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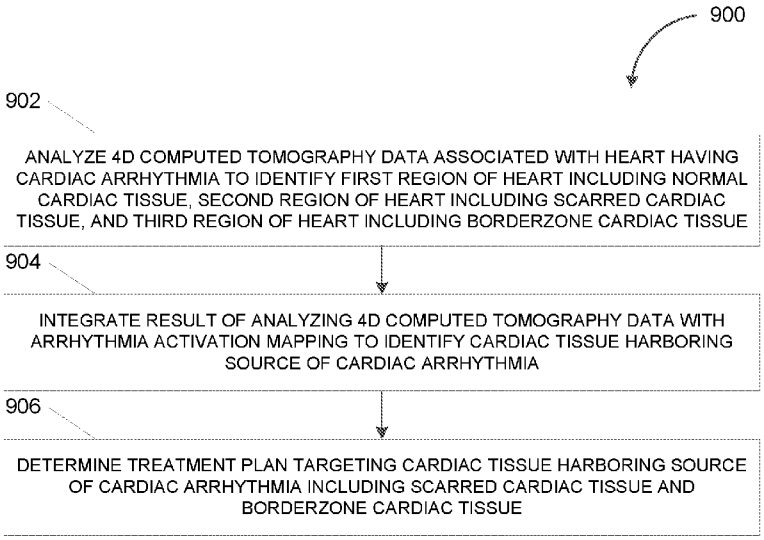

FIG. 9

(57) Abstract: A method to enhance the localization and treatment of cardiac arrhythmia sources are provided. The method may include analyzing a 4-dimensional computed tomography data associated with a heart having cardiac arrhythmia to identify regions of the heart including normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue. The result of analyzing the 4-dimensional computed tomography data may be integrated with an arrhythmia activation mapping to identify cardiac tissue harboring the source of the cardiac arrhythmia. A treatment plan targeting the cardiac tissue harboring the source of the cardiac arrhythmia may be generated. The treatment may include ablation targeting scarred cardiac tissue and borderzone cardiac tissue while avoiding normal cardiac tissue. Related systems and articles of manufacture are also provided.

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FUNCTIONAL COMPUTED TOMOGRAPHY FOR IDENTIFYING ARRHYTHMOGENIC CARDIAC SUBSTRATE

RELATED APPLICATION

[0001] This application claims priority to U.S. Provisional Application No. 62/972,602 entitled "FUNCTIONAL CT TO IDENTIFY ARRHYTHMOGENIC CARDIAC SUBSTRATE" and filed on February 10, 2020, the disclosure of which is incorporated herein by reference in its entirety. This application also incorporates by reference U.S. patent 10,319,144 "Computational Localization of Fibrillation Sources" regarding the computational model and the computational simulation library.

TECHNICAL FIELD

[0002] The subject matter described herein relates generally to medical imaging and more specifically to computed tomography for identifying cardiac substrate harboring sources of cardiac arrhythmias.

BACKGROUND

[0003] Cardiac arrhythmias are common medical disorders in which abnormal electrical signals in the heart cause the heart to contract in a suboptimal manner. The resulting abnormal heartbeat, or arrhythmia, can occur in the atria of the heart (e.g., atrial fibrillation (AF)) and/or the ventricles of the heart (e.g., ventricular tachycardia (VT) or ventricular fibrillation (VF)). Treatments for cardiac arrhythmias attempt to address the mechanisms driving sustained and/or clinically significant episodes including, for example, stable electrical rotors, recurring electrical focal sources, reentrant electrical circuits, and/or the like. Left untreated, cardiac arrhythmias may cause serious complications including morbidity (e.g., syncope, stroke, and/or the like) and mortality (e.g. sudden cardiac death (SCD)).

SUMMARY

[0004] Systems, methods, and articles of manufacture, including computer program products, are provided for identifying arrhythmogenic cardiac substrate. In some example embodiments, there is provided a system that includes at least one processor and at least one memory. The at least one memory may include program code that provides operations when executed by the at least one processor. The operations may include: analyzing 4-dimensional computed tomography (CT) data associated with a heart having cardiac arrhythmia to identify a first region of the heart including a normal cardiac tissue, a second region of the heart including a scarred cardiac tissue, and a third region of the heart including a borderzone cardiac tissue; identifying, based at least on a result of analyzing the 4-dimensional computed tomography data, a cardiac tissue harboring a source of the cardiac arrhythmia, the cardiac tissue harboring the source of the cardiac arrhythmia including the scarred cardiac tissue and the borderzone cardiac tissue; and determining a treatment plan targeting the cardiac tissue harboring the source of the cardiac arrhythmia.

[0005] In some variations, one or more features disclosed herein including the following features can optionally be included in any feasible combination. The result analyzing the 4-dimensional computed tomography data may be integrated with an arrhythmia activation mapping in order to identify the cardiac tissue harboring the source of the cardiac arrhythmia.

[0006] In some variations, the arrhythmia activation mapping may include a patient-specific and/or a non-patient specific computational simulation.

[0007] In some variations, the arrhythmia activation mapping may be derived from an electrophysiology (EP) study.

[0008] In some variations, the treatment plan may be configured to target the second region of the heart including the scarred cardiac tissue and/or the third region of the heart

including the borderzone cardiac tissue while avoiding the first region of the heart including the normal cardiac tissue.

[0009] In some variations, the third region of the heart including the borderzone cardiac tissue may occupy an area between the first region of the heart including the normal cardiac tissue and the second region of the heart including the scarred cardiac tissue.

[0010] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the first region of the heart exhibiting a normal or above-threshold level of contraction, the first region of the heart as including the normal cardiac tissue.

[0011] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the second region of the heart exhibiting a below-threshold level of contraction, severely reduced, akinetic, or dyskinetic motion; the second region of the heart as including the scarred cardiac tissue.

[0012] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the third region of the heart exhibiting a hypokinesis, the third region of the heart as including the borderzone cardiac tissue.

[0013] In some variations, the third region of the heart may be determined to exhibit hypokinesis and/or significant angular deformation, based at least on the third region of the heart having a greatest angle of deformation from systole to diastole, as including the borderzone tissue.

[0014] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on a plurality of strain measurements associated with the heart, the first region of the heart as including the normal cardiac tissue, the second region of the heart as including the scarred cardiac tissue, and the third region of the heart as including the borderzone cardiac tissue.

[0015] In some variations, the plurality of strain measurements may be taken at different locations on a surface of the heart and during different phases of a cardiac cycle.

[0016] In some variations, a machine learning model trained to differentiate, based at least on the plurality of strain measurements, between the normal cardiac tissue, the scarred cardiac tissue, and the borderzone cardiac tissue may be applied.

[0017] In some variations, the machine learning model may include a support vector machine (SVM) trained to map, based at least on the plurality of strain measurements, the 4-dimensional computed tomography data in a 2-dimensional space in which clusters of data points corresponding to normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue are disposed with maximum-width gaps therebetween.

[0018] In some variations, a dimensionality reduction technique may be applied to the 4-dimensional computed tomography data and the plurality of strain measurements prior to applying the machine learning model.

[0019] In some variations, the treatment plan may include an ablation.

[0020] In some variations, the treatment plan may include a radiofrequency ablation, a cryogenic ablation, an ultrasound ablation, and/or a stereotactic ablative radiotherapy (SAbR).

[0021] In some variations, the 4-dimensional computed tomography data may include a time-lapse sequence of 3-dimensional volume renderings of the heart.

[0022] In some variations. the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the first region of the heart exhibiting a normal or above-threshold level of wall thickness, the first region of the heart as including the normal cardiac tissue.

[0023] In some variations. the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the second region of the heart exhibiting a

severely decreased, or below-threshold level of wall thickness, the second region of the heart as including the scarred cardiac tissue.

[0024] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the third region of the heart exhibiting an intermediate decrease in wall thickness, the third region of the heart as including the borderzone cardiac tissue.

[0025] In some variations, the third region of the heart may be determined to exhibit intermediately decreased level of wall thickness based at least on the third region of the heart having a wall thickness measuring between the threshold values of normal tissue and dense scar.

[0026] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the third region of the heart exhibiting a narrow channel of intermediate-threshold level of wall thickness surrounded by an area with a low or below-threshold level of wall thickness, the third region of the heart as including the borderzone cardiac tissue surrounded by scar, and an area of increased statistical probability to harbor arrhythmia-sustaining mechanisms.

[0027] In some variations, the narrow channel of intermediate wall thickness may traverse a region with neighboring tissue having a low, or below-threshold level of wall thickness.

[0028] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on a plurality of wall thicknesses associated with the heart, the first region of the heart as including the normal cardiac tissue, the second region of the heart as including the scarred cardiac tissue, and the third region of the heart as including the borderzone cardiac tissue.

[0029] In some variations, the plurality of wall thicknesses may be measured at different locations throughout the heart by segmenting the endocardial surface and epicardial surfaces of the heart based on Hounsfield units.

[0030] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the first region of the heart exhibiting a normal or above-threshold level of wall thickening, the first region of the heart as including the normal cardiac tissue.

[0031] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the second region of the heart exhibiting a severely decreased, or below-threshold level of wall thickening, the second region of the heart as including the scarred cardiac tissue.

[0032] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the third region of the heart exhibiting an intermediate decrease in wall thickening, the third region of the heart as including the borderzone cardiac tissue.

[0033] In some variations, the third region of the heart may be determined to exhibit intermediately decreased level of wall thickness based at least on the third region of the heart having a wall thickness measuring between the threshold values of normal tissue and dense scar.

[0034] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the third region of the heart exhibiting a narrow channel of intermediate-threshold level of wall thickness surrounded by an area with a low or below-threshold level of wall thickness, the third region of the heart as including the borderzone cardiac tissue surrounded by scar, and an area of increased statistical probability to harbor arrhythmia-sustaining mechanisms.

[0035] In some variations, the narrow channel of intermediate wall thickness may traverse a region with neighboring tissue having a low, or below-threshold level of wall thickness.

[0036] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on a plurality of wall thicknesses associated with the heart, the first region of the heart as including the normal cardiac tissue, the second region of the heart as including the scarred cardiac tissue, and the third region of the heart as including the borderzone cardiac tissue.

[0037] In some variations, the plurality of wall thicknesses may be measured at different locations throughout the heart by segmenting the endocardial surface and epicardial surfaces of the heart based on Hounsfield units.

[0038] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the first region of the heart exhibiting a normal or above-threshold level of wall thickening, the first region of the heart as including the normal cardiac tissue.

[0039] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the second region of the heart exhibiting a severely decreased, or below-threshold level of wall thickening, the second region of the heart as including the scarred cardiac tissue.

[0040] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the third region of the heart exhibiting an intermediate decrease in wall thickening, the third region of the heart as including the borderzone cardiac tissue.

[0041] In some variations, the third region of the heart may be determined to exhibit intermediately decreased level of wall thickness based at least on the third region of the heart

having a wall thickening measuring between the threshold values of normal tissue and dense scar.

[0042] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the third region of the heart exhibiting a narrow channel of intermediate-threshold level of wall thickening surrounded by an area with a low or below-threshold level of wall thickening, the third region of the heart as including the borderzone cardiac tissue surrounded by scar, and an area of increased statistical probability to harbor arrhythmia-sustaining mechanisms.

[0043] In some variations, the narrow channel of intermediate wall thickening may traverse a region with neighboring tissue having a low, or below-threshold level of wall thickening.

[0044] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on a plurality of wall thicknesses associated with the heart, the first region of the heart as including the normal cardiac tissue, the second region of the heart as including the scarred cardiac tissue, and the third region of the heart as including the borderzone cardiac tissue.

[0045] In some variations, the plurality of wall thickening may be measured at different locations throughout the heart by segmenting the endocardial surface and epicardial surfaces of the heart based on Hounsfield units.

[0046] In some variations, the identification of the first region, the second region, and/or the third region may be used to facilitate a non-invasive ECG computational simulation library activation mapping.

[0047] In some variations, the identification of the first region, the second region, and/or the third region may be used to facilitate a non-invasive ECG computational simulation

library activation mapping and non-invasive stereotactic ablative radiotherapy (SAbR) procedure.

[0048] In some variations, the identification of the first region, the second region, and/or the third region may be used to facilitate a non-invasive ECG computational simulation library activation mapping and invasive catheter ablation procedure.

[0049] In some variations, the identification of the first region, the second region, and/or the third region may be used to facilitate an invasive catheter-based activation mapping.

[0050] In some variations, the identification of the first region, the second region, and/or the third region may be used to facilitate an invasive catheter-based activation mapping and invasive catheter ablation procedure.

[0051] In another aspect, there is provided a method for identifying arrhythmogenic cardiac substrate. The method may include: analyzing 4-dimensional computed tomography (CT) data associated with a heart having cardiac arrhythmia to identify a first region of the heart including a normal cardiac tissue, a second region of the heart including a scarred cardiac tissue, and a third region of the heart including a borderzone cardiac tissue; identifying, based at least on a result of analyzing the 4-dimensional computed tomography data, a cardiac tissue harboring a source of the cardiac arrhythmia, the cardiac tissue harboring the source of the cardiac arrhythmia including the scarred cardiac tissue and the borderzone cardiac tissue; and determining a treatment plan targeting the cardiac tissue harboring the source of the cardiac arrhythmia.

[0052] In some variations, one or more features disclosed herein including the following features can optionally be included in any feasible combination. The result analyzing the 4-dimensional computed tomography data may be integrated with an arrhythmia activation mapping in order to identify the cardiac tissue harboring the source of the cardiac arrhythmia.

[0053] In some variations, the arrhythmia activation mapping may include a patient-specific and/or a non-patient specific computational simulation.

[0054] In some variations, the arrhythmia activation mapping may be derived from an electrophysiology (EP) study.

[0055] In some variations, the treatment plan may be configured to target the second region of the heart including the scarred cardiac tissue and/or the third region of the heart including the borderzone cardiac tissue while avoiding the first region of the heart including the normal cardiac tissue.

[0056] In some variations, the third region of the heart including the borderzone cardiac tissue may occupy an area between the first region of the heart including the normal cardiac tissue and the second region of the heart including the scarred cardiac tissue.

[0057] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the first region of the heart exhibiting a normal or above-threshold level of contraction, the first region of the heart as including the normal cardiac tissue.

[0058] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the second region of the heart exhibiting a below-threshold level of contraction, severely reduced, akinetic, or dyskinetic motion; the second region of the heart as including the scarred cardiac tissue.

[0059] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the third region of the heart exhibiting a hypokinesis, the third region of the heart as including the borderzone cardiac tissue.

[0060] In some variations, the third region of the heart may be determined to exhibit hypokinesis and/or significant angular deformation, based at least on the third region of the

heart having a greatest angle of deformation from systole to diastole, as including the borderzone tissue.

[0061] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on a plurality of strain measurements associated with the heart, the first region of the heart as including the normal cardiac tissue, the second region of the heart as including the scarred cardiac tissue, and the third region of the heart as including the borderzone cardiac tissue.

[0062] In some variations, the plurality of strain measurements may be taken at different locations on a surface of the heart and during different phases of a cardiac cycle.

[0063] In some variations, a machine learning model trained to differentiate, based at least on the plurality of strain measurements, between the normal cardiac tissue, the scarred cardiac tissue, and the borderzone cardiac tissue may be applied.

[0064] In some variations, the machine learning model may include a support vector machine (SVM) trained to map, based at least on the plurality of strain measurements, the 4-dimensional computed tomography data in a 2-dimensional space in which clusters of data points corresponding to normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue are disposed with maximum-width gaps therebetween.

[0065] In some variations, a dimensionality reduction technique may be applied to the 4-dimensional computed tomography data and the plurality of strain measurements prior to applying the machine learning model.

[0066] In some variations, the treatment plan may include an ablation.

[0067] In some variations, the treatment plan may include a radiofrequency ablation, a cryogenic ablation, an ultrasound ablation, and/or a stereotactic ablative radiotherapy (SAbR).

[0068] In some variations, the 4-dimensional computed tomography data may include a time-lapse sequence of 3-dimensional volume renderings of the heart.

[0069] In some variations. the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the first region of the heart exhibiting a normal or above-threshold level of wall thickness, the first region of the heart as including the normal cardiac tissue.

[0070] In some variations. the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the second region of the heart exhibiting a severely decreased, or below-threshold level of wall thickness, the second region of the heart as including the scarred cardiac tissue.

[0071] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the third region of the heart exhibiting an intermediate decrease in wall thickness, the third region of the heart as including the borderzone cardiac tissue.

[0072] In some variations, the third region of the heart may be determined to exhibit intermediately decreased level of wall thickness based at least on the third region of the heart having a wall thickness measuring between the threshold values of normal tissue and dense scar.

[0073] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the third region of the heart exhibiting a narrow channel of intermediate-threshold level of wall thickness surrounded by an area with a low or below-threshold level of wall thickness, the third region of the heart as including the borderzone cardiac tissue surrounded by scar, and an area of increased statistical probability to harbor arrhythmia-sustaining mechanisms.

[0074] In some variations, the narrow channel of intermediate wall thickness may traverse a region with neighboring tissue having a low, or below-threshold level of wall thickness.

[0075] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on a plurality of wall thicknesses associated with the heart, the first region of the heart as including the normal cardiac tissue, the second region of the heart as including the scarred cardiac tissue, and the third region of the heart as including the borderzone cardiac tissue.

[0076] In some variations, the plurality of wall thicknesses may be measured at different locations throughout the heart by segmenting the endocardial surface and epicardial surfaces of the heart based on Hounsfield units.

[0077] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the first region of the heart exhibiting a normal or above-threshold level of wall thickening, the first region of the heart as including the normal cardiac tissue.

[0078] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the second region of the heart exhibiting a severely decreased, or below-threshold level of wall thickening, the second region of the heart as including the scarred cardiac tissue.

[0079] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the third region of the heart exhibiting an intermediate decrease in wall thickening, the third region of the heart as including the borderzone cardiac tissue.

[0080] In some variations, the third region of the heart may be determined to exhibit intermediately decreased level of wall thickness based at least on the third region of the heart

having a wall thickness measuring between the threshold values of normal tissue and dense scar.

[0081] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the third region of the heart exhibiting a narrow channel of intermediate-threshold level of wall thickness surrounded by an area with a low or below-threshold level of wall thickness, the third region of the heart as including the borderzone cardiac tissue surrounded by scar, and an area of increased statistical probability to harbor arrhythmia-sustaining mechanisms.

[0082] In some variations, the narrow channel of intermediate wall thickness may traverse a region with neighboring tissue having a low, or below-threshold level of wall thickness.

[0083] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on a plurality of wall thicknesses associated with the heart, the first region of the heart as including the normal cardiac tissue, the second region of the heart as including the scarred cardiac tissue, and the third region of the heart as including the borderzone cardiac tissue.

[0084] In some variations, the plurality of wall thicknesses may be measured at different locations throughout the heart by segmenting the endocardial surface and epicardial surfaces of the heart based on Hounsfield units.

[0085] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the first region of the heart exhibiting a normal or above-threshold level of wall thickening, the first region of the heart as including the normal cardiac tissue.

[0086] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the second region of the heart exhibiting a

severely decreased, or below-threshold level of wall thickening, the second region of the heart as including the scarred cardiac tissue.

[0087] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the third region of the heart exhibiting an intermediate decrease in wall thickening, the third region of the heart as including the borderzone cardiac tissue.

[0088] In some variations, the third region of the heart may be determined to exhibit intermediately decreased level of wall thickness based at least on the third region of the heart having a wall thickening measuring between the threshold values of normal tissue and dense scar.

[0089] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on the third region of the heart exhibiting a narrow channel of intermediate-threshold level of wall thickening surrounded by an area with a low or below-threshold level of wall thickening, the third region of the heart as including the borderzone cardiac tissue surrounded by scar, and an area of increased statistical probability to harbor arrhythmia-sustaining mechanisms.

[0090] In some variations, the narrow channel of intermediate wall thickening may traverse a region with neighboring tissue having a low, or below-threshold level of wall thickening.

[0091] In some variations, the analyzing of the 4-dimensional computed tomography data may include identifying, based at least on a plurality of wall thicknesses associated with the heart, the first region of the heart as including the normal cardiac tissue, the second region of the heart as including the scarred cardiac tissue, and the third region of the heart as including the borderzone cardiac tissue.

[0092] In some variations, the plurality of wall thickening may be measured at different locations throughout the heart by segmenting the endocardial surface and epicardial surfaces of the heart based on Hounsfield units.

[0093] In some variations, the identification of the first region, the second region, and/or the third region may be used to facilitate a non-invasive ECG computational simulation library activation mapping.

[0094] In some variations, the identification of the first region, the second region, and/or the third region may be used to facilitate a non-invasive ECG computational simulation library activation mapping and non-invasive stereotactic ablative radiotherapy (SAbR) procedure.

[0095] In some variations, the identification of the first region, the second region, and/or the third region may be used to facilitate a non-invasive ECG computational simulation library activation mapping and invasive catheter ablation procedure.

[0096] In some variations, the identification of the first region, the second region, and/or the third region may be used to facilitate an invasive catheter-based activation mapping.

[0097] In some variations, the identification of the first region, the second region, and/or the third region may be used to facilitate an invasive catheter-based activation mapping and invasive catheter ablation procedure.

[0098] In another aspect, there is provided a computer program product including a non-transitory computer readable medium storing instructions. The instructions may cause operations which may be executed by at least one data processor. The operations may include: analyzing 4-dimensional computed tomography (CT) data associated with a heart having cardiac arrhythmia to identify a first region of the heart including a normal cardiac tissue, a second region of the heart including a scarred cardiac tissue, and a third region of the heart including a borderzone cardiac tissue; identifying, based at least on a result of analyzing the 4-

dimensional computed tomography data, a cardiac tissue harboring a source of the cardiac arrhythmia, the cardiac tissue harboring the source of the cardiac arrhythmia including the scarred cardiac tissue and the borderzone cardiac tissue; and determining a treatment plan targeting the cardiac tissue harboring the source of the cardiac arrhythmia.

[0099] In another aspect, there is provided an apparatus for identifying arrhythmogenic cardiac substrate. The apparatus may include: means for analyzing 4-dimensional computed tomography (CT) data associated with a heart having cardiac arrhythmia to identify a first region of the heart including a normal cardiac tissue, a second region of the heart including a scarred cardiac tissue, and a third region of the heart including a borderzone cardiac tissue; means for identifying, based at least on a result of analyzing the 4-dimensional computed tomography data, a cardiac tissue harboring a source of the cardiac arrhythmia, the cardiac tissue harboring the source of the cardiac arrhythmia including the scarred cardiac tissue and the borderzone cardiac tissue; and means for determining a treatment plan targeting the cardiac tissue harboring the source of the cardiac arrhythmia.

[0100] Implementations of the current subject matter can include systems and methods consistent including one or more features are described as well as articles that comprise a tangibly embodied machine-readable medium operable to cause one or more machines (e.g., computers, etc.) to result in operations described herein. Similarly, computer systems are also described that may include one or more processors and one or more memories coupled to the one or more processors. A memory, which can include a computer-readable storage medium, may include, encode, store, or the like one or more programs that cause one or more processors to perform one or more of the operations described herein. Computer implemented methods consistent with one or more implementations of the current subject matter can be implemented by one or more data processors residing in a single computing system or multiple computing systems. Such multiple computing systems can be connected

and can exchange data and/or commands or other instructions or the like via one or more connection including, for example, a connection over a network (e.g. the Internet, a wireless wide area network, a local area network, a wide area network, a wired network, or the like), a direct connection between one or more of the multiple computing systems, and/or the like.

[0101] The details of one or more variations of the subject matter described herein are set forth in the accompanying drawings and the description below. Other features and advantages of the subject matter described herein may be apparent from the description and drawings, and from the claims. While certain features of the currently disclosed subject matter are described for illustrative purposes in relation to computed tomography for identifying arrhythmogenic cardiac substrate, it should be readily understood that such features are not intended to be limiting. The claims that follow this disclosure are intended to define the scope of the protected subject matter.

DESCRIPTION OF THE DRAWINGS

[0102] The accompanying drawings, which are incorporated in and constitute a part of this specification, show certain aspects of the subject matter disclosed herein and, together with the description, help explain some of the principles associated with the disclosed implementations. In the drawings,

[0103] FIG. 1 depicts a system diagram illustrating an example of a cardiac arrhythmia mapping workflow, in accordance with some example embodiments;

[0104] FIG. 2 depicts an example of a voltage map, in accordance with some example embodiments;

[0105] FIG. 3A depicts an example of a 3-dimensional volume rendering forming 4-dimensional computed tomography (CT) data, in accordance with some example embodiments;

[0106] FIG. 3B depicts an example of a 3-dimensional CT volume rendering of a heart illustrating areas corresponding to borderzone cardiac tissue;

[0107] FIG. 3C depicts an example of a 3-dimensional volume rendering of a heart illustrating areas corresponding to borderzone cardiac tissue;

[0108] FIG. 3D depicts a 2-dimensional axial slice rendering of a heart illustrating areas corresponding to borderzone cardiac tissue;

[0109] FIG. 4A depicts an example of surface map illustrating ventricular strain, in accordance with some example embodiments;

[0110] FIG. 4B depicts an example of a bullseye plot illustrating ventricular strain through the phases of cardiac cycle, in accordance with some example embodiments;

[0111] FIG. 5A depicts an example of a computational simulation library mapping result, in accordance with some example embodiments;

[0112] FIG. 5B depicts an example of an activation map, in accordance with some example embodiments;

[0113] FIG. 6 depicts an example of a noninvasive cardiac arrhythmia treatment, in accordance with some example embodiments;

[0114] FIG. 7 depicts a 3-dimensional volume rendering of a heart subjected to an example of an invasive cardiac arrhythmia treatment, in accordance with some example embodiments;

[0115] FIG. 8 depicts an example of an electrocardiogram illustrating ablation-related termination of ventricular tachycardia, in accordance with some example embodiments;

[0116] FIG. 9 depicts a flowchart illustrating an example of a process for treating cardiac arrhythmia, in accordance with some example embodiments;

[0117] FIG. 10 depicts a block diagram illustrating a computing system, in accordance with some example embodiments.

[0118] When practical, similar reference numbers denote similar structures, features, or elements.

DETAILED DESCRIPTION

[0119] Cardiac arrhythmias (e.g., atrial fibrillation, ventricular tachycardia, ventricular fibrillation) may be treated by targeting the mechanisms driving sustained and/or clinically significant episodes including, for example, stable electrical rotors, recurring electrical focal sources, reentrant electrical circuits, and/or the like. Ablation is one example treatment for cardiac arrhythmias in which radiofrequency, cryogenic temperatures, ultrasound, and/or radiation (e.g. stereotactic ablative radiotherapy (SAbR)) may be applied to the source of the cardiac arrhythmia. The resulting lesions may alleviate the cardiac arrhythmia by disrupting and/or eliminating the diseased tissue and/or the erratic electric signals causing the abnormal heart activation. Nevertheless, the outcome of ablation may depend on a variety of factors including a correct localization of the source of cardiac arrhythmia and/or the associated myocardial structural abnormalities which sustain the arrhythmia. Correctly localizing the source of cardiac arrhythmia may include identifying normal cardiac issue without scarring; scarred cardiac tissue from different pathological processes such as myocardial infarction, myocarditis, or surgery; and borderzone cardiac tissue existing in isolation or at the interface between normal cardiac tissue and scarred cardiac tissue, where small channels of slow electrical conduction, or spontaneously firing cells may be found that cause reentrant arrhythmias

[0120] Regarding the management of cardiac arrhythmias, localizing the source of cardiac arrhythmia and identifying the arrhythmia-sustaining substrate are separate but related tasks which both present challenges to the clinician. For example, some techniques which identify the arrhythmia source (for example the source of a ventricular tachycardia due to triggered activity) may merely identify a small portion of borderzone or scarred cardiac tissue,

such as the location where arrhythmic electrical wavefronts originate, but not the full extent of scarred cardiac tissue (e.g., not the entire extent of the borderzone and scarred cardiac tissue) that ablation should ideally target. Other conventional techniques may be less ideal because they are invasive, time consuming, and complex procedures. Voltage mapping, for example, is performed as part of an invasive electrophysiology procedure to map the arrhythmia-sustaining substrate using invasive catheters which are inserted and manipulated under fluoroscopic guidance, thus potentially subjecting the patient to harmful radiation or the risk of cardiac perforation. Absent a correct identification of normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue, subsequent therapy may fail to target scarred cardiac tissue and borderzone cardiac tissue or may incorrectly target normal cardiac tissue. Furthermore, scar and borderzone myocardial tissue may harbor sources of other potential sources of arrhythmia in different locations than the clinical arrhythmia. Identifying, localizing and destroy such diseased tissue may reduce the recurrence of arrhythmia without destroying healthy tissue.

[0121] In some example embodiments, an analysis engine may be configured to analyze computed tomography (CT) data associated with a heart to identify normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue existing alone or occupying an area between normal cardiac tissue and scarred cardiac tissue. For example, the analysis engine may analyze 4-dimensional computed tomography (CT) data of the heart, which may include a time-lapse sequence of 3-dimensional volume renderings of the heart.

[0122] In some example embodiments, the analysis engine may analyze the 4-dimensional computed tomography data to differentiate, based at least on a motion, a cardiac wall thickness, and/or a change in the cardiac wall thickness exhibited by various regions of the heart, normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue. Alternatively and/or additionally, the analysis engine may perform a strain and/or deformation

analysis in order to differentiate normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue. For example, the strain analysis may include applying a machine learning model, such as a support vector machine (SVM), to longitudinal or radial strain measurements and/or deformation analysis taken across at least a portion of the surface of the heart. One or more dimensionality reduction techniques, including principal component analysis (PCA) and/or the like, may be applied in order to improve the performance of the machine learning model operating on the high dimensional raw data such as the strain measurements associated with the 4-dimensional computed tomography data. Quantitative longitudinal strain, radial strain, feature tracking, and similar analyses may be accomplished using computational feature tracking.

[0123] In some example embodiments, the results of the analysis of 4-dimensional computed tomography data, which identifies potential arrhythmia-sustaining substrate, may be integrated with an arrhythmia activation and/or pace mapping system, which localizes the source of the cardiac arrhythmia, may be combined to better inform subsequent treatment such as ablation. The result of analyzing the 4-dimensional computed tomography data may include, as noted, an identification of normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue. Meanwhile, the arrhythmia activation or pace mapping may identify a probable source of the cardiac arrhythmia (e.g., the origin of arrhythmic electrical wavefronts). The arrhythmia activation mapping may be a patient specific computational simulation and/or a non-patient specific computational simulation (e.g., selected from computational simulation library such as the one described in U.S. Patent No. 10,319,144 entitled “Computational Localization of Fibrillation Sources”). The arrhythmia activation and/or pace mapping may also be derived from an electrophysiology procedure using point-by-point or multielectrode mapping.

[0124] Integrating the result of the 4-dimensional computed tomography data analysis and the arrhythmia activation mapping may enable treatments that precisely target diseased cardiac tissue (e.g., scarred cardiac tissue and borderzone cardiac tissue) with minimal impact on (e.g. avoidance of) normal cardiac tissue. Examples of treatments for cardiac arrhythmia may include ablation such as radiofrequency ablation (e.g., externally-irrigated radiofrequency catheter ablation), cryogenic ablation (e.g., cryoablation), ultrasound ablation, laser ablation, stereotactic ablative radiotherapy (SAbR), and/or the like. For example, when analysis of 4-dimensional computed tomography data is combined with noninvasive computational simulation library arrhythmia mapping and stereotactic ablative radiotherapy (SAbR), the entire substrate mapping, arrhythmia source localization, and treatment workflow for cardiac arrhythmia management may be noninvasive.

[0125] FIG. 1 depicts a system diagram illustrating an example of a cardiac arrhythmia management workflow 100, in accordance with some example embodiments. Referring to FIG. 1, the cardiac arrhythmia control system 100 may include an analysis engine 110 that is communicatively coupled with a client device 120 via a network 130. The client device 120 may be a processor-based computing device such as, for example, a smartphone, a personal computer, a tablet computer, a wearable apparatus, and/or an Internet-of-Things (IoT) appliance. The network 130 may be a wired network and/or a wireless network including, for example, a local area network (LAN), a virtual local area network (VLAN), a wide area network (WAN), a public land mobile network (PLMN), the Internet, and/or the like.

[0126] In some example embodiments, the analysis engine 110 may be configured to identify arrhythmogenic cardiac substrate harboring sources of cardiac arrhythmia. For example, the analysis engine 110 may identify arrhythmogenic cardiac substrate by at least differentiating normal cardiac tissue, scarred cardiac tissue rendered by nonviable by scarring, and borderzone cardiac tissue occupying an area between normal cardiac tissue and scarred

cardiac tissue. It should be appreciated that arrhythmogenic cardiac substrate may include scarred cardiac tissue and borderzone cardiac tissue as arrhythmia sources often exist in scarred cardiac tissue and borderzone cardiac tissue. Treatment for cardiac arrhythmias, such as various forms of ablation, should therefore target scarred cardiac tissue and borderzone cardiac tissue. Accordingly, the analysis engine 110 may be configured to localize the source of cardiac arrhythmia including by identifying the full extent of scarred cardiac tissue, up to and including the borderzone cardiac tissue.

[0127] Conventional techniques for localizing arrhythmia sources may be less ideal due to their complexity and invasive nature. Voltage mapping, for example, requires an invasive electrophysiology procedure during which catheters are inserted and manipulated under fluoroscopic guidance. Creation of a voltage map is very time consuming and may be subject to data acquisition errors, such as poor tissue contact or errors from electrogram artifact. FIG. 2 depicts an example of a voltage map 200 providing a visualization of the voltage measured at various regions of a heart. Normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue may be differentiated based at least on voltage. For example, in the example of the voltage map 200 shown in FIG. 2, areas of scarred cardiac tissue are shown in a first color, areas of normal cardiac tissue are shown in a second color, and areas of borderzone cardiac tissue are shown in a third color. Although the voltage map 200 may enable an identification of normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue, generating the voltage map 200 may require an invasive electrophysiology procedure.

[0128] Instead of conventional techniques for localizing arrhythmia sources, the analysis engine 110 may analyze computed tomography (CT) data associated with a heart to identify normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue occupying an area between normal cardiac tissue and scarred cardiac tissue. For example, the analysis engine 110 may analyze 4-dimensional computed tomography (CT) data of the heart (e.g., from

a data store 150 or another data source), which may include a time-lapse sequence of 3-dimensional volume renderings of the heart. FIG. 3A depicts an example of a 3-dimensional volume rendering 300 of a heart, which may form 4-dimensional computed tomography (CT) data associated with the heart.

[0129] In some example embodiments, the analysis engine 110 may analyze the 4-dimensional computed tomography data to differentiate, based at least on the motion exhibited by various regions of the heart, normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue. For example, the analysis engine 110 may analyze 4-dimensional computed tomography data to detect areas of the heart exhibiting normal motion, areas of the heart exhibiting poor motion or hypokinesis, and areas of the heart exhibiting severely reduced, absent motion (akinesis), or dyssynergic motion (dyskinesis). Areas of the heart exhibiting normal motion, such as a normal or above threshold level of contraction, may be identified as normal cardiac tissue. Contrastingly, areas of the heart exhibiting severely reduced, akinetic, dyskinetic motion, such as a poor or below threshold level of contraction, may be identified as scarred cardiac tissue. Furthermore, areas of the heart exhibiting hypokinesis or motion consistent with a "hinge" between normal tissue and scar may be identified as borderzone cardiac tissue.

[0130] Hypokinesis and/or significant angular deformation may refer to a quality of motion (e.g. angular motion) akin to a "hinge", and this area may represent the borderzone of tissue between dense scar and normal tissue. The analysis engine 110 may quantitatively identify one or more such hinge points by at least measuring an angle of deformation from systole to diastole. Areas with the greatest deformation angle may be identified as "hinge points" corresponding to borderzone cardiac tissue. In other words, the analysis engine 110 may identify a first area of the heart as being borderzone cardiac tissue based at least on the

first area of the heart having a greater angle of deformation from systole to diastole than at least a second area of the heart.

[0131] To further illustrate, FIGS. 3B-C depict 3-dimensional volume renderings of a heart during ventricular diastole. A corresponding 2-dimensional slice of the heart is shown in FIG. 3D. Referring to FIGS. 3B-D, dots denote borderzone cardiac tissue, which is located between scarred cardiac tissue and normal cardiac tissue. It should be appreciate that the area within the red dots, which corresponds to scarred cardiac tissue, may exhibit a relative lack of motion.

[0132] Instead of and/or in addition to the motion exhibited by different regions of the heart, the analysis engine 110 may also perform a strain analysis in order to differentiate normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue. For example, the strain analysis may include applying a machine learning model, such as a support vector machine (SVM), to strain measurements taken across at least a portion of the surface of the heart. FIG. 4A depicts an example of surface map 400 illustrating strain measurements made across a ventricular surface. FIG. 4B depicts an example of a bullseye plot 450 illustrating ventricular strain through the phases of cardiac cycle. To improve the performance of the machine learning model operating on the high dimensional raw data such as the strain measurements associated with the 4-dimensional computed tomography data, the analysis engine 110 may apply one or more dimensionality reduction techniques, such as principal component analysis (PCA) and/or the like.

[0133] In some example embodiments, the machine learning model may be trained to differentiate, based at least on a strain measurement, normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue. For example, a multi-class support vector machine (SVM) may be trained to classify, based at least on strain measurements made over time (e.g., different phases of the cardiac cycle), one or more regions of a heart as normal cardiac tissue,

scarred cardiac tissue, and borderzone cardiac tissue. For example, the support vector machine may be trained as a binary classifier to differentiate between two different types of cardiac tissue including, for example, normal cardiac tissue and abnormal cardiac tissue that includes scarred cardiac tissue as well as borderzone cardiac tissue.

[0134] The support vector machine may be trained in a supervised manner with training data in which various locations on the surface of the heart and the corresponding strain measurements are labeled, for example, as normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue. For instance, the support vector machine may be configured to operate on data points including a strain measurement, a time unit (e.g., a cardiac cycle phase) associated with the strain measurement, and the 3-dimensional spatial coordinates (e.g., x-coordinate, y-coordinate, and z-coordinate) of a location at which the strain measurement was made. Alternatively, the support vector machine may be trained in an unsupervised manner, with unlabeled training data.

[0135] The support vector machine may be trained to map, based at least on strain measurements, 4-dimensional computed tomography data in a 2-dimensional space in which clusters of data points corresponding to normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue are disposed with maximum-width gaps therebetween. The accuracy and robustness of the support vector machine may be improved by applying one or more dimensionality reduction techniques (e.g., principal component analysis (PCA) and/or the like) because the high-dimensionality of 4-dimensional computed tomography data tends to prevent a proper clustering of the data points to enable a differentiation between normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue. Referring again to FIG. 4B, for example, the bullseye graph 450 during Phase 2 of the cardiac cycle depicts normal tissue, scarred cardiac tissue, and borderzone cardiac tissue.

[0136] In some example embodiments, the localization of arrhythmia sources may be performed based on the analysis of the 4-dimensional computed tomography data combined with an arrhythmia activation or pace mapping (e.g., from the data store 150 or another data source). The result of analyzing the 4-dimensional computed tomography data may include, as noted, an identification of normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue. Meanwhile, the arrhythmia activation mapping may identify a probable source of the cardiac arrhythmia (e.g., the origin of arrhythmic electrical wavefronts). For example, in some example embodiments, the arrhythmia activation mapping may be a computational simulation selected from computational simulation library such as the one described in U.S. Patent No. 10,319,144 entitled "Computational Localization of Fibrillation Sources." Referring to FIG. 5A, the computationally simulated arrhythmia activation mapping may analyze a 12-lead electrocardiogram (ECG) and match the resulting vectorcardiogram with vectorcardiograms from simulations of cardiac arrhythmias to identify a probable arrhythmia source (e.g., the red hotspot on ventricular surface shown in FIG. 5A). Alternatively, an arrhythmia activation mapping derived from an invasive procedure, such as an electrophysiology (EP) study, may be used. FIG. 5B depicts an example of an activation map showing a yellow electrical wavefront corresponding to an activation from an arrhythmia-sustaining substrate that lies close to the tip of the ablation catheter (e.g., a silver tipped catheter with a green-tipped arrow denoting its force vector).

[0137] In some example embodiments, the results of analyzing the 4-dimensional computed tomography data may be combined with a computationally simulated arrhythmia activation mapping that is patient-specific or non-patient specific. In some cases, a non-patient specific computational model may be enhanced using the results of analyzing the 4-dimensional computed tomography data, thereby obviating the need for generating a patient-specific computational simulation. For example, the analysis engine 110 may be configured to

modify, based at least on the analysis of the 4-dimensional computed tomography data, one or more of the non-patient specific computationally simulated arrhythmia activation maps. The non-patient specific computationally simulated model may be adjusted to account for the size and orientation the patient's heart as well as the locations of normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue.

[0138] In some example embodiments, the result of analyzing the 4-dimensional computed tomography data may be integrated with an arrhythmia activation mapping to localize the source of cardiac arrhythmia and to inform subsequent treatment such as ablation. For example, the analysis engine 110 may integrate the result of the 4-dimensional computed tomography data analysis and the arrhythmia activation mapping to generate a treatment plan that precisely targets diseased cardiac tissue (e.g., scarred cardiac tissue and borderzone cardiac tissue) with minimal impact on normal cardiac tissue. Examples of treatments for cardiac arrhythmia may include ablation such as radiofrequency ablation (e.g., rhiztomy), cryogenic ablation (e.g., cryoablation), ultrasound ablation (e.g., thermal ablation), stereotactic ablative radiotherapy (SAbR), and/or the like. FIG. 6 depicts a patient undergoing stereotactic ablative radiotherapy (SAbR), an example of a non-invasive treatment in which gamma rays are used for treating cardiac arrhythmia. Alternatively, FIG. 7 depicts a 3-dimensional volume rendering 700 of a heart subjected to catheter ablation, an example of an invasive treatment for cardiac arrhythmia with various ablation lesions denoted with white, red, and pink spheres within the ventricular geometry.

[0139] In some example embodiments, when the analysis of 4-dimensional computed tomography data is combined with computationally simulated arrhythmia mapping and stereotactic ablative radiotherapy (SAbR), the entire diagnostic and treatment workflow for cardiac arrhythmia may be noninvasive. The result of ablation is shown in FIG. 8, which

depicts an example of an electrocardiogram 800 illustrating the electrical activities of a heart afflicted with ventricular tachycardia prior and subsequent to ablation.

[0140] FIG. 9 depicts a flowchart illustrating an example of a process 900 for treating cardiac arrhythmia, in accordance with some example embodiments. Referring to FIGS. 1-9, the process 900 may be performed by the analysis engine 110 to generate, based at least on an analysis of 4-dimensional computed tomography (CT) data, a treatment plan for cardiac arrhythmia.

[0141] At 902, the analysis engine 110 may analyze a 4-dimensional computed tomography (CT) data associated with a heart having cardiac arrhythmia to identify a first region of the heart including a normal cardiac tissue, a second region of the heart including a scarred cardiac tissue, and a third region of the heart including a borderzone cardiac tissue. In some example embodiments, the analysis engine 110 may analyze the 4-dimensional computed tomography data to differentiate, based at least on the motion exhibited by various regions of the heart, normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue. For example, normal cardiac tissue may exhibit normal motion (e.g., a normal level of contraction) whereas scarred cardiac tissue may exhibit abnormal motion (e.g., severely reduced, akinetic, or dyskinetic contraction) and borderzone cardiac tissue may exhibit hypokinesis and/or significant angular deformation, which is a quality of motion (e.g. angular motion) corresponding to a "hinge."

[0142] Alternatively and/or additionally, the analysis engine 110 may also perform a strain analysis in order to differentiate normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue. The strain analysis may be performed by applying a machine learning model, such as a support vector machine (SVM), trained to differentiate normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue based on strain measurements made over time (e.g., different phases of the cardiac cycle) and across various

regions of the heart. According to some example embodiments, the accuracy and robustness of the machine learning model (e.g., the support vector machine and/or the like) may be improved by applying one or more dimensionality reduction techniques (e.g., principal component analysis (PCA) and/or the like) at least because the high-dimensionality of 4-dimensional computed tomography data tend to prevent a proper clustering of the data points to differentiate between normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue.

[0143] Other machine learning methods may also involve time-series-based classification of well-defined, discrete regions of the heart as "normal", "scarred", and "border-zone" based on the measured strain features. Time-series classification methods such as K-nearest neighbors with Dynamic Time Warping, Time Series Forest, Shapelet-Based classification, Gradient Boosting methods, or specialized neural networks (e.g. long short-term memory architectures) may be used to characterize a given region as "normal", "scarred", or "borderzone" based on strain feature measurements over discrete (i.e. cardiac cycle phases) or continuous (i.e. absolute or beat-relative) time measurements. For example, data point clusters in a 2D space representing the cardiac surface can be grouped according to cardiac region and quantified according to a strain-based feature measured at that point in space.

[0144] The results of the above strain analysis can be mapped to standard geometric model of the heart comprised of 1) a well-defined set of discrete cardiac regions (e.g. AHA cardiac segment model) and/or 2) a continuous 3D structural model of the heart. The mapping can be performed by 1) assigning to the standard geometric model the classification results of normal, scarred, and border-zone tissue on a per-region basis, and/or 2) applying regression techniques (e.g. least-squares fit) on the strain analysis feature(s) (e.g., angular motion, rate of wall thickening, etc) to a 3D structural model, thereby producing a weighting function of strain analysis feature(s).

[0145] At 904, the analysis engine 110 may integrate the result of analyzing the 4-dimensional computed tomography data with an arrhythmia activation mapping to identify cardiac tissue harboring a source of the cardiac arrhythmia. In some example embodiments, the results of analyzing the 4-dimensional computed tomography data may be combined with an arrhythmia activation mapping to determine a precise location of the source of the cardiac arrhythmia, including the scarred cardiac tissue and up to the borderzone cardiac tissue. This may be accomplished by weighting one with the other, such as through Boolean operations (i.e. a discrete cardiac region is classified as ("scarred" OR "abnormal) AND has an arrhythmia source hotspot) or a continuous weighting function.

[0146] The arrhythmia activation mapping may be simulated computationally or derived from an invasive procedure, such as an electrophysiology (EP) study. Moreover, a computationally simulated arrhythmia mapping may be patient-specific or non-patient specific. In the latter case, the results of analyzing the 4-dimensional computed tomography data may enhance the non-patient specific computational model to obviate the need for generating a patient-specific computational simulation.

[0147] At 906, the analysis engine 110 may determine, based at least on the localization of the source of the cardiac arrhythmia, a treatment plan targeting the cardiac tissue harboring the source of cardiac arrhythmia including scarred cardiac tissue and/or borderzone cardiac tissue. In some example embodiments, a treatment plan for cardiac arrhythmia may be determined based on the localization of the source of the cardiac arrhythmia. Arrhythmogenic cardiac substrate harboring sources of cardiac arrhythmia may include, as noted, scarred cardiac tissue as well as borderzone cardiac tissue occupying an area between normal cardiac tissue and scarred cardiac tissue. A correct localization of the arrhythmia source may therefore include identifying the full extent of the scarred cardiac tissue, up to and including the borderzone cardiac tissue, and not just a portion of the cardiac tissue where arrhythmic

electrical wavefronts originate. Without a correct localization of the arrhythmia source, subsequent therapy may fail to target scarred cardiac tissue and borderzone cardiac tissue or may incorrectly target normal cardiac tissue.

[0148] The result of analyzing the 4-dimensional computed tomography data may be integrated with an arrhythmia activation mapping to provide a correct localization of the arrhythmia source such that subsequent treatment may target scarred cardiac tissue and borderzone cardiac tissue with minimal impact on normal cardiac tissue. Moreover, when the analysis of 4-dimensional computed tomography data is combined with computationally simulated arrhythmia mapping and stereotactic ablative radiotherapy (SAbR), the entire diagnostic and treatment workflow for cardiac arrhythmia may be noninvasive.

[0149] FIG. 10 depicts a block diagram illustrating a computing system 1000, in accordance with some example embodiments. Referring to FIGS. 1 and 10, the computing system 1000 can be used to implement the analysis engine 110 and/or any components therein.

[0150] As shown in FIG. 10, the computing system 1000 can include a processor 1010, a memory 1020, a storage device 1030, and input/output device 1040. The processor 1010, the memory 1020, the storage device 1030, and the input/output device 1040 can be interconnected via a system bus 1050. The processor 1010 is capable of processing instructions for execution within the computing system 1000. Such executed instructions can implement one or more components of, for example, the analysis engine 110. In some implementations of the current subject matter, the processor 1010 can be a single-threaded processor. Alternately, the processor 1010 can be a multi-threaded processor. The processor 1010 is capable of processing instructions stored in the memory 1020 and/or on the storage device 1030 to display graphical information for a user interface provided via the input/output device 1040.

[0151] The memory 1020 is a computer readable medium such as volatile or non-volatile that stores information within the computing system 1000. The memory 1020 can store

data structures representing configuration object databases, for example. The storage device 1030 is capable of providing persistent storage for the computing system 1000. The storage device 1030 can be a floppy disk device, a hard disk device, an optical disk device, or a tape device, or other suitable persistent storage means. The input/output device 1040 provides input/output operations for the computing system 1000. In some implementations of the current subject matter, the input/output device 1040 includes a keyboard and/or pointing device. In various implementations, the input/output device 1040 includes a display unit for displaying graphical user interfaces.

[0152] According to some implementations of the current subject matter, the input/output device 1040 can provide input/output operations for a network device. For example, the input/output device 1040 can include Ethernet ports or other networking ports to communicate with one or more wired and/or wireless networks (e.g., a local area network (LAN), a wide area network (WAN), the Internet).

[0153] In some implementations of the current subject matter, the computing system 1000 can be used to execute various interactive computer software applications that can be used for organization, analysis and/or storage of data in various (e.g., tabular) format. Alternatively, the computing system 1000 can be used to execute any type of software applications. These applications can be used to perform various functionalities, e.g., planning functionalities (e.g., generating, managing, editing of spreadsheet documents, word processing documents, and/or any other objects, etc.), computing functionalities, communications functionalities, and/or the like. The applications can include various add-in functionalities or can be standalone computing products and/or functionalities. Upon activation within the applications, the functionalities can be used to generate the user interface provided via the input/output device 1040. The user interface can be generated and presented to a user by the computing system 1000 (e.g., on a computer screen monitor, etc.).

[0154] One or more aspects or features of the subject matter described herein can be realized in digital electronic circuitry, integrated circuitry, specially designed application specific integrated circuits (ASICs), field programmable gate arrays (FPGAs) computer hardware, firmware, software, and/or combinations thereof. These various aspects or features can include implementation in one or more computer programs that are executable and/or interpretable on a programmable system including at least one programmable processor, which can be special or general purpose, coupled to receive data and instructions from, and to transmit data and instructions to, a storage system, at least one input device, and at least one output device. The programmable system or computing system may include clients and servers. A client and server are generally remote from each other and typically interact through a communication network. The relationship of client and server arises by virtue of computer programs running on the respective computers and having a client-server relationship to each other.

[0155] These computer programs, which can also be referred to as programs, software, software applications, applications, components, or code, include machine instructions for a programmable processor, and can be implemented in a high-level procedural and/or object-oriented programming language, and/or in assembly/machine language. As used herein, the term "machine-readable medium" refers to any computer program product, apparatus and/or device, such as for example magnetic discs, optical disks, memory, and Programmable Logic Devices (PLDs), used to provide machine instructions and/or data to a programmable processor, including a machine-readable medium that receives machine instructions as a machine-readable signal. The term "machine-readable signal" refers to any signal used to provide machine instructions and/or data to a programmable processor. The machine-readable medium can store such machine instructions non-transitorily, such as for example as would a non-transient solid-state memory or a magnetic hard drive or any

equivalent storage medium. The machine-readable medium can alternatively, or additionally, store such machine instructions in a transient manner, such as for example, as would a processor cache or other random-access memory associated with one or more physical processor cores.

[0156] The subject matter described herein can be embodied in systems, apparatus, methods, and/or articles depending on the desired configuration. The implementations set forth in the foregoing description do not represent all implementations consistent with the subject matter described herein. Instead, they are merely some examples consistent with aspects related to the described subject matter. Although a few variations have been described in detail above, other modifications or additions are possible. In particular, further features and/or variations can be provided in addition to those set forth herein. For example, the implementations described above can be directed to various combinations and subcombinations of the disclosed features and/or combinations and subcombinations of several further features disclosed above. In addition, the logic flows depicted in the accompanying figures and/or described herein do not necessarily require the particular order shown, or sequential order, to achieve desirable results. Other implementations may be within the scope of the following claims.

WHAT IS CLAIMED IS

1. A system, comprising:

at least one processor; and

at least one memory including program code which when executed by the at least one processor provides operations comprising:

analyzing 4-dimensional computed tomography (CT) data associated with a heart having cardiac arrhythmia to identify a first region of the heart including a normal cardiac tissue, a second region of the heart including a scarred cardiac tissue, and a third region of the heart including a borderzone cardiac tissue;

identifying, based at least on a result of analyzing the 4-dimensional computed tomography data, a cardiac tissue harboring a source of the cardiac arrhythmia, the cardiac tissue harboring the source of the cardiac arrhythmia including the scarred cardiac tissue and the borderzone cardiac tissue; and

determining a treatment plan targeting the cardiac tissue harboring the source of the cardiac arrhythmia.

2. The system of claim 1, further comprising integrating the result analyzing the 4-dimensional computed tomography data with an arrhythmia activation mapping in order to identify the cardiac tissue harboring the source of the cardiac arrhythmia.

3. The system of claim 2, wherein the arrhythmia activation mapping comprises a patient-specific and/or a non-patient specific computational simulation.

4. The system of any one of claims 2-3, wherein the arrhythmia activation mapping is derived from an electrophysiology (EP) study.

5. The system of any one of claims 1-4, wherein the treatment plan is configured to target the second region of the heart including the scarred cardiac tissue and/or the third region of the heart including the borderzone cardiac tissue while avoiding the first region of the heart including the normal cardiac tissue.

6. The system of any one of claims 1-5, wherein the third region of the heart including the borderzone cardiac tissue occupy an area between the first region of the heart including the normal cardiac tissue and the second region of the heart including the scarred cardiac tissue.

7. The system of any one of claims 1-6, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the first region of the heart exhibiting a normal or above-threshold level of contraction, the first region of the heart as including the normal cardiac tissue.

8. The system of any one of claims 1-7, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the second region of the heart exhibiting a below-threshold level of contraction, severely reduced, akinetic, or dyskinetic motion; the second region of the heart as including the scarred cardiac tissue.

9. The system of any one of claims 1-8, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the third region of the heart exhibiting a hypokinesis, the third region of the heart as including the borderzone cardiac tissue.

10. The system of claim 9, wherein the third region of the heart is determined to exhibit hypokinesis and/or significant angular deformation, based at least on the third region of the

heart having a greatest angle of deformation from systole to diastole, as including the borderzone tissue.

11. The system of any one of claims 1-10, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on a plurality of strain measurements associated with the heart, the first region of the heart as including the normal cardiac tissue, the second region of the heart as including the scarred cardiac tissue, and the third region of the heart as including the borderzone cardiac tissue.

12. The system of claim 11, wherein the plurality of strain measurements are taken at different locations on a surface of the heart and during different phases of a cardiac cycle.

13. The system of any one of claims 11-12, further comprising applying a machine learning model trained to differentiate, based at least on the plurality of strain measurements, between the normal cardiac tissue, the scarred cardiac tissue, and the borderzone cardiac tissue.

14. The system of claim 13, wherein the machine learning model comprises a support vector machine (SVM) trained to map, based at least on the plurality of strain measurements, the 4-dimensional computed tomography data in a 2-dimensional space in which clusters of data points corresponding to normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue are disposed with maximum-width gaps therebetween.

15. The system of any one of claims 13-14, wherein the machine learning model comprises the time-series-based classification K-nearest neighbors with Dynamic Time Warping to characterize a given region as “normal”, “scarred”, or “borderzone” based on strain feature measurements over discrete time measurements to map, based at least on the

plurality of strain measurements, the 4-dimensional computed tomography data in a 2-dimensional space in which clusters of data points corresponding to normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue are identified.

16. The system of any one of claims 13-15, wherein the machine learning model comprises the methodology of a Time Series Forest to characterize a given region as "normal", "scarred", or "borderzone" based on strain feature measurements over discrete time measurements to map, based at least on the plurality of strain measurements, the 4-dimensional computed tomography data in a 2-dimensional space in which clusters of data points corresponding to normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue are identified.

17. The system of any one of claims 13-16, wherein the machine learning model comprises the Shapelet-Based classification to characterize a given region as "normal", "scarred", or "borderzone" based on strain feature measurements over discrete time measurements to map, based at least on the plurality of strain measurements, the 4-dimensional computed tomography data in a 2-dimensional space in which clusters of data points corresponding to normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue are identified.

18. The system of any one of claims 13-17, wherein the machine learning model comprises a Gradient Boosting method to characterize a given region as "normal", "scarred", or "borderzone" based on strain feature measurements over discrete time measurements to map, based at least on the plurality of strain measurements, the 4-dimensional computed

tomography data in a 2-dimensional space in which clusters of data points corresponding to normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue are identified.

19. The system of any one of claims 13-18, wherein the machine learning model comprises a specialized neural network consisting of a deep learning feedforward network, structured as alternating convolutional layers and max-pooling layers, topped by pure classification layers to map, based at least on the plurality of strain measurements, the 4-dimensional computed tomography data in a 2-dimensional space in which clusters of data points corresponding to normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue.

20. The system of any one of claims 13-19, wherein a dimensionality reduction technique is applied to the 4-dimensional computed tomography data and the plurality of strain measurements prior to applying the machine learning model.

21. The system of any one of claims 1-20, wherein the treatment plan includes an ablation.

22. The system of any one of claims 1-21, wherein the treatment plan includes a radiofrequency ablation, a cryogenic ablation, an ultrasound ablation, and/or a stereotactic ablative radiotherapy (SAbR).

23. The system of any one of claims 1-22, wherein the 4-dimensional computed tomography data includes a time-lapse sequence of 3-dimensional volume renderings of the heart.

24. The system of any one of claims 1-23, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the first region of the heart exhibiting a normal or above-threshold level of wall thickness, the first region of the heart as including the normal cardiac tissue.

25. The system of any one of claims 1-24, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the second region of the heart exhibiting a severely decreased, or below-threshold level of wall thickness, the second region of the heart as including the scarred cardiac tissue.

26. The system of any one of claims 1-25, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the third region of the heart exhibiting an intermediate decrease in wall thickness, the third region of the heart as including the borderzone cardiac tissue.

27. The system of claim 26, wherein the third region of the heart is determined to exhibit intermediately decreased level of wall thickness based at least on the third region of the heart having a wall thickness measuring between the threshold values of normal tissue and dense scar.

28. The system of any one of claims 1-27, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the third region of the heart exhibiting a narrow channel of intermediate-threshold level of wall thickness surrounded by an area with a low or below-threshold level of wall thickness, the third region of the heart as including the borderzone cardiac tissue surrounded by scar, and an area of increased statistical probability to harbor arrhythmia-sustaining mechanisms.

29. The system of claim 28, wherein the narrow channel of intermediate wall thickness traverses a region with neighboring tissue having a low, or below-threshold level of wall thickness.

30. The system of any one of claims 1-29, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on a plurality of wall thicknesses associated with the heart, the first region of the heart as including the normal cardiac tissue, the second region of the heart as including the scarred cardiac tissue, and the third region of the heart as including the borderzone cardiac tissue.

31. The system of claim 30, wherein the plurality of wall thicknesses are measured at different locations throughout the heart by segmenting the endocardial surface and epicardial surfaces of the heart based on Hounsfield units.

32. The system of any one of claims 1-31, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the first region of the heart exhibiting a normal or above-threshold level of wall thickening, the first region of the heart as including the normal cardiac tissue.

33. The system of any one of claims 1-32, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the second region of the heart exhibiting a severely decreased, or below-threshold level of wall thickening, the second region of the heart as including the scarred cardiac tissue.

34. The system of any one of claims 1-33, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the third region of the heart

exhibiting an intermediate decrease in wall thickening, the third region of the heart as including the borderzone cardiac tissue.

35. The system of any one of claims 27-34, wherein the third region of the heart is determined to exhibit intermediately decreased level of wall thickness based at least on the third region of the heart having a wall thickening measuring between the threshold values of normal tissue and dense scar.

36. The system of any one of claims 1-35, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the third region of the heart exhibiting a narrow channel of intermediate-threshold level of wall thickening surrounded by an area with a low or below-threshold level of wall thickening, the third region of the heart as including the borderzone cardiac tissue surrounded by scar, and an area of increased statistical probability to harbor arrhythmia-sustaining mechanisms.

37. The system of claim 36, wherein the narrow channel of intermediate wall thickening traverses a region with neighboring tissue having a low, or below-threshold level of wall thickening.

38. The system of any one of claims 1-37, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on a plurality of wall thicknesses associated with the heart, the first region of the heart as including the normal cardiac tissue, the second region of the heart as including the scarred cardiac tissue, and the third region of the heart as including the borderzone cardiac tissue.

39. The system of claim 38, wherein the plurality of wall thickening are measured at different locations throughout the heart by segmenting the endocardial surface and epicardial surfaces of the heart based on Hounsfield units.

40. The system of any one of claims 1-39, wherein the identification of the first region, the second region, and/or the third region are used to facilitate a non-invasive ECG computational simulation library activation mapping.

41. The system of any one of claims 1-40, wherein the identification of the first region, the second region, and/or the third region are used to facilitate a non-invasive ECG computational simulation library activation mapping and non-invasive stereotactic ablative radiotherapy (SAbR) procedure.

42. The system of any one of claims 1-41, wherein the identification of the first region, the second region, and/or the third region are used to facilitate a non-invasive ECG computational simulation library activation mapping and invasive catheter ablation procedure.

43. The system of any one of claims 1-42, wherein the identification of the first region, the second region, and/or the third region are used to facilitate an invasive catheter-based activation mapping.

44. The system of any one of claims 1-43, wherein the identification of the first region, the second region, and/or the third region are used to facilitate an invasive catheter-based activation mapping and invasive catheter ablation procedure.

45. A non-transitory computer readable medium storing instructions, which when executed by at least one data processor, result in operations comprising:

analyzing 4-dimensional computed tomography (CT) data associated with a heart having cardiac arrhythmia to identify a first region of the heart including a normal cardiac tissue, a second region of the heart including a scarred cardiac tissue, and a third region of the heart including a borderzone cardiac tissue;

identifying, based at least on a result of analyzing the 4-dimensional computed tomography data, a cardiac tissue harboring a source of the cardiac arrhythmia, the cardiac tissue harboring the source of the cardiac arrhythmia including the scarred cardiac tissue and the borderzone cardiac tissue; and

determining a treatment plan targeting the cardiac tissue harboring the source of the cardiac arrhythmia.

46. A computer-implemented method, comprising:

analyzing 4-dimensional computed tomography (CT) data associated with a heart having cardiac arrhythmia to identify a first region of the heart including a normal cardiac tissue, a second region of the heart including a scarred cardiac tissue, and a third region of the heart including a borderzone cardiac tissue;

identifying, based at least on a result of analyzing the 4-dimensional computed tomography data, a cardiac tissue harboring a source of the cardiac arrhythmia, the cardiac tissue harboring the source of the cardiac arrhythmia including the scarred cardiac tissue and the borderzone cardiac tissue; and

determining a treatment plan targeting the cardiac tissue harboring the source of the cardiac arrhythmia.

47. The method of claim 46, further comprising integrating the result analyzing the 4-dimensional computed tomography data with an arrhythmia activation mapping in order to identify the cardiac tissue harboring the source of the cardiac arrhythmia.

48. The method of any one of claims 46-47, further comprising integrating the result analyzing the 4-dimensional computed tomography data with an arrhythmia activation mapping via the technique of weighting one with the other through Boolean operations in order to identify the cardiac tissue harboring the source of the cardiac arrhythmia.

49. The method of any one of claims 46-48, further comprising integrating the result analyzing the 4-dimensional computed tomography data with an arrhythmia activation mapping via a continuous weighting function in order to identify the cardiac tissue harboring the source of the cardiac arrhythmia.

50. The method of any one of claims 49, wherein the arrhythmia activation mapping comprises a patient-specific and/or a non-patient specific computational simulation.

51. The method of any one of claims 49-50, wherein the arrhythmia activation mapping is derived from an electrophysiology (EP) study.

52. The method of any one of claims 46-51, wherein the treatment plan is configured to target the second region of the heart including the scarred cardiac tissue and/or the third region of the heart including the borderzone cardiac tissue while avoiding the first region of the heart including the normal cardiac tissue.

53. The method of any one of claims 46-52, wherein the third region of the heart including the borderzone cardiac tissue occupy an area between the first region of the heart including the normal cardiac tissue and the second region of the heart including the scarred cardiac tissue.

54. The method of any one of claims 46-53, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the first region of the heart exhibiting a normal or above-threshold level of contraction, the first region of the heart as including the normal cardiac tissue.

55. The method of any one of claims 46-54, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the second region of the heart exhibiting a below-threshold level of contraction, severely reduced, akinetic, or dyskinetic motion; the second region of the heart as including the scarred cardiac tissue.

56. The method of any one of claims 46-55, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the third region of the heart exhibiting a hypokinesis, the third region of the heart as including the borderzone cardiac tissue.

57. The method of claim 56, wherein the third region of the heart is determined to exhibit hypokinesis and/or significant angular deformation, based at least on the third region of the heart having a greatest angle of deformation from systole to diastole, as including the borderzone tissue.

58. The method of any one of claims 46-57, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on a plurality of strain measurements associated with the heart, the first region of the heart as including the normal cardiac tissue, the second region of the heart as including the scarred cardiac tissue, and the third region of the heart as including the borderzone cardiac tissue.

59. The method of claim 58, wherein the plurality of strain measurements are taken at different locations on a surface of the heart and during different phases of a cardiac cycle.

60. The method of any one of claims 46-59, further comprising applying a machine learning model trained to differentiate, based at least on the plurality of strain measurements, between the normal cardiac tissue, the scarred cardiac tissue, and the borderzone cardiac tissue.

61. The method of claim 60, wherein the machine learning model comprises a support vector machine (SVM) trained to map, based at least on the plurality of strain measurements, the 4-dimensional computed tomography data in a 2-dimensional space in which clusters of data points corresponding to normal cardiac tissue, scarred cardiac tissue, and borderzone cardiac tissue are disposed with maximum-width gaps therebetween.

62. The method of any one of claims 60-61, wherein a dimensionality reduction technique is applied to the 4-dimensional computed tomography data and the plurality of strain measurements prior to applying the machine learning model.

63. The method of any one of claims 46-62, wherein the treatment plan includes an ablation.

64. The method of any one of claims 46-63, wherein the treatment plan includes a radiofrequency ablation, a cryogenic ablation, an ultrasound ablation, and/or a stereotactic ablative radiotherapy (SAbR).

65. The method of any one of claims 46-64, wherein the 4-dimensional computed tomography data includes a time-lapse sequence of 3-dimensional volume renderings of the heart.

66. The method of any one of claims 46-65, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the first region of the heart exhibiting a normal or above-threshold level of wall thickness, the first region of the heart as including the normal cardiac tissue.

67. The method of any one of claims 46-66, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the second region of the heart exhibiting a severely decreased, or below-threshold level of wall thickness, the second region of the heart as including the scarred cardiac tissue.

68. The method of any one of claims 46-67, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the third region of the heart exhibiting an intermediate decrease in wall thickness, the third region of the heart as including the borderzone cardiac tissue.

69. The method of claim 68, wherein the third region of the heart is determined to exhibit intermediately decreased level of wall thickness based at least on the third region of the heart having a wall thickness measuring between the threshold values of normal tissue and dense scar.

70. The method of any one of claims 46-69, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the third region of the heart exhibiting a narrow channel of intermediate-threshold level of wall thickness surrounded by

an area with a low or below-threshold level of wall thickness, the third region of the heart as including the borderzone cardiac tissue surrounded by scar, and an area of increased statistical probability to harbor arrhythmia-sustaining mechanisms.

71. The method of claim 70, wherein the narrow channel of intermediate wall thickness traverses a region with neighboring tissue having a low, or below-threshold level of wall thickness.

72. The method of any one of claims 46-71, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on a plurality of wall thicknesses associated with the heart, the first region of the heart as including the normal cardiac tissue, the second region of the heart as including the scarred cardiac tissue, and the third region of the heart as including the borderzone cardiac tissue.

73. The method of claim 72, wherein the plurality of wall thicknesses are measured at different locations throughout the heart by segmenting the endocardial surface and epicardial surfaces of the heart based on Hounsfield units.

74. The method of any one of claims 46-73, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the first region of the heart exhibiting a normal or above-threshold level of wall thickening, the first region of the heart as including the normal cardiac tissue.

75. The method of any one of claims 46-74, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the second region of the heart exhibiting a severely decreased, or below-threshold level of wall thickening, the second region of the heart as including the scarred cardiac tissue.

76. The method of any one of claims 46-75, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the third region of the heart exhibiting an intermediate decrease in wall thickening, the third region of the heart as including the borderzone cardiac tissue.

77. The method of claim 76, wherein the third region of the heart is determined to exhibit intermediately decreased level of wall thickness based at least on the third region of the heart having a wall thickening measuring between the threshold values of normal tissue and dense scar.

78. The method of any one of claims 46-77, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on the third region of the heart exhibiting a narrow channel of intermediate-threshold level of wall thickening surrounded by an area with a low or below-threshold level of wall thickening, the third region of the heart as including the borderzone cardiac tissue surrounded by scar, and an area of increased statistical probability to harbor arrhythmia-sustaining mechanisms.

79. The method of claim 78, wherein the narrow channel of intermediate wall thickening traverses a region with neighboring tissue having a low, or below-threshold level of wall thickening.

80. The method of any one of claims 46-79, wherein the analyzing of the 4-dimensional computed tomography data includes identifying, based at least on a plurality of wall thicknesses associated with the heart, the first region of the heart as including the normal cardiac tissue, the second region of the heart as including the scarred cardiac tissue, and the third region of the heart as including the borderzone cardiac tissue.

81. The method of claim 80, wherein the plurality of wall thickening are measured at different locations throughout the heart by segmenting the endocardial surface and epicardial surfaces of the heart based on Hounsfield units.

82. The method of any one of claims 46-81, wherein the identification of the first region, the second region, and/or the third region are used to facilitate a non-invasive ECG computational simulation library activation mapping.

83. The method of any one of claims 46-82, wherein the identification of the first region, the second region, and/or the third region are used to facilitate a non-invasive ECG computational simulation library activation mapping and non-invasive stereotactic ablative radiotherapy (SAbR) procedure.

84. The method of any one of claims 46-83, wherein the identification of the first region, the second region, and/or the third region are used to facilitate a non-invasive ECG computational simulation library activation mapping and invasive catheter ablation procedure.

85. The method of any one of claims 46-84, wherein the identification of the first region, the second region, and/or the third region are used to facilitate an invasive catheter-based activation mapping.

86. The method of any one of claims 46-85, wherein the identification of the first region, the second region, and/or the third region are used to facilitate an invasive catheter-based activation mapping and invasive catheter ablation procedure.

87. An apparatus, comprising:

means for analyzing 4-dimensional computed tomography (CT) data associated with a heart having cardiac arrhythmia to identify a first region of the heart including a normal cardiac tissue, a second region of the heart including a scarred cardiac tissue, and a third region of the heart including a borderzone cardiac tissue;

means for identifying, based at least on a result of analyzing the 4-dimensional computed tomography data, a cardiac tissue harboring a source of the cardiac arrhythmia, the cardiac tissue harboring the source of the cardiac arrhythmia including the scarred cardiac tissue and the borderzone cardiac tissue; and

means for determining a treatment plan targeting the cardiac tissue harboring the source of the cardiac arrhythmia.

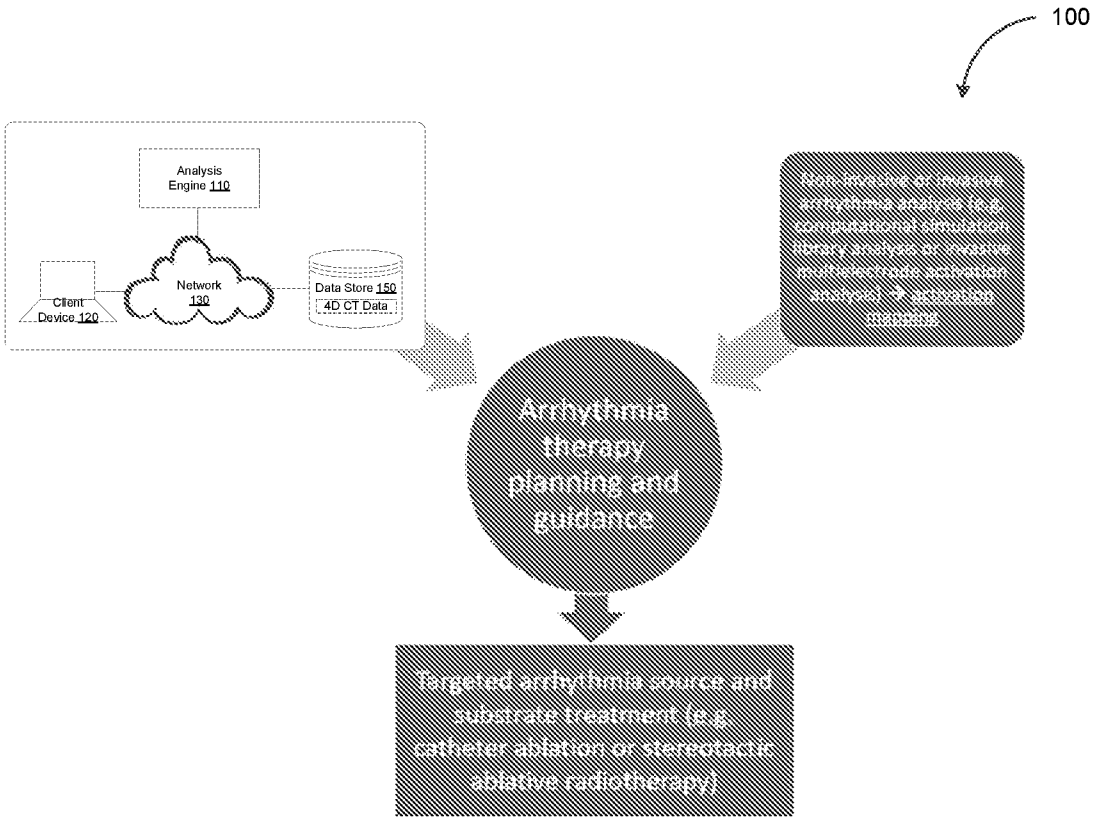
100
Analysis Engine 110
Client Device 120
Network 130
Data Store 150
4D CT Data
Arrhythmia therapy planning and guidance
Targeted arrhythmia source and substrate treatment (e.g. catheter ablation or stereotactic ablative radiotherapy)

FIG. 1

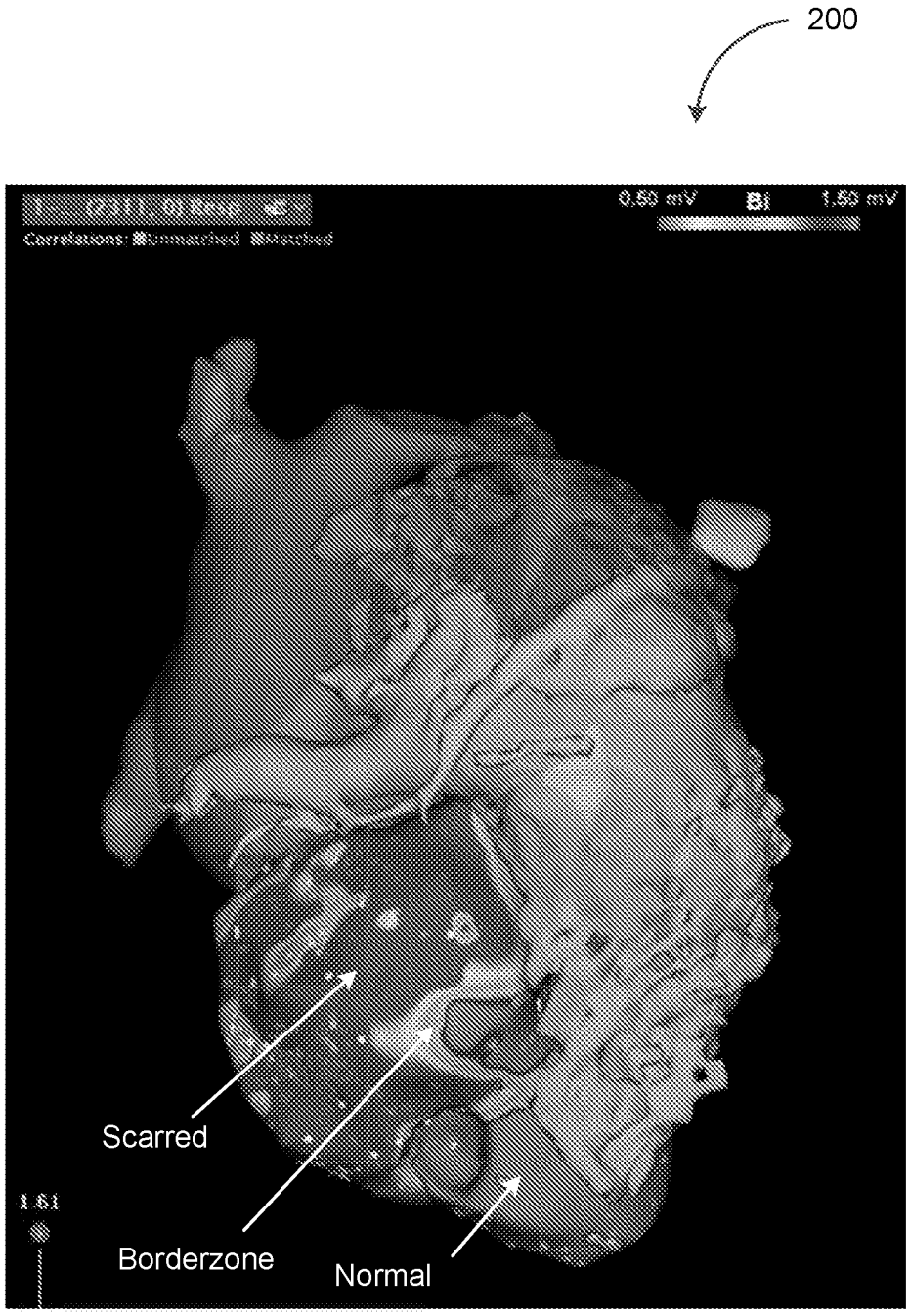

FIG. 2

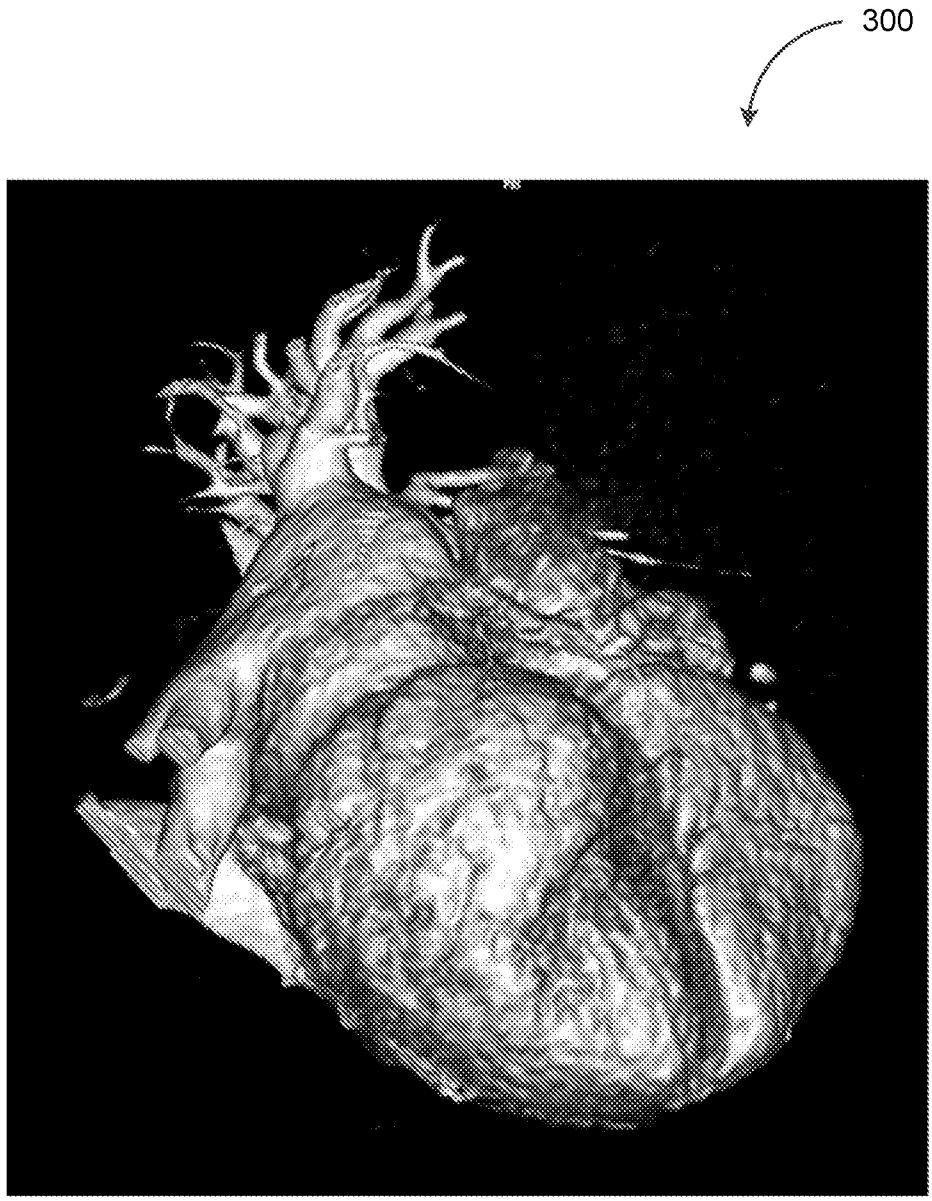

FIG. 3A

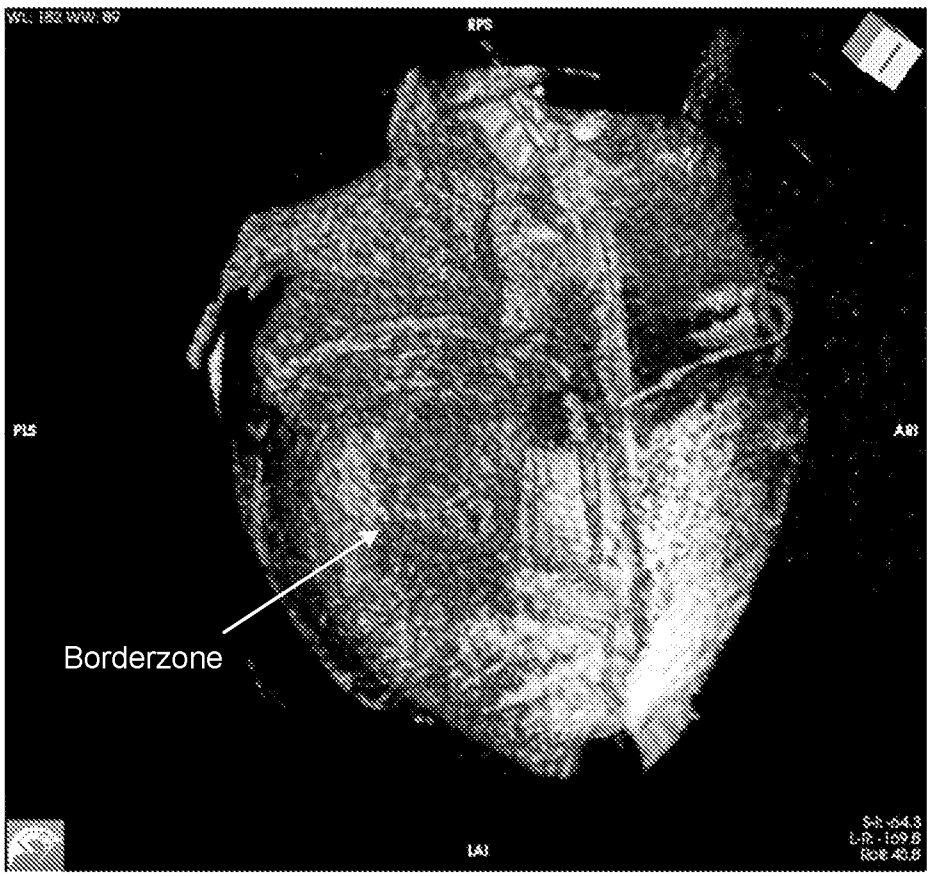

FIG. 3B

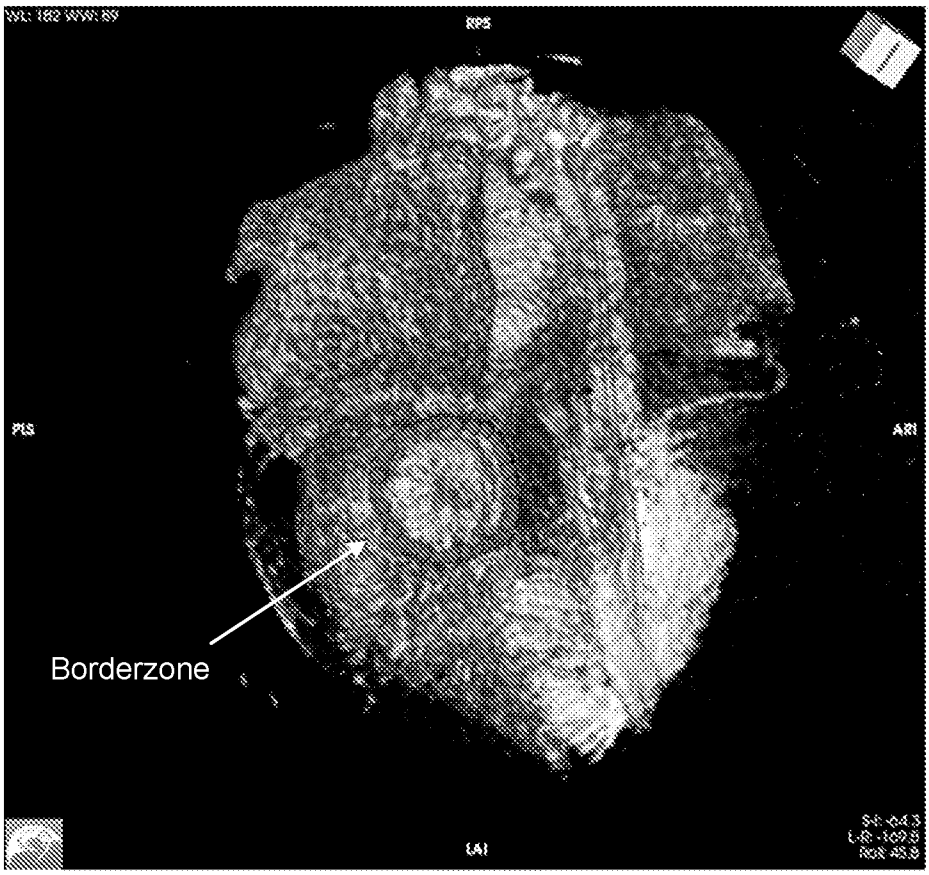

FIG. 3C

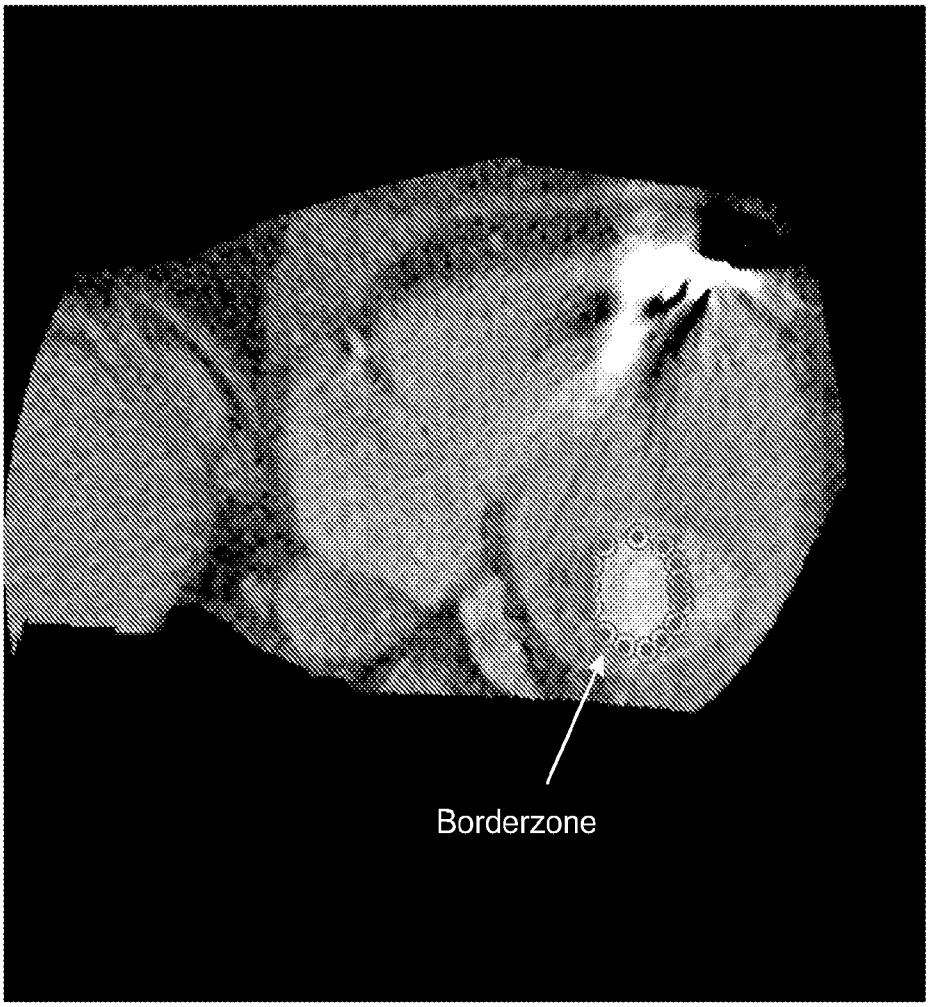

FIG. 3D

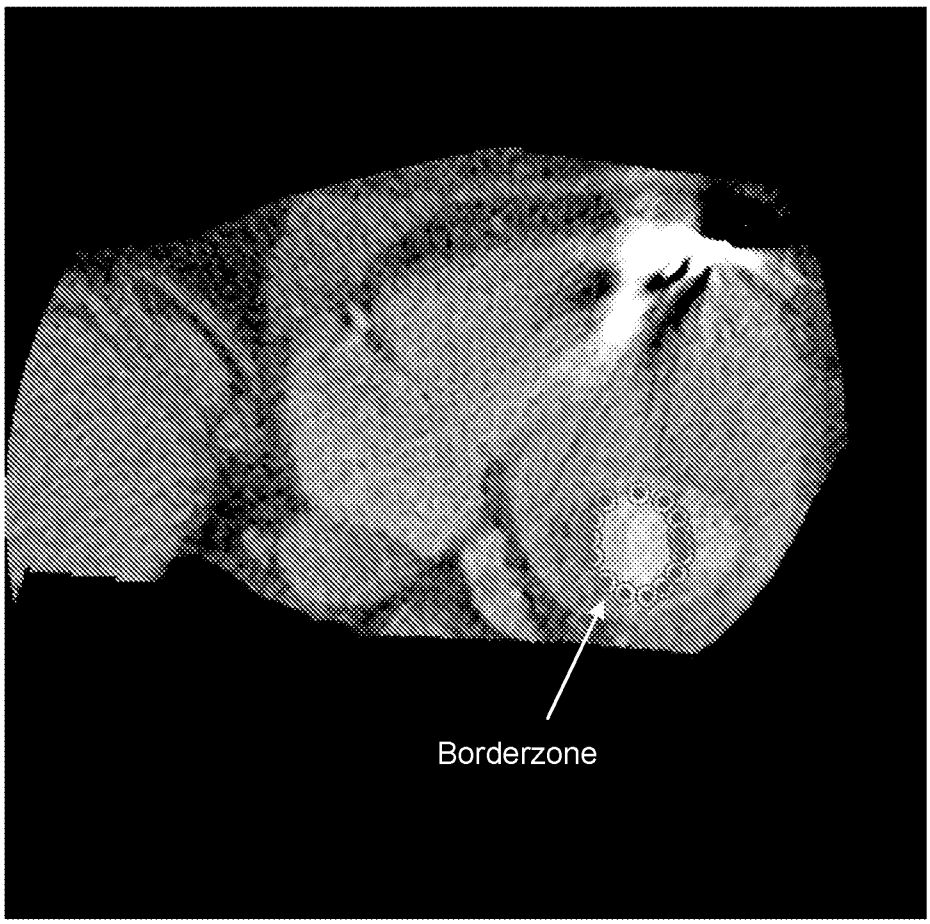

FIG. 4C

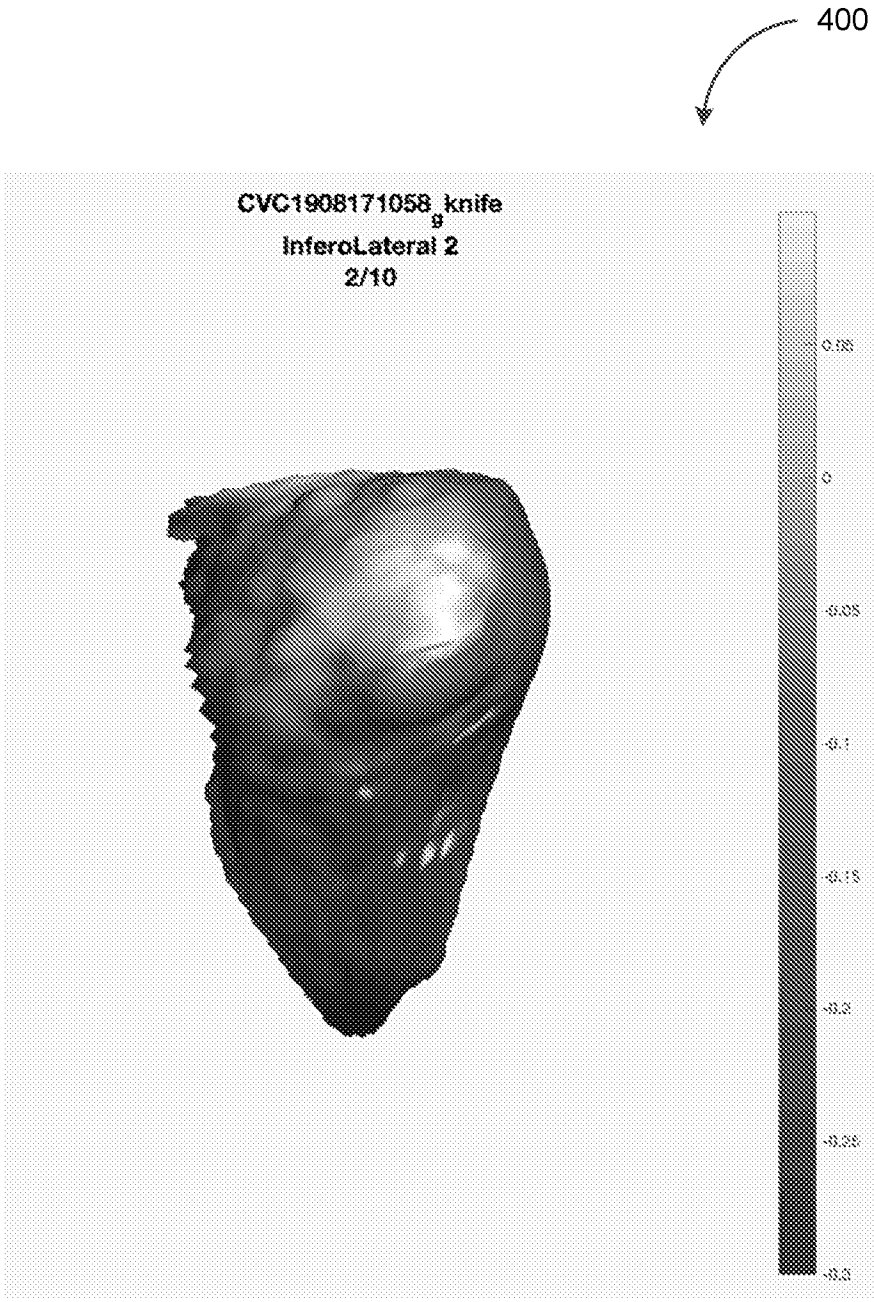
400
CVC1908171058_g_knife
InferoLateral 2
2/10
0.05
0
-0.05
-0.1
-0.15
-0.2
-0.25
-0.3

FIG. 4A

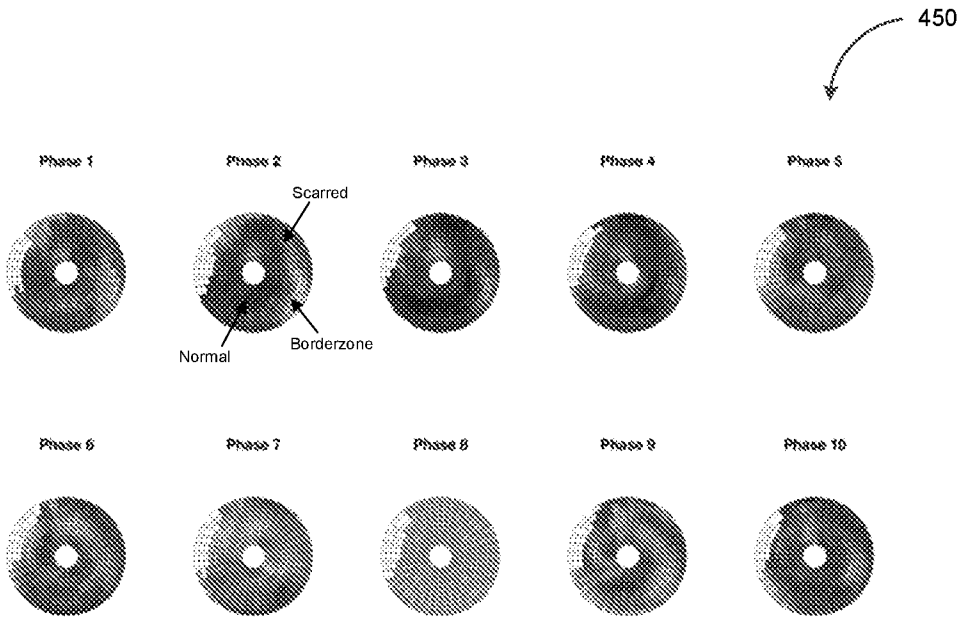
450
Phase 1
Phase 2
Phase 3
Phase 4
Phase 5
Scarred
Normal
Borderzone
Phase 6
Phase 7
Phase 8
Phase 9
Phase 10

FIG. 4B

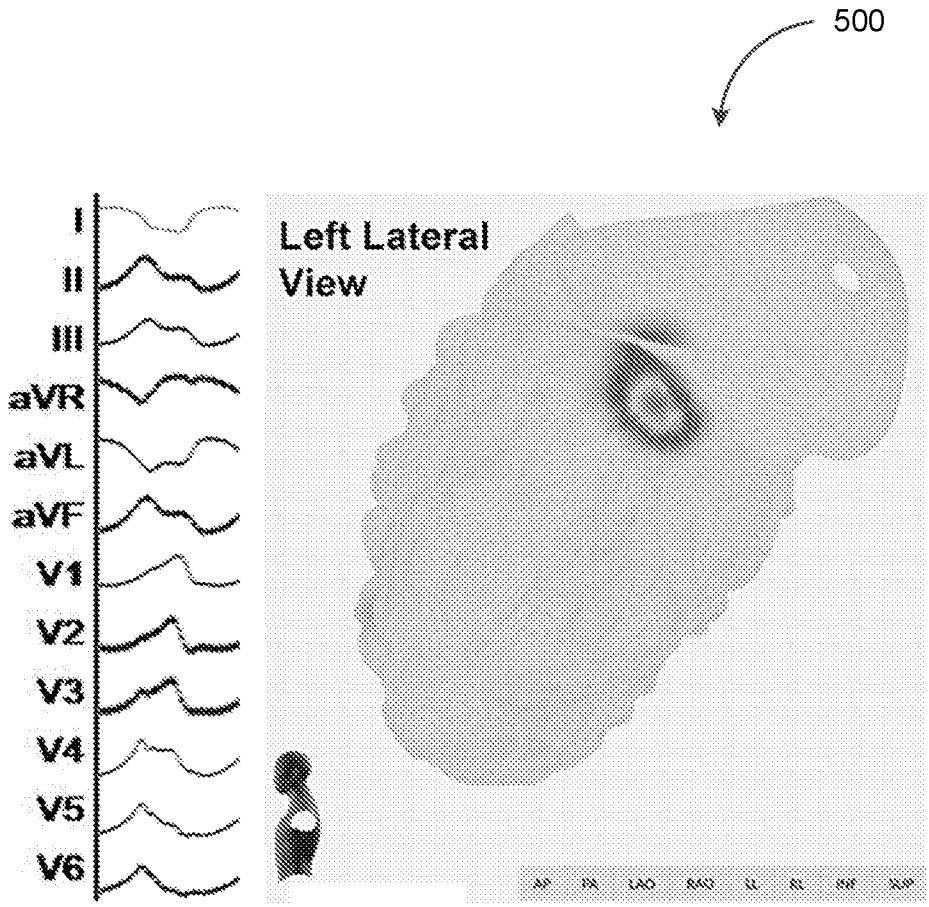

FIG. 5A

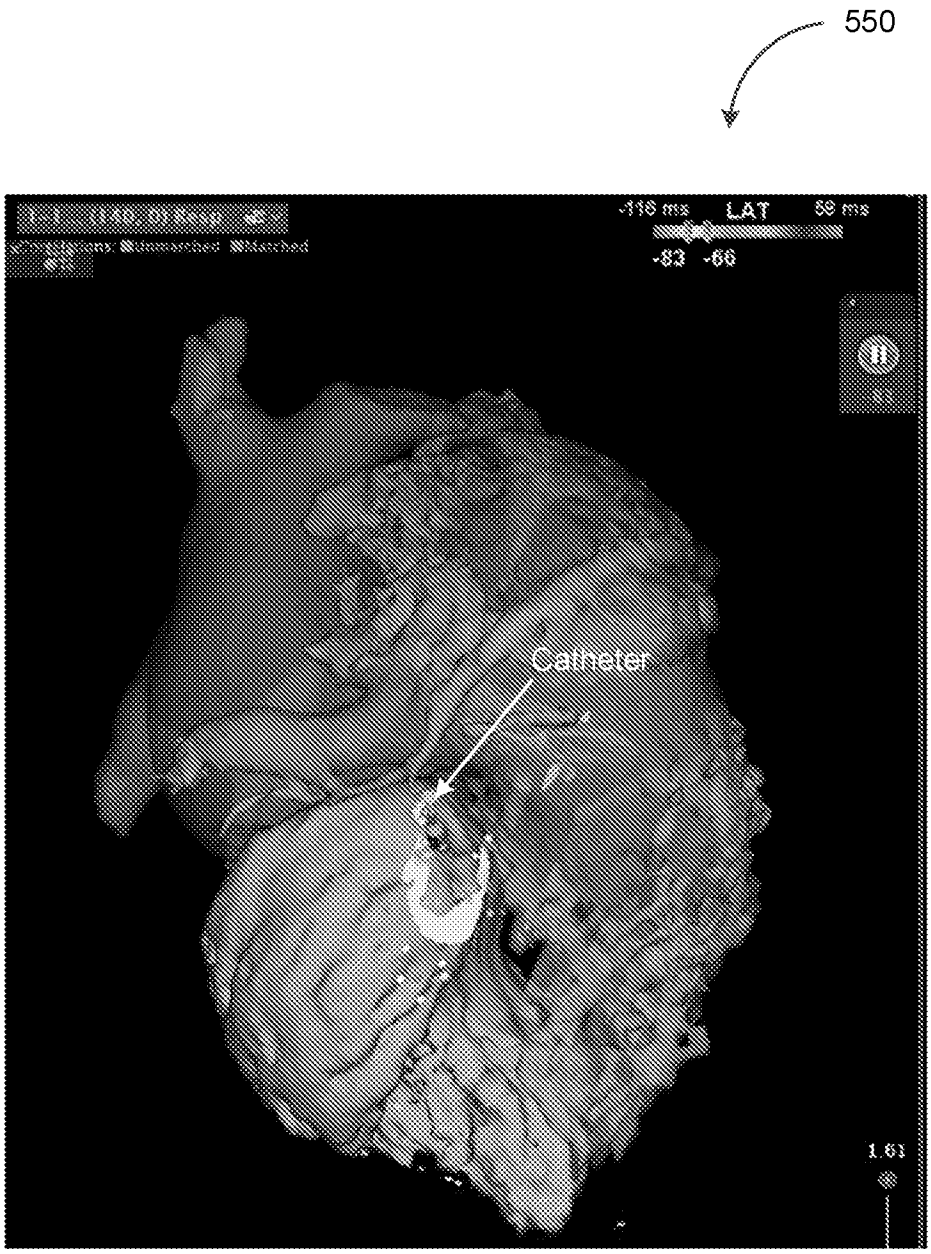

FIG. 5B

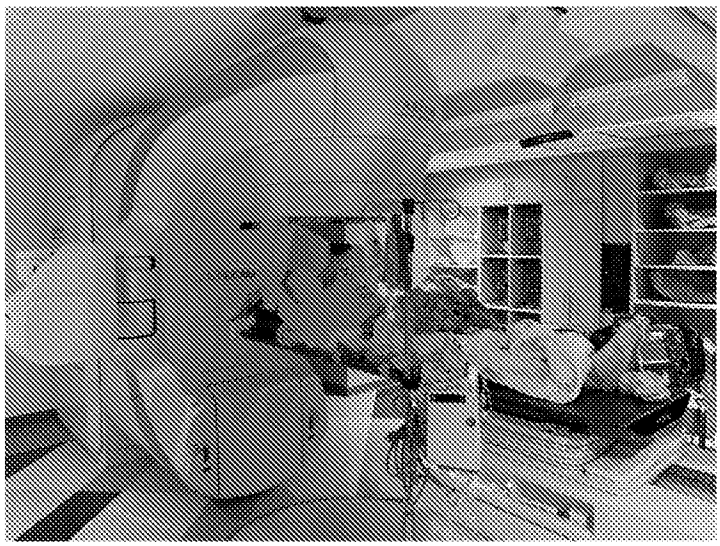

FIG. 6

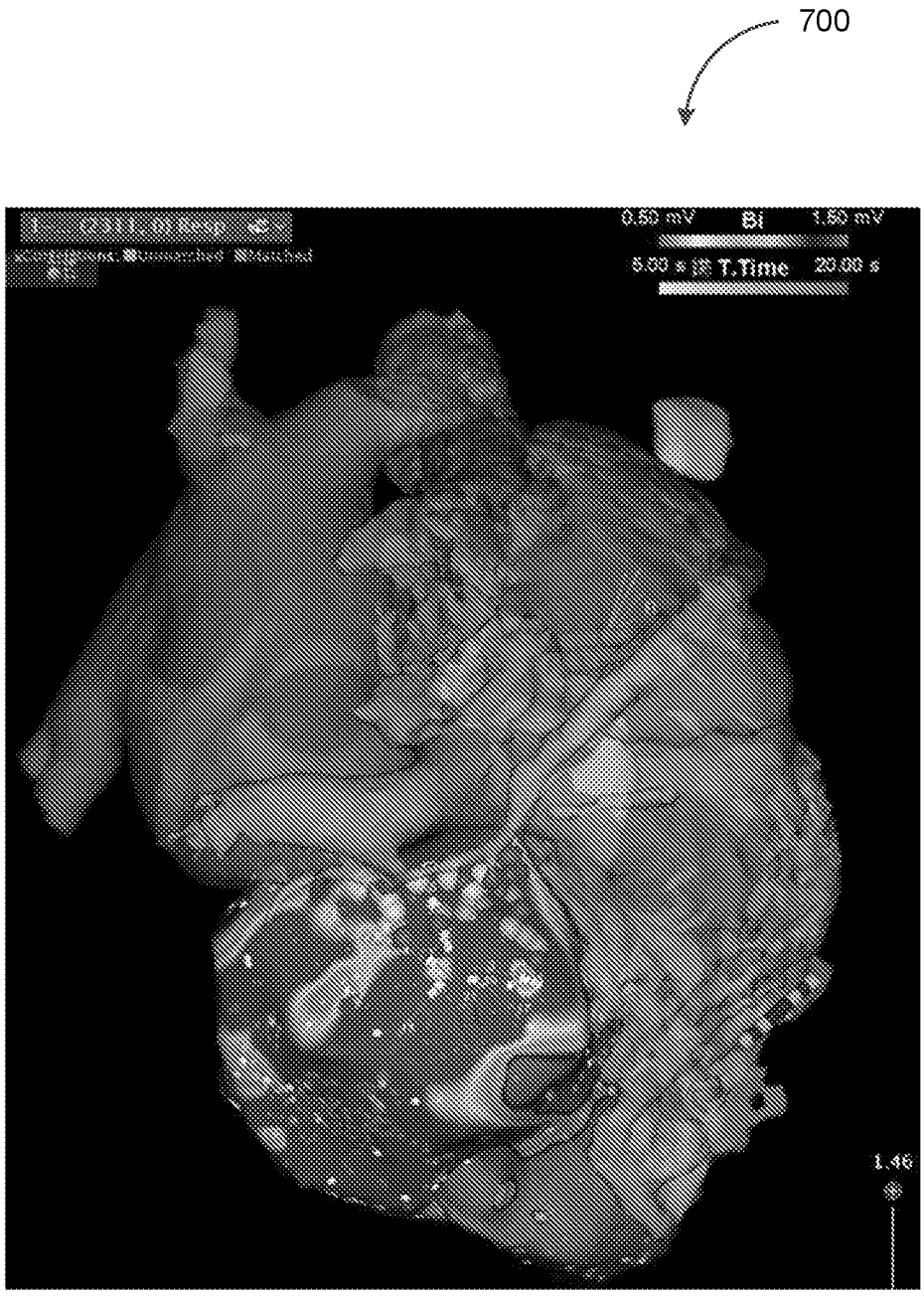

FIG. 7

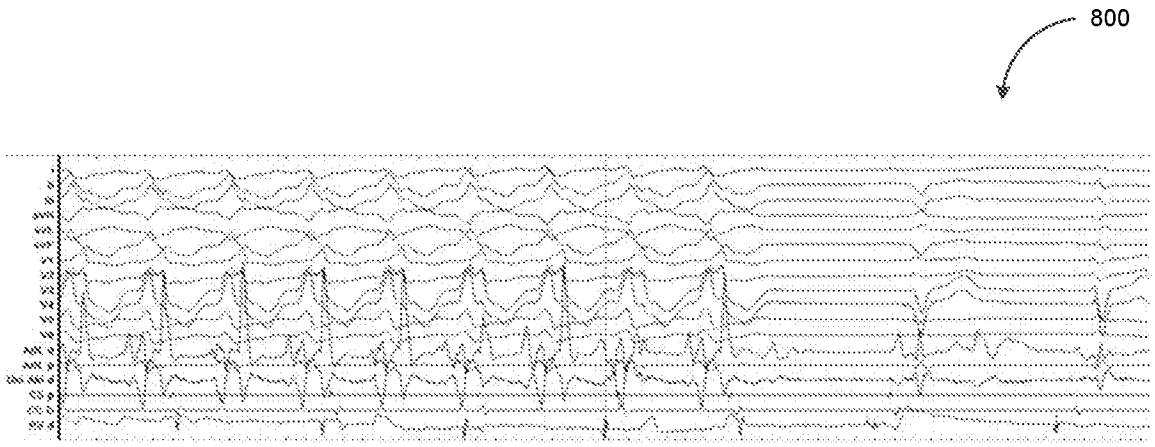

FIG. 8

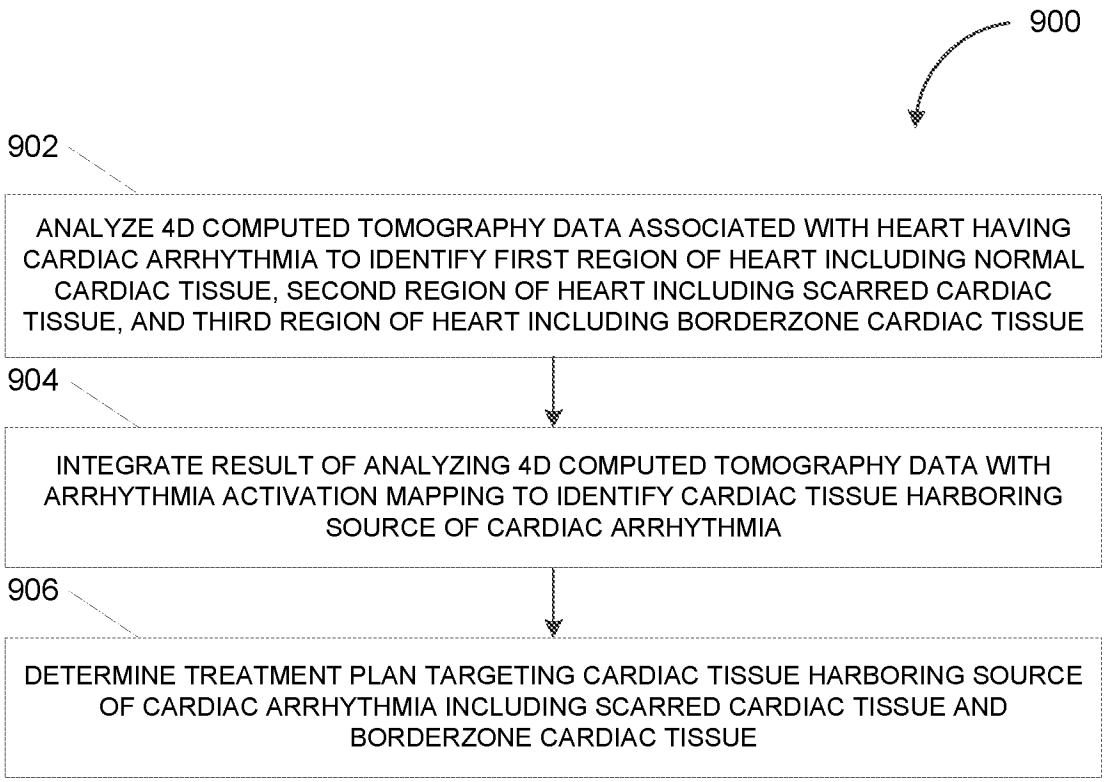
900
902
ANALYZE 4D COMPUTED TOMOGRAPHY DATA ASSOCIATED WITH HEART HAVING CARDIAC ARRHYTHMIA TO IDENTIFY FIRST REGION OF HEART INCLUDING NORMAL CARDIAC TISSUE, SECOND REGION OF HEART INCLUDING SCARRED CARDIAC TISSUE, AND THIRD REGION OF HEART INCLUDING BORDERZONE CARDIAC TISSUE
904
INTEGRATE RESULT OF ANALYZING 4D COMPUTED TOMOGRAPHY DATA WITH ARRHYTHMIA ACTIVATION MAPPING TO IDENTIFY CARDIAC TISSUE HARBORING SOURCE OF CARDIAC ARRHYTHMIA
906
DETERMINE TREATMENT PLAN TARGETING CARDIAC TISSUE HARBORING SOURCE OF CARDIAC ARRHYTHMIA INCLUDING SCARRED CARDIAC TISSUE AND BORDERZONE CARDIAC TISSUE

FIG. 9

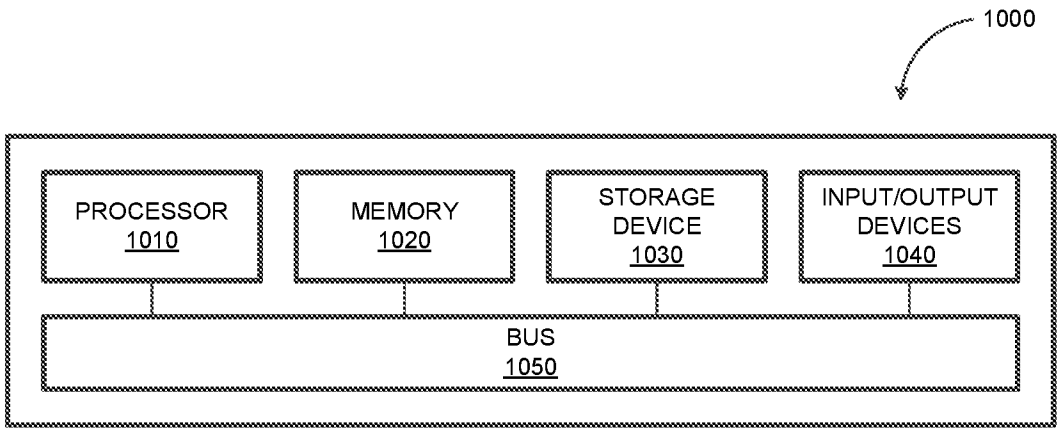
1000
PROCESSOR
1010
MEMORY
1020
STORAGE
DEVICE
1030
INPUT/OUTPUT
DEVICES
1040
BUS
1050

FIG. 10

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 21/17511

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61B 6/03 (2021.01)

CPC - G06T 2207/10076; A61B 6/03; A61B 6/032; G06T 7/11; G06T 2207/10081; G06T 2207/20112; G06T 2207/30048

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)
See Search History document

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2019/118640 A1 (WASHINGTON UNIVERSITY) 20 June 2019 (20.06.2019) Fig 1A, 4, abstract, para [0005], [0071], [0074], [0076], [0085], [00137], [00141]	1-4, 45-48, 87
Y	US 2017/0178403 A1 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) 22 June 2017 (22.06.2017) Fig 5B, abstract, para [0004], [0064], [0065], [0076]	1-4, 45-48, 87
Y	US 2008/0045815 A1 (DERCHAK et al.) 21 February 2008 (21.02.2008) abstract, para [0073], [0074], [0090]	48

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"D" document cited by the applicant in the international application
"E" earlier application or patent but published on or after the international filing date
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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
16 April 2021	MAY 04 2021
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Lee Young Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 21/17511

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 5-44, 49-86
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.