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(54) **Title**: TRACKED IMAGERY OPTICAL BIOPSY SYSTEM

(57) **Abstract**: An imaging system includes an optical probe to generate imaging data, a tracking system to track the optical probe, a light source operatively coupled to the optical probe, and a processing device communicably coupled to the tracker. The light source enables optical sectioning by the imaging system. The processing device applies optical sectioning to generate a first image based on a subset of the imaging data. The processing device further determines first position data and first orientation data associated with the optical probe as the subset of the imaging data was generated and applies a geometric transformation to the first position data and the first orientation data to determine a first position in a virtual three dimensional space. Furthermore, the processing device generates a three dimensional model comprising the first image placed at the first position in the virtual three dimensional space.

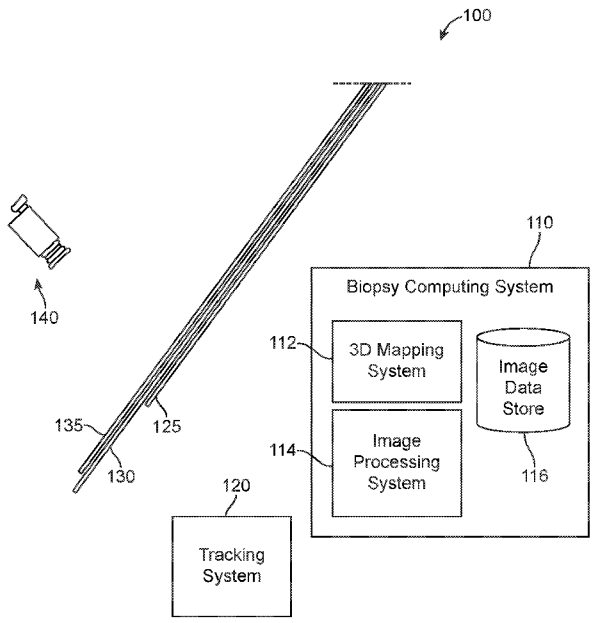


FIG. 1

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TRACKED IMAGERY OPTICAL BIOPSY SYSTEM

CROSS-REFERENCE TO RELATED APPLICATION

[0001] This application claims the benefit under 35 U.S.C. § 119(e) of U.S. Provisional Application 62/263,809 filed on December 7, 2015, which is hereby incorporated by reference in its entirety.

FIELD OF THE INVENTION

[0002] This document relates generally to optical probe-based assessment of biological tissues.

BACKGROUND OF THE INVENTION

[0003] There were an estimated 1.7 million new cancer patients in the US in 2014. Most of these patients will undergo initial biopsy for diagnostic confirmation, followed by surgery with the goal of removing all traces of abnormal or at-risk tissue. The accuracy with which these procedures can be achieved has a major effect on the patient's long-term outlook. A pathology diagnosis is only as good as the original specimen; in many cases, the biopsy sample may miss abnormal cells. At present, in many fields of medicine, the physician uses his or her judgment and experience to visually determine the most appropriate site to remove tissue for histopathologic analysis.

[0004] Following surgery, a key prognostic indicator is the status of tissue at the surgical margin, with positive margins universally associated with poor outcomes. The challenge facing the surgeon is then to balance the use of wide margins to ensure complete removal of tumor, against preserving as much healthy tissue as possible to retain cosmetic appearance and function. This challenge is particularly acute with the shift towards more conservative procedures, such as lumpectomy versus mastectomy in breast cancer. Surgeons are challenged to work to as narrow a margin as possible, but this is difficult without access to the type of cellular level detail usually only available under the microscope to a pathologist. In addition, diagnosticians may also face the challenge of using visual inspection to determine the most appropriate site to biopsy, and to determine whether a biopsy is even necessary.

[0005] To address this clinical need of more precise surgical margins, some procedures may employ intra-operative frozen section histopathology, or touch-prep cytology to try and provide the surgeon with near-real-time feedback which can be used to guide their incisions. Both methods involve rapidly processing a tissue or cell sample while the

patient remains on the operating table. Unfortunately, these approaches provide margin status at only a few selected locations, lengthen procedure times, and raise costs. Nevertheless, intra-operative frozen-section pathology for guidance on margin location continues to be used, indicating a desire for data at the microscopic scale despite the recognized limitations. In addition, to address the clinical need of determine the site for biopsy, as well as whether (or when) to biopsy for a diagnosis, information from microscopic scale would be useful.

DESCRIPTION OF THE DRAWINGS

[0006] Embodiments will be described with reference to the following drawing figures, in which like numerals represent like items throughout the figures, and in which:

[0007] Figure is a block diagram illustrating components of an optical biopsy system, according to an embodiment.

[0008] Figure 2 is a block diagram illustrating components of an optical biopsy system using optical sectioning, according to an embodiment.

[0009] Figure 3 is an example three dimensional model generated by an optical biopsy system, according to an embodiment.

[0010] Figure 4 is an example two dimensional model generated from a three dimensional model by an optical biopsy system, according to an embodiment.

[0011] Figure 5 is an example user interface generated by an optical biopsy system, according to an embodiment.

[0012] Figure 6 is an example user interface generated by an optical biopsy system, according to an embodiment.

[0013] Figure 7 is a flow chart depicting processes performed by an optical biopsy system, according to an embodiment.

[0014] Figure 8 is a block diagram depicting a computer system of an optical biopsy system, according to an embodiment.

DETAILED DESCRIPTION OF THE INVENTION

[0015] Described herein are systems and methods for performing optical biopsies. In some embodiments, systems described herein may include an optical probe, a tracking system to track the position of the optical probe, and a system for optical sectioning to improve diagnostic performance of the optical probe.

[0016] Non-invasive fiber-optic imaging and/or spectroscopy probes may provide clinicians with the ability to assess tissue status in real-time. This information can be used to help the user decide which site(s) to take a biopsy from, whether a biopsy is even necessary, or where a resection margin should be during surgery. Current optical biopsy imaging (OBI) probes (including epi-fluorescence, scanning confocal, and multiphoton variations) only provide discrete images from each site examined. This requires the user to remember the appearance of images from multiple sites, and to return to the specific site(s) of interest via cognitive memory. Marking or tagging optical measurement sites for subsequent biopsy may include creating a dimple on the tissue by pressing the probe against the mucosa or using a cauterizing laser to physically mark the site. Embodiments of the optical biopsy systems described herein may integrate fiber-optic OBI hardware with a tracking device to acquire both optical imaging information as well as the precise 3D location of the imaging probe.

[0017] Various probe-based optical imaging and spectroscopy devices may provide microscopic level information about target portions of a subject. These optical probes have demonstrated good diagnostic accuracy in laboratory and pilot clinical studies but face practical challenges in gaining widespread clinical acceptance. One challenge is cost. Some confocal platforms are expensive due to the need for a rapidly scanned beam from a laser source. Multi-photon systems may also be cost-prohibitive as an optical probe. A second challenge which is common to these devices relates to how they are used in practice. For instance, when performing a biopsy, a medical practitioner may collect biopsy specimens from precisely documented anatomical locations. The specimens could then be sent to a pathology lab for processing and interpretation by a trained pathologist. The emergence of optical probes and other diagnostic instruments that provide a real-time ability to explore a tissue field prior to committing to biopsy, raises new challenges for integration within the clinical workflow. A medical practitioner must obtain clinical data from optical probes while documenting individual sites, interpret the images received from the optical probe, and return to specific sites where an image was taken by an optical probe. Furthermore, in some implementations a practitioner may wish to use multiple images in a region to gather sufficient information to make a diagnosis or map a region of diagnosis.

[0018] In some embodiments, the systems described herein incorporate an optical probe to provide detailed microscopic level information with a tracking device to track the location of images and optical sectioning technology. The optical sectioning technology

may improve the images provided by the optical probe by blocking out of focus light from the image.

[0019] In some embodiments, an optical biopsy system may integrate an in-vivo Optical Biopsy Imaging ("OBI") with electromagnetic (EM) tracking hardware, and three dimensional ("3D") data registration systems. In some embodiments, a tracking system other than an EM tracking system may be used to determine a position of the optical probe. Together, the optical biopsy system may allow users to examine tissue at the cellular scale in living patients and log the spatial location(s) of imaged sites. This may enable the user to precisely return to areas of interest (e.g., high-risk sites for biopsy collection) based on the logged spatial location(s). The logged spatial location(s) may also be stitched together into a single large area image for improved diagnostic ability or guidance on surgical margin status. In some embodiments, the spatial locations corresponding to images may be mapped into a three dimensional space for viewing or analysis.

[0020] In some embodiments, an optical probe may be implemented as a handheld probe for use during minimally invasive procedures, open surgeries, or dermatologic applications. The location of the optical probe may be tracked using a tracking device. The optical biopsy system may then execute 3D tracking and image integration systems for data processing/display and may allow a clinician to return to previous potential biopsy locations for biopsy/treatment. In various embodiments, the optical biopsy system may be used in a variety of applications. For example, the present solution can be used in Gastrointestinal ("GI"), urinary, reproductive, respiratory, skin and other tissue/organ systems. The handheld probe may also be used in conjunction with an endoscope, laparoscope, or the like to perform respective procedures.

[0021] Various embodiments described herein may provide a variety of advantages. For example, in some embodiments, a tracking device may be integrated with an optical probe and provide improved imaging with optical sectioning. Some embodiments may further accurately map an image from the optical probe to a 3D location in a virtual space. An optical biopsy system may then provide a view of the 3D space with captured images. In some embodiments, an optical biopsy system may generate 2D views of the captured images from a perspective in the 3D space. In some embodiments, the optical biopsy system may stitch together images from the 3D space to generate a 2D view of a portion of the 3D space. In some embodiments, a practitioner may use a 2D or 3D model

generated by the system to return the optical probe, or another instrument, to a previously logged position that is identified as an area of interest.

[0022] In some embodiments, the tracking system may include an EM tracker that tracks the position of an EM device attached to the optical probe. However, in various embodiments, other tracking devices and systems may be used. Any known or to be known tracker can be used herein which provides position and/or orientation values. For example, a mechanical tracker can be used in addition to or alternative to an EM tracker. In some embodiments, the tracking devices may provide tracking with 6 degrees of freedom (e.g., an x value, a y value, a z value, a roll value, a pitch value, and a yaw value). In some embodiments, a tracking device may provide fewer degrees of position or orientation values if they can be inferred by other means. For example, if an orientation of a subject is known, the position of the tracker relative to the subject may provide sufficient data without additional orientation data. Furthermore, in some embodiments, more than one tracker may be used to provide position and/or orientation values when combined. For example, one tracker may provide position data and a second tracker (potentially of a different kind) may provide orientation data. In addition, two trackers providing position data may use their relative positions to determine orientation data. Moreover, the data from multiple trackers may be combined (for example by averaging) in order to reduce variability or other sources of inaccurate tracking information from a single tracker. Additionally, several tracking values from a single tracker may be combined (for example by a weighted average of the data from a preceding time interval) as an alternative method for reducing variability or other sources of inaccuracies. Various trackers may include EM trackers, gyroscopes, accelerometers, potentiometers, proximity sensors, or the like.

[0023] In some embodiments, an optical biopsy system as described herein may be used as a handheld imaging probe, for applications in an open area of tissue (such as the skin) or surgical field. However, such an optical biopsy system may also be used in minimally-invasive procedures. In particular, the handheld imaging probe may be designed to fit through a standard endoscope or laparoscope accessory channel.

[0024] To assess a wider area than the field of view of an optical probe, a practitioner may move the probe to a new location. In some embodiments, the tracking system may record the location of the tracker as the images are collected from the optical probe. The optical biopsy system may then use the position of the tracker to determine a position of the optical probe as an image is taken. Thus, a position in 3D space of an image received from an optical probe

may be determined. The optical biopsy system may generate a 3D map of the captured images using the position and image data. Furthermore, because the images have associated position data from the tracker, the 3D map may be generated without using overlapping portions of the optical biopsy data to determine the positions.

[0025] In some embodiments, an optical biopsy system as described herein may include hardware and processing to provide optical sectioning. Using optical sectioning, an optical biopsy system may block out of focus light from distorting the images received by the optical probe. For example, a light source may provide structured illumination to a target area of an optical probe. The light received by the optical probe may then be processed by the optical biopsy system to block out of focus light received by the optical probe from distorting the received images. In some embodiments, optical sectioning may be performed by confocal methods, nonlinear optical methods, coherent illumination methods, coherence gating methods, or other approaches.

[0026] In addition to imaging data from an optical probe, in some embodiments, the optical biopsy system may include a wide-field imaging device. The wide-field image device may provide wide-field images or video. For example, the wide-field device may be a camera that provides a view of an area including the areas viewed by the optical probes. In some embodiments, the wide-field images may be used by the optical biopsy system to generate wide field images that include images from the optical probe. For example, the position of a tracker relative to the wide-field imaging device may be used to determine a location in the field of view of the wide-field imaging device of the optical probe. The images received from the optical probe may then be superimposed onto the images received from the wide-field imaging device. The view may therefore be improved to include a wide-field view of a patient with additional data received from an optical probe.

[0027] Some embodiments of the disclosure are described herein in with reference to endoscopic and dermatologic applications. However, other applications of using optical probe data may incorporate systems as describe herein. Furthermore, in some embodiments, devices or systems described herein may fit into an auxiliary port on an endoscope, but could also be used in a laproscope and/or handheld device, and is not limited to endoscopic or dermatologic diagnosis systems.

[0028] The systems, methods, and device described herein are described with reference to use by medical professionals. However, it will be understood that the embodiments described herein may be used in other applications. For example, the embodiments described herein may be used as training for lab technicians, researchers, education

purposes (e.g., anatomy students), or any applications of tracking the position of optical data.

[0029] It will be readily understood that the components of the embodiments as generally described herein and illustrated in the appended figures could be arranged and designed in a wide variety of different configurations. Thus, the description of various embodiments, as represented in the figures, is not intended to limit the scope of the present disclosure, but is merely representative of various embodiments. While the various aspects of the embodiments are presented in figures, the figures are not necessarily drawn to scale. Furthermore, in some embodiments, the systems, devices, and methods set forth in the figures may include fewer or additional components than are shown.

[0030] The present disclosure may be embodied in other specific forms without departing from its spirit or essential characteristics. The described embodiments are to be considered in all respects only as illustrative and not restrictive. The scope of the disclosure is, therefore, indicated by the appended claims rather than by this detailed description. All changes which come within the meaning and range of equivalency of the claims are to be embraced within their scope.

[0031] Reference throughout this specification to features, advantages, or similar language does not imply that all of the features and advantages that may be realized with the described embodiments should be or are in any single embodiment of the invention. Rather, language referring to the features and advantages is understood to mean that a specific feature, advantage, or characteristic described in connection with an embodiment is included in at least one embodiment. Thus, discussions of the features and advantages, and similar language, throughout the specification may, but do not necessarily, refer to the same embodiment.

[0032] Furthermore, the described features, advantages and characteristics of the invention may be combined in any suitable manner in one or more embodiments. One skilled in the relevant art will recognize, in light of the description herein, that the invention can be practiced without one or more of the specific features or advantages of a particular embodiment. In other instances, additional features and advantages may be recognized in certain embodiments that may not be present in all embodiments.

[0033] Reference throughout this specification to "one embodiment", "an embodiment", "some embodiments," or similar language means that a particular feature, structure, or characteristic described in connection with the indicated embodiment is included in at least one embodiment of the present invention. Thus, the phrases "in one embodiment",

"in an embodiment", "in some embodiments," and similar language throughout this specification may, but do not necessarily, refer to the same embodiment.

[0034] As used in this document, the singular form "a", "an", and "the" include plural references unless the context clearly dictates otherwise. Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art. As used in this document, the term "comprising" means "including, but not limited to."

[0035] Figure 1 depicts an optical biopsy system 100, according to an embodiment. In some embodiments, the optical biopsy system may include a biopsy computing system 110 in communication with a tracking system 120 and an optical probe 130. The tracking system 120 may track the position of a tracker 125. The optical probe 130 may provide imaging data. In some embodiments, a light source 135 may provide light that is captured by the optical probe 130 when reflected (or fluorescent light generated by the light from the light source). The optical computing system 110 may receive input streams from the optical probe 130 and the tracking system 120. In some embodiments, the optical biopsy system 100 may also communicate with a wide-field imaging device 140 that provides wide-field imaging. In some embodiments, the optical biopsy system 100 may include fewer or additional components. For example, the optical biopsy system 100 may not have a wide-field imaging device 140, or may have more than one optical probe 130, light source 135, or tracker 125.

[0036] The optical probe 130 may generate imaging data of a field of view in front of the optical probe 130. The imaging data provided by the probe may be raw images in the field of view of the optical probe 130. In some embodiments, other methods of acquiring photoelectric data may be used by the optical probe. For instance, the optical probe may provide imaging data based on spectroscopy or other imaging methods. In some embodiments, the optical probe 130 may be a coherent optical fiber bundle. The optical fibers may generate imaging data that can then be processed by the biopsy computing system 110. In some embodiment, other types of optical probes 130 may be used instead of optical fiber probes. For example, other types of optical probes may use conventional or micro-optical components, or gradient index (GRIN) lens based probes. The optical probe 130 may provide a stream of imaging data do the biopsy computing system 110. In some embodiments, the stream of imaging data may be provided to the biopsy computing system 110 in response to a command from the biopsy computing system 119 or it may be provided constantly. In some embodiments, the optical probe may provide the imaging

data with additional information, such as a time stamp, a count indicating a frame number of the imaging data, or the like.

[0037] In some embodiments, the optical probe 130 may be coupled to a light source 135 that provides light to the field of view of the optical probe 130. In some embodiments, the light source 135 may provide light at a specific wavelength that is calibrated to provide information about a target in the field of view of the optical probe. For instance certain wavelengths of light may be provided that cause fluorescence in particular tissues of a patient. In some embodiments, a light source may be provided at 450 nm, 488 nm, 790 nm, or 830 nm, that will provide reflected or fluoresced light from tissue in the field of view of the optical probe. Depending on the embodiment, any type of light source 135 may be used.

[0038] In some embodiments, the light source 135 may provide light in a manner to improve the images received by the optical probe 130. For example, the light source 135 may provide light in a manner to enable optical sectioning. In optical sectioning the light that is generated from locations that are out of focus from a plane of interest to the optical probe 130 may be blocked out. Generally, the optical probe 130 may generate a 2D image of the tissue of a subject. The 2D image may be in a particular plane in the tissue of the subject. However, the optical probe 130 may also receive other interfering light that is reflected from other planes. Thus, to improve the clarity of images generated from imaging data from the optical probe 130, the light source 135 may provide light to enable optical sectioning. In some embodiments, the out of focus light may be blocked at the optical probe. In some embodiments, the light source 135 may provide structured illumination. For example, illumination that is uneven. The imaging data generated by the optical probe 130 may then be processed by the biopsy computing system 110 to block out of focused light received by the optical probe 130 in the imaging data. Techniques for optical sectioning that may be used by the optical probe 130 and light source 135 are discussed further below with reference to Figure 2.

[0039] While shown as a separate component in Figure 1, in some embodiments, the light source 135 may be provided as part of optical probe 130. In some embodiments, the optical probe 130 is a fiber optic bundle, and the light source 135 may provide light to the fiber optic bundle that is then transmitted to the end of the fiber optic bundle. Thus, the optical probe 130 may provide light as a light source 135 and provide imaging data as an optical probe 130. Furthermore, in some embodiments, the light source 135 may be separate and/or independent from the optical probe 130 and the tracker 125.

[0040] In some embodiments, the tracking system 120 tracks the tracker 125. The tracker may be an EM tracker, or any other type of tracker that provides position and/or orientation data. In some embodiments, an EM tracking system 120 may generate a magnetic field in the vicinity of the tracker 125. The tracker 125 may cause changes in the magnetic field that can then be sensed by the tracking system 120 and used to generate position and/or orientation data of the tracker 125. In some embodiments, the tracking system 120 may track more than one tracker 125. For example, additional trackers (not shown) may provide more accurate information, or may be used together to provide different information. A first tracker may be used to track position while a second tracker is used to track an orientation, for instance. In some embodiments, the tracking system 120 may be integrated with the biopsy computing system 110, or other components of the optical biopsy system 100. In some embodiments, the tracking system 120 is stationary within the vicinity of a subject. The tracking system 120 may then track the position of tracker 125 relative to the position of the tracking system 120. In some embodiments, the tracking system 120 may track the tracker 125 relative to another component. For example, the position of tracker 125 may be tracked relative to a second tracker located on the body of a patient. This may enable the location of the tracker 125 on or within a patient to be determined even if the patient moves during the procedure. For instance, if the tracker 125 is tracked relative to a component on a patient's chest, the position of the tracker 125 may be relative to the patient's body even if the patient sits up, rolls over, or otherwise moves. Furthermore, in some embodiments, the tracking system 120 may be placed on the patient's body (e.g., on the patient's chest) to determine a position of the tracker 125 relative to the patient's body instead of relative to a space the patient occupies.

[0041] In some embodiments, the tracking system 120 outputs position and orientation data for the tracker 125 data with six (6) degrees of freedom. The six (6) degrees of freedom are described in terms of x, y, and z locations as well as yaw, pitch, and roll angles. The position of the optical probe 130 may then be derived from the position and orientation of the tracker 125. In some embodiments, the tracking system 120 may output the location and orientation of the tracker 125 to the biopsy computing system 110. In some embodiments, the tracking system 120 may output the position of an image captured by the optical probe 130 to the biopsy computing system 110.

[0042] In some embodiments, a wide-field imaging device 140 may have a tracker that determines the position of the wide-field imaging device 140 relative to the tracker 125 or

the optical probe 130. Tracking the wide-field imaging device 140 may enable the biopsy computing system 110 to determine a perspective matrix for the imaging device (which maps 3D input locations onto 2D perspective locations to be displayed on a computer monitor). Any stored OBI image locations may also be mapped onto the 2D display relative to the perspective matrix of the wide-field imaging device 140. In some embodiments, the biopsy computing system 110 may generate 2D locations for the optical biopsy images from the position and orientation of the tracker 125, the perspective matrix of the wide-field imaging device 140, and the previously stored positions of optical biopsy images.

[0043] In some embodiments, the biopsy computing system 110 may include a 3D mapping system 112, and an image processing system 114. The biopsy computing system 110 may receive two input data streams. A first input stream may be received from tracking system 120. The second input stream may be received from the optical probe 130. The input stream received from the tracking system 120 may be processed by the 3D mapping system to determine a position in a virtual 3D space of an optical probe 130 based on position and/or orientation data of the tracker 125. The input stream received from the optical probe 130 may be processed by an image processing system 114 to generate optical biopsy images. The biopsy computing system 110 may then combine the 3D mapping information with the optical biopsy images to generate a virtual 3D map of optical biopsy images.

[0044] The 3d mapping system 112 of the biopsy computing system 110 may determine a position of an optical probe 130 from data received from a tracking system 120. In some embodiments, the tracking system 120 outputs position and orientation data for a tracker 125. The 3D mapping system 112 may use the position and orientation data of the tracker 125 to determine a position and/or orientation of the optical probe 130 or a position of imaging data provided by the optical probe 130. For example, the position of the end of optical probe 130 may be known relative to the position of the tracker 125, and the orientation of the optical probe may also be known. Thus, the 3D mapping system 112 may use the received position data and orientation data to generate a position and orientation of an image. For instance, the 3D mapping system 112 may receive x, y, and z coordinates, and yaw, pitch, and roll angles of a tracker 125. The 3D mapping system may then use the orientation data (yaw, pitch, and roll angles) to determine a position of the imaging data relative to the x, y, and z coordinates of the tracker 125. Thus, in an example, the 3D mapping system may determine that the optical scope 130 is in a position

x', y', z' in response to determining a position x, y, z for the tracker 125. The position x', y', z' may be determined based on a transformation of the yaw, pitch, and roll of the tracker 125 and a set distance from the tracker 125 to the optical probe 130. For example, if the tracker 125 is rigidly attached to the optical probe 130, the distance between the two may be a set distance. The position of the optical probe 130 (x', y', z') may be determined as being the set distance in a direction defined by the yaw, pitch, and roll of the tracker 125 from the position (x, y, z) of the tracker 125.

[0045] In some embodiments, other transformations may be performed by 3D mapping system 112 to determine a location in a virtual 3D space of imaging data. For example, in some embodiments, the 3D mapping system 112 may receive tracking data for more than one tracker 125. The location of multiple trackers may then be used to determine a position and/or orientation of the optical probe 130. For example, in one embodiment, position data of three trackers may be used to determine yaw, pitch, and roll of the probe. The position of the optical probe 130 may be derived from the position of one of the trackers and the yaw, pitch, and roll, as discussed above. In some embodiments, two trackers may be aligned such that an optical probe 130 is known to be located a set distance along an axis formed by the position of the two trackers. Thus, a location x', y', z' of the optical probe 130 may be determined based on a geometric transformation a set distance along the axis from a point x, y, z that is one of the trackers. In various embodiments, the 3D mapping system 112 may determine a position of optical probe 130 (and associated imaging data) in different manners. In some embodiments, the 3D mapping system 112 may also determine an orientation of the imaging data. For example, the direction the optical probe 130 is facing may be used to determining an orientation of imaging data provided by the optical probe.

[0046] The image processing system 114 generates images based on the imaging data received by optical probe 130. In some embodiments, generating images may include recording images received directly from the optical probe 130. In some embodiments, image processing system 114 may improve the quality of images before storing them for viewing by a practitioner. For example, imaging data received from an optical probe 130 may have irregularities based on the type of optical probe 130. A fiber optic bundle may have distortions from the individual fibers, for instance. In addition, the imaging data received by the image processing system 114 may have images that have reflectance from structured illumination of the subject. Thus, the image process system 114 may perform image processing operations to generate an image by blocking out of focus light from one

or more received images. In some embodiments, the image processing system 114 may process the imaging data to highlight specific cellular attributes in addition to improving quality. In addition, in some embodiments, imaging data associated with multiple wavelengths of light may be combined into a color image.

[0047] The biopsy computing system 110 may store the images generated by the image processing system 114 in an image data store 116. The biopsy computing system 110 may include position and/or orientation data associated with the imaging data in image data store 116. For example, the stream of imaging data received by the image processing system 114 may be correlated with the stream of position and/or orientation data received by the 3D mapping system. The biopsy images output by the image processing system 114 may then be associated with the corresponding output of the 3D mapping system. In some embodiments, the position and/or orientation data may be stored as metadata for the images, possibly for future retrieval. In some embodiments, the images and position and/or orientation data may be stored separately, but may be stored with an identifier indicating that the two are associated.

[0048] In some embodiments, the optical probe 130 is a flexible fiber-optic bundle to deliver illumination light to the tissue and to transmit an image back to an external camera unit. In some embodiments, the fiber optic bundle may have an outer diameter of 0.45 mm to 1.70 m. In some embodiments, the optical probe 130 and tracking device 125 may be designed to fit through an auxiliary port of a standard endoscope (typically 2.8-3.2 mm). In some embodiments, the outer diameter for a handheld imaging probe comprising the optical probe 130 and the tracker 125 may be approximately 2 mm which may be achieved through integration of a 0.96 mm outer diameter imaging fiber with a 16-gauge (0.9 mm outer diameter) EM tracker. A tracked probe with this diameter may be used in standard diameter colonoscopes and gastroscopes, and is compatible with some smaller Ear Node Throat ("ENT") scopes and bronchoscopes. In some embodiments, the outer diameter of a tracked probe may be smaller or larger than described. For example, the tracked probe may have an outer diameter of approximately 0.5mm, 1mm, 1.5mm, 2.5mm, or other diameters depending on the application.

[0049] Figure 2 depicts an example of optical sectioning performed by an optical biopsy system, according to an embodiment. Using optical sectioning, an optical biopsy system may block out of focus light from reducing the quality of light on a plane being observed by an optical probe. In Figure 2, an optical probe 230 observes a tissue specimen 210. The optical probe 230 may be similar or the same as the optical probe 130 described above with reference to Figure 1. For instance, the optical probe 230 may be connected to an

optical biopsy system and may be coupled to a tracker to determine the position of optical probe 230. In some embodiments, the optical probe 230 is a bundle of fiber optic fibers.

[0050] The optical probe 230 may have as a light source, or another light source may provide incident light 240 to the tissue sample 210. In some embodiments, the incident light 240 may be of a particular frequency that promotes diagnosis in imaging data received by the optical probe 230. In some embodiments, the incident light may provide structured illumination that enables optical sectioning by the optical probe 230 or a connected image processing system.

[0051] The incident light may illuminate a portion 220 of the tissue specimen 210 and reflected light 250 may return from portion 220. As shown in Figure 2, the illuminated portion 220 may extend through a depth 222 of the tissue specimen 210. However, the optical probe 230 may be focused on a particular plane of the tissue specimen 210. Accordingly, the light reflected from the illuminated portion 220 of the tissue specimen 210 that is not within the in focus area 225 may provide out of focus light to the optical probe 230. Thus, to improve image quality, the optical probe 230 may block out of focus light from generated imaging data. In some embodiments, the optical sectioning may be performed by processing of one or more images generated by the optical probe 230. For instance, the optical probe 230 may take multiple images of the tissue specimen 210 while incident light 240 provides structured illumination. For example the structured illumination may provide an illumination pattern with stripes of light that are phase shifted at 0, 120, and 240 degrees. The optical probe may then acquire images of a sample when the illumination pattern is at the phase shifted 0, 120, and 240 degree positions. The imaging data provided by the optical probe 230 may then include multiple images. An optical biopsy system, image processing system, or other system may then use the images captured under structured illumination to generate a composite image that blocks out of focus light. In some embodiments, other structured illumination patterns may be provided by the light source and additional images may be acquired by the optical probe.

[0052] In some embodiments optical sectioning may be achieved through scanning confocal microscopy which uses a point-source of light with a pinhole, both conjugate to the specimen plane, to prevent out of focus light from reaching the detector of the optical probe. In some embodiments, optical sectioning may be achieved through nonlinear microscopy. In nonlinear microscopy, light is generated only at the (in focus) sample plane, and therefore does not require a physical pinhole to block out of focus light. In some embodiments, optical sectioning may be achieved using speckle (coherent)

illumination. Coherent illumination may be provided by a light source providing a defined pattern of light to the sample. Then an image processing system may process multiple images to produce a sectioned image with the out of focus light removed.

[0053] Figure 3 depicts an example of a virtual 3D model 300 with images 310 generated from imaging data received from an optical probe. The images may be generated by an optical biopsy system. For example, the images may be generated by the optical biopsy system 100 described with reference to Figure 1 above. A biopsy computing system may generate the virtual 3D model 300 based on images and position and/or orientation data associated with the images. The images may be retrieved from a data store that includes images and position and/or orientation data associated with the images.

[0054] The optical biopsy system may then generate a virtual 3D space that shows the images 310 in their corresponding coordinates and orientation planes. In some embodiments, the images 310 may be placed in the virtual 3D space as 2D images oriented in the direction they were captured from by an optical probe. In some embodiments, the images 310 may be placed in the virtual 3D space as a 2D image oriented in the direction of a perspective of a user. The generated 3D space may be displayed to a medical practitioner or other user on a display screen. In some embodiments, the generated 3D model 300 may be provided as a 2D representation of the 3D space from a particular perspective. In some embodiments, the user may be able to manipulate the orientation of the 3D model. For example, a user interface may enable a user to change the position and orientation from which the 3D model is viewed. In some embodiments, a 2D plane 320 may be used to generate a 2D perspective view of the 3D model.

[0055] As shown in Figure 3, the 3D model 300 includes a number of images 310. The images may be placed into 3D space based on the position and/or orientation determined by an optical biopsy system. In addition, the images may be placed into the 3D model without determining positions based on overlap of the images. Thus the images 310 may be placed into a 3D model without flattening the images and aligning one image with a neighboring image to generate an overlapping mosaic of a number of different images. The images 310 may be displayed following filtering, being otherwise processed, shown with various levels of opacity or colors, or the like. The images 310 may be cropped. In some embodiments, only a subset of the images 310 may be displayed.

[0056] Figure 4 depicts an example of generating a 2D perspective view 450 from a 3D model 450 with images received from an optical probe. The 3D model 410 may be generated in a similar manner as discussed above with respect to Figure 3. In addition, a

user interacting with the 3D model 410 may be able to manipulate the position and/or orientation of a cross section 420. Thus, the user can select a 2D plane 420 through which the user can view a perspective view of the 2D model 450.

[0057] A biopsy computing system may then generate a 2D perspective view 450 of the 3D model 410 based on the selected plane. For example, in Figure 4, the 3D model 410 includes images 411, 412, 413, and 414. The biopsy computing system may then determine the position of the images 411, 412, 413, and 414 from the perspective of a selected 2D plane 420. The positions of the images 411, 412, 413, and 414 may then be mapped from the 3D space to positions on a 2D plane. The biopsy computing system may then generate a 2D perspective view 450 with the images 411, 412, 413, and 414 shown on the 2D plane as images 451, 452, 453, and 454. In some embodiments, the images 411, 412, 413, and 414 may be cropped, transformed, filtered, processed, displayed with various levels of opacity, or the like, for easier viewing. In some embodiments, the 2D plane 450 of the 3D model 410 may be generated to correspond to the perspective of a wide-field image capture device. Thus, the images 451, 452, 453, and 453 may be superimposed onto a wide-field image to show the positions of the images relative to a wide-field image of a subject.

[0058] Figure 5 is an example user interface 500 showing images received from an optical probe mapped to a wide-field image of a subject. In some embodiments, the optical probe may be part of an optical biopsy system as discussed with reference to Figure 1 above. The user interface 500 provides a real-time view 510 from a wide-field camera, as well as a current view 520 from an optical probe. The physical location of the currently streaming image from the optical probe is represented by an indicator 525 (in this case a circle) at the tip of an imaging probe visible in the wide-field view 510.

[0059] The user interface may include a user interface element that enables a user to capture an image from the optical probe. In Figure 5, the user interface element 530 is a "Capture" button that captures the current image. In some embodiment, an optical biopsy system may store the imaging data from the optical probe and a location associated with the imaging data. For example, as discussed above, position and/or orientation data of the optical probe may be generated from a tracker coupled to the optical probe

[0060] The operator may continue to take optical biopsies as different locations by moving the optical probe and capturing new imaging data. Locations of previously stored biopsy images may be overlaid onto the wide-field images. For example, images of previous optical biopsies may be shown in a list of images 540, 542, 544. The location of the images taken may

be shown as an overlay in the wide-field image 510 as well. For example, an optical biopsy system may overlay indicators 550, 552, 554 corresponding to previously recorded biopsy images 540, 542, 544 respectively. In some embodiments, the indicators may have different colors, shapes, or other indications that associate the list of images with their associated indicators on the screen. The location of the previously recorded biopsy images may be determined by tracking the wide-field image capture device. The position of the image capture device may then be used to determine a perspective of the image capture device. The perspective may then be used to generate a 2D view of capture images as discussed above with respect to Figure 4. Finally, the optical biopsy system may overlay the generated 2D view on the wide-field image captured by the wide-field image capture device. When the user has finished collecting optical biopsies, the user may select a user interface element 550 to terminate the session.

[0061] Figure 6 is an example user interface 600 showing images received from an optical probe mapped to a wide-field image of a subject. Similar to the example user interface shown in Figure 5, the user interface shown in Figure 6 includes a wide-field image 610 and an insert showing a current view of an optical probe 620. The example user interface 600 in Figure 6 is used in reference to an optical biopsy system for dermatological procedures. Previously recorded biopsy images may be recorded along with position and/or orientation data as discussed above. Furthermore, the current position of the imaging data may be indicated by a user interface element 630 and previously recorded biopsy images may be indicated by user interface elements 640.

[0062] Figure 7 is a flow chart illustrating processes to generate a model based on images taken by an optical probe. Beginning in block 710, an optical biopsy system may receive imaging data from an optical probe. In some embodiments, the optical biopsy system may be similar to that described with reference to Figure 1, and the image data may be received by the image processing system 114. The optical probe may be a fiber optic bundle, or any other type of optical probe. In some embodiments, the imaging data may be raw imaging data from the optical probe. For example, the raw imaging data may include multiple signals from different components of an optical probe. In some embodiments, the raw imaging data may include imaging data taken at multiple points in time. For instance, the raw imaging data may include the output of sensors at different times that may then be used to generate a composite image. In some embodiments, the imaging data may be provided by an optical probe that blocks out of focus light to provide better clarity through optical sectioning. In some embodiments, the imaging data may include spectroscopic data or other photoelectric data from the tissue.

[0063] In block 720, the optical biopsy system generates an image from the imaging data. The image may be generated by an image processing system. In some embodiments, the image may be generated by applying optical sectioning to the imaging data. For example, an image processing system may use one or more components of imaging data to block the out of focus light received from the optical probe. This optical sectioning may improve the clarity of the generated images. In some embodiments, an image processing system may generate an image that is in a different color scheme, frequency of light, brightness, or having other characteristics. In some embodiments, generating an image from the imaging data may comprise filtering one or more defects from the raw imaging data received by the optical biopsy system. In some embodiments, generating an image from the imaging data may comprise displaying the imaging data as waveforms or other numerical or graphical representations generated from the raw imaging data.

[0064] While the optical biopsy system is generating an image from the imaging data, it may also receive position and/or orientation data in block 730. For example, the position and/or orientation data may be received by a 3D mapping system as discussed above with reference to Figure 1. As discussed above, the position and orientation data may include six degrees of position or orientation data. In some embodiments, the position and/or orientation data may be received from a tracking system that tracks a tracker or a plurality of trackers.

[0065] In block 740, the optical biopsy system determines a position of an optical probe based on the position and/or orientation data. In some embodiments, the position of the optical probe may be determined based on a geometric transformation from the position and orientation of a tracker to a position of the optical probe. In some embodiments, the optical biopsy system may determine an orientation of the optical probe in addition to the position of the optical probe. For example, the optical biopsy system may determine that a direction that the optical probe is facing based on the yaw, pitch, and/or roll indicated in the position and/or orientation data. Furthermore, alternatively or additional to determining a position and/or orientation of the optical probe, in some embodiments, the optical biopsy system may determine a position and/or orientation of imaging data that would be received by the optical probe. For instance, the position of the imaging data may be slightly in front of the optical probe, and the imaging data may have an orientation in an opposite direction of the orientation of the optical probe.

[0066] In block 750, the optical biopsy system may store the generated image with a determined position. For example, as the optical biopsy system receives a stream of imaging data in block 710, it may receive a corresponding stream of position and/or orientation data in block 730. The optical biopsy system may then correlate the image generated from the

received imaging data with the position determined from the corresponding stream of position and/or orientation data. In some embodiments, the correlation may be determined by time-stamps associated with each stream of data. The optical biopsy system may then store the generated image and the associated position data in a data store.

[0067] In block 760, the optical biopsy system may generate a 3D model with the generated image at the determined position. For example, the generated image may be placed in a virtual 3D space in the determined position. In some embodiments, the optical biopsy system may output the generated to a display at the determined position. During operation of the optical biopsy system, many images may be generated. The optical biopsy system may then map each of the images to a position in the 3D space. The images may then be displayed as a 3D model with each of the images in a determined position in the 3D space. To display the images as a 3D model, the optical biopsy system may provide the images as facing the perspective through which the model is viewed. In some embodiments, the images may be provided in an orientation that is associated with the image. In some embodiments, one or more of the images may overlap in 3D space. In response to determining that one or more of the images overlap in 3D space, the images may be flattened into 2D images. The 2D images may then be compared to identify components of the images that are the same. The 2D images may then be stitched together to generate a composite 2D image. Thus, the overlapping images may be displayed together in the 3D space accounting for the overlap. The composite 2D image may use image similarity metrics such as Normalized Cross Correlation, Mutual Information, or the like, in order to determine the optimal overlap between the components of such images. Image registration algorithms may slightly reposition the raw images into the composite 2D image in order to maximize this overlap. In some embodiments, the overlapping regions between contiguous images may be blended together by an image processing system. In some embodiments, one image may be displayed atop another image (rather than blending). In some embodiments, perspective transforms such as shearing may be performed in order to maximize the image similarity metric in the composite 2D image. In some embodiments, the outer edges (or other portions) of the images may be displayed with varying levels of opacity to yield a higher quality composite image. In some embodiments, an imaging system may be employed to predict the data between images, thus filling in empty space between the images in the composite image.

[0068] Figure 8 depicts an example computer system 800 which can perform any one or more of the methods described herein for performing optical biopsies. In one example, computer system 800 may correspond to optical biopsy system 100 or biopsy computing system 110

described with reference to Figure 1. The computer system may be connected (e.g., networked) to other computer systems in a LAN, an intranet, an extranet, or the Internet. The computer system 800 may operate in the capacity of a server in a client-server network environment. The computer system 800 may be a personal computer (PC), a set-top box (STB), a server, a network router, switch or bridge, or any device capable of executing a set of instructions (sequential or otherwise) that specify actions to be taken by that device. Further, while only a single computer system is illustrated, the term "computer" shall also be taken to include any collection of computers that individually or jointly execute a set (or multiple sets) of instructions to perform any one or more of the methods discussed herein. In addition, the computer may reside in a geographically separated area (such as in a data center), providing only a set of display instructions to a second clinical device, such as a tablet or web browser.

[0069] The exemplary computer system 800 includes a processing device 802, a main memory 804 (e.g., read-only memory (ROM), flash memory, dynamic random access memory (DRAM) such as synchronous DRAM (SDRAM)), a static memory 806 (e.g., flash memory, static random access memory (SRAM)), and a secondary memory 816 (e.g., a data storage device), which communicate with each other via a bus 808.

[0070] The processing device 802 represents one or more general-purpose processors such as a microprocessor, central processing unit, or the like. The term "processing device" is used herein to refer to any combination of one or more integrated circuits and/or packages that include one or more processors (e.g., one or more processor cores). Therefore, the term processing device encompasses a single core CPU (computer processing unit), a multi-core CPU and a massively multi-core system that includes many interconnected integrated circuits, each of which may include multiple processor cores. The processing device 802 may therefore include multiple processors. The processing device 802 may include a complex instruction set computing (CISC) microprocessor, reduced instruction set computing (RISC) microprocessor, very long instruction word (VLIW) microprocessor, processor implementing other instruction sets, or processors implementing a combination of instruction sets. The processing device 802 may also be one or more special-purpose processing devices such as an application specific integrated circuit (ASIC), a field programmable gate array (FPGA), a digital signal processor (DSP), network processor, system on chip (SoC), or the like. The computer system 800 may include a graphics processing unit 822, a video processing unit 828, and an audio processing unit 832. In some instances, the graphics processing unit 822 may be used to

perform image processing instead of, or in conjunction with, the general-purpose CPU 802.

[0071] The computer system 800 may further include a network interface device 808. The computer system 800 also may include a video display unit 810 (e.g., a liquid crystal display (LCD) or a cathode ray tube (CRT)), an alphanumeric input device 812 (e.g., a keyboard), a cursor control device 814 (e.g., a mouse), and a signal generation device 820 (e.g., a speaker). In some embodiments, the computer system 800 may include or be in communication with other input and output device. For example, the computer system 800 may receive input signals from a foot pedal, a haptic device, or the like.

[0072] The secondary memory 816 may include a machine-readable storage medium (or more specifically a computer-readable storage medium (CRM)) 824 on which is stored one or more sets of instructions embodying any one or more of the methodologies or functions described herein (e.g., 3D mapping system 112, image processing system 114, or the like). The main memory 804 may also store, completely or partially, instructions 854 embodying any one or more of the methodologies or functions described herein (e.g., 3D mapping system 112, image processing system 114, or the like). Furthermore, the processing device 802 may include instructions to implement 3D mapping system 112, image processing system 114, or the like during execution thereof by the computer system 800. The main memory 804 and the processing device 802 may also include machine-readable storage media.

[0073] While the computer-readable storage medium 824 is shown in an exemplary implementation to be a single medium, the term "computer-readable storage medium" (or "computer-readable medium") should be taken to include a single medium or multiple media (e.g., a centralized or distributed database, and/or associated caches and servers) that store the one or more sets of instructions. The term "computer-readable storage medium" shall also be taken to include any medium other than a carrier wave that is capable of storing or encoding a set of instructions for execution by the machine that cause the machine to perform any one or more of the methodologies of the present disclosure. The term "computer-readable storage medium" shall accordingly be taken to include, but not be limited to, non-transitory media such as solid-state memories, and optical and magnetic media.

[0074] The modules, components and other features described herein (for example in relation to Figures 1) can be implemented as discrete hardware components or integrated in the functionality of hardware components such as ASICS, FPGAs, DSPs, SoCs, or

similar devices. In addition, the modules can be implemented as firmware or functional circuitry within hardware devices. Further, the modules can be implemented in any combination of hardware devices and software components, or only in software.

[0075] Some portions of the detailed descriptions which follow are presented in terms of algorithms and symbolic representations of operations on data bits within a computer memory. These algorithmic descriptions and representations are the means used by those skilled in the data processing arts to most effectively convey the substance of their work to others skilled in the art. An algorithm is here, and generally, conceived to be a self-consistent sequence of steps leading to a desired result. The steps are those requiring physical manipulations of physical quantities. Usually, though not necessarily, these quantities take the form of electrical or magnetic signals capable of being stored, transferred, combined, compared, and otherwise manipulated. It has proven convenient at times, principally for reasons of common usage, to refer to these signals as bits, values, elements, symbols, characters, terms, numbers, or the like.

[0076] It should be borne in mind, however, that all of these and similar terms are to be associated with the appropriate physical quantities and are merely convenient labels applied to these quantities. Unless specifically stated otherwise, as apparent from the following discussion, it is appreciated that throughout the description, discussions utilizing terms such as “creating”, “receiving”, “determining”, “executing”, “performing”, “transferring,” “translating,” “assigning,” “reassigning,” “identifying,” “providing,” “associating,” “retrieving,” or the like, refer to the action and processes of a computer system, or similar electronic computing device, that manipulates and transforms data represented as physical (electronic) quantities within the computer system’s registers and memories into other data similarly represented as physical quantities within the computer system memories or registers or other such information storage, transmission or display devices.

[0077] The terms “first”, “second”, “third”, “fourth”, etc. as used herein are meant as labels to distinguish among different elements and may not necessarily have an ordinal meaning according to their numerical designation.

[0078] Implementations of the present disclosure also relate to an apparatus for performing the operations herein. This apparatus may be specially constructed for the required purposes, or it may comprise a general purpose computer system selectively programmed by a computer program stored in the computer system. Such a computer program may be stored in a computer readable storage medium, such as, but not limited to,

any type of disk including floppy disks, optical disks, CD-ROMs, and magnetic-optical disks, read-only memories (ROMs), random access memories (RAMs), EPROMs, EEPROMs, magnetic disk storage media, optical storage media, flash memory devices, other type of machine-accessible storage media, or any type of media suitable for storing electronic instructions, each coupled to a computer system bus.

[0079] The algorithms and displays presented herein are not inherently related to any particular computer or other apparatus. Various general purpose systems may be used with programs in accordance with the teachings herein, or it may prove convenient to construct more specialized apparatus to perform the required method steps. The required structure for a variety of these systems will appear as set forth in the description above. In addition, the present disclosure is not described with reference to any particular programming language. It will be appreciated that a variety of programming languages may be used to implement the teachings of the disclosure as described herein.

[0080] It is to be understood that the above description is intended to be illustrative, and not restrictive. Many other implementations will be apparent to those of skill in the art upon reading and understanding the above description. Although the present disclosure has been described with reference to specific exemplary implementations, it will be recognized that the disclosure is not limited to the implementations described, but can be practiced with modification and alteration within the spirit and scope of the appended claims. Accordingly, the specification and drawings are to be regarded in an illustrative sense rather than a restrictive sense. The scope of the disclosure should, therefore, be determined with reference to the appended claims, along with the full scope of equivalents to which such claims are entitled.

CLAIMS

What is claimed is:

1. An imaging system comprising:

an optical probe to generate imaging data;

a tracking system to generate position data and orientation data associated with the optical probe;

a light source operatively coupled to the optical probe, the light source to provide light enabling optical sectioning to an area in a field of view of the optical probe; and

a processing device operatively coupled to the tracking system, the processing device to:

apply optical sectioning to generate a first image based on a subset of the imaging data received from the optical probe;

determine first position data and first orientation data associated with the subset of imaging data received from the optical probe;

apply a geometric transformation to the first position data and the first orientation data to determine a first position of the first image in a virtual three dimensional space; and

generate a three dimensional model of images comprising the first image placed at the first position in the virtual three dimensional space.

2. The imaging system of claim 1, further comprising a tracker coupled to the optical probe, wherein the tracking system determines a position of a tracker relative to a receiver.

3. The imaging system of claim 2, wherein the tracker is an electromagnetic (EM) tracker, and wherein the tracking system generates the position data and the orientation data based on changes to an EM field caused by the tracker.

4. The imaging system of claim 2, the processing device to:

determine a direction of the optical probe relative to the tracker based on a yaw, a pitch, and a roll provided in the first orientation data; and

determine the first position based on a predetermined distance from the tracker to the optical probe in the direction.

5. The imaging system of claim 1, wherein the tracking system tracks a plurality of trackers coupled to the optical probe.

6. The imaging system of claim 1, wherein the optical probe is a coherent fiber optic bundle.

7. The imaging system of claim 1, the processing device to:

obtain a plurality of images of a sample, wherein each of the images is acquired with a relative spatial phase shift in an illumination pattern generated by the light source; and

process the plurality of images to reduce out-of-focus light.

8. The imaging system of claim 1, the processing device to:

generate a second image based on a second subset of the imaging data;

determine a second position of the second image in the virtual three dimensional space; and

update the three dimensional model to comprise the second image placed at the second position in the virtual three dimensional space.

9. The imaging device of claim 8, the processing device to:

determine the first image and the second image overlap in the three dimensional space;

generate a composite image based on the first image and the second image;

determine a composite position for the composite image based on the first position and the second position; and

output the composite image at the determined composite position.

10. The imaging system of claim 1, the processing device to:

receive wide-field imaging data from a wide-field imaging device; determine a two dimensional position in the wide-field imaging data corresponding to the first position; and

display the wide-field imaging data with an indication of the first image at the two dimensional position.

11. A method comprising:

receiving, by a processing device, imaging data from an optical probe;

applying, by the processing device, optical sectioning to generate a first image based on a subset of the imaging data;

receiving, by the processing device, tracking data from a tracking system, the tracking data comprising an indication of a first position of a tracker coupled to the optical probe;

determining, by the processing device, a second position of the optical probe based on the tracking data received from the tracking system; and

generating, by the processing device, a three dimensional model of images comprising the first image placed at the second position in a virtual three dimensional space.

12. The method of claim 11, wherein determining the second position of the optical probe comprises:

determining, based on the tracking data, first position data and first orientation data associated with the tracker; and

applying a geometric transformation to the first position data and the first orientation data to determine the second position of the optical probe.

13. The method of claim 11, further comprising:

generating a second image based on a second subset of the imaging data;

determining a third position in the virtual three dimensional space associated with the second image; and

updating the three dimensional model to comprise the second image placed at the third position in the virtual three dimensional space.

14. The method of claim 13, further comprising:

determining the first image and the second image overlap in the three dimensional space;

generating a composite image based on the first image and the second image;

determining a composite position for the composite image based on the first position and the second position; and

updating the three dimensional model to comprise the composite image at the composite position.

15. The method of claim 11, wherein applying optical sectioning to generate a first image comprises:

obtaining a plurality of images of a sample, wherein each of the plurality of images has a relative spatial phase shift in an illumination pattern generated the light source; and

processing the plurality of images to reduce out-of-focus light.

16. The method of claim 11, further comprising:

receiving wide-field imaging data from a wide-field imaging device;

determining a two dimensional position in the wide-field imaging data corresponding to the position of the optical probe; and

displaying the wide-field imaging data with an indication of the first image at the two dimensional position.

17. An apparatus comprising:

a memory device; and

a processing device operatively coupled to the memory device, the processing device to:

receive imaging data from an optical probe;

apply optical sectioning to generate a first image based on a subset of the imaging data;

receive tracking data from a tracking system, the tracking data comprising an indication of a first position of a tracker coupled to the optical probe;

determine a second position of the optical probe based on the tracking data received from the tracking system; and

generate a three dimensional model of images comprising the first image placed at the second position in a virtual three dimensional space.

18. The apparatus of claim 17, wherein to determine the position of the optical probe the processing device is to:

determine, based on the tracking data, first position data and first orientation data associated with the tracker from the tracking data; and

apply a geometric transformation to the first position data and the first orientation data to determine the second position of the optical probe.

19. The apparatus of claim 17, wherein the processing device is further to:

generate a second image based on a second subset of the imaging data;

determine a third position in the virtual three dimensional space associated with the second image; and

update the three dimensional model to comprise the second image placed at the third position in the virtual three dimensional space.

20. The apparatus of claim 17, wherein the processing device is further to:

determine the first image and the second image overlap in the three dimensional space;

generate a composite image based on the first image and the second image;

determine a composite position for the composite image based on the first position and the second position; and

update the three dimensional model to comprise composite image at the composite position.

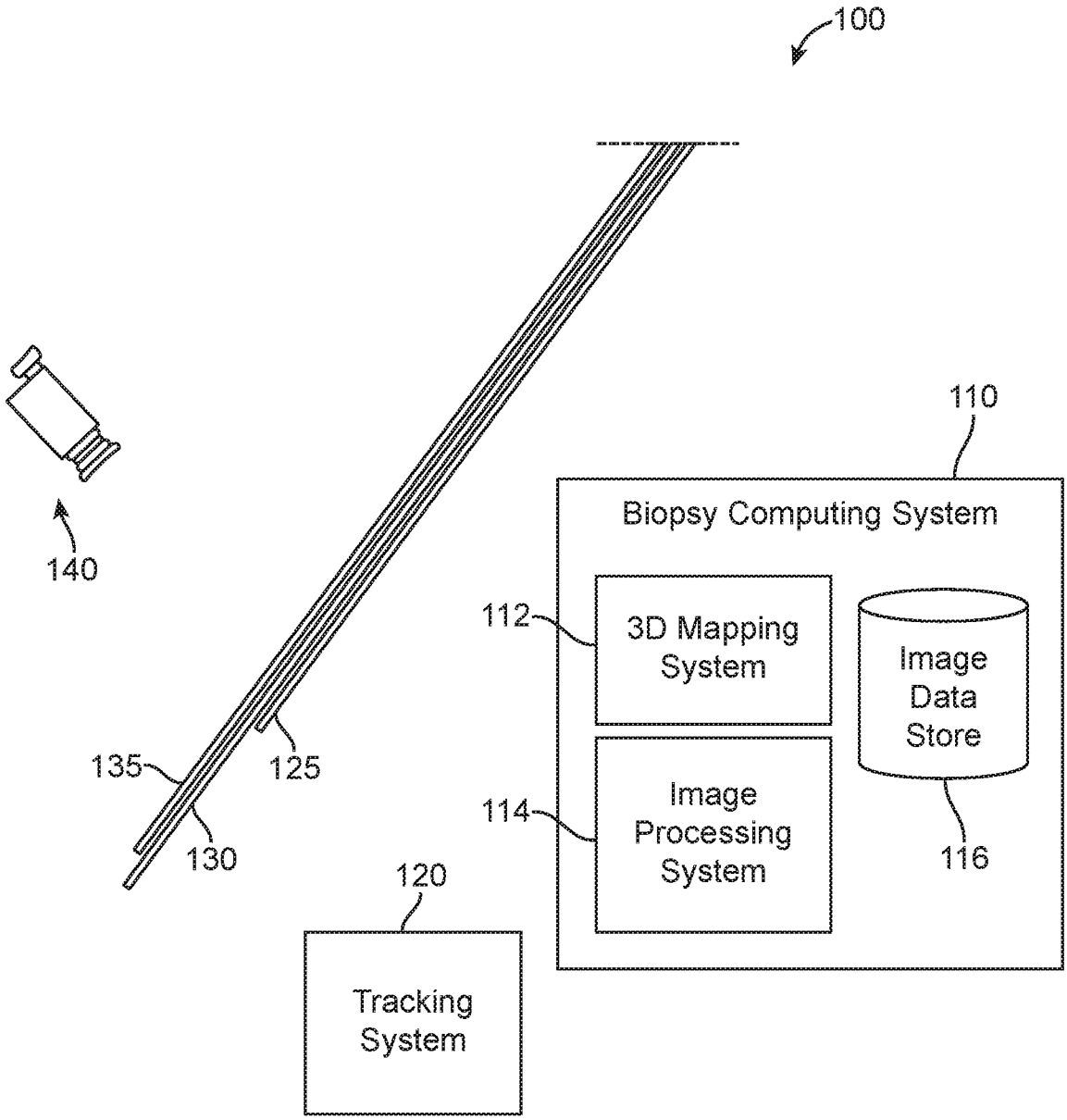

100
110
Biopsy Computing System
112
3D Mapping System
Image Data Store
114
Image Processing System
116
120
Tracking System
140
135
125
130

FIG. 1

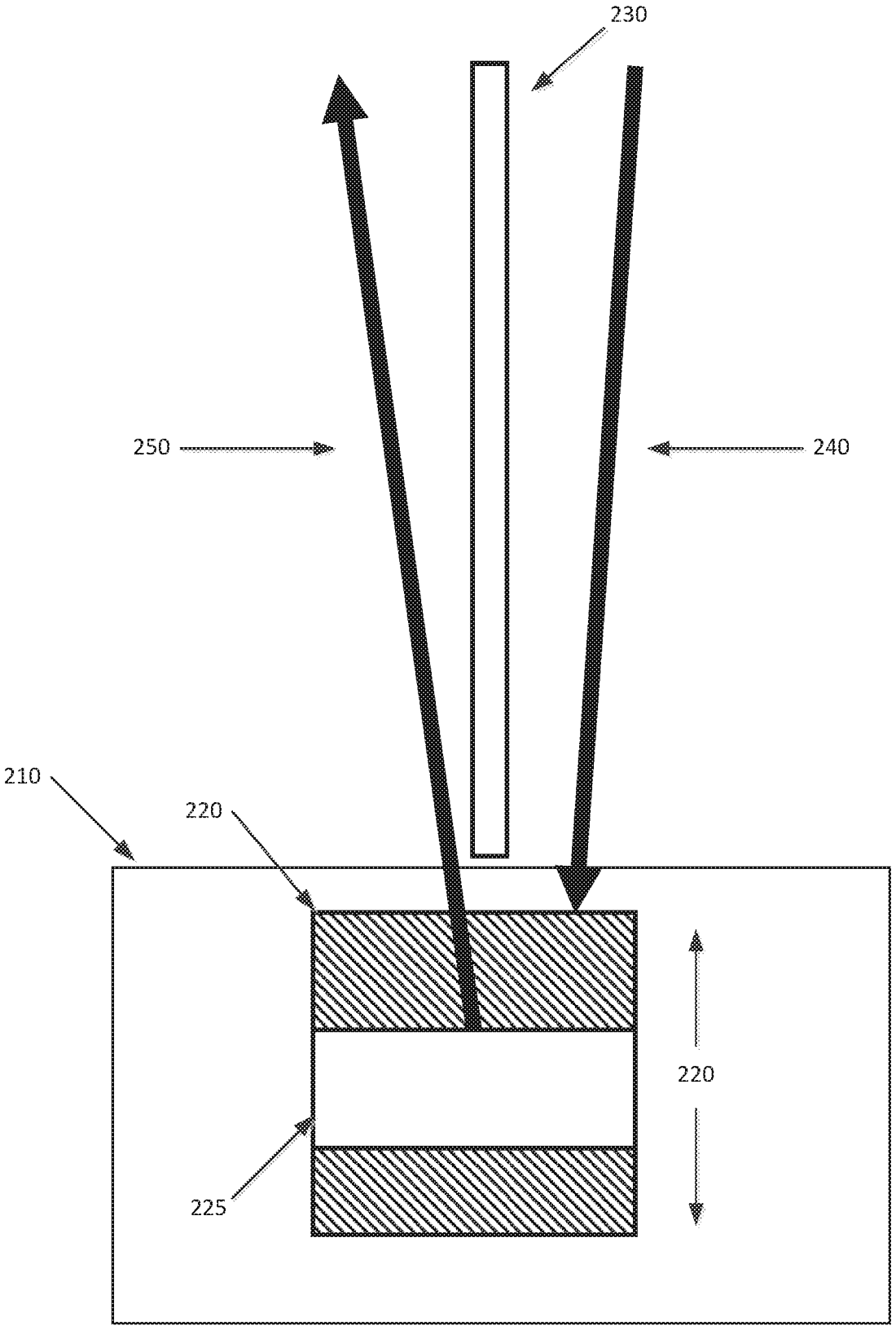


Fig. 2

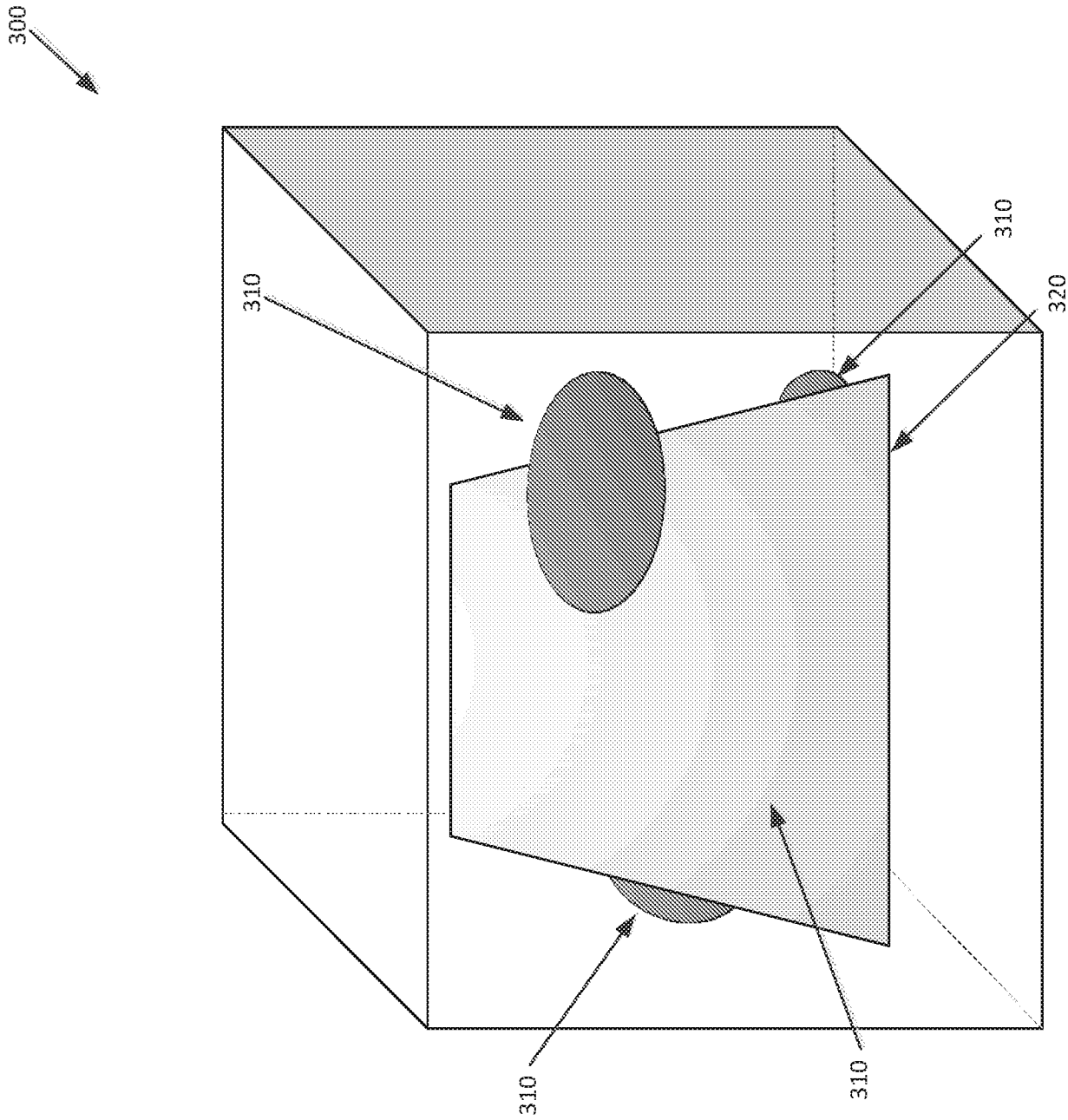


Fig. 3

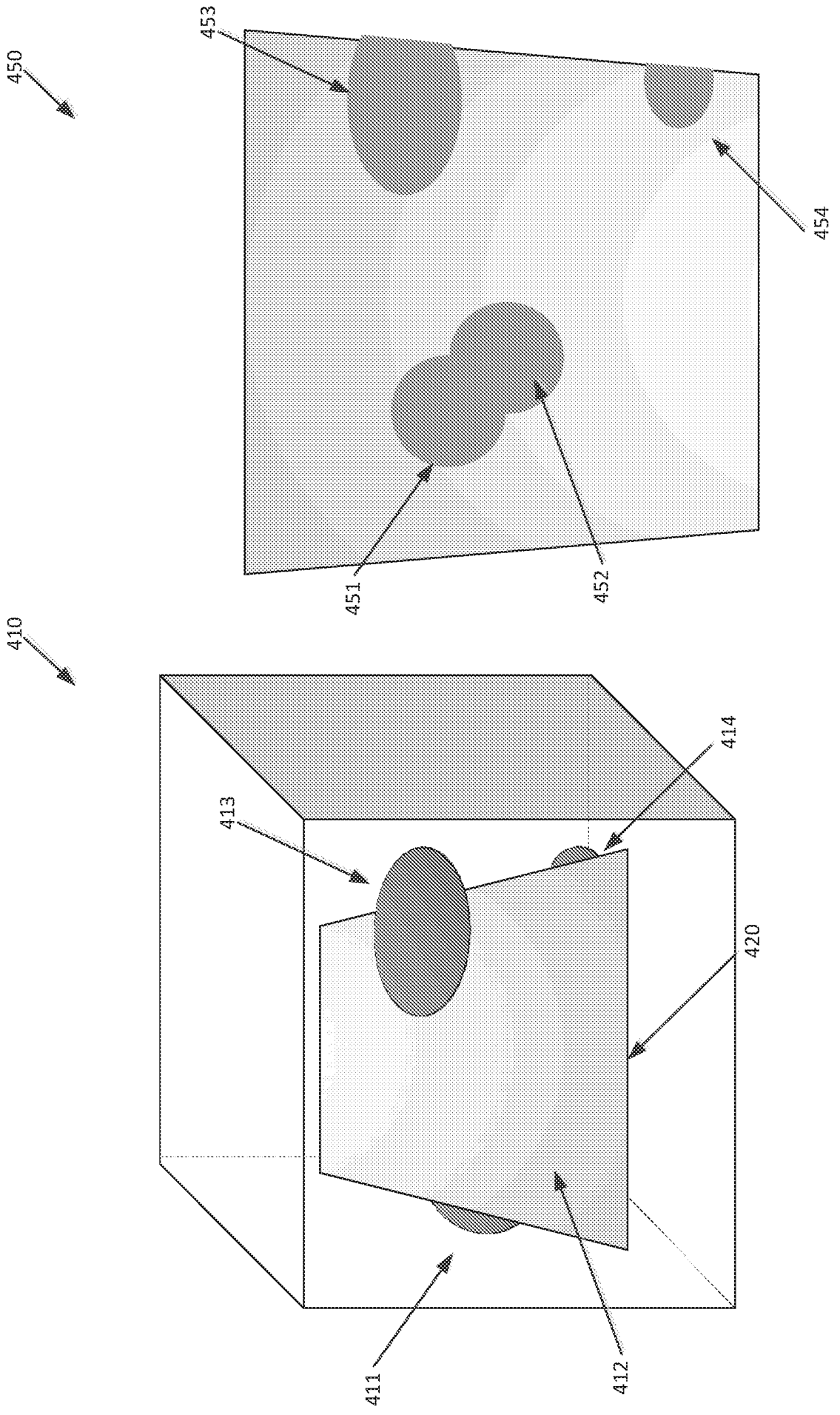


Fig. 4

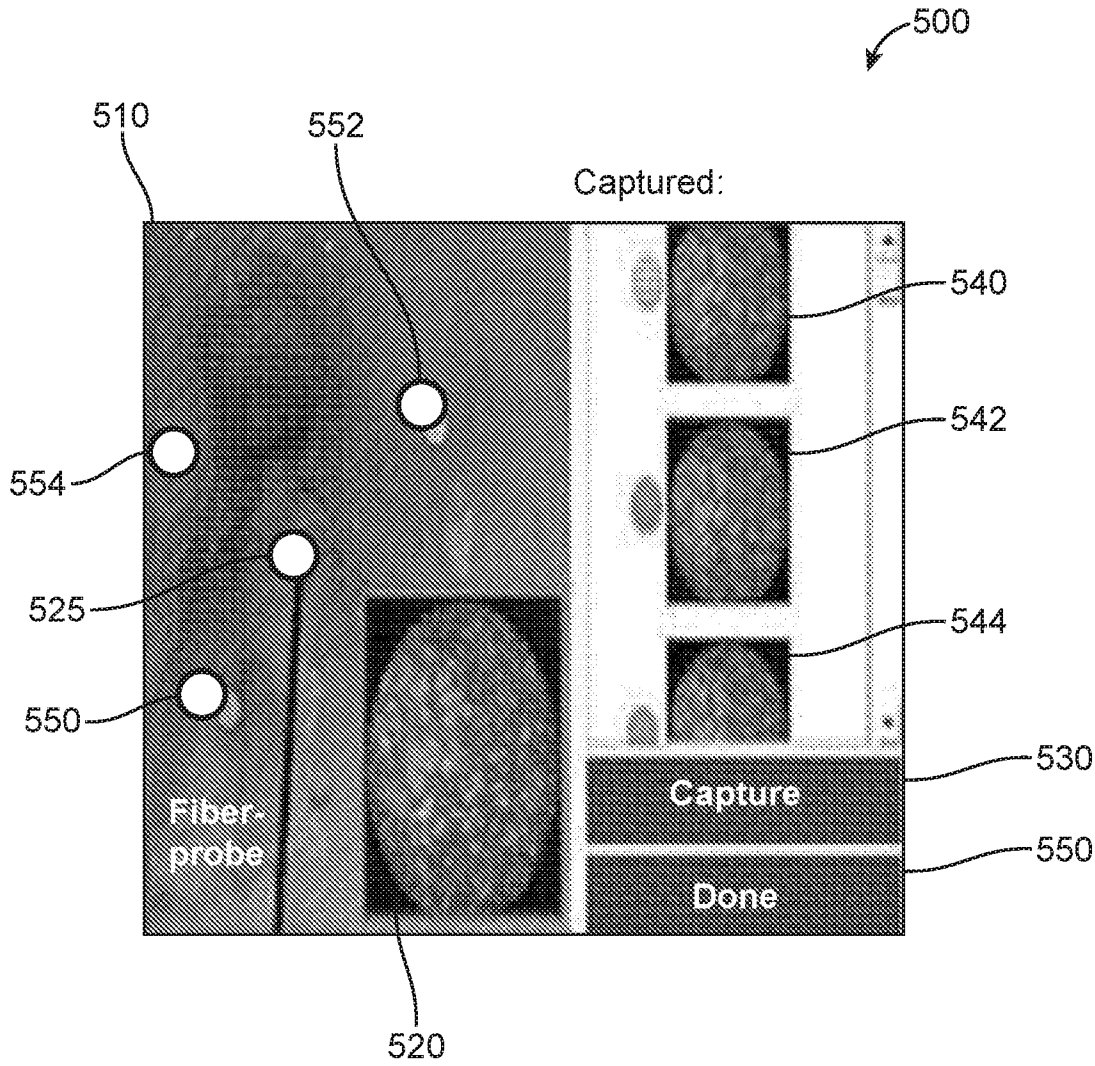

500
510
552
Captured:
540
542
554
525
544
550
530
Capture
Done
Fiber probe
520

FIG. 5

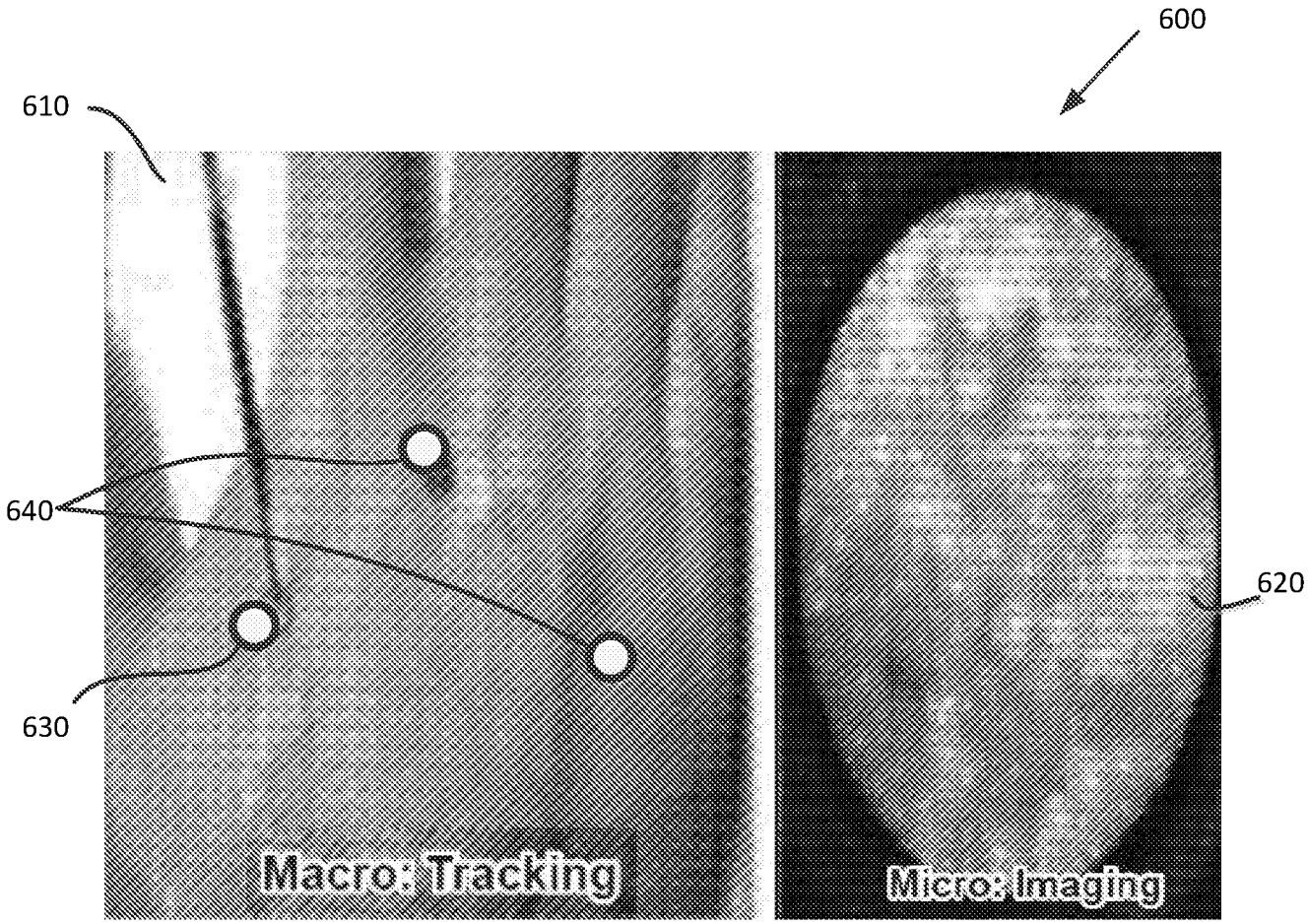


Fig. 6

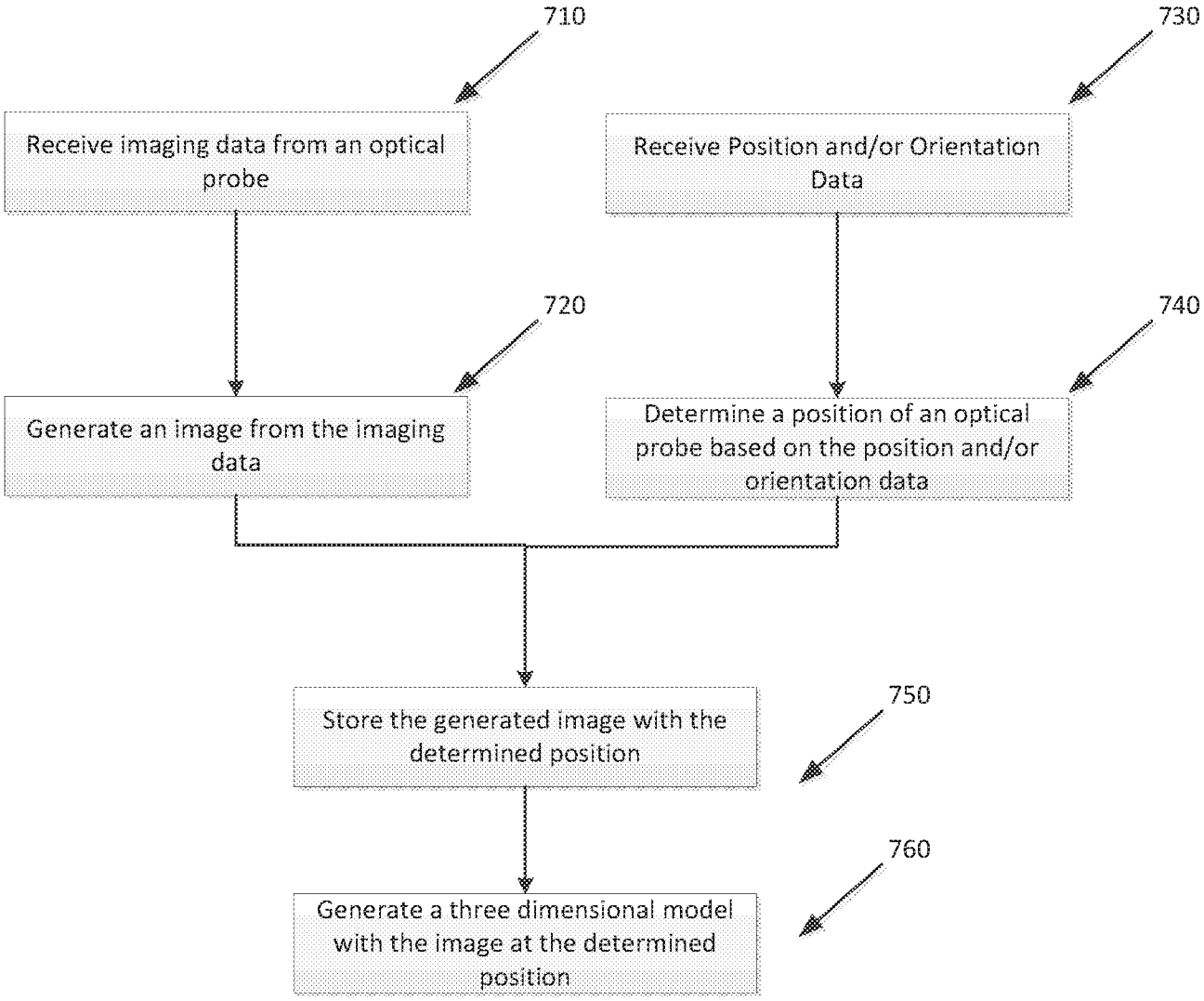

710
Receive imaging data from an optical probe
730
Receive Position and/or Orientation Data
720
Generate an image from the imaging data
740
Determine a position of an optical probe based on the position and/or orientation data
Store the generated image with the determined position
750
760
Generate a three dimensional model with the image at the determined position

Fig. 7

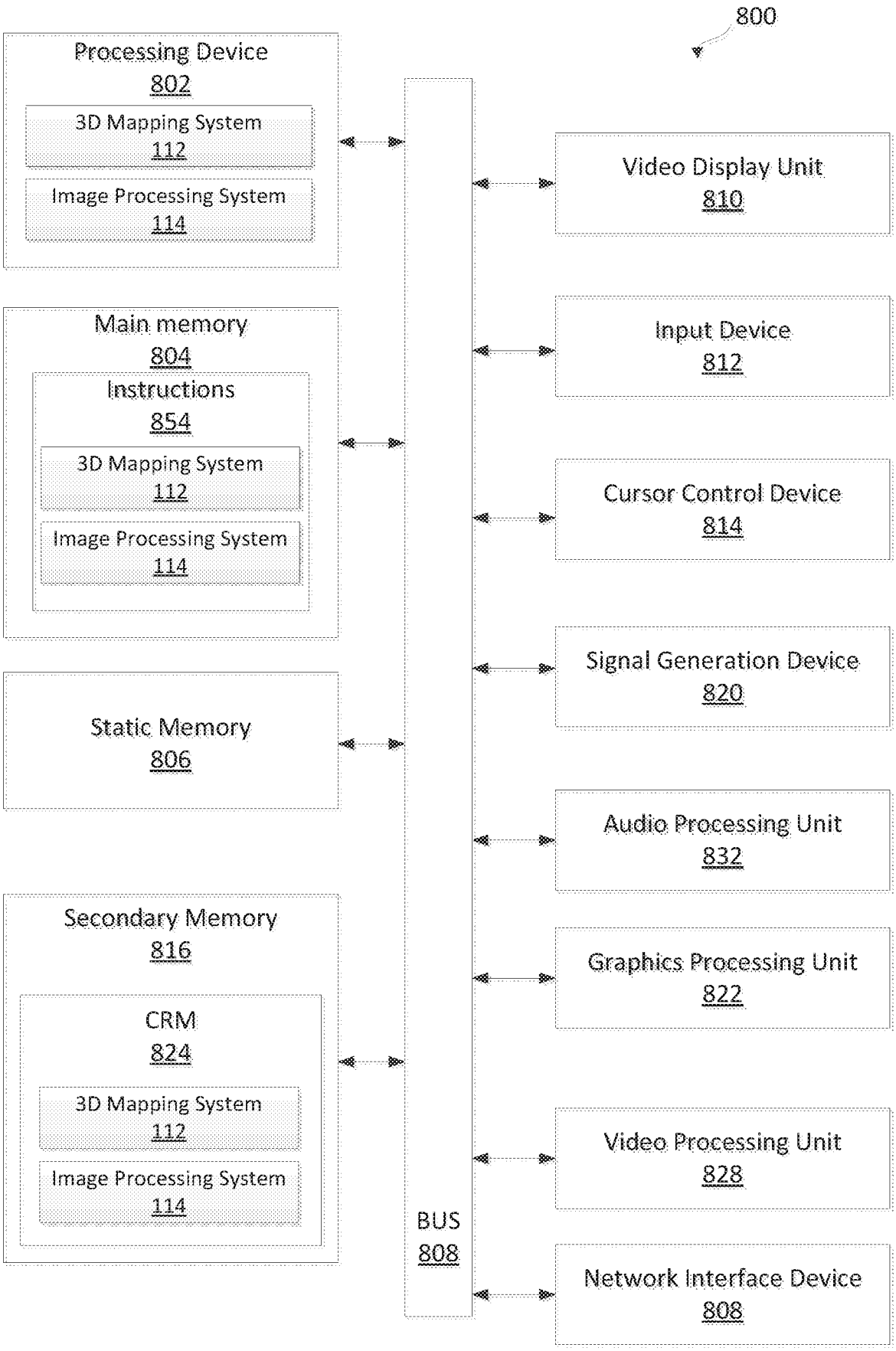

800
Processing Device
802
3D Mapping System
112
Image Processing System
114
Main memory
804
Instructions
854
3D Mapping System
112
Image Processing System
114
Static Memory
806
Secondary Memory
816
CRM
824
3D Mapping System
112
Image Processing System
114
BUS
808
Video Display Unit
810
Input Device
812
Cursor Control Device
814
Signal Generation Device
820
Audio Processing Unit
832
Graphics Processing Unit
822
Video Processing Unit
828
Network Interface Device
808

Fig. 8

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US16/65014

A. CLASSIFICATION OF SUBJECT MATTER
IPC - G06T 3/00, 7/00; A61B 10/02, 10/04, 1/06, 17/94 (2017.01)
CPC - G06T 3/00, 7/00, 7/10; A61B 10/04

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History document

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2015/0045648 A1 (UC-CARE LTD.) February 12, 2015; figure 1; paragraphs [0017]-[0018], [0037], [0052], [0066]	1-10
Y	WO 2015/074018 A1 (VOLCANO CORPORATION) May 21, 2015; figure 8; page 11, paragraph 1; page 13, paragraphs 2-3	1-10
Y	EP 1 611 457 B1 (KONINKLIJKE PHILIPS N.V.) September 10, 2014; paragraphs [0008], [0009], [0012], [0024]	10

☐ 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 application or patent 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
31 January 2017 (31.01.2017)	05 APR 2017
Name and mailing address of the ISA/ Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US16/65014

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

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

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

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

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

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

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

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

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

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

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-10

Remark on Protest

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

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

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US16/65014

-***-Continued from Box No. III Observations where unity of invention is lacking -***-

The application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fee must be paid.

Group I: Claims 1-10 are directed toward an imaging system with a light source applying and applying a geometric transformation.

Group II: Claims 11-20 are directed toward an imaging system with a memory device and determining a second position of the optical probe.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features.

Group I has at least a light source operatively coupled to the optical probe and applying a geometric transformation to the first position data and the first orientation data that Group II does not have. Group II has at least a memory device, determine a second position of the optical probe based on the tracking data received from the tracking system that Group I does not have.

The common technical features of Groups I-II are an optical probe to generate imaging data; a tracking system to generate position data and orientation data associated with the optical probe, a processing device operatively coupled to the tracking system, determine first position data and first orientation data associated with the subset of imaging data received from the optical probe, generate a three dimensional model of images comprising the first image placed at the first position in the virtual three dimensional space.

The common technical features are disclosed by US 2015/045648 A1 to UC-CARE LTD. ("UC-CARE"). UC-CARE discloses an imaging system (imaging system; abstract), comprising: an optical probe to generate imaging data (imaging probe forms image data; paragraph [0017]); a tracking system to generate position data and orientation data associated with the optical probe (tracking system has tracking sensor that is spatially fixed to imaging probe to provide location and orientation data; paragraphs [0016]-[0018]); and a processing device operatively coupled to the tracking system (processing unit receives position data from the tracking sensor; paragraph [0018]), the processing device to: apply optical sectioning to generate a first image based on a subset of the imaging data received from the optical probe (cross-sectioning image data from a portion of the imaging probe forming 2D images; paragraphs [0052], [0066]); determine first position data and first orientation data associated with the subset of imaging data received from the optical probe (position data, corresponding to location and orientation, is assigned to image data from the imaging probe, relating by time collected (being a subset of imaging data); paragraphs [0017]-[0018]); and generate a three dimensional model of images comprising the first image placed at the first position in the virtual three dimensional space (generating a 3D model based on the images transformed into the volume of space; paragraphs [0066], [0072], [0074]).

Since the common technical features are previously disclosed by the UC-CARE reference, these common features are not special and so Groups I-II lack unity.