

# 4D Strain: Advanced research application for quantitative echocardiography

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## Introduction

4D Strain is a post-processing research tool that tracks inherent features in a 3D image called “natural acoustic markers” from frame to frame in three dimensions over time.

According to Luigi P. Badano, M.D. at the Department of Cardiac, Thoracic and Vascular Sciences, University of Padua, Italy, “4D Strain has the potential to become the reference method to assess myocardial function and detect early, subclinical myocardial involvement in many heart diseases as well as to quantify regional myocardial function in ischemic heart disease. The present software is very robust, reproducible and user friendly. Its clinical value remains to be established”.

GE Healthcare has introduced many breakthrough quantitative ultrasound tools based on innovative technologies, such as Tissue Velocity Imaging (TVI), Tissue Tracking, Strain and Strain Rate Imaging, Tissue Synchronization Imaging (TSI), as well as 2D Strain and Automated Function Imaging (AFI). These well-established Doppler- or 2D feature tracking-based techniques (for reviews see reference <sup>1-5</sup>) provide detailed measurements of regional wall motion and function, while adding new parametric imaging displays. Applications include studies of regional and global function, stress echocardiography, diastolic function analysis, cardiomyopathy, cardiac resynchronization imaging and more.

Doppler-only-based techniques are limited due to angle dependence of the signal. As a result, certain myocardial areas are excluded, for example, the apex in the apical views, as well as large portions of the myocardium in the parasternal views and especially the short-axis views. 2D feature tracking techniques overcome some of these limitations, by allowing tracking in any direction within the 2D image. However, out-of-plane motion is still a limitation.

4D Strain performs tracking over time in three dimensions, which also means there is no out-of-plane motion issue. 4D Strain can therefore be seen as a natural extension of 2D

Strain. Compared to alternative three dimensional strain measurement tools, like MRI tagging, ultrasound 4D Strain has advantages in availability, feasibility, and affordability. (Figure 1.)

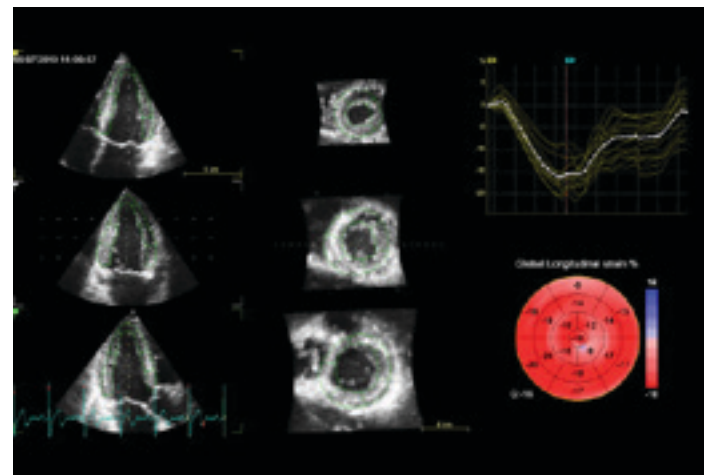
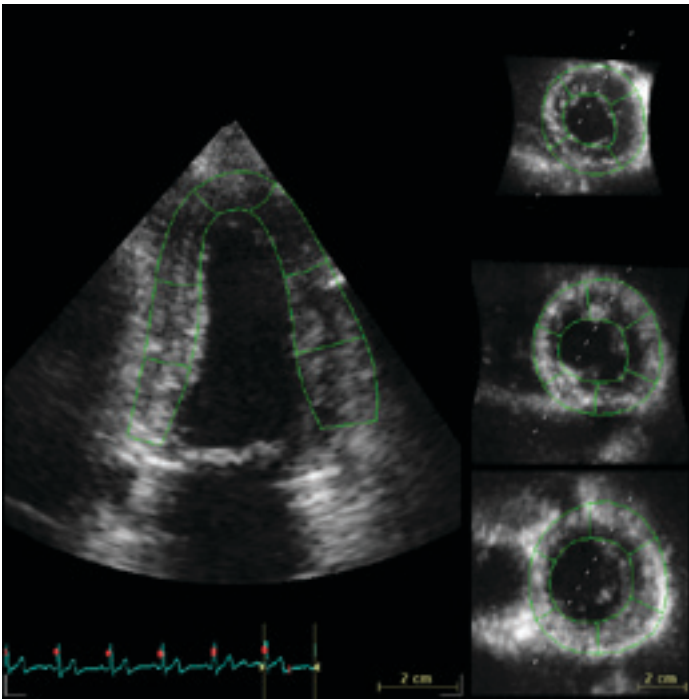


Figure 1. 4D Strain results from a normal heart, showing longitudinal strain.

## Region of interest

The 4D Strain tracking is performed starting from a region of interest (ROI) defined at end-systole. 4D Strain analysis is integrated as the last step in the 4D Auto Left Ventricular Quantification tool, which also includes volume and LV mass measurements<sup>6</sup>. The meshes created for these two measurements are re-used for the 4D Strain ROI. The 4D Strain ROI is automatically generated in the end diastolic frame and is built up from an endocardial and an epicardial mesh. The endocardial mesh is based on the one used for the end-diastolic volume measurement. The epicardial mesh is automatically generated from the epicardial mesh used in the LV mass stage, by propagating it from end diastole to end systole. The user can correct the ROI shape by placing attractor points to pull the nearby ROI border towards where the user wishes it to go. (Figure 2.)

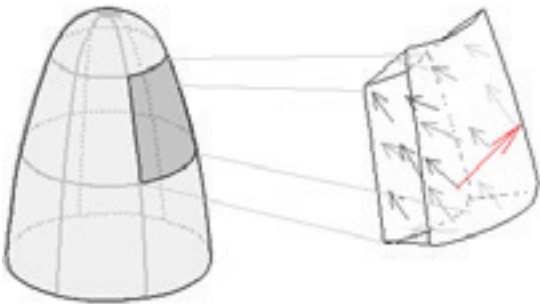




**Figure 2.** The 4D Strain ROI shown in an alternative layout with a large 2-chamber slice and three SAX slices through the 4D dataset. This display allows the user to see if the ROI is placed correctly and also to easily assess the tracking quality.

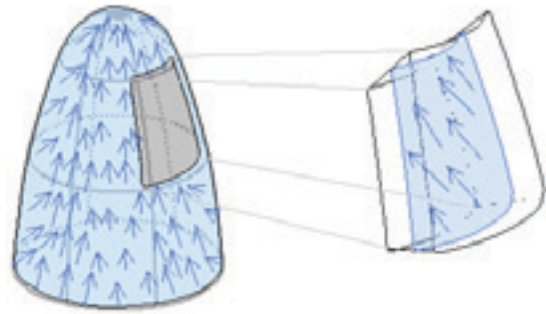
## 4D tracking algorithm

4D Strain uses a tracking algorithm based on frame-to-frame block matching performed in three dimensions. This involves successively searching for a match between 3D patterns found in one 3D frame and in the next. Calculation is performed after defining a region of interest (ROI) that covers the left ventricular myocardium. All areas inside the ROI are tracked, i.e., from endocardium to epicardium, as illustrated in Figure 3.



**Figure 3.** Illustration of a segment of the left ventricle with tracking results from all areas through the heart wall from endocardium to epicardium. The arrows indicate the estimated displacement from one frame to the next. The arrow in red color illustrates an outlier caused by an erroneous match.

The quality of each match is calculated, and each tracking result is also compared to its neighborhood to detect outliers. These are removed before performing weighted spatial averaging of the results. The results are next mapped to an average myocardial mesh, to represent the entire myocardium in a robust way, as illustrated in Figure 4. In this way, the shape of the mesh model of the left ventricle is updated for all frames. All quantitative results are derived from this model.



**Figure 4.** Illustration of the averaged myocardial mesh model of the left ventricle

Note that the longer time there is between successive frames, the longer the tissue may have moved, and the larger the search areas for each block matching has to be. Since the search is performed in three dimensions, the search region grows with a power of three compared to the time between frames. Therefore, one may observe the perhaps counter-intuitive effect that processing time decreases as frame rate goes up. It is, however, not advisable to increase the frame rate to maximum, as this will reduce the line density in the images. The frame rate has to be above a minimum level for the natural acoustic markers to be recognizable in successive frames. As a rule of thumb, the frame rate should be at least 40% of the heart rate, e.g. 24 fps at 60 bpm and 40 fps at 100 bpm. Multibeat acquisition is the preferred way to achieve these frame rates.

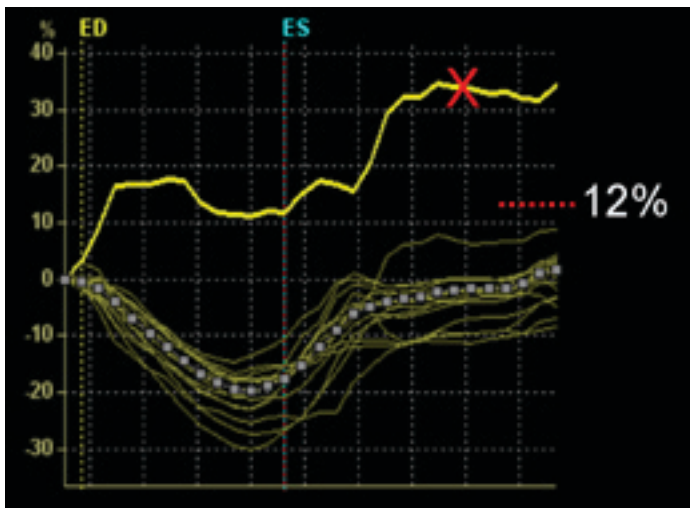
## Tracking quality

For the calculated strain results to be valid, it is crucial that the tracking algorithm has been able to track the tissue correctly. Factors that affect the tracking accuracy include image quality, frame rate and line density. A display that allows visual inspection of tracking correctness is therefore used, so that the user can manually approve or reject the results from individual segments. The 4D dataset is sliced to show three apical and three short axis slices, allowing inspection of the tracking of each segment both in apical and short axis directions. Additional layouts for closer inspection are also available. In addition, strain traces are available to allow evaluation of trace shape.

The user interface allows the user to reject segments with sub-optimal tracking. The results for these segments will then be removed. Furthermore, global strain values will not take these into the calculation. If more than three segments are rejected, global strain values will not be calculated.

## Drift

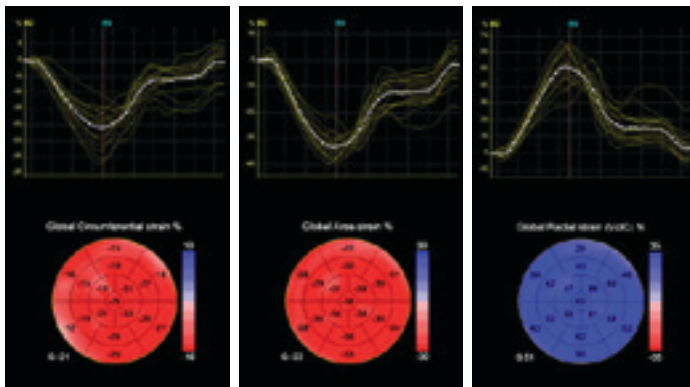
Since the heart moves in a cyclic manner, it is expected that the strain at the beginning and end of the heart beat shall be the same. Any drift is an indication of errors in the tracking. The algorithm automatically rejects segments that show a drift of more than 12 percentage points, as illustrated in Figure 5. This limit is chosen since it may correspond to an error of at least 4 percentage points at end systole assuming that the tracking error is evenly distributed throughout the cardiac cycle.



**Figure 5.** Illustration of a longitudinal strain trace with more than 12 percent drift. In this example one could wonder if the +11% end systolic strain is a real deformation or an artifact, but by looking at the strain at the end of the cycle, one sees that this is an artifact. The corresponding segment will automatically be excluded from the analysis. However, the user may override this and include it despite the drift. In general, the user should check the whole trace as well as how well the ROI follows the tissue in the slice images to decide whether or not to exclude a segment.

## Parameters

From the tracking results, 4D Strain derives several parameters, including longitudinal (Figure 1), circumferential and radial strain, as well as area strain. (Figure 6.)



**Figure 6.** 4D Strain results from a normal heart, showing circumferential strain (left), area strain (middle) and radial strain (right). In each panel, the upper part shows a plot with yellow traces for each of the 17 segments, in addition to a white trace for the global strain. The lower part shows a color coded bull's eye plot with instantaneous strain values. The instantaneous global strain is shown marked with a "G:" to the lower left of the bull's eye plot.

## Longitudinal and circumferential strain

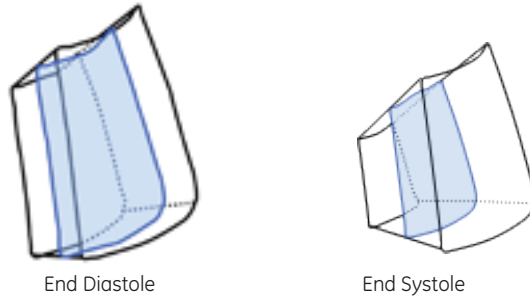
Strain is a measure of the relative deformation of an object. In the left ventricular myocardium, the strain can be measured in different directions, including longitudinal and circumferential.

Longitudinal strain is defined as  $SL = 100 \cdot (L - L_0) / L_0$ , where  $L$  is the instantaneous longitudinal length of the segment and  $L_0$  is the initial length at end diastole (QRS). The length is measured as the average midwall longitudinal length of the segment. Circumferential strain,  $SC$ , is defined in exactly the same manner, only using the circumferential length of the segment instead.

## Area strain

Area strain is a measure of relative area change that combines the effect of longitudinal and circumferential strain.<sup>7</sup> In MRI tagging, area strain has been shown to discriminate normal and ischemic zones better than most other strain indexes.<sup>8</sup>

Area strain is defined as  $SA = 100 \cdot (A - A_0) / A_0$ , where  $A$  is the instantaneous segmental area and  $A_0$  is the initial area at end diastole (QRS). In other words, area strain is the relative change in the area of the segment. (Figure 7.)



**Figure 7.** Illustration of the change in area in a segment over time. Notice that as the area is reduced, the thickness of the muscle is increased. If volume conservation is assumed, radial strain can be calculated from the area strain.

## Radial strain assuming volume conservation (VoIC)

Radial strain is estimated from the area strain assuming that the segment has a constant volume  $V$ . Radial strain is found as  $SR = 100 \cdot (R - R_0) / R_0$ , where  $R = V/A$  is the radial length of the segment, and  $A$  is the segmental area.  $R_0$  is the initial length at end diastole (QRS). By substitution, the radial strain formula can also be written  $SR = -100 \cdot SA / (SA + 100)$ , where  $SA$  is the area strain.

## Global strain

In 4D Strain, global strain is calculated as a weighted average of the segmental strain values. The initial segmental areas ( $A_0$ ) are used as weights. Rejected segments are not included in the calculation of global strain in 4D Strain. Also, the global strain is not calculated if more than three segments are rejected.

Global strain values in 4D Strain are available for all four parameters: Longitudinal, Circumferential, Area and Radial.

The instantaneous global strain value is shown marked as "G:" to the lower left of the Bull's Eye plot. For example, in Figure 8, the global area strain at the time marked with a red line in the trace plot is -23%.

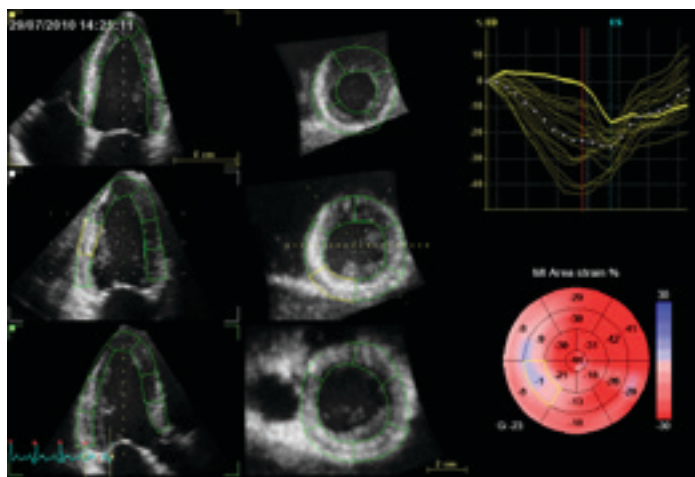
For global longitudinal strain, peak detection is performed. This means that in addition to the instantaneous value, typically the end diastolic value, next to the Bull's eye plot, a Global Peak Longitudinal Strain (GPSL) value is available in the measurement result window. Note that these two values might be different if the currently displayed frame is not at the peak in the global longitudinal strain trace. Also note that in AFI, global strain is calculated in a slightly different manner.

## Bull's eye plot

The calculated parameters can be presented in various ways, including a color coded bull's eye plot. The ventricle is divided into 17 segments, and the instantaneous strain throughout the cardiac cycle is displayed numerically and using color coding in the bull's eye plot. Care should be taken when comparing 2D AFI and 4D Strain, as the strain values in 2D AFI are the peak systolic values, including positive peaks, while in 4D Strain it is the strain values from the current frame, typically the end systolic frame, that are used.

## Example

Figure 8 shows the area strain in a patient with inferior myocardial infarction.



**Figure 8.** 4D Strain results from a patient with inferior wall myocardial infarction, showing the area strain. The Mid Inferior segment is highlighted. Data courtesy of Dr Badano, University of Padua.

## Research tool

Numerical data for all parameters, including numerical trace data, can be exported in HDF5 format for further analysis. HDF5 (Hierarchical Data Format) is a free data format supported by several post processing tools. A tool for viewing HDF files can be downloaded from <http://www.hdfgroup.org/hdf-java-html/hdfview/>.

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## Validation

The 4D Strain tool has been validated in a study using 22 simulated datasets with known deformation<sup>9</sup>. The 4D Strain results were compared to the theoretical value using Bland and Altman analysis and as shown in Table 1, the results showed very good agreement between measured and expected values for all parameters.

	Bias and limit (1.96 std)	Correlation R
<b>Global Strain n=22</b>		
Longitudinal	0.20 ± 0.78	0.998
Circumferential	0.57 ± 1.62	0.992
Area	0.96 ± 1.56	0.997
<b>Segmental Strain n=374</b>		
Longitudinal	0.24 ± 2.37	0.982
Circumferential	0.59 ± 3.85	0.953
Area	0.98 ± 3.75	0.984

**Table 1.** Results of comparison between known deformation in simulated datasets and 4D Strain analysis results on the same datasets. Data courtesy of S. Langeland.<sup>9</sup>

## References

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