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Declaration under Rule 4.17:

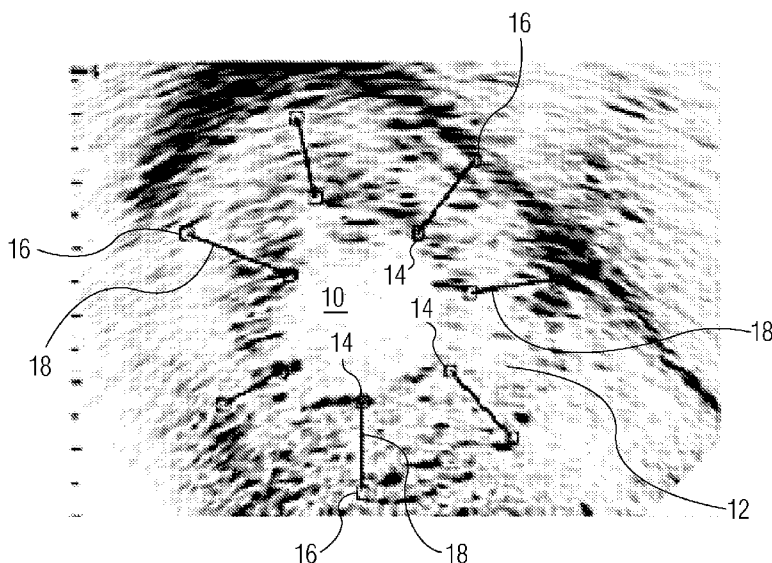
— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))

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[Continued on next page]

(54) Title: QUANTIFICATION AND DISPLAY OF CARDIAC CHAMBER WALL THICKENING



(57) Abstract: An ultrasonic imaging system and method are described for quantification and display of myocardial wall thickening. The endocardial and epicardial borders in an image sequence are defined over a heart cycle and changes in the distance between the borders are tracked at specified locations around the myocardium over the heart cycle. The changes in distance are presented to the user in a graphical format, preferably together with another measure of the cardiac cycle such as chamber volume variation, ejection fraction, or the ECG waveform. The changes in the distance of chord lengths across the myocardium provide a direct indication of wall thickness variation at the specified locations. Preferably the tracking of the specified locations over the heart cycle is done by speckle tracking. The inventive technique can also represent strain at the specified locations of the myocardium.

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QUANTIFICATION AND DISPLAY OF CARDIAC CHAMBER WALL THICKENING

5 This application claims the benefit of US
provisional patent applications serial numbers
60/803,148, filed May 25, 2006, and 60/823,114, filed
August 22, 2006.

10 This invention relates to medical diagnostic
ultrasound systems and, in particular, to ultrasound
systems which perform quantified measurements of
echocardiographic images.

15 There exist many ultrasonic methods to quantify
cardiac chamber function. Ventricular wall motion
indicative of myocardial infarction and ejection
fraction are basic diagnostic tools for
echocardiographers. These diagnostic tools require
that the heart chamber be defined and tracked over a
series of images over the cardiac cycle so that
20 measurements of the delineated myocardium and heart
chamber can be made. Techniques for delineating the
heart wall in an ultrasound image include for example
automated border tracking of blood tissue interfaces
and tissue Doppler imaging of cardiac wall motion to
quantify velocity of contraction, among others. The
25 ability to delineate and track myocardial motion is
also important for diagnosing the synchronicity of
the electrical stimulation of the heart, referred to
as electromechanical transduction. The heart is
commanded to contract by electrochemical signals
30 passed by sodium and potassium channels in the muscle
cells of the myocardium. These signals, dispersed as
they are over the entire heart muscle, should command
the heart muscle cells to contract at the same
instant in time. When this happens the heart
35 contracts from a relaxed, full volume to a contracted

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minimal volume, thereby pumping a maximal volume of blood with each heartbeat. This is a characteristic of a healthy heart. However, when the signals that stimulate this contraction cause different regions of the heart to contract at different times, the erratic contraction will pump less than the maximal volume of blood, producing reduced efficiency and taxing the heart over time. It is desirable to be able to diagnose this condition so that the necessary treatment regime, generally the implantation of a pacemaker with leads placed to force synchronous contractions, can be performed if needed. This diagnosis and its treatment is referred to as cardiac resynchronization therapy, or CRT.

A disease condition which can affect electromechanical transduction of the heart is left bundle branch block. Left bundle branch block occurs when transmission of the cardiac electrical impulse is delayed or fails to conduct along the rapidly conducting fibers of the main left bundle branch or in both left anterior and posterior fascicles. This can cause the left ventricle to depolarize slowly via cell-to-cell conduction spreading from the right ventricle to the left ventricle. This condition results in a loss of synchronicity of chamber contraction and a consequent inefficient ejection of blood volume from the chamber. Accordingly it is desirable to be able to effectively and accurately identify and quantify indications and effects of this condition such as heart wall thickening. Heretofore, wall thickening has been assessed by subjective measurements by experts.

Identifying wall thickening requires delineation of the endocardium and the epicardium. At present, there are no reliable methods to extract epicardial

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borders by the usual expedient of extracting image gradients. Furthermore, while wall thickening can in theory be assessed by tissue Doppler methods, the Doppler effect is subject to orientation limitations of the acoustic beam, with detected velocities varying in proportion to the relation between the direction of motion and the direction of the interrogating ultrasound beams. For instance, if the myocardium is moving at right angles to the acoustic line (the beam direction), no motion will be detected. Doppler methods can also only indirectly measure thickening. They measure velocities which must be then be integrated, introducing noise and potential error, in order to determine displacements and hence thickening. Thus it is desirable to be able to directly identify and quantify myocardial wall thickening.

In accordance with the principles of the present invention, a region of interest (ROI) in a cardiac ultrasound image is defined with points on the endocardium and the epicardium for a frame at a point in the cardiac cycle. These points are then speckle/texture tracked over the cardiac cycle. The distance between corresponding endo- and epicardial tracked points is calculated for each frame, yielding direct measures for length and Lagrangian strain or other fractional changes in length from initial value. Both measures are direct measurements of wall thickening and are displayed in graphs as a function of time. The inventive technique is not limited to gradient detection methods (blood-tissue interface), is not subject to angular deviations of tissue motion relative to the ultrasound beam characteristic of Doppler measurements, and provides a direct measurement of displacements and hence thickening.

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In the drawings:

FIGURE 1 illustrates in block diagram form an ultrasound system with an automatic border detection processor constructed in accordance with the principles of the present invention.

FIGURE 2 illustrates a portion of the ultrasound system of FIGURE 1 in greater detail.

FIGURES 3a-3c illustrate a technique for detecting the endocardial border of the left ventricle in an ultrasound image.

FIGURE 4 illustrates an extension of the technique of FIGURES 3a-3c for detection of the epicardial border of the left ventricle in an ultrasound image.

FIGURE 5 illustrates an ultrasound image with graphics used to measure wall thickening in accordance with the principles of the present invention.

FIGURE 6 illustrates a graphical plot of wall thickness measurements over a heart cycle in accordance with a further embodiment of the present invention.

Referring first to FIGURE 1, an ultrasonic diagnostic imaging system constructed in accordance with the principles of the present invention is shown in block diagram form. A probe or scanhead 410 which includes a one dimensional (1D) or two dimensional (2D) array 412 of transducer elements transmits ultrasonic waves and receives ultrasonic echo signals. This transmission and reception is performed under control of a beamformer 420 which processes received echo signals to form coherent beams of echo signals from the anatomy being scanned. The echo information is Doppler processed by a Doppler processor 430 when Doppler information is to

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be presented, and the processed Doppler information is coupled to an image processor 440 which forms 2D or 3D Doppler images. For B mode imaging of tissue structure the echo signals are image processed by
5 amplitude detection and scan converted into the desired image format for display. The images pass through a Cineloop® memory 460 from which they may be coupled directly to a video processor 470 for display on an image display 480. The Cineloop memory can
10 also be operated to capture a sequence of recently acquired real time images for storage and later inspection and diagnosis. The sequence of captured images, referred to as a "loop" of images, can extend over one or more heart cycles. The images may also
15 be applied to an automatic border detection (ABD) processor 490 which operates on the 2D or 3D images to define anatomical borders and boundaries in the images as described below. The defined borders are graphically overlaid on the images which are coupled
20 to the video processor 470 for display. The system may operate to define and display borders on loops of images saved in the Cineloop memory 460, or to display borders drawn on real time images produced during live scanning of a patient.

25 FIGURE 2 is a detailed block diagram of the portion of the ultrasound system between the image processor 440 and the video processor 470 of FIGURE 1. The image processor 440 produces scanline data of an image which is stored in image data memory 140. A
30 first, starting point image of a sequence of heart images is analyzed by border detection of a heart chamber by an ABD processor 144 as described more fully below. When the border is defined in this first image its location is tracked through
35 subsequent images by a speckle tracker 142. The

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initially defined border and the border in subsequent images are drawn by a graphics processor 148. The ultrasound images of the sequence are converted to the desired display format (e.g., sector, linear, 3D, etc.) by a scan converter 50 which displays the graphically produced borders over the defined border locations in the ultrasound images. The image with its graphic border overlay are stored in a Cineloop memory 460. The images are then coupled to the video processor 470 for display.

Specific points on the identified borders of the successive images are tracked by the speckle tracker 142. which tracks the starting anatomical positions of the points by the speckle pattern produced by the local tissue at the image locations of the points. The speckle tracker 142 identifies regions of pixels around the reference points in the adjacent myocardium. The speckle patterns of these pixels are saved and compared with speckle patterns in the same regions of the successive images and the speckle patterns matched by block matching, as described in US patent 6,442,289 (Olsson et al.) The difficulty and precision of the matching is determined by establishing a maximum correlation for the matching. The reference point locations in the images are thus tracked from image to image by following the speckle patterns around the points. When the speckle tracker 142 locates the reference points in a new image the reference point locations are coupled to the graphics processor 148, the border redrawn using the newly identified point locations, and a graphic overlay produced for the new image. The new image and its graphic overlay are scan converted and displayed on image display 480.

Speckle tracking is preferred over extraction of

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image gradients at the myocardial border by reason of its lower sensitivity to noise in the image. In addition there is no well-defined gradient for the epicardial border which, unlike the endocardial border is not defined by an adjacent blood pool. Furthermore, image noise can cause dropouts in the delineated border, causing estimates of the border to appear deeper into the myocardium rather than at the tissue boundary. A fairly well defined speckle patten has been found to track with reasonable accuracy from frame to frame in the presence of noise. However it has been found that the speckle pattern will change over time. This tendency can be countered by seeding the speckle pattern location at multiple locations in the stored images of a heart cycle, then tracking backward and forward in time from the two defined borders to cause convergence of a drifting speckle pattern. The seeding is performed by delineating two borders at, for example, the beginning and ending of the heart cycle using the automated or semi-automated border detection techniques described below or by manually defining the border by hand. Once the endocardial border has been defined this border can be expanded uniformly outward in all directions, then manually adjusting the border to the epicardial border viewed in the image. The convergence technique has been found to perform well over frame sequences of 80-300 frames, with 30-100 frames contained within one heart cycle.

Instead of tracking the speckle pattern of the myocardial tissue surrounding, underlying, or adjacent to the reference points, it may be appreciated that the reference point locations may be tracked by means other than speckle tracking, that is, by tracking image characteristics which are

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greater than a wavelength in size. For instance, the movement of specific anatomical features may be tracked. As another example, tissue texture may be tracked. It will also be appreciated that the targeted characteristics may be tracked in either pre-scan converted or post-scan converted image data.

FIGURES 3a, 3b, and 3c illustrate contrast-enhanced long axis images of the left ventricle (LV) in which the border of the LV is traced. The user designates a first landmark in the image with a pointing device such as a mouse or a trackball, usually located on the ultrasound system control panel 150 or with a workstation keyboard, which manipulates a cursor over the image. In the example of FIGURE 3a, the first landmark designated is the medial (septal) mitral annulus (MMA). When the user clicks on the MMA in the image, a graphic marker appears such as the white control point indicated by the number "1" in the drawing. The user then designates a second landmark, in this example the lateral mitral annulus (LMA), which is marked with the second white control point indicated by the number "2" in FIGURE 3b. A line produced by the ABD processor then automatically connects the two control points, which in the case of this long axis view of the left ventricle indicates the mitral valve plane. The user then moves the pointer to the endocardial apex, which is the uppermost point within the left ventricular cavity. As the user moves the pointer to this third landmark in the image, a template shape of the left ventricular endocardial cavity dynamically follows the cursor, distorting and stretching as the pointer seeks the apex of the LV chamber. This template, shown as a white line in FIGURE 3c, is anchored by the first and second control points 1 and

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2 and passes through the third control point "3", which is positioned at the apex when the user clicks the pointer at the apex. When positioned, the endocardial cavity template provides an approximate tracing of the endocardium as shown in FIGURE 3c. In the embodiment of FIGURE 3c a black line which bisects the left ventricle follows the pointer as it approaches and designates the apex. This black line is anchored between the center of the line indicating the mitral valve plane and the left ventricular apex, essentially indicating a center line between the center of the mitral valve and the apex of the cavity. In commercial implementations the ABD processor 144 is available onboard ultrasound systems or in offline workstation form from Philips Medical Systems of Andover, MA in an image analysis package known as "QLAB™." This feature of the QLAB package is more fully described in US patent publication 2005/0075567 (Skyba et al.) The automated border processing can be fully automated by other means, such as that described in US Pat. 6,491,636 (Chenal et al.)

In accordance with a further aspect of the present invention the ABD processor 144 is also capable of tracing the epicardial border of the myocardium as shown in FIGURE 4. The epicardial border tracing can be done in a continuous process starting with the endocardial identification steps illustrated in FIGURES 3a, 3b, and 3c. With the endocardial border thus defined, the user moves the cursor to the epicardial apex, the uppermost point on the outer surface of the myocardium. The user then clicks on the epicardial apex and a fourth control point marked "4" is positioned. A second trace then automatically appears which approximately delineates

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the epicardial border as shown in FIGURE 4. This second trace, shown by the outer white border line in FIGURE 4, is also anchored by the first and second control points and passes through the positioned fourth control point at the epicardial apex. The two traces are an approximate outline of the myocardial border.

As a final step, the user may want to adjust the traces shown in FIGURE 4 so that they precisely outline the border of the myocardium. Located around each tracing are a number of small control points shown in the drawing as "+" symbols. The number and spacing of these small control points is a system design choice or may be a variable that the user can set. Using a control on the user interface or control panel 150, the user can point at or near these control points and click and drag the outline to more precisely delineate the myocardial boundary in the image. This process of stretching or dragging the border is known as "rubberbanding", and is described more fully in the aforementioned 6,491,636 patent, with particular reference to Fig. 9 of that patent. As an alternative to rubberband adjustment, in a more complex embodiment the approximated borders may automatically adjust to the image borders by image processing which uses the intensity information of the pixels at and around the approximated tissue borders. When finished, the border can precisely delineate the boundary of the myocardium by enclosing the image pixels of the myocardium in the image.

FIGURE 5 illustrates a short axis cardiac image produced by an ultrasound system constructed in accordance with the principles of the present invention. The heart chamber 10 is shown in the center of the short axis image, surrounded by the

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myocardium 12. The endocardial and epicardial borders are defined using the techniques described above or those described in US Pat. 5,797,396 (Geiser et al.), for instance. A number of reference points are defined on both the endo- and epi-cardial borders. Each pair of endo- and epi-cardial reference points 14,16 in this example comprises two points positioned at a separate radius of the short axis view. Each pair of reference points is joined by a graphically drawn chord line 18 produced by the graphics processor 148 which connects the points and is orthogonal to the borders in the initial image. In this example the border tracing graphics are not displayed; only the endo- and epi-cardial reference points 14,16 and their connecting chords 18 are displayed. In this example the reference points for seven lines are positioned around the myocardium and seven chord lines are drawn, although in a given implementation a greater or lesser number of chords can be used or user- defined by means of the user interface 150. As the reference point locations are modified by the user their values in the reference point data file 146 are correspondingly updated. The chord lines can be continuous between the associated reference points or can be segmented between the points for more detailed analysis of the line segment variations.

As the sequence of images moves from frame to frame through the cardiac cycle, the endo- and epi-cardial borders will change from image to image as the heart muscle contracts during systole, then relaxes during diastole. The reference points 14,16 continue to track the same positions on the respective borders due to the speckle tracking of their locations. As the heart muscle contracts to

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eject blood from the chamber, the endocardium should relatively uniformly move toward the center of the chamber and the lengths of the chords 18 should lengthen: the endo- to epi-cardial thickness increases. The variation in the lengths of the wall thickness chords can then be compared as shown by the seven corresponding transmural wall thickening curves 30 in FIGURE 6, which are produced by the wall thickening curve calculator 20. In this example the wall thickening curves 30 are plotted against an acoustic quantification curve 32-38 which shows the changing heart chamber volume. The acoustic quantification (AQ) curve may be produced as described in US Pat. 5,195,521 (Melton Jr. et al.) During the initial portion 32 of the AQ curve this heart chamber is ejecting blood until a point 34 of minimum chamber volume is reached. During this time the heart wall should be thickening until a point of maximum thickness 40 is attained. In this example all of the wall thickening curves attain a maximum at approximately the same time 40, characteristic of a healthy heart. If a heart is diseased such as occurs with an infarction, the chord at the infarcted location may not attain its maximum thickness at the same time as the healthy locations or will attain a lesser maximum thickness as the infarcted region is dragged along by the neighboring healthy regions, as shown by wall thickness curve 42.

From the point 34 of maximum contraction the heart muscle of the LV will begin to relax during portion 36 of the AQ curve as the heart refills with blood from the lungs, and the wall thickness will decrease as shown by the decreasing curves 30 during this time. The relaxed heart will plateau during the latter portion of diastole until a final atrial

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"kick" 38 is experienced when the left atrium contracts.

It is not strictly necessary for the chord reference points to be located exactly on the epi- and endo-cardial borders. An ROI can be defined by a user selected number of reference points 14 located some distance into the myocardium from the endocardial border (the ROI endocardium). Corresponding points are defined a further user-selected distance into the myocardium (the ROI epicardium). The ROI points are freehand refined if desired so that its endo- and epicardial points match the perceived tissue regions. Locating the point some distance into the tissue rather than exactly on the border will better assure their placement in a speckle pattern susceptible to tracking over the subsequent frames of the cardiac cycle. The ROIs need rely only on definition for a single frame at the beginning of the cardiac cycle and are subsequently re-defined by the updates from the tracking.

Alternatively or in addition to tracking the chord length variation as shown in FIGURE 6, the Lagrangian strain (fractional change in length relative to initial length) may be calculated by the wall thickening curve calculator 20 and graphically displayed. Strain is a measure of deformation in tissue and is an indicator of the mechanical effects of muscle tissue. See, for instance, US Pat. 6,537,221 (Criton et al.) In accordance with a further aspect of the present invention the accumulated strain from the endocardium to the epicardium may be displayed and analyzed. The length and strain calculations for each endo- and epicardial pair of reference points 14,16 in the ROIs are

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displayed in graphs versus time with reference graphs
of ventricular area, ejection fraction, or the ECG
displayed for comparison, as shown in the graph of
FIGURE 6. In other implementations the length and
5 strain variations may be displayed in a parametric
image in colors or graphical representations over the
tissue image of FIGURE 5, enabling the clinician to
readily identify abnormal variations in relation to
their positions in the myocardial tissue.

10

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WHAT IS CLAIMED IS:

1. An ultrasonic diagnostic imaging system for diagnosing heart wall thickening comprising:
 - 5 a probe which acts to transmit ultrasonic waves into a heart and receives echoes in response;
 - an image processor responsive to the echoes which operates to produce an image of the myocardium;
 - 10 a myocardial wall thickness delineator which delineates distance between the endocardium and epicardium of the myocardium; and
 - 15 a wall thickness analyzer, responsive to the delineated distance, which operates to produce an indication of variation in myocardial wall thickness over at least a portion of a cardiac cycle.
2. The ultrasonic diagnostic imaging system of Claim 1, further comprising an image tracker which acts to track the delineated distance from frame to frame through at least a portion of a cardiac cycle.
- 20 3. The ultrasonic diagnostic imaging system of Claim 2, wherein the image tracker further comprises a speckle tracker.
- 25 4. The ultrasonic diagnostic imaging system of Claim 2, wherein the image tracker further comprises an anatomical feature tracker.
- 30 5. The ultrasonic diagnostic imaging system of Claim 2, wherein the image tracker further comprises a texture tracker.
- 35 6. The ultrasonic diagnostic imaging system of Claim 1, wherein the wall thickness analyzer further

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operates to produce an indication of the variation of the lengths of chords directed across the myocardium.

5 7. The ultrasonic diagnostic imaging system of Claim 6, wherein the wall thickness analyzer further operates to produce an indication of the variation of the distance between the endocardium and the epicardium.

10 8. The ultrasonic diagnostic imaging system of Claim 1, further comprising:

 an anatomical border detector, responsive to images of the myocardium, which operates to delineate the endocardial and epicardial borders of the
15 myocardium,

 wherein the wall thickness analyzer operates to produce an indication of variation between the endocardial and epicardial borders.

20 9. The ultrasonic diagnostic imaging system of Claim 8, wherein the wall thickness analyzer further operates to produce an indication of variation between the endocardial and epicardial borders at selected locations around the heart chamber.

25 10. The ultrasonic diagnostic imaging system of Claim 9, wherein the wall thickness analyzer further operates to produce a quantified measure of variation between the endocardial and epicardial borders at
30 selected locations around the heart chamber over at least a portion of a cardiac cycle.

 11. The ultrasonic diagnostic imaging system of Claim 10, wherein the quantified measure comprises a
35 graphical display.

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12. The ultrasonic diagnostic imaging system of Claim 1, wherein the wall thickness analyzer operates to produce an indication of strain across at least a portion of the myocardium.

13. The ultrasonic diagnostic imaging system of Claim 12, wherein the wall thickness analyzer operates to produce an indication of Lagrangian strain across at least a portion of the myocardium.

14. The ultrasonic diagnostic imaging system of Claim 13, wherein the wall thickness analyzer operates to produce a quantified measure of Lagrangian strain across at least a portion of the myocardium over at least a portion of a cardiac cycle.

15. The ultrasonic diagnostic imaging system of Claim 14, wherein the quantified measure comprises a graphical display.

16. A method of measuring myocardial wall thickness comprising:

acquiring a sequence of ultrasound images of the myocardium over at least a portion of a cardiac cycle;

defining a distance between the endocardium and epicardium in at least one of the images;

tracking changes in the defined distance over at least a portion of the cardiac cycle; and

displaying a quantified measure of the changes over at least a portion of the cardiac cycle.

17. The method of Claim 16, wherein defining a

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distance further comprises defining a plurality of lengths across the myocardium; and

wherein tracking changes further comprises tracking changes in the defined lengths.

5

18. The method of Claim 17, wherein displaying further comprises displaying a graphical display of changes in the defined lengths.

10

19. The method of Claim 16, further comprising tracing the endocardial and epicardial borders in at least one of the images,

wherein tracking further comprises tracking the endocardial and epicardial borders over at least a portion of the cardiac cycle.

15

20. The method of Claim 19, wherein tracking further comprises tracking the endocardial and epicardial borders by speckle tracking.

20

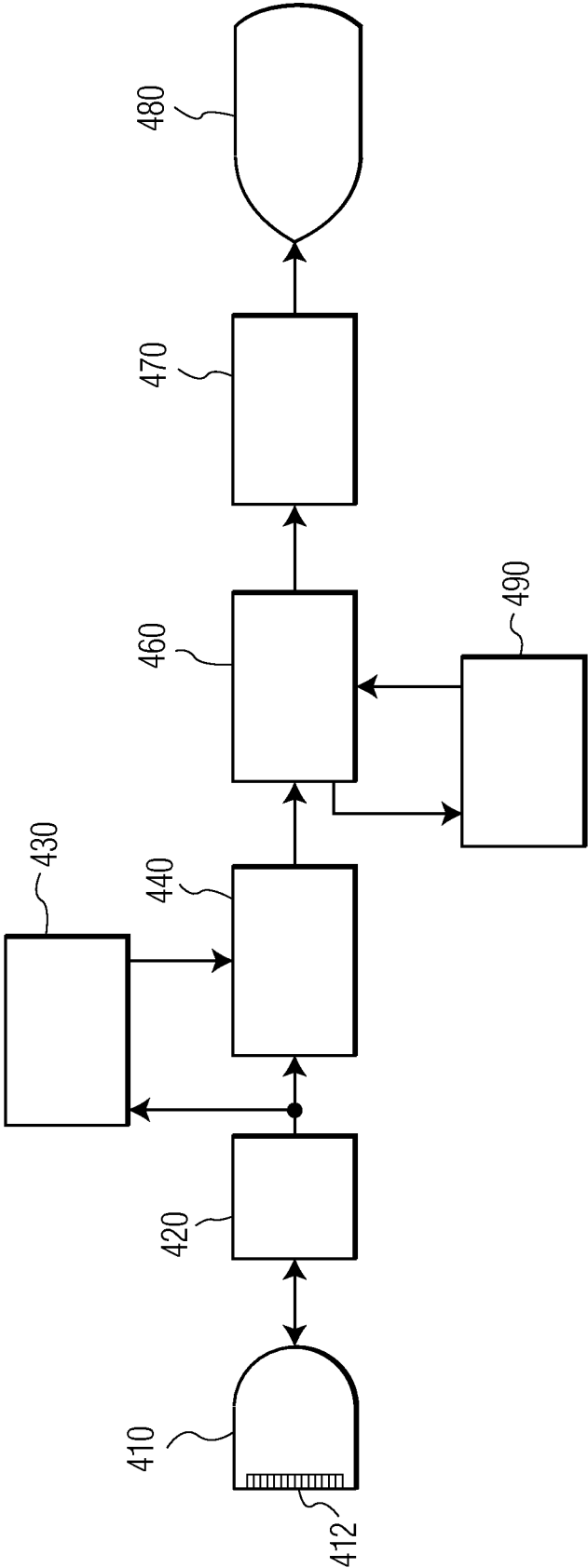


FIG. 1

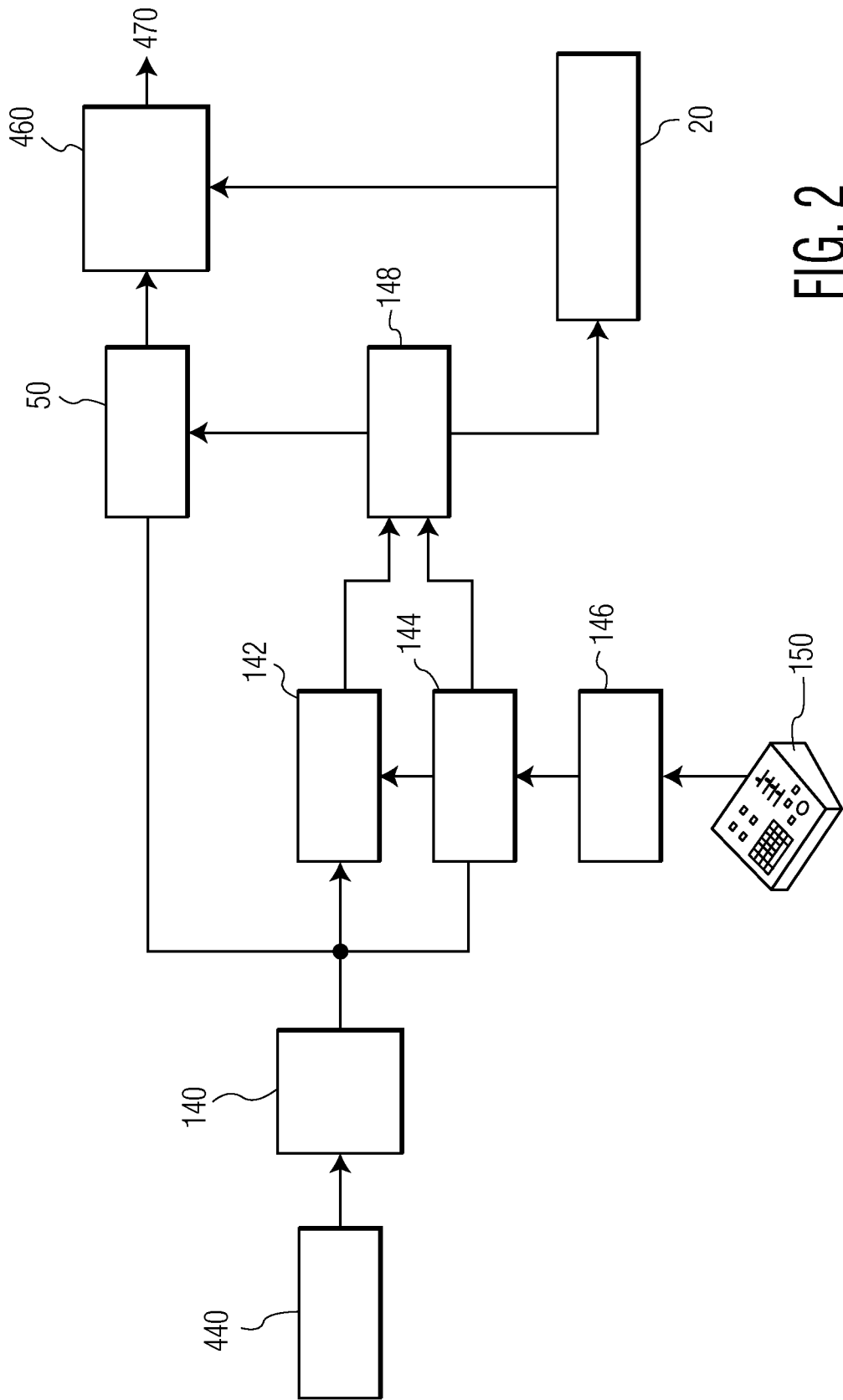


FIG. 2

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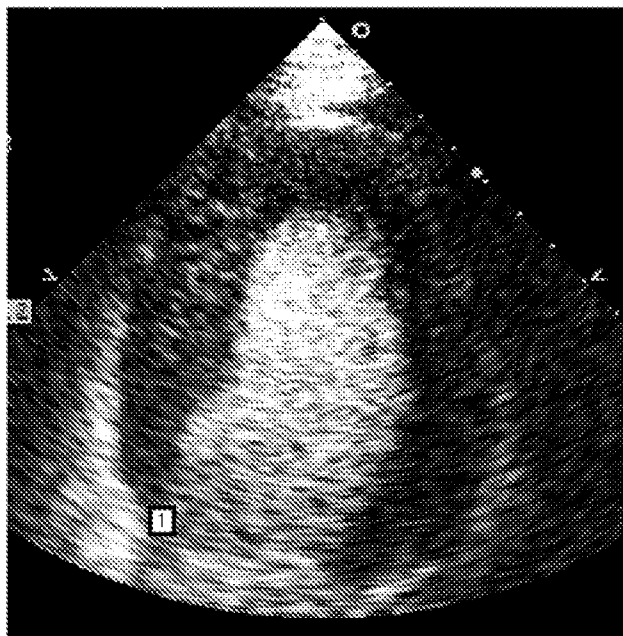


FIG. 3A

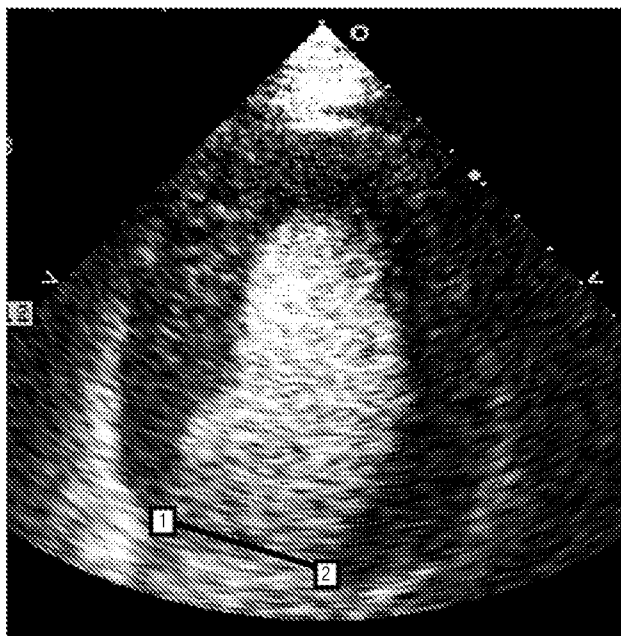


FIG. 3B

4/6

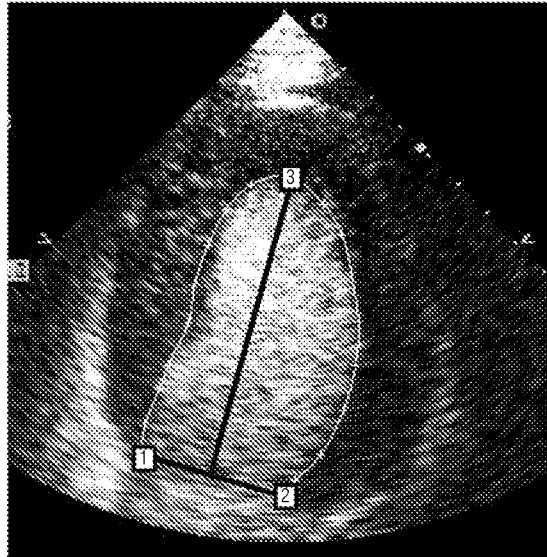


FIG. 3C

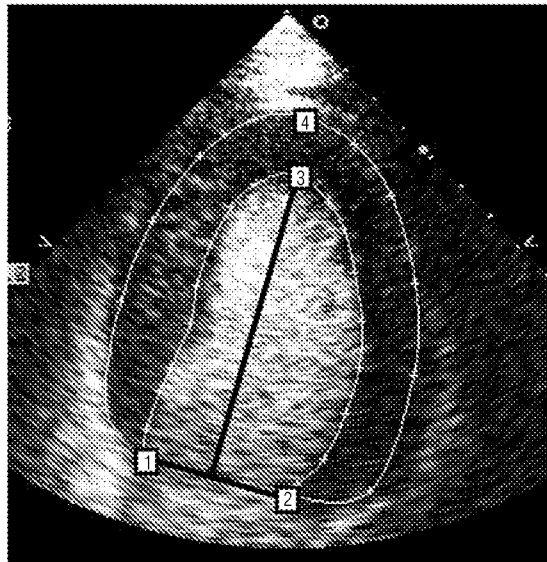


FIG. 4

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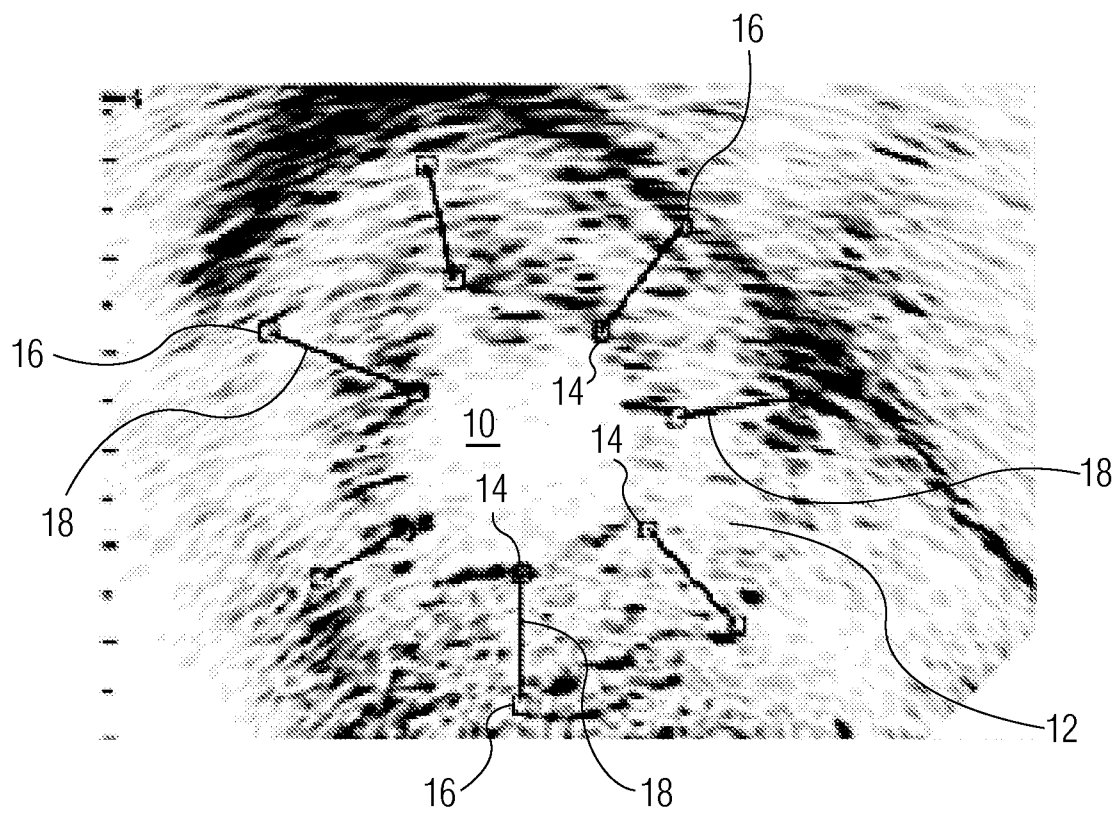


FIG. 5

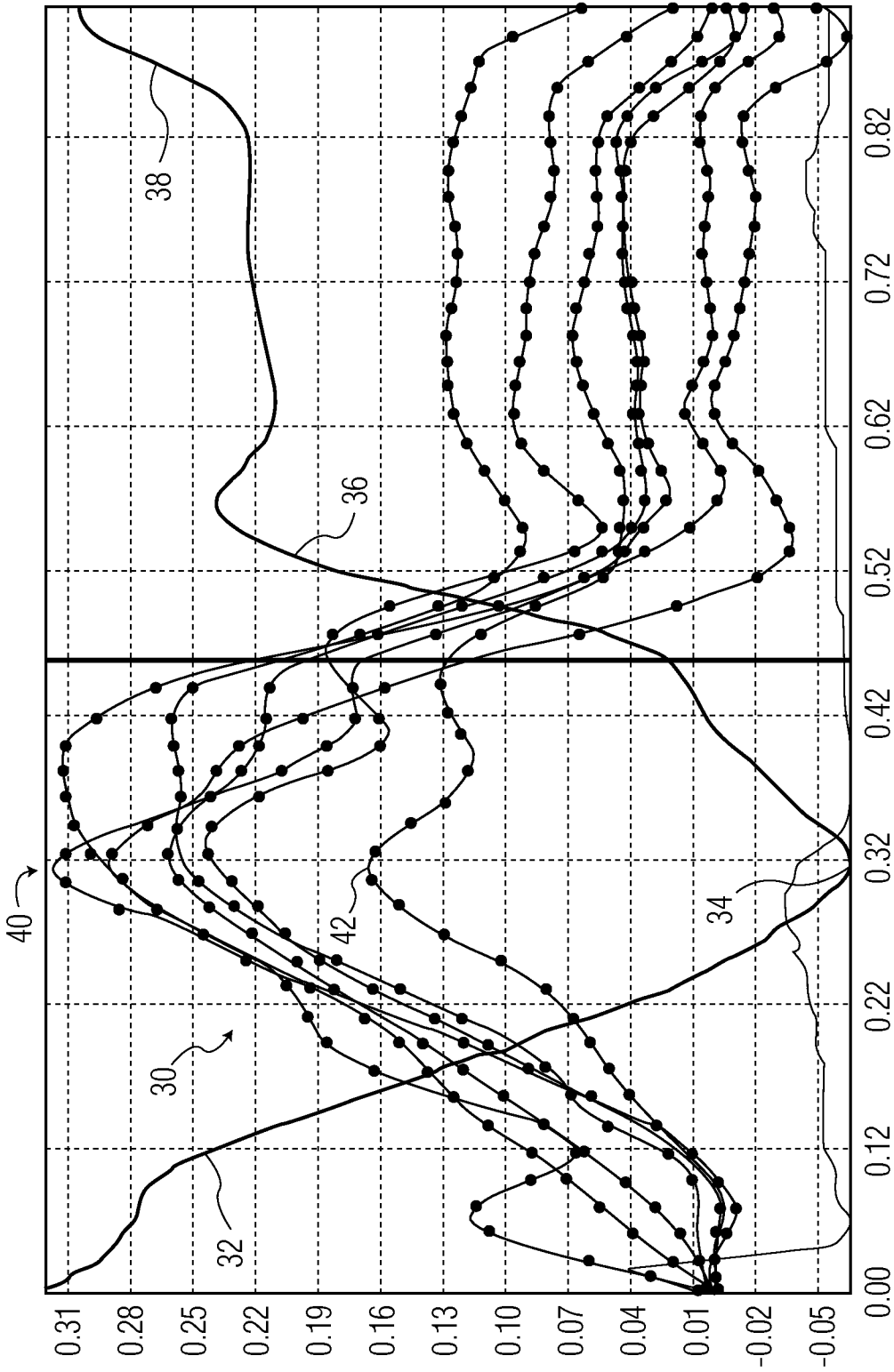


FIG. 6

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2007/051895

A. CLASSIFICATION OF SUBJECT MATTER
INV. G01S7/52

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
G01S A61B G06T

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	STANLEY T E ET AL INSTITUTE OF ELECTRICAL AND ELECTRONICS ENGINEERS: "QUANTITATIVE ANALYSIS OF TRANSESOPHAGEAL ECHOCARDIOGRAMS FOR THE INTRAOPERATIVE SETTING: CLINICAL NEED AND INITIAL EXPERIENCE" IMAGES OF THE TWENTY FIRST CENTURY. SEATTLE, NOV. 9 - 12, 1989, PROCEEDINGS OF THE ANNUAL INTERNATIONAL CONFERENCE OF THE ENGINEERING IN MEDICINE AND BIOLOGY SOCIETY, NEW YORK, IEEE, US, vol. PART 5 CONF. 11, 9 November 1989 (1989-11-09), pages 1569-1570, XP000129522	1,2, 6-11, 15-19
Y	abstract; figures 1-4 Sections "Introduction", "Methods" ----- -/--	3-5, 12-14,20

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

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"A" document defining the general state of the art which is not considered to be of particular relevance

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