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Hermann Blessberger and Thomas Binder

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NON-INVASIVE IMAGING

Two dimensional speckle tracking echocardiography: basic principles

Hermann Blessberger,[1] Thomas Binder[2]

[1]AKH Linz, Department of Internal Medicine I - Cardiology, Krankenhausstrasse, Austria
[2]Department of Cardiology, Medical University of Vienna, Internal Medicine II, AKH, Waehringerguertel, Vienna, Austria

Correspondence to
Professor Dr Thomas Binder, Department of Cardiology, Medical University of Vienna, Internal Medicine II, AKH, Waehringerguertel 18-20, 1090 Vienna, Austria; thomas.binder@meduniwien.ac.at

Two dimensional (2D) speckle tracking echocardiography (STE) is a promising new imaging modality. Similar to tissue Doppler imaging (TDI), it permits offline calculation of myocardial velocities and deformation parameters such as strain and strain rate (SR). It is well accepted that these parameters provide important insights into systolic and diastolic function, ischaemia, myocardial mechanics and many other pathophysiological processes of the heart. So far, TDI has been the only echocardiographic methodology from which these parameters could be derived. However, TDI has many limitations. It is fairly complex to analyse and interpret, only modestly robust, and frame rate and, in particular, angle dependent. Assessment of deformation parameters by TDI is thus only feasible if the echo beam can be aligned to the vector of contraction in the respective myocardial segment. In contrast, STE uses a completely different algorithm to calculate deformation: by computing deformation from standard 2D grey scale images, it is possible to overcome many of the limitations of TDI. The clinical relevance of deformation parameters paired with an easy mode of assessment has sparked enormous interest within the echocardiographic community. This is also reflected by the increasing number of publications which focus on all aspects of STE and which test the potential clinical utility of this new modality. Some have already heralded STE as 'the next revolution in echocardiography'. This review describes the basic principles of myocardial mechanics and strain/SR imaging which form a basis for the understanding of STE. It explains how speckle tracking works, its advantages to tissue Doppler imaging, and its limitations.

BACKGROUND

Deformation parameters—strain and strain rate

Strain is a dimensionless quantity of myocardial deformation. The so-called Langrangian strain (ϵ) is mathematically defined as the change of myocardial fibre length during stress at end-systole compared to its original length in a relaxed state at end-diastole=$(l-l_0)/l_0$ (figure 1).[1] Strain is usually expressed in per cent (%). The change of strain per unit of time is referred to as strain rate (SR). Negative strain indicates fibre shortening or myocardial thinning, whereas a positive value describes lengthening or thickening.

As SR (1/s) is the spatial derivative of tissue velocity (mm/s), and strain (%) is the temporal integral of SR, all of these three parameters are mathematically linked to each other (figure 2).[1 2]

Basically, strain measures the magnitude of myocardial fibre contraction and relaxation. In contrast to TDI, it only reflects active contraction since the STE derived deformation parameters are not influenced by passive traction of scar tissue by adjacent vital myocardium (tethering effect) or cardiac translation.[3] Since contraction is three dimensional and myocardial fibres are oriented differently throughout the myocardial layers, deformation can also be described with respect to the different directional components of myocardial contraction. To truly understand deformation it is therefore essential to consider myocardial mechanics.

Basics of myocardial mechanics

The sophisticated myocardial fibre orientation of the left ventricular (LV) wall provides an equal distribution of regional stress and strains.[4] In healthy subjects, the left ventricle undergoes a twisting motion which leads to a decrease in the radial and longitudinal length of the LV cavity. During isovolumetric contraction the apex initially performs a clockwise rotation. During the ejection phase the apex then rotates counterclockwise while the base rotates clockwise when viewed from the apex.[5] In diastole relaxation of myocardial fibres and subsequent recoiling (clockwise apical rotation) contributes to active suction.[5] Thus, the contraction of the heart is similar to the winding (and unwinding) of a towel. From a mathematical point of view several parameters of myocardial mechanics can be described (figure 3):

- *Rotation* (degrees)=angular displacement of a myocardial segment in short axis view around the LV longitudinal axis measured in a single plane.
- *Twist* or *torsion* (degrees) which is the net difference between apical and basal rotation (calculated from two short axis cross-sectional planes of the LV).[6 7]
- *Torsional gradient* (degrees/cm) which is defined as twist/torsion normalised to ventricular length from base to apex and accounts for the fact that a longer ventricle has a larger twist angle.[8]

LV twist can be quantified in short axis views by measuring both apical and basal rotation with the help of STE (figure 4). In addition, it is possible to calculate time intervals of contraction/relaxation with respect to torsion or rotation and therefore measure the speed of ventricular winding and unwinding. In particular, the speed of apical recoil

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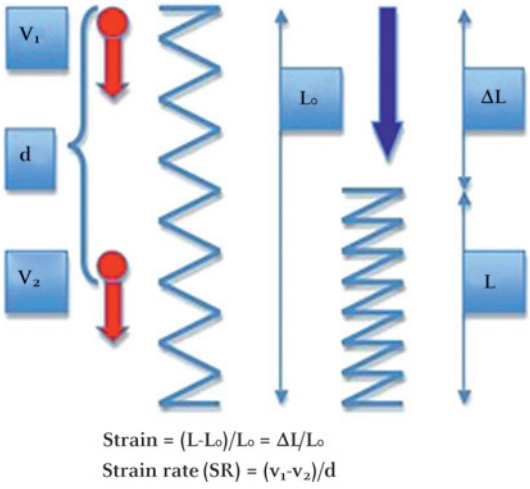

Figure 1 Elastic deformation properties. Strain=change of fibre length compared to original length, strain rate=difference of tissue velocities at two distinctive points related to their distance. ΔL, change of length; L_o, unstressed original length; L, length at the end of contraction; blue arrow, direction of contraction; v_1, velocity point 1; v_2, velocity point 2; d, distance.

during early diastole seems to reflect diastolic dysfunction.[9 10]

Several studies have demonstrated that disturbed rotational mechanics can be found in many cardiac disease states and that specific patterns describe specific pathologies.[9–14]

While these parameters are assessed with the help of STE derived deformation parameters and describe the 'mechanics' of the entire heart, deformation parameters can also be calculated for individual segments and specific vectors of direction. Three different components of contraction have been defined: radial, longitudinal, and circumferential (figure 5).

- *Longitudinal* contraction represents motion from the base to the apex.
- *Radial* contraction in the short axis is perpendicular to both long axis and epicardium. Thus, radial strain represents myocardial thickening and thinning.
- *Circumferential* strain is defined as the change of the radius in the short axis, perpendicular to the radial and long axes.

Longitudinal deformation is assessed from the apical views while circumferential and radial deformation are assessed from short axis views of the left ventricle. The description of these three aforementioned 'normal strains'—which can be measured using current STE technology—allows a good approximation of active cardiac motion. However, they still represent a simplification. When considering myocardial deformation during contraction in three dimensional space, six more 'shear strains' can be defined in addition to the normal strains.[1] Normal strains are caused by forces that act perpendicular to the surface of a virtual cylinder within the myocardial wall, resulting in en bloc stretching or contraction without skewing of the volume. Conversely, forces causing shear strain act parallel to the surface of such a myocardial block and lead to a shift of volume borders relative to one another as delineated by a shear angle α (figure 6).

Reference values for segmental strain were established for the left ventricle and the left atrium.[15–19] Normal paediatric strain values are also available.[18] However, clear cut-offs for peak systolic strain to define pathologic conditions are still missing. Marwick *et al* enrolled 242 healthy individuals without cardiovascular risk factors or a history of cardiovascular disease in their multicentre study and defined normal LV longitudinal strain values as displayed in table 1.[19] Global reference values (mean±SEM) for the longitudinal peak systolic strain (GLPSS: −18.6±0.1%), peak systolic SR (−1.10±0.01/s), early diastolic SR (1.55±0.01/s), as well as for the global late diastolic SR (1.02±0.01/s) were also established.[19] Circumferential and radial LV strain reference values were determined by Hurlburt *et al* (table 2).[15] It appears that longitudinal strain values in the basal segments are less than in the mid and apical segments. It remains unclear if this truly reflects less contractility or if it is a methodological issue. According to current data, it does not seem necessary to adjust STE based strain or SR parameters for sex or indices of LV morphology. Studies investigating this issue only found a weak relationship or yielded conflicting results.[15 19–21] However, it has been shown that with age, LV twisting motion increases, whereas diastolic untwisting is delayed and reduced when compared to young individuals.[22] Possibly this is caused by the higher incidence of diastolic dysfunction with age.

Strain and SR change throughout the cardiac cycle. To describe systolic myocardial function, it is best to use peak systolic strain (which reflects

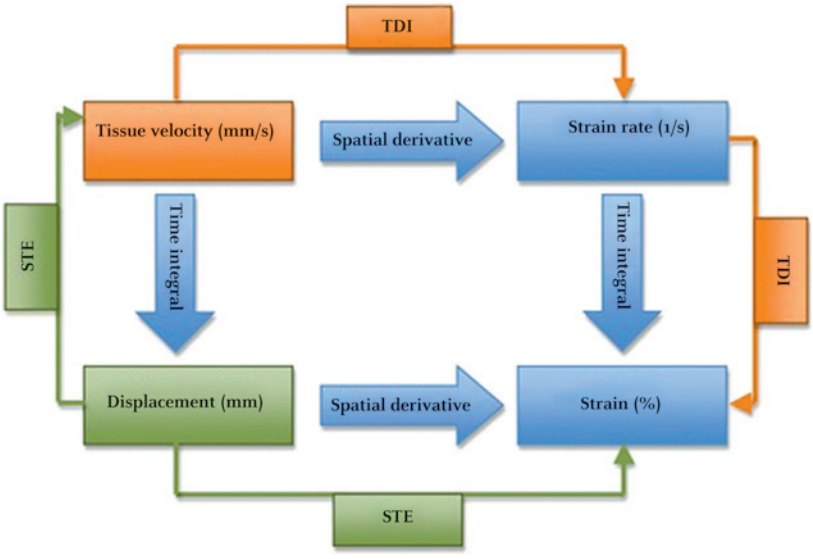

Figure 2 Mathematical relationship between different deformation parameters and mode of calculation for speckle tracking echocardiography (STE) and tissue Doppler imaging (TDI). STE primarily assesses myocardial displacement, whereas TDI primarily assesses tissue velocity. Modified from Pavlopoulos *et al*.[1]

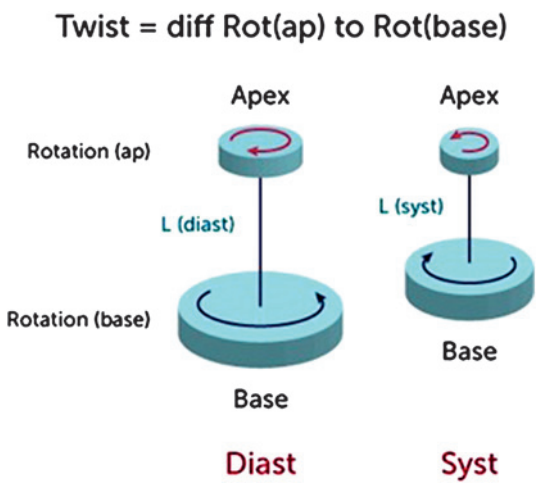

Figure 3 Rotation of left ventricular apex and base during the heart cycle. Rot, rotation; l, length; diast, diastole; syst, systole; ap, apical; diff, difference.

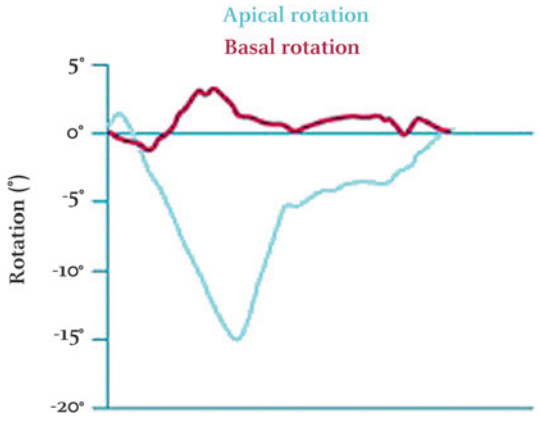

Figure 4 Apical and basal rotation during heart cycle. Ordinate, rotation in degrees; abscissa, time.

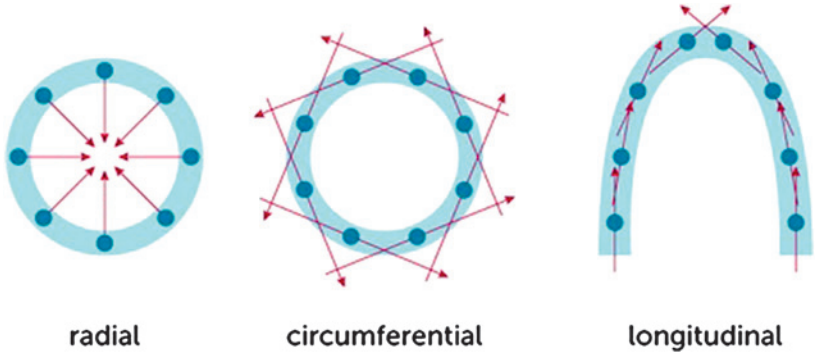

Figure 5 Different types of left ventricular myocardial wall strains.

systolic shortening fraction) and peak systolic SR.[23] For timing of contraction the time to peak systolic strain and SR have been used (beginning of QRS complex to max peak of strain/SR curve, see figure 7). By defining the time of aortic valve closure it is also possible to determine if peak strain in certain regions occurs before or after the end of systole. This may be particularly important for the assessment of dyssynchrony.[24]

Such computations can be made for radial, circumferential, and longitudinal function, either for individual segments, a cut plane or the entire ventricle (using averaged values). Thus, strain and SR provide valuable information on both global and regional systolic and diastolic function and their timing.

Basic principles of 2D speckle tracking echocardiography (STE): key points

- STE is a novel imaging modality that overcomes many of the limitations associated with tissue Doppler imaging.
- STE allows easy assessment of segmental and global longitudinal, radial, and circumferential strain and strain rate as well as LV rotation, torsion, and dyssynchrony.
- Reference values for all LV segments are already available.
- STE is a valuable tool in evaluating LV systolic function and provides information on top of ejection fraction.
- STE also proved useful to investigate LV diastolic dysfunction.
- Application of STE is limited by image quality, out-of-plane motion of speckles, lack of clear cut-off values for clinical decision making, and software issues (correct definition of ROI, inter-vendor comparability of values).

How does 2D speckle tracking work?

STE was introduced by Reisner, Leitman, Friedman, and Lysyansky in 2004.[25 26] It is performed as an offline analysis from digitally recorded and ECG triggered cine loops. The algorithm uses speckle artefacts in the echo image which are generated at random due to reflections, refraction, and scattering of echo beams. Such speckles in the LV wall are tracked throughout the cardiac cycle. Some of these speckles stay stable during a part of the heart cycle and can be used as natural acoustic markers for tagging the myocardial motion during the cardiac cycle. The post-processing software defines a 'cluster of speckles' (called a 'kernel') and follows this cluster frame to frame (figure 8).[1] Detection of spatial movement of this 'fingerprint' during the heart cycle now allows direct calculation of Langrangian strain. Tissue velocity is estimated from the shift of the individual speckles divided by the time between successive frames. Strain rate can be calculated from tissue velocity as well (figure 2). Before strain analysis can be performed, it is essential to correctly track the endocardial and epicardial borders of the left ventricle, and thereby correctly define the region of interest (ROI) (figure 9). After definition of ROI in the long or short axis view, the post-processing software automatically divides the ventricle into six equally distributed

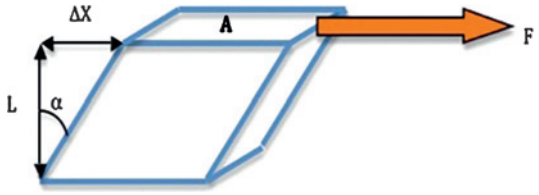

Figure 6 Shear strain. A, surface area; F, force; Δx, border shift; L, height; α, shear angle.

segments. Several different approaches and varying degrees of user interaction are required depending on the scanner type and the echocardiographic view (parasternal vs apical). Endocardial tracking also allows computation of LV area changes during the cardiac cycle and can, thus, also be used to define end-systole and end-diastole.

The raw data are filtered and mathematical algorithms are applied to generate values. Several different display formats have been used to represent the data both using strain and SR curves and graphical colour encoded displays. STE proved to be highly robust and reproducible.[27] Intra- as well as inter-observer variability between skilled echo examiners were negligible.[27] From a practical point it is essential to choose a sector width and transducer position which provides visibility of the apical and lateral segments, but which still guarantees frame rates above 30 Hz, ideally around 50 Hz.

Speckle tracking versus tissue Doppler imaging and MRI

STE has several important advantages compared to other modalities which are able to measure deformation. In contrast to MRI, STE is much more available, cost efficient, can be used 'bedside', and has a shorter procedure and post-processing time. In comparison to TDI, STE is insonation angle independent and does not require such high frame rates, is not subjected to the tethering effect, and allows straightforward measurement of radial and circumferential strain in addition to longitudinal strain.[2] The 'tethering effect' is a phenomenon encountered when TDI is used to assess strain. Scar tissue which is unable to contract is 'dragged' by adjacent viable myocardium during systole. Since TDI strain is calculated on the basis of tissue velocities, this motion is falsely assigned with a negative strain value, and thus assumed to be actively contracting tissue. In STE, this effect does not occur as strain is directly calculated from the frame to frame motion of speckle patterns and not from myocardial velocities.

Strain and systolic function

While both strain and LV ejection fraction (LVEF) measure LV function, there is a fundamental difference between the two: strain calculates the contractility of the myocardium, while LVEF is a surrogate parameter that describes myocardial pump function. Even if contractility is reduced, compensatory mechanisms (ie, ventricular dilatation, geometry changes) can still assure that stroke volume remains normal (at least at rest). Thus, STE is especially suited for the assessment of global and regional systolic function in patients with heart failure and apparently normal ejection fraction (HFNEF).[28] Furthermore, regional dysfunction is not as apparent when using a global parameter such as LVEF. In addition, exact calculation of LVEF requires good image quality, operator experience, and has a large error of measurement. LVEF is also much more load dependent than strain.[29] Hooke's law[30] summarises the relationship between the forces contributing to tissue deformation:

$$\text{Passive wall stress}_{(t)} - \text{contractile force}_{(t)} = \text{elasticity} \times \text{deformation}_{(t)}$$

According to this law, passive wall stress and elasticity both interfere with direct translation of segmental contractile force into deformation (strain). Passive wall stress is influenced by LV loading conditions (LV pressure), ventricle geometry, and segment to segment interaction, whereas elasticity is defined by tissue properties.

In summary, strain could be an important parameter for LV function which can display cardiac dysfunction on a more fundamental level in an early stage of disease.

STE longitudinal strain and EF correlate well in healthy individuals; however, in ST elevation myocardial infarction survivors and heart failure patients, for example, the correlation is less strong.

Table 1 Reference values for segmental longitudinal peak systolic strain

LV segment (apical 4 chamber view)	Mean peak systolic longitudinal strain (%)±SD*	Mean peak systolic longitudinal strain (%)±SD†	LV segment (apical 2 chamber view)	Mean peak systolic longitudinal strain (%)±SD*	LV segment (apical 3 chamber view)	Mean peak systolic longitudinal strain (%)±SD*
Basal septal	−13.7±4.0	−17±4	Basal anterior	−20.1±4.0	Basal anteroseptal	−18.3±3.5
Mid septal	−18.7±3.0	−19±4	Mid anterior	−18.8±3.4	Mid anteroseptal	−19.4±3.2
Apical septal	−22.3±4.8	−23±6	Apical anterior	−19.4±5.4	Apical anteroseptal	−18.8±5.9
Apical lateral	−19.2±5.4	−21±7	Apical inferior	−22.5±4.5	Apical posterior	−17.7±6.0
Mid lateral	−18.1±3.5	−19±6	Mid inferior	−20.4±3.5	Mid posterior	−16.8±5.0
Basal lateral	−17.8±5.0	−19±6	Basal inferior	−17.1±3.9	Basal posterior	−14.6±7.4

*Mean left ventricular longitudinal peak systolic segmental strain values calculated from 242 healthy subjects aged 51±12 years (between 18 and 80 years) by Marwick *et al*.[19] Scanner: Vivid 7, GE Medical Systems, Horten, Norway. Software: EchoPAC PC, version 6.0.0, GE Healthcare, Chalfont St Giles, UK.
†Mean left ventricular longitudinal peak systolic segmental strain values calculated from 60 healthy subjects aged 39±15 years by Hurlburt *et al*.[15] Scanner: Vivid 7, GE Medical Systems, Milwaukee, Wisconsin, USA. Software: EchoPac Advanced Analysis Technologies, GE Medical Systems.
LV, left ventricular.

Table 2 Mean left ventricular circumferential and radial peak systolic segmental strain values calculated from 60 healthy subjects aged 39±15 years by Hurlburt *et al*[15]

LV segment (short axis view at a basal level, just below mitral valve)	Mean peak systolic circumferential strain (%)±SD	Mean peak systolic radial strain (%)±SD
Anterior	−24±6	39±16
Lateral	−22±7	37±18
Posterior	−21±7	37±17
Inferior	−22±6	37±17
Septal	−24±6	37±19
Anteroseptal	−26±11	39±15

Scanner: Vivid 7, GE Medical Systems. Software: EchoPac Advanced Analysis Technologies, GE Medical Systems.

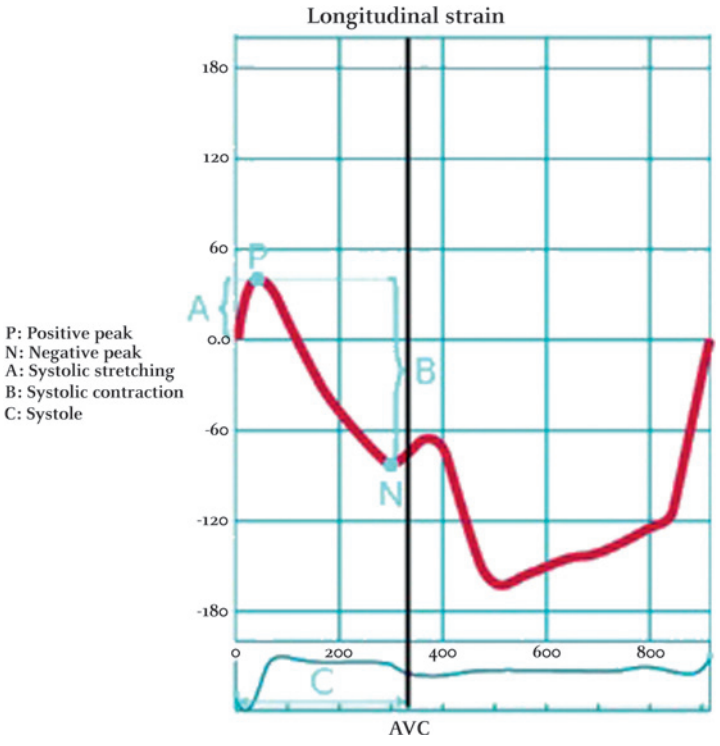

Figure 7 Longitudinal strain curve with peak longitudinal strain occurring in early diastole. AVC, aortic valve closure; N, peak systolic longitudinal strain.

This suggests that EF and STE strain reflect different parameters of systolic LV function. Thus, STE strain provides information on top of LVEF.[31]

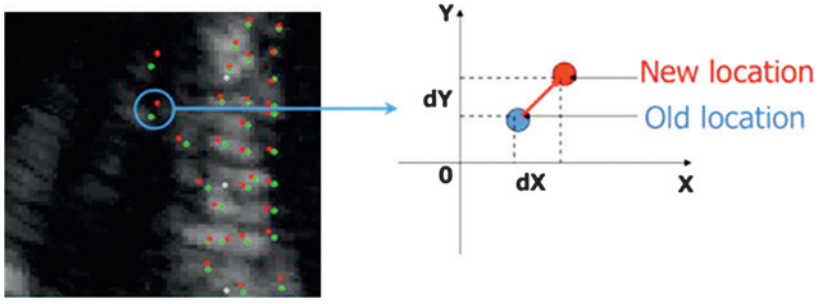

Figure 8 Displacement of acoustic markers from frame to frame. Green dots represent the initial position and red the final position of the speckles.

Deformation and diastolic function

Diastolic dysfunction in patients with normal systolic function results in impaired myocardial relaxation and reduced filling of the left ventricle during early diastole. This state is reflected by a change of the early diastolic LV (un-) twist pattern.[9] A decrease of early diastolic apical untwisting rate (rotR) as well as a shortening or negativity of time from peak apical diastolic untwist to mitral valve opening ($t_{rotR\ to\ MVO}$) can be observed (figure 10).[10]

Thereby, rotR and $t_{rotR\ to\ MVO}$ both become less as diastolic dysfunction progresses. RotR correlates well with established parameters of diastolic dysfunction like early diastolic tissue velocity of septal mitral annulus (e') and ratio of early diastolic mitral inflow to tissue velocity of septal mitral annulus (e:e').[10]

LIMITATIONS OF 2D STRAIN

- **Image quality:** Even though 2D STE is fairly robust, image quality is still an issue. In young healthy subjects, approximately 6% of all LV segments cannot be analysed due to poor image quality.[15]
- **Out of plane motion** caused by movement of the heart during the cardiac cycle: It is unclear how out of plane motion of speckles and frame

Figure 9 Semi-automated definition of left ventricular endocardial and epicardial borders (ROI) in an apical four chamber view.

FUTURE PERSPECTIVES

STE is rapidly evolving both on the investigational and the technological front. It will be necessary to clearly define normal values and clinical settings where STE is useful. A primary goal will be the definition of cut-off values for medical decision making and to correlate these with hard end points. This will also require standardisation among different scanners to assure cross platform reproducibility and clear guidelines for the integration of STE into routine echocardiography.

Optimisation of the algorithms for strain and SR assessment will certainly occur. This will include a more flexible endo- and epicardial border detection algorithm that accounts for differences in myocardial thickness and enhanced mathematical models and filtering techniques.

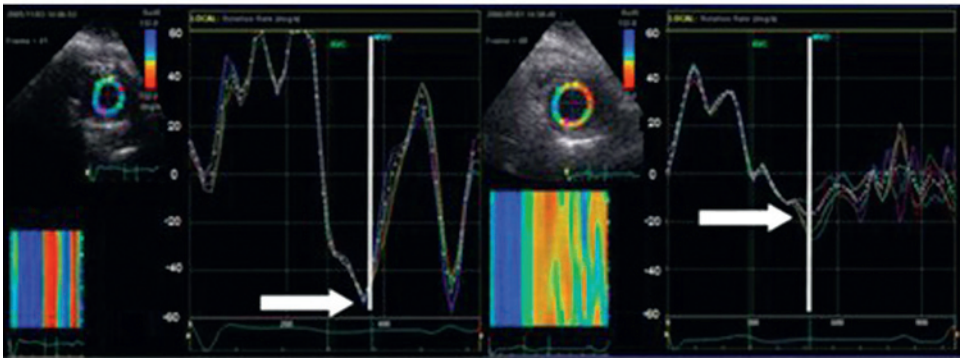

Figure 10 Speckle tracking derived apical rotation rate of a subject with normal diastology (A) and with pseudonormal filling pattern. White lines indicate mitral valve opening, arrows indicate peak rotation rate during early diastole. Reproduced with permission from Perry *et al*.[10]

rate affect the accuracy of STE. This shortcoming could be overcome by the use of 3D speckle tracking technology.

- **Unknown software algorithms:** To track speckles and compute strain and SR values, filtering algorithms are used. The effect of this filtering on the results represents a 'black box' and may vary from vendor to vendor. It is, thus, unclear how values from different scanners and software versions compare. Cross platform comparisons and a clear definition of global and regional norm values are essential for a broad application of STE.
- **Correct tracing of myocardial region of interest:** One of the major limitations is the exact detection of borders. Even though speckle tracking itself seems to enhance the capabilities of endocardial delineation, it is still necessary to correct contours manually. In addition, assessment of strain and SR also requires definition of the epicardial borders. In most software versions a uniform thickness of the myocardium is assumed—an assumption which is not true.
- **Size of left ventricle:** A further limitation, encountered in large ventricles, is that it is often difficult to image the entire myocardium, especially the apical segments.

Three dimensional STE applications will help to improve the understanding of myocardial motion. The current practice of just measuring longitudinal, radial, and circumferential strain is a simplification of the complex myocardial fibre contraction pattern, and neglects 'shear strains' and out-of-plane motion. These problems may be overcome with three dimensional technology.[32–35]

Finally, more advanced technologies will allow LV rotation/torsion and strain/SR measurement of the endocardial, midwall, and epicardial myocardial layers and thus deliver a deeper insight into the physiology of myocardial mechanics, and permit the study of global and local processes within the LV wall.[36]

CONCLUSION

STE has developed rapidly from a research tool to a technique which is on the verge of becoming an important part of routine echocardiography. STE uses the 2D image to calculate deformation parameters and is in many aspects superior to TDI. STE is easy to use, robust and provides a multitude of new insights into the mechanics and deformation processes of the myocardium. In particular, STE could provide important information on regional and global systolic and diastolic function

which could translate into improved diagnostics of heart disease.

Competing interests In compliance with EBAC/EACCME guidelines, all authors participating in Education in *Heart* have disclosed potential conflicts of interest that might cause a bias in the article. The authors have no competing interests.

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