(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
28 July 2016 (28.07.2016)

WIPO | PCT

(10) International Publication Number
WO 2016/118947 A1

(51) International Patent Classification:
A61B 8/00 (2006.01) *G01N 29/06* (2006.01)

(21) International Application Number:
PCT/US2016/014685

(22) International Filing Date:
25 January 2016 (25.01.2016)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/107,321 23 January 2015 (23.01.2015) US

(71) Applicant: **THE UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL** [US/US]; 100 Europa Drive, Suite 430, Chapel Hill, NC 27517 (US).

(72) Inventors: **DAYTON, Paul, Alexander**; 101 Riverwalk Lane, Carrboro, NC 27510 (US). **GESSNER, Ryan, Christopher**; 812 Perkins Drive, Chapel Hill, NC 27514 (US). **BUTLER, James, Owen**; 2033 Copper Leaf Parkway (apt 305), Durham, NC 27703 (US). **HARLACHER, Max, Stephen**; 105 Timber Hollow Court (apt 325), Chapel Hill, NC 27514 (US). **NORMAN, Nicholas, Allan**; 3801 S. Congress Avenue (apt 312), Austin, TX 78704 (US).

(74) Agent: **HUNT, Gregory, A.**; Jenkins, Wilson, Taylor & Hunt, P.A., Suite 1200, University Tower, 3100 Tower Boulevard, Durham, NC 27707 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: APPARATUSES, SYSTEMS, AND METHODS FOR PRECLINICAL ULTRASOUND IMAGING OF SUBJECTS

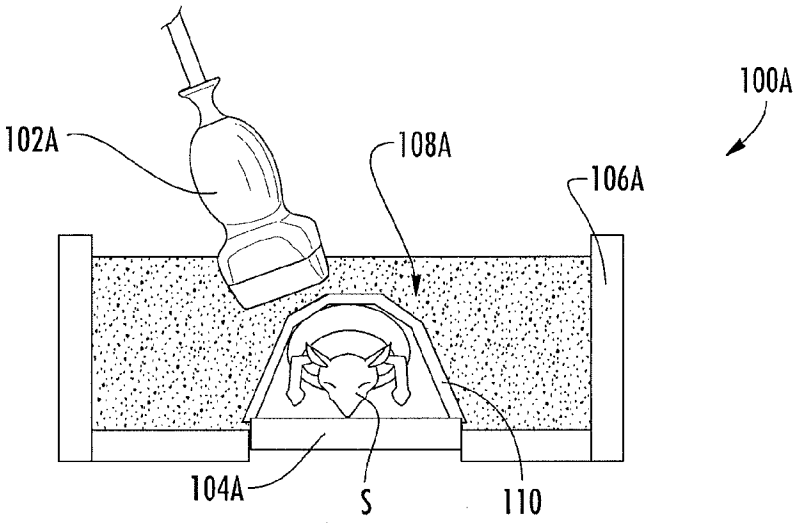

FIG. 1A

(57) Abstract: Apparatuses, systems, and methods for preclinical ultrasound imaging of subjects are provided. In one aspect, the apparatus can include a platform on which a subject is positionable and at least one motion stage for controlling a spatial position of at least one ultrasound transducer relative to the platform in order to acquire ultrasound image data of the subject. Methods for preclinical ultrasound raster scanning of at least one organ or tissue in a subject are also provided, where the at least one organ or tissue is a heart.

WO 2016/118947 A1

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

DESCRIPTION

APPARATUSES, SYSTEMS, AND METHODS FOR PRECLINICAL ULTRASOUND IMAGING OF SUBJECTS

PRIORITY

This application claims the priority benefit of U.S. Provisional Patent Application Serial No. 62/107,321, filed January 23, 2015, which is incorporated by reference herein in its entirety.

GRANT INFORMATION

This invention was made with government support under Grant Nos. CA170665 and CA192482 awarded by the National Institutes of Health and Grant Nos. IIP-1346336 and IIP-1533978 awarded by the National Science Foundation. The government has certain rights in the invention.

TECHNICAL FIELD

The subject matter described herein relates to apparatuses, systems, and methods for use in ultrasound imaging. More particularly, the subject matter described herein relates to apparatuses, systems, and methods for preclinical ultrasound imaging of subjects.

BACKGROUND

Preclinical drug development researchers in both industry and academia rely on a variety of imaging techniques to visualize the effects caused by their novel therapeutic candidates within rodent disease models. "Molecular" or "functional" imaging techniques allow researchers to visualize processes occurring at the cellular level, which are indicative of a presence of disease. These imaging strategies - such as optical, Single Photon Emission Computed Tomography (SPECT), and Positron Emission Tomography (PET) - are extremely sensitive to contrast agents designed to target various disease processes of interest, though are not well suited to visualize anatomical features, such as tumor boundaries. Conversely, anatomical imaging strategies - such as magnetic resonance imaging (MRI),

computed tomography (CT), and ultrasound - enable researchers to visualize the physical boundaries of anatomical structures, as well as the relative locations and morphologies of disease sites and healthy anatomy. These anatomical imaging approaches are less proficient, however, at detecting any processes not occurring at a gross phenotypic scale. Combining these two complimentary strategies is an intuitive approach to maximizing sensitivity for disease detection or for monitoring therapeutic response, and is widely implemented in both clinical and preclinical settings worldwide in the form of SPECT-CT and PET-CT systems.

Though not widely produced, a combination of MRI and PET (MR-PET) systems has recently been developed and offer a lower radiation-dose alternative to the CT approaches (albeit in exchange for an increase in financial and time expenses). Of the anatomical imaging approaches, ultrasound is often the most attractive because of the following: (a) it is innocuous for both user and patient, (b) it is the most portable of any of the modalities, (c) it is real-time, and (d) significantly the least expensive. Despite these attractive advantages, products to enable ultrasound-based multimodality clinical and preclinical imaging are scarce.

Accordingly, an efficient, flexible, and customizable platform that enables researchers to acquire whole-body anatomical images of their preclinical animal models using either primary or after-market ultrasound systems and probes which may already be in use, and if necessary, allowing for immediate registration of their anatomical ultrasound data with the functional imaging acquisition method of their choice: PET, SPECT, or optical is needed.

SUMMARY

Apparatuses, systems, and methods for preclinical ultrasound imaging of subjects are provided herein. In some aspects, an apparatus for preclinical ultrasound imaging of a subject may comprise a platform on which a subject (e.g., a rodent) is positionable, and at least one motion stage for controlling a spatial position of at least one ultrasound transducer relative to the platform in order to acquire ultrasound image data of the subject.

In some aspects, a system for preclinical ultrasound imaging of a subject may comprise at least one ultrasound imaging system, at least one ultrasound transducer associated with the ultrasound imaging system and positionable relative to a subject (e.g., a rodent), and an apparatus. In some aspects, the apparatus may a platform on which the subject is positionable, and at least one motion stage for controlling a spatial position of at least one ultrasound transducer relative to the platform in order to acquire ultrasound image data of the subject.

In some aspects, a method for preclinical ultrasound imaging of a subject may comprise movably positioning a platform, on which a subject (e.g., a rodent) is positionable, controlling, by at least one motion stage, a spatial position of at least one ultrasound transducer relative to the platform, and acquiring ultrasound image data of the subject.

In some aspects, the present subject matter may provide a system and method for preclinical ultrasound raster scanning of at least one organ or tissue in a subject. The system may comprise at least one ultrasound imaging system, at least one ultrasound transducer associated with the at least one ultrasound imaging system and positionable relative to a subject, an apparatus comprising a platform on which the subject is positionable, and at least one motion stage for controlling a spatial position of the at least one ultrasound transducer relative to the platform in order to acquire ultrasound image data of the subject, and a computing platform having a hardware processor and a memory and being associated with the at least one ultrasound imaging system and the apparatus, wherein the computing platform is configured to collect one-dimensional (1D) ultrasound scan lines through translation of the at least one ultrasound transducer through a raster scan grid aligned over an approximation of a location of at least one organ or tissue in the subject, and to analyze the 1D ultrasound scan lines to build a two-dimensional (2D) or three-dimensional (3D) mesh of relevant surfaces of the at least one organ or tissue.

The method may comprise positioning a subject on a platform, controlling a spatial position of at least one ultrasound transducer relative to the platform in order to acquire ultrasound image data of the subject,

collecting one-dimensional (1D) ultrasound lines by translating the at least one ultrasound transducer through a raster scan grid aligned over an approximation of a location of at least one organ or tissue in the subject, and analyzing the 1D ultrasound lines to build a two-dimensional (2D) or three-dimensional (3D) mesh of relevant surfaces of the at least one organ or tissue.

BRIEF DESCRIPTION OF THE DRAWINGS

Preferred embodiments of the subject matter described herein will now be explained with reference to the accompanying drawings, wherein like reference numerals represent like parts, of which:

Figure 1A is a front view illustrating an exemplary embodiment of an apparatus including a rigid reservoir for preclinical ultrasound imaging of a subject, wherein an imaging transducer scans substantially above the subject, according to the subject matter disclosed herein;

Figure 1B is a front view illustrating an exemplary embodiment of an apparatus including a reservoir membrane for preclinical ultrasound imaging of a subject, wherein an imaging transducer scans substantially above the subject, according to the subject matter disclosed herein;

Figure 2A is a front view illustrating an exemplary embodiment of an apparatus for preclinical ultrasound imaging of a subject, wherein an imaging transducer scans substantially below the subject, according to the subject matter disclosed herein;

Figure 2B is a perspective view illustrating the exemplary embodiment of Figure 2A;

Figure 3 is a front view illustrating a rotational stage and two linear stages of an apparatus for preclinical ultrasound imaging of a subject according to the subject matter disclosed herein;

Figure 4 is a perspective view illustrating an exemplary reservoir for an exemplary embodiment of an apparatus for preclinical ultrasound imaging of a subject according to the subject matter disclosed herein;

Figure 5 is a perspective view illustrating an exemplary reservoir, support structure, and x and y-axis motion stages for an exemplary

embodiment of an apparatus for preclinical ultrasound imaging of a subject according to the subject matter disclosed herein;

Figure 6 is a cross-sectional view illustrating an exemplary transducer aligned with an I-beam for an exemplary embodiment of an apparatus for preclinical ultrasound imaging of a subject according to the subject matter disclosed herein;

Figure 7A is a cross-sectional view illustrating an exemplary cross-coupling clamp disposed between a transducer and a rigid reservoir for an exemplary embodiment of an apparatus for preclinical ultrasound imaging of a subject according to the subject matter disclosed herein;

Figure 7B is a cross-sectional view illustrating an exemplary cross-coupling clamp disposed between a transducer and a reservoir membrane for an exemplary embodiment of an apparatus for preclinical ultrasound imaging of a subject according to the subject matter disclosed herein;

Figure 8 is a perspective view illustrating an exemplary z-axis and rotational motion stage for an exemplary embodiment of an apparatus for preclinical ultrasound imaging of a subject according to the subject matter disclosed herein;

Figure 9 is a perspective view illustrating an exemplary embodiment of an apparatus for preclinical ultrasound imaging of a subject according to the subject matter disclosed herein;

Figure 10 is a perspective view illustrating an exemplary subject transfer platform for an exemplary embodiment of an apparatus for preclinical ultrasound imaging of a subject according to the subject matter disclosed herein;

Figures 11A is a line drawing illustrating an apparatus used in an exemplary process flow for generating an atlas using fiducial landmarks for preclinical ultrasound imaging of a subject according to the subject matter disclosed herein;

Figures 11B-11G are computer generated images illustrating an exemplary process flow for generating an atlas using fiducial landmarks for preclinical ultrasound imaging of a subject according to the subject matter disclosed herein;

Figure 12 is a schematic illustrating an exemplary system for preclinical ultrasound imaging of a subject according to the subject matter disclosed herein;

Figures 13A-13C are screenshots illustrating an exemplary workflow for spatial mapping of a subject system for preclinical ultrasound imaging of a subject according to the subject matter disclosed herein;

Figure 14A is a diagram illustrating a first scan plane relative to a subject for preclinical ultrasound imaging of a subject according to the subject matter disclosed herein;

Figure 14B is a photograph illustrating the first scan plane relative to the platform according to Figure 14A;

Figure 14C is a screenshot illustrating a two-dimensional (2D) ultrasound image of the subject taken along the first scan plane according to Figure 14A, where a bladder, a liver, and a heart of the subject are visible;

Figure 15A is a diagram illustrating a second scan plane relative to a subject for preclinical ultrasound imaging of a subject according to the subject matter disclosed herein;

Figure 15B is a screenshot illustrating a 2D ultrasound image of the subject taken along the second scan plane according to Figure 15A, where a bladder, a liver, and a heart of the subject are visible;

Figure 16A is a diagram illustrating a third scan plane relative to a subject for preclinical ultrasound imaging of a subject according to the subject matter disclosed herein;

Figure 16B is a screenshot illustrating a 2D ultrasound image of the subject taken along the third scan plane according to Figure 16A, where a bladder of the subject is visible;

Figure 17 is a screenshot illustrating a three-angled composite 2D ultrasound image of the bladder of the subject using the 2D ultrasound images of Figures 14C, 15B, and 16B;

Figure 18A is a screenshot illustrating a single 2D ultrasound image of a subject;

Figure 18B is a screenshot illustrating a three-angled composite 2D ultrasound image of a subject for preclinical ultrasound imaging of a subject

according to the subject matter disclosed herein, where a field of view in Figure 18A is smaller than a field of view in Figure 18B;

Figure 19 is a computer generated image illustrating at least one exemplary ultrasound transducer raster scanning a subject according to the subject matter disclosed herein;

Figure 20A is a computer generated image illustrating an exemplary raster scan grid over a subject according to the subject matter disclosed herein;

Figure 20B is a computer generated image illustrating a detailed view of the raster scan grid of Figure 20A;

Figure 21A is a screenshot illustrating an exemplary m-mode trace line from the raster scan grid of Figure 20B according to the subject matter disclosed herein;

Figure 21B is a set of line drawing illustrating automated segmentations from four surfaces extracted from the screenshot of the m-mode trace line of Figure 21A;

Figure 22 is a 3D model illustrating an exemplary 3D mesh built from at least a portion of the automated segmentations of Figure 21B;

Figure 23A is a 3D model of Figure 22 illustrating optimal long and short axes;

Figures 23B is a computer generated image of the subject in Figure 19 illustrating 2D scan planes about the heart of the subject;

Figure 24 is a process flow diagram illustrating a method for raster scanning a subject according to the subject matter disclosed herein; and

Figure 25 is a process flow diagram illustrating a method for preclinical ultrasound imaging of a subject according to the subject matter disclosed herein.

DETAILED DESCRIPTION

In accordance with the subject matter herein apparatuses, systems, and related methods for preclinical ultrasound imaging of subjects, as well as a method for raster scanning a subject, are disclosed. The apparatuses, systems, and related methods for preclinical ultrasound imaging of subjects

may provide an efficient, flexible, and customizable platform that enables researchers to acquire whole-body anatomical images of preclinical animal models using any ultrasound systems and/or probes, while allowing for immediate registration of anatomical ultrasound data with functional imaging acquisition method of their choice: Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT), optical, cryoimaging, etc.

Small animal models, specifically rodents, serve as models for human disease across a broad spectrum of pathologies. Animal models offer scientists a way to uncover underlying mechanisms for disease process, as well as study drug efficacy and toxicity profiles in living organisms. Until the advent of non-invasive imaging, large numbers of animals expressing a given disease phenotype were required for preclinical studies, as the only method to assess disease presence or response to a candidate therapeutic was through terminal strategies (necropsy, histology, etc.). By comparison, non-invasive imaging methods enable researchers to interrogate the structure and function of bodily tissues without the need to sacrifice for each assessment time-point, and thus drastically reduce number of animals needed for preclinical studies.

There are two principal types of imaging modalities: structural (i.e., anatomical) and functional. Structural imaging modalities allow for the visualization and assessment of physical properties (i.e., morphology, shape, size, texture, density, etc.) of tissue. Functional imaging modalities allow for the visualization and assessment of sub-resolution biological processes (i.e., inflammation, angiogenesis, metabolic demand, etc.) through the implementation of a contrast agent or reporter compound. Magnetic Resonance Imaging (MRI), Computed Tomography (CT), and Ultrasound (US) are examples of imaging modalities that are primarily used for anatomical imaging purposes. In vivo optical (bioluminescence and fluorescence) imaging, cryoimaging, SPECT, and PET are examples of functional imaging modalities.

Ultrasound offers several advantages over the other anatomical imaging modalities: it acquires real-time images, is non-invasive, is relatively

portable, and is inexpensive. Accordingly, the apparatuses, systems, and methods described herein offer a novel approach to anatomical imaging of small animals using ultrasound (synonymous with "preclinical ultrasound imaging"). There are several existing tools available to researchers interested in using ultrasound to image small animals, including clinical imaging scanners, and specialized preclinical imaging systems. These tools enable either two-dimensional (2D) cross sections of tissue or small three-dimensional (3D) volumes of tissue. As used herein, "small subvolumes" do not encompass a significant portion of the animal's anatomy (e.g., >50% by volume). The consequence of this is comparisons between image acquisitions captured at different times are difficult to make, since relative orientations between tissue structures are unknown, as transducer orientation and scan angle is very difficult to identically recapitulate at two separate timepoints. This problem of one-to-one mapping between timepoints is further exacerbated when tissue structures are not in the same relative positions in the image data, which can be caused by multiple factors including: 3D non-linear warping that takes place when tissues are distended by physical contact between an ultrasound transducer and the tissue, a tumor growing and changing the tissue morphology within its neighborhood, one or more tumors arriving between timepoints, animal weight gain or loss, causing a spatial re-scaling between corresponding anatomical points, etc.

Accordingly, apparatuses, systems, and methods that circumvent these current deficiencies of preclinical ultrasound imaging are disclosed, which allow widefield imaging of tissue volumes. The apparatuses, systems, and methods may allow over 50% of a subject's body to be imaged, and thus better enable longitudinal comparisons. In addition to allowing an increased field of view, the quality of the image data will be improved by the apparatuses, systems, and methods described herein, as these apparatuses, systems, and methods may allow spatial compounding approaches to be implemented. Furthermore, these apparatuses, systems, and methods do not require direct contact to be made between transducer

and tissue, and thus no tissue warping may be caused by the image acquisitions of these apparatuses, systems, and methods, better enabling image registration.

In addition, the present subject matter is based on the idea that one can acquire both anatomical and functional images with the same device or platform. Ultrasound imaging may be used to acquire anatomical images using the presently disclosed apparatus, system and method, while the specific functional imaging modality (SPECT, PET, optical, photoacoustics, optoacoustics, fluorescence, bioluminescence, cryoimaging, etc.,) may be coupled with the presently disclosed apparatuses, systems, and methods for a complimentary approach to preclinical image acquisition.

In some aspects, the present subject matter described herein is directed to acquiring whole-body images with preclinical ultrasound imaging. Most current clinical and preclinical ultrasound transducers acquire 2D images and display the result on a computer monitor. To buildup a 3D image volume, the user must move the probe or transducer in a controlled manner to make a stack of 2D images into a cohesive 3D volume. Currently, there are already available methods of moving a transducer in a single linear path to construct a single subvolume of a target (i.e., an image of a preclinical animal model's tumor). Notably, the present subject matter proposes to extend this idea over a significantly larger area by using apparatuses, systems, and methods comprising two or more one-dimensional (1D) linear motion stages capable of controlling a spatial position of at least one ultrasound transducer's position to enable a cohesive volumetric image to be formed from a series of 2D images using the spatial coordinates of the ultrasound transducer's spatial position. It is contemplated that 3D functional images may be acquired using a functional imaging modality to fuse with the anatomical image acquired using the apparatuses, systems, and methods described herein. In some aspects, the 3D functional images may also be acquired using said apparatuses, systems, and methods disclosed herein. Any major functional imaging technique may be used to acquire the 3D images, such as, for example, photoacoustics, optoacoustics, fluorescence, bioluminescence, PET, SPECT, cryoimaging, x-ray, MRI, etc.

Figures 1A-1B and 2A-2B are illustrations of two separate, exemplary embodiments of apparatuses for preclinical imaging of a subject where the ultrasound transducer is configured to move relative to both the subject and the reservoir. In either embodiment, the apparatus may comprise an ultrasound transducer or plurality of ultrasound transducers, at least one motion stage, and/or one or more individual platforms. In some aspects, at least one motion stage may comprise a combination of at least one linear motion stage and at least one rotational computerized stage for moving and supporting ultrasound transducer(s) (see, e.g., Fig. 3). In a first example, at least one transducer may be configured to scan a subject at position(s) above the subject (see, e.g., Figs. 1A and 1B), while in a second example, a transducer may be configured to scan a subject at position(s) below the subject (see, e.g., Figs. 2A-2B).

Referring to Figure 1A, an apparatus, generally designated **100A**, may be configured such that at least one transducer **102A** is movable via an actuating arm (see, e.g., **312**, Figure 3) relative to both subject **S** positioned on a platform **104A** and a reservoir **106A**. As illustrated in Figure 1A, reservoir **106A** may be in the form of a stand-alone tank with structured walls to contain a coupling medium **108A**, which may be liquid or gel-based. The walls of reservoir **106A** may be removable, either by complete detachment from platform **104A**, or by mechanically lowering platform **104A** into a recessed cavity. A coupling medium impermeable membrane **110** may be disposed between subject **S** and coupling medium **108A** to provide a seal between the two.

Alternatively, as illustrated in Figure 1B, an apparatus, generally designated **100B**, may be configured in a manner similar to that of Figure 1A with a transducer **102B** movable via an actuating arm (see, e.g., **312**, Figure 3) relative to both a subject **S** positioned on a platform **104A** and a reservoir **106A**. However, in comparison with Figure 1A, reservoir **106B** may be in the form of a bag that hangs from the same actuating arm. In this embodiment, a coupling medium impermeable membrane does not need to be utilized because reservoir bag **106B** acts as its own coupling medium impermeable membrane in between a coupling medium **108B** and subject **S**.

In addition, as illustrated in Figure1B, reservoir bag **106B** may be coupleable to the one or more individual platform **104B**. For example, reservoir bag **106B** may be anchored to platform **104B** supporting subject **S**. Consequently, where an apparatus is configured to include a reservoir, the reservoir may, itself, either act as a partition between the subject being imaged and the coupling medium or may further comprise a coupling medium impermeable membrane between the coupling medium and the subject being imaged to prevent the subject from being submerged in the coupling medium.

As in Figures 1A and 1B, where a reservoir is configured such that a separate or integral a coupling medium impermeable membrane, or other type of partition, is necessary to separate the subject from being imaged from the coupling medium, sufficient downward pressure may be generated by the coupling medium to ensure that the seal between the membrane and platform is coupling medium impermeable. In some aspects, the membrane may be sealed to the platform using a rectangular rigid frame, or other geometrically shaped frame, bearing magnetic material which may be activated by alternating a polarity of magnets disposed below the platform on which the subject is positionable. In some aspects, the membrane maybe sealed to the platform by using a rectangular rigid frame, or other geometrically shaped frame, which may be mechanically forced downward by one or more clamps (see, e.g., Figures 7A-7B). In some aspects, the membrane may be sealed to the platform by using a rectangular rigid frame, or other geometrically shaped frame, which may be mechanically forced downward via a vacuum seal. Regardless of the specific method for generating downward pressure between the membrane and animal platform, the two components can be quickly unattached for quick removal of the membrane after the imaging session has concluded.

In another alternative, not shown, a reservoir containing coupling medium is not needed in the apparatus in order to perform preclinical ultrasound imaging of a subject. For example, a REXOLITE® stage may be used, instead, and the at least one transducer may be scanned across the stage.

Referring to the above-referenced exemplary embodiment, Figure 2A illustrates an apparatus, generally designated **200**, comprising at least one transducer **202** positioned below a subject **S** that is configured to movably scan subject **S** from underneath the subject. For example, transducer **202** may scan subject **S** below a platform **204** on which the subject is placed. In some aspects, apparatus **200** may comprise a reservoir **206** in the form of a stand-alone tank or a bag, as discussed above. For example, reservoir **206** may be in the form of an acoustic coupling reservoir. As illustrated in Figure 2A, reservoir **206** is in the form of a bag that contains a coupling medium **208**. Reservoir **206** may be suspended from or otherwise affixed to platform **204**. In such a configuration, a coupling medium impermeable membrane does not need to be utilized because the acoustic coupling reservoir acts as its own coupling medium impermeable membrane in between coupling medium **208** and subject **S**. In the alternative, apparatus **200** does not need reservoir **206** containing coupling medium **208** in order to perform preclinical ultrasound imaging.

Still referring to the second embodiment, Figure 2B illustrates apparatus **200** from a perspective view, where at least one motion stage, generally designated **210** is visible. Motion stage **210** may be connectably attached to transducer **202** and may thus move transducer **202** (not visible in Figure 2B) relative to an imaging area underneath a subject, as indicated by arrow $\mathbf{A_1}$ in Figure 2A. Although arrow $\mathbf{A_1}$ in Figure 2A is illustrated as moving in a semi-circular manner relative to subject **S**, it is contemplated that motion stage **210** may also move transducer **202** substantially horizontally, vertically, etc., with regard to subject **S**, which will be described in greater detail below.

Still referring to an embodiment of an apparatus, system, and/or method of preclinical imaging of a subject where a transducer moves relative to both a subject and a reservoir, Figure 3 illustrates an exemplary apparatus **300** including one transducer **302** movable relative to a platform **304** and a reservoir (not illustrated in this Figure). Notably, more than one

transducer moveable in a similar or different manner to the one illustrated in Figure 3 may also be included in the apparatuses, systems, and/or methods described herein.

In Figure 3, transducer **302** may be movable about three stages, one of which is rotational and the other two being linear, and each comprising its own individual axis on which transducer **302** may be independently movable. For example, the individual axes of the three stages may include a y-axis motion stage **306**, a z-axis motion stage **308**, and a Θ-axis motion stage **310**, y-axis motion stage **306** and z-axis motion stage **308** allowing for linear movement of transducer **302** and Θ-axis motion stage **310** allowing for rotational movement of transducer **302**. Notably, there may be more stages or fewer stages, as well, for different degrees of movement of transducer **302**. In some embodiments, transducer **302** may be positioned on an actuating arm **312** that is coupled to the three stages. Thus, movement of each of the three stages individually moves the position of actuating arm **312** along that axis with respect to a subject, and thereby translates into movement of transducer **302** into various spatial positions relative to platform **304**. For example, motion stages **306-310** may be configured to position transducer **302** above a subject in order to scan the subject from above (i.e., above platform **304**), while the motion stages **306-310** may also be configured to position transducer **304** below the subject in order to scan the subject from below (i.e., below platform **304**). The ability to move each of the three stages **306-310**, independently, enables apparatus **300** to be configured in either the first exemplary position (i.e., Figures 1A-1B) or the second exemplary position (i.e., Figures 2A-2B) of the apparatus described above.

In some aspects, transducer **302** may be moved in any of the three directions (x, y, Θ) manually and/or automatically using a motion control system associated with a computing platform (see, e.g., Figure 12), such that transducer **302** is movable 360 degrees around a subject positioned on platform **304**. For example, a motion control system may enable one or more users to enter a mode of operation (e.g., jogging mode) where a spatial position of transducer **302** is controlled by a computing platform, or

an external joystick or keypad, and transducer **302** is moved to a specified location. In some aspects, a spatial position or positions of transducer **302** may be determined *a priori* by a computing platform in order to control the linear and rotational stages' **306-310** positions. Regardless, this mode may be useful for users wanting to explore tissue volume to locate features of interest in a subject. Consequently, movability of transducer(s) in the manner described above may enable whole-body images to be acquired by the disclosed apparatuses, systems, and/or methods, since the transducer(s) may be translatable around a body of a subject in order to acquire images at different and various angles.

Referring now to another embodiment, Figures 4-9 are illustrations of another exemplary embodiment of an apparatus and a system for preclinical imaging of a subject where an ultrasound transducer and a reservoir are configured to move together relative to a subject being imaged in comparison to the embodiments illustrated in Figures 1A-3, where a transducer is configured to move relative to both a subject and a reservoir.

Figure 4 illustrates a perspective view of an exemplary embodiment of an apparatus, generally designated **400**, for preclinical imaging of a subject. Apparatus **400** may be configured with at least one movable transducer **402** that is coupled to a bottom surface of a reservoir **404**. In some aspects, reservoir **404** may be a rigid box or stand-alone tank with structured walls rather than a flexible bag. For example, Figure 4 illustrates reservoir **404** as a rigid, rectangular box having a bottom surface and four structured walls that are substantially perpendicular to the bottom surface of reservoir **404**. Reservoir **404** may be composed of an acoustically attenuating material to limit reflection and reverberation of ultrasound waves during imaging. An orifice having a diameter sufficient to receive transducer **402** may be provided in the bottom surface of reservoir **404**. In such a manner, transducer **402** may be introduced under reservoir **404** through the bottom surface and removably coupled to reservoir **404** via a mechanism (e.g., **706A**, **706B**, Figures 7A-7B). Thus, movement of transducer **402** once coupled to reservoir **404** results in movement of reservoir **404** relative to an imaging chamber on which a subject is placed (see, e.g., Figure 9).

Although not illustrated in Figure 4, a coupling medium impermeable membrane may be provided with respect to reservoir **404** in order to provide a seal between the coupling medium and a subject to be imaged, although it may be unnecessary for contact-free imaging. In order to retain the coupling medium impermeable membrane, reservoir **404** may include a spray skirt, or other similar mechanism, disposed around its perimeter. For example, as illustrated in Figure 4, a spray skirt **406** is disposed along each of the side walls of reservoir **404** and is configured to retain a coupling medium impermeable membrane to create a seal between any coupling medium contained in reservoir **404** and a subject being imaged, above. Spray skirt **406** may be clamped, bolted, pinched, screwed, and/or otherwise brought into close contact with the inside surface of respective side walls on which spray skirt **406** is disposed, with the coupling medium impermeable membrane sandwiched in between spray skirt **406** and the side walls of reservoir **404** for a tight seal.

In some aspects, a heating mechanism may be disposed along an interior surface of one or more side walls of reservoir **404**. For example, reservoir **404** may comprise a U-shaped thermal rod **408** disposed along three of the side walls for immersion heating. In this manner, the coupling medium may be heated while it is already contained within reservoir **404**. In some aspects, the temperature of the coupling medium within reservoir **404** may be adjusted (e.g., either automatically or using real time user input) via an input to U-shaped thermal rod **408**. For example, a feedback controller (e.g., a proportional–integral–derivative controller) may be used for passively regulating the temperature of the coupling medium within reservoir **404** to a desired temperature, e.g., a body temperature of a subject, throughout an imaging session.

Further temperature adjustment functionality is also contemplated for reservoir **404**. In some aspects, where a coupling medium impermeable membrane is provided, a coupling medium may be heated outside of reservoir **404**. For example, reservoir **404** may comprise an attachable pump (not shown) to circulate liquid between reservoir **404** and a separate temperature controlled reservoir where the coupling medium is regulated to

a desired temperature. In some aspects, a surface of reservoir **404** may be heated directly from an outside, rather than through thermal rod **408**, to passively heat coupling medium. For example, a heating lamp or heating plate may be used. Temperature adjustment functionality for heating a coupling medium disposed within a reservoir may also be implemented in any other manner and in any of the other embodiments described herein, (i.e., a reservoir configured as in **106A**, **106B**, **206**).

One or more ports **410** may be provided in one or more side walls of reservoir **404**. As illustrated in Figure 4, two ports **410** are provided in a first side wall of reservoir **404**. Ports **410** may provide an entry and/or exit for sensors. In some aspects, a sensor may be provided for apparatus **400** to detect a temperature, height, presence, etc., of a coupling medium within reservoir **404**. For example, one or more thermocouples (not shown) may be threaded through port(s) **410** to measure a temperature of a coupling medium. The thermocouple may be used as feedback to an acquisition model associated with a computing platform that may implement control software to adjust the temperature of the reservoir appropriately, using, for example, thermal rod **408**. Ports for providing sensors of any type into a reservoir may also be implemented in any of the other embodiments described herein, (i.e., a reservoir configured as in **106A**, **106B**, **206**).

In some aspects, reservoir **404** may also comprise an input/output for delivering and/or draining reservoir **404** of a coupling medium. For example, Figure 4 illustrates an input/output **412** disposed in between the two ports **410** on the first side wall that is configured to fill/drain reservoir **404** with coupling medium. One or both filling and draining reservoir **404** may be controlled manually or automatically by a computing platform associated with apparatus **400**. An input/output for delivering and/or draining a reservoir may also be implemented in any of the other embodiments described herein, (i.e., a reservoir configured as in **106A**, **106B**, **206**). Notably, it may be desirable to drain water from a reservoir after each imaging session in order to avoid damaging the transducer.

Referring now to Figure 5, a front perspective view of an apparatus, generally designated **500**, which includes a transducer **402** and a reservoir

404 as described above is provided. Apparatus **500** includes an I-beam **502** that connects both transducer **402** and reservoir **404** to an x-axis motion stage **504** and a y-axis motion stage **506**, and a U-shaped platform **508** with one or more blocks **510** for supporting the extra weight from reservoir **404**. In comparison with embodiments of apparatuses, systems, and methods for preclinical imaging where the transducer moves relative to both a subject and a reservoir, in the embodiment provided in Figure 5, the transducer and the reservoir move simultaneously relative to a subject. As a result, the motion stages that are configured to move the transducer must be configured to simultaneously translate a reservoir containing a quantity of coupling medium in two dimensions.

In some aspects, I-beam **502** comprises a non-weight bearing structure that may be configured to couple reservoir **404** to motion stages **504**, **506**. For example, I-beam is rigidly fixed to a bottom surface of reservoir **404** at a first end and is rigidly fixed to both motion stages **504**, **506** at a second end. In some aspects, I-beam **502** may also comprise a ring (e.g., **602**, Figure 6) that is configured to rigidly receive a bottom surface of transducer **402**. For example, transducer **402** may be inserted into an orifice in a bottom surface of reservoir **404** and then rigidly received by the ring of I-beam **502**. In this manner, transducer **402** is retained in a rigid relationship (i.e., precise spatial location) relative to reservoir **404** during translation of I-beam **502** along one or both of the x-axis or the y-axis.

X-axis motion stage **504** and y-axis motion stage **506** provide linear translation of transducer **402** and reservoir **404** via translation of I-beam **502**. Each of x-axis motion stage **504** and y-axis motion stage **506** are independently movable relative to a stationary subject (not shown in this Figure) in order to scan the subject from a variety of desired spatial positions in a horizontal plane. Thus, transducer **402** may be moved in x, y manually and/or automatically using a motion control system associated with a computing platform (see, e.g., Figure 12), such that transducer **402** is movable in a horizontal plane relative to a subject positioned above reservoir **404**. For example, a motion control system may enable one or more users to enter a mode of operation (e.g., jogging mode) where a spatial position of

transducer **402** is controlled by the computing platform, or an external joystick or keypad, and transducer **402** is moved to a specified location via motors controlling x, y stages **504**, **506**. In some aspects, a spatial position or positions of transducer **402** may be determined *a priori* by the computing platform in order to control the linear stages' **504-506** positions. Regardless, this mode may be useful for users wanting to explore tissue volume to locate features of interest.

In order to support reservoir **404** and coupling medium contained within, apparatus **500** includes a weight bearing apparatus. In some aspects, the weight bearing apparatus may comprise a plurality of blocks configured to distribute the weight across a platform, a suspension configuration from above the reservoir, rollers below the reservoir, or other strain relieving methods. As illustrated in Figure 5, the weight bearing apparatus may comprise platform **508**, contact blocks **510**, rods **512**, sleeve bearing blocks **514**, and anchored corner blocks **516**. Platform **508** may comprise a U-shaped platform with a center removed to receive I-beam **502** and transducer **402**. Platform **508** may be composed of a rigid material, such as aluminum.

In some aspects, one or more contact blocks **510** may be fixedly attached to a bottom surface of reservoir **404**. For example, four T-shaped contact blocks **510** may be fixedly attached to reservoir **404**, where two blocks **510** are provided on one longitudinally extending side and two blocks **510** are parallelly provided on an opposing longitudinally extending side of a bottom surface of reservoir **404** so that they are not in contact with platform **508**. In some aspects, screws, bolts, and/or any other type of fastener may be used to fixedly attach contact blocks **510** to reservoir **404**. Each of contact blocks **510** may be provided with a through-hole through which greased rods **512** may be slideably threaded. Greased rods **512** may terminate at each end in sleeve bearing blocks **514** suspended over platform **508**. For example, a first end of a first rod **512** may be fixed in a first sleeve bearing block **514** and be slideably threaded through two contact blocks **510** disposed on a first longitudinally extending side of a bottom surface of reservoir **404** and a second end of the first rod **512** may terminate in a

second sleeve bearing block **514**, while a first end of a second rod **512** may be fixed in a third sleeve bearing block **514** and be slideably threaded through two contact blocks **510** disposed on a second, opposing longitudinally extending side of the bottom surface of reservoir **404** and terminate in a fourth sleeve bearing block **514**. The first and third sleeve bearing blocks and the second and fourth bearing blocks **514** may be parallel to one another, while the first and second bearing blocks and the third and fourth bearing blocks **514** may also be parallel to one another. In this way, when x-axis motion stage **504** translates reservoir **404** along the x-axis, contact blocks **510** translate along rods **512** a corresponding magnitude and direction along the x-axis.

Each of sleeve bearing blocks **514** may be suspended over platform **508** by one or more greased rods **518** being provided through through-holes in each of sleeve bearing blocks **514** and terminating at each end in anchored corner blocks **516** fixed onto platform **508**. Axes of through-holes through which greased rods **518** extend in sleeve bearing blocks **514** are substantially orthogonal to a surface in sleeve bearing blocks **514** at which ends of rods **512** terminate. For example, a first end of a first rod **518** may be fixed in a first anchored corner block **516** and be slideably threaded through two sleeve bearing blocks **514** and a second end of the first rod **518** may terminate in a second anchored corner block **516** and a first end of a second rod **518** may be fixed in a third anchored corner block **516** and be slideably threaded through two sleeve bearing blocks **514** and terminate in a fourth anchored corner block **516**. Where there are more than two rods **518** in each of sleeve bearing blocks **514**, rods **518** may extend in parallel to one another. The first and third anchored corner blocks and the anchored corner blocks **516** may be parallel to one another, while the first and second anchored corner blocks and the third and fourth anchored corner blocks **516** may also be parallel to one another. In this way, when y-axis motion stage **506** translates reservoir **404** along the y-axis, sleeve bearing blocks **514** translate along rods **518** a corresponding magnitude and direction along the y-axis.

Now referring to Figure 6, a cross-sectional view of an exemplary embodiment of an apparatus, generally designated **600**, including transducer **402**, reservoir **404**, and I-beam **502** as described above, is provided. As noted, I-beam **502** may comprise a ring **602** configured to rigidly receive a bottom surface of transducer **402**, while a top surface of transducer **402** may be securely received in a bottom surface of reservoir **404**. For example, ring **602** may comprise an indented bottom surface sized to receive a bottom surface of transducer, such that transducer **402** may be able to be stabilized and cannot be misaligned. In other examples, ring **602** may be configured to retain transducer **602** using other contemplated methods. Regardless, transducer **402** may be rigidly aligned (i.e., in a precise spatial location) relative to reservoir **404** during translation of I-beam **502** along either the x-axis or the y-axis.

While a bottom surface of transducer **402** may be secured to ring **602** of I-beam **502**, a top surface of transducer **402** may be coupled to a bottom surface of reservoir **402** in a substantially water-tight manner. Now referring to Figures 7A-7B, a coupling mechanism may be provided which may be configured to act as a seal between the transducer and the reservoir and thereby prevent substantial leakage therebetween. In Figure 7A, a cross-sectional view of a first embodiment, generally designated **700A**, provides for a transducer **702A** and a reservoir **704A** similar to transducer **402** and reservoir **404** described with regard to earlier embodiments. For example, reservoir **704A** is a rigid tank, rather than a bag reservoir (see, e.g., **704B**, Figure 7B). In some aspects, a coupling mechanism or cross-coupling clamp **706A**, may be an annular clamp disposed around an outer circumference of transducer **702A** having a top surface substantially abutting a bottom surface of reservoir **704A**. Clamp **706A** may comprise a radial or inward pressure to seal around transducer **702A**, using, for example, a fastening element. Upward clamping pressure may be applied from clamp **706A** towards reservoir **704A** to seal between transducer **702A** and reservoir **704A**, using similar fastening elements. As illustrated in Figure 7A, two fastening screws are used to provide inward pressure on clamp **706A**, while two fastening screws are used to provide upward clamping pressure

on reservoir **704A**. One or more o-rings, generally designated **OR**, may be utilized to provide radial pressure on transducer **702A**. For example, three o-rings **OR** may be utilized as illustrated in Figure 7A. However, using o-rings **OR** may cause slight misalignment of transducer **702A** in which case a secondary method of positioning transducer **702A** may be required. One such secondary method may be, for example, to include a secondary stabilization point at a distal or bottom end of transducer **702A**.

In some aspects, a coupling mechanism for a reservoir comprising a flexible bag is provided. Figure 7B is a second embodiment, generally designated **700B**, of a transducer **702B** and a reservoir **704B** that differs from the first embodiment **700A** in that reservoir **704B** is a flexible bag or membrane containing coupling medium **CM**. Additionally, a coupling mechanism or cross-coupling clamp **706B** may be an annular clamp disposed around an outer circumference of transducer **702B** having a top surface substantially abutting a bottom surface of reservoir **704B** in order to add additional clamping pressure onto coupling medium **CM** contained within reservoir **704B**. In such a manner, clamp **706B** allows transducer **702B** to enter through a bottom of reservoir **704B** without leakage of coupling medium **CM**. A bracket **708** provided on a side of clamp **706B** may enable movement of transducer **702B**.

Now referring to Figure 8, a perspective view of an apparatus, generally designated **800**, for providing z-axis and rotational movement of a subject into an imaging chamber over a reservoir, such as reservoir **404** in Figure 4, is provided. Where apparatus **800** is used in conjunction with an apparatus, such as apparatus **500** (see, e.g., Figure 5), the resulting configuration will be an apparatus such as apparatus **900**, Figure 9, where apparatus **800** is provided above apparatus **500** in the z-axis.

Z-axis movement of apparatus **800** may be achieved by a z-motion stage comprising a primary motor, generally designated **802**, which is configured to drive vertical motion of a lead screw **804** along the z-axis on which a middle block **806** is rotatingly attached and coupled to a platform **808** on which a subject may be placed. In this manner, motor **802** may drive lead screw **804** either clockwise or counterclockwise, which will in turn drive

middle block **806**, and platform **808**, either up or down in a z-axis direction along lead screw **804**. Alternatively, motor **802** may drive a pulley system (not shown) in order to move platform **808** along the z-axis direction. Where apparatus **800** is configured to be disposed over a reservoir having a transducer disposed therein, as in any of the configurations described above, a subject positioned on platform **808** may be automatically raised and/or lowered into an imaging chamber over the reservoir through actuation of motor **802**.

Notably, platform **808** is advantageously configured to be rotational about an x-axis, such that a subject placed belly up on platform **808** may be automatically rotated 180 degrees into a belly down position relative to an x-plane as the platform is lowered. More particularly, a rotational motion stage comprising a secondary motor, generally designated **810**, may be utilized to actuate rotation of platform **808** via rotating a rotational shaft **812** in either a clockwise or counterclockwise manner a predetermined number of degrees (e.g., 180 degrees). Alternatively, a rack and pinion (not shown) may be used to rotate platform **808**. Arrow A_2 illustrates rotation of shaft **812** about the x-axis. In some aspects, primary motor system **802** and secondary motor system **810** may simultaneously be actuated so that platform **808** is lowered along the z-axis at a same time as the platform is being rotated from a first position (i.e., belly up position – illustrated in Figure 8) to a second position (i.e., belly down position) about the x-axis. Conversely, primary motor system **802** and secondary motor system **810** may simultaneously be actuated so that platform **808** is raised along the z-axis at a same time as the platform is being rotated from the second position to the first position about the x-axis.

In some aspects, one or more stationary optical cameras **814** may be provided on apparatus **800**. Cameras **814** may be linked to a computing platform that may be used to control motors **802**, **810** such that images of a subject on platform **808** may be automatically acquired at specific intervals while the subject is being lowered and/or raised and/or rotated on platform **808**. Advantageously, acquiring images during movement and/or rotation of a subject is advantageous for combining pre-clinical ultrasound imaging with

other modalities, especially bioluminescence imaging, because images of the subject at a number of different angles may be beneficial in constructing one or more projections of the subject for surface mapping.

Referring now to Figure 9, an apparatus generally designated **900** for preclinical ultrasound imaging of a subject is provided. Apparatus **900** comprises a plurality of components described in reference to Figures 4-8, including a transducer **402**, reservoir **404**, I-beam **502**, x and y motion stages **504**, **506**, a z-motion stage **802**, a rotational motion stage **810**, and an animal platform **808**. Reservoir **404** is coupled to x and y motion stages **504**, **506** via I-beam **502** which, in turn, rigidly affixes transducer **402**, to a bottom surface of reservoir **404**, as described in Figures 4-7A. A removable housing **902** is provided to encase transducer **402**, reservoir **404**, I-beam **502**, x and y motion stages **504**, **506**, as well as other components of apparatus **900**. Removable housing **902** may be composed of a rigid material to add stability to apparatus **900** and may be removable in parts so that apparatus may be quickly assembled and disassembled, as necessary.

In some aspects, removable housing **902** may comprise a removable stage **904**. Stage **904** may be configured as a removable lid to housing **902**. For example, stage **904** is disposed over reservoir **404** such that a coupling medium disposed within reservoir **404** is substantially covered by stage **904**. In this example, transducer **402**, reservoir **404**, I-beam **502**, and x and y motion stages **504**, **506** are disposed below stage **904**, while z-motion stage **802**, rotational motion stage **810**, and animal platform **808** are provided above. In some aspects, stage **904** comprises an opening in which an imaging chamber **906** is defined. For example, the opening may be sized to receive platform **808** when platform **808** is in the lowered, second position. In such a position, platform **808** may be configured to be in close proximity to the coupling medium contained within reservoir **404**. Accordingly, for example, a membrane **908** disposed on a bottom surface of imaging chamber **906** may be used as a barrier between coupling medium in reservoir **404** and imaging chamber **906** in order to protect a subject from the coupling medium contained within reservoir **404**.

Accordingly, apparatus **900** may be utilized by an operator to translate transducer **402** along the x and y-axes by x and y motion stages **504**, **506** and acquire pre-clinical ultrasound images of a subject positioned in a lowered, second position on platform **808**. After acquisition of preclinical ultrasound images is complete, platform **808** may be raised and rotated back into a first position away from imaging chamber **906**. Stage **904** may be removed and housing **902** may be disassembled in order to, for example, drain the coupling medium from reservoir **404** and/or remove transducer **402**.

Referring now to Figure 10, an exemplary embodiment of a subject transfer platform, generally designated **1000**, is provided. Specifically, subject transfer platform **1000** may be similar to platform **808** (Figure 8) and may be configured to allow registration of images acquired during preclinical ultrasound imaging of a subject to other imaging modalities via one or more fiducial landmarks. Subject transfer platform **1000** may comprise a cassette **1002** that may be slidable and/or removable with regard to a rigid structure, such that cassette **1002** may be consistently and reliably positioned in a same spatial position for each imaging session. In some aspects, cassette **1002** may be a transferable item that can transfer to any number of imaging modalities (e.g., bioluminescence, cryoimaging, etc.)

As illustrated in Figure 10, for example, cassette **1002** may be slideable along a groove **1004** that corresponds in width to a protrusion **1006** extending in each of a pair of guide rails **1008** in platform **1000**. Thus, cassette **1002** may be configured to be slid completely onto guide rails **1008** so that a first end of cassette **1002** is coplanar with first end of guide rails **1008** and a second end of cassette **1002** substantially abuts a far wall of platform **1000**. Thus, guide rails **1008** may be used to ensure vertical and lateral alignment of cassette **1002** in platform **1000**.

In some aspects, cassette **1002** may comprise elements for interacting with a subject positioned thereon. For example, a nose cone **1010** for which a subject's nose is positioned, which is connectable and/or disconnectable with anesthesia tubes **1012** via valves **1014**, is provided. Valves **1014** may be connected with nose cone **1010** and may be

connectable and/or disconnectable to anesthesia tubes **1012** upon complete insertion of cassette **1002** in guide rails **1008**. In Figure 10, for example, cassette **1002** is illustrated in an intermediate position where the cassette is only partially slid onto guide rails **1008**. Therefore, when cassette **1002** is completely slid onto guide rails **1008** so that cassette **1002** is considered completely inserted onto the guide rails, valves **1014** will be in a position to be connected to anesthesia tubes **1012** so that an uninterrupted flow of anesthesia may pass from anesthesia tubes **1012** to nose cone **1010**. Additionally, connection of anesthesia tubes **1012** to nose cone **1010** acts as securing cassette **1002** at an appropriate position in a z-axis direction.

In other aspects, cassette **1002** may include an integrated heating mechanism (not shown) to ensure animal homeostasis during an imaging study. For example, cassette **1002** may include an embedded electrical heating pad, a recessed pocket for a chemical heating pad (e.g., a hand warmer, microwavable heating pad, etc.)

Cassette **1002** may also comprise one or more fiducial landmarks **1016** disposed on a top surface thereof. For example, in Figure 10, cassette **1002** comprises a checkerboard pattern rendered in two distinct colors on a top surface of cassette **1002**. A subject may be placed on this surface and then both optical images and ultrasound images may be acquired of the subject on the cassette **1002** against the fiducial landmarks **1016**. For example, an optical camera (not shown in this Figure) may be utilized to acquire images of a subject and register those images with a modality other than ultrasound in order to provide more accurate and/or precise 2D or 3D images.

Referring now to Figures 11A-11G, computer generated images of an exemplary process flow for generating an atlas using fiducial landmarks, such as those depicted in Figure 10, is illustrated. Figure 11A illustrates a subject platform **1100A** similar to **1000** illustrated in Figure 10 and configured to include a subject **S** positioned thereon. Subject platform **1100A** may be configured to include a cassette **1102** having one or more fiducial landmark **1104** disposed on a surface on which subject **S** is positioned. Fiducial landmark **1104** may comprise a checkerboard pattern

rendered in two distinct colors similar to pattern **1016** in Figure 10. Cassette **1102** may be movable with regard to platform **1100A** in a z-axis and/or a rotational x-axis direction towards and/or away from an imaging chamber **1106**, similar to the imaging chamber described in reference to Figure 9, where a transducer (not shown) may be provided.

One or more optical cameras may be provided on animal platform **1100A**. For example, two optical cameras **1108** and **1110** are provided in two disparate locations on platform **1100A**. In some aspects, one or more optical camera **1108** and **1110** may be utilized to coarsely map (i.e., one to one spatially map) a spatial position of subject **S** on cassette **1102** in order to facilitate ultrasound imaging scan boundaries and subsequent positioning of subject **S** in later imaging sessions. One or more optical camera **1108** and **1110** may be actuated by a computing platform associated with platform **1100A** to acquire images as cassette **1102** moves in either one or both a rotational and/or vertical manner towards imaging chamber **1106**. Figures 11B-11C each illustrate exemplary computer generated images that may be acquired by each camera at a first time period. For example, Figure 11B provides for image **1100B** acquired by first camera **1108** during a first time period, while Figure 11C provides for image **1100C** acquired by second camera **1110** during the first time period. Thus, as can be seen from a comparison of images **1100B** and **1100C**, different angular views of subject **S** may be acquired at a same time period. Subsequent images may be acquired for each of cameras **1108** and **1110** for subsequent time periods.

Figure 11D illustrates a computer generated image, generally designated **1100D**, of a topographic surface model formation based on the angular images acquired from cameras **1108** and **1110**. Notably, the more images may be acquired at different time periods, the more precise the topographic surface models may be.

Figure 11E illustrates a computer generated image, generally designated **1100E**, of a surface model registered to a 3D atlas. The 3D atlas may be a 3D probability model of a subject that includes locations of specific features within a subject, e.g., a heart, stomach, bladder, etc. By registering a surface model of a subject to a 3D atlas of a generic subject, an operator

may be able to determine an approximate location of where a specific organ is on a subject currently being imaged and then robotically translate a transducer in a preclinical ultrasound imaging system to that position relative to the platform, keeping in mind a surface geometry and contours of the subject For example, if the operator was interested in viewing the subject at line **P** the 3D atlas would enable precise positioning of the transducer at that point on the subject currently being imaged. In this manner, a 3D scan region of a region of interest (ROI) of a subject may also be displayed prior to acquisition of ultrasound images.

Figures 11F-11G each illustrate a computer generated image of a targeted ultrasound using the spatial positioning information achieved from the 3D atlas. Specifically, a screenshot of a targeted ultrasound image at line **P** in a B-mode scan **1100F** and using acoustic angiography **1100G** are illustrated in Figures 11F-11G, respectively.

Contact free imaging may thus be achieved by any of the embodiments illustrated in Figures 1A-11G, since the ultrasound probe may be coupled to the target without physical contact being made between the probe and the tissue of the subject.

Figure 12 is a schematic illustrating a system generally designated **1200** for preclinical ultrasound imaging of a subject. System **1200** may comprise an ultrasound transducer **1202**, which may be an ultrasound transducer similar to transducers described herein. An ultrasound imaging system **1204** may be communicatively connected to ultrasound transducer **1202** for controlling acquisition of preclinical ultrasound images of a subject.

Transducer **1202** may be movable relative to both a subject and a reservoir or just a subject, as transducer **1202** may be coupled to the reservoir. In some aspects, transducer **1202** may be moved via one or more robotic motion stage **1206**. For example, motion stage **1206** comprises two linear motion stages to independently translate transducer **1202** along an x and y axis. In another example, motion stage **1206** comprises two linear motion stages to independently translate transducer **1202** along an x and z axis and one rotational computerized stage for rotating transducer **1202** along a Θ axis. Each motion stage of the one or more robotic motion stage

1206 may be independently controllable by a motion control system, generally designated **1208**, for either automatic and/or manual control by an operator.

Other entities that may be associated with system **1200** may include a reservoir for containing a coupling medium, a platform, more than one robotic stage configured to move and/or rotate the platform, a reservoir support structure, seals, membranes, one or more optical cameras, heating elements, sensors, etc., as well as any structure comprising functionality for capturing, regulating and/or storing acquired data.

In some aspects, a computing platform, generally designated **1210** may be in communication with and/or otherwise associated with motion control system **1208** and/or ultrasound imaging system **1204**. In some aspects, computing platform **1210** may include functionality for configuring an apparatus to operate one or more robotic stage **1206** via motion control system **1208** (e.g., through acquisition software or by an external joystick or keypad.

Computing platform **1210** may be used for acquiring preclinical ultrasound images of a subject. Computing platform **1210** may represent any suitable entity or entities (e.g., an acquisition platform or a server farm) for acquiring preclinical ultrasound images of a subject. For example, computing platform **1210** may acquire preclinical ultrasound images associated with an apparatus, such as apparatus **300**, **900**, etc., using one or more ultrasound transducers.

In some aspects, computing platform **1210** may be configured to perform one or more functions associated with acquiring preclinical ultrasound images. In some embodiments, computing platform **1210** may be a stand-alone acquisition tool, an ultrasound acquisition device, or software executing on a processor. In some embodiments, computing platform **1210** may be a single node or may be distributed across multiple computing platforms or nodes.

Computing platform **1210** may include an acquisition module (AM) **1212**. AM **1212** may be any suitable entity (e.g., software executing on a processor) for performing one or more aspects associated with preclinical

ultrasound image acquisition and processing. AM **1212** may include functionality for acquiring preclinical ultrasound image(s) during one imaging session or multiple sessions and for processing these images. For example, AM **1212** may acquire one or more ultrasound images of a subject for processing. In this example, an AM user (e.g., a device or computing platform usable by a user or an operator) may acquire one or more preclinical ultrasound images of the subject via ultrasound imaging system **1204** associated with computing platform **1210**, which may be subsequently processed by AM **1212**. In addition to providing functionality for acquiring and/or processing the preclinical ultrasound images of a subject, AM **1212** may include functionality for storing the images for future use. In some embodiments, AM **1212** may include functionality for instantiating or initializing images and/or for providing the images to other computing platforms or devices. For example, AM **1212** may acquire the ultrasound images and process those images or may provide the acquired ultrasound images to other nodes to process the images.

In some aspects, AM **1212** may include or access data storage **1214** containing data and/or images related to preclinical ultrasound imaging. For example, AM **1212** may access data storage **1214** containing previous image acquisitions, mapped coordinate systems, image data, profiles, settings, or configurations. Exemplary data storage may include non-transitory computer readable media, such as flash memory, random access memory, or other storage devices. In some embodiments, data storage **1214** may be external to and/or integrated with the computing platform **1210** and/or AM **1212**.

In some aspects, AM **1212** may include one or more communications interfaces **1216** for interacting with users and/or nodes. For example, AM **1212** may provide a communications interface for communicating with an AM user. In some embodiments, the AM user may be an automated system or may be controlled or controllable by a human user. The AM user may acquire and/or process the ultrasound images acquired during preclinical imaging. In some embodiments, processing the ultrasound images may

include registering a currently acquired image set acquired at a second time point to a previous acquired image set acquired at a first time point.

In some aspects, the AM user may include one or more communications interfaces **1216** for interacting with one or more systems and/or devices. Such systems and/or devices may include, but are not limited to, an apparatus for acquiring preclinical ultrasound images (see, Figures 1A-9), an ultrasound imaging system **1204**, a motion control system **1208**, a video recording device (e.g., one or more webcam **1218**) for capturing images regarding the positioning of the subject on the platform, thermal management system (e.g., fluid coupling reservoir thermal regulation **1220**) with any sensors for regulating temperature of the coupling medium, and/or any other suitable entity or entities (e.g., storage devices containing animal physio-data **1222**) implementing, acquiring, or otherwise using preclinical ultrasound images. For example, such suitable entity or entities may comprise an enterprise data storage system including multiple physical storage devices or components.

In some aspects, computing platform **1210** may include functionality for configuring an apparatus to maintain a specific offset relative to the platform during acquisition of preclinical ultrasound images. For example, where computing platform **1210** communicates with transducer **1202** via ultrasound imaging system **1204**, computing platform **1210** may control movement of transducer **1202** to specified locations relative to a subject. In this example, computing platform **1210** may control movement of transducer **1202** to predetermined transducer-body offset such that transducer **1202** may be maintained and/or controlled at a predetermined (optimal) offset from a body of a subject during an imaging session, e.g., a 1-1.5 cm offset, whether a subject is moved relative to transducer **1202** or vice versa. In this example, a surface atlas of the subject may be saved to data storage **1214** that may be accessed by computing platform **1210** during the imaging session and may be utilized by computing platform **1210** to aid in maintaining the offset.

In another aspect, computing platform **1210** may include functionality to configure an ultrasound imaging system **1204** to acquire the images from

positioned transducer **1202**. In another aspect, computing platform **1210** may include functionality to modify conditions within the apparatus; for example, regulating temperature of a coupling medium held within a reservoir, movement of transducer **1202** to multiple spatial positions within one imaging session, etc. In some aspects, computing platform **1210** may include functionality to generate content (e.g., compounded image data using previously acquired preclinical ultrasound images) and/or retrieve stored content associated with a preclinical imaging session and may send or provide the content to other suitable entities (e.g., subject physio-data **1222** regarding the subject being imaged that has been logged in previous sessions). In some aspects, computing platform **1210** may be configured to monitor subject physiological homeostasis, including but not limited to heart rate, breathing rate, and body temperature, where this physio-data may be logged throughout an imaging study. Consequently, any physio-data logged during an imaging study may be used to retroactively gate images to remove image frames in which a subject was moving.

In some aspects, the AM user may be configured to acquire and/or process acquired ultrasound images based on existing content. For example, during preclinical image acquisition, the AM user may import transducer positioning data from a previous imaging session in order to replicate positioning of transducer **1202** in a current and/or subsequent imaging session. Consequently, computing platform **1210** may be associated with different aspects of system **1200** for acquiring preclinical ultrasound images.

In some aspects, a system for preclinical ultrasound imaging may be utilized to coarsely map (i.e., one to one spatially map) a subject's spatial position on a platform of an apparatus for preclinical ultrasound imaging in order to facilitate ultrasound imaging scan boundaries and subsequent positioning of the subject in later imaging sessions. Such a system and/or apparatus may include a system, such as system **1200**, described with respect to Figure 12, as well as any of the apparatuses described in conjunction with Figures 1A-9. Users of a system for preclinical ultrasound imaging may be enabled to manually and/ or automatically define angular

and linear regions over which to scan, how many passes to make at each location, and then execute this set of parameters. The system may update a user how much time remains for the scan. This may be achieved in one or more axes (e.g., the Z and Y axis) using one or more of the following options including but not limited to: laser-based ranging, segmentation based on webcam image feedback, pressure feedback of a subject on a platform, and/or acoustic ranging based on *a priori* knowledge of platform distance. Other options may also be utilized. In addition, a transducer used for acquiring the preclinical images may include a laser indicating where the transducer is currently aimed in order to allow visual feedback for the user in positioning it. This may include non-visible wavelengths which an optical detection device may detect in order to prevent reflections from endangering a user's eyes).

Mapping a subject's spatial position may be performed by acquiring an image of an organ, such as the heart, at a first time point. Location of a 2D ultrasound image acquired may be recorded in XYZ space and subsequently stored using, for example, AM **1212** of computing platform **1210**. A 3D ultrasound scan showing tissue surrounding a region of interest at the first time point may then be acquired. Features of interest (e.g., organ(s), rib(s), a surface of the skin, or feature(s) that can serve as landmarks), which have at least four XYZ points associated with them, may be segmented from the 3D ultrasound scan. In some instances, four XYZ points may be the minimum number of points needed to uniquely define a coordinate system in 3D space to determine a location of the 2D ultrasound plane relative to the landmarks.

In some aspects, a spatial position of a subject at a first time point may be used to exactly position a transducer in order to acquire a 2D ultrasound image (i.e., position the scan plane) at a second time point. This may be useful in evaluating predetermined regions in a subject's body in a different imaging session. In order to use previous locations of a scan plane in XYZ space in a subsequent session, another 3D image of that subject may be acquired at a second time point. The same features of interest acquired at the first time point may be segmented out of the 3D image in

order to determine a location of a 2D ultrasound plane relative to the landmarks in the second time point. The segmented landmarks may then be aligned from the data, and once this transformation is known the image data between the time points may be mapped, such that the ultrasound scan plane may be exactly positioned where the scan plane was at the first time point.

Slight adjustments may be needed for replicating positioning of a scan plane from a first time point to a second time point once image data between the time points is mapped. However, in one aspect, this may be done very precisely and iteratively by comparing two 2D images (a current image from a second time point, which updates every time a transducer is moved, compared with a previous image from a first time point, which is static) and stopping when a maximum value of correlation between the frames is reached. This may ensure more accuracy than is capable from the human eye.

In another aspect, instead of having a user define and/or segment landmarks, a whole image dataset at a second time point may be registered (manually or automatically) to an image dataset at a first time point. This may result in a same coordinate transform, as described above.

In another aspect, an optical recording device (e.g., a webcam) looking down on a subject may result in calibrated locations of XY locations. This may enable a user to come very close to an original scan plane location and/or orientation. For example, a user may add a suitable marking (e.g., fiducial landmark) to a subject's skin, one that is not likely to move very much over time, so that a location of the marking may be selected in the webcam image and transmit the transducer to that specific location.

For example and in reference to Figures 13A-13C, an exemplary process flow for one to one spatial mapping is illustrated, where an image set of an imaging session at a second time point is registered to an image set of either the same or different modality at a first time point. Figure 13A illustrates a screenshot, **1300A**, of a first image set at a first time point in a first coordinate system. In some aspects, the first image set may include, for example, an ultrasound image, a 2D webcam image, a 3D contour map of

the animal derived by one or more webcam images, a photoacoustics image, a bioluminescence image, an x-ray image, an MRI image, a fluorescence image, a SPECT image, a PET image, an anatomical atlas, or any multimodality combination thereof. Figure 13B illustrates a screenshot, **1300B**, of a second image set at a second time point using a different coordinate system. In some aspects, the second image set may include, for example, a widefield ultrasound image volume, a 2D webcam image, or a 3D contour map of the subject derived by one or more webcam images. Figure 13C illustrates a screenshot of the resulting registration **1300C** of the image set from the second time point in Figure 13B to the image set from the first time point in Figure 13A, where the coordinate system between the image sets has been mapped one-to-one. Notably, once registration has been performed, a user can provide a ROI somewhere in the first image set (i.e., in Figure 13A) that is viewable in the registered set (i.e., in Figure 13C). Thus, the presently disclosed subject matter enables the automatic localization of one or more organ systems of interest based on the registration between image data from a first time point and a second time point.

In addition, the presently disclosed subject matter is advantageous because it enables widefield imaging of tissue volumes. More specifically, over 50% of a subject's body may be imaged, which may enable better longitudinal comparisons, thereby increasing the quality of image data. This is made possible by the system physically positioning an ultrasound transducer at different angles relative to the same tissue, and imaging the tissue without physically contacting it directly (i.e., no tissue warping). This may allow the resulting images to be rigidly registered together to ensure accurate alignment between the ultrasound image data and the secondary image data set (i.e., sampling the same tissue regions) so that measurements made within the ultrasound image data and the secondary image data set have one to one correspondence. Alignment may be performed in an automated or manual fashion, and may occur simultaneously with or subsequently to image generation.

For example, an ultrasound transducer may be positioned at three different angles relative to a same tissue (see, e.g., Figures 14A-C, 15A-B, and 16A-B). These angles may be +/- 20 degrees and 0 degrees, with a z range of 5 cm and a z resolution of 150 μm, and 333 image frames per stack. A transducer may be positioned at more angles or less angles relative to the same tissue, as well. Referring to Figures 14A-C, a first angle at which an ultrasound transducer is positioned and subsequent image plane at which an ultrasound image of the subject is acquired is provided. Specifically, Figure 14A provides a diagram of an imaging session, generally designated **1400A**, of a transducer **1402** in a first spatial position relative to a subject **S** positioned on a platform **1404**. Subject **S** is prepped and positioned on platform **1404** over a reservoir holding a coupling medium (not shown) in an apparatus similar to one or more apparatus described hereinabove. Transducer **1402** may be positioned in the first spatial position in either a manual or automated manner in order to scan a certain region of subject **S** in a first scan plane $\mathbf{P_1}$ (e.g., a rectangular region right to left). Notably, the first spatial position of transducer **1402** may be chosen in order to image certain organs or tissues of subject **S**. Figure 14B is an exemplary photograph, generally designated **1400B**, of an image of transducer **1402** in the first spatial position relative to subject **S** as described in Figure 14A. First scan plane $\mathbf{P_1}$ is provided in photograph **1400B** to illustrate the ROI in subject **S** in which transducer **1402** will acquire a 2D ultrasound image. Accordingly, Figure 14C is an exemplary screen shot of a 2D ultrasound image, generally designated **1400C**, acquired of subject **S**, where a bladder **1406**, a liver **1408**, and a heart **1410** are all visible.

Referring now to Figures 15A-15B a second angle at which an ultrasound transducer is positioned and subsequent image plane at which an ultrasound image of the subject is acquired is provided. Specifically, Figure 15A provides a diagram of an imaging session, generally designated **1500A**, of a transducer **1502** in a second spatial position relative to a subject **S** positioned on a platform **1504**. Notably, the imaging session illustrated in Figure 15A may be a same imaging session as that illustrated in Figure 14A. The only difference may be that the transducer has been moved from a first

spatial position to a second spatial position relative to a subject **S**. Transducer **1502** may be positioned in the second spatial position in either a manual or automated manner in order to scan a certain region of subject **S** in a second scan plane P_2 (e.g., a rectangular region superior to interior) in order to image the same organs or tissues from Figures 14A-C at a different angle. Figure 15B is an exemplary screen shot of a 2D ultrasound image, generally designated **1500B**, acquired of subject **S**, where a bladder **1506**, a liver **1508**, and a heart **1510** are all visible; albeit at a different angle than in Figure 14C.

Referring now to Figures 16A-B, a third angle at which an ultrasound transducer is positioned and subsequent image plane at which an ultrasound image of the subject is acquired is provided. Specifically, Figure 16A provides a schematic illustration of an imaging session, generally designated **1600A**, of a transducer **1602** in a third spatial position relative to a subject **S** positioned on a platform **1604**. Notably, the imaging session illustrated in Figure 16A may be a same imaging session(s) as that illustrated in either one or both of Figures 14A and 15A. The only difference may be that the transducer has been moved from first and/or second spatial position(s) to a third spatial position relative to a subject **S**. Transducer **1602** may be positioned in the third spatial position in either a manual or automated manner in order to scan a certain region of subject **S** in a third scan plane P_3 (e.g., a rectangular region anterior to posterior) in order to image the same organs or tissues from Figures 14A-C and 15A-B at a different angle. Figure 16B is an exemplary screen shot of a 2D ultrasound image, generally designated **1600B**, acquired of subject **S**, where only a bladder **1606**, is visible; albeit at a different angle than in Figures 14C and15B.

Accordingly, once images at different reference angles of a transducer have been acquired, the images at different angles may then be compounded into a multi-angle composite image. For example, Figure 17 is a screenshot of a three-angle composite image, generally designated **1700**, of the 2D ultrasound images of the bladder acquired in Figures 14C, 15B, and 16B. Such a resulting composite image may have a direct and advantageous impact on a field of view (FOV), as it may be dramatically

increased when compared to a single angle FOV. Such a comparison is illustrated in Figures 18A-B. Figure 18A is a screenshot of a single angle 2D ultrasound image, generally designated **1800A**, of a subject with a FOV having a width of X_1, while Figure 18B is a screenshot of a three angle composite 2D ultrasound image, generally designated **1800B**, of a same subject with a FOV having a width of X_2. In the example provided in screenshots **1800A** and **1800B**, X_1 is equal to approximately 1.8 cm, while X_2 is equal to approximately 3.7 cm. Thus, the single acquisition image in Figure 18A has a FOV that is approximately two times less than the FOV of the three angle composition image of Figure 18B, such that compounding multiple images acquired of a subject from different angles into a single image may provide a larger FOV for analysis and study.

In addition, the apparatuses, systems, and methods described herein enable users to specify a desired signal to noise ratio (SNR) in their final image. This may achieved by computing how many angular projections would be acquired to result in the specified SNR, and then automatically determining the angular range over which to acquire the data, and displaying the required time for the user. In some aspects, the system may enable the user to specify a desired acquisition time, and then SNR is maximized given the time constraint and spatial area being scanned.

The apparatuses, systems, and/or methods according to the present subject matter may also include functionality for producing values for cardiac function, such as, for example, left ventricular (LV) wall thicknesses - proximal and distal, LV chamber dimensions at systole and diastole, fractional shortening, ejection fraction, heart rate, and cardiac output. Traditionally, capturing values for cardiac function has proven difficult using conventional imaging techniques. This is because of the technical challenge in placing a sampling line or plane in exactly the same position within the body between subjects or time points, leading to increased variance. Additionally, data samples of the heart can be corrupted by the ribs, respiratory motion, and other reasons. However, the following presents an advantageous approach that reduces time, cost, and the effect of inter-user variability.

Specifically, an amount of time that a user has to actively interact with the apparatus and/or system may be reduced by the subject matter described herein. By positioning, a raster scan grid approximately near the heart (e.g., as indicated by a laser or light to show the user where the scan will be), the user may configure the apparatus and/or system, actuate the apparatus and/or system, and let the apparatus and/or system collect data, without the need for continual supervision by the user. During the time that the apparatus and/or system may be automatically acquiring data, the user may be able to prepare the next subject, thereby increasing the efficiency of the workflow. In addition, the effect of inter-user variability is reduced because the user may not have control over the placement of the scan plane, since movement of the linear and/or rotational stages (which position the transducer) of the apparatus and/or system may be controllable automatically by a computing platform associated with the apparatus and/or system.

Moreover, reducing the overall cost of the technology may be enabled by using a single ultrasound transducer (or small number of ultrasound transducers) and moving the single transducer around using the above-described apparatus, compared to a conventional ultrasound probes which attempt to produce 2D or 3D images for user interface. Such "image-producing" transducer arrays significantly increase the price of heart-analysis tools, while the apparatus or system according to the present subject matter collects individual lines of data about how the heart walls are moving in different areas of the organ and then interpolates between those lines to create a model of the heart beating in 3D. Although, the apparatus or system of the present subject matter could be used to create a 2D image of the heart, it may be relatively slow (several seconds per image due to the necessity that the transducer be physically translated along the subject).

As mentioned above, the system and/or apparatus used to produce values for cardiac function may be an m-mode line, pulse wave Doppler, or tissue Doppler, and/or any other mode of ultrasound which acquires a 1D spatial sampling region over time. Illustrated below is an exemplary

workflow for raster scanning and acquiring data of a subject using an apparatus and/or system of the type described above.

Figures 19-23B each illustrates a process for producing values for cardiac function as described above. Referring now to Figure 19, a computer generated image of an exemplary setup, generally designated **1900**, is provided where a transducer **1902** (e.g., a 30 MHz piston) may be aligned to an approximate location on a subject **S**. For example, transducer **1902** may be aligned to an approximate location on subject's chest where heart **1904** is expected to be. Transducer **1902** may be translated over heart **1904** along x and y axes using one or more motion stages coupled to transducer **1902**.

Figure 20A is a computer generated image, generally designated **2000A**, illustrating a subject **S** with an exemplary sampling grid **2002** provided thereon. Further to Figure 19, sampling may be performed in an XY grid **2002** in the approximate location of where heart **1904** is expected to be on a chest of subject **S**. This may be estimated or it may be more precisely determined using, for example, lasers to indicate where the ultrasound grid will appear on a chest of subject **S**. Additionally, an even more precise approach of determining where heart **1904** may be comprises acquiring a picture of subject **S** (e.g., in the prone position while the subject is on a platform, registering the image to an "atlas", which is able to detail where the heart is located in a subject when it is positioned in the current manner photographed, etc). Additionally, a 3D ultrasound volume, or "scout scan" may be used to localize the boundaries of the desired organ or tissue, and positioning of the raster grid.

Once the approximate area of heart **1904** is determined, a motion stage (not shown) may move transducer **1902** to a center of grid **2002**, and then move it iteratively through a plurality of XY locations across a chest of subject **S** at predetermined spacings (e.g., 0.05 mm - 1 mm), over a predetermined grid size (e.g., 0.5 cm – 2 cm) and for a predetermined amount of time at each location (e.g., 0.5-5 seconds). Thus, grid **2002** is composed of a plurality of 1D ultrasound lines **2004**, which may be collected at a predetermined line-sampling rate (e.g., 100 Hz – 5,000 Hz) and stored

in memory. For example, there may be 400 total sample lines **2004** in a grid **2002**, although this number may be larger or smaller depending on a size of grid **2002**. Figure 20B is a computer generated image, generally designated **2000B**, including a detailed view of grid **2002** having a plurality of sampling lines **2004**. Notably, although some of sampling lines **2004** may be corrupted by ribs **2006** of subject **S**, these may be automatically removed from the dataset (see Figure 20A). In order to achieve enough data samples at each location (e.g., 4 heart beats) a total time for a grid **2002** may be approximately between three and four minutes; preferably 3 minutes and 35 seconds. However, it is noted that less data samples may require less time for the grid and larger data samples may require more time for the grid.

While the 1D ultrasound data is being collected, electrocardiogram (ECG) data of a subject's heartbeat may also be collected by any computing platform and/or nodes (e.g., computing platform **1210**, Figure 12). Any respiration-induced motion may be removed after acquisition using passive gating, or another technique. For example, passive gating may be accomplished by determining if a cross correlation function has a strong frequency component at the rate at which a normal subject breathes (e.g., less than 1 Hz, where a mouse heart is usually around 8 Hz). Once data has been acquired, it may be determined which lines of data correspond to valid data captured from the heart. This may be done by determining a cross correlation function between lines of data at each location, and creating a scoring system which increases a location's score if the cross correlation function at given location has the same frequency and phase as the ECG signal recording the heart's motion. In other words, if the ECG signal says the heart should be beating, and the ultrasound data shows something happening at the same exact point in time, that's a strong indicator that the location is on the heart. For example, in Figures 20A-B, the acquired 1D ultrasound image (i.e., lines **2004**) may be considered valid data because they were taken from a location on heart **1904**, rather than a location that was not on heart **1904** of subject **S**.

Using valid data (i.e., data that is indicative that a scan location is on the heart (or on a desired organ)), relevant walls of heart **1904** may be

segmented or "localized" in each m-mode trace line. A screenshot of the acquired 1D ultrasound image, generally designated **2100A**, of a portion of lines **2004**, is illustrated in Figure 14, where there are four clear trace lines **2102A-2108A**. Depending on an angle of the ultrasound beam, screenshot **2100A** may be representative of a right ventricle wall (posterior or anterior), left ventricle wall (posterior or anterior), or a septum, among other surfaces or interfaces in heart **1904** of subject **S**. Segmentation of trace lines **2102A-2108A** may be accomplished either manually or in an automated manner. For example, Figure 21B provides a set of line drawings, generally designated **2100B**, where each line drawing is an automated segmentation **2102B-2108B** that corresponds to the curvature of one of the four surfaces extracted from each m-mode line **2102A-2108A** in Figure 21A. For example, automated segment **2102B** corresponds to m-mode line **2102A**, automated segment **2104B** corresponds to m-mode line **2104A**, automated segment **2106B** corresponds to m-mode line **2106A**, and automated segment **2108B** corresponds to m-mode line **2108A**.

Accordingly, a sparsely sampled grid of heart wall locations at all times during the cardiac cycle may be modeled by fit to the sparse-spatial/high-temporal sampled segmentations of each m-mode trace line (see, e.g., Figures 21A-B). For example, Figure 22 illustrates a 3D model of a heart, generally designated **2200**, fit to sparse-spatial/high-temporal sampled segmentations. Notably, by interpolating between these points at each time step through the cardiac cycle, a 3D mesh of the relevant surfaces of the heart (the epicardium and endocardium walls, for example) may be built up. This interpolation may be done very simply using a spline based approach, although it may also be done using a more complex image-to-atlas registration approach, where movement of the heart is watched and attempted to be aligned with how a heart normally moves during the cardiac cycle. The 3D mesh may be refined and corrected. In addition, several quantitative outputs may be determined from the model of the heart, such as: LV wall thicknesses (proximal and distal), LV chamber dimensions (systole and diastole), fractional shortening, ejection fraction, heart rate,

and/or cardiac output. However, strain calculations and Doppler of flow or tissue may not be determined from the fitted heart model.

Once the 3D mesh of the heart is obtained, optimal long and short axes positions/orientations of the subject's heart may be determined using the 3D model. In Figure 23A, a 3D model, generally designated **2300A**, of the heart **1904** of subject **S** with optimal long **2302A** and short axes **2304A** indicate the short axis end systole, short axis end diastole, long axis end systole, and long axis end diastole. Using optimal long **2302A** and short **2304A** axes modeled on the 3D model **2300A**, 2D scan plans may be defined in order to acquire b-mode images. The b-mode images may be acquired by translating the 1D sampling lines along a predetermined trajectory to build up a 2D image by slowly translating the beam laterally through tissue of the subject. Translation of the beam may be accomplished through several cardiac cycles in order to acquire a video of the heart beating.

In some aspects, the scan planes may be manually defined and selected, or may be automated once a model of the heart is created. As illustrated in Figure 23B, a computer generated image illustrating the location of the heart on the subject, generally designated **2300B** is provided, where the 3D model of the heart **2300A** is used to define 2D scan planes **2302B** and **2304B**.

Consequently, producing values for cardiac function for one subject may be accomplished in approximately less than 13 minutes and 30 seconds. Figure 24 is an example flow chart, generally designated **2400**, for such a process. In comparison, conventional workflows for producing values for cardiac function, which include raster scanning and acquiring data, have taken as long as 28 minutes for one subject. Exemplary flow chart **2400** illustrates a first step **2402**, during which time subject prep and positioning may occur. For example, a subject may be prepared and placed in an apparatus, for example a SonoVol device, used for preclinical ultrasound imaging in approximately five minutes. Five minutes may be a typical preparation and positioning time for a subject in a study.

In a second step **2404**, a transducer may be positioned near a region of interest over the subject. For example, a transducer may be positioned over a heart in approximately thirty seconds to one minute. Such a range of time, i.e., thirty seconds to one minute, may be a dramatic decrease in positioning in time compared to typical positioning times which may be up to approximately five minutes.

In a third step **2406**, an m-mode raster scan may be performed over a region of interest of the subject. For example, a raster scan grid in x-y axes may be performed in approximately three minutes and thirty seconds. Typical raster scan times may be approximately five minutes.

In a fourth step **2408**, datasets may be processed. For example, data obtained from the m-mode raster scan may be processed in approximately less than one minute. Advantageously, this is where the most significant time savings in producing values for cardiac functions may be achieved as typically dataset processing may take up to thirteen minutes per imaging session per subject.

In a fifth step **2410**, quantitative outputs may be transmitted. For example, any analysis of the datasets from the fourth step **2408** may be transmitted and saved to a database (e.g., database **1214**, Figure 12).

In an optional step **2412**, an orthogonal b-scan may be acquired. For example, a high resolution b-scan image may comprise a lateral FOV of approximately 1.5 cm with a lateral resolution of 120 μm and an acquisition time of approximately one minute and thirty seconds. Alternatively, prior to acquiring the b-mode images, another round of data in addition to step **2406**, may be collected having a finer sampling density over the area where it has been validly determined that the heart is located on the subject. Doing so may further increase the accuracy of determining the location of the subject's heart.

In an optional step **2414**, manual definition of one or more ROI may be performed. For example, an operator may define one or more ROI in approximately two minutes.

After step **2412**, in step **2416**, qualitative outputs based on the b-scan image acquired may be transmitted and saved to a database (e.g., database **1214**, Figure 12).

Accordingly, a preclinical ultrasound imaging session for a single subject may be dramatically reduced to approximately ten minutes in comparison to typical sessions which may take approximately twenty eight minutes. Reduction of subject preparation time may be further reduced in order to further reduce workflow time. For example, anesthesia induction/subject preparation may be accomplished while the apparatus and/or system described above is raster-scanning and acquiring data, which may reduce the time for each imaging session by three to four minutes, thereby resulting in completion of an entire days worth of work using conventional methods to less than three hours.

Referring now to Figure 25, a process flow diagram, generally designated **2500**, for preclinical ultrasound imaging of a subject is provided. In a first step, **2502**, a platform, on which a subject is positionable is movably positioned. For example, a subject **S** may be movably positioned on a platform (e.g., **808**, Figure 8).

In a second step, **2504**, a spatial position of at least one ultrasound transducer relative to the platform may be controlled by at least one motion stage. For example, a spatial position of an ultrasound transducer **402** relative to a subject **S** may be controlled by two linear stages, an x-axis motion stage **504** and a y-axis motion stage **506** (Figure 5). In other examples, a spatial position of an ultrasound transducer **302** relative to a subject **S** may be controlled by two linear stages, a y-axis stage **306** and a z-axis stage **308** and a rotational stage, a Θ-axis stage **310** (Figure 3).

In a third step, **2506**, ultrasound image data of the subject may be acquired. For example, ultrasound image data of a subject may be acquired and transmitted to a computing platform for data processing and/or analysis.

It will be understood that various details of the subject matter described herein may be changed without departing from the scope of the subject matter described herein. Furthermore, the foregoing description is for the purpose of illustration only, and not for the purpose of limitation.

CLAIMS

What is claimed is:

1. An apparatus for preclinical ultrasound imaging of a subject, the apparatus comprising:

a platform on which a subject is positionable; and

at least one motion stage for controlling a spatial position of at least one ultrasound transducer relative to the platform in order to acquire ultrasound image data of the subject.

2. The apparatus of claim 1, further comprising an ultrasound imaging system, wherein the at least one ultrasound transducer is associated with the ultrasound imaging system.

3. The apparatus of claim 1, wherein the at least one motion stage is configured to move the at least one ultrasound transducer into at least a first spatial position and at least a second spatial position to acquire ultrasound image data of the subject at each spatial position.

4. The apparatus of claim 1, further comprising a computing platform associated with the apparatus and configured to register the ultrasound image data to a secondary image data set, of either a same or a different modality from the ultrasound image data, acquired prior to acquisition of the ultrasound image data in order to ensure accurate alignment between the ultrasound image data and the secondary image data set so that measurements made within the ultrasound image data and the secondary image data set have one to one correspondence.

5. The apparatus of claim 1, further comprising a reservoir, movable in relation to the platform, for containing a coupling medium.

6. The apparatus of claim 5, wherein the at least one ultrasound transducer is coupled to a bottom surface of the reservoir, such that

the reservoir and the at least one ultrasound transducer are configured to move relative to the platform on which the subject is positionable.

7. The apparatus of claim 5, wherein the at least one ultrasound transducer is configured to translate substantially either above and/or below the platform on which the subject is positionable.

8. The apparatus of claim 5, wherein the reservoir comprises a tank having a coupling medium impermeable membrane creating a seal between the subject and the coupling medium, or the reservoir comprises a bag creating a seal between the subject and the coupling medium in order to provide contact-free imaging between the at least one ultrasound transducer and the subject.

9. The apparatus of claim 1, wherein the at least one motion stage comprises a plurality of motion stages and the apparatus further comprises a motion control system configured to independently control motion of each of the plurality of motion stages.

10. The apparatus of claim 1, wherein the platform comprises fiducial landmarks for enabling registration of the ultrasound image data to at least one functional imaging modality.

11. The apparatus of claim 10, wherein the at least one functional imaging modality comprises at least one modality selected from the group consisting of: bioluminescence, fluorescence, cryoimaging, single-photon emission computerized tomography (SPECT), and positron emission tomography (PET).

12. The apparatus of claim 1, wherein the subject comprises a small animal, and wherein the at least one motion stage is movable to allow generation of a full body three-dimensional (3D) volume ultrasound image of the small animal.

13. A system for preclinical ultrasound imaging of a subject, the system comprising:

at least one ultrasound imaging system;

at least one ultrasound transducer associated with the at least one ultrasound imaging system and positionable relative to a subject; and

an apparatus comprising:

a platform on which the subject is positionable, and

at least one motion stage for controlling a spatial position of the at least one ultrasound transducer relative to the platform in order to acquire ultrasound image data of the subject.

14. The system of claim 13, wherein the at least one motion stage is configured to move the at least one ultrasound transducer into at least a first spatial position and at least a second spatial position to acquire ultrasound image data of the subject at each spatial position.

15. The system of claim 14, further comprising a computing platform associated with the apparatus and configured to register the ultrasound image data to a secondary image data set, of either a same or a different modality from the ultrasound image data, acquired prior to acquisition of the ultrasound image data in order to ensure accurate alignment between the ultrasound image data and the secondary image data set so that measurements made within the ultrasound image data and the secondary image data set have one to one correspondence.

16. The system of claim 13, wherein the apparatus comprises a reservoir, movable in relation to the platform, for containing a coupling medium.

17. The system of claim 16, wherein the reservoir comprises a tank having a coupling medium impermeable membrane creating a seal between the subject and the coupling medium, or the reservoir

comprises a bag creating a seal between the subject and the coupling medium in order to provide contact-free imaging between the at least one ultrasound transducer and the subject.

18. The system of claim 13, wherein the at least one motion stage comprises a plurality of motion stages and the apparatus further comprises a motion control system configured to independently control motion of each of the plurality of motion stages.

19. The system of claim 13, wherein the platform comprises fiducial landmarks for enabling registration of the ultrasound image data to at least one functional imaging modality.

20. The system of claim 19, wherein the at least one functional imaging modality comprises at least one modality selected from the group consisting of: bioluminescence, fluorescence, cryoimaging, single-photon emission computerized tomography (SPECT), and positron emission tomography (PET).

21. The system of claim 13, wherein the subject comprises a small animal, and wherein the at least one motion stage is movable to allow generation of a full body three-dimensional (3D) volume ultrasound image of the small animal.

22. A method for preclinical ultrasound imaging of a subject, the method comprising:

movably positioning a platform, on which a subject is positionable;

controlling, by at least one motion stage, a spatial position of at least one ultrasound transducer relative to the platform; and

acquiring ultrasound image data of the subject.

23. A system for preclinical ultrasound raster scanning of at least one organ or tissue in a subject, the system comprising:

at least one ultrasound imaging system;

at least one ultrasound transducer associated with the at least one ultrasound imaging system and positionable relative to a subject;

an apparatus comprising:

a platform on which the subject is positionable, and

at least one motion stage for controlling a spatial position of the at least one ultrasound transducer relative to the platform in order to acquire ultrasound image data of the subject; and

a computing platform having a hardware processor and a memory and being associated with the at least one ultrasound imaging system and the apparatus, wherein the computing platform is configured to collect one-dimensional (1D) ultrasound scan lines through translation of the at least one ultrasound transducer through a raster scan grid aligned over an approximation of a location of at least one organ or tissue in the subject, and to analyze the 1D ultrasound scan lines to build a two-dimensional (2D) or three-dimensional (3D) mesh of relevant surfaces of the at least one organ or tissue.

24. The system of claim 23, wherein the at least one organ or tissue in the subject is a heart.

25. The system of claim 23, wherein the computing platform is configured to localize walls of surfaces or interfaces in the at least one organ or tissue to build the 3D mesh of the relevant surfaces of the at least one organ or tissue.

26. The system of claim 23, wherein the computing platform is configured to acquire b-mode images by translating the collected 1D ultrasound lines along a predetermined trajectory to build a 2D ultrasound image.

27. The system of claim 26, wherein the computing platform is configured to register the acquired ultrasound image to previously acquired

functional images of the at least one organ or tissue in the subject from at least one functional imaging modality in order to target the at least one organ or tissue in the subject at a same location of the at least one organ or tissue in the subject as indicated in the previously acquired functional images, via controlling the spatial position of the at least one ultrasound transducer relative to the platform.

28. The system of claim 27, wherein the platform comprises fiducial landmarks for registering the ultrasound image to the previously acquired functional images from the at least one functional imaging modality.

29. The system of claim 28, wherein the at least one functional imaging modality comprises at least one modality selected from the group consisting of: bioluminescence, fluorescence, cryoimaging, single-photon emission computerized tomography (SPECT), and positron emission tomography (PET).

30. The system of claim 23, wherein there is at least one motion stage for controlling the at least one ultrasound transducer over the raster scan grid.

31. The system of claim 23, wherein the computing platform is configured to perform passive gating on the acquired 1D ultrasound images to remove physio-induced motion.

32. The system of claim 23, wherein the computing platform is configured to refine the 3D mesh.

33. A method for preclinical ultrasound raster scanning of at least one organ or tissue in a subject, the method comprising:

positioning a subject on a platform;

controlling a spatial position of at least one ultrasound transducer relative to the platform in order to acquire ultrasound image data of the subject;

collecting one-dimensional (1D) ultrasound scan lines by translating the at least one ultrasound transducer through a raster scan grid aligned over an approximation of a location of at least one organ or tissue in the subject; and

analyzing the 1D ultrasound scan lines to build a two-dimensional (2D) or three-dimensional (3D) mesh of relevant surfaces of the at least one organ or tissue.

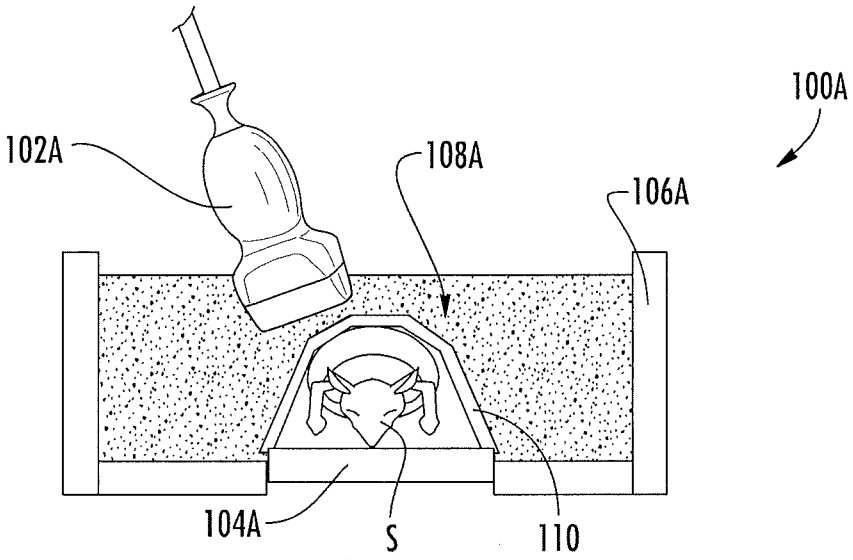

FIG. 1A

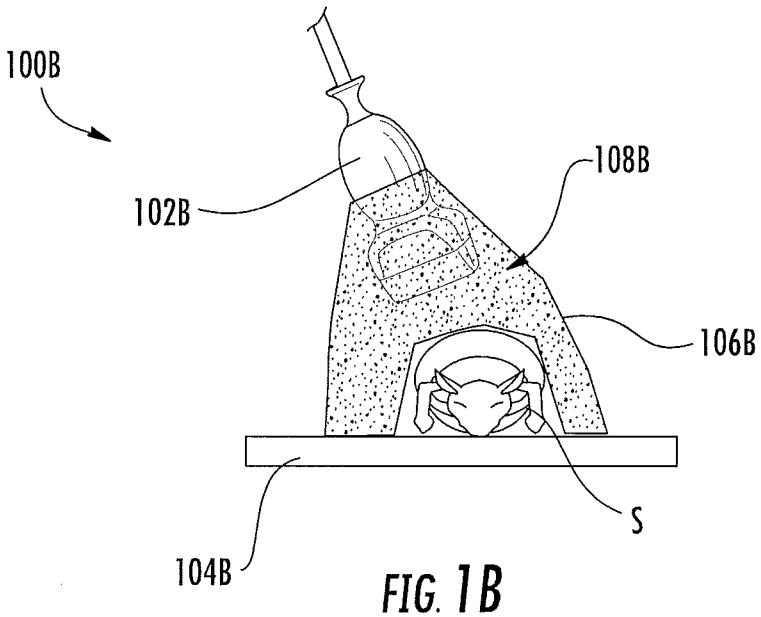

FIG. 1B

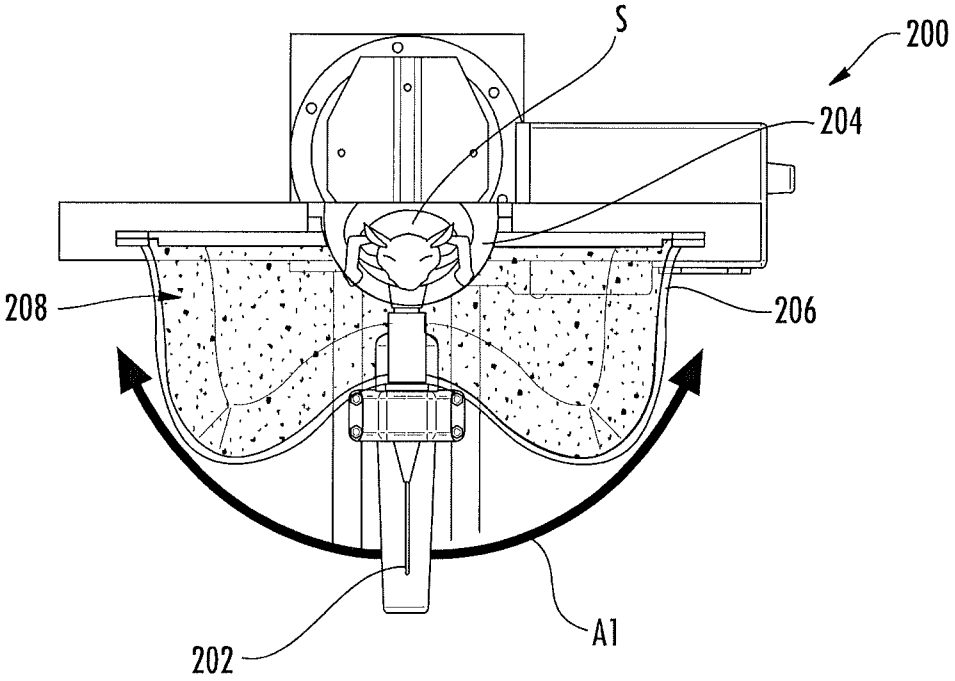

FIG. 2A

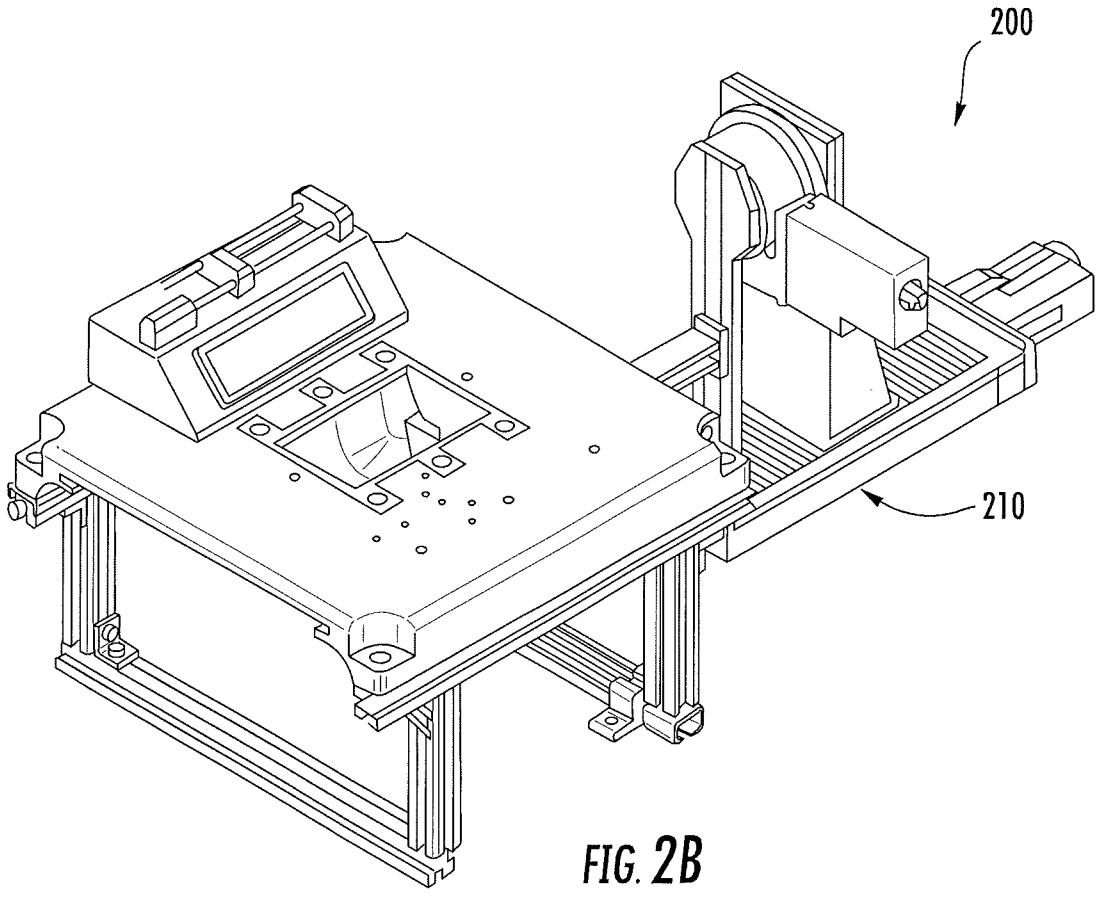

FIG. 2B

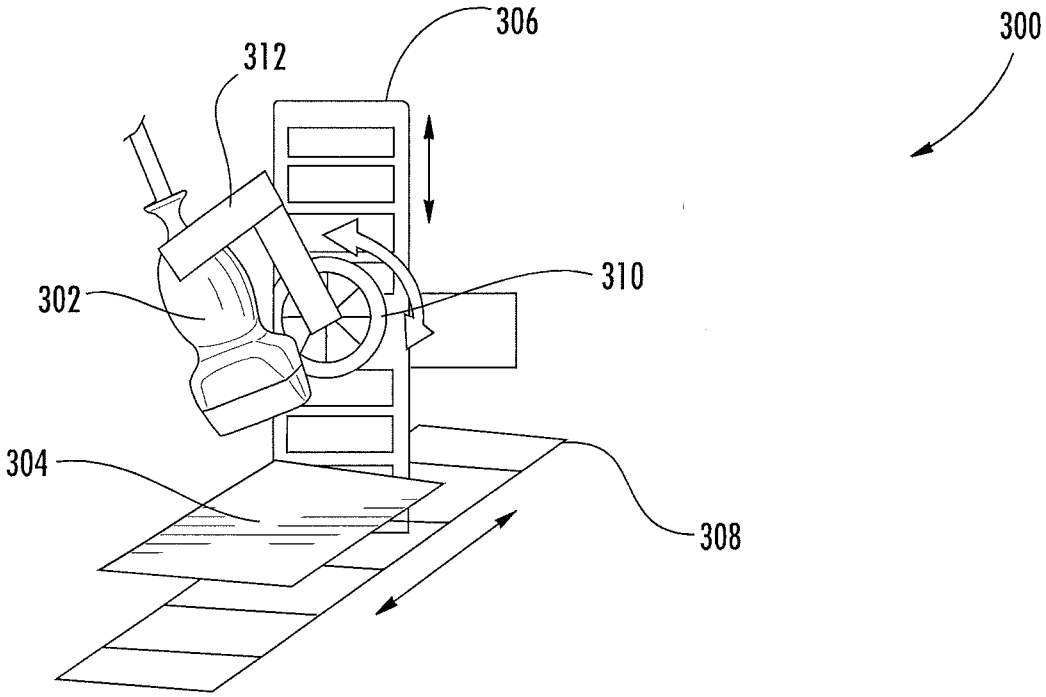

FIG. 3

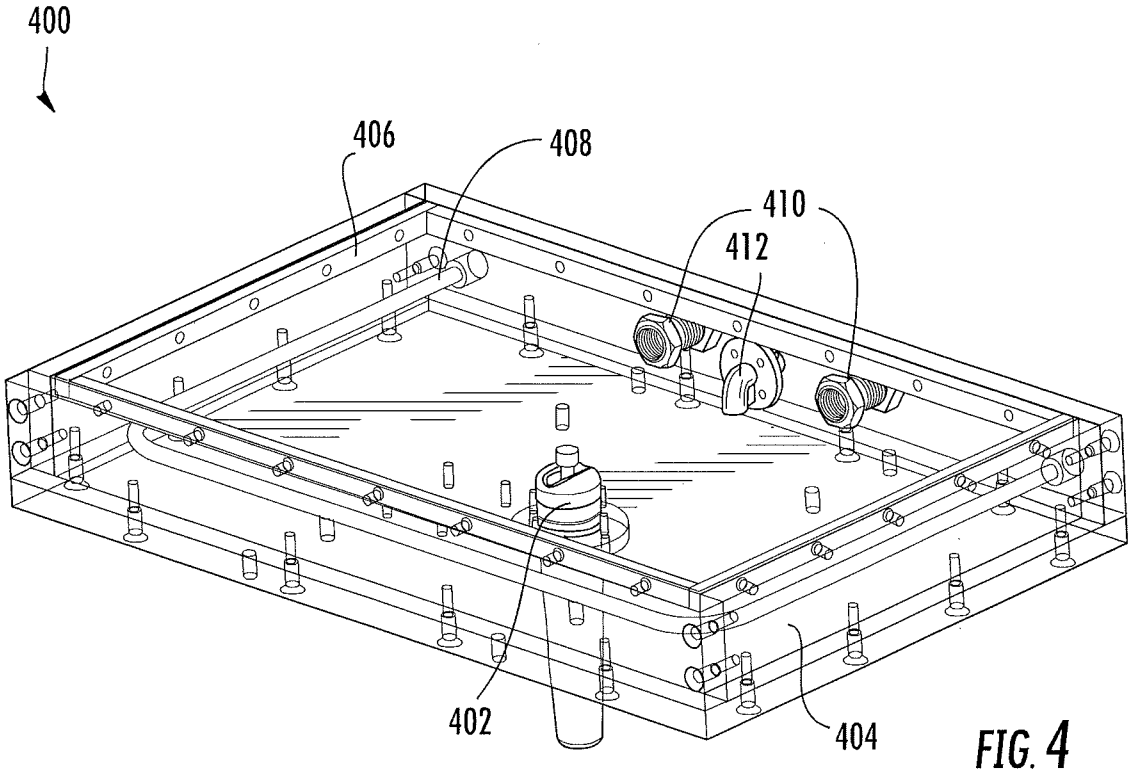
400
406
408
410
412
402
404

FIG. 4

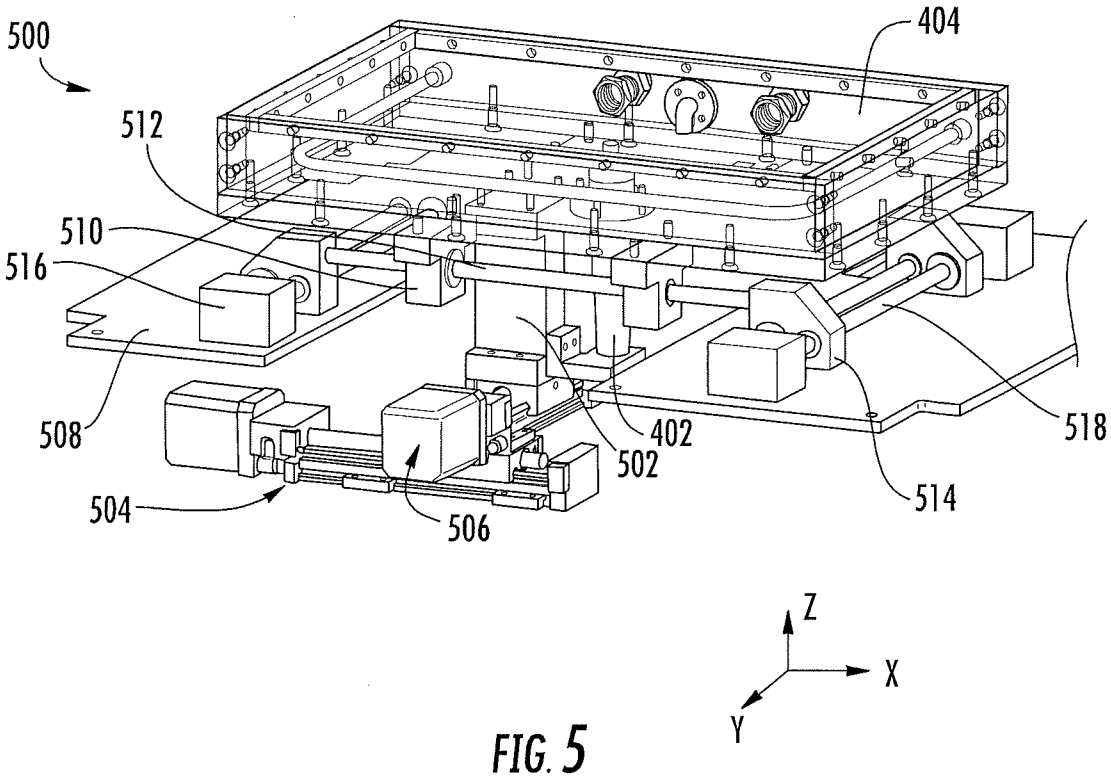
500
404
512
510
516
508
504
506
402
502
514
518
Z
X
Y

FIG. 5

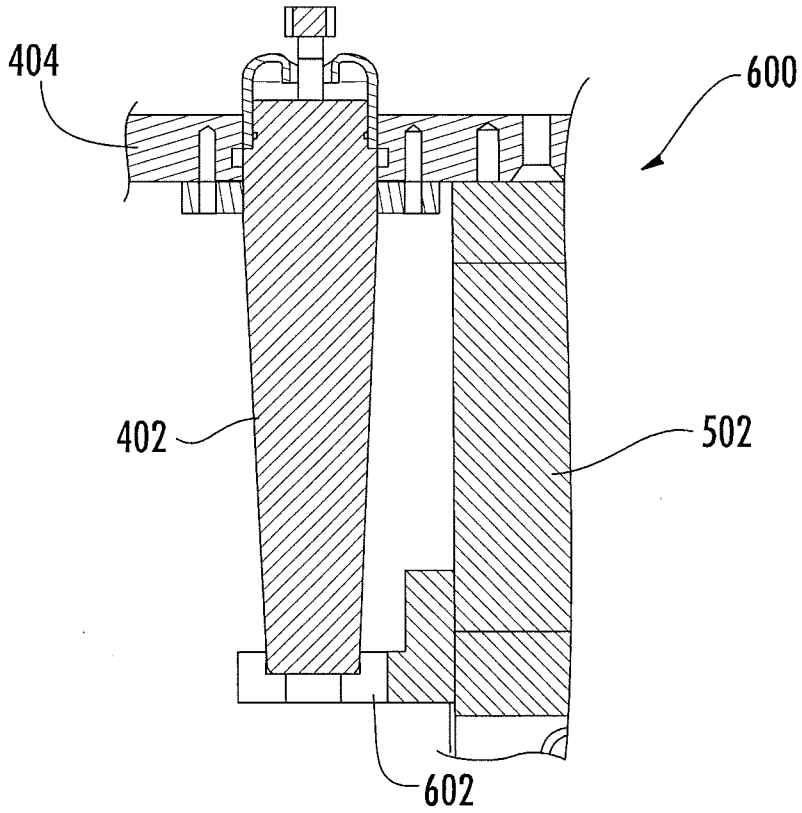

FIG. 6

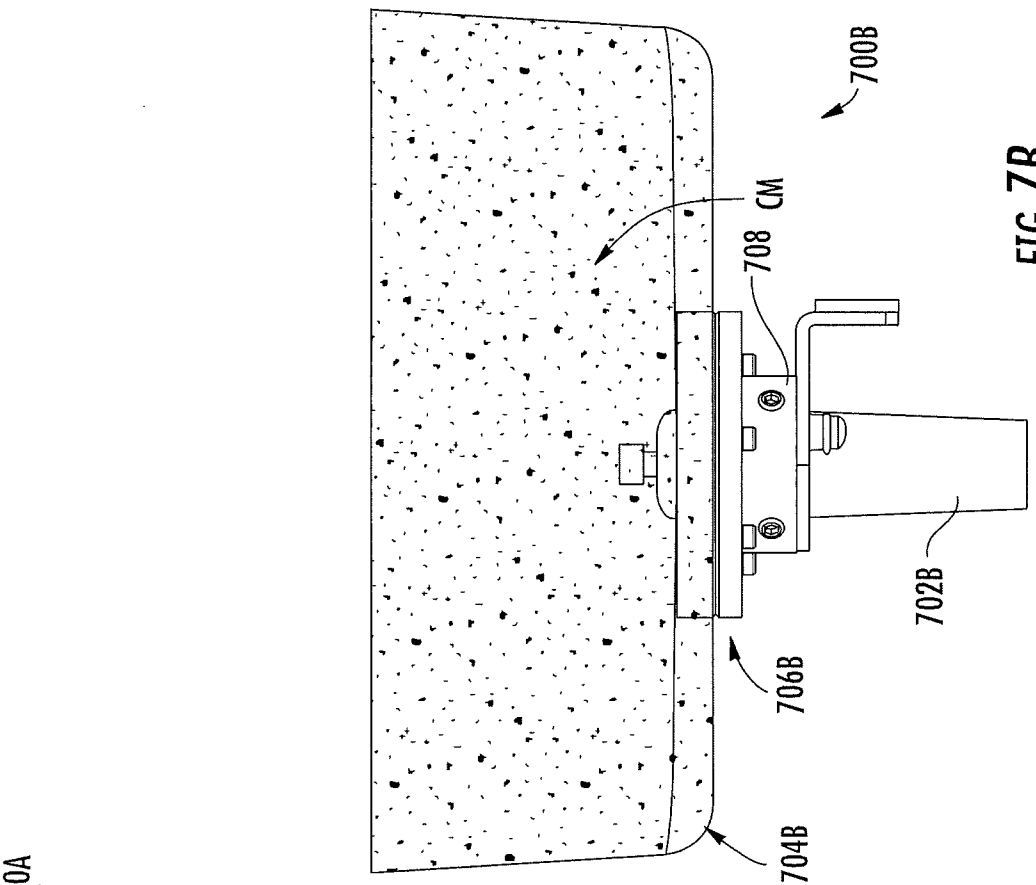

FIG. 7B

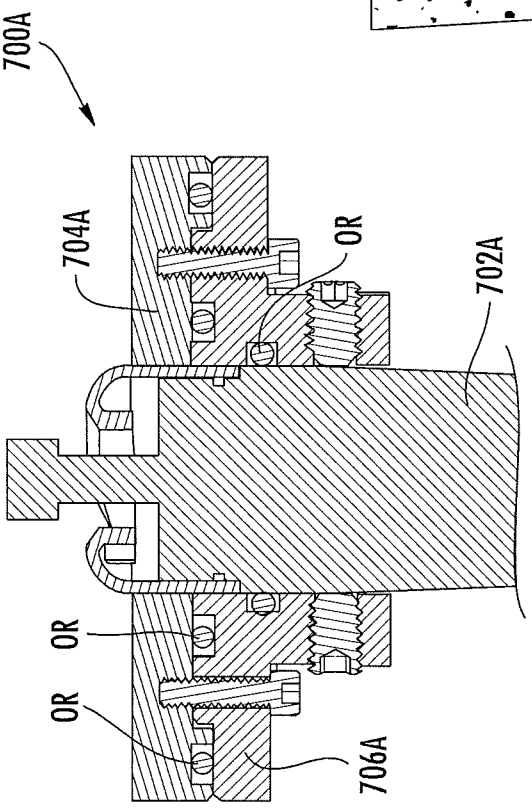

FIG. 7A

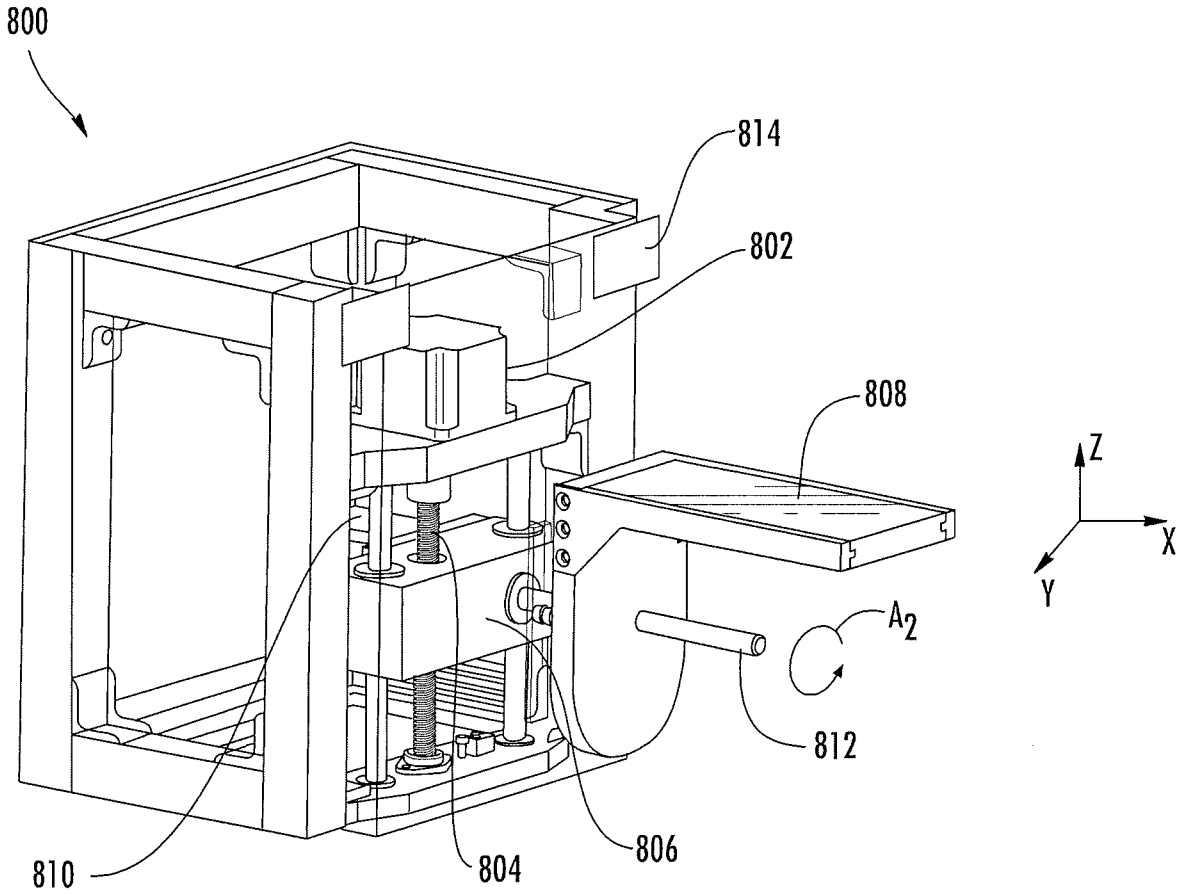

FIG. 8

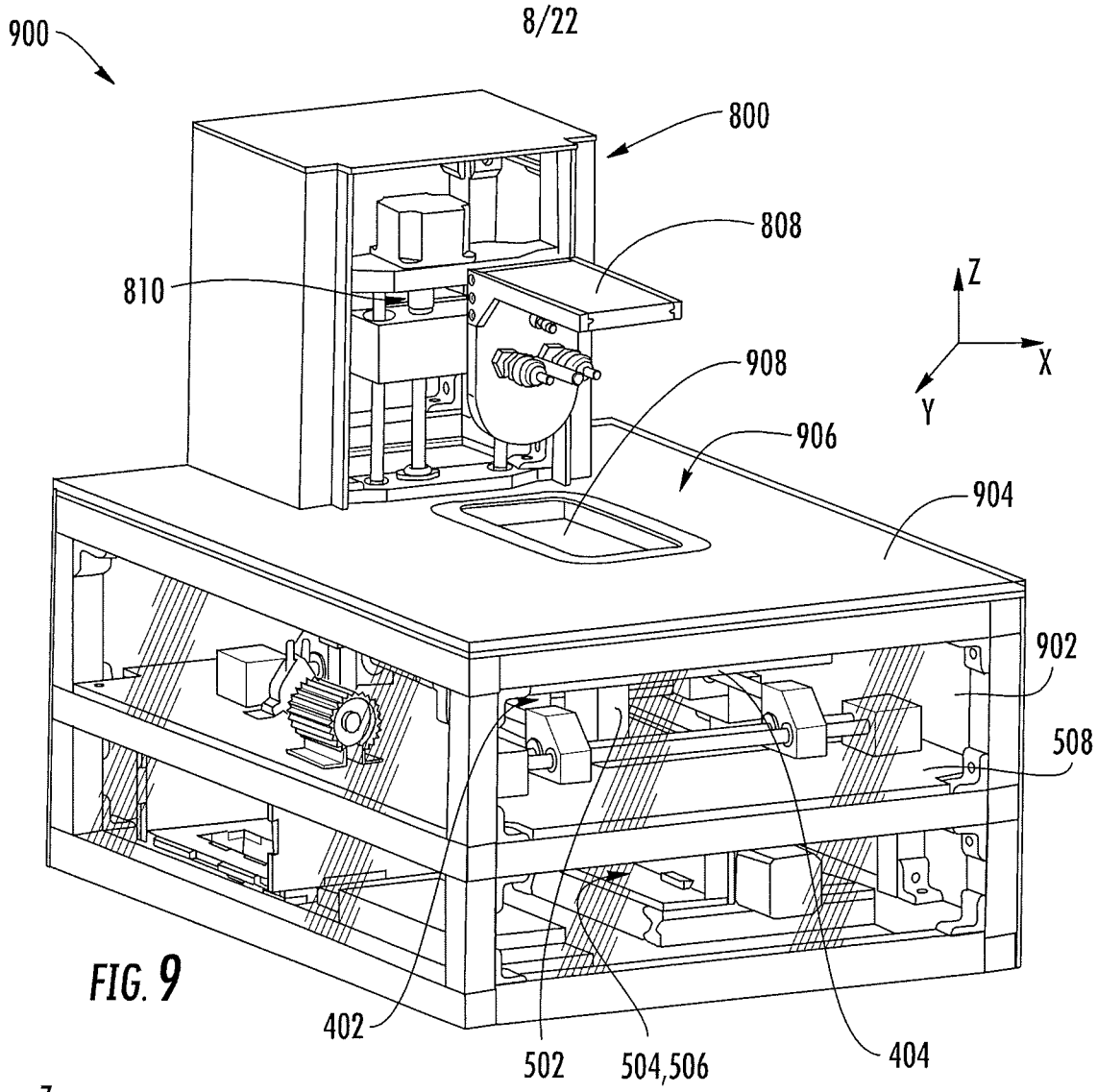
900
800
808
810
908
906
904
902
508
Z
X
Y
402
502
504,506
404

FIG. 9

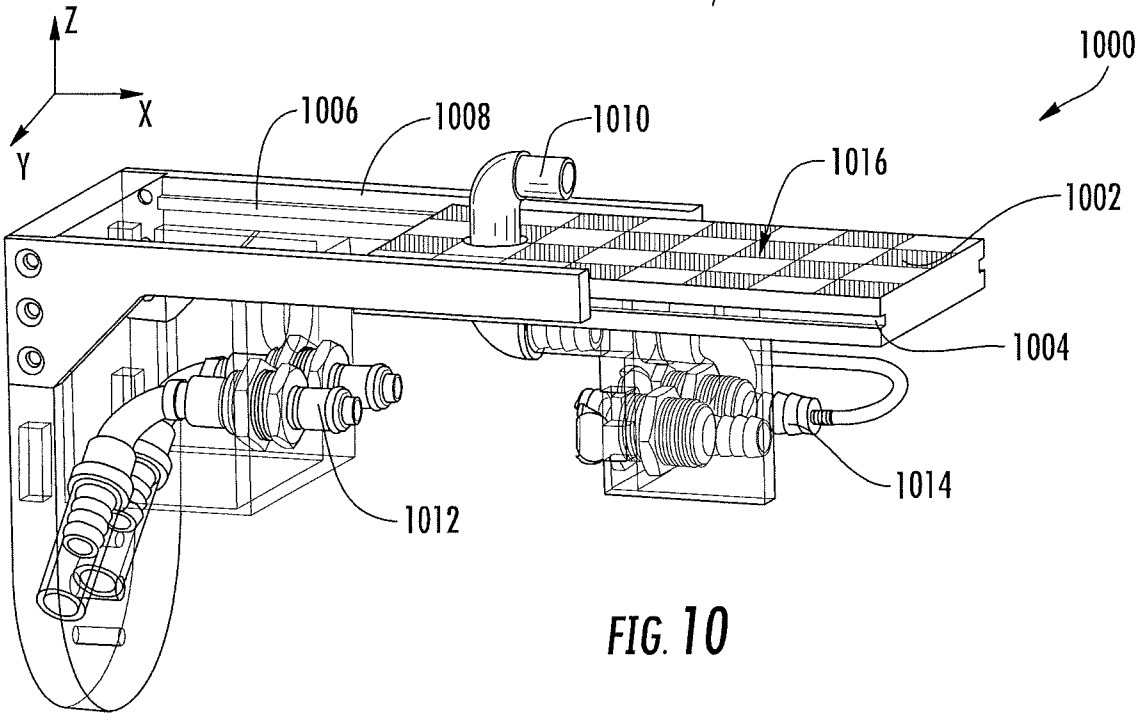
Z
X
Y
1000
1006
1008
1010
1016
1002
1004
1012
1014

FIG. 10

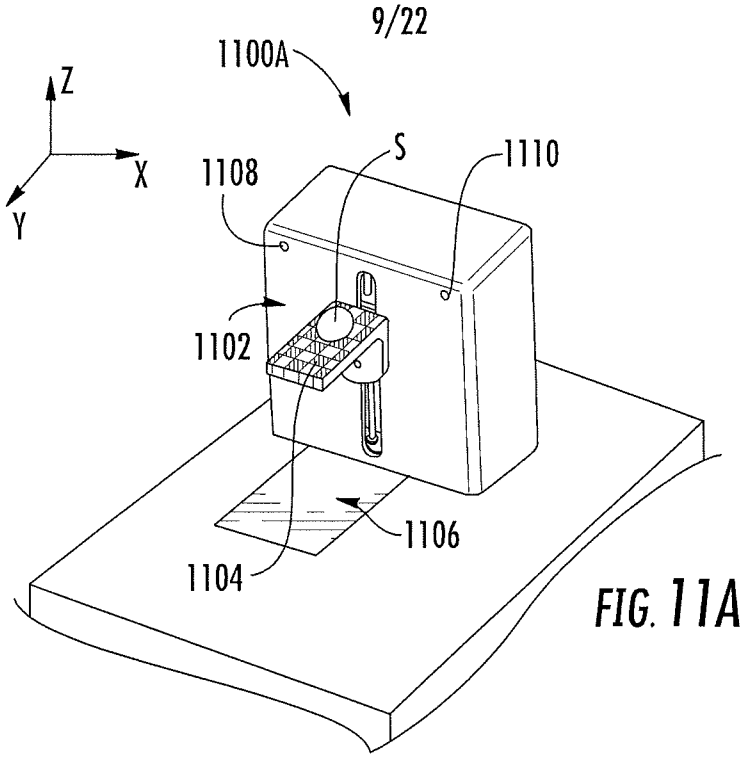

FIG. 11A

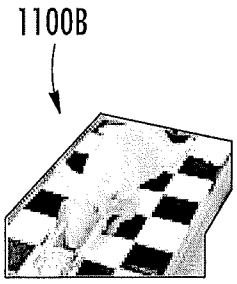

FIG. 11B

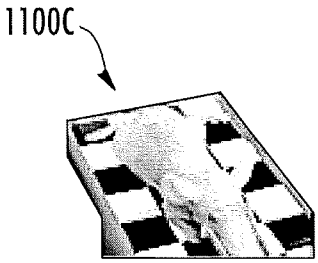

FIG. 11C

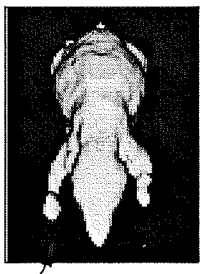

FIG. 11D

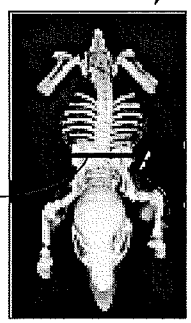

FIG. 11E

FIG. 11F

FIG. 11G

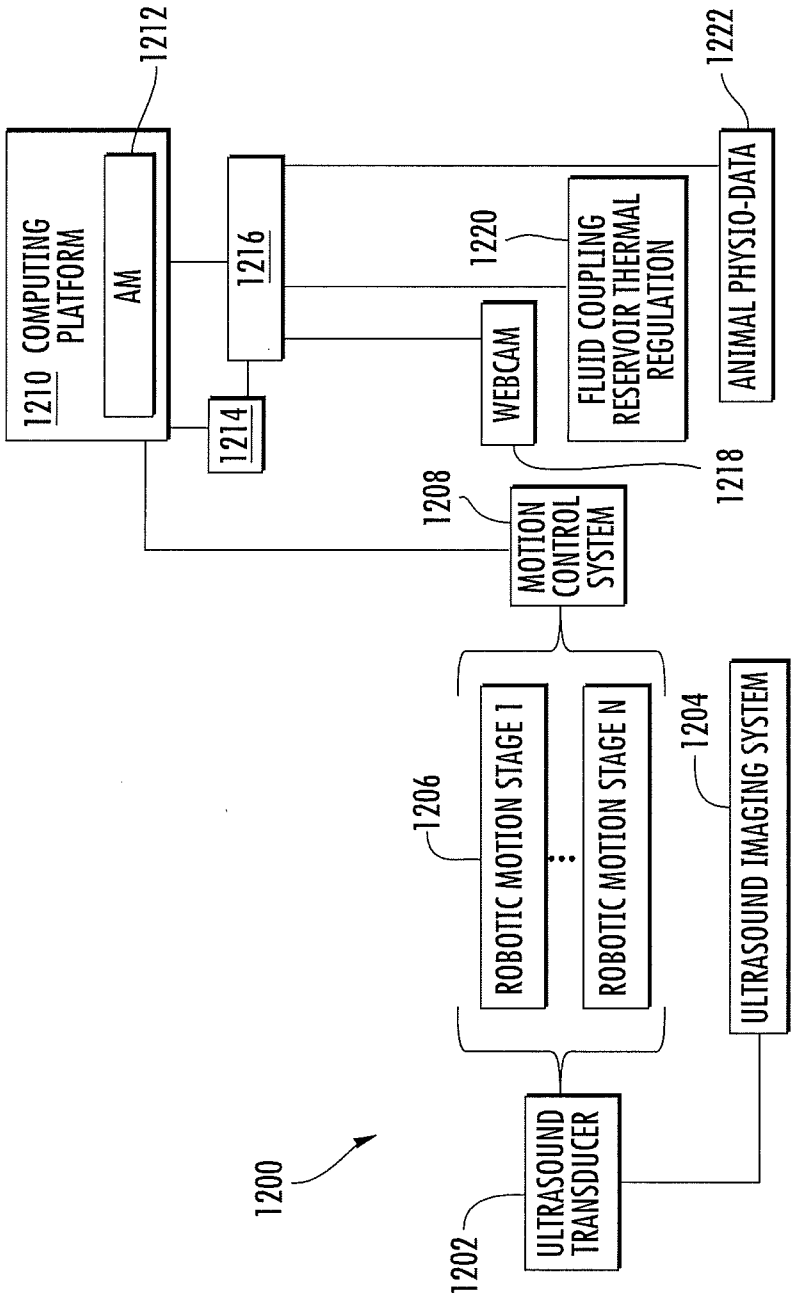
1200
1202
ULTRASOUND TRANSDUCER
1204
ULTRASOUND IMAGING SYSTEM
1206
ROBOTIC MOTION STAGE 1
ROBOTIC MOTION STAGE N
1208
MOTION CONTROL SYSTEM
1210 COMPUTING PLATFORM
AM
1212
1214
1216
1218
WEBCAM
1220
FLUID COUPLING RESERVOIR THERMAL REGULATION
1222
ANIMAL PHYSIO-DATA

FIG. 12

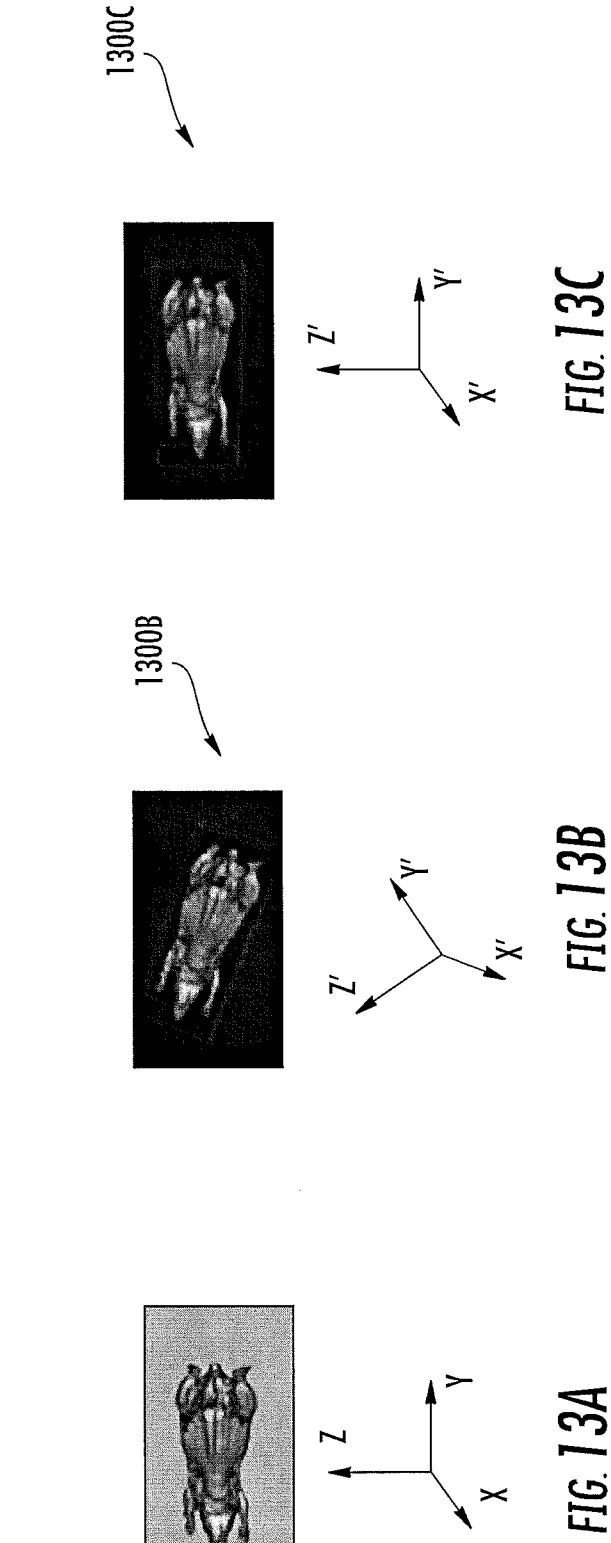

FIG. 13C

FIG. 13B

FIG. 13A

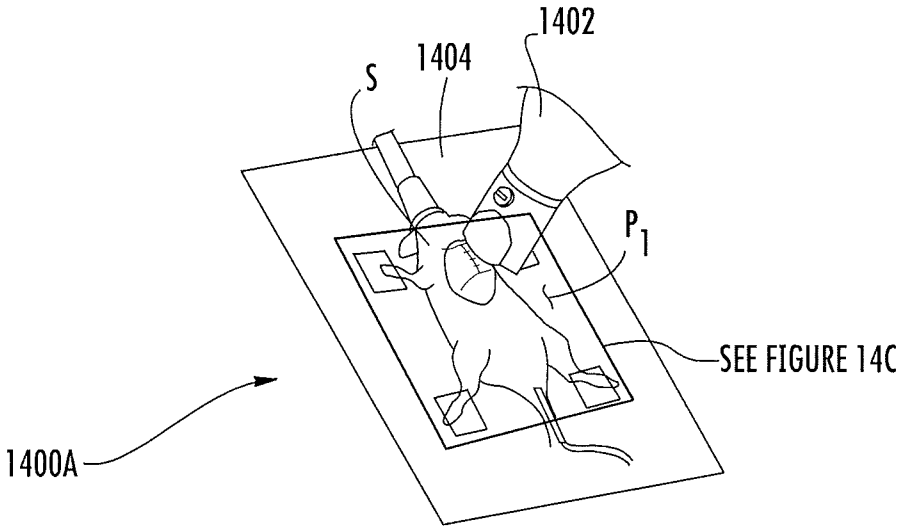

FIG. 14A

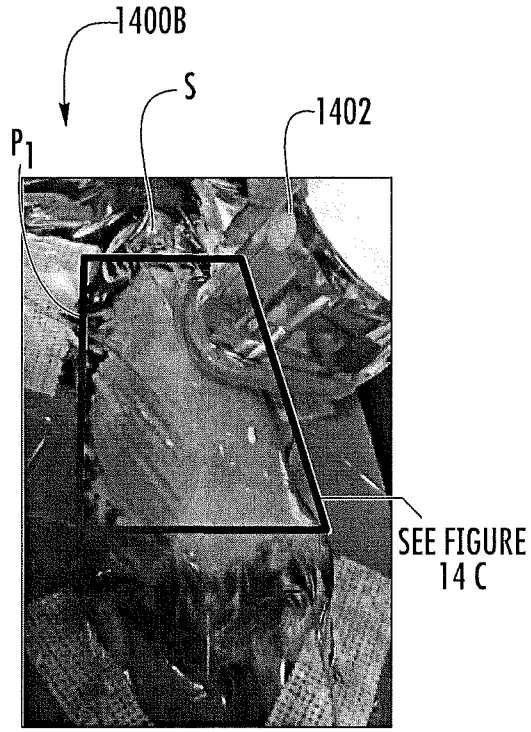

FIG. 14B

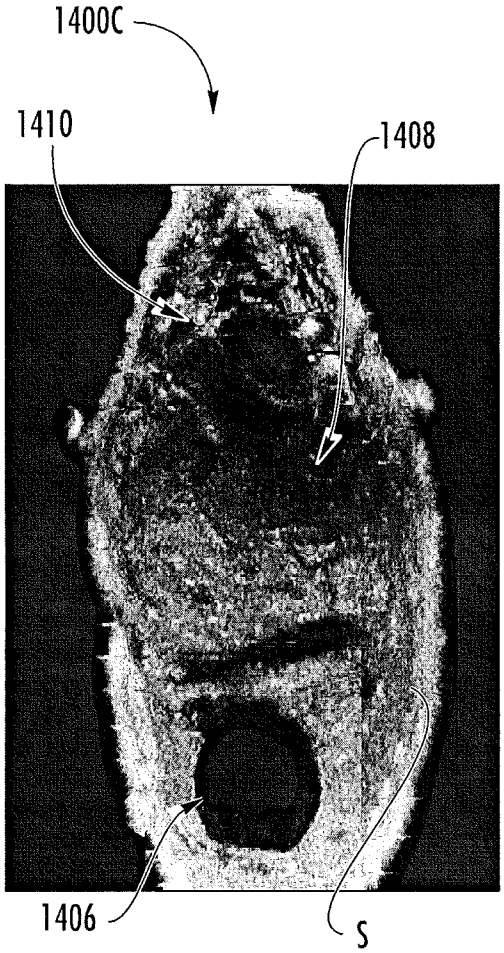

FIG. 14C

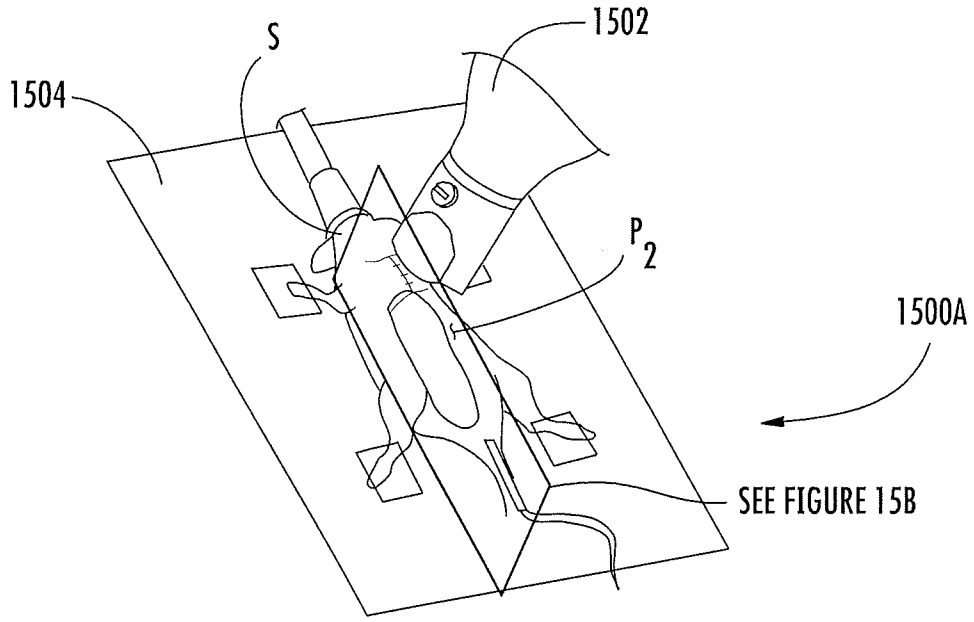

FIG. 15A

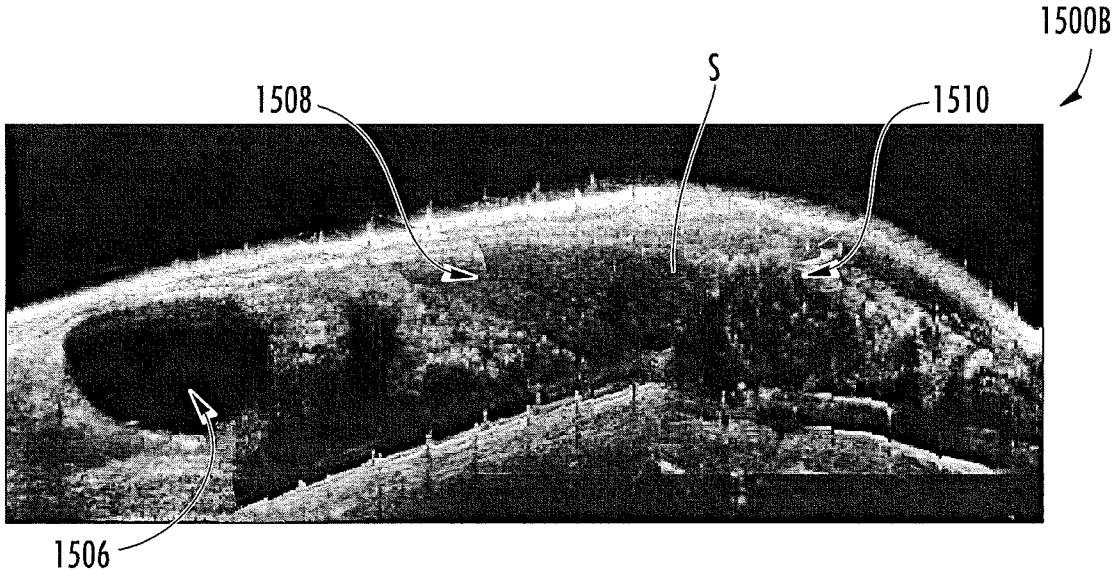

FIG. 15B

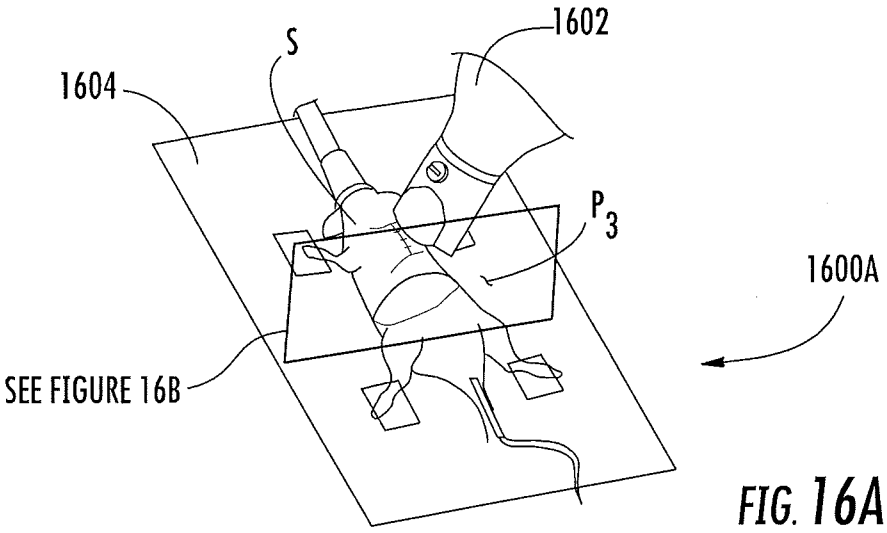

FIG. 16A

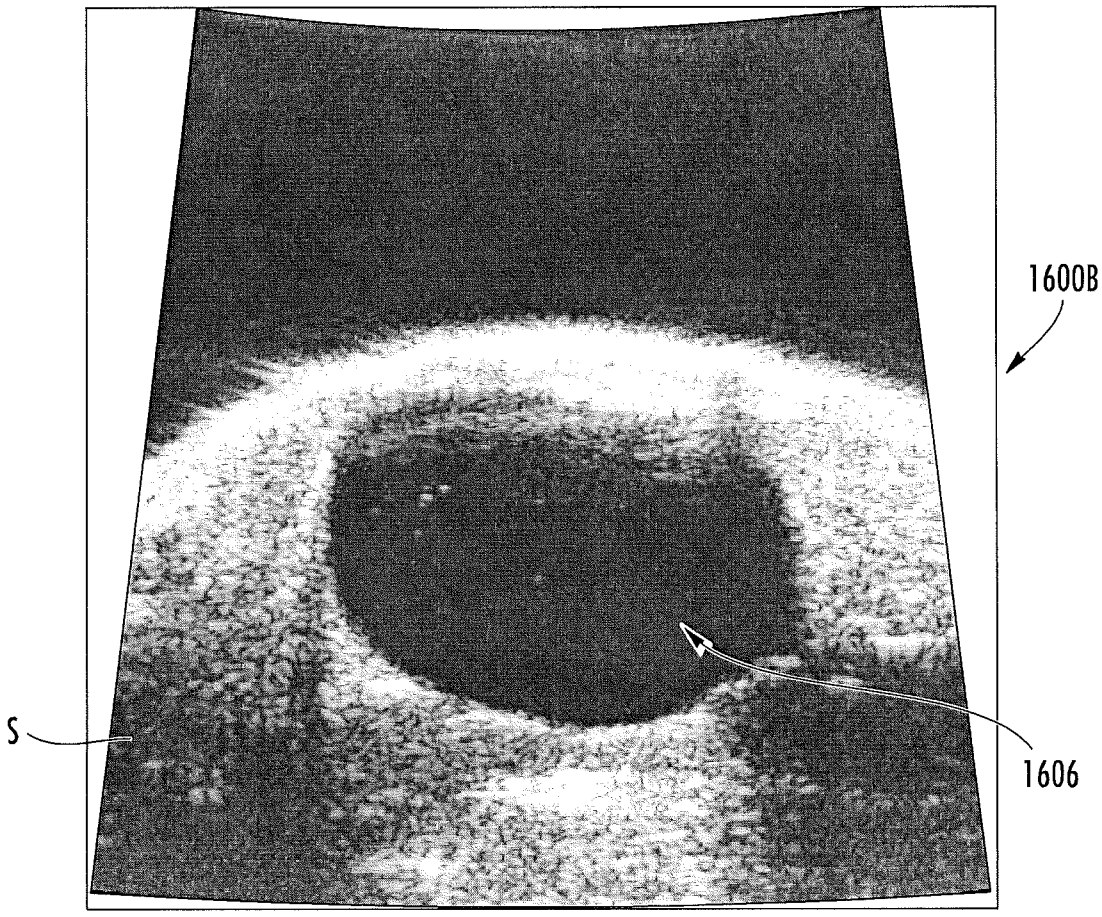

FIG. 16B

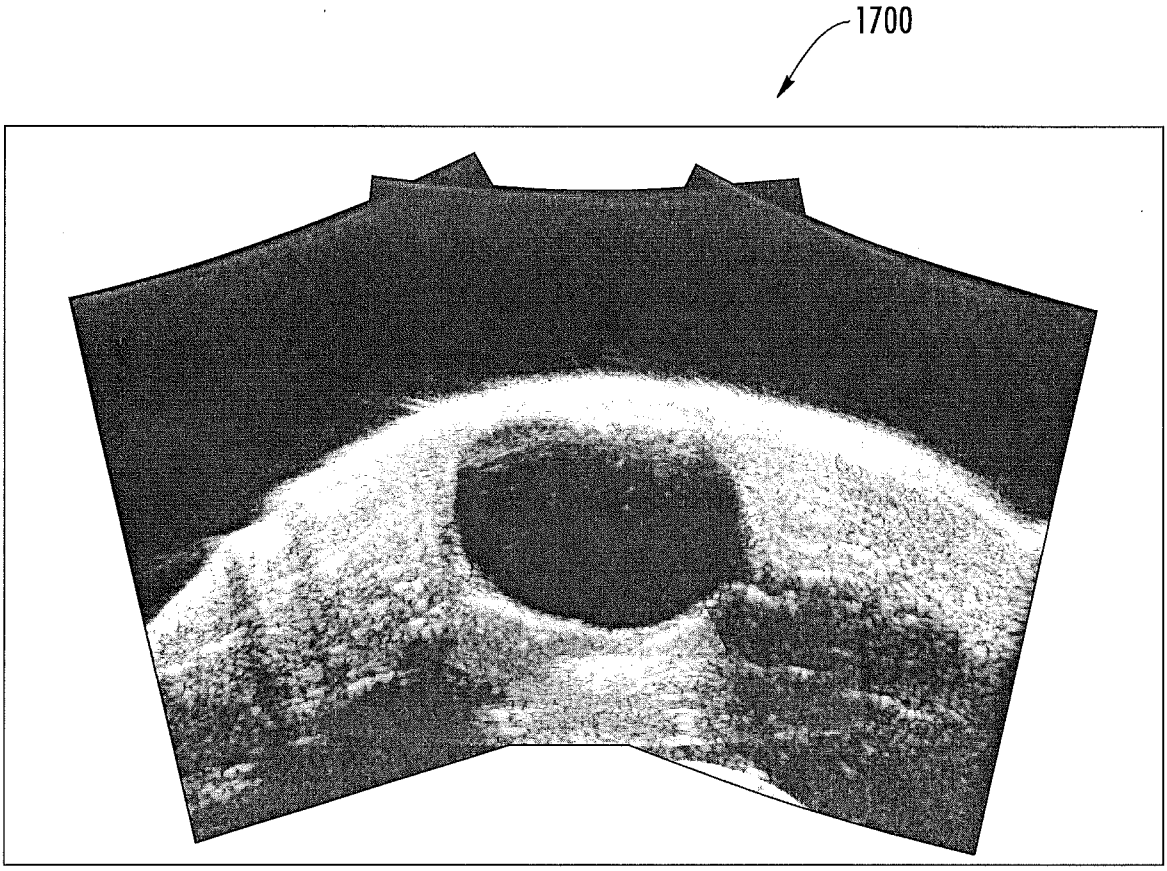

FIG. 17

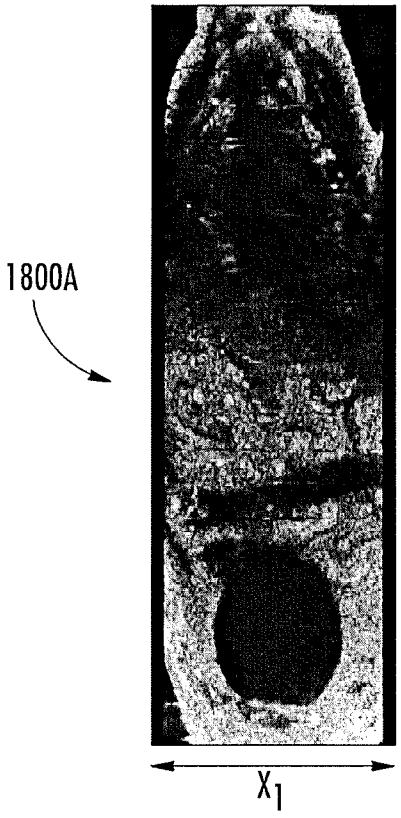

FIG. 18A

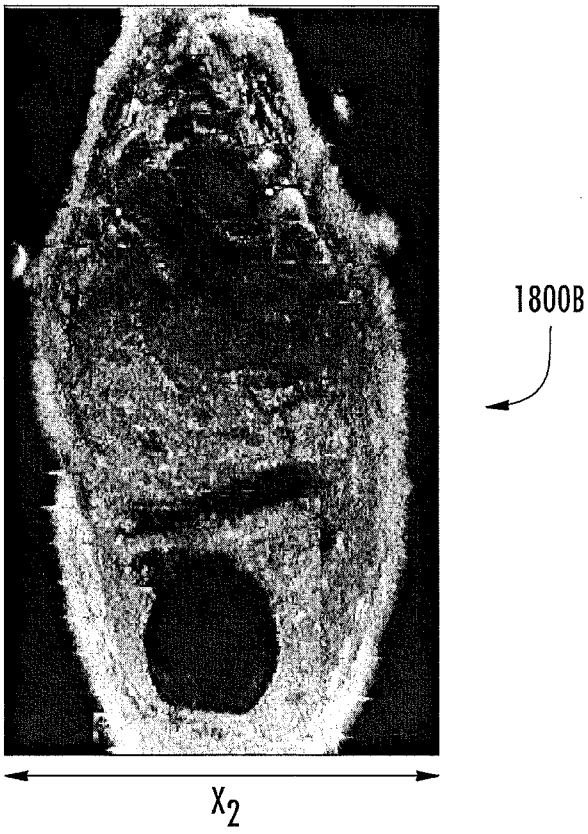

FIG. 18B

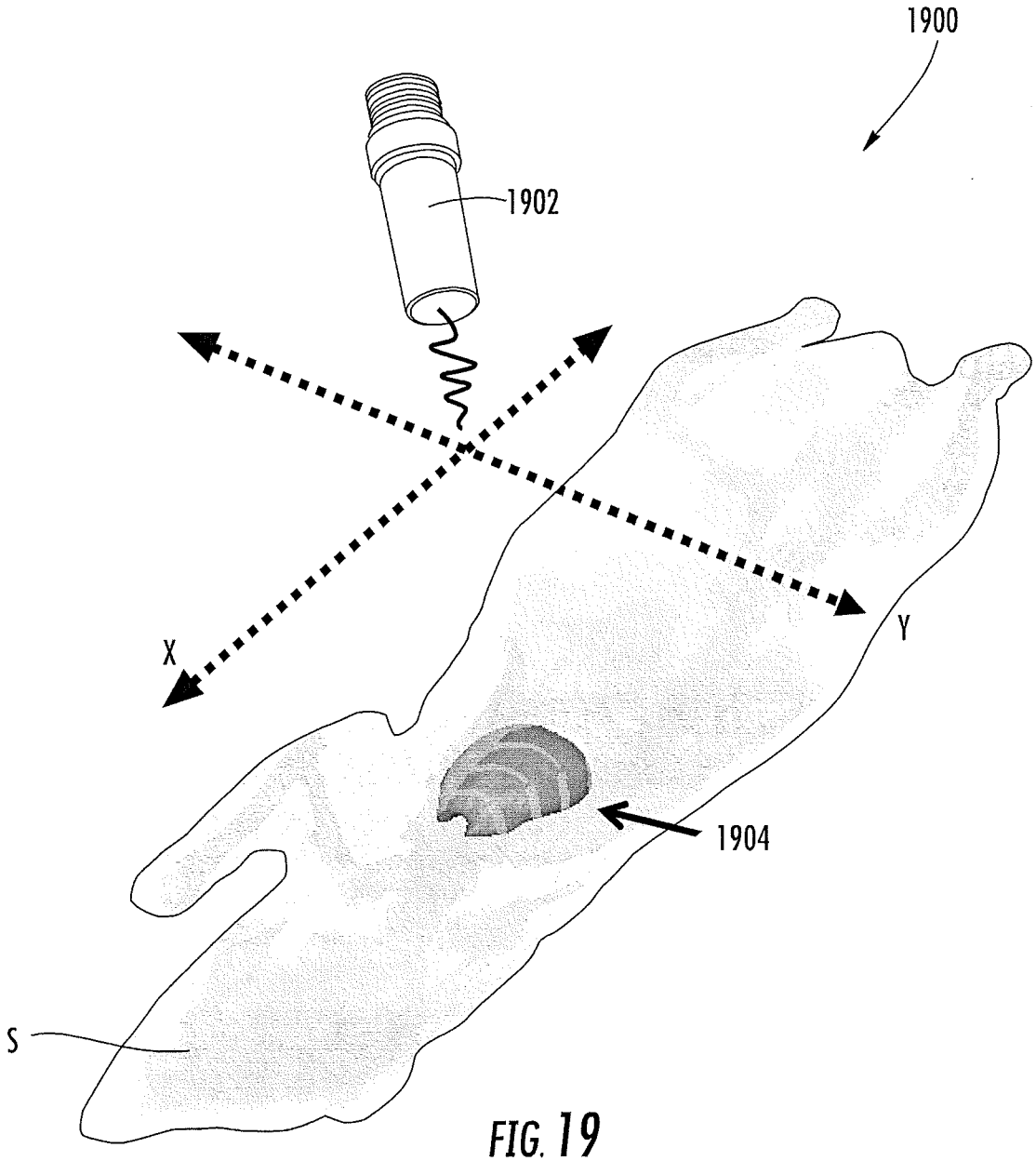

FIG. 19

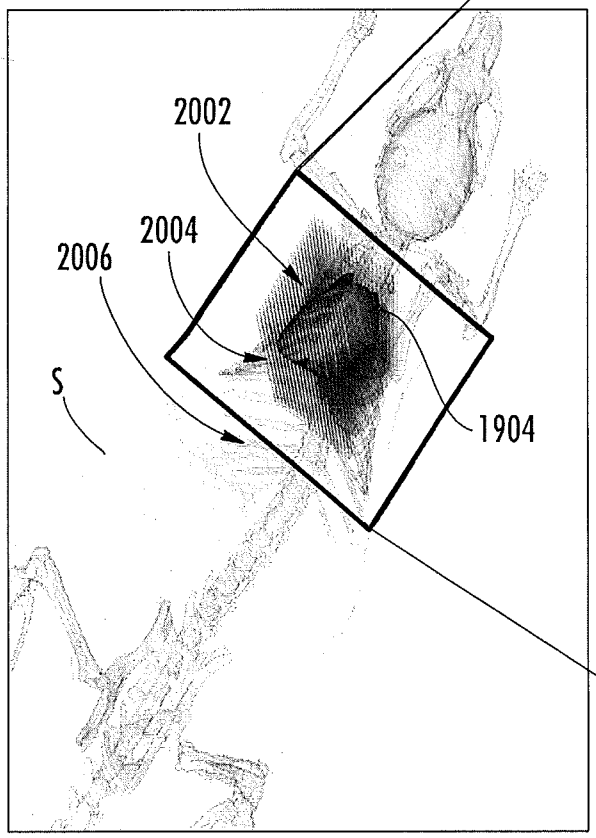

FIG. 20A

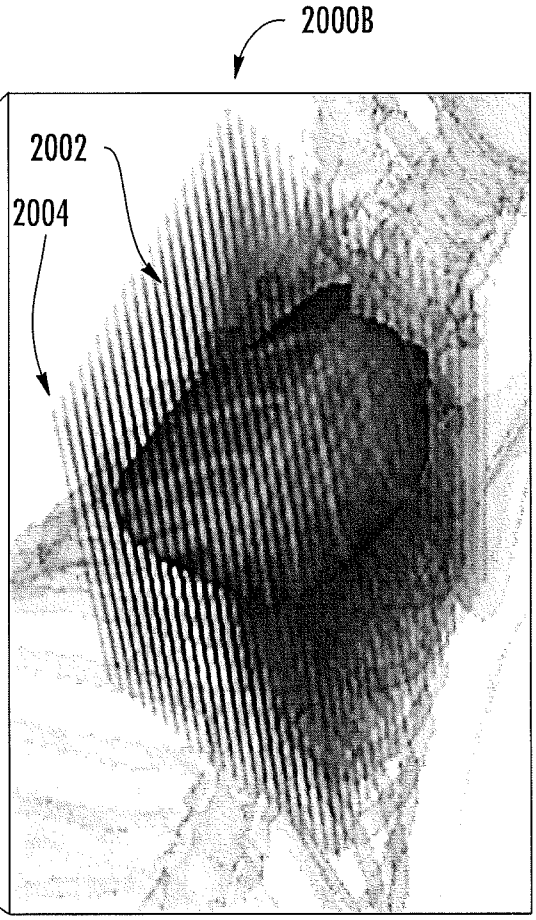

FIG. 20B

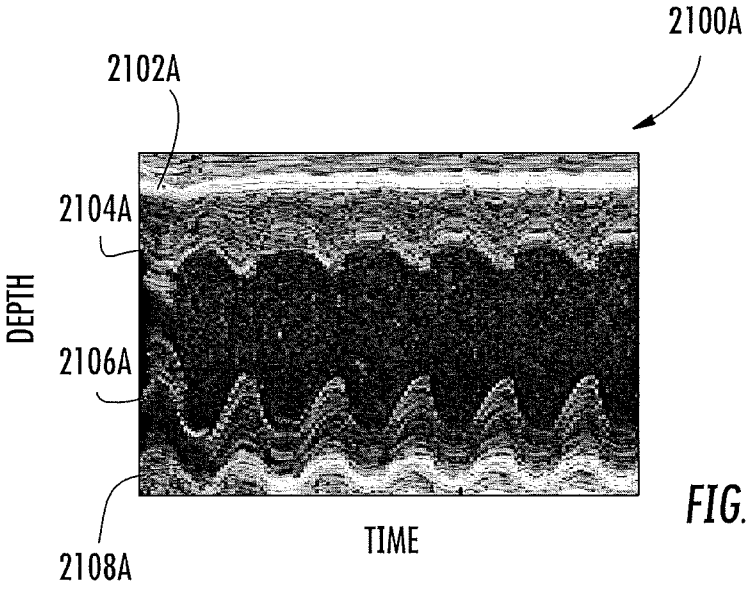

FIG. 21A

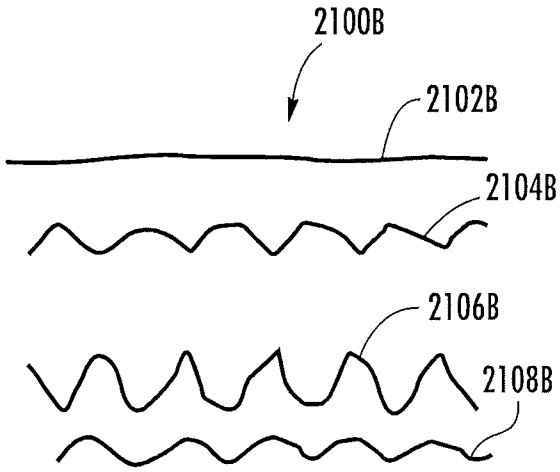

FIG. 21B

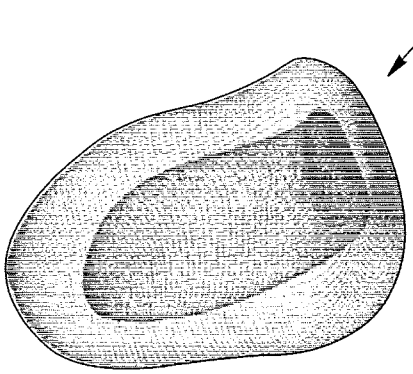

FIG. 22

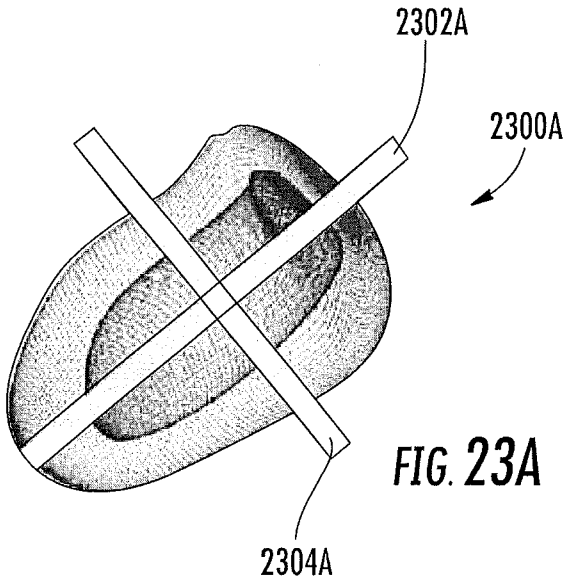

FIG. 23A

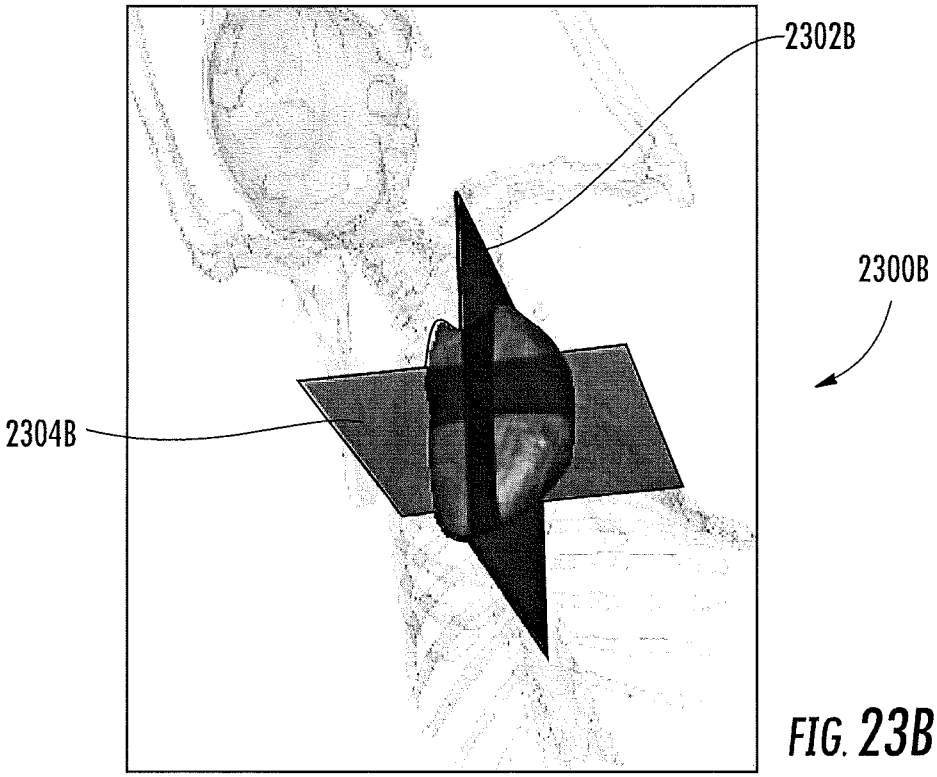

FIG. 23B

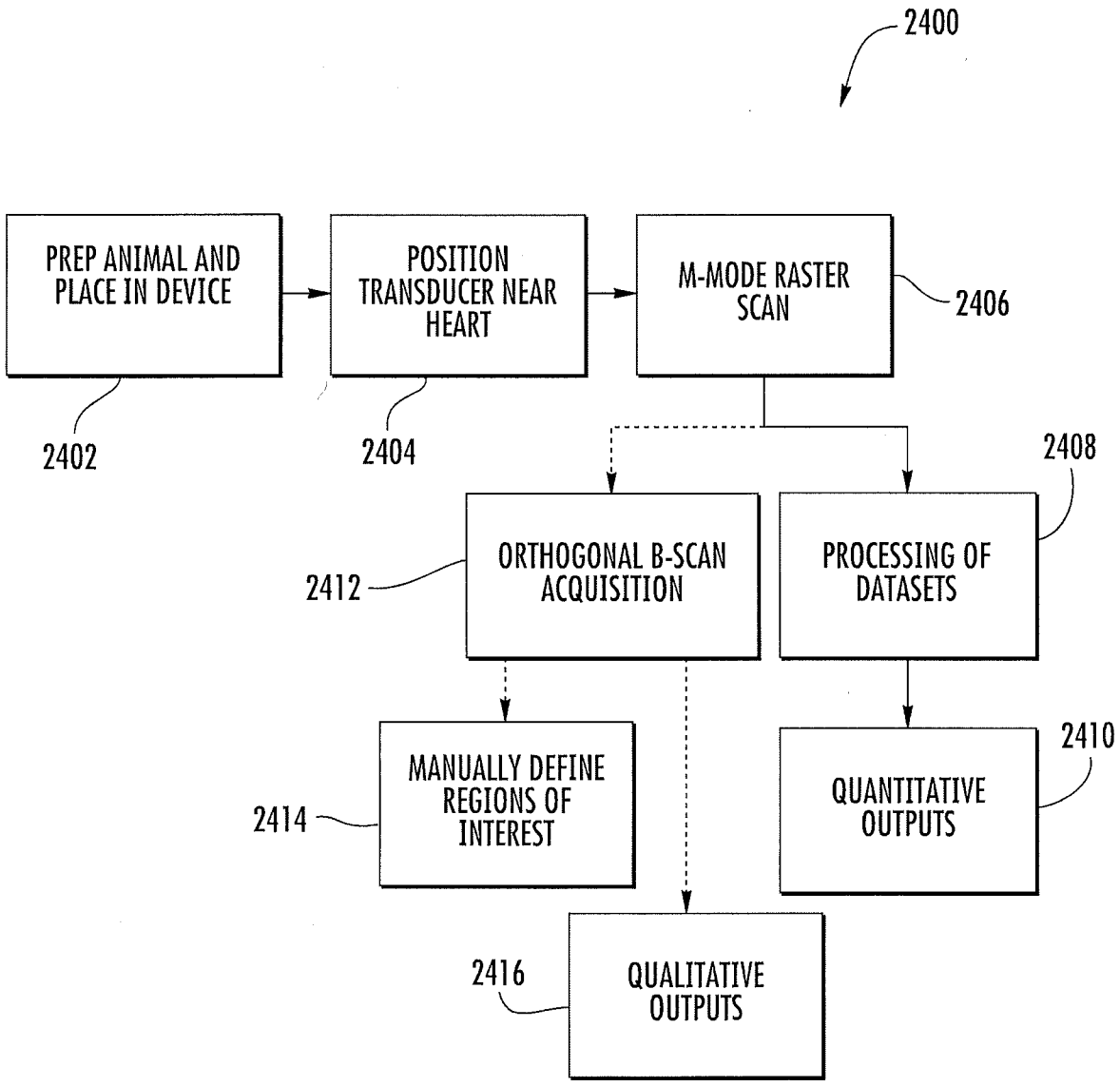
2400
PREP ANIMAL AND PLACE IN DEVICE
POSITION TRANSDUCER NEAR HEART
M-MODE RASTER SCAN
2406
2402
2404
2408
2412
ORTHOGONAL B-SCAN ACQUISITION
PROCESSING OF DATASETS
2410
MANUALLY DEFINE REGIONS OF INTEREST
2414
QUANTITATIVE OUTPUTS
2416
QUALITATIVE OUTPUTS

FIG. 24

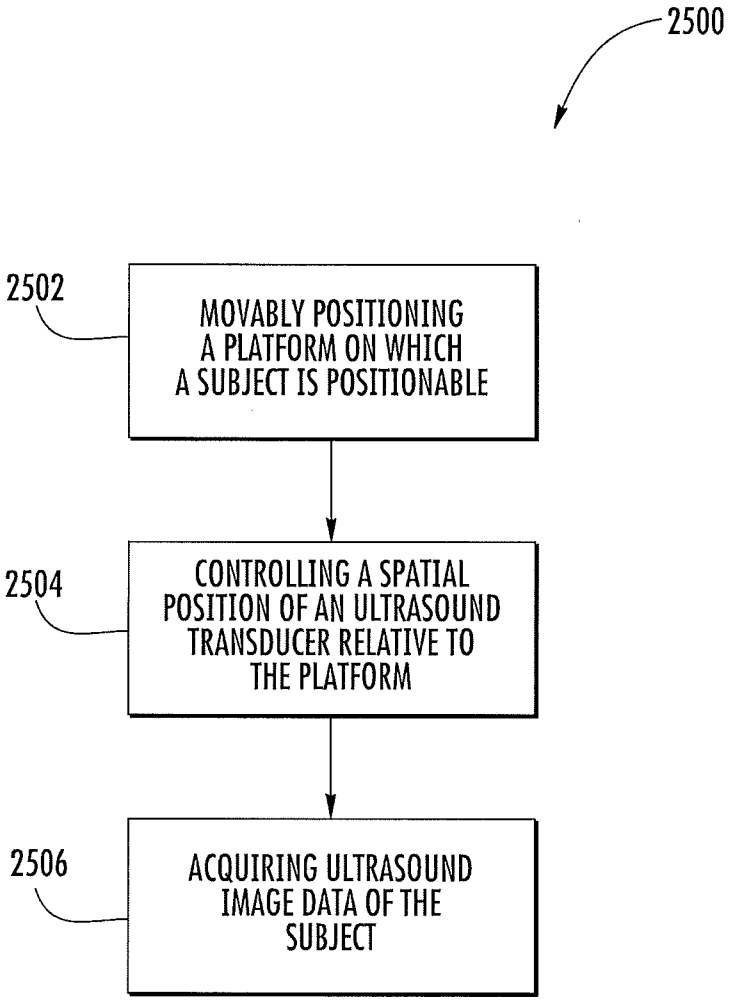
2500
2502
MOVABLY POSITIONING A PLATFORM ON WHICH A SUBJECT IS POSITIONABLE
2504
CONTROLLING A SPATIAL POSITION OF AN ULTRASOUND TRANSDUCER RELATIVE TO THE PLATFORM
2506
ACQUIRING ULTRASOUND IMAGE DATA OF THE SUBJECT

FIG. 25

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 2016/014685

A. CLASSIFICATION OF SUBJECT MATTER

A61B 8/00 *(2006.01)*
G01N 29/06 *(2006.01)*

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)

A61B 8/00, G01N 29/06

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

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

Google Patents, Patentscope, USPTO DB, Espacenet, DWPI, CIPO (Canada PO), SIPO DB, AIPN, DEPATISnet, VINITI, SCSML.FSSI.RU, PatSearch (RUPTO internal)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2002/0099290 A1 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) 25.07.2002, abstract, paragraphs [0017], [0018], [0023], [0025], [0045], claims 1, 22, fig. 1	1-3, 5-7, 8, 10, 13, 14, 16, 17, 19, 22, 23, 25, 26, 30, 33
Y		9, 11, 12, 18, 20, 21, 24
A		4, 15, 27, 28, 29, 31, 32
Y	US 2008/0208044 A1 (SUPERSONIC IMAGINE et al.) 28.08.2008, paragraph [0003]	11, 12, 20, 21, 24
Y	US 2010/0224782 A1 (NATIONAL CENTRAL UNIVERAITY) 09.09.2010, claim 1	9, 18

☐ 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

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"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

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
20 June 2016 (20.06.2016)	30 June 2016 (30.06.2016)
Name and mailing address of the ISA/RU: Federal Institute of Industrial Property, Berezhkovskaya nab., 30-1, Moscow, G-59, GSP-3, Russia, 125993 Facsimile No: (8-495) 531-63-18, (8-499) 243-33-37	Authorized officer A. Ilyin Telephone No. (495)531-64-81

专利名称(译)	用于受试者的临床前超声成像的装置，系统和方法		
公开(公告)号	EP3247281A4	公开(公告)日	2018-10-03
申请号	EP2016740894	申请日	2016-01-25
[标]申请(专利权)人(译)	北卡罗来纳大学查珀尔希尔分校		
申请(专利权)人(译)	教堂山北卡罗来纳大学		
当前申请(专利权)人(译)	教堂山北卡罗来纳大学		
[标]发明人	DAYTON PAUL ALEXANDER GESSNER RYAN CHRISTOPHER BUTLER JAMES OWEN HARLACHER MAX STEPHEN NORMAN NICHOLAS ALLAN		
发明人	DAYTON, PAUL, ALEXANDER GESSNER, RYAN, CHRISTOPHER BUTLER, JAMES, OWEN HARLACHER, MAX, STEPHEN NORMAN, NICHOLAS, ALLAN		
IPC分类号	A61B8/00 G01N29/06		
CPC分类号	A61B8/08 A61B6/4417 A61B6/508 A61B8/0883 A61B8/4218 A61B8/4281 A61B8/4416 A61B8/52		
优先权	62/107321 2015-01-23 US		
其他公开文献	EP3247281A1		
外部链接	Espacenet		

摘要(译)

提供了用于受试者的临床前超声成像的装置，系统和方法。在一个方面，该装置可包括其上可定位对象的平台和用于控制至少一个超声换能器相对于平台的空间位置的至少一个运动台，以便获取对象的超声图像数据。还提供了用于对象中的至少一个器官或组织的临床前超声光栅扫描的方法，其中所述至少一个器官或组织是心脏。