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(57) Abstract: Methods, devices, and systems for accurately steering a biopsy needle into a lung region of interest via devices delivered through the bronchial tree.



WO 2015/123350 A2

METHODS AND DEVICE FOR BRONCHIAL INTERVENTION**CROSS REFERENCE TO RELATED APPLICATIONS**

[0001] This application claims priority to the following U.S. provisional patent applications, the disclosures of which are incorporated by reference herein: 61/938,352 filed Feb. 11, 2014; 61/954,529, filed March 17, 2014; 61/969,067, filed March 21, 2014; and 61/977,576, filed April 9, 2014.

INCORPORATION BY REFERENCE

[0002] All publications and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference.

BACKGROUND

[0003] A small swelling or aggregation of cells in the body is referred to as a nodule. A nodule can be a collection of benign tissue or even cancerous cells. In an effort to identify the nature of the nodule common procedures are biopsy and needle aspiration, herein referred to as biopsy. During this procedure a needle is advanced to the nodule where it is used to pierce it and obtain a sample of the tissue within it. The size, location and varying density of nodules can make accessing them and obtaining the correct tissue sample difficult. Correct tissue sampling is critical when performing a biopsy on any nodule found in the body.

SUMMARY OF THE DISCLOSURE

[0004] This disclosure describes methods, devices, and systems for obtaining a sample of tissue from a tissue volume of interest. Some aspects of this disclosure include methods, devices, and systems for verifying the location of a biopsy or aspiration needle, herein referred to as an aspiration needle, in relation to the region of interest, such as a nodule or other target tissue, prior to obtaining the sample, to ensure the correct tissue sample is obtained. Current catheter and mapping technologies provide ways to identify and access the general nodule area but fail to provide needle tip location information as the needle is advanced. Without this ability, it is up to the operator to determine when he believes that that needle is within the nodule in order to obtain a sample of the correct tissue. Misdiagnoses can result from improper sampling.

[0005] One aspect of this disclosure is a steerable biopsy needle with a sharpened distal end. The steerable needle includes an inner and an outer member that are axially fixed relative to one another at a location distal to a steerable section of the biopsy needle. The system can be

configured with an external steering controller that is configured to cause relative axial displacement of the inner and outer members at a location proximal to the steerable portion, which causes bending, or steering, of the biopsy needle in the steerable section. One aspect of the disclosure is a system, and method for using the system, for obtaining a sample of lung tissue for biopsy, comprising: a plurality of impedance mapping spines; a plurality of inflatable members such as balloons, each of the inflatable members being coupled to one of the plurality of spines; a plurality of impedance electrodes secured on each of the plurality of inflatable members; and a biopsy needle adapted to be steered relative to the plurality of inflatable members. The biopsy needle can include first and second impedance electrodes, and it can also include a tissue sample collection member. This system and method of use can include any of the structurally features herein and can be used according to the any of the methods herein.

[0006] One aspect of the disclosure is a system, and method for using the system, for obtaining a sample of lung tissue for biopsy, comprising: a plurality of impedance mapping spines each with a plurality of impedance electrodes secured thereto, each of the plurality of impedance mapping spines including an expandable anchor, optionally disposed at the distal end region; and a biopsy needle adapted to be steered relative to the plurality of impedance mapping spines. The biopsy needle can include first and second impedance electrodes thereon, and optionally a tissue sample collection member. This system and method of use can include any of the structurally features herein and can be used according to the any of the methods herein. The spines may or may not have pre-set expanded configurations which they are adapted to assume.

BRIEF DESCRIPTION OF THE DRAWINGS

[0007] Figures 1, 2 and 3 illustrate an exemplary sequence of using infrared to determine nodule location.

[0008] Figures 4, 5, 6, 7 and 8 illustrate an exemplary sequence of using ultrasound to determine nodule location.

[0009] Figure 9 illustrates an exemplary graph of a measured tissue back scatter signal relative to needle position.

[00010] Figures 10A, 10B, and 10C illustrate an exemplary sequence of monitoring electrical impedance that utilizes the inherent difference in electrical impedance between healthy parenchymal tissue and that of the target lesion.

[00011] Figure 11 illustrates an exemplary graph of a measured tissue impedance signal relative to needle position.

[00012] Figure 12 illustrates an example of a biopsy needle having more than two impedance electrodes.

[00013] Figures 13A and 13B illustrate an exemplary method of using a device configured to determine nodule location with a mechanical mechanism.

5 [00014] Figures 14 and 15 illustrate imagery of exemplary tracking technology.

[00015] Figures 16 and 17 illustrate an exemplary biopsy needle that comprises electrodes.

[00016] Figures 18, 19, 20 and 21 illustrate an exemplary method of using a biopsy needle to obtain a tissue sample.

10 [00017] Figures 22, 23 and 24 illustrate an exemplary steerable biopsy needle.

[00018] Figures 25, 26 and 27 illustrate an exemplary steerable biopsy needle.

[00019] Figures 28, 29 and 30 illustrate an exemplary method of steering a biopsy tissue towards a region of interest.

15 [00020] Figure 31 illustrates an exemplary graph representing a measured impedance signal versus position of the biopsy needle.

[00021] Figures 32 and 33 illustrate an exemplary sequence of steering a biopsy needle from a bronchi into a nodule.

20 [00022] Figures 34A-34L illustrate an exemplary sequence of steering a biopsy needle into a lung tissue region of interest based on measured impedance signals using electrodes on the biopsy needle.

[00023] Figures 35, 36, 37, 38, 39, 40 and 41 illustrate an exemplary steerable biopsy needle configured to obtain a sample of tissue.

25 [00024] Figures 42, 43, 44, 45, 46 and 47 illustrate an exemplary method of steering a biopsy needle based on measured impedance signals and obtaining a tissue sample when the impedance signals indicate the biopsy needle is in a desired location.

[00025] Figure 48 illustrates an exemplary system and method of creating an impedance map of a region of interest, and steering a biopsy needle into a nodule.

[00026] Figures 49 and 50 illustrate an exemplary system and method of use in which the spines have expandable balloons secured thereon.

30 [00027] Figure 51 illustrates an exemplary system and method of use in which the spines are secured to expandable anchors.

DETAILED DESCRIPTION

[00028] There are various ways in which a biopsy needle can be located around and within a nodule. One way of doing this is to integrate an infrared source and receiver tip into the biopsy needle. For example, infrared can be projected from the tip of the needle and it is absorbed differently depending on tissue density and composition. By monitoring the backscatter of the infrared the tissue density can be approximated and compared to the density of the surrounding tissue. Figures 1-3 illustrate an exemplary sequence of using infrared to determine nodule location. In figure 1, needle 103 is advanced through healthy tissue 102 and up to nodule 101. As the infrared 104 projects from needle 103, it is absorbed while some remains as backscatter 105. Figures 2 and 3 show the theoretical behavior of the infrared as the needle is advanced into the nodule and then past it. By monitoring this backscatter and tissue absorption, the behavior of the system, an example of which is shown in figure 9, can be evaluated and used to determine when the needle is within the nodule.

[00029] Another method of navigating a needle into a nodule is by utilizing ultrasound to evaluate tissue density. Figures 4-8 illustrate an exemplary sequence of using ultrasound to determine nodule location. Figure 4 shows a burst of ultrasound 204 moving through tissue 202 and up to nodule 201. Figure 5 shows the ultrasound being reflected back 205 to needle 203 where it is evaluated and again used to evaluate the tissue density. Figure 6 shows the ultrasound burst 204 while within nodule 201. Figure 7 shows the ultrasound bounce back 205 to the tip of the needle. Figure 8 shows the ultrasound burst 204 when needle 203 has moved past nodule 201.

[00030] An alternative embodiment in which a needle is used utilizes the inherent difference in electrical impedance between healthy parenchymal tissue and that of a target lesion in this case a more vascularized tissue such as a cancerous lesion. Figures 10A-10C illustrate an exemplary sequence of monitoring electrical impedance. As shown in Figures, 10A-10C needle 1003 is advanced through the lung in the direction of target lesion 1001. Needle 1003 includes at least two electrodes 1009 and 1010. The electrical impedance is continuously monitored as needle 1003 is advanced through the lung tissue. In healthy parenchymal tissue (as shown in figure 10A), the impedance is of a first value 1111 as illustrated in figure 11. Upon both electrodes entering the lesion (as shown in figure 10B), a second impedance 1112 is achieved as illustrated in figure 11. Further passage of needle 1003 completely through tumor 1001 will result in the electrodes 1009 and 1010 re-entering healthy tissue as shown in Fig. 10C, with a corresponding change in the electrical impedance 1113 illustrated in figure 11. It is important to note that the number of electrodes may be

greater than two, and the impedance between any two of those electrodes may be monitored. It is possible to monitor the impedances between electrodes at such a frequency that the progress of the needle through the lesion could be monitored in real time by the user, with the position of the lesion relative to the needle determined by which electrode is returning an impedance characteristic of the lesion. An example of a needle 1203 having a plurality of electrodes greater than two is shown in figure 12, where the electrodes are illustrated 1209'. In this merely exemplary embodiment there are nine electrodes 1209'.

[00031] In some embodiments the needle includes a heating element and sensor within the needle tip which can be used to evaluate for a target tissue by variations in thermal mass or conductivity. In such a system, any of the following can be used to ascertain the whether the needle tip is in a target tissue: the power required to maintain the needle at a constant temperature; the change in temperature associated with a constant delivery of power to the needle tip; or the time required for a peak temperature to reach the sensor after a temperature pulse is applied to the source.

[00032] An alternative method of determining tissue density and nodule location includes using a mechanical method of sensing density at the needle tip. This mechanical method could include a strain gauge, a compression spring, or a push rod or fluid chamber, for example, used to show a change in the force required to advance the needle. As the needle is advanced through the tissue and it comes into contact with the nodule more force is required to move the needle into the denser nodule tissue. This increase in force could be sensed via the mechanical sensor which would inform the operator that he or she has encountered the denser tissue. An example of a mechanical method is illustrated in figure 13A and 13B.

[00033] In figure 13A, needle 1303 is comprised of outer shaft 1314 and inner shaft 1315. Spring element 1316 connects, or indirectly or directly, inner shaft 1315 and outer shaft 1314, and provides a degree of movement between the two. As force is applied to the needle tip, the spring element is compressible, and the degree of compression is presented to the user as a scale 1317 provided on the proximal end of inner shaft 1315. Figure 13A shows the needle passing through parenchyma tissue, which has low resistance to the needle's passage. As a result, the scale 1317 reads little or no force. In Figure 13B, however the needle is passing through lesion 1301, which provides significant resistance to the needle's passage, resulting in compression of spring element 1316, and a corresponding display on the scale 1317.

[00034] In some embodiments needle biopsy can benefit from tracking technology that provides feedback to the user as to where the needle has passed previously, and what the

likelihood is that a good biopsy sample has been obtained. Figure 14 and Figure 15 show imagery of a tracking technology. The imagery includes a series of needle tracks 1418 that pass through the outline of the target lesion 1419. The outline of the target lesion may be obtained from CT scans used to plan the procedure. The needle track position and direction can be obtained from 3-D positioning sensors that are known in the art (Superdimension now owned by Covidien, and the like). The needle track is divided into a series of segments 1420, and the color of each segment is determined based on whatever measure is used to differentiate the lesion from surrounding healthy tissue (e.g. force, impedance, ultrasound, thermal conduction, I.R. reflectance and the like). By providing this data in a graphical representation, the user can more easily see a pattern within the tissue that measures within an individual needle track, and also across multiple needle tracks. In this way, providing graphical representation of the previous needle passes can help direct, and improve the outcome of, subsequent needle passes. As an example, figure 15 shows three needle tracks 1418 that pass through the outline of lesion 1419, and one needle track 1418' that passes below the outline of the lesion. It can be appreciated, even if the outline of the lesion was not present, that the measure used to differentiate between healthy tissue and the lesion forms a pattern (e.g. dark segments grouped together in a specific region) that illustrates to the user that the lesion has been biopsied. Additionally, it can be appreciated that the one needle track that does not pierce the outline of the lesion 1418' does not have the dark segments, and therefore should not be assumed to have passed through the lesion, nor be a good biopsy candidate for analysis of the lesion.

[00035] Figures 16 and 17 illustrate an exemplary biopsy needle that comprises electrodes. Figure 17 shows a cross section of the device shown in figure 16, with equivalent parts having the same last two numbers in the reference numbers. The biopsy needle utilizes outer 1625 an inner 1623 shafts or hypotubes. A first electrode 1626 is integrated into the distal tip of outer tube 1625 and the second electrode 1622 is integrated into the distal tip of the inner actuating tube. The uniqueness of this design is that the electrodes are positioned on either end of needle lancing orifice 1624, which collects the tissue sample when actuated. This configuration means that as the needle is advanced into the nodule, not only is the nodule engagement confirmed with this needle but the correct tissue sample can be collected since the electrodes set a boundary condition for the tissue sample to be collected and confirm its nature. More specifically, by monitoring the impedance of the tissue between the two electrodes the needle can be navigated into position to ensure that the tissue sample collected within the tip 1624 is truly from the nodule, as shown in by the placement in figure 21. The cross sectional view of the needle shown in figure 17 illustrates how inner tube 1623

travels within the inner diameter of outer tube 1625. Once in position the device can be aspirated and the inner tube withdrawn slightly, trapping and collecting a tissue sample within the tip, as shown in figure 21. If the two tubes of the needle are made of a conductive material the electrodes of the device can be integrated by insulating the majority of the surface and exposing only the desired portion that will function as the electrode.

[00036] Figures 18-21 illustrate a sequence of positioning a biopsy needle, as shown in figure 16 and 17, for sampling tissue that utilizes the inherent difference in electrical impedance between healthy parenchymal tissue and that of an aberrant target lesion. As shown in figure 18, biopsy needle 1621 is advanced through the lung in the direction of the target lesion 1819. The electrical impedance is continuously monitored as the needle is advanced through the lung tissue. In healthy parenchymal tissue 1827 shown in figure 18, the impedance is of a first value 3111, as shown in the exemplary graph in figure 31. Upon both electrodes entering the lesion, as shown in figure 19, a second impedance 3112 is achieved, as illustrated in figure 31. Further passage of the needle completely through the tumor will result in the electrodes re-entering healthy tissue, as shown in Fig. 20, with a corresponding change in the electrical impedance 3113, as illustrated in figure 31. The needle can then be withdrawn back to the position shown in figure 21, and based on impedance measurements that indicate the needle lancing orifice (not labeled) is within the target lesion, a sample can then be taken by activating the needle. It is possible to monitor the impedances between electrodes at such a frequency that the progress of the needle through the lesion could be monitored in real time by the user, with the position of the lesion relative to the needle determined by impedance between the electrodes. By integrating the electrodes into the components comprising the needle, the profile of the needle can be reduced and the volume of the tissue sample collected maximized.

[00037] In some embodiments herein the biopsy is configured to be steerable, which may also be described herein as controlled bending, or derivatives of those phrases. One embodiment of such a design is shown in figures 22-24. Figure 23 shows a cross section of the embodiment in figure 22, while figure 24 shows a detailed sectional view of the distal end of the biopsy needle. The biopsy needle includes inner hypotube 2223 positioned within outer hypotube 2225, and fixed to the outer hypotube at the distal tip 2232, which is shown in greater detail in figure 24. In this embodiment, by advancing or retracting inner tube 2223, motion is imparted to outer tube 2225. The series of cutouts 2231 in outer tube 2225 allow the tube to flex axially and deflect with this inner tube motion. Other exemplary devices in which outer and inner members, which are axially affixed distal to a steerable section, can be

steered by moving the members axially relative to one another can be found in U.S.

Publication No. 2014/0107623, published April 17, 2014, incorporated by reference herein.

Electrodes can be integrated into this embodiment by, for example, utilizing nonconductive coverings 2234 and insulating all but the desired portion on the outer 2225 tubes at the distal tip, as shown in figure 24. The same or similar, not shown, coverings are applied on the inside tube 2223. This sharpened needle could be advanced into a nodule and aspirated in order to take a tissue sample, exemplary methods of which are described herein.

[00038] Figures 25-27 illustrates an alternative embodiment, with figure 26 being a sectional view, and figure 27 being detailed sectional view of the distal end of the biopsy needle. The same parts are referred to in the different figures with the same last two digits. As opposed to a needle that uses an inner tube motion to steer the needle, this embodiment utilizes pull wire 2535 within outer tube 2525 to deflect, or steer, the tip. A conductive wire could be used for the pull wire and an exposed distal end of the wire 2522 could serve as one of the electrodes. Another electrode could again be the exposed end of the tube, as seen in figure 27.

[00039] The steerability of some of the needles herein can prevent incorrect sampling by allowing the operator to approach the nodule. Figures 28-30 illustrate an exemplary method of steering a steerable needle. In figure 29 the distal end of biopsy needle 2821 is not positioned in target tissue 2819. Based on any of the methods herein that allow a user to determine where lung tissue of interest is located, biopsy needle 2821 is then steered so that the distal region of needle 2821 is disposed in the nodule 2819. The actuating lance of the inner tube shown in the design in Fig. 16 could be integrated into this and other steerable needles as well, in order to set a sensing boundary around the biopsy sample in question while still maintaining the capacity to steer to the nodule. This boundary means that if any of the electrodes are not within the nodule the signal to the operator would indicate as such and the needle could be steered in a different direction or moved.

[00040] In addition to integrating a steerable feature into the physical biopsy needle itself, as described above, it could also be leveraged across additional variations of the design. One option would be to use the steerable design described above as a steerable delivery channel through which a separate biopsy needle could be delivered. This needle could actuate and integrate a lancing orifice as described in the design in figure 16. The working channel of this steerable element could also be used to deliver equipment designed for therapeutic purposes. This means that not only could the position within a nodule be confirmed, but any biopsy needle or therapeutic equipment could then be delivered to correct location for sampling or

treatment.

[00041] Regardless of the configuration of the biopsy needles or steerable delivery elements within the biopsy needle, the change in the signal measured from the electrodes, shown in the exemplary signal of figure 31, could be used to signal true nodule engagement while moving through the healthy lung tissue. This accurate indicator would greatly improve the yield and accuracy of a needle biopsy, preventing potential misdiagnosis and ensuring therapeutic treatment of the correct tissue.

[00042] Additional to the needle embodiments described above, needle biopsy and steerable elements for therapeutics can benefit from tracking technology that provides feedback to the user as to where the tip has passed previously. This could suggest the likelihood a good biopsy sample has been obtained or therapy performed on the correct tissue. The track position and direction can be obtained from 3-D positioning sensors that are known in the art (Superdimension now owned by Covidien and the like). While these mapping software products help the operator move the majority of the way there by guiding them through bronchi 3229 as shown in theoretical path in figures 32 and 33, the mapping is limited and doesn't guide the operator past the walls of the bronchi. The needles and steerable elements described herein would allow the operator to move past the bronchi 3229 and through to the nodule 3219 by following an extended path 3236 until the unit confirms nodule engagement and positioning, exemplary methods of which are described herein. This would greatly improve the yield and accuracy of any procedure performed in or around the nodule in question.

[00043] In addition to the integration of electrodes into the needle or steerable element, other means of looped feedback for positioning could include, for example, infrared, ultrasound, resistance heating and heat capacity. As with the electrodes, any of these methods integrated into the design could be coupled with the mapping software to improve yield and accuracy of sampling and therapeutics.

[00044] Figures 34A - 34L depict an exemplary procedure using an exemplary embodiment of a steerable needle biopsy apparatus, which can include any of the features described in any of the biopsy needle embodiments herein. Steerable biopsy needle assembly 3416 is delivered, within the bronchial tree 3430, to the vicinity of a nodule 3401 as delineated via CT, PET, MRI or other appropriate imaging means as indicated in figure 34A. The steerable biopsy needle 3400 is then pushed through the wall of the bronchi into the parenchymal tissue 3427 and steered along a path such as that depicted in figures 34B and 34C. As the needle assembly 3400 is moved through the tissue, the local tissue

impedance is measured between electrodes 3444 and 3458 using methods described herein. As depicted in figures 34B and C, the local impedance never drops below a threshold level indicating that nodule 3401 has not been traversed by the needle tip. The needle is then retracted as indicated in figure 34E and then steered through an alternate path, as depicted in figures 34F and 34G. Again as depicted, no nodule is identified, and so the needle is retracted back to the position as depicted in figure 34H. The needle is then steered along a new path as depicted in figures 34I and 34J. As depicted in figures 34J, the need has passed into nodule 3401, which is known due to a change in monitored impedance noted by an indicator at impedance monitor 3438. A tissue biopsy jaw is then extended into the body of the nodule, then retracted back into the needle assembly, thereby capturing a volume of tissue for biopsy as depicted in figures 34K and 34L. In alternative methods, a needle distal tip can be actuated, such as described herein, the capture the tissue to be sampled.

[00045] Figures 35-41 illustrate an exemplary steerable biopsy needle comprising electrodes. Figure 36 illustrates a sectional view of figure 35, and figure 37 illustrates a sectional detailed view of the distal end of the biopsy needle. The biopsy needle includes outer hypotube 3550 and inner push rod 3551. The distal tip of the hypotube could be honed to a needle point 3548 and a series of channels 3540 could be cut into one side of the part to allow for flexibility. A lancing orifice 3545 is cut into this hypotube just proximally of the needle tip 3548. Figure 36 and the detailed view of the tip in figure 37 also show the biopsy needle in an open condition, and how push rod 3551 is fixed to the proximal end of the actuating scissor 3528 of the biopsy needle 3521. By advancing push rod 3551 the scissor element 3528 is also advanced past the lancing orifice 3545 and up to stopper 3554 into a closed position, shown in figure 38. Figures 39 and 40 also show the closed position, with the same sectional and detail views as in figures 36 and 37 respectively. By advancing push rod 3551 further, as shown in cross section in figure 41, the scissor element 3528 bottoms out on the stopper 3554 and a deflection is imparted on the needle 3521. The push rod 3551 biases towards the outer edge of the bend radius by the channels 3540 of the outer hypotube 3550.

[00046] When advancing a needle only in a straight path, the ability of the needle to accurately access the nodule can be limited and could result in misdiagnoses. As a steerable needle is advanced it can be directed in slightly different trajectories to greatly improve yield and the accuracy of tissue sampling. Figures 42-47 illustrate an exemplary method of using steerable biopsy needle 3521 to obtain a tissue sample. Figures 43 and 44 show the approach of needle 3521 through the healthy parenchyma tissue 4227 and up to the nodule 4201 with the ability to deflect to access the tissue in question. Once positioned within nodule 4201,

push rod 3551 is withdrawn slightly to open the lancing orifice 3545. The device is then aspirated through the area between outer hypotube 3550 and the push rod 3551. This draws the nodule tissue 4201 into the lancing orifice 3540, at which point the push rod 3551 is advanced forcing the scissor element 3528 forward which cuts off a sample of tissue and traps it within the now closed lancing orifice 3545. The configuration of this needle design is as such that when the push rod 3551 is advanced to capture a tissue sample, the needle tip deflects further which puts the tissue above the sample in tension 4252 and the tissue beneath the sample in compression 4241. This additional motion towards the tissue sample within the orifice can be utilized to maximize the volume of sample collected by forcing more tissue into the orifice 3545 as it is being closed to capture the sample. The steerability of biopsy needles can prevent incorrect sampling by allowing the operator to approach the nodule and deflect the tip to direct the needle into the nodule. Once positioned,, an accurate sample can be collected prior to withdrawing the sample and the needle 3521 from the sample location 4252, as shown in figure 47.

[00047] Just as with previous designs the two primary elements of the biopsy needle can be comprised of conductive materials that are insulated over their length with the exception of a specific area desired to serve as an electrode. The impedance between the electrodes for the two elements can be used to indicate tissue impedance and density by setting a sensing boundary condition for the tissue around the needle tip. This ability to sense and differentiate between different tissue types could help provide the operator with real-time feedback about the tissue they are travelling through. By integrating the electrodes into the distal end of the outer hypotube and the proximal end of the scissoring element, the tissue sample can be evaluated prior to collection. The profile of the needle could also be reduced and the volume of the tissue sample collected maximized by removing the need to add electrodes to the surface and instead integrating it into two main components of the needle to reduce profile.

[00048] In addition to integrating this steerable feature into the biopsy needle itself, as described above, it could also be leveraged across additional variations of the design. One option would be to use the steerable design listed above as a steerable delivery channel through which equipment designed for therapeutic purposes can be delivered. The configuration described above could be used to position the distal end of the hypotube within the nodule, the push rod could be withdrawn and the hypotube inner channel could be used to deliver any equipment. This means that not only could the position within a nodule be confirmed, but any biopsy needle or therapeutic equipment could then be delivered to correct location for sampling or treatment.

[00049] The measured impedance signal from the electrodes can be used to signal true nodule engagement while moving through the healthy lung tissue. This accurate indicator greatly improves the yield and accuracy of a needle biopsy, preventing potential misdiagnosis and ensuring therapeutic treatment of the correct tissue.

5 [00050] Figure 48 illustrates an additional exemplary system, device, and methods for accurately obtaining a lung tissue sample for biopsy. As described herein target tissues of interest have different impedances than non-target tissues.

[00051] Figure 48 illustrates a needle biopsy system 4800 comprising an electrical impedance mapping system 4843 and a steerable biopsy needle 4833. The steerable needle
10 comprises a tip steering feature 4857 facilitating needle steerability, a steering electrode 4853, and a nodule verification feature 4846. The electrical impedance mapping system as illustrated comprises a set of three mapping needles or spines 4847, each comprising five mapping electrodes 4846. Mapping spines are flexible and have a curved configuration such that on deployment they follow a curved path as illustrated. The system may additionally
15 comprise a delivery sheath 4842. Typically the system will be delivered via the working channel of a bronchoscope, but it is not limited in this use or adaptation.

[00052] In use, the mapping needles are delivered to an area near and proximal to the target tissue 4855, which can be a region of lung tissue. The mapping needles are then extended out of the delivery catheter and/or bronchoscope working channel through the
20 tissue either all at once or serially. Once deployed, as shown in figure 48, mapping electrodes 4846 are used to create an impedance map of the volume of tissue surrounded by the mapping needles. The biopsy needle is then steered towards the target tissue, and examples of steerable needles are described herein. Steering is facilitated by using the mapping system to report on where in the electrical impedance map the biopsy needle steering electrode 4853 is and its location relative to the target tissue 4855. Once it is
25 believed that the biopsy needle has been steered to the site of the target tissue or while steering the biopsy needle, the biopsy needle verification 4846 and steering electrodes 4853 can be used to evaluate the electrical impedance of the local tissue to verify proper biopsy needle positioning, and that the biopsy or aspiration aspect of the biopsy needle is placed
30 within the target tissue. Once the position is confirmed, the biopsy or aspiration aspects of the procedure may be performed, examples of which are described herein.

[00053] In exemplary methods mapping is performed by sequentially exciting each electrode and monitoring the impedance between it and each of the other electrodes, as is known in the art. In the case of needle steering, the steering electrode will generally be used

as the excitation source. This electrical data in combination with data on the physical position of the needles and electrodes comprised thereon provide an electrical impedance map of the surrounded tissue.

[00054] The mapping system may comprise two or more spines with two or more electrodes per spine. In some preferred embodiments the system includes three spines. Spines may be shape set such that on deployment they assume a pre-determined curve such that the distance between spine distal tips increase as the length of the deployed section is increased. In this fashion the volume of tissue mapped increases non-linearly on increased deployment and the distance between electrodes may be estimated.

10 [00055] Steering of the biopsy needle may be accomplished by any number of the mechanisms described herein or using any type of steerable devices known in the art. The biopsy needles as described herein may comprise biopsy capability and/or an aspiration capability.

[00056] The method above described in reference to figure 48 is an example of a method of obtaining a sample of lung tissue for biopsy, comprising: delivering a plurality of impedance mapping spines through the bronchial tree; advancing a delivery device comprising a plurality of impedance mapping spines proximate a lung region of interest; advancing a plurality of impedance mapping spines from within the delivery device such that the volume of lung surrounded by the mapping spines encompasses a lung region of interest; mapping the impedance of lung tissue in the lung region of interest using the plurality of impedance mapping spines; identifying target lung tissue within the region of interest; steering a biopsy needle from within the bronchial tree towards the target lung tissue by determining where the biopsy needle is within the lung region of interest and relative to the target lung tissue; and obtaining a sample of the target lung tissue once the biopsy needle has been determined to be in a desired location relative to the target lung tissue. The embodiment in figure 48 also includes, at a time prior to the obtaining step, measuring local tissue impedance between two electrodes on the biopsy needle to verify the position of the biopsy needle relative to the target lung tissue. In some embodiments of the method, advancing the plurality of impedance mapping spines proximate a lung region of interest comprises advancing the plurality of impedance mapping spines into lung tissue outside of the bronchial tree. In some embodiments of the method advancing the plurality of impedance mapping spines proximate a lung region of interest comprises advancing the plurality of impedance mapping spines through the bronchial tree without advancing the plurality of spines into lung tissue. In the embodiment in figure 48, advancing the plurality of impedance mapping spines proximate a lung region of interest comprises allowing the

plurality of impedance mapping spines to expand such that the distance between corresponding points on different spines are further apart than corresponding points on the proximal ends of the spines. In the embodiment in figure 48 the lung region of interest comprises a nodule identified from a previous lung imaging process. In the embodiment in figure 48, mapping the impedance of lung tissue in the lung region of interest using the plurality of impedance mapping spines comprises sequentially exciting each electrode on each of the spines and monitoring the impedance between each excited electrode and each of the other electrodes on the spines. In the embodiment in figure 48, identifying target lung tissue within the region of interest comprises identifying target lung tissue that has an impedance that is different than impedance of healthy lung tissue. In the embodiment in figure 48, determining where the biopsy needle is within the lung region of interest and relative to the target lung tissue comprising exciting a steering electrode on the needle and monitoring impedance between the exciting electrode and electrodes on the plurality of impedance mapping spines. In some embodiments of the method steering comprising actuating a pull-wire within the biopsy needle. In some embodiments of the method obtaining a sample comprising activating a tissue sample collection mechanism on the biopsy needle. In some embodiments of the method obtaining a sample comprising aspirating the sample through the biopsy needle.

[00057] The system above described in reference to figure 48 is an exemplary system for obtaining a sample of lung tissue for biopsy, comprising: a plurality of impedance mapping spines each with a plurality of impedance electrodes, the spines having expanded configurations; a biopsy needle adapted to be steered relative to the plurality of impedance mapping spines in their expanded configurations, the biopsy needle comprising first and second impedance electrodes thereon and a tissue sample collection member. In some embodiments the system further comprises a lumen defined by a delivery sheath, the plurality of impedance mapping spines and biopsy needle disposed with the delivery sheath. In some embodiments the system further comprises a bronchoscope, wherein the plurality of impedance mapping spines and biopsy needle are configured to be advanced through a working channel of the bronchoscope. In some embodiments the first and second impedance electrodes are proximal to the tissue sample collection member.

[00058] Figures 49 - 51 describe alternative embodiments to that of figure 48, in which a plurality of spatial mapping elements have been incorporated and paired with the plurality of electrical impedance electrode mapping elements. In these configurations, the plurality of spatial mapping electrodes are adapted to provide the spatial location of the plurality of electrical impedance electrodes such that the spatial distance between each electrode can be

mapped. This is in contrast to the design of figure 48, wherein distance between electrodes can be inferred from the expected deployed configuration of the mapping spines and electrodes comprised thereon, and/or a 3 dimensional map of the spines created via a conventional imaging means such as CT or MRI. Additionally, the system and methods of figures 49 - 51 provide mapping and steering capabilities with components that are configured to be used in a manner that is atraumatic to the lungs, as the mapping components may be placed and used within the bronchi. This is in contrast to the design of figure 48, which requires the mapping spines to be deployed through the bronchi walls and into the lung parenchymal tissue.

[00059] Figure 49 illustrates the distal configuration of an electrical impedance mapping electromagnetic hybrid mapping system 4900. The system, as depicted, is comprised of three mapping members 4966 each comprised of three mapping balloons 4960, each comprising five mapping sensors 4961 (sensors 4961 are labeled on only one of the three balloons 4960). Each mapping sensor 4961, as illustrated in figure 50, is comprised of a spatial mapping sensor 4946 and an electrical impedance electrode 4909. The spatial mapping sensors are depicted as a coil for use in an electromagnetic mapping system such as those described in the following US patents: 6,574,492; 5,713,946; and 5,983,126. However, in actual use, the component will be configured in a fashion best suited to the particular spatial mapping system. In this embodiment, the use of the mapping balloons, as opposed to the mapping spines discussed elsewhere herein, assures electrical contact between the electrical impedance electrodes 4009 and the bronchi 4929, whose diameters decrease the more distal they are located, as the balloon may be inflated to assure proper contact. In addition the balloon provides another benefit in that it anchors the mapping elements to the tissue, hence the mapping elements will better follow the perimeter of the mapped volume as it moves during normal breathing. Although as illustrated each mapping balloon is in a particular bronchial branch, in practice the mapping balloons could span multiple branches of different generation. More or fewer balloons may be used.

[00060] An exemplary procedure for deployment and use of the mapping system 4900 is as follows. The mapping balloons are delivered down the bronchial tree to locations believed to surround the target tissue as defined by an alternate imaging means such as CT. A system such as the Super Dimensions™ pulmonary mapping system may be used to facilitate the placement of the mapping balloons. Once the mapping balloons are located, a mapping procedure may be initiated to determine if the mapped volume contains the target tissue. The procedure will comprise the steps of creating a spatial map of the contained volume and an electrical impedance map to the volume. Using the electrical impedance map it will be

ascertained if the target tissue is within the mapped volume. If not, one or more of the mapping balloons will be relocated and the procedure repeated. Once the target tissue is located within an electrical impedance map, the biopsy needle will be delivered to the target tissue. As illustrated, a steerable biopsy needle 4933, comprising impedance electrodes as described elsewhere herein, is steered to the target tissue using the electrical impedance volume map and mapping components as described elsewhere herein. In an alternate embodiment not illustrated here, the steerable needle may comprise a spatial mapping component and the steerable needle may be steered using feedback from the spatial mapping system within the spatial map. In such a procedure the information in the impedance map regarding the location of the target tissue will be mapped into the spatial map. Once samples of the target tissues have been collected and evaluated, the balloon may be deflated and the system removed.

[00061] In an alternate procedure, multiple mapping balloons may be placed randomly within a lung lobe and subsets of mapping balloons and associated contained volume, queried to see if aberrant tissue is contained within the queried volume. By proper sequencing a large part of the total volume of a lobe may be evaluated in a non-traumatic way. Such a procedure can obviate the need for a CT or other imaging procedure and the associated radiation risks and or costs.

[00062] Figure 51 illustrates the distal configuration of an electrical impedance mapping electromagnetic hybrid mapping system 5100, similar to that described in figures 49 and 50. The mapping system 5100 relies on distal anchors 5163 (three shown but only one is labeled), but does not comprise balloons that comprise mapping elements. In this embodiment the diameter of the plurality of the mapping spines is large enough to assure that each impedance mapping element in mapping sensors 5161 (only one sensor 5161 is labeled on one of the three spines shown) properly contacts the bronchi wall. Anchors 5163 may comprise balloons as illustrated, braids, or any other suitable structure as is known in the art. In yet other alternate embodiments, the impedance mapping element comprised in the mapping sensor may be comprised of an expandable structure such as a braid, a helical spring, an individual balloon, or any other expandable structure known in the art.

[00063] The following patents are incorporated by reference herein for all that they describe, and aspects of their disclosure can be incorporated into any of the systems, devices, and methods herein: U.S. Pat. Nos. 6,962,587; 5,536,267; 8,287,531; 7,561,907; and 7,089,045.

CLAIMS

What is claimed is:

1. A method of obtaining a sample of lung tissue for biopsy, comprising:
 - 5 advancing a delivery device comprising a plurality of impedance mapping spines through the bronchial tree and proximate a lung region of interest;
 advancing the plurality of impedance mapping spines from within the delivery device such that the volume of lung surrounded by the mapping spines encompasses a lung region of interest;
 - 10 mapping the impedance of lung tissue in the lung region of interest using the plurality of impedance mapping spines;
 identifying target lung tissue within the region of interest;
 steering a biopsy needle from within the bronchial tree towards the target lung tissue by determining where the biopsy needle is within the lung region of interest and relative to the
 - 15 target lung tissue; and
 obtaining a sample of the target lung tissue once the biopsy needle has been determined to be in a desired location relative to the target lung tissue.
2. The method of claim 1 further comprising, at a time prior to the obtaining step,
 - 20 measuring local tissue impedance between two electrodes on the biopsy needle to verify the position of the biopsy needle relative to the target lung tissue.
3. The method of claim 1 wherein advancing the plurality of impedance mapping spines
25 advancing the plurality of impedance mapping spines into lung tissue.
4. The method of claim 1 wherein advancing the plurality of impedance mapping spines
 comprises advancing the plurality of impedance mapping spines through the bronchial tree without advancing the plurality of spines into lung tissue.
- 30 5. The method of claim 1 wherein advancing the plurality of impedance mapping spines
 comprises allowing the plurality of impedance mapping spines to expand such that the distance between corresponding points on different spines are further apart than corresponding points on the proximal ends of the spines.

6. The method of claim 1 wherein the lung region of interest comprises a nodule identified from a previous lung imaging process.

7. The method of claim 1 wherein mapping the impedance of lung tissue in the lung region of interest using the plurality of impedance mapping spines comprises sequentially exciting each electrode on each of the spines and monitoring the impedance between each excited electrode and each of the other electrodes on the spines.

8. The method of claim 1 wherein identifying target lung tissue within the region of interest comprises identifying target lung tissue that has an impedance that is different than impedance of healthy lung tissue.

9. The method of claim 1 determining where the biopsy needle is within the lung region of interest and relative to the target lung tissue comprising exciting a steering electrode on the needle and monitoring impedance between the exciting electrode and electrodes on the plurality of impedance mapping spines.

10. The method of claim 1 wherein steering comprising actuating a pull-wire within the biopsy needle.

11. The method of claim 1 wherein obtaining a sample comprising activating a tissue sample collection mechanism on the biopsy needle.

12. The method of claim 1 wherein obtaining a sample comprising aspirating the sample through the biopsy needle.

13. A system for obtaining a sample of lung tissue for biopsy, comprising:
a plurality of impedance mapping spines each with a plurality of impedance electrodes, the spines having expanded configurations;
a biopsy needle adapted to be steered relative to the plurality of impedance mapping spines in their expanded configurations, the biopsy needle comprising first and second impedance electrodes thereon and a tissue sample collection member.

14. The system of claim 13 further comprising a lumen defined by a delivery sheath, the plurality of impedance mapping spines and biopsy needle disposed with the delivery sheath.

15. The system of claim 13 further comprising a bronchoscope, wherein the plurality of impedance mapping spines and biopsy needle are configured to be advanced through a working channel of the bronchoscope.

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16. The system of claim 13 wherein the first and second impedance electrodes are proximal to the tissue sample collection member.

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17. The system of claim 13 wherein the plurality of impedance mapping spines are at least three spines.

18. The system of claim 13 wherein the plurality of impedance mapping spines each comprise at least four impedance electrodes.

1 / 30

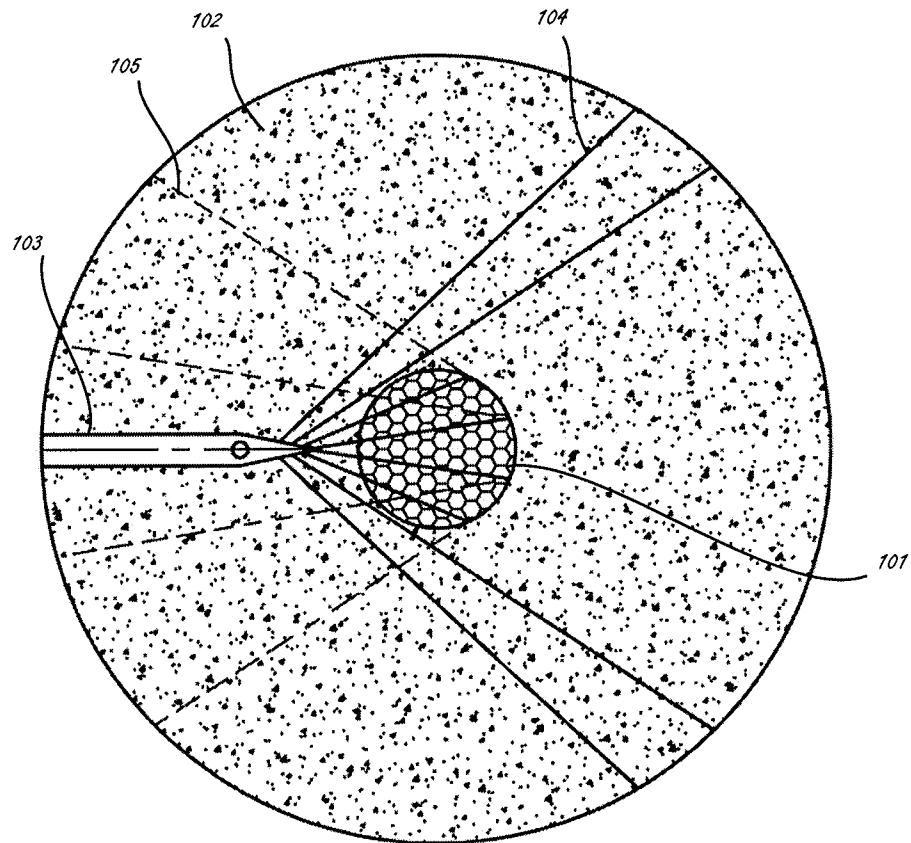


Fig. 1

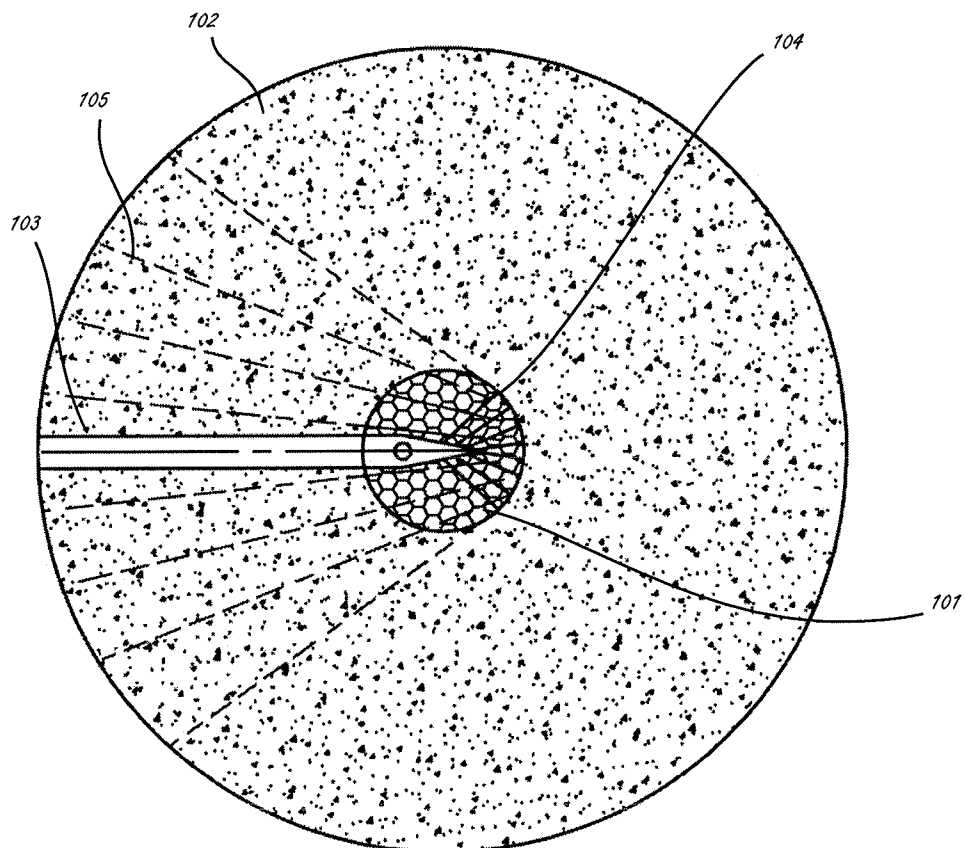
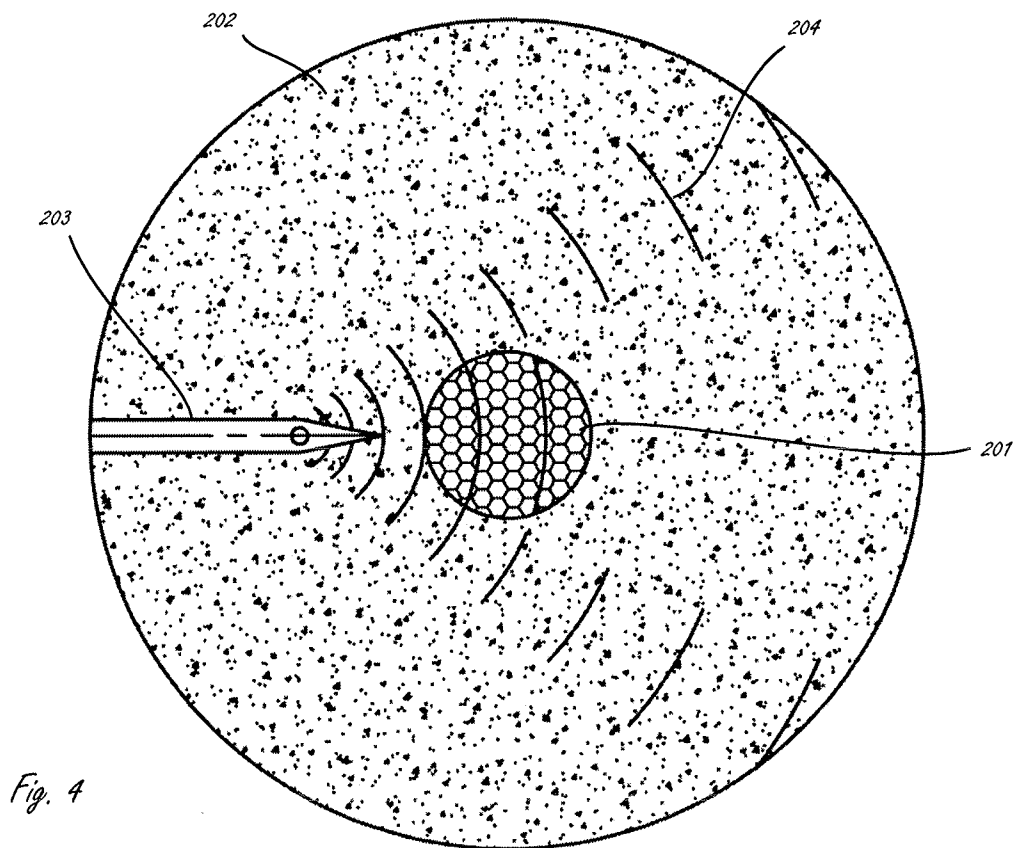
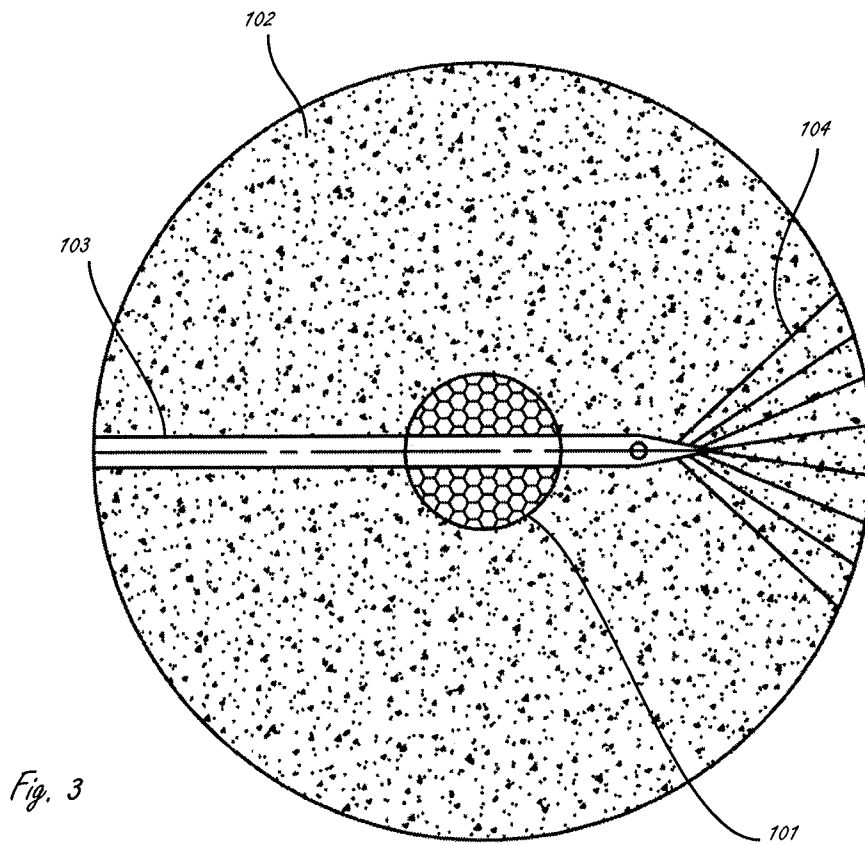


Fig. 2

2 / 30



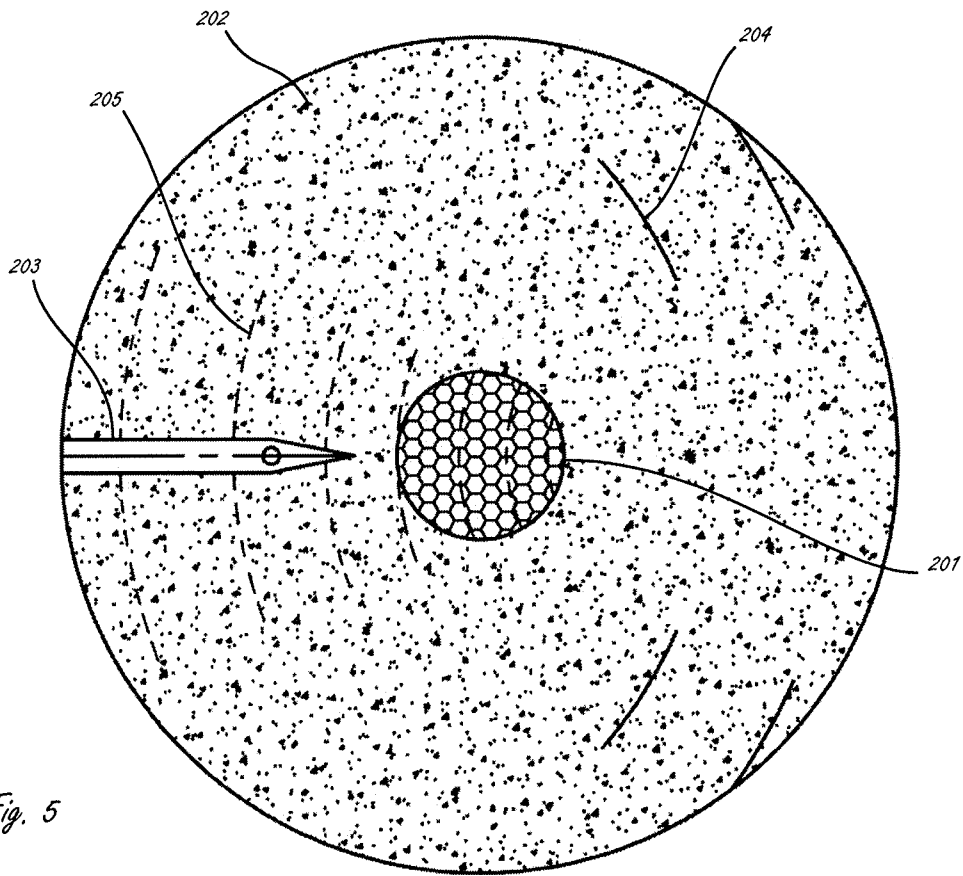


Fig. 5

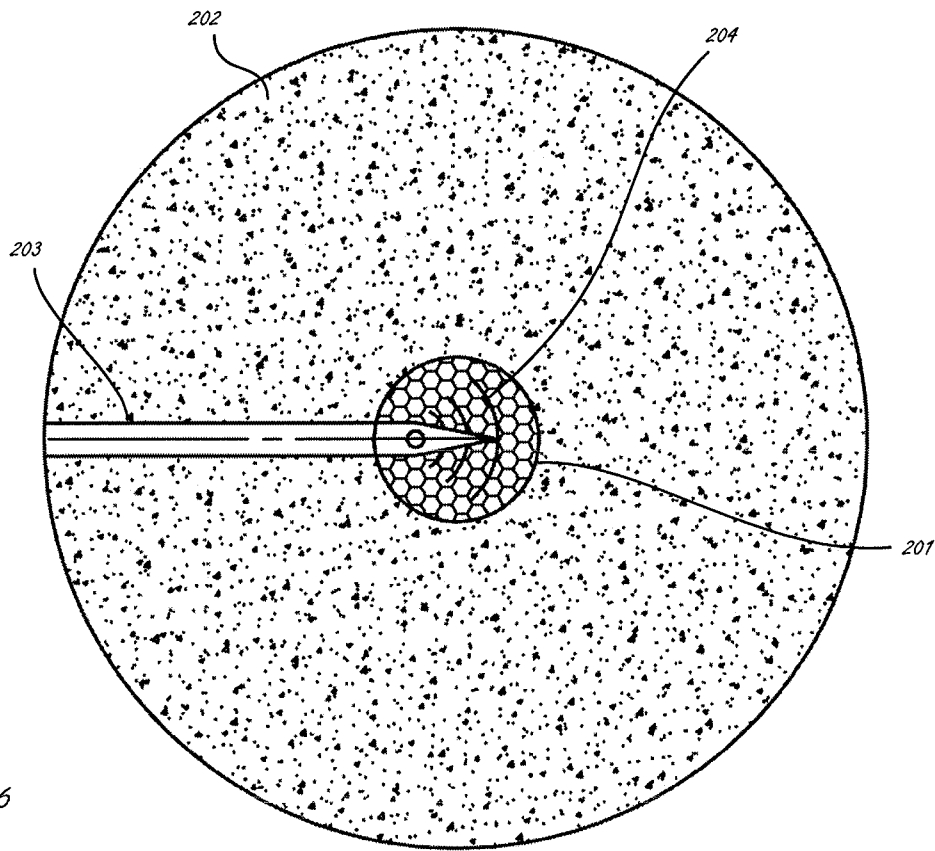


Fig. 6

4 / 30

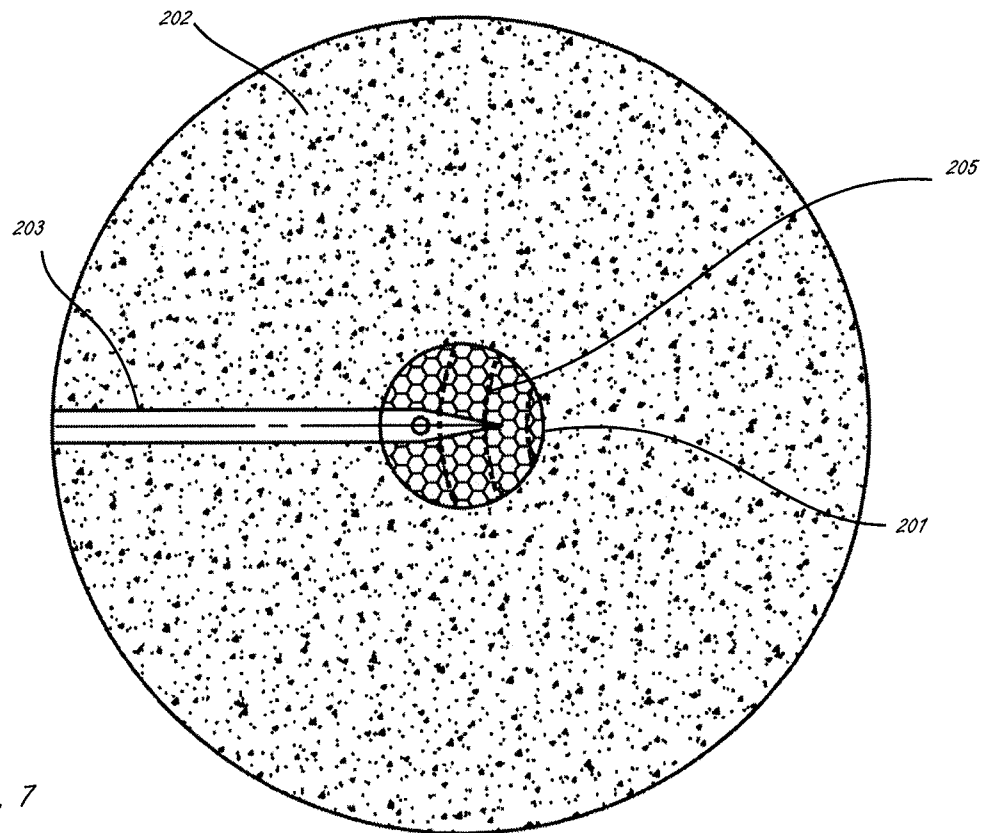


Fig. 7

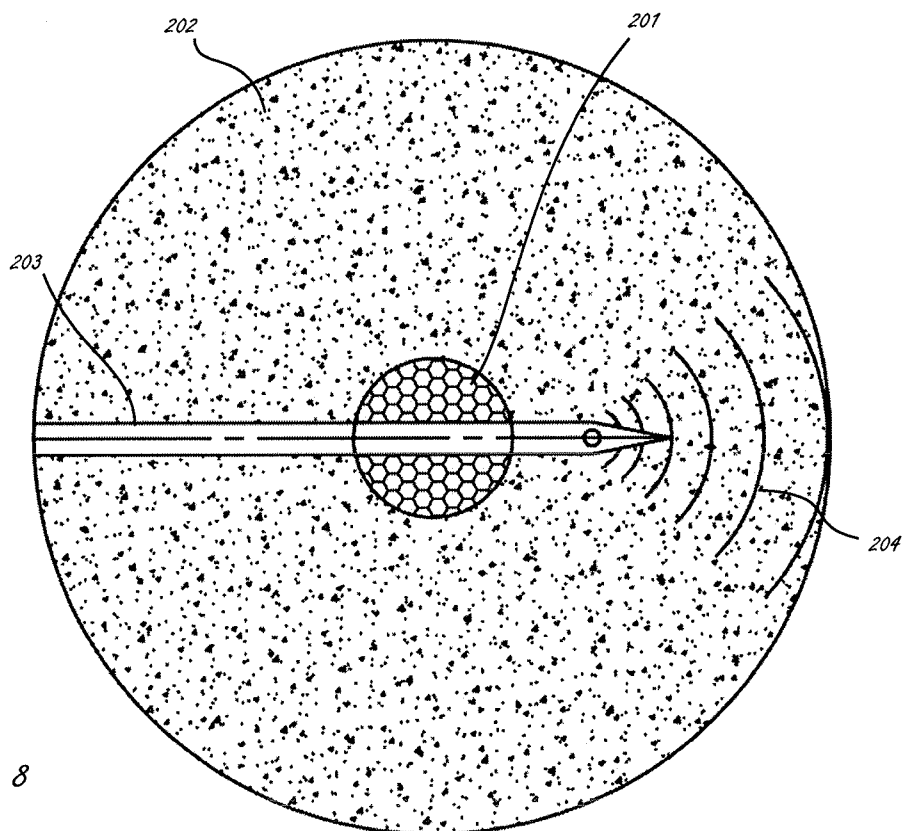


Fig. 8

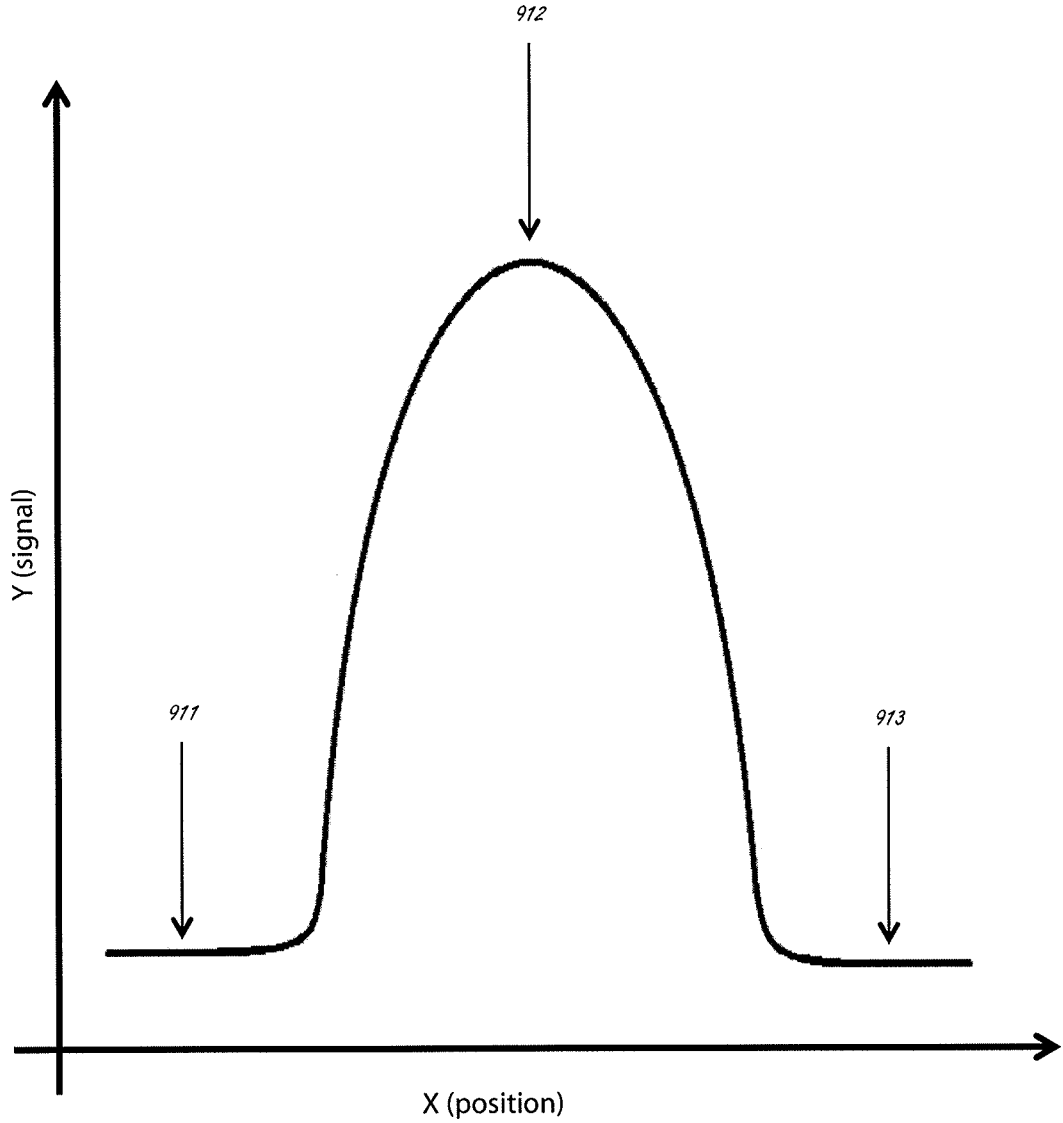


Fig. 9

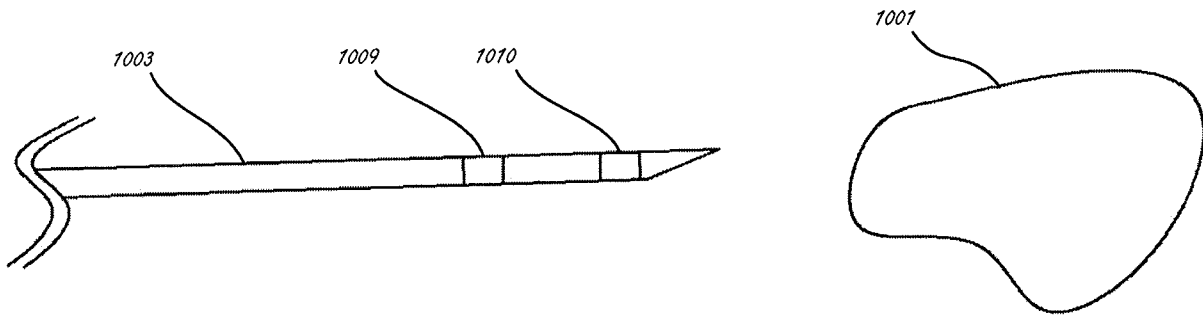


Fig. 10A

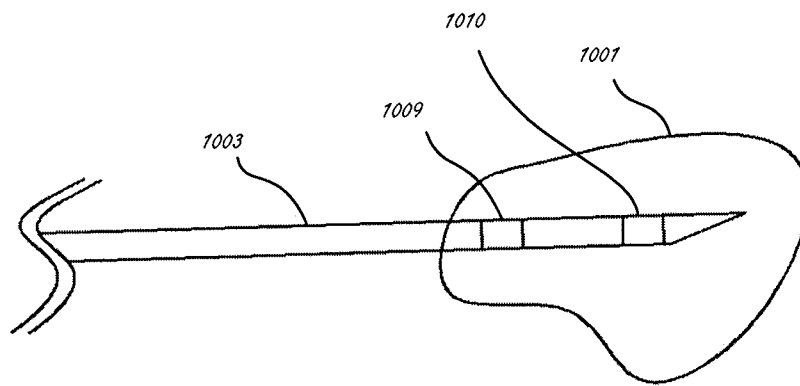


Fig. 10B

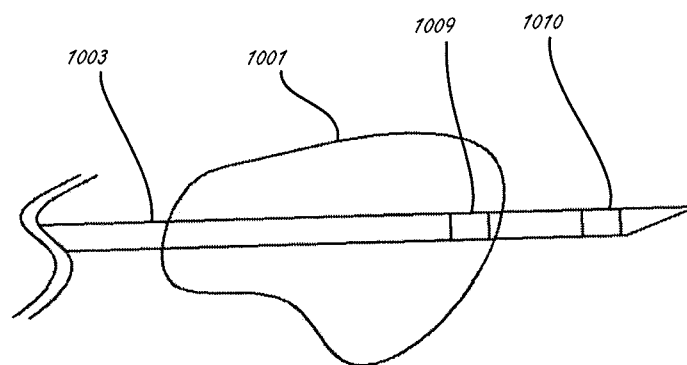


Fig. 10C

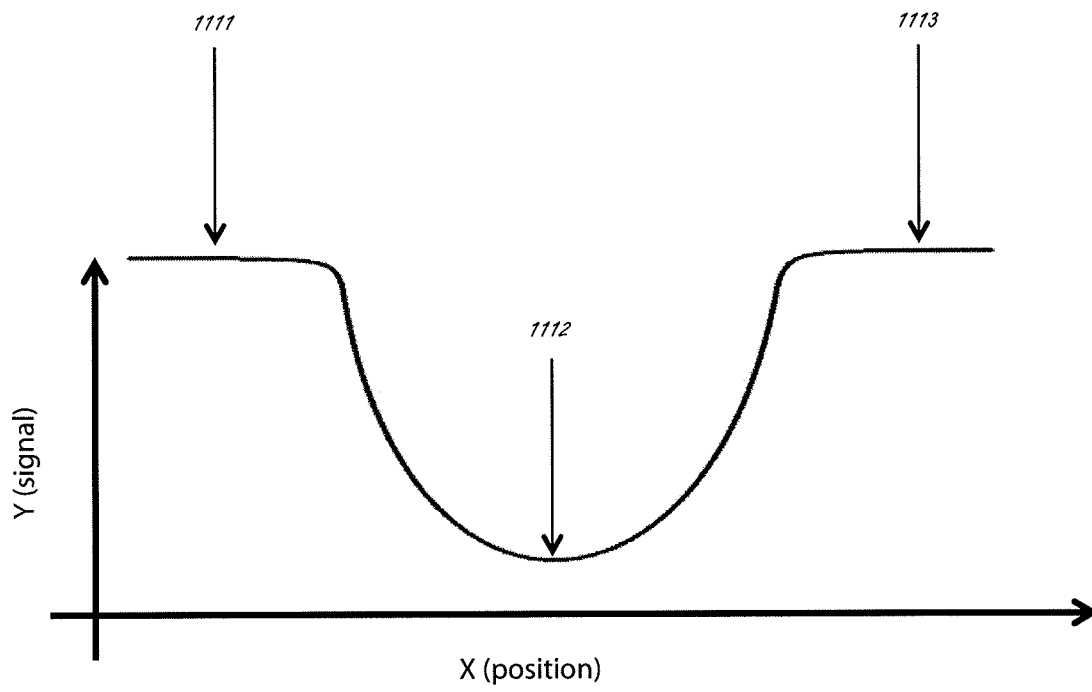


Fig. 11

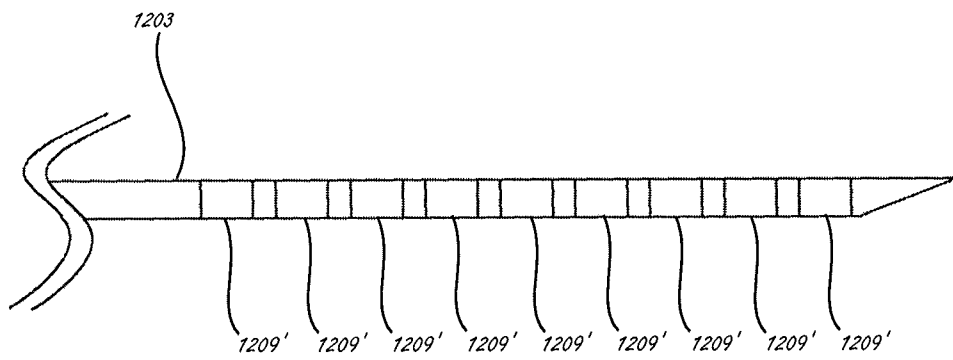


Fig. 12

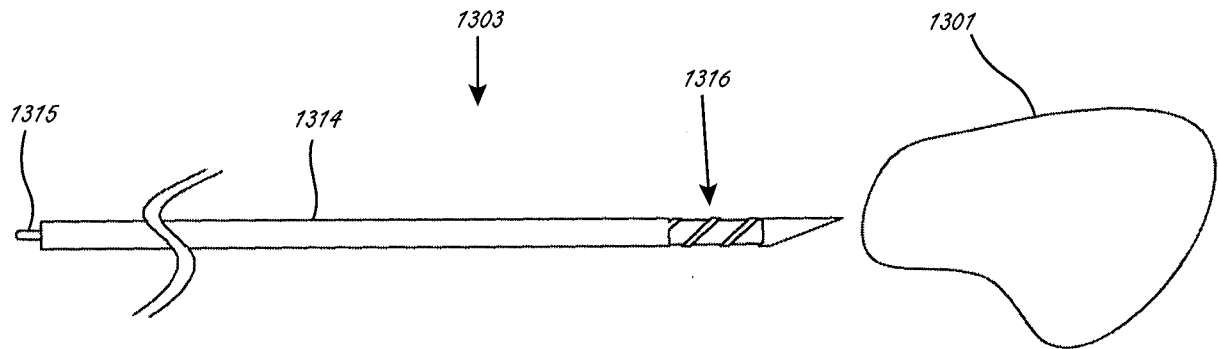


Fig. 13A

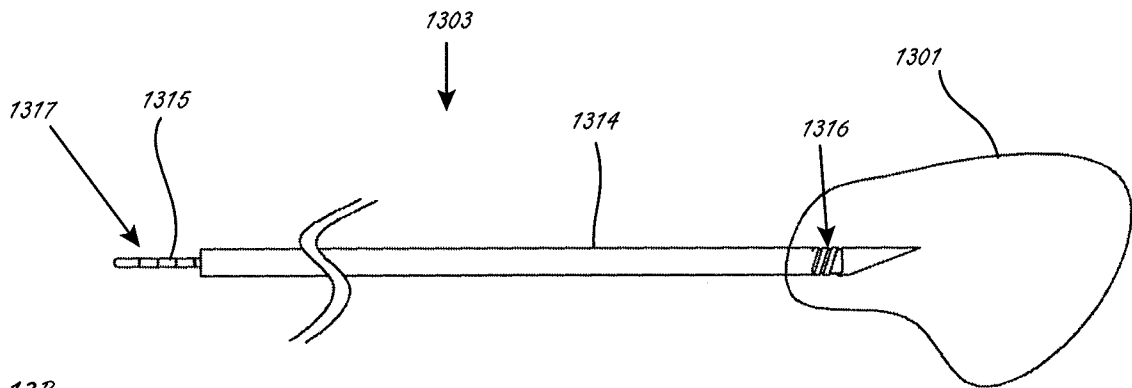
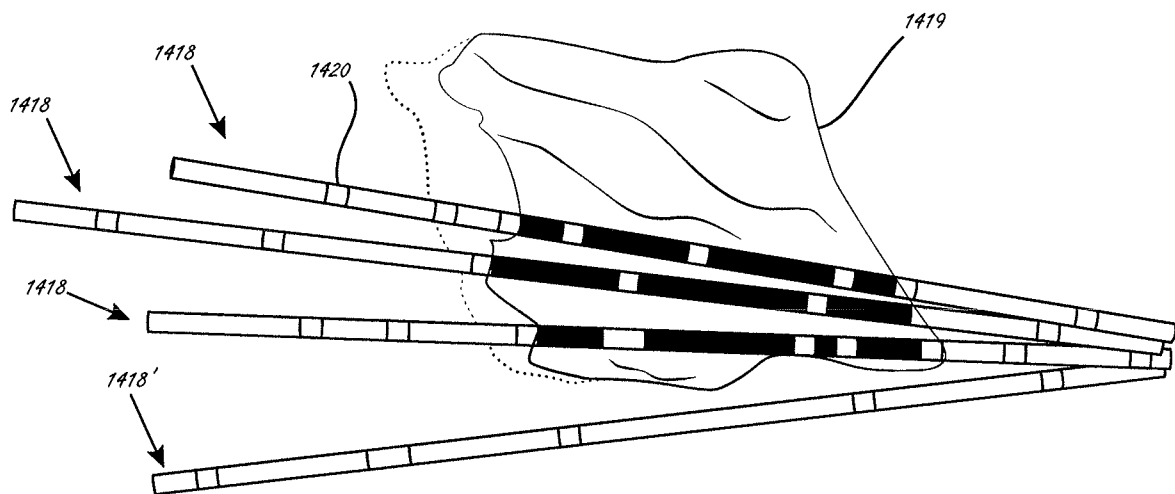
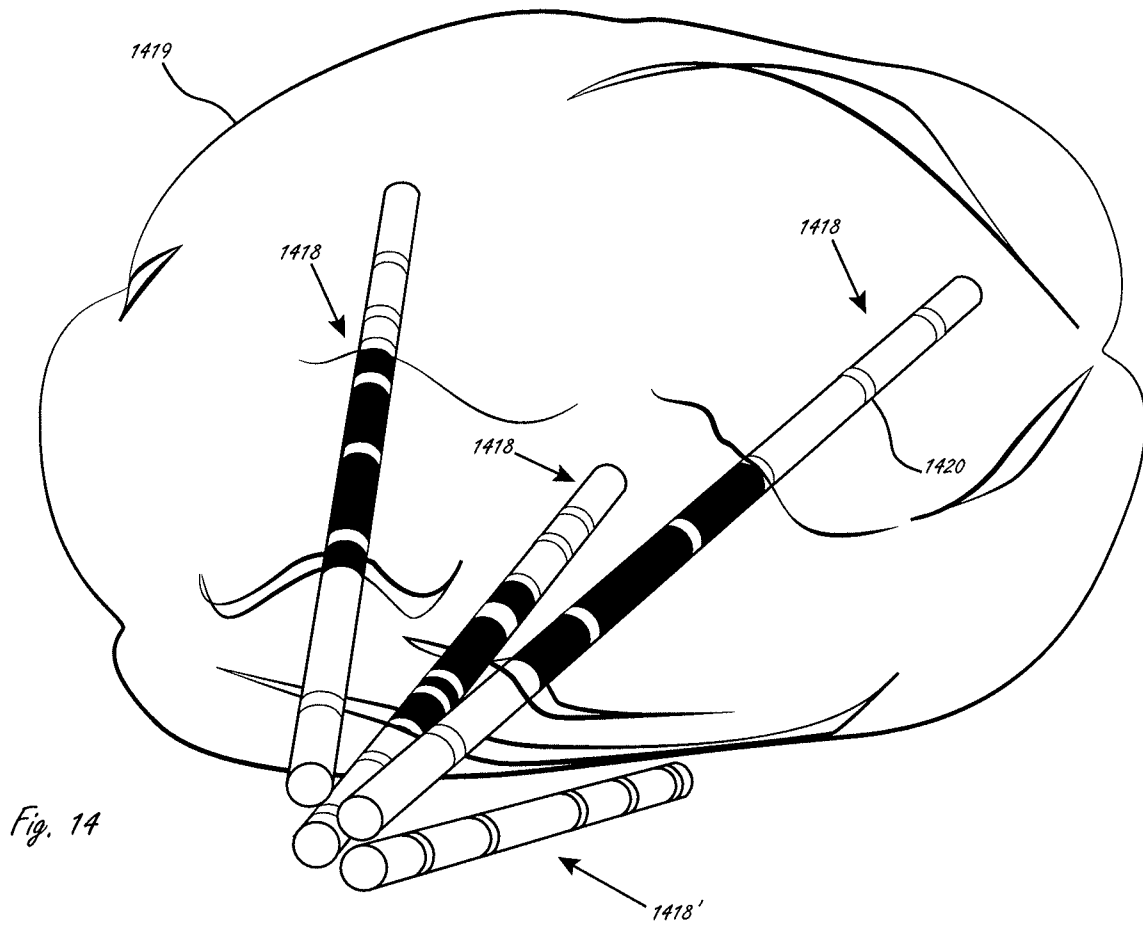
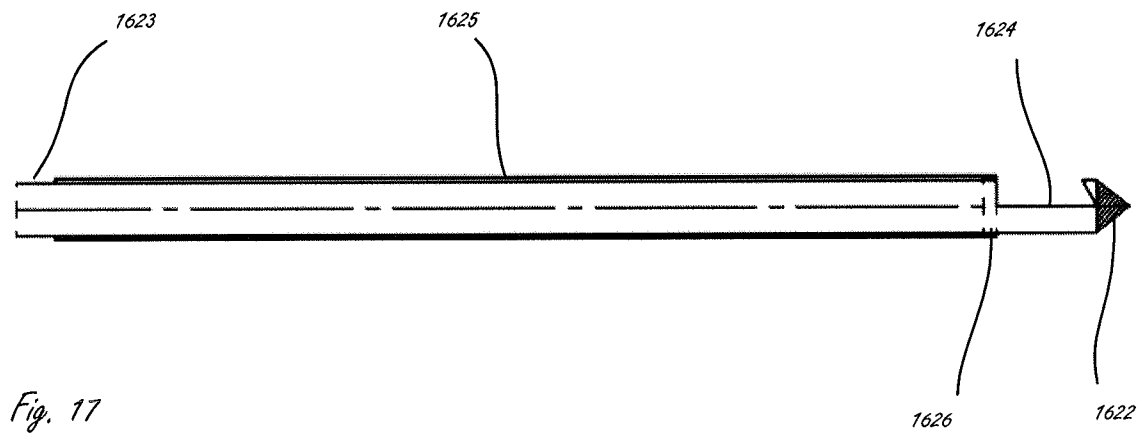
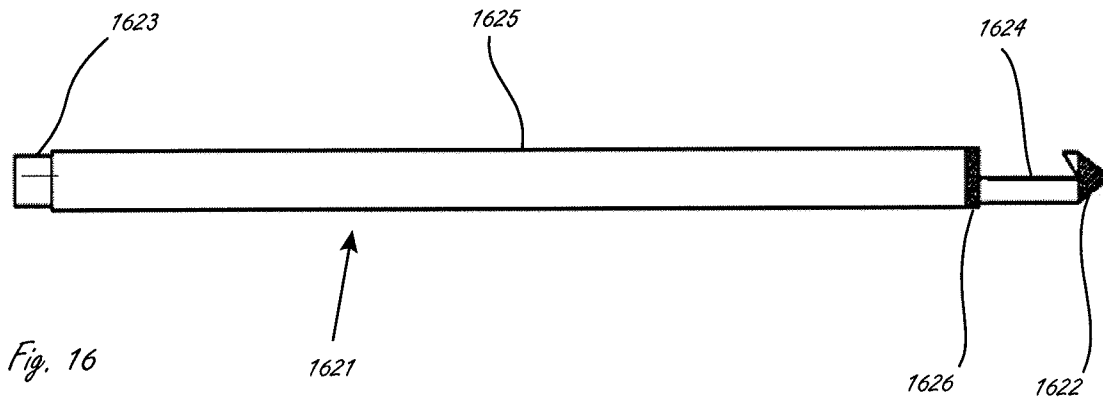
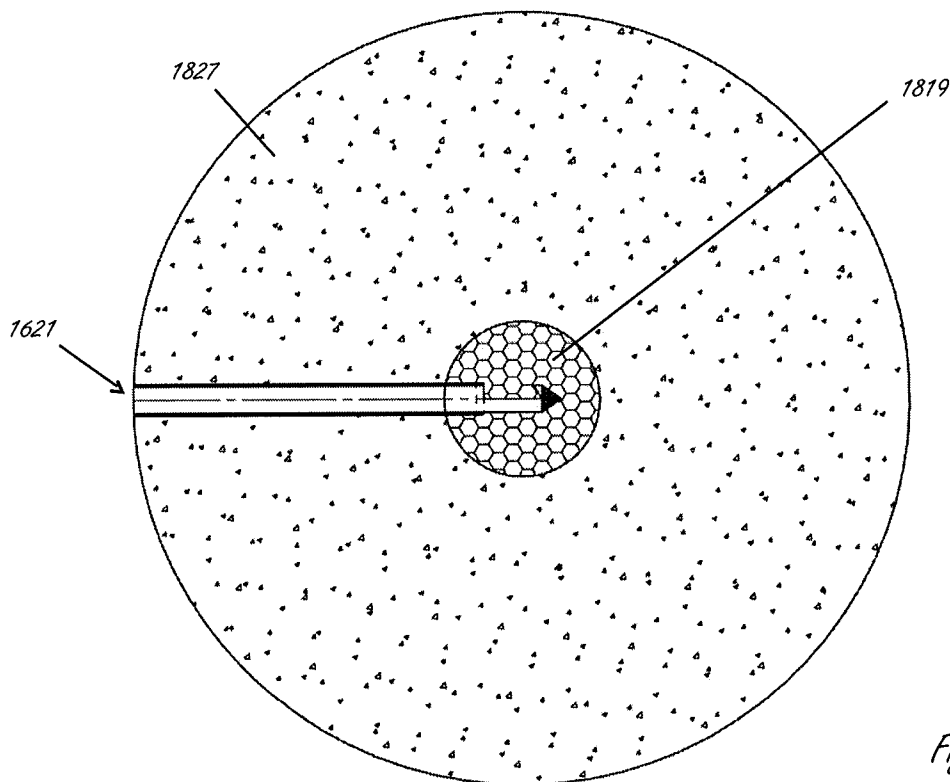
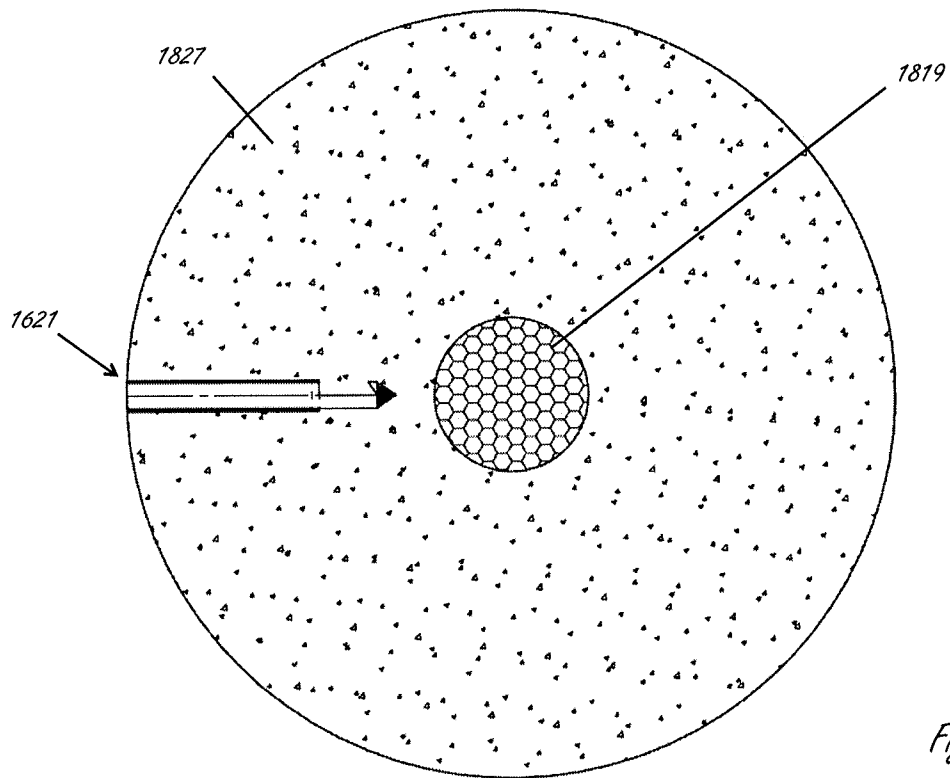


Fig. 13B





11 / 30



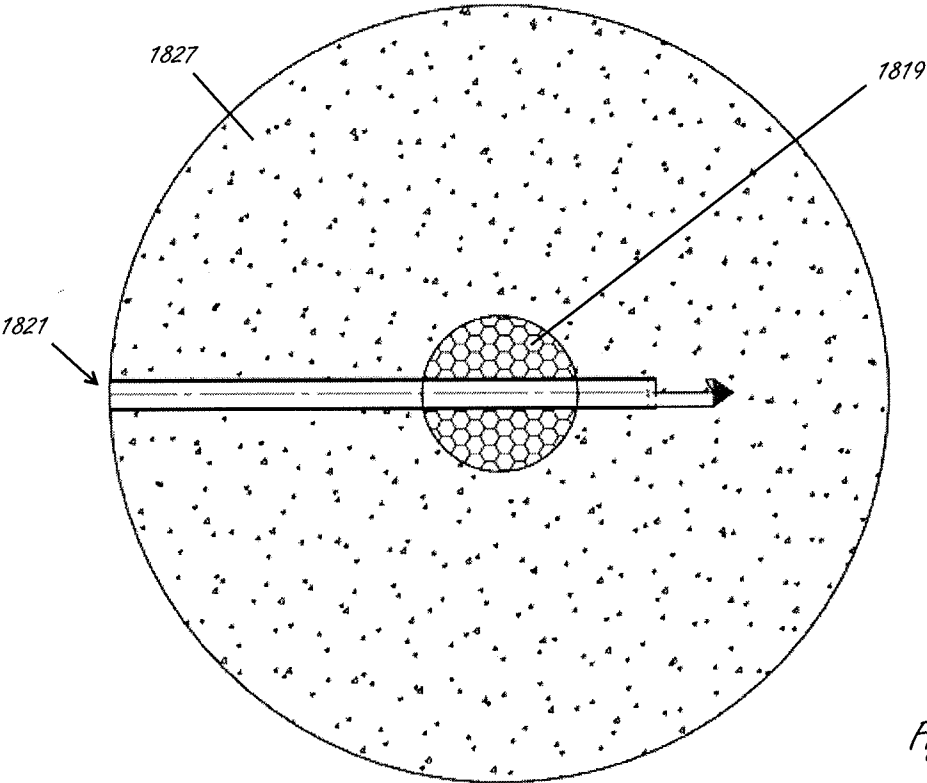


Fig. 20

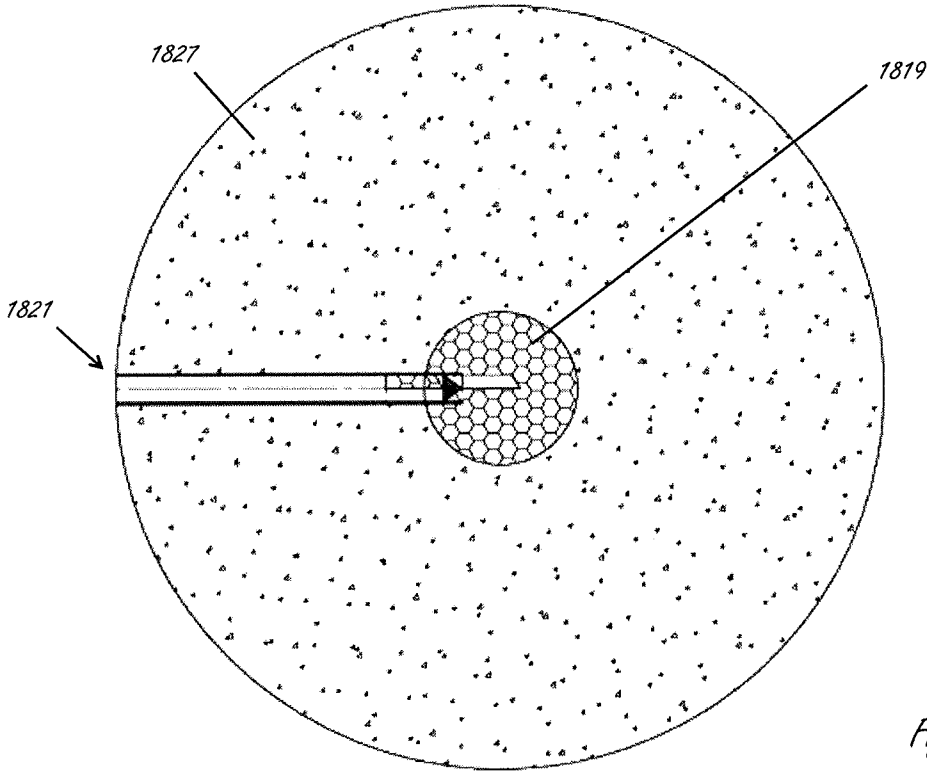
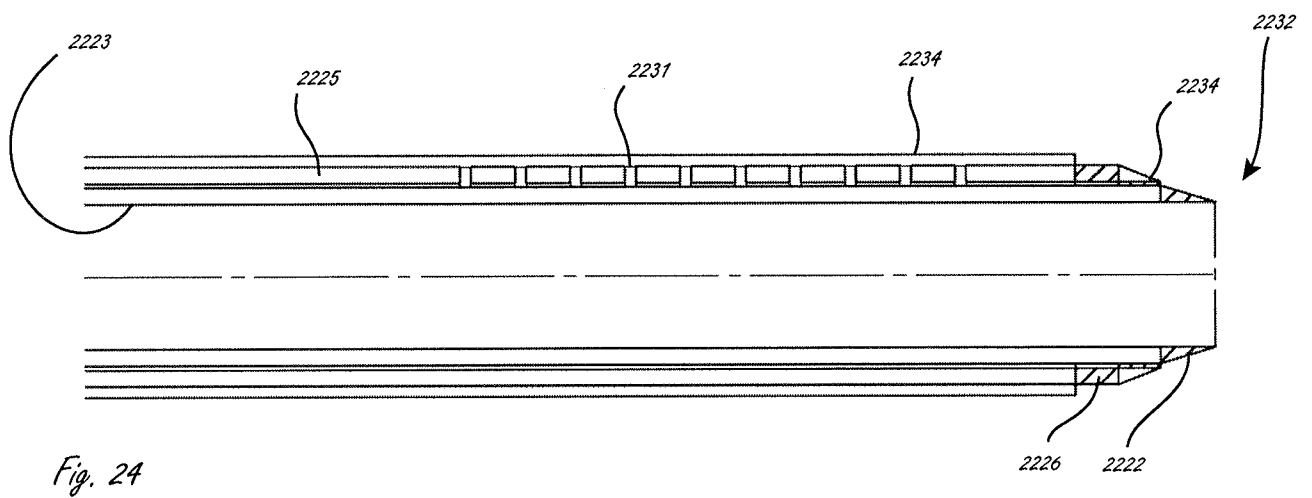
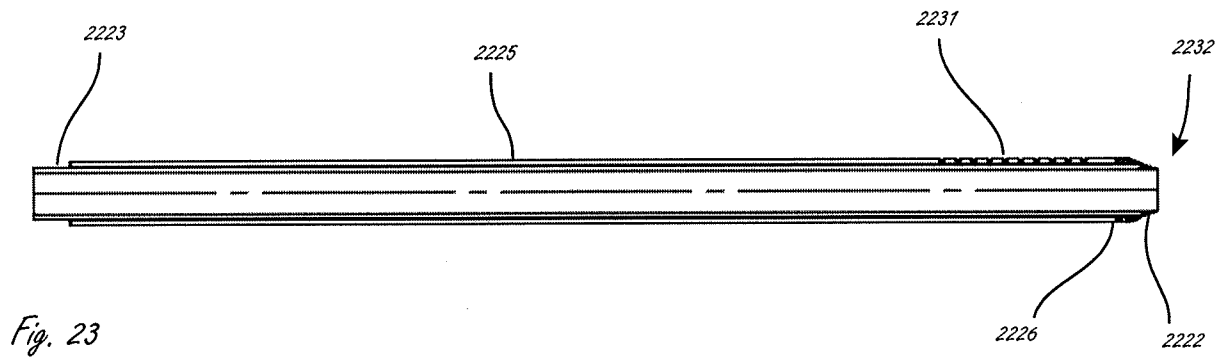
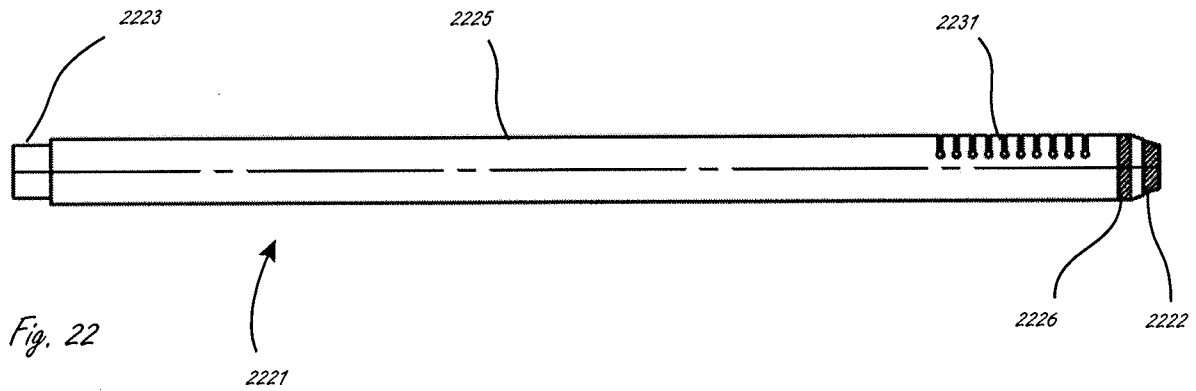
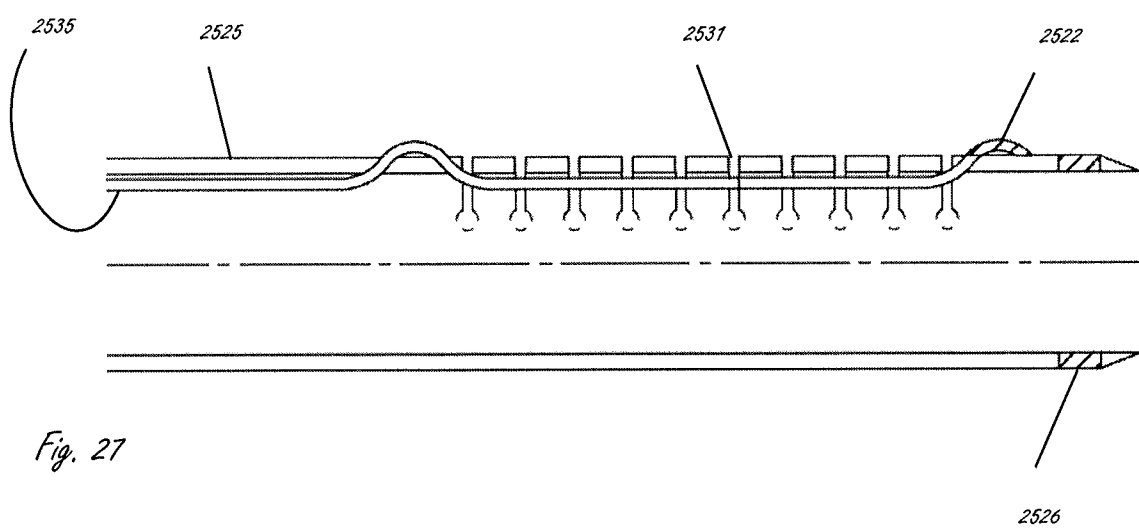
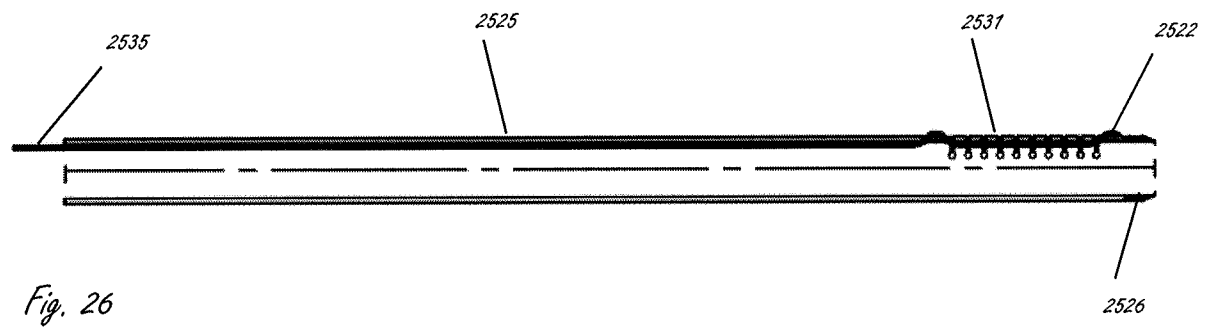
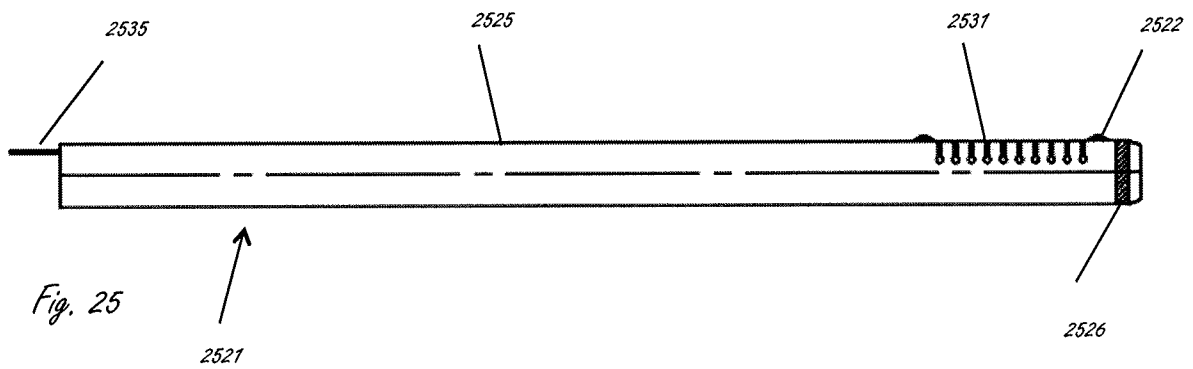


Fig. 21





15 / 30

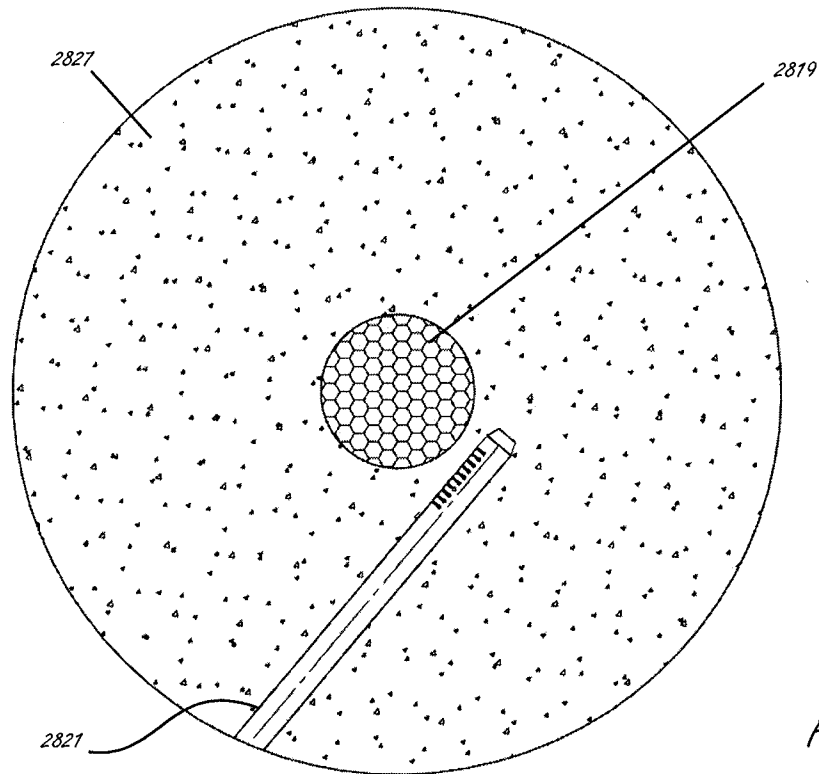


Fig. 28

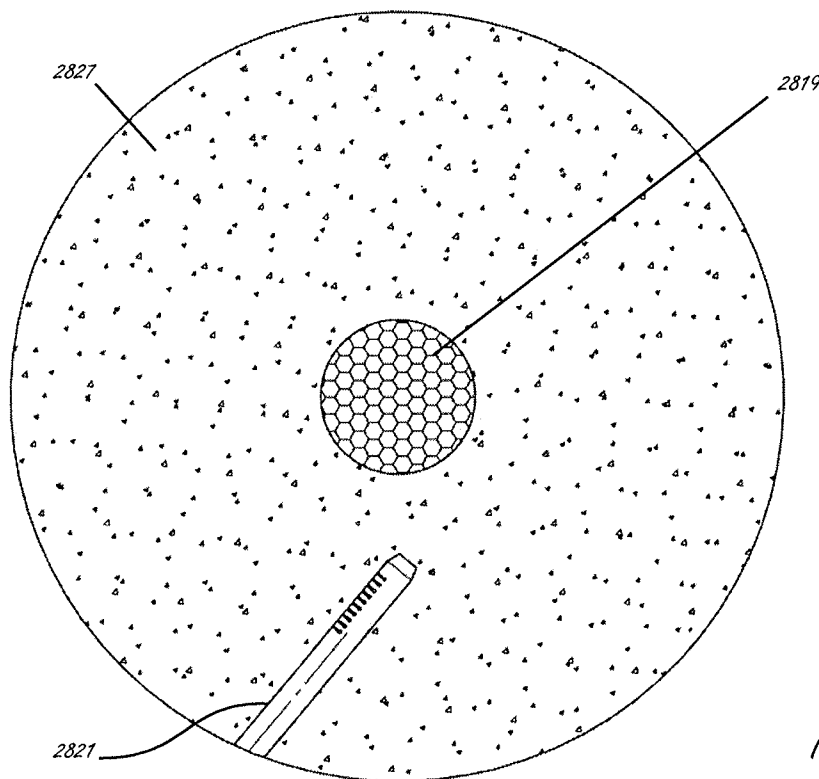


Fig. 29

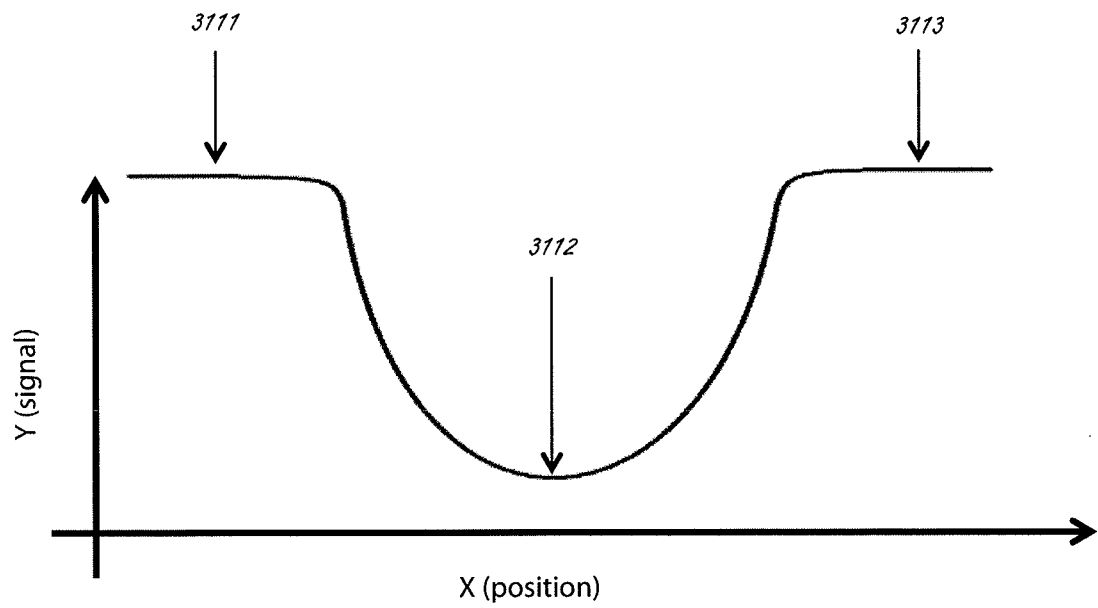
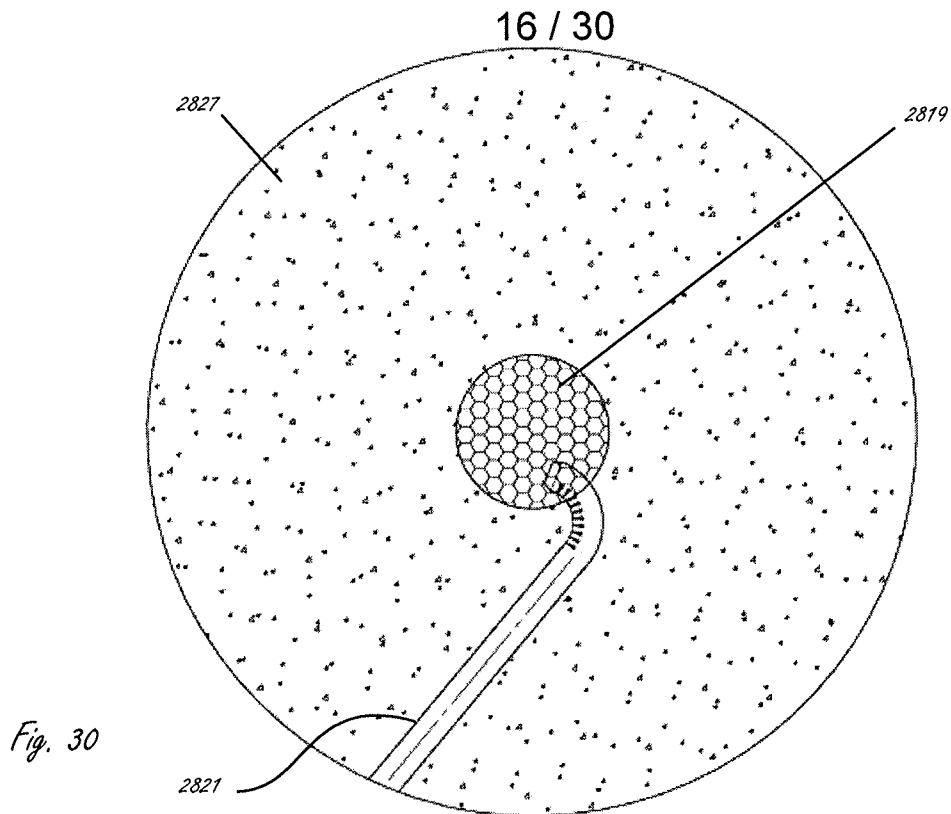


Fig. 31

17 / 30

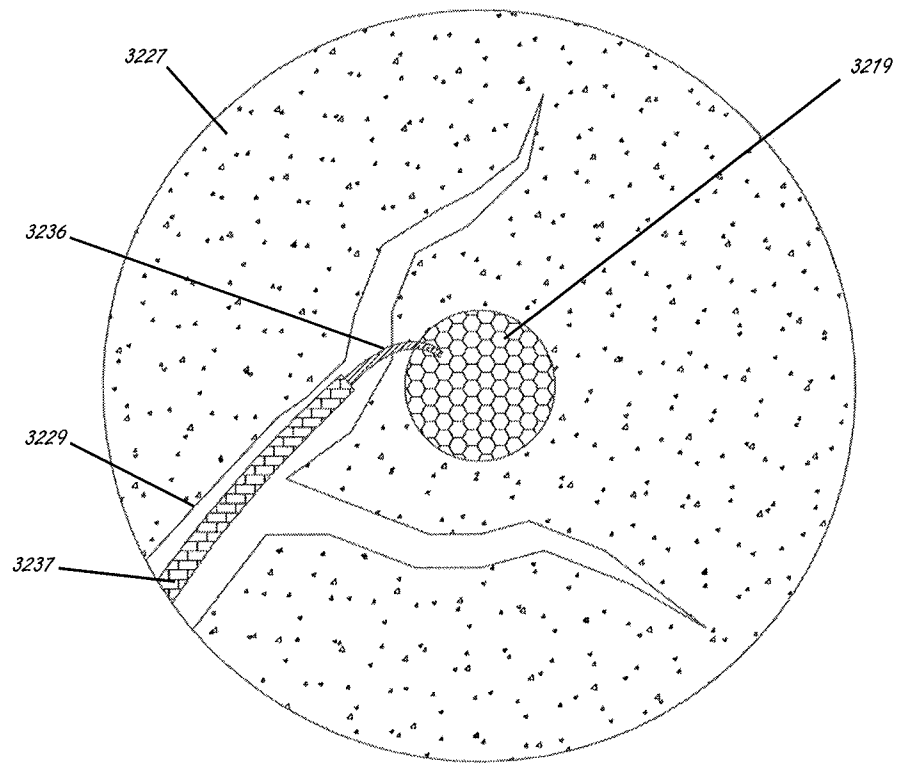


Fig. 32

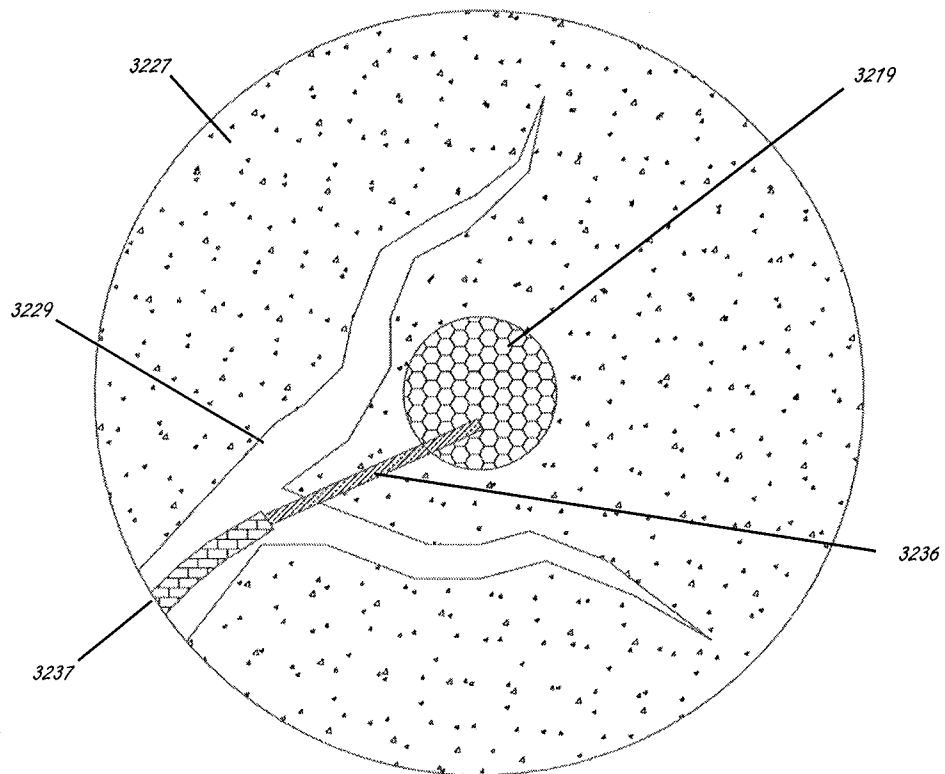
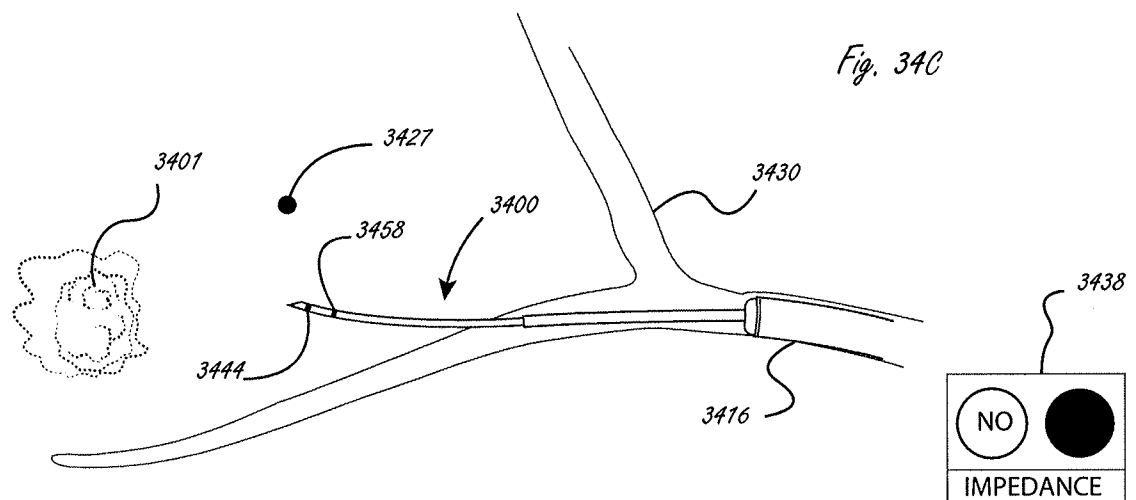
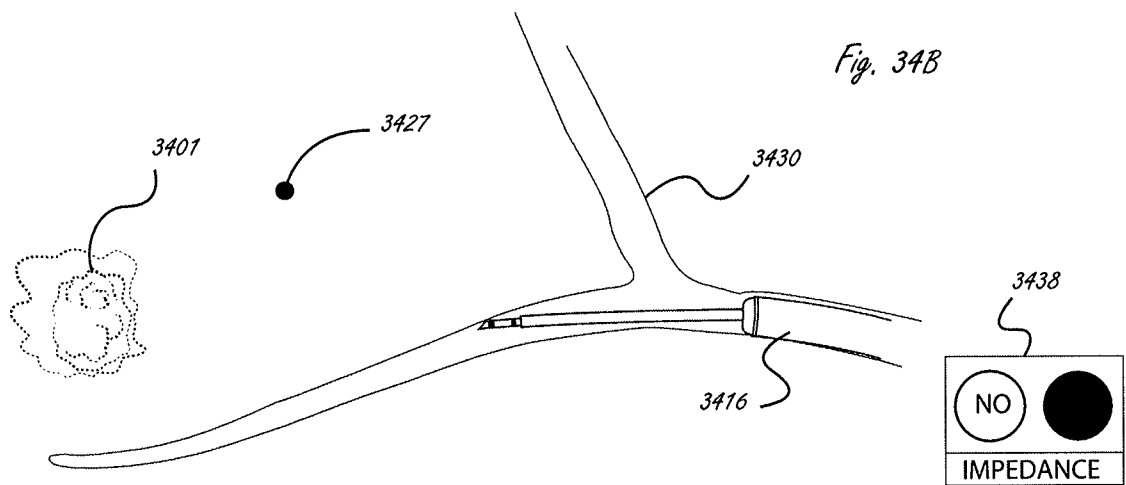
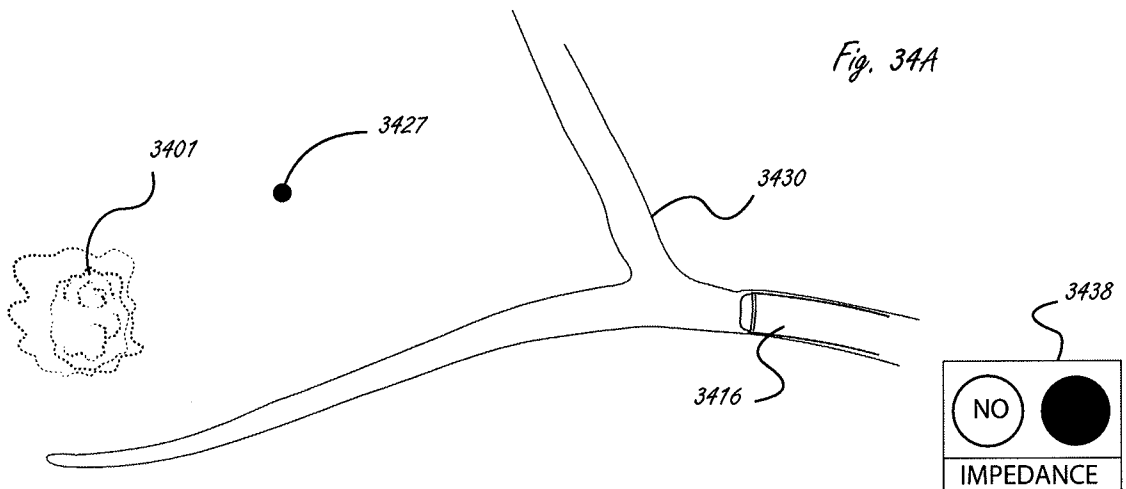
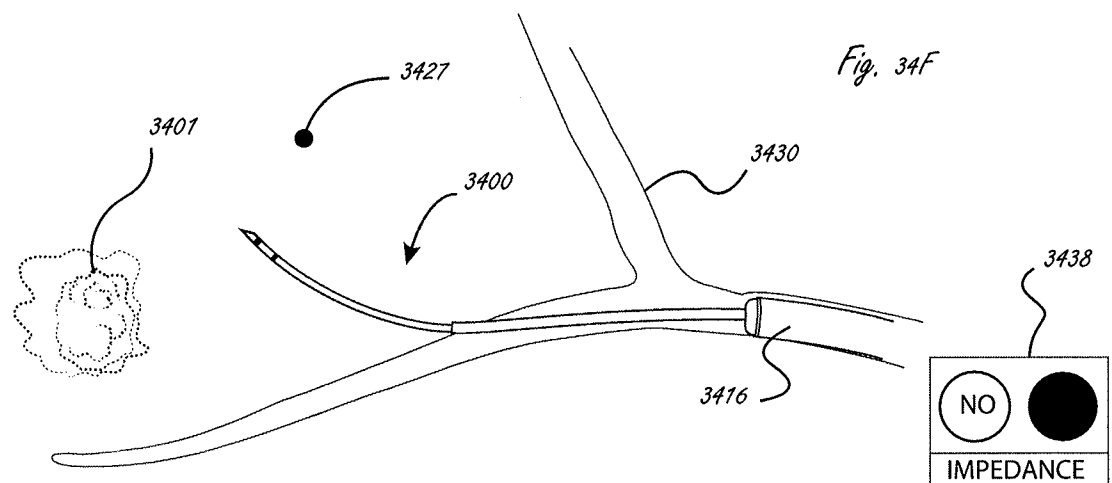
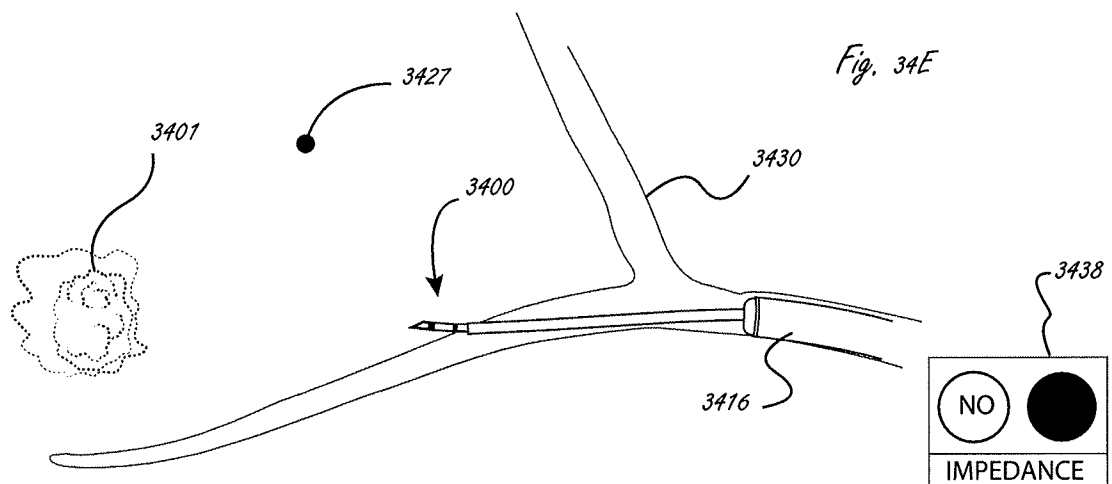
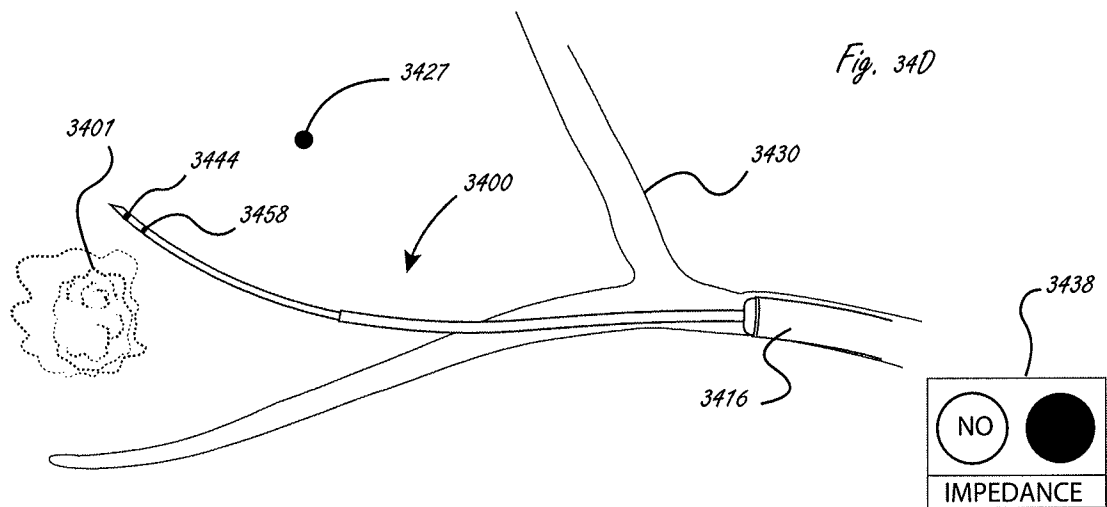


Fig. 33

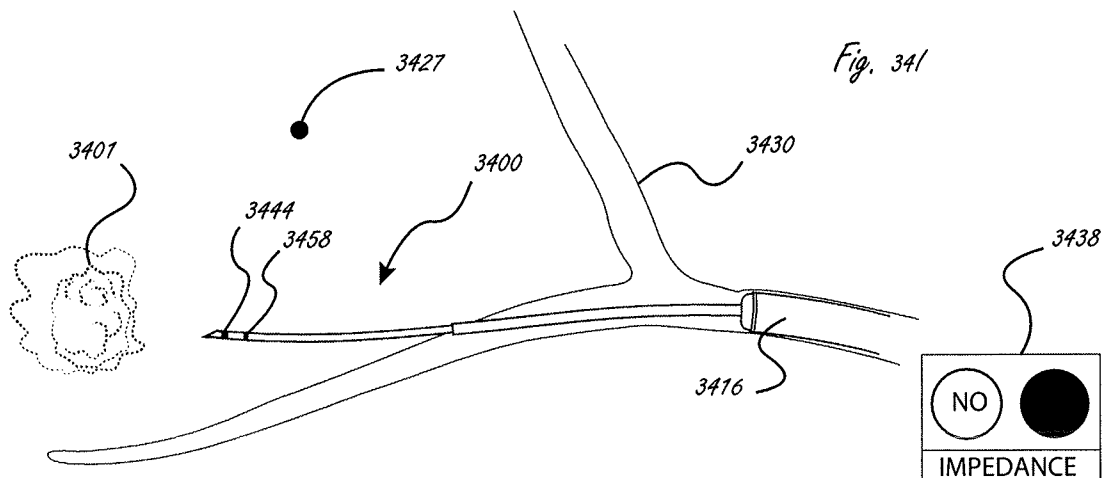
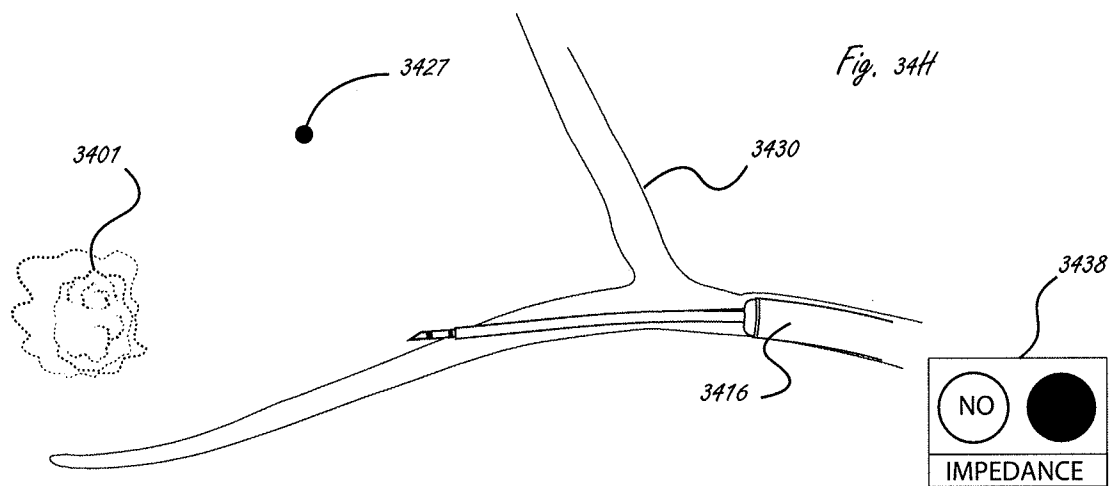
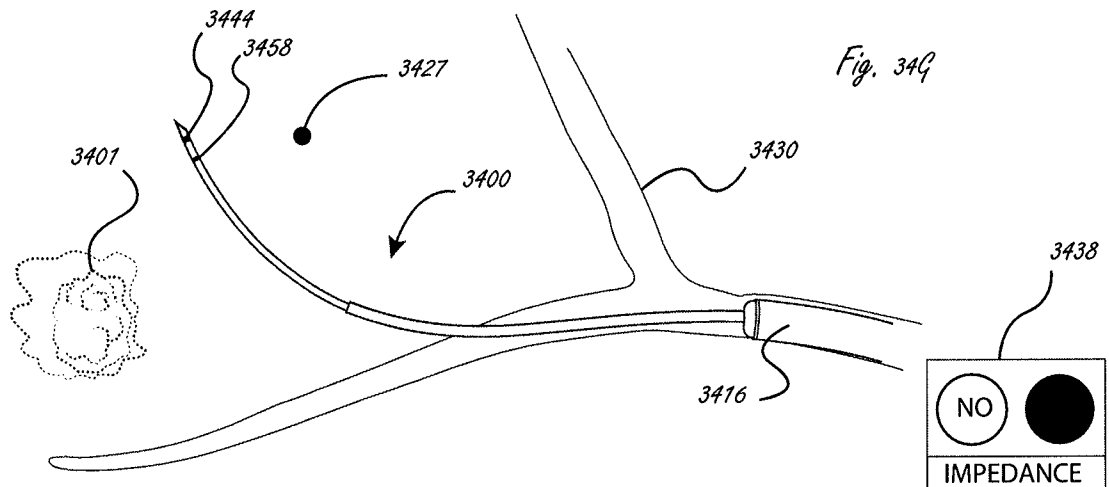
18 / 30



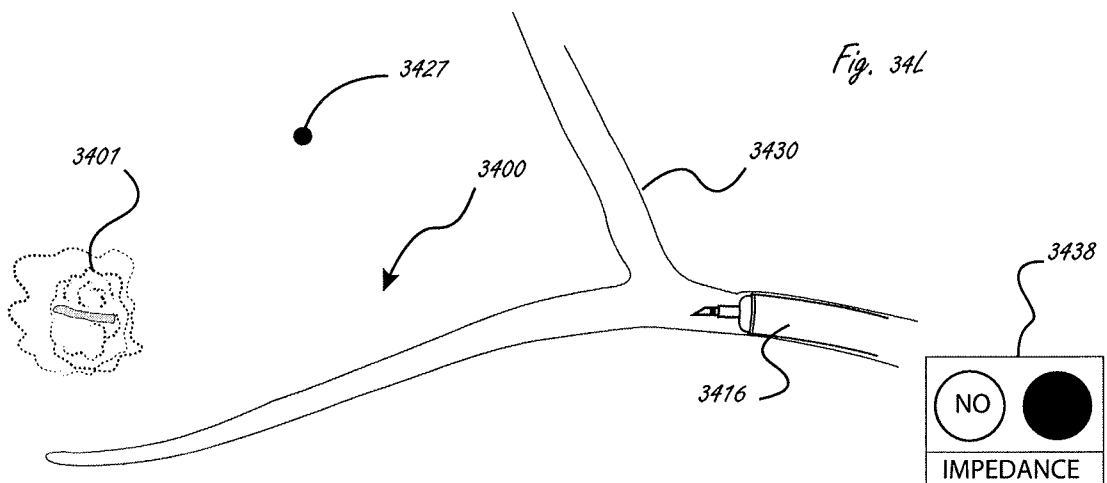
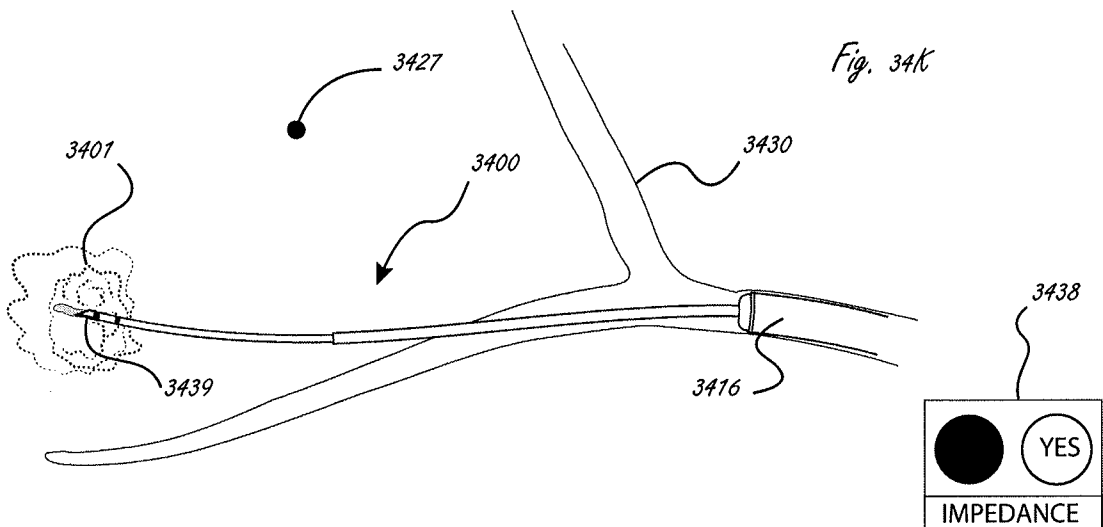
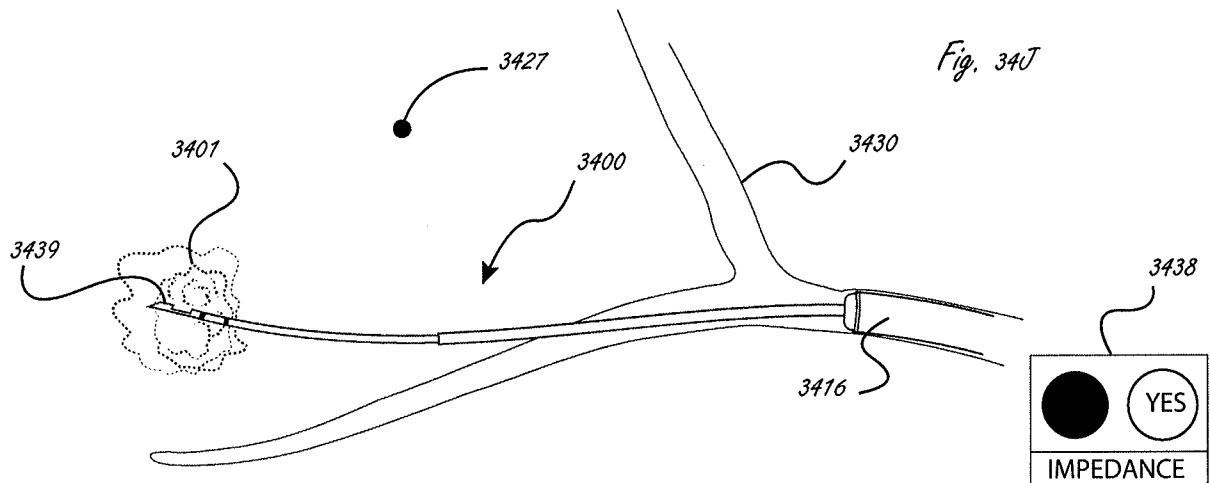
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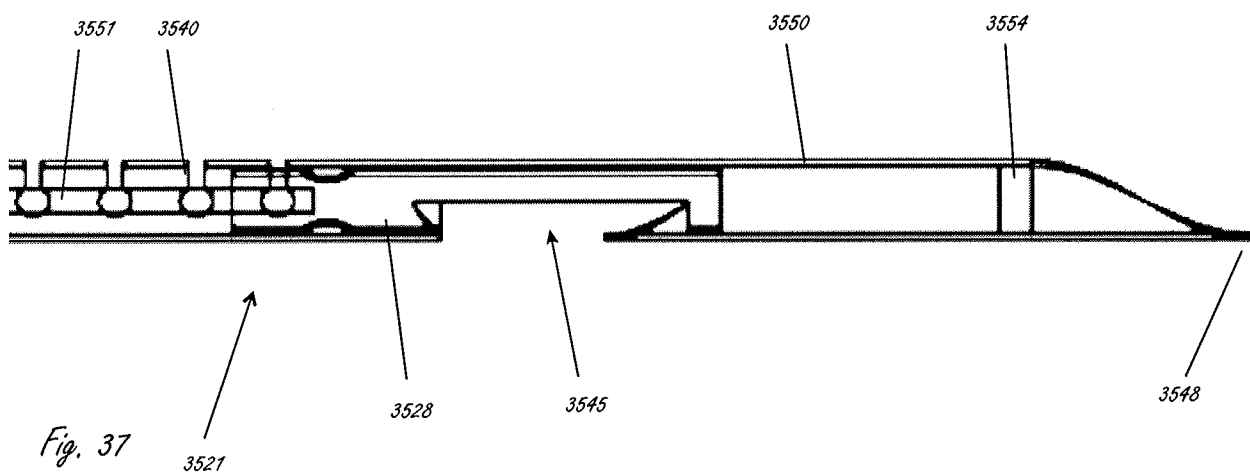
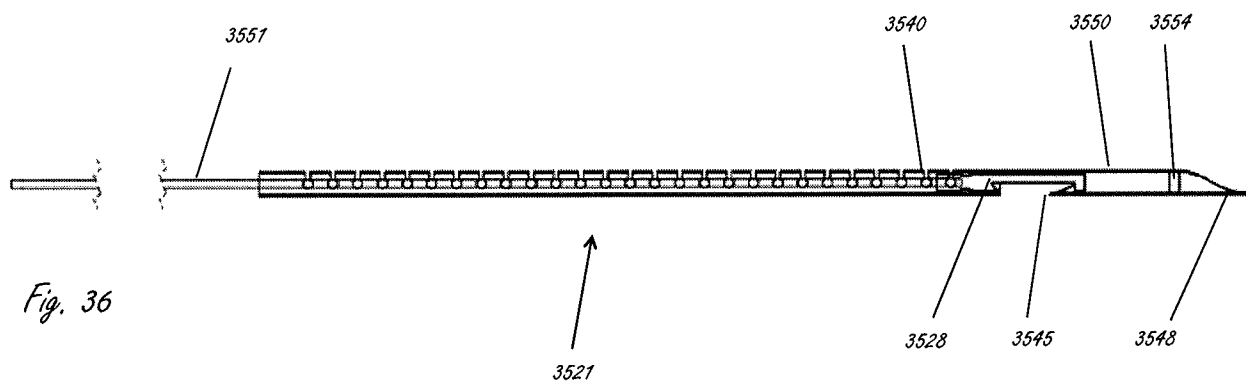
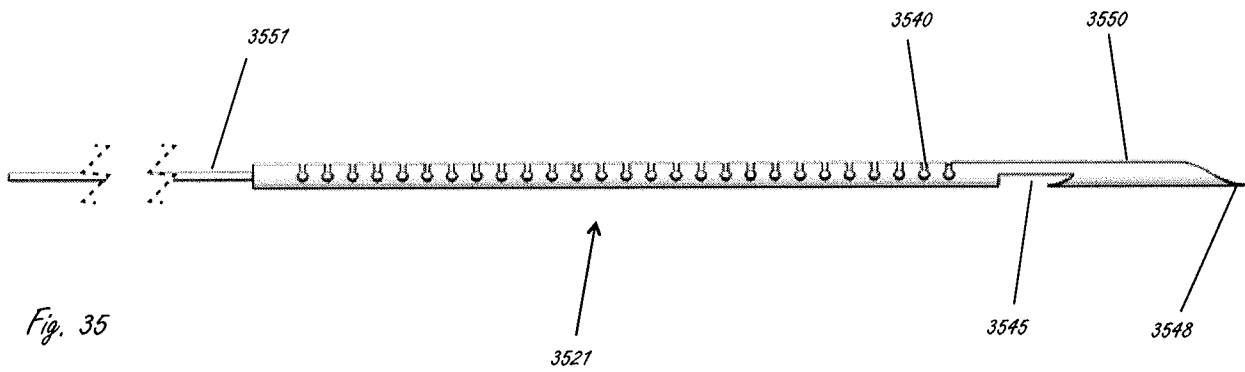


20 / 30

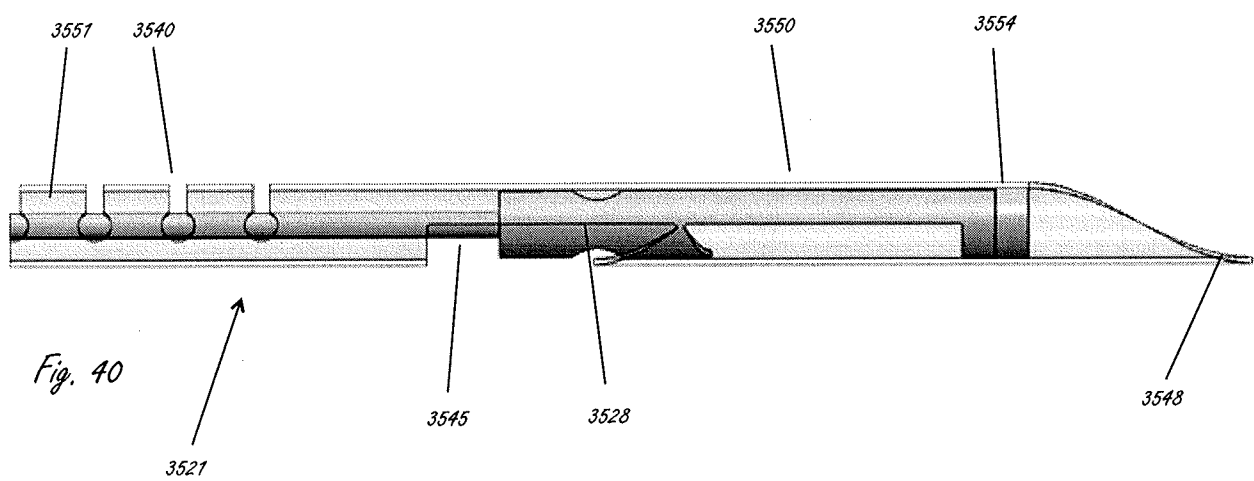
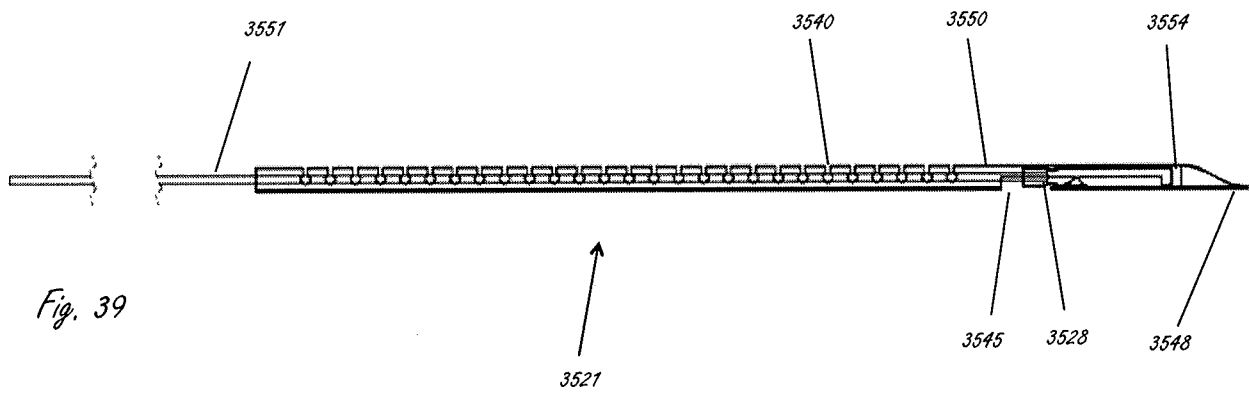
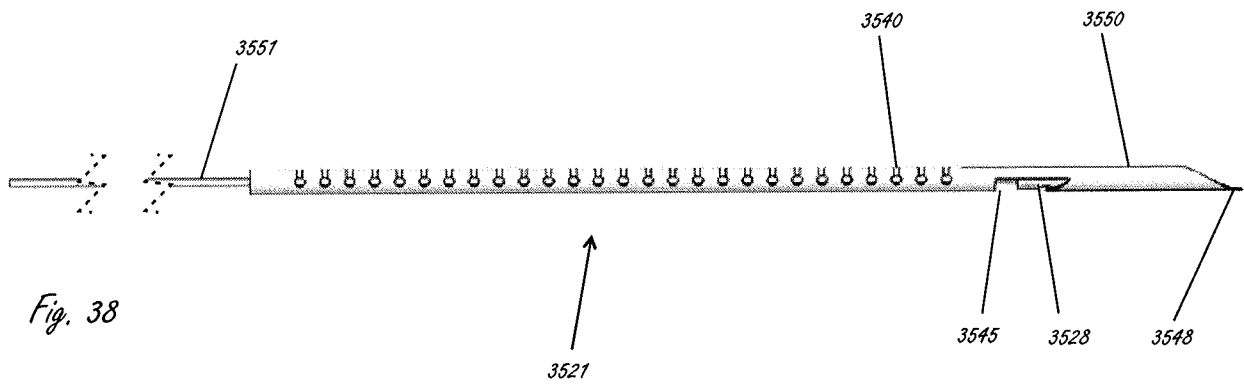


21 / 30

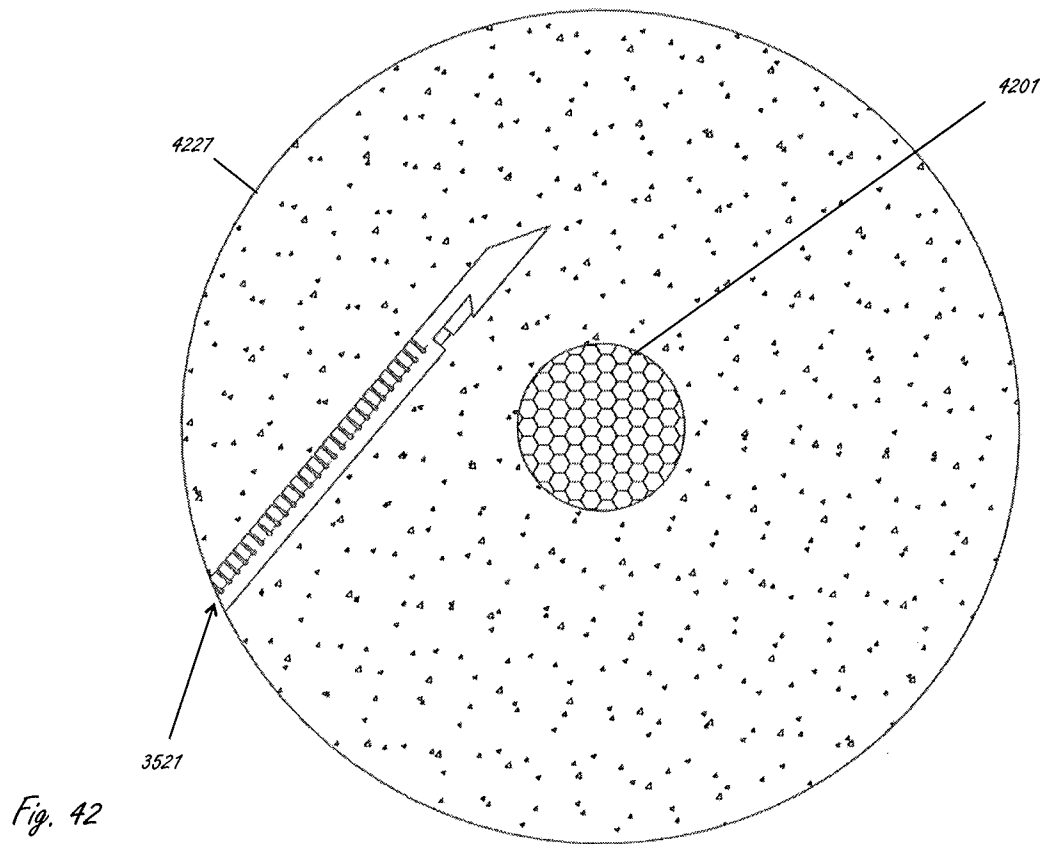
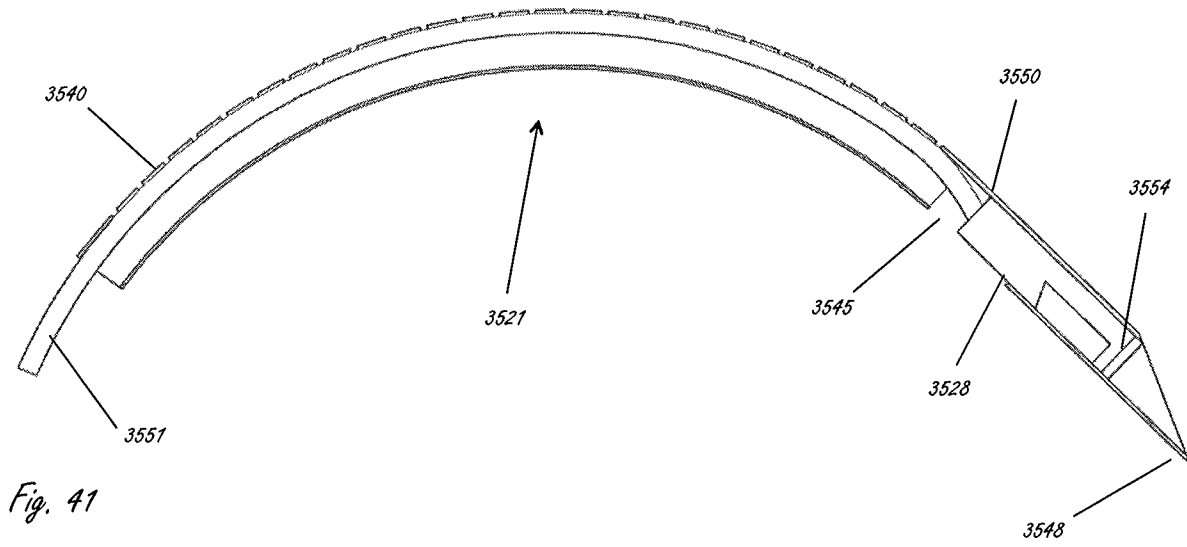




23 / 30



24 / 30



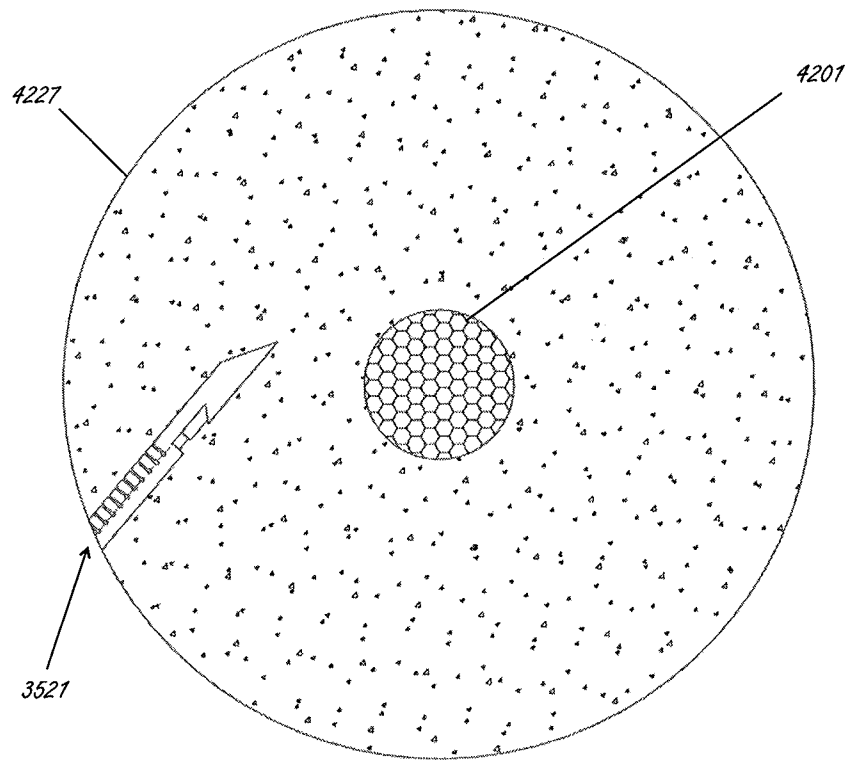


Fig. 43

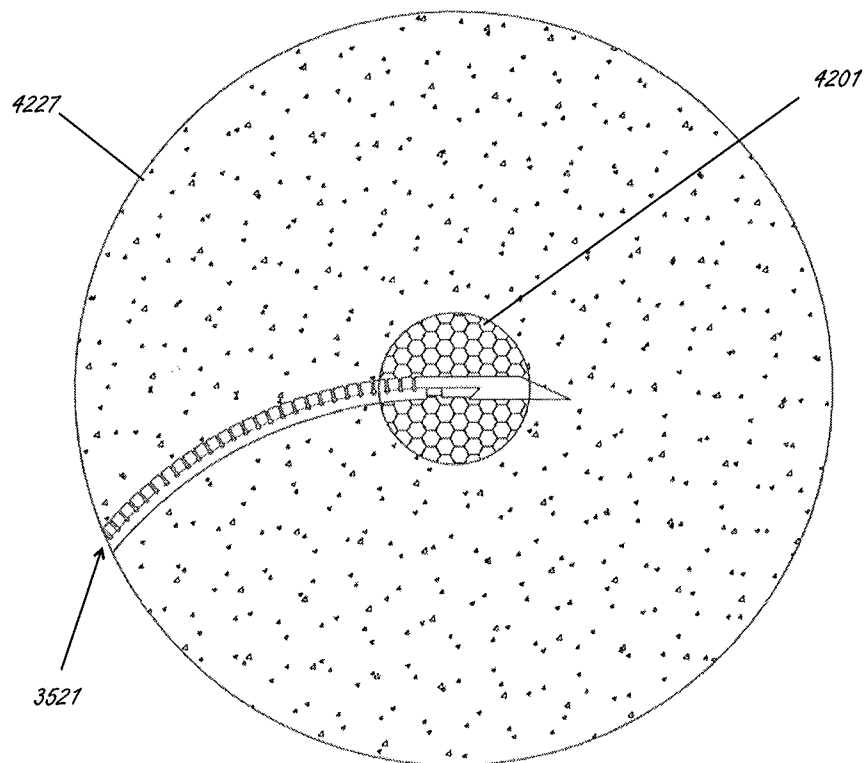


Fig. 44

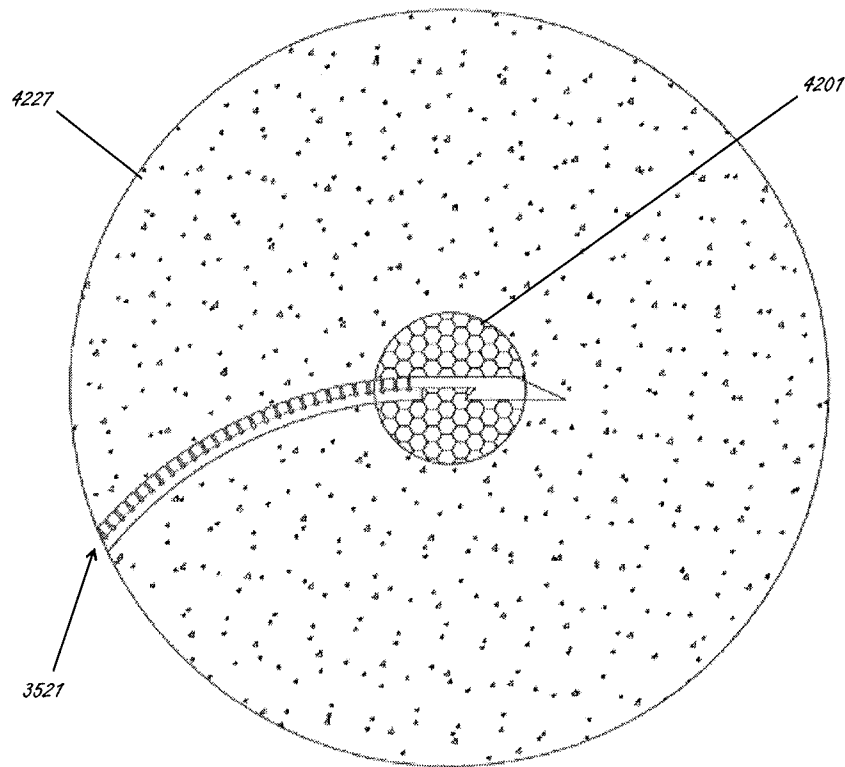


Fig. 45

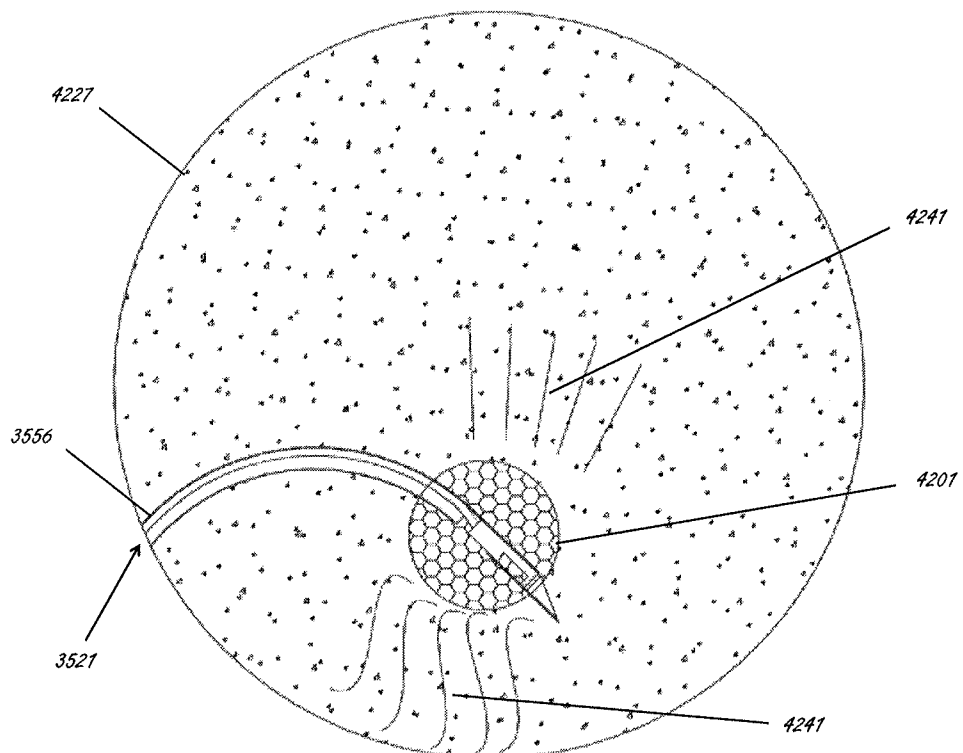


Fig. 46

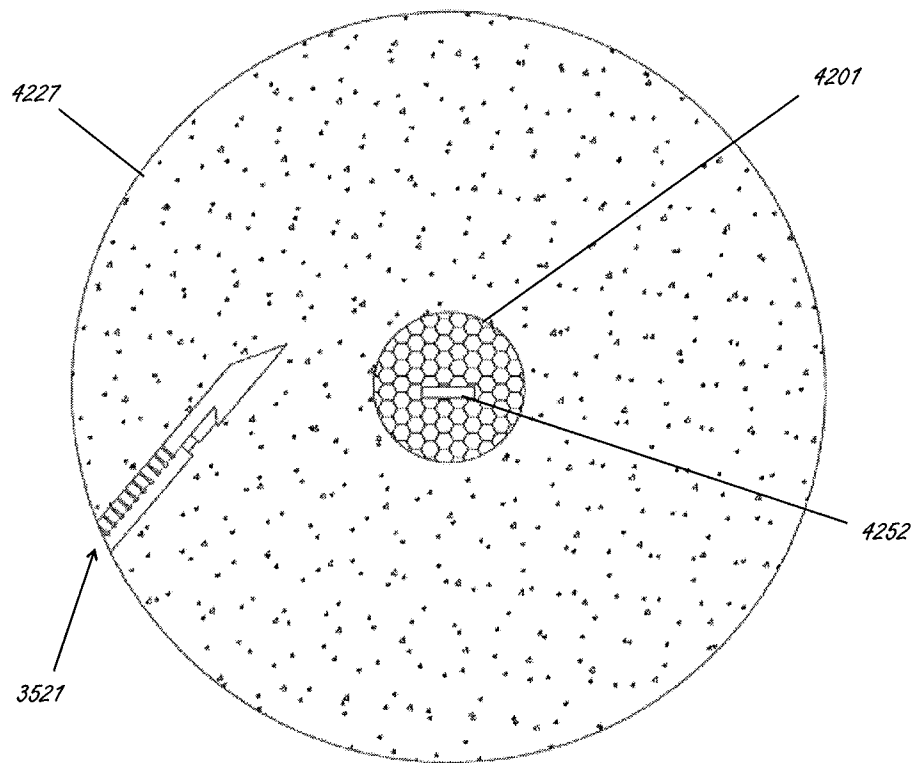
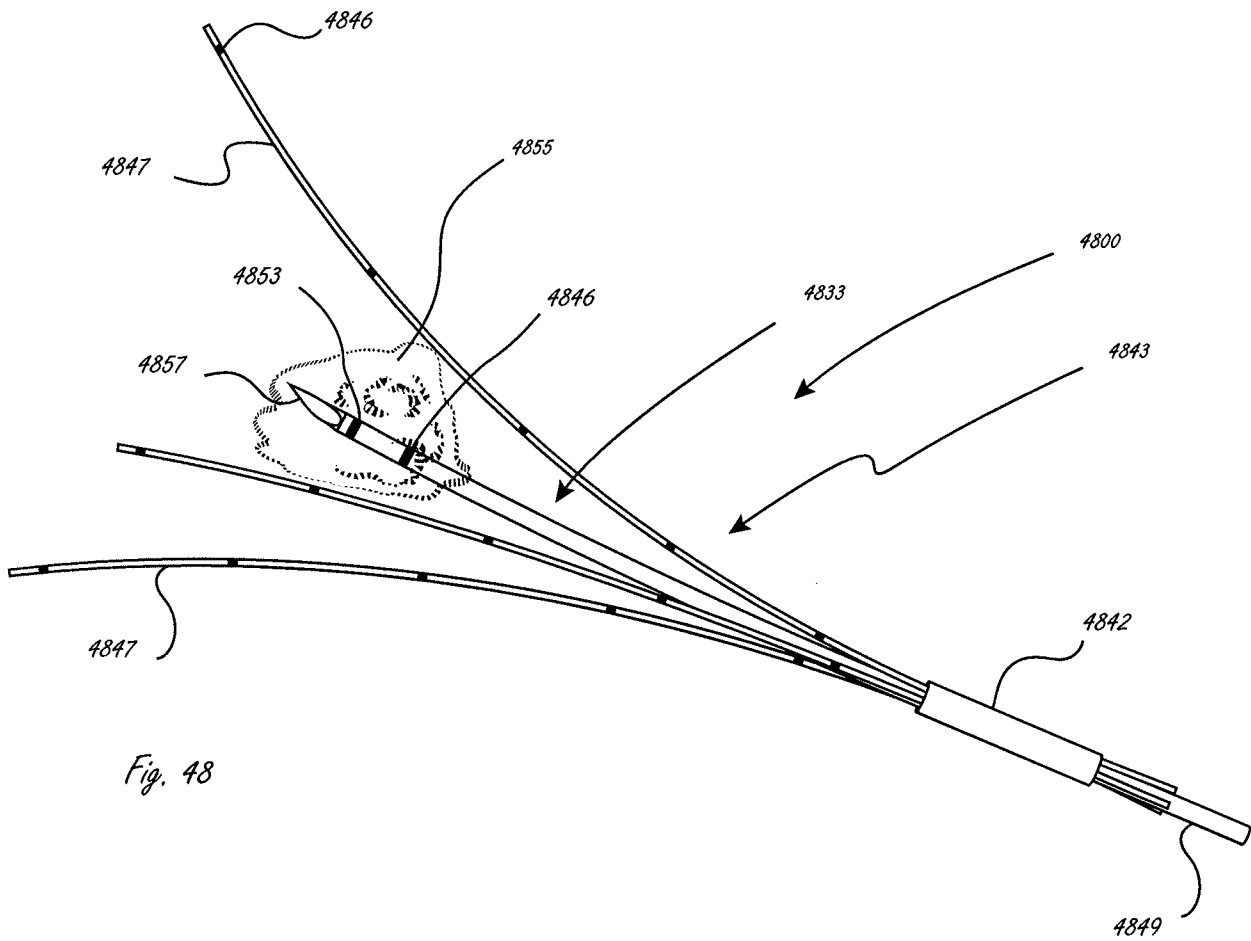


Fig. 47



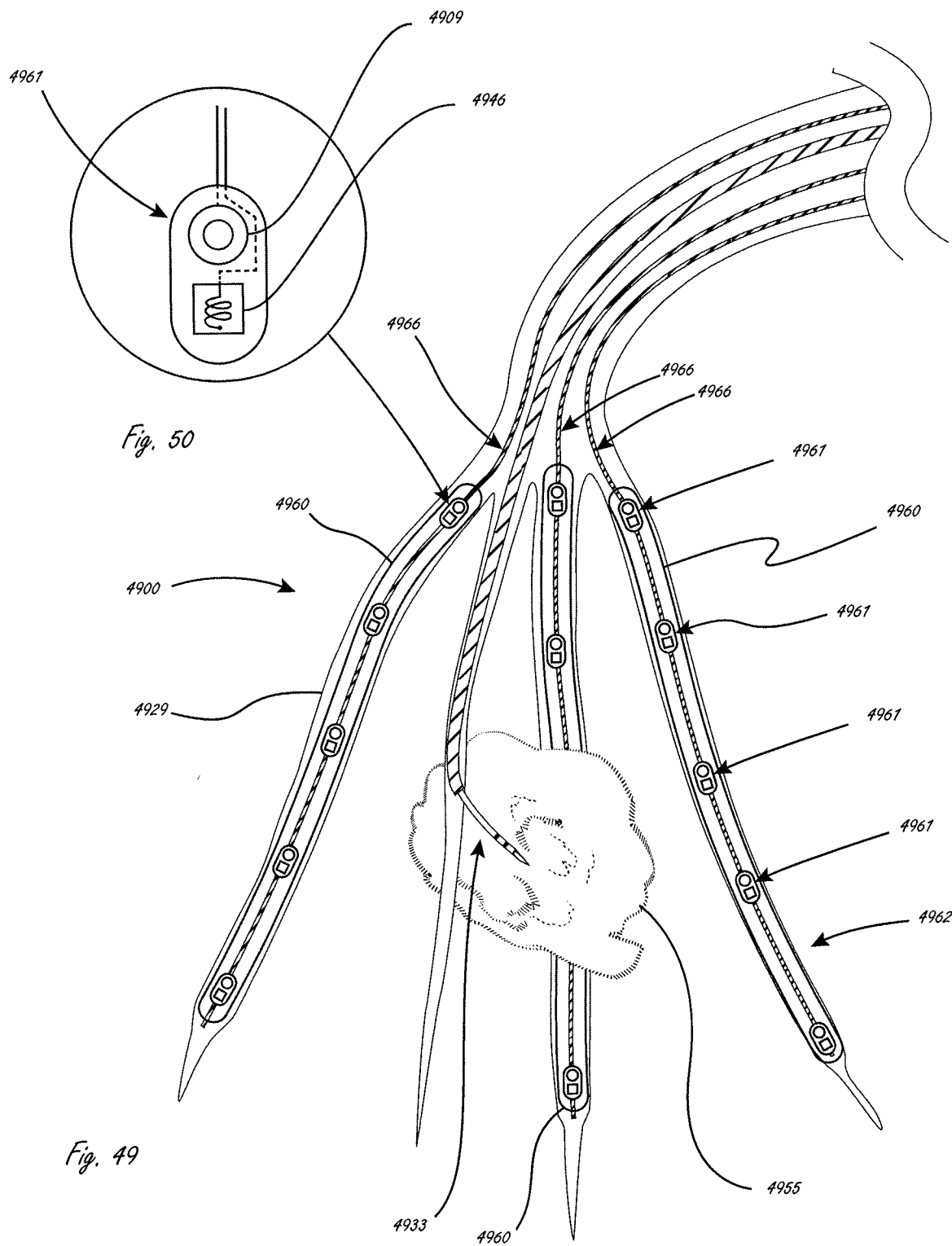


Fig. 49

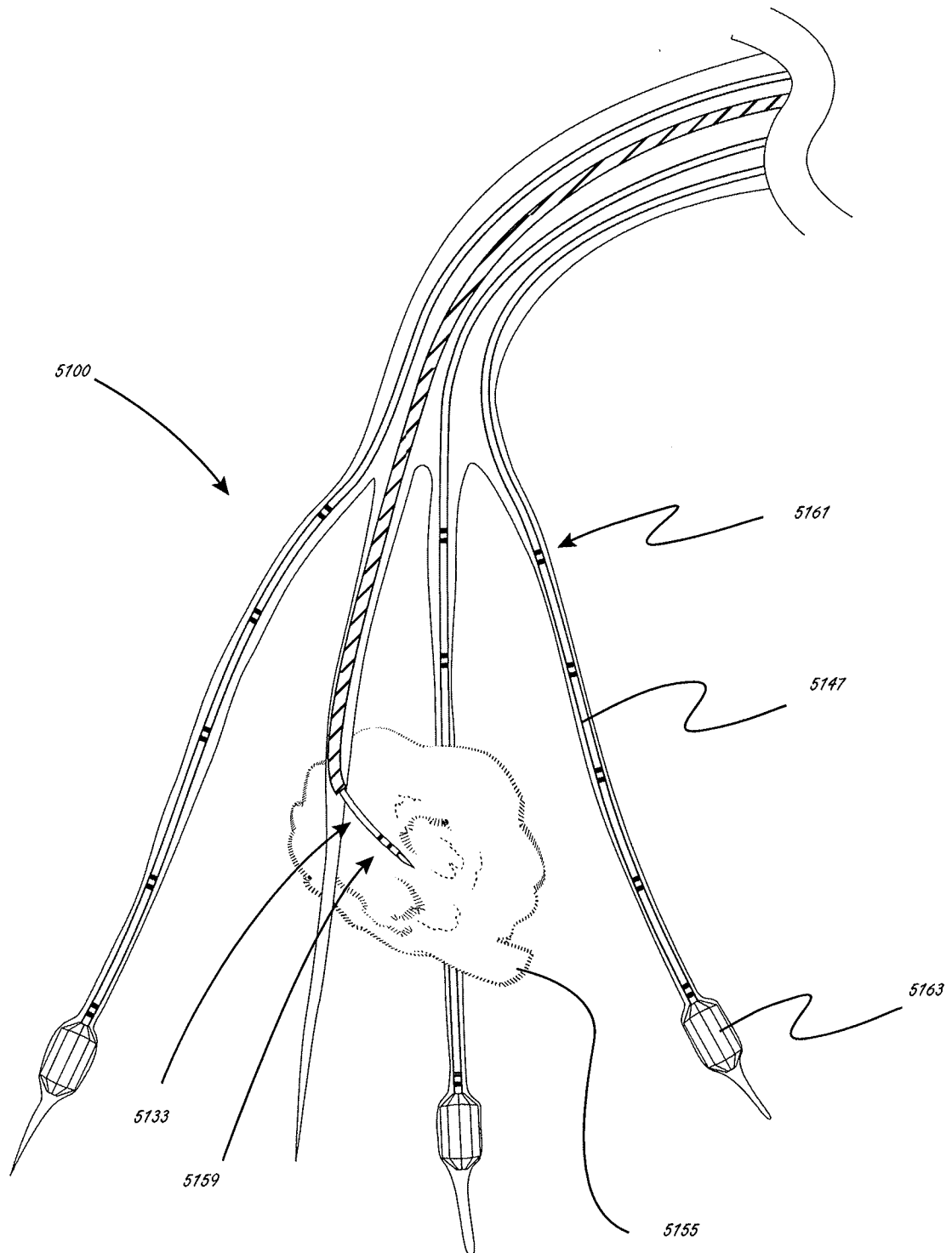


Fig. 51