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(12) **United States Patent**
Long

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

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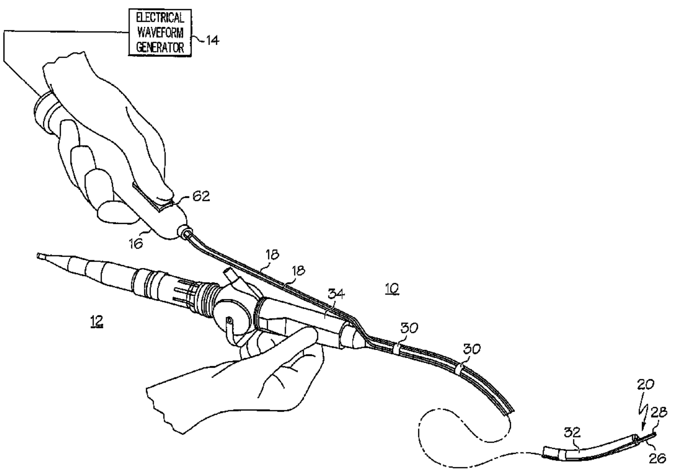
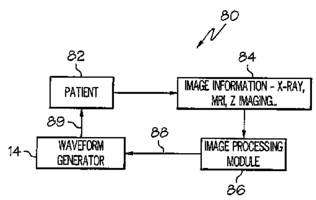
(57) **ABSTRACT**

A surgical instrument, such as an endoscopic or laparoscopic instrument, includes an ablation device. The ablation device includes an elongate relatively flexible member having a proximal end and a distal end, the flexible member includes at least a first working channel. A first and second electrode extends from a working channel at the distal end of the flexible member. The first and second electrodes are adapted to be endoscopically located in a tissue treatment region. The first and second electrodes are 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. The waveform parameters of the irreversible electroporation electrical waveform are determined based on image information received from the tissue treatment region.

19 Claims, 12 Drawing Sheets





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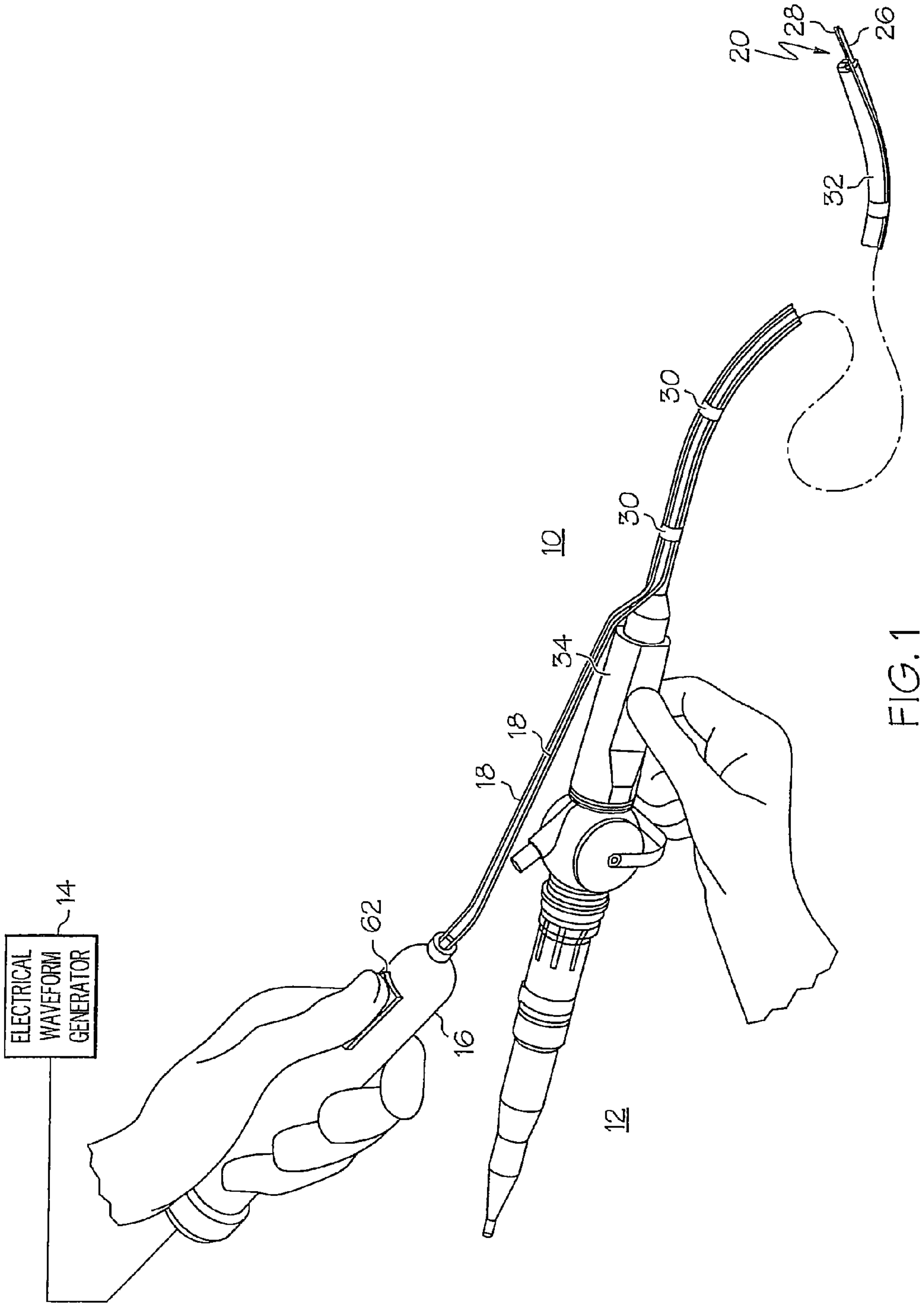
20
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32
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62
14
ELECTRICAL WAVEFORM GENERATOR
16
12

FIG. 1

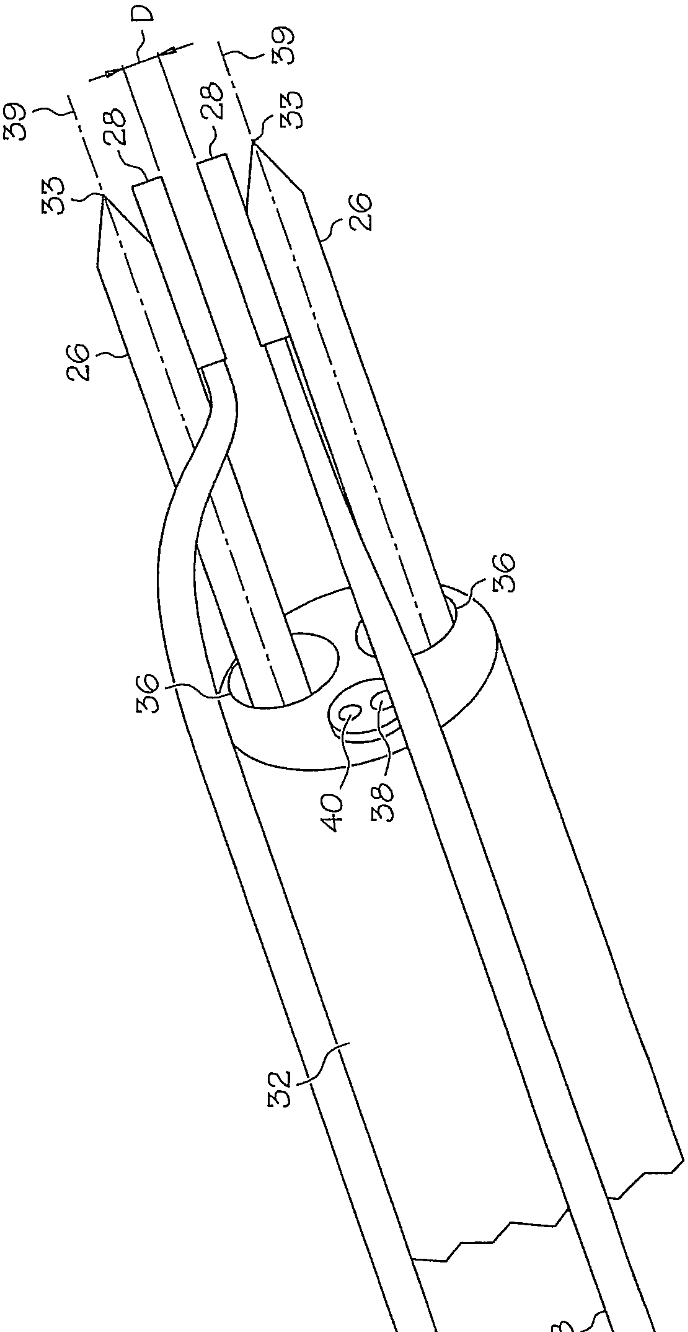


FIG. 2

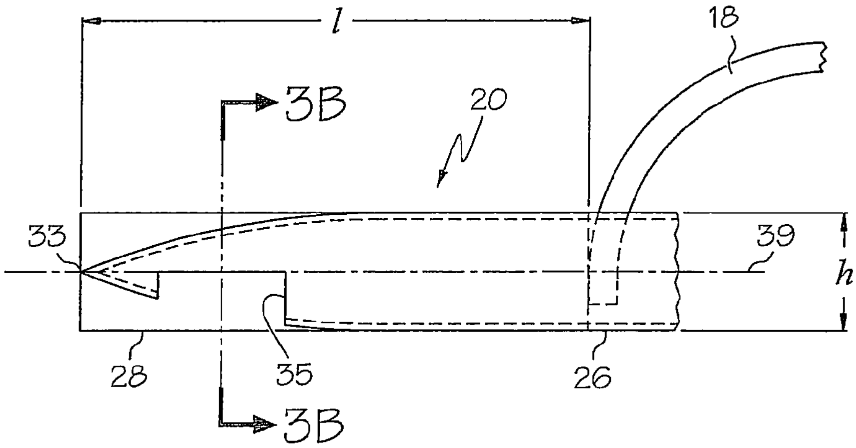


FIG. 3A

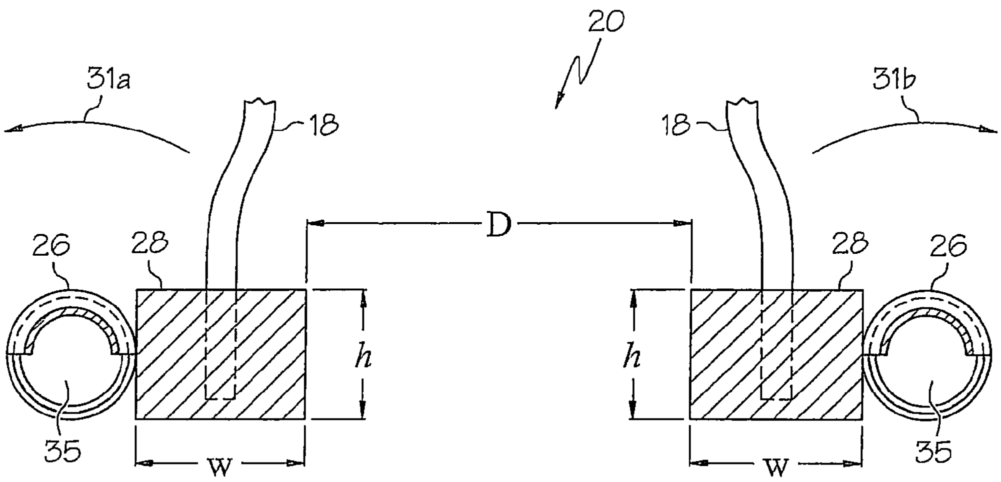


FIG. 3B

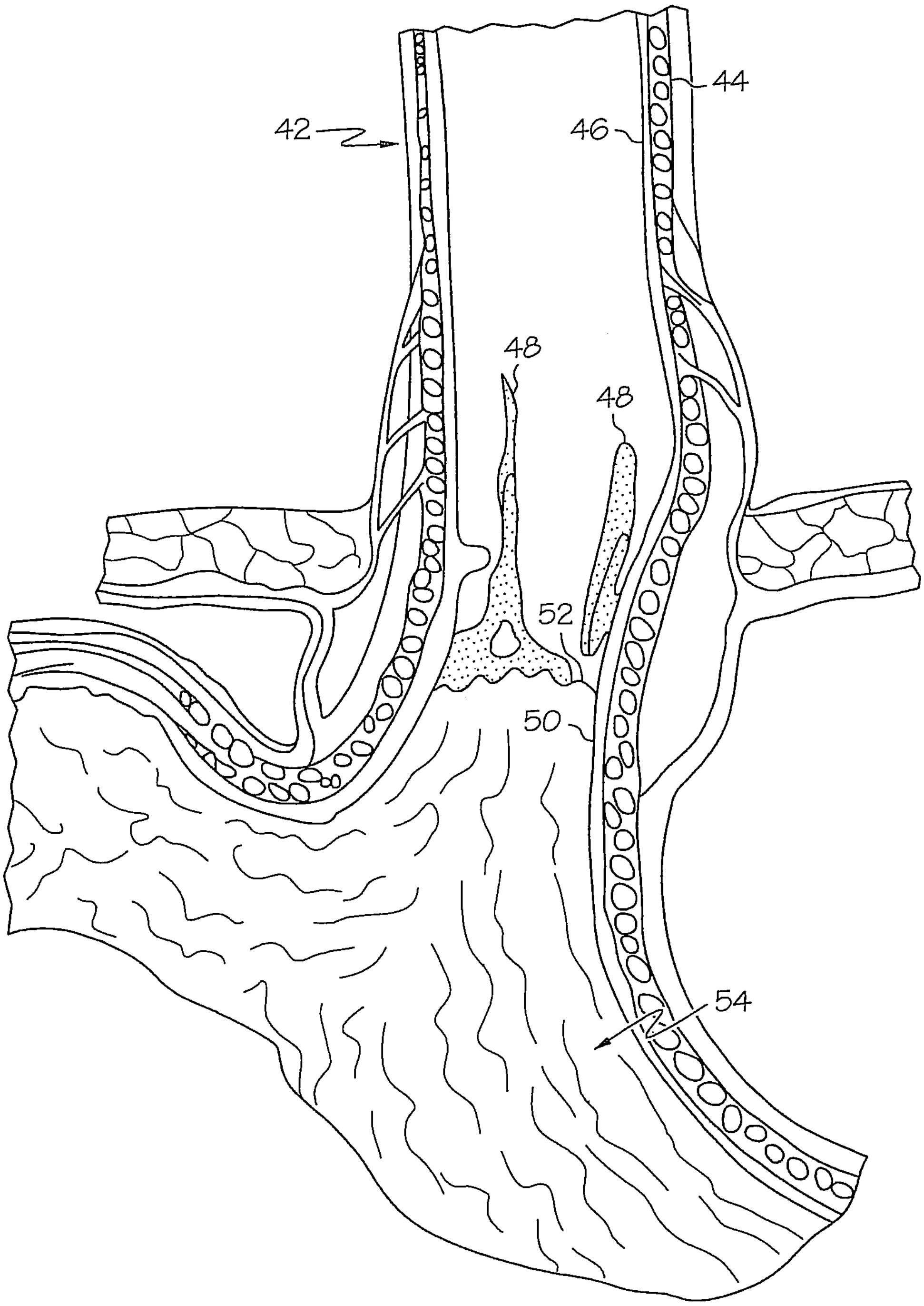


FIG. 4

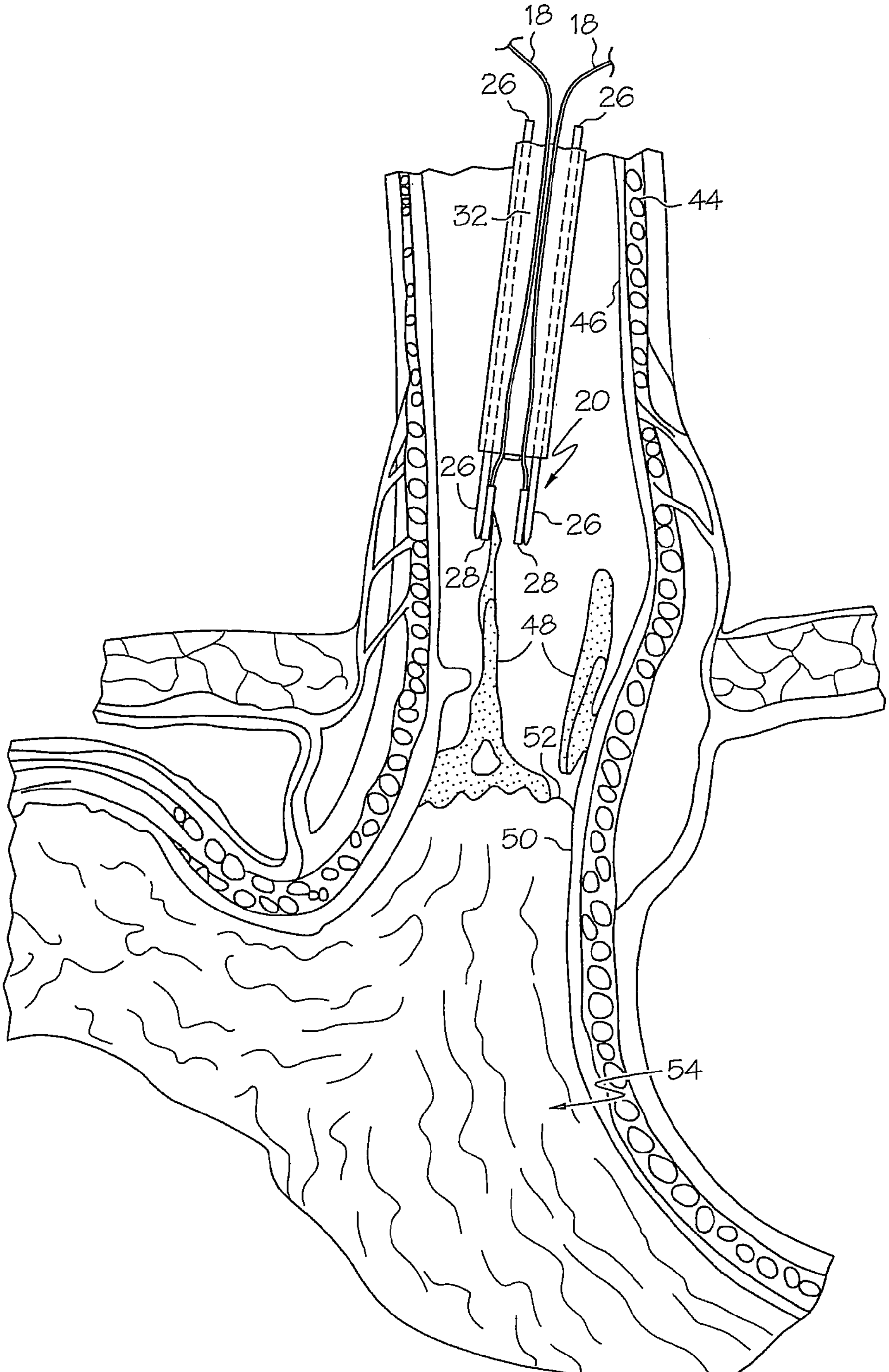


FIG. 5

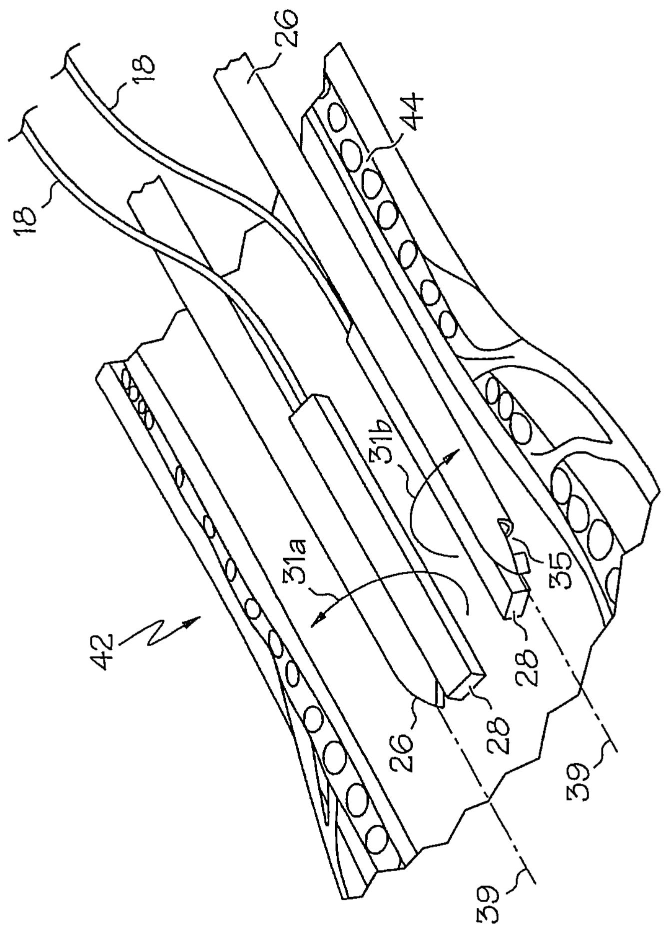


FIG. 6

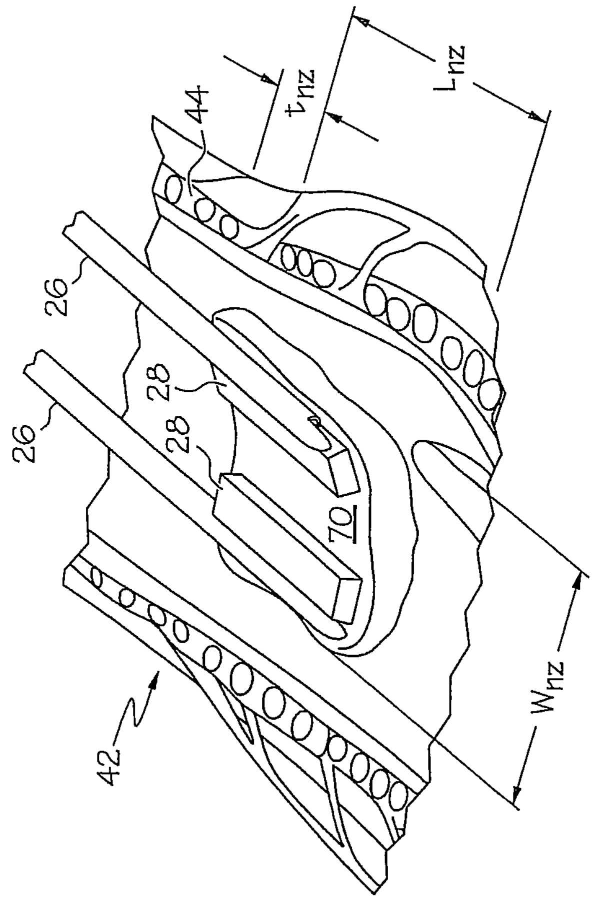


FIG. 7

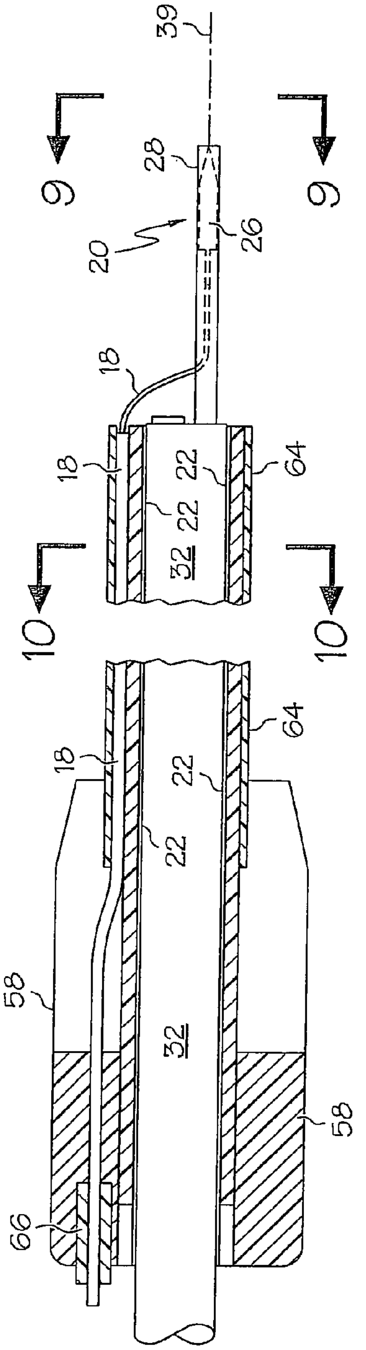


FIG. 8

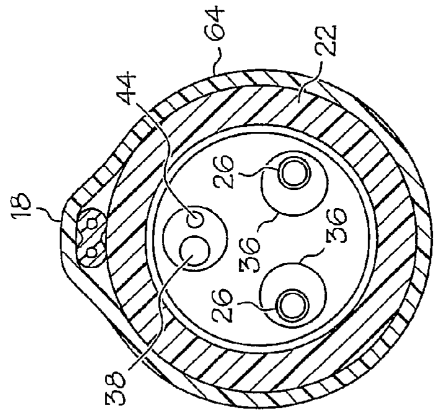


FIG. 10

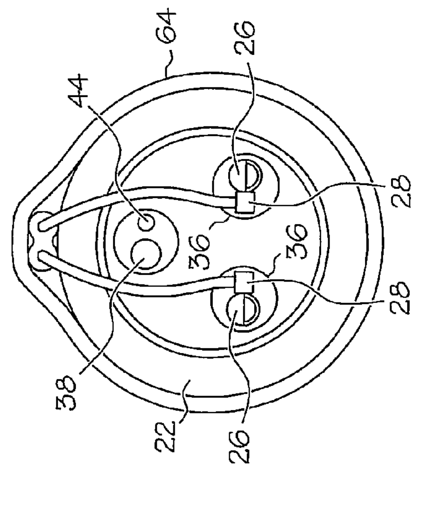


FIG. 9

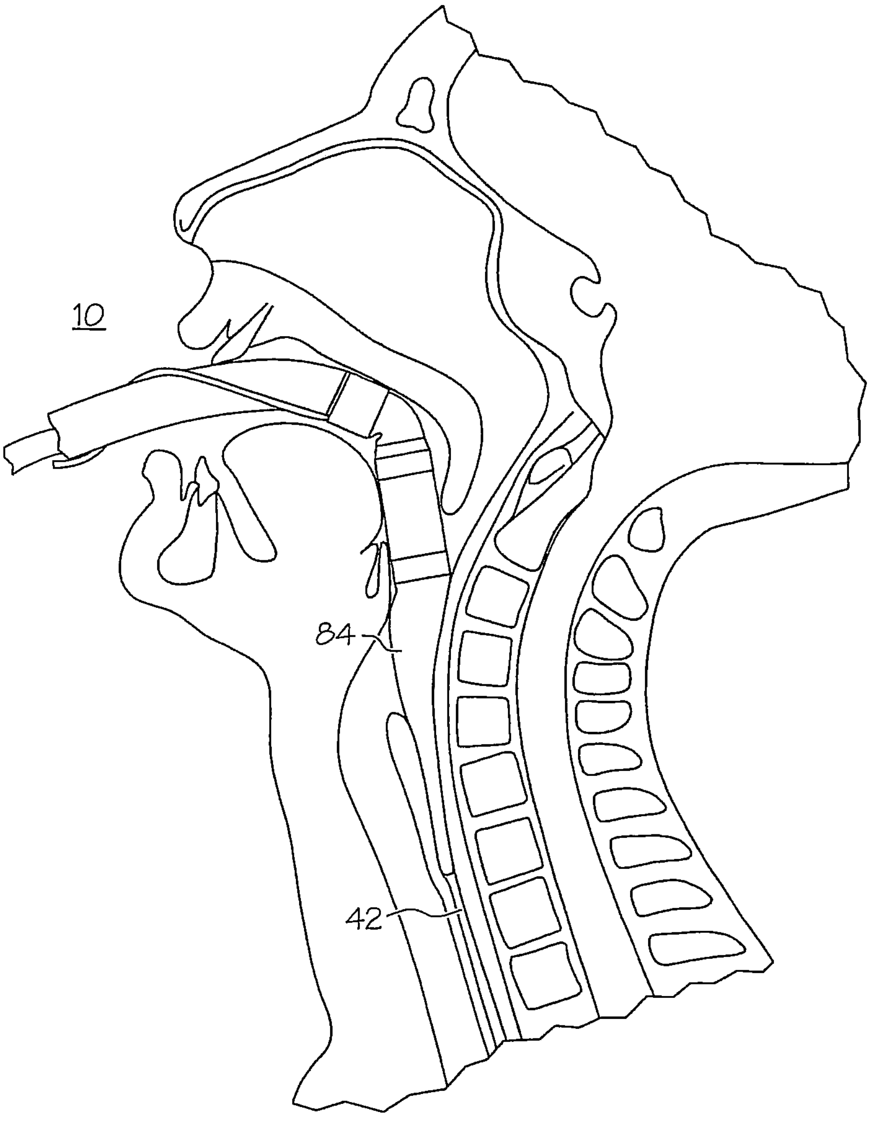
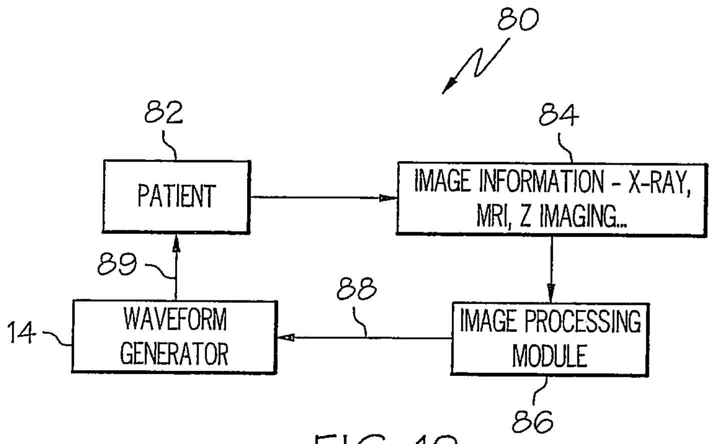


FIG. 11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82
PATIENT
84
IMAGE INFORMATION - X-RAY, MRI, Z IMAGING...
89
14
WAVEFORM GENERATOR
88
IMAGE PROCESSING MODULE
86

FIG. 12

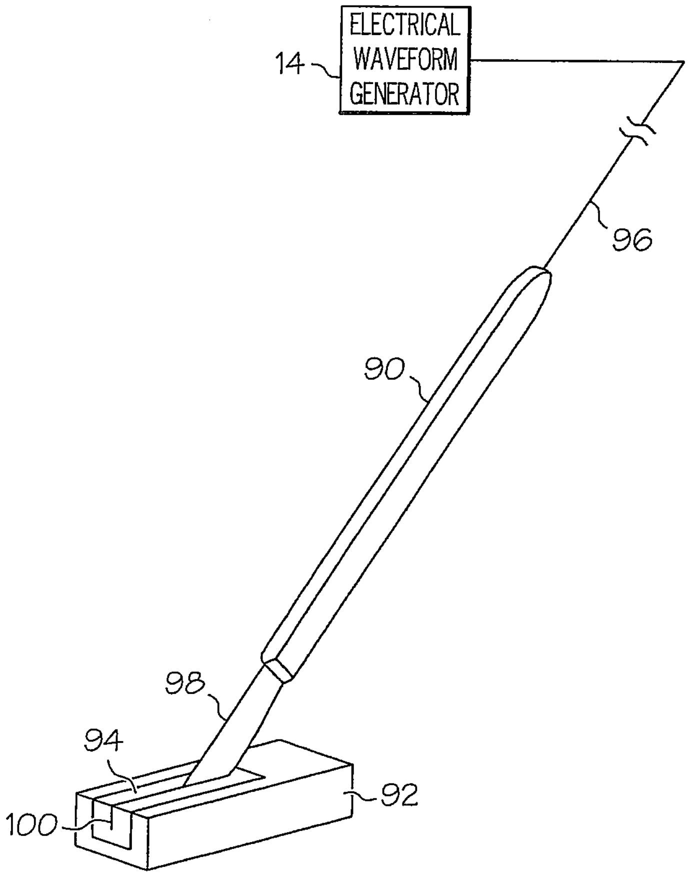
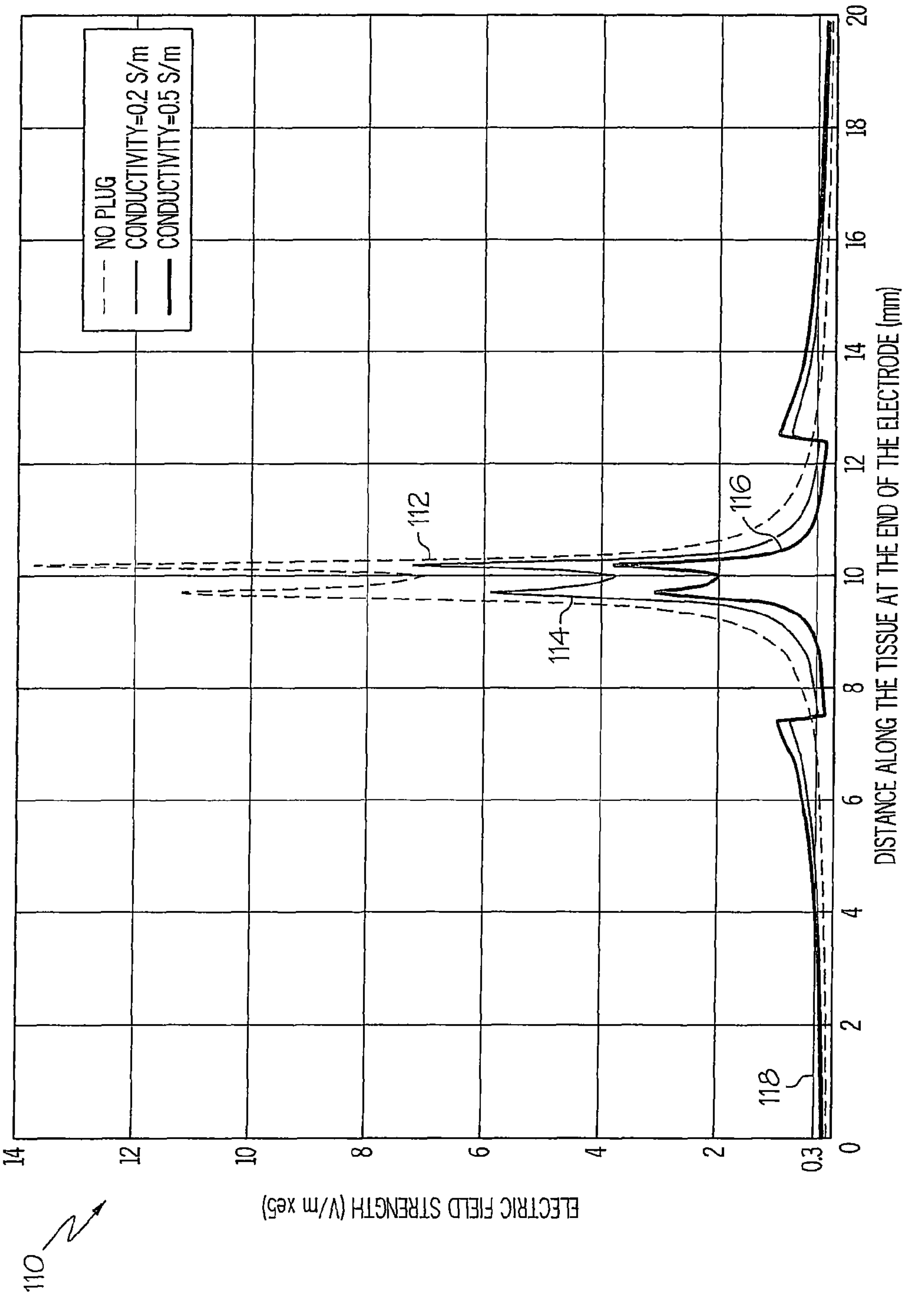
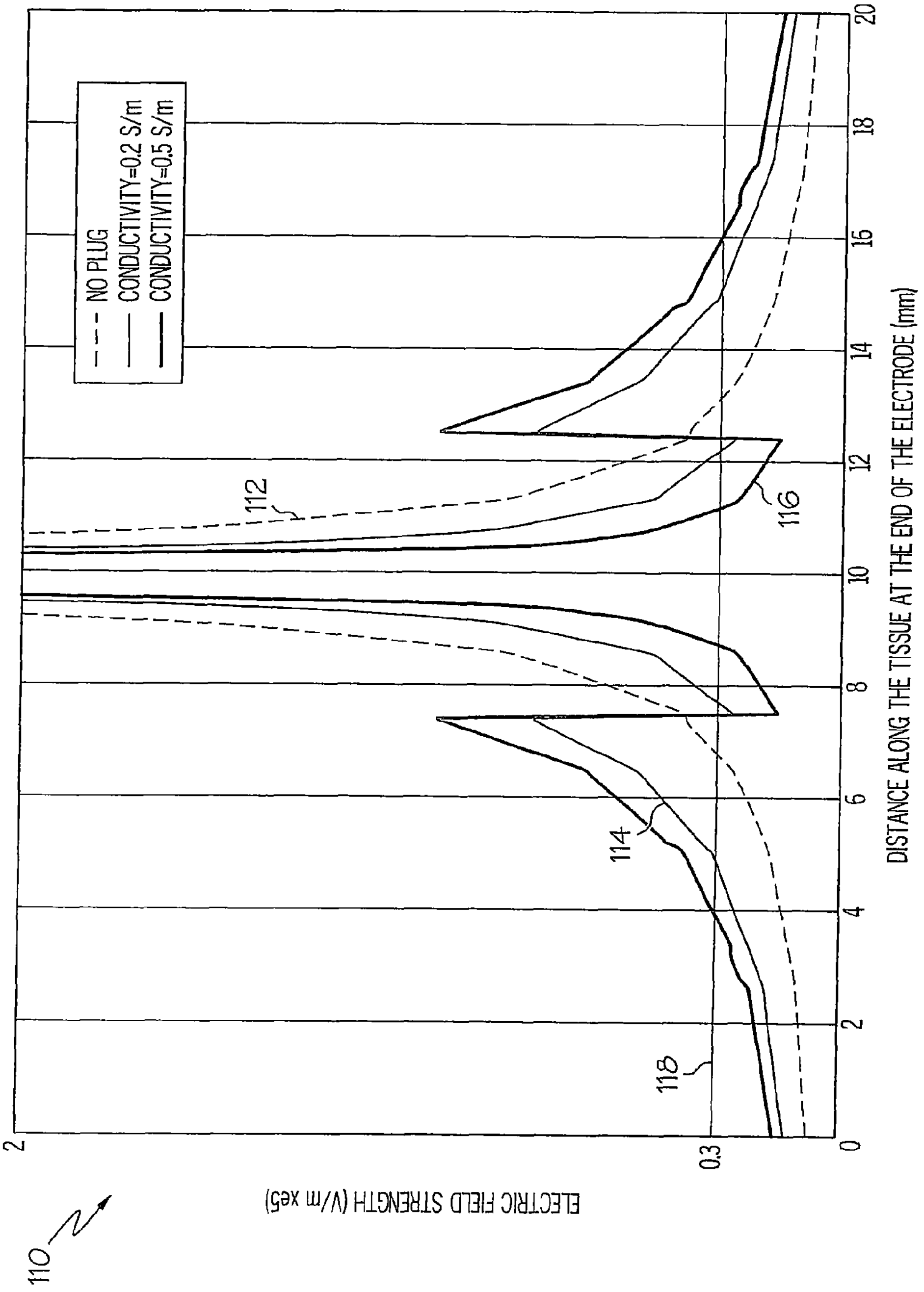

14
ELECTRICAL WAVEFORM GENERATOR
96
90
98
94
100
92

FIG. 13



NO PLUG
CONDUCTIVITY=0.2 S/m
CONDUCTIVITY=0.5 S/m
ELECTRIC FIELD STRENGTH (V/m xe5)
DISTANCE ALONG THE TISSUE AT THE END OF THE ELECTRODE (mm)
0.3
2
4
6
8
10
12
14
0
2
4
6
8
10
12
14
16
18
20
110
112
114
116
118

FIG. 14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0.3
0
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CONDUCTIVITY=0.2 S/m
CONDUCTIVITY=0.5 S/m
112
114
116
118
0
2
4
6
8
10
12
14
16
18
20
DISTANCE ALONG THE TISSUE AT THE END OF THE ELECTRODE (mm)

FIG. 15

ELECTROPORATION ABLATION APPARATUS, SYSTEM, AND METHOD

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a divisional application, under 35 U.S.C. §121, of U.S. patent application Ser. No. 11/706,766, filed Feb. 15, 2007, entitled ELECTROPORATION ABLATION APPARATUS, SYSTEM, AND METHOD, now U.S. Pat. No. 7,655,004, which is related to U.S. patent application Ser. No. 12/635,298, filed Dec. 10, 2009, entitled ELECTROPORATION ABLATION APPARATUS, SYSTEM, AND METHOD, now U.S. Pat. No. 8,029,504 and U.S. patent application Ser. No. 11/706,591, filed Feb. 15, 2007, entitled ELECTRICAL ABLATION APPARATUS, SYSTEM, AND METHOD, now U.S. patent. application Publication No. 2008/0200911, each of which is incorporated herein by reference in its entirety.

BACKGROUND

Electrical therapy techniques have been employed in medicine 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 another general aspect, the various embodiments are directed to a method comprising receiving image information of a diseased tissue region in a patient, determining a volume and outline of a necrotic zone required to treat the diseased tissue based on the image information. Waveform parameters to be generated by an electrical waveform generator suitable to destroy the diseased tissue located between first and second electrodes are determined. The first and second electrodes are adapted to couple to the electrical waveform generator to receive an irreversible electroporation electrical waveform sufficient to ablate tissue located between the first and second electrodes.

In yet another general aspect, the various embodiments are directed to an ablation system. In one embodiment, the ablation system comprises an elongate member having a proximal end and a distal end, and comprising first and second working channels formed within the flexible member. The ablation system may comprises a first electrode extending from the first working channel at the distal end of the flexible member, and second electrode extending from the second working channel, the first and second electrodes are adapted to be endoscopically located in a diseased tissue region. In one embodiment, the ablation system comprises an image processing module and an electrical waveform generator electrically coupled to the first and second electrodes and the image processing module, to generate an irreversible electroporation electrical (IRE) waveform based on waveform parameters, where the IRE waveform is sufficient to ablate tissue

located between the first and second electrodes, where the electrical waveform generator is adapted to receive the waveform parameters from the image processing module, and where the waveform parameters are determined based on image information of the diseased tissue region in a patient.

In another general aspect, the various embodiments are directed to a method comprising receiving first image information of a diseased tissue in a patient and creating a virtual model of the diseased tissue. A first size of a necrotic zone required to treat the diseased tissue based on the first image information is determined. A first set of waveform parameters of an irreversible electroporation electrical waveform to be generated by an electrical waveform generator suitable to destroy the diseased tissue located between first and second electrodes is determined. The first and second electrodes are adapted to couple to the electrical waveform generator to receive the irreversible electroporation electrical waveform.

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 ablation system.

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

FIG. **3**A 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. **3**B is a sectional view of one embodiment of a therapeutic/diagnostic probe taken along section line **3**B-**3**B showing the geometric relationship between the electrodes and the diagnostic probes.

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 endoscopic ablation system to treat diseased tissue in the lower esophagus.

FIG. **6** illustrates the use of one embodiment of an endoscopic 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 embodiment 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 diagnostic 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 endoscopically. 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 current 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, legions, 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)™.

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 ostepathologies 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 trans-anally 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 though 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. **3**A, 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. **3**A, 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. **3**A is a side view of the distal end of one embodiment of the therapeutic/diagnostic probe **20** comprising a biopsy probe **26** and an electrical therapy electrode **28** assembly. FIG. **3**B is a sectional view of one embodiment of a therapeutic/diagnostic probe **20** taken along section line **3**B-**3**B showing the geometric relationship between the electrodes **28** and the diagnostic probes **26**. In the embodiment illustrated in FIGS. **3**A, 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 **31***a* and **31***b*.

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 **31***a* and **31***b*. 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. **3**A, 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 they 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 Multiphysics 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. **14**A. 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. A method comprising:

receiving image information of a diseased tissue region in a patient;

determining a volume and outline of a necrotic zone required to treat the diseased tissue based on the image information;

displaying an image of a virtual model of the diseased tissue on a monitor;

displaying an image of the diseased tissue based on the image information overlaid with the image of the virtual model of the diseased tissue;

determining waveform parameters to be generated by an electrical waveform generator suitable to destroy the diseased tissue located between first and second electrodes wherein the first and second electrodes are adapted to couple to the electrical waveform generator to receive an irreversible electroporation electrical waveform sufficient to ablate tissue located between the first and second electrodes; and

determining whether the generated waveform parameters are suitable to destroy the diseased tissue based on the image of the diseased tissue overlaid on the image of the virtual model.

2. The method of claim **1**, comprising:

extracting geometric information from the image information; and

determining the volume and outline of the necrotic zone required to treat the diseased tissue based on the geometric information.

3. The method of claim **1**, comprising:

providing the waveform parameters to an electrical waveform generator.

4. The method of claim **1**, comprising:

determining amplitude, frequency, and pulse width waveform parameters suitable to destroy the diseased tissue.

5. An ablation system comprising:

an elongate member having a proximal end and a distal end, and comprising first and second working channels formed within the elongate member;

a first electrode extending from the first working channel at the distal end of the flexible member, and second electrode extending from the second working channel, the first and second electrodes are adapted to be endoscopically located in a diseased tissue region;

an image processing module configured to receive image information and a virtual model of the diseased tissue region and to display an image of the diseased tissue region overlaid with an image of the virtual model on a monitor;

an electrical waveform generator electrically coupled to the first and second electrodes and the image processing module, to generate an irreversible electroporation electrical (IRE) waveform based on waveform parameters, wherein the IRE waveform is sufficient to ablate tissue located between the first and second electrodes, wherein the electrical waveform generator is adapted to receive the waveform parameters from the image processing module, and wherein the waveform parameters are determined based on image information of the diseased tissue region in a patient overlaid with the image of the virtual model.

6. The ablation system of claim **5**, wherein the waveform parameters are determined based on a volume and outline of a necrotic zone required to treat diseased tissue in the diseased tissue region based on the image information.

7. The ablation system of claim **5**, wherein the volume and outline of the necrotic zone are determined from geometric information extracted from the image information.

8. The ablation system of claim **5**, wherein the waveform parameters comprise amplitude, frequency, and pulse width of an electrical waveform suitable to destroy the diseased tissue.

9. The ablation system of claim **5**, comprising: an image sensor coupled to the image processing module and positioned to image tissue therethrough.

10. The ablation system of claim **9**, comprising: at least one illuminator positioned to illuminate tissue.

11. The ablation system of claim **5**, comprising:

first and second probes disposed within the respective first and second channels, the first and second probes each defining a central axis;

wherein the first and second electrodes are coupled to distal ends of the respective first and second probes;

wherein a distance between the first and second electrodes is adjustable by rotating at least one of the first and second probes about the central axis of the at least one of the first and second probes.

12. The ablation system of claim **5**, wherein the elongate member is flexible.

13. A method comprising:

receiving first image information of a diseased tissue in a patient;

creating a virtual model of the diseased tissue;

displaying an image of the virtual model of the diseased tissue on a monitor;

displaying an image of the diseased tissue based on the first image information overlaid with the image of the virtual model of the diseased tissue;

determining a first size of a necrotic zone required to treat the diseased tissue based on the first image information; and

determining a first set of waveform parameters of an irreversible electroporation electrical (IRE) waveform based on the image of the diseased tissue overlaid with the image of the virtual model of the diseased tissue to be generated by an electrical waveform generator suitable to be generated by an electrical waveform generator suitable to destroy the diseased tissue located between first and second electrodes wherein the first and second electrodes are adapted to couple to the electrical waveform generator to receive the irreversible electroporation electrical waveform.

14. The method of claim **13**, comprising:

extracting geometric information from the first image information; and

determining the first size of the necrotic zone required to treat the diseased tissue based on the geometric information.

15. The method of claim **13**, comprising:

providing the first set of waveform parameters to an electrical waveform generator.

16. The method of claim **13**, comprising:

determining amplitude, frequency, and pulse width waveform parameters suitable to destroy the diseased tissue.

17. The method of claim **13**, comprising:

after treating the diseased tissue with the IRE waveform, receiving second image information of the diseased tissue.

18. The method of claim **17**, comprising:

determining a second size of the necrotic zone required to treat the diseased tissue based on the second image information.

19. The method of claim **18**, comprising:

determining a second set of waveform parameters to be generated by an electrical waveform generator suitable to destroy the diseased tissue located between first and second electrodes.

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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。消融装置包括细长的相对柔性的构件，该构件具有近端和远端，柔性构件包括至少第一工作通道。第一和第二电极从柔性构件的远端处的工作通道延伸。第一和第二电极适于内窥镜定位在组织治疗区域中。第一和第二电极适于耦合到电波形发生器，以接收足以消融位于第一和第二电极之间的组织的不可逆电穿孔电波形。基于从组织治疗区域接收的图像信息确定不可逆电穿孔电波形的波形参数。