



- (51) **International Patent Classification:**
A61B 17/04 (2006.01) *A61B 90/00* (2016.01)
- (21) **International Application Number:**
PCT/US2019/058708
- (22) **International Filing Date:**
30 October 2019 (30.10.2019)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
62/756,907 07 November 2018 (07.11.2018) US
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(81) **Designated States** (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States** (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,

(54) **Title:** SYSTEM FOR DELIVERY OF A FIDUCIAL MARKER

(57) **Abstract:** A transurethral system for delivering and depositing fiducial markers usable to delineate the prostate during radiation therapy.

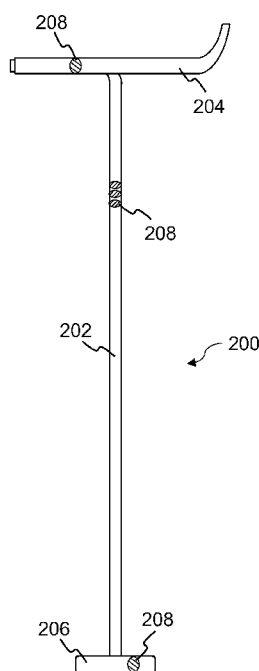


FIG. 6



EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,
MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
KM, ML, MR, NE, SN, TD, TG).

Published:

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

SYSTEM FOR DELIVERY OF A FIDUCIAL MARKER

BACKGROUND OF THE INVENTION

[0001] The present invention relates generally to medical devices, and more particularly to systems for delivering fiducial markers to an interventional site within the body of a human or animal subject.

[0002] Prostate cancer is the second most common cancer, as well as the second leading cause of cancer-related deaths, among men in the United States. Presently, one in nine men in the United States is diagnosed with prostate cancer in their lifetime. The American Cancer Society estimates about 165,000 new cases of prostate cancer and 29,000 deaths from prostate cancer will occur in 2018.

[0003] External Beam Radiation Therapy (EBRT) is a core treatment modality for patients with non-metastatic prostate cancer and is used for nearly one third of all patients receiving prostate cancer therapy.

[0004] Three-dimensional (3D) conformal radiation therapy (3DCRT) is an individualized, image-guided EBRT technique whereby a radiation dose is planned and delivered such that the high-dose volume is restricted to a predetermined target volume. 3DCRT utilizes 3D digital data sets representative of patient tumors and adjacent anatomy. These data sets are then used to select the number, direction, and arrangement of radiation beams to deliver the high-dose radiation to a volume of tissue. This targeting process allows higher doses of radiation to be delivered to cancer cells while reducing the amount of off-target radiation received by adjacent, healthy tissue. Accordingly,

effective delivery of conformal radiation therapy (RT) relies on accurately locating the prostate gland and its boundaries.

[0005] Fiducial markers, small radiopaque objects typically made from gold or platinum, can be implanted in the prostate gland prior to RT and subsequently used to localize the prostate gland and associated tumor and to accurately deliver the radiation dose during treatment. Fiducial markers known in the prior art are designed to be biologically inert. Fiducial markers are typically delivered using a needle applicator, whose length can range from 20 cm to 30 cm. Ideally, fiducial markers are implanted 3 mm to 5 mm from the edge of the prostate gland, which is covered by a tissue capsule.

[0006] Fiducial markers are typically implanted using a transrectal or transperineal approach. In both approaches, the fiducials are implanted from a few days to a week before the initial scans that are then used to plan the radiation treatment. The transrectal procedure carries with it a risk of rectal bleeding and both procedures carry the risk of infection, and of urosepsis in particular. Other complications of fiducial marker placement include pain, fever, voiding issues, hematuria, hematospermia, inflammatory bowel disease, and complications related to migration of the markers.

[0007] Patients with prostate cancer frequently experience lower urinary tract symptoms (LUTS) including urinary hesitancy, chronic urinary retention, and nocturia. Furthermore, patients undergoing EBRT are more likely to experience LUTS, particularly if the patient also suffers from Benign Prostatic Hyperplasia (BPH), a condition characterized by noncancerous enlargement of the prostate.

[0008] BPH can be treated by a variety of surgical and nonsurgical procedures including a minimally invasive transurethral procedure that implants small prostatic anchors to hold the prostate lobes in compression and relieve blockage of the urethra.

[0009] Such a system could also be used to deliver fiducial markers for EBRT as the placement of the anchors can be used to delineate the prostate during the planning and execution of RT. In this way, fiducial markers could be implanted without the need for an additional procedure and/or in a way that identifies the boundary of the prostate. Embodiments of the invention disclosed herein address various aspects of such as system and the methods of use of that system.

SUMMARY OF THE INVENTION

[0010] Embodiments of the present invention are directed towards a system for transurethral delivery of fiducial markers to the prostate gland that can be used to visualize and target the prostate during radiation therapy. One embodiment of the system includes a device having at least one fiducial marker, an anchor assembly with a first and second anchoring component and a connector, and a delivery device.

[0011] The fiducial markers can be made of materials that are detectable by suitable medical imaging equipment. The fiducial markers can be formed integrally with or are attached to various portions of the anchor assembly by swaging, molding, plating, or embedding during formation of the anchor assembly.

[0012] In some embodiments, the fiducial marker is a dye or contrast agent deposited on the connector or delivered by a needle advanceable from the fiducial delivery device. The needle can be used to inject or release the dye or contrast agent into the prostatic lobes or extra-prostatic space.

[0013] Various embodiments of the anchor assembly with fiducial markers are disclosed and described herein. Moreover, various ways in which fiducial markers can

be deposited to an interventional site by the fiducial delivery device independent of the anchor assembly are discussed.

[0014] Other features and advantages of embodiments of the present invention will become apparent from the following description, taken in conjunction with the accompanying drawings, which illustrate, by way of example, certain principles of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

[0015] FIG. 1 is a top view of an assembled anchor assembly.

[0016] FIG. 2 is a cross-sectional view through the prostatic urethra with the anchor assembly applied to the prostate.

[0017] FIG. 3A is a top view of one embodiment of an anchor assembly with fiducial marker(s).

[0018] FIG. 3B is an enlarged, top view of one embodiment of an anchor assembly with fiducial marker(s).

[0019] FIG. 3C is an enlarged, top view of one embodiment of a fiducial marker.

[0020] FIG. 4A is a top view of another embodiment of an anchor assembly with fiducial marker(s).

[0021] FIG. 4B is an enlarged, top view of another embodiment of an anchor assembly with fiducial marker(s).

[0022] FIG. 4C is an enlarged, top view of another illustrative embodiment of an anchoring component with fiducial marker(s).

[0023] FIG. 5 is a top view of an embodiment of an anchor assembly with fiducial marker(s).

[0024] FIG. 6 is a top view of an embodiment of an anchor assembly with fiducial marker(s).

[0025] FIG. 7A is a top view of an embodiment of an anchor assembly with a fiducial tag.

[0026] FIG. 7B is an enlarged, top view of an embodiment of an anchor assembly with a fiducial tag.

[0027] FIG. 8A is a top view of another illustrative embodiment of a connector with a fiducial marker.

[0028] FIG. 8B is a top view of another illustrative embodiment of an anchoring component with a fiducial marker.

[0029] FIG. 9 is a top view of an illustrative embodiment of an anchor assembly with a radiopaque wire.

[0030] FIG. 10A is a top view of another illustrative embodiment of an anchoring component with a fiducial marker.

[0031] FIG. 10B is a top view of still another illustrative embodiment of an anchoring component with a fiducial marker.

DETAILED DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

[0032] The present disclosure is directed to a system for transurethral delivery of fiducial markers to the prostate that can be used to visualize and target the prostate during radiation therapy. The figures herein are provided by way of example and not limitation, and the description of the various embodiments of the invention includes all aspects of the figures.

[0033] Generally, embodiments of the system according to the present disclosure include an anchor assembly that modifies, contours, or otherwise manipulates prostatic tissue and includes material or one or more features detectable by medical targeting and/or imaging modalities. Such modalities presently include, but are not limited to, ultrasound, magnetic resonance imaging (MRI), and radiography (such as x-ray imaging and including computed tomography). For radiography, the suitable materials are radiopaque and include, but are not limited to, gold, platinum, or tantalum. To the extent an embodiment refers to a fiducial marker as being radiopaque, it should be understood that fiducial markers having properties detectable by other medical targeting and/or imaging modalities are also included in such an embodiment. Further, the shape, size, and surface texture (including roughness) of an anchor assembly can be altered improve the ability for targeting and/or imaging modalities to detect the anchor assembly.

[0034] FIG. 1 is a top view of an assembled anchor assembly. As shown in FIG. 1, implant or anchor assembly 10 includes connector 12 situated between first anchoring component 14 and second anchoring component 16. Connector 12 can be formed from suitable material that provides a desired holding force between the first and second anchoring components. In some embodiments, connector 12 can be formed

from conventional suture material. In preferred embodiments, connector 12 is monofilament polyethylene terephthalate (PET). The flexible material of connector 12 can accommodate access and placement of anchor assembly 10 to various positions in the prostate and transmit necessary forces between the first and second anchoring components. First anchoring component 14 can be attached to connector 12 by various means including, but not limited to, adhesive bonding or thermal bonding or can include tabs or other structures capable of forming a locking arrangement with connector 12. Alternatively, first anchoring component 14 can be crimped or secured directly to connector 12. In some embodiments, connector 12 includes a structure(s) which is complementary to first anchoring component 14 to facilitate attachment.

[0035] Similar approaches can be used to secure connector 12 to second anchoring component 16. However, in preferred embodiments, second anchoring component is secured to connector 12 during the time of placement of anchor assembly 10 within a patient. That is, in preferred embodiments, first anchoring component 14 can be attached to connector 12 during the manufacturing process, and second anchoring component is left unsecured to connector 12. An unassembled anchor assembly is loaded into a delivery system. First anchoring component 14 and attached connector 12 are delivered to a location within or near the prostate gland. Second anchoring component 16 is then secured to connector 12 by the delivery system within or near the prostate gland.

[0036] Various embodiments of an anchor assembly or selected portions thereof and an anchor assembly delivery device are detailed or contemplated in U.S. Patent No. 7,896,891 entitled "Apparatus and Method for Manipulating or Retracting Tissue and Anatomical Structure" and U.S. Patent No. 7,914,542 entitled "Devices, Systems

and Methods for Treating Benign Prostatic Hyperplasia and Other Conditions” which are hereby incorporated by reference in their entireties.

[0037] First anchoring component 14 and second anchoring component 16 can be formed from conventional biocompatible materials such as, but not limited to, stainless steel and nitinol. First anchoring component 14 includes a first portion 18 and a second portion 20. In some preferred embodiments, first portion 18 is a generally cylindrical structure while second portion 20 is at least partially cylindrical and includes a curved, angled, or otherwise bent structure or leg.

[0038] The lumen within the generally cylindrical portion of first anchoring component 14 can facilitate attachment of connector 12 by placing connector 12 coaxially within the lumen of the generally cylindrical portion of first anchoring component 14. Once connector 12 is within the lumen of the generally cylindrical portion of first anchoring component 14, connector 12 can be secured via various means including, but not limited to, adhesive bonding or thermal bonding. First anchoring component 14 can include tabs or other structures capable of forming a locking arrangement with connector 12.

[0039] In one preferred embodiment, the process for attaching first anchoring component 14 and connector 12 can include creating a fiducial marker at or near the junction of first anchoring component 14 and connector 12. In the case of bonding connector 12 to first anchoring component 14, the bonding process can introduce a fiducial marker material. For example, a radiopaque adhesive material can be used to bond first anchoring component 14 and connector 12. A radiopaque foil, sheet, or other thin structure can be used to form an interference fit between first anchoring component 14 and connector 12 by sandwiching the foil between first anchoring

component 14 and connector 12. A radiopaque cap, plug, or similar structure can be used to anchor the end of connector 12 to first anchoring component.

[0040] Still further, a radiopaque material can be introduced during a thermal bonding step to bond first anchoring component 14 and connector 12. For example, when connector 12 is within the lumen of the generally cylindrical portion of first anchoring component 14, a fiducial marker can be embedded at or near the joint between first anchoring component 14 and connector 12 by heating the joint and introducing the fiducial marker. The heating step can be used form a cap on a portion of connector 12 that extends outside the the lumen of the generally cylindrical portion of first anchoring component 14, thereby forming a secure connection between first anchoring component 14 and connector 12. This cap could contain a fiducial marker.

[0041] While one embodiment of anchor assembly 10 is illustrated in FIG. 1 with a single first anchoring component 14, in other embodiments, an anchor assembly can include a plurality of first anchoring components spaced to suit a particular application. When a plurality of first anchoring components are included, the first anchoring components can be spaced at time of deployment, or can be spaced after deployment with subsequent manipulation. The first anchoring components can be provided at fixed, spaced positions, or can be provided such that the first anchoring components are able to be moved into the desired spaced arrangement.

[0042] FIG. 2 is a cross-sectional view through the prostatic urethra (the portion of the urethra that passes through the prostate gland) with the anchor assembly applied to the prostate. As shown in FIG. 2, an anchor assembly can be employed to manipulate the prostate gland (PG) by positioning first anchoring component 14 at the outer surface of the prostatic capsule and second anchoring component 16 at or near

the inner surface of the urethra (UT) such that the tissue captured between the anchors is held in a compressed state by tensioned connector 12. While a single anchor assembly is shown on each lateral lobe of FIG. 2, it will be understood that multiple anchor assemblies can be applied to each lateral lobe depending on the application. The length of the connector element can also be customized for various applications.

[0043] In preferred embodiments, the anchor assembly is part of a transurethral system that localizes fiducial markers to the prostate for the purpose of marking and/or delineating the prostate, or a portion thereof, during x-ray imaging, MRI, CT scan, and/or radiotherapy. This can be achieved by incorporating or connecting plates, bands, or seeds of markers made of inert, radiopaque material such as, but not limited to, gold, platinum, or tantalum to various portions of the anchor assembly during manufacture or formation of the anchor assembly.

[0044] Markers can be various shapes and sizes. In some preferred embodiments, markers are spherical or cylindrical in shape with a diameter in the range of 0.5 - 1.5 mm and a length in the range of 2 - 5 mm that are easily identified during targeting and/or imaging.

[0045] In some embodiments, radiopaque markers (subsequently referred to as “markers”) are incorporated by swaging, molding, plating, or embedding radiopaque material onto a portion of the anchor assembly. In preferred embodiments, at least three markers are used during the procedure to establish the required number of fiducial targets. More than one marker can be present on an anchor component, connector, or anchor assembly. To the extent the markers are included on the connector, the number of markers should be such that the flexibility of the connector is maintained.

[0046] FIG. 3A is a top view of one embodiment of an anchor assembly with fiducial marker(s). FIG. 3B is an enlarged, top view of one embodiment of an anchor assembly with fiducial marker(s). As shown in FIGS. 3A-3B, anchor assembly 50 includes connector 52 with markers 58. Markers can be clustered together and biased toward the end of connector 52 that contacts first anchoring component 54 or second anchoring component 56. Alternatively, markers 58 can be spaced at equidistant intervals along the length of connector 52.

[0047] In other embodiments, radiopaque markers can be included in the anchoring portions of the anchor assembly. FIG. 4A is a top view of another embodiment of an anchor assembly with fiducial marker(s). FIG. 4B is an enlarged, top view of another embodiment of an anchor assembly with fiducial marker(s). FIG. 4C is an enlarged, top view of another illustrative embodiment of an anchoring component with fiducial marker(s). FIGS. 4A and 4B illustrate anchor assembly 100 with a plurality of markers 108 incorporated in first anchoring component 104. Alternatively, as shown in FIG. 4C, anchor assembly 100 can include an anchoring component 104 with a second radiopaque leg 120 in lieu of or in addition to markers 108. FIG. 5 is a top view of an embodiment of an anchor assembly with fiducial marker(s). FIG. 5 illustrates anchor assembly 150 with a plurality of markers 158 in second anchoring component 156. It is also contemplated that the first and second anchoring components or portions thereof can be manufactured from radiopaque material or include coils, anchors, or other suitable structures that confer the ability of the anchor assembly to manipulate the prostate and function as fiducial markers.

[0048] FIG. 6 is a top view of an embodiment of an anchor assembly with fiducial marker(s). FIG. 6 shows an embodiment of anchor assembly 200 in which markers

208 are included in first anchoring component 204, connector 202, and/or second anchoring component 206. Use of markers 208 on the first and/or second anchoring components, in addition to the markers on connector 202, can allow for additional positional information of the prostate to be obtained and further refine the boundaries of the prostate when during imaging and/or radiotherapy.

[0049] In some embodiments, rather than using distinct fiducial markers, the connector or suture can be coated, filled, or saturated with radiopaque dye or contrast agent such as barium sulfate. It is contemplated that the anchoring components of the anchor assembly can also be configured with reservoirs filled with radiopaque dye or contrast agent.

[0050] Alternatively, co-delivery of the radiopaque dye or contrast agent could be achieved by including an internal reservoir filled with radiopaque dye or contrast agent housed in the delivery device such that when the anchor assembly is advanced from the device, it picks up a desired quantity of the dye or agent.

[0051] FIG. 7A is a top view of an embodiment of an anchor assembly with a fiducial tag. FIG. 7B is an enlarged, top view of an embodiment of an anchor assembly with a fiducial tag. In FIGS. 7A and 7B, rather than swaging a radiopaque marker onto a component of the anchor assembly, an embodiment with a separate radiopaque tag is shown. Here, radiopaque tag 258 is a thin sheet of radiopaque material situated between second anchoring component 256 and connector 252. Tag 258 can be attached to second anchoring component 256 and connector 252 by conventional means.

[0052] In embodiments of the anchor assembly in which a plurality of markers are used, each marker can have the same dimensions and thickness or be of varying

dimensions and thicknesses. Varying the thickness of radiopaque markers can provide directionality or orientation-related information of the prostate.

[0053] Alternative embodiments of anchor assemblies incorporating radiopaque material are shown in FIGS. 8A and 8B. FIG. 8A is a top view of another illustrative embodiment of a connector with a fiducial marker. FIG. 8B is a top view of another illustrative embodiment of an anchoring component with a fiducial marker. FIG. 8A shows connector 262 in which radiopaque marker 264 has been incorporated into a rounded tip of the connector that extends beyond cylindrical end 266 of first anchoring component 260. This allows marker 264 to be situated in the extra-prostatic space when the anchor assembly is implanted and prevents or minimizes the creation of imaging artifacts. Markers may be placed in the intra-prostatic space in order to localize specific features within the prostate. FIG. 8B shows a partial view of an anchor assembly that includes bullet tip 274 made of radiopaque material. Tip 274 can be secured to the end of first anchoring component 270 or configured to be continuous with connector 272.

[0054] FIG. 9 is a top view of an illustrative embodiment of an anchor assembly with a radiopaque wire. Another embodiment of an anchor assembly is shown in FIG. 9. Anchor assembly 300 includes first anchoring component 314, second anchoring component 316, and connector 312. In this embodiment, connector 312 is a wire made from or coated with suitable radiopaque material such as gold.

[0055] Application of the anchor assembly to the prostate can also impart information on prostate health. For example, the system can be configured to supply data on tissue stiffness or other characteristics during implantation of the anchor assembly. Such data could be used to distinguish normal, healthy tissue from

abnormal tissue. After implantation, movement or other behavior of the markers over time may provide further information on prostate health, including, but not limited to, changes in size.

[0056] Fiducial markers can also be delivered to the prostate by the anchor assembly delivery device independent of the anchor assembly. Various embodiments of an anchor delivery system are detailed or contemplated in U.S. Patent No. 9,504,461 entitled "Anchor Delivery System" which is hereby incorporated by reference in its entirety. The delivery device includes various subassemblies configured to deploy one or more anchor assemblies and/or deliver therapeutic or diagnostic agents to an interventional site within the body of a patient. In one aspect, the delivery device can include a cartridge carrying the anchor assembly or therapeutic/diagnostic agent and a handle assembly configured to couple with the cartridge such that mechanical energy loaded in at least one spring mechanism within the handle is transferred to the cartridge to deploy the anchor assembly or agent. The device includes an actuator configured to initiate transfer of the mechanical energy to the spring mechanisms.

[0057] The delivery device can also include an elongate member connected to a handle assembly that can be inserted into the urethra of a patient and advanced to establish contact with the prostate gland. The elongate member can house components to construct an anchor assembly. The elongate member can also house tools controllable by an actuator and advanceable from the elongate member such as a needle or other penetrating member that deploy one or more anchor assemblies and/or deliver therapeutic or diagnostic agents to the prostate.

[0058] It is contemplated that the hollow needle or penetrating member can be used to deliver radiopaque dye or contrast agent to the extra-prostatic space or to inject dye or agent into the prostatic lobes or urethral tissue for radiotherapy or imaging. Alternatively, the needle exit point can include tape or other adhesives configured to deposit radiopaque material onto the needle, anchor assembly, implant, or other penetrating members when the tape is pierced or otherwise contacted.

[0059] The delivery device can also be used to deliver and deposit radiopaque or therapeutic seeds, coils, or anchors into the tissue of the prostate, urethra or bladder. In some embodiments, the delivery device includes a fiducial cartridge, separate from the anchor assembly-delivering cartridge that delivers the fiducial marker as part of the actuator deployment sequence.

[0060] The delivery device can also be used to modify an existing or previously implanted anchor assembly by affixing radiopaque seeds or other radiopaque material to the anchoring components and/or connector.

[0061] In each of the detailed and contemplated embodiments, the fiducial markers can be used to delineate the prostate for, at least, the planning and execution of radiation therapy to treat prostate cancer or other cancers. The number and placement of fiducial markers can be optimized to allow triangulation and measurement of anatomical position in different planes. For procedures in which multiple anchor assemblies are used to manipulate each of the lateral prostatic lobes, fiducial markers need not be incorporated into every anchor assembly. Fiducial markers can be used to identify tissue planes or other tissue features within an organ, gland, or other collection of tissue.

[0062] In a typical procedure, the physician places implants in the anterior portion of the prostate. The physician does not place implants in the posterior aspect of the prostate because implants positioned in the posterior aspect could compress the neurovascular bundles, which are located at nearby. Similarly, placing implants in the trust your aspect of the prostate could result in damage to the rectum. However, for use as a fiducial marker, implants can be deployed in the posterior aspect of the prostate. In such an embodiment, only the distal section of the anchor assembly would be implanted. With only the distal section implanted, there would be no compression on the neurovascular bundles because the proximal anchor would not be placed, and it is this anchor that typically facilitates holding compression on tissue. Thus, it is possible to delineate the outer capsule of the prostate gland in the posterior aspect, which is often where cancerous tissue is located.

[0063] An exemplary embodiment of the invention disclosed herein is a system for delivering and depositing a fiducial marker to tissue at an interventional site within the body of a human patient, where the system includes: a first fiducial marker made of radiopaque material; at least two anchor assemblies, the anchor assemblies including a first anchoring component, a second anchoring component, and a connector; and a fiducial delivery device, the fiducial delivery device carrying the anchor assembly and comprising an actuator usable to deploy the anchor assembly and an elongate member to be inserted and advanced to the interventional site.

[0064] The exemplary embodiment includes an aspect wherein the fiducial marker is attached to a portion of each anchor assembly by swaging, molding, plating, or embedding during formation of the anchor assembly.

[0065] The exemplary embodiment includes an aspect wherein the first fiducial marker is attached to the first anchoring component.

[0066] The exemplary embodiment includes an aspect wherein the system includes a second fiducial marker and a third fiducial marker wherein the second and third fiducial markers are made of radiopaque material and attached to the first anchoring component.

[0067] The exemplary embodiment includes an aspect wherein the first fiducial marker is attached to the connector and wherein the second and third fiducial markers are made of radiopaque material and attached to the connector.

[0068] The exemplary embodiment includes an aspect wherein the first fiducial marker is attached to the second anchoring component and wherein the second and third fiducial markers are made of radiopaque material and attached to the second anchoring component.

[0069] The exemplary embodiment includes an aspect wherein the radiopaque material of the first fiducial marker is a dye or contrast agent. The exemplary embodiment includes an aspect wherein the dye or contrast agent coats the length of the connector. The exemplary embodiment includes an aspect wherein the first anchoring component and/or the second anchoring component further comprises a reservoir to hold the dye or contrast agent.

[0070] The exemplary embodiment includes an aspect wherein the first fiducial marker is made of metal. The exemplary embodiment includes an aspect wherein the first fiducial marker is made of gold, platinum, or tantalum. The exemplary embodiment includes an aspect wherein the first fiducial marker is a band or a seed.

[0071] The exemplary embodiment includes an aspect wherein first anchoring component, the second anchoring component, the connector, or a portion thereof is made of radiopaque material and serves as the first fiducial marker.

[0072] The exemplary embodiment includes an aspect wherein first anchoring component, the second anchoring component, the connector, or a portion includes features that increase radiopacity.

[0073] The exemplary embodiment includes an aspect wherein the first fiducial marker is a tag made of radiopaque material situated between the second anchoring component and the connector.

[0074] The exemplary embodiment includes an aspect wherein the system includes a plurality of fiducial markers wherein the plurality of fiducial markers are made of metal. The exemplary embodiment includes an aspect wherein the plurality of fiducial markers are made of gold, platinum, or tantalum.

[0075] The exemplary embodiment includes an aspect wherein the first anchoring component comprises a leg made of radiopaque material that serves as the first fiducial marker.

[0076] The exemplary embodiment includes an aspect wherein the connector includes a rounded tip that extends into the extra-prostatic space when the anchor assembly is implanted into a prostatic lobe of a patient, wherein the rounded tip includes radiopaque material and serves as the first fiducial marker.

[0077] The exemplary embodiment includes an aspect wherein the fiducial delivery device further comprises a needle advanceable from the elongate member.

[0078] The exemplary embodiment includes an aspect wherein the fiducial marker is manipulated after being delivered.

[0079] The exemplary embodiment includes an aspect wherein the fiducial marker is placed in intra-prostatic space, extra-prostatic space, on the prostatic capsule, or combinations thereof.

[0080] The exemplary embodiment includes an aspect wherein the fiducial marker is biodegradable.

[0081] The exemplary embodiment includes an aspect wherein the fiducial marker delivers therapy to tissue.

[0082] The exemplary embodiment includes an aspect wherein the needle is configured to deliver the first fiducial marker. The exemplary embodiment includes an aspect wherein the system includes a second fiducial marker and a third fiducial marker wherein the second and third fiducial markers are delivered to the interventional site by the needle. The exemplary embodiment includes an aspect wherein the first fiducial marker is a dye or contrast agent delivered by the needle. The exemplary embodiment includes an aspect wherein the needle injects the dye or contrast agent into tissue adjacent to the prostate. The exemplary embodiment includes an aspect wherein the needle injects the dye or contrast agent into the prostatic lobes. The exemplary embodiment includes an aspect wherein the needle injects the dye or contrast agent into the extra-prostatic space.

[0083] The exemplary embodiment includes an aspect wherein at least two of the first, second, or third fiducial marker span a gland or organ. The exemplary embodiment includes an aspect wherein the fiducial marker is placed at a tissue plane.

[0084] The exemplary embodiment includes an aspect wherein the system delivers fiducial markers to the prostate for the purpose of delineating the prostate during radiotherapy.

[0085] While particular elements, embodiments and applications of the present invention have been shown and described, it will be understood that the invention is not limited thereto since modifications can be made by those skilled in the art without departing from the scope of the present disclosure, particularly in light of the foregoing teachings.

We claim:

1. A system for delivering and depositing a fiducial marker to tissue at an interventional site within the body of a human patient, comprising:
 - a fiducial marker made of radiopaque material;
 - at least two anchor assemblies, the anchor assemblies including a first anchoring component, a second anchoring component, and a connector; and
 - a fiducial delivery device, the fiducial delivery device carrying the anchor assembly and comprising an actuator usable to deploy the anchor assembly and an elongate member to be inserted and advanced to the interventional site.
2. The system of claim 1, wherein the fiducial marker is attached to the first anchoring component.
3. The system of claim 2, further comprising a second fiducial marker and a third fiducial marker wherein the second and third fiducial markers are made of radiopaque material and attached to the first anchoring component.
4. The system of claim 1, wherein the fiducial marker is attached to the connector.
5. The system of claim 4, further comprising a second fiducial marker and a third fiducial marker wherein the second and third fiducial markers are made of radiopaque material and attached to the connector.

6. The system of claim 1, wherein the fiducial marker is attached to the second anchoring component.

7. The system of claim 6, further comprising a second fiducial marker and a third fiducial marker wherein the second and third fiducial markers are made of radiopaque material and attached to the second anchoring component.

8. The system of claim 1, wherein the radiopaque material of the fiducial marker is a dye or contrast agent.

9. The system of claim 8, wherein the dye or contrast agent coats the length of the connector.

10. The system of claim 9, wherein the first anchoring component and/or the second anchoring component further comprises a reservoir to hold the dye or contrast agent.

11. The system of claim 1, wherein the fiducial marker is a tag made of radiopaque material situated between the second anchoring component and the connector.

12. The system of claim 1, wherein the connector includes a rounded tip that extends into the extra-prostatic space when the anchor assembly is implanted into a prostatic lobe of a patient, wherein the rounded tip includes radiopaque material and serves as the fiducial marker.

13. The system of claim 1, wherein the first fiducial delivery device further comprises a needle advanceable from the elongate member.

14. The system of claim 1, wherein the fiducial marker is placed in intra-prostatic space, extra-prostatic space, on the prostatic capsule, or combinations thereof.

15. The system of claim 1, wherein the fiducial marker is biodegradable.

16. The system of claim 1, wherein the fiducial marker delivers therapy to tissue.

17. The system of claim 13, wherein the needle is configured to deliver the fiducial marker.

18. The system of claim 13, wherein the fiducial marker is a dye or contrast agent delivered by the needle.

19. The system of any one of the preceding claims, wherein at least two fiducial markers are present and the fiducial markers are delivered to span a gland or organ.

20. The system of claim 1, wherein the fiducial marker is placed at a tissue plane.

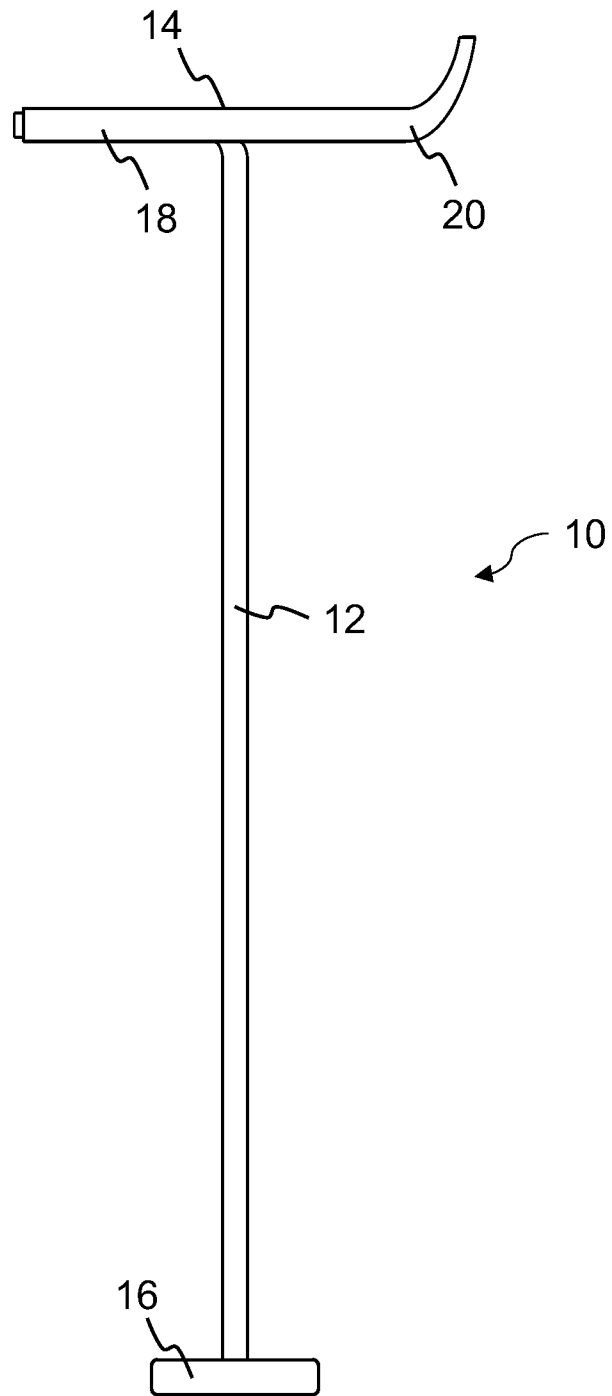


FIG. 1

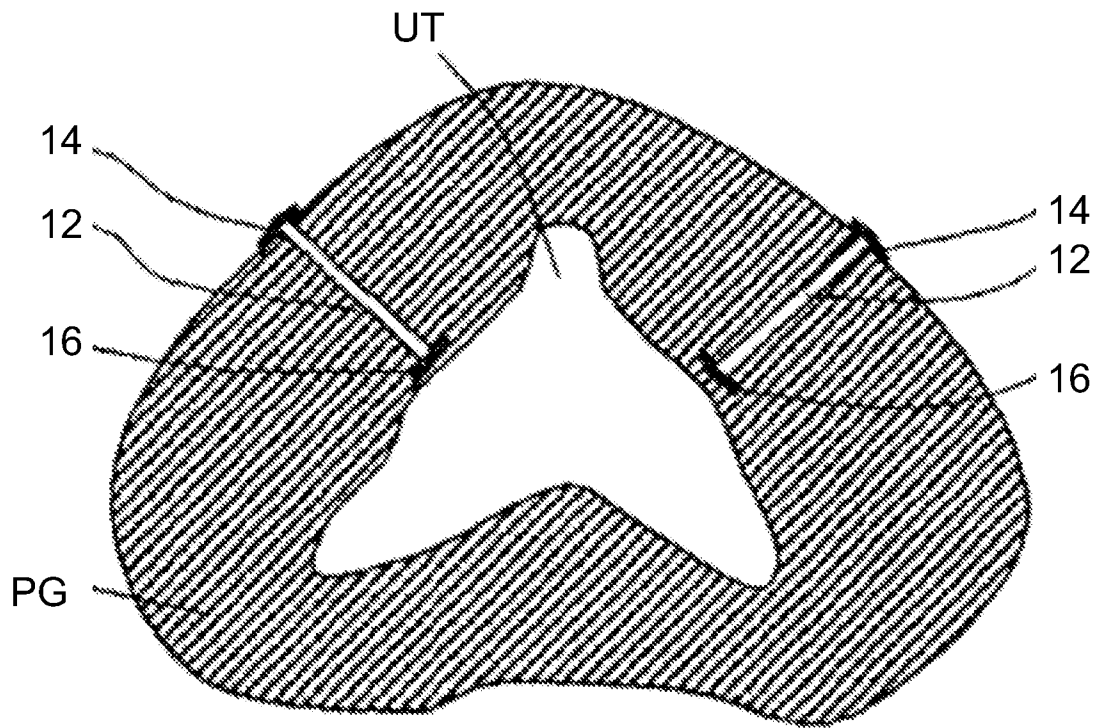


FIG. 2

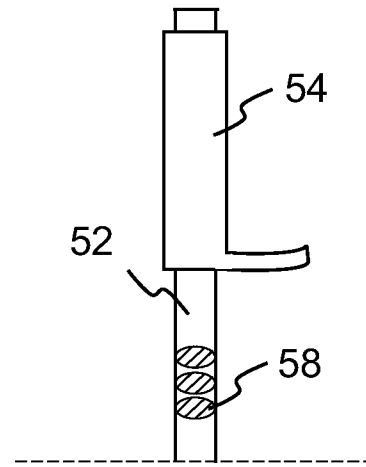
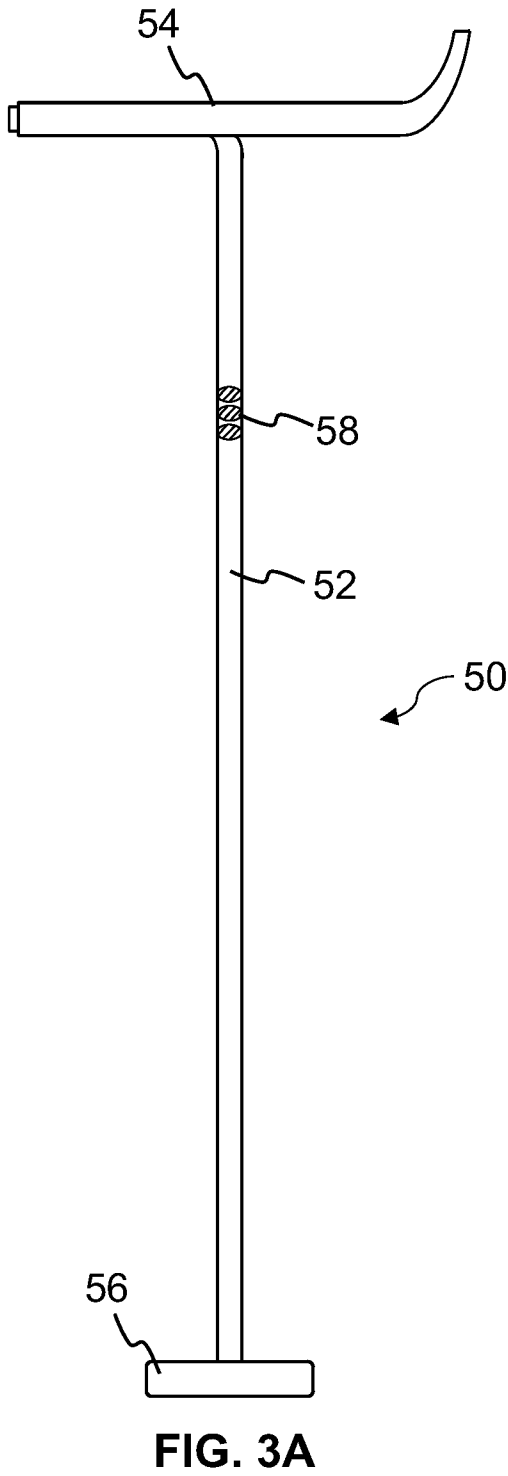


FIG. 3B

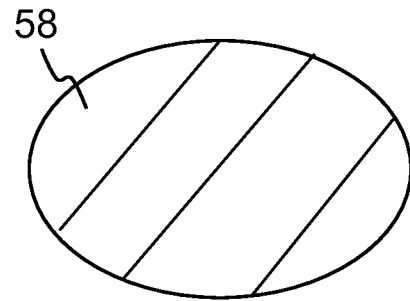


FIG. 3C

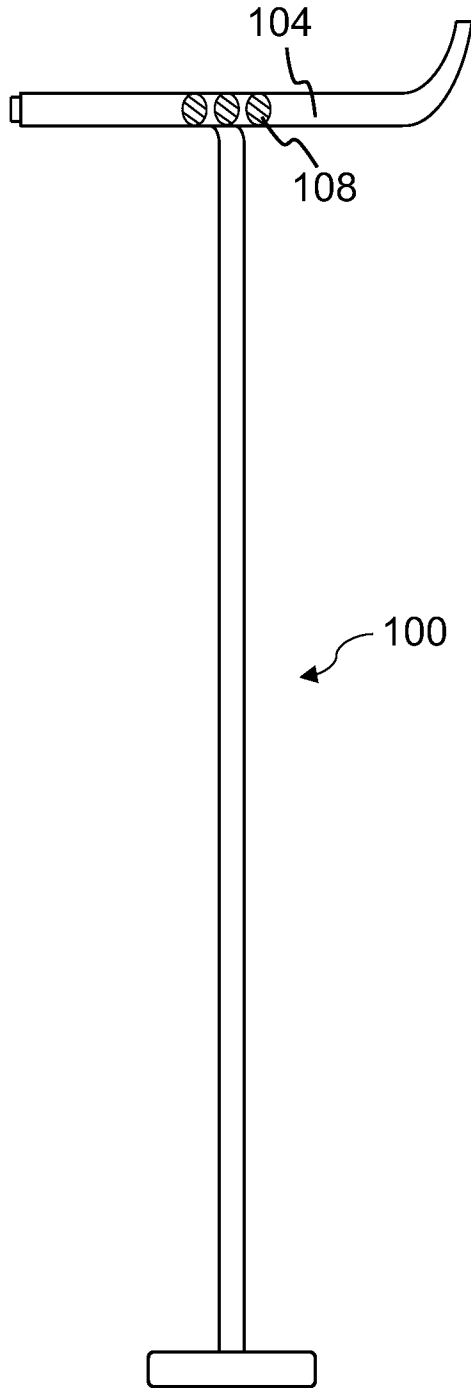


FIG. 4A

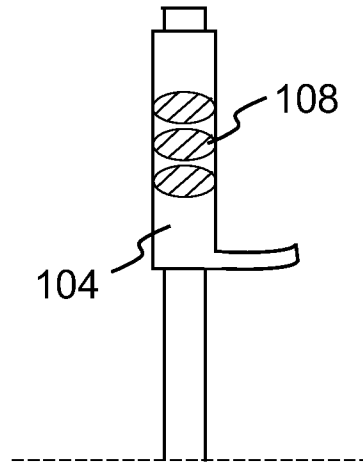


FIG. 4B

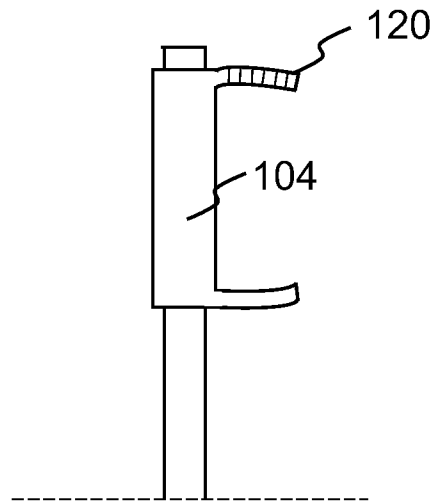


FIG. 4C

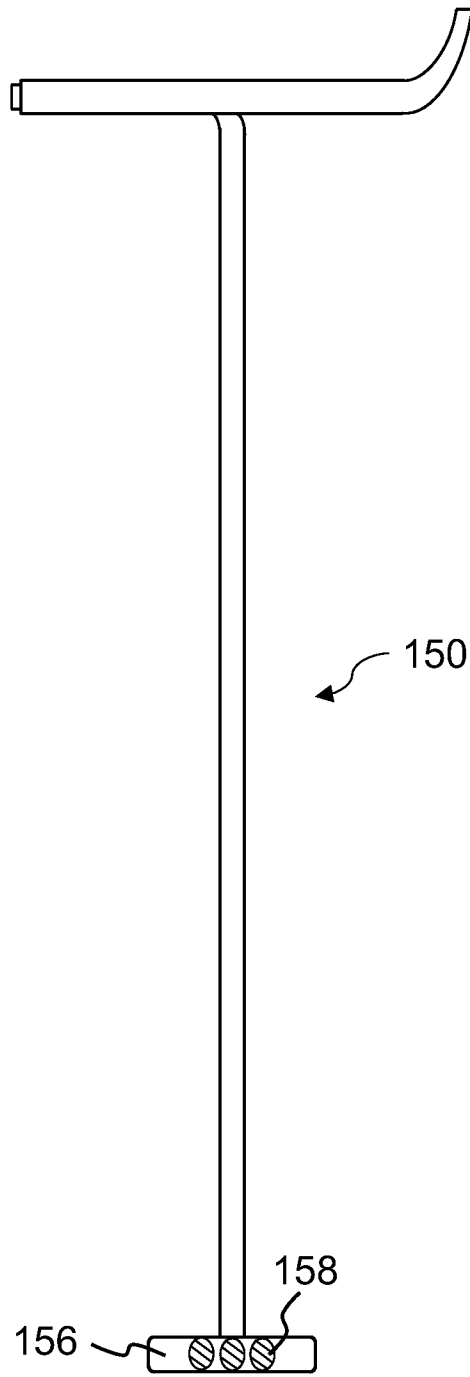


FIG. 5

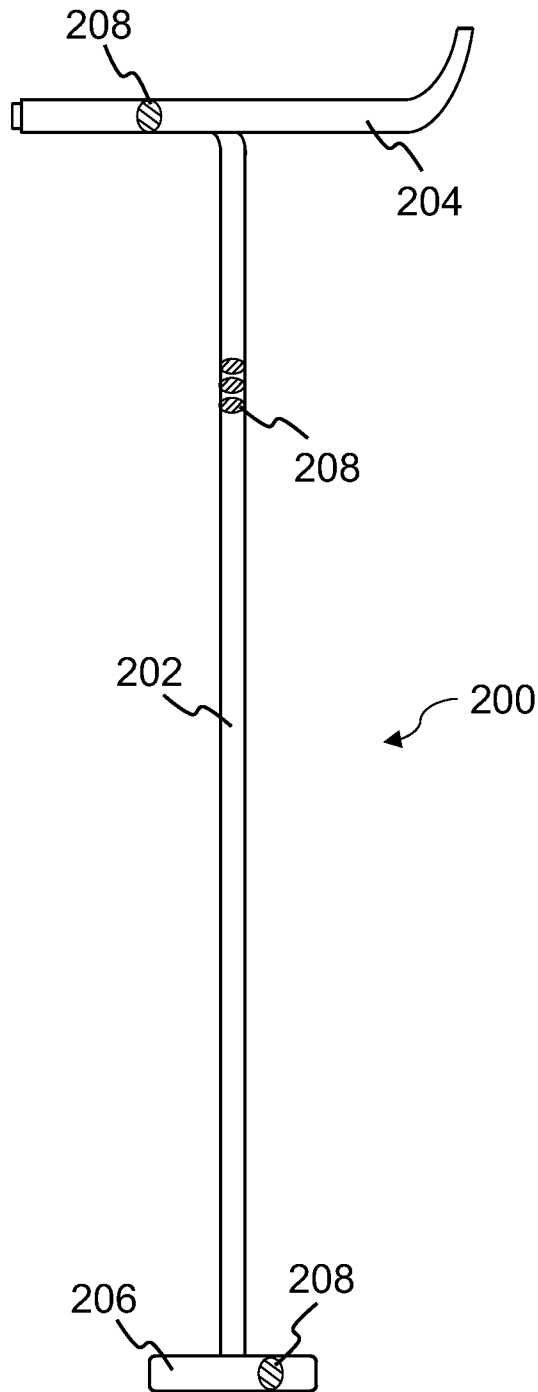


FIG. 6

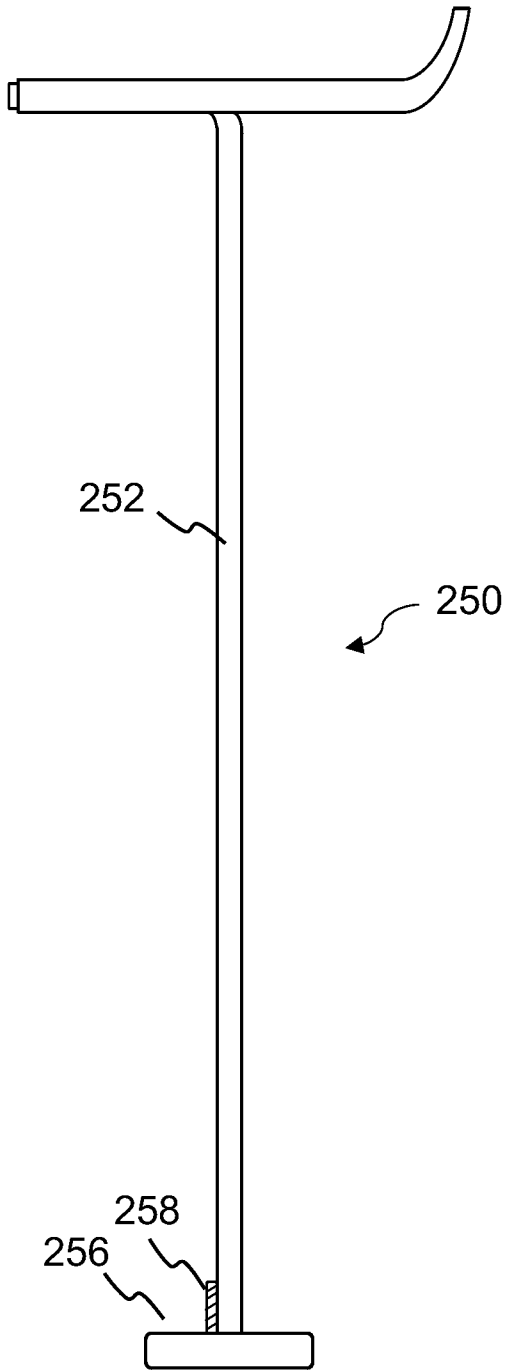


FIG. 7A

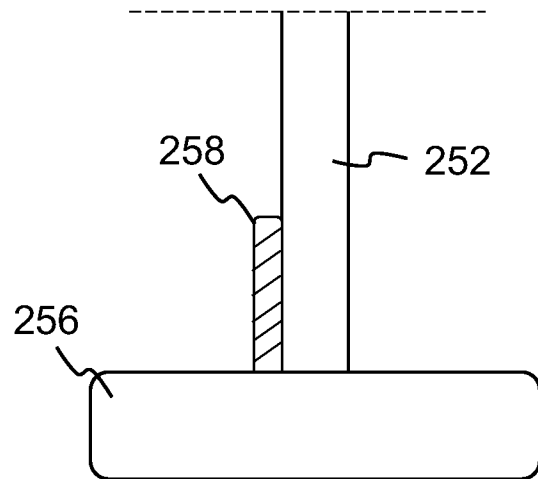


FIG. 7B

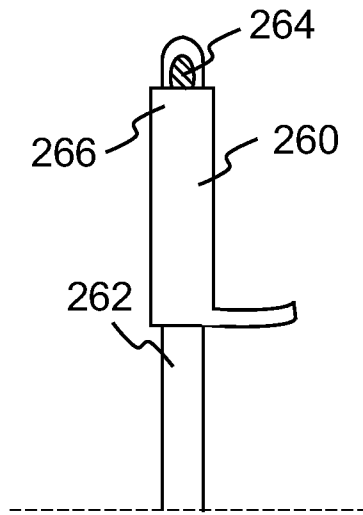


FIG. 8A

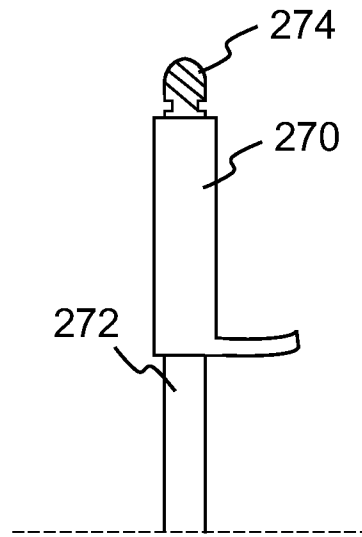


FIG. 8B

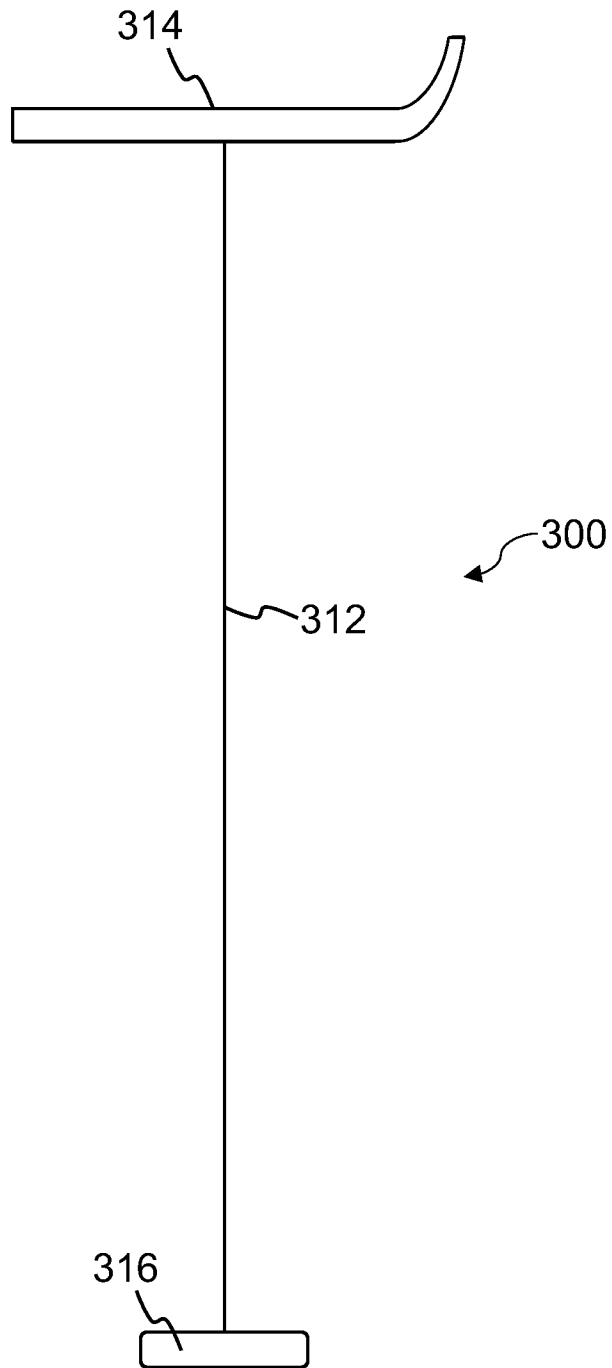


FIG. 9

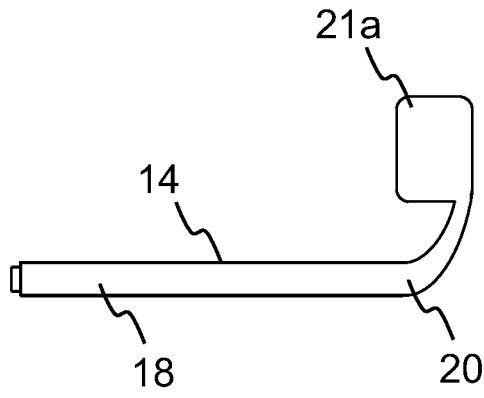


FIG. 10A

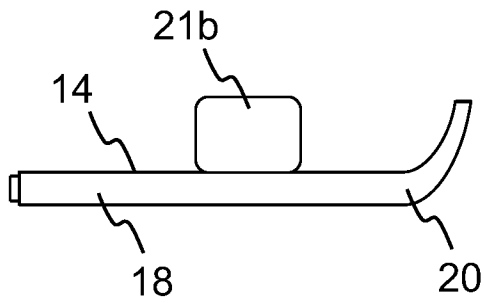


FIG. 10B

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2019/058708

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B17/04 A61B90/00
ADD.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
Minimum documentation searched (classification system followed by classification symbols)
A61B
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 7 914 542 B2 (NEOTRACT INC [US]) 29 March 2011 (2011-03-29) cited in the application	1,8,14, 16
Y	column 17, line 6; figures 3A-3C column 19, lines 62-65; figure 4H column 31, line 65; figure 17F column 32, line 67 - column 33, line 1 claim 31	15
X	----- US 2016/317304 A1 (SPENCE PAUL A [US] ET AL) 3 November 2016 (2016-11-03) paragraphs [0071], [0072], [0075]; figures 9-16 ----- -/--	1-7,19, 20

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	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"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
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search 30 January 2020	Date of mailing of the international search report 10/02/2020
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Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Christen, Jérôme
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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2019/058708

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2015/006729 A2 (SHIFAMED HOLDINGS LLC [US]) 15 January 2015 (2015-01-15)	1-3,6,7, 19
Y	paragraph [0148]; figures 10,11 paragraph [0149] paragraph [0158]; figure 28 -----	9,12,15
Y	WO 2018/027145 A1 (SHIFAMED HOLDINGS LLC [US]) 8 February 2018 (2018-02-08) page 26, lines 2-3; figure 43 -----	9,12
Y	EP 1 185 317 A1 (AMERICAN MED SYST [US]) 13 March 2002 (2002-03-13) claim 1 -----	15

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2019/058708

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.: 10, 11, 13, 17, 18
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:
see FURTHER INFORMATION sheet PCT/ISA/210

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

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

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

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 an 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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 10, 11, 13, 17, 18

The description and the claims below do not provide support and disclosure in the sense of Article 5 PCT. The subject-matter below is not disclosed in a manner sufficiently clear and complete to be carried out by a person skilled in the art.

1. Claim 10:

The "reservoir" is not disclosed in a manner sufficiently clear and complete to be carried out by a person skilled in the art.

According to the teaching of claim 9, which forms part of the subject-matter of claim 10, the dye or contrast agent coats the length of the connector. However, according to the features of claim 10, the same dye or contrast agent is comprised in a reservoir which is comprised at the first and/or second anchoring component, not at the connector. This is not clear.

Secondly, the description brings even more doubt as how the reservoir should be embodied. According to the sole passage of the description, not reciting the wording of the claims, i.e. the paragraph [0050] on page 12 ("[0050]: Alternatively, co-delivery of the radiopaque dye or contrast agent could be achieved by including an internal reservoir filled with radiopaque dye or contrast agent housed in the delivery device such that when the anchor assembly is advanced from the device, it picks up a desired quantity of the dye or agent."), the said reservoir is housed in the delivery device, not at the first and/or second anchoring component or connector as explained in claim 10.

As a result, the "reservoir" is not disclosed in a manner sufficiently clear and complete to be carried out by a person skilled in the art.

2. Claim 11:

The "tag" is not disclosed in a manner sufficiently clear and complete to be carried out by a person skilled in the art.

According to the teaching of claim 11, the tag is situated between the second anchoring component and the connector. Paragraph [0051] teaches the same. However, according to the figure 7A and 7B which are to be read with said paragraph, the tag 258 is not located between the second anchoring component and the connector but at an edge connecting the said second anchoring component and connector. A location between would be below the connector 252 as seen on figure 7B and at the same time above the second anchoring component 256.

As a result, the "tag" is not disclosed in a manner sufficiently clear and complete to be carried out by a person skilled in the art.

3. Claim

13 (with dependent claims 17, 18):

The "needle" is not disclosed in a

INTERNATIONAL SEARCH REPORT

International Application No. PCT/ US2019/ 058708

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

manner sufficiently clear and complete to be carried out by a person skilled in the art.

The application is silent about any figure showing such a needle. While the provision of a needle advanceable from an elongated member per se is not an issue as such (claim 13), it becomes unclear when studying claims 17 and 18 and the teaching of the corresponding description. The solution according to these claims would be to have e.g. a tape at the needle exit (see [0058] of the description). It is however unclear how e.g. such a tape could be embodied. The lack of figures showing such a mechanism enhances this problem, i.e. lack of support.

As a result, the "needle" (claim 13) and the marker delivered by the said needle (claims 17, 18) is not disclosed in a manner sufficiently clear and complete to be carried out by a person skilled in the art.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guidelines C-IV, 7.2), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/US2019/058708

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