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(54) **TUNED RF ENERGY FOR SELECTIVE TREATMENT OF ATHEROMA AND OTHER TARGET TISSUES AND/OR STRUCTURES**

(60) Provisional application No. 60/666,766, filed on Mar. 28, 2005.

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Publication Classification

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A61B 18/00 (2006.01)

(52) **U.S. Cl.** **606/33; 606/41**

(73) Assignee: **Vessix Vascular, Inc.**, Laguna Hills, CA (US)

(57) **ABSTRACT**

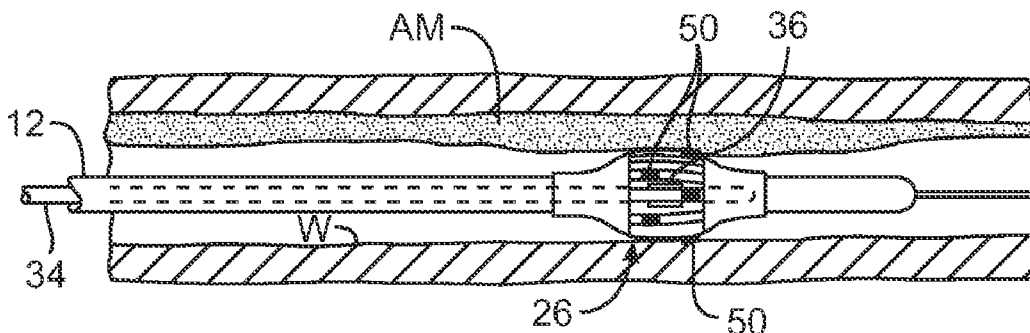
(21) Appl. No.: **13/406,458**

(22) Filed: **Feb. 27, 2012**

A catheter and catheter system can use energy tailored for remodeling and/or removal of target material along a body lumen, often of atherosclerotic material of a blood vessel of a patient. An elongate flexible catheter body with a radially expandable structure may have a plurality of electrodes or other electrosurgical energy delivery surfaces to radially engage atherosclerotic material when the structure expands. An atherosclerotic material detector system may measure and/or characterize the atherosclerotic material and its location, optionally using impedance monitoring.

Related U.S. Application Data

(60) Continuation of application No. 12/660,515, filed on Feb. 26, 2010, which is a division of application No. 11/392,231, filed on Mar. 28, 2006, now Pat. No. 7,742,795.



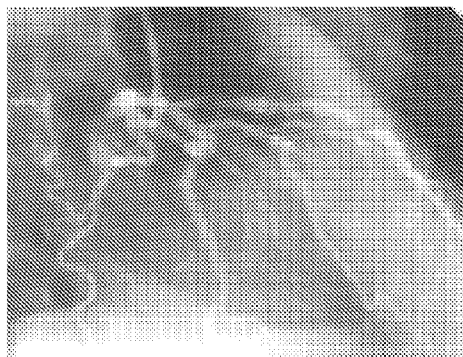


FIG. 1a



FIG. 1b

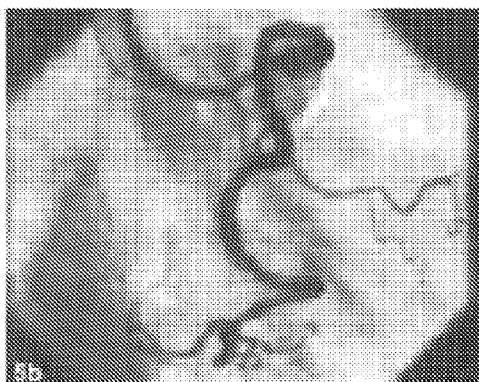


FIG. 1c

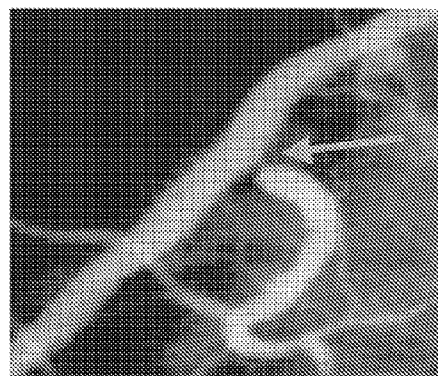


FIG. 1d



FIG. 1e

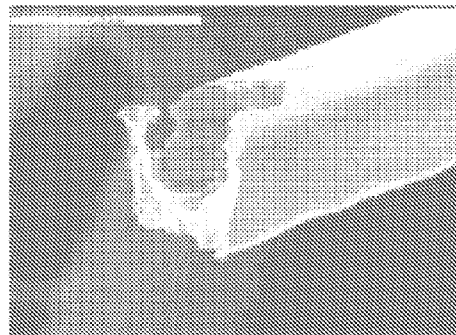


FIG. 1f

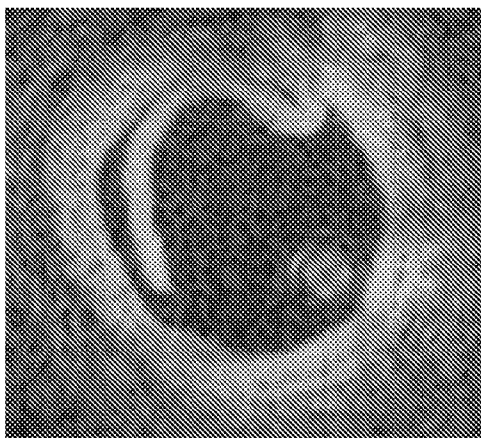


FIG. 1G

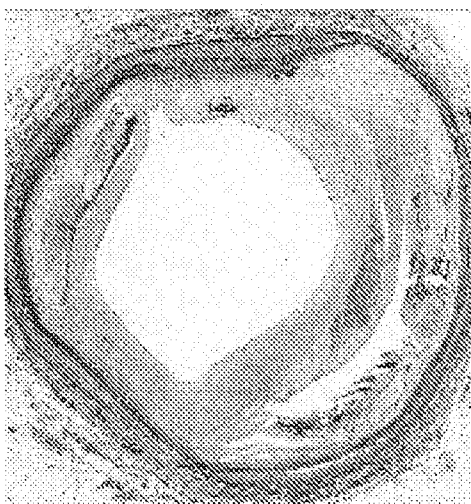


FIG. 1H

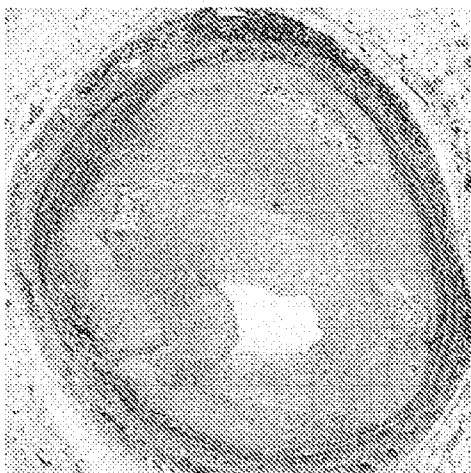
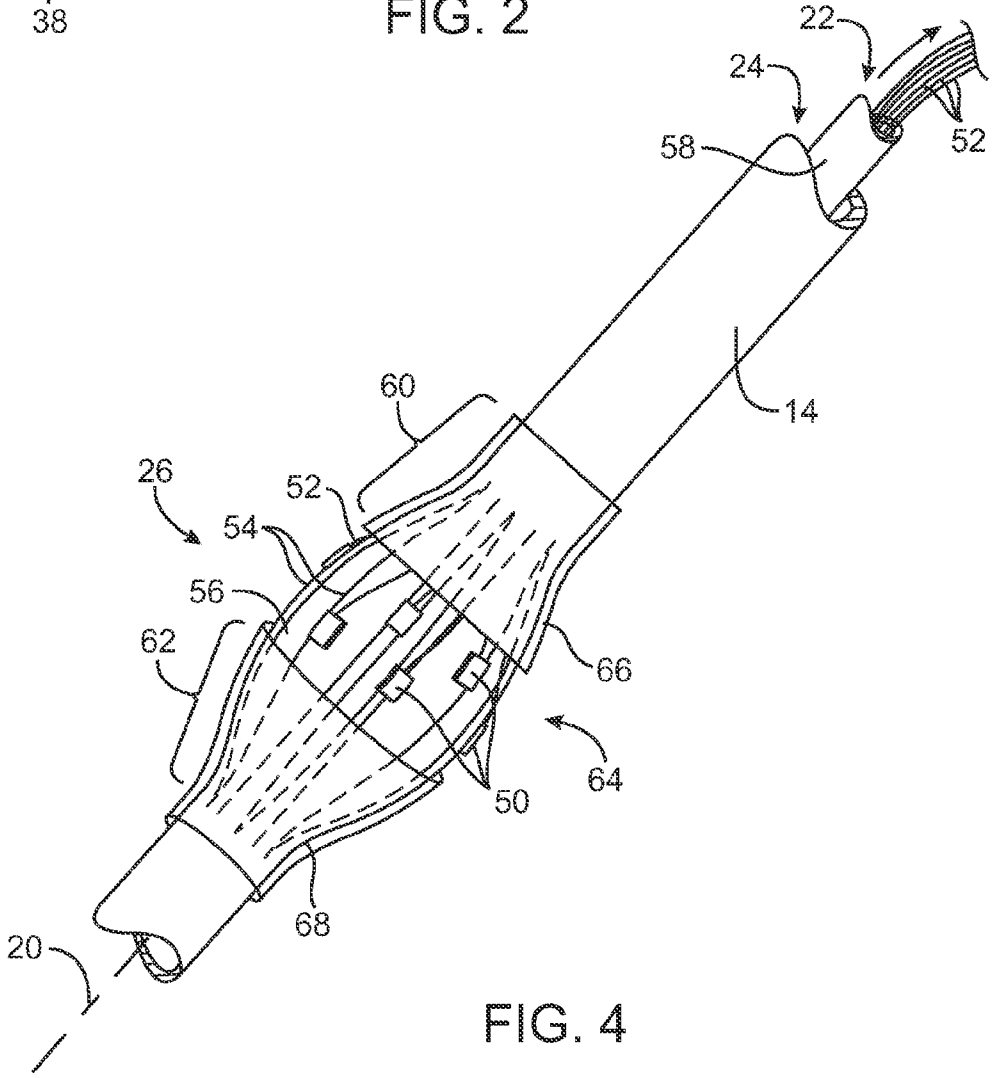
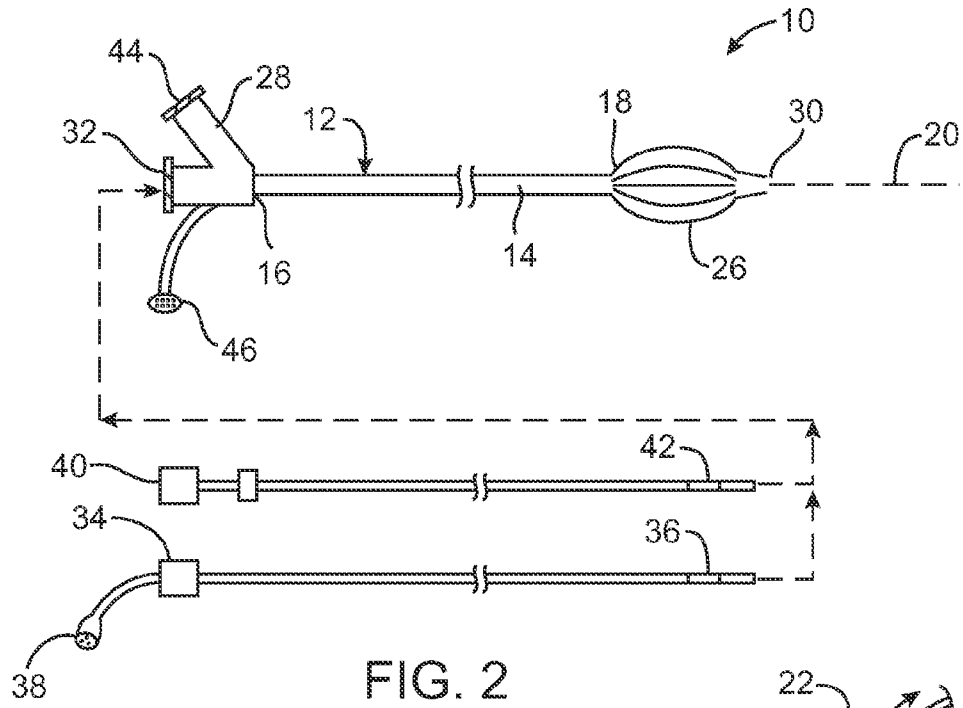


FIG. 1I



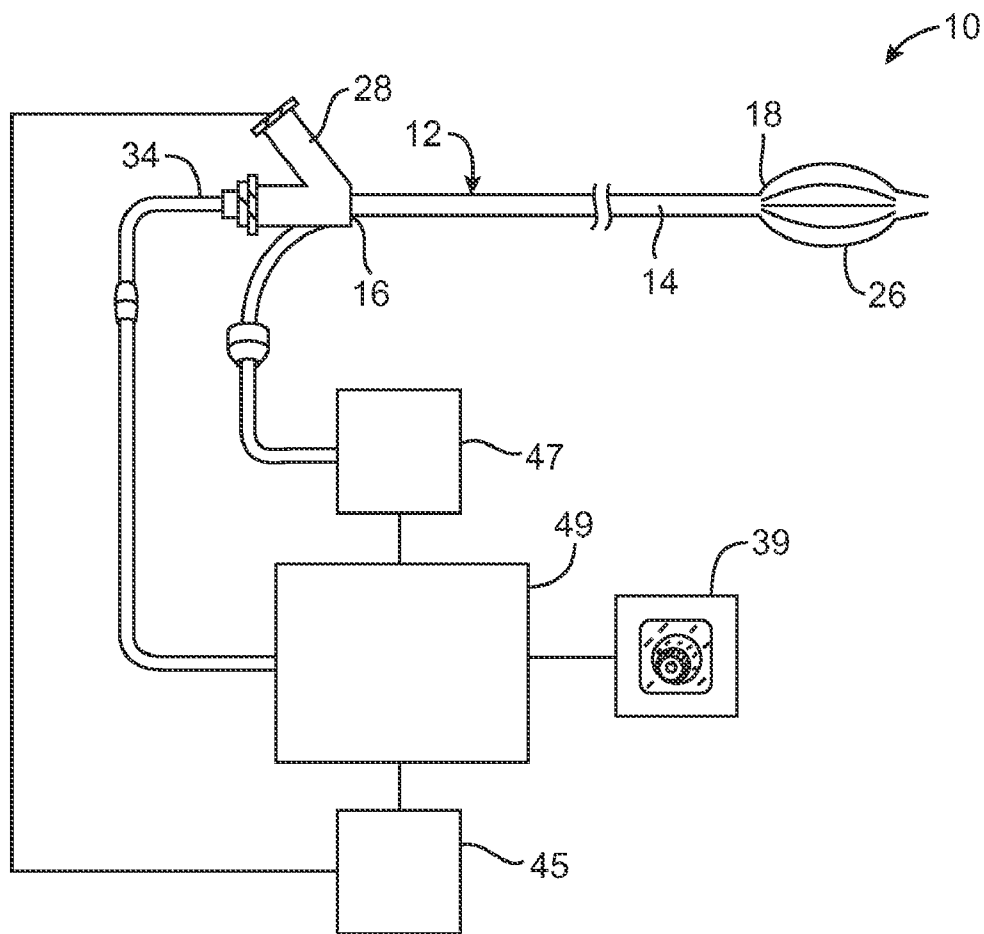
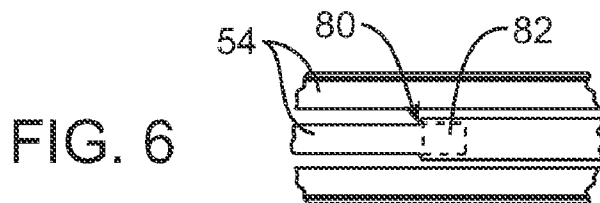
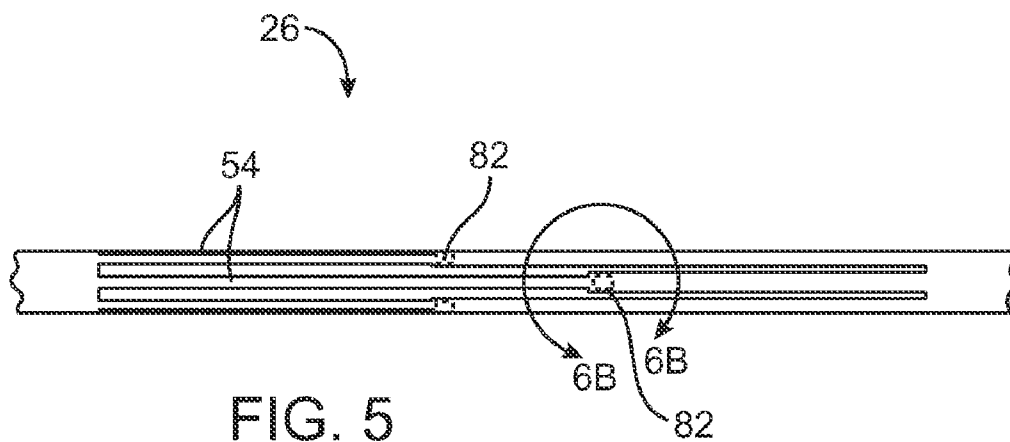


FIG. 3



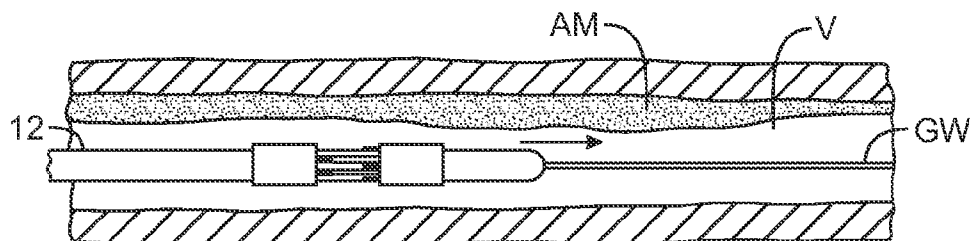


FIG. 7A

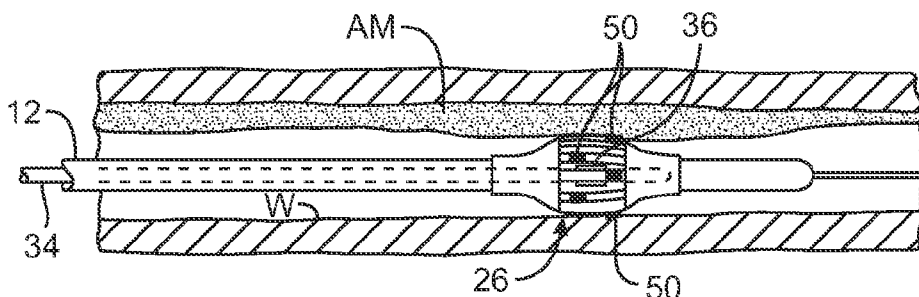


FIG. 7B

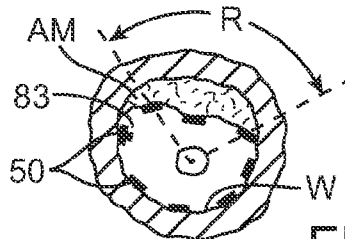


FIG. 7C

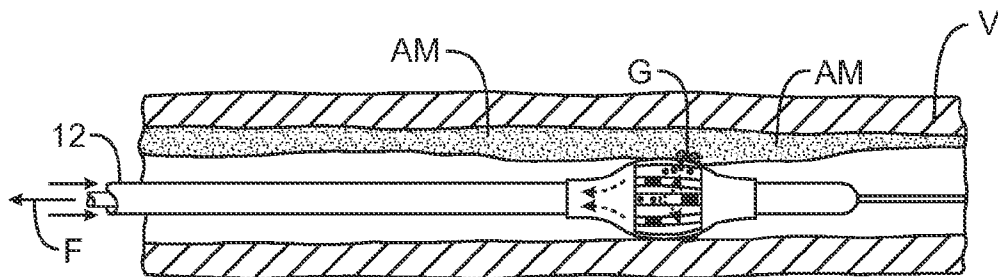


FIG. 7D

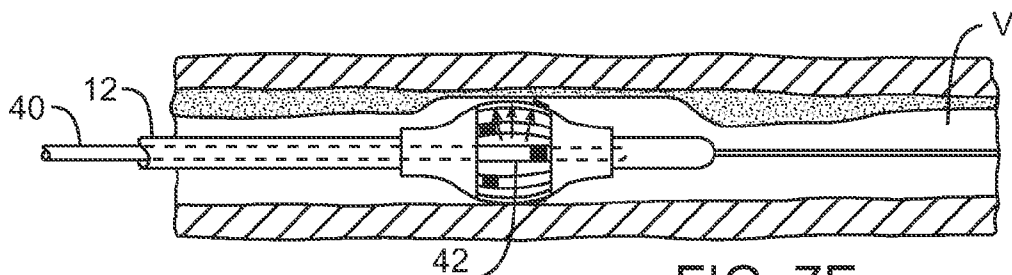


FIG. 7E

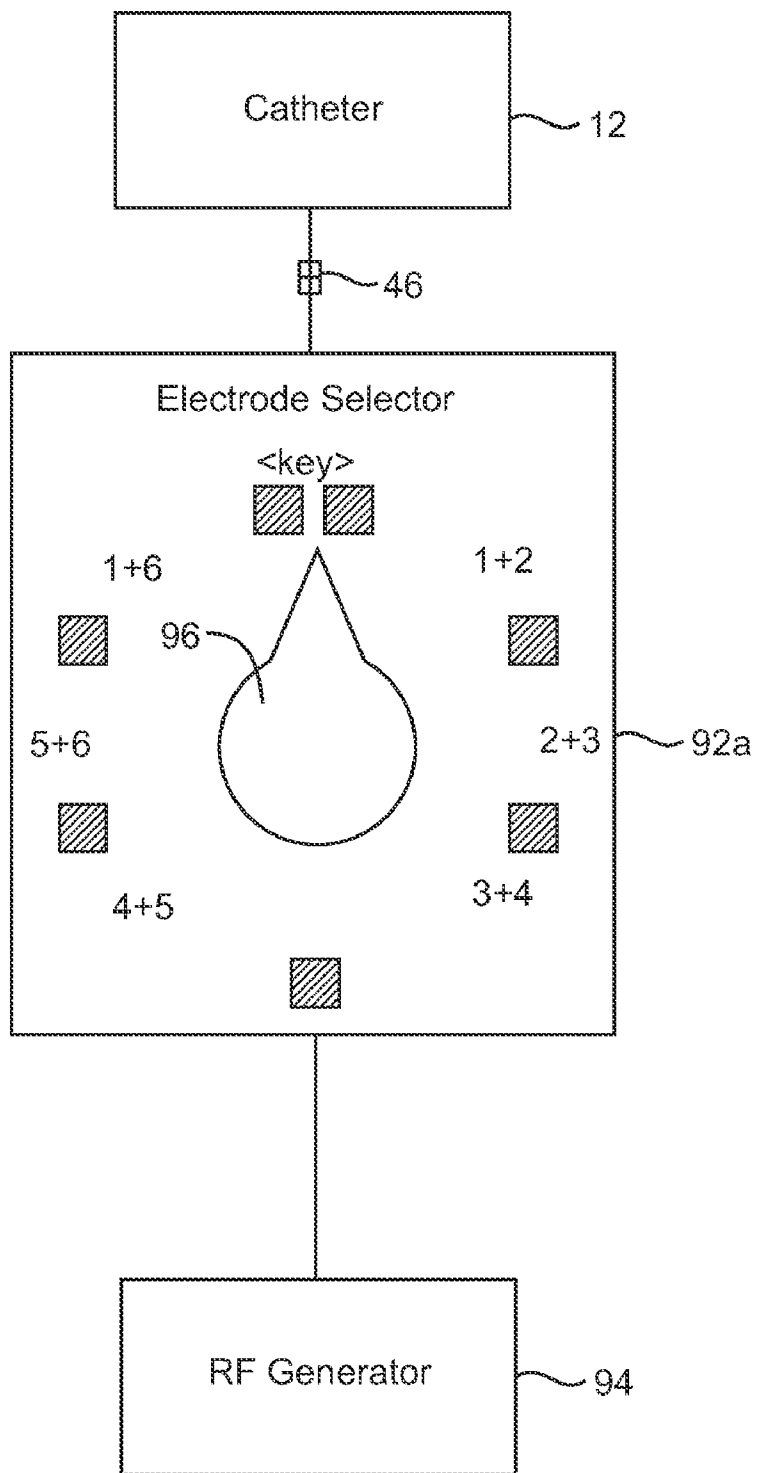


FIG. 8

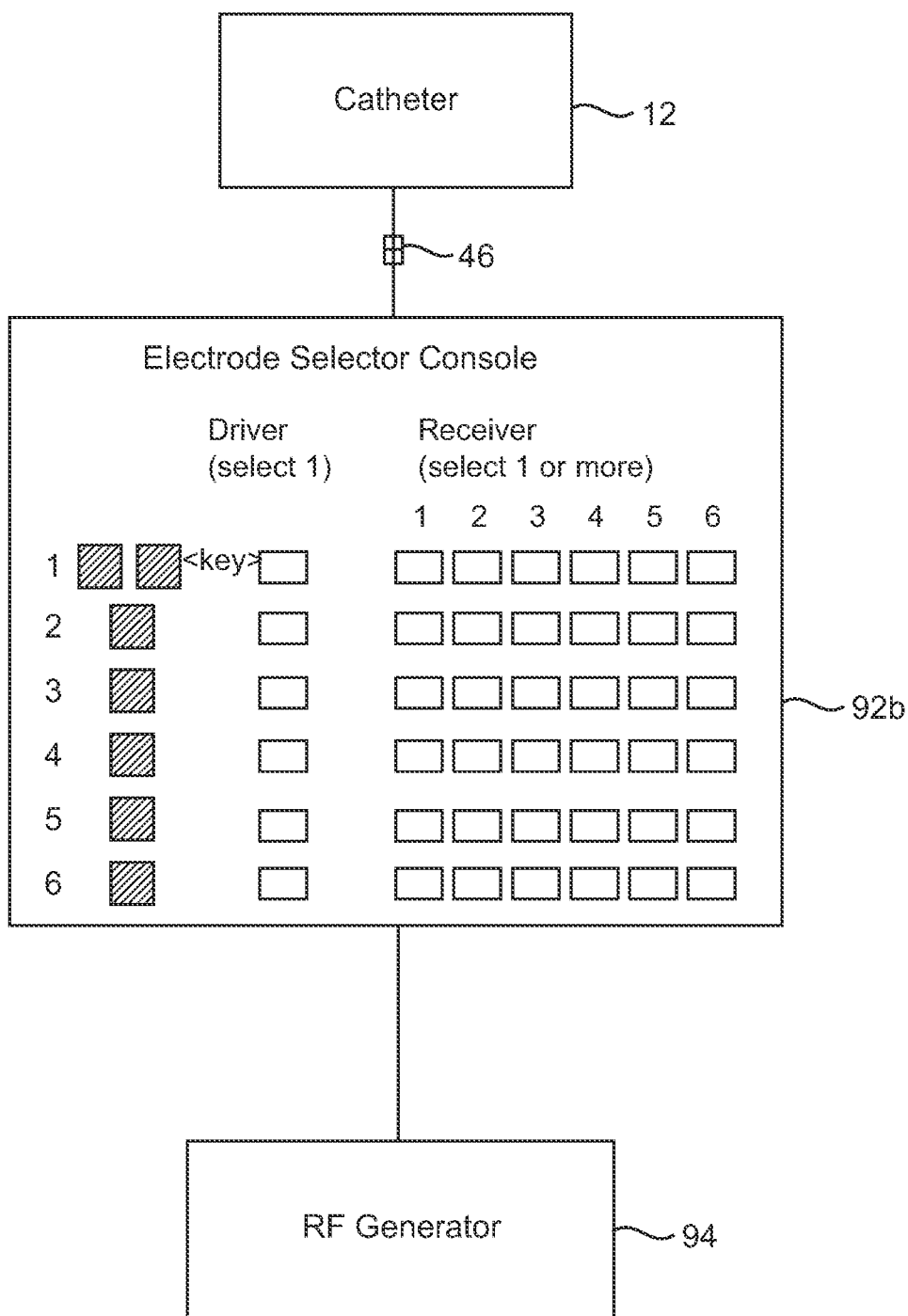


FIG. 9

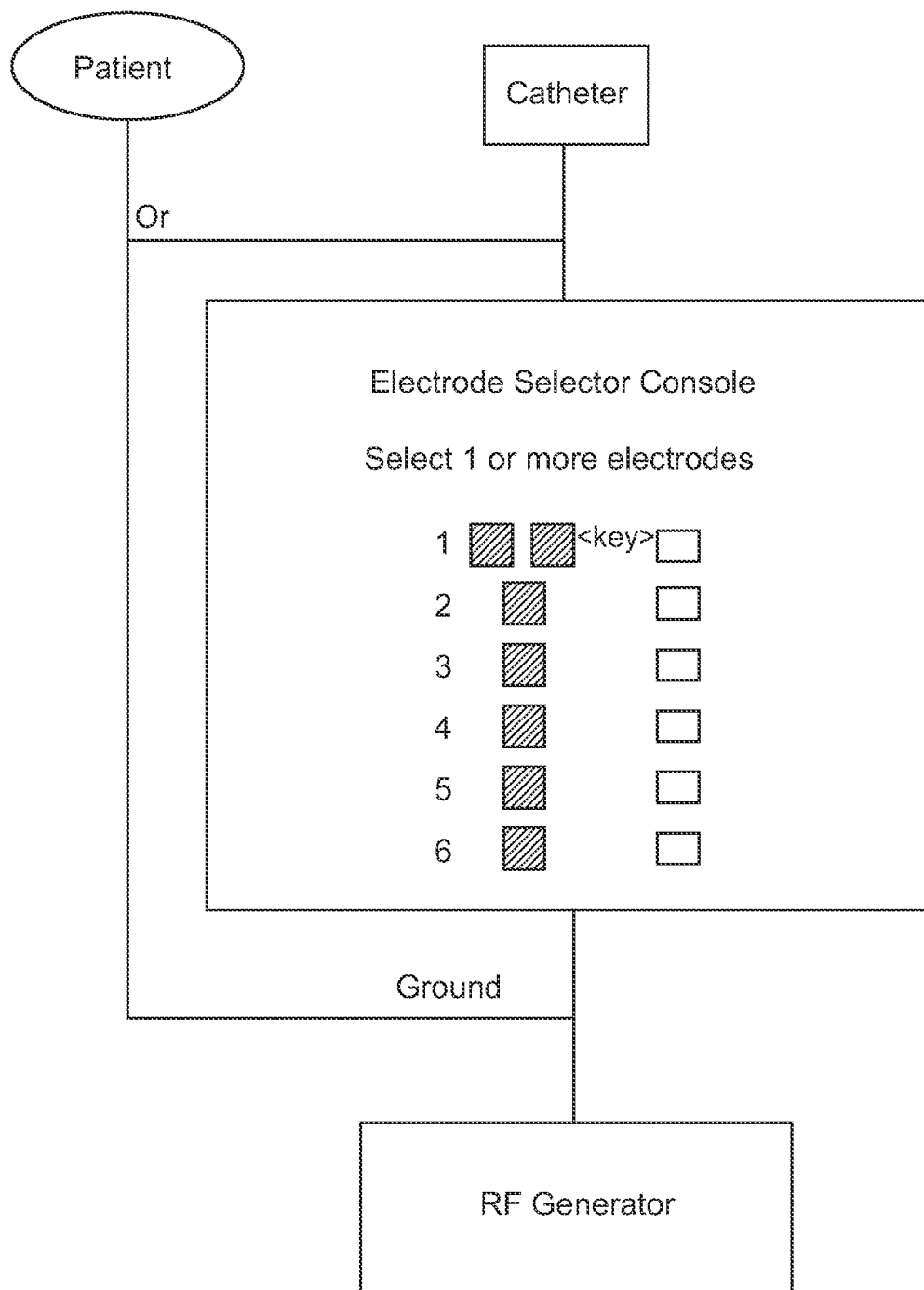


FIG. 10

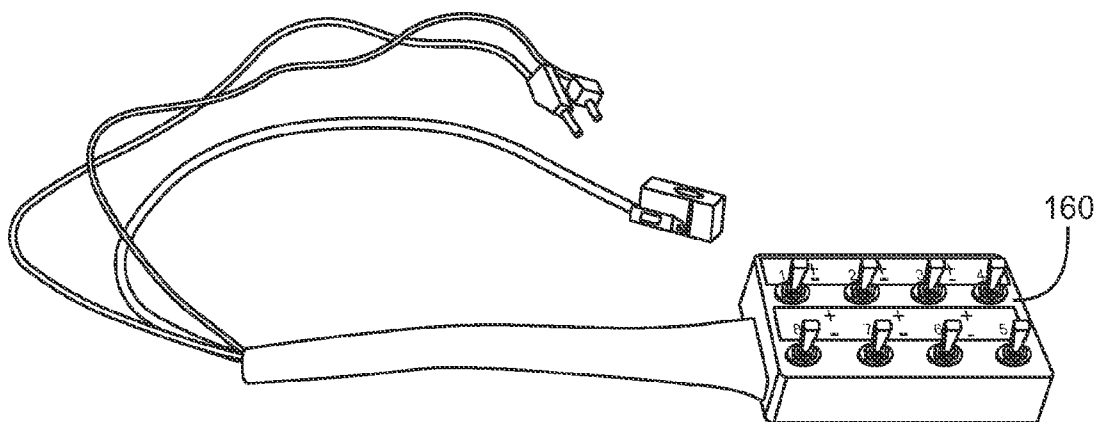


FIG. 11

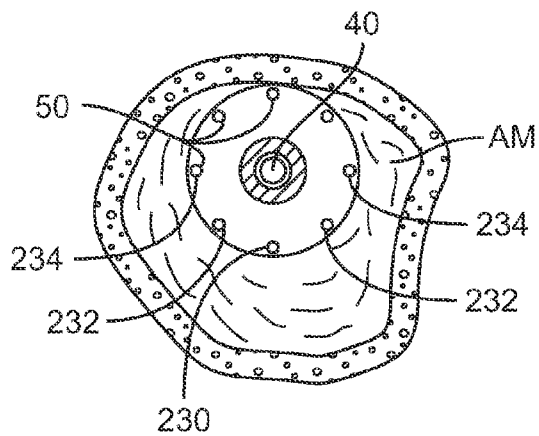


FIG. 13

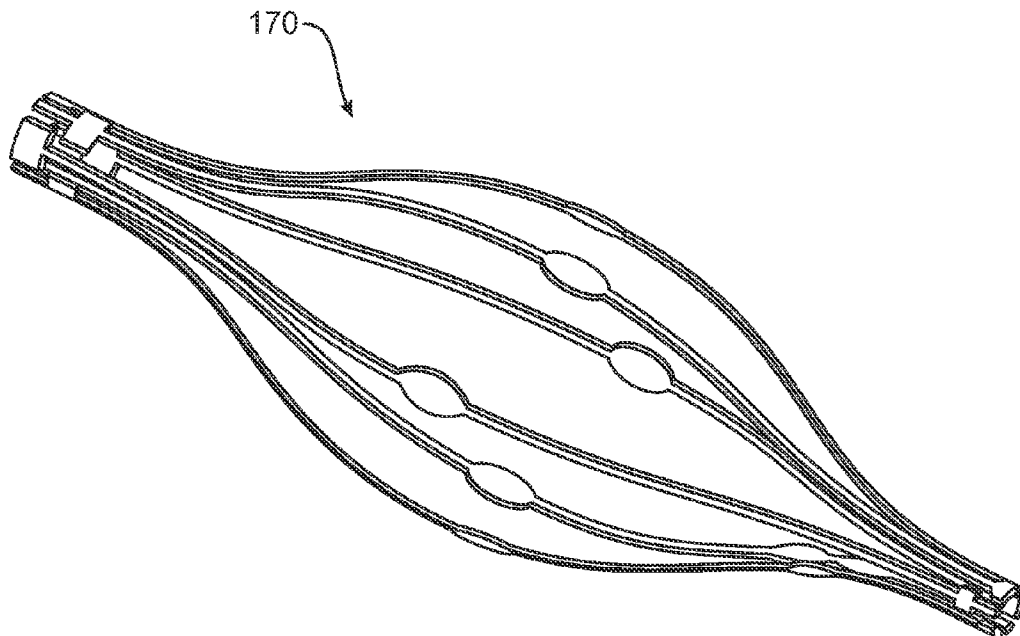


FIG. 12A

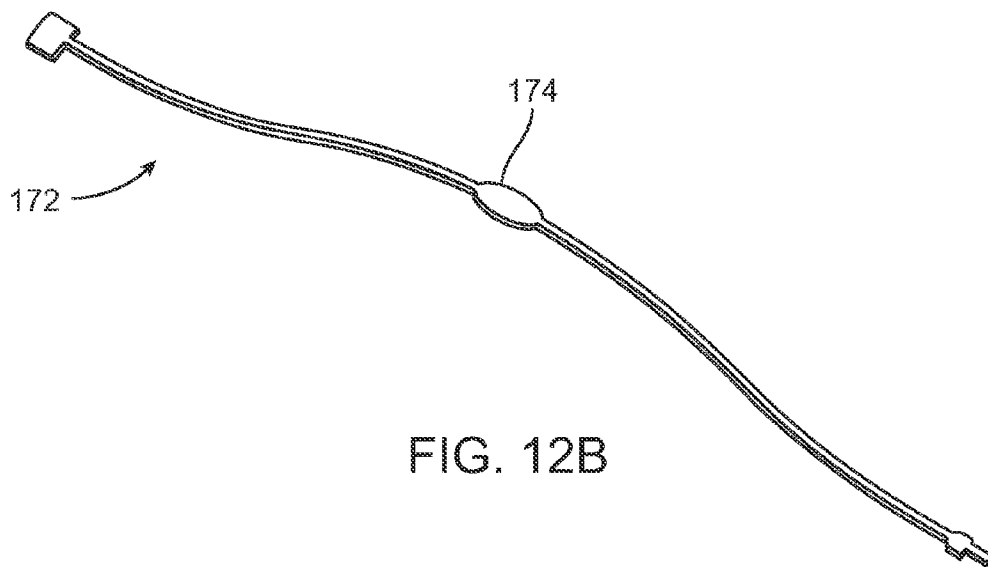


FIG. 12B

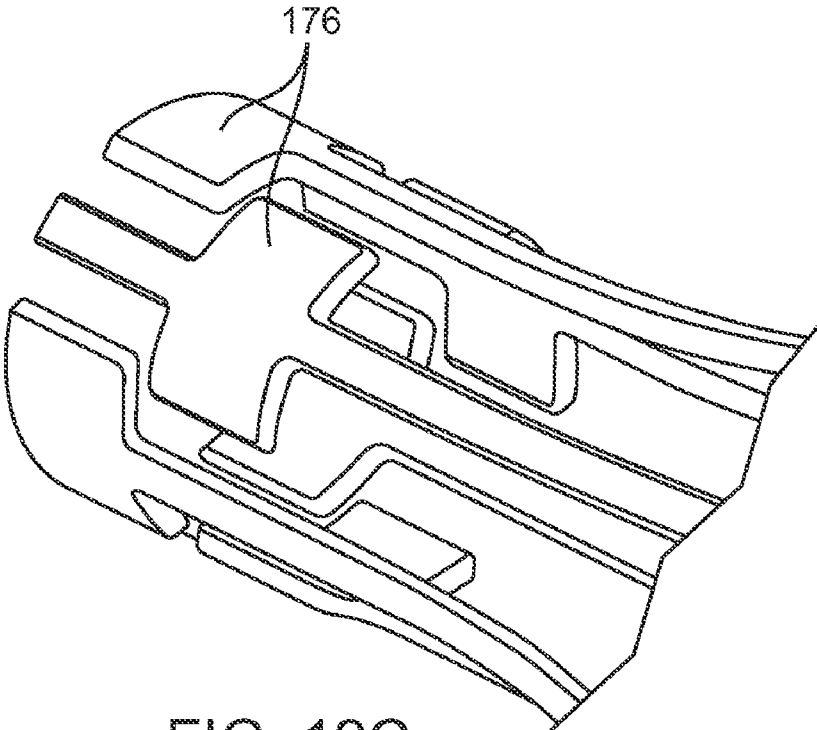


FIG. 12C

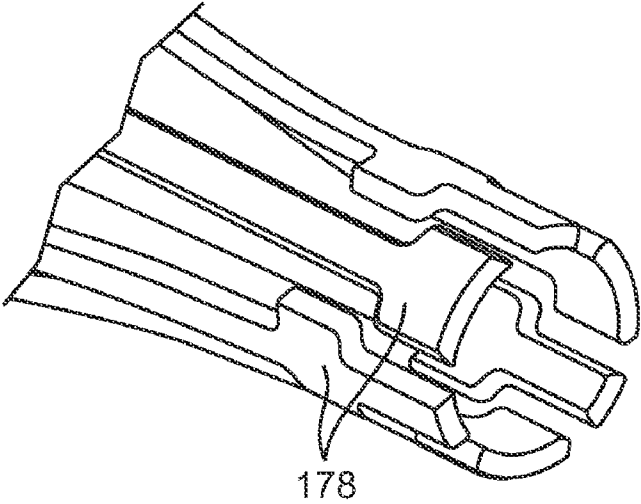


FIG. 12D

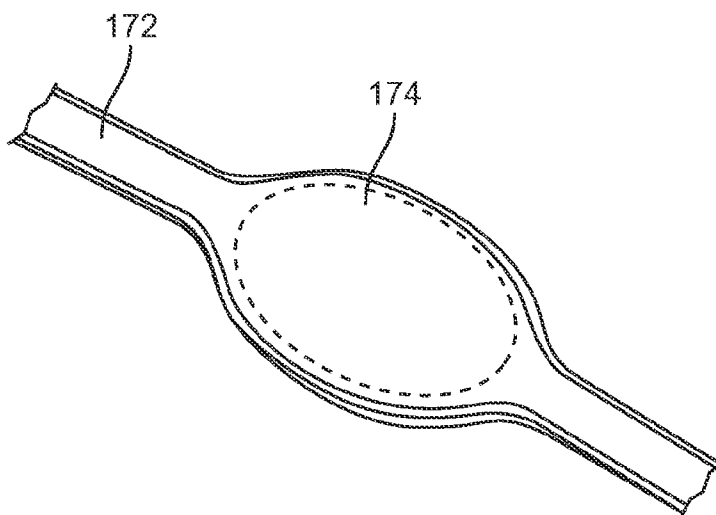


FIG. 12E

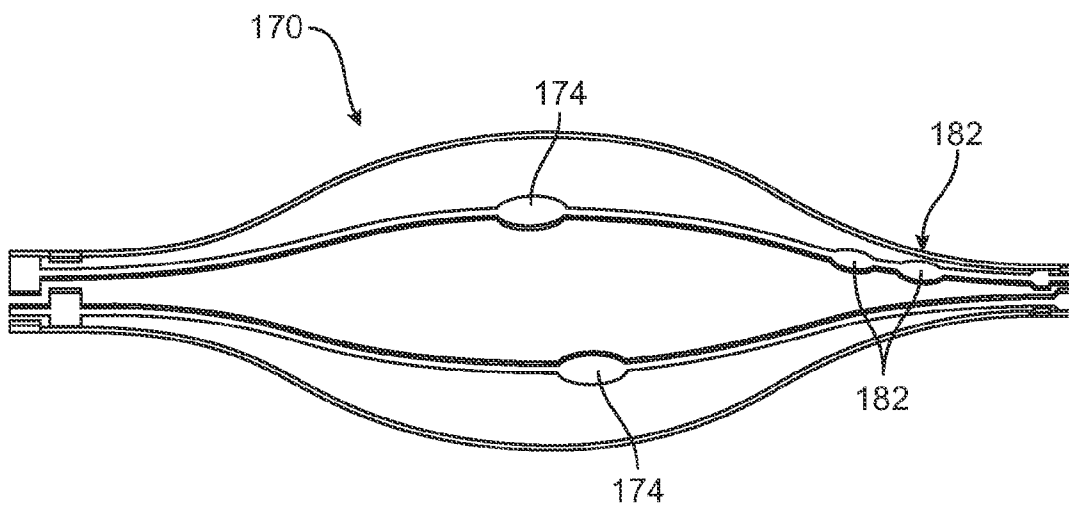


FIG. 12F

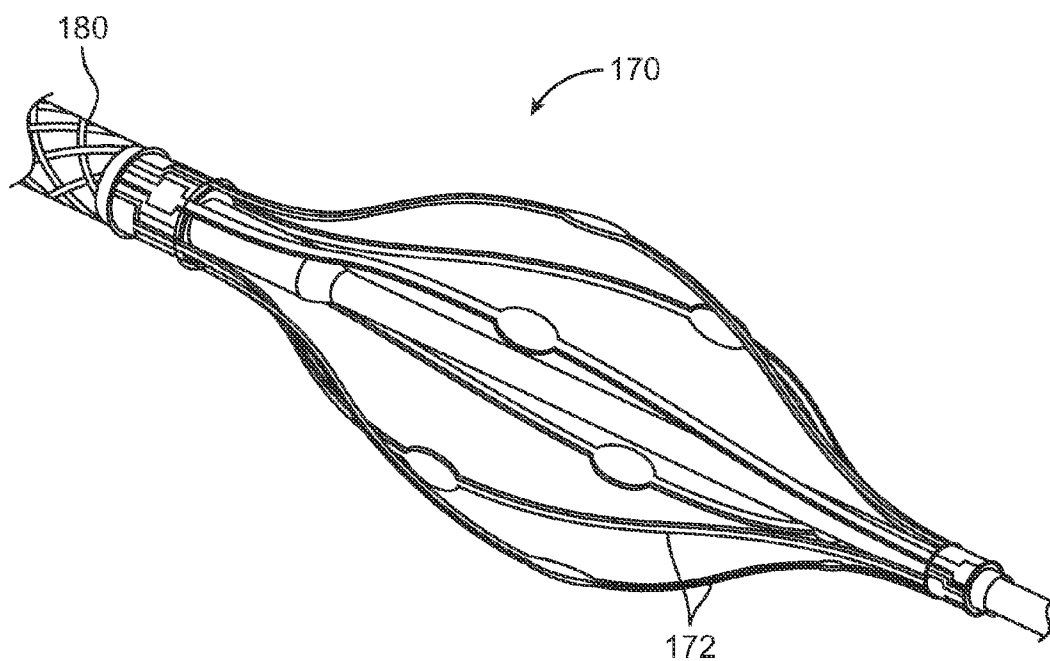


FIG. 12G

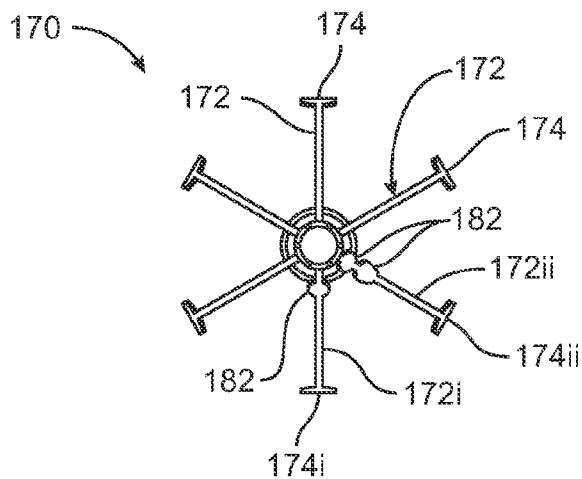


FIG. 12H

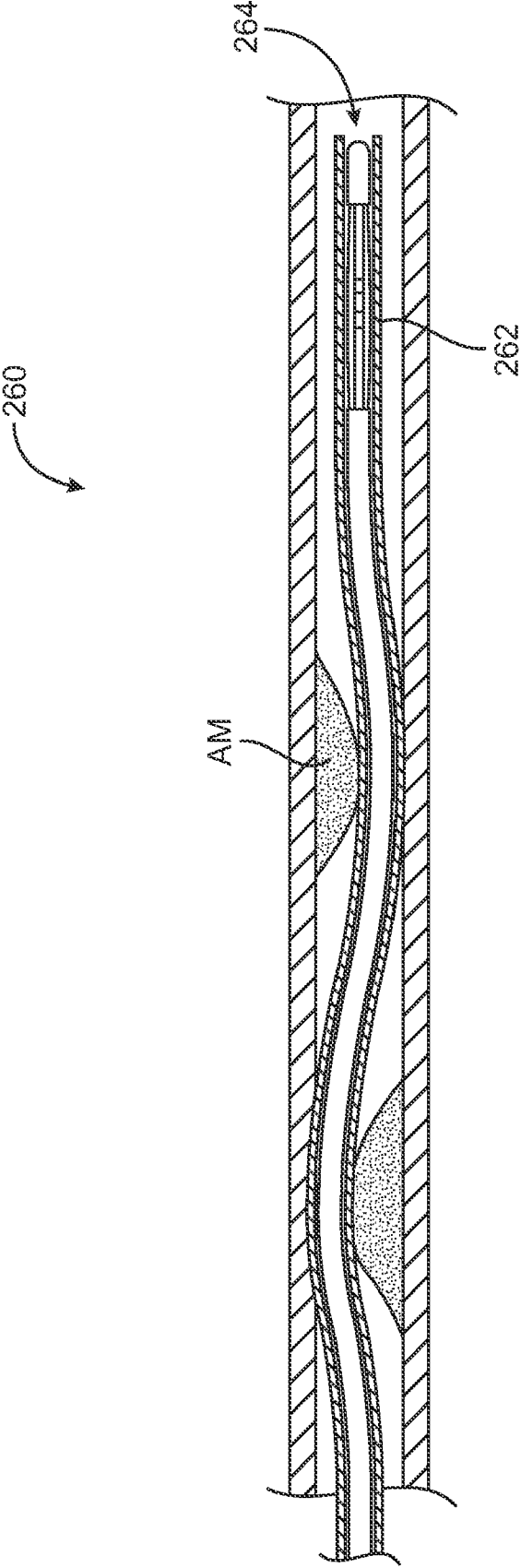


FIG. 14A

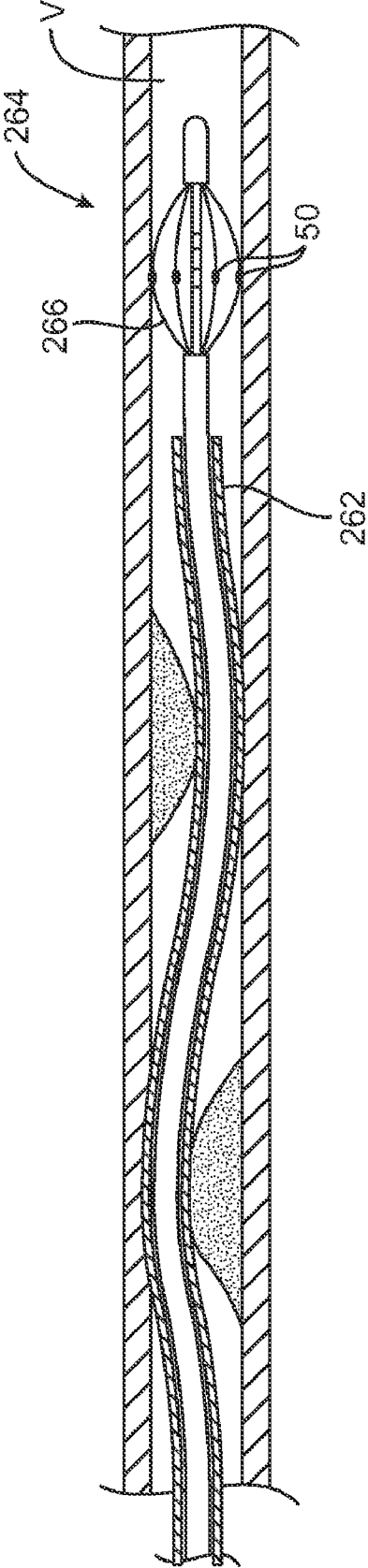


FIG. 14B

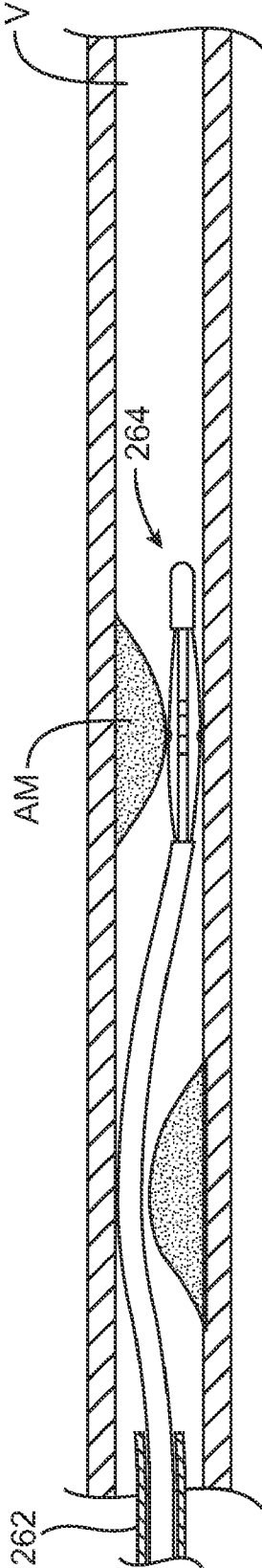


FIG. 14C

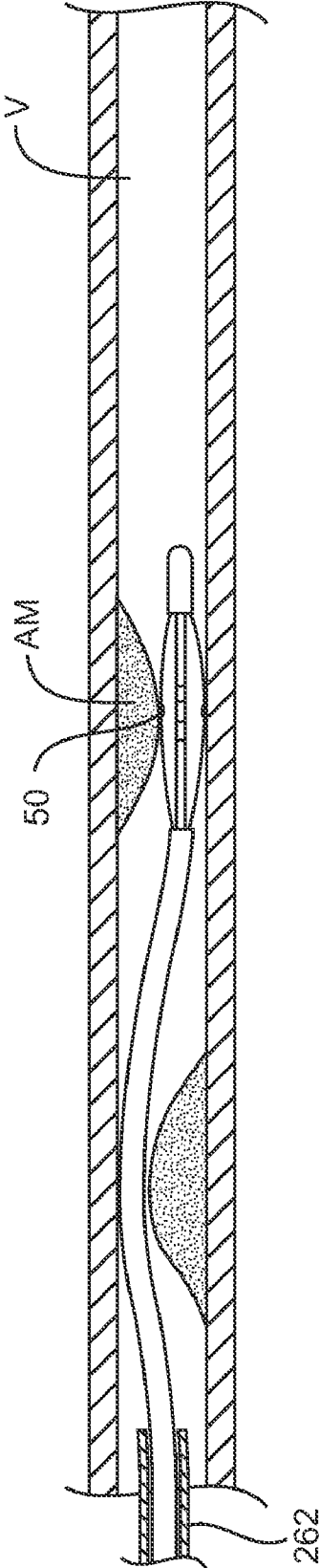


FIG. 14D

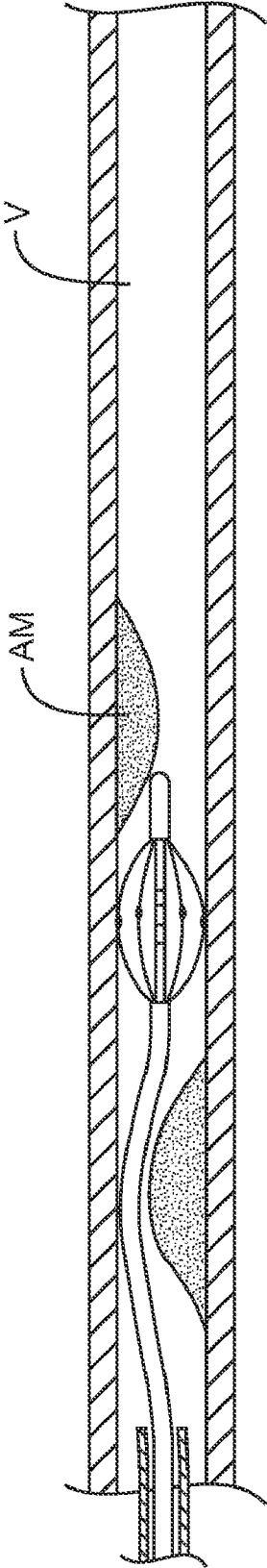


FIG. 14E

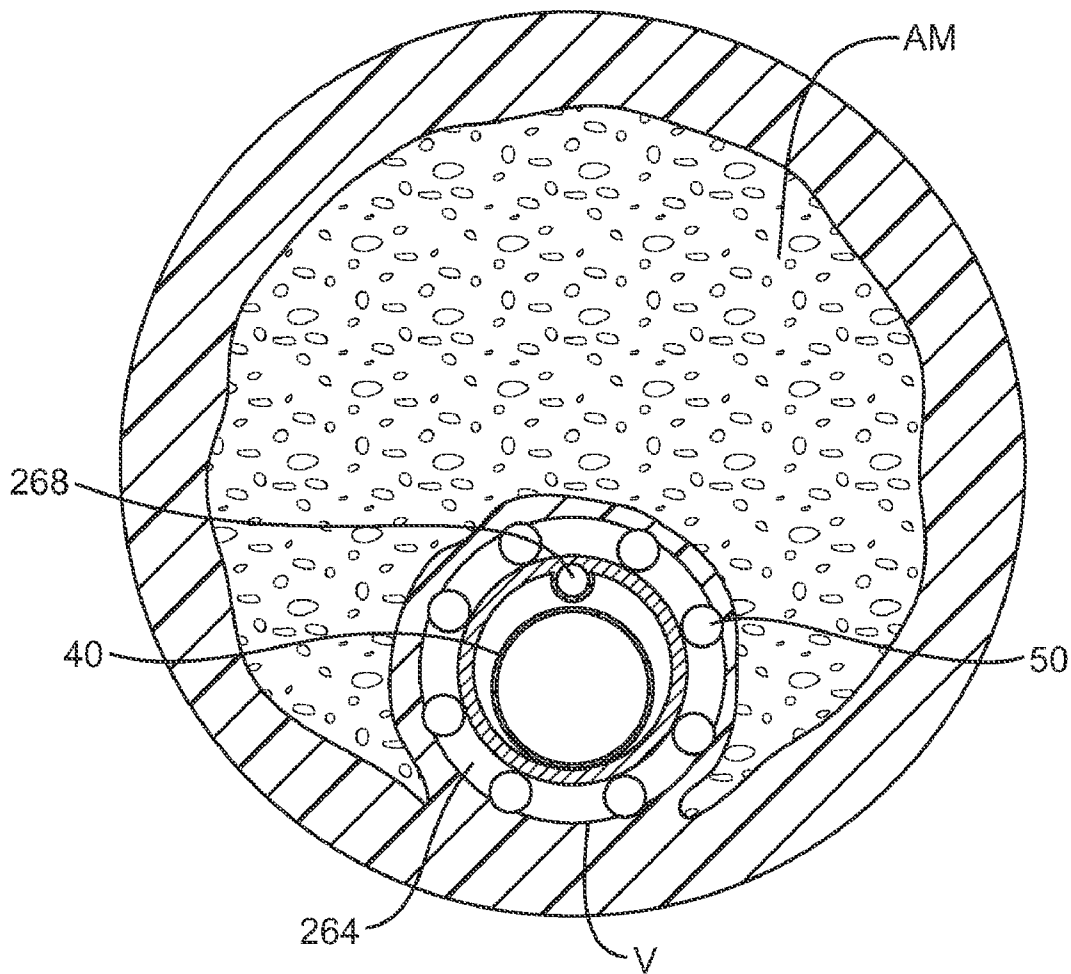


FIG. 14F

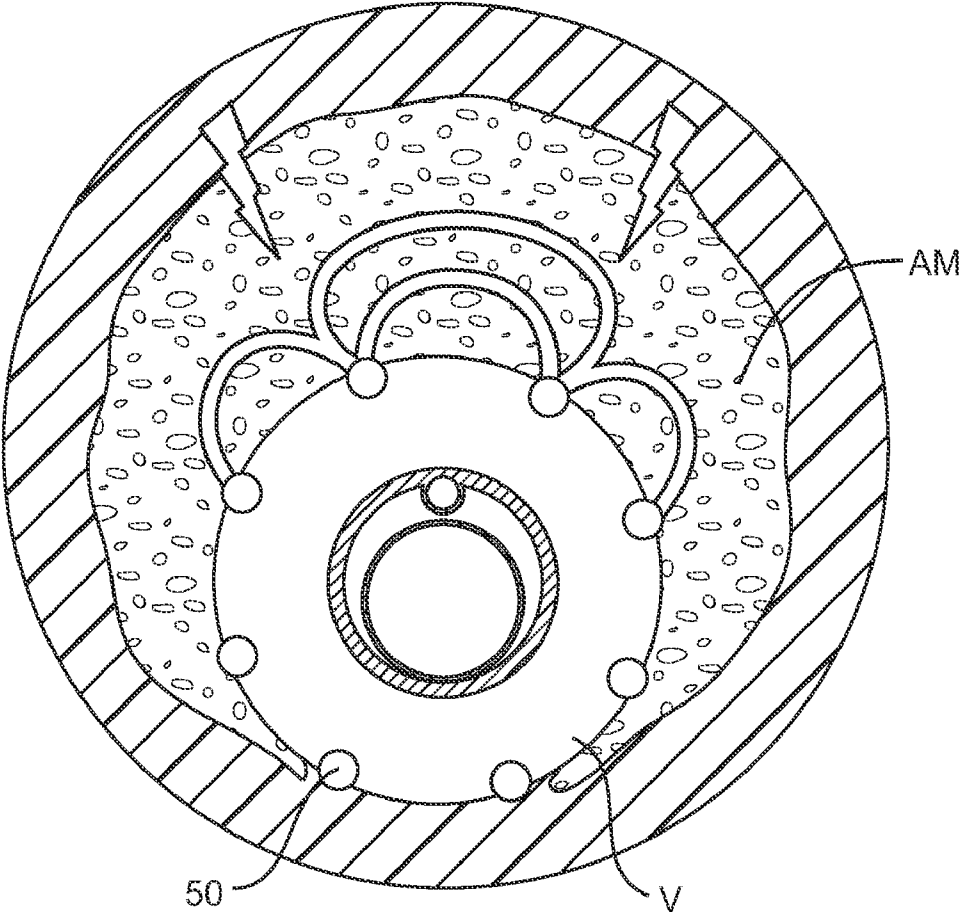


FIG. 14G

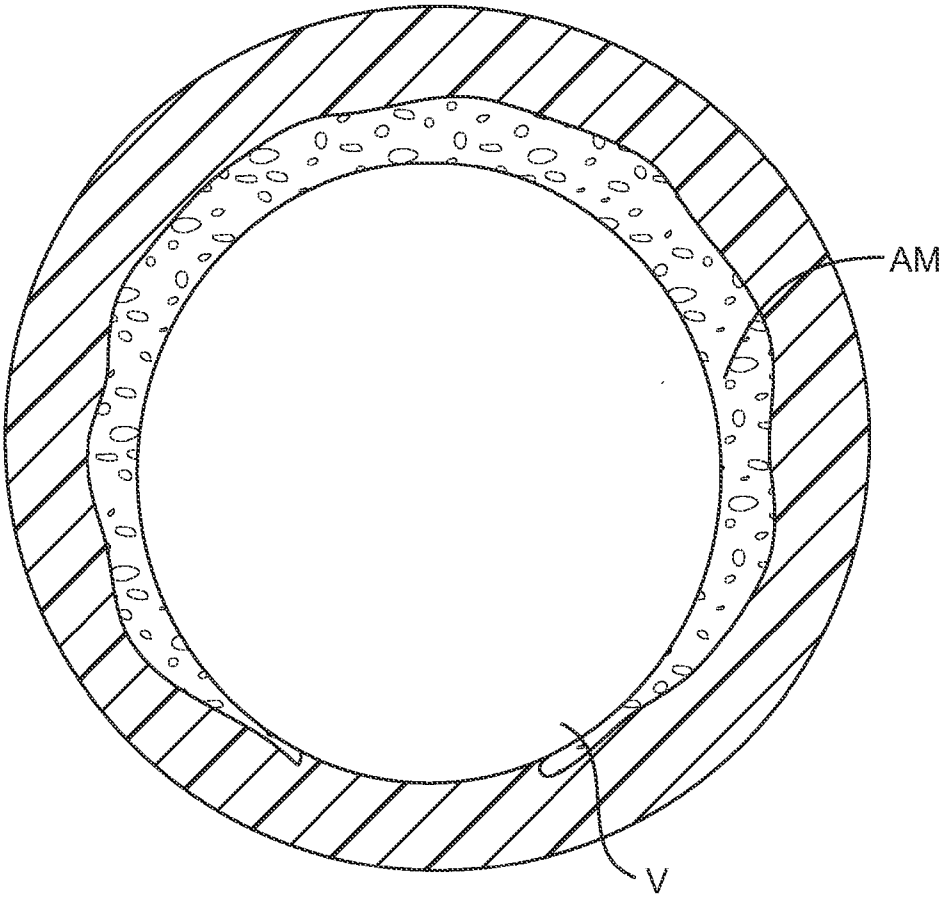


FIG. 14H

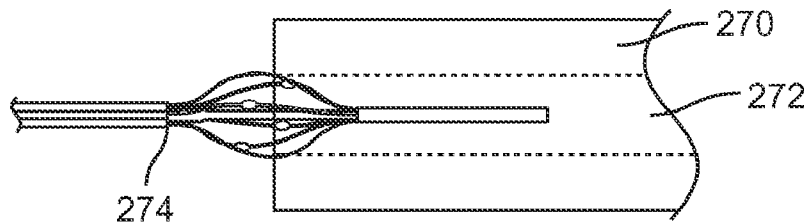


FIG. 15A

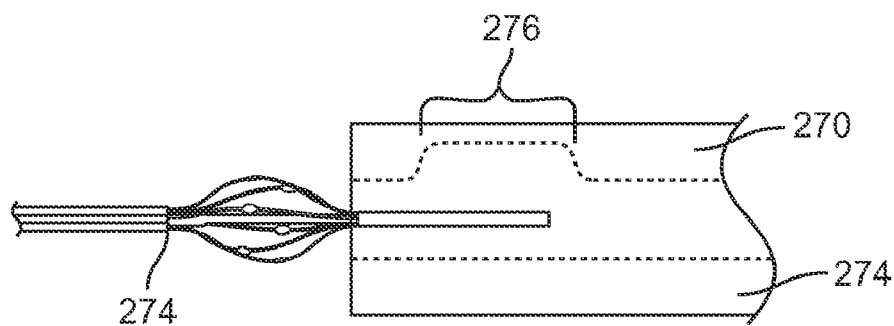


FIG. 15B

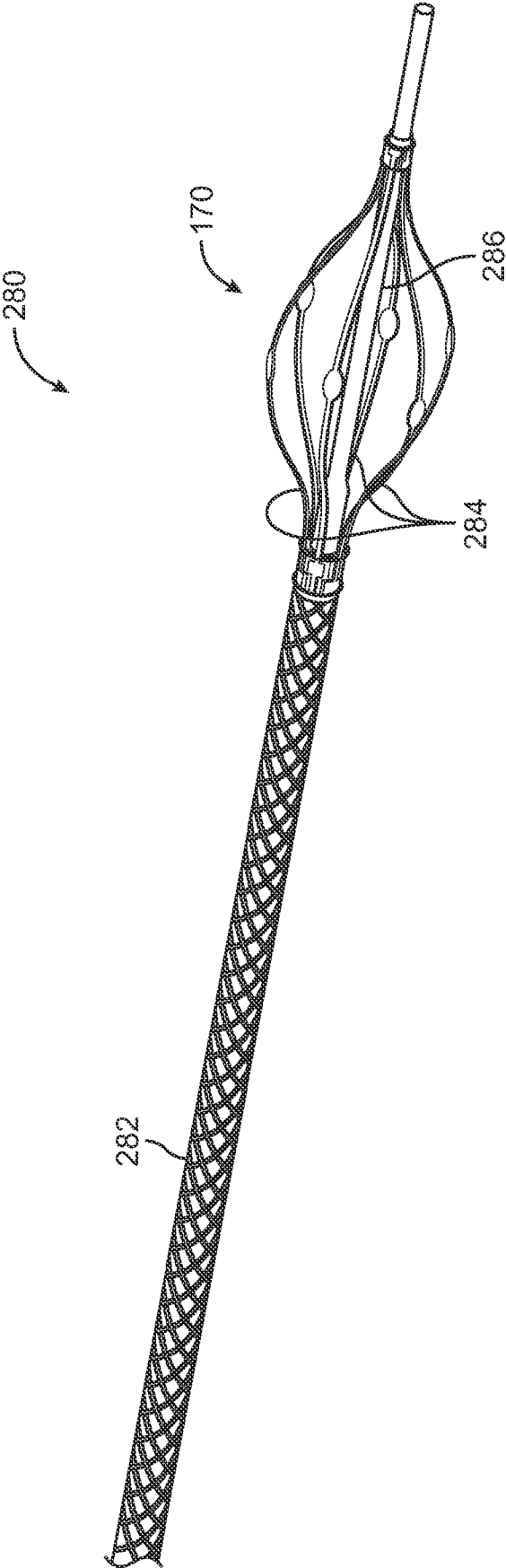


FIG. 16

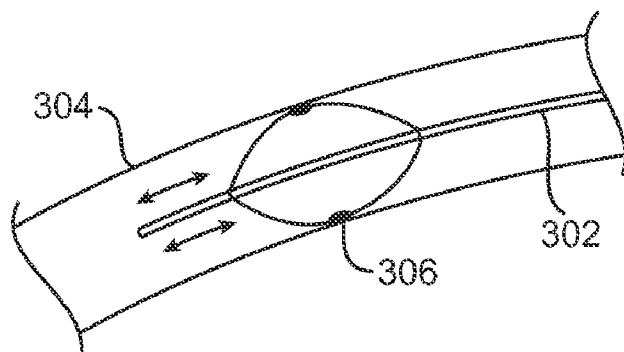


FIG. 17A

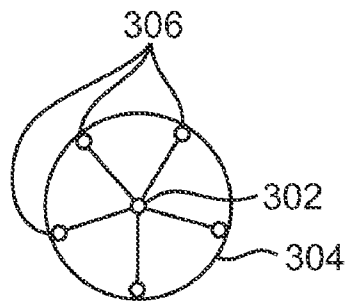


FIG. 17B

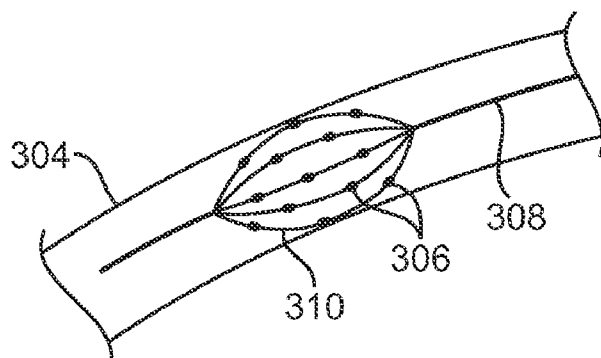
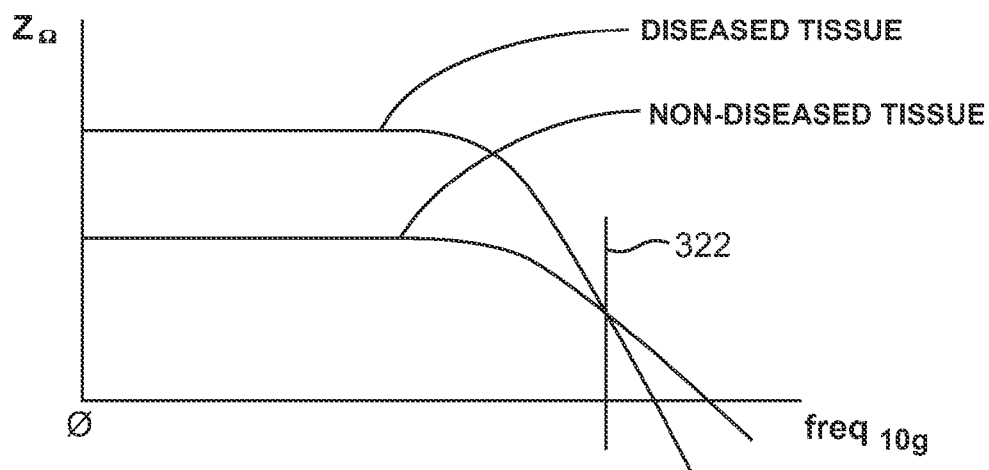


FIG. 17C



IMPEDANCE OF DISEASED AND NON-DISEASED TISSUE

FIG. 18

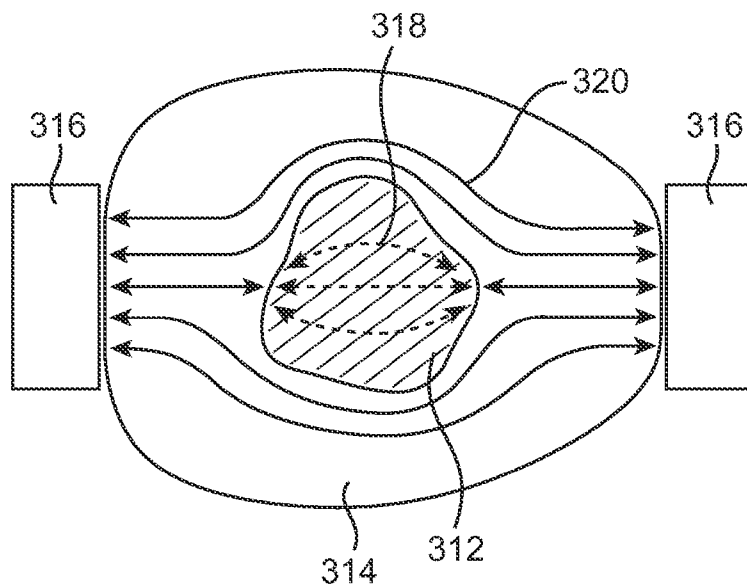


FIG. 19

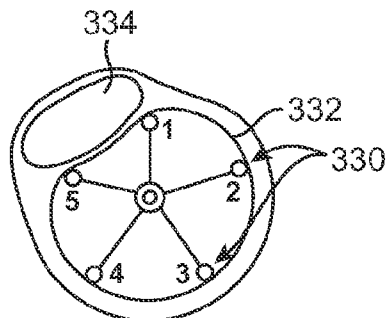


FIG. 20

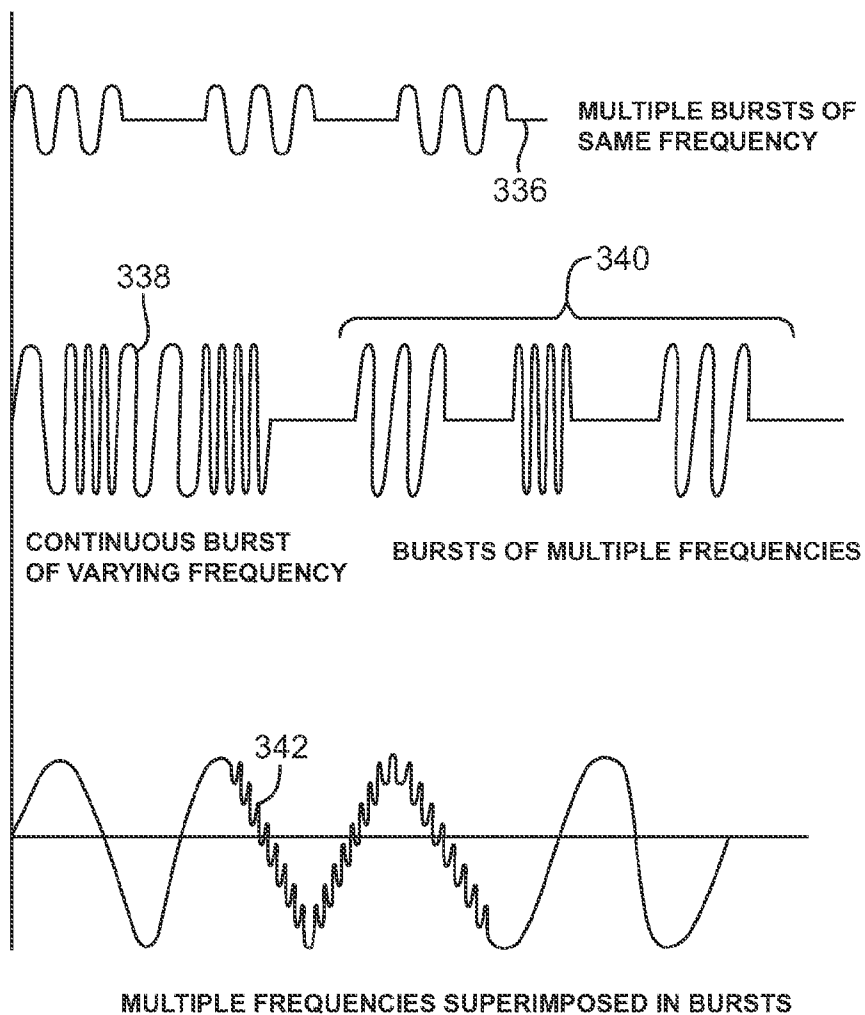


FIG. 21

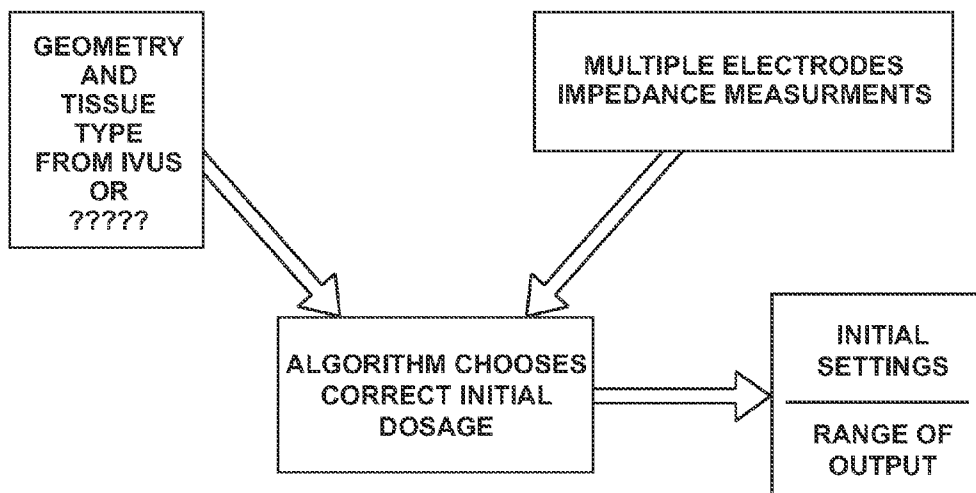


FIG. 22

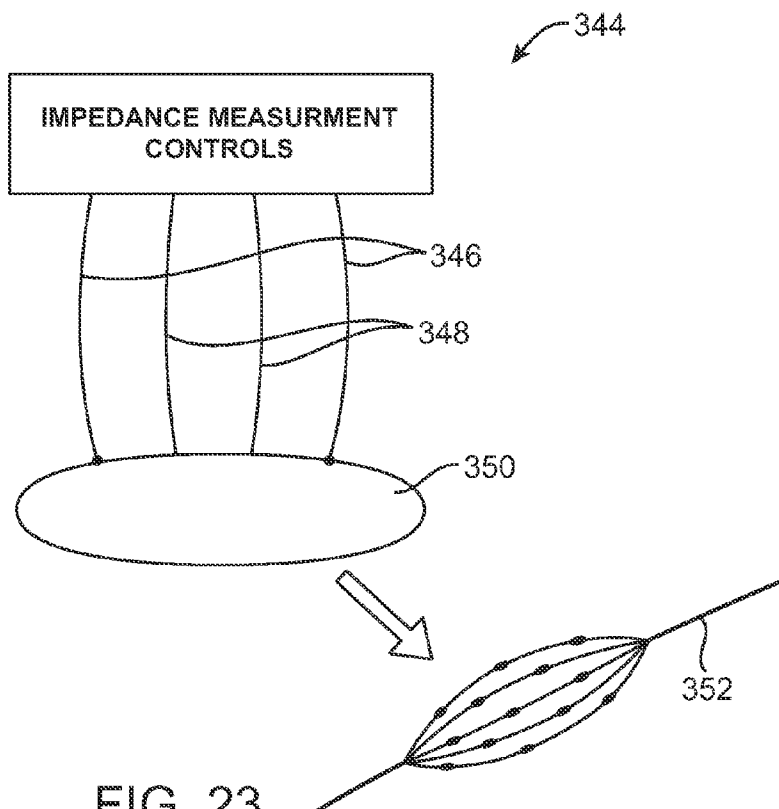


FIG. 23

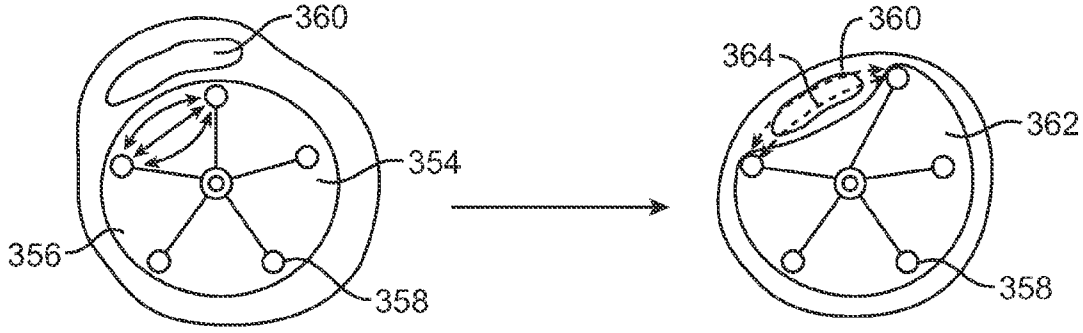


FIG. 24

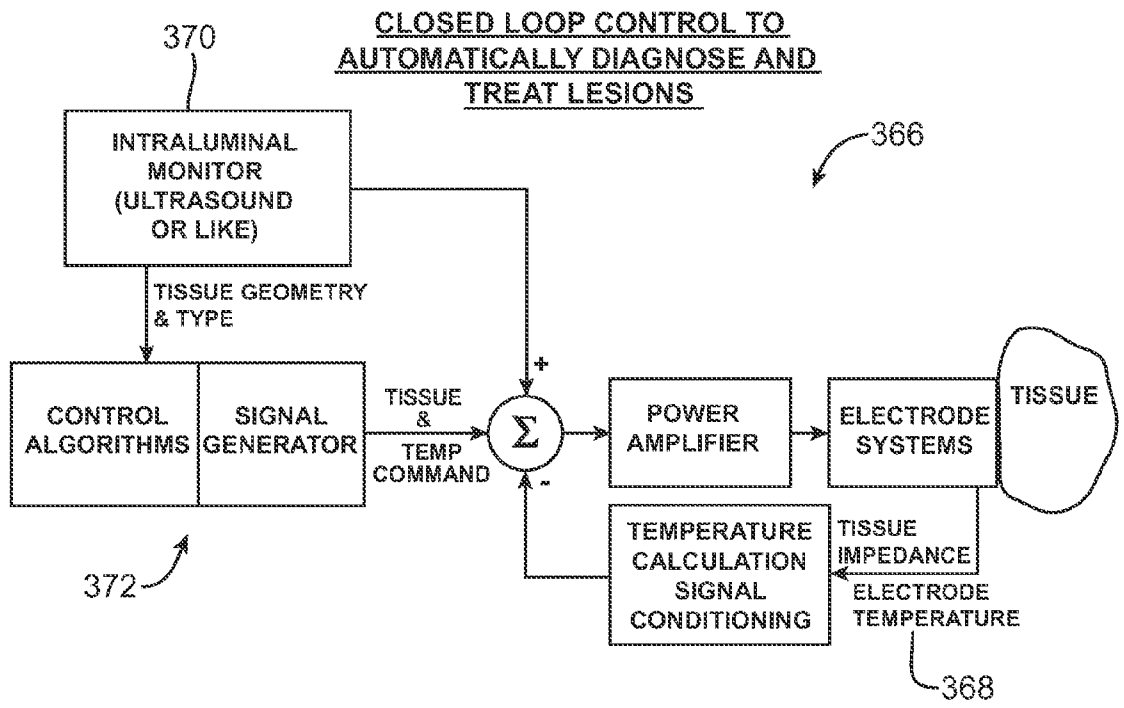


FIG. 25

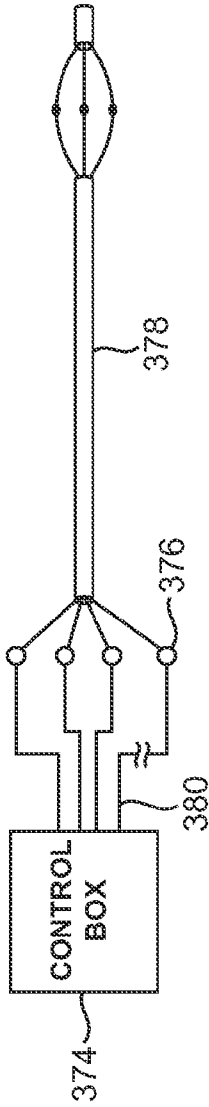


FIG. 26A

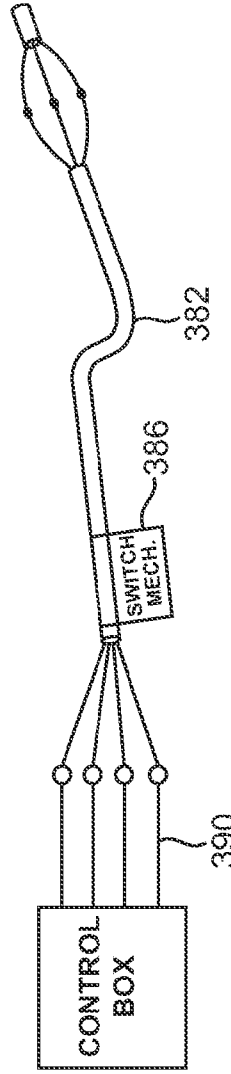


FIG. 26B

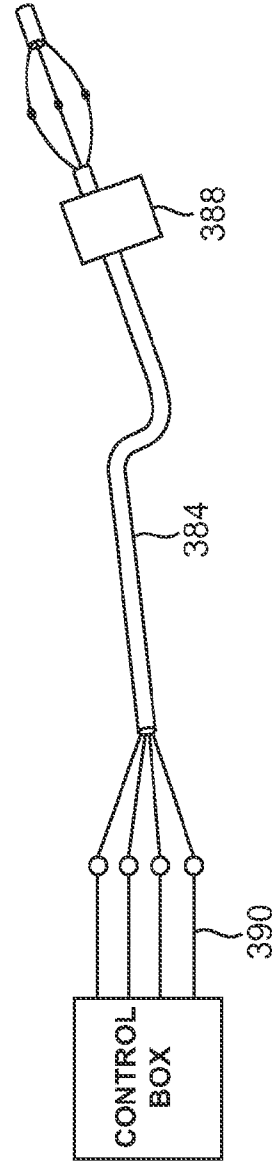


FIG. 26C

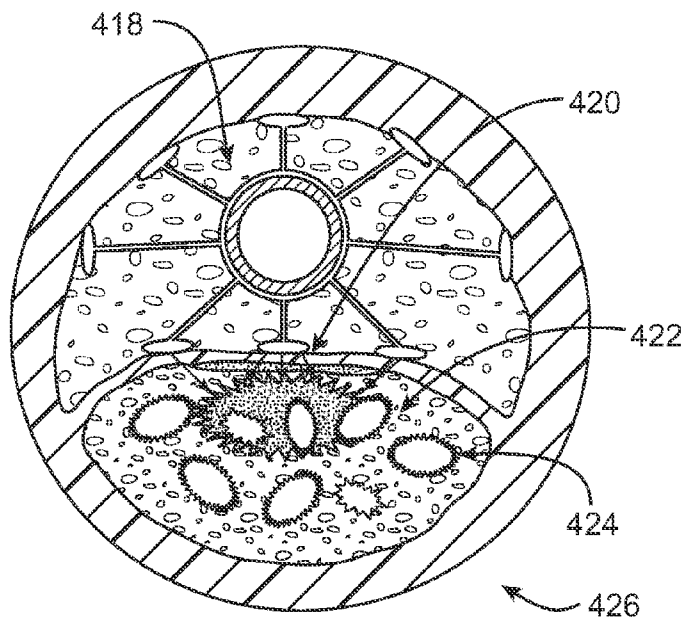


FIG. 27

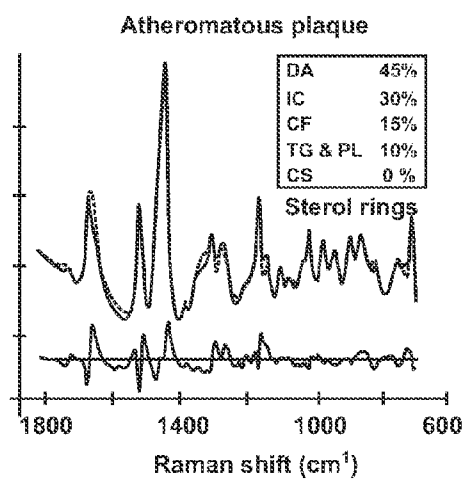


FIG. 27A

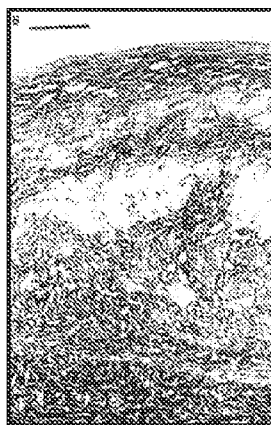


FIG. 27B



FIG. 27C

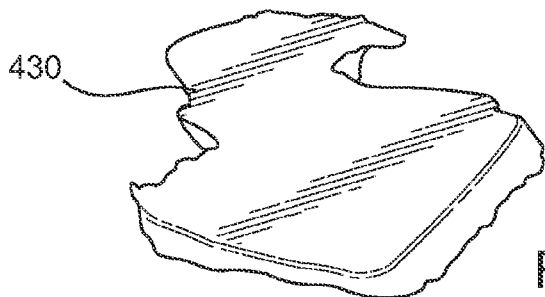


FIG. 28A

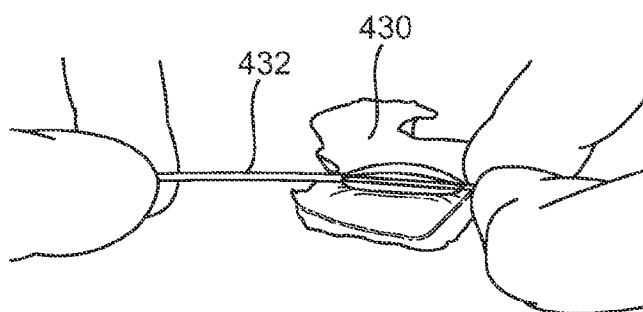


FIG. 28B

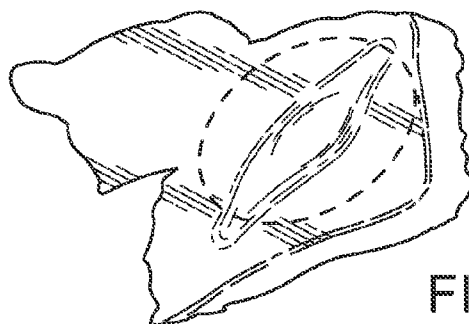


FIG. 28C

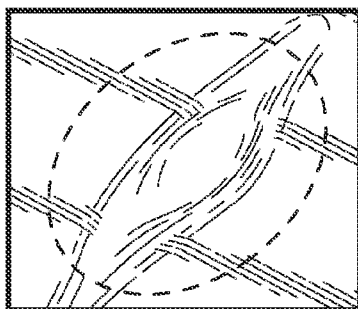


FIG. 28D

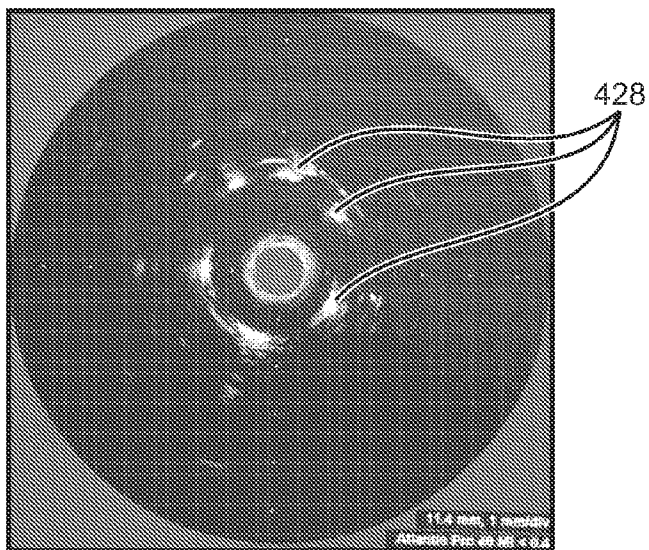


FIG. 29A

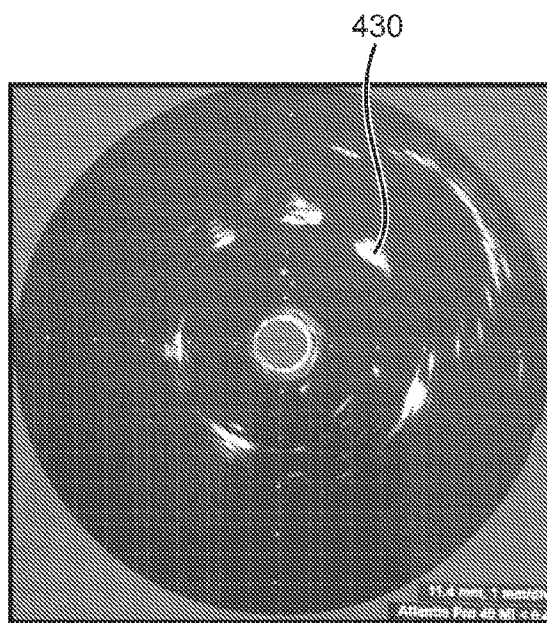


FIG. 29B

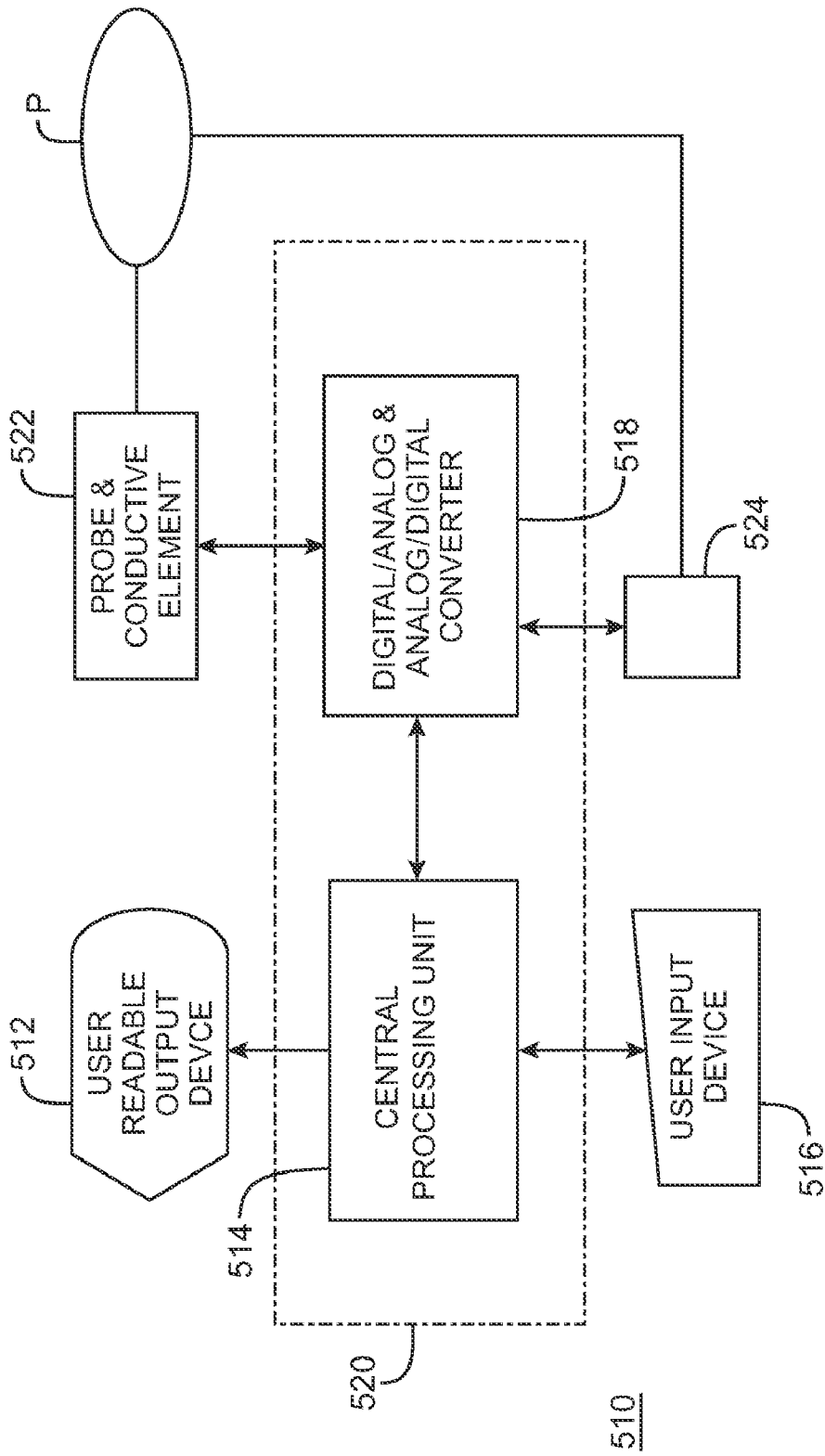


FIG. 30

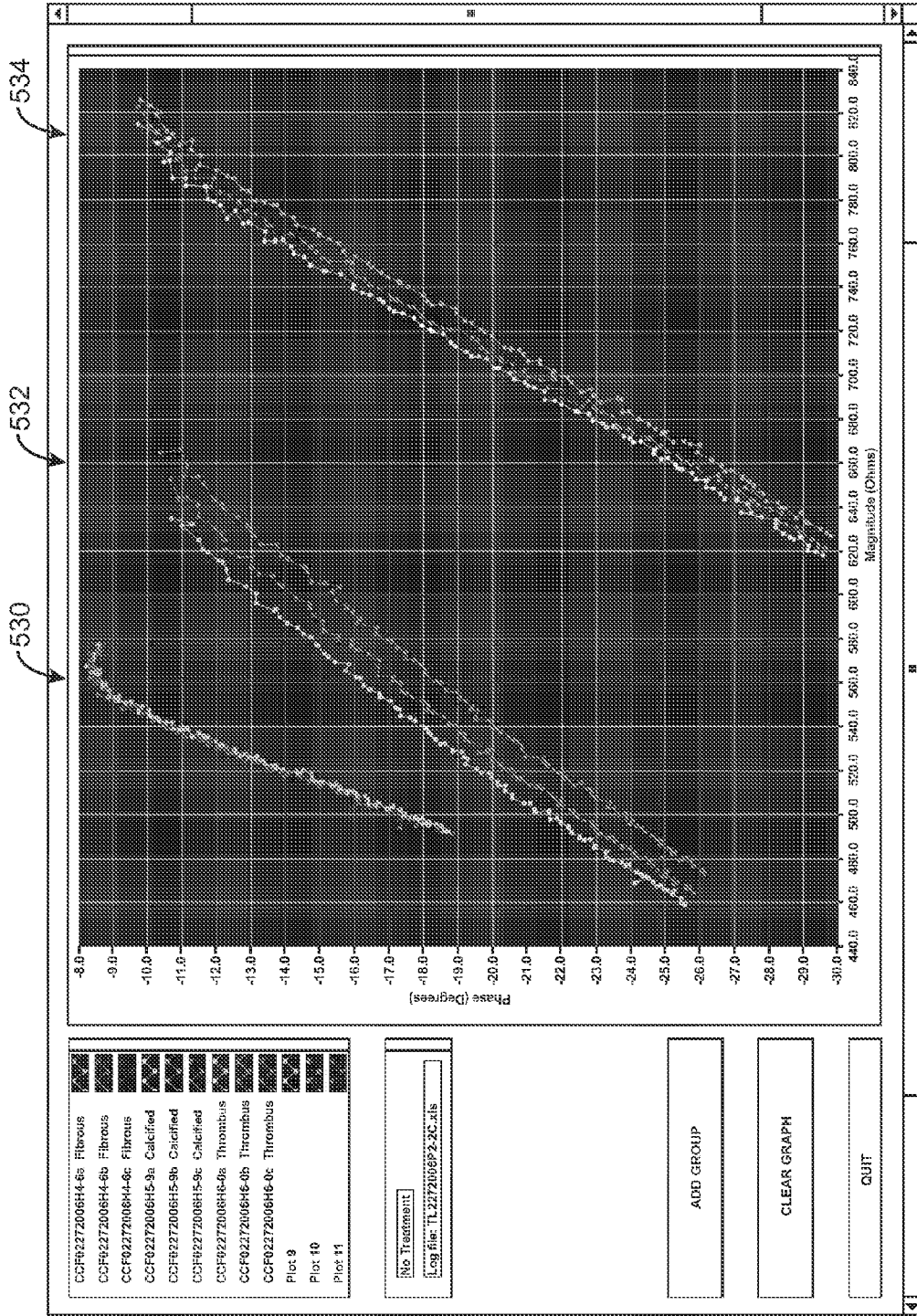


FIG. 31A

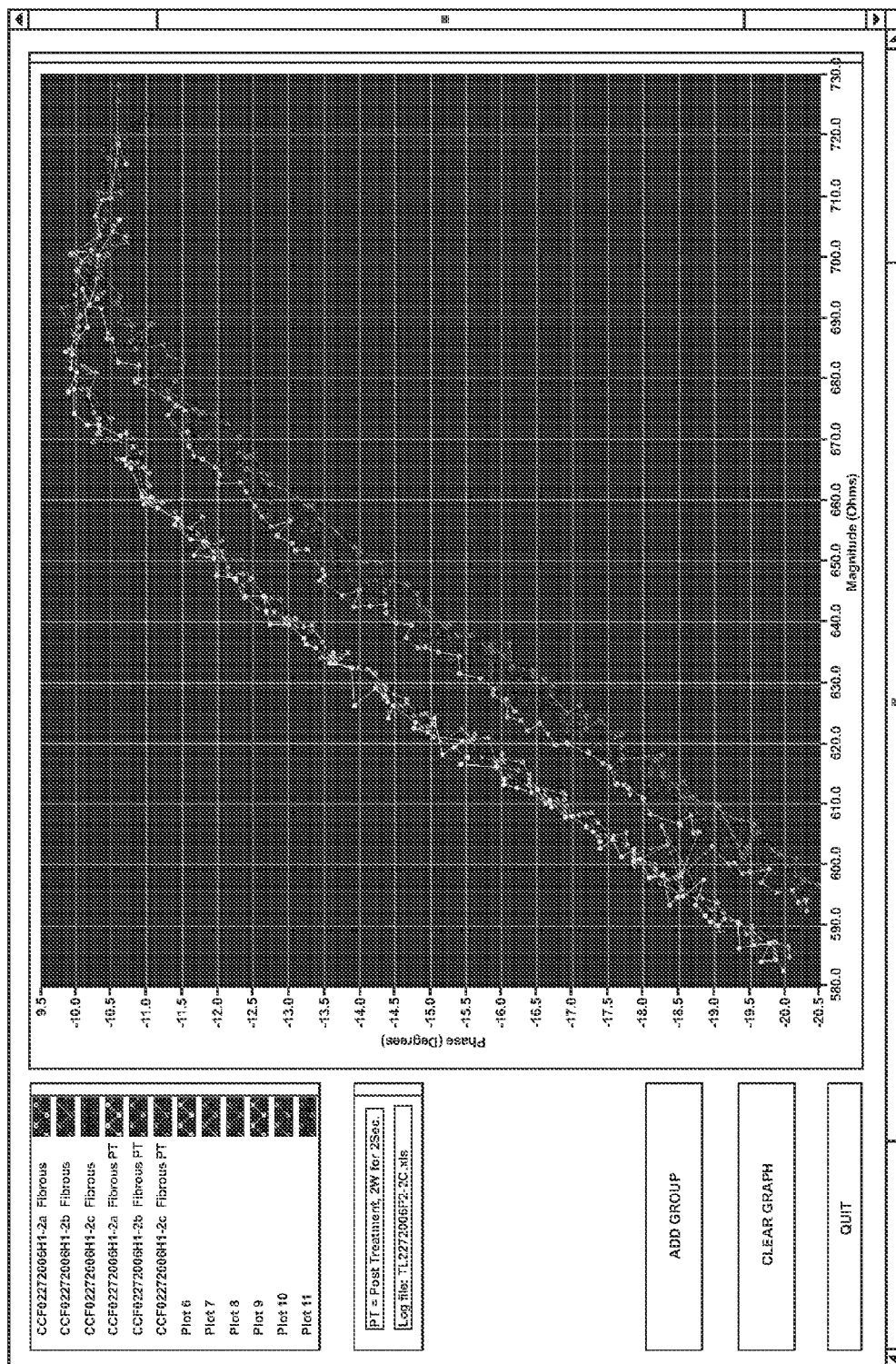


FIG. 31B

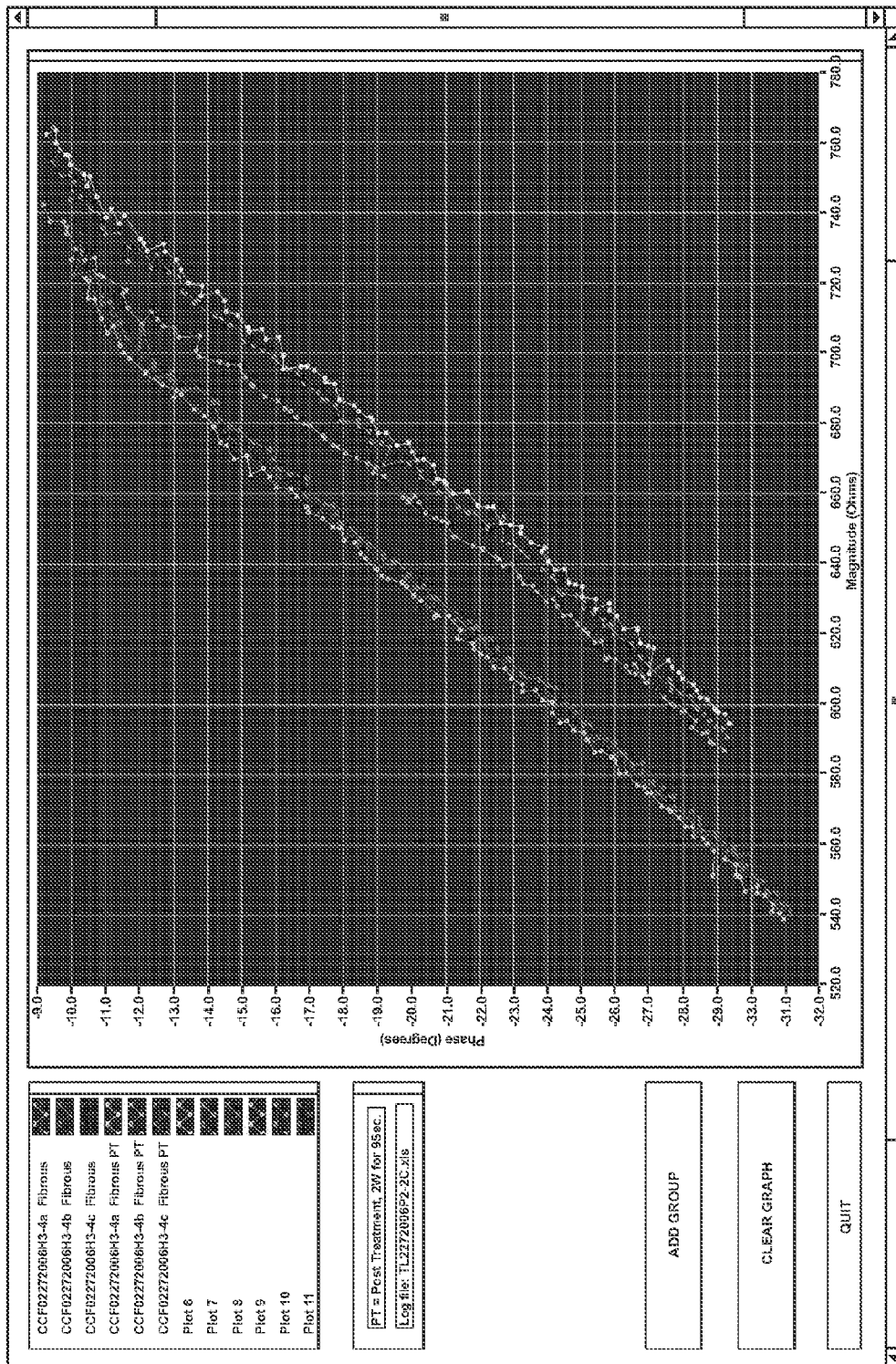


FIG. 31C

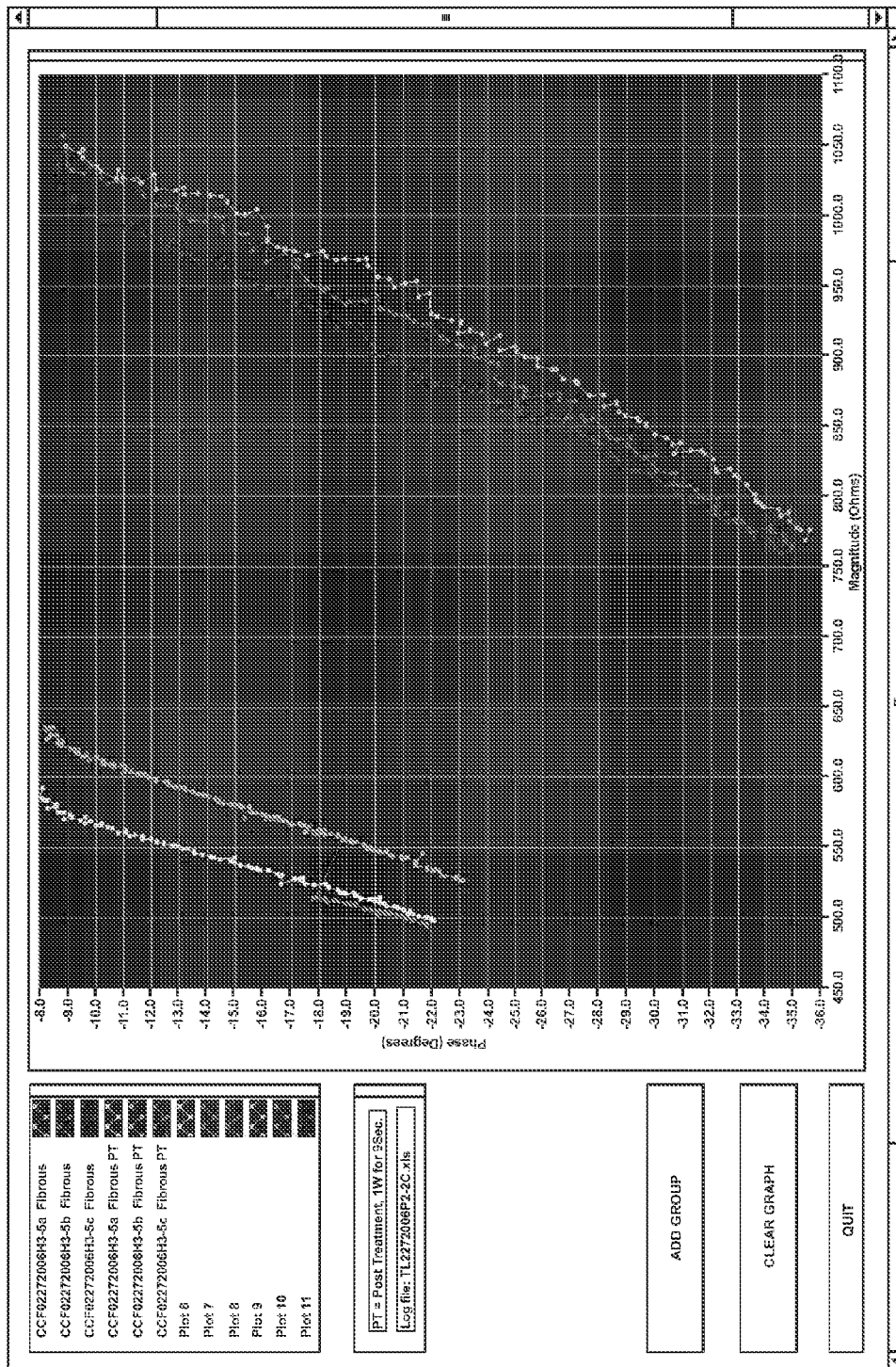


FIG. 31D

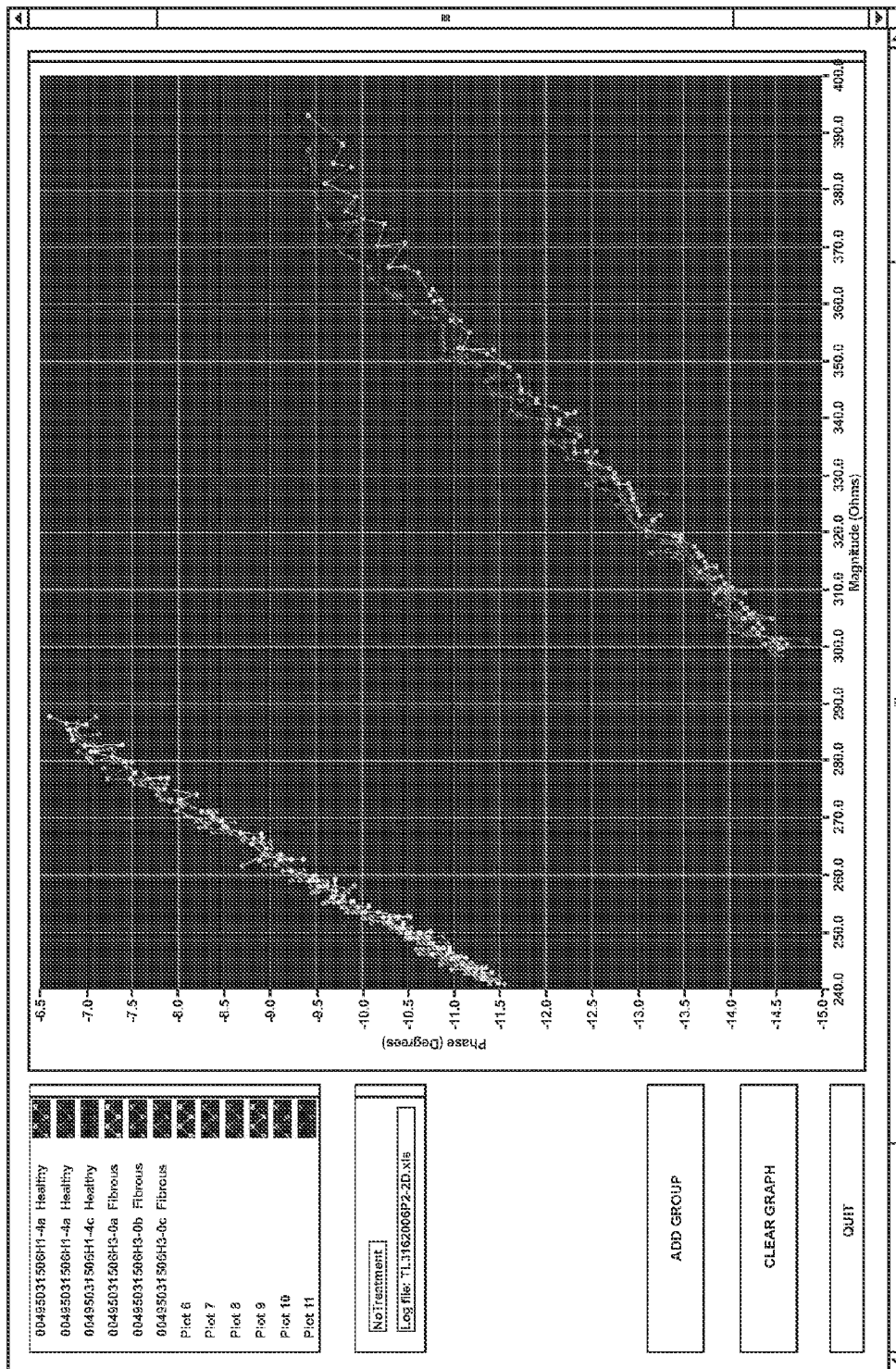


FIG. 31E

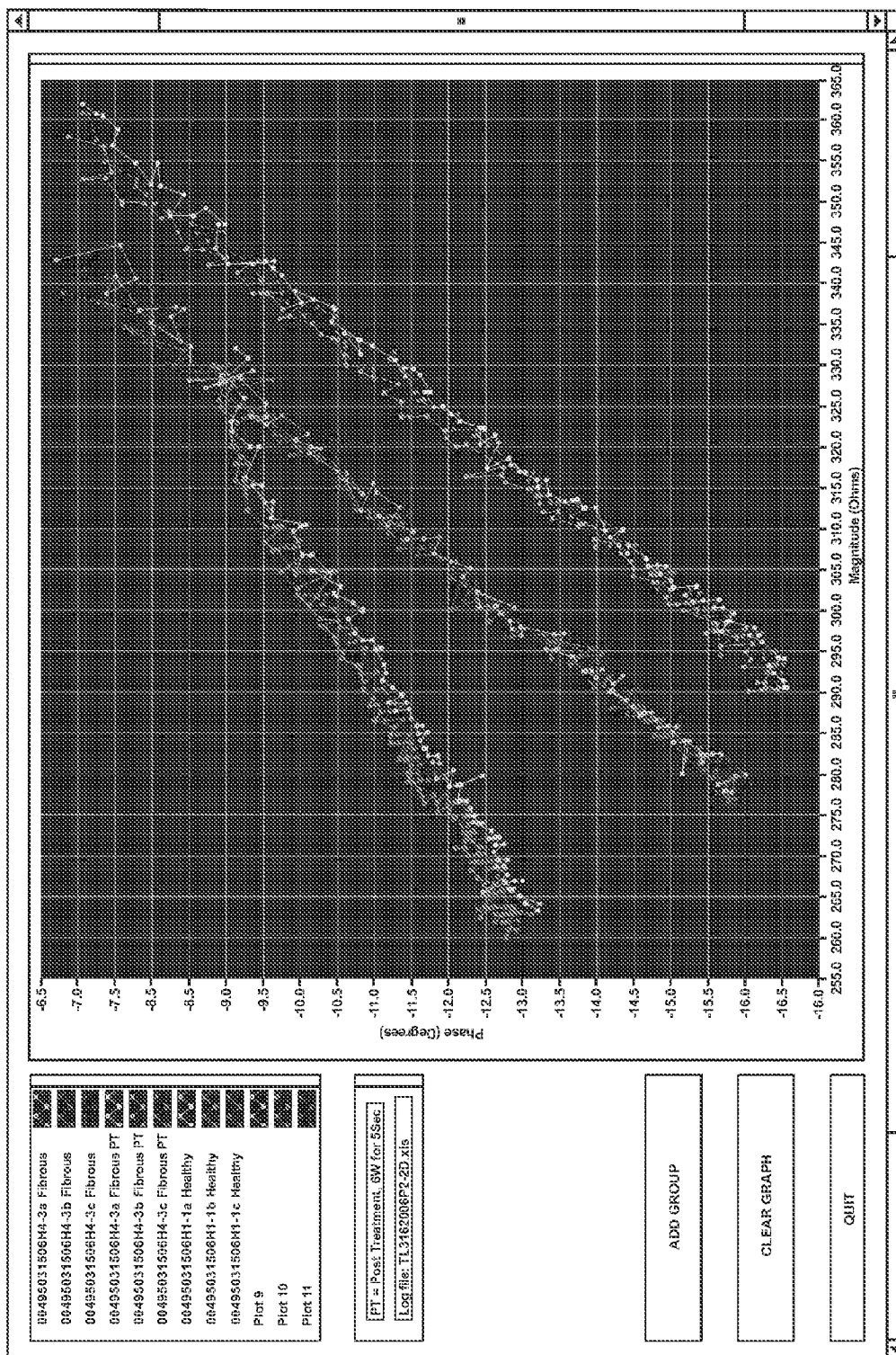


FIG. 31F

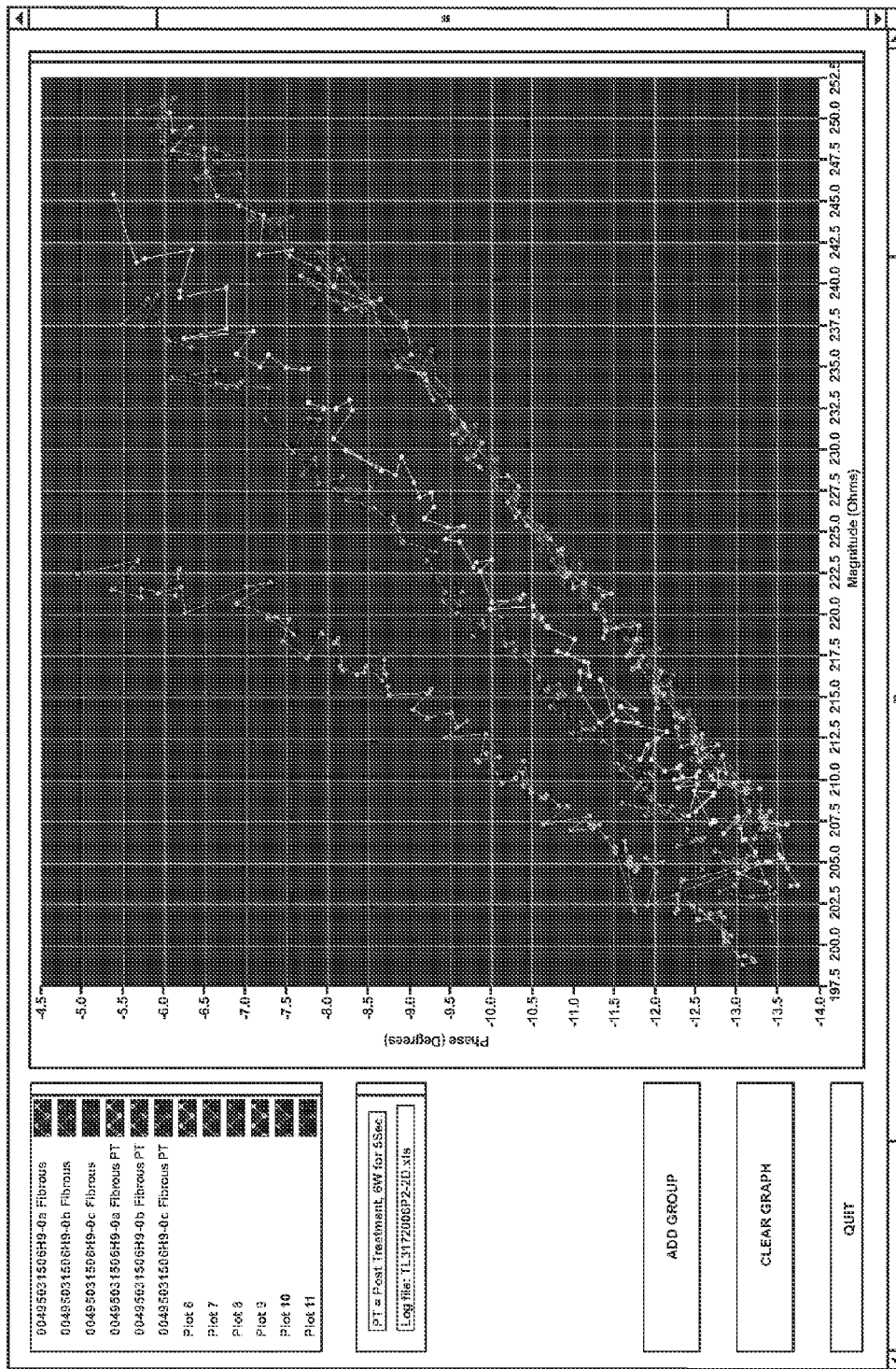


FIG. 31G

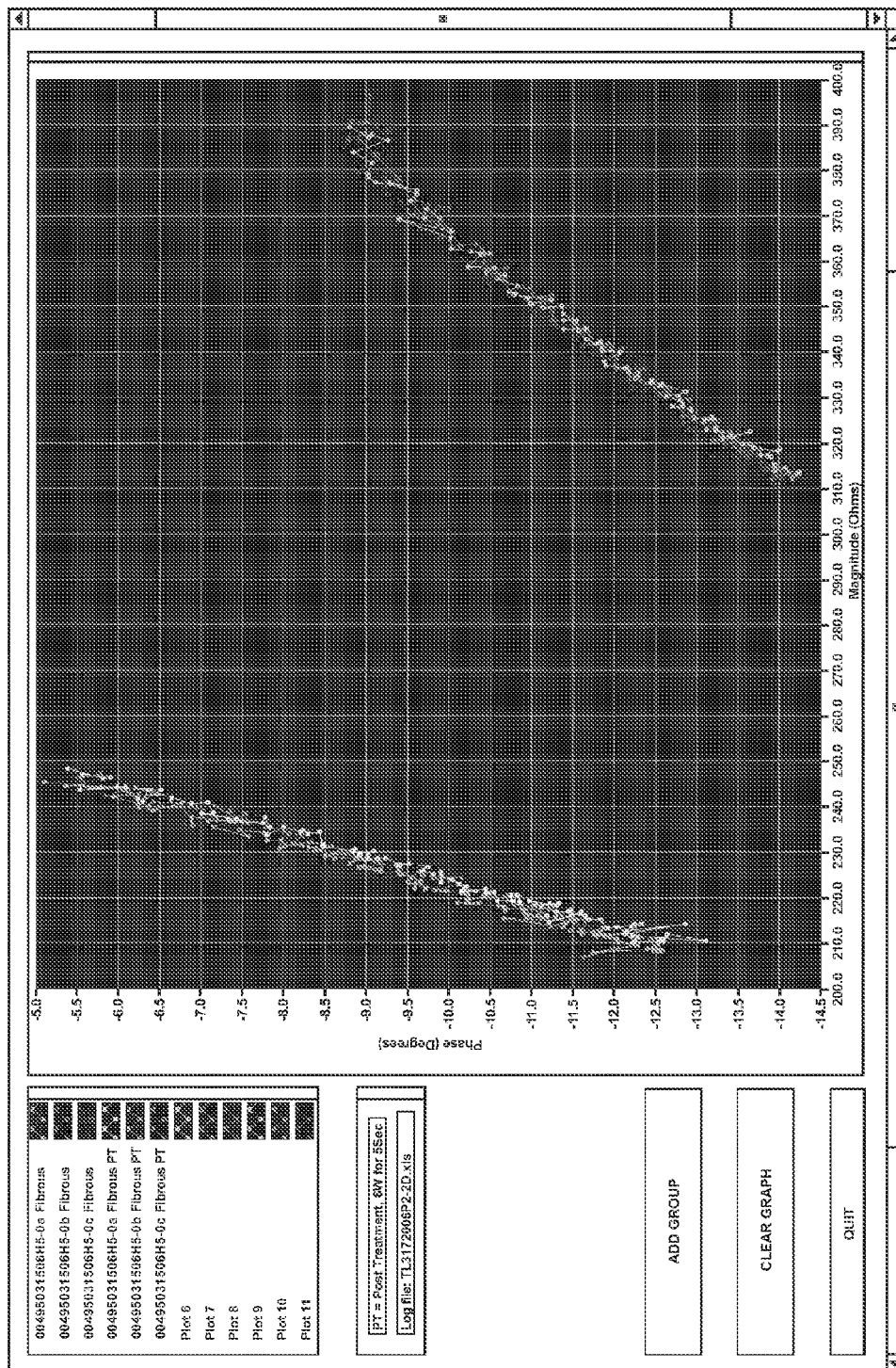


FIG. 31H

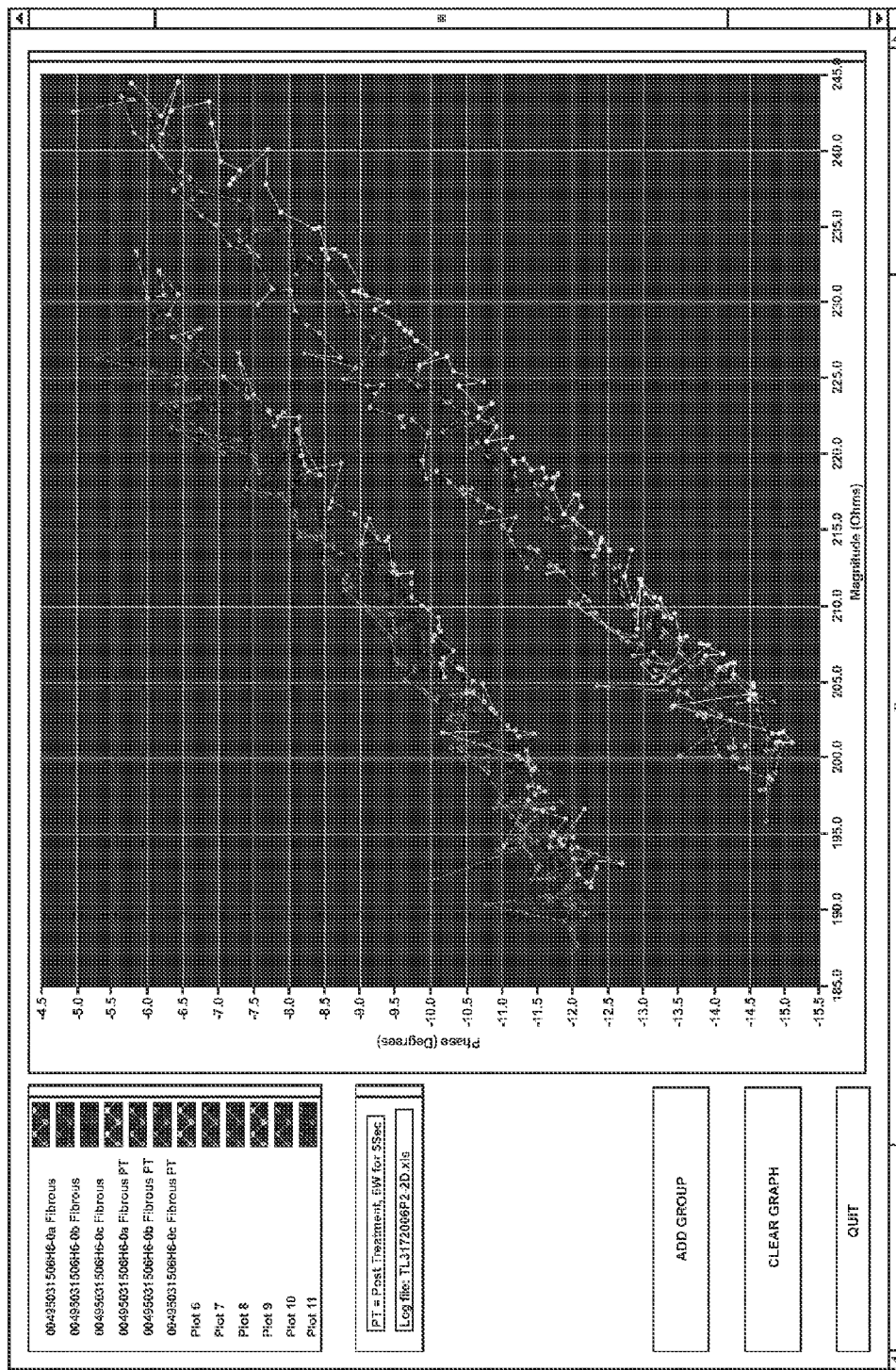


FIG. 31I

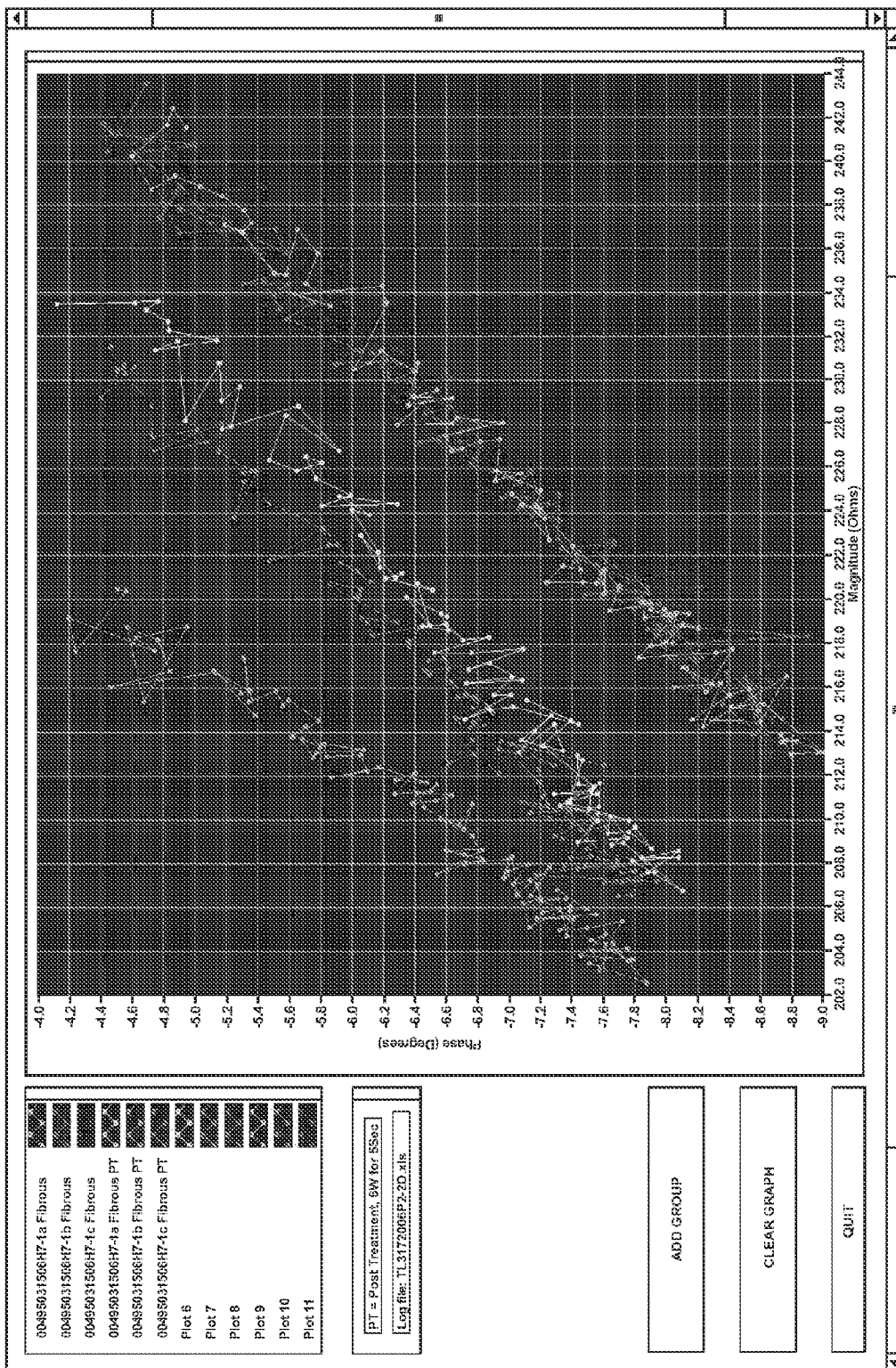


FIG. 31J



FIG. 32

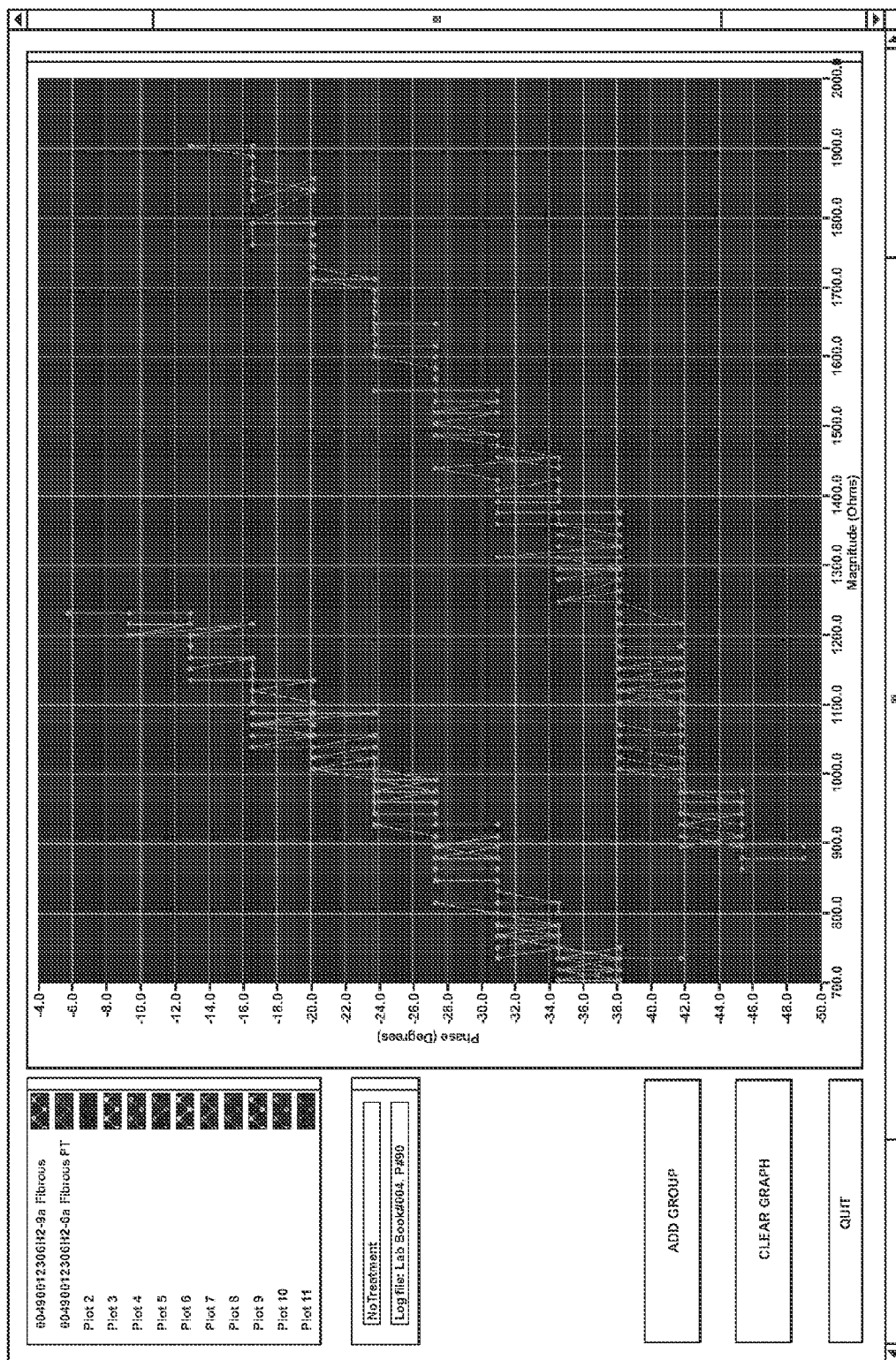


FIG. 32A

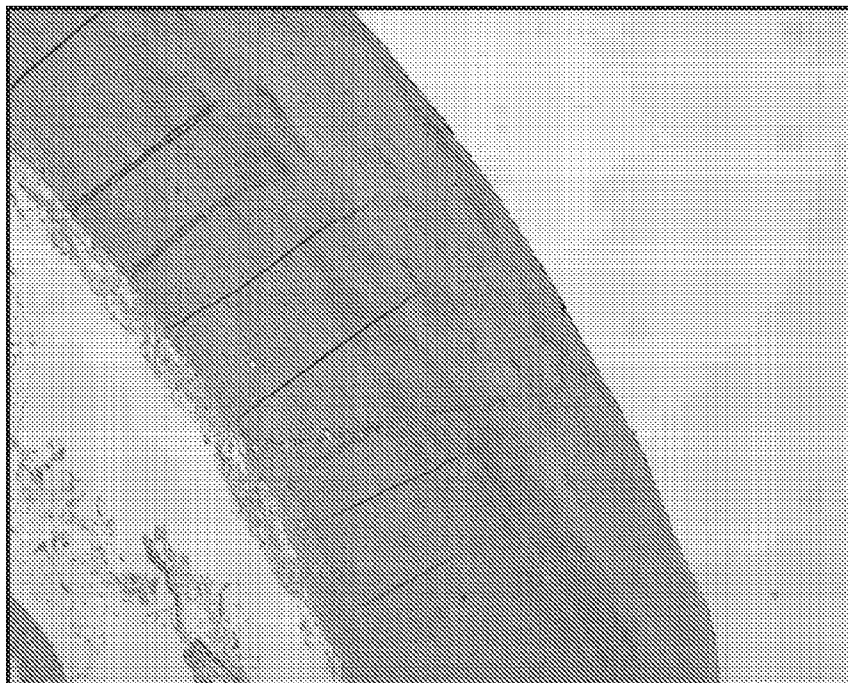


FIG. 32B



FIG. 32C

**TUNED RF ENERGY FOR SELECTIVE
TREATMENT OF ATHEROMA AND OTHER
TARGET TISSUES AND/OR STRUCTURES**

CROSS-REFERENCES TO RELATED
APPLICATIONS

[0001] This application is a Continuation of U.S. patent application Ser. No. 12/660,515 filed on Feb. 26, 2010, which is a Divisional of U.S. patent application Ser. No. 11/392,231 filed Mar. 28, 2006 (now U.S. Pat. No. 7,742,795); which application claims the benefit of priority from U.S. Provisional Application No. 60/666,766 filed Mar. 28, 2005 and is related to U.S. patent application Ser. No. 10/938,138 filed on Sep. 10, 2004 (now U.S. Pat. No. 7,291,146) entitled "Selectable Eccentric Remodeling and/or Ablation of Atherosclerotic Material;" the full disclosures, all of which are incorporated herein by reference in their entirety.

STATEMENT AS TO RIGHTS TO INVENTIONS
MADE UNDER FEDERALLY SPONSORED
RESEARCH OR DEVELOPMENT

[0002] Not Applicable

BACKGROUND OF THE INVENTION

[0003] 1. Field of the Invention

[0004] The present invention is generally related to medical devices, systems, and methods. In exemplary embodiments, the invention provides catheter-based diagnosis and/or treatment for luminal diseases, particularly for atherosclerotic plaque, vulnerable or "hot" plaque, and the like. The structures of the invention allow guided eccentric atherosclerotic material analysis, remodeling and/or removal, often using both electrical diagnostic signals and electrosurgical energy.

[0005] Physicians use catheters to gain access to and repair interior tissues of the body, particularly within the lumens of the body such as blood vessels. For example, balloon angioplasty and other catheters often are used to open arteries that have been narrowed due to atherosclerotic disease.

[0006] Balloon angioplasty is often effective at opening an occluded blood vessel, but the trauma associated with balloon dilation can impose significant injury, so that the benefits of balloon dilation may be limited in time. Stents are commonly used to extend the beneficial opening of the blood vessel.

[0007] Stenting, in conjunction with balloon dilation, is often the preferred treatment for atherosclerosis. In stenting, a collapsed metal framework is mounted on a balloon catheter which is introduced into the body. The stent is manipulated into the site of occlusion and expanded in place by the dilation of the underlying balloon. Stenting has gained widespread acceptance, and produces generally acceptable results in many cases. Along with treatment of blood vessels (particularly the coronary arteries), stents can also be used in treating many other tubular obstructions within the body, such as for treatment of reproductive, gastrointestinal, and pulmonary obstructions.

[0008] Restenosis or a subsequent narrowing of the body lumen after stenting has occurred in a significant number of cases. More recently, drug coated stents (such as Johnson and Johnson's Cypher™ stent, the associated drug comprising Sirolimus™) have demonstrated a markedly reduced restenosis rate, and others are developing and commercializing alternative drug eluting stents. In addition, work has also been

initiated with systemic drug delivery (intravenous or oral) which may also improve the procedural angioplasty success rates.

[0009] While drug eluting stents appear to offer significant promise for treatment of atherosclerosis in many patients, there remain many cases where stents either cannot be used or present significant disadvantages. Generally, stenting leaves an implant in the body. Such implants can present risks, including mechanical fatigue, corrosion, and the like, particularly when removal of the implant is difficult and involves invasive surgery. Stenting may have additional disadvantages for treating diffuse artery disease, for treating bifurcations, for treating areas of the body susceptible to crush, and for treating arteries subject to torsion, elongation, and shortening.

[0010] A variety of modified restenosis treatments or restenosis-inhibiting occlusion treatment modalities have also been proposed, including intravascular radiation, cryogenic treatments, ultrasound energy, and the like, often in combination with balloon angioplasty and/or stenting. While these and different approaches show varying degrees of promise for decreasing the subsequent degradation in blood flow following angioplasty and stenting, the trauma initially imposed on the tissues by angioplasty remains problematic.

[0011] A number of alternatives to stenting and balloon angioplasty so as to open stenosed arteries have also been proposed. For example, a wide variety of atherectomy devices and techniques have been disclosed and attempted. Despite the disadvantages and limitations of angioplasty and stenting, atherectomy has not gained the widespread use and success rates of dilation-based approaches. More recently, still further disadvantages of dilation have come to light. These include the existence of vulnerable plaque, which can rupture and release materials that may cause myocardial infarction or heart attack.

[0012] In light of the above, it would be advantageous to provide new devices, systems, and methods for diagnosing, characterizing, remodeling, and/or removal of atherosclerotic material and occlusions of the lumens of the body, and particularly of the blood vessels. It would further be desirable to avoid significant cost or complexity while providing structures which could both characterize and remodel or remove plaques and other occlusive materials without having to resort to the trauma of dilation, and to allow the opening of blood vessels and other body lumens which are not suitable for stenting. It would also be helpful if diagnosing and treating systems could provide some feedback on the progress of treatment.

BRIEF SUMMARY OF THE INVENTION

[0013] The present invention generally provides improved devices, systems, and methods for treating diseases of body lumens. Embodiments of the invention may allow analysis and/or treatment of the materials along these body lumens, optionally allowing plaque and other lesions to be characterized using a variable frequency electrical power or signal source. By radially expanding an electrode array-supporting basket within (for example) a blood vessel, and by monitoring electrical characteristics (and particularly frequency, impedance phase angle, and impedance magnitude) of circuits formed using selected electrodes of the array, plaque, fibrous vulnerable or "hot" plaques, healthy tissues, treated tissues, and/or the like along the blood vessel may be locally ana-

lyzed. Optionally, the same electrodes may be used to selectively (and often eccentrically) treat the tissues per the results of the analysis.

[0014] Embodiments of the invention may employ electrical energy to selectively heat target tissues and/or other structures. For example, the electrical energy waveforms, application cycles, potentials, delivery systems, and the like may be tailored to help direct therapeutic energy into atheroma and other disease tissues of the vasculature while inhibiting injury to collateral tissue structures. As the electrical characteristics of at least some diseased tissues (and particularly their impedances relative to those of surrounding tissues) may tend to urge known electrosurgical treatment energy into healthy adjacent tissues, such tailoring may improve the efficacy of luminal therapies and/or decrease collateral tissue damage. Exemplary treatment systems and methods for physical targeting (for example, axial and/or radial targeting of occlusive tissues from within a blood vessel) and/or frequency targeting may make use of disease localization information (for example, from intravascular imaging, impedance measurement, or the like) and may optionally employ cooling to protect at least some tissues along a luminal wall.

[0015] In a first aspect, the invention provides a catheter system for remodeling and/or reduction of material of or adjacent to a body lumen of a patient. The system comprises an elongate flexible catheter body having a proximal end and a distal end with an axis therebetween. At least one energy delivery surface is disposed near the distal end. A power source is electrically coupled to the energy delivery surface(s). The power source energizes the energy delivery surface(s) with an electrical energy form that helps the energy heat the material and inhibits collateral tissue damage.

[0016] In another aspect, the invention provides a method for analyzing a vessel wall of a blood vessel. The method comprises engaging the vessel wall with an electrode of a probe, and energizing the electrode with a variable frequency power source. A frequency of the power source is varied, and a target plaque of the vessel wall is characterized by monitoring a frequency-dependent characteristic of an electrical circuit. The electrical circuit comprises the power source, the electrode, and the engaged vessel wall.

[0017] Optionally, the probe expands radially within the blood vessel so as to engage a plurality of electrodes against the vessel wall. The electrodes of the expanded probe generally define a circumferentially distributed electrode array, and the electrodes of the array can be supported by associated struts of the probe. The struts may expand resiliently and independently within the blood vessel so as to couple the array to the vessel wall within non-circular lumens. An eccentric subset of the array (optionally a single electrode or an adjacent pair of electrodes) adjacent the target plaque may be energized to characterize tissues locally, and/or to eccentrically remodel the characterized target plaque using a remodeling electrical potential. Feedback on the remodeling may be obtained by monitoring the characteristic of the electrical circuit while applying an appropriate variable-frequency signal, either during remodeling or by halting remodeling at least temporarily.

[0018] In exemplary embodiments, the characterized target plaque may comprise a vulnerable plaque, and the remodeling may be halted in response to the electrical characteristics of the circuit. For example, the remodeling may be halted in response to a change in a tissue signature signal (such as an impedance phase angle and magnitude at a selected fre-

quency or range of frequencies), particularly when the change is associated with heating of lipids of the vulnerable plaque to 85° C. or more. More generally, the target plaque can be characterized using tissue signature and/or tissue signature profiles, with the signature profiles comprising curves or sets of data representing a plurality of tissue signature measurements at different frequencies throughout a frequency range. The target plaque may be characterized by comparison of a measured tissue signature profile to at least one other tissue signature profile, and may allow identification of the measured signature profile as being associated with at least one of healthy tissue, calcified plaque, or vulnerable plaque, with exemplary embodiments able to identify at least two of these. Beneficial embodiments may allow differentiation between plaques and other tissues that have not been treated, have been partially treated, and been appropriately treated, optionally by checking changes of a subset of the tissue signature measurements of the signature profiles (such as at an appropriate frequency or the like).

[0019] Many embodiments will be suitable for characterizing a plurality of localized materials distributed axially and/or eccentrically about the blood vessel, and optionally for selectively treating the different characterized materials with different remodeling treatments using the electrodes. Tissue signature profiles may be normalized and/or benchmarked to a known tissue of the patient (such as a healthy tissue identified using intravascular ultrasound or other known techniques), and target plaques may be characterized using relative slopes of tissue signature profiles or offsets between tissue signature profiles (and preferably both). The frequency range of the profiles will often extend below 50 KHz, typically extending from below about 50 KHz to over 1 MHz, and in some embodiments extending from about 4 Hz to about 2 MHz.

[0020] In another aspect, the invention provides a system for analyzing a vessel wall of a blood vessel. The system comprises a vascular probe having a proximal end, a distal end, and an electrode disposed near the distal end for engaging the vessel wall. A variable frequency power source can be coupled to the electrode such that, when the electrode engages the vessel wall, an electrical circuit (including the power source, the electrode, and the engaged vessel wall) can be established. A processor is coupled with the variable frequency power source, the processor configured to characterize a target plaque of the vessel wall by monitoring a frequency-dependent characteristic of the electrical circuit.

BRIEF DESCRIPTION OF THE DRAWINGS

[0021] The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

[0022] FIG. 1A illustrates diffuse atherosclerotic disease in which a substantial length of multiple blood vessels has limited effective diameters.

[0023] FIG. 1B illustrates vulnerable plaque within a blood vessel.

[0024] FIG. 1C illustrates the sharp bends or tortuosity of some blood vessels.

[0025] FIG. 1D illustrates atherosclerotic disease at a bifurcation.

[0026] FIG. 1E illustrates a lesion associated with atherosclerotic disease of the extremities.

[0027] FIG. 1F is an illustration of a stent fracture or corrosion.

[0028] FIG. 1G illustrates a dissection within a blood vessel.

[0029] FIG. 1H illustrates a circumferential measurement of an artery wall around a healthy artery.

[0030] FIG. 1I illustrates circumferential distribution of atheroma about a restenosed artery.

[0031] FIG. 2 schematically illustrates an atherosclerotic material catheter system according to the present invention.

[0032] FIG. 3 schematically illustrates a catheter system for remodeling atherosclerotic material, the system including the catheter of FIG. 2.

[0033] FIG. 4 illustrates an expandable basket and an associated electrode array of the catheter system of FIG. 2.

[0034] FIGS. 5 and 6 illustrate an exemplary basket structure having alternating axially offset electrodes in a circumferential array.

[0035] FIGS. 7A-E illustrate an exemplary atherosclerotic material remodeling and/or removal method using the catheter system of FIG. 2.

[0036] FIGS. 8-10 schematically illustrate controllers for selectively energizing electrodes in the system of FIG. 2.

[0037] FIG. 11 illustrates an alternative controller for selectively energizing electrodes in the system of FIG. 2.

[0038] FIGS. 12A-12H illustrate an alternative basket structure formed with independent struts having a localized enhanced width for use as an electrode surface, along with components thereof.

[0039] FIG. 13 is a schematic cross sectional view showing the application of different power levels through different electrodes so as to eccentrically remodel atherosclerotic materials.

[0040] FIGS. 14A-14E are cross sectional side views through a body lumen showing additional aspects of treatment methods and devices described herein.

[0041] FIGS. 14F-14H are cross sectional views taken across a body lumen and treatment device to show additional aspects of the eccentric treatment methods and devices.

[0042] FIGS. 15A and 15B illustrate an eccentric treatment device and method in a gelatin artery model.

[0043] FIG. 16 is a perspective view of an exemplary catheter assembly.

[0044] FIG. 17A illustrates physical targeting within vessel by longitudinal movement.

[0045] FIG. 17B illustrates physical targeting within vessel by radial electrode activation.

[0046] FIG. 17C illustrates physical targeting by activation of radial and longitudinal electrode combinations.

[0047] FIG. 18 illustrates electrical impedance versus frequency characteristic of diseased and non-diseased tissue.

[0048] FIG. 19 illustrates shielding of high impedance tissue from electrical current by surrounding lower impedance tissue.

[0049] FIG. 20 illustrates electrical impedance measurement utilizing multiple radial spaced electrodes.

[0050] FIG. 21 illustrates variations of multiple frequency therapy.

[0051] FIG. 22 illustrates use of physical tissue characteristics from external sources, combined with electrical impedance measurements to determine a desired or optimum energy setting.

[0052] FIG. 23 illustrates four electrode measurement system distributed across multiple electrodes to measure contact and tissue impedance.

[0053] FIG. 24 illustrates flooding of vessel with non-ionic fluid to direct energy to vessel wall and surrounding tissue, reducing losses in native fluid.

[0054] FIG. 25 illustrates one embodiment of a closed loop control system to automatically diagnose and treat lesions within a vessel utilizing tissue information from an external source such as IVUS.

[0055] FIG. 26A illustrates the switching mechanism in an external control box.

[0056] FIG. 26B illustrates the switching mechanism at the distal end of the catheter.

[0057] FIG. 26C illustrates the switching mechanism at the proximal end of the catheter.

[0058] FIG. 27 illustrates selective treatment of plaque.

[0059] FIGS. 27A-27C illustrate spectral correlations of tissues, as may be used to analyze or characterize plaques.

[0060] FIGS. 28A-28C illustrate bench top remodeling of tissue using an animal fat model treated with an exemplary embodiment of the catheter system.

[0061] FIGS. 29A and 29B illustrate intravascular imaging and eccentric remodeling with an exemplary embodiment of the catheter system.

[0062] FIG. 30 is a simplified schematic illustrating components of the system of FIG. 2 that can be used for intraluminal tissue and other material analysis and characterization.

[0063] FIGS. 31A-31J graphically illustrate relationships between phase angles and impedance in a frequency range as can be used to electrically analyze and characterize materials engaging and disposed between electrodes of the system of FIG. 2.

[0064] FIG. 32 illustrate a variety of tissues for characterization and selective treatment by the system of FIG. 2.

[0065] FIGS. 32A-32C illustrate changes in a relationship between phase angle and impedance in a frequency range associated with treatment of a tissue, along with histological images of the tissue before and after treatment.

DETAILED DESCRIPTION OF THE INVENTION

[0066] The present invention provides devices, systems, and methods to analyze and/or treat a luminal tissue. The invention will be particularly useful for characterizing and remodeling materials along a partially occluded artery in order to open the artery lumen and increase blood flow. Remodeling may involve the application of electrosurgical energy, typically in the form of RF and/or microwave electrical potentials to energy delivery surfaces such as electrodes, antennas, and the like. This energy will optionally be controlled so as to limit a temperature of target and/or collateral tissues, for example, limiting the heating of a fibrous cap of a vulnerable plaque or the intimal layer of an artery structure to a maximum temperature in a range from about 50 to about 60° Celsius. In many embodiments, the energy will be controlled to limit the maximum temperature of an outer layer or adventitia of the blood vessel to no more than about 63° Celsius. Limiting heating of a lipid-rich pool of a vulnerable plaque sufficiently to induce melting of the lipid pool while inhibiting heating of other tissues (such as an intimal layer or fibrous cap) to less than a temperature in a range from about 50 to about 60° Celsius may inhibit an immune response that might otherwise lead to restenosis, or the like. Many embodiments may apply sufficient heat energy to heat the lipids to about 85°

Celsius or more while inhibiting collateral damage through selective application of heating energy. Relatively mild heating energies may be sufficient to denature and shrink atherosclerotic material during treatment, immediately after treatment, and/or more than one hour, more than one day, more than one week, or even more than one month after the treatment through a healing response of the tissue to the treatment so as to provide a bigger vessel lumen and improved blood flow.

[0067] In some embodiments, remodeling of the atherosclerotic plaque may comprise the use of higher energies to ablate and remove occlusive material from within body lumens, and particularly to remove atherosclerotic material from a blood vessel in order to improve blood flow. Ablation debris may be generated by such ablation, and the ablation debris may be thrombotic or non-thrombotic. Where thrombotic debris is generated by ablation, that debris may be restrained, captured, and/or evacuated from the treatment site. Non-thrombotic debris produced by ablation may not have to be restrained and/or evacuated from the vessel. The analysis and/or treatment region of the body lumen may be at least partially (or effectively fully) isolated for ablative or other remodeling treatments so as to allow the treatment environment to be modified (for example, by cooling the lumen and/or altering the electrical characteristics of fluid within the lumen using cooled fluid irrigation, non-isotonic fluid irrigation, and/or the like), to limit the release of any remodeling debris, and the like. The techniques of the invention will often provide electrosurgical capabilities, sensing or imaging suitable for measuring atheroma and/or vascular walls, and/or an emboli inhibitor. As atherosclerosis may be eccentric relative to an axis of the blood vessel over 50% of the time, possibly in as much as (or even more than) 75% of cases, the devices and methods of the present invention will often be particularly well suited for directing treatment eccentrically, often in response to circumferential atherosclerotic material detecting or imaging. While the methods and devices described herein allow such eccentric treatments, the devices can also be used for treatment of radially symmetric atherosclerosis by selectively directing energy in a radially symmetric pattern about an axis of the catheter or the like.

[0068] Hence, remodeling of atherosclerotic materials may comprise ablation, removal, shrinkage, melting, and the like of atherosclerotic and other plaques. Optionally, atherosclerotic material within the layers of an artery may be denatured so as to improve blood flow, so that debris will not necessarily be generated. Similarly, atherosclerotic materials within the arterial layers may be melted and/or treatment may involve a shrinking of atherosclerotic materials within the artery layers, again without necessarily generating treatment debris. The invention may also provide particular advantages for treatment of vulnerable plaques or blood vessels in which vulnerable plaque is a concern. Such vulnerable plaques may comprise eccentric lesions, and the present invention may be particularly well suited for identifying an orientation (as well as axial location) of the vulnerable plaque structure. The invention will also find applications for targeting the cap structure for mild heating (to induce thickening of the cap and make the plaque less vulnerable to rupture) and/or heating of the lipid-rich pool of the vulnerable plaque (so as to remodel, denature, melt, shrink, and/or redistribute the lipid-rich pool).

[0069] While the present invention may be used in combination with stenting and/or balloon dilation, the present invention is particularly well suited for increasing the open

diameter of blood vessels in which stenting and balloon angioplasty are not a viable option. Potential applications include treatment of diffuse disease, in which atherosclerosis is spread along a significant length of an artery rather than being localized in one area. The invention may also provide advantages in treatment of vulnerable plaque or blood vessels in which vulnerable plaque is a concern, both by potentially identifying and avoiding treatment of the vulnerable plaque with selected eccentric and/or axial treatments separated from the vulnerable plaque, and by intentionally ablating and aspirating the cap and lipid-rich pool of the vulnerable plaque within a controlled environmental zone or region within the blood vessel lumen. The invention may also find advantageous use for treatment of tortuous, sharply-curved vessels, as no stent need be advanced into or expanded within the sharp bends of many blood vessel. Still further advantageous applications include treatment along bifurcations (where side branch blockage may be an issue) and in the peripheral extremities such as the legs, feet, and arms (where crushing and/or stent fracture failure may be problematic).

[0070] Embodiments of the invention may measure impedance of a circuit, and particularly of a circuit that includes an electrode coupled with a luminal wall or other tissue. Such impedance measurements of alternating current (AC) circuits will often include a measurement of both a real portion or magnitude of the impedance, and an imaginary portion or phase angle of the impedance. The impedance magnitude and phase angle generated at an appropriate frequency by a tissue coupled to the electrode may provide a tissue signature. To enhance the accuracy of tissue signature measurements, a plurality of individual measurements (often three or more) may be taken and averaged. By measuring tissue signatures at a plurality of different frequencies (for example, at about 100 different frequencies) within a frequency range, a signature profile for the tissue may be generated, with the signature profiles optionally comprising a curve or curve-fit of phase angles and magnitudes throughout a frequency range. In some embodiments, signal tissue signature measurements may be compared, and/or a smaller number (2-10 or 5-50) of such measurements may be included in a tissue signature profile. Tissue signature measurements may depend on the measurement conditions (including the configuration of the electrodes/tissue coupling), particularly, when the measurements are performed by transmitting bipolar tissue sensing current between two electrodes that are supported by a flexible and/or radially expandable support structure. Nonetheless, the relative tissue signatures and/or signature profiles (particularly the relative offsets between signature profiles, relative slopes of signature profiles, and the like) of different tissues of different patients will often be sufficiently consistent to allow the tissue signatures and signature profiles to be used to distinguish between healthy tissue, calcified plaque, fibrous plaque, lipid-rich plaques, untreated tissue, partially treated tissue, fully treated tissue, and the like.

[0071] Optionally, baseline measurements of tissues (which may be characterized via intravascular ultrasound, optical coherence tomography, or the like) may be taken to help differentiate adjacent tissues, as the tissue signatures and/or signature profiles may differ from person to person. Additionally, the tissue signatures and/or signature profile curves may be normalized to facilitate identification of the relevant slopes, offsets, and the like between different tissues. Once sufficient correlations have been established between tissue signatures (including impedance magnitude, phase

angle, and frequency) and signature profiles of different tissues for a number of different patients and measurement conditions, tissue characterization of at least some patients may be provided without having to resort to other baseline tissue characterization methodologies.

[0072] Diffuse disease and vulnerable plaque are illustrated in FIGS. 1A and 1B, respectively. FIG. 1C illustrates vascular tortuosity. FIG. 1D illustrates atherosclerotic material at a bifurcation, while FIG. 1E illustrates a lesion which can result from atherosclerotic disease of the extremities.

[0073] FIG. 1F illustrates a stent structural member fracture which may result from corrosion and/or fatigue. Stents may, for example, be designed for a ten-year implant life. As the population of stent recipients lives longer, it becomes increasingly likely that at least some of these stents will remain implanted for times longer than their designed life. As with any metal in a corrosive body environment, material degradation may occur. As the metal weakens from corrosion, the stent may fracture. As metal stents corrode, they may also generate foreign body reaction and byproducts which may irritate adjoining body tissue. Such scar tissue may, for example, result in eventual reclosure or restenosis of the artery.

[0074] Arterial dissection and restenosis may be understood with reference to FIGS. 1G through 1I. The artery comprises three layers, an endothelial layer, a medial layer, and an adventitial layer. During angioplasty, the inside layer may delaminate or detach partially from the wall so as to form a dissection as illustrated in FIG. 1G. Such dissections divert and may obstruct blood flow. As can be understood by comparing FIGS. 1H and 1I, angioplasty is a relatively aggressive procedure which may injure the tissue of the blood vessel. In response to this injury, in response to the presence of a stent, and/or in the continuing progression of the original atherosclerotic disease, the opened artery may restenose or subsequently decrease in diameter as illustrated in FIG. 1I. While drug eluting stents have been shown to reduce restenosis, the efficacy of these new structures several years after implantation has not been fully studied, and such drug eluting stents are not applicable in many blood vessels.

[0075] In general, the present invention provides a catheter which is relatively quick and easy to use by the physician. The catheter system of the present invention may allow arteries to be opened to at least 85% of their nominal or native artery diameter. In some embodiments, arteries may be opened to about 85%, and/or acute openings may be less than 85%. Rapid occlusive material removal may be effected using sufficient power to heat tissues locally to over about 100° C. so as to vaporize tissues, or more gentle remodeling may be employed.

[0076] The desired opening diameters may be achieved immediately after treatment by the catheter system in some embodiments. Alternatively, a milder ablation may be implemented, for example, providing to no more than a 50% native diameter when treatment is complete, but may still provide as much as 80 or even 85% or more native vessel open diameters after a subsequent healing process is complete, due to resorption of injured luminal tissues in a manner analogous to left ventricular ablation for arrhythmia and transurethral prostate treatments. Such embodiments may heat at least some occlusive tissue to a temperature in a range from about 55° C. to about 80° C. In some embodiments, occlusive tissues may be heated to a maximum temperature in a range between about 93 and 95° C. In other embodiments described herein, heating

may be controlled so as to provide tissue temperatures in a range between about 50 and 60° C., with some embodiments benefiting from maximum tissue temperatures of about 63° C. Still further treatments may benefit from treatment temperatures of about 90° C. Advantageously, the catheter systems and methods of the invention may be used without balloon angioplasty, thereby avoiding dissections and potentially limiting restenosis. Optionally, treatments of tissues described herein may be repeated during a single surgical session, or after a month or more (even after a year or more) if appropriate to provide or maintain a desired opening of the lumen.

[0077] An exemplary catheter system 10 is schematically illustrated in FIGS. 2 and 3. A remodeling and/or ablation catheter 12 includes a catheter body 14 having a proximal end 16 and a distal end 18. Catheter body 14 is flexible and defines a catheter axis 20, and includes an aspiration lumen 22 and an irrigation lumen 24 (see FIG. 3). Still further lumens may be provided for a guidewire, imaging system, or the like as described below. Lumen 22 may be used for sensing and/or imaging of atheroma as well as aspiration.

[0078] Catheter 12 includes a radially expandable structure 26 adjacent distal end 18 and a housing 28 adjacent proximal end 16. A distal tip 30 may include an integral tip valve to seal aspiration lumen 22 and allow passage of guidewires, imaging and/or restenosis inhibiting catheters, and the like.

[0079] Proximal housing 28 includes a first connector 32 in fluid communication with aspiration lumen 22. Aspiration lumen 22 may have an aspiration port within expandable structure 26 so as to allow aspiration or aspiration of debris and gasses from within the expandable structure. Aspiration lumen 22 may also be used as an access lumen for guidewires, intravascular imaging catheters, and/or distally advancing intravascular radiation treatment catheters or restenosis inhibiting drugs. Hence, connector 32 may selectively accommodate an imaging catheter 34 having an atherosclerotic material detector 36 advancable within catheter body 14 adjacent to and/or beyond distal end 18, the detector often comprising an intravascular ultrasound transducer, an optical coherent tomography sensor, an MRI antenna, or the like. An imaging connector 38 of imaging catheter 34 transmits imaging signals allowing circumferential measurement of atherosclerotic thicknesses about axis 20 to a display 39.

[0080] Connector 32 also accommodates a restenosis inhibiting treatment catheter 40, the treatment catheter here comprising an intravascular radiation catheter. Such a radiation catheter may include a radiation source 42 which can again be advanced distally within catheter body 14 to or beyond expandable structure 26.

[0081] A second connector 44 of proximal housing 28 is in fluid communication with irrigation lumen 24 (see FIG. 4). Second connector 44 may be coupled to an irrigation fluid source for introducing conductive or non-conductive liquids, gases, or the like, ideally for introducing gas or heparinized saline. Both first and second connectors 32, 44 may optionally comprise a standard connector such as a Luer-Loc™ connector. In FIG. 3 connector 44 is schematically shown coupled to an aspiration vacuum source/infusion fluid source 45.

[0082] Referring now to FIGS. 2, 3, and 4, proximal housing 28 also accommodates an electrical connector 46. Connector 46 includes a plurality of electrical connections, each electrically coupled to an electrode 50 via a dedicated conductor 52. This allows a subset of electrodes 50 to be easily

energized, the electrodes often being energized with bipolar or monopolar RF energy. Hence, electrical connector 46 will often be coupled to an RF generator via a controller 47, with the controller allowing energy to be selectively directed to an eccentric portion of an engaged luminal wall. When monopolar RF energy is employed, patient ground may (for example) be provided by an external electrode or an electrode on catheter body 14. A processor 49 may manipulate signals from imaging catheter 34 to generate an image on display 39, may coordinate aspiration, irrigation, and/or treatment, and may automatically register the treatment with the image.

[0083] Processor 49 will typically comprise computer hardware and/or software, often including one or more programmable processor unit running machine readable program instructions or code for implementing some or all of one or more of the methods described herein. The code will often be embodied in a tangible media such as a memory (optionally a read only memory, a random access memory, a non-volatile memory, or the like) and/or a recording media (such as a floppy disk, a hard drive, a CD, a DVD, a memory stick, or the like). The code and/or associated data and signals may also be transmitted to or from the processor via a network connection (such as a wireless network, an Ethernet, an internet, an intranet, or the like), and some or all of the code may also be transmitted between components of catheter system 10 and within processor 49 via one or more bus, and appropriate standard or proprietary communications cards, connectors, cables, and the like will often be included in the processor. Processor 49 will often be configured to perform the calculations and signal transmission steps described herein at least in part by programming the processor with the software code, which may be written as a single program, a series of separate subroutines or related programs, or the like. The processor may comprise standard or proprietary digital and/or analog signal processing hardware, software, and/or firmware, and will typically have sufficient processing power to perform the calculations described herein during treatment of the patient, the processor optionally comprising a personal computer, a notebook computer, a tablet computer, a proprietary processing unit, or a combination thereof. Standard or proprietary input devices (such as a mouse, keyboard, touchscreen, joystick, etc.) and output devices (such as a printer, speakers, display, etc.) associated with modern computer systems may also be included, and processors having a plurality of processing units (or even separate computers) may be employed in a wide range of centralized or distributed data processing architectures. Hence, any or all of the

[0084] Expandable structure 26 is illustrated in more detail in FIG. 4. Expandable structure 26 may expand resiliently when released from within a restraining sheath, or may expand by pulling tip 30 toward distal end 18 (see FIG. 2), optionally using a pullwire, an inner catheter body 58, or the like. Expandable structure 26 here comprises a perforate structure or basket having a series of structural struts or elements 54 with opening or perforations 56 therebetween. Perforations 56 may be formed, for example, by cutting elongate slits in a flexible tube material, or the basket may be formed by braiding elongate wires or ribbons or the like.

[0085] Expandable structure 26 generally includes a proximal portion 60, a distal portion 62, and an intermediate portion 64 therebetween. Each electrode 50 is mounted on an associated basket element 54 along intermediate portion 64, with an associated conductor 52 extending proximally from the electrode. Electrodes 50 are distributed circumferentially

about axis 20 in an array, adjacent electrodes preferably being axially offset, ideally being staggered or alternating between proximal and distal axial locations. This allows bipolar energy to be directed between adjacent circumferential (axially offset) electrodes between adjacent distal electrodes, between adjacent proximal electrodes, and the like.

[0086] In the exemplary embodiment, proximal and distal barriers 66, 68 expand radially with proximal and distal portions 60, 62 of expandable structure 26. Barriers 66, 68 inhibit any ablation debris and gases generated adjacent electrodes 50 from traveling within the body lumen beyond catheter 12. Barriers 66, 68 also allow an at least partially isolated ablation environment to be established within the body lumen, for example, by replacing blood within a blood vessel with a more advantageous fluid environment for limiting charring of the electrodes and the like. Alternative barriers may be provided instead of (or in combination with) barriers 66, 68, including one or more balloons axially offset from expandable member 26, elastic lips, or the like. In other embodiments remodeling may be effected without generating significant thermolytic ablation debris and/or a desired treatment environment may be provided with localized irrigation and/or aspiration flows so that some systems may forego the use of barriers.

[0087] An exemplary expandable structure 26 is formed by cutting slots in a superelastic alloy tube such as a nickel titanium alloy or Nitinol™ tube. As can be understood with reference to FIG. 6, expandable structures 54 may have circumferential widths 80 which are enhanced adjacent an electrode and/or electrode mounting location 82. As can be seen in FIG. 5, the localized enhancement of the width 80 adjacent electrode mounting pads 82 may be axially offset, as described above. The slots forming expandable members 54, and hence the expandable members themselves may, for example, be 0.8 inches in length, with the expandable members having a circumferential width of about 0.25 inches.

[0088] Referring now to FIGS. 7A and 7B, side and end views of an expandable barrier in the form of a collapsible cone can be seen. Barrier 66 here comprises a braided Nitinol™ wire 84 coated in silicone, for example, by dipping a braid of a superelastic alloy such as a Nitinol™ braid in liquid silicone and allowing it to harden. Such cones may then be mounted over the proximal and distal portions of the expandable structure. As noted above, a variety of alternative barrier membranes may be employed. FIG. 7C illustrates a basket 75 with an integral barrier 77 coated directly on the basket. Barrier 77 comprises a polyurethane, which may be quite tear resistant. Alternative barrier membranes may comprise other materials such as PTFE or the like.

[0089] Referring now to FIGS. 8 and 9, exemplary electrodes 50 supported by polyimide alloy expandable members 54 may be coated with a high-temperature polymer. Conductors 52 extend proximally from electrodes 50 as described above. High contrast radiopaque markers such as gold, platinum, platinum/iridium alloy, and the like may be attached to or near these struts. The markers could also be used as the electrodes.

[0090] The use of catheter system 10 for remodeling and/or removal of eccentric atheroma from within a blood vessel can be understood with reference to FIGS. 7A through 7E. As seen in FIG. 7A, accessing of a treatment site will often involve advancing a guidewire GW within a blood vessel V at, and more often distally beyond a target region of atherosclerotic material AM. A wide variety of guidewires may be used.

For accessing a vessel having a total occlusion, guidewire GW may comprise any commercially available guidewire suitable for crossing such a total occlusion, including the Safe-Cross™ RF system guidewire having forward-looking optical coherence reflectometry and RF ablation. Where atherosclerotic material AM does not result in total occlusion of the lumen, such capabilities need not be provided in guidewire GW, although other advantageous features may be provided. For example, guidewire GW may include a distal balloon to hold the guidewire in place and further inhibit movement of ablation debris and the like. Guidewire GW may be positioned under fluoroscopic (or other) imaging.

[0091] Catheter **12** is advanced distally over guidewire GW and positioned adjacent to atherosclerotic material AM, often toward a distal portion of the occlusion as can be understood with reference to FIGS. 7A and 7B. Expandable structure **26** expands radially within the lumen of the blood vessel so that electrodes **50** radially engage atherosclerotic material AM. Expandable structure **26** may be expanded by, for example, pulling a pullwire extending through catheter body **14** to the coupled (directly or indirectly) to distal portion **62** of expandable body **26** (see FIG. 4). Alternatively, an inner catheter body **58** may be moved proximally relative to outer catheter body **14**, with the inner catheter again being coupled to the distal portion of the expandable body. Still further alternatives are possible, including withdrawing a sheath from around the expandable body and allowing the expandable body to flex radially outwardly. In at least some embodiments, whether actuated from the proximal end of catheter **12** or simply by releasing the expandable body, the structural members defining the expandable body may comprise elastic or superelastic materials treated to expand radially outwardly, such as by heat-setting a superelastic Nitinol™ metal, polyimide, or the like. In some embodiments, guidewire GW may be removed after the ablation catheter is positioned and/or the basket is expanded. As atherosclerotic material AM is distributed eccentrically about catheter **12**, some of electrodes **50** directly engage a luminal wall W, as can be understood with reference to FIGS. 7B and 7C.

[0092] Imaging catheter **34** is positioned within a lumen of catheter **12** so that detector **42** extends to adjacent atherosclerotic material AM. The imaging catheter operates within and/or through catheter **12** so as to measure a thickness of atherosclerotic material concentrically about catheter **12** as illustrated in FIG. 7C with measurements often being taken at a plurality of axial locations so as to measure axial variation of the atherosclerotic material AM within the blood vessel, such measurements often progressing proximally. In many cases, atherosclerotic material AM will be distributed eccentrically within the vessel wall as shown in FIG. 7C. It should be noted that no portion of the vessel wall need be completely uncovered by atherosclerotic material for the measurement distribution to indicate that the obstruction is eccentric, as a relatively thin layer of atheroma along one portion or side of the blood vessel may be much different in thickness than a very thick layer of atherosclerotic material on an opposite side of the blood vessel V. In some methods, remodeling and/or ablation of all atheroma along one side may result in electrode/vessel wall engagement only after treatment begins.

[0093] In some cases, imaging catheter **34** may allow identification and/or characterization of atherosclerotic materials, plaques, tissues, lesions, and the like from within a blood vessel. For example, imaging catheter **34** may determine an

axial and/or circumferential localization of a target plaque for treatment. Where treatments are intended for atherosclerotic plaques so as to enhance blood flow through the lumen, the treatment may be tailored to provide short term and/or long term increases in lumen diameter and blood flow. Where catheter **34** identifies a circumferentially and/or axially localized vulnerable plaque, that vulnerable plaque may be targeted for a suitable treatment to inhibit deleterious release of thrombotic materials, often by thickening a fibrous cap of the vulnerable plaque, making the plaque less vulnerable to rupture, decreasing a size or danger of release from a lipid-rich pool of the vulnerable plaque, or the like. Hence, catheter **34** may be used to provide information similar to that available through histology so as to indicate a composition of an atheroma (by identifying and location, for example, a fibrous cap, smooth muscle cells, a lipid pool, calcifications, and the like.) Intravascular ultrasound catheters may now be capable of such atheroma characterizations, and these characterizations may also be provided by optical coherence tomography intravascular catheters, intravascular MRI antennas, and other catheter-based imaging systems, or by non-invasive imaging modalities such as MRI systems, and the like.

[0094] Suitable imaging catheters for use in the present catheter system are commercially available from a wide variety of manufacturers. Suitable technology and/or catheters may, for example, be commercially available from SciMed Life Systems and Jomed-Volcano Therapeutics (providers of intravascular ultrasound catheters), Light Lab™ Imaging (developing and commercializing optical coherence tomography catheters for intravascular imaging), Medtronic CardioRhythm, and the like. Still further alternative technologies may be used, including ultra fast magnetic resonance imaging (MRI), electrical impedance atheroma depth measurements, optical coherence reflectometry, and the like.

[0095] The systems, devices, and methods described herein may optionally make use of imaging techniques and/or atherosclerotic material detector devices which are at least in part (optionally being entirely) disposed outside of the body lumen, optionally being disposed outside of the patient body. Non-invasive imaging modalities which may be employed include X-ray or fluoroscopy systems, MRI systems, external ultrasound transducers, and the like. Optionally, external and/or intravascular atherosclerotic material detectors may also be used to provide temperature information. For example, a system having an MRI antenna may detect tissue temperatures such that a graphical indication of treatment penetration may be presented on the system display. Tissue temperature information may also be available from ultrasound and/or optical coherence tomography systems, and the temperature information may be used as feedback for directing ongoing treatments, for selecting tissues for treatment (for example, by identifying a hot or vulnerable plaque), and the like.

[0096] As with positioning of guidewire GW and advancement of catheter **12**, positioning of sensor **30** of imaging catheter **34** may be facilitated by fluoroscopic or other imaging modalities. Location of sensor **36** relative to expandable structure **26** may be facilitated by radiopaque markers of catheter **34** adjacent sensor **36**, and by the radiopaque structure (or corresponding radiopaque markers placed on or near) expandable structure **26**, and/or by the use of radiopaque electrodes.

[0097] By expanding expandable structure **26** within blood vessel V, optional proximal and distal barriers **66**, **68** (see FIG. 4) may form an at least partially, and preferably a substan-

tially isolated environment within the blood vessel. That environment may be adapted to improve subsequent remodeling and/or ablation by aspirating blood from a port of aspiration lumen 22 disposed between proximal and distal barriers 66, 68, and by irrigating the isolated environment with a desired fluid, as described above. When provided, aspiration and/or irrigation may be performed, optionally simultaneously, so as to generate a flow within the controlled environment for removal of any vaporization gases, ablation debris, and the like.

[0098] Referring now to FIGS. 7C and 7D, circumferential imaging often indicates that remodeling and/or ablation should be targeted to an eccentric portion or region R of the vessel wall W. To aid in registering the electrodes with the circumferential atheroma distribution, one strut of expandable structure 26 has an identifiable image, allowing the strut to serve as a rotational alignment key. Registering the electrodes may be achieved using intravascular imaging such as intravascular ultrasound (IVUS), optical coherence tomography (“OCT”), intravascular MRI, and/or the like, optionally using external imaging such as fluoroscopy, magnetic resonance imaging (“MRI”), or the like. Electronic registration may also be used. In response to this information, RF energy is directed to electrodes within region R. These actively energized electrodes define a subset of the overall array of electrodes, and selection of this subset of electrodes may be implemented using a controller as described hereinbelow.

[0099] The mechanisms of ablating atherosclerotic material within a blood vessel have been well described, including by Slager et al. in an article entitled, “Vaporization of Atherosclerotic Plaque by Spark Erosion” in *J. of Amer. Cardiol.* (June, 1985), on pp. 1382-6; and by Stephen M. Fry in “*Thermal and Disruptive Angioplasty: a Physician’s Guide*,” Strategic Business Development, Inc., (1990) the full disclosures of which are incorporated herein by reference. Suitable vaporization methods and devices for adaptation and/or use in the present system may also be described in U.S. Pat. Nos. 5,098,431; 5,749,914; 5,454,809; 4,682,596; and 6,582,423, among other references. The full disclosure of each of these references is incorporated herein by reference.

[0100] Referring now to FIG. 7E, as described above, it may not be necessary to completely remove all atheroma or atherosclerotic material from within the blood vessel. Providing an open lumen having an effective diameter of at least 80 or 85% of a nominal native lumen diameter may be sufficient. Remodeling treatments may provide acute effective open diameters in a range from about 30% to about 50%. In some embodiments, injury caused to the atherosclerotic material with the energized electrodes or other energy directing surfaces may result in subsequent resorption of the injured tissue lesions so as to provide further opening of the vessel after termination of treatment as part of the healing process.

[0101] To promote long term efficacy and inhibit restenosis of a treated region of blood vessel V, a restenosis inhibiting catheter 40 may be advanced through a lumen of catheter 12, so that a radiation source 42 irradiates the treated region of the blood vessel. Suitable intravascular radiation catheters are commercially available from Novoste™, Guidant, Johnson & Johnson, and the like. Restenosis inhibiting drugs similar to those now being employed on drug eluting stents may also be advanced through a lumen of catheter 12, optionally while the proximal and distal barriers again help to maintain a controlled environmental zone within the blood vessel, so that systemic drug delivery might be limited or avoided. In addition

to known restenosis inhibiting drugs used on drug eluting stents, drugs which cause vasodilation might be employed. Known restenosis inhibiting drugs such as Rapamycin™ may also be used.

[0102] In some embodiments, expandable structure 26 may remain expanded against the vessel wall W and/or atherosclerotic material AM while catheter 12 moves within the blood vessel, the catheter often being drawn proximally during or between ablation treatments. Analogous movement of a radially expanded perforate basket is employed, for example, when measuring temperatures of blood vessels so as to detect vulnerable plaque in systems now being developed and/or commercialized by Volcano Therapeutics. Alternatively, the basket may be repeatedly contracted, axial movement of the catheter 12 employed to reposition the basket, with subsequent expansion of the basket at each of a plurality of treatment locations along atherosclerotic material AM. Repeated intravascular imaging or other atherosclerotic material thickness measurements circumferentially about catheter 12 may be employed, with the remodeling and/or ablation often being halted temporarily so as to allow an image to be acquired intermittently during an ablation procedure. A final image may be taken to verify remodeling and/or ablation has been successful.

[0103] Referring now to FIGS. 8 and 9, alternative controllers 92a, 92b selectively energize electrodes of catheter 12 with RF power supplied from an RF generator 94. A wide range of RF energy types may be employed, including burst of 500 Khz, different types of waveforms, and the like. In controller 92a, a simple dial 96 is turned to point to a desired electrode pair to be energized. A “key” electrode may be registered with the intravascular imaging system, either electronically or by providing an electrode, electrode support member, or attached marker which presents a distinct image on the intravascular imaging display. This simplifies selection of one or more eccentric electrode pair along atheroma. Advantageously, catheter 12 need not be rotated into a proper orientation to accurately remodel and/or ablate the desired eccentric atherosclerotic material. Controller 92b includes similar capabilities, but allows the operator to select multiple electrodes for driving bipolar RF energy therebetween, providing greater flexibility in allowing multiple electrodes to be simultaneously energized. Monopole control arrangements similar to those of FIGS. 8 and 9 may also be employed, as can be understood with reference to FIG. 10. Patient grounding may be effected by a patient grounding plate, a ring electrode 2 to 5 cm proximal to basket 26, or the like. Once again, no catheter rotation is required to orient an active side of the catheter adjacent to the targeted atheroma since various eccentric ablation orientations can be selected through the electrode selection controller.

[0104] An alternative controller is illustrated in FIG. 11. This controller allows an operator to choose, for each electrode, whether to keep that electrode inactive, electrically couple that electrode to a first pole (sometimes referred to as pole A) of an energy source (such as an RF generator or the like), or to electrically couple that electrode to a second pole or pole B of the energy source. This controller allows a wide range of energized electrode configurations, including pseudo-monopolar modes where all electrodes except one are connected to one pole of the energy source (pole A) and one electrode is connected to the other pole (pole B). Each electrode (in this embodiment, up to eight electrodes) is electrically coupled to a 3-way switch numbered from 1 to 8. A

switch disposed in the middle position indicates the electrode is not coupled to either pole, while a switch pushed toward the plus sign indicates the associated electrode is coupled to a red RF connector with the controller. Similarly, a switch pushed toward the minus sign indicates the associated electrode is electrically coupled to a black RF connector of the control box.

[0105] An exemplary self-expandable basket is illustrated in FIGS. 12A-12H. As can be understood from these drawings, electrodes may be fabricated as part of the struts 172 from which the basket is formed, for example, using a radially outwardly oriented surface of a localized widening 174 of each strut disposed in axially central portion of the strut, as can be seen in FIGS. 12B and 12E. Each arm may be formed from one piece of material, optionally comprising a Nitinol™ nickel-titanium shaped memory alloy, with the struts optionally being laser cut from a Nitinol™ tube. The electrode/basket may be, for example, coated with a high temperature polymer such as a polyimide. Electrodes 174 may be formed by inhibiting coating or removing coating from the desired portion of the associated strut 172 (as illustrated in FIG. 12E) so that the electrode surface is exposed for contact with atherosclerotic material. At least the active electrode surfaces may be coated with a highly conductive metal such as gold, silver, an alloy of copper, or the like, and the coating will preferably maintain and withstand flexibility of the basket structure, with coating materials optionally being rolled or the like. By limiting the conductive electrode to a properly configured (often radially outwardly oriented), electrical coupling between the electrode and blood or other conductive fluids within the lumen may be limited. The struts may be separated from each other and structurally supported with an insulated material such as ultraviolet (“UV”) cure or heat shrink sleeve, a polyethylene, Nylon™, or the like to form basket 170.

[0106] Each strut 172 may be used to conduct energy between electrode surface 174 and an electrical conductor extending proximally from the strut toward a controller. Proximal pads for connecting such conductors are illustrated in FIG. 12C, while distal structural pads 178 are illustrated in FIG. 12D. Adjacent electrodes 174 may be axially offset or staggered as can be seen in FIG. 12F. Insulating coating along each strut 172 may be inhibited or removed from an inner surface of proximal pads 176 so as to facilitate connecting of an associated conductive wire, such as by spot welding or the like. Alternative polymer or non-polymer insulating materials may also be used, including parylene coatings, while alternative methods for attaching struts 172 to a catheter body may be employed, including adhesive bonding using insulating UV cure, embedding the pad structures in polyethylene, and the like.

[0107] Exemplary structures for fixing struts 172 of basket 170 to a catheter body 180 are illustrated in FIG. 12G.

[0108] Referring now to FIGS. 12F and 12H, an alternative indicia providing a distinguishable image for rotationally registering selected electrodes 174 of basket 170 to images or other atherosclerotic material measurements can be understood. In this embodiment, an electrode 174*i* referenced as electrode 1 may have a radiopaque marker 182 disposed on the associated strut 172*i*. A strut 172*ii* supporting an associated second electrode 174*ii* may have two radiopaque markers 182 provide a circumferentially asymmetric count indicator allowing all electrodes to be referenced without ambiguity. The shape of electrodes 50 may vary, for example,

electrodes 174 may be wider than other portions of struts 172 as illustrated in FIGS. 12A-G.

[0109] Remodeling will often be performed using irrigation and/or aspiration flows. In many embodiments, an irrigation port directs fluid, such as a saline solution, from an irrigation lumen to an interior of the basket. An aspiration port may provide fluid communication between an aspiration lumen and an interior of the basket. One or both of these fluid flows may be driven continuously, or may alternatively pulsate before, during, and/or after treatment. In some embodiments, aspiration and/or irrigation flow may occur acutely or concurrently so as to circulate between the irrigation port and the aspiration port. Optionally, the flow may carry ablation debris to the aspiration port, where the debris may be evacuated through the aspiration lumen. There may be coordination between the irrigation system and the aspiration system such that the irrigation fluid may remain confined in an area closely adjacent the basket so as to inhibit embolization of ablation debris when the basket is expanded within the blood vessel. Such coordination, for example, may inhibit distal movement of ablation debris, and/or may obviate any need for a distal and/or proximal barrier or membrane. In some embodiments, the circulation of fluid between an irrigation port and an aspiration port may create an effectively bloodless environment adjacent the electrodes to facilitate remodeling and/or ablation, imaging of atherosclerotic tissue, and the like.

[0110] Referring now to FIG. 13, controllers of the catheter systems described herein may allow distribution of differing power levels to differing pairs of electrodes. For example, in response to a circumferential distribution of atherosclerotic material AM such as that illustrated in FIG. 13, a controller may direct 50 watts of energy to a first electrode 230, 30 watts of energy to a pair of second electrodes 232 and only 10 watts of energy to a pair of third electrodes 234. Other electrodes may have no energy directed thereto, as described above. In some embodiments, a differing power directed to the differing electrodes may be provided by controlling the duty cycle, for example, with 50 watts being provided by energizing one or more electrode for 50% of the time, 30 watts being provided by energizing an electrode 30% of the time, and the like.

[0111] Many imaging modalities (including intravascular ultrasound, optical coherence tomography, intravascular MRI, and the like) may be at least in part blocked or degraded by positioning the image detecting structure within a metallic structure such as a basket formed of Nitinol™. Hence, there may be advantages in producing alternative expandable structures such as baskets comprising plastics or a polymer. In light of the heat generated by the electrodes of the systems described herein, it may be advantageous for such polymer basket structures to comprise a high temperature polymer such as a polyimide. Alternative basket structures may comprise HDPE, PET, Nylon™, PEBAX™, and the like. The basket may be formed by cutting struts from a tube of the polymer material.

[0112] Exemplary treatment methods are illustrated in FIGS. 14A-14H. In FIG. 14A, the catheter system 260 includes a basket covering sheath 262 over an atherosclerotic material detecting and treating catheter 264 as described above. In this embodiment, outer basket sheath 262 radially restrains the basket 266, which is biased to expand radially when released from the outer sheath, as illustrated in FIG. 14B. In some embodiments, the basket may be expanded after the outer sleeve is retracted, such as by pulling pullwires, rotating one portion of the catheter relative to the other, or the

like. Regardless, as the basket expands within the vessel V, electrodes 50 of the basket engage the surrounding vessel wall. An imaging transducer near basket 266 of an imaging catheter disposed in a lumen of the treatment catheter evaluates the vessel V, and the detection/treatment catheter system 264 is pulled proximally along the artery or vessel V.

[0113] When the imaging catheter detects atherosclerotic material AM as illustrated in FIG. 14C, an appropriate subset (possibly including only a single electrode 50) is activated to remodel the atherosclerotic material AM, as illustrated in FIG. 14D, and the open vessel lumen size increases moderately during treatment. The catheter is pulled proximally to the next atheroma, which is again detected and treated. A cross section of the limited open lumen prior to treatment is schematically illustrated in FIG. 14F, which also illustrates a saline flush or irrigation lumen 268 of the catheter 264. Treatment energy and the moderate increase in the open lumen diameter of the vessel V are schematically illustrated in the cross section of FIG. 14G. After a healing response gradually increases the open lumen diameter, the longer term open lumen results schematically illustrated in FIG. 14H may then be provided.

[0114] Referring now to FIGS. 15A and B, eccentric material removal in a gelatin artery model 270 are presented. Prior to the test, the artery model includes a consistent lumen 272 as seen in FIG. 15A. A test eccentric treatment catheter 274 having an expandable basket supporting a circumferential array of electrodes is introduced into lumen 272, with the expandable basket supporting the electrodes in engagement with the luminal wall. Selected electrodes of test catheter 274 were energized so as to eccentrically treat the gelatin artery model 274, thereby effecting eccentric remodeling of the gelatin model, in this case by removing an eccentric volume 276 from along one side of lumen 272. The orientation and amount of the material removed was controlled by selectively energizing electrodes of test catheter 274.

[0115] Referring now to FIG. 16, an exemplary catheter system 280 is illustrated. In this embodiment, catheter body 282 includes only a single lumen, which is large enough to accommodate an imaging catheter therein and also to be used as an irrigation lumen to bring irrigation fluid to irrigation ports 284. The lumen may decrease in diameter distally of irrigation ports 284, with the decreased diameter portion 286 fittingly receiving the imaging catheter within the lumen thereof so as to direct the irrigation fluid radially outward through the plurality of irrigation ports. This embodiment may be particularly useful when remodeling atherosclerotic materials using the methods illustrated in FIGS. 14A-14H, in which mild heating improves vessel size, optionally without requiring aspiration.

[0116] Catheter body 282 may include a braided shaft in which conductive wires (for example copper wires or beryllium-copper wires) are coated with a high temperature and/or high strength insulation material such as a layer of polyimide or the like. The braided wires may be sandwiched between layers of materials forming the shaft of catheter body 282. The shaft may, for example, comprise a plurality of layers of polyethylene, an inner Teflon™ PTFE layer, an outer nylon layer, and the like.

[0117] The wires of shaft 282 may be braided so as to inhibit capacitive losses between wires when electrical currents run through them. Capacitive losses may be decreased when a wire that carries a current from an energy source to an electrode of the catheter system and a wire that carries a

current from an electrode back to the energy source are not parallel, but at an angle, ideally being perpendicular. This may be achieved by braiding the wires with appropriate pitch or a number of peaks per inch. The basket structure 170 of catheter system 280 may be included, with the basket structure being described in more detail with reference to FIGS. 12A-12H. Guide 286 may extend through basket 170 and may comprise a material transparent to the imaging catheter, optionally comprising HDPE, PET, or the like.

[0118] Still further alternatives are available. For example, another way to employ RF energy to remodel atherosclerotic material may be to energize a plurality of the adjacent electrodes with differing RF signals so as to employ the adjacent electrodes as a phase-array. A phase array can direct or steer an electromagnetic signal in a desired direction using constructive and destructive interferences between signals of adjacent elements of the array. By controlling phases of the adjacent signals, a phase array of electrodes may provide a focused and/or steerable RF signal.

[0119] Along with controlling steering and directionality, adjusting phases of adjacent RF electrodes may allow focusing of some or most of the RF energy at a desired depth D inside the atherosclerotic material while inhibiting RF energy delivery between the electrode surfaces and depth D using constructive and destructive interference between the signals. For example, such a system may be employed to preserve the cap of a plaque so as to reduce restenosis. Inhibiting heating of the cap while focusing energy toward an internal portion of the plaque may lower an immune response to heat that could otherwise lead to restenosis. Hence, inhibiting heating of the cap may reduce restenosis.

[0120] In general, the present invention may make use of highly elastic, expandable structures, particularly of expandable structures formed from structural members separated by perforations so as to define a basket. Such structures can conform to an artery diameter before, during, and/or after atherosclerotic material removal. This expandability allows for direct contact of the electrodes against atheroma, although the systems of the present invention may also make use of conductive fluid environments to complete an RF energy path, or conversely, use non-conductive fluid to enhance energy directed through tissue. Multiple electrodes can be distributed circumferentially around an intermediate portion of the expandable structure, and a subset of these electrodes can be activated to allow for eccentric tissue remodeling and/or ablation.

[0121] Atheroma may be identified and targeted by intravascular imaging, and these capabilities may be integrated into the remodeling and/or ablation catheter. Preferably, the intravascular imaging capabilities will be deployed in a separate catheter which can be advanced within, and removed from the ablation catheter. In general, this intravascular imaging capability allows the progress of the therapy to be monitored so that wall perforation can be avoided, while ideally reducing occlusion to no more than 15% of the overall native vessel diameter (either upon completion of the treatment or after subsequent tissue healing). The ablation catheter may further allow the use of localized radiation or drug delivery for antirestenosis treatments. The ablation catheter may include a relatively large lumen allowing selective use of an intravascular imaging system, a radiation delivery or other treatment catheter, an aspiration of debris and vaporization gases, with these uses often being employed sequentially. A

guidewire may make use of this or a separate lumen, and the guidewire may be removed to allow access for the restenosis and/or imaging catheters.

[0122] The devices, systems, and methods described above are well suited for application of electrical energy that is tailored to target tissues and materials along a body lumen.

[0123] The exemplary catheter devices and methods for their use described herein are intended for application in the lumen of vessels of the human anatomy. The anatomical structure into which the catheter is placed may be, for example, the esophagus, the oral cavity, the nasopharyngeal cavity, the auditory tube and tympanic cavity, the sinus of the brain, the arterial system, the venous system, the heart, the larynx, the trachea, the bronchus, the stomach, the duodenum, the ileum, the colon, the rectum, the bladder, the ureter, the ejaculatory duct, the vas deferens, the urethra, the uterine cavity, the vaginal canal, and the cervical canal.

[0124] As can be understood with reference to FIG. 17A-17C, physical targeting of eccentric disease can be accomplished by positioning of electrodes by moving longitudinally in vessel until positioned in the vicinity of targeted tissue. As schematically illustrated in FIG. 17A, axial movement of a distal end of probe in the form of a catheter 302 within a body lumen 304 allows different axial portions of the lumen wall to be targeted for analysis and treatment. An additional method to physically target eccentric disease in a radial manner is to apply bipolar energy selectively to specific electrodes 306 so as to direct energy through the targeted tissue, as can be understood with reference to FIG. 17B. In some embodiments, radial and longitudinal physical targeting may be effected by selective activation of electrodes distributed both radially and longitudinally on an expandable body 310, as illustrated in FIG. 17C

[0125] Frequency targeting of tissues is illustrated in FIGS. 18 and 19. As graphically illustrated in FIG. 18, different tissue types have different characteristic electrical impedances that cause the tissue to absorb energy of certain frequencies or frequency ranges more readily than others. By applying energy at the specific frequency or range of frequencies that the tissue is more conductive, energy penetrates the tissue more readily. In general, it has been shown that samples of diseased tissue exhibit higher impedance characteristics than samples of healthy tissue. As illustrated in FIG. 19, in the case where a diseased area of tissue 312 is surrounded by relatively healthy tissue 314, the healthy tissue is likely to shield the diseased tissue from electrical current flow due to the lower impedance of the healthy tissue. Hence, minimal (or less than the desired) current flow 318 may pass through diseased tissue 312, and heavier current flow 320 may be seen in low impedance healthy tissue 314 when bipolar current is transmitted between electrodes 316. Typically, the frequency ranges in which tissue impedance varies to a useful degree occur between 100 kilohertz and 10 Megahertz.

[0126] Frequency targeting seeks to deliver more energy to the diseased tissue by determining the frequency or range of frequencies at which the impedance of the diseased tissue is equal to or less than that of the healthy tissue, such as by operation at or above a threshold frequency 322 as illustrated in FIG. 18. Energy delivered at the specified frequency or range of frequencies will cause more heat to be dissipated in the diseased tissue than energy delivered outside of those specific frequencies.

[0127] The use of impedance measurements to determine a location and/or state of tissue may be generally understood

with reference to FIG. 20. First, impedance measurements utilizing an array of radially spaced electrodes 330 within lumen 332 can be used to analyze diseased tissue 334. Impedance measurements between the five electrodes of the array, and particularly impedance measurements between pairs of adjacent electrodes (and/or between pairs of separated electrodes), may differ when the current path passes through diseased tissue 334, and when it passes through healthy tissues of the luminal wall. Hence, impedance measurements between the electrodes on either side of diseased tissue 334 may indicate a lesion, while measurements between other pairs of adjacent electrodes indicate healthy tissue. The impedance characterizes the molecular state of a tissue. The state of a tissue can be affected/changed by temperature: for instance, lipids start denaturing at 85 C and turn into a new state, fatty acids, which may be 90% more compact in volume than the original lipids

[0128] If one knows the temperatures of state change for a tissue, and the impedance of the different states of the tissue, then by measuring the tissue impedance, it is possible to detect a state change, and or to estimate what the temperature is, thereby allowing one to monitor the progress of the therapy. E.g.: if impedance of lipids were 100 Ohms, and impedance of fatty acids were 90 Ohms (here using hypothetical values), and knowing that lipids turn into fatty acids at around 85 C, then detecting a change in impedance from 100 Ohms to 90 Ohms indicates that the lipids turned into fatty acids and therefore that the temperature should be around 85 C. Analysis of diseased luminal tissues may use specific frequencies to verify a type and condition of tissue based on electrical impedance measurement. Normal use will include the discovery and characterization of diseased tissue using intraluminal ultrasound or other methods. Measurement of tissue electrical impedances over radially spaced electrodes will allow for verification of the existence of diseased tissue and knowledge of the location of the electrodes relative to specific tissue.

[0129] Multiple Frequency Therapies and signals are schematically illustrated in FIG. 21. Therapy can consist of the application of electrical energy at a single frequency or at multiple frequencies. Depending on the composition of the target tissue and surrounding tissue, the optimum treatment may consist of a single frequency to target a single tissue type, multiple frequencies to target multiple tissue types, or multiple frequencies applied to a single tissue type. Multiple bursts of the same frequency 336, varying frequencies, such as a continuous burst of varying frequency 338, bursts of multiple frequencies 340, and multiple frequencies superimposed (optionally in bursts 342) may be employed.

[0130] Multiple frequencies can be applied in any sequence from any combination of electrodes in contact with the target tissue or surrounding tissue. Multiple frequencies can be applied as discrete frequencies or can be applied as a frequency sweep across a range in a linear, logarithmic, or other manner.

[0131] An energy Control arrangement is schematically illustrated in FIG. 22. In general, impedance and physical tissue characteristics may be utilized to set the output or treatment parameters. Geometry and tissue type may be determined as described herein using IVUS or other similar detector techniques. Electrode impedance measurements from multiple electrodes may be taken. An algorithm of the system processor may choose a correct initial dosage, and initial settings and/or range output.

[0132] Regarding setting up the correct initial dosage, the shape and type of diseased tissue to be treated is generally diagnosed and characterized by ultrasonic, optical, or other types of intraluminal sensing devices. Using the multi-electrode approach, electrical impedance measurements can be used to understand the electrical characteristics of atherosclerotic tissue of varying geometries and types previously diagnosed. Using that data, the initial therapy dosage setting can be optimized.

[0133] Regarding controlling the dosage, the electrical impedance characteristics of tissues vary due to temperature variations and the molecular state of a tissue. Dynamic measurement of electrical impedance of the tissue during application of energy can be used to monitor the changes in the tissue and the progress of the therapy. A four electrode implementation of the electrode system would allow for measurement of the electrical impedance of the electrode to tissue interface and therefore, measurement of the change in temperature of the tissue at the contact surface and that of the contact tissue.

[0134] Regarding determination of proper dosage during therapy, the pattern of energy delivery can be a single pulse or multiple pulses of varying duration separated by resting periods of varying duration. The measurement of electrical impedance of the tissue and of the electrode to tissue interface during energy delivery and between energy pulses can be used to determine the optimum durations of energy delivery and resting periods. Pre-treatment bursts of RF energy can be applied to condition the target tissue. Conditioning may be utilized to activate Heat-Shock Proteins (HSPs) in healthy tissue prior to treatment to get better protection of healthy tissue. Post-treatment bursts of RF energy can be applied to control the cool down time of the tissue. Interim treatment bursts of RF energy can be applied to control the temperature of the target and surrounding tissue between multiple therapy bursts. Energy can be delivered in any combination of amplitude and frequency from any combination of electrodes.

[0135] Impedance measurement on multiple electrodes can also be employed. When a multi electrode design is used it is likely that some of the electrodes will be in contact with the lumen wall and others will be suspended in the blood or other existing fluid or thrombus, or existing stents, or foreign materials of the like. The measurement of impedance at various radial locations allows the determination of which electrodes are in contact with the lumen wall and which ones are in contact with fluid such as blood. This contact determination can be used in combination with an intraluminal viewing device such as ultrasound to determine the physical orientation of electrodes.

[0136] Utilizing the impedance measurements between multiple electrodes, the determination of the contact status of each electrode with tissue or blood can be utilized to determine if the electrode carrying mechanism (catheter) is in the proper location for therapy. Impedance measurements between multiple electrodes can be used to determine contact quality of electrodes to tissue. Poor contact quality can cause excessive or unwanted localized heating or can otherwise prevent optimum treatment. Determination of contact quality can be utilized to minimize this type of problem.

[0137] In some situations the choice of electrode may be determined by a combination of position and quality of contact. Impedance measurements between multiple electrodes

can be utilized to better understand which electrodes are in better contact or a better position to treat a specific area or lesion.

[0138] In some situations the determination of energy level and frequency to be applied to the target can be based on quality of contact. Impedance measurements between multiple electrodes can be utilized to determine the optimum energy level and frequency.

[0139] In some situations energy may be applied to a single pair of electrodes, between multiple pairs of electrodes, or from a single electrode to multiple electrodes, or any combination thereof. Impedance measurements between multiple electrodes can be utilized to determine the optimum pattern.

[0140] Different embodiments may employ impedance measurement using two vs four electrodes, as can be understood with reference to FIG. 23. Four electrode systems have been used for the measurement of electrical impedance in many applications. Four electrode systems are inherently more accurate than two electrode systems due to inaccuracies created in the two electrode systems by excessive contact impedance and electrical polarization reactions created in the contact area. In the four electrode system 344 energy is delivered to the target by two energy delivery electrodes 346 and an impedance measurement is taken between the other two high impedance electrodes 348 shown schematically in contact with the tissue 350 in the energy path. In this multiple electrode application any two electrodes can be utilized to deliver energy while any other two electrodes can be utilized for impedance measurement, thus forming a four electrode measurement system. A probe or catheter 352 may include a circumferential and/or longitudinally distributed array of electrodes may be used to contact the tissue, and any four electrodes of the catheter can be configured for energy delivery or impedance measurement. Thus, the electrode array can be utilized as a two or four electrode system.

[0141] In many applications it is helpful to know how much energy is being delivered to the target tissue and how much is being dissipated in the interface between the electrodes and tissue. By taking measurements as a two electrode system and then as a four electrode system the electrode to tissue interface can be characterized and that data can be utilized to determine how much energy is being dissipated in the electrode to tissue interface and how much is actually delivered to the target tissue.

[0142] Measurement of the electrical impedance in two or four electrode configurations can be performed statically utilizing small excitation signals or can be measured dynamically during the application of energy at the normal therapy levels. Using this technique, tissue electrical impedance can be measured dynamically during the application of energy to determine the state of the treated tissue and surrounding tissue.

[0143] Impedance measurement may optionally be performed in mono-polar configuration. It is possible to utilize multiple electrode systems in a mono-polar configuration where the return electrode is an electrically conductive pad applied to the external surface of the patient or the like. In this configuration impedance measurements can be performed between any one of the internally applied electrodes and the external return pad in the two electrode mode or any one of the internally applied electrodes can apply energy that flows to the external return pad while any other two internally applied electrodes is used to measure impedance.

[0144] Regarding temperature measurements, impedance measurements taken prior to therapy can be utilized to calculate a normalized value to be used in further calculations to determine the change in temperature from that initial value. Dynamic monitoring of the electrical impedance of target and surrounding tissue during therapy can be utilized to calculate the change in temperature of tissue. In some embodiments, dynamic monitoring of the electrical impedance of interface between electrodes and tissue can be utilized to prevent tissue charring or coagulation of blood at the interface.

[0145] Temperature change during therapy can be utilized to determine the effectiveness of energy delivery settings and to determine the condition of the tissue being treated.

[0146] Temperature measurement can be performed by intraluminal ultrasound or other mechanism and verified by data derived from impedance measurements.

[0147] Use of the systems described herein with ionic and non-ionic fluid can be understood with reference to FIG. 24. When electrical current flows in an ionic fluid such as blood filling a lumen 356, at least a portion of the current may pass through the blood when electrodes 358 are energized. Even when electrodes on either side of a target tissue 360, heating of the target tissue may be reduced by the current flow within the blood.

[0148] When used in a fluid filled lumen such as an artery, this device can be used in combination with a non-ionic fluid flooding the area 362 to displace or partially displace the native fluid to modify the conductivity of the environment around the electrodes. This action can be desirable in order to direct the energy, in form of electrical current 364, into lumen walls instead of through the native fluid, thereby delivering energy to the tissue of the surrounding walls with minimal dissipation into the fluid filling the lumen.

[0149] A second purpose of the non-ionic fluid or an ionic fluid may be to provide cooling to the electrodes and to the tissue on the surface and just below the surface of the lumen wall.

[0150] Electrical impedance measurements at the electrodes can be utilized to determine the conductivity of the surrounding fluid, thus measuring the concentration of non-ionic fluid in the native fluid. This data can be fed to the control system to allow for adjustment of ionic fluid concentration to optimize delivery of energy to the target tissue and minimize undesired effects to surrounding tissue.

[0151] Use of blood as contact interface is also an option. Blood is a conductive ionic fluid that may be used as an interface between electrodes and tissue to ensure a good electrode-tissue contact and low contact impedance.

[0152] Closed loop control can be understood with reference to FIG. 25. Impedance measurements over frequency ranges and across multiple electrodes can be utilized to verify electrode location relative to tissue landmarks, optionally by correlation to companion intraluminal measurement devices such as IVUS prior to and during therapy.

[0153] Impedance measurements using a closed loop treatment controller 366 making use of hardware and/or software of the system processor may facilitate treatment control. Such control over frequency ranges and across multiple electrodes can be utilized to monitor and to verify physical changes such as tissue shrinkage or denaturing of tissue in the application area. This data can be utilized to verify physical changes observed by other intraluminal observation techniques such as ultrasound.

[0154] Data from impedance measurements 368 combined with inputs from intraluminal measurement devices 370 such as ultrasound can be used to determine electrode selection from a predetermined set of rules of a controller or processor module 372. This type of control system could potentially be utilized in an automatic mode to diagnose and treat diseased intraluminal tissue.

[0155] Data about the condition of the tissue, optionally including temperature change, electrode to tissue interface impedance, tissue impedance, electrode to tissue or blood contact, and intraluminal geometry and tissue type from ultrasound or other sources, can be utilized by a controller as inputs to a closed loop control system 366.

[0156] Implementation of electrode switching may employ any of a wide variety of selective energizing electrode circuits, switch types, and switch locations, and the like, some of which are schematically illustrated in FIGS. 26A-26C.

[0157] Electrode switches can be located in an external instrument or external control box 374, so that one external connector point 376 is provided for each electrode of catheter of catheter 378, with one wire per electrode 380 extending to, in and/or along the body of the catheter. Alternatively, electrode switch mechanisms 386, 388 may be embedded in a catheter 382, 384, respectively, either near the proximal end of the catheter for external switching or near the distal end of the catheter for internal switching. A limited number (e.g., 4) wires 390 may run proximally of the switching mechanism, while one wire per electrode may extend distally of the switching mechanism. Connection of discrete electrodes to RF generator or impedance measuring device can be accomplished by either electromechanical or solid state means.

[0158] Switching mechanisms disposed at distal end of catheter may have advantages. If located on the catheter, the switching mechanism can be located at the distal end to decrease the number of wires in the body of the catheter or at the proximal end. In embodiments of switching mechanism located at distal end of catheter the external control circuit optionally communicates with the switching mechanism via the same wires used for impedance measurements.

[0159] Switching mechanism at proximal end or other location on catheter may also be employed. The switching mechanism can be located at proximal end or any other location on the catheter if it provides advantage in performance or cost.

[0160] Referring now to FIG. 27, the catheter devices 418, systems and methods described herein will often be used to treat plaques having fibrous tissue 420. Fibrous tissue 420 may be heated to a target tissue to a temperature in a range from about 90 to about 95 C, which may provide shrinkage of up to about 50%. Lipids 424 may be heated to target temperatures in a range from about 80-85 C, providing up to about 90% shrinkage. Damage to adventitial layer 426 may be inhibited or the layer protected by limiting heating to below about 62 C. These and other temperatures and shrinkage estimates can be determined by appropriate empirical testing or the like, from unpublished and/or published work, or from other sources. Referring to FIGS. 27A-27C, spectral correlations to diseased tissue may allow tissue characterization using techniques such as those described in an article by Tjeerd J. Romer et al. entitled "Histopathology of Human Coronary Atherosclerosis by Quantifying Its Chemical Composition with Raman Spectroscopy," *Circulation* 97:878-885 (1998).

[0161] Referring now to FIGS. 28A-28D, feasibility of tissue shrinkage may be seen in a bench top experiment using a

catheter system such as those described herein. An animal fat tissue model **430** (shown before the treatment in FIG. **28A**) can be treated by manually holding the expandable structure and associated electrodes of the catheter in contact with a surface of the tissue during treatment with tissue remodeling electrosurgical energy (see FIG. **28B**). After treatment, as seen in FIG. **28C** and the close up of FIG. **28D**, visible shrinkage of the tissue can be verified. Feasibility of the use of intravascular imaging with the methods and systems described herein can be verified by images of the six individual electrode-supporting struts **428** of the expandable structure of the catheter in FIG. **29A**, as well as by viewing an eccentric void **430** that is created using a benign guided reshaping energy delivery targeted so as to increase effective artery diameter for better blood flow, as seen in FIG. **29B**.

[0162] Referring now to FIG. **30**, advantageous embodiments may employ aspects of electrical tissue discrimination techniques and devices described in U.S. Pat. No. 6,760,616 to Hoey et al., entitled "Tissue Discrimination and Applications in Medical Procedures," the full disclosure of which is incorporated herein by reference. As more fully described in that reference, tissue identification system **510** includes a user readable output device **512**, a user input device **516**, a processor **520**, and a probe **522**. The processor **520** includes a central processing unit ("CPU") **514**, a Digital to Analog converter ("D/A"), and an Analog to Digital converter ("A/D") **518**. Processor **520** may be included in processor **49** (see FIGS. **2** and **3**), and probe **522** may comprise any of the catheter structures described herein, so that tissue identification system **510** may be embodied in system **10**.

[0163] Referring now to FIGS. **30** and **31A**, tissue identification system **510** may apply a sliding or variable frequency electrical signal by energizing the electrode with a variable frequency power source **524**. Power source **524**, the electrode of probe **522**, and the engaged tissue of patient P can thus generally be included in a circuit, and an electrical characteristic of the circuit can be measured at different frequencies. In exemplary embodiments, an impedance (both phase angle and magnitude) of the circuit are measured at a plurality of frequencies within a frequency range of about 4 KHz to about 2 MHz. Each frequency/magnitude/phase angle datapoint may represent a tissue signature measurement, with a series of individual datapoints often being taken under similar conditions (for example, at a given frequency and without moving the electrodes) and averaged for enhanced accuracy. The tissue signature datapoints may be measure at a plurality of frequencies throughout a range of frequencies so as to generate frequency/phase angle/phase magnitude curves representing a tissue signature profile or correlation **530**, **532**, or **534**, which may be used to characterize the tissue of the circuit.

[0164] The signals used to derive the tissue signature profiles **530**, **532**, **543** will often be driven between electrodes of the catheters described herein. Conveniently, the tissue included in the circuit may be controlled by selecting different electrode pairs for testing, with or without repositioning of the electrodes. There may be significant patient-to-patient differences (or even region to region differences within a patient) for individual tissue signature measurements, and these differences may, at least in part, be caused by the different configurations of the electrodes during testing, different distances between electrodes, and the like. Nonetheless, the relationships (and particularly the relative slopes of the profile correlations, the offsets between correlations, and the

like will be sufficiently consistent to allow tissue characterization, particularly where a baseline tissue signature profile for the patient or tissue region is obtained using IVUS, OCT, or the like. Where a region of (for example) healthy tissue can be identified using IVUS and used to generate a baseline tissue signature profile for the patient, other nearby tissue signature measurements or profiles can then be normalized to that baseline, compared to the baseline, and/or the like. From the offsets, the differences in slope, and the like, the tissue can be analyzed.

[0165] Referring now to FIGS. **31A-31J**, the relationships between tissue signature profile curves or correlations can be used to analyze and characterize the tissues engaged by the electrodes of the probe. For example, a correlation **530** associated with fibrous plaque (seen on the left side of the graph of FIG. **31A**) has both a slope and a magnitude that differs significantly from that of a calcified plaque **534** (seen in the right side of the plotted data) and from a correlation **532** associated with thrombus (generally between **530** and **534**). The offsets between the correlations here encompasses a difference in phase for a given impedance, a difference in impedance for a given phase, or the like. As can be understood with reference to the graphical plots, the relationships between correlations may be determined by fitting curves to the data, by statistical analysis, by lookup tables, or the like. In exemplary embodiments, tissue signature measurements may be taken by (for example) a commercially available vector impedance meter such as a Hewlett-Packard Model No. 4193A, and the correlations may be captured using Lab-View™ Software and plotted or manipulated using Excel™ spreadsheet software from Microsoft, or the like. Once sufficient benchmarked data has been obtained and repeatability under different probe configurations has been established, electrical circuit measurements tissue characterization without benchmarking of each patient may avoid the expense of IVUS measurements.

[0166] Referring now to FIG. **31B**, along with characterizing different tissues, the relationships can also be used as feedback on treatments of luminal walls. A fibrous plaque correlation or profile before treatment (toward the right side of the plot) changes in magnitude during treatment to a post-treatment correlation or profile (toward the left side). The treatment here comprised 2 W of electrosurgical energy for 2 seconds, showing that moderate remodeling or partial treatments can be monitored, verified, and/or controlled using the electrical characteristics of the circuit of tissue identification system **510**. Advantageously, once an appropriate frequency or range of frequencies has been determined, the entire tissue signature profile need not be generated for analysis of ongoing tissue treatments and/or characterization of tissues, as offsets can be readily identified. Such measurements may, for example, allow tissue temperatures to be determined, particularly where the temperature is a treatment temperature that alters an offset of the tissue signatures. The energy of the electrical signals used for tissue analysis will typically be less than the remodeling treatments. A similar plot is shown in FIGS. **31C** and **31D**, with the post-treatment correlation here being after treatment with 2 W for 9 seconds and 1 W for 9 seconds, respectively.

[0167] Referring now to FIG. **31E**, relationships between healthy tissue (toward the right) and fibrous plaques (toward the left) can be identified from their associated tissue signature profiles or correlations, which differ significantly in both slope and magnitude. FIG. **31F** shows relationships between

correlations or profiles for fibrous tissue before treatment (left), fibrous tissue after treatment (right), and healthy tissue (center). FIGS. 31G-31J illustrate additional plots of relationships between profiles or correlations associated with fibrous tissues and treated fibrous tissues.

[0168] Referring to FIG. 32 a severely diseased blood vessel with three basic categories of plaque can be seen: lipid rich (fatty) plaque, fibrous plaque, and calcified plaque or tissue. All may be present in one sample, and may also be present in the diseased tissue of (or adjacent to) one lesion, making the lesion hard to treat using conventional techniques. Through the tissue analysis techniques described herein, the correct prescription and dosage of energy can be targeted and delivered to effect a safe and appropriate (and often different) remodeling of the different tissue categories or types, at the appropriate locations of the constituent parts that make up each lesion.

[0169] Referring now to FIG. 32A, this graph shows tissue signature measurements and tissue signature profile results obtained from a human aorta specimen, with these results for an engaged fibrous plaque before and after treatment. FIGS. 32B and 32C show histopathology slides of the tissue. The cracks visible on each slide may be artifacts of the mounting process. The nucleation or voids that show up in FIG. 32C, however, may indicate a remodeling of the tissue itself.

[0170] While the exemplary embodiments have been described in some detail, by way of example and for clarity of understanding, those of skill in the art will recognize that a variety of modification, adaptations, and changes may be employed. Hence, the scope of the present invention should be limited solely by the appending claims.

What is claimed is:

1. A catheter system for remodeling a tissue adjacent a blood vessel, the system comprising:

a catheter including an elongate flexible catheter body having a proximal end and a distal end with an axis therebetween, a radially expandable support structure disposed near the distal end of the catheter body, and a plurality of electrodes disposed on the radially expandable support structure for engaging a luminal wall of the blood vessel;

a power source coupled to the electrodes such that, when the one or more electrodes engage the luminal wall and energized by the power source, the power source, the electrode, and engaged luminal wall defines an electrical circuit;

a processor coupled with the power source, the processor configured to control delivery of remodeling energy from the power source to the target tissue adjacent the blood vessel while inhibiting collateral tissue damage by monitoring and controlling a temperature of the electrical circuit.

2. The system of claim 1, wherein the plurality of electrodes are distributed circumferentially about the support structure to define an electrode array.

3. The system of claim 2, wherein the processor is configured to remodel the tissue with the electrode array by energizing a subset of the electrodes with the remodeling energy.

4. The system of claim 2, wherein the electrodes are axially offset on the radially expandable support structure.

5. The system of claim 2, wherein the electrode array comprises a plurality of bipolar electrode pairs.

6. The system of claim 2, wherein the power source comprises a variable frequency power source, and wherein the

processor is configured to regulate the remodeling energy in response to a measurement of impedance phase angle.

7. The system of claim 6, wherein the processor, in response to feedback signals generated by monitoring the phase angle, alters the delivery of the remodeling energy to the target tissue.

8. The system of claim 7, wherein the processor is configured to respond to feedback on the target tissue by monitoring a characteristic of the electrical circuit after applying at least a portion of the therapeutic energy.

9. The system of claim 8, wherein the processor is configured to halt the remodeling energy in response to a change in at least one of temperature, frequency range, impedance magnitude, impedance phase angle of the circuit, the change associated with heating of tissue to 62° C. or more.

10. The system of claim 9, wherein the variable frequency power source generates bipolar RF energy, and wherein a frequency range of the variable frequency power source extends from below about 50 KHz to over 1 MHz.

11. The system of claim 6, wherein the processor is further configured to determine a specific frequency or range of frequencies at which the target tissue is more conductive by monitoring the temperature and/or frequency-dependent characteristic of the electrical circuit.

12. The system of claim 11, wherein the processor is configured to selectively heat the target tissue adjacent the body lumen while inhibiting injury to collateral tissue by applying energy in a range of frequencies for which the target tissue is more conductive.

13. The system of claim 1, wherein the processor is configured to control energy delivery as a closed loop control system, wherein inputs to the closed loop control system include tissue impedance and/or temperature change.

14. The system of claim 1, wherein the processor is configured so that dosage of energy delivery is controlled using dynamic measurement of change in temperature of tissue contacting the catheter.

15. The system of claim 1, wherein the processor is configured to asymmetrically deliver energy of differing power levels to differing bipolar pairs of the electrodes.

16. The system of claim 1, wherein the processor is configured to deliver pulsed energy.

17. The system of claim 1, wherein the processor is configured to control delivery of energy so as to provide tissue temperatures in a range between 55° C. and about 80° C.

18. The system of claim 1, wherein the processor is configured so that energy delivery includes multiple bursts of the same frequency.

19. The system of claim 1, wherein the processor is configured to control delivery of energy by energizing differing electrodes according to a duty cycle.

20. A system for remodeling a tissue material adjacent a body lumen, the system comprising:

an elongate flexible catheter body having a proximal end and a distal end with an axis therebetween;

a radially expandable member disposed near the distal end and supporting a plurality of electrodes distributed circumferentially about the axis to define an electrode array for engaging the lumen wall; and

a power source electrically coupled to the plurality of electrodes and configured to energize the electrodes with a remodeling energy that heats the tissue material and inhibits damage of collateral tissues.

21. A method for remodeling of a tissue adjacent a body lumen, the method comprising:

engaging a vessel wall of a blood vessel with a radially expandable array of electrodes supported by an expandable member near a distal end of a catheter, the electrodes being circumferentially distributed and axially offset;

energizing the engaged electrodes with a power source so as to define an electrical circuit with the power source, the electrodes and the engaged vessel wall; and

remodeling the tissue by delivering a controlled remodeling energy to the tissue with the electrodes so as to heat the tissue with the remodeling energy while inhibiting damage to collateral tissues.

22. The method of claim **21** wherein delivering remodeling energy with the electrodes comprises energizing selected electrodes of the array with bipolar RF energy.

23. The method of claim **21** wherein the remodeling energy is controlled by monitoring and controlling a characteristic of the electrical circuit.

24. The method of claim **23** wherein the characteristic comprises a temperature of the electrical circuit.

25. The method of claim **23** wherein the characteristic comprises a load impedance.

26. The method of claim **21** wherein delivery of remodeling energy is controlled so as to provide tissue temperatures in a range between 55° C. and about 80° C.

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