”
- “Left/right ROIs.”

Vendors have incorporated tools to help users identify tracking reliability. Various methods are utilized. Some vendors have introduced protocols that identify segments where tracking is suboptimal and is excluded from the final results. In addition, some vendors provide accuracy indices to guide the user in tracking performance estimates.

Longitudinal strain is more robust and reproducible than other parameters. The values tend to be partly different for different walls and segments. There is a gradient of longitudinal strain values from base to apex (higher values for apical segments) as well as from endo to epicardium (higher values of strain in the subendocardial region).

No Conflict of interest.

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