

Vevo[®] Strain

User Guide

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Introduction

This document is designed as a user guide for processing and analyzing clips of B-Mode and EKV (700 Hz) images acquired by a Vevo Imaging System. Vevo Strain Analysis Software is available on Vevo LAB and on the Vevo 2100 and Vevo LAZR Imaging Systems. It is not available on the Vevo 1100 Imaging System, nor can it be used to analyze images acquired with the Vevo 1100 Imaging System. Images from the Vevo 3100 Imaging System can be analyzed with Vevo Strain in Vevo LAB.

Vevo Strain is a multifunctional cardiac analysis application with advanced speckle tracking. The software enables calculations of velocity, displacement, strain and strain rate over a selected period of cardiac cycles, based on an acquired B-Mode image (please refer to "[Appendix 1](#)" on page 29 for further details on strain and strain rate calculations). Data are illustrated in parametric and graph displays, and are exportable as multiple formats. Global Longitudinal Strain (GLS) or Global Circumferential Strain (GCS) (for long axis or short axis image analysis, respectively) values are automatically displayed to summarize results and expedite comparisons within studies. Strain and strain rate can not only be measured across the entire left ventricle, but also for specific regions of interest (depending on the model being used and the outcomes desired). To identify regions of interest users can choose specific points across the left ventricular (LV) wall for tracking.

To begin, prepare the Vevo Imaging System by choosing the highest frequency probe appropriate for your model, a Cardiology scanning application package, and an optimized image. Speckle tracking requires very fast sampling for animals with high heart rates, so the highest possible frame rate for image acquisition is desirable. The animal should be on the handling platform with limbs fixed to the electrodes to enable recording of ECG signals. A good ECG signal (with the entire signal visible in the physiological data trace) will assist with correctly marking R-Waves during the first step of Vevo Strain. Optimize the parasternal long axis (PSLAX) for analysis and ensure the image is as narrow as possible, without cutting out any of the ventricle. The

quality of the image determines the quality of the data resulting from Vevo Strain. Therefore, it is best to optimize the image so that the entire wall can be seen clearly, with minimal image artifacts.

Note: For long-term studies, users may find it useful to save a B-Mode or EKV preset specifically for acquiring images destined for Vevo Strain.

The first part of Vevo Strain allows selection of the cycles that will be used for measurement and analysis. The second part of Vevo Strain involves tracing the endocardial and epicardial borders—tracing both allows for endocardial and epicardial strain/strain rate measurements, as well as calculations of the radial motion components. In addition to strain and strain rate calculations, traditional long and short axis functional calculations are provided (please refer to "[Appendix 2](#)" on page 35 for the reference used in these calculations).

Note: Similar to using the parasternal long axis (PSLAX) protocol to optimize the image for analysis, a similar optimization can be performed with the short axis (SAX) protocol.

Data for Vevo Strain Analysis

Only B-Mode and certain EKV Mode images acquired on the appropriate Vevo Imaging System can be analyzed with Vevo Strain.

The following types data are not suitable for Vevo Strain Analysis:

- Single frames.
- 3D Mode cine loops.
- EKV Mode images acquired with a frame rate other than 700 Hz.
- EKV Mode images acquired on a Vevo 3100 Imaging System using a software version earlier than v2.1.x.
- EKV Mode images acquired on a Vevo 2100 Imaging System using a software version earlier than v2.1.x.
- B-Mode cine loops acquired using ECG Triggering.
- B-Mode cine loops acquired using respiratory gating.
- B-Mode cine loops acquired with the Vevo 1100 Imaging System.
- B-Mode cine loops acquired with a heart rate greater than 1000 bpm
- B-Mode images acquired at low frame rates (i.e. below 120 frames per second).
- B-Mode loops or sub-ranged cine loops of less than 10 frames or greater than 300 frames.

Typical Vevo Strain Workflow

The following is an overview of Vevo Strain Analysis workflow.

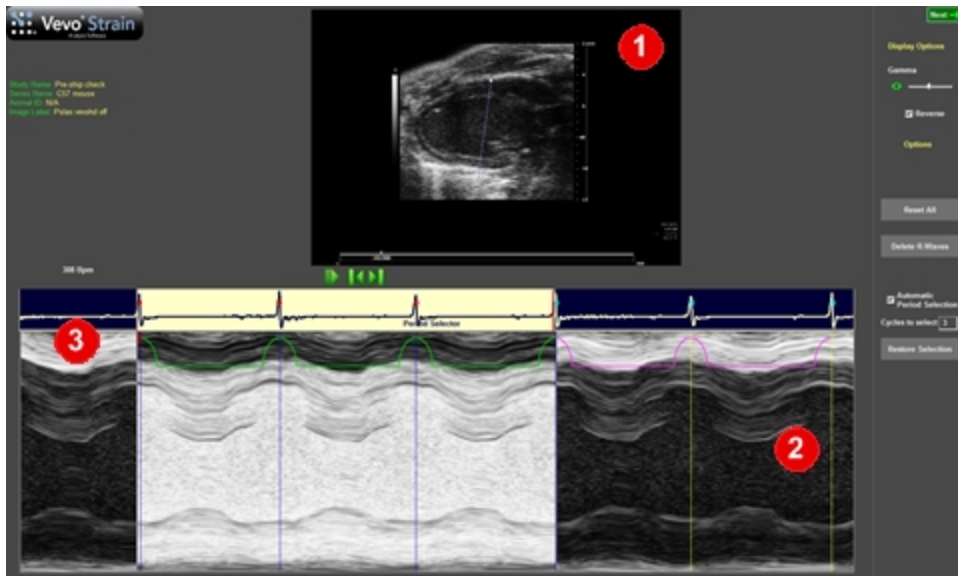
To perform an analysis in Vevo Strain

1 Select up to 5 cine loops, according to "[Data for Vevo Strain Analysis](#)" on the previous page.

2 From the Study Browser, click **Vevo Strain** in the main tool bar or from the mode window, go to the measurement panel and click **Vevo Strain**.

The software processes the cine loop and then displays it within the Vevo Strain Analysis Workspace.

The selected image will be displayed in the image area (see **1** in the image below)



- 3 Within the image area click above the anterior LV epicardial wall and drag the pointer down across the chamber to beyond the opposite (posterior) wall at an angle that optimizes visualization of the walls in M-mode.
- 4 Then right-click to set the Anatomical(A)M-mode cross-section. The selected axis will then appear in the AM-Mode spectrum area (see **2** above).
- 5 Use the playback controls below the B-Mode image to locate the cardiac cycles you would like included in the analysis. Select the **Reverse** check box if you want to switch the grayscale assignment values for either a white or black background.
- 6 In the AM-Mode image area (see **2** above), manually select the best cycles for analysis from within the physiological data or ECG trace.

- a. On the left side drag the single red slider to the position where you would like the analysis area to begin (see **3** above).
- b. On the right side drag the double red slider to the end of the desired data area. In the example above, the desired area includes three R-Waves.

Note: The area chosen for analysis must include at least one complete cardiac cycle.

- 7 If the ECG signal is clear, the software will automatically place blue vertical lines demarcating all R-Waves.

These markers should line up with the end diastole on the AM-Mode image. If the R-Wave markers do not appear or are misaligned with the end-diastole, they should be moved to better reflect the AM-Mode image.

- 8 If all markers are incorrectly placed, click the **Delete R-Waves** button on the right side of the screen, then manually insert them:

- a. Click on the R-Waves from all cardiac cycles within your desired analysis area. The system applies a blue line with every click and connects adjacent blue vertical lines (marking R-Waves) with a green line.

For best results, your desired AM-Mode area should not include cardiac cycles during inspiration, as movement of anatomy during inspiration distorts the normal pattern.

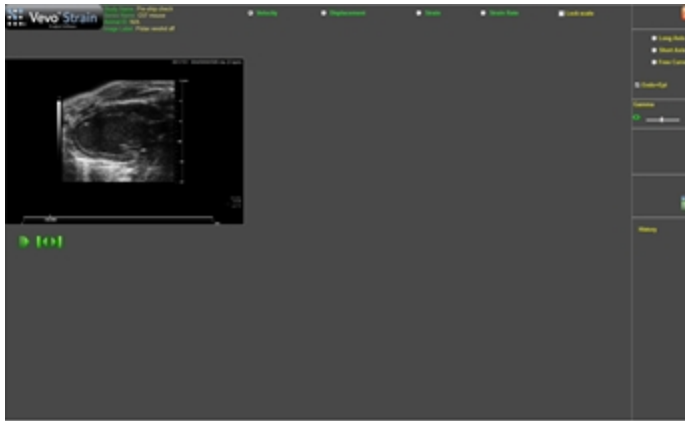
- b. If you want to change the position of a line, double-click it to delete, and then click again at the new position.
- c. If you want to return to the automatically defined R-Wave selection, click **Reset All**.

9 As an alternative to the manual period selection process outlined above, **Automatic Period Selection** is available.

Define the number of cardiac cycles you would like to include in your desired analysis area automatically. This setting will be saved and re-applied each time the software is used. An automatically selected window can be shifted right or left by manually deleting or adding R-Waves on the AM-Mode trace.

10 Once your cycles of interest are selected and all R-Waves are labeled, in the upper-right corner click **Next**.

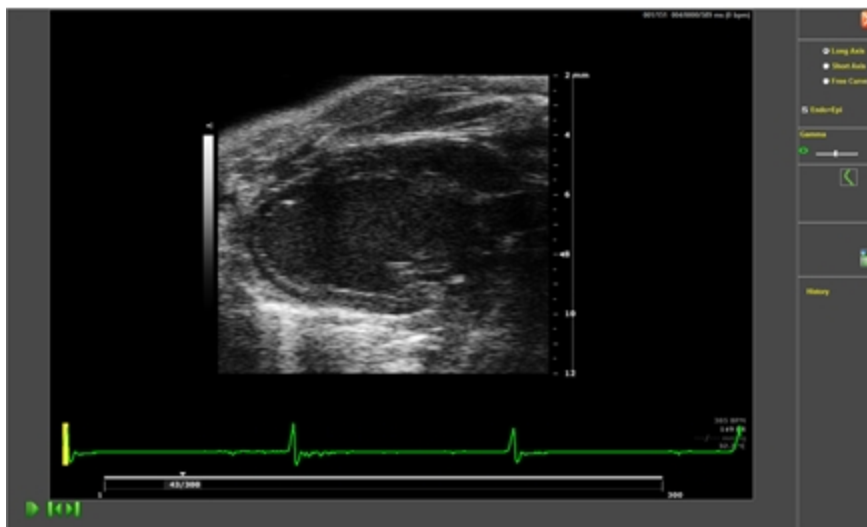
The cine loop will then appear in the tracing workspace.



11 At the top right of the screen, select the type of trace you will create based on the type of image you are analyzing: Short Axis, Long Axis, or Free Curve.



Free Curve can be used for right ventricular measurements (if visible), non-traditional views, or measurement of motion and deformity in other tissue. The displayed image will become larger to allow for more accurate placement of the trace. Adjust the gamma settings as needed to change the grey scale brightness and improve your ability to accurately see and trace the walls.



12 If you select **Endo/Epi** at the top right of the screen, the system will simultaneously trace both the endocardium and the epicardium (based on your trace of the endocardium).

Note: This setting is on by default. After tracing the endocardium, the automatic outer wall trace can be expanded or contracted to fit the outer wall using the +/- arrow control or by clicking on and dragging individual points in the trace. Applying both traces is recommended.

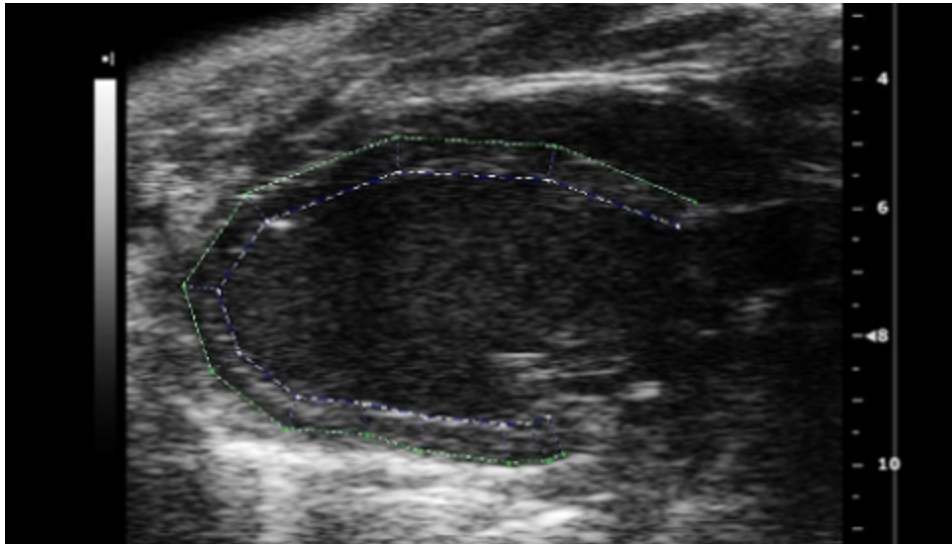
13 Use the playback controls at the bottom left of the screen to select a frame where the endocardial and epicardial walls are most visible/clear.

The frame selected can be anywhere in the cardiac cycle (it does not matter if it is in systole versus diastole).

14 Within the image, click to add points all along the endocardial wall. Right-click to complete the trace.

Optimize the width to ensure the outer line is tracing the epicardium accurately. Individual points can be moved by clicking and dragging them to a new location.

Note: For a trace in the long-axis view, it is recommended to start at the anterior and place points around to the posterior. For the short-axis view, it is recommended to start at the top dead-center of the anterior and place points in a counter-clockwise direction.



15 (Optional) To delete the entire trace and start again select the **New Trace**

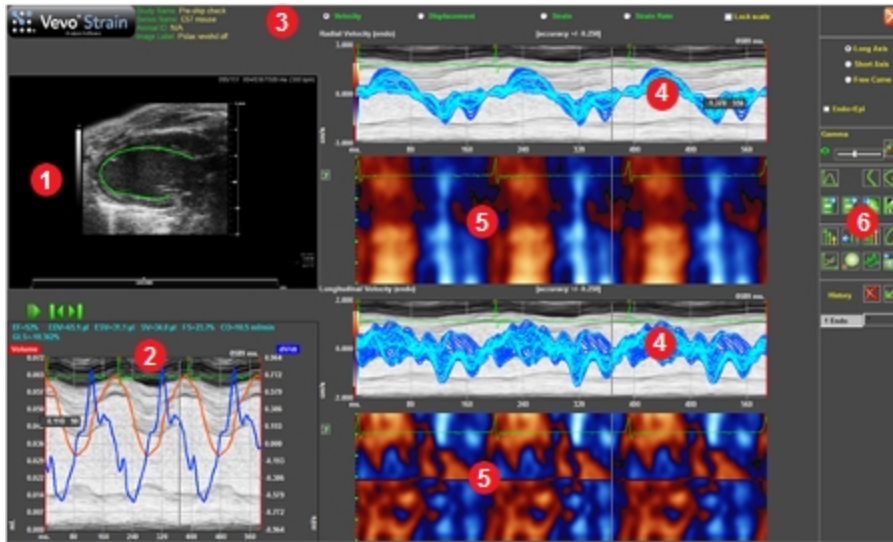
button .

16 (Optional) To return to the AM-Mode view to select a new cardiac period,

click the **Sequence** button .

17 Once you are satisfied with your trace click the **Start Analysis** button .

18 For a comprehensive view, Vevo Strain builds the dynamic LV wall trace for all selected frames in the cine loop and displays the results in the analysis workspace.

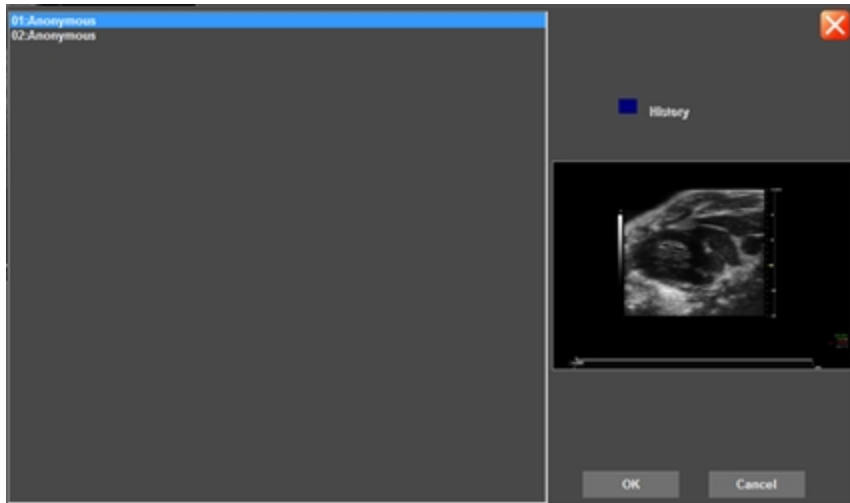


Up to five B-Mode loops can be loaded into Vevo Strain at one time. This is done by selecting multiple B-Mode cine loops in the Vevo LAB Study Browser and then clicking the Vevo Strain button.

Note: You will only be able to analyze data for one cine loop at a time. To switch to one of the other loaded cine loops, within the Vevo Strain Trace

workspace click **Select Clip** .

19 The Select Clip dialog then opens. Within the dialog is a list of the loaded cine loops, the current history/state of the selected cine loop and a thumbnail of the selected cine loop is displayed.



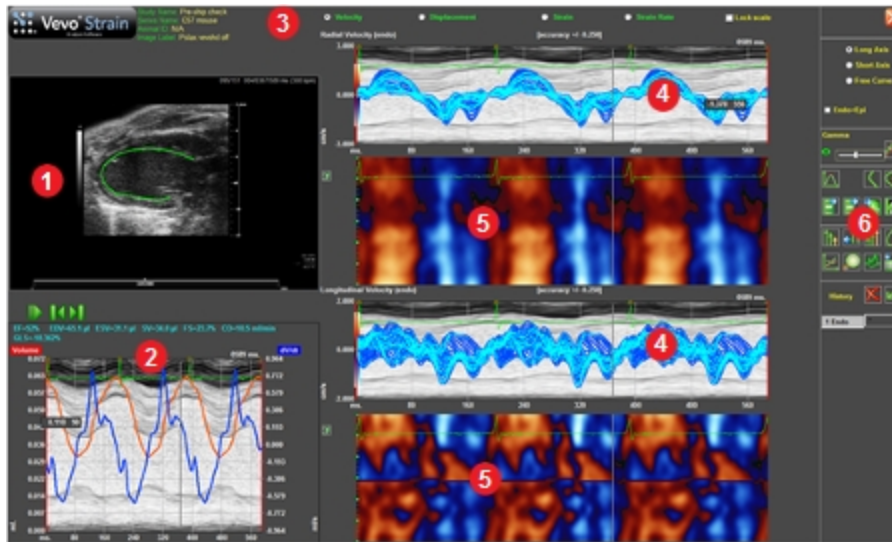
When the History box in the above dialog is **blue**, this indicates that an analysis has not been completed on the selected cine loop.

When the History box in the above dialog is **green**, this indicates that an analysis has been successfully completed on the selected cine loop.

Analyzing Data

Vevo Strain Analysis software window workspace

The following illustration describes the information and features in the Vevo Strain Analysis software window workspace.



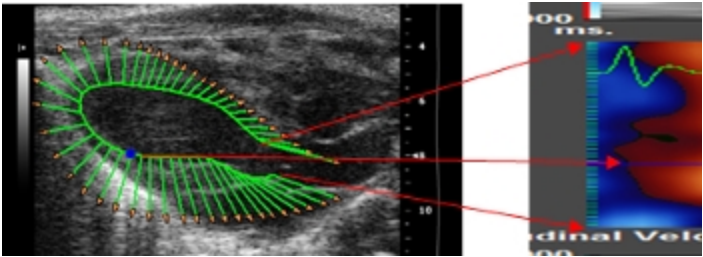
Vevo Strain Workspace Descriptions

Number	Description
1	LV wall trace on cine loop. This area features the automatic endocardial (and epicardial) wall trace through all frames. Use the playback controls to move through the cine loop frames. As you move through the cine loop, the time lines in the other graphs match that position.

Vevo Strain Workspace Descriptions

Number	Description
2	<p>Derivative distribution graph. For the long axis, the graph displays the volume and volume derivative. For the short axis, the graph displays the area and area derivative. Above this graph is a list of functional and structural parameters measured.</p> <p>In PSLAX the following measurements are provided: EF (ejection fraction), EDLVM (end diastolic left ventricular mass), ESLVM (end systolic left ventricular mass), EDV (end diastolic volume), ESV (end systolic volume), SV (stroke volume), FS (fractional shortening), CO (cardiac output) and GLS (global longitudinal strain).</p> <p>In SAX the following measurements are provided: FAC (fractional area change), A(s) (Area in systole), A(d) (area in diastole) and GCS (global circumferential strain).</p>
3	<p>Graph type/analysis options. Includes Velocity, Displacement, Strain, and Strain Rate as options for output parameters.</p>
4	<p>Velocity distribution along the radial axis (top graph), and longitudinal/circumferential axis (for PSLAX/SAX, respectively) (bottom graph). This graph displays velocity/displacement/strain/strain rate (depending on which parameter is selected in 3 above) tracings (y-axis) for each point along the traced contour over time (x-axis).</p>

Vevo Strain Workspace Descriptions

Number	Description
5	<p>Parametric distribution for data in the radial axis (top graph), and longitudinal/circumferential axis (for PSLAX/SAX, respectively) (bottom graph). The parametric graphs give an idea of wall motion along each point of the contour. For the radial graph, movement at each point is displayed as blue (moving away from the center of the heart) or red (moving towards the center of the heart) over time (x-axis). For the longitudinal graph, movement at each point is displayed as blue when the tissue is moving away from the apex and red when the tissue is moving towards the apex. For the circumferential graph, movement at each point is displayed as blue when the movement is clockwise and red when the movement is counter-clockwise.</p> <p>White areas represent fast movement while black areas represent slow movement. Each point along the traced contour is displayed horizontally on the graph. The first anterior point at the base of the heart is represented at the top of the graph, and the last posterior point at the base of the heart represented at the bottom of the graph. When individual points are selected they appear as color-matched horizontal lines on the graph.</p> <div style="text-align: right;">  </div>
6	<p>Analysis tools, see "Vevo Strain Analysis software window workspace" on page 18.</p>

Analysis tools



Vevo Strain analysis tools

Number	Tools
1	Restore Gamma Settings, Gamma slider, Toggle Filtered/Unfiltered Plots.
2	Time-to-Peak Analysis, New Trace, Edit Trace.
3	Export AVI, Export Picture, Export Data, Export Graph to Vevo Report. Note: You can export images, videos and data from Vevo Strain independently from Vevo LAB or a Vevo Imaging System.

Vevo Strain analysis tools


Number	Tools
4	Decrease vector size, Reset Vector Size, Increase Vector Size, Toggle contour/vector/orbit line/B-Mode.
5	Reset graphs display, Zoom in/out, background M-Mode display, sequence/M-Mode selection.
6	Delete selected contour, undo.

Visualizing wall trace tendencies

Every point used for calculations is displayed with an associated vector. As the cine loop is played, directional tendencies for different parts of the cardiac contour at different points in the cardiac cycle can be visualized.

To view the directional tendencies of the LV wall trace

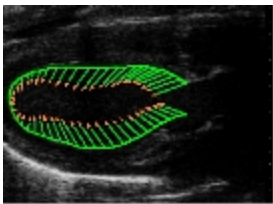
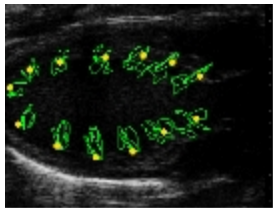
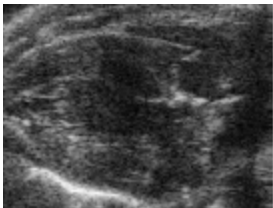


◆ Click the  button and toggle the button as needed to display the required wall trace tendency.

Wall Trace Tendency Display Options

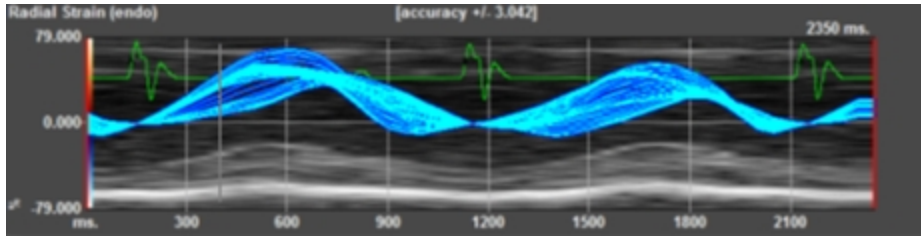
Image	Toggle description
	Contour

Wall Trace Tendency Display Options

Image	Toggle description
	Vector
	Orbit line
	B-Mode

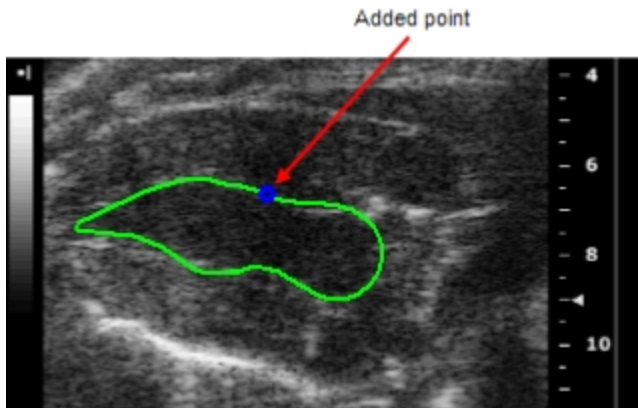
Displaying individual curves for specific points on the trace

By default, the system displays all the curves for all of the individual points along the trace.

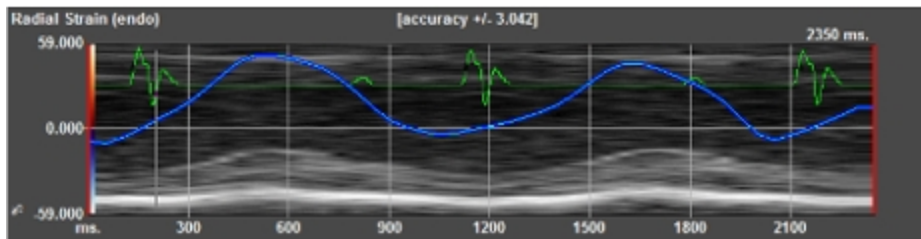


To assess specific regions of interest

- 1 Click on the contour to create a point (or points).

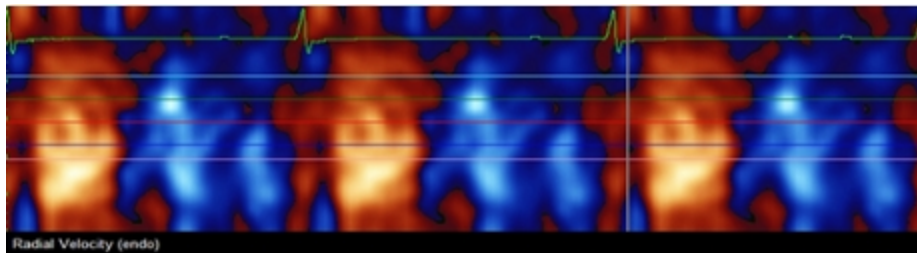
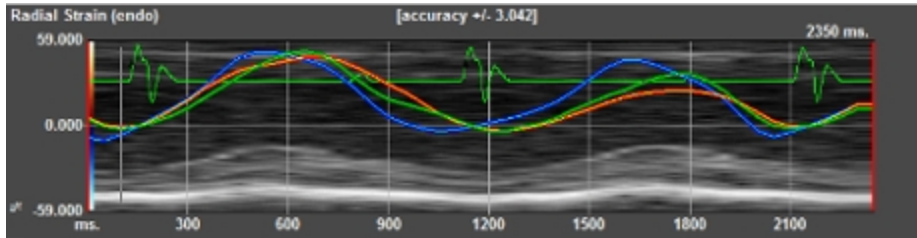


The graph displays a curve for the individual point.



- 2 (Optional) Add additional points onto the trace.

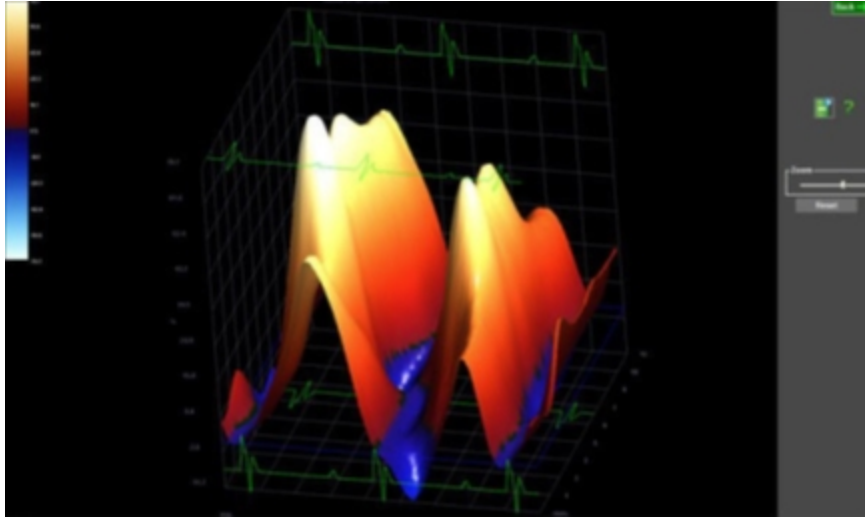
The software will apply unique colors to the additional points and to the corresponding curves and horizontal lines on the graphs



Visualizing data in 3D

To visualize data in 3D

- 1 From the Vevo Strain Analysis window, click the **3^d** button that is located to the left of the parametric distribution graph system displays the parametric data in three dimensions



2 (Optional) Modify your view of the data by dragging the image to rotate it on any axis, or move the zoom slider as needed.

Note: The data being viewed in 2D (i.e. velocity, displacement, strain, or strain rate) determines what is shown in 3D.

3 Click  to save the 3D image.

Analyzing Time-to-Peak

Time-to-Peak analysis displays the segmental synchronicity and phase for different segments of the heart, as well as globally. The display for the segments varies depending on the view of the heart: long or short axis. Only the first cardiac cycle is initially selected for Time-to-Peak analysis (indicated in the red box). Other cardiac cycles can be added, excluded, or assessed individually using buttons in the upper right of the screen.

Time-to-Peak is calculated as the time from the reference axis, 0.000 (the R-wave is considered the reference point), to the maximum peak velocity, for each of the segments of the heart.

Low Time-to-Peak is displayed in blue and high in red in the segmental C-graphs in the middle of the screen.


The phase measures the synchronicity between regions of the heart for a selected time interval (For more information on time-to-peak and phase calculations see ["Analyzing Time-to-Peak"](#) on the previous page).

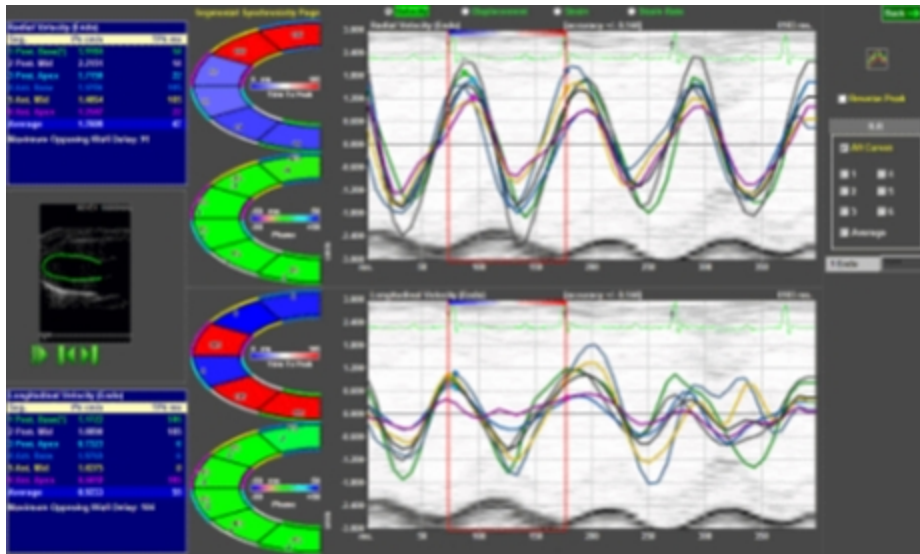
Each of the heart sectors is represented by a corresponding graph and a designated color. You can display all of the curves simultaneously or select them separately using the curve options on the right side of the screen.

Time-to-peak and phase are quantified on the pictographs displayed to the right of the charts. The minimum and maximum range displayed in the center of the pictographs is calculated based on the contour that is traced on the B-Mode image.

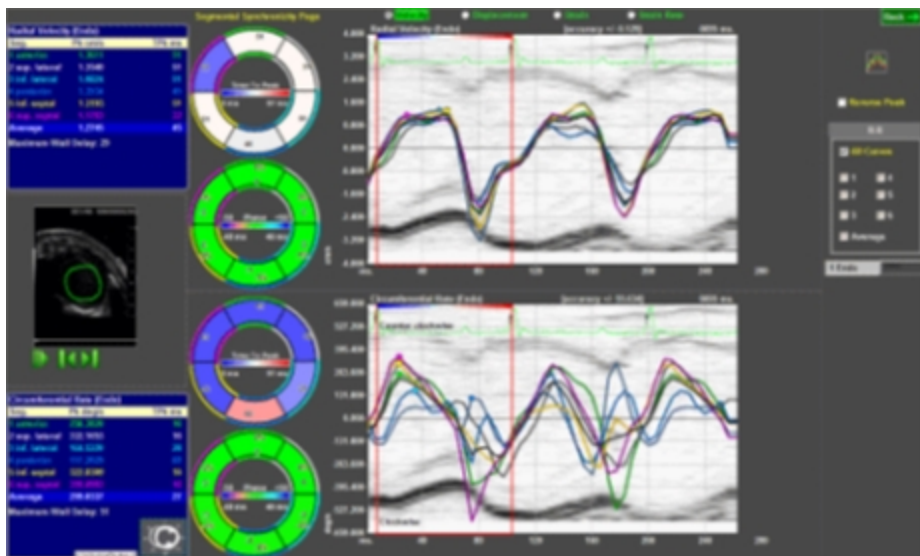
Time-to-Peak analysis can be applied for velocity, displacement, strain, and strain rate.

To view the Time-to-Peak analysis

- ◆ Click . The Time-to-Peak window will appear for your selected cardiac period.



Time-to-Peak window for long axis wall data.



Time-to-Peak window for short axis wall data.

Appendix 1

Vevo Strain calculations

Introduction

Vevo Strain was developed as a sensitive and reproducible method of quantifying cardiac function and contractility. Using speckle-tracking technology on ultrasound images, the software analyzes LV wall motion, deformation and synchrony in multiple axes over the cardiac cycle. Regional and global measures of velocity, displacement, strain, and strain rate are calculated. These measures are able to detect subtle and early changes in myocardial performance.

Strain and strain rate

Strain is a measure of the extent of deformation (lengthening or shortening of the tissue) the heart undergoes throughout the cardiac cycle, relative to its original shape. Deformation occurs when various parts of the heart wall are not moving with the same velocity throughout the cardiac cycle. Strain rate (**SR**) represents the measure of strain per unit of time, or the rate at which deformation occurs.

To calculate strain at a particular point along the endocardium, the distance/length between that point and a secondary point inside the myocardium (outside of the endocardium) is measured at the baseline time-point in the cardiac cycle (always the R-Wave). This is then compared to the distance between the same two points at another instant in the cardiac cycle. The difference between these distances is then represented as a percentage of the original distance; this percentage is the strain.

The equations used to calculate strain (S) and strain rate (SR) are as follows:

$$S = \frac{\Delta L}{L_0} = \frac{L-L_0}{L_0} \quad SR = \frac{S}{\Delta t} = \frac{(\Delta L/L_0)}{\Delta t} = \frac{(\Delta L/\Delta t)}{L_0} = \frac{\Delta V}{L_0}$$

where:

S is the longitudinal strain

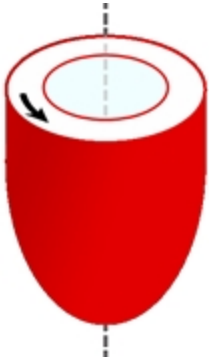


ΔL is the absolute change in length

L_0 is the baseline length (at end diastole/ the R-Wave)

ΔV is the velocity gradient in the segment.

The speckle-tracking algorithms used in strain analysis involve tracking natural acoustic markers (called speckles) in the B-Mode cine loop across the cardiac cycle and estimating velocity vectors. The tracing pattern delineated on the B-Mode image is replicated within the cardiac cycle and across all cycles included in the analysis. As such strain analysis is considered angle independent with lower inter-user variability than other echocardiographic measures of cardiac function.

Due to the dynamic nature of the natural movement of the heart, strain and strain rate can be measured in 3 different planes, based on 3 different directions of deformity that is detected and see in the table below.

	<p>Circumferential of a normal heart.</p> <p>Circumferential strain can only be measured from SAX images.</p>
	<p>Radial of a normal heart.</p> <p>Radial strain can be measured from both SAX and PSLAX images.</p>
	<p>Longitudinal of a normal heart.</p> <p>Longitudinal strain can only be measured from PSLAX images.</p>

Strain can be measured either globally throughout the entire LV, or in specific regions of the heart wall. Global longitudinal strain (**GLS**) and Global

Circumferential Strain (**GCS**) are calculating taking into consideration the entire LV wall throughout the entire cardiac cycle. The equations to calculate **GLS** and **GCS** are as follows:

$$\frac{GLS=L_{ES}-L_{ED}}{L_{ED}} \qquad \frac{GCS=C_{ES}-C_{ED}}{C_{ED}}$$

where:

L_{ED} represents the original length of the LV contour (at the R-Wave in diastole) and **L_{ES}** represents the length of the LV contour in systole.

GLS as a measure of cardiac function (mathematically correlated with ejection fraction (**EF**) in vivo:

$$GLS = (1 - EF)^{2/3} (1 + SF) - 1$$

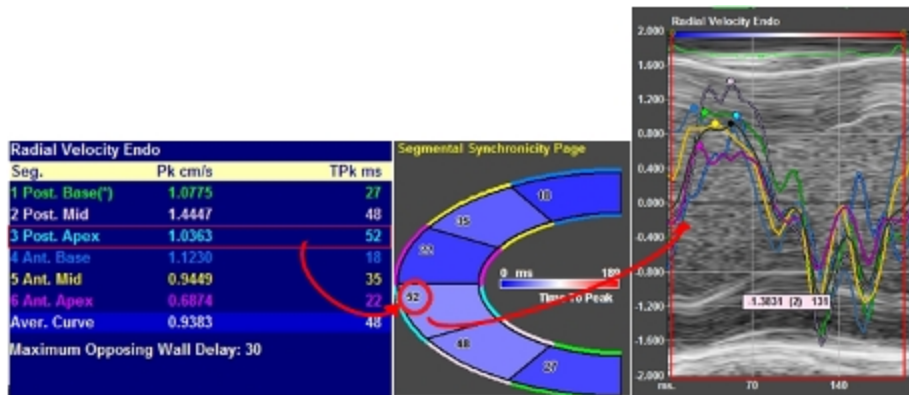
where:

SF is a shape function representing a change in shape from end -diastole to end systole.

Time-to-Peak

Time-to-Peak is defined as the time from the R-Wave (baseline) to when the maximum peak is reached for each of 6 automatically determined segments of the LV wall. This can be calculated for velocity, displacement, strain or strain rate, depending on which parameter is selected. Each pre-determined LV segment considers 9 individual points within. The time it takes for each segment to reach its peak (for the parameter selected) is displayed on the C-graph (below). The graph is also color-coded according to the scale depicted in the center of the graph. The colors along the inner and outer borders of each segment correspond to the tracings on the graph (on the right, below). The data is also included in the table (on the left, below). In the table, Pk is the highest point achieved for that segment in the parameter chosen (the units

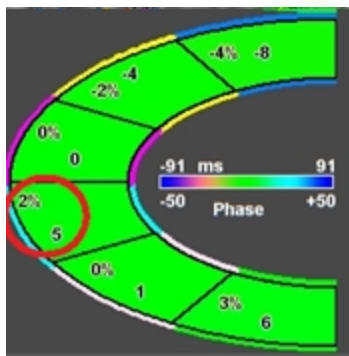
will change depending on the parameter); TPk ms is the time it took to achieve that highest point from the baseline time-point (R-Wave). The table also lists an Average Pk and TPk ms, which takes into account all 6 segments and averages the Time-to-Peak data. Maximum Opposing Wall Delay (MOWD) is calculated by looking at the difference between the highest and lowest segmental TPk ms values. The units for this measure are also ms. MOWD, therefore, represents a lag between one segment of the LV and another, and indicates level of asynchronicity.



Phase

Phase calculations look at the entire cardiac cycle rather than just one point (as is used in Time-to-Peak analysis with the point of maximum velocity/displacement/strain/strain rate). The system calculates Phase for each velocity curve using a Fourier Transformation, which essentially involves using a calculation to deconstruct each waveform into its sinusoidal components. Segmental Phase looks at the deconstructed sinusoids from the velocity waveforms of each segment, as well as their average velocity waveform. The times at which a component of each segmental sinusoid reaches their peak are then compared to the peak of the average sinusoid component (of all LV segments) and each segment is assigned an absolute value (in ms.). This value is also presented as a percentage (from -50 to +50%) and both values are displayed on the segmental Phase C-graph (below).

Similar to the Time-to-Peak analysis, the color along the borders of the segments corresponds to each particular segment, however, the data are not presented in a table. The color filling in each segment is based on the scale illustrated in the center of the C-graph.



Appendix 2

Key Vevo Strain References

Cardiac Functional Measurements Calculated Using Vevo Strain

Otto, Catherine M. (2013). Cardiac Functional Measurements Calculated Using Vevo Strain, *Textbook Of Clinical Echocardiography* (5th ed.) Philadelphia: Saunders, ISBN: 978-1-4557-2857-2.

Global Longitudinal and Circumferential Strain Calculations

Pedrizzetti G, Mangual J, Tonti G. (2014). Global Longitudinal and Circumferential Strain Calculations. On the geometrical relationship between global longitudinal strain and ejection fraction in the evaluation of cardiac contraction. *J Biomech*: 47:746-9.

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