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(54) **Title:** CATHETER WITH IMAGING CAPABILITY ACTS AS GUIDEWIRE FOR CANNULA TOOLS

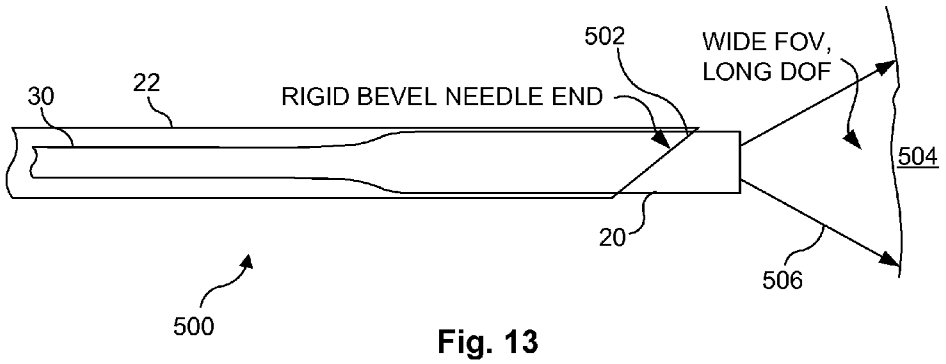

Fig. 13

(57) **Abstract:** A catheter having an imaging device on its distal end serves as a guidewire for cannula tools, enabling the tools to be advanced to a desired site in a patient's body. One exemplary embodiment of such a catheter is a scanning fiber endoscope. The images facilitate navigation through linked body lumens and also enable an operator to view a site where a biopsy sample is to be taken with a cannula tool. Exemplary cannula tools include bristles or sharp points that scrub cells from adjacent tissue, a biopsy needle that can be thrust into tissue, a loop that cuts away tissue, a cutting edge that slices tissue from a site, and forceps. The sample can be carried by a bodily or introduced fluid to a proximal end of the catheter through an annular gap between the catheter and the cannula tool, or the cannula tool can retain the sample.

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CATHETER WITH IMAGING CAPABILITY ACTS AS GUIDEWIRE FOR CANNULA TOOLS

Background

[0001] A cannula is a hollow flexible tube used in medicine to introduce or open a lumen or to insert medical devices and can be introduced into the human body over a guidewire. Typically this guidewire is a highly-flexible metal coiled wire less than 0.5 mm in diameter and is used extensively in cardiovascular medicine. A catheter has very low flexural rigidity but is able to be pushed from the vein in the leg all the way through the heart. A guidewire can be inserted into the body of a patient in a generally conventional manner and advanced to a desired location where a biopsy of cells and tissue is to be taken. The process of advancing the guidewire can be done purely by exercising the touch and feel of an experienced physician, or can be carried out with visualization technologies, such as fluoroscopy, X-ray or computed tomography (CT) imaging, magnetic resonance imaging (MRI), ultrasound imaging, optical tomography, etc. Clearly, it would be desirable to advance a device that serves as a guidewire by imaging the lumen in the body of a patient through which the device is being advanced.

[0002] Catheters with cannula tools that are introduced into a patient's body by means of slipping the catheter with its cannula tools over a guidewire that has previously been maneuvered to a desired location in the body are well developed for cardiovascular applications. In these applications, the task of taking a biopsy for disease diagnosis was not required, so tools for cell sampling have not previously been developed. In contrast, one of the primary purposes of endoscopy and bronchoscopy is disease diagnosis, which often requires taking cell samples and tissue biopsies. It is likely that appropriate tools for taking cell and tissue samples will be useful in the endoscopy and bronchoscopy fields, along with urology and other medical fields that require cell sampling for disease diagnosis. It would clearly be desirable to develop a variety of different types of guidewire-based tools for use in collecting samples from an internal site in a patient's body for cytopathological diagnosis, so that these tools can be advanced over a guidewire that has imaging capability.

[0003] After a guidewire has been inserted and advanced to a desired site, it would further be desirable to introduce a multifunction tool over the guidewire as a cannula, or otherwise couple the tool to the guidewire so that it can be advanced to the site over the guidewire and be employed to obtain a biopsy sample at the site. It would also be desirable to develop multifunctional cannula tools that can be employed to carry out more than one function, for example, dislodging cells and tissue, and then capturing and withdrawing the cells and tissue for diagnostic evaluation, to detect disease by applying conventional cytological and pathological procedures.

[0004] An endoscope can be made that has only a single optical fiber, for example, 0.1 to 0.3 mm in diameter. Typically, optical fibers made from fused silica, silicon-dioxide, or quartz have the ability to withstand compressive forces and can be used in a way similar to a catheter guidewire, since the distal tip can be steered, e.g., by bending it as it is advanced through a body lumen. Accordingly, it would be desirable to provide a "guidewire with eyes" for introducing cannula tools to a treatment site within a patient's body. Such a device should have many more uses than as a simple guidewire or catheter, since the ability to image as the device is being advanced (and while it is being withdrawn) through a lumen would enable a medical practitioner to introduce the cannula tools to a desired site without the need for external imaging. Such a device would enable cannula tools to be introduced for many different medical applications, and to be used more effectively at a desired site by providing a visual image showing the medical practitioner what is occurring as the cannula tools are being used.

Summary

[0005] As described below, a number of advantages arise from using an ultrathin and flexible catheter having an imaging device, as a guidewire for a cannula tool. For example, both a hollow cell sampling tool (i.e., a cannula tool) can be used concurrently with such a catheter having a small overall diameter by simply threading the cell sampling tool over the catheter and advancing it with the distal end of the catheter or sliding it distally along the shaft of the catheter once the distal end of the catheter (with the imaging device) has been positioned at a desired site. A much larger and non-circular cross-sectional shape would be required if the two functions

were implemented side-by-side in separate channels, which is typical of the approach currently used in flexible endoscopy. While not intended to be considered limiting, an initial exemplary embodiment of a catheter with imaging capability described herein as “scanning fiber endoscope” has been developed and is ideally suited to serve as a guidewire with eyes for cannula tools. However, it should be stressed that other types of imaging devices can be included on the distal end of a catheter, so that the catheter is usable as a “guidewire with eyes.” Thus, the following discussion, which repeatedly uses the term “scanning fiber endoscope” is intended to generally represent one type of catheter with imaging capability, but should not be viewed to limit the technology to that type of scanning device.

[0006] The smaller overall circular diameter of an endoscope is ideal for reaching previously inaccessible regions of the human body such as the more peripheral airways, to enable sight-directed cytological sampling in these small lumens. Current practice that relies on a larger sized bronchoscope with separate biopsy or working channels for cell sampling often blindly use the cell sampling tool after it has been extended beyond the view from the standard bronchoscope, and deep into the peripheral airways. This blind cell sampling (or sampling that relies on CT, fluoroscopy, or MRI imaging to guide the biospy) either produces very low diagnostic yields or adds cost and complexity to the procedure, when used for diagnosing suspected disease in the lungs. This problem also applies to many other regions of the human body, such as the urinary tracts, pancreatic and biliary ducts, sinus cavities, ear canal, etc.

[0007] The following discusses several different cannula tools and means for employing these tools to take cell or tissue samples for diagnosis while imaging the tissue. The mechanisms for applying the cannula tool can be one or a combination of:

1. pushing the cannula tool over a more stationary scanning fiber endoscope;
2. retracting a scanning fiber endoscope while holding the cannula tool stationary;
3. using a helical thread for advancing/retracting the cannula tool with respect to the scanning fiber endoscope;
4. releasing a spring-loaded, previously retracted cannula tool over a scanning fiber endoscope, so that the cannula tool is propelled, for example, with a helical spring;

5. employing a pneumatic or fluid push mechanism, such as a balloon, for applying pressure to stabilize an endoscope during use of a cannula tool;

6. applying a vacuum to fluid that draws the cannula tool forward relative to the scanning fiber endoscope;

7. applying a vacuum to the tissue that brings the tissue closer to the cannula tool/endoscope;

8. applying an active force electrically proximate to the distal end of the scanning fiber endoscope/cannula tool to release a trigger or apply a force that causes the cannula tool to interact with adjacent tissue;

9. applying an active force with a piezoelectric actuator coupled with a mechanical lever mechanism to increase a displacement of the cannula tool; or

10. applying an active force with a prime mover, such as a rotational electric motor, linear electric motor, etc.

[0008] A portion of the cannula tool, for example, a balloon that can be inflated, can be used as an anchor to stabilize the cannula tool and scanning fiber endoscope relative to adjacent tissue. Especially for high-resolution imaging, slow-frame-rate imaging, or where the tissue is moving due to blood flow, muscle contraction, breathing, etc., it can be important to stabilize the tissue with respect to the endoscope and cannula tool. If a cannula tool needle or forceps is being used to take a biopsy, the needle or forceps can be inserted into or onto the tissue to help stabilize the endoscope for imaging, diagnosis, and/or administration of therapy. The same needle or forceps can also be used to take cell or tissue samples for cytological or pathological analysis. As another example of a stabilizing feature on a cannula tool, one or more balloons like those sometimes used with a catheter can be inflated to stabilize the endoscope and the cannula tool inside a lumen of a patient’s body, so that when the tissue of the lumen moves, the endoscope and cannula tool move together so no relative motion is apparent. In addition, the endoscope and/or cannula tool can be provided with barbs that engage adjacent tissue, to hold the cannula tool in place. Alternatively, when a tissue sample that has been cut away at a site is removed for biopsy, the barbs can hold the released biopsy sample as the cannula tool is withdrawn.

[0009] This Summary has been provided to introduce a few concepts in a simplified form that are further described in detail below in the Description. However, this Summary is not intended to identify key or essential features of the claimed subject matter, nor is it intended to be used as an aid in determining the scope of the claimed subject matter.

Drawings

[0010] Various aspects and attendant advantages of one or more exemplary embodiments and modifications thereto will become more readily appreciated as the same becomes better understood by reference to the following detailed description, when taken in conjunction with the accompanying drawings, wherein:

[0011] FIGURE 1A (Prior Art) is a schematic end view of a conventional multi-channel bronchoscope, showing the multiple channels used for carrying out different functions;

[0012] FIGURE 1B is a cross-sectional schematic view of a flexible endoscope inside a cannula tube, in accord with the present approach;

[0013] FIGURE 2A is a simple schematic diagram of a flexible endoscope being used as a guidewire-with-eyes for a cannula tube, defining an annular passage between the two components;

[0014] FIGURE 2B is a simple schematic diagram of a cannula tool with a bristle brush that is guided by a flexible endoscope;

[0015] FIGURE 2C is a simple schematic diagram of a cannula tool comprising a biopsy needle that is guided by a flexible endoscope;

[0016] FIGURE 3 is a schematic diagram illustrating portions of an exemplary scanning fiber endoscope used for guiding a cannula tool to a desired site;

[0017] FIGURE 4 is a cut-away schematic view of an exemplary scanning mechanism usable in the scanning fiber endoscope that is employed to guide cannula tools to a desired site;

[0018] FIGURE 5A is a schematic block diagram of an exemplary multifunctional cannula tool and scanning fiber endoscope for collecting a biopsy sample from an internal site in a body of a patient;

[0019] FIGURE 5B is an enlarged cut-away schematic view of an exemplary embodiment of a distal end of a cannula tool that includes an abrasive surface for abrading cells from adjacent tissue;

[0020] FIGURE 5C is a schematic block diagram of an exemplary system used by the scanning fiber endoscope for imaging, performing diagnostic evaluation, and rendering therapy to a site within a patient's body;

[0021] FIGURE 6 is an enlarged cut-away schematic view of a distal end of an exemplary embodiment of a cannula tool that includes a loop for snaring tissue that is cut away for a biopsy sample;

[0022] FIGURE 7 is an enlarged cut-away schematic view of a distal end of an exemplary embodiment of a cannula tool that includes a helical ribbon having a cutting edge for cutting away a piece of tissue for a biopsy sample;

[0023] FIGURE 8 is an exploded view of an exemplary rotational driver that is disposed externally and is configured to drivingly rotate a cannula tool about a longitudinal axis;

[0024] FIGURE 9 is a schematic view of an exemplary embodiment of a cannula tool having an inflatable balloon with an abrasive surface, within a body lumen, illustrating the inflatable balloon in a deflated state;

[0025] FIGURE 10 is a schematic view of the exemplary embodiment of FIGURE 9 after the balloon has been selectively inflated and either rotated or moved longitudinally so that the abrasive surface frees cells from tissue on the inner surface of the body lumen, enabling the cells to be drawn into an annular passage between a guidewire and inner surface of the cannula lumen;

[0026] FIGURES 11A and 11B are schematic views illustrating an exemplary embodiment of a cannula tool that includes a bristle brush for collecting a biopsy sample, respectively showing the bristle brush exposed and covered;

[0027] FIGURES 12A and 12B are schematic views illustrating another exemplary embodiment of a cannula tool that includes a bristle brush for collecting a biopsy sample, respectively showing the bristle brush exposed and covered;

[0028] FIGURE 13 is a schematic view of an exemplary cannula tool that includes a bevel needle end, illustrating how the scanning fiber endoscope can image a prospective site with a wide field of view and a long depth of field;

[0029] FIGURE 14 is a schematic view of the exemplary cannula tool of FIGURE 13, illustrating how the scanning fiber endoscope can image the tissue inside the bevel end needle with a small field of view and long depth of field, after the bevel needle end has been plunged into the tissue;

[0030] FIGURE 15 is a schematic view of the exemplary cannula tool of FIGURE 13, illustrating how cells comprising a biopsy sample can be drawn from the tissue within the bevel needle end;

[0031] FIGURE 16 is a schematic cut-away view of an exemplary cannula tool that includes a helical thread for advancing a bevel needle end into adjacent tissue and a balloon that is inflated for stabilizing the cannula tool/scanning fiber endoscope while imaging the site;

[0032] FIGURES 17 and 18 are schematic views of an exemplary cannula tool that includes a compressed helical spring for thrusting a bevel needle end into adjacent tissue, in which the compressed spring is selectively released, wherein FIGURE 17 shows the cannula tool before the helical spring is released, and FIGURE 18 shows it after the helical spring is released;

[0033] FIGURES 19, 20, and 21 show three different exemplary embodiments of bevel needle ends that respectively include barbs, backward angled teeth, and helically angled barbs, for holding the cannula tool engaged with tissue, and for retaining cells and tissue as a biopsy sample;

[0034] FIGURES 22A, 22B, 22C, 22D and 22E respectively illustrate a side view, a distal end view, a side view with jaw open, a side view with jaws open and the guidewire with eyes retracted, and a side view with jaws grasping tissue, for a first exemplary embodiment of forceps that are used with a guidewire with eyes;

[0035] FIGURE 23 is a side view of another exemplary embodiment of forceps adapted to slide over a guidewire with eyes and are used to grasp tissue;

[0036] FIGURES 24A, 24B, 24C, 24D, and 24E respectively illustrate a side view, a side view with jaws open, a distal end view, a phantom side view showing a cannula shaft used to force the jaws to open, and an alternative embodiment where the cannula shaft is used in a different manner to force the jaws open, for forceps mounted on a guidewire with eyes, for use in grasping tissue;

[0037] FIGURE 25 is a schematic view of an exemplary embodiment of a cannula tool that includes a piggyback guide collar that is adapted to slide over a scanning fiber endoscope, and which has a cutting edge on a leading distal end of a lumen, so that a piece of tissue cut from tissue can be drawn into the lumen for collection at the proximal end of the cannula tool; and

[0038] FIGURE 26 is a schematic diagram of an exemplary cannula tool that includes an annular passage for conveying cells that are released from tissue by explosive thermal heating caused by a focused laser pulse.

Description

FIGURES and Disclosed Embodiments Are Not Limiting

[0039] Exemplary embodiments are illustrated in referenced Figures of the drawings. It is intended that the embodiments and Figures disclosed herein are to be considered illustrative rather than restrictive. No limitation on the scope of the technology and of the claims that follow is to be imputed to the examples shown in the drawings and discussed herein.

[0040] FIGURE 1A (Prior Art) shows an end-view of the distal tip of a typical conventional multi-channel bronchoscope 10 with the capability of being selectively bent and having four channels within a 6.2 mm outer diameter. The approach used in this embodiment employs two illumination channels 12 and one camera channel 14. For image-guided interventions like cell/tissue sampling, a working channel 16 having a 2.8 mm diameter is used, as in this example (which uses a PENTAX, type EB-1970K bronchoscope), while smaller working channels of 2.0 mm diameter can be used in smaller 5.2 mm OD bronchoscopes (e.g., those available from Olympus). Surrounding the four channels is an articulated tube 18 that is manipulated by side wires (not shown), which extend proximally outside a patient's body and are pulled to bend the tip of the tube. Care must be taken not to bend the structure too sharply, since doing so might damage the optical fiber bundles in illumination channels 12 that are used for illumination, to enable imaging with a camera through cameral channel 14.

[0041] Simply by combining all three imaging channels into one, a scanning fiber endoscope, which is used as an exemplary embodiment of a "guidewire with eyes" saves about 2/3 of the diameter of a conventional bronchoscope. Details of an exemplary scanning mechanism used in the flexible scanning endoscope are discussed below in connection with FIGURE 4. As noted above, other imaging devices can be used with a catheter that also serves as a guidewire for cannula tools, within the scope of the approach described below, and it is not intended that the following description, which focuses on the use of a scanning fiber endoscope for such a device should in any way limit the scope of the present approach.

[0042] An exemplary scanning fiber endoscope 20 within a cannula tube 22 is shown in FIGURE 1B. As will be evident from the Figure, the flexible scanning fiber endoscope of this embodiment is only 0.95 mm in diameter and readily fits within the 1.5 mm outer diameter of cannula tube 22. The cannula tube is thus sized and shaped to readily slide over an elongate flexible shaft of the scanning fiber endoscope. The relatively small size of this configuration enables it to be advanced into much smaller body lumens, such as the smaller passages within a patient’s lungs, than conventional bronchoscopes, such as bronchoscope 10. Also, by using the scanning fiber endoscope as a guidewire for cannula tube 22, various types of cannula tools can be employed adjacent to the distal end of the scanning fiber endoscope. In many cases, such tools will be used to free cells or tissue from the internal site and then to facilitate collection of the cells or tissues, which comprise a biopsy sample.

[0043] FIGURE 2A shows a simple cannula tube over the sub-millimeter guidewire-with-eyes for taking cells from an internal site through an annular gap 23 defined between the outer surface of the endoscope and the inner surface of the cannula tube, for example, using lavage to wash the cells free and then extract them through the annular gap. Annular gap 23 is formed because cannula tube 22 is sized sufficiently larger in diameter than the flexible shaft of the scanning fiber endoscope to provide such a generally annular passage. This exemplary embodiment can also be used for applying a vacuum to adjacent tissue that draws the tissue closer to the distal end of the cannula tool or draws the cannula tool closer to the tissue. FIGURE 2B shows a tubular-style cytology brush 24, which can be made from clear plastic and is useful for image-guided cell sampling by abrasion when extended beyond the guidewire-with-eyes and moved over tissue, e.g., the tissue on the inner surface of a lumen. FIGURE 2C shows a sharpened tip 26 (i.e. a beveled end) on the distal end of cannula tube 22, which comprises a biopsy needle. The sharpened distal tip slides over endoscope 20, i.e., over the guidewire-with-eyes, and can be image-guided to a desired spot on tissue within a patient’s body. The biopsy needle can be thrust into adjacent tissue, to stabilize the guidewire-with-eyes, while imaging or to ensure that the imaging is not adversely affected by movement of the tissue due to cardiovascular motion, or respiratory motion. Those knowledgeable of this art will appreciate that the use of image-guided cannula tools such as these for cell sampling has not previously been accomplished in the bronchoscopy field. Further details and other types of cannula tools that are useable in connection with an endoscope that also serves as the guidewire for the cannula tools are discussed below.

Further Details of Exemplary Scanning Fiber Endoscope

[0044] FIGURE 3 illustrates other portions of exemplary scanning fiber endoscope 20. The central technical advance is an optical fiber scanner 28, which is coupled to a flexible shaft 30. The distal end of the scanning fiber endoscope is rigid, housing the micro-fiber scanning mechanism and lenses, as discussed below in connection with FIGURE 4. In one exemplary embodiment, the rigid tip length is about 12 mm, while the flexible shaft 30 length can be more than 2 meters long. The flexible shaft holds the fine electrical wires that are coupled to the piezoelectric tube actuator, and a plurality of optical detectors spaced-apart around the distal end of the housing to receive light from internal tissue, producing a signal corresponding to the intensity of the light that is conveyed proximally, for display as an image. Alternatively, a ring of 6 to 12 plastic collection optical fibers (for example, arranged in a 250 micron thick ring) can be deployed around the scanning mechanism to receive light from tissue within a patient's body that is illuminated with light from the scanning mechanism. Both the quartz singlemode optical fiber and plastic optical fibers are very flexible, and their sharp bend angles with a bend radius of up to about 5 mm cause no detrimental physical or optical effects.

[0045] Scanning fiber endoscope images are generated one pixel at a time as a scanned spot of RGB illumination illuminates the internal tissue with light having an intensity of less than 6 mW. The backscattered light is collected in a non-confocal geometry by the optical detectors (or by the plastic collection optical fibers surrounding the 1 mm optical fiber scanning system, with final detection at the base station). As a further alternative, by using a singlemode optical fiber with dual cladding as the optical fiber scanner, high-efficiency collection of the backscattered light within the inner cladding can be achieved. As a further alternative, a side-viewing optical fiber scanning endoscope can be employed that illuminates tissue at the side(s) (and optionally forward) of the endoscope and collects light scattered from the tissue for imaging. The scanning fiber endoscope is portable and has been used for *in vivo* imaging of pig airways as a daughter scope through a working channel of a flexible bronchoscope.

Exemplary Scanning Mechanism

[0046] FIGURE 4 shows an exemplary scanning mechanism 90 for use in the scanning fiber endoscope described above. Scanning mechanism 90 comprises flexible single mode optical fiber 98 that is supported by a tube 94 of piezoelectric material, which serves to drive a distal end 96 of the optical fiber to move in a desired scanning pattern. Distal end 96 extends distally beyond the tube of piezoelectric material and is cantilevered from it, generally within the center of the flexible scanning fiber endoscope and adjacent to its distal end. This tube of piezoelectric material is held in the endoscope by a base 92. Quadrant electrodes 102, 104, and 106 (and one other that is not visible in this view) are plated onto the tube of piezoelectric material and can be selectively energized with an applied voltage in order to generate two axes of motion in distal end 96 of optical fiber 98. Lead wires 100 carry electrical voltage signals to each of the quadrant electrodes to energize the piezoelectric material relative to each axis of motion. In this exemplary embodiment, the two axes are generally orthogonal to each other. An amplified sine wave applied to one axis and a cosine wave applied to the other axis of the tube piezoelectric material generate a circular scan, although those of ordinary skill in the art will understand that a variety of different scan patterns can be produced by appropriately moving distal end 96 of optical fiber 98. An appropriate modulation of the amplitudes of the electrical voltage signals applied to the quadrant electrodes can create a desired area-filling two dimensional pattern for imaging with light emitted from distal end 96 of the optical fiber. A few examples of the various scan patterns that can be achieved include a linear scan, a raster scan, a sinusoidal scan, a toroidal scan, a spiral scan, and a propeller scan. In some exemplary embodiments, the distal end is driven so that it moves at about a resonant (or near-resonant) frequency of the cantilevered distal end of optical fiber 98, which enables a greater scan amplitude to be achieved for the given drive signals applied. FIGURE 4 shows the first mode of lateral vibratory resonance of the cantilevered distal end of the optical fiber.

[0047] Other types of scanning mechanisms can alternatively be used for the guidewire with eyes approach. For example, a micro-mechanical electrical systems (MEMS) scanner (not shown) that has a scanning beam used to optically scan an internal site with light to produce an image of the internal site might instead be used. An example of a MEMS scanner for imaging is shown in commonly assigned U.S. Patent No. 6,975,898, the disclosure and specification of which are specifically hereby incorporated herein by reference.

[0048] Light emitted from distal end 96 as it moves in the desired scan pattern travels through a lens assembly 108 and is directed at the tissue forward of the scanning fiber endoscope. Light reflected or scattered by the tissue illuminated with the scanning light is then detected. In this exemplary embodiment, an annular ring 110 on which a plurality of spaced-apart optical detectors 112 are mounted is disposed around the distal end of the scanning fiber endoscope. Optical detectors 112, which may comprise photodiodes or other light sensitive devices, produce output signals indicative of the intensity of the light that they receive from the internal tissue, and these output signals are conveyed proximally through flexible shaft 30 of the scanning fiber endoscope over conductive leads 114. The output signals conveyed by these conductive leads are then used to produce an image of the internal tissue proximate to the distal end of the scanning fiber endoscope, for example on a monitor. As noted above, a side-viewing scanning fiber endoscope having a reflective surface (not shown) can optionally be used to image tissue at one or more sides of the scanning fiber endoscope.

Exemplary Cannula Tools

[0049] FIGURE 5A illustrates an exemplary cannula tool system 116 that includes an exemplary cannula tool 118. In this schematic illustration, flexible cannula tube 22 is illustrated extending through a dermal interface 130 and into a body 132 of a patient. Elongate flexible cannula tube 22 is guided to a desired location within body 132 by scanning fiber endoscope 20, which has been inserted through an incision or other opening in dermal interface 130 and has already been advanced to the desired location or site. Flexible cannula tube 22 is then slid over scanning fiber endoscope 20 and is thus guided to the desired location within the patient's body.

[0050] After thus being advanced to the desired location, cannula tool 118 can be employed to carry out a plurality of functions. Specifically, cannula tool 118 is employed to dislodge cells or tissue at the desired location, and then facilitates withdrawal of the dislodged cells or tissue from the site as a biopsy sample, for collection to enable further processing or analysis. The dislodged cells or tissue are conveyed from the site at the distal end of the cannula tube through annulus 23 toward the proximal end of the cannula tube. As noted above, annulus 23 is formed between the outer surface of scanning fiber endoscope 20 and the interior surface of cannula tube 22. In this exemplary embodiment, a port 120 is formed at or adjacent to the proximal end of cannula tube 22, in fluid communication with the annulus, and is coupled to one end of a fluid line 122. The other end of fluid line 122 is connected to a three-way valve 123, which selectively provides direct communication to a vacuum pump 128 for applying negative pressures or to a fluid pump 125 for applying positive pressures. Optionally, a biopsy trap 124 is disposed between the three-way valve and vacuum pump (or other source of a vacuum). Vacuum pump 128, which is coupled through a fluid line 126 to the opposite side of biopsy trap 124 produces a negative pressure that draws the biopsy sample, e.g., along with a bodily fluid such as blood, mucus, or an introduced fluid (e.g., air or saline), into the biopsy trap. The biopsy sample can then be removed from the biopsy trap so that the processing and analysis can be carried out. Fluid pump 125 can provide saline solution (from a source reservoir – not shown) to suspend the dislodged cells or tissue for easier retrieval. Furthermore, the introduced fluid under positive pressure can help to dislodge cells, mucus, blood, or other bodily fluid from the tool, scanning fiber endoscope, or wall of the body lumen. It should also be noted that vacuum pump 128 can be employed to draw tissue closer to the distal end of a cannula tool or alternatively to draw the distal end of the cannula tool closer to the tissue, using the force exerted by ambient pressure that is greater than the reduced pressure created by the vacuum pump.

[0051] Further details of cannula tool 118 are illustrated in FIGURE 5B. Cannula tool 118, which is shown being guided by scanning fiber endoscope 20, includes a plurality of spaced-apart outwardly extending points 230 disposed around the exterior surface of cannula tube 22. Points 230 are shaped so that they tend to abrade cells from tissue adjacent to the outer surface on which the points are disposed when the cannula tube is moved longitudinally back-and-forth a few centimeters (and/or rotated back and forth around) its longitudinal axis. A plurality of orifices 232 are interspersed between the plurality of points providing a number of fluid communication paths through which the bodily fluid and cells dislodged from the adjacent tissue can be drawn into an annulus 23, which is disposed between the outer surface of scanning fiber endoscope 20 and the inner surface of cannula tube 22. As explained above in connection with FIGURE 5A, the bodily fluid conveys the dislodged cells or tissue through annulus 23 from the distal end of the elongate flexible tube to the proximal end where port 120 is disposed, so that the cells or tissue comprising the biopsy sample can be drawn into biopsy trap 124 and collected for processing.

[0052] A seal comprising annular rings 234a and 234b is disposed at the distal end of cannula tube 22 to ensure that vacuum pump 128 draws the bodily fluid and dislodged cells or tissue through orifices 232, rather than simply drawing bodily fluid without the cells or tissue from around scanning fiber endoscope 20 at the distal end of the cannula tube. It will be understood that the shape or configuration of points 230 are intended to be exemplary and not in any way limiting, since it should be apparent that a number of other different shapes or configurations can be employed for such points comprising an abrasive surface, such as short bristles (e.g., a tubular brush). Further, either more or fewer points 230 can be disposed on cannula tool 118, over either a longer or shorter length section of cannula tube 22.

[0053] FIGURE 5C is a schematic block diagram of an exemplary system 140 for use by the scanning fiber endoscope for imaging an internal site 142 using the signals produced by scanning mechanism 90 (details of which are shown in FIGURE 4). To simplify this Figure, details of the components involved in providing fluid, vacuum, and collecting the biopsy sample that are discussed above in connection with FIGURE 5A are not replicated in this view. A high-power laser 144 that can be used for spectroscopy analysis of internal site 142 is optionally included in system 140. Also provided as light sources are red, green, and blue (RGB) lasers 146, 148, and 150, respectively. These lasers are selectively controlled with electro-mechanical shutters (not shown) and their output laser light beams are combined with a fiber optic combiner for transmission down the optical fiber to the scanning mechanism. In connection with the optional high-power laser for spectroscopy, a spectrophotometer and spectrum analyzer 152 is also optionally included in system 140. This system includes a block 154, which comprises several electrical sources and control electronics for fiber optic scanning and data sampling, which are used for imaging internal site 142 with scanning mechanism 90. Optionally, one or more infrared (IR) thermal photodetectors and a temperature monitor 156 can be included, to track the temperature of the internal site, which can be important if therapy is being rendered, or for diagnostic purposes. An interactive computer workstation and monitor 158 and a high-resolution color monitor 160 are also included to enable an operator to view images of internal site 142 and to facilitate advancing the scanning fiber endoscope to a desired location in a patient's body. The imaging capability can be particularly important if advancing the scanning fiber endoscope through a labyrinth of linked passages, e.g., the bronchial passages in a patient's respiratory system. The images of anatomical features and tissue enable the medical practitioner to readily select a path along which to manipulate and control the direction along a path being followed by the distal end of the endoscope to reach a desired location in a patient's body. An endoscope controller for tip navigation and stabilization 162 is schematically illustrated and is intended to indicate that means are provided for controlling the endoscope as it is navigated through one or more lumens or along a path in a patient's body.

[0054] In FIGURE 6, an exemplary cannula tool 240 is illustrated for use in connection with an elongate flexible tube 242. This same outer tube can also be used to shield the internal tissues of the body from cannula tool 118 during insertion to the desired location within the body. This outer elongate flexible tube or sheathing can then be withdrawn to reveal a biopsy tool distal tip when the tip is disposed at the desired biopsy site within the body. As in cannula tool 118, cannula tool 240 is configured to be advanced to a desired site by sliding along scanning fiber endoscope 20. Cannula tool 240 includes a wire loop 246 that extends distally of a ring 244, which is disposed just inside the distal end of elongate flexible tube 242. Loop 246 is sized to ensnare a biopsy sample of tissue, such as a polyp 254 growing from adjoining tissue 256 at the desired site, as shown in this Figure.

[0055] Two different techniques can be employed to cut away the piece of tissue comprising the biopsy sample from adjoining tissue. One option is to supply an electrical current so that loop 246 is heated sufficiently to burn through adjacent tissue 256, freeing the biopsy sample, such as polyp 254. The electrical current can be applied to loop 246 through conductive wires 248 and 250, which extend proximally of the elongate flexible tube 242 and are connected through a switch to a conventional electrical current supply (neither shown). Alternatively, one or both of wires 248 and 250 can be pulled proximally of the proximal end of elongate flexible tube 242, which tightens loop 246 around the tissue sufficiently to cut through the tissue, freeing it from the adjacent tissue. To help stabilize the tool over the sample and possibly help to ensnare the tissue, a vacuum can be applied within outer elongate flexible tube 242. Once the biopsy sample is freed, it can be drawn with bodily fluid into an annulus 252 formed between the outer surface of scanning fiber endoscope 20 and the inner surface of the elongate flexible tube 242. For example, vacuum pump 128 (shown in FIGURE 5A) can be used to draw the bodily fluid and the dislodged tissue comprising the biopsy sample to the proximal end of the elongate flexible tube 242. This biopsy sample that has thus been freed and withdrawn from inside the body of a patient can then be collected for processing and analysis by medical personnel.

[0056] An exemplary embodiment of a cannula tool 260 shown in FIGURE 7 is also configured to be advanced to a desired site within the body of the patient over scanning fiber endoscope 20. Cannula tool 260 includes an outer elongate flexible tube 262 that extends between a distal end and a proximal end. The proximal end is disposed outside the body of the patient. Within the outer elongate flexible tube is disposed a middle flexible tube 265. On the outer surface of the middle flexible tube, at its distal end, is affixed a helical coil 264. The helical coil is in contact with the inner surface of the outer elongate flexible tube and terminates on its leading end at a sharp cutting edge 266, which extends just beyond the distal end of elongate flexible tube 262. Sharp cutting edge 266 is thus configured to slice a ribbon of tissue from the desired site as middle flexible tube 265 is rotated about its longitudinal axis in the appropriate direction with respect to outer elongate flexible tube 262 to bring the sharp cutting edge into the adjacent tissue. This ribbon of tissue, which comprises a biopsy sample, is carried between helical coils 264 and conveyed with bodily or introduced fluid through an annulus 268 formed between the outer surface of scanning fiber endoscope 20 and the inner surface of middle flexible tube 265. A smaller annular gap 263 is provided between the outer surface of middle flexible tube 265 and the inner surface of outer elongate flexible tube 262, which may facilitate capture of the tissue ribbon when negative pressure is applied at the proximal end of the elongate flexible tube or may facilitate removal of the tissue ribbon from the helical coil with introduced fluid applied at the proximal end. As discussed above, the vacuum pump shown in FIGURE 5A can be used to draw the biopsy sample and bodily fluid through the annulus toward the proximal end of the elongate flexible tube, where the biopsy sample can be collected.

[0057] FIGURE 8 illustrates a rotational driver 270 that is configured to rotate a cannula tube or scanning fiber endoscope 20 about a longitudinal axis of the scanning fiber endoscope. Attached to the distal end of the cannula tube or scanning fiber endoscope can be one of the multifunctional cannula tools discussed herein. The cannula tube should be viewed as a specific type of "elongate flexible tube," which is used with each of the exemplary embodiments of the cannula tools discussed herein. However, this exemplary embodiment happens to match the ribbon cutting tool in FIGURE 7, which optionally can provide fluid communication in both annular gaps around the middle flexible tube.

[0058] In connection with rotational driver 270, a prime mover 274 (for example, an electric motor) is included to rotate a driven shaft 276, thereby providing a rotational force that rotates and drives middle flexible tube 265, which holds the biopsy tool, forward and backward. An outer sheath sleeve 278 is fitted over guidewire or endoscope 272. Sealing "O" rings 290 are provided on outer sheath sleeve 278, as well as on each side 288 of a driven gear 286, and on a guidewire or endoscope sleeve 280, which is near a proximal end 284 of the scanning fiber endoscope and attached to a strain relief boot 282. End caps 292 and 294 are fitted over and sealingly engage "O" rings 290, when securely coupled to a bearing body 300 by fasteners 295. End caps 292 and 294 include ports 296 and 298, to provide fluid paths in fluid communication with exposed portions of the scanning fiber endoscope. At each of these exposed portions, the elongate flexible tube is open for withdrawing or injecting either gases or liquids into one or two annular gaps formed for use with cannula tool 272. When combining the components of FIGURES 7 and 8, port 298 can be used to withdraw a biopsy sample that is conveyed with a bodily or introduced fluid from the distal end of the guidewire or endoscope with cannula tool 272, through annulus 268 formed between scanning fiber endoscope 20 and the inner surface of middle flexible tube 265. Port 296 is in fluid communication with small annular gap 263 that is formed between the outer surface of middle flexible tube 265 and the inner surface of outer elongate flexible tube 262. For example, a vacuum can be applied to both ports 296 and 298 in FIGURE 8, which will help pull the tissue up against the cutting edge of the cannula tool in FIGURE 7. After cutting is completed by advancing helical coil 264 on middle flexible tube 265 toward the tissue by rotating the drive gear that is mechanically coupled with the middle flexible tube, the vacuum can be removed from only the outer annular gap, i.e., from port 296. By applying a saline solution to port 296, any tissue and cells within the helical coil can be flushed and then sucked into the larger inner annulus 268, with negative pressure applied to port 298, e.g., with vacuum pump 125 (FIGURE 5A).

[0059] Driven shaft 276 is drivingly coupled to a drive gear 302, which is rotatably mounted in bearing block 300 and affixed to an end of driven shaft 276. A gear slide fork 304 is mounted on the side of bearing block 300 and is configured to engage driven gear 286, so as to move the driven gear into meshing relationship with drive gear 302 when gear slide rod 306 is appropriately pushed (or pulled) longitudinally. By thus moving gear slide rod 306, a user can selectively engage driven gear 286 with drive gear 302 to apply a rotational force that begins turning driven gear 286, which is in mechanical communication with middle flexible tube 293, so that the middle flexible tube turns in one direction versus the opposite direction, about its longitudinal axis. Rotational motion of the cannula tool shaft can be used either for abrading or for cutting cells and tissue from adjacent tissue at a desired location in a body of a patient. For example, the rotational driver can be used to rotate a cannula tool having an abrasive surface, such as exemplary cannula tool 118, or can turn a cannula tool that has a sharp cutting edge, which is able to cut away a ribbon of tissue to form a biopsy sample, such as exemplary cannula tool 260.

[0060] In FIGURE 9, a cannula tool 310 is illustrated and is disposed adjacent to the distal end of a flexible elongate tube 316. As explained above, flexible elongate tube 316 has an internal lumen that is sized to be guided over scanning fiber endoscope 20 to a desired site within a body of a patient. For example, as shown in this Figure, scanning fiber endoscope 20 has been advanced through a body lumen 312 and has been used to guide elongate flexible tube 316 so that a balloon 318 (currently deflated) is advanced to a site where cells comprising a biopsy sample is to be taken. Balloon 318 is sealingly attached to the outer surface of the flexible elongate tube at each end of the balloon (for example, by thermal bonding or using an appropriate adhesive). A pressurized fluid tube 320 extends within an annulus formed between the outer surface of scanning fiber endoscope 20 and the inner surface of elongate flexible tube 316, from the proximal end of the flexible elongate tube to a port 322. Port 322 provides an opening through elongate flexible tube 316 to add or remove fluid volume inside balloon 318. The proximal end of the pressurized fluid tube is coupled to a pressurized fluid source, such as fluid pump 125, and to a negative pressure source, such as vacuum pump 128, both of which are shown in FIGURE 5A.

[0061] Pressurized fluid provided by the pressurized fluid source can be selectively applied through pressurized fluid tube 320 and port 322 to inflate balloon 318, as shown in FIGURE 10. When balloon 318 is thus inflated, an abrasive coating 324 that extends over the outer surface of balloon 318 comes into contact with tissue on the wall of body lumen 312. When the elongate flexible tube 316 is then rotated around its longitudinal axis or pushed/pulled longitudinally back-and-forth within body lumen 312, cells 326 are abraded from the tissue lining the body lumen by the abrasive coating. The abraded cells and bodily fluid within body lumen 312 are together drawn into an annulus 328 formed between the inner surface of the lumen extending through elongate flexible tube 316 and the outer surface of scanning fiber endoscope 20, as shown in FIGURE 10. These cells, which comprise a biopsy sample, can be withdrawn from the annulus at the proximal end of flexible elongate tube 316, generally as explained above. An elongate sheath 325 (shown in FIGURES 9 and 10 after the elongate sheath has been pulled back) can be disposed around the abrasive balloon during insertion and retraction and then pulled back proximally to expose the abrasive surface of the balloon when the cannula tool is disposed at a desired site for taking a biopsy sample. The proximal end of elongate sheath 325 is accessible outside the body of a patient and can be separately manipulated to move it longitudinally, relative to balloon 318 (or other embodiments of the cannula tool). For other types of cannula tools, it may be preferable to rotate the elongate sheath about its longitudinal axis between first and second positions, so that an opening at its distal end (not shown) selectively either protects or exposes the portion of the cannula tool that is used to dislodge cells or tissue comprising the biopsy sample.

[0062] An exemplary cannula tool 400 is illustrated in FIGURES 11A and 11B, which includes bristles 402 disposed over an area of cannula tube 22, proximate the distal end of the cannula tube. These bristles can be used to abrade a biopsy sample comprising cells and tissue, from an interior surface of a body lumen or other adjacent tissue inside a patient's body. When advancing cannula tool 400 into a body over scanning fiber endoscope 20, a protective cover 404 is moved forward over bristles 402, as shown in FIGURE 11B, and the protective cover is pulled back using an internal wire or other flexible lead (not shown) that extends through the cannula tube, exposing bristles 402, as shown in FIGURE 11A. Alternatively, the protective cover 404 is the distal portion of an outer elongate flexible tube that provides mechanical communication to the proximal end of the cannula tool over guidewire system. Similarly, after a biopsy sample is taken at a desired site, protective cover 404 is drawn forward to again cover bristles 402 and to also cover and protect the biopsy sample that has been collected on the bristles, so that the biopsy sample remains intact as cannula tube 22 and cannula tool 400 are withdrawn from the body of the patient.

[0063] Another related exemplary cannula tool 420 that includes bristles 402 on the distal end of cannula tube 22 is shown in FIGURES 12A and 12B. When inserting cannula tool 420 into a patient's body and while advancing it to a desired site where a biopsy sample is to be taken, cannula tube 22 is positioned so that bristles 402 are covered by a fixed protective cover 424, as shown in FIGURE 12B. After the distal end of cannula tube 22 has reached the desired site where the biopsy sample is to be taken, the cannula tube is pushed forward (i.e., distally), while scanning fiber endoscope 20 is held in a fixed position, which exposes bristles 402, as shown in FIGURE 12A. Once the bristles have been scrubbed against the adjacent tissue so that cells are scrubbed away and left on the bristles, the cannula tube is drawn backward (i.e., proximally), so that fixed protective cover again covers bristles 402 and the biopsy sample collected there. The cannula tube and scanning endoscope can then be removed from the patient's body together so that the biopsy sample remains covered by the fixed protective cover. Once outside the patient's body, the biopsy sample can be recovered from bristles 402 for further processing and analysis.

[0064] FIGURES 13, 14, and 15 illustrate an exemplary embodiment of a cannula tool 500 that includes a bevel needle end 502, which is rigid and can be forcefully thrust into adjacent tissue 504 to take a biopsy sample comprising cells or tissue that are cut free when bevel needle end 502 is withdrawn from the tissue, or which can be used to cut free a biopsy sample comprising cells that can be flushed from the tissue and carried to the proximal end of cannula tube 22 for collection with a bodily fluid or an introduced fluid, as discussed above. As cannula tool 502 is approaching a potentially desired site 504, scanning fiber endoscope can image the surface of the site using a relatively wide field of view (FOV) and long depth of field (DOF) 506, as illustrated in FIGURE 13. If the site appears appropriate to take a biopsy sample, cannula tube 22 is forcibly advanced in the distal direction over scanning fiber endoscope 20, so that bevel needle end 502 pierces the surface of the tissue at site 504, as shown in FIGURE 14. A plug of tissue can then be withdrawn with bevel needle end 502 as the cannula tool is pulled proximally, or alternatively, as shown in FIGURE 15, site 504 can be washed with a lavage using an introduced a pressurized fluid 512 that is conveyed through cannula tube 22 from fluid pump 125 (FIGURE 5A). Pressurized fluid 512 is applied to the tissue through bevel needle end 502, causing cells 510 to be freed from the tissue within the bevel needle end. These cells are then conveyed through the needle and into annular gap 23, drawn by vacuum pump 128 (FIGURE 5A), and collected as the biopsy sample.

[0065] An exemplary embodiment of a cannula tool 520 is illustrated in FIGURE 16. In this Figure, cannula tool 520 is shown in a body lumen 522 that is defined by surfaces 524 and is adjacent to a site 534 that is being imaged to determine if it is appropriate to take a biopsy sample. Cannula tool 520 includes a bevel needle end 532 formed on the distal end of cannula tube 22. A helical thread 528 is provided inside the distal portion of cannula tube 22, and the helical thread engages a corresponding helical threaded collar 530 that is affixed on the exterior surface of scanning fiber endoscope 20, a few centimeters from its distal end. As cannula tube 22 is rotated relative to scanning fiber endoscope 20, e.g., by rotational driver 270 (FIGURE 8), bevel needle end 532 is advanced forward from the distal end of the scanning fiber endoscope and into the tissue at site 534, enabling a biopsy sample to be taken from the tissue at the site, as generally explained herein. The direction of rotation of cannula tube 22 by rotational driver 270 (or other suitable mechanism – including manual rotation) can be reversed to draw the bevel needle end from the tissue at site 534.

[0066] Optionally, a balloon 536 can be inflated inside body lumen 520 to stabilize the scanning fiber endoscope, for example, while imaging site 534. To inflate balloon 536, a pressurized fluid is supplied through a fluid line 538 that extends from a source of pressurized fluid at the proximal end of cannula tube 22 and through a port (too small to be visible in this Figure) in cannula tube 22, which is in fluid communication with the interior of balloon 536. Balloon 356 can be deflated by releasing the pressure within balloon 536 after site 534 has been imaged. By enabling the site to be imaged before a decision is made to take a biopsy sample, scanning fiber endoscope provides clear advantages over conventional approaches that employ touch or external imaging to determine where a biopsy sample should be taken inside a patient's body.

[0067] An exemplary embodiment of a cannula tool 540 that uses a different approach for taking a biopsy sample with a bevel needle end 548 is illustrated in FIGURES 17 and 18. FIGURE 17 shows how a cannula tube 542 includes a compressed helical coil spring 544 that can be selectively released (for example, by pulling a trip lead that extends proximally inside cannula tube 542 – not shown, or by applying an electrical signal to leads (not shown) that extend through inside the cannula tube to an electrically actuated trigger (also not shown)). The cannula tube and scanning fiber endoscope would be advanced with the helical spring pre-compressed, until imaging by the scanning fiber endoscope indicates that it is disposed adjacent a site 550 where it is appropriate to take a biopsy sample of cells and tissue. Cannula tube 542 is constrained with scanning fiber endoscope 20 when the helical spring is selectively released so that expansion of compressed helical spring 544 acts on a tubular segment 546 of the cannula tool, forcing it forward of the distal end of scanning fiber endoscope 20, as shown in FIGURE 18. The force of the expanding helical spring thus causes bevel needle end 548 on the distal end of tubular segment 546 to pierce tissue at adjacent site 550, enabling cells and tissue to be freed from the site and withdrawn as a biopsy sample when cannula tube 542, tubular segment 546, and scanning fiber endoscope 20 are withdrawn from the patient's body.

[0068] Unless the biopsy sample is carried by a fluid through the annular gap between the interior surface of the cannula tube and the exterior surface of the scanning fiber endoscope, as explained in regard to some of the exemplary embodiments, it may be important to ensure that cells and tissue are retained by the bevel needle end that pierces tissue at a desired site, so that the cells and tissue are not lost as the bevel needle end is withdrawn from the patient's body. FIGURES 19, 20, and 21 illustrate different exemplary embodiments for anchoring the cannula tool to tissue, for example, to stabilize the cannula tool and the scanning fiber endoscope while carrying out high-resolution imaging or slow-imaging or to minimize the effects of respiration motion or other biological motion while imaging. In addition, these different embodiments can ensure that tissue and cells usable as a biopsy sample are retained by the bevel needle end when it is withdrawn from the tissue at an internal site. FIGURE 19 shows a plurality of barbs 566, which are formed just inside a bevel needle edge 564 of a cannula tool 560. Barbs 566 can engage tissue and tear it away when a cannula tube 562 is rotated so that the barbs on the inside of the bevel needle end are turned into the tissue pierced by the bevel needle edge, at the internal site. Cells and tissue trapped by barbs 566 can then be collected after cannula tool 560 is withdrawn, or optionally, can be flushed free of the barbs and drawn with a bodily fluid or an introduced fluid into an annular gap 568, which is formed between the inner surface of cannula tool 562 and the outer surface of scanning fiber endoscope 20 and collected at the proximal end of cannula tube 562.

[0069] In FIGURE 20, backward angled teeth 576 formed just inside the distal end of a cannula tool 570 can also tear away cells and tissue from an internal site as the cannula tool is pulled back from a site pierced by a bevel needle edge 574. The cells and tissue torn away by backward angled teeth 576 will be retained behind the teeth and can be collected after the cannula tool is removed from the body, or optionally can be flushed into and withdrawn through an annular gap 578, carried by a bodily fluid or introduced fluid. Vacuum pump 128 (FIGURE 5A) can pull the tissue and cells with the fluid to the proximal end of cannula tube 572, through the annular gap.

[0070] A portion of a set of angled barbs 582 on a cannula tool 580 are illustrated in FIGURE 21. These angled barbs are configured in a helical array inside the opening formed by a bevel needle end 574, disposed at the distal end of a cannula tube 584. As the cannula tool is turned or rotated after bevel needle end 574 has pierced tissue, the angled barbs slice away tissue and retain it on the angled barbs so that the tissue can be removed from the patient's body and collected as a biopsy sample. Again, optionally, the biopsy sample can be drawn through an annular gap 578 with fluid and extracted from the proximal end of the cannula tube, as explained above.

[0071] A forceps cannula tool can also be used to grasp tissue and remove a biopsy sample. An exemplary hollow head portion of forceps 600 is shown in FIGURE 22A (side view) and FIGURE 22B (distal end view). Other views of this exemplary embodiment are illustrated in FIGURES 22C, 22D, and 22E. Scanning fiber endoscope 20, which can be moved longitudinally relative to the hollow head portion of forceps 600, is shown passing through the center of the jaws of forceps 600 and out of a distal tip 624 of the jaws, via a channel 622 formed between an upper jaw 642 and a lower jaw 644 of the forceps, which are pivotally coupled together by hinge pins 650, which also attach to longitudinally extending arms 626, at each side of the forceps. An outer sheathing 620 encompasses the closed forceps to hold them closed and also provides a fluid communication path around the forceps through which fluid can flow into or from a body lumen in which the jaws of the forceps can be disposed. Longitudinally extending arms 626 are coupled to an internal tube 628 that extends externally from the proximal end of the system and is used to longitudinally push or pull forceps 600 so that the forceps move relative to outer sheathing 620 and/or scanning fiber endoscope 20. In this exemplary embodiment, both upper jaw 642 and lower jaw 644 can be biased open by a helical or other type of spring (not shown) or other suitable means, so that the distal ends of the jaws spread apart, as shown in FIGURE 22C, when the jaws are extended beyond the outer sheathing or when the outer sheathing is drawn proximally relative to the forceps, so that the jaws are no longer encompassed by outer sheathing 620. In order to grasp tissue, the central scanning fiber endoscope is retracted relative to forceps 600, as shown in FIGURE 22D. Once the forceps are closed, for example by advancing outer sheathing 620 over the jaws (thereby causing the jaws of the forceps to grasp and thereby remove a biopsy sample 660 of tissue from a site in a patient's body), the forceps and scanning fiber endoscope can be withdrawn from the patient's body together, with the outer sheath sheathing. The outer sheathing extends over the forceps when the forceps and biopsy sample are being withdrawn, as shown in

FIGURE 22E, to protect the biopsy sample and retain the jaws closed and grasping the biopsy sample.

[0072] In an alternative exemplary embodiment, a forceps 670, the jaws of the forceps can be configured so that they extend parallel with scanning fiber endoscope 20, as shown in FIGURE 23. A lower jaw 684 of the forceps is rigidly attached to a flexible tubular conduit 680 that is sized and configured to readily slide over scanning fiber endoscope 20, which thus can be used as a guidewire to guide forceps 670 to a desired site in a patient's body. An upper jaw 682 can be opened with a draw wire 672 or by using an actuator (not shown), for example, an actuator that is formed of a shape memory metal such as Nitinol™, which changes shape in response to resistive heating caused by an electrical current supplied to the actuator through electrical leads (also not shown). Upper jaw 682 can be then closed toward lower jaw 684 by a further shape change of the actuator or by a helical or other type of spring (not shown) disposed at a hinge 686, so that the jaws grasp tissue for taking a biopsy sample. (It should be apparent that the relative operation and function of the upper and lower jaws can alternatively be reversed.) The biopsy sample can be taken from an internal site in a patient's body while imaging the site with scanning fiber endoscope 20, and the images can assist a medical practitioner in identifying the desired site and the tissue to be retrieved as the biopsy sample.

[0073] Several other exemplary mechanisms for opening and closing the jaws of the forceps tools are illustrated in FIGURES 24A through 24E. The simplest method is to provide very thin wires that pull the two rearwardly extending ends of jaws 712 and 714 together, as shown for an exemplary embodiment of forceps 700 in FIGURE 24A. For example, wires 718 and 719 are coupled to the rearwardly extending ends of jaws 712 and 714 and then pass through a wire loop 716 that is coupled by a wire 717 to hinge 650 that pivotally couples the jaws together. Longitudinally extending arms 702 are coupled to an internal tube 704 that extends externally from the proximal end of the system and is used to longitudinally push or pull forceps 700 so that the forceps move relative to scanning fiber endoscope 20. By using internal tube 704 to hold forceps 700 in place while pulling wires 718 and 719 proximally, serrated distal ends 646 and 648 of the jaws can be opened, as shown in FIGURE 24B. Alternatively, wires (not shown) connected to jaws 712 and 714 can be formed of a shape memory alloy wire (e.g., such as wire formed from Nintinol™) that is activated by selectively resistively heating the wire with an electrical current (or other heat source) to change shape from a straight to a foreshortened state. In both mechanisms, a helical spring (not shown) can be used to force the jaws closed when the opening force provided by the shape memory alloy wires is released.

[0074] A third exemplary embodiment, a forceps 780 is shown in FIGURES 24C (distal end view), 24D (side phantom view with the jaws closed), and 24E (side view with the jaws open). In this embodiment, a cannula shaft 720 is shown attached to the forceps by pins 722 and 724 at hinge 650 where jaws 712 and 714 are pivotally coupled together. The jaws are opened by pushing an inner cannula 728 having angled ramp distal ends 730 forward against the rearwardly extending portions of the jaws, so that the angled ramp distal ends force the rearwardly extending ends of the jaws together, opening the distal ends of the jaws. The forceps are held stationary by simultaneously applying a restoring force on cannula shaft 720. Outer sheathing 620 can again optionally be used for providing fluid communication around forceps 780. When the inner cannula is pushed forward, a helical spring 726 disposed on the proximal end of the forceps jaws is compressed, as illustrated in FIGURE 24E. Helical spring 726 supplies the force necessary to close the distal serrated ends of the jaws when the inner cannula is retracted away from the jaws so that it no longer applies force to the rearwardly extending portions of the jaws. Alternative configurations can be used for actuating the jaws, such as forcing the jaws closed with the inner cannula and providing a spring to open the jaws, and those skilled in the art of forceps design and manufacture will readily understand how these and other mechanisms can be employed to open/close the jaws of the forceps.

[0075] Yet another exemplary embodiment of a cannula tool is illustrated in FIGURE 25. A cannula tool 740 shown in this Figure is intended to cut away a ribbon of tissue with a sharpened cutting edge 744, which is formed over at least a portion of the distal leading edge of the elongate flexible tube. Unlike the other exemplary embodiments of cannula tools discussed above, cannula tool 740 has a flexible elongate tube 742 with an internal lumen 746 that does not slide over scanning fiber endoscope 20. Lumen 746 instead defines a passage through which a ribbon of tissue that is cut away by sharpened cutting edge 744 from adjacent tissue within the body of a patient can be drawn with bodily fluid toward the proximal end of the elongate flexible tube. While not shown in this Figure, it is contemplated that a protective cover can be provided that overlies sharpened cutting edge 744 until the distal end of the cannula tool is disposed where it is desired to cut away a ribbon of tissue as a biopsy sample. A pull wire (not shown) that is coupled to the protective cover can then be pulled proximally, enabling the protective cover to be pulled away from the sharpened cutting edge and out through the proximal end of lumen 746. Alternatively, during insertion and retraction, flexible elongate tube 742 can be rotated so that cutting edge 744 is disposed close to the guidewire and away from the tissue, then rotated outwardly toward the tissue, to cut away the biopsy sample.

[0076] The distal end of the cannula cutting tool is guided to a desired location by a piggyback collar 748, which is attached to one side of the flexible elongate tube with a stanchion 750. Piggyback collar 748 includes an internal open guide lumen that is sized to readily slide along scanning fiber endoscope 20, and thus, to be guided to a desired site within the body of a patient where a biopsy sample is to be taken. Stanchion 750 may enable elongate tube 742 to rotate but prevent it from sliding longitudinally to enable cutting edge 744 to be turned away from the tissue during insertion and retraction of the tool through the body lumen.

[0077] The simple cannula tool comprising annular gap 23 that is formed between the outer surface of scanning fiber endoscope and the inner surface of cannula tube 22, as shown in FIGURE 2A, can be employed to assist in collecting a biopsy sample comprising cells that are released from tissue. The cells are released from the tissue as a result of an explosive thermal heating caused by a focused laser light that is emitted by the scanning fiber endoscope, as shown in regard to an exemplary embodiment 800 illustrated in FIGURE 26. In this embodiment, cannula tube 22 is advanced over scanning fiber endoscope 20 within a body lumen 802 that is defined by walls 804. At an internal site 810, the scanning fiber endoscope is used to emit pulses of laser light 808 that are focused on the internal site where a biopsy sample is to be taken. The laser pulses cause rapid heating, disrupting the cells and tissue at the internal site so that cells 812 are freed and can be drawn with bodily fluid or by introduced fluid into annular gap 23 by vacuum pump 128 (FIGURE 5A) and collected at the proximal end of the cannula tube.

[0078] Each of the exemplary embodiments of cannula tools discussed above is characterized by performing at least two functions. The first function is to dislodge or cutaway cells or tissue from within the body of a patient. The second function is to enable the cells or tissue that have been dislodged to be collected as a biopsy sample for further processing or analysis. A multi-functional capability and relatively compact size of these cannula tools enable them to be readily used in many applications where conventional cannula tools cannot be.

Fabricating the Cannula Tool System

[0079] The cannula tube is a hollow tube that slips over the sub-mm scanning fiber endoscope. Based on experience threading a 1.6 mm OD sheathing with 12 plastic optical fibers around a 1 mm diameter optical fiber scanner, the material surface properties of the contacting plastics must be controlled to reduce friction. In one exemplary embodiment, the outer sheathing of the sub-mm scanning fiber endoscope is fabricated of slick polyethylene plastic (e.g., having a coefficient of friction < 0.3), and the inner surface of the cannula tube is formed of PolyTetraFluoroEthylene (PTFE – sold under the mark TEFLON™) coated polyurethane plastic. If necessary, an annular gap of about 0.2 mm can be maintained with small TEFLON™ standoff fins (not shown) adhered to the outside of the pre-assembled scanning fiber endoscope, reducing the area of contact and friction. The standoff fins formed from loops of plastic are expected to be attached to the scanning fiber endoscope by a friction fit.

[0080] At a proximal end, a water-tight seal between the interior surface of the cannula tube and the outer surface of the scanning fiber endoscope can be achieved by applying saline under pressure, as well as by removal of fluids by suction. Difficulties in extending the cannula beyond the scanning fiber endoscope may occur when the cannula is bent, either temporarily by the bending mechanism discussed above, or permanently, when using a bent-tip endoscope design. These difficulties can be minimized by maintaining the distal end of the cannula tool nearly flush with the distal end face of the scanning fiber endoscope during all image-guided cell sampling. A practical difficulty is that the saline used for lavage will cover the distal end of the scanning fiber endoscope lenses. Since the distal surface of the objective lens can be designed for both air and saline media, the forward-view (or side-view) image should not be distorted unless water droplets or bubbles are within the field of view. Previous scanning fiber endoscope lens designs optimized for air immersion have modeled the scanning fiber endoscope when immersed in saline, and the optimum focal length shifts slightly, but there is no apparent distortion in the scanning fiber endoscope image because of the long working distance objective lens assembly that has been provided for use in this exemplary embodiment by PENTAX Corporation. The annular gap in the cannula tools will be used to control the air/saline medium for immersion.

[0081] The cannula brush is a hollow tube constructed in a manner similar to the cannula for lavage except that the cannula brush includes short radial bristles at the distal tip for abrading the bronchiole lumen. At the proximal end of the cannula brush, there is an option for the lavage handling equipment since a lavage may be employed after brushing to insure that a sufficient quantity and quality of cells are collected. Since brushing captures cells within the bristles, the brush is likely to be a single-use device. A second site for cell sampling within a subject will require removal of the first cannula brush and insertion of a new, second cannula brush. Therefore, up to 10 cannula brushes will be fabricated once the optimal design is determined through consultations with the clinical collaborators.

[0082] The cannula tool for needle biopsy (like that shown in FIGURE 2C) will be the most novel tool for the clinicians since the bore size will be greater than standard needles used for fine needle aspirates (FNA) and core biopsies. The needle is required for sampling cells that are not exposed on the lumens inner surface. Since the distal tip of the scanning fiber endoscope is rigid for about 12 mm in one exemplary embodiment, the rigid needle stock can be this long without affecting the scanning fiber endoscope navigation. One difficulty can arise when extending the needle past the scanning fiber endoscope and into tissue. An induced cough may be required during the procedure, which is often used for assisting the penetration of needles for minimally-invasive FNA sampling in humans. In addition, threaded outer needle stock may be tested *in vivo*. Another difficulty can arise when extracting the needle with a tissue sample, which can be assisted by applying suction to the needle at the proximal end or by twisting a customized needle having small barbs. Due to the unique scanned light illumination of the scanning fiber endoscope, the bronchial tissue can be observed much further down the peripheral airways than current bronchoscopes that use more diffuse illumination. Thus, as in the case of cannula tools for lavage and brushing, the image of the distal tissue surface will stay in focus as the needle is advanced over the guidewire-with-eyes toward the tissue, although the field of view will be greatly reduced. Although the bore size is greater than standard needles, it is expected that the ability to perform biopsy under direct vision will reduce the incidence of pneumothorax.

[0083] Although the concepts disclosed herein have been described in connection with the preferred form of practicing them and modifications thereto, those of ordinary skill in the art will understand that many other modifications can be made thereto within the scope of the claims that follow. Accordingly, it is not intended that the scope of these concepts in any way be limited by the above description, but instead be determined entirely by reference to the claims that follow.

The invention in which an exclusive right is claimed is defined by the following:

1. A catheter system with an imaging capability, for guiding a tool to a desired location within a body of a patient, comprising:

(a) an elongate flexible catheter shaft having proximal end and a distal end, said elongate flexible catheter shaft being adapted to be advanced within a body of a patient, to a desired location;

(b) an imaging scanner for imaging within a body of a patient, the imaging scanner being disposed within and at the distal end of the elongate flexible shaft, to enable imaging at least during one of:

(i) while the elongate flexible catheter shaft is being advanced within the body of a patient;

(ii) while the distal end of the elongate flexible body is disposed at a desired location within a body of a patient; and

(iii) while the elongate flexible catheter shaft is being withdrawn from within the body of a patient; and

(c) a cannula that includes a lumen sized and shaped to readily slide over the elongate flexible catheter shaft toward the distal end of the elongate flexible shaft, the cannula being adapted to be slid over the elongate flexible shaft and toward the desired location, the elongate flexible shaft thus serving as a guidewire for positioning the cannula at a desired location within a body of a patient.

2. The catheter system of Claim 1, wherein the cannula is sized sufficiently larger than the elongate flexible catheter shaft to provide a generally annular passage around an outer perimeter of the elongate flexible shaft, so that the annular passage is adapted to convey a lavage fluid for collecting cells from a desired location within a body of a patient.

3. The catheter system of Claim 2, further comprising a pump in fluid communication with the annular passage, said pump being configured for extracting cells comprising a biopsy sample through the annular passage from a distal end of the cannula by drawing the biopsy sample with a fluid through the lumen, toward the proximal end of the elongate flexible catheter shaft.

4. The catheter system of Claim 3, wherein when the cannula is disposed proximate to tissue, the pump applies a negative pressure that draws the tissue and the cannula toward each other.

5. The catheter system of Claim 3, wherein the cannula includes a plurality of outwardly extending abrasive points disposed at spaced-apart positions on the exterior surface of the cannula, proximate to a distal end thereof, said abrasive points abrading cells from an internal site within a body of a patient for collection as a biopsy sample.

6. The catheter system of Claim 5, further comprising a plurality of orifices formed in the cannula proximate to the spaced-apart positions where the plurality of outwardly extending abrasive points are disposed, so that the plurality of orifices provide fluid communication paths for cells conveyed with a fluid to pass into the annular passage and be drawn by the pump through the annular passage toward the proximal end of the cannula.

7. The catheter system of Claim 3, further comprising a biopsy trap disposed between and in fluid communication with the pump and the proximal end of the cannula, the biopsy trap serving to trap cells and tissue comprising a biopsy sample after the biopsy sample exits from the cannula.

8. The catheter system of Claim 3, wherein the cannula includes a balloon that is disposed around an exterior of the cannula adjacent to the distal end of the cannula, an outer surface of the balloon having an abrasive coating so that when the balloon is selectively inflated while the distal end of the cannula is disposed at an internal site with a body of a patient, and the cannula is moved while the abrasive coating is in contact with tissue at the internal site, cells are dislodged from the tissue by the abrasive coating on the balloon and are drawn with a fluid into and through the annular passage by the pump, toward the proximal end of the cannula.

9. The catheter system of Claim 1, wherein the cannula includes a plurality of short bristles that extend outwardly of an outer surface of the cannula to provide a brush that dislodges cells and collects the cells dislodged from tissue at a desired location within a body of a patient.

10. The catheter system of Claim 1, wherein the cannula has a sharpened distal end adapted to pierce tissue and collect cells dislodged from tissue at a desired location within a body of a patient.

11. The catheter system of Claim 1, wherein the cannula comprises forceps that include jaw that can selectively be opened and closed, the jaws being configured so that when closed on tissue, the tissue can be withdrawn with the cannula as a biopsy sample, from an internal site within a body of a patient.

12. The catheter system of Claim 1, wherein the cannula comprises a snare loop that extends generally distal of a distal end of the cannula, the snare loop being employed to cut away tissue comprising a biopsy sample from an internal site within a body of a patient.

13. The catheter system of Claim 12, wherein the snare loop is coupled to a power supply that is selectively activated to heat the snare loop with an electrical current sufficiently to cut through tissue, thereby freeing the biopsy sample from adjacent tissue.

14. The catheter system of Claim 12, wherein the snare loop is coupled to a line that extends proximally and is pulled to tighten the snare loop around tissue to cut the tissue from adjacent tissue.

15. The catheter system of Claim 1, wherein the cannula tool includes a helical member having a cutting blade formed on its distal end and disposed in the cannula, within an annular gap defined between an interior surface of the cannula and an outer surface of the elongate flexible catheter shaft, rotation of the cannula causing the cutting blade to cut free a piece of tissue comprising a biopsy sample at an internal site within a body of a patient, the piece of tissue being then drawn into and through the annular gap toward a proximal end of the cannula.

16. The catheter system of Claim 15, further comprising a prime mover, and a rotational driver that is configured to drivingly couple with the cannula where exposed outside a body of a patient, the prime mover causing the rotational driver to rotate the cannula about the elongate flexible catheter shaft so that the cutting blade is rotated into tissue to cut away the piece of tissue.

17. The catheter system of Claim 1, further including a passage for conveying a pressurized fluid, wherein the passage is configured to direct the pressurized fluid at a velocity sufficient to dislodge cells from tissue at a desired location within a body of a patient, the cells that are dislodged being withdrawn through the passage when a suction at a sub-ambient pressure is applied in fluid communication with a proximal end of the passage.

18. The catheter system of Claim 1, wherein the imaging scanner includes a scanning device selected from the group consisting of:

(a) a scanning optical fiber that is driven by actuators to move in a specific scanning pattern to optically scan an internal site with light to produce an image of the internal site; and

(b) a micro-mechanical electrical systems (MEMS) that has a scanning beam used to optically scan an internal site with light to produce an image of the internal site.

19. The catheter system of Claim 1, wherein the cannula includes an outer elongate sheath that is movable between a first position that protects a tool portion of the cannula during insertion and retraction of the cannula within a body of a patient, and a second position that exposes the tool portion, when the tool portion is disposed at the desired internal site.

20. The catheter system of Claim 1, wherein the cannula includes a guide collar disposed proximate to a distal end of the cannula, the guide collar being attached to one side of the cannula and having the lumen formed within the guide collar, the lumen being sized and configured to slide over the elongate flexible catheter shaft.

21. The catheter system of Claim 3, wherein the annular passage serves to convey cells toward a proximal end of the cannula after the cells are released from tissue at a desired site as a result of an explosive thermal heating caused by a focused light beam transmitted from the imaging scanner toward the tissue.

22. A system for guiding a cannula that includes a tool, to a desired position within a body of a patient while imaging a path along which the system is being advanced or withdrawn, comprising:

(a) a flexible elongate catheter;

(b) an imaging device disposed at a distal end of the flexible elongate catheter, the imaging device being adapted to produce an image signal corresponding to an image of tissue along the path followed as the flexible elongate catheter is introduced through a passage within a body of a patient, the imaging device enabling details of the path to be observed to assist introduction of the flexible elongate catheter along the path, to a desired position within a body of a patient; and

(c) a cannula having a lumen that is sized to slide freely along the flexible elongate catheter toward a desired position within a body of a patient, enabling the cannula to be guided by the flexible elongate catheter when advanced to a desired position within a body of a patient or while the flexible elongate catheter is being withdrawn from a body of a patient.

23. The system of Claim 22, wherein the tool comprising the cannula includes means for freeing a biopsy sample from tissue at a desired position within a body of a patient, the biopsy sample comprising cells or a piece of the tissue.

24. The system of Claim 23, wherein the cannula includes a passage for carrying the biopsy sample toward a proximal end of the passage, for collection external to a body of a patient.

25. The system of Claim 22, further comprising a prime mover that applies a rotational force to the cannula to rotate the tool so that it interacts with tissue adjacent to the tool to free a biopsy sample from the tissue.

26. The system of Claim 22, wherein the imaging device comprises a scanning device selected from the group consisting of:

(a) a scanning optical fiber that is driven by actuators to move in a specific scanning pattern to optically scan an internal site with light to produce an image of the internal site; and

(b) a micro-mechanical electrical systems (MEMS) that has a scanning beam used to optically scan an internal site with light to produce an image of the internal site.

27. A system for guiding a tool to a desired location in a body of a patient, comprising:

(a) an elongate flexible catheter extending between a proximal end and a distal end;

(b) a scanning fiber device disposed at the distal end of the elongate flexible catheter, said scanning fiber device including an actuator that drives the scanning fiber in a desired pattern to scan a region, the scanning fiber device producing an output signal that is usable to produce an image of an internal site consisting of at least one of:

(i) tissue and anatomical structures while the elongate flexible catheter is being advanced along a path through a body of a patient, the image assisting in maneuvering the distal tip of the elongate flexible catheter to a desired location; and

(ii) tissue and anatomical structure after a distal tip of the elongate flexible catheter has been advanced to a desired location within a body of a patient; and

(c) a cannula having a lumen that is configured to be advanced over the elongate flexible catheter and guided thereby to a desired location within a body of a patient to which the distal tip of the elongate flexible catheter has been advanced.

28. The system of Claim 27, wherein the tool is adapted to free cells or a piece of tissue from a desired location within a body of a patient, the cells or the piece of tissue comprising a biopsy sample.

29. The system of Claim 28, wherein the cannula includes a passage through which the biopsy sample is drawn toward a proximal end of the cannula, for collection.

30. The system of Claim 29, further comprising:

(a) a pump for drawing the biopsy sample toward the proximal end of the cannula; and

(b) a trap disposed adjacent to the proximal end of the cannula, for collecting the biopsy sample.

31. The system of Claim 28, further comprising a rotational driver for rotating the cannula and the tool, so that the tool interacts with adjacent tissue to free the biopsy sample from the adjacent tissue.

32. The system of Claim 27, wherein the cannula includes a balloon disposed around an exterior surface of the cannula, adjacent to a distal end of the cannula, and a fluid passage through which a pressurized fluid is selectively communicated to an interior volume of the balloon to selectively inflate the balloon so that the balloon provides stabilization for the elongate flexible catheter while imaging an internal site with the scanning fiber device.

33. The system of Claim 27, wherein the tool includes a needle at a distal end of the cannula that is selectively thrust into tissue, said needle being used to carry out at least one function selected from the group consisting of:

(a) stabilizing the elongate flexible catheter while imaging with the scanning fiber device; and

(b) taking a biopsy sample from tissue at an internal site.

34. The system of Claim 33, wherein the needle includes angled points disposed around a bevel edge of the needle that engage the tissue as the needle is thrust into the tissue.

35. The system of Claim 28, wherein the tool comprises forceps having jaws that can be selectively closed to grasp tissue.

36. A system for guiding a tool to a desired location in a body of a patient, comprising:

(a) an elongate flexible catheter extending between a proximal end and a distal end;

(b) a resonant scanning beam device disposed at the distal end of the elongate flexible catheter, said resonant scanning beam device including an actuator that drives a scanning beam to move at about its resonant frequency, in a desired pattern, to optically scan a region, the scanning beam device producing an output signal that corresponds to an image of tissue; and

(c) a cannula that is configured to be advanced over the elongate flexible catheter and to be guided thereby to a desired location within a body of a patient to which the distal tip of the elongate flexible catheter has been advanced.

37. The system of Claim 36, wherein the cannula includes a tool for taking a biopsy sample comprising either cells or a piece of tissue from the desired location.

38. A system for carrying out an image-guided biopsy at a desired location in a body of a patient, comprising:

(a) a flexible elongate catheter having a distal end and a proximal end, a cross-sectional diameter of the flexible elongate catheter being less than 2 millimeters;

(b) an imaging system disposed at the distal end of the flexible elongate catheter, the imaging system being configured to produce a high resolution image of a site proximate to the distal end of the flexible elongate catheter; and

(c) a cannula that is sized and shaped to slide freely over the flexible elongate catheter and to be guided by the flexible elongate catheter toward a desired location in a body of a patient, the imaging system producing an image of tissue at a desired location to provide visual guidance for taking a biopsy sample of tissue at the desired location.

39. The system of Claim 38, wherein the cannula includes a tool for taking the biopsy sample.

AMENDED CLAIMS
received by the International Bureau on 04 August 2008 (04.08.2008).

1. A catheter system with an imaging capability, for guiding a tool to a desired location within a body of a patient, comprising:

(a) an elongate flexible catheter shaft having proximal end and a distal end, said elongate flexible catheter shaft being adapted to be advanced within a body of a patient, to a desired location;

(b) an imaging scanner for imaging within a body of a patient, the imaging scanner being disposed within and at the distal end of the elongate flexible shaft, to enable imaging at least during one of:

(i) while the elongate flexible catheter shaft is being advanced within the body of a patient;

(ii) while the distal end of the elongate flexible catheter shaft is disposed at a desired location within a body of a patient; and

(iii) while the elongate flexible catheter shaft is being withdrawn from within the body of a patient; and

(c) a cannula that includes a lumen sized and shaped to readily slide over the elongate flexible catheter shaft toward the distal end of the elongate flexible shaft, the cannula being adapted to be independently slid over the elongate flexible shaft and toward the desired location such that any advancement beyond the distal end of the elongate flexible shaft is not restricted, the elongate flexible shaft thus serving as a guidewire for positioning the cannula at a desired location within a body of a patient.

2. The catheter system of Claim 1, wherein the cannula is sized sufficiently larger than the elongate flexible catheter shaft to provide a generally annular passage around an outer perimeter of the elongate flexible shaft, so that the annular passage is adapted to convey a lavage fluid for collecting cells from a desired location within a body of a patient.

3. The catheter system of Claim 2, further comprising a pump in fluid communication with the annular passage, said pump being configured for extracting cells comprising a biopsy sample through the annular passage from a distal end of the cannula by drawing the biopsy sample with a fluid through the lumen, toward the proximal end of the elongate flexible catheter shaft.

4. The catheter system of Claim 3, wherein when the cannula is disposed proximate to tissue, the pump applies a negative pressure that draws the tissue and the cannula toward each other.

5. The catheter system of Claim 3, wherein the cannula includes a plurality of outwardly extending abrasive points disposed at spaced-apart positions on the exterior surface of the cannula, proximate to a distal end thereof, said abrasive points abrading cells from an internal site within a body of a patient for collection as a biopsy sample.

6. The catheter system of Claim 5, further comprising a plurality of orifices formed in the cannula proximate to the spaced-apart positions where the plurality of outwardly extending abrasive points are disposed, so that the plurality of orifices provide fluid communication paths for cells conveyed with a fluid to pass into the annular passage and be drawn by the pump through the annular passage toward the proximal end of the cannula.

7. The catheter system of Claim 3, further comprising a biopsy trap disposed between and in fluid communication with the pump and the proximal end of the cannula, the biopsy trap serving to trap cells and tissue comprising a biopsy sample after the biopsy sample exits from the cannula.

8. The catheter system of Claim 3, wherein the cannula includes a balloon that is disposed around an exterior of the cannula adjacent to the distal end of the cannula, an outer surface of the balloon having an abrasive coating so that when the balloon is selectively inflated while the distal end of the cannula is disposed at an internal site with a body of a patient, and the cannula is moved while the abrasive coating is in contact with tissue at the internal site, cells are dislodged from the tissue by the abrasive coating on the balloon and are drawn with a fluid into and through the annular passage by the pump, toward the proximal end of the cannula.

9. The catheter system of Claim 1, wherein the cannula includes a plurality of short bristles that extend outwardly of an outer surface of the cannula to provide a brush that dislodges cells and collects the cells dislodged from tissue at a desired location within a body of a patient.

10. The catheter system of Claim 1, wherein the cannula has a sharpened distal end adapted to pierce tissue and collect cells dislodged from tissue at a desired location within a body of a patient.

11. The catheter system of Claim 1, wherein the cannula comprises forceps that include jaw that can selectively be opened and closed, the jaws being configured so that when closed on tissue, the tissue can be withdrawn with the cannula as a biopsy sample, from an internal site within a body of a patient.

12. The catheter system of Claim 1, wherein the cannula comprises a snare loop that extends generally distal of a distal end of the cannula, the snare loop being employed to cut away tissue comprising a biopsy sample from an internal site within a body of a patient.

13. The catheter system of Claim 12, wherein the snare loop is coupled to a power supply that is selectively activated to heat the snare loop with an electrical current sufficiently to cut through tissue, thereby freeing the biopsy sample from adjacent tissue.

14. The catheter system of Claim 12, wherein the snare loop is coupled to a line that extends proximally and is pulled to tighten the snare loop around tissue to cut the tissue from adjacent tissue.

15. The catheter system of Claim 1, wherein the cannula tool includes a helical member having a cutting blade formed on its distal end and disposed in the cannula, within an annular gap defined between an interior surface of the cannula and an outer surface of the elongate flexible catheter shaft, rotation of the cannula causing the cutting blade to cut free a piece of tissue comprising a biopsy sample at an internal site within a body of a patient, the piece of tissue being then drawn into and through the annular gap toward a proximal end of the cannula.

16. The catheter system of Claim 15, further comprising a prime mover, and a rotational driver that is configured to drivingly couple with the cannula where exposed outside a body of a patient, the prime mover causing the rotational driver to rotate the cannula about the elongate flexible catheter shaft so that the cutting blade is rotated into tissue to cut away the piece of tissue.

17. The catheter system of Claim 1, further including a passage for conveying a pressurized fluid, wherein the passage is configured to direct the pressurized fluid at a velocity sufficient to dislodge cells from tissue at a desired location within a body of a patient, the cells that are dislodged being withdrawn through the passage when a suction at a sub-ambient pressure is applied in fluid communication with a proximal end of the passage.

18. The catheter system of Claim 1, wherein the imaging scanner includes a scanning device selected from the group consisting of:

(a) a scanning optical fiber that is driven by actuators to move in a specific scanning pattern to optically scan an internal site with light to produce an image of the internal site; and

(b) a micro-mechanical electrical systems (MEMS) that has a scanning beam used to optically scan an internal site with light to produce an image of the internal site.

19. The catheter system of Claim 1, wherein the cannula includes an outer elongate sheath that is movable between a first position that protects a tool portion of the cannula during insertion and retraction of the cannula within a body of a patient, and a second position that exposes the tool portion, when the tool portion is disposed at the desired internal site.

20. The catheter system of Claim 1, wherein the cannula includes a guide collar disposed proximate to a distal end of the cannula, the guide collar being attached to one side of the cannula and having the lumen formed within the guide collar, the lumen being sized and configured to slide over the elongate flexible catheter shaft.

21. The catheter system of Claim 3, wherein the annular passage serves to convey cells toward a proximal end of the cannula after the cells are released from tissue at a desired site as a result of an explosive thermal heating caused by a focused light beam transmitted from the imaging scanner toward the tissue.

22. A system for guiding a cannula that includes a tool, to a desired position within a body of a patient while imaging a path along which the system is being advanced or withdrawn, comprising:

(a) a flexible elongate catheter;

(b) an imaging device disposed at a distal end of the flexible elongate catheter, the imaging device being adapted to produce an image signal corresponding to an image of tissue along the path followed as the flexible elongate catheter is introduced through a passage within a body of a patient, the imaging device enabling details of the path to be observed to assist introduction of the flexible elongate catheter along the path, to a desired position within a body of a patient; and

(c) a cannula having a lumen that is sized to slide freely and independently along the flexible elongate catheter toward a desired position within a body of a patient, configured such that a portion of it can be advanced past the distal end of the catheter if necessary, enabling the cannula to be guided by the flexible elongate catheter when advanced to a desired position within a body of a patient or while the flexible elongate catheter is being withdrawn from a body of a patient.

23. The system of Claim 22, wherein the tool comprising the cannula includes means for freeing a biopsy sample from tissue at a desired position within a body of a patient, the biopsy sample comprising cells or a piece of the tissue.

24. The system of Claim 23, wherein the cannula includes a passage for carrying the biopsy sample toward a proximal end of the passage, for collection external to a body of a patient.

25. The system of Claim 22, further comprising a prime mover that applies a rotational force to the cannula to rotate the tool so that it interacts with tissue adjacent to the tool to free a biopsy sample from the tissue.

26. The system of Claim 22, wherein the imaging device comprises a scanning device selected from the group consisting of:

(a) a scanning optical fiber that is driven by actuators to move in a specific scanning pattern to optically scan an internal site with light to produce an image of the internal site; and

(b) a micro-mechanical electrical systems (MEMS) that has a scanning beam used to optically scan an internal site with light to produce an image of the internal site.

27. A system for guiding a tool to a desired location in a body of a patient, comprising:

(a) an elongate flexible catheter extending between a proximal end and a distal end;

(b) a scanning fiber device disposed at the distal end of the elongate flexible catheter, said scanning fiber device including an actuator that drives the scanning fiber in a desired pattern to scan a region, the scanning fiber device producing an output signal that is usable to produce an image of an internal site consisting of at least one of:

(i) tissue and anatomical structures while the elongate flexible catheter is being advanced along a path through a body of a patient, the image assisting in maneuvering the distal tip of the elongate flexible catheter to a desired location; and

(ii) tissue and anatomical structure after a distal tip of the elongate flexible catheter has been advanced to a desired location within a body of a patient; and

(c) a cannula having a lumen that is configured to be independently advanced over the elongate flexible catheter and guided thereby to a desired location within a body of a patient to which the distal tip of the elongate flexible catheter has been advanced, said cannula configured such that it can be advanced forward of the distal tip of the catheter.

28. The system of Claim 27, wherein the tool is adapted to free cells or a piece of tissue from a desired location within a body of a patient, the cells or the piece of tissue comprising a biopsy sample.

29. The system of Claim 28, wherein the cannula includes a passage through which the biopsy sample is drawn toward a proximal end of the cannula, for collection.

30. The system of Claim 29, further comprising:

(a) a pump for drawing the biopsy sample toward the proximal end of the cannula; and

(b) a trap disposed adjacent to the proximal end of the cannula, for collecting the biopsy sample.

31. The system of Claim 28, further comprising a rotational driver for rotating the cannula and the tool, so that the tool interacts with adjacent tissue to free the biopsy sample from the adjacent tissue.

32. The system of Claim 27, wherein the cannula includes a balloon disposed around an exterior surface of the cannula, adjacent to a distal end of the cannula, and a fluid passage through which a pressurized fluid is selectively communicated to an interior volume of the balloon to selectively inflate the balloon so that the balloon provides stabilization for the elongate flexible catheter while imaging an internal site with the scanning fiber device.

33. The system of Claim 27, wherein the tool includes a needle at a distal end of the cannula that is selectively thrust into tissue, said needle being used to carry out at least one function selected from the group consisting of:

(a) stabilizing the elongate flexible catheter while imaging with the scanning fiber device; and

(b) taking a biopsy sample from tissue at an internal site.

34. The system of Claim 33, wherein the needle includes angled points disposed around a bevel edge of the needle that engage the tissue as the needle is thrust into the tissue.

35. The system of Claim 28, wherein the tool comprises forceps having jaws that can be selectively closed to grasp tissue.

36. A system for guiding a tool to a desired location in a body of a patient, comprising:

(a) an elongate flexible catheter extending between a proximal end and a distal end;

(b) a resonant scanning beam device disposed at the distal end of the elongate flexible catheter, said resonant scanning beam device including an actuator that drives a scanning beam to move at about its resonant frequency, in a desired pattern, to optically scan a region, the scanning beam device producing an output signal that corresponds to an image of tissue; and

(c) a cannula that is configured to be independently advanced over the elongate flexible catheter and to be guided thereby to a desired location within a body of a patient to which the distal tip of the elongate flexible catheter has been advanced, such that a portion of the cannula can extend beyond the distal tip of the elongate flexible catheter.

37. The system of Claim 36, wherein the cannula includes a tool for taking a biopsy sample comprising either cells or a piece of tissue from the desired location.

38. A system for carrying out an image-guided biopsy at a desired location in a body of a patient, comprising:

(a) a flexible elongate catheter having a distal end and a proximal end, a cross-sectional diameter of the flexible elongate catheter being less than 2 millimeters;

(b) an imaging system disposed at the distal end of the flexible elongate catheter, the imaging system being configured to produce a high resolution image of a site proximate to the distal end of the flexible elongate catheter; and

(c) a cannula that is sized and shaped to independently slide freely over the flexible elongate catheter and to be guided by the flexible elongate catheter toward a desired location in a body of a patient, said independent sliding motion enabling a portion of the cannula to be disposed at a point beyond the distal end of the catheter, if required, the imaging system producing an image of tissue at a desired location to provide visual guidance for taking a biopsy sample of tissue at the desired location.

39. The system of Claim 38, wherein the cannula includes a tool for taking the biopsy sample.

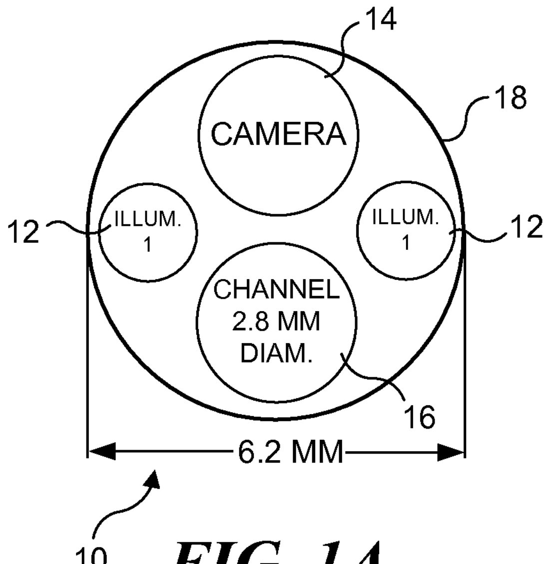


FIG. 1A (PRIOR ART)

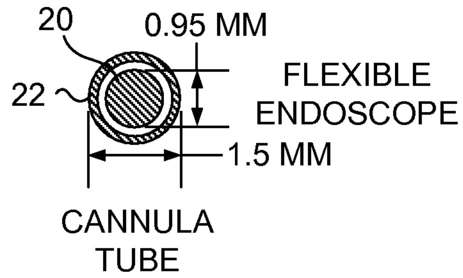


FIG. 1B

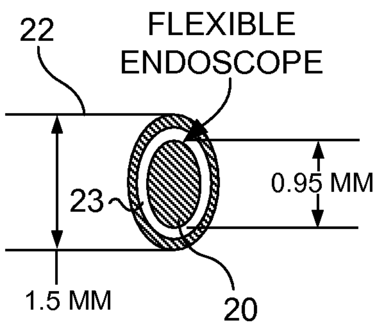


FIG. 2A

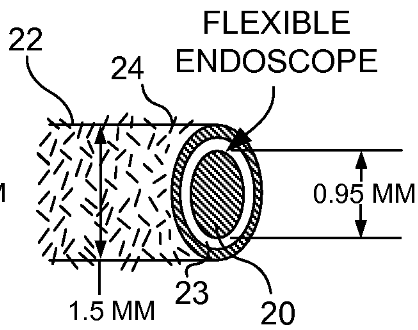


FIG. 2B

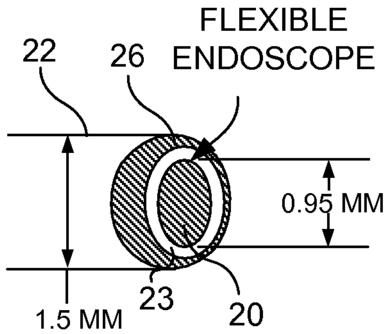


FIG. 2C

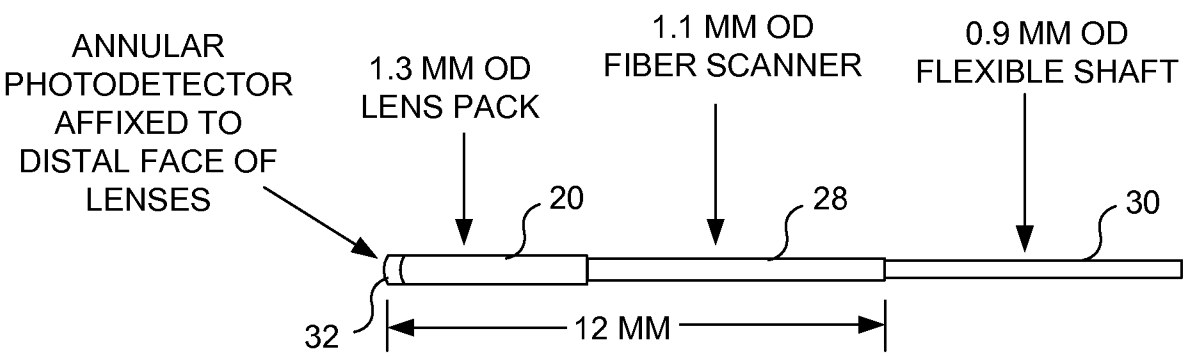


FIG. 3

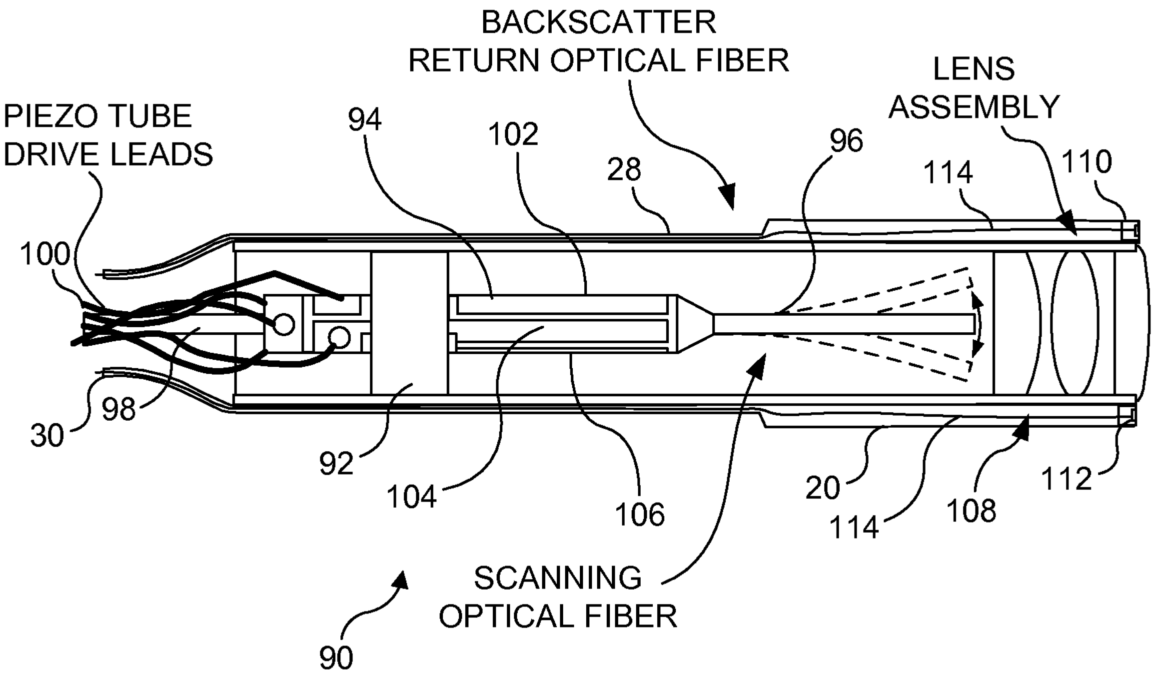

BACKSCATTER
RETURN OPTICAL FIBER
LENS
ASSEMBLY
PIEZO TUBE
DRIVE LEADS
94
102
96
28
114
110
100
30
98
92
104
106
20
114
108
112
SCANNING
OPTICAL FIBER
90

FIG. 4

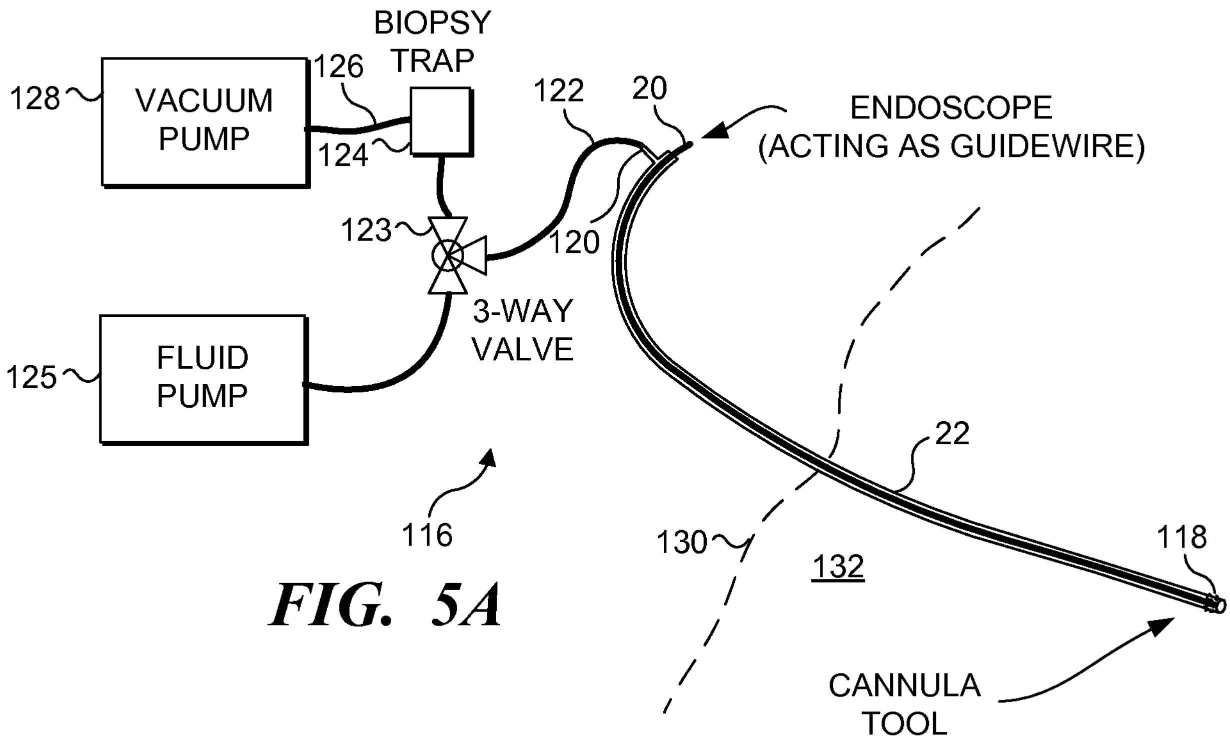
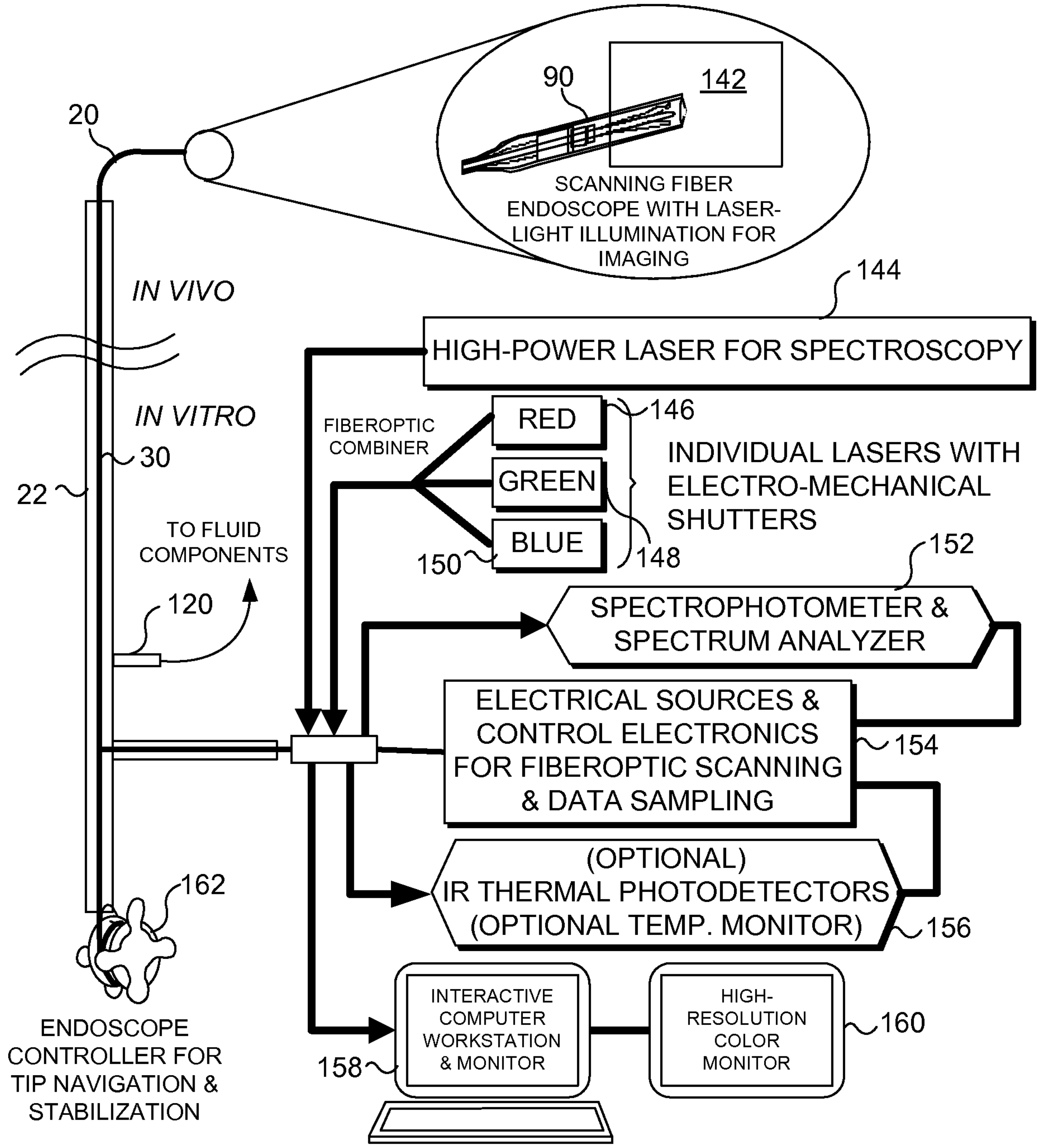

BIOPSY
TRAP
128
VACUUM
PUMP
126
124
122
20
ENDOSCOPE
(ACTING AS GUIDEWIRE)
123
120
3-WAY
VALVE
125
FLUID
PUMP
22
116
130
132
118
CANNULA
TOOL

FIG. 5A



COMPUTER WORKSTATION IS PROGRAMMED TO DETERMINE THE SITES FOR OPTICAL DIAGNOSIS AND ASSIST IN LASER DOSIMETRY, THEN AUTOMATICALLY DELIVER THE CORRECT OPTICAL RADIATION ON BOTH SPATIALLY & TEMPORALLY WHILE IMAGING. REAL-TIME MONITORING OF THERAPY IS DONE BY THERMAL OR SPECTRAL IMAGING.

FIG. 5C

140

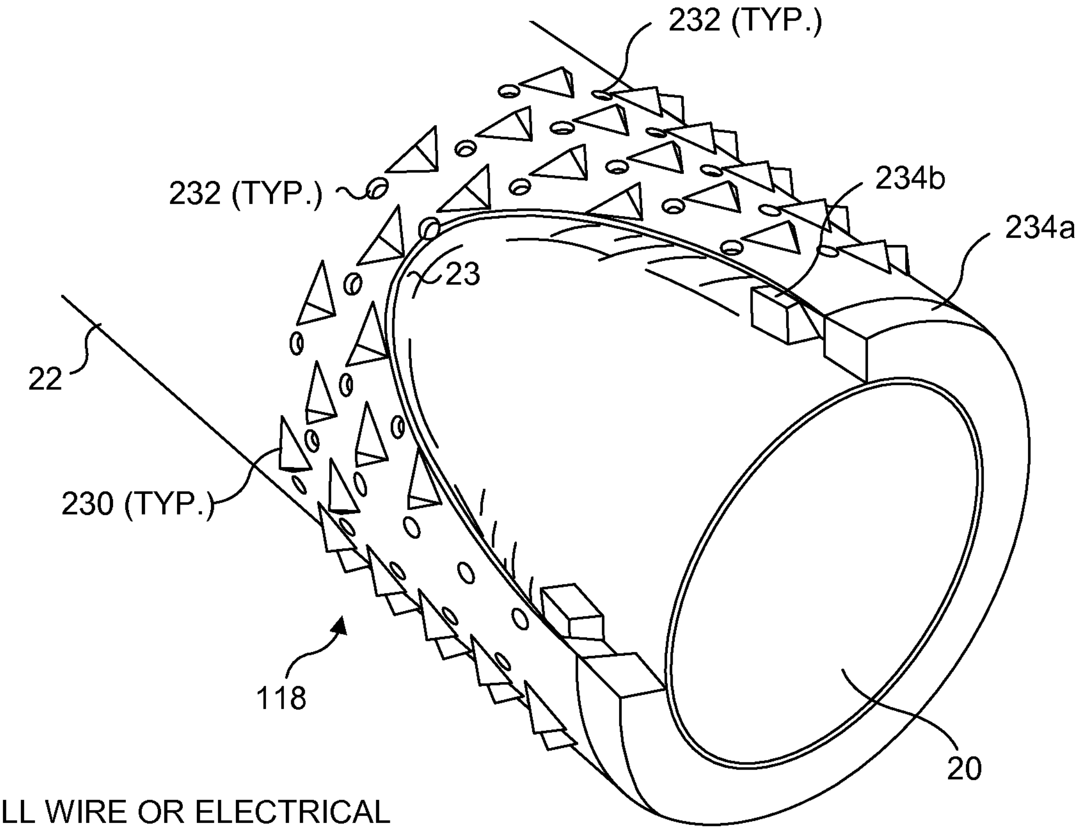

232 (TYP.)
232 (TYP.)
234b
234a
23
22
230 (TYP.)
118
20

FIG. 5B

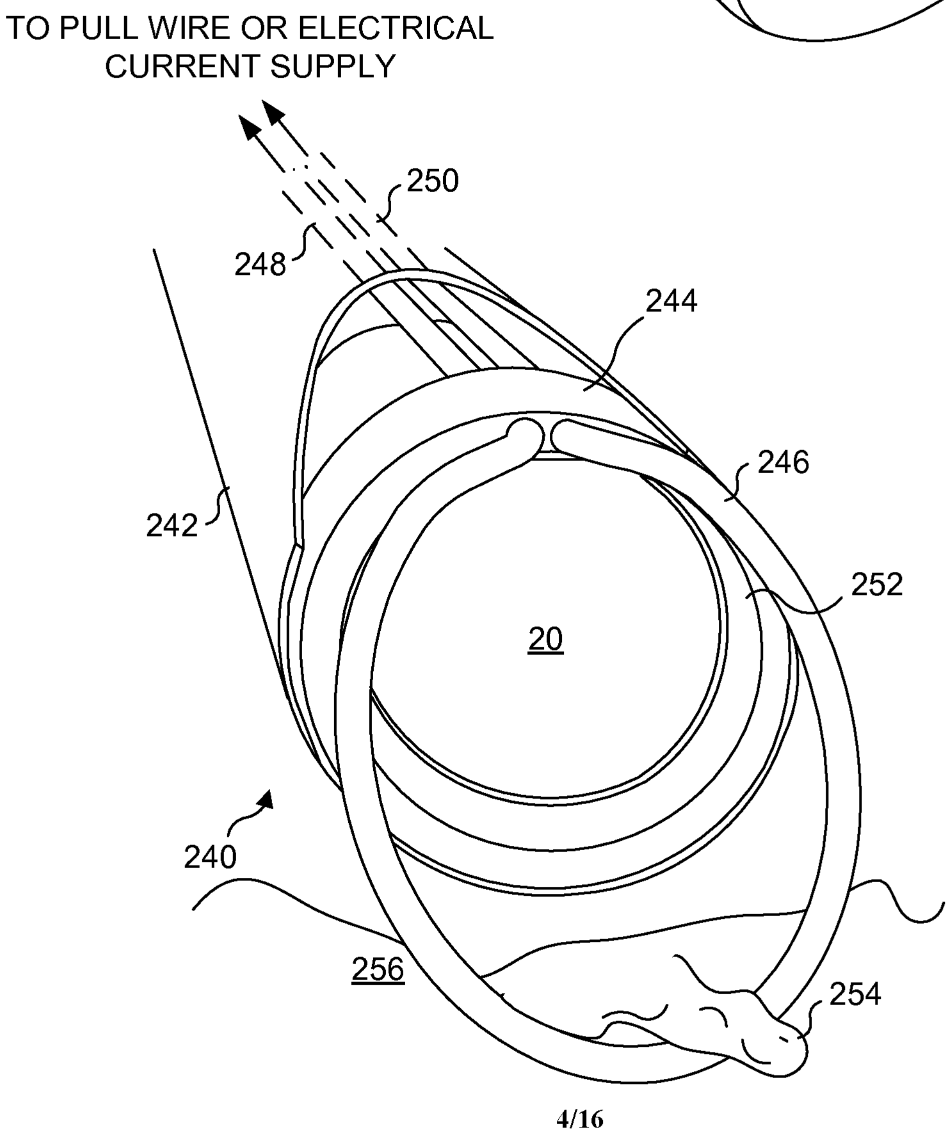

TO PULL WIRE OR ELECTRICAL CURRENT SUPPLY
250
248
244
246
242
252
20
240
256
254

FIG. 6

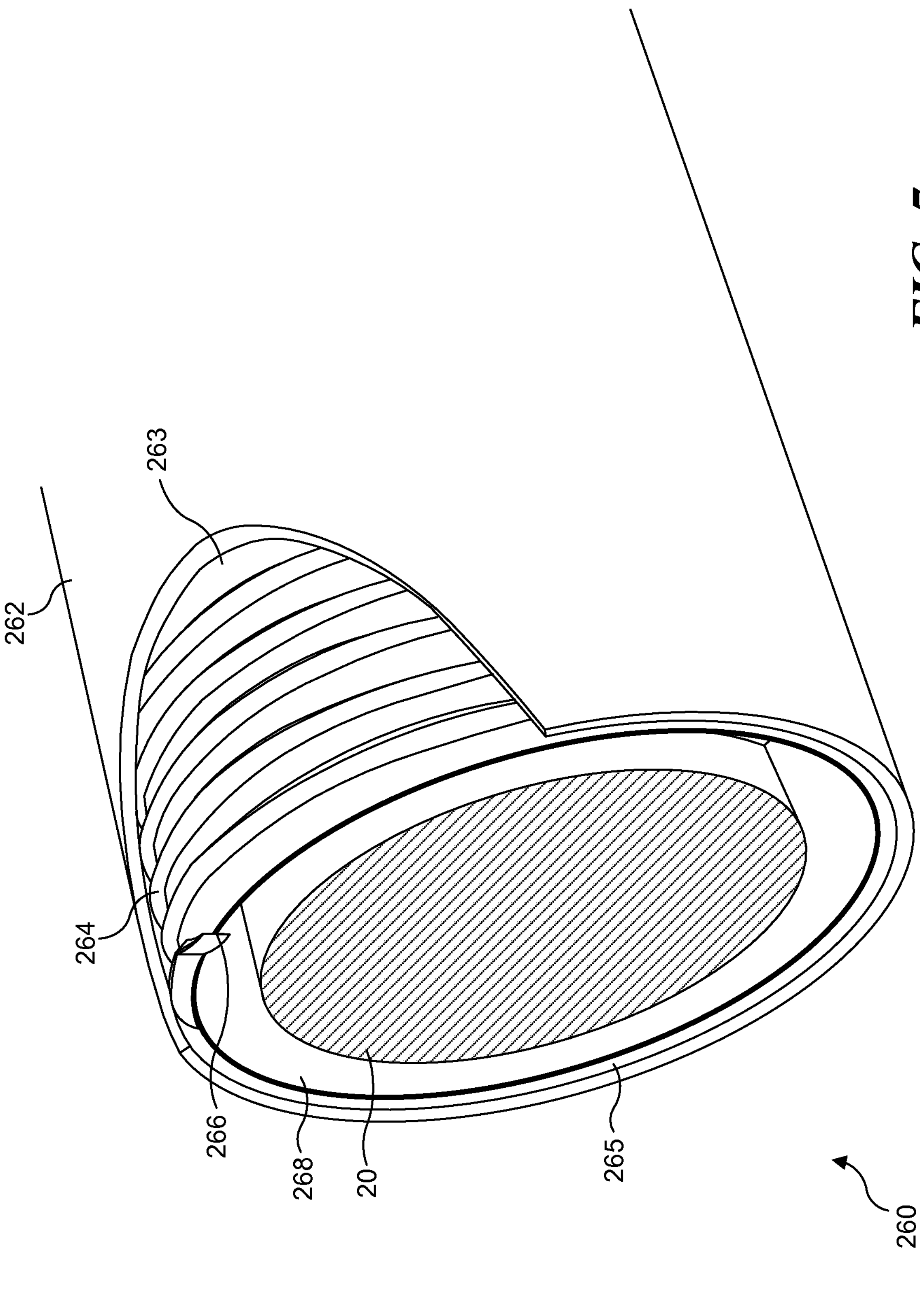


FIG. 7

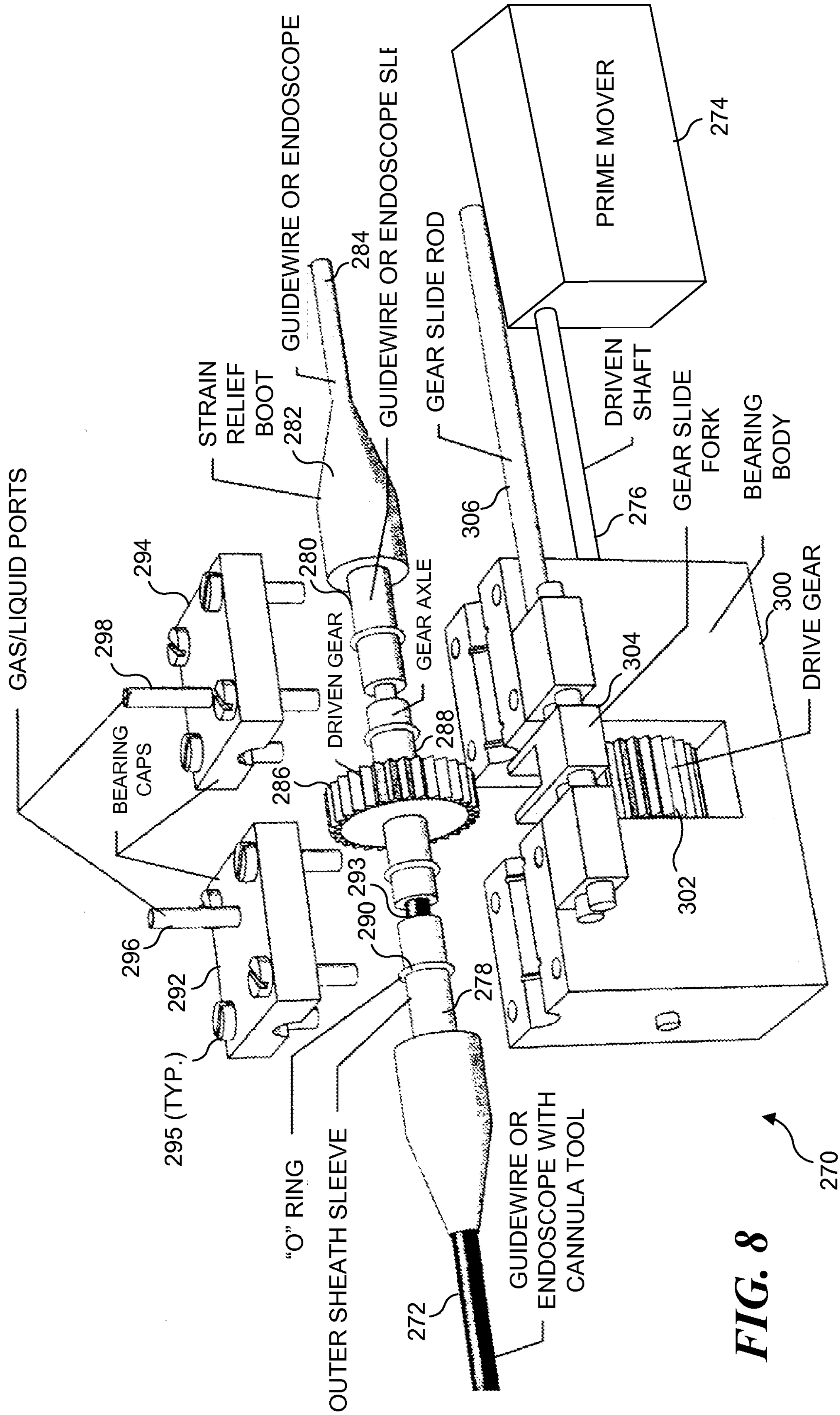

GUIDEWIRE OR ENDOSCOPE
GUIDEWIRE OR ENDOSCOPE SL
PRIME MOVER
274
284
GEAR SLIDE ROD
STRAIN
RELIEF
BOOT
282
DRIVEN
SHAFT
GEAR SLIDE
FORK
BEARING
BODY
306
276
GAS/LIQUID PORTS
294
280
GEAR AXLE
300
DRIVE GEAR
298
DRIVEN GEAR
304
BEARING
CAPS
288
286
302
293
296
290
292
278
295 (TYP.)
"O" RING
OUTER SHEATH SLEEVE
GUIDEWIRE OR
ENDOSCOPE WITH
CANNULA TOOL
272
270

FIG. 8

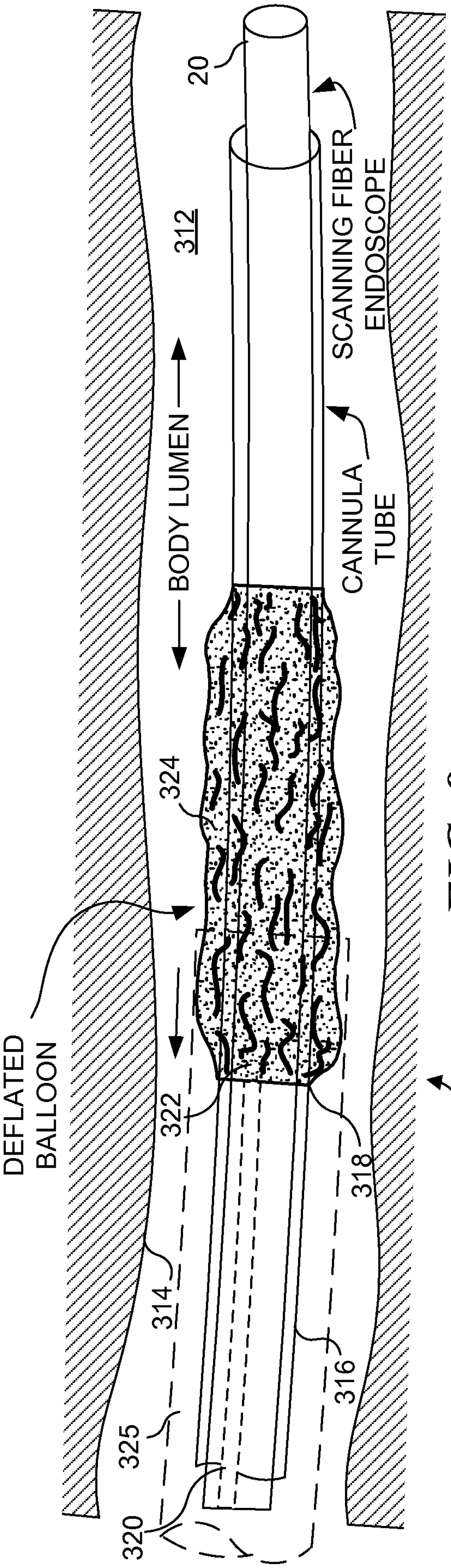

DEFLATED
BALLOON
20
SCANNING FIBER
ENDOSCOPE
312
BODY LUMEN
CANNULA
TUBE
324
322
318
310
314
316
325
320

FIG. 9

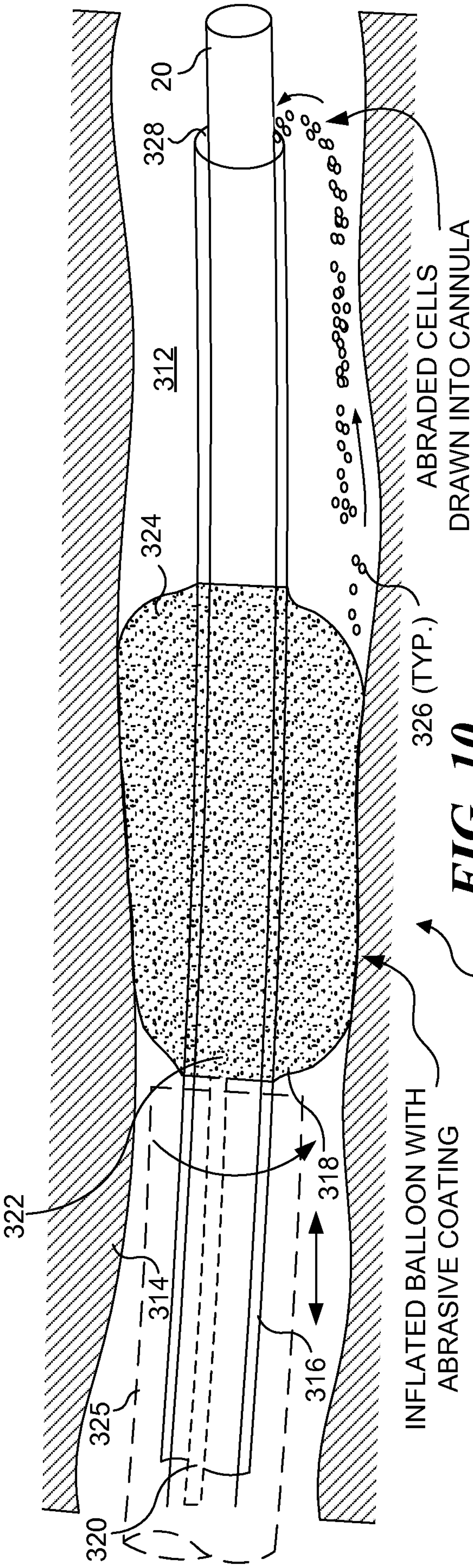

20
328
312
ABRADED CELLS
DRAWN INTO CANNULA
324
326 (TYP.)
310
INFLATED BALLOON WITH
ABRASIVE COATING
322
318
314
316
325
320

FIG. 10

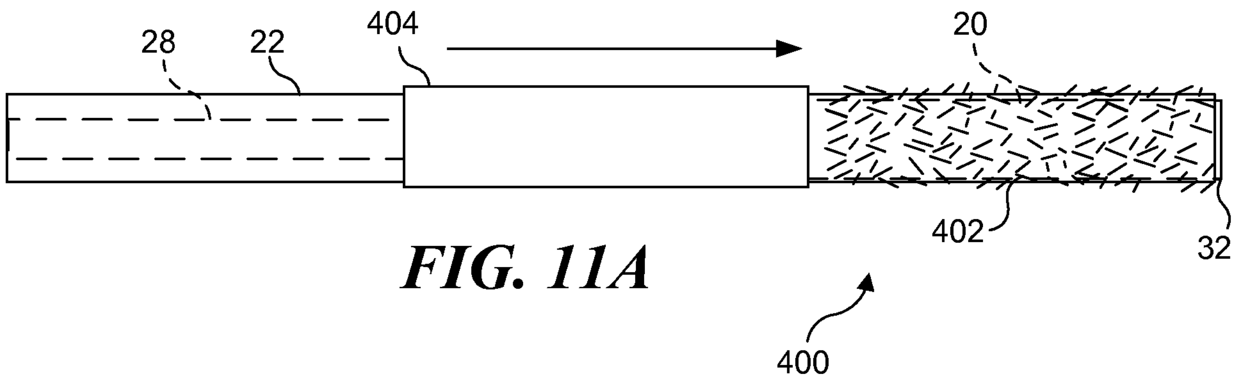


FIG. 11A

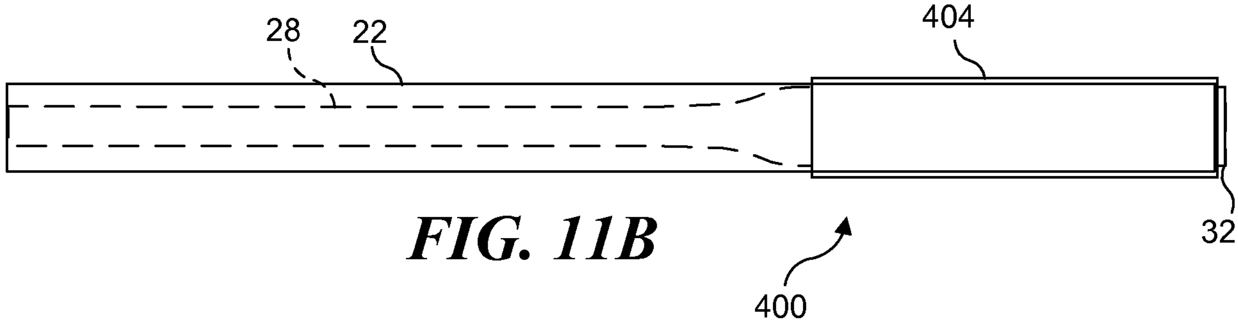


FIG. 11B

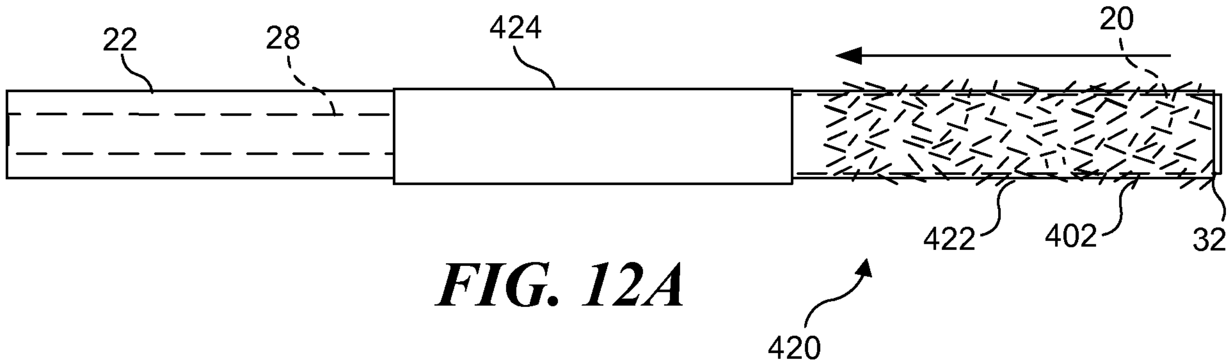


FIG. 12A

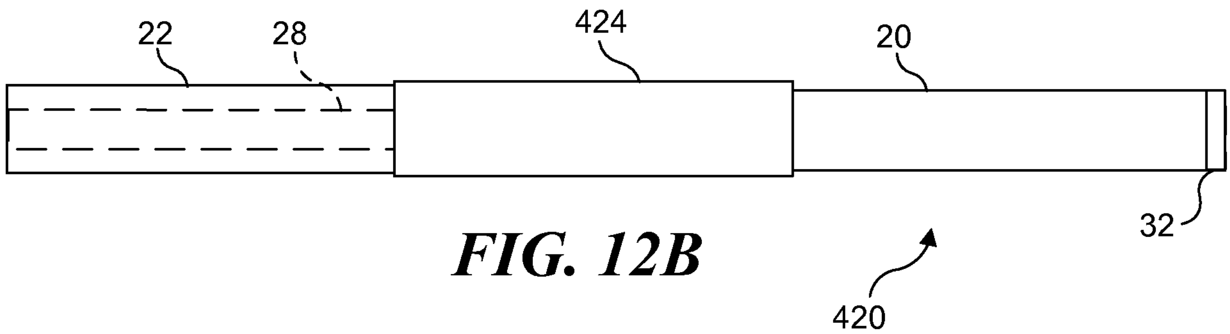


FIG. 12B

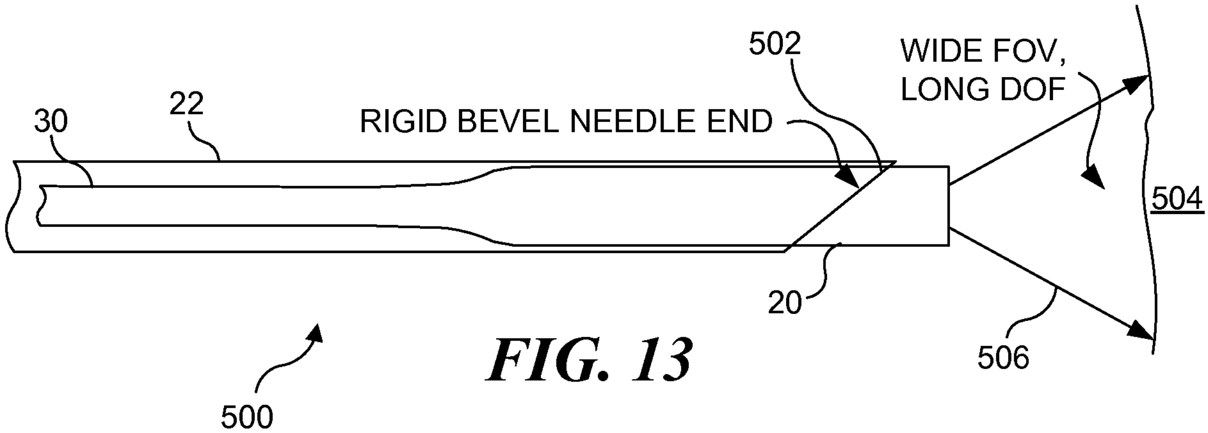


FIG. 13

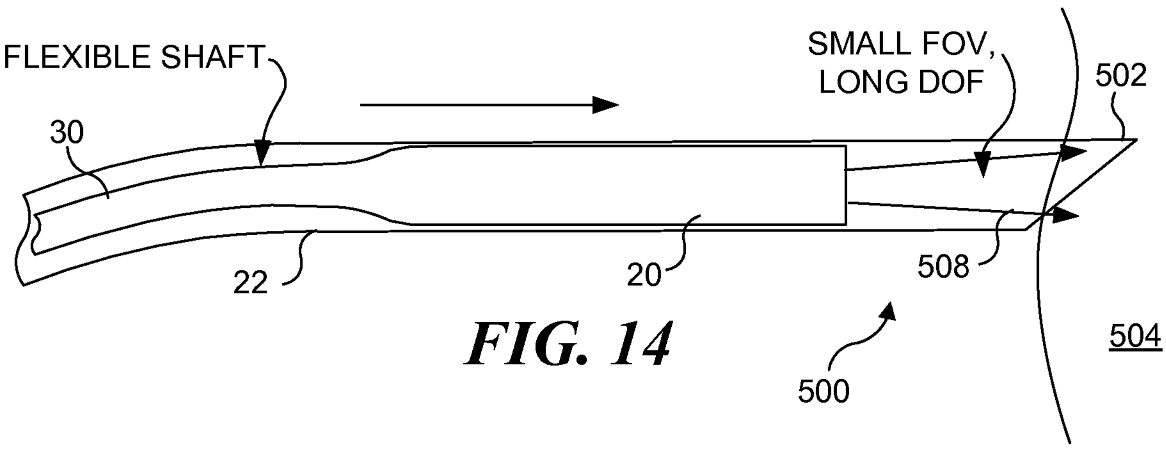


FIG. 14

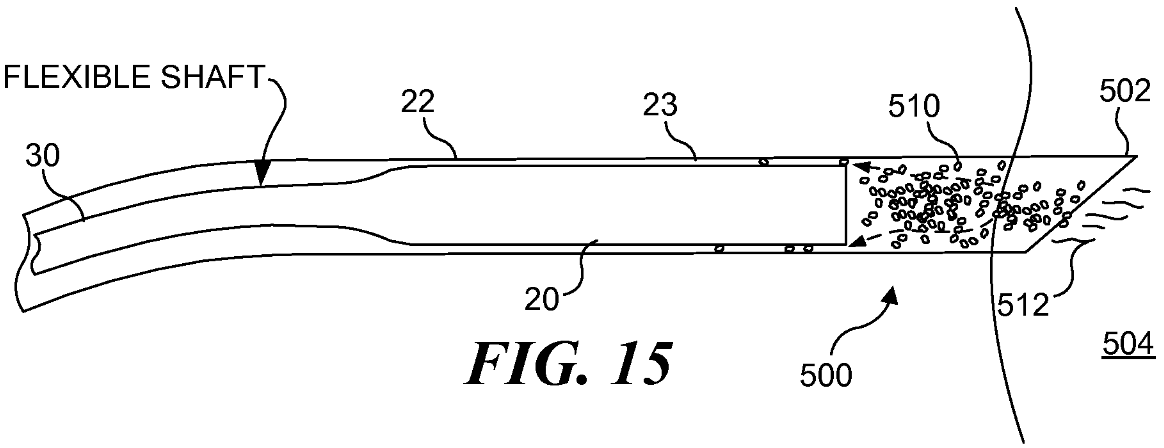


FIG. 15

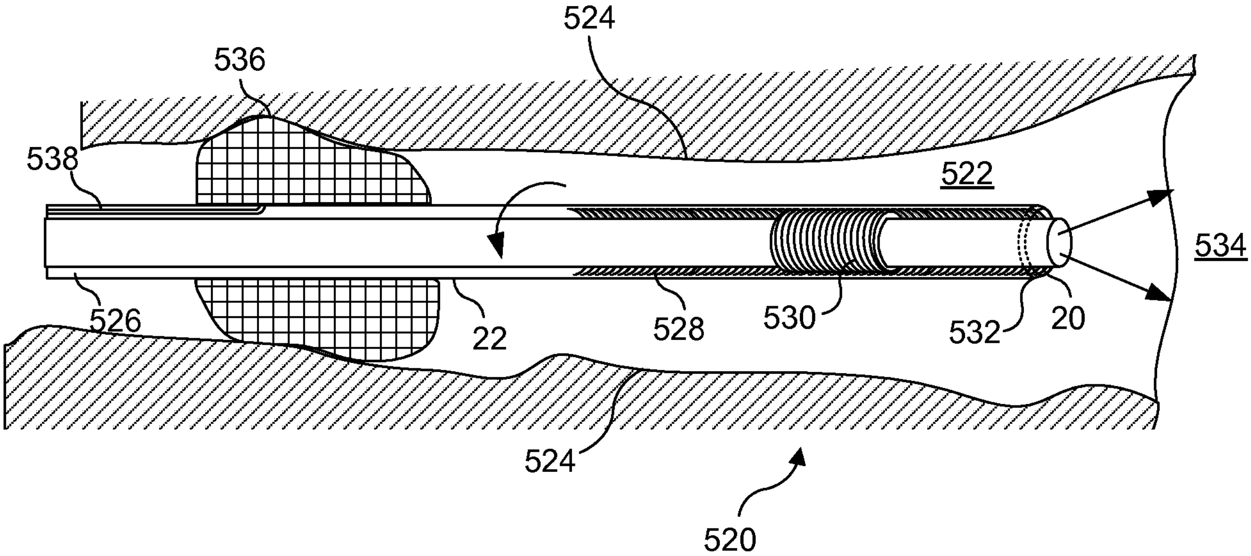


FIG. 16

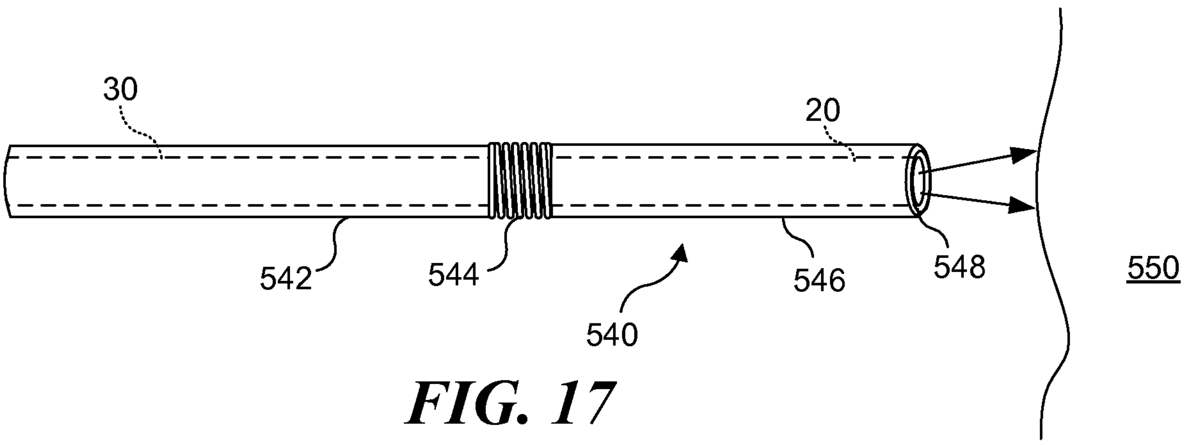


FIG. 17

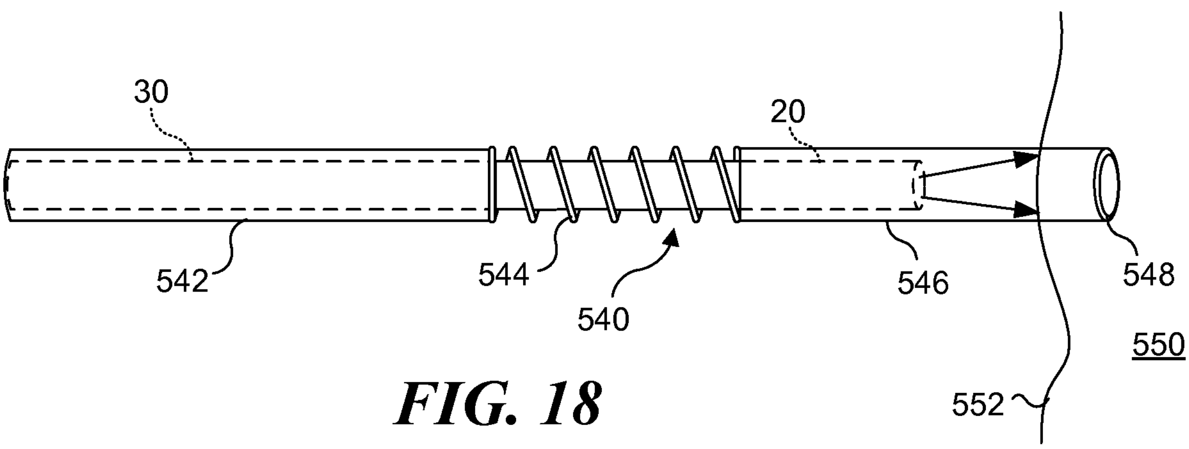


FIG. 18

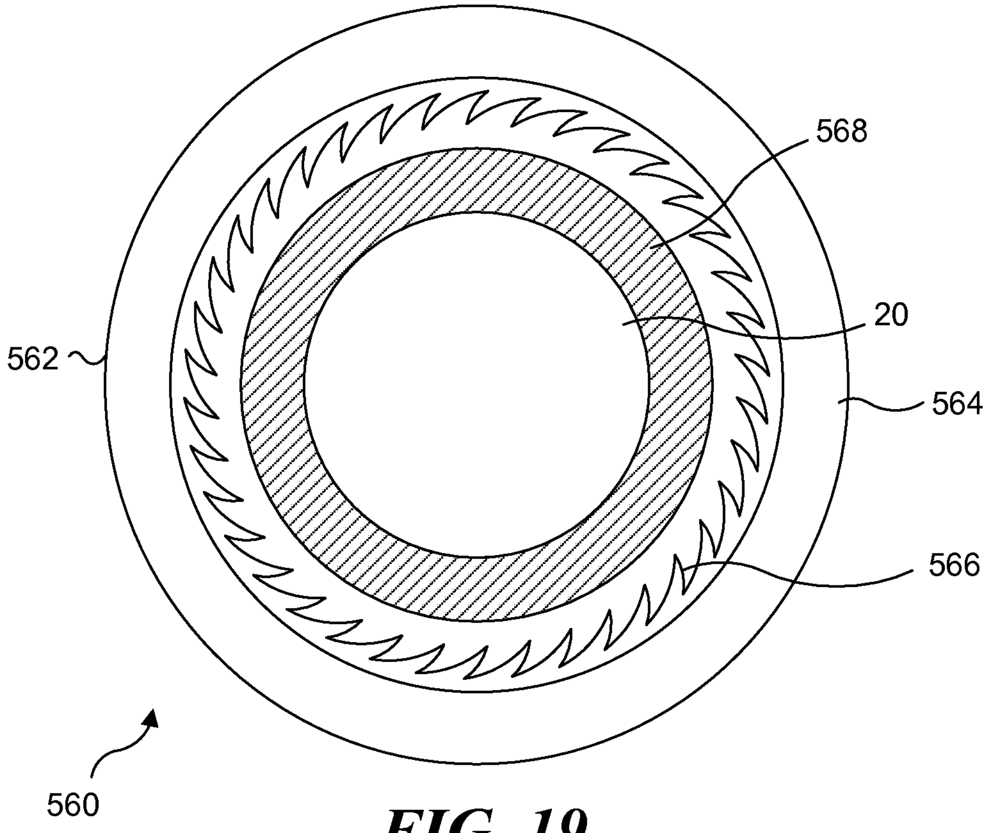


FIG. 19

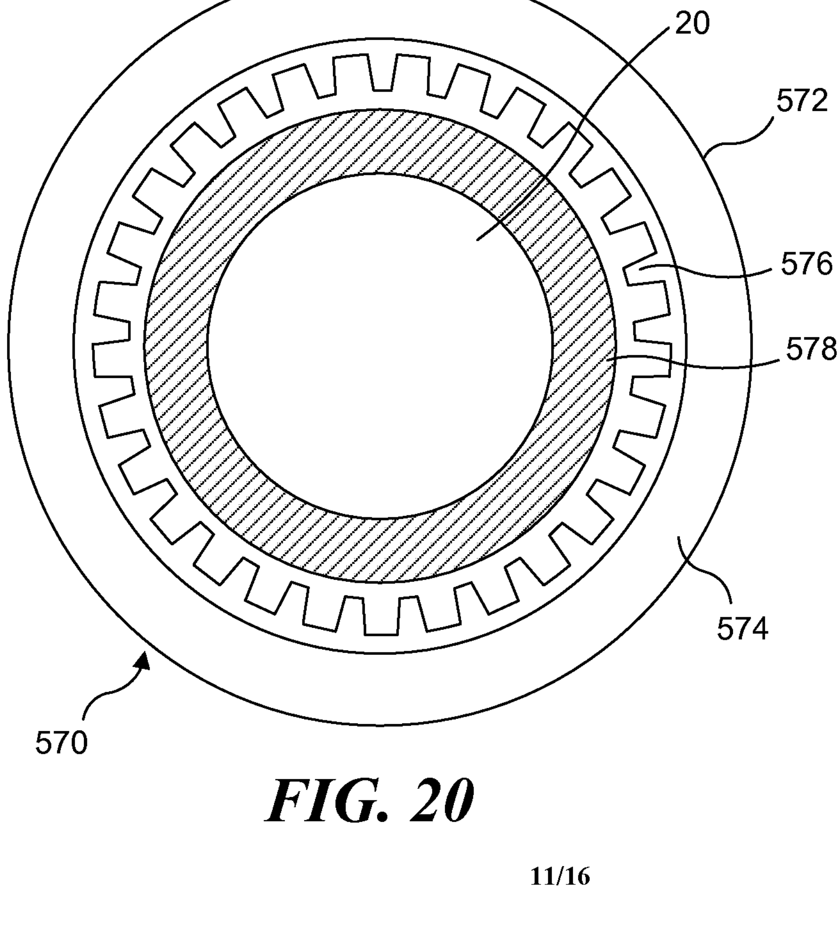


FIG. 20

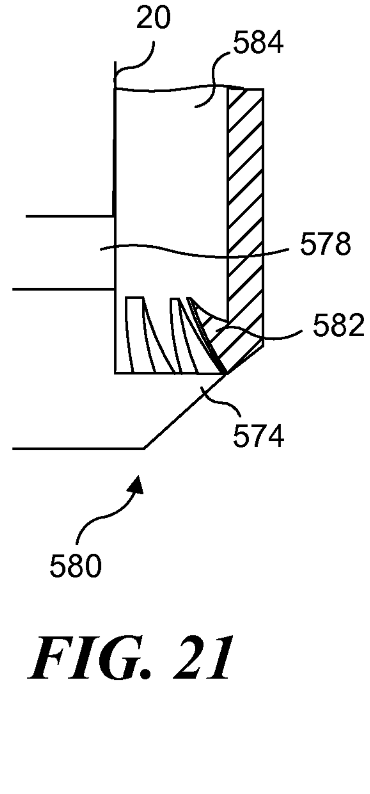


FIG. 21

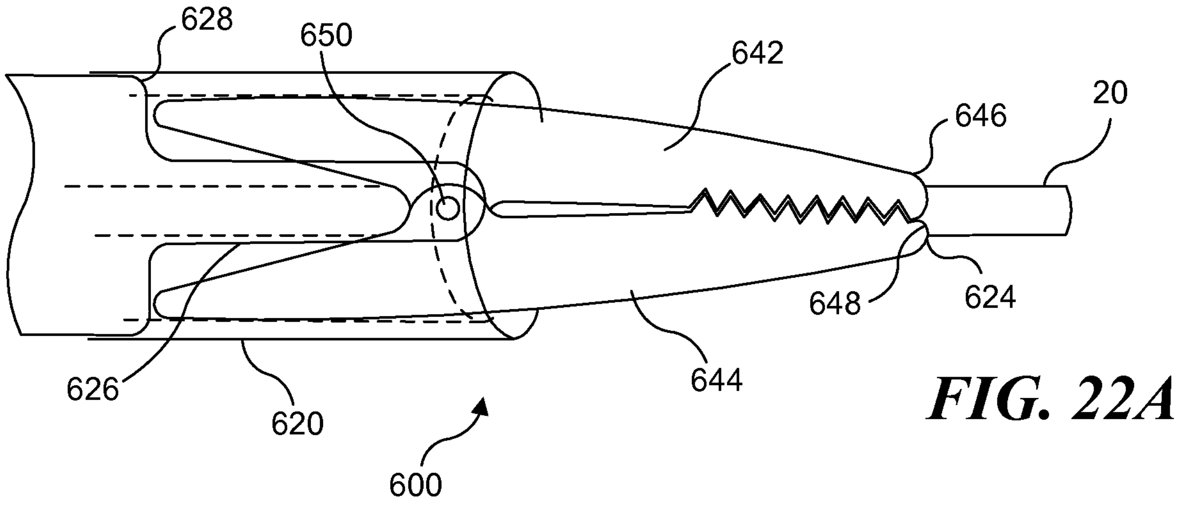


FIG. 22A

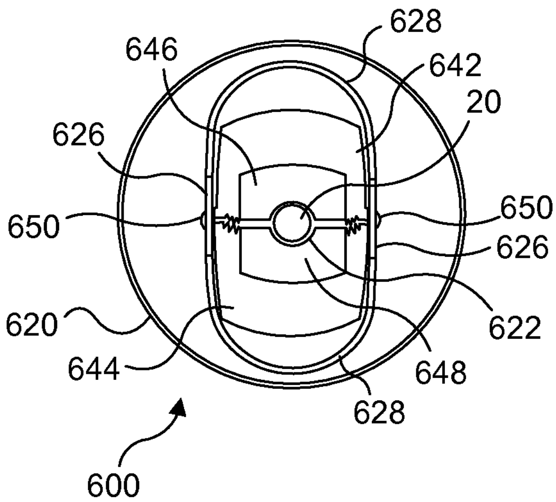


FIG. 22B

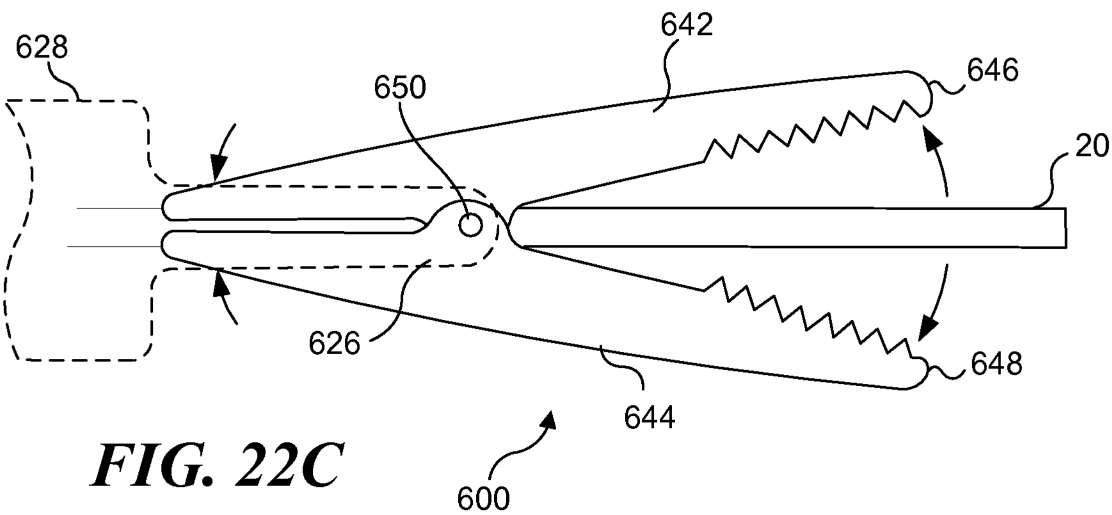


FIG. 22C

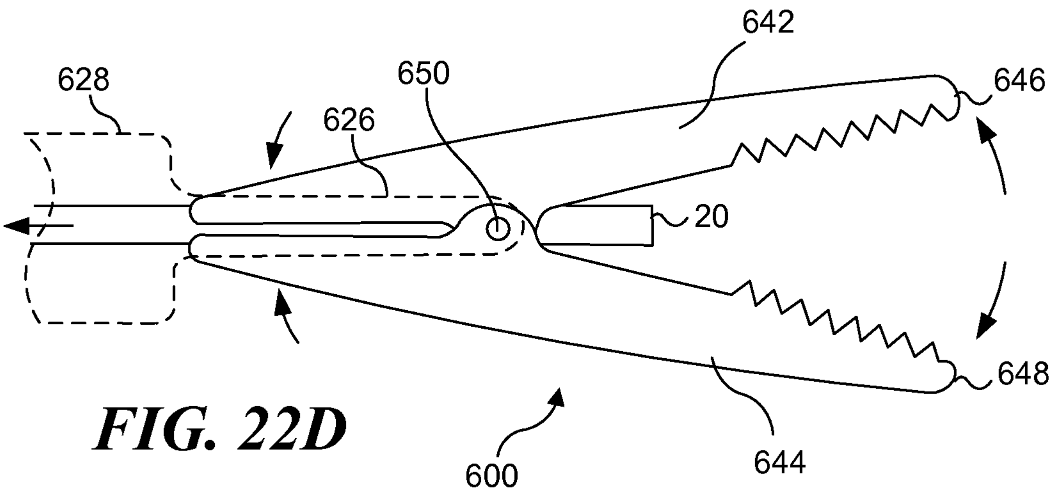


FIG. 22D

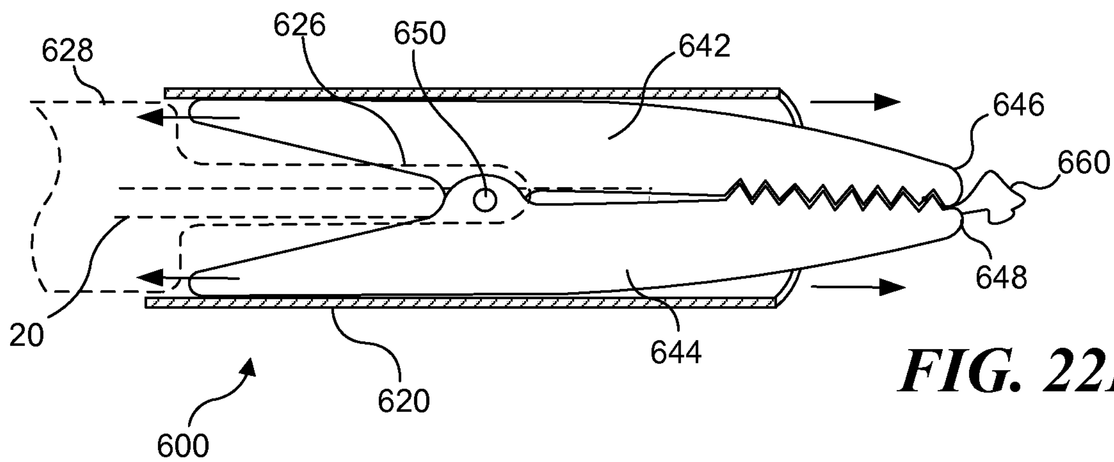


FIG. 22E

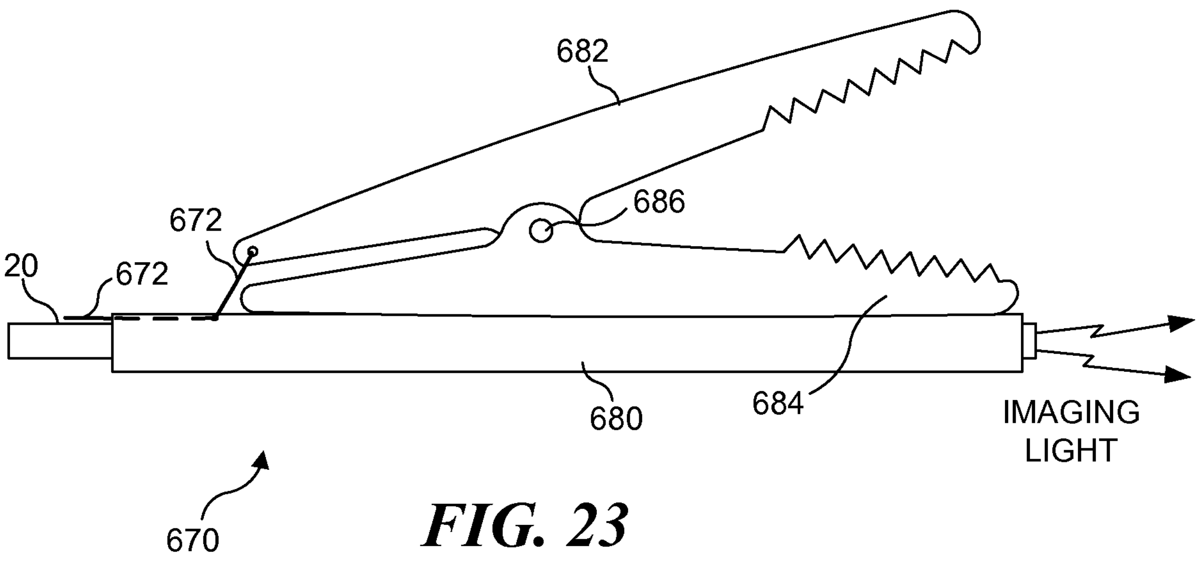


FIG. 23

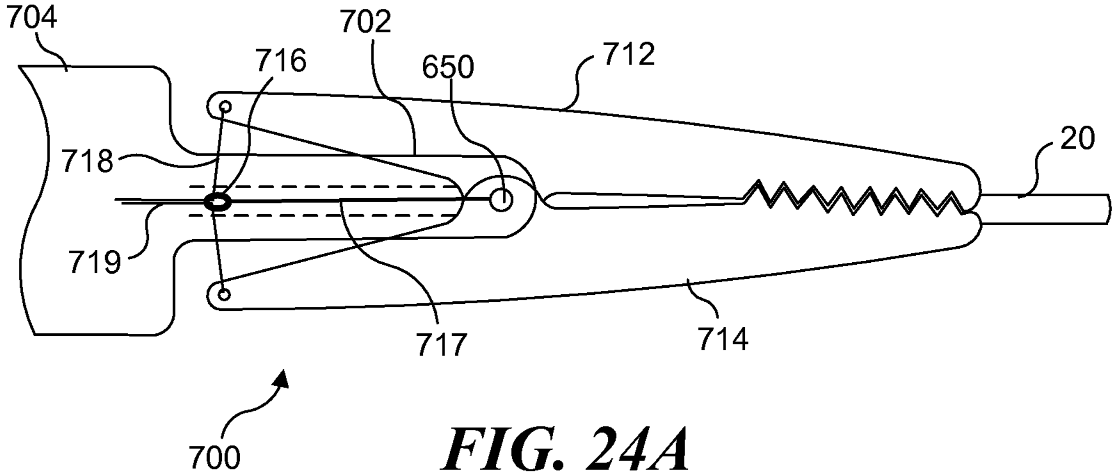


FIG. 24A

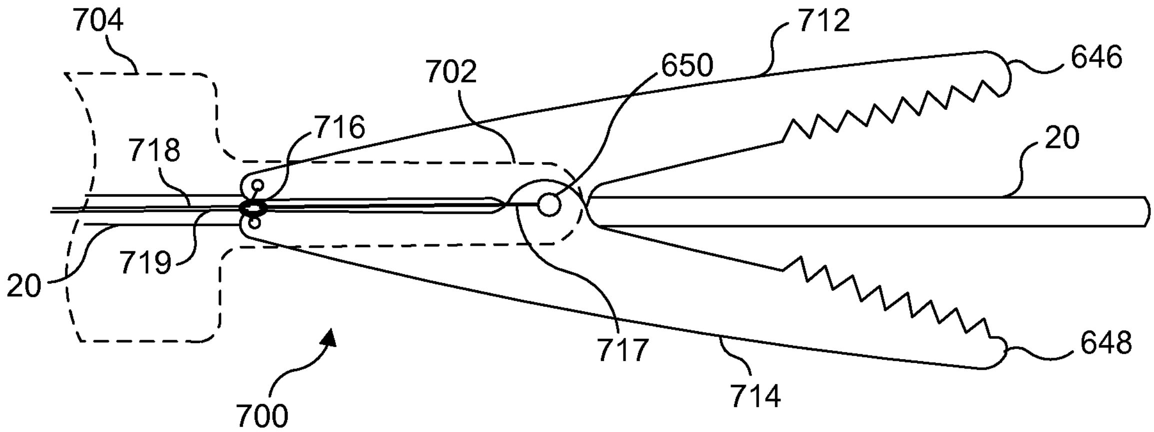


FIG. 24B

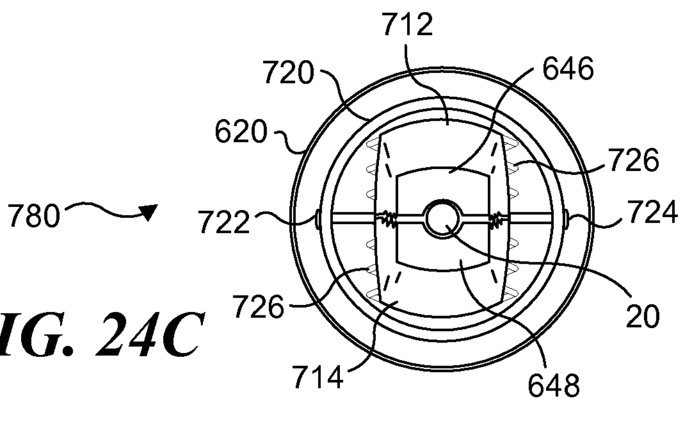


FIG. 24C

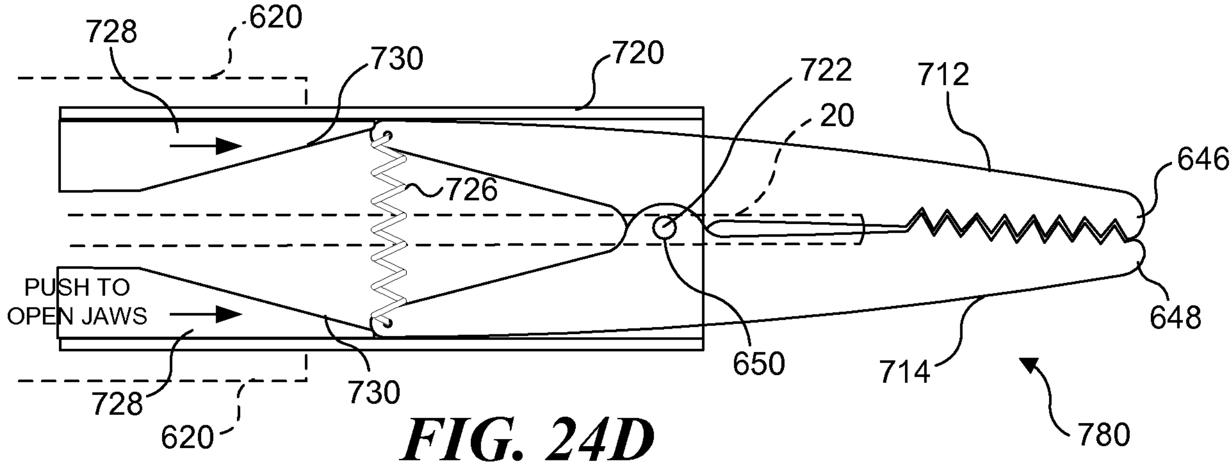


FIG. 24D

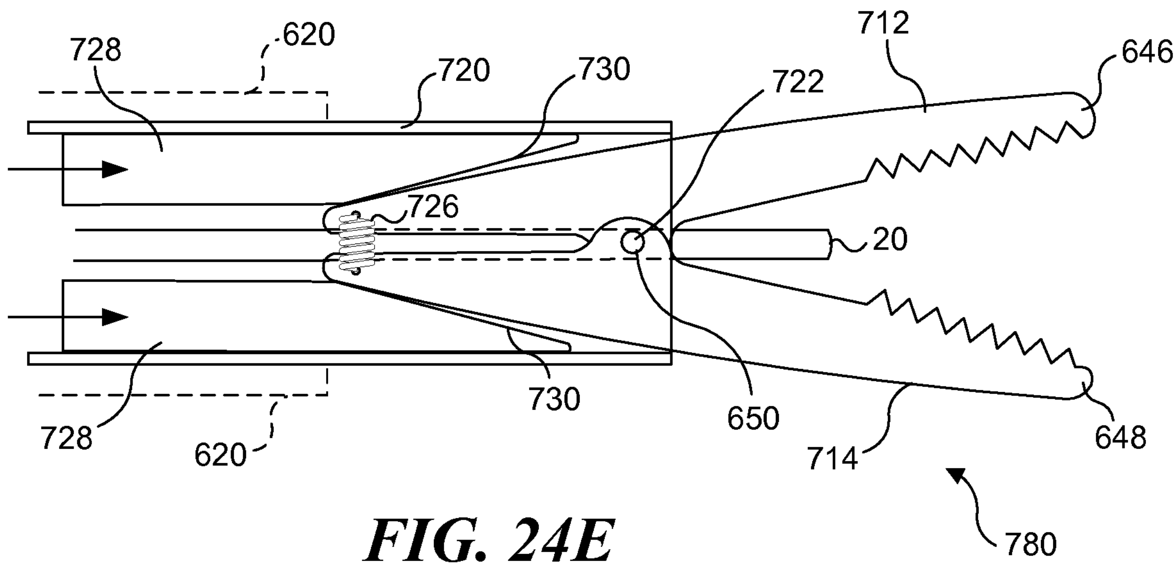


FIG. 24E

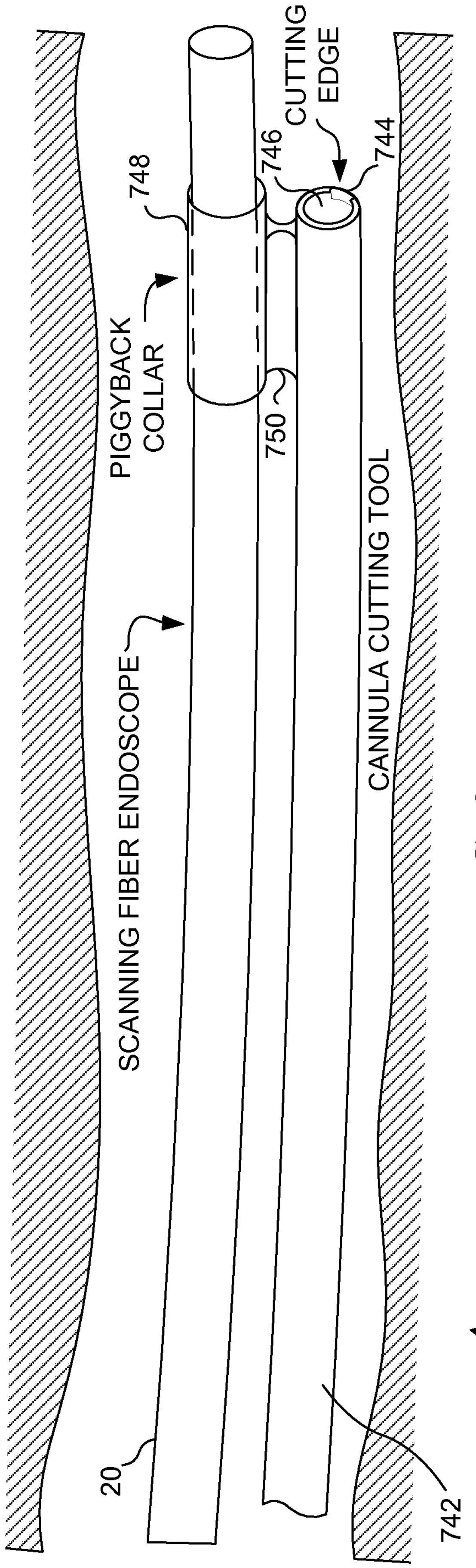

PIGGYBACK COLLAR
748
746
CUTTING EDGE
744
750
SCANNING FIBER ENDOSCOPE
CANNULA CUTTING TOOL
20
742
740

FIG. 25

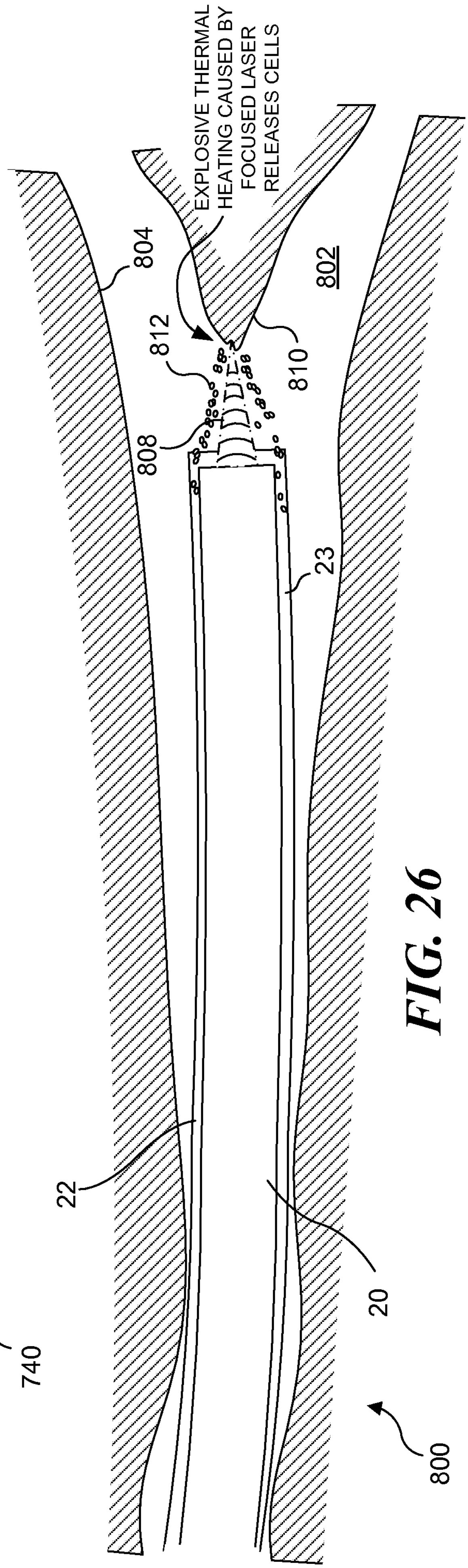

EXPLOSIVE THERMAL HEATING CAUSED BY FOCUSED LASER RELEASES CELLS
804
802
812
810
808
23
22
20
800

FIG. 26

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US07/65781

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61M 25/04 (2007.10)
USPC - 606/159; 604/528
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)
IPC(8) - A61M 25/04 (2007.10)
USPC - 606/159; 604/528

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)
USPTO EAST System (US, USPG-PUB, EPO, DERWENT), MicroPatent.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	US 2006/0015126 A1 (SHER) 19 January 2006 (19.01.2006) entire document	1-6, 10, 13-22, 26-29, 32-33, 38 -------- 7-9, 11-12, 23-25, 30-31, 34-37, 39
Y	US 2004/0199052 A1 (BANIK et al) 07 October 2004 (07.10.2004) entire document	7, 9, 11-12, 30
Y	US 2007/0066983 A1 (MASCHKE) 22 March 2007 (22.03.2007) entire document	25, 31, 37, 39
Y	US 5,919,200 A (STAMBAUGH et al) 06 July 1999 (06.07.1999) entire document	8, 23-24
Y	US 7,004,173 B1 (SPARKS et al) 28 February 2006 (28.02.2006) entire document	34-35
Y	US 2006/0195014 A1 (SEIBEL et al) 31 August 2006 (31.08.2006) entire document	36-37

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search
29 November 2007

Date of mailing of the international search report
28 DEC 2007

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450
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PCT OSP: 571-272-7774