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Long

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(54) **ELECTROPORATION ABLATION
APPARATUS, SYSTEM, AND METHOD**

4,491,132 A 1/1985 Aikins

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(Continued)

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(58) **Field of Classification Search** 600/101,
600/104, 153, 160, 106, 137; 606/32-50;
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(57) **ABSTRACT**

See application file for complete search history.

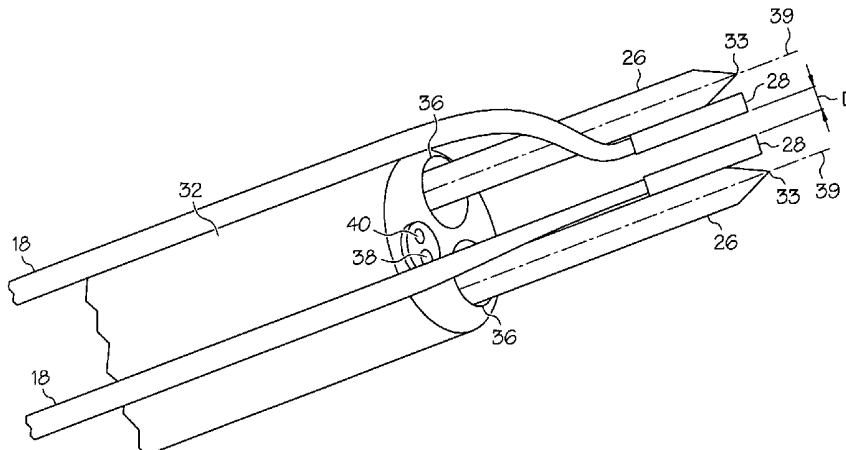
A surgical instrument, such as an endoscopic or laparoscopic instrument, includes an ablation device. The ablation device includes an elongate flexible member having a proximal end and a distal end. A first working channel is formed within the flexible member. A first diagnostic probe having a proximal end and distal end is located within the first working channel and extends through the distal end of the flexible member. A first electrode is connected to the distal end of the first diagnostic probe electrode is adapted to be endoscopically located in a tissue treatment region. The first electrode is adapted to couple to an electrical waveform generator to receive an irreversible electroporation electrical waveform sufficient to ablate tissue located proximate to the first electrode. A system further includes an electrical waveform generator electrically coupled to the first electrode of the ablation device to generate an IRE waveform sufficient to ablate tissue located proximate to the first electrode.

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12 Claims, 12 Drawing Sheets



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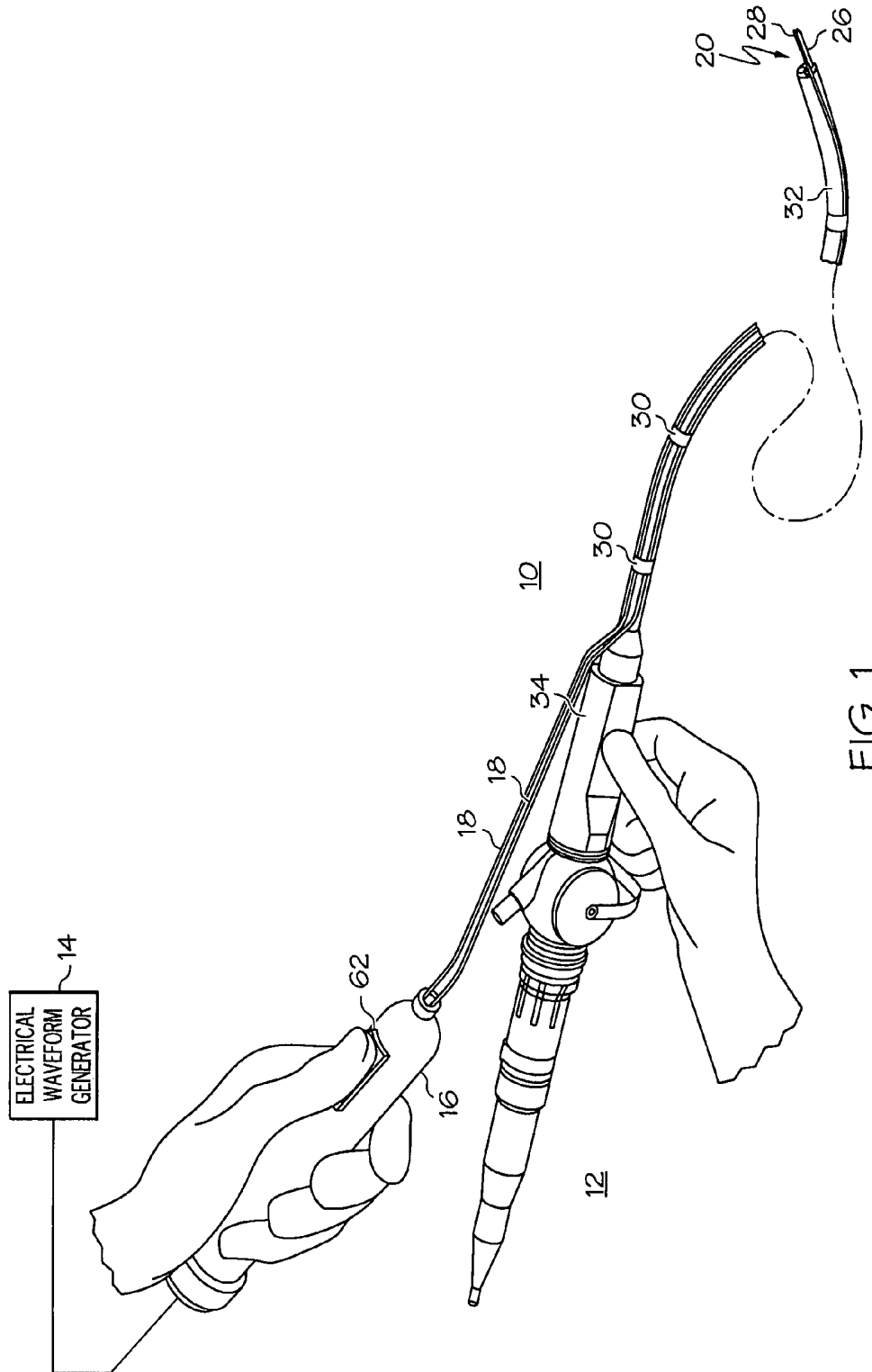
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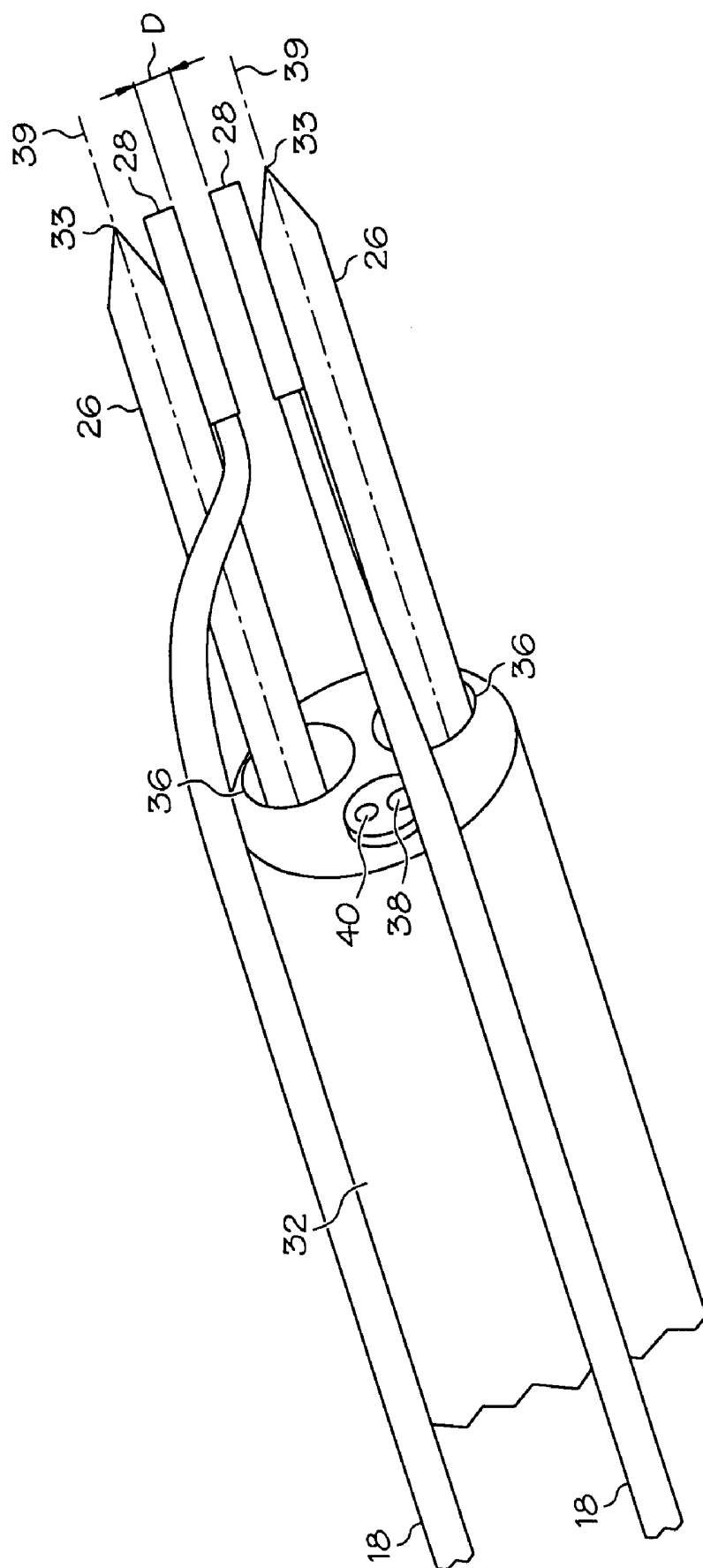


FIG. 2

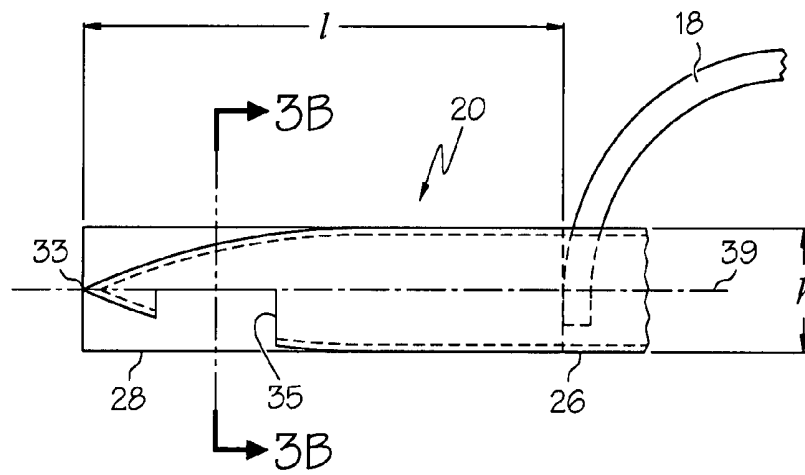


FIG. 3A

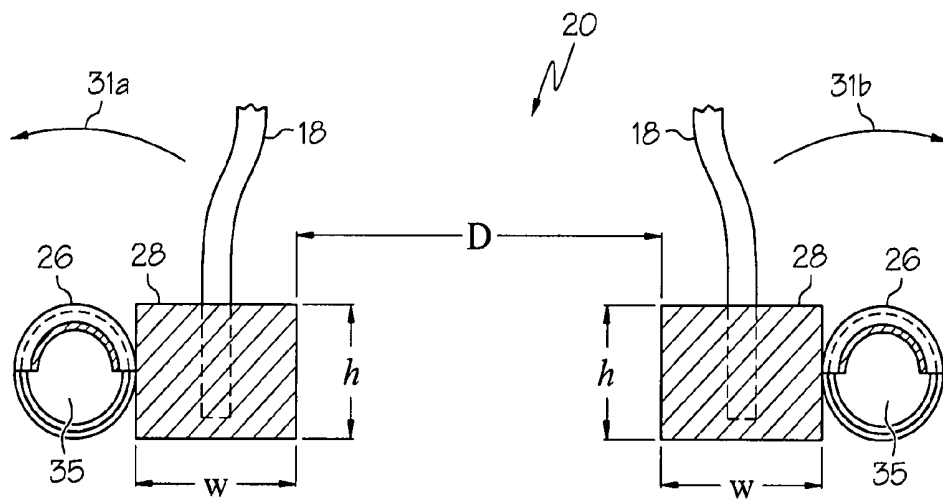


FIG. 3B

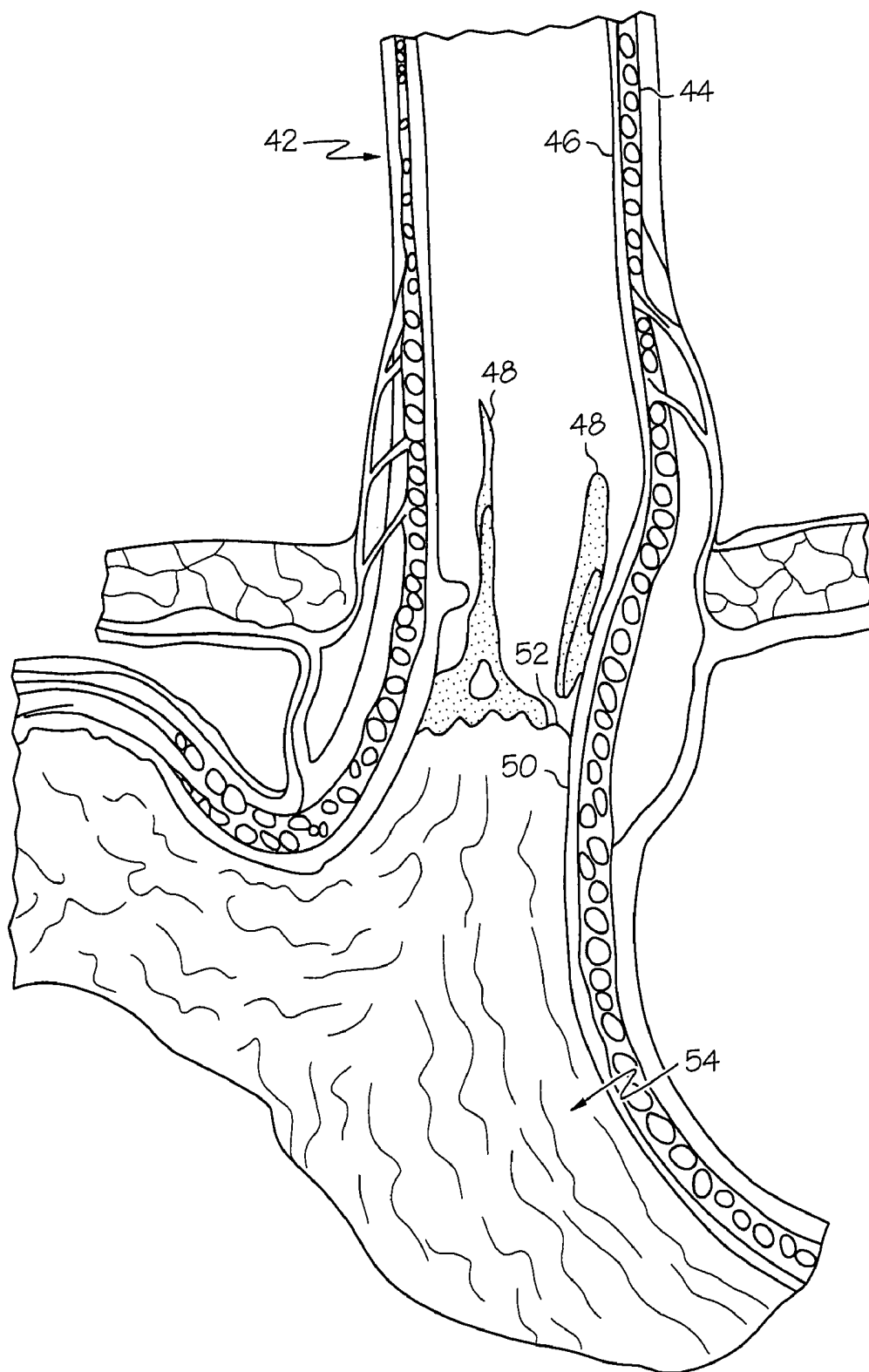


FIG. 4

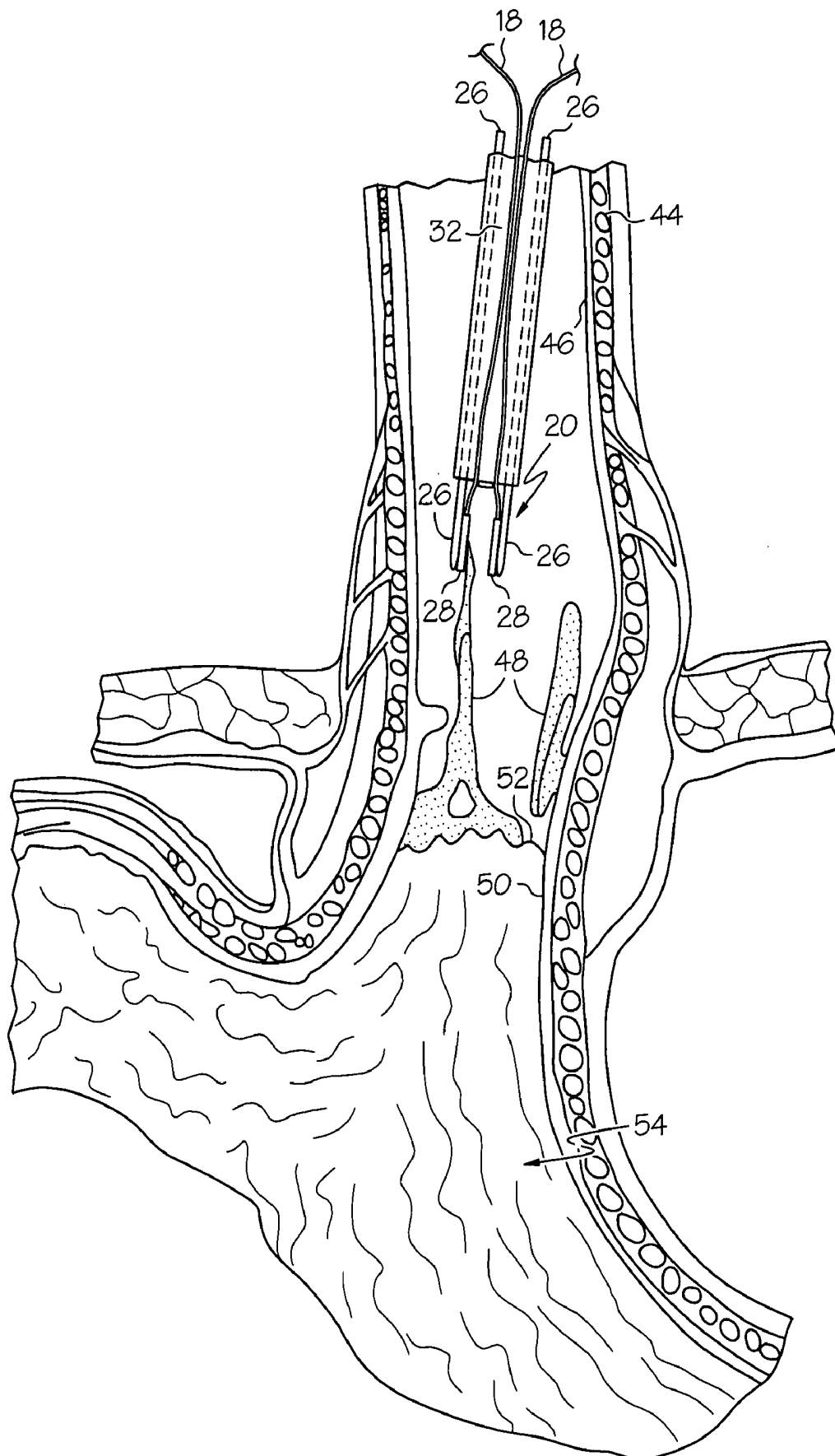


FIG. 5

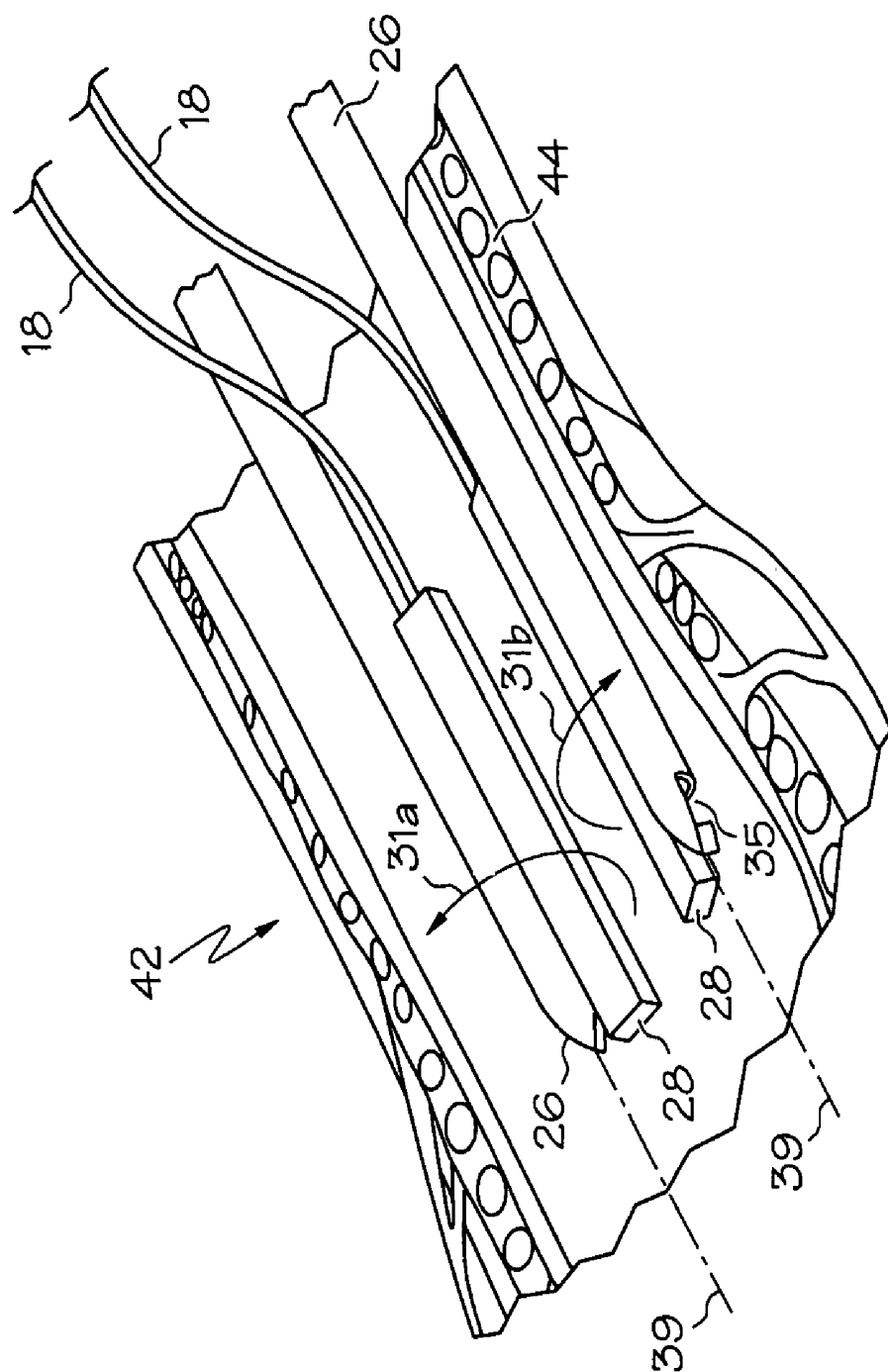


FIG. 6

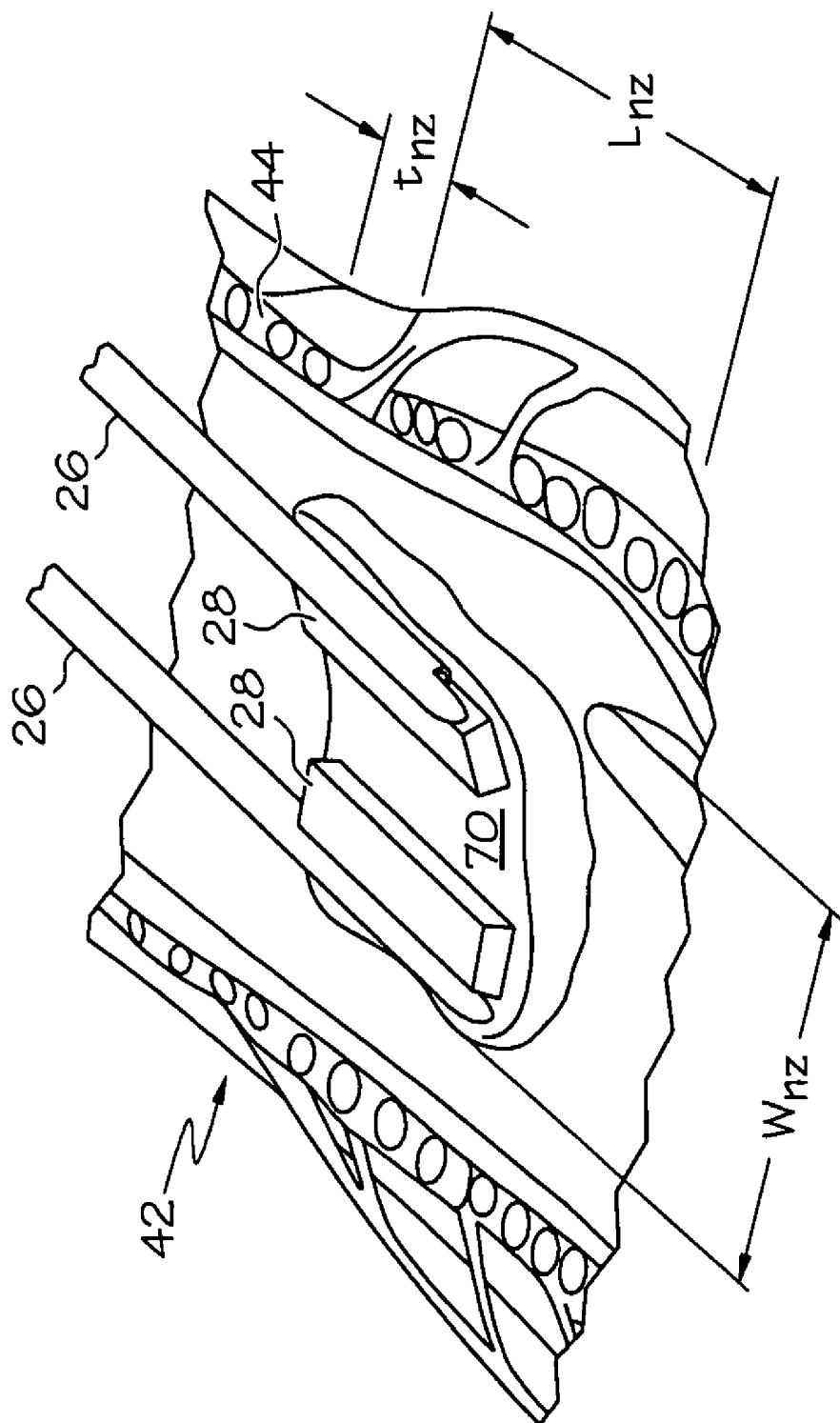


FIG. 7

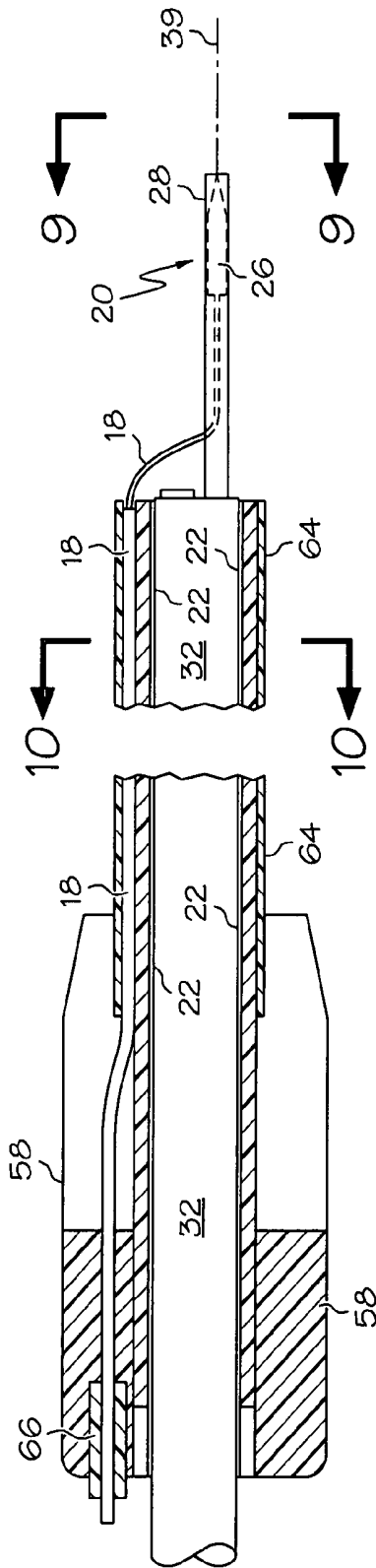


FIG. 8

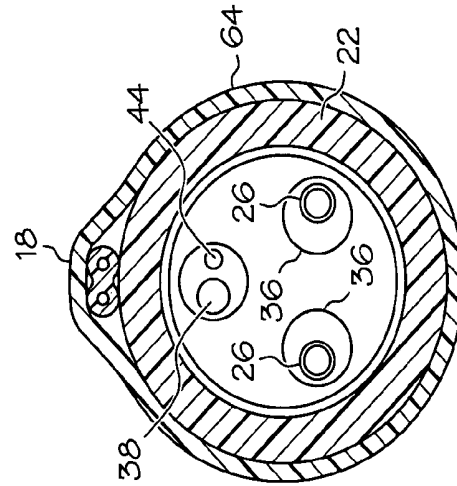


FIG. 10

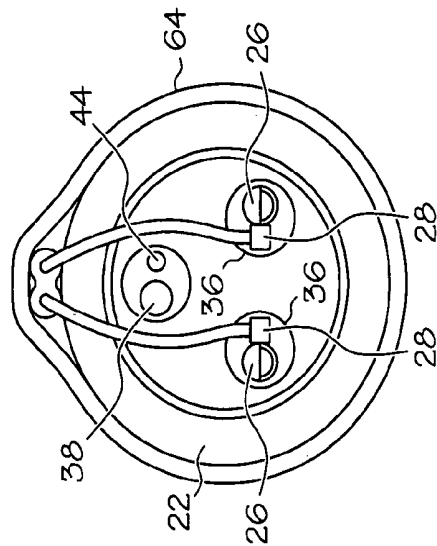


FIG. 9

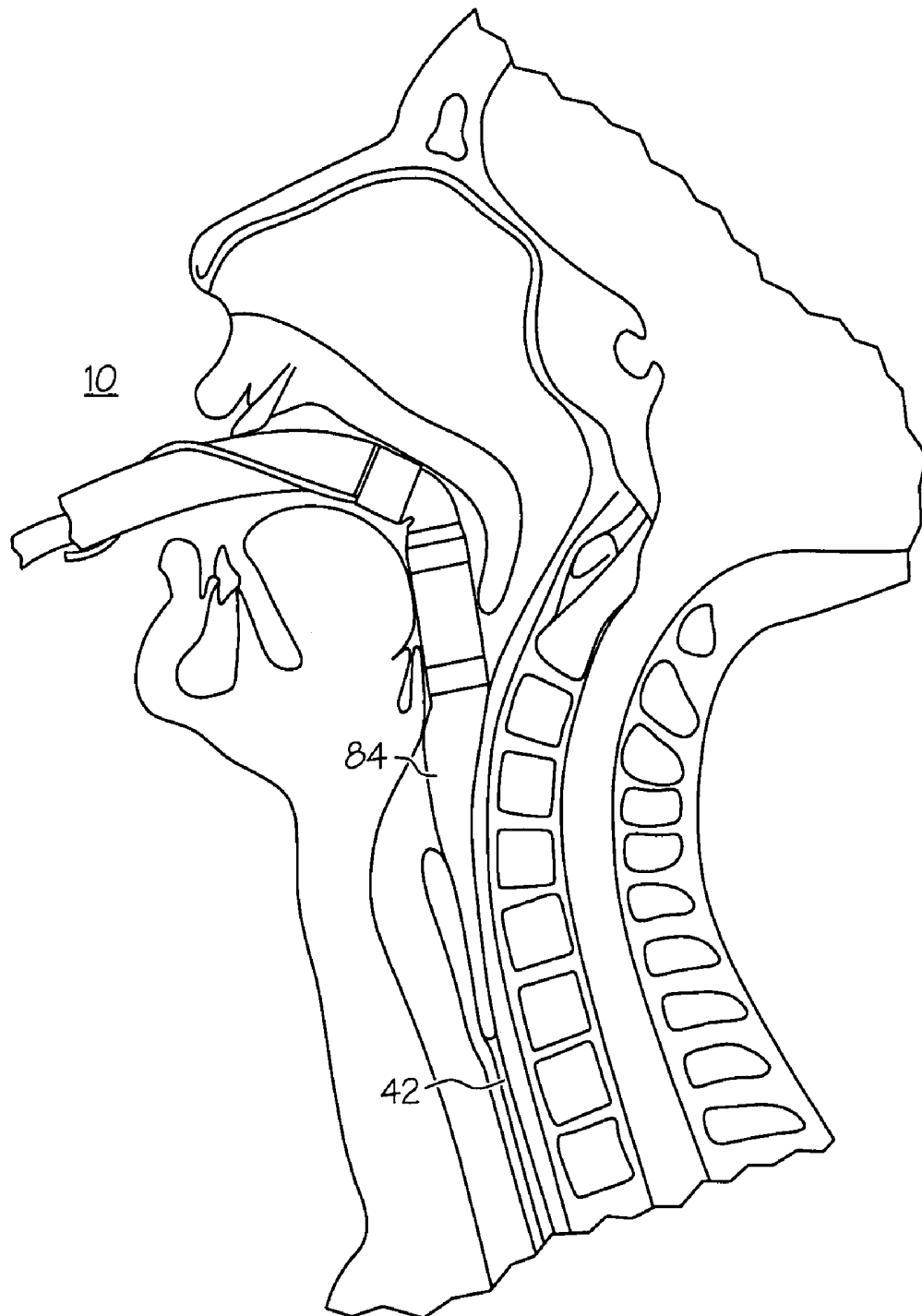


FIG. 11

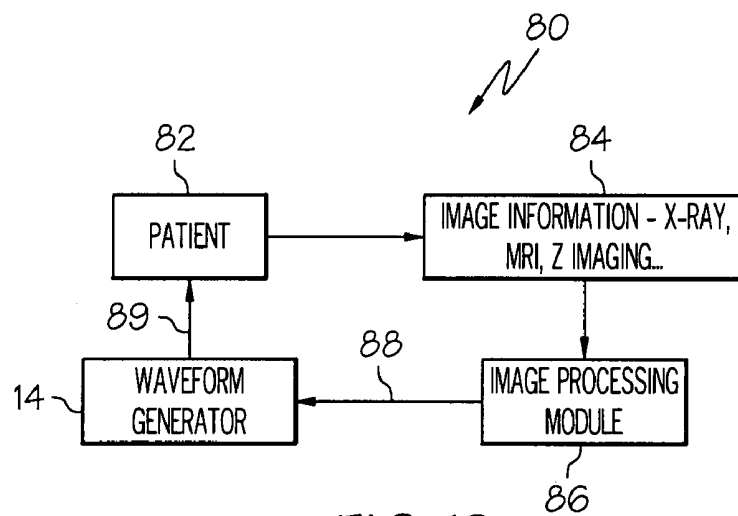


FIG. 12

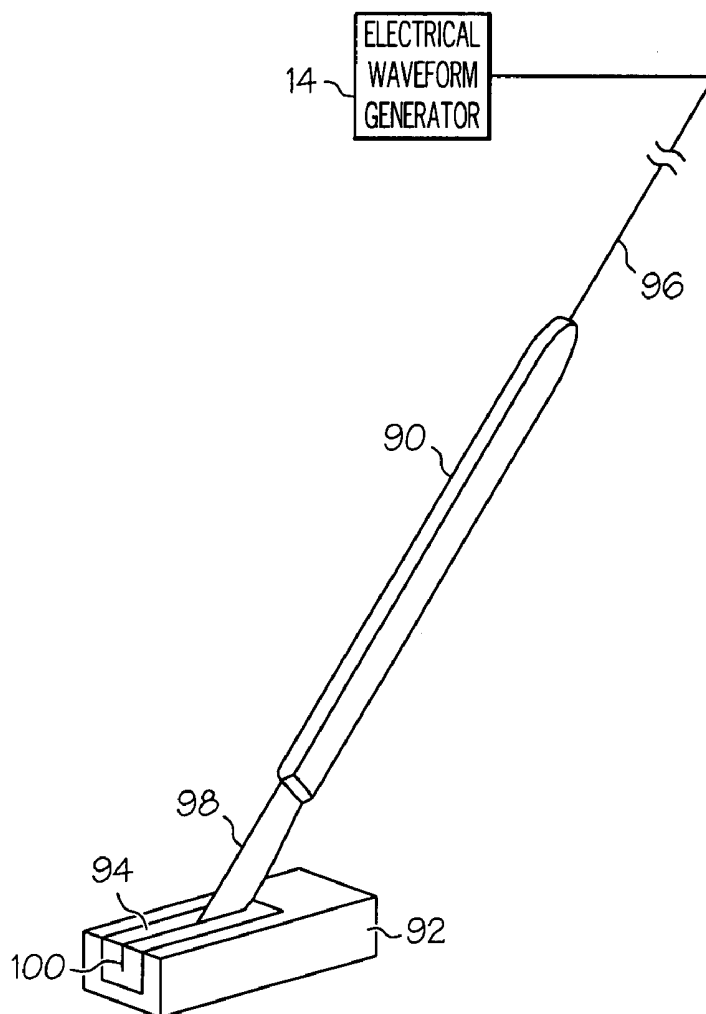


FIG. 13

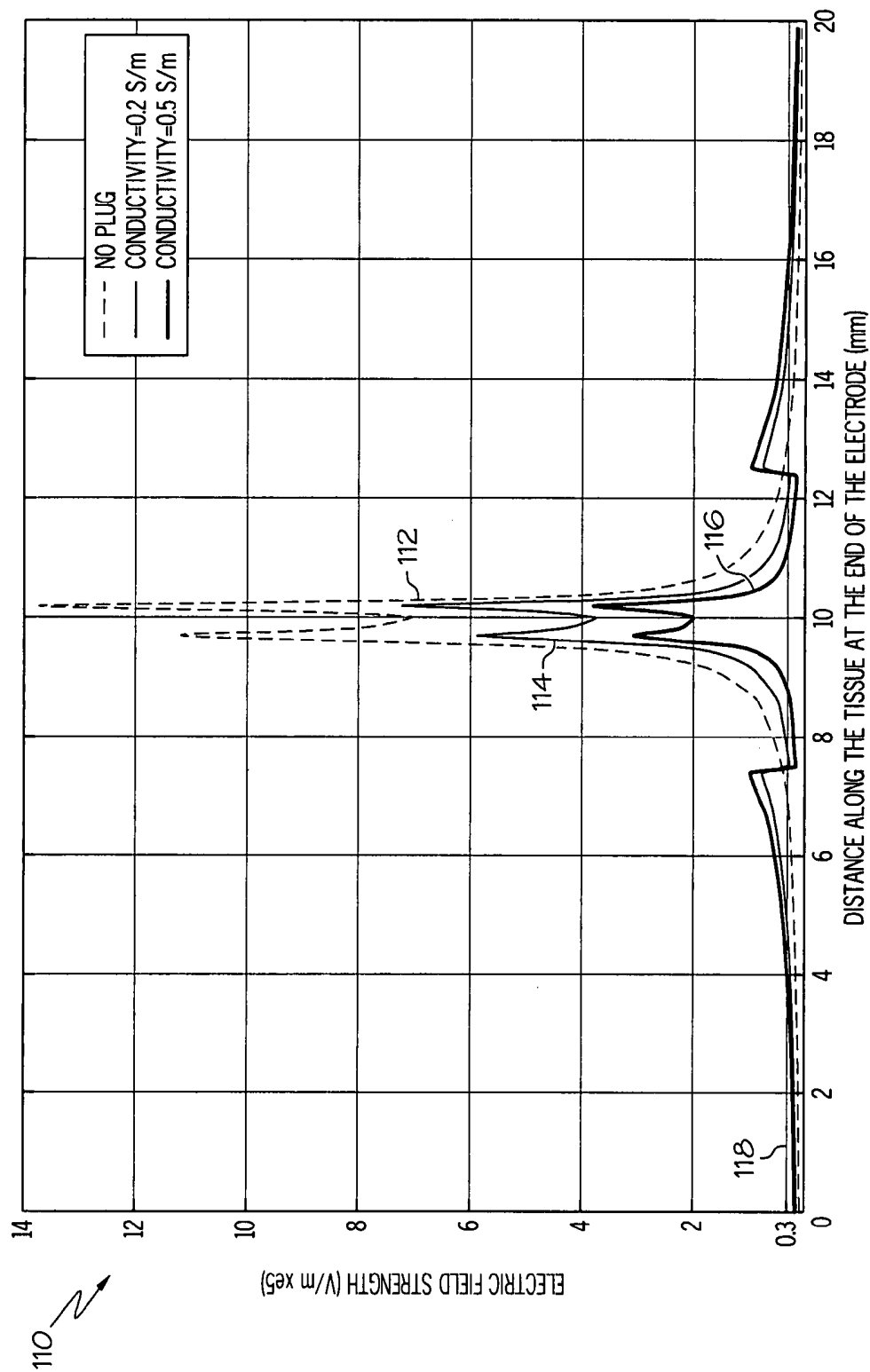


FIG. 14

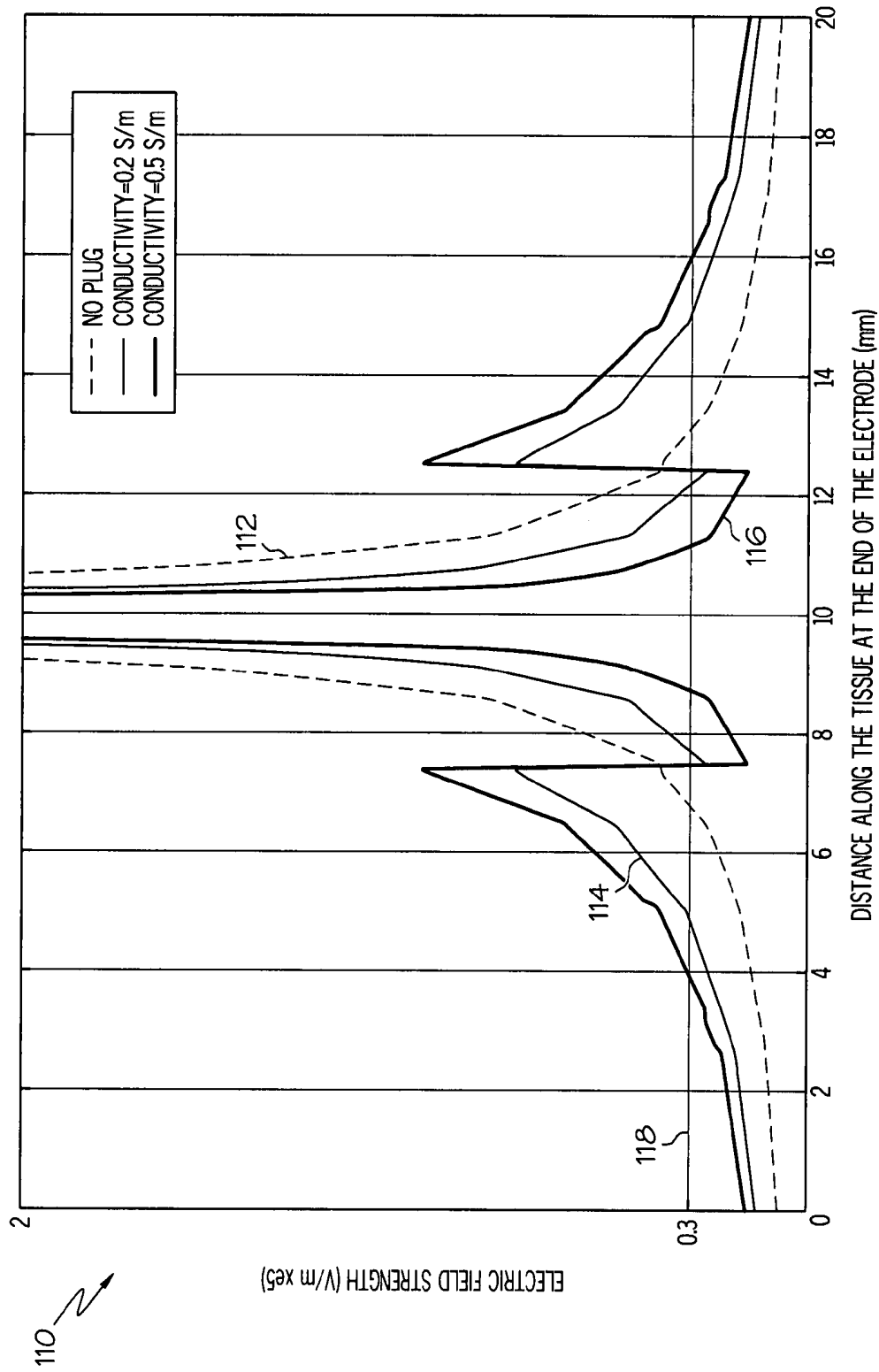


FIG. 15

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ELECTROPORATION ABLATION APPARATUS, SYSTEM, AND METHOD

CROSS REFERENCE TO RELATED APPLICATION

The present application is related to concurrently-filed U.S. patent application Ser. No. 11/706,591, entitled ELEC-
TRICAL ABLATION APPARATUS, SYSTEM, AND
METHOD, which is incorporated herein by reference in its
entirety.

BACKGROUND

Electrical therapy techniques have been employed in medi-
cine to treat pain and other and other conditions. Electrical
ablation techniques have been employed in medicine for the
removal of diseased tissue or abnormal growths from the
body. Nevertheless, there is a need for improved medical
instruments to electrically ablate or destroy diseased tissue or
abnormal growths from the body, such as cancer tissue. There
may be a need for such electrical therapy techniques to be
performed endoscopically.

Electrical therapy probes comprising electrodes may be
required to electrically treat diseased tissue. The electrodes
may be introduced into the patient endoscopically to the
tissue treatment region by passing the electrodes through the
working channel of an endoscope.

SUMMARY

In one general aspect, the various embodiments are
directed to an ablation device. In one embodiment, the abla-
tion device comprises an elongate flexible member having a
proximal end and a distal end. A first working channel is
formed within the flexible member. A first diagnostic probe
having a proximal end and distal end is located within the first
working channel and extends through the distal end of the
flexible member. A first electrode is connected to the distal
end of the first diagnostic probe, the first electrode is adapted
to be endoscopically located in a tissue treatment region. The
first electrode is adapted to couple to an electrical waveform
generator to receive an irreversible electroporation electrical
waveform sufficient to ablate tissue located proximate to the
first electrode.

FIGURES

The novel features of the various embodiments of the
invention are set forth with particularity in the appended
claims. The various embodiments of the invention, however,
both as to organization and methods of operation, together
with further objects and advantages thereof, may best be
understood by reference to the following description, taken in
conjunction with the accompanying drawings as follows.

FIG. 1 illustrates one embodiment of an endoscopic abla-
tion system.

FIG. 2 is an enlarged view of one embodiment of a thera-
peutic/diagnostic probe of one embodiment of the endoscopic
ablation system shown in FIG. 1.

FIG. 3A is a side view of a distal end of one embodiment of
a therapeutic/diagnostic probe comprising a biopsy probe and
an electrical therapy electrode assembly.

FIG. 3B is a sectional view of one embodiment of a thera-
peutic/diagnostic probe taken along section line 3B-3B show-
ing the geometric relationship between the electrodes and the
diagnostic probes.

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FIG. 4 is a sectional view of the lower end of an esophagus
and the upper portion of a stomach of a human being.

FIG. 5 illustrates the use of one embodiment of an endo-
scopic ablation system to treat diseased tissue in the lower
esophagus.

FIG. 6 illustrates the use of one embodiment of an endo-
scopic ablation system to treat diseased tissue in the lower
esophagus.

FIG. 7 illustrates one embodiment of a necrotic zone
defined by the geometry and placement of the electrical
therapy electrodes.

FIG. 8 is a sectional view taken along the longitudinal axis
of one embodiment of an endoscopic ablation system shown
in FIG. 1.

FIG. 9 is an end view taken along line 9-9 of one embodi-
ment of a therapeutic/diagnostic probe of the endoscopic
ablation system shown in FIG. 8.

FIG. 10 is a sectional view taken along line 10-10 of a
rotation tube of the endoscopic ablation system shown in FIG.
8.

FIG. 11 shows one embodiment of a distal portion of an
endoscopic ablation system shown in FIG. 1 partially inserted
into the esophagus of a patient.

FIG. 12 is a diagram of one embodiment of a control loop
for one embodiment of an irreversible electroporation therapy
procedure to treat diseased tissue as described herein.

FIG. 13 illustrates one embodiment of an electrical scalpel
for dissecting tissue.

FIG. 14 is a graphical representation (graph) of electric
field strength (along the y-axis) as a function of distance from
an electrical therapy electrode under various conductivity
environments near diseased tissue.

FIG. 15 is a close up of the graph shown in FIG. 14.

DESCRIPTION

The various embodiments described herein are directed to
diagnostic and electrical therapy ablation devices. The diag-
nostic devices comprise biopsy probes. The electrical therapy
ablation devices comprise probes and electrodes that can be
positioned in a tissue treatment region of a patient endosco-
pically. An endoscopic electrode is inserted through a working
channel of an endoscope. The placement and location of the
electrodes can be important for effective and efficient therapy.
Once positioned, the electrical therapy electrodes deliver
electrical current to the treatment region. The electrical cur-
rent is generated by a control unit or generator external to the
patient and typically has particular waveform characteristics,
such as frequency, amplitude, and pulse width. Depending on
the diagnostic or therapeutic treatment rendered, the probes
may comprise one electrode containing both a cathode and an
anode or may contain a plurality of electrodes with at least
one serving as a cathode and at least one serving as an anode.

Electrical therapy ablation may employ electroporation, or
electropermeabilization, techniques where an externally
applied electrical field significantly increases the electrical
conductivity and permeability of a cell plasma membrane.
Electroporation is the generation of a destabilizing electric
potential across biological membranes. In electroporation,
pores are formed when the voltage across the cell plasma
membrane exceeds its dielectric strength. Electroporation
destabilizing electric potentials are generally in the range of
several hundred volts across a distance of several millimeters.
Below certain magnitude thresholds, the electric potentials
may be applied across a biological membrane as a way of
introducing some substance into a cell, such as loading it with
a molecular probe, a drug that can change the function of the

cell, a piece of coding DNA, or increase the uptake of drugs in cells. If the strength of the applied electrical field and/or duration of exposure to it are properly chosen, the pores formed by the electrical pulse reseal after a short period of time, during which extra-cellular compounds have a chance to enter into the cell. Thus, below a certain threshold, the process is reversible and the potential does not permanently damage the cell membrane. This process may be referred to as reversible electroporation (RE).

On the other hand, the excessive exposure of live cells to large electrical fields (or potentials) can cause apoptosis and/or necrosis—the processes that result in cell death. Accordingly, this may be referred to irreversible electroporation (IRE) because the cells die when exposed to excessive electrical potentials across the cell membranes. The various embodiments described herein are directed to electrical therapy ablation devices such as electroporation ablation devices. In one embodiment, the electroporation ablation device may be an IRE device to destroy cells by applying an electric potential to the cell membrane. The IRE potentials may be applied to cell membranes of diseased tissue in order to kill the diseased cells. The IRE may be applied in the form of direct current (DC) electrical waveforms having a characteristic frequency, amplitude, and pulse width.

Electroporation may be performed with devices called electroporators, appliances which create the electric current and send it through the cell. The electroporators may comprise two or more metallic (e.g., Ag, AgCl) electrodes connected to an energy source to generate an electric field having a suitable characteristic waveform output in terms of frequency, amplitude, and pulse width.

Endoscopy means looking inside and refers to looking inside the human body for medical reasons. Endoscopy may be performed using an instrument called an endoscope. Endoscopy is a minimally invasive diagnostic medical procedure used to evaluate the interior surfaces of an organ by inserting a small tube into the body, often, but not necessarily, through a natural body opening. Through the endoscope, the operator is able to see abnormal or diseased tissue such as lesions and other surface conditions. The endoscope may have a rigid or a flexible tube or member and in addition to providing an image for visual inspection and photography, the endoscope enables taking biopsies, retrieving foreign objects, and introducing medical instruments to a tissue treatment region. Endoscopy is the vehicle for minimally invasive surgery.

The embodiments of the electrical therapy ablation devices may be employed for treating diseased tissue, tissue masses, tissue tumors, and lesions (diseased tissue). More particularly, the electrical therapy ablation devices may be employed in minimally invasive therapeutic treatment of diseased tissue. The electrical therapy ablation devices may be employed to deliver energy to the diseased tissue to ablate or destroy tumors, masses, lesions, and other abnormal tissue growths. In one embodiment, the electrical therapy ablation devices and techniques described herein may be employed in the treatment of cancer by quickly creating necrosis of live tissue and destroying cancerous tissue in-vivo. These minimally invasive therapeutic treatment of diseased tissue where medical instruments are introduced to a tissue treatment region within the body of a patient through a natural opening are known as Natural Orifice Translumenal Endoscopic Surgery (NOTES)TM.

A biopsy is a medical procedure involving the removal of cells or tissues for examination. The tissue is often examined under a microscope and can also be analyzed chemically (for example, using polymerase chain reaction [PCR] techniques). When only a sample of tissue is removed, the procedure

is called an incisional biopsy or core biopsy. When an entire lump or suspicious area is removed, the procedure is called an excisional biopsy. When a sample of tissue or fluid is removed with a needle, the procedure is called a needle aspiration biopsy. A procedure called “optical biopsy” may be employed where optical coherence tomography may be adapted to allow high-speed visualization of tissue in a living animal with a catheter-endoscope 1 millimeter in diameter. Optical biopsy may be used to obtain cross-sectional images of internal tissues.

Biopsy specimens may be taken from part of a lesion when the cause of a disease is uncertain or its extent or exact character is in doubt. Vasculitis, for instance, is usually diagnosed on biopsy. Additionally, pathologic examination of a biopsy can determine whether a lesion is benign or malignant, and can help differentiate between different types of cancer.

FIG. 1 illustrates one embodiment of an endoscopic ablation system 10. The endoscopic ablation system 10 may be employed to electrically treat diseased tissue such as tumors and lesions. The endoscopic ablation system 10 may be configured to be positioned within a natural opening of a patient such as the colon or the esophagus and can be passed through the opening to a tissue treatment region. The illustrated endoscopic ablation system 10 may be used to treat diseased tissue via the colon or the esophagus of the patient, for example. The tissue treatment region may be located in the esophagus, colon, liver, breast, brain, and lung, among others. The endoscopic ablation system 10 can be configured to treat a number of lesions and osteopathologies including but not limited to metastatic lesions, tumors, fractures, infected site, inflamed sites, and the like. Once positioned at the target tissue treatment region, the endoscopic ablation system 10 can be configured to treat and ablate diseased tissue in that region. In one embodiment, the endoscopic ablation system 10 may be employed as a diagnostic instrument to collect a tissue sample using a biopsy device introduced into the tissue treatment region via an endoscope (e.g., the endoscopic ablation system 10). In one embodiment, the endoscopic ablation system 10 may be adapted to treat diseased tissue, such as cancers, of the gastrointestinal (GI) tract or esophagus that may be accessed orally. In another embodiment, the endoscopic ablation system 10 may be adapted to treat diseased tissue, such as cancers, of the liver or other organs that may be accessible transanally through the colon and/or the abdomen.

One embodiment of the endoscopic ablation system 10 may be mounted on a flexible endoscope 12 (also referred to as endoscope 12), such as the GIF-100 model available from Olympus Corporation. The flexible endoscope 12 includes an endoscope handle 34 and a flexible shaft 32. The endoscopic ablation system 10 generally comprises one or more therapeutic/diagnostic probe 20, a plurality of conductors 18, a handpiece 16 having a switch 62, and an electrical waveform generator 14. In one embodiment, the electrical waveform generator 14 may be a high voltage direct current (DC) irreversible electroporation (IRE) generator. The therapeutic/diagnostic probe 20 is located at a distal end of the flexible shaft 32 and the conductors 18 attach to the flexible shaft 32 using a plurality of clips 30. The therapeutic/diagnostic probe 20 comprises an elongate member attached to an electrical energy delivery device comprising one or more electrical therapy electrodes 28. In one embodiment, the therapeutic/diagnostic probe 20 extends through a bore in the flexible shaft 32 such as a working channel 36 (FIG. 2). In one embodiment, the therapeutic/diagnostic probe 20 may comprise elongate diagnostic probes 26 attached or joined to the electrodes 28 that extend through the working channel 36. In another embodiment, the flexible shaft 32 may comprise two

working channels 36 and a first diagnostic probe 26 joined to a first electrode 28 that extends through the distal end of a first working channels 36 and a second diagnostic probe 26 joined to a second electrode 28 that extends through the distal end of a second working channel 36. In one embodiment, the diagnostic probe comprises one or more diagnostic probes 26 attached or joined in any suitable manner to the electrodes 28. For example, the diagnostic probes 26 may be joined or attached to the electrodes 28 by welding, soldering, brazing or other well known techniques. Many different energy sources may be used for welding, soldering, or brazing such as, for example, a gas flame, an electric arc, a laser, an electron beam, friction, and ultrasound. Thus, in one embodiment, the therapeutic/diagnostic probe 20 may be employed in a diagnostic mode to take a biopsy sample of the diseased tissue using the diagnostic probes 26 and, in one embodiment the therapeutic/diagnostic probe 20 may be employed in a therapeutic mode by treating diseased tissue with electrical current delivered by the electrodes 28. In other embodiments, the therapeutic/diagnostic probe 20 may be employed in a combination of therapeutic and diagnostic modes. The therapeutic/diagnostic probe 20 may be passed through the one or more working channels 36 located within the flexible shaft 32. The therapeutic/diagnostic probe 20 is delivered to the tissue treatment region endoscopically and is located on top of the diseased tissue to be electrically treated. Once the therapeutic/diagnostic probe 20 is suitably located by the operator, manual operation of the switch 62 on the handpiece 16 electrically connects or disconnects the electrodes 28 to the electrical waveform generator 14. Alternatively, the switch 62 may be mounted on, for example, a foot switch (not shown).

In one embodiment, the electrical waveform generator 14 may be a conventional, bipolar/monopolar electrosurgical generator (ICC200 Erbe Inc.) or an IRE generator such as one of many models commercially available, including Model Number ECM800, available from BTX Boston, Mass. The IRE generator generates electrical waveforms having predetermined frequency, amplitude, and pulse width. The application of these electrical waveforms to the cell membrane causes the cell to die. The IRE electrical waveforms are applied to the cell membranes of diseased tissue in order to kill the diseased cells and ablate the diseased tissue. IRE electrical waveforms suitable to destroy the cells of diseased tissues energy are generally in the form of direct current (DC) electrical pulses delivered at a frequency in the range of 1-20 Hz, amplitude in the range of 100-1000 VDC, and pulse width in the range of 0.01-100 ms. For example, an electrical waveform having amplitude of 500 VDC and pulse duration of 20 ms may be delivered at a pulse repetition rate or frequency of 10 HZ can destroy a reasonably large volume of diseased tissue. Unlike RF ablation systems which require high power and energy input into the tissue to heat and destroy the tissue, IRE requires very little energy input into the tissue, rather the destruction of the tissue is caused by high electric fields. It has been determined that in order to destroy living tissue, the waveforms have to generate an electric field of at least 30,000V/m in the tissue treatment region. In one embodiment, the IRE generator 14 may generate voltages from about 100-1000 VDC. The IRE generator 14 may generate voltage pulses from 0.01-100 ms. These pulses may be generated at a suitable pulse repetition rate. The electrical current depends on the voltage amplitude, pulse width, pulse repetition rate, and the volume of tissue being treated. In one embodiment, the IRE generator 14 generates 20 ms pulses of 500 VDC amplitude between the electrodes 28. The embodiments, however, are not limited in this context.

When using the IRE generator 14 in monopolar mode with two or more electrical therapy electrodes 28, a grounding pad is not needed on the patient. Because a generator will typically be constructed to operate upon sensing connection of ground pad to the patient when in monopolar mode, it can be useful to provide an impedance circuit to simulate the connection of a ground pad to the patient. Accordingly, when the electrical ablation system 10 is used in monopolar mode without a grounding pad, an impedance circuit can be assembled by one skilled in the art, and electrically connected in series with one of the electrical therapy electrodes 28 that would otherwise be used with a grounding pad attached to a patient during monopolar electrosurgery. Use of an impedance circuit allows use of the IRE generator 14 in monopolar mode without use of a grounding pad attached to the patient.

FIG. 2 is an enlarged view of one embodiment of the therapeutic/diagnostic probe 20 of one embodiment of the endoscopic ablation system 10 shown in FIG. 1. The therapeutic/diagnostic probe 20 extends through the distal end of the flexible shaft 32. In one embodiment, the therapeutic/diagnostic probe 20 protrudes from the distal end of an internal lumen extending between the proximal and distal ends of the flexible endoscope 12. In one embodiment, the therapeutic/diagnostic probe 20 may comprise a biopsy device adapted and configured to remove sample tissue using an incisional, core, needle aspiration, or optical biopsy techniques. In one embodiment, the biopsy device comprises one or more diagnostic probes 26. As previously discussed, the electrical therapy electrodes 28 may be joined or attached to the diagnostic probes 26 in any suitable manner.

As previously discussed, the electrical therapy electrodes 28 are connected to the diagnostic probes 26 in any known suitable manner and are located in a spaced-apart relationship so as to define a distance D between the electrodes. The distance D is adjustable and can be increased or decreased by rotating one or both of the diagnostic probes 26. The therapeutic/diagnostic probe 20 are rotatable about a central axis 39. Thus, the diagnostic probes 26 and the electrodes 28 are rotatable about the central axis 39. The electrodes 28 may be rotated to increase or decrease the relative distance D between the electrode 28 either to focus the energy in a smaller tissue region or to enlarge the tissue treatment region. In this manner, the operator can surround the diseased tissue such as a cancerous lesion, a polyp, or a tumor. The electrodes 28 are energized with the electrical waveform generator 14 to treat the diseased tissue. The diagnostic probes 26 have a sharp tooth 33 at the distal end and are moveable from the distal end to the proximal end of the flexible shaft 32 capable of slicing a thin section of the tissue to obtain a biopsy sample (shown in more detail below). The diagnostic probes 26 may comprise a bore 35 (FIGS. 3A, B) at the distal end extending from a proximal end to the distal end of the diagnostic probes 26. Suction may be applied at the proximal end of the probes to remove a tissue sample before and/or after treatment through the bore 35 (FIGS. 3A, B) formed through the diagnostic probes 26.

The electrical therapy electrodes 28 may be positioned in any orientation relative to the diagnostic probes 26. The electrodes 28 and the diagnostic probes 26 may have any suitable shape. In the illustrated embodiment, the electrodes 28 may have a generally cuboidal shape and the diagnostic probes 26 may have an elongate cylindrical shape with a sharp tooth 33 and a bore 35 formed therein at the distal end. The electrical conductors 18 are electrically insulated from each other and surrounding structure except for the electrical connections the electrodes 28. The distal end of the flexible shaft 32 of the flexible endoscope 12 may comprise a light source 40, a

viewing port 38, and one or more working channels 36. The viewing port 38 transmits an image within its field of view to an optical device such as a charge coupled device (CCD) camera within the flexible endoscope 12 so that an operator may view the image on a display monitor (not shown). In the embodiment shown in FIG. 2, the distal end of flexible shaft 32 is proximal to the electrodes 28 and is within the viewing field of the flexible endoscope 12 to enable the operator to see the diseased tissue to be treated between the electrodes 28.

FIG. 3A is a side view of one embodiment of the therapeutic/diagnostic probe 20 comprising a biopsy probe 26 and an electrical therapy electrode 28 assembly. FIG. 3B is a sectional view of one embodiment of a therapeutic/diagnostic probe 20 taken along section line 3B-3B showing the geometric relationship between the electrodes 28 and the diagnostic probes 26. In the embodiment illustrated in FIGS. 3A, B, the cuboidal electrodes 28, each have a width "w," a length "l," and a thickness or height "h." The electrodes 28 have parallel, adjacent edges 8 separated by a distance "D." This geometry of the electrodes 28, the distance D between them, and the electrical waveform may be used to calculate an ablation index, which has particular significance to the location, size, shape, and depth of ablation achievable, as will be described later. The diagnostic probes 26 may be juxtaposed with the electrodes 28. In this embodiment, the two cylindrically elongate diagnostic probes 26 have a bore 35 for removing ablated tissue or taking biopsy samples of the tissue by way of suction. The length of the diagnostic probes 26 may extend through the entire length of the flexible endoscope 12. The conductors 18 are attached to the electrodes 28 in any suitable manner including welding, soldering, or brazing and may employ many different energy sources such as, for example, a gas flame, heat source, an electric arc, a laser, an electron beam, friction, and ultrasound. The electrodes 28 are attached to the diagnostic probes 26 and may be rotated about the central axis 39 in the directions indicated by arrows 31a and 31b.

FIG. 4 is a sectional view of the lower end of an esophagus 42 and the upper portion of a stomach 54 of a human being. The esophagus 42 has a mucosal layer 46, a muscular layer 44, and a region of diseased tissue 48. The boundary between the mucosal layer 46 of the esophagus 42 and a gastric mucosa 50 of the stomach 54 is a gastro-esophageal junction 52, which is approximately the location for the lower esophageal sphincter (LES). The LES allows food to enter the stomach 54 while preventing the contents of the stomach 54 from refluxing into the lower esophagus 42 and damaging the mucosal layer 46. The diseased tissue 48 can develop when chronic reflux is not treated. In one form, the diseased tissue 48 may be, for example, intestinal metaplasia, which is an early stage of Barrett's esophagus. As can be seen in FIG. 4, the esophagus 42 is relatively flaccid and contains numerous folds and irregularities on the interior lining.

FIG. 5 illustrates the use of one embodiment of the endoscopic ablation system 10 to treat the diseased tissue 48 in the lower esophagus 42. The operator positions the therapeutic/diagnostic probe 20 using endoscopic visualization so that the diseased tissue 48 to be treated is within the field of view of the flexible endoscope 12. Once the operator positions the therapeutic/diagnostic probe 20 such that the electrical therapy electrodes 28 are located above the diseased tissue 48, the operator may energize the electrodes 28 with the electrical waveform generator 14 to destroy the diseased tissue 48 in the tissue treatment region. For example, the electrodes 28 may be energized with an electrical waveform having amplitude of approximately 500 VDC and a pulse width of approximately 20 ms at a frequency of approximately 10 Hz. In this manner,

the diseased tissue 48 in the tissue treatment region may be destroyed. This procedure may take very little time and may be repeated to destroy relatively larger portions of the diseased tissue 48. Suction may be applied to remove the treated tissue sample through the bore 35 formed in the diagnostic probes 26.

FIG. 6 illustrates the use of the endoscopic ablation system 10 to treat the diseased tissue 48 in the lower esophagus 42. As shown in the illustrated embodiment, the electrical therapy electrodes 28 can be rotated about the central axis 39 in the direction indicated by arrows 31a and 31b. The treated tissue can be sucked into the bore 35 of the biopsy probe 26 by applying suction to thereto.

FIG. 7 illustrates one embodiment of a necrotic zone 70 defined by the geometry and placement of the electrical therapy electrodes 28. The energy delivered by the waveform to the electrodes 28 in terms of frequency, amplitude, and pulse width should be suitable to destroy the tissue in the necrotic zone 70. Based on the location and geometry of the electrodes 28, and the energy delivered thereto, the necrotic zone 70 in the illustrated embodiment may be approximated generally as a volume of width "wnz," a thickness "tnz," and a length "lnz." Energizing the electrodes 28 destroys the diseased tissue 48 within the necrotic zone 70. In one embodiment, electrodes 28 with a width "w=0.5 mm," a length "l=10 mm," and a thickness "h=0.5 mm" (as shown in FIGS. 3A, B) and a waveform of approximately 500 VDC, a pulse width of 20 ms, and a frequency of 10 Hz, would define a necrotic zone 70 with dimensions of approximately wnz=6 mm wide, lnz=10 mm long, and hnz=2 mm deep. If a biopsy indicates that the treatment region includes dysplastic or malignant cells, or if the treatment region is larger than the necrotic zone 70, the process may be repeated until all the diseased tissue 48 is destroyed in the treatment region and clean margins are recorded. In one embodiment, optical biopsy may be used as an alternative to the vacuum diagnostic probes 26 shown in the illustrated embodiments.

FIG. 8 is a sectional view taken along the longitudinal axis of one embodiment of an endoscopic ablation system 10 shown in FIG. 1. The distal portion of the flexible shaft 32 is located inside a rotation tube 22 of the endoscopic ablation system 10. The pair of electrical conductors 18 pass through a strain relief 66 of a rotation knob 58. In the illustrated embodiment an external tube 64 may be located over the flexible shaft 32 such that the conductors 18 pass between the external tube 64 and the rotation tube 22. Each of the conductors 18 connect electrically to the electrical therapy electrodes 28 in the therapeutic/diagnostic probe 20. The rotation tube 22 rotatably joins the rotation knob 58. The operator can rotatably orient the electrodes 28, even after insertion into the esophagus, by remotely rotating the diagnostic probes 26 about the central axis 39 of each of the therapeutic/diagnostic probe 20. The therapeutic/diagnostic probe 20 is within the field of view of the flexible endoscope 12, thus enabling the operator to see on a display monitor the tissue that is located between the electrodes 28. Optionally, in one embodiment, a valve element (not shown) may extend from the distal end of therapeutic/diagnostic probe 20 to prevent tissue or fluids from entering the therapeutic/diagnostic probe 20.

FIG. 9 is an end view taken along line 9-9 of one embodiment of the therapeutic/diagnostic probe 20 of the endoscopic ablation system 10 shown in FIG. 8. The electrical conductors 18 connect to the electrical therapy electrodes 28. The rotation tube 22 retains the flexible shaft 32. The inside diameter of the rotation tube 22 is larger than the outer diameter of the flexible endoscope 12 to allow rotation of the rotation tube 22 while holding the flexible endoscope 12 stationary, or vice

versa. Each of the therapeutic/diagnostic probe 20 comprising the diagnostic probes 26 attached to the electrodes 28 extend outwardly from the distal end of the flexible shaft 32 through each of the working channels 36. In this embodiment, the operator may endoscopically view the tissue between the electrodes 28. The flexible endoscope 12 includes the light source 40, the viewing port 38, and the one or more working channels 36.

FIG. 10 is a sectional view taken along line 10-10 of the rotation tube 22 of the endoscopic ablation system 10 shown in FIG. 8. The external tube 64 and the rotation tube 22 assemble and retain the electrical conductors 18 as already described. The light source 40, the viewing port 38, and the one or more working channels 36 of the flexible endoscope 12 are shown.

FIG. 11 shows one embodiment of the distal portion of the endoscopic ablation system 10 shown in FIG. 1 partially inserted into the esophagus 42 of a patient. A tapered end cover 84 dilates the esophagus 42 as the operator gently inserts the therapeutic/diagnostic probe 20 for positioning near the diseased tissue 48 to be ablated. A flexible coupling 88 flexes as shown, reducing the required insertion force and minimizing trauma (and post-procedural pain).

The operator may treat the diseased tissue 48 using the embodiment of the endoscopic ablation system 10 comprising the therapeutic/diagnostic probe 20 shown in FIGS. 1-3 and 5-11 as follows. The operator inserts the flexible shaft 32 of the endoscope 12 into the lower esophagus 42 trans-orally. A rigid support member at the distal end of the endoscope 12 holds the lower esophagus 42 open as the operator uses endoscopic visualization through the therapeutic/diagnostic probe 20 to position the electrical therapy electrodes 28 next to the diseased tissue 48 to be treated. The rigid support member opens and supports a portion of the flaccid, lower esophagus 42 and helps to bring the diseased tissue 48 to be treated into intimate contact with the electrodes 28 and within the field of view of the flexible endoscope 12. While watching through the viewing port 38, the operator actuates the switch 62, electrically connecting the electrodes 28 to the electrical waveform generator 14 through the electrical conductors 18. Electric current then passes through the portion of the diseased tissue 48 positioned between the electrodes 28 and within the field of view. When the operator observes that the tissue in the field of view has been ablated sufficiently, the operator deactuates the switch 62 to stop the ablation. The operator may reposition the electrodes 28 for subsequent tissue treatment, or may withdraw the therapeutic/diagnostic probe 20 (together with the flexible endoscope 12).

FIG. 12 is a diagram of one embodiment of a control loop 80 for one embodiment of an IRE therapy procedure to treat diseased tissue as described herein. As previously discussed, the IRE therapy may be effective in quickly creating necrosis of live tissue and destroying diseased (e.g., cancerous) tissue in-vivo. Real time information feedback about the size in volume of a necrotic zone may be helpful during an IRE therapy procedure for focal treatment of diseased tissue 48.

Prior to an IRE therapy procedure, a patient 82 will have an image of the diseased tissue 48 taken for clinical purposes in an effort to reveal, diagnose, or examine the diseased tissue 48 and to identify its location more precisely. The image information 84 will generally include geometric information about the volume of the diseased tissue 48. The image information 84 is provided to an image processing module 86 to calculate the volume of the diseased tissue 48 and to display a virtual model of the diseased tissue 48 on a monitor. The image processing module 86 may comprise, for example, image processing software applications such as Comsol Multiphys-

ics available by Comsol, Inc. to receive the image information 84, extract the geometric information, and determine (e.g., calculate) the voltage required to treat the proper volume and outline of the necrotic zone required to treat the diseased tissue 48. The image processing module 86 creates a virtual model of a treatment zone necessary to treat the diseased tissue 48. The image processing module 86 then determines waveform parameters 88 of a suitable electrical waveform necessary to destroy the diseased tissue 48. The waveform parameters 88 include the frequency, amplitude, and pulse width of the electrical waveform to be generated by the waveform generator 14. The waveform generator 14 would then generate the suitable electrical waveform to destroy the diseased tissue 48 based on the calculated waveform parameters 88.

The image processing module 86 also comprises image processing software applications such as Matlab available by MathWorks, Inc. to receive the image information 84 and the virtual model and display an image of the diseased tissue 48 overlaid with an image of the virtual model. The overlaid images enable the operator to determine whether the calculated electrical waveform parameters 88 are suitable for destroying the diseased tissue 48, whether too strong or too weak. Thus, the IRE waveform parameters 88 may be adjusted such that the virtual model image substantially overlays the entire diseased tissue image. The calculated parameters 88 are provided to the waveform generator 14 and the diseased tissue may be treated with an electrical waveform 89 based on the calculated parameters 88 as discussed herein. After the diseased tissue 48 is treated with the electrical waveform 89, a new image of the diseased tissue 48 can be generated to determine the extent or effectiveness of the treatment. The cycle may be repeated as necessary to ablate the diseased tissue 48 as much as possible.

FIG. 13 illustrates one embodiment of an electrical scalpel 90 for dissecting tissue 92. In one embodiment, the electrical scalpel 90 may be driven by an IRE waveform previously described. The scalpel 90 comprises a blade 98 that is formed of metal such as hardened and tempered steel (and/or stainless in many applications). The blade 98 is connected to the electrical waveform generator 14 by multiple electrical conductors 96. The electrical waveform generator 14 may generate an IRE waveform (e.g., 10 Hz frequency, 500 VDC amplitude, and 20 ms pulse). As the blade 98 dissects the tissue 92 along an incision 100, the electrical waveform generator 14 may be activated or pulsed to create a tissue destruction zone 94 surrounding the blade 98. Accordingly, as the blade 98 dissects the diseased tissue 92 it generates the tissue destruction zone 94 beyond the incision 100. This may help to ensure the destruction of any diseased tissue cells left behind. The pulse repetition rate or frequency of the electrical waveform generated by the generator 14 may be selected to provide a continuous zone of tissue destruction 94 as the blade 98 moves through the diseased tissue 92. In one embodiment, a feedback signal (e.g., audio, visual, or cut-off of electrical power to the blade 98) may be provided to the operator to indicate that the scalpel 90 is moving too quickly.

FIG. 14 is a graphical representation 110 (graph) of electric field strength (along the y-axis) as a function of distance from an electrical therapy electrode 28 under various conductivity environments near the diseased tissue 48. FIG. 15 is a close up of the graph 110 shown in FIG. 14A. In electrical therapy of diseased tissue 48, the volume of tissue that can be destroyed by an electrical waveform (e.g., the necrotic zone) may be defined by a minimum electric field strength applied to the tissue treatment region. The electric field strength in the tissue treatment region varies throughout the tissue as a function of

the applied electrical waveform parameters frequency, amplitude, and pulse width as well as the conductivity of the tissue in the treatment region. When a single electrical therapy electrode **28** is located in a first position in the tissue treatment region of interest and a return pad is placed at a distance relatively far from the first position, an electric field is generated around the electrode **28** when it is energized with a particular electrical waveform. The magnitude of the electric field, however, diminishes rapidly in the radial direction away from the electrode **28**. When two electrodes **28** are placed relatively close together, a larger pattern of tissue can be destroyed. Injecting a fluid having a higher conductivity than the tissue into the tissue treatment region extends the electric field of sufficient strength to destroy the tissue radially outwardly from the electrode **28**. Thus, the addition of a fluid having higher conductivity than the tissue to be treated creates a larger tissue destruction zone by extending the electric field radially outwardly from the electrodes **28**.

The graph **110** illustrates the electric field strength, along the y-axis, as a function of the radial distance from the electrical therapy electrode **28**. The y-axis is labeled in units of volts/meter ($V/m \times e^5$) and the x-axis is labeled in units of mm. The graph **110** illustrates a family of three functions with conductivity as a parameter. A first function **112** illustrates the electric field strength as a function of the radial distance from one of the electrodes **28** with no conductivity plug introduced into the tissue treatment region. A second function **114** illustrates the electric field strength as a function of the radial distance from one of the electrodes **28** with a conductivity plug of 0.2 S/m introduced in the tissue treatment region. A third function **116** illustrates the electric field strength as a function of the radial distance from one of the electrodes **28** with a conductivity plug of 0.5 S/m introduced in the tissue treatment region. As shown in the graph **110**, the peak electric field strength of each of the functions **112**, **114**, **116** decreases with increased conductivity in the tissue treatment region in proximity to the electrode **28**. However, the threshold **118** of each of the functions **112**, **114**, **116** where the electric field strength drops below the minimum threshold **118** of electric field strength required to destroy tissue becomes wider as the conductivity increases. In other words, increasing the conductivity of the tissue in the tissue treatment region extends the range of an effective electric field to destroy tissue or creates a larger necrotic zone. In one embodiment, the minimum electric field strength threshold **118** is approximately 30,000V/m.

The devices disclosed herein can be designed to be disposed of after a single use, or they can be designed to be used multiple times. In either case, however, the device can be reconditioned for reuse after at least one use. Reconditioning can include any combination of the steps of disassembly of the device, followed by cleaning or replacement of particular pieces, and subsequent reassembly. In particular, the device can be disassembled, and any number of the particular pieces or parts of the device can be selectively replaced or removed in any combination. Upon cleaning and/or replacement of particular parts, the device can be reassembled for subsequent use either at a reconditioning facility, or by a surgical team immediately prior to a surgical procedure. Those skilled in the art will appreciate that reconditioning of a device can utilize a variety of techniques for disassembly, cleaning/replacement, and reassembly. Use of such techniques, and the resulting reconditioned device, are all within the scope of the present application.

Preferably, the various embodiments of the invention described herein will be processed before surgery. First, a new or used instrument is obtained and if necessary cleaned.

The instrument can then be sterilized. In one sterilization technique, the instrument is placed in a closed and sealed container, such as a plastic or TYVEK bag. The container and instrument are then placed in a field of radiation that can penetrate the container, such as gamma radiation, x-rays, or high-energy electrons. The radiation kills bacteria on the instrument and in the container. The sterilized instrument can then be stored in the sterile container. The sealed container keeps the instrument sterile until it is opened in the medical facility.

It is preferred that the device is sterilized. This can be done by any number of ways known to those skilled in the art including beta or gamma radiation, ethylene oxide, steam.

Although the various embodiments of the invention have been described herein in connection with certain disclosed embodiments, many modifications and variations to those embodiments may be implemented. For example, different types of end effectors may be employed. Also, where materials are disclosed for certain components, other materials may be used. The foregoing description and following claims are intended to cover all such modification and variations.

Any patent, publication, or other disclosure material, in whole or in part, that is said to be incorporated by reference herein is incorporated herein only to the extent that the incorporated materials does not conflict with existing definitions, statements, or other disclosure material set forth in this disclosure. As such, and to the extent necessary, the disclosure as explicitly set forth herein supersedes any conflicting material incorporated herein by reference. Any material, or portion thereof, that is said to be incorporated by reference herein, but which conflicts with existing definitions, statements, or other disclosure material set forth herein will only be incorporated to the extent that no conflict arises between that incorporated material and the existing disclosure material.

What is claimed is:

1. An ablation device, comprising:

an elongate flexible member having a proximal end and a distal end and comprising:

a first working channel formed within the flexible member;
a first diagnostic probe having a proximal end and a distal end, the first diagnostic probe located within the first working channel and extending through the distal end of the flexible member; and

a first electrode connected to the distal end of the first diagnostic probe;

wherein the first electrode is adapted to be endoscopically located in a tissue treatment region; and

wherein the first electrode is adapted to couple to an electrical waveform generator to receive an irreversible electroporation electrical waveform sufficient to ablate tissue located proximate to the first electrode;

a second working channel formed within the flexible member;

a second diagnostic probe having a proximal end and a distal end, the second diagnostic probe located within the second working channel and extending through the distal end of the flexible member; and

a second electrode connected to the distal end of the second diagnostic probe;

wherein the second electrode is adapted to be endoscopically located in a tissue treatment region;

wherein the second electrode is adapted to couple to an electrical waveform generator to receive an irreversible electroporation electrical waveform sufficient to ablate tissue located between the first and second electrodes; and

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wherein the first and second electrodes are rotatable about a central axis defined through each of the first and second diagnostic probes, wherein a distance between the first and second electrodes is adjustable by rotating either one or both of the first and second diagnostic probes. 5

2. The ablation device of claim 1, wherein the first diagnostic probe comprises a sharp distal end and an aperture in communication with a bore formed within the first diagnostic probe to receive a tissue sample therethrough.

3. The ablation device of claim 1, wherein the second diagnostic probe comprises a sharp distal end and an aperture in communication with a bore formed within the second diagnostic probe to receive a tissue sample therethrough. 10

4. The ablation device of claim 1, comprising:

at least one illuminator supported on the device and positioned to illuminate tissue; and 15
an image sensor supported on the device and positioned to image tissue therethrough.

5. An ablation system, comprising:

an ablation device comprising:

an elongate flexible member having a proximal end and a distal end and comprising:

a first working channel formed within the flexible member;
a first diagnostic probe having a proximal end and a distal end, the first diagnostic probe located within the first working channel and extending through the distal end of the flexible member; and 25

a first electrode connected to the distal end of the first diagnostic probe;

wherein the first electrode is adapted to be endoscopically located in a tissue treatment region; and 30

wherein the first electrode is adapted to receive an irreversible electroporation electrical (IRE) waveform sufficient to ablate tissue located proximate to the first electrode;

a second working channel formed within the flexible member; 35

a second diagnostic probe having a proximal end and a distal end, the second diagnostic probe located within the second working channel and extending through the distal end of the flexible member; and 40

a second electrode connected to the distal end of the second diagnostic probe;

wherein the second electrode is adapted to be endoscopically located in a tissue treatment region;

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wherein the second electrode is adapted to couple to an electrical waveform generator to receive an IRE waveform sufficient to ablate tissue located between the first and second electrodes; and

wherein the first and second electrodes are rotatable about a central axis defined through each of the first and second diagnostic probes to adjust a distance between the first and second electrodes by rotating either one or both of the first and second diagnostic probes; and

an electrical waveform generator electrically coupled to the first and second electrodes of the ablation device to generate an IRE waveform sufficient to ablate tissue located proximate to the first and second electrodes.

6. The ablation system of claim 5, wherein the first diagnostic probe comprises a sharp distal end and an aperture in communication with a bore formed within the first diagnostic probe to receive a tissue sample therethrough.

7. The ablation system of claim 5, wherein second diagnostic probe comprises a sharp distal end and an aperture in communication with a bore formed within the second diagnostic probe to receive a tissue sample therethrough. 20

8. The ablation system of claim 5, wherein the ablation device comprises at least one illuminator supported on the device and positioned to illuminate tissue; and an image sensor supported on the device and positioned to image tissue therethrough. 25

9. The ablation system of claim 8, wherein the electrical waveform generator is adapted to receive IRE electrical waveform parameters from an image processing module; wherein the IRE electrical waveform parameters are determined based on image information of the diseased tissue region in a patient. 30

10. The ablation system of claim 9, wherein the IRE electrical waveform parameters are determined based on a volume and outline of a necrotic zone required to treat the diseased tissue based on the image information. 35

11. The ablation system of claim 10, wherein the volume and outline of the necrotic zone are determined from geometric information extracted from the image information.

12. The ablation system of claim 9, wherein the IRE electrical waveform parameters comprise amplitude, frequency, and pulse width of an electrical waveform suitable to destroy the diseased tissue. 40

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摘要(译)

诸如内窥镜或腹腔镜器械的手术器械包括消融装置。消融装置包括细长柔性构件，该细长柔性构件具有近端和远端。第一工作通道形成在柔性构件内。具有近端和远端的第一诊断探针位于第一工作通道内并延伸穿过柔性构件的远端。第一电极连接到第一诊断探针电极的远端，适于内窥镜定位在组织治疗区域中。第一电极适于耦合到电波形发生器以接收足以消融位于第一电极附近的组织的不可逆电穿孔电波形。系统还包括电波形发生器，其电耦合到消融装置的第一电极以产生足以消融位于第一电极附近的组织的IRE波形。

