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7480 Flying Cloud Drive, Suite 110, Eden Prairie, Minnesota 55344 (US).

(74) Agent: **BRADLEY, Brian F.**; Casimir Jones, S.C., 2275 Deming Way, Ste 310, Middleton, Wisconsin 53562 (US).

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(71) Applicant: **ELUCENT MEDICAL, INC.** [US/US]; 7480 Flying Cloud Drive, Suite 110, Eden Prairie, Minnesota 55344 (US).

(72) Inventors: **HILTNER, Jason**; c/o Elucient Medical, Inc., 7480 Flying Cloud Drive, Suite 110, Eden Prairie, Minnesota 55344 (US). **DEAN, Bryan**; c/o Elucient Medical, Inc.,

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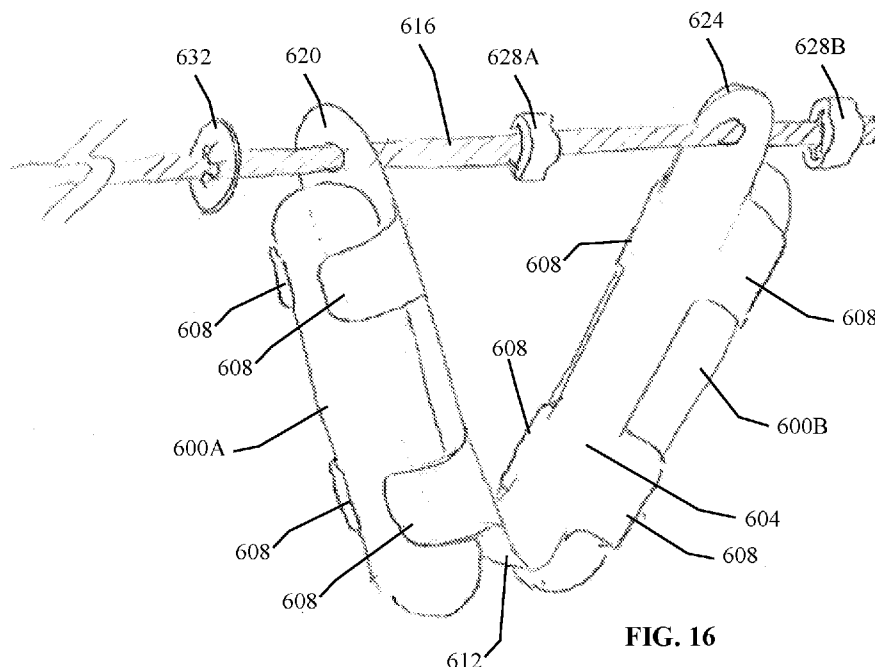


FIG. 16

(57) Abstract: Provided herein are systems and methods comprising two or more localization agents that are linked together by a linker. For example, provided herein are systems and methods for the placement of two or more linked localization devices within biological systems and the detection of such localization devices for targeted surgeries or other medical procedures. For example, provided herein are systems comprising one or more miniature detectable devices that are linked together, that are placed into a target location and activated by remote introduction of a magnetic field.



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SYSTEMS AND METHODS COMPRISING LINKED LOCALIZATION AGENTS

CROSS REFERENCE TO RELATED APPLICATIONS

The present application claims the benefit of U.S. Provisional Application No.
5 63/078,971 filed on September 16, 2020, the contents of which are hereby incorporated by
reference in their entirety.

FIELD

Provided herein are systems and methods comprising two or more localization agents
10 that are linked together by a linker. For example, provided herein are systems and methods
for the placement of two or more linked localization devices within biological systems and
the detection of such localization devices for targeted surgeries or other medical procedures.
For example, provided herein are systems comprising one or more miniature detectable
devices that are linked together, that are placed into a target location and activated by remote
15 introduction of a magnetic field.

BACKGROUND

A common and serious challenge for many medical procedures is the accurate
localization of treatment areas. For example, the location of lesions, such as tumors that are
20 to undergo treatment, including surgical resection, continues to present a challenge to the
medical community. Existing systems are expensive, complex, time-consuming, and often
unpleasant for the patient.

Recent methods for tissue localization for medical procedures involve the use of
localization agents, such as RFID tags, that may be placed within the patient. However, these
25 tags may migrate within the patient in between placement and the performance of the surgical
procedure, leading to a failure to properly mark the desired location within the patient.
Furthermore, the orientation of the tags may shift after placement within the patient, leading
to a loss of accuracy in identifying the 3-dimensional location of the tag within the patient.
Additional problems with efficacy may arise with larger patients, where the strength of signal
30 generated by a single tag is insufficient to be detected due to the volume of tissue present.

Accordingly, improved systems and methods are needed for tissue localization for
medical procedures.

SUMMARY

Provided herein are systems and methods comprising two or more localization agents (e.g. “tags”) that are linked together by a linker. For example, provided herein are systems and methods for the placement of two or more linked tags within biological systems and the detection of such tags for targeted surgeries or other medical procedures. While the description below illustrates the invention using examples of human surgical procedures, it should be appreciated that the invention is not so limited and includes veterinary applications, agricultural applications, industrial applications, mechanical applications, military applications (e.g., sensing and removal of dangerous materials from an object or region), aerospace applications, and the like.

In some embodiments, provided herein are systems comprising one or more of each of: a) at least two tags, b) a linker attached to each of the at least two tags; c) a remote activating device (e.g., exciter assembly) that generates a magnetic field (e.g., time varying magnetic field) within a region of each tag, and d) a plurality of sensors configured to detect a signal from the at least two tags when the tags are exposed to the magnetic field.

Each of the at least two tags are attached to at least one other tag (e.g. linked) by a linker. Tags connected to each other by a linker are referred to herein as “linked tags”.

In some embodiments, the linker is a flexible linker. In some embodiments, the linker comprises plastic. In other embodiments, the linker comprises a shape-memory alloy. For example, the linker may comprise a nickel-titanium alloy (e.g., Nitinol 60 or Nitinol 55).

In some embodiments, the at least two tags are positioned to form an angle within a range of 15 degrees to 40 degrees. In some embodiments, the angle is 25 degrees.

In some embodiments, the linker includes a grip that is graspable by a surgical tool. In some embodiments, the grip is a sphere. In some embodiments, the linker is positioned within a packaging that includes a notch that exposes the grip.

In some embodiments, the linker comprises a torsion spring. In some embodiments, each of the tags is attached to the linker via heat shrink tubing.

In some embodiments, the linker is configured to hold the at least two tags in a first position when the tags are present in an insertion device. In some embodiments, the linker is configured to hold the at least two tags in a second position when present in tissue, wherein at least one of the tags in the second position points approximately in the X dimension, and at least one of the tags points approximately in the Y dimension. In some embodiment, the at least two tags comprises first, second, and third tags. In such embodiments, in said second position: i) said first tag points approximately in the X dimension, ii) said second tag points

in approximately the Y dimension, and iii) and said third tag points in approximately in the Z dimension.

In some embodiments, the system further comprises a wire or a line. The wire or line may be attached to, and/or pass through, the linker at two or more points on the linker. For example, the wire or line may be attached to, and/or pass through, the linker such that the two or more tags are held in a first position with respect to each other. The linker may be configured to hold the two or more tags in a second position when the wire or line is not attached to, and/or does not pass through, the linker. The second position may be different from the first position.

In some embodiments, the tags are programmed to respond to a signal from the magnetic field with an offset frequency compared to the signal. In some embodiments, the tags comprise a non-dielectric resonant antenna capacitor.

In some embodiments, each of the at least two tags comprise an antenna, wherein each tag emits sidebands at defined frequencies upon activation by a magnetic field. In some embodiments, each tag antenna comprises a coil antenna. For example, each coil antenna may comprise a ferrite-core coil antenna.

In some embodiments, each coil antenna resonates at 100-200 kHz. Each coil antenna may resonate at the same or substantially the same frequency. Alternatively, each coil antenna may resonate at a different frequency.

In some embodiments, the remote activating device comprises at least one excitation coil. In some embodiments, the remote activating device comprises two or more excitation coils configured to flow current in either a clockwise or counterclockwise direction such that the magnetic field generated by the remote activating device may be selectively generated in one or more of X, Y, and Z directions, (e.g., to ensure that the tags can be excited for multiple or any angle that it may be placed). In some embodiments, the magnetic field is generated in two or more of X, Y, and Z directions. In some embodiments, the magnetic field is generated in each of the X, Y, and Z directions.

In some embodiments, the remote activating device comprises four or more exciter coils. In some embodiments, the exciter coils are connected in series. In some embodiments, four of the exciter coils are in a layout of two rows centered at coordinates (X1, Y1), (X1, Y2), (X2, Y1), and (X2, Y2). In some embodiments, the remote activating device (e.g., exciter assembly) comprises at least one of three current flow configurations: a) all current clockwise to simulate an exciter coil aligned with a direction normal to the Z axis; b) exciter coils centered at (X2, Y1), (X2, Y2) running current counter-clockwise to simulate an exciter

coil aligned to the X axis; and c) exciter coils centered at (X1, Y2), (X2, Y2) running current counter-clockwise to simulate an exciter coil aligned substantially to the Y axis. In some embodiments, the remote activating device comprises all three of the above current flow configurations.

5 In some embodiments, the remote activating device (e.g., exciter assembly) comprises a plurality of relays that provide a switching function to accomplish the current direction change (polarity) yet maintain an excitation frequency by switching additional capacitive reactance. In some embodiments, the switching function inserts additional series capacitive reactance via a capacitance element when total inductance is increased so that a tuning center
10 frequency is maintained at said excitation frequency (e.g., the total inductance of the 4 coils, when 4 coils are employed, varies as the current direction is changed within each coil or coil pair). In some embodiments, the capacitance element is comprised of multiple capacitors (e.g., to better accommodate the voltage potential at resonance and/or to provide greater flexibility on frequency tuning). In some embodiments, the remote activating device further
15 comprises a balun in proximity to the exciter coils. The balun eliminates common mode current that would otherwise produce unwanted electric field components that could otherwise reduce accuracy. It also provides impedance transformation to match the real component of the coil impedance to that of the transmission line, typically 50 Ohms. In some embodiments, the balun has eight turns on a primary side (amplifier side) and four turns on a
20 secondary side (coil side). In some embodiments, the system further comprises an amplifier in electronic communication with the remote activating device. In some embodiments, the system further comprises a computer that controls magnetic field generation and sensor detection. In some embodiments, the computer comprises a hunting algorithm (e.g., embodied in software running on the processor) that adjusts the magnetic field orientation to
25 identify (and power) optimal detection of at least two tags.

Also provided herein are uses of any of the above systems (e.g., for detecting the positions of two or more linked tags in an object; for detecting a position of two or more linked tags relative to a medical device; etc.).

Further provided herein are methods of identifying a position of two or more linked
30 tags, comprising: a) providing any of the systems described herein; b) placing the at least two tags in an object; c) generating a magnetic field with the activating device; and d) identifying a position of the tags in said object by collecting information emitted from each tag with the witness stations. In some embodiments, the position or comprises relative location or distance of the tags to a medical device.

In some embodiments, placing the at least two tags in an object comprises positioning the at least two tags into said object using an introduction device. In some embodiments, the at least two tags are arranged in a first position within said introduction device. In some embodiments, the at least two tags migrate into a second position when placed in said object.

5 In some embodiments, at least one of said tags in said second position points approximately in the X dimension, and at least one of said tags points approximately in the Y dimension. In some embodiments, the at least two tags comprises first, second, and third tags, and wherein, when in said second position: i) said first tag points approximately in the X dimension, ii) said second tag points in approximately the Y dimension, and iii) and said third tag points in
10 approximately in the Z dimension.

DEFINITIONS

As used herein, the terms “processor” and “central processing unit” or “CPU” are
15 used interchangeably and refer to a device that is able to read a program from a computer memory (e.g., ROM or other computer memory) and perform a set of steps according to the program.

As used herein, the terms “computer memory” and “computer memory device” refer to any storage media readable by a computer processor. Examples of computer memory
20 include, but are not limited to, RAM, ROM, computer chips, digital video discs (DVD), compact discs (CDs), hard disk drives (HDD), optical discs, and magnetic tape. In certain embodiments, the computer memory and computer processor are part of a non-transitory computer (e.g., in the control unit). In certain embodiments, non-transitory computer readable media is employed, where non-transitory computer-readable media comprises all
25 computer-readable media with the sole exception being a transitory, propagating signal.

As used herein, the term “computer readable medium” refers to any device or system for storing and providing information (e.g., data and instructions) to a computer processor. Examples of computer readable media include, but are not limited to, DVDs, CDs, hard disk drives, magnetic tape and servers for streaming media over networks, whether local or distant
30 (e.g., cloud-based).

As used herein, the term “in electronic communication” refers to electrical devices (e.g., computers, processors, etc.) that are configured to communicate with one another through direct or indirect signaling. Likewise, a computer configured to transmit (e.g.,

through cables, wires, infrared signals, telephone lines, airwaves, etc.) information to another computer or device, is in electronic communication with the other computer or device.

As used herein, the term “transmitting” refers to the movement of information (e.g., data) from one location to another (e.g., from one device to another) using any suitable means.

As used herein, the term “alloy” refers to a combination of a metal with at least one other metal or nonmetal. The term “shape-memory alloy” refers to an alloy that can be deformed when cold but returns to its pre-deformed (e.g., “remembered”) shape when heated.

As used herein, the term “subject” or “patient” refers to any animal (e.g., a mammal), including, but not limited to, humans, non-human primates, companion animals, livestock, equines, rodents, and the like, which is to be the recipient of a particular treatment. Typically, the terms “subject” and “patient” are used interchangeably herein in reference to a human subject.

As used herein, the term “subject/patient suspected of having cancer” refers to a subject that presents one or more symptoms indicative of a cancer (e.g., a noticeable lump or mass) or is being screened for a cancer (e.g., during a routine physical). A subject suspected of having cancer may also have one or more risk factors. A subject suspected of having cancer has generally not been tested for cancer. However, a “subject suspected of having cancer” encompasses an individual who has received an initial diagnosis (e.g., a CT scan showing a mass) but for whom the stage of cancer is not known. The term further includes people who once had cancer (e.g., an individual in remission).

As used herein, the term “biopsy tissue” refers to a sample of tissue (e.g., breast tissue) that is removed from a subject for the purpose of determining if the sample contains cancerous tissue. In some embodiments, biopsy tissue is obtained because a subject is suspected of having cancer. The biopsy tissue is then examined (e.g., by microscopy; by molecular testing) for the presence or absence of cancer.

As used herein, the term “linker” herein refers to a suitable material which connects one tag to another tag. The linker may comprise any suitable material. For example, the linker may comprise plastic. Alternatively, the linker may comprise a shape-memory alloy.

As used herein, the term “linked tags” refers to a group of at least two tags, wherein at least one tag is attached to at least one other tag via a linker. The term may refer to two attached tags. The term may refer to three or more tags, wherein each tag is attached to at least one other tag via one or more linkers.

As used herein, the term “tag” or “marker tag” refers to the small implantable marker that, when excited by an exciter’s time varying magnetic field, will emit a “homing beacon” spectrum of frequency(ies) received by the witness coil(s) and used to determine its location. It may be programmed to produce a unique spectrum, thus permitting multiple tags to be
 5 implanted and located simultaneously.

DESCRIPTION OF DRAWINGS

FIG. 1 shows an exemplary positioning of an exciter assembly, a medical device with display component attached, and a patient with a tag implanted next to a tumor.

10 FIG. 2 shows an attachment component 10 that is attached to a medical device 20, which has a device tip 25. The attachment component 10 has two location emitters 70 located therein. The attachment component 10 is attached to, or integral, with a display component 40.

FIG. 3 shows an exemplary coil configuration of an exciter assembly.

15 FIG. 4A shows an exemplary exciter assembly 250 attached to controller 210 via a cable bundle 200. FIG. 4B shows an exemplary witness coil assembly (aka witness station assembly) 161. FIG. 4C shows an exemplary witness coil 160, including the three directions in which wire is wound to form coils 167 over the metal core 166.

FIG. 5 shows an exemplary exciter assembly with four exciter coils (Coils A-D),
 20 where the current is flowing in the clockwise direction in all four exciter coils.

FIG. 6 shows an exemplary exciter assembly with four exciter coils (Coils A-D), where the current is flowing in the clockwise direction in Coils A and B, and flowing in the counterclockwise direction in Coils C and D.

FIG. 7 shows an exemplary exciter assembly with four exciter coils (Coils A-D),
 25 where the current is flowing in the clockwise direction in Coils A and C, and flowing in the counterclockwise direction in Coils B and D.

FIG. 8 shows an exemplary exciter assembly 250 with the top cover 230 on. The exciter assembly 250 is shown with cable bundle 200 leading therein.

FIG. 9 shows an exemplary attachment component 10, with an angled distal end 300
 30 that the distal tip 25 of the medical device 20 is inserted through.

FIG. 10A shows the distal end 25 of a medical device 20 after it is initially inserted through the angled distal end 300 of attachment component 10. FIG. 10B shows attachment component wire 60 prior to being attached to the cable management component 315 of the display component housing 330. FIG. 10B shows attachment component wire 60 prior to

being attached to the cable management component 315 of the display component housing 330. FIG. 10B also shows the housing tapered connection 340 that the proximal end tapered connection 350 of the attachment component 10 is inserted into. The cable management component 315 has two clips that attached to and align both the attachment component wire 60 and the medical device wire 50.

FIG. 11 shows an exemplary attachment component 10 attached to a display component housing 330. The attachment component 10 has a pair of location emitters 70, which are linked to location emitter wires leads 72 which are inside tube 360. The attachment component also has an angled distal end 300 with a distal end opening 305, which allows the tip of a surgical or other device to be inserted therethrough. The display component housing 330 has a cable management component 315, composed of a pair of clips for holding insulated wires.

FIG. 12 shows an exemplary attachment component 10 attached to a display component housing 330 with a display component 40 located therein. A display cover 370 is shown, which is used to secure the display component 40 inside the display component housing 330. Also shown is an adhesive strip 380, which is shaped and sized to fit inside the attachment component and help secure a medical device to the attachment component.

FIG. 13A shows the proximal end tapered connection 350 of the attachment component 10, which is configured to push-fit into housing tapered connection 340 of the display component housing 330. FIG. 13B shows a close up of section A of FIG. 13A, including cable management tapered connection 317 that is part of cable management component 315 and designed to be inserted into tapered connection hole 319 of display component housing 330. Cable management tapered connection 317 includes a flat part 318 to lock angular position.

FIG. 14 shows an exemplary system for localizing a tag that is implanted in a patient. The system is composed of an exciter assembly that emits signals that activate the tag(s) in the patient. A systems electronics enclosure is shown as a mobile cart, which delivers signals to the exciter assembly and receives and processes signals from the tag(s) in the patient. Guidance for a surgeon is displayed on the display component, as well as on a screen on the systems electronics enclosure.

FIG. 15 shows an exemplary arrangement of two tags connected by a Nitinol linker.

FIG. 16 shows an exemplary arrangement of two tags connected by a Nitinol linker and a wire or line containing crimps and a self-cinching washer.

FIG. 17 shows an exemplary arrangement of two tags connected by a linker.

FIG. 18 shows the arrangement of FIG. 17 in a packaging.

DETAILED DESCRIPTION

5 Provided herein are systems, devices, assemblies, and methods for localization two or tags connected by a linker, for example, in a tissue of a patient. For example, provided herein are systems, devices, and methods employing one or more or all of: a) two or more linked tags placed into an object, such as a patient; b) a remote activating device that generates an electromagnetic field within a region of the tags; c) a plurality of sensors (e.g. witness
10 stations) that receive information from the tags that have been exposed to the electromagnetic field; d) one or more emitters positioned on a medical device that are exposed to the electromagnetic field and that emit information received by the sensors (e.g. witness stations); and e) a computer system for analyzing information received by the sensors and generating and displaying information about the positions of the medical device and/or tag or
15 tags (e.g., relative location, relative distance, orientation, etc.).

 The systems, devices, assemblies, and methods find use in a variety of application including medical applications for locating the linked tags in a subject. While the specification focuses on medical uses in human tissues, it should be understood that the systems and methods find broader use, including non-human uses (e.g., use with non-human
20 animals such as livestock, companion animals, wild animals, or any veterinary settings). For example, the system may be used in environmental settings, agricultural settings, industrial settings, or the like. In some embodiments, the systems, devices, assemblies, and methods find use in electromagnetic navigation systems that power a remote tag device with a sinusoidal magnetic field (see e.g., U.S. Pat. No. 9,730,764 and U.S. Appln. Ser. Nos.
25 15/281,862 and 15/674,455, herein incorporated by reference in their entireties).

 In some embodiments, provided herein are systems comprising at least two tags, wherein each tag is attached to at least one other tag via a linker, a remote activating device that generates a magnetic field within a region of each tag, and a plurality of sensors configured to detect a signal from each tag while each tag is exposed to said magnetic field.

30 In some embodiments, the tag is wireless and ideally minimally sized. In some embodiments, while powered, the tag generates its own time varying magnetic field at one or more sideband frequencies. The shape of the magnetic field is approximately that of a magnetic dipole positioned at the tag. By monitoring the magnetic field at several positions with receiving antenna coils, also called sensors, sensing coils, witness coils, or witness

stations, the location of the tag is identified. In some embodiments, the systems, devices, assemblies, and methods further comprise an electrosurgical tool. In some embodiments, the electrosurgical tool, or a component attached to or in physical proximity to the tool, comprises two or more location emitters that also generate a magnetic field similar to a magnetic dipole. In some embodiments, the location emitters are driven with two different frequency signals that are also different from both the exciter frequency and the tag response frequencies. In certain embodiments, the location emitters are wired to a signal supply source.

In some embodiments, a single exciter assembly is employed (e.g., as shown in Figure 4A) to generate signals that interact with the tag and the location emitters in the attachment component associated with the electrosurgical tool. In some embodiments, the exciter assembly is contained in a single thin assembly. In some embodiments, the assembly comprising the exciter further comprises sensors (e.g., the receiving antenna/sensing/witness station coils). In some embodiments, the exciter assembly is configured to be deployed under a patient that is undergoing a medical procedure. An exemplary procedure configuration is shown in FIG. 1 with patient 90 positioned on a surface 95 (e.g., mattress or operating table). The surface 95 is held by a surface frame 97. The patient 90 has a lesion (e.g., tumor) 110 and an implanted tag 100 positioned near, on, or in the tumor. An exciter assembly 250 is positioned beneath the patient, and beneath the surface (e.g., on the surface frame 97), and generates an electromagnetic field (not shown) in a region around the patient encompassing the position of the tag 100 and a medical device 20 (e.g., surgical device) in the operating field above the patient.

FIG. 2 shows an exemplary electrocautery surgical device (e.g., BOVIE) that finds use in some embodiments of the invention. The device 20 includes a tip 25 providing an operating surface for treatment of tissues, two embedded location emitters 70 allows the system to sense the location and position of the device 20, and a display unit 40 that provides visual information to a user (e.g., surgeon) about the location of a tag in the patient.

In some embodiments, the exciter assembly is configured to provide enhanced detection of remote objects (e.g., tags and surgical devices) under a number of different settings that would otherwise complicate location, position, and distance assessment, particularly real-time assessment of such factors.

In some embodiments, the systems and methods comprise a plurality of components. In some embodiments, a first component comprises at least two linked tags (which may be used interchangeably with the term “marker”) whose location, position, distance, or other

properties are to be assessed. The linked tags described herein find use in a variety of systems and methods, such as those disclosed in WO2018031826A1, WO2017059228A1, WO2019236600A1, and WO2015112863A1, the entire contents of each of which are incorporated herein by reference. In some embodiments, the systems and methods may comprise two linked tags, three linked tags, four linked tags, five linked tags, or more than five linked tags. In some embodiments, the systems and methods comprise two linked tags. For example, the systems and methods may comprise two linked tags “A” and “B” that are attached to each other via a linker. Alternatively, the systems and methods may comprise three or more linked tags. In such embodiments, the tags are linked in the sense that each tag is attached to at least one other tag via the same or different linkers. For example, three tags may be linked, wherein tag “A” is attached to tag “B” via a linker and tag “B” is attached to tag “C” via a linker. In some embodiments, at least one tag may be attached to two or more tags. For example, three tags may be linked, wherein tag “A” is attached to tag “B” and tag “B” is attached to tag “C” and tag “C” is attached to tag “A”.

The tags are linked by a suitable linker. The linker may comprise any suitable material that connects one tag to another. For example, the linker may comprise plastic. Alternatively, the linker may comprise a shape-memory alloy. In some embodiments, the shape-memory alloy linker may comprise any one or more metals selected from copper, iron, aluminum, nickel, titanium, manganese, silicon, zinc, or gold. For example, the shape-memory alloy may be a nickel-titanium alloy (e.g. Nitinol). As another example, the shape-memory alloy may be a copper-aluminum-nickel alloy. The metals in the shape-memory alloy may be present in any suitable amount to achieve the desired alloy characteristics. For example, for Nitinol, nickel and titanium are typically present in atomic percentages ranging from 55%-60% nickel and 40-45% titanium (by weight). For example, Nitinol 55 comprises 55% nickel and 45% Titanium. Alternatively, Nitinol 60 comprises 60% nickel and 40% titanium (wt%).

With reference to FIG. 15, a first tag 500A and a second tag 500B are coupled to a linker 504. The first tag 500A and the second tag 500B are glass tag that are mechanically coupled to the linker 504 by a heat shrink tubing 508 (or other similar means of retention). The linker 504 is made of Nitinol wire and includes a torsion spring 512 positioned between the first tag 500A and the second tag 500B.

In some embodiments, the linker holds the two or more linked tags in a first position prior to being placed within a subject, and the linked tags subsequently form into a second position after being placed within the subject. For example, the linked tags may be held in a

first, constrained arrangement prior to being placed within the subject such that the linked tags fit within the introduction device used to position the linked tags within the subject. This may be accomplished by the use of a plastic linker that folds or bends to allow the linked tags to fit within the introduction device. Alternatively, this may be accomplished by using a
5 shape-memory alloy linker, which may be chilled and molded to a first position to allow for placement within the introduction device. For example, the first position may comprise a linear shape, such that each of the at least two tags are oriented in a straight line to fit within the introduction device (e.g. cannula). The linked tags may subsequently enter into a second position after positioning within the subject. For example, the shape-memory alloy (e.g.
10 nitinol) linker could re-fold to a remembered shape (e.g. L-shape, T-shape, V-shape, etc.) after positioning within the subject. As another example, the linker may be plastic which is folded or bent to allow the linked tags to fit within the introduction device (e.g. cannula), and the plastic linker could un-fold upon positioning within the subject to allow for the linked devices to enter into a second position. Alternatively, a shape-memory alloy linker would be
15 heated to the body temperature of the subject upon positioning within the subject, thus allowing the alloy to return to its “remembered” shape.

The second position (e.g. the arrangement of the linked tags after positioning within the subject) maybe any suitable arrangement. For example, for embodiments with two linked tags the second position may be an L-shape, T-shape, V-shape, or X-shape. As another
20 example, for embodiments with three or more linked tags the second arrangement may be a shape such as triangle, square, rectangle, etc. depending on the number of linked tags. Any of the above-described arrangements would allow for improved anchoring of the linked tags within the tissue of the subject. In some embodiments, the linked tags are configured to be placed in a subject at a surgical location or other clinically relevant location to mark a target
25 region within a body.

In some embodiments, when in the second position, the tags are separated by an angle within a range of approximately 15° to approximately 40° (i.e., the angle of tag separation). In some embodiments, the tags are separated by approximately 30° in the second position for improved six degrees of freedom localization. In some embodiments, the tags are separated
30 by approximately 25° in the second position for improved six degrees of freedom localization. The tags are advantageously angled large enough with respect to each other to establish a full six degrees of freedom coordinate system, while also angled small enough with respect to each other such that both tags can be powered at the same time. A 0° angle between tags would not allow a full six degrees of freedom coordinate system to be

established because the tag signal(s) would not vary as the tag is rotated about its long axis. Likewise, a 90° angle between tags is not preferred because when one tag is fully aligned to the exciter field and receiving full power, the other tag will receive no power. The 90° angle between tags is also not preferred if one tag is pointed at the center of the other tag, because it is ambiguous when the entire structure is flipped (i.e., a T has mirror symmetry, whereas a L does not).

In some embodiments, the second position may be achieved by the use of one or more additional facilitating features (e.g. wires, lines, crimps, washers, etc.). For example, the at least two tags may be linked by a shape-memory alloy. The linker and/or tag(s) may be attached to a wire or a line, which may further comprise crimps, washers, etc. to ensure that the at least two tags achieve the desired arrangement. For example, the wire or line may contain crimps and the spacing between crimps would determine the angle at which the at least two tags are linked (e.g. the angle of the shape memory alloy linking the tags). In some embodiments, the first position of the at least two tags (e.g. the arrangement within the introduction device) may be a straight line, and the wire/line may be pulled after placement of the device into the subject such that the crimps apply the appropriate pressure on the linked tags/shape alloy, thus causing the alloy to bend in order to achieve the desired second position within the subject. In some embodiments, upon achieving the second position the wire/line may be cut and subsequently removed from the subject. Exemplary embodiments using these additional facilitating features are shown in FIG. 16.

With reference to FIG. 16, a first tag 600A and a second tag 600B are mechanically coupled to a linker 604. The first tag 600A and the second tag 600B are glass tags that are retained by clips 608 cut and formed into the linker 604. In the illustrated embodiment, the linker 604 is cut and formed Nitinol tubing with a bend 612 positioned between the first tag 600A and the second tag 600B. A wire 616 (or line) extends between a first end 620 of the linker 604 and a second end 624 of the linker 604. In the illustrated embodiment, the wire 616 passes through bores formed in both the first and second ends 620, 624. Crimps 628A, 628B are positioned along the wire 616 to create positional stops, and a self-cinching washer 632 is adjustably positioned along the wire 616. The self-cinching washer 632 is configured to slide along the wire 616 to adjust the relative position the first end 620 along the wire 616 with respect to the second end 624.

With reference to FIG. 17, a first tag 700A and a second tag 700B are mechanically coupled to a linker 704. The first tag 700A and the second tag 700B are retained to the linker 704 by corresponding clips 708 formed on the linker 704. The linker 704 is a Nitinol linkage

with a bending portion 712 positioned between the first tag 700A and the second tag 700B. In the illustrated embodiment, the linker 704 includes a grip 716 at a first end 720 of the linker 704. In the illustrated embodiment, the grip 716 is a sphere configured to be graspable by a surgical forceps, for example. As such, the tags 700A, 700B and the linker 704 are easily manipulated by surgical tools or instruments.

With reference to FIG. 18, the first tag 700A, the second tag 700B, and the linker 704 are positioned within a packaging 724 (a sheath) for easy deployment into a bronchoscope, endoscope, or the like. The packaging 724 is configured to fit into the scope working channel. Typically, scope working channels include discontinuities and the packaging 724 prevents the linker 704 and tags 700A, 700B from becoming caught or stuck on those discontinuities. The packaging 724 is long enough to extend past features in the scope working channel, but short enough to not extend where the working channel is bending into anatomy. In some embodiments, the packaging 724 includes a length within a range of approximately 100 cm to approximately 180 cm. The packaging 724 surrounds the linker 704 (holding the linker 704 in a first position) except for the grip 716 is exposed. The grip 716 is graspable by a surgeon's forceps. In other words, the packaging 724 includes notch 728 that exposes the grip 716. Once grasped, the forceps are used to push the tags 700A, 700B and linker 704 to a deployment site. Before reaching the deployment site, the tags 700A, 700B and linker 704 are retrievable until released into position. As such, the linker 704 is retrievable if difficulties are encountered before the linker 704 is in position.

The use of at least two linked tags provides an advantage over only a single tag in that fewer exciter field directions can be generated while still ensuring detection of at least one tag. Accordingly, the tags may be placed within the subject at different orientations without risking loss of detection of at least one of the two linked tags. In some embodiments, the linker is configured to hold the at least two tags in a second position when present in tissue, wherein at least one of said tags in said second position points approximately in the X dimension, and at least one of said tags points approximately in the Y dimension. In some embodiments, 3 tags are used, and in said second position: i) the first tag points approximately in the X dimension, ii) the second tag points in approximately the Y dimension, and iii) and the third tag points in approximately in the Z dimension.

Any suitable spacing between each of the two or more linked tags may be used. For example, the two or more linked tags may be spaced from each other at a suitable distance to allow the tags to mark a target region (e.g. a tumor) within the body. In such embodiments, the appropriate spacing between each of the at least two tags may be determined based upon

the estimated size and shape of the target (e.g. tumor). In some embodiments, the spacing between each of the linked tags is the same. In some embodiments, the spacing between two or more of the linked tags is variable (e.g. the distance between tag A and B may differ between the distance between tag A and C, or the distance between tag B and C). In some
5 embodiments, the first tag and the second tag are separated by at least approximately 2 mm to reduce cross-coupling affects.

In some embodiments, a second component comprises a remote activating device (e.g., exciter assembly) that generates a magnetic field. In some embodiments, the second component is located in a device positioned near (e.g., below) a subject containing the linked
10 tags. In some embodiments, a third component comprises a plurality of sensors (e.g. witness stations) configured to receive a signal generated by the tags upon being exposed to the magnetic field generated by the second component. In some embodiments, the second and third components are physically contained in the same device (e.g., as shown in Figure 4A). In some embodiments, a fourth component comprises a medical device location emitter. The
15 fourth component can be integrated into a medical device or attached or otherwise associated with an attachment component (e.g., sheath). The fourth component comprises one or more location emitters (e.g., antennas that emit signals or other types of emitters) that generate signals via electrical wire feeds or upon exposure to the magnetic field generated by the second component, said signals detectable by the third component. In some embodiments, a
20 fifth component comprises a computing device comprising a processor that receives information from the witness stations of the third component and generates information about the relative locations, distances, or other characteristics of the tags, the medical device, and the witness stations. In some embodiments, the fifth component comprises a display that displays such generated information to a user of the system.

25 In some embodiments, the first component is two or more tags (e.g., 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, etc.). In some embodiments, the tags are of identical type. In other embodiments, the tags are of different type.

Any number of tag designs may be employed. In some embodiments, at least one of the linked tags comprises or consists of a ferrous pellet or particle. When the ferrous object is
30 introduced within a magnetic field, the object creates an irregularity in the alternating magnetic field which is detectable by sense coils contained within witness stations, producing a phase and amplitude shift from null. The null is restored when the ferrous object is physically equidistant to two sense coils.

In some embodiments, at least one of the linked tags comprises a ferrite-core coil antenna (e.g., resonant at 100-200 kHz) coupled to an integrated circuit (IC), which is powered by an AC magnetic field at resonance. In some embodiments, the core is contained in an enclosure (e.g., a cylindrical glass or plastic housing). In some embodiments, the exciter antenna(s) is/are driven by a conventional oscillator and power amplifier at a level sufficient to power the tag(s). In some embodiments, the implanted tag amplitude-modulate (AM's) the continuous wave (CW) carrier power from the exciter, thus emitting sidebands at frequencies defined by a number programmed into the tag's counter. In some embodiments, these sidebands, as well as the much stronger CW carrier, are ultimately detected by the third component.

In some embodiments, at least one of the linked tags comprises a self-resonant object (e.g., a small ferrite core with a wound inductor). The wound inductor possesses inter-winding capacitance that in combination with the inductance produces a high frequency resonant circuit. In some embodiments, at least one of the linked tags comprises a resonant object (e.g., the self-resonant object is equipped with a chip capacitor to produce resonance at a prescribed frequency). In certain embodiments, the chip capacitor is not a dielectric resonant antenna, and instead is a standard thin film capacitor, or a multi-layer ceramic capacitor (MLCC). Dielectric resonant antenna capacitors may not be well suited for use in the present methods, as dielectric resonant antenna capacitors are less effective at low frequencies (e.g. 100-200kHz). In contrast, standard thin film capacitors or MLCCs may be created to have consistent functionality at low frequencies (e.g. 100-200kHz). Moreover, standard thin film capacitors or MLCCs may be manufactured to provide consistent functionality independent of temperature, such that they will work effectively both at ambient temperature and at body temperature (e.g. once placed within a subject). In addition, standard thin film capacitors or MLCCs are less expensive than dielectric resonant antennas.

In some embodiments, the tag(s) comprise a resonant or self-resonant object with a diode. A diode in combination with an LC circuit produces a sub-harmonic frequency when immersed in a magnetic field of sufficient strength (imposed voltage exceeds the diode's band-gap potential). In some embodiments, the tag(s) comprise a resonant object or self-resonant object with an active modulator (e.g., integrated circuit amplitude modulates resonant circuit). In some embodiments, detection occurs similar to a full duplex (FDX) radio frequency identification (RFID) except that the modulation pattern is a simple sub-harmonic rather than a coded binary pattern; in some embodiments, the detection occurs after excitation similar to a half-duplex (HDX) mode of operation.

In some embodiments, at least one of the linked tags are configured for single-use. In some such embodiments, the linked tag(s) can be disabled or deactivated (e.g., like an EAS tag). This is particularly useful where multiple tags are used in a procedure where individual tags are turned off to make detection of other tags easier (e.g., to avoid or reduce interference
 5 between multiple tags). In some embodiments, a burst of energy from an external device is used to disable or deactivate a tag. In other embodiments, at least one of the linked tags has an internal control component that, upon receiving instruction from an external device, turns the tag on or off (e.g., the tag stops “talking” temporarily or permanently).

In some embodiments, each of the linked tags has an exterior length, width, and
 10 depth, wherein the length is 30 mm or less (e.g., 20 mm or less, . . . , 10 mm or less, . . . , 9 mm or less, . . . , 8 mm or less, . . . , 5 mm or less, . . . , 3 mm or less, . . . , etc.), the width is 5 mm or less (e.g., 4 mm or less, . . . , 3 mm or less, . . . , 2 mm or less, . . . , 1 mm or less, . . . 0.5 mm or less, . . . , etc.), and the depth is 5 mm or less (e.g., 4 mm or less, . . . , 3 mm or less, . . . , 2 mm or less, . . . , 1 mm or less, . . . 0.5 mm or less, . . . , etc.).

In some embodiments, each of the linked tags is contained in a housing or sheath. In some embodiments, no housing is employed. In some embodiments, at least one of the linked tags is contained in a housing and at least one of the linked tags is not contained in a housing. In some embodiments, the housing comprises a biocompatible material. In some embodiments, the housing provides a liquid and/or gas resistant barrier separating the signal
 20 source from the exterior of the housing. In some embodiments, the housing is small, permitting administration of the linked tags through a needle, cannula, endoscope, catheter, or other medical device. In some such embodiments, the housing has an exterior length, width, and depth, wherein the length is 30 mm or less (e.g., 20 mm or less, . . . , 10 mm or less, . . . , 9 mm or less, . . . , 8 mm or less, . . . , 5 mm or less, . . . , 3 mm or less, . . . , etc.), the width is 5 mm or less (e.g., 4 mm or less, . . . , 3 mm or less, . . . , 2 mm or less, . . . , 1 mm or less, . . . 0.5 mm or less, . . . , etc.), and the depth is 5 mm or less (e.g., 4 mm or less, . . . , 3 mm or less, . . . , 2 mm or less, . . . , 1 mm or less, . . . 0.5 mm or less, . . . , etc.). The housing can be of any desired shape. In some embodiments, the housing is cylindrical along the length axis. In some embodiments, the housing is shaped like a grain of rice (e.g., cylindrical with rounded
 30 ends). In some embodiments, the housing is shaped like a pillar (e.g., cylindrical with flat ends). In some embodiments, the housing is polygonal along the length axis (e.g., triangular, square, rectangular, trapezoidal, pentagonal, etc., in cross-section). In some embodiments the housing has struts or other fasteners to keep the tag in place, avoiding migration in tissue.

These struts may deploy upon placement in tissue. In some embodiments the fastener may be

a biocompatible material that bonds with surrounding tissue. Advantageously, embodiments of the two linked tags that do not include a sheath are able to be positioned with a tighter bend radius.

In some embodiments, the housing is a single uniform component synthesized around the interior components of the tag. In other embodiments, the housing is made of two or more separate segments that are sealed together after introduction of the interior components of the tag. In some embodiments, the tag is completely or partially covered in a coating. In some embodiments, the coating comprises a biocompatible material (e.g., parylene-C, etc.).

In some embodiments, one or more of the linked tags does not comprise any power source. In some embodiments, each of the linked tags do not comprise any power source. For example, in some embodiments, the signal is generated from the signal source in response to a magnetic field as the activation event (i.e., electromagnetic induction).

In some embodiments, at least one of the linked tags comprise a radio-frequency identification (RFID) chip (e.g., in a housing). For example, each of the linked tags may comprise an RFID chip. In some embodiments, the RFID chip comprises a radio-frequency electromagnetic field coil that modulates an external magnetic field to transfer a coded identification number and/or other coded information when queried by a reader device. In some embodiments, the RFID chip collects energy from an EM field generated by the second component (or other device) and then acts as a passive transponder to emit microwaves or UHF radio waves. In some embodiments, the RFID chip is read-only. In other embodiments, it is read/write. The technology is not limited by the nature of the information provided by the RFID chip. In some embodiments, the information includes a serial number, lot or batch number, time information (e.g., production date; surgery date; etc.); patient-specific information (e.g., name, family history, drugs taken, allergies, risk factors, procedure type, gender, age, etc.); procedure-specific information; etc. The technology is not limited by the frequency used. In some embodiments, the RFID frequency is in the 120-150 kHz band (e.g., 134 kHz), the 13.56 MHz band, the 433 MHz band, the 865-868 MHz band, the 902-928 MHz band, the 2450-5800 MHz band, or the like. In some embodiments, the RFID chip is incorporated with browser-based software to increase its efficacy. In some embodiments, this software allows for different groups or specific hospital staff, nurses, and patients to see real-time data relevant to the tag, procedure, or personnel. In some embodiments, real-time data is stored and archived to make use of historical reporting functionality and to prove compliance with various industry regulations. In some embodiments, the RFID chip reports sensor data (e.g., temperature, movement, etc.). In some embodiments, the RFID chip

contains or collects information that is read at a later time (e.g., after surgery). In some embodiments, information is reviewed during surgery. For example, a message may be provided to the surgeon (e.g., “the chip is just to the left of the tumor”) to assist in guiding the surgeon (e.g., optimizing removal of a tumor with the appropriate margins).

5 In some embodiments, each of the two or more linked tags is composed of the same components. In other words, each of the linked tags does not need to be composed of components with different electrical properties in order for the tags to be uniquely identifiable. In some embodiments, each of the linked tags consists of or consists essentially of the signal source and the housing or the signal source, the housing, and the RFID chip. In
10 some embodiments, the tag (e.g., via the chip) emits an ultrasound signal (e.g., gray scale, spectral, or color Doppler) such that the signal is detectable by an ultrasound probe or a hand-held Doppler unit.

 In some embodiments, a tag is heated during a procedure (e.g., via exposure to an external energy source). In some such embodiments, heating may be used to assist in
15 coagulation or precoagulation of tissue or to provide thermotherapy (see e.g., U.S. Pat. Publ. No. 2008/0213382, herein incorporated by reference in its entirety). Heating may also be used to improve the efficacy of radiation therapy.

 In some embodiments, the second component provides a remote activating device. In some embodiments, the remote activating device comprises at least one excitation coil. In
20 some embodiments, the remote activating device comprises two or more excitation coils (e.g., exciter assembly shown in Figure 4A). In some embodiments, the at least one excitation coil is provided on a base substrate. The base substrate may be composed of any suitable material, which may be, for example, polycarbonate or the like and is typically nonmagnetic and non-electrically conducting.

25 In some embodiments, the excitation coils are provided in a patch or pad that is placed on the patient or on the operating table, although it can be positioned in any desired location within functional distance of the tags. In some embodiments, the remote activating device provides an AC magnetic field originating from one or more exciter antennas. In some embodiments, where the system is used to locate breast tumors, the patch encircles the treated
30 breast or is placed otherwise near the breast. Similar approaches may be used for other targeted areas of a body. In some embodiments, a pad containing the excitation coil(s) are placed beneath the patient. In such embodiments, a large coil or multiple coils are employed. The excitation coil(s) may comprise or consist of several turns of a flat conductor patterned on a dielectric substrate, or may comprise or consist of magnet wire wound around a suitable

mandrel; the coil is powered by an external frequency source, and the magnetic field emanating from the coil penetrates the patient's body to excite the tags, whose emissions are detected by a detection component.

In some embodiments, the excitation coil or coils are contained in a belt that is placed around the subject or a portion of the subject. In some embodiments, the external excitation coil may further be used for other aspects of the patient care, such as for radiotherapy or to act as a ground current return pad used in electrosurgery. In some embodiments, the remote activating device emits light (e.g., laser light). In some embodiments, the remote activating device is configured for single use (e.g., is disposable).

In some embodiments, the remote activating device employs an unmodulated constant frequency activation (i.e., the activation signal has constant amplitude and frequency). In some embodiments, the remote activating device employs an unmodulated swept frequency (i.e., the activation signal has constant amplitude and swept frequency between two endpoints). Such devices find use with resonant-type tags such that a detectable change in the activation signal's amplitude occurs when the transmitted frequency coincides with the tag's resonant frequency. In some embodiments, the remote activating device employs a pulsed frequency (i.e., the activation signal comprises brief excitation pulses at a periodic frequency, which may be comprised of two closely-related frequencies whose sum or difference is the response frequency of the tag). The pulsed activation produces a post-pulse sinusoidal decay signal. A tag alters the characteristic of the decaying signal, either in amplitude or time.

The system provided herein is advantageous in that each of the at least two linked tags may respond to a single transmitted frequency (e.g. activation signal), such as the activation signal provided by the remote activating device. In other words, the transmitted frequency is common to all tags. For example, each of the at least two linked tags may be programmed to generate a unique frequency in response to the single transmitted frequency provided by the activation device. The at least two linked tags may be programmed to respond to a broad range of frequencies (e.g. 100-150kHz), with the response frequency of each tag scaling according to the stimulating frequency.

In some embodiments, the remote activating device comprises a hand-held component. In some embodiments, the hand-held component is lightweight to allow a surgeon to hold and manipulate the component over the course of a procedure (e.g., 5 kg or less, 4 kg or less, 3 kg or less, 2 kg or less, 1 kg or less, 0.5 kg or less, 0.25 kg or less, or any range therein between, e.g., 0.5 to 5 kg, 1 to 4 kg, etc.). In some embodiments, the hand-held

component is shaped like a wand, having a proximal end that is held by the physician and a distal end that is pointed towards the treated subject or tissue harboring the linked tags. In some embodiments, the hand-held component is shaped like an otoscope, having a distal end that terminates at an angle (e.g., right angle) from the body of the component. In some
5 embodiments, the remote activating device comprises an antenna that generates a magnetic field. In some embodiments, the remote activating device has only a single antenna (i.e., is monostatic). In some embodiments, the remote activating device has only two antennas (i.e., is bistatic).

In some embodiments, the magnetic field of the remote activating device (e.g., exciter
10 assembly shown in Figure 4A) is controlled by a processor running a computer program. In some embodiments, the remote activating device comprises a display or user interface that allows the user to control the remote activating device and/or monitor its functions while in use. In some embodiments, the remote activating device provides a visual, audio, numerical, symbol (e.g., arrows), textual, or other output that assists the user in locating the linked tags
15 or identifying the distance to or direction of the tags from the remote activating device.

In some embodiments, the plurality of witness coils of the third component collectively provide several antennas (e.g. witness antennas) at multiple defined locations relative to the tags and configured to receive a signal generated by one or more tags upon being exposed to the magnetic field generated by the second component.

In some embodiments, each witness coil feeds a receiver channel, which is time-
20 division multiplexed (TDM'd) to reduce the receiver complexity. Fixed witness stations of defined locations relative to the tag(s) and each other (e.g., arrayed along the patient) contain one or more (e.g., one to three) witness coils arranged in a locally orthogonal manner to sense various components of the AC magnetic field from the tag(s). In some embodiments, one or
25 more or all of these witness coils in the witness stations is also TDM'd into a receiver channel, reducing complexity, as well as cross-talk between antennas.

In some embodiments, witness coils comprise or consist of a ferrite-loaded cylindrical coil antenna (e.g., witness antenna), tuned (e.g., with one or more capacitors in parallel) for resonance at the frequency of an exciter (e.g., tag or emitter), (e.g., 100-200 kHz). Typical
30 dimensions of a witness coils are 3-5 mm diameter and 8-12 mm length, although both smaller and larger dimensions may be employed. In some embodiments, witness station antenna has a ferrite core size of 0.25 x 1 inch and contains 75-80 turns of a 10/46 (10 strands of #46) Litz wire which provides 0.157mH (Q=53) (75 Turns).

In some embodiments, each witness coil is symmetrically wound about a ferrite core and connected to the secondary of a small balun transformer through two series capacitances, one for each wire from the coil. The total series capacitance is selected to resonate with the inductance of the coil, and the turns ratio of the balun transformer may be chosen to match the real impedance of the resonant coil/capacitor circuit to the transmission line, typically 50 Ohms. The real impedance of the resonant coil/capacitor circuit is typically 10 to 25 Ohms but may vary from just a couple Ohms to greater than 50 Ohms and may be adequately matched by appropriate choice of balun transformer primary and secondary turns. In addition to its role as impedance transformer, the balun minimizes any electric field generation/susceptibility from the witness coil assembly; alternately, it may be thought of as removing common mode effects.

In some embodiments, each witness station contains 1-3 witness antennas oriented orthogonally to each other and further arranged to have minimum cross-talk (i.e., interference with one another). The component housing the witness stations further comprises one or more receiver channels for collecting information obtained by the antennas of the witness stations. In some embodiments, the receiver comprises or consists of one or more channels, each channel fed by one or more (via a multiplexing switch) witness antennas.

In some embodiments, the witness stations are provided below the patient (e.g., in a pad, garment, or other device positioned below the patient). In some embodiments, the witness stations are integrated into a surgical table or imaging device in which a patient is placed during a medical procedure. In some embodiments, the witness stations are placed on the floor, wall, or ceiling of the operating room or in a medical transport vehicle. In some embodiments, the witness stations are integrated into or attached to a medical device used in the medical procedure.

In some embodiments, a fourth component provides a medical device location emitter in an attachment component (see Figures 9-12) to allow the system to determine the location, position, distance, or other characteristic of a medical device relative to the tag or tags. In some embodiments, the medical device location emitter or emitters are integrated into a medical device or into an attachment component. In other embodiments, they are attachable to a medical device. In some such embodiments, the location emitters are provided in an attachment component (e.g., sleeve) that slips over a portion of a medical device. The location emitters may operate as and/or comprise the same materials as the tags, but are positioned on or near a medical device rather than within tissue. For example, in some embodiments, the emitters comprise coils that are excited with both carrier and/or sidebands,

enabling the emitters to emit signals as though it were a tag. In other embodiments, the location emitters are wired to a power and signal source.

In some embodiments, location of the location emitters is accomplished geometrically by measuring the quasi-simultaneous power detected from the emitters at a plurality of
5 witness stations (e.g., four or more stations), and using the power differences to perform vector math that determines the location of the emitter without ambiguity. This process is facilitated by a preliminary calibration using a known tag in a known location prior to the procedure.

In some embodiments, the component (e.g., attachment component) that contains the
10 location emitters may further comprise a display to assist the user in directing the medical device to the linked tags during a surgical procedure. In some such embodiments, a visual or audio display is provided on or associated with the medical device that receives location information about one or more of the linked tags from the computer system. The display may be one or more directional indicators such as LEDs, that indicate direction and/or distance to
15 the tag(s). Color changes may be employed to indicate “on target” versus “off target” positions. In certain embodiments, the display comprises a first display for presenting distance to tag information (e.g., visual, audible, lights, color, vibration, tactile, etc.); a second display for presenting vertical axis orientation, such as a preset preferred angle for approaching the linked tags in a patient (e.g., a visual, audible, lights, colors, vibration,
20 tactile, etc. display); and/or a third display for presenting horizontal orientation (e.g., left to right information so the surgical device can be centered when approaching the tags). In some embodiments, the display comprises a plurality of displays (e.g., visual, audible, sensory, etc.) that allow the correct pitch and yaw axes to be employed (to minimize non-target tissue damage), and/or further a display that provides distance to tag information. In certain
25 embodiments, a series of lights and/or sounds are provided on the display that guide the surgeon (e.g., the surgeon attempts to keep the lights in a center of an “X” series of lights, and/or to keep the volume of warning sounds off or as low as possible).

Vectors describing the location of the location emitters are used to provide visualization guidance to the surgeon about the spatial relationship of a medical device (e.g.,
30 particularly its tip) to an implanted tag, or (e.g., with computational guidance) to a lesion boundary. Use of multiple location emitters on an attachment component attached to a medical device provides vectors to determine the device’s principal axis using the same vector math. Where a more complex medical device, such as a robotic surgical system (e.g., da Vinci surgical system) is employed, multiple location emitters located on multiple

different locations of the device are employed to provide location, orientation, and other position information of multiple components (e.g., arms) of the device. In some embodiments, the location emitters are also used as detectors (e.g., provide witness stations on the medical device).

5 In some embodiments, a fifth component provides one or more computing systems comprising one or more computer processors and appropriate software to analyze, calculate, and display tag and emitter position information (see, part 210 in Figure 4A). In some embodiments, the display provides a graphical representation of the tag(s), patient, and/or medical device on a monitor. In other embodiments, the display provides directional
10 information for moving or positioning the medical device. In some embodiments, the system automatically (e.g., robotically) controls the medical device or one or more functions thereof. In some embodiments, the display integrates tag and/or medical device information with previously obtained or concurrently obtained medical images of the patient or target tissue (e.g., CT, MRI, ultrasound, or other imaging modalities). For example, in some
15 embodiments, an image indicating a tag or tags is fused with an image of the subject's tissue or body region obtained from an imaging device. In some embodiments, information is analyzed in real-time. In some embodiments, information is analyzed at one or more discrete time points.

In some embodiments, the fifth component provides command and control functions
20 for a user of the system. In some embodiments, the fifth component has information stored thereon that helps guide the information displayed on the attachment component. For example, the information may include data on the type of medical device the attachment component is attached to, or what tip or cutting implement is being used with a particular medical device. In this regard, the precise location of the cutting tip of a medical device and
25 its relation to the tag(s) (e.g., distance to the tag(s)) is communicated to the surgeon (e.g., for very precise instructions on cutting tissue). Such information is, for example in some embodiments, manually entered into a control unit or attachment component by the user, or automatically found (e.g., by a barcode or other indicator) when a detection component is attached to a particular medical device.

30 The system finds use with a wide variety of medical devices and procedures. In some embodiments, the surgical device comprises an electrical surgical device that is turned on and off by a user, wherein a control unit that is part of the fifth component allows the remote activating device to generate the magnetic field when the electrical surgical device is off, and prevents the remote activating device from generating the magnetic field when the electrical

surgical device is on (e.g., ensuring that the surgical device and detection system do not interfere with one another). In other embodiments, the surgical device comprises a power cord, wherein an AC current clamp is attached to the power cord, wherein the AC current clamp is electrically-linked or wirelessly linked to the control unit, wherein the AC current
5 clamp senses when the electrical surgical device is on or off and reports this to the control unit (e.g., such that the control unit can ensure that the magnetic field from the surgical device and from the remote activating device are not active at the same time).

In certain embodiments, the surgical device comprises an electrocautery device, a laser cutting device, a plasma cutting device, or a metal cutting device (e.g., a surgical device
10 manufactured by BOVIE MEDICAL). Additional examples of medical devices that find use in embodiments of the system are found, for example, in the following U.S. Patents: 9,144,453; 9,095,333; 9,060,765; 8,998,899; 8,979,834; 8,802,022; 8,795,272; 8,795,265; 8,728,076; 8,696,663; 8,647,342; 8,628,524; 8,409,190; 8,377,388; 8,226,640; 8,114,181; 8,100,897; 8,057,468; 8,012,154; 7,993,335; 7,871,423; 7,632,270; 6,361,532; all of which
15 are herein incorporated by reference in their entireties, and particularly with respect to the hand-held medical devices disclosed therein.

In some embodiments, the attachment component has thereon, or attached thereto, a display component for directing the surgeon to the tag or tags. In some embodiments, the display component provides: i) a spatial orientation indicator (e.g., visual, audible, etc.),
20 and/or ii) a distance-to-tag indicator (e.g., visual, audible, etc.). In some embodiments, the display component comprises a first display for presenting distance to tag information (e.g., visual, audible, lights, color, vibration, tactile, etc.), a second display for presenting vertical axis orientation, such as a preset preferred angle for approaching a tag in a patient (e.g., a visual, audible, lights, colors, vibration, tactile, etc. display); and/or a third display for
25 presenting horizontal orientation (e.g., left to right information so the surgical device can be centered when approaching the tag). In some embodiments, the display component comprises a plurality of displays (e.g., visual, audible, sensory, etc.) that allow the correct pitch and yaw axes to be employed (to minimize non-target tissue damage), and/or further a display that provides distance to tag information. In certain embodiments, the medical device
30 is moved around the patient's body prior to surgery to orient the emitters and the display component. In certain embodiments, a series of lights and/or sounds is provided on the display component that guides the surgeon (e.g., the surgeon attempts to keep the lights in a center of an "X" series of lights, and/or to keep the volume of warning sounds off or as low as possible).

The linked tags disclosed herein are not limited to placement within a particular body region, body part, organ, or tissue. For example, in some embodiments, the tags are placed in the cephalic, cervical, thoracic, abdominal, pelvic, upper extremities, or lower extremities region of the body. In some embodiments, the tags are placed within an organ system, such as the skeletal system, muscular system, cardiovascular system, digestive system, endocrine system, integumentary system, urinary system, lymphatic system, immune system, respiratory system, nervous system or reproductive system. In some embodiments, the tags are placed within an organ. Such organs may include the heart, lungs, blood vessels, ligaments, tendons, salivary glands, esophagus, stomach, liver, gallbladder, pancreas, intestines, rectum, anus, hypothalamus, pituitary gland, pineal gland, thyroid, parathyroid, adrenal glands, skin, hair, fat, nails, kidneys, ureters, bladder, urethra, pharynx, larynx, bronchi, diaphragm, brain, spinal cord, peripheral nervous system, ovaries, fallopian tubes, uterus, vagina, mammary glands, testes, vas deferens, seminal vesicles, and prostate. In some embodiments, the tags are placed within tissues, such as connective, muscle, nervous, and epithelial tissues. Such tissues may include cardiac muscle tissue, skeletal muscle tissue, smooth muscle tissue, loose connective tissue, dense connective tissue, reticular connective tissue, adipose tissue, cartilage, bone, blood, fibrous connective tissue, elastic connective tissue, lymphoid connective tissue, areolar connective tissue, simple squamous epithelium, simple cuboidal epithelium, simple columnar epithelium, stratified epithelium, pseudostratified epithelium, and transitional epithelium.

In some embodiments, the tissue region where the tags are located comprises a lesion. In some embodiments, the lesion is a tumor or a tissue region identified as being at risk for forming a tumor. For example, one tag may be placed at a boundary of a tumor and another tag may be placed at a second boundary of a tumor, such that the linked tags delineate the outer edges of the tumor. In some embodiments, the lesion is fibrotic tissue. In some embodiments, the lesion is an inflamed or infected region. In some embodiments, the tags are placed within a lumen to detect function or other process of the organ or provide localizing information. For example, the tags could be swallowed, or placed into a hollow organ via endoscopy. In some embodiments, the tissue region is healthy tissue. In some embodiments, the two linked tags are positioned offset from a lesion. In some embodiments, the two linked tags are positioned within an airway up to approximately 5 mm.

In some embodiments, the linked tags are placed within a solid tumor. Examples of solid tumors into which the tags may be placed include carcinomas, lymphomas, and sarcomas, including, but not limited to, aberrant basal-cell carcinoma, acinar cell neoplasms,

acinic cell carcinoma, adenocarcinoma, adenoid cystic carcinoma, adenoid/pseudoglandular
 squamous cell carcinoma, adnexal neoplasms, adrenocortical adenoma, adrenocortical
 carcinoma, apudoma, basal cell carcinoma, basaloid squamous cell carcinoma, carcinoid,
 cholangiocarcinoma, cicatricial basal-cell carcinoma, clear cell adenocarcinoma, clear cell
 5 squamous-cell carcinoma, combined small cell carcinoma, comedocarcinoma, complex
 epithelial carcinoma, cylindroma, cystadenocarcinoma, cystadenoma, cystic basal-cell
 carcinoma, cystic neoplasms, ductal carcinoma, endometrioid tumor, epithelial neoplasms,
 extramammary Paget's disease, familial adenomatous polyposis, fibroepithelioma of Pinkus,
 gastrinoma, glucagonoma, Grawitz tumor, hepatocellular adenoma, hepatocellular carcinoma,
 10 hidrocystoma, Hurthle cell, infiltrative basal-cell carcinoma, insulinoma, intraepidermal
 squamous cell carcinoma, invasive lobular carcinoma, inverted papilloma, keratoacanthoma,
 Klatzkin tumor, Krukenberg tumor, large cell keratinizing squamous cell carcinoma, large
 cell nonkeratinizing squamous cell carcinoma, linitis plastica, liposarcoma, lobular
 carcinoma, lymphoepithelial carcinoma, mammary ductal carcinoma, medullary carcinoma,
 15 medullary carcinoma of the breast, medullary thyroid cancer, micronodular basal-cell
 carcinoma, morpheaform basal-cell carcinoma, morphoeic basal-cell carcinoma, mucinous
 carcinoma, mucinous cystadenocarcinoma, mucinous cystadenoma, mucoepidermoid
 carcinoma, multiple endocrine neoplasia, neuroendocrine tumor, nodular basal-cell
 carcinoma, oncocytoma, osteosarcoma, ovarian serous cystadenoma, Paget's disease of the
 20 breast, pancreatic ductal carcinoma, pancreatic serous cystadenoma, papillary carcinoma,
 papillary hidradenoma, papillary serous cystadenocarcinoma, papillary squamous cell
 carcinoma, pigmented basal-cell carcinoma, polypoid basal-cell carcinoma, pore-like basal-
 cell carcinoma, prolactinoma, pseudomyxoma peritonei, renal cell carcinoma, renal
 oncocytoma, rodent ulcer, serous carcinoma, serous cystadenocarcinoma, signet ring cell
 25 carcinoma, signet-ring-cell squamous-cell carcinoma, skin appendage neoplasms, small cell
 carcinoma, small cell keratinizing squamous cell carcinoma, somatostatinoma, spindle cell
 squamous cell carcinoma, squamous cell carcinoma, squamous cell lung carcinoma,
 squamous cell thyroid carcinoma, superficial basal-cell carcinoma, superficial multicentric
 basal-cell carcinoma, syringocystadenoma papilliferum, syringoma, thymoma, transitional
 30 cell carcinoma, verrucous carcinoma, verrucous squamous cell carcinoma, VIPoma, and
 Warthin's tumor.

In some embodiments, placing the linked tags comprises the steps of inserting an
 introduction device into the subject and introducing the linked tags through the introduction
 device into the subject. In some embodiments, the introduction device is a needle, cannula,

or endoscope. In some embodiments, the linked tags are forced through the introduction device (e.g., via physical force, pressure, or any other suitable technique) and released into the subject at the distal end of the introduction device. After the tags are placed, the introduction device is withdrawn, leaving the tags at the desired location with the subject. In some embodiments, the introduction of the tags is guided by imaging technology. In some
5 embodiments, the linked tags are positioned within a packaging while being moved into the desired position.

In the embodiments provided herein, multiple tags are placed into the subject. The tags are linked together (e.g. by a linker). The tags may be of identical type or may differ
10 (e.g., differ in signal type). The tags may be placed in proximity to one another or at distant locations. Multiple tags are used, in some embodiments, to triangulate the location intended for medical intervention.

In some embodiments, the tags are further used as fiducials for radiotherapy (or other targeted therapy). The location of the tags is identified with an external reader and used to
15 place, for example, laser light on the skin surface exactly where the chip is located. This eliminates the need to use X-ray, CT, or fluoroscopy to see the fiducials. This also decreases or eliminates the need to put skin markers (e.g., tattoos) on patients. This also helps in respiratory compensation as the fiducial moves up and down with a tumor in the lung or abdomen. Therefore, one can conduct real-time radiation only when the tumor is in the
20 correct position and decrease damage to the background tissue (e.g., avoid burning a vertical stripe in the patient as the tumor moves up and down). The use as fiducials for director therapy (e.g., radiation therapy) also enhances triangulation as depth information (based on signal strength) assists in localization of the tumor to minimize collateral damage.

In some embodiments, provided herein are systems and methods employing one or
25 more or all of: a) two or more linked tags (e.g., comprising an antenna; e.g., a coil antenna; e.g., a ferrite-core coil antenna; e.g., that resonates at 100-200 kHz; e.g., coupled to an integrated circuit); b) a remote activating device that generates a magnetic field within a region of the tag; and c) a plurality of sensors (e.g. witness stations), each of the witness stations comprising an antenna configured to detect information generated by the tags or a
30 change in a magnetic field generated by the remote activating device caused by said tags. In some embodiments, at least one of the linked tags emits sidebands at defined frequencies upon activation by a magnetic field and the witness stations detect such sidebands. In some embodiments, at least one of the linked tags emits the sidebands at frequencies defined by a number programmed into a counter in the tag(s).

In some embodiments, the remote activating device comprises an excitation coil that is, for example, powered by a generator electrically connected to the remote activating device. In some embodiments, the remote activating device comprises a pad configured to be placed in proximity to (e.g., under, above, beside) a patient having the linked tags embedded in the patient. In some embodiments, the pad also contains the witness stations.

In particular embodiments, provided herein are devices and systems comprising: a remote activating device that generates a magnetic flux within a region of a tag, wherein the remote activating device comprises: a) a base substrate, b) at least one exciter coil attached to the base substrate that generates the magnetic flux, and c) a plurality of witness station assemblies attached to the base substrate, wherein each of the witness station assemblies comprises a witness coil having a sensing axis and comprising: i) a core having a coil-free proximal end, a coil-free distal end, and a central region, wherein the core comprises metal, and ii) coil windings wound around the central region of the core, wherein each of the witness station assemblies is oriented on the base substrate such that the sensing axis of each of the witness coils: A) runs from the proximal end to the distal end of the core, and B) is orthogonal to, or substantially orthogonal to: i) the magnetic flux, and/or ii) the at least one exciter coil. In particular embodiments, the at least one exciter coil is configured to selectively flow current in a clockwise or counterclockwise direction. In other embodiments, the sensing axis of each of the witness coils is substantially orthogonal to the magnetic flux for both the clockwise, and the counterclockwise, directions.

In certain embodiments, each of the exciter coils comprises a central plane, and wherein each of the witness station assemblies is further oriented on the base substrate such that the sensing axis of each of the witness coils: C) is co-planar with the central plane of each of the exciter coils. In particular embodiments, the magnetic flux does not induce a signal in the witness coils when generated in substantially the X and/or Y directions.

In other embodiments, each of the witness station assemblies further comprises: i) first and second witness coil brackets, and ii) first and second elastomeric parts, and wherein the coil-free proximal end of the core is secured between the first witness coil bracket and the first elastomeric part, and wherein the coil-free distal end of the core is secured between the second witness coil bracket and the second elastomeric part. In further embodiments, the first and second witness coil brackets each comprises at least one adjustment part. In other embodiments, the at least one adjustment part comprises at least one screw and/or at least one rod. In particular embodiments, provided herein are methods of employing the adjustment

parts to adjust the witness coils such that their sensing axes are orthogonal to, or substantially orthogonal to the magnetic flux, and/or the at least one exciter coils.

In some embodiments, the at least one adjustment part allows the sensing axis of each of the witness coils to be adjusted such that it is orthogonal to, or substantially orthogonal to, the magnetic flux in one or more of the X, Y, or Z directions. In some embodiments, the sensing axis of each of the witness coils may be adjusted such that it is orthogonal to the X and Y directions. In further embodiments, the magnetic flux may be further selectively generated in substantially the Z direction, and wherein each of the witness station assemblies is oriented on the base substrate such that the sensing axis of each of the witness coils is orthogonal to, or substantially orthogonal to, the magnetic flux the Z direction. In further embodiments, the magnetic flux does not induce a signal in the witness coils when generated in substantially the Z direction. In further embodiments, the at least one adjustment part allows the sensing axis of each of the witness coils to be adjusted such that it is orthogonal to, or substantially orthogonal to, the magnetic flux in each of the X, Y, and Z directions. In some embodiments, the metal comprises ferrite.

In other embodiments, each of the witness station assemblies is oriented on the base substrate such that the sensing axis of each of the witness coils is orthogonal to, or substantially orthogonal to the at least one exciter coil. For example, each of the witness station assemblies may be oriented on the base substrate such that the sensing axis is orthogonal to, or substantially orthogonal to, the at least two exciter coils, the at least three exciter coils, or the at least four exciter coils. In some embodiments, each of the witness station assemblies is oriented on the base substrate such that the sensing axis of each of the witness coils is orthogonal to, or substantially orthogonal to the magnetic flux in each of the X and Y directions. In further embodiments, the four or more exciter coils is four exciter coils or six exciter coils. In other embodiments, the four exciter coils are in a layout of two rows centered at coordinates (X1, Y1), (X1, Y2), (X2, Y1), and (X2, Y2). In additional embodiments, the remote activating device comprises three current flow configurations: a) all current clockwise to simulate an exciter coil aligned, or substantially aligned, with a plane normal to the Z axis; b) exciter coils centered at (X2, Y1), (X2, Y2) running current counter-clockwise to simulate an exciter coil aligned, or substantially aligned, to the X axis; and c) exciter coils centered at (X1, Y2), (X2, Y2) running current counter-clockwise to simulate an exciter coil aligned, or substantially aligned, to the Y axis.

In some embodiments, the sensing axis of the witness coil is substantially orthogonal when isolation between the at least four exciter coils and the witness coil is 60dB or greater

in the X and Y directions. In other embodiments, the sensing axis of the witness coil is substantially orthogonal when isolation between the at least four exciter coils and the witness coil is 60dB or greater in the X, Y, and Z directions.

In certain embodiments, provided herein are systems and devices comprising: an
5 exciter assembly that cycles between generating at least first, second, and third magnetic fields (e.g., first, second, third, fourth, fifth, sixth, seventh, and/or eighth magnetic fields) for causing a tag to generate a signal, wherein the exciter assembly comprises A) a base substrate, B) a first exciter coil attached to the base substrate, wherein current in the first exciter coil travels clockwise when the first, second, and third magnetic fields are generated.

10 In some embodiments, the exciter further comprises C) a second exciter coil attached to base substrate, wherein current in the second exciter coil travels clockwise when the first and second magnetic fields are generated, and travels counterclockwise when the third magnetic field is generated. In some embodiments, the exciter assembly further comprises D) a third exciter coil attached to the base substrate, wherein current in the third exciter coil travels
15 clockwise when the first and third magnetic fields are generated, and travels counterclockwise when the second magnetic field is generated. In some embodiments, the exciter assembly further comprises E) a fourth exciter attached to the base substrate, wherein current in the fourth exciter coil travels clockwise when the first magnetic field is generated, and travels counterclockwise when the second and third magnetic fields are generated.

20 Exciter coils, for example, may be wound using Litz wire to minimize resistive losses due to the skin effect that occurs as frequency increases. The number of turns is generally chosen to maximize coil “Q” (the ratio of inductance/resistance). An exemplary coil example is 63 turns of Litz wire comprised of 100 strands of 38 AWG wire. Inductance of an individual coil measures about 1.1 mH and Q (ratio of inductive reactance to resistance)
25 measures over 500 at 134.5KHz. Other coil constructions using other wire with different values of inductance and Q may be used. However, it is generally desired to keep “Q” as high as possible to minimize resistive losses that result in loss of efficiency and greater thermal heating.

In some embodiments, provided herein are systems and devices comprising: a) a base
30 substrate, b) a first exciter coil attached to the substrate and configured to generate a magnetic field for causing a tag to generate a signal, and c) a balun circuit electrically linked to the first exciter coil. In some embodiments, the systems and devices further comprise a second exciter coil attached to the substrate and configured to generate a magnetic field for causing a tag to generate a signal, and c) a balun circuit electrically linked to the second exciter coil. In

some embodiments, the systems and devices further comprise a third exciter coil, or a third and fourth exciter coil, attached to the substrate and configured to generate a magnetic field for causing a tag to generate a signal, and c) a balun circuit electrically linked to the third exciter coil or a third and fourth exciter coil.

5 In particular embodiments, the second exciter coil, the second and third exciter coil, or each of the second, third, and fourth exciter coils are operatively connected to a switch that controls the direction of current through a coil. In certain embodiments, each switch comprises a relay element, a PIN diode, a Field Effect Transistor, or other solid-state switching device. In particular embodiments, each switch additionally switches at least one
10 capacitor (e.g., two capacitors) into the circuit to keep the resonant frequency of the series combination of exciter coils constant regardless of the change in overall coil inductance that results from changing coil polarity.

The inductance of an exemplary exciter coil system measures 1.1mH with $Q > 500$ for each individual coil. The inductance of the series combination coils, such as of 4 coils (e.g.,
15 as shown in Figure 4A) varies with polarity (current direction) of the coils because of the interaction of the magnetic flux produced by each coil. The inductance of the series combination of all 4 exemplary coils measures 3.9mH with $Q = 435$ for the current direction depicted in FIG. 5 where all coils have current flowing in the clockwise direction. The inductance of the series combination of all 4 exemplary coils measures 4.6mH with $Q = 500$
20 for the current direction depicted in FIG 6 where coils A and B have current in the clockwise direction and coils C and D have current flowing in the counterclockwise direction. The inductance of the series combination of all 4 exemplary coils measures 4.3mH with $Q = 473$ for the current direction depicted in FIG 7 where coils A and C have current in the clockwise direction and coils B and D have current flowing in the counterclockwise direction. This
25 variation in total inductance necessitates switching in appropriate compensation capacitors when the coil polarity is changed.

In some embodiments, the components of the relay or switch and associated capacitors may be placed on a ceramic substrate to provide secure mounting, excellent dielectric properties, and also serve as a heat spreader to reduce localized heating of
30 individual components.

In some embodiments, the systems and devices further comprise: a plurality of witness coils or witness station assemblies attached to the substrate and configured to detect the signal from the tags. In some embodiments, the witness coils are placed such that the axis of the coil is co-planar with the central plane of the exciter coil(s). In this plane, the magnetic

flux produced by the exciter is orthogonal to the sensing axis of the witness coils for every combination of coil current direction described previously. The orthogonal exciter current does not induce a signal into the witness coils and thus provides isolation between the exciter coil and witness coils. This isolation is generally needed to achieve the needed system
5 dynamic range so that the very weak tag signal may be detected in the presence of the very large exciter magnetic field. This isolation is also important because crosstalk between the exciter coil and witness coils would otherwise greatly impede navigation because the crosstalk term would contribute significant signal arising from the same magnetic dipole (the exciter) to all witness coils and therefore the witness coils would lose their spatial
10 independence. An additional point is that the presence of the z-oriented exciter significantly distorts the z-component of the tag (and emitter) magnetic field, making it less useful for navigation.

In further embodiments, the plurality of witness coils, or plurality of witness station assemblies, comprises six to thirty witness coils (e.g., 6 ... 9 ... 12 ... 20 ... or 30). In
15 additional embodiments, the plurality of witness coils: i) are located on opposing sides of said base substrate, but not adjacent to said opposing sides, and/or ii) are each positioned to alternate opposite orientation along x and y axes with respect to other witness coils. This positioning minimizes crosstalk between witness coils and thereby reduces the degree that crosstalk compensation that is applied (e.g., by a mathematic solver software).

In some embodiments, the systems and devices further comprise a plurality of printed
20 circuit boards, wherein each of the plurality of witness coils is operably linked to one of the plurality of circuit boards. In certain embodiments, each circuit board comprises at least two capacitors and at least one balun circuit. In particular embodiments, the systems and devices further comprise the linked tags.

In certain embodiments, the systems and devices further comprise a balun circuit that
25 is electrically linked each of the at least one exciter coils. In further embodiments, the systems and devices further comprise a cable bundle that is electrically linked to the balun circuit. In additional embodiments, the systems and devices further comprise a plurality of witness coils attached to the substrate and configured to detect the signal from the linked tags,
30 wherein the plurality of witness coils are electrically linked to the cable bundle.

In some embodiments, the systems and devices further comprise at least one self-test emitter. In other embodiments, the systems and methods further comprise a top cover, wherein the top cover mates with the base substrate to enclose each of the exciter coils therein.

In other embodiments, the systems and devices further comprise a system electronics enclosure which is configured to provide a signal to the exciter coil(s). In other embodiments, the center of each of the exciter coils is separated from each other by at least 5 centimeters (e.g., 5 ... 10 ... 15 ... 25 ... 100 ... 1000 cm). In other embodiments, the center
5 of each of the exciter coils is separated from each other by 2-5 times the largest dimension of the coils themselves. In certain embodiments, the fourth exciter coil is positioned next to the second exciter coil, and wherein the third exciter coil is positioned next to the first exciter coil and diagonal from the second exciter coil.

In some embodiments, provided herein are methods comprising: a) positioning the
10 systems or devices disclosed herein below or near a patient that has at least two linked tags located therein, and b) activating the system or device such that a magnetic field is generated, thereby causing the each of the linked tags to generate a signal.

In some embodiments, provided herein are systems and devices comprising a witness station assembly, wherein the witness station assembly comprises: a) a witness coil, wherein
15 the witness coil comprises: i) a metal core having a coil-free proximal end, a coil-free distal end, and a central region, and ii) coil windings wound around the central region of the metal core, b) first and second witness coil brackets, and c) first and second elastomeric parts, wherein the coil-free proximal end of the metal core is secured between the first witness coil bracket and the first elastomeric part, and wherein the coil-free distal end of the metal core is
20 secured between the second witness coil bracket and the second elastomeric part. In certain embodiments the systems or devices further comprise a remote activating device (e.g., as described herein), wherein the remote activating device comprises at least one exciter coil. In further embodiments, the systems and devices further comprise: an exciter assembly (e.g., as described herein), wherein the exciter assembly comprises at least one exciter coil.

In further embodiments, the first and second witness coil brackets each comprises at
25 least one adjustment part (e.g., two adjustment screws). In some embodiments, the at least one adjustment part comprises at least one screw and/or at least one rod. In other embodiments, the witness station assembly further comprises an electronics part electrically linked to the witness coil. In other embodiments, the electronics part comprises at least one
30 capacitor and/or at least one balun circuit. In further embodiments, the electronics part comprises a printed circuit board.

In certain embodiments, the witness station assembly further comprises a faraday shield. In other embodiments, the witness station assembly further comprises: i) an electronics part electrically linked to said witness coil, and ii) a faraday shield. In additional

embodiments, the first and second elastomeric parts comprise a material selected from: an elastomer polymer and a spring.

In some embodiments, the metal core comprises a ferrite core. In other embodiments, the metal core has a diameter of 4 to 25 mm (4 ... 8 ... 12 ... 14 ... 16 ... 25 mm). In certain
5 embodiments, the metal core has a length of 15 to 75 mm (e.g., 15 ... 30 ... 45 ... 58 ... 75 mm). In particular embodiments, the coil windings comprise metal wire. In other embodiments, the metal wire is wound around said metal core 150-300 times. In further embodiments, the first and second witness coil brackets each comprises a notch configured to fit the wire-free proximal end and/or the wire-free distal end of said metal core.

10 In particular embodiments, provided herein are devices and systems comprising: a) an attachment component (e.g., a sheath) configured to be attached to a hand-held medical device with a device tip, wherein the attachment component comprises: i) a proximal end, ii) an angled distal end, wherein the angled distal end comprises a distal end opening configured to allow the device tip, but not the remainder of the medical device, to pass therethrough, and
15 iii) a main body stretching between the proximal end and the angled distal end, and b) first and second location emitters attached to the attachment component.

In certain embodiments, the angled distal end has an angle of at least 35 degrees with respect to the longitudinal axis of the attachment component (e.g., at least 35 ... 45 ... 65 ...
20 85 ... or 95 degrees). In some embodiments, the angled distal end has an angle of about 90 degrees with respect to the longitudinal axis of the attachment component. In further embodiments, the first and second location emitters are attached to the main body of the attachment component (e.g., spaced apart).

In other embodiments, systems and devices further comprise: c) a display component housing, wherein the display component housing is attached to, or attachable to, the proximal
25 end of the attachment component. In additional embodiments, the systems and devices further comprise a display component attached to the display component housing, wherein the display component comprises a display screen (e.g., LCD screen) for displaying the location of an implanted tag in a patient relative to the device tip on a medical device. In other embodiments, the display component housing comprises a cable management
30 component. In additional embodiments, the display component housing comprises a housing tapered connection. In further embodiments, the proximal end of the attachment component comprises a proximal tapered connection.

In other embodiments, the devices and systems further comprise first and second location emitter wire leads, wherein the first location emitter wire lead is electrically linked to

the first location emitter (e.g., small coil), and the second location emitter wire lead is electrically linked to the second location emitter (e.g., small coil). In other embodiments, the systems and devices further comprise: c) an adhesive strip sized and shaped to cover at least 50% (e.g., 50% ... 75% ... 90%) of the attachment component main body, and configured to
5 adhere the attachment component to the medical device. In certain embodiments, the systems and devices further comprise: c) the medical device. In other embodiments, the medical device comprises an electro-cautery surgical device.

A. Addressing variable alignment of an external coil (e.g., tag coil) with the exciter assembly

10 In some embodiments, the exciter is configured to provide power to a tag, independent of the alignment of the coil of the tag with the exciter. For example, in some embodiments, power transfer to a tag may be dependent on the relative orientation of the exciter magnetic field to the tag. In some such embodiments, absent a corrective measure,
15 the tag may only collect power from the portion of field aligned to the tag's coil (e.g., a ferrite-core coil contained in the tag). This issue could be resolved by including multiple exciters capable of producing all three orthogonal directions of the magnetic field. This, however, leads to a thicker assembly and prevents both rejection of primary exciter coil (e.g., located in the exciter assembly) to sensing coil coupling (also located in the exciter assembly)
20 (see section B below) and rejection of secondary field coupling between the tags/emitters and exciter coil that subsequently couple to the sensing coils and impair localization of the tags or emitters (see section C below). To address this challenge, provided herein are configurations of the exciter assembly that provide a mechanism of changing the orientation of the magnetic field with exciter coils that can be deployed in only one magnetic direction.

25 In some embodiments, this is accomplished by having multiple coils in the exciter assembly (see, e.g., Figure 4A), and setting the direction of current within each coil to either clockwise or counterclockwise (see, e.g., Figures 5-7). In some embodiments, the coils are connected in series so that the same current is running in each. In some embodiments, a coil layout comprises four coils in two rows, centered at (X1, Y1), (X1, Y2), (X2, Y1), and (X2, Y2) coordinates with three sets of current flow configurations: Configuration 1: all current
30 clockwise to simulate an exciter coil aligned with its plane normal to the Z axis; Configuration 2: coils centered at (X2, Y1), (X2, Y2) running current counter-clockwise to simulate an exciter coil aligned to the X axis; and Configuration 3: coils centered at (X1, Y2), (X2, Y2) running current counter-clockwise to simulate an exciter coil aligned to the Y axis.

Any number of other coil configurations may be employed. For efficiency, it is desired (although not required) to minimize the number of components and overall complexity of the design. However, in some embodiments, it may be desirable to have more than four coils (e.g., 6, 8, 10, 16, etc.) in the exciter assembly to provide more flexibility for changing field directionality, albeit at the expense of system complexity.

Tuning of the coils in the exciter assembly for each configuration requires less change between configurations when the same current is flowing through all the coils in every configuration. This is because the effect of one exciter coil on the others is dependent on the state of the first exciter coil (open circuit, current-carrying, etc.).

To provide optimal performance, the area of the exciter coils should be maximized, and the distance between the centers of the coils should be maximized. A larger area coil provides a higher field for the same applied current. Coils separated by larger distances provide a larger directional change for Configurations 2 and 3.

FIG. 3 provides an exemplary schematic of a four-coil exciter assembly in some embodiments of the invention, with the four coils labeled Coil A, Coil B, Coil C, and Coil D (see Figure 4A).

For medical uses, where the exciter assembly is provided in a flat planar mode (e.g., pad) beneath a patient, a clinically preferred system geometry entails that all four coils are placed very close to each other. As a result, the magnetic coupling between each coil varies with individual coil polarity and therefore the total inductance of all four coils in series varies with coil polarity combinations. Thus, optimal performance will necessarily balance competing factors. To compensate for this, in some embodiments, a system of switching is employed in which additional series capacitive reactance is inserted when the total inductance is increased so that the tuning center frequency is maintained at the desired excitation frequency. In a preferred embodiment shown in FIG. 3, relays are utilized for switching. Other embodiments may employ solid state switching approaches such as PIN diodes. Any suitable mechanism that achieves the switching may be employed.

In some embodiments, the centers of the coils are separated by 10 ... 50 ... 100 ... 500 ... or 1000 cm. In some embodiments, each coil is from 25 ... 625 ... 2500 ... 62,500 ... or 250,000 cm² in area. The largest total series capacitance is needed for a condition when all four coils have the same polarity. In some embodiments, this series capacitance is distributed equally among all four coils, balanced on each side of the switching relay as shown in FIG. 3. Distributing capacitance this way keeps the contact voltage present at the switch to a

minimum. Otherwise, the high “Q” of the coils could result in excessively high voltage, exceeding 10KV for some configurations, present at the switches and interconnects.

Additional capacitance useful for maintaining a desired resonant frequency as described above (e.g., adding capacitors in series to reduce the capacitance) is switched in by the polarity switching relay or a separate switch that may be energized when needed. In some embodiments, this capacitance is distributed among the polarity switching relays to both minimize terminal voltage and minimize common mode coupling by achieving best symmetry.

In some embodiments, each capacitance element is comprised of multiple capacitors to minimize the voltage across each capacitor to ensure the voltage capability of the capacitors is not exceeded and to minimize heating due to losses that might otherwise cause the resonant frequency to drift.

In some embodiments, a balun is incorporated as close as possible to the exciter coils (see Section D below and FIG. 3). The balun described below accomplishes common mode rejection to reduce or eliminate electric field generation and also provides an impedance transformation to optimally match the coil assembly impedance to that of the transmission line and power amplifier. In some embodiments, the primary (amplifier side) of the balun has 8 turns and the secondary (coil side) has 4 turns, thus providing a 4 to 1 change in impedance that nicely matches, for example, a 50-ohm generator output impedance to a 12-ohm coil impedance at resonance. Other turns ratio may be employed for optimal impedance transformation to other characteristic impedance transmission lines and amplifiers.

FIG.3 provides an exemplary embodiments of the coil system employed in the exciter assembly. In this figure, a plurality of capacitors is identified by number (e.g., C1, C5, C11, C40 etc.; pF (picofarads)) and their relative position to Coils A, B, C, and D (see, e.g., Figure 4A). A balun with a 7:4 turn ratio is shown (Balun transformer ratio matches impedance to 50 Ohms, employing 7:4 ratio, with 7 turns on the 50 ohm side and 4 turns on the coil side). The system may be configured or adjusted to optimize performance based on the manner in which the coils are utilized. For example, as shown in the exemplary embodiment in FIG. 3:

Field: Z-plane (++++) capacitors C9 and C10 are 25,600 pF (20,000 in parallel with 5,600 pF);

Field: X-plane (+-+-) capacitors C19 and C20 are 27,235 pF (used 27,000 pF in parallel with series combination of (2) 470 pF capacitors);

Field: Y-plane (++--) capacitors C29 and C30 are 6,050 pF (2,700 parallel with 3,300 pF in parallel with series combination of (2) 100 pF capacitors);

Common (all fields): capacitors C39 and C40 are 9,000 pF (parallel combination of (3) 3,000 pF capacitor); and

5 C39 and C40 capacitors (value XY-fixed) are 9,000 pF (18,000 pF in series with 18,000 pF; could be 9,220 pF; 8,200 in parallel with 820 pF or other combinations; total voltage is 660 Vrms).

Other specific values of capacitance may be utilized to provide the desired resonance frequency or frequencies with different values of inductance that may result from different
10 coil constructions.

B. Addressing exciter field strength near sensors

The exciter field strength used to power the tags, in general, is close to the exciter in order to create a large volume in which a tag or tags can be powered. This field is much
15 larger than the field provided by the tag or tags or the emitters associated with a surgical tool (the tags and emitters collectively and individually referred to herein as “the beacons”). Also, since a single excitation assembly device is preferred to both provide excitation and sensing, the sensing components should be in close proximity to the exciter components. Therefore, the magnetic field sensors would normally sense a magnetic field at the exciter frequency that
20 is very large, on the order of 160dB or larger than the signals of interest (from the beacons).

This issue can be partially resolved by means of electronic filters. However, the rejection capabilities of these filters are limited, they are expensive, and they are physically large. Filters may be active or passive. However, active electronic filters have an inherent noise floor that limits dynamic range and filtering effectiveness for this very high dynamic
25 range situation so passive filters may be employed in some embodiments.

An alternative (or additive) solution takes advantage of the coil system described in Section A above. In such embodiments, one can reduce the exciter field pickup by the sensors by taking advantage of the vector nature of the magnetic field. In some embodiments, an exciter coil with an orientation generating only magnetic flux substantially perpendicular
30 to the X-Y plane containing the sensing coils is selected. In some embodiments, ferrite-core coils, which are also highly directional in nature, are then aligned to that plane, such that magnetic flux orthogonal to the plane is not sensed. This produces rejection of the exciter field by more than 40 dB. In a preferred geometry, greater than 70 dB of isolation has been achieved for all sensing coils in all three polarity configurations described above. Both the

height and tilt of each witness coil is adjusted to achieve the alignment needed to achieve this level of isolation for all three coil polarity conditions. Isolation is typically measured using a Vector Network Analyzer by connecting the exciter coil to port 1 and a specific witness coil to port 2. The magnitude and phase of S_{21} is then measured at the receive frequency. In a preferred embodiment, the receive frequency chosen is 130.2KHz.

In such embodiments, the system therefore uses one magnetic field direction for excitation, and the two remaining directions (orthogonal to the excitation direction) for sensing. In other embodiments, one can use two orthogonalities for excitation and one orthogonality for sensing. However, it may be preferable to use two orthogonalities for sensing to provide faster estimates of the beacon position(s).

C. Addressing exciter/beacon coupling

In some embodiments, the exciter is a highly resonant coil. Because, in some embodiments, the beacon's frequency is close to the resonant frequency of the exciter, a portion of the beacon's AC magnetic field aligned to the exciter coil orientation may induce current flow in the exciter and therefore produce a magnetic field in the exciter coil orientation at the beacon frequency. This effect distorts the original field from the beacon, making it more difficult to localize the beacon. In a clinically preferred geometry, this distortion masks the true location of the beacon such that navigation may become difficult or impossible.

This coupling can be diminished by choosing a different beacon frequency less close to the exciter resonance. However, because, in some preferred embodiments, the beacons utilize a single ferrite core RF coil for both reception and transmission, the available bandwidth is limited.

Using the exciter configuration described in Sections A and B above, instead, since the sensing system comprised of sensing coils is oriented orthogonal to the exciter coil, the distorted field is not sensed. In other words, distortion is limited to the magnetic field direction that is substantially aligned to the exciter coil, which is orthogonal to the sensing system. The true location of the beacon is thus no longer masked by the field distortion produced by the exciter current flow at the beacon frequency so accurate navigation is achievable without artifact.

D. Addressing electric field magnitude produced by the system

The exciter and associated circuitry should be designed to minimize the electric field magnitude produced by the system. If produced, electric fields can couple capacitively into the sensing system and degrade system accuracy. Electric fields also interact with the patient and the environment much more significantly than magnetic fields.

5 In some embodiments, this challenge is addressed by incorporating a balun as close as possible to the exciter coils. The balun, which can also act as an impedance transformer, minimizes electric field by eliminating asymmetric current flow with respect to ground. Another way to think of this is that the balun eliminates common mode coupling. In some embodiments, on the exciter side of the balun, the circuit design and layout should be as
10 symmetric as possible to maintain balance.

In addition to reducing electric field effects, the transformer allows off the shelf 50-ohm coaxial transmission line to be used without mismatch. This scales transmission line voltage and current to optimally transmit power to the exciter assembly with the best efficiency and the smallest, most flexible, coaxial cable.

E. Identifying and managing locations of multiple beacons

In accordance with the methods described herein, two or more beacons (e.g., tags, emitters associated with one or more surgical devices, or other objects whose location, position, relative position, or other spatial information desired) are employed. The two or
20 more beacons (e.g. tags) are linked together by a linker (e.g. "linked tags"). In some embodiments, each beacon generates the same frequency. Such embodiments may be advantages because the signal strength could be up to 2x larger (assuming two tags are used, 3x larger if three tags are used, 4x larger if 4 tags are used, etc.) than with one beacon alone. Accordingly, such embodiments may be useful in large patients, wherein tissue volume of the
25 patient would otherwise limit the ability to detect a signal from a single beacon.

In some embodiments, each beacon generates the same frequency and the two signals can be deconvoluted to improve overall accuracy in detection. In some embodiments, the tags are programmed to respond with an offset frequency compared to the frequency of the stimulating frequency. In some embodiments, the tags are programmed to respond with an
30 offset frequency and a stable phase locked to the phase of the stimulating signal. This strategy allows the response signal(s) to be easily decoupled from the stimulating signals. In particular, a stable phase locked to the stimulating signal allows for precise localization of the signal of each of the at least two linked tags. In some embodiments, each of the two or more tags generates the same frequency, but are programmed to have a set phase offset. In some

embodiments, each beacon generates the same frequency, but the phase of each beacon can be a random factor of 11.25 degrees, which can be exploited to deconvolute the two signals.

In some embodiments, each different beacon (e.g. tag) generates a unique frequency, spectrum of frequencies or otherwise distinguishable signal. In some such embodiments, a hunting algorithm is employed to identify the spatial information of one or more of the beacons. In some embodiments, the optimal exciter polarity and power level is identified for each beacon (e.g., accounting for any relative orientation of beacon to the exciter) by cycling the exciter through different planes. Based on this information, an optimal exciter pattern is calculated to maximize the quality of the procedure and accuracy of information conveyed to a user (e.g., treating physician). In some such embodiments, a first optimal pattern is utilized to provide spatial information about a first tag and a first portion of a procedure is conducted. Next, a second optimal pattern (which may be the same or different) is utilized to provide spatial information about a second tag and a second portion of a procedure is conducted. Further cycles may be conducted for additional tags. Alternatively, the exciter pattern (polarity and power) may cycle between multiple, different optimal patterns during a procedure to provide near real-time optimal spatial information of multiple beacons. In some such embodiments, rapid switching of coil polarity in the emitter is employed to simultaneously or near-simultaneously power two or more beacons.

F. Exemplary Protocol

The technology is not limited by the mode of tag placement and a wide variety of placements techniques are contemplated including, but not limited to, open surgery, laparoscopy, endoscopy, via endovascular catheter, etc. The tags may be placed by any suitable device, including, but not limited to, syringes, endoscopes, bronchoscopes, extended bronchoscopes, laparoscopes, thorascopes, etc. An exemplary protocol is provided below.

A patient previously identified as having a breast tumor is admitted to a medical facility. The patient is initially sent to radiology. The radiologist examines prior imaging information identifying the target tumor. The subject is administered a local anesthetic, usually lidocaine or a derivative, using a needle introduced percutaneously. The subject is positioned in an imaging device, generally either ultrasound, conventional mammography, or a stereotactic unit. The location of the tumor is determined. An introducer needle (usually 6-20 gauge) is inserted either into or just proximal to the tumor and a biopsy needle is placed through the introducer needle and a specimen is obtained using a variety of methods (suction,

mechanical cutting, freezing to fix the position of the tissue followed by mechanical cutting). After the specimen is obtained and sent for pathologic examination, a 6-20 gauge tag delivery needle is inserted into the coaxial introducer needle to the tissue with the distal open end positioned at the lesion. Two linked tags are inserted into the proximal end of the delivery
5 needle and delivered by plunger through the opening at the distal end of the needle and into the tissue. Likewise, the tags could have been pre-positioned at the distal end of the delivery needle. Proper location of the linked tags is confirmed via imaging. The delivery needle is withdrawn, leaving the tags in place in the breast tissue.

This type of procedure can be performed in an analogous manner in virtually any
10 body space, organ, or pathologic tissue with the intent of localizing that tissue or space for further diagnosis or treatment of any kind. Areas of particular interest include but are not limited to the following organs, and disease processes that take place within them: brain, skull, head and neck, thoracic cavity, lungs, heart, blood vessels, gastrointestinal structures, liver, spleen, pancreas, kidneys, retroperitoneum, lymph nodes, pelvis, bladder, genitourinary
15 system, uterus, ovaries, and nerves.

In some embodiments, during surgery, the patient is placed onto an operating table with the surgical area exposed and sterilized. The surgeon is provided with the imaging information showing the location of the target tissue (e.g., tumor) and tags. An incision is made at the location of the entry point of the placement needle. The remote activating device
20 is placed in proximity to the tissue to activate the tags. The detection component comprising the witness stations (e.g., as shown in Figure 4A) detects a signal from the tags and allows the surgeon to guide the direction of the medical device toward the tumor. Once the tumor is localized, the surgeon removes the appropriate tissue and, optionally, removes the tags.

In some embodiments, the system finds use in surgery with the tags placed as
25 fiducials on or in the body. The relative position of the tags and any surgical instruments is located using the electromagnetic field. This information is communicated to a physician in real-time using a variety of methods including by not limited to visual (computer screens, direction and depth indicators using a variety of methods, haptic feedback, audio feedback, holograms, etc.), and the position of the instruments displayed on any medical images such as
30 CT, MRI, or PET scans in 2D or 3D. This data finds use to guide the physician during a procedure, or is used as a training method so that physicians can perform a virtual procedure. Such system may be integrated into or provide alternative approaches to existing surgical systems, such as the STEALTH system (Medtronic) for applications such as neurosurgeries.

In some embodiments, information about the location of the tags or the surgical paths or routes to the tags is conveyed to a surgeon or other user in a manner that comprises one or more augmented reality or virtual reality components. For example, in some embodiments, a surgeon wears or accesses a virtual reality device (e.g., goggles, glasses, helmet, etc.) that shows a partial or complete virtual image of the patient or surgical landscape. Tag position information collected and calculated by the systems described herein are represented by one or more visual components to the surgeons to assist in accurate targeting of the tag or tags. For example, the tissue containing the linked tags may be represented with a virtual image of the tags location shown. Likewise, in some embodiments, a surgical pathway is visually presented, for example, as a colored line to be followed. In some embodiments employing augmented reality features, a display, presents a graphical or video capture of the patient representative of what the surgeon would visualize if the monitor were not present and overlays one or more augmented features on the display. The graphical or video display data may be captured by one or more cameras in the surgical field. The augmented features include, but are not limited to, a representation of the location of the tags in the target tissue, a projected surgical path, a target point to which the surgeon aligns the tip of the surgical device, a simulated surgical margin zone to treat, arrows or other location indicators that recommend movement if the optimal pathway is deviated from, or the like.

An exemplary exciter assembly 250 is shown in Figures 4, 5, 6, and 7. This exciter assembly, as shown in Figure 1, can be positioned under the mattress of a patient lying on a surface, such as an operating table or mattress. The exemplary exciter assembly in these figures provides the excitation signal, via four exciter coils 150, for the tag(s) in the patient. The exemplary exciter assembly in Figure 4A provides a plurality of witness coil assemblies (aka witness station assembly) 161, each with a witness coil 160, in order to detect the signal from implanted tag(s) and the tags in the attachment component that is attached to the surgical device. The exciter assembly is composed of a base substrate 140 to which other components are generally attached or integrated into. The base substrate is composed of any suitable material, which may be, for example, polycarbonate or the like and is typically nonmagnetic and non-electrically conducting. Not pictured in Figure 4A is a top cover 230 (see Figure 8) that mates with the base substrate, enclosing all the internal components therein. The top cover is composed of any suitable material, including Kevlar and/or other rigid materials, again typically nonmagnetic and non-electrically conducting. Foam or other type of padding may be included on top of the top cover.

Attached to the base substrate are four large exciter coils 150, which are labeled “Coil A,” “Coil B,” “Coil C,” and “Coil D,” in Figure 4A. Each exciter coil 150 can be wound around four exciter coil mounts 155. In certain embodiments, the exciter coils are not wound in any particular form and instead employ wires that bond to themselves to create the coil shape. While not shown in Figure 4A, in certain embodiments, coil covers (e.g., plastic coil covers) are situated over each of the four exciter coils. Between the four exciter coils, generally centrally located, is a large central balun circuit 180.

On the interior of exciter coils B, C, and D is a switch 190. The switch 190 contains a component, such as a relay or multiple PIN diodes (e.g., at least four PIN diodes), or field effect transistor, that controls the directionality of the current (clockwise or counterclockwise) in the respective exciter coils. In the particular embodiment in Figure 4A, excited Coil A does not have a switch 190 as the direction in this coil is not changed. The switch 190 is linked to difference capacitors employed to correctly match the different inductance resulting from changing the directionality of current flow. If a relay(s) (e.g., four SPST, two SPDT type or one DPDT) is employed in the switch, it generally directs an input to one of two outputs. If multiple PIN diodes are employed (to create relay function) in the switch 190, this provides a very high impedance when “off” and low impedance when “on.” Each switch 190 also is linked to one or more capacitors to modify the capacitance that, along with the exciter coil inductor, forms the resonant circuit. This is necessary because the effective total series inductance of all exciter coils changes when the current flow direction is changed. Also on the interior of Coils A-D are a pair of capacitor assemblies 195, composed of a central capacitor 197, flanked by metal leads 199. In certain embodiments, the metal leads 199, are affixed to ceramic heat spreaders, in order to dissipate heat that builds up during operation.

In operation, the exciter assembly in Figure 4A is configured, in certain embodiments, to cycle between three configurations, called Configuration 1 (shown in Figure 5), Configuration 2 (shown in Figure 6), and Configuration 3 (shown in Figure 7). In Configuration 1, as shown in Figure 5, the current from all four exciter coils is clockwise in order to simulate an exciter coil generally aligned with its plane normal to the Z axis. In Configuration 2, as shown in Figure 6, the current from Coil A and Coil B is clockwise, while the current from Coil C and Coil D is counterclockwise, in order to simulate an exciter coil generally aligned to the Y axis. In configuration 3, as shown in Figure 7, the current from Coil A and Coil C is clockwise, while the current from Coil B and Coil D is counterclockwise, in order to simulate an exciter coil generally aligned to the X axis.

Although this is a preferred embodiment, other combinations of coil polarities with other values of additional series capacitance may be advantageous for certain tag orientations. For example, the current in coil A, instead of being clockwise, could be counterclockwise, and then all of the other 3 coils (Coils B, C, and D) could have the current flow as shown in
5 Figures 5, 6, or 7, or the other 3 coils (Coils B, C, and D) would have the opposite current flow as shown in Figures 5, 6, and 7. In other embodiments, the current arrangement is as shown in Figure 6, except the current in Coil B is counterclockwise, and the current in Coil D is clockwise. Every different combination of clockwise and counterclockwise for the Coils A-D is contemplated (i.e., all sixteen combinations).

10 The exemplary exciter assembly 250 in Figure 4A is also shown with twelve witness station assemblies 161 (each with a witness coil 160). The twelve witness coils 160 alternate opposite orientation (along x and y axes) to reduce crosstalk. In other embodiments, software may also or alternatively be used to reduce cross talk. In certain embodiments, rather than alternating orientation, all of the witness coils point toward the center, which would increase
15 crosstalk, but may have the advantage of shifting the location of inflection points in the witness coil signal pickups as a beacon is transitioned across the perimeter of the exciter assembly. It is generally preferably for the wires that feed into the exciter coils not be in close proximity to any of the witness coils, to prevent reduction in isolation and noise pickup. In Figure 4A, the wires from the center balun circuit to each of the four exciter coils are in a
20 location away from the twelve witness coils 160. Also, as shown in Figure 4A, the witness coils run down the left and right side of the exciter assembly, and do not run across the top or bottom of the exciter assembly. Adding witness stations across the top and/or bottom can cause strong crosstalk to occur. Alternatively, software applications can be used to reduce cross talk if witness coils are placed in positions that induce crosstalk. The witness coils 160
25 are held in place by a pair of witness coil brackets 165.

Next to each witness coil 160 is a printed circuit board 170. Each printed circuit board 170 contains capacitors and a small balun circuit. The capacitors, along with the witness coil, are employed to create a resonant circuit. The balun serves to eliminate common mode effects that would otherwise make the witness coil assembly susceptible to
30 electric field interaction. It also may serve as an impedance matching element that matches the real impedance of the coil/capacitor resonant circuit to the transmission line characteristic impedance, typically 50 Ohms, by optimally selecting the number of primary and secondary turns.

The exciter assembly 250 in Figure 4A is also shown with a pair of self-test emitters 220. These self-test emitters 220 are present such that one can apply known signals and check the response on all witness coils. If a witness coils does not show the expected signal, it indicates a system problem, or could indicate the presence of an interfering magnet or piece of metal which is distorting the field and degrading overall localization accuracy. It is noted that another self-test that can be employed is to generate a signal on the exciter coils that is normally applied to one of the emitters on the attachment component (e.g., sheath on hand held surgical device). By measuring the signal passed from the exciter to each witness coils, one can confirm the level of isolation between them. In still another self-test, a signal may be applied to each witness coil individually and the remaining witness coils may be used to detect the signal. In other embodiments, field witness coil crosstalk may also be measured this way and used to calibrate the system.

Figure 4A shows various wire connections between the various components of the exciter assembly. Each witness coil 160 is attached to a coaxial cable which is connected to the system electronics enclosure (labelled "controller," 210) via the cable bundle 200. The exciter signal comes from the cable bundle 200 into the central balun circuit 180. From there, wires carry the signal to the switches 190 and/or capacitor assemblies 195. The system electronics enclosure (controller 210) performs signal processing (e.g., filtering, mixing, amplification, digitization, and demodulation of multiple frequency 'channels') on the witness coil signals. Generally, no A/C main power is applied to the witness coils.

In regard to the capacitors employed in each capacitor assembly 195, and in the printed circuit boards 170, in general, the capacitors are chosen to be COG/NPO type where the capacitance value does not change with temperature, so that the resonant frequency of the exciter does not change with temperature. The capacitors also provide a tuning network which can selectively add capacitance in series to change the resonant frequency, which helps reduce tolerances during manufacturing, as well as makes it more tolerant of tuning changes due to temperature and other factors. In general, all the materials employed should have high dielectric strength and high stability over temperature to prevent geometric changes as the exciter assembly is used and the temperature is raised.

An exemplary witness coil assembly (aka witness station assembly) 161 is shown in Figure 4B. Witness coil assembly 161 includes witness coil two witness coil brackets 165, which are used to clamp a secure witness coil 160 against elastomer 162. The witness coil 160, as shown in Figures 4B and 4C, is composed of a metal core (e.g., ferrite core) 166 and coils 167 formed from wire. As shown in exemplary figure 4C, the metal core 166 is

composed of a central region 173 (under the wires in Figure 4C), with a wire-free proximal end 171 and a wire-free distal end 172. Only the ferrite core (using the proximal and distal ends that are wire-free) is clamped by bracket 165 and elastomer 162 (e.g., to provide best registration and eliminate the possibility of damaging the coil windings 167 of witness coil 160). The height of each end of witness coil 160 may be adjusted up or down by adjustment screws 163 (present in each witness coil bracket 165) while a restoring force is provided by elastomer 162. Elastomer thickness and durometer is chosen to provide the needed restoring force over the desired range of adjustment so that the adjustment screws will be easily adjusted yet hold the desired setting once the optimal position is achieved. Additionally, coil brackets 165 each has a "V" or "U" shaped feature that allows them to secure the proximal and distal ends of the metal core 166. This allows, for example, the brackets 165 to precisely register the witness coil core (e.g., ferrite core) in the desired direction so it cannot rotate about an axis perpendicular to the plane containing exciter coils. The witness coil assembly 161 also includes a printed circuit board 170 (with capacitors and balun circuit) and a faraday shield 168. The faraday shield may be composed of conductive material, such as brass or copper.

In certain embodiments, the exciter coil (e.g., as shown in Figure 4A) is connected to port 1 of a vector network analyzer or VNA. The witness coil output is generally connected to port 2 of the VNA and transmission (S21) is measured and displayed. This measurement is a direct measurement of the signal present at port 2 resulting from excitation provided to port 1 and is, therefore, a direct measurement of isolation. The lower S21 (more negative) the better. The more negative S21 the better. Typical isolation values (S21) achieved with the generally preferred embodiment are -70dB with usable ranges including -50dB to more than -100dB (e.g., the noise floor of the VNA).

In general, to achieve the best isolation between exciter coil and witness coil for the best accuracy over the largest navigation volume, it is generally important to position the witness coils orthogonal (e.g., precisely orthogonal) to the magnetic flux produced by the exciter coil. Figure 4A shows such an orthogonal arrangement of the twelve witness coils. Small offsets to height or tilt of the witness coil from this optimal position will generally result in signal coupling to the witness coil from the exciter coil that undermines isolation. Accordingly, in certain embodiments, the screws (or other connectors) on the witness coil brackets are employed to make fine adjustments.

Figure 4C shows an exemplary witness coil 160, including how the coils 167 are formed by wire being wound around the metal core in three stages: i) wind direction 1, where

wire is wound around most of a first half of the metal core; ii) wind direction 2, where wire is wound over the top of the wire wound over the first half, as well as over most of the second half of the metal core; and iii) wind direction 3, where wire is wound back over the wire on the second half. In certain embodiments, 80-140 windings (e.g., 80 ... 90 ... 112 ... 140) are on each half of the metal core (e.g., for total of 160-280 windings (e.g., 160 ... 200 ... 224 ... 280). In certain embodiments, the wire is 32 AWG copper magnet wire with a single layer polyester enamel and bond coat (e.g., 0.011 inches in diameter), and heat is used during wrapping to secure wire wraps. In certain embodiments, the metal core is a ferrite core part number #4077484611 from FAIR-RITE products corporation. In certain embodiments, the metal core (e.g., ferrite core) has a diameter of about 10-15 mm (e.g., 10 ... 12 ... 14 ... 15 mm), and is about 30-50 mm in length (e.g., 30 ... 35 ... 45 ... 50 mm). In certain embodiments, the metal core has a diameter of about 12.7 mm and a length of about 41.5 mm.

The wire is also connected to the secondary of a small balun transformer (in the printed circuit board, part 170 in Figure 4B) through two series capacitances (e.g., in the printed circuit board), one for each wire from the coil. In general, in certain embodiments, the total series capacitance is selected to resonate with the inductance of the coil in the tags, and the turns ratio of the balun transformer may be chosen to match the real impedance of the resonant coil/capacitor circuit to the transmission line (e.g., around 50 Ohms). In certain embodiments, the real impedance of the resonant coil/capacitor circuit is typically 10 to 25 Ohms, but may vary from just a couple Ohms to greater than 50 Ohms and may be adequately matched by appropriate choice of balun transformer primary and secondary turns. In addition to its role as impedance transformer, the balun minimizes any electric field generation/susceptibility from the witness coil assembly; alternately, it may be thought of as removing common mode effects. To further reduce the electric field susceptibility, the use of a conductive faraday shield 168 over the balun and capacitors is employed. This faraday shield (e.g., Faraday cage) reduces the observed electric field to components under the shield. Typically a Faraday shield is used to reduce the emission of electric fields of components under the shield, in this case it is also reducing the reception of electric fields.

Figure 8 shows an emitter component 250 with the top cover 230 on. The top cover 230 may be composed of Kevlar or other suitably tough material. The exciter assembly 250 is shown with cable bundle 200 leading therein.

Figure 9 shows an attachment component 10, with an angled distal end 300 that the distal tip 25 of the medical device 20 is inserted through. The display component 40 is attached to an attachment component control unit 310 via attachment component wire 60.

Figure 10A shows the distal end 25 of a medical device 20 after it is initially inserted
5 through the angled distal end 300 of attachment component 10. This view is prior to the attachment component wire 60 being inserted into the cable management component 315. Figure 10B shows attachment component wire 60 prior to being attached to the cable management component 315 of the display component housing 330. FIG. 10B also shows the housing tapered connection 340 that the proximal end tapered connection 350 of the
10 attachment component 10 is inserted into. The cable management component 315 has two clips that align both the attachment component wire 60 and the medical device wire 50.

Figure 11 shows an attachment component 10 attached to a display component housing 330. The attachment component 10 has a pair of location emitters 70, which are linked to location emitter wires leads 72 which are inside tube 360. The location emitters 70
15 are powered by the wire leads 72 to generate a signal which is detected by the witness coils. The attachment component also has an angled distal end 300 with a distal end opening 305, which allows the tip of a medical or other device to be inserted therethrough. The display component housing 330 has a cable management component 315, composed of a pair of clips for holding the attachment component wire and the medical device wire.

Figure 12 shows an exemplary attachment component 10 attached to a display component housing 330 with a display component 40 located therein. A display cover 370 is shown, which is used to secure the display component 40 inside the display component housing 330. Also shown is an adhesive strip 380 (e.g., a two sided strip with strong adhesive on both sides), which is shaped and sized to fit inside the attachment component and
25 help secure a medical device to the attachment component.

Figure 13A shows the proximal end tapered connection 350 of the attachment component 10, which is configured to push-fit into housing tapered connection 340 of the display component housing 330. Figure 13B shows a close up of section A of FIG. 13A, including cable management tapered connection 317 that is part of cable management
30 component 315 and designed to be inserted into tapered connection hole 319 of display component housing 330. Cable management tapered connection 317 includes a flat part 318 to lock angular position.

Figure 14 shows an exemplary system for localizing tags that are implanted in a patient. The system is composed of an exciter assembly that emits signals that activate the

tags in the patient. A systems electronics enclosure is shown as a mobile cart, which delivers signals to the exciter assembly and receives and processes signals from the tag(s) in the patient and the location emitters in the attachment component. Guidance for a surgeon is displayed on the display component, as well as on a screen on the systems electronics enclosure.

5

CLAIMS

We claim:

1. A system comprising:
 - a) at least two tags,
 - 5 b) a linker attached to said at least two tags;
 - c) a remote activating device that generates a magnetic field within a region of each tag; and
 - d) a plurality of sensors configured to detect a signal from each tag while each tag is exposed to said magnetic field.
- 10 2. The system of claim 1, wherein the tags are programmed to respond to a signal from said magnetic field with an offset frequency compared to said signal.
- 15 3. The system of claim 1, wherein the tags comprise a non-dielectric resonant antenna capacitor.
4. The system of claim 3, wherein the tags comprise a standard thin film capacitor or a multi-layer ceramic capacitor.
- 20 5. The system of claim 1, further comprising a wire or line, wherein said wire or line is attached to, and/or passes through, said linker at two or more points on said linker.
- 25 6. The system of claim 5, wherein said wire or line is attached to, and/or passes through, said linker such that said two or more tags are held in a first position with respect to each other, and wherein said linker is configured to hold said two or more tags in a second position when said wire or line is not attached to, and/or does not pass through, said linker, wherein said second position is different from said first position.
- 30 7. The system of claim 1, wherein the linker comprises a torsion spring.
8. The system of claim 1, wherein each of the tags is attached to the linker via heat shrink tubing.

9. The system of claim 1, wherein said linker is configured to hold said at least two tags in a first position when said tags are present in an insertion device.
- 5 10. The system of claim 1, wherein said linker is configured to hold said at least two tags in a second position when present in tissue, wherein at least one of said tags in said second position points approximately in the X dimension, and at least one of said tags points approximately in the Y dimension.
- 10 11. The system of claim 1, wherein said at least two tags comprises first, second, and third tags, and wherein, when in said second position: i) said first tag points approximately in the X dimension, ii) said second tag points in approximately the Y dimension, and iii) and said third tag points in approximately in the Z dimension.
- 15 12. The system of claim 1, wherein the linker is a flexible linker.
13. The system of claim 1, wherein the linker comprises plastic.
14. The system of claim 1, wherein the linker comprises a shape-memory alloy.
- 20 15. The system of claim 14, wherein the shape-memory alloy comprises a nickel-titanium alloy.
16. The system of claim 15, wherein the nickel-titanium alloy is Nitinol 55 or Nitinol 60.
- 25 17. The system of claim 1, wherein the at least two tags are positioned to form an angle within a range of 15 degrees to 40 degrees.
18. The system of claim 17, wherein the angle is 25 degrees.
- 30 19. The system of claim 1, wherein the linker includes a grip that is graspable by a surgical tool.
20. The system of claim 19, wherein the grip is a sphere.

21. The system of claim 19, wherein the linker is positioned within a packaging with a notch that exposes the grip.

5 22. The system of any of the preceding claims, wherein each tag comprises an antenna, wherein each tag emits sidebands at defined frequencies upon activation by said magnetic field.

23. The system of claim 22, wherein each tag antenna comprises a coil antenna.

10

24. The system of claim 23, wherein each coil antenna comprises a ferrite-core coil antenna.

25. The system of claim 24, wherein each coil antenna resonates at 100-200 kHz.

15

26. The system of claim 25, wherein each coil antenna resonates at the same or substantially the same frequency.

27. The system of claim 25, wherein each coil antenna resonates at a different frequency.

20

28. The system of any one of claims 24-27, wherein each coil antenna is coupled to an integrated circuit.

29. The system of any of the preceding claims, wherein each tag comprises an enclosure around said tag antenna.

25

30. The system of any of the preceding claims, wherein the remote activating device comprises at least one excitation coil.

30 31. The system of claim 30, wherein the remote activating device comprises two or more exciter coils each configured to flow current in a clockwise or counterclockwise

direction such that the magnetic field generated by said remote activating device may be selectively generated in one or more of X, Y, and Z directions.

5 32. The system of claim 30, wherein the remote activating device comprises four or more exciter coils.

33. The system of any one of claims 30-32, wherein the exciter coils are connected in series.

10 34. The system of any one of claims 31-33, wherein the exciter coils are configured such that the magnetic field is generated in two or more of X, Y, and Z directions.

15 35. The system of claim 34, wherein the exciter coils are configured such that the magnetic field is generated in the X, Y, and Z directions.

36. The system of claim 32, comprising four exciter coils in a layout of two rows centered at coordinates (X1, Y1), (X1, Y2), (X2, Y1), and (X2, Y2).

20 37. The system of claim 36, wherein the remote activating device comprises one or more of the following current flow configurations:

- a) all current clockwise to simulate an exciter coil aligned, or substantially aligned, with a plane normal to the Z axis;
- b) exciter coils centered at (X2, Y1), (X2, Y2) running current counter-clockwise to simulate an exciter coil aligned, or substantially aligned, to
25 the X axis; and
- c) exciter coils centered at (X1, Y2), (X2, Y2) running current counter-clockwise to simulate an exciter coil aligned, or substantially aligned, to
the Y axis.

30 38. The system of any one of claims 30-37, wherein the remote activating device comprises a plurality of relays, at least one PIN diode, or a field effect transistor, that provide a switching function to maintain an excitation frequency.

39. The system of claim 38, wherein the switching function inserts additional series capacitive reactance via a capacitance element when total inductance is increased so that a tuning center frequency is maintained at the excitation frequency.

5 40. The system of claim 39, wherein the capacitance element is comprised of multiple capacitors.

41. The system of any one of claims 30-40, wherein the remote activating device further comprises a balun in proximity to the exciter coils.

10

42. The system of any of the preceding claims, wherein said system further comprises an amplifier in electronic communication with the remote activating device.

15 43. The system of any of the preceding claims, wherein the remote activating device comprises a pad configured to be placed under a patient having the at least two tags embedded in the patient.

44. The system of any one of claims 30-43, wherein plurality of sensors comprises a plurality of witness stations.

20

45. The system of claim 44, further comprising a lock-in amplifier, wherein said lock-in amplifier lock-in amplifier is configured for narrow-band detection to provide omnidirectional detection for determining the location of said at least two tags.

25 46. The system of claim 44 or 45, wherein each witness station comprises a plurality of antennas.

47. The system of claim 46, wherein each of said witness station antennas feeds a receiver channel that is time-division multiplexed.

30

48. The system of claim 46 or 47, wherein said plurality of antennas within a witness station are arranged in an orthogonal manner to each other.

49. The system of any one of claims 46-48, wherein said witness station antennas comprise a ferrite-loaded cylindrical coil antenna tuned for resonance at the frequency of at least one of the tags.

5 50. The system of any of the preceding claims, further comprising a medical device.

51. The system of claim 50, wherein the medical device is a hand-held surgical tool.

10 52. The system of claim 51, further comprising one or more location emitters configured for attachment to the hand-held surgical tool.

53. The system of claim 52, wherein the one or more location emitters are positioned on a sheath that slides over a portion of the hand-held surgical tool.

15 54. The system of claim 51 or 52, wherein the one or more location emitters comprise an antenna, wherein the one or more location emitters emits sidebands at defined frequencies upon activation by a magnetic field.

20 55. The system of any of the preceding claims, further comprising a computer system that controls magnetic field generation and sensor detection.

56. The system of claim 55, wherein the computer system receives information from the plurality of sensors and generates information about the position of the tags.

25 57. The system of claim 55, wherein the computer system applies a hunting algorithm that adjusts the magnetic field orientation to identify optimal detection of one or more tags.

30 58. The system of any one of claims 51-57, further comprising a display screen attached to the hand-held surgical tool.

59. The system of claim 58, wherein the display screen displays information about the position of the tags to a user.

5 60. Use of a system of any one of claims 1-59 for detecting a position of a tag in an object.

61. The use of claim 60, wherein the object is human.

10 62. The use of claim 60, wherein the object is tissue near or on a tumor.

63. Use of the system of any one of claims 1-62 for detecting a position of a tag relative to a medical device.

15 64. A method of identifying a position of two linked tags, comprising:
a) providing the system of any of claims 1-59;
b) placing the at least two tags in an object;
c) generating a magnetic field with the remote activating device; and
d) identifying the positions of the at least two tags in the object by collecting
information emitted from the at least two tags with the plurality of sensors.

20 65. The method of claim 64, wherein the positions of the at least two tags comprises the relative locations of each tag to a medical device.

25 66. The method of claim 64, wherein the positions of the at least two tags comprises the distance of each tag to a medical device.

67. The method of any one of claims 64-66, wherein the object is human.

30 68. The method of any one of claims 64-66, wherein the object is tissue near or in a tumor.

69. The method of claim 59, wherein placing the at least two tags in an object comprises positioning the at least two tags into said object using an introduction device.

70. The method of claim 69, wherein the at least two tags are arranged in a first position within said introduction device.

5 71. The method of claim 70, wherein the at least two tags migrate into a second position when placed in said object.

72. The method of claim 71, wherein at least one of said tags in said second position points approximately in the X dimension, and at least one of said tags points
10 approximately in the Y dimension.

73. The method of claim 71, wherein said at least two tags comprises first, second, and third tags, and wherein, when in said second position: i) said first tag points approximately in the X dimension, ii) said second tag points in approximately the Y
15 dimension, and iii) and said third tag points in approximately in the Z dimension.

74. The method of any one of claims 69-73, wherein said introduction device comprises a cannula.

20

25

30

FIG. 1

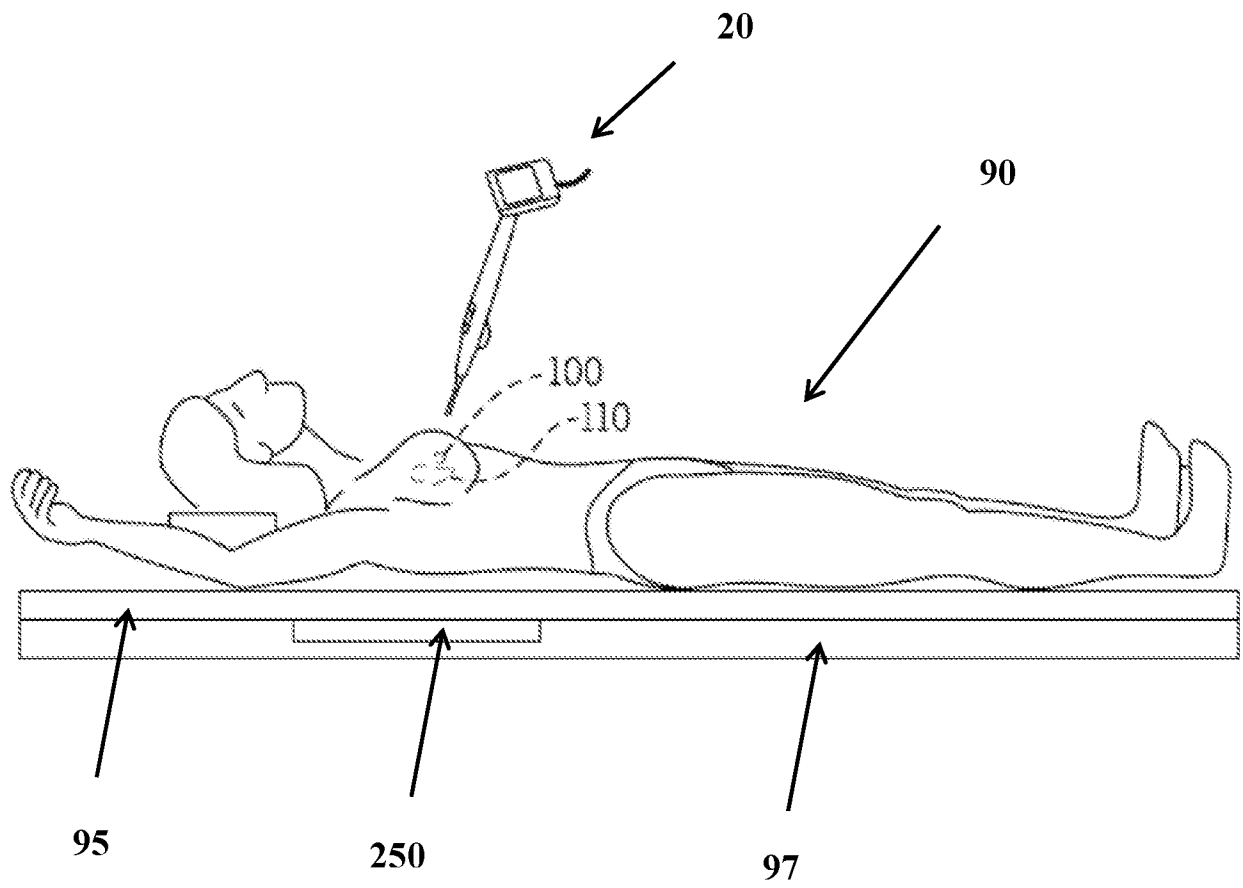


FIG. 2

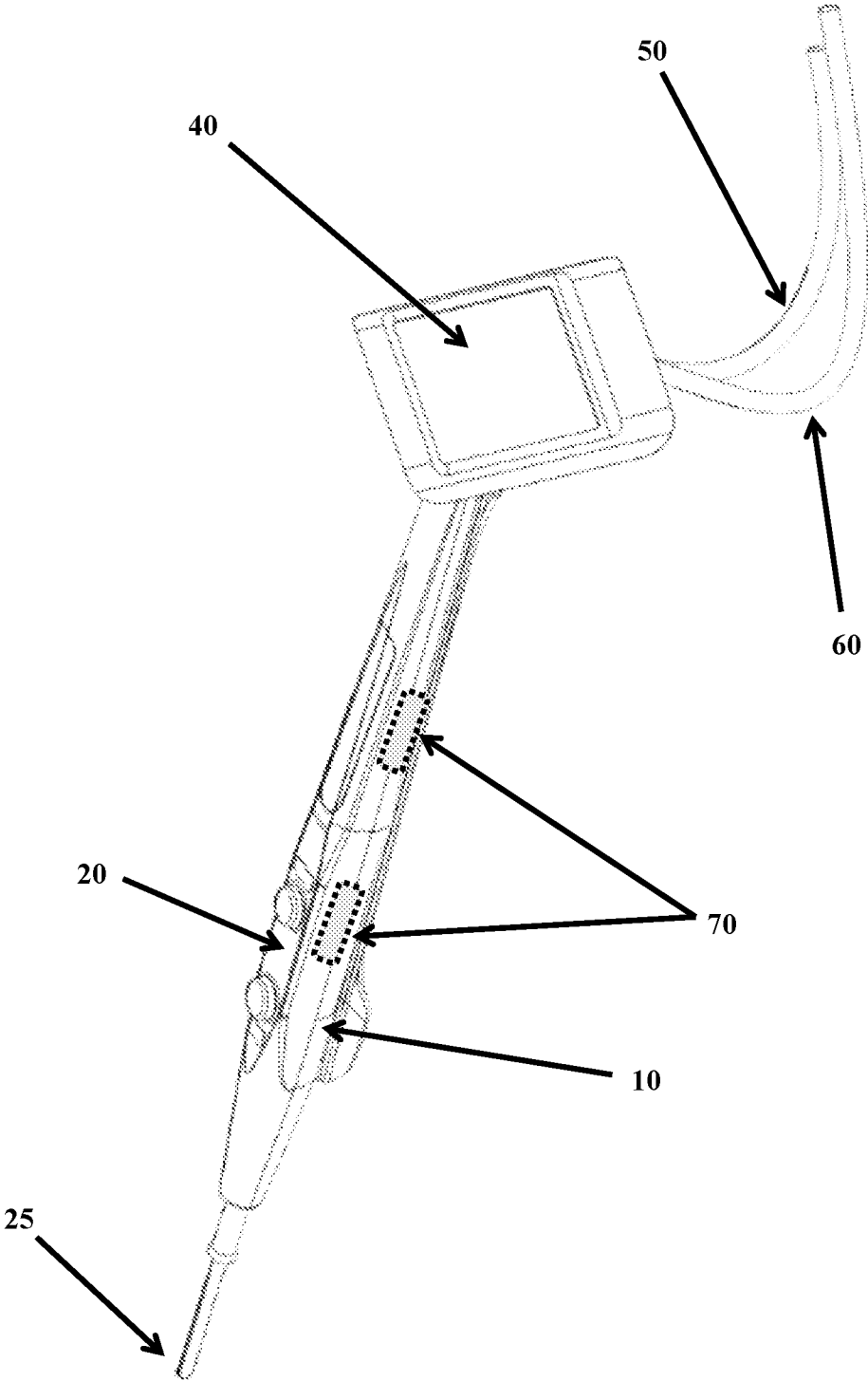


FIG. 3

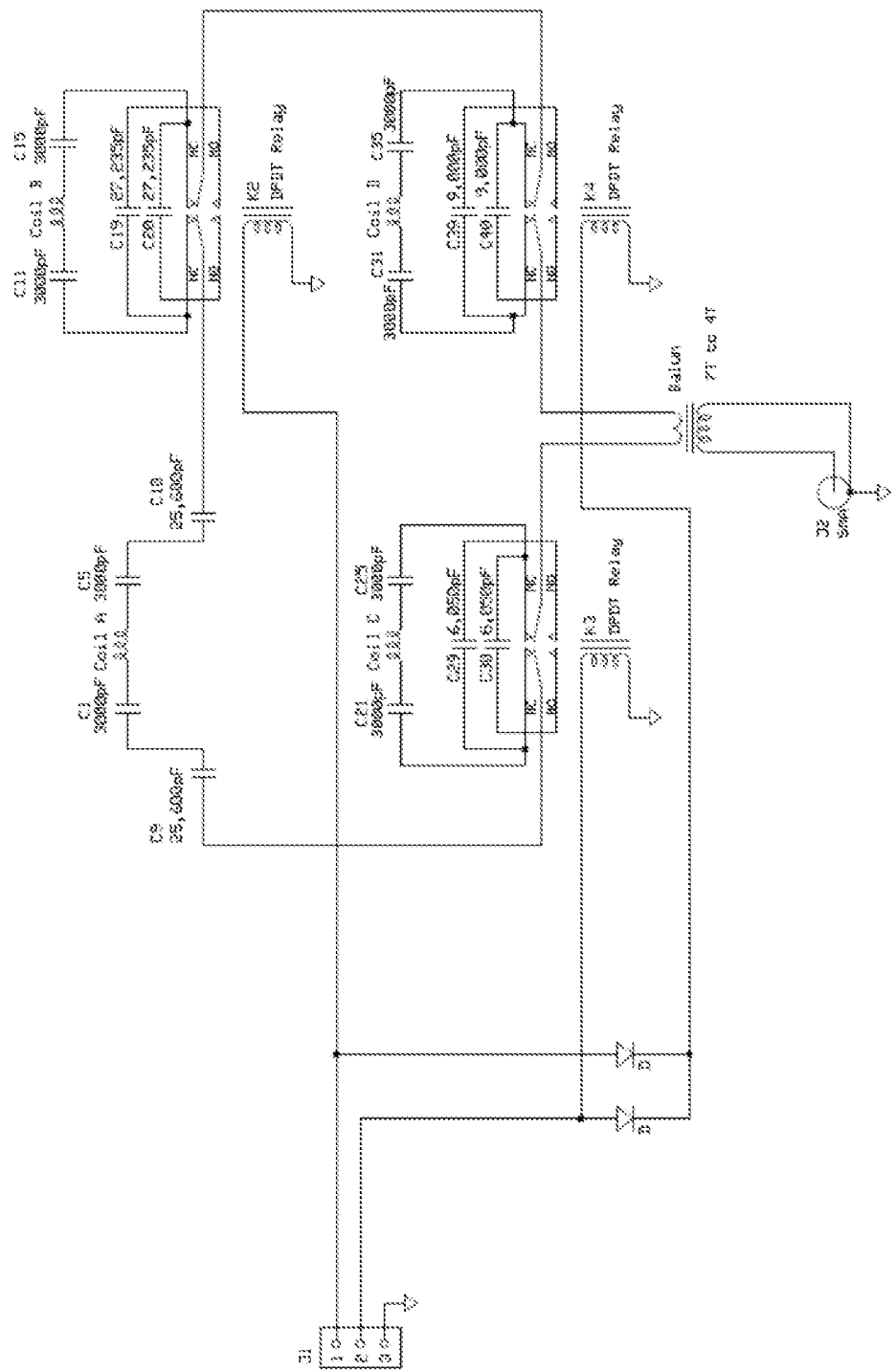


FIG. 4A

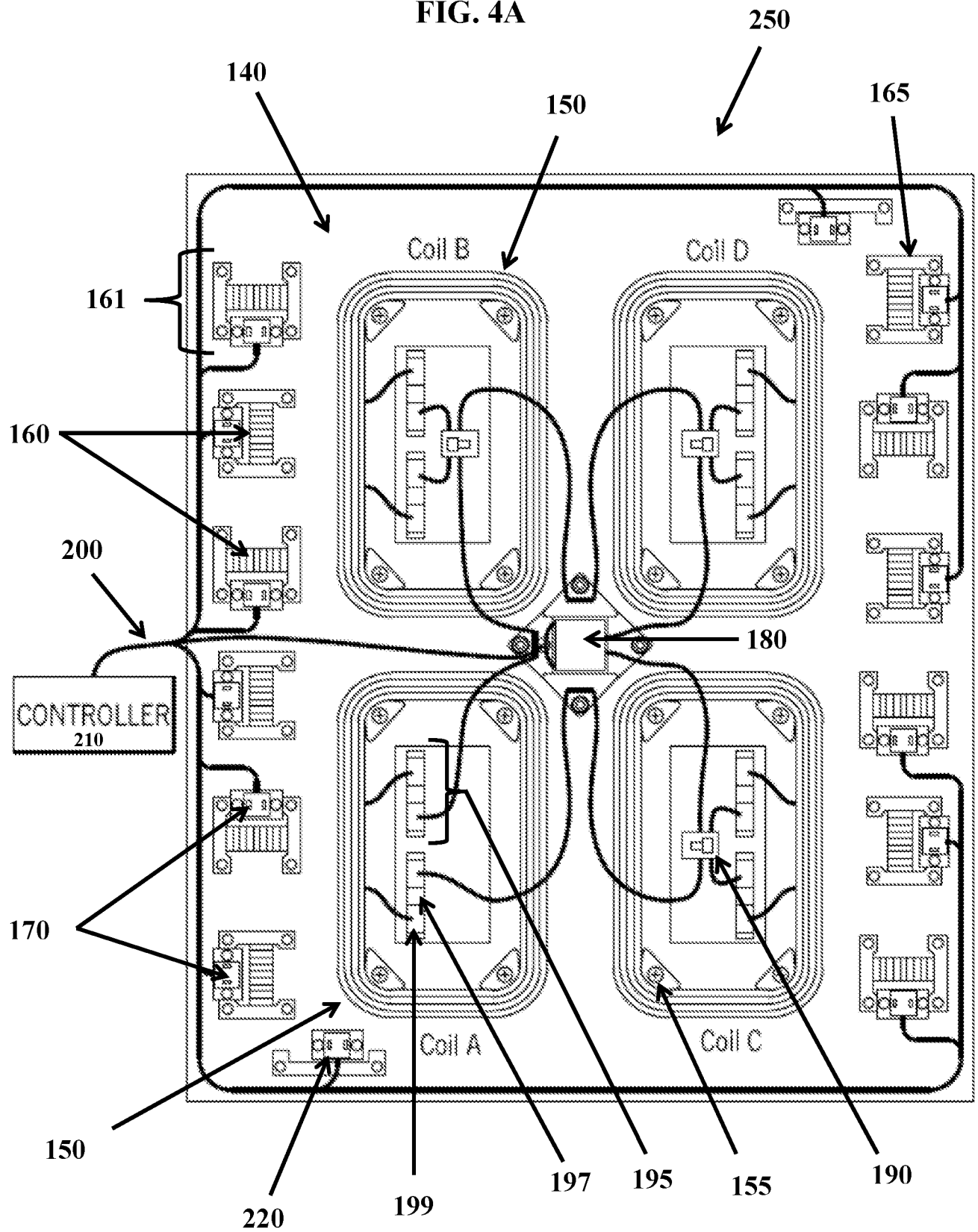


FIG. 4B

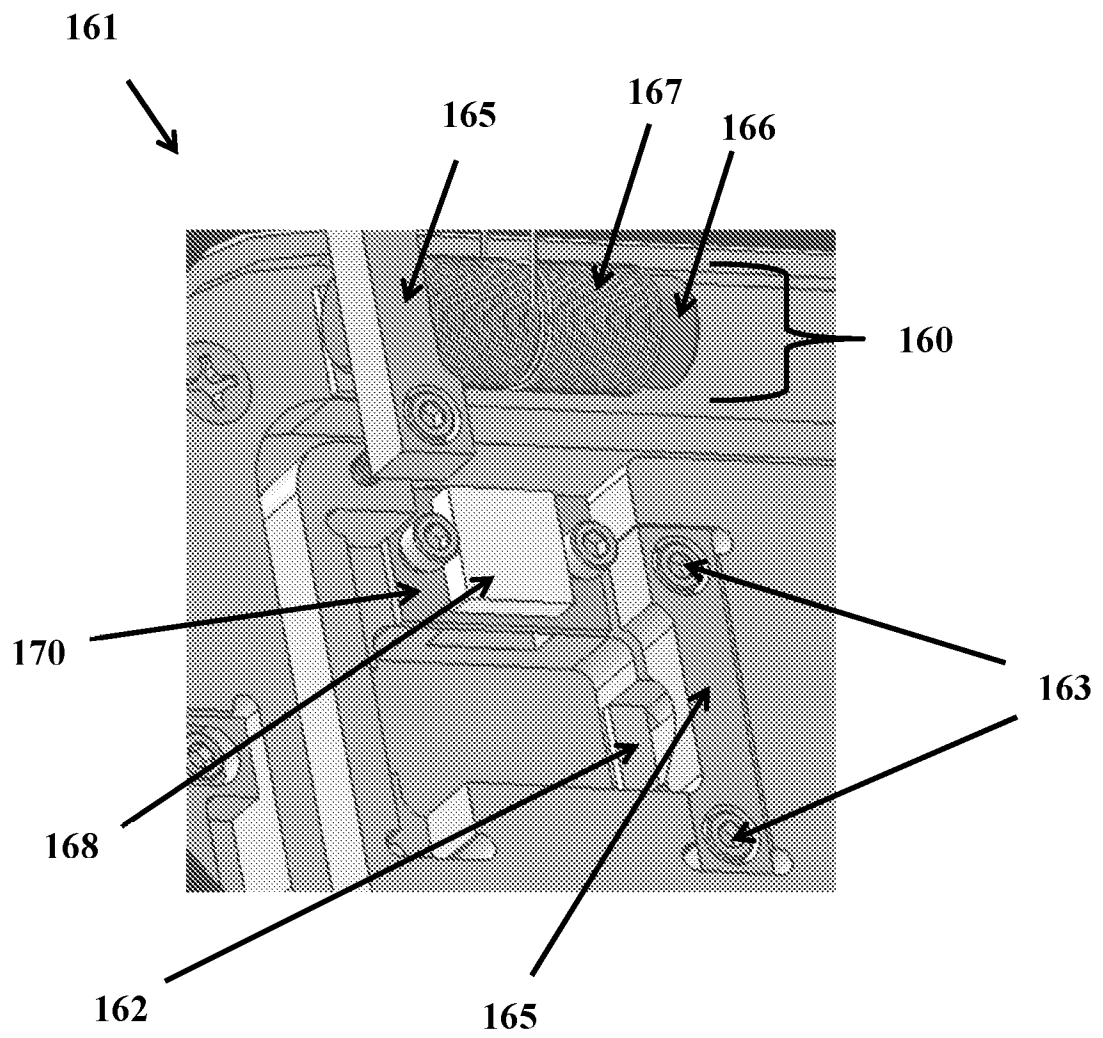


FIG. 4C

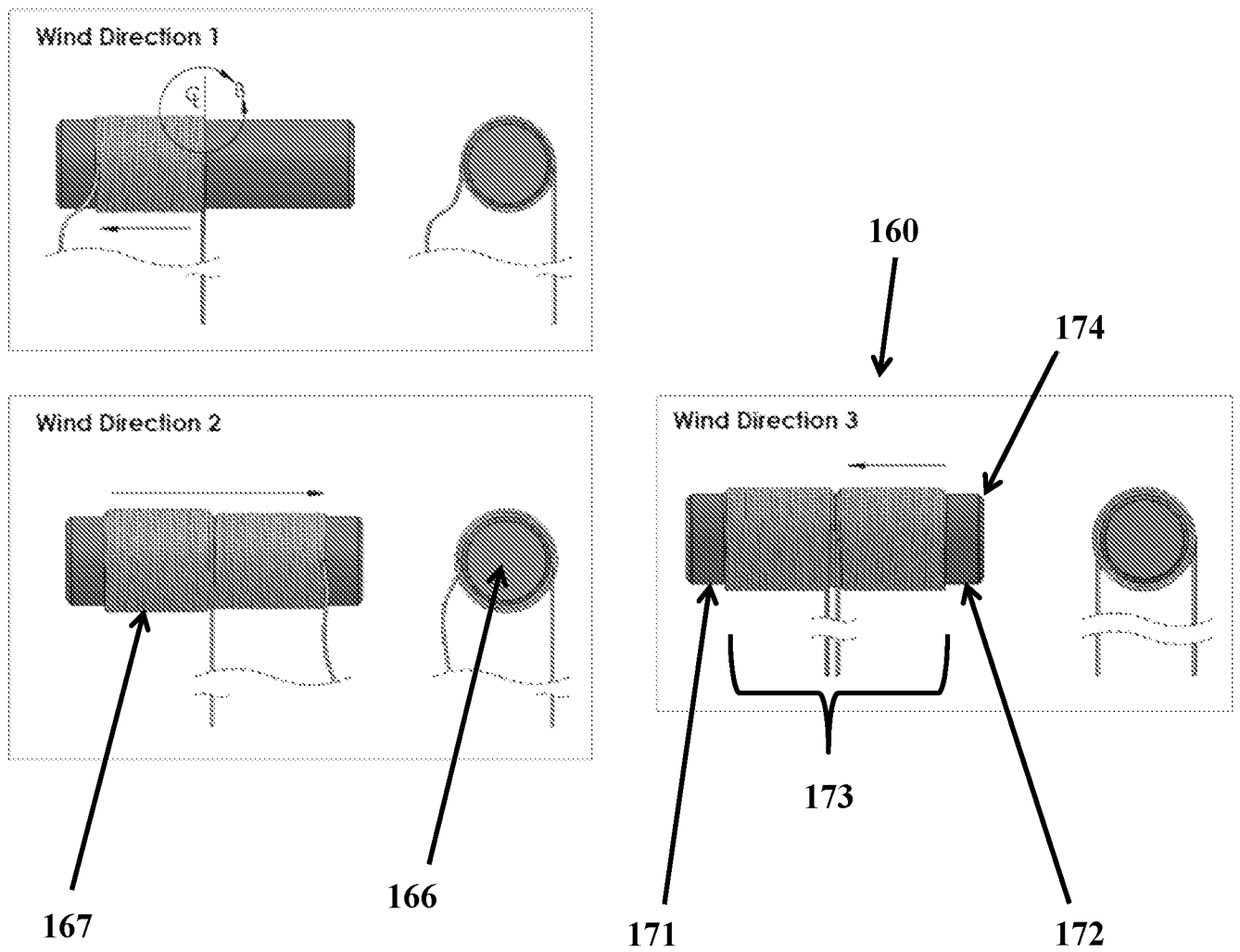


FIG. 5

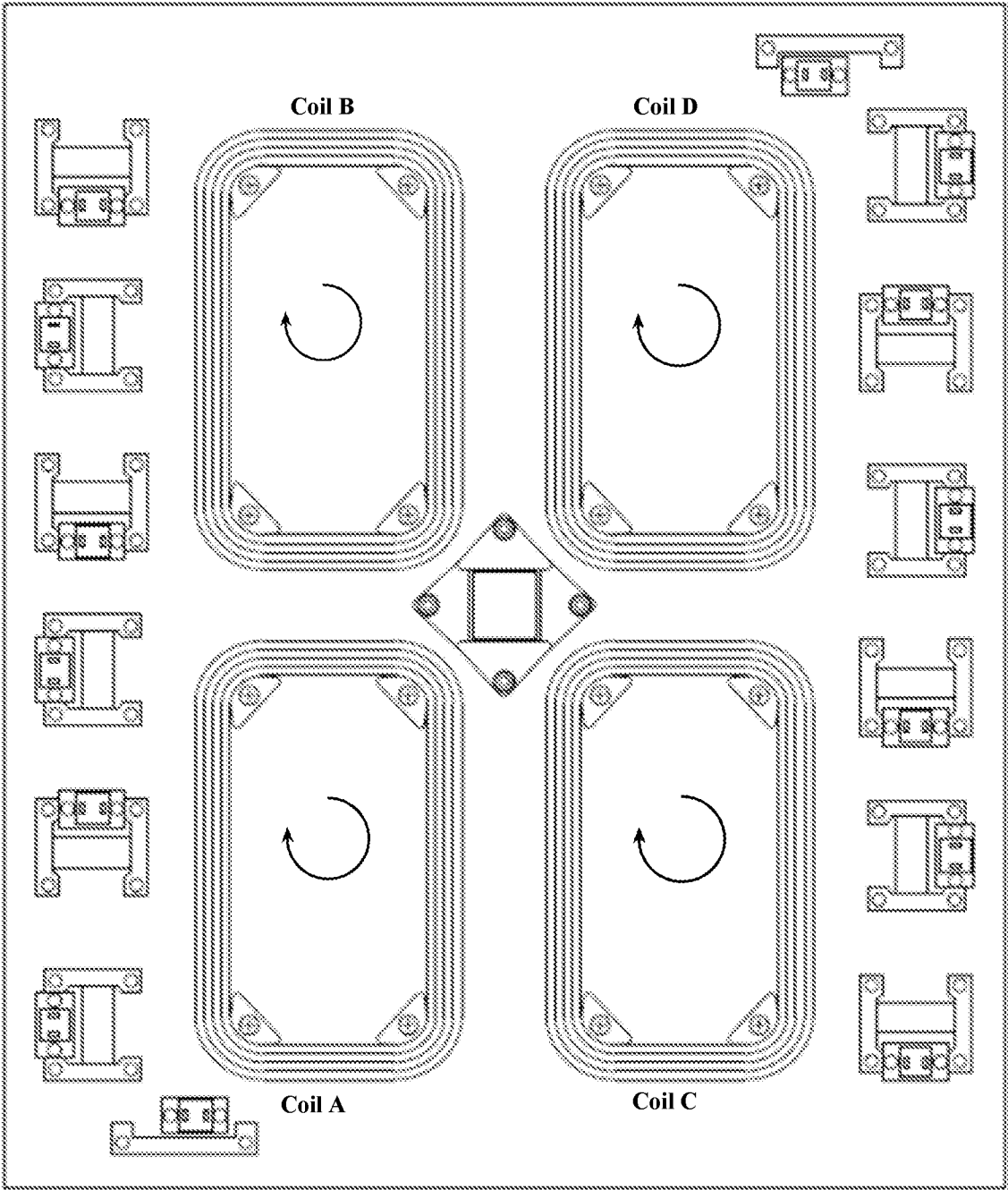


FIG. 6

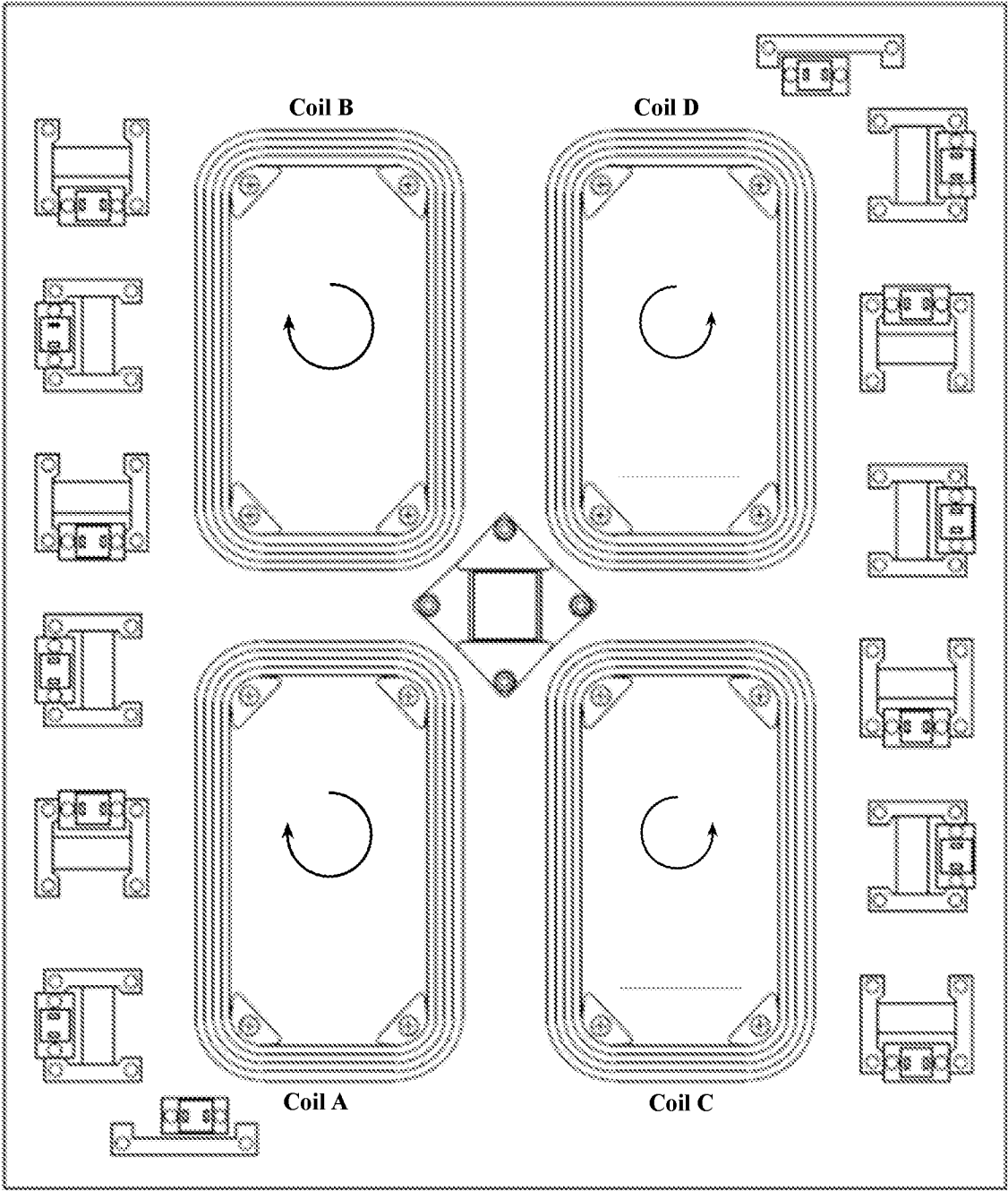


FIG. 7

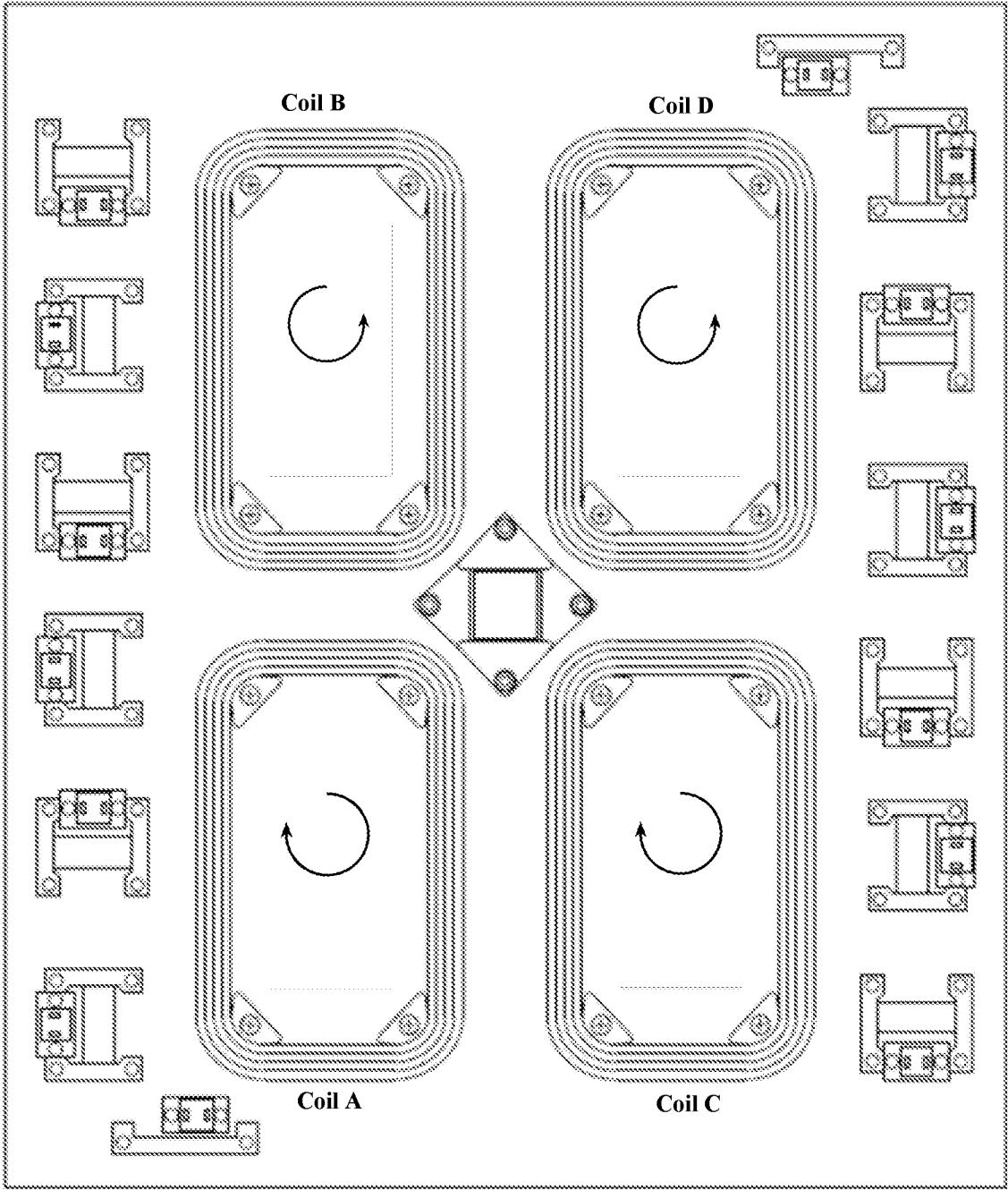


FIG. 8

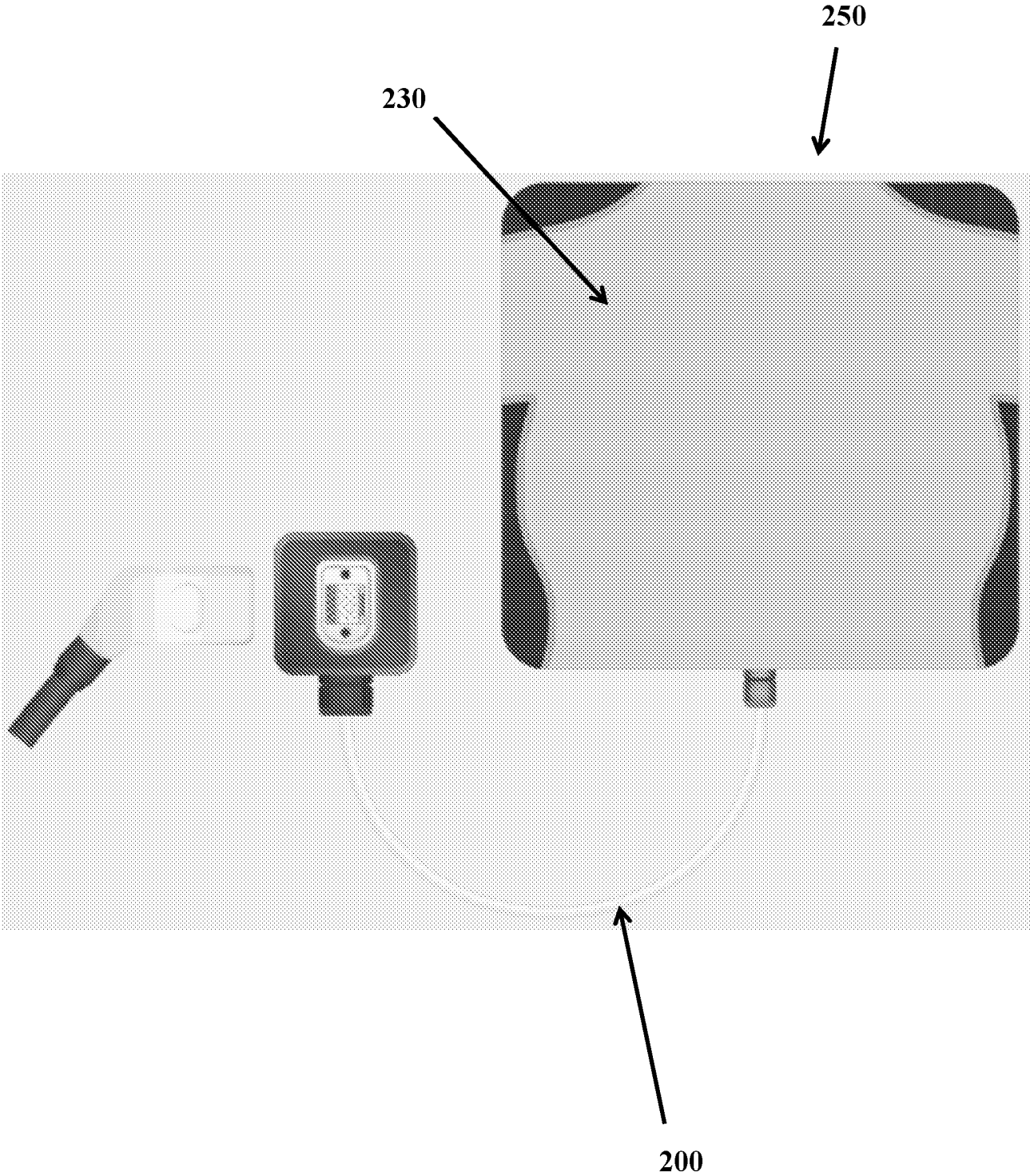


FIG. 9

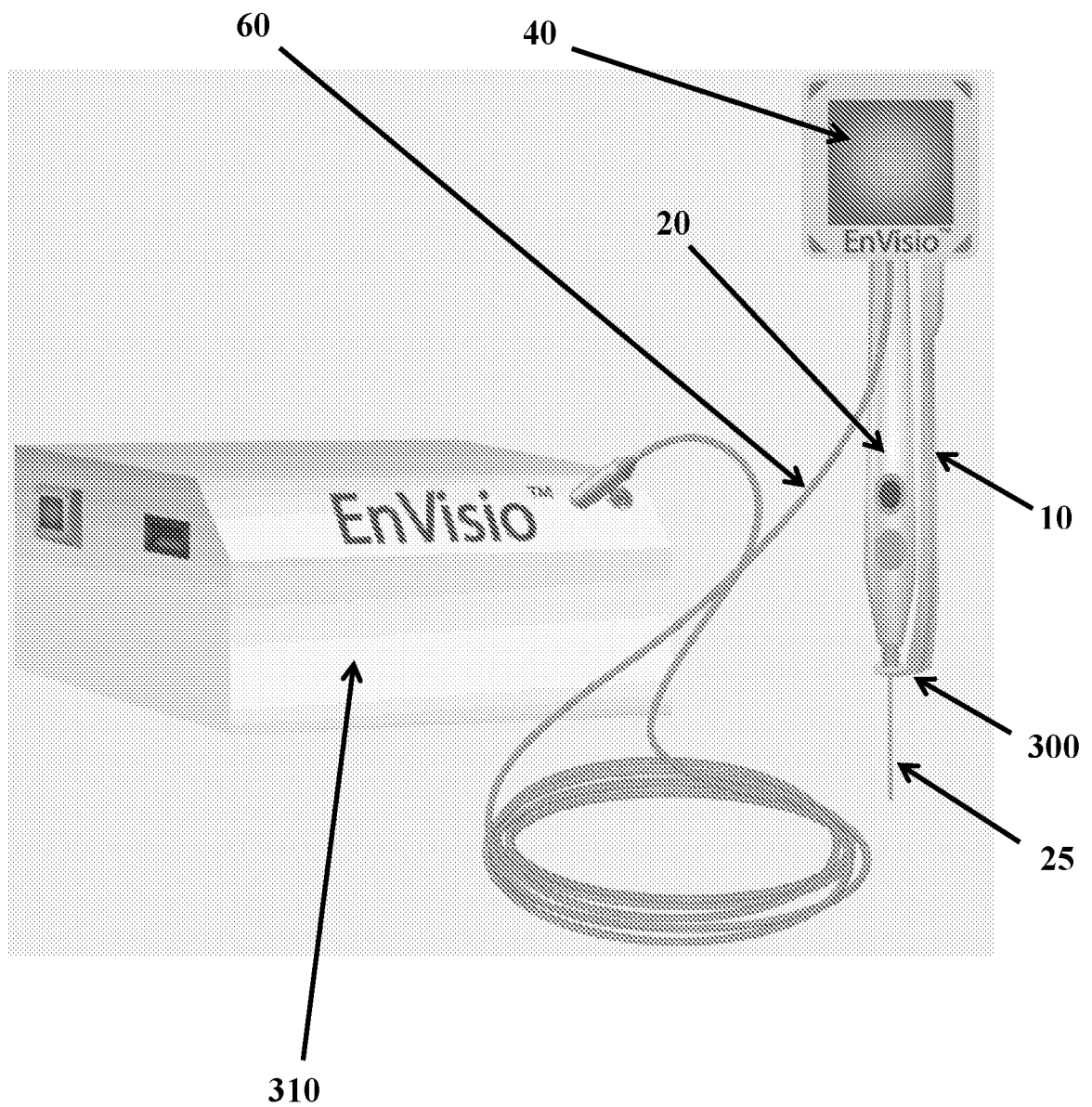


FIG. 10

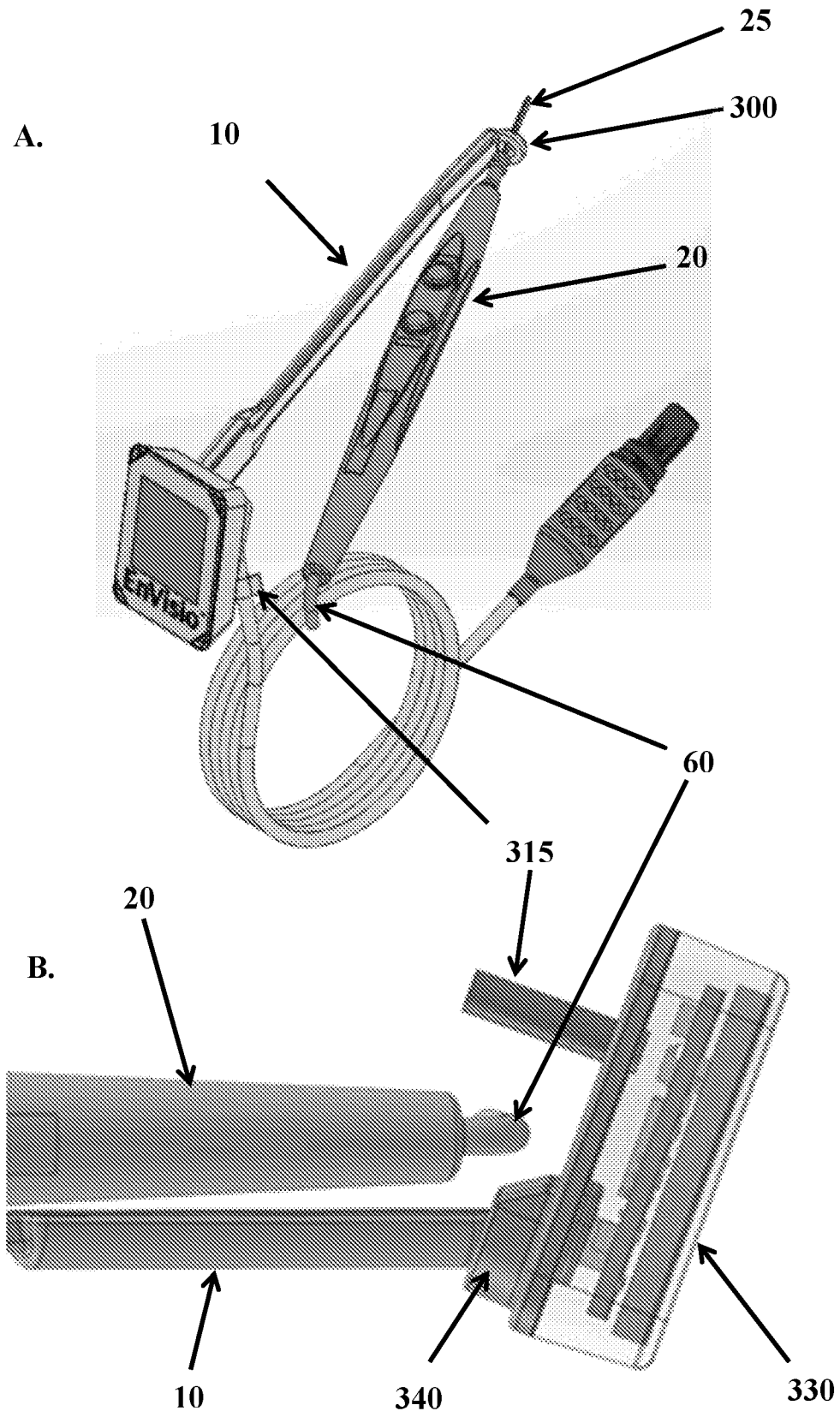


FIG. 11

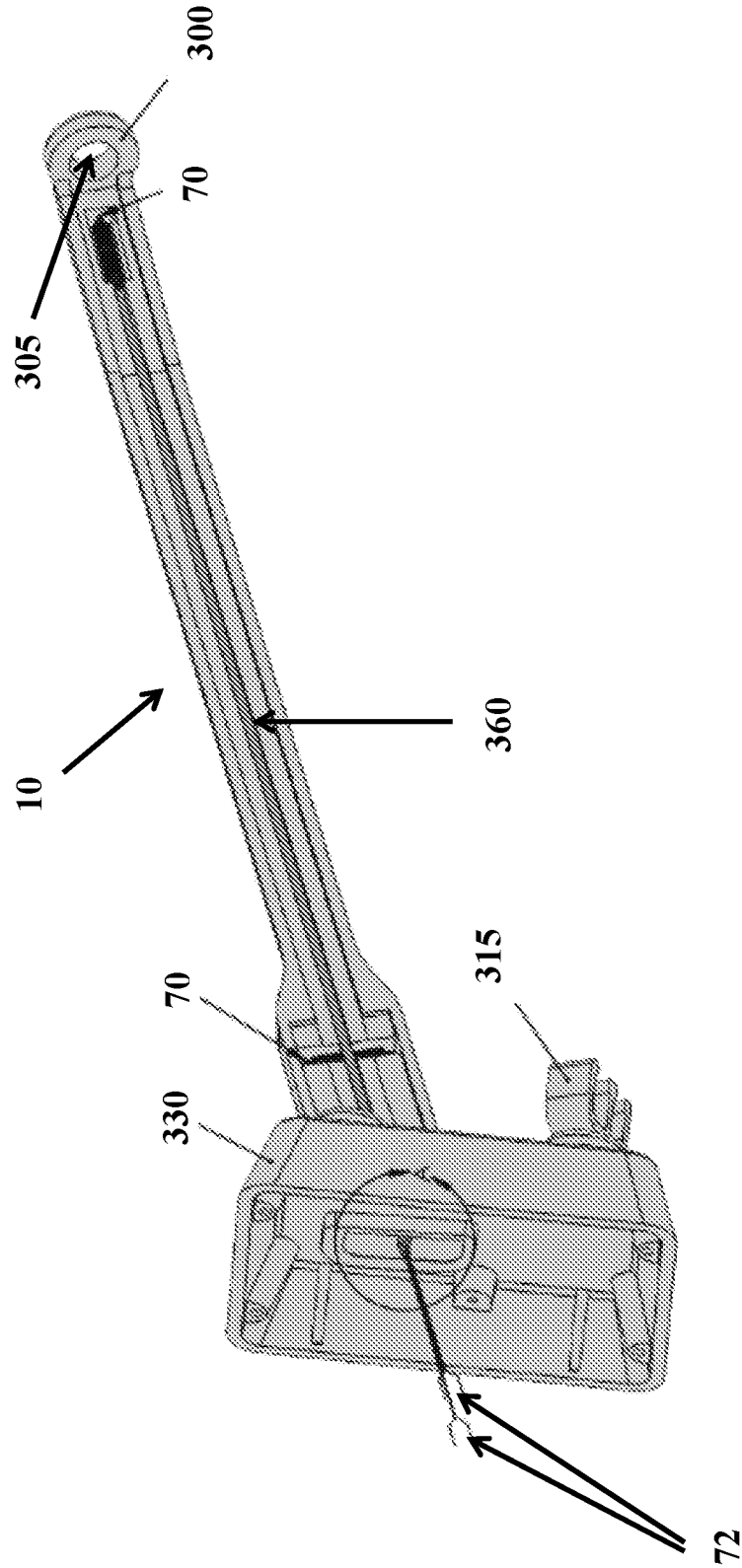


FIG. 12

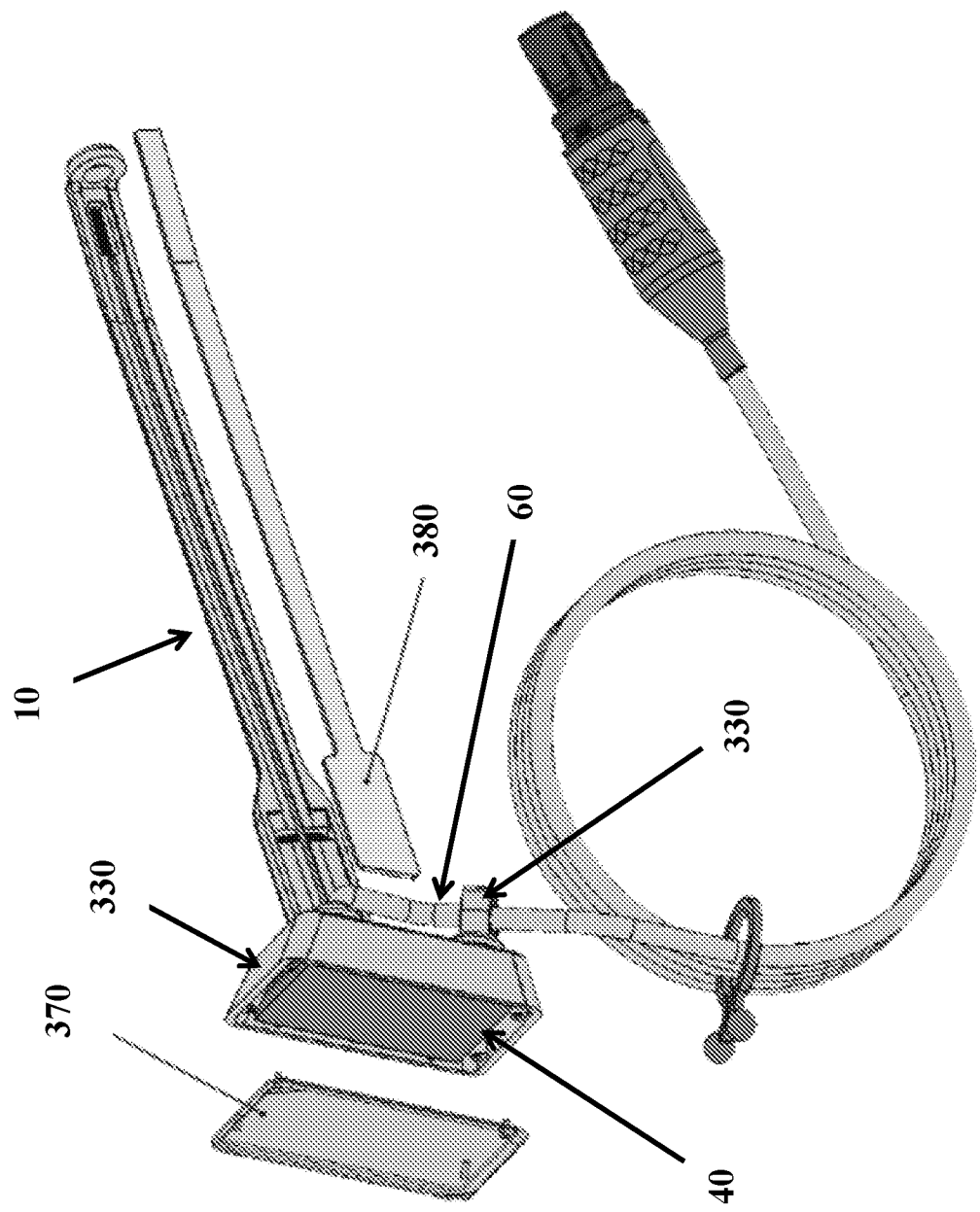


FIG. 13

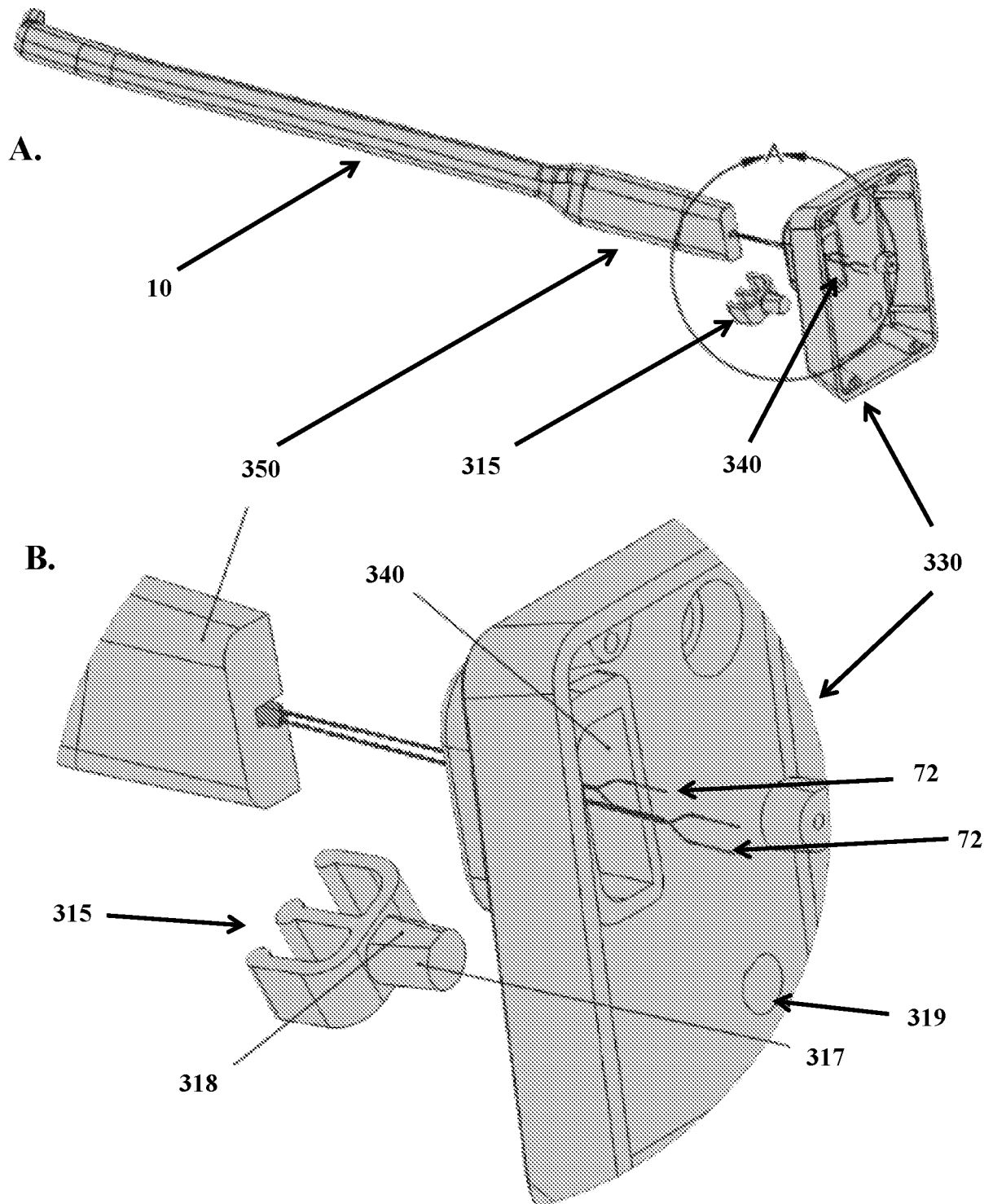
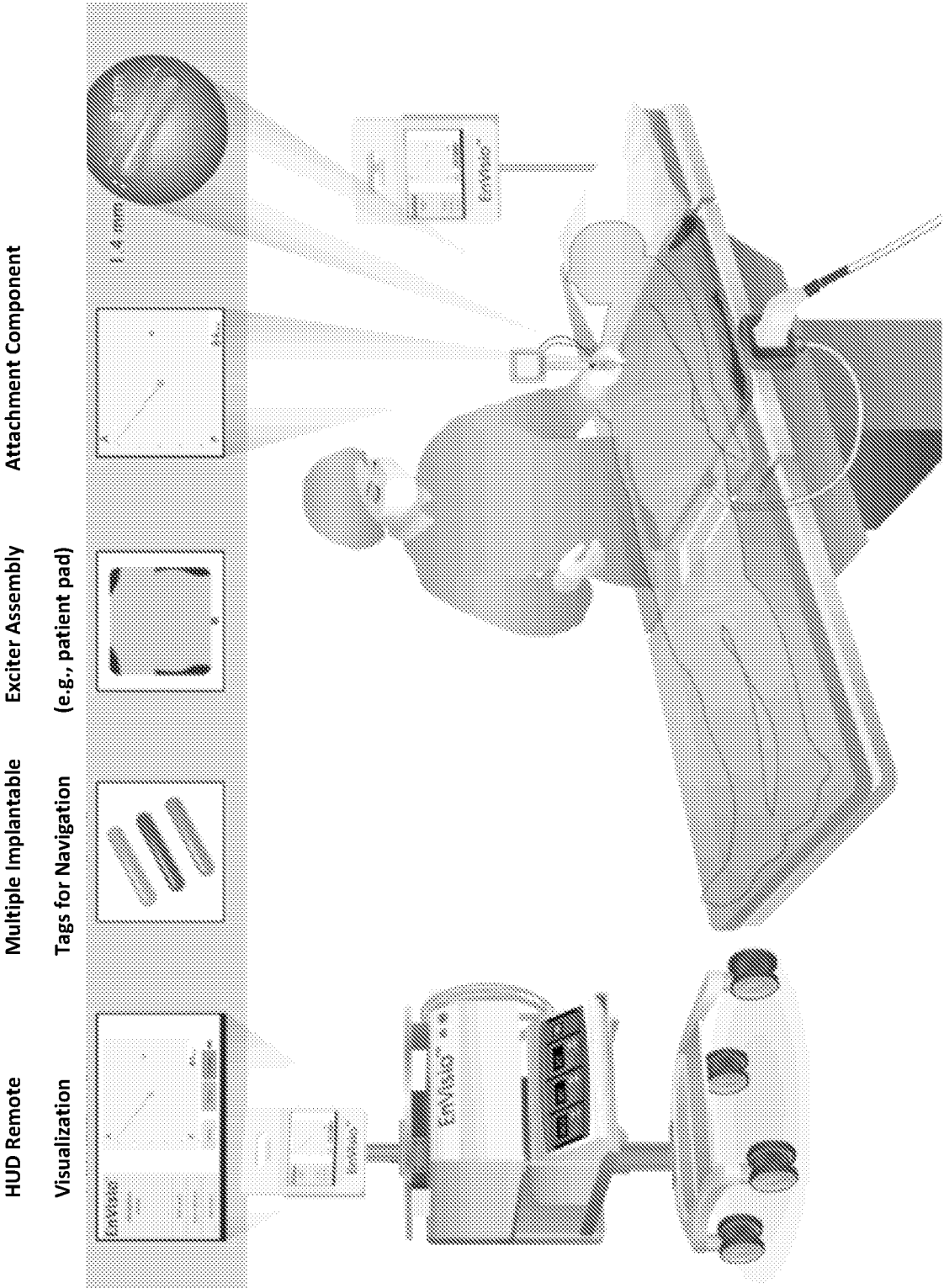


FIG. 14



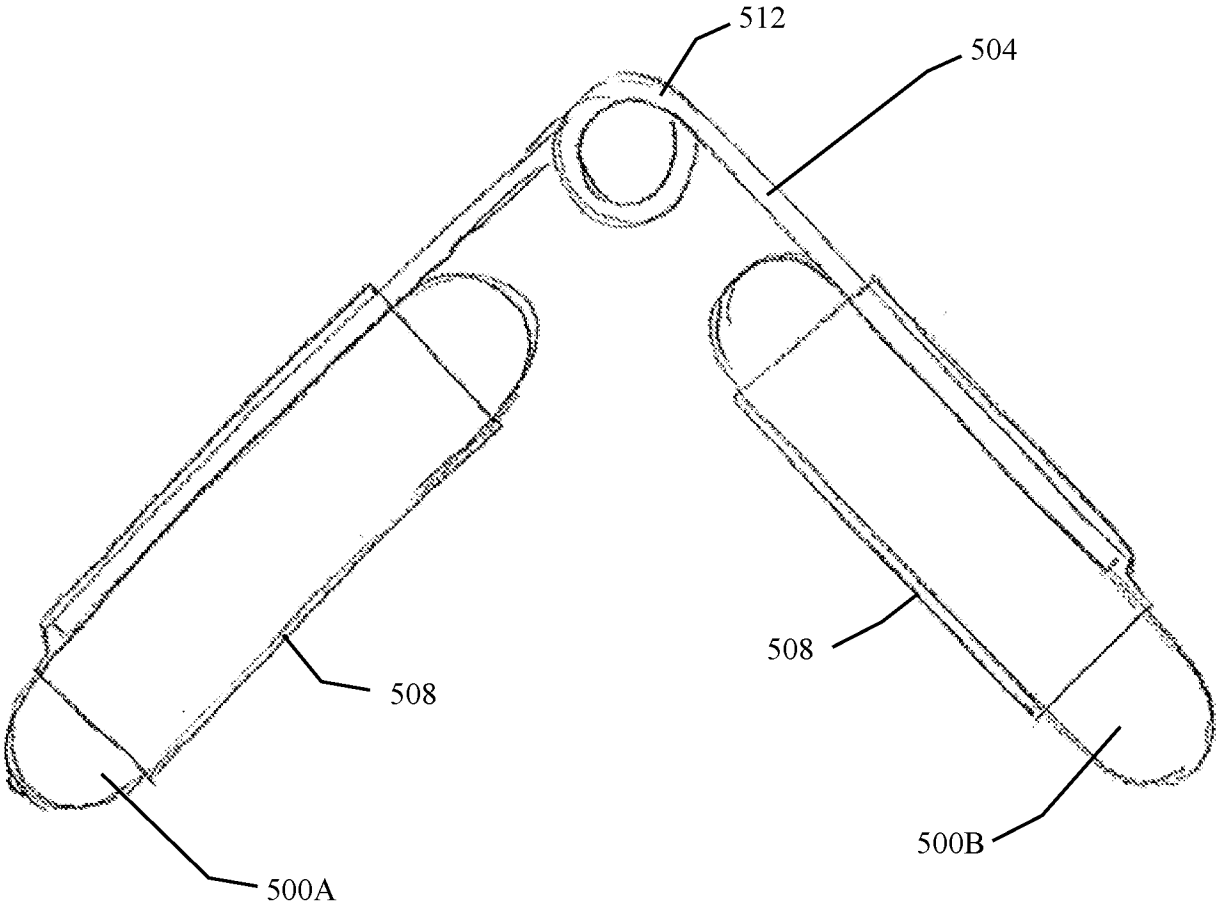


FIG. 15

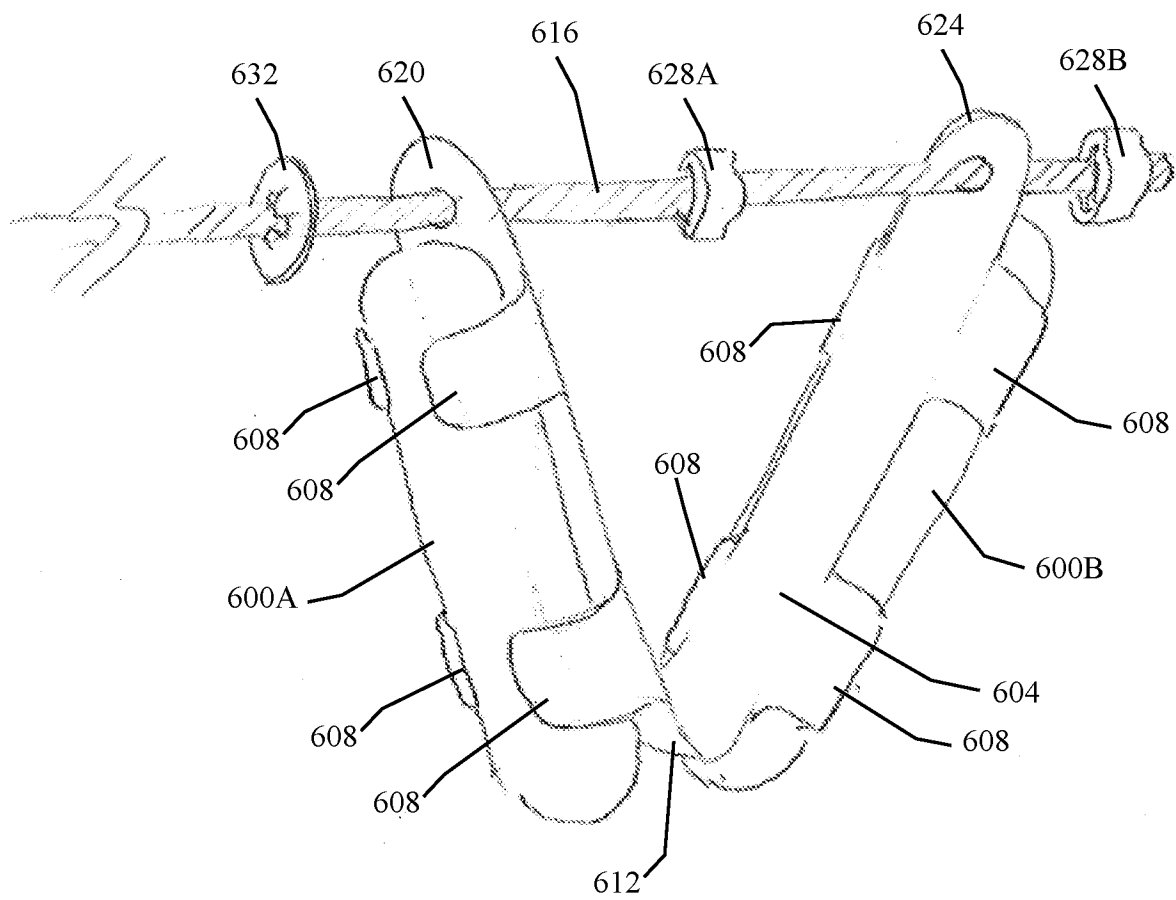


FIG. 16

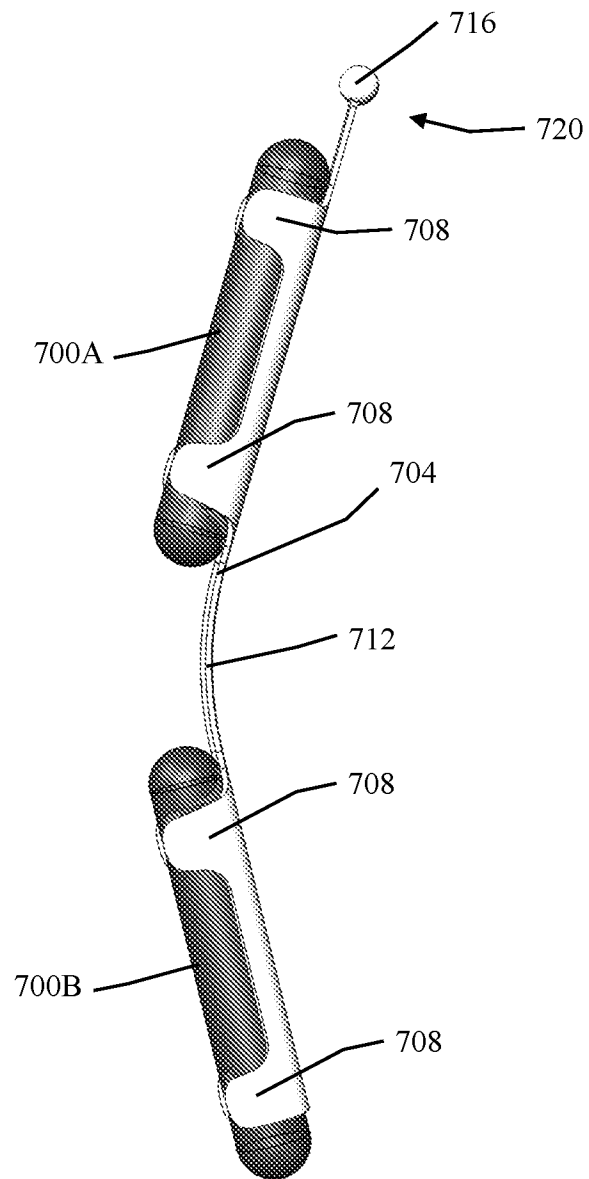


FIG. 17

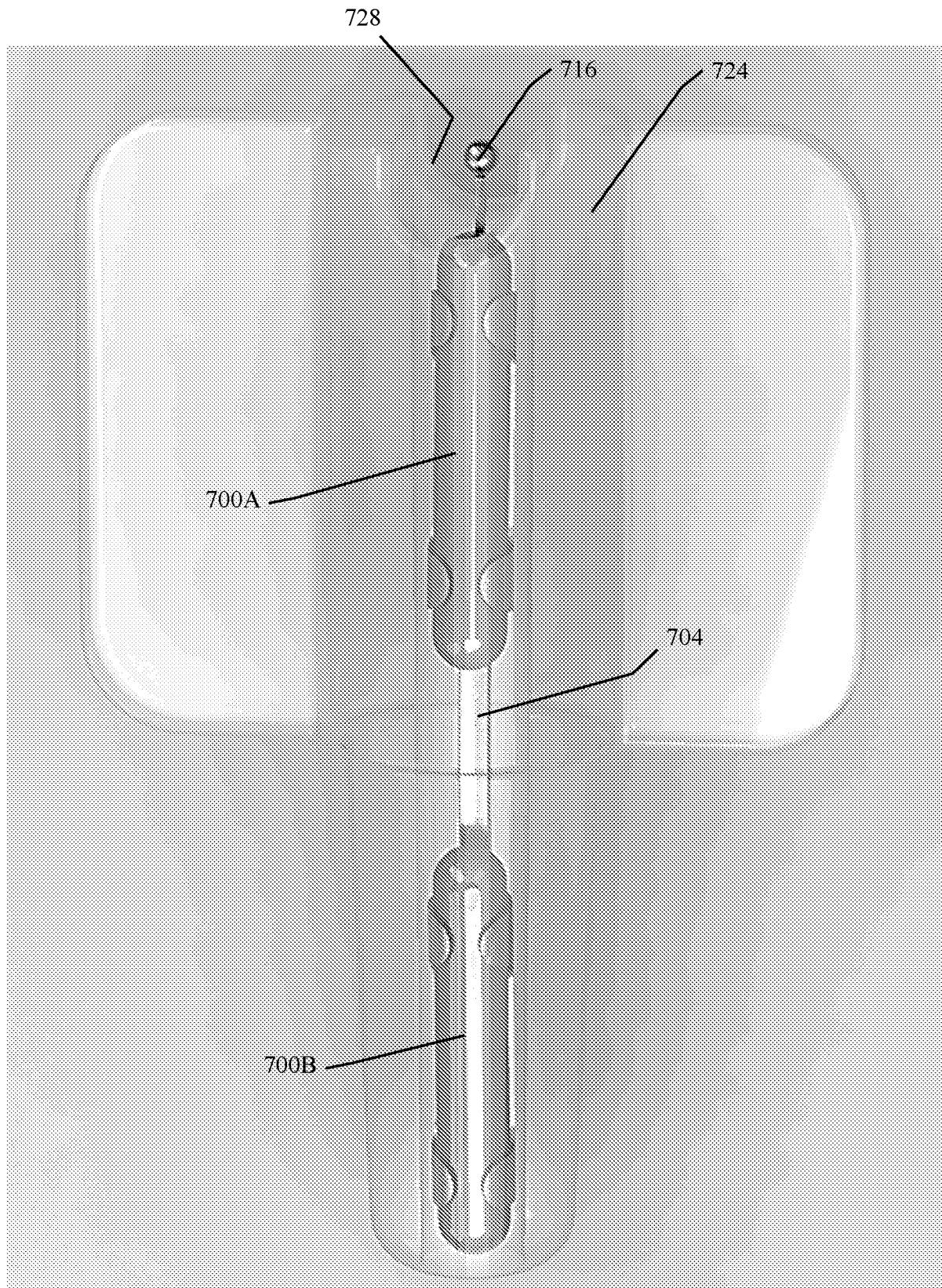


FIG. 18

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 21/49796

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61B 90/90, A61B 90/98, A61B 5/06, G06K 19/07, G06K 19/12 (2021.01)

CPC - A61B 90/90, A61B 90/98, A61B 90/39, A61B 5/064, A61B 5/0031, A61B 5/062, A61B 34/20, A61B 2034/2051, A61B 2090/397, G06K 19/0723, G06K 9/12, G08B 13/2434

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.
X --- Y --- A	US 2013/0257595 A1 (TROSSEN et al.) 03 October 2013 (03.10.2013), Fig. 1; para [0030], [0031], [0038]	1-2 8, 9, 12, 13, 17, 18, (22-27)/(1-2, 8, 9, 12, 13, 17, 18) 3-7, 10, 11, 14-16, 19-21, (22-27)/(3-7, 10, 11, 14-16, 19-21)
Y --- A	US 9,198,654 B1 (HEALTH BEACON, INC.) 01 December 2015 (01.12.2015), Fig 4-6; col 5, ln 12-22; col 6, ln 4-12; col 6, ln 62-col 7, ln 3	8, 9, 12, 13, 17, 18, (22-27)/(8, 9, 12, 13, 17, 18) 11
Y A	US20170095315 (ELUCENT MEDICAL, INC.) 06 April 2017 (06.04.2017), para [0010]-[0014], [0047]	(22-27)/(1-2, 8, 9, 12, 13, 17, 18)
A	US 2012/0004023 A1 (HSU) 05 January 2012 (05.01.2012), para [0036]	11
A	US20070210923 A1 (BUTLER et al.) 13 September 2007 (13.09.2007), entire document	1-27
A	US 2007/0257799 A1 (BAUCHOT et al.) 08 November 2007 (08.11.2007), entire document	1-27

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

* Special categories of cited documents:

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

"D" document cited by the applicant in the international application

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

"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

04 November 2021

Date of mailing of the international search report

DEC 07 2021

Name and mailing address of the ISA/US

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P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-8300

Authorized officer

Kari Rodriguez

Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 21/49796

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2019/147857 A1 (BARD PERIPHERAL VASCULAR INC) 26 November 2019 (26.11.2019), entire document	1-27
A	WO 2015/187857 A1 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) 10 December 2015 (10.12.2015), entire document	1-27

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 21/49796

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.: 28-74
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

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

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

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

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

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.