



US00RE42016E

(19) **United States**  
(12) **Reissued Patent**  
**Chornenky et al.**

(10) **Patent Number:** **US RE42,016 E**  
(45) **Date of Reissued Patent:** **Dec. 28, 2010**

(54) **APPARATUS AND METHOD FOR THE TREATMENT OF BENIGN PROSTATIC HYPERPLASIA**

(75) Inventors: **Victor I. Chornenky**, Minnetonka, MN (US); **Ali Jaafar**, Eden Prairie, MN (US)

(73) Assignee: **AngioDynamics, Inc.**, Latham, NY (US)

(21) Appl. No.: **12/572,047**

(22) Filed: **Oct. 1, 2009**

**Related U.S. Patent Documents**

Reissue of:

(64) Patent No.: **7,130,697**  
Issued: **Oct. 31, 2006**  
Appl. No.: **10/668,775**  
Filed: **Sep. 23, 2003**

U.S. Applications:

(63) Continuation-in-part of application No. 10/217,749, filed on Aug. 13, 2002, now Pat. No. 6,994,706.

(60) Provisional application No. 60/412,705, filed on Sep. 23, 2002, provisional application No. 60/325,994, filed on Oct. 1, 2001, and provisional application No. 60/311,792, filed on Aug. 13, 2001.

(51) **Int. Cl.**  
**A61F 2/00** (2006.01)  
**A61B 18/18** (2006.01)

(52) **U.S. Cl.** ..... **607/101; 606/41; 607/116**

(58) **Field of Classification Search** ..... **606/27-31, 606/41, 47-50; 607/101, 102, 115, 116, 143; 604/22**

See application file for complete search history.

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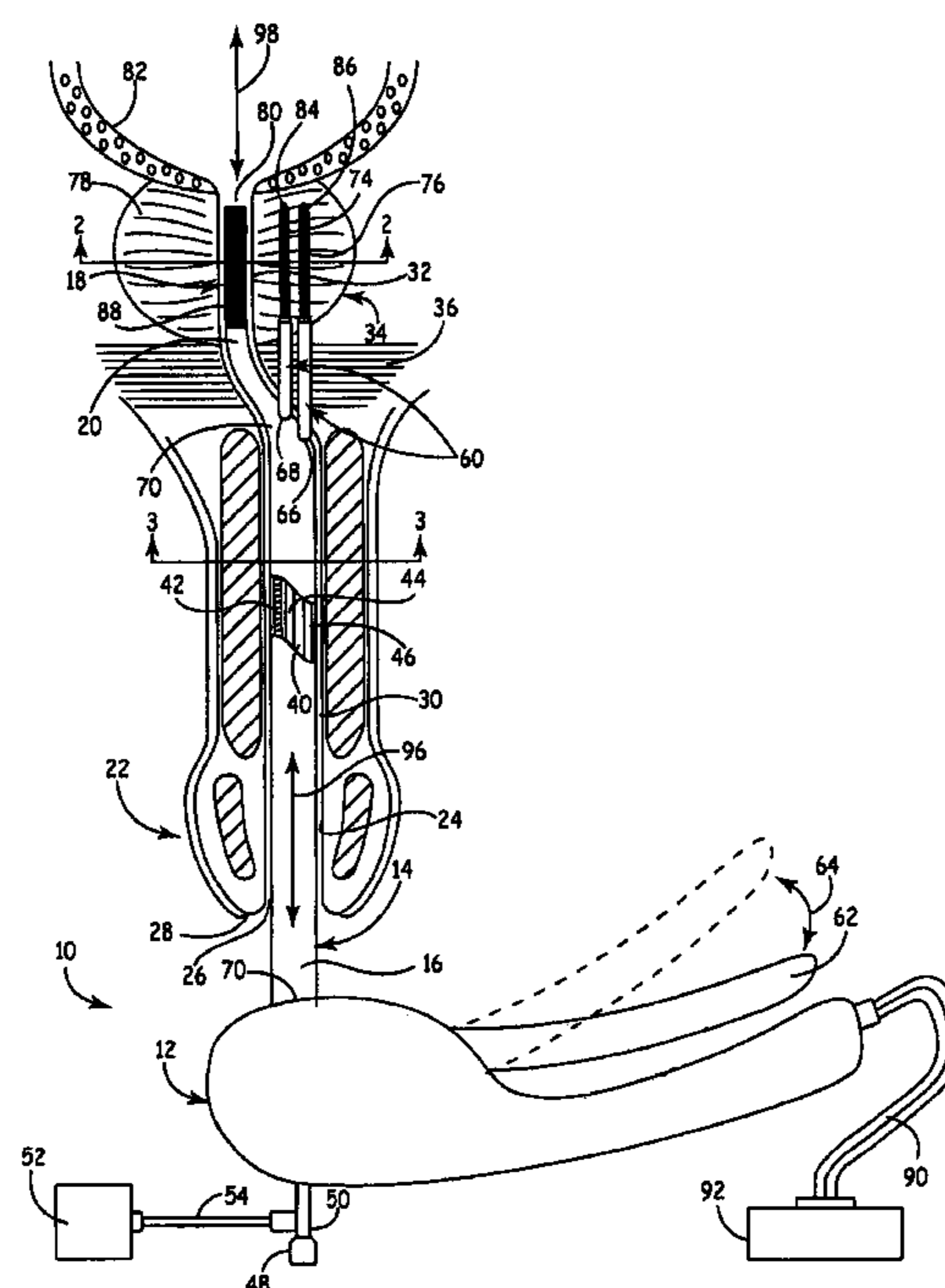
*Primary Examiner*—Michael Peffley

(74) *Attorney, Agent, or Firm*—Harry K. Ahn; Abelman Frayne & Schwab

(57) **ABSTRACT**

An apparatus and method for treatment of benign prostatic hyperplasia is disclosed wherein the apparatus includes an applicator having a probe having proximal and distal probe sections wherein the proximal and distal probe sections each define an axis and wherein the axes are not collinear.

**16 Claims, 2 Drawing Sheets**



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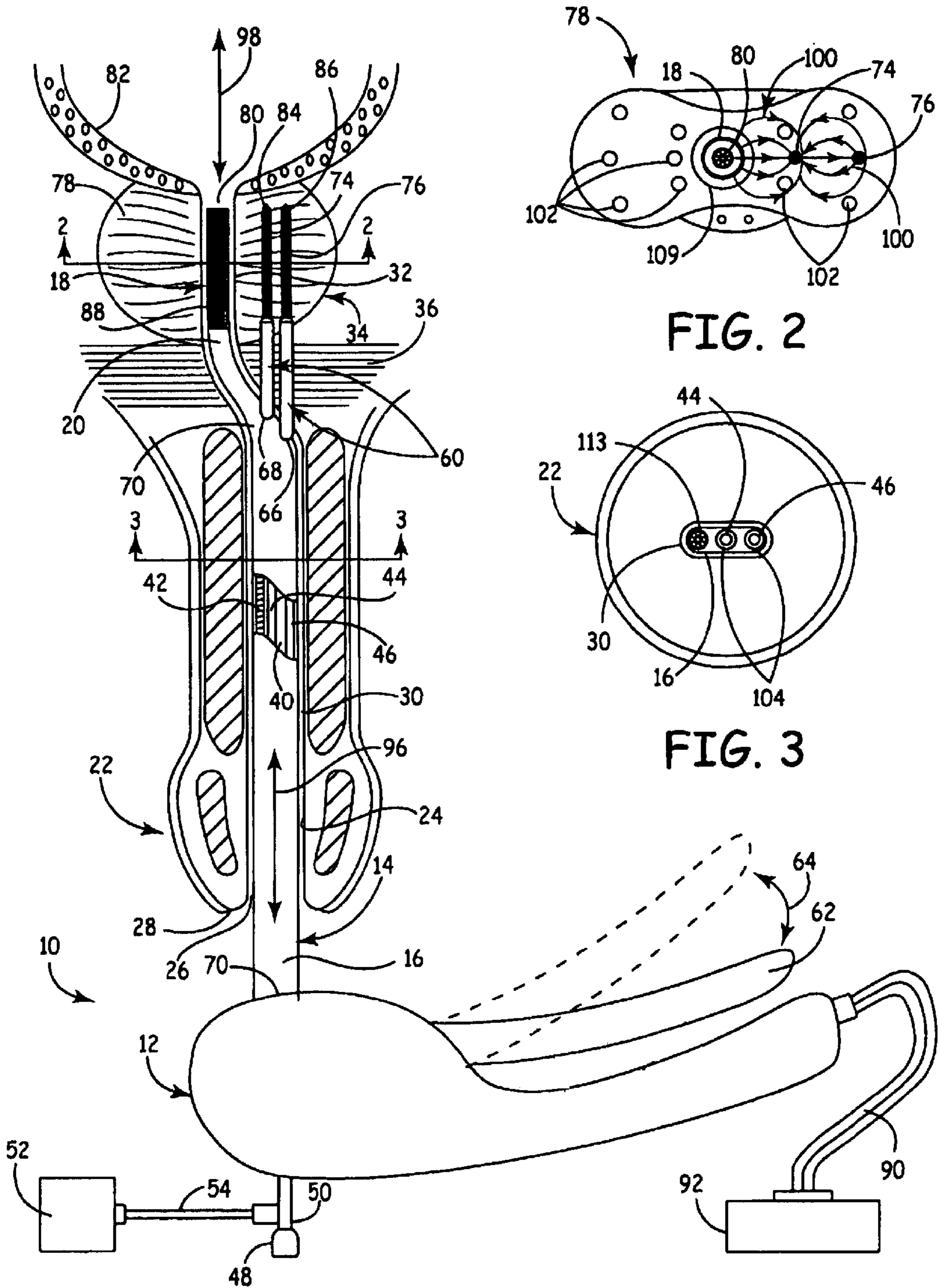


FIG. 1

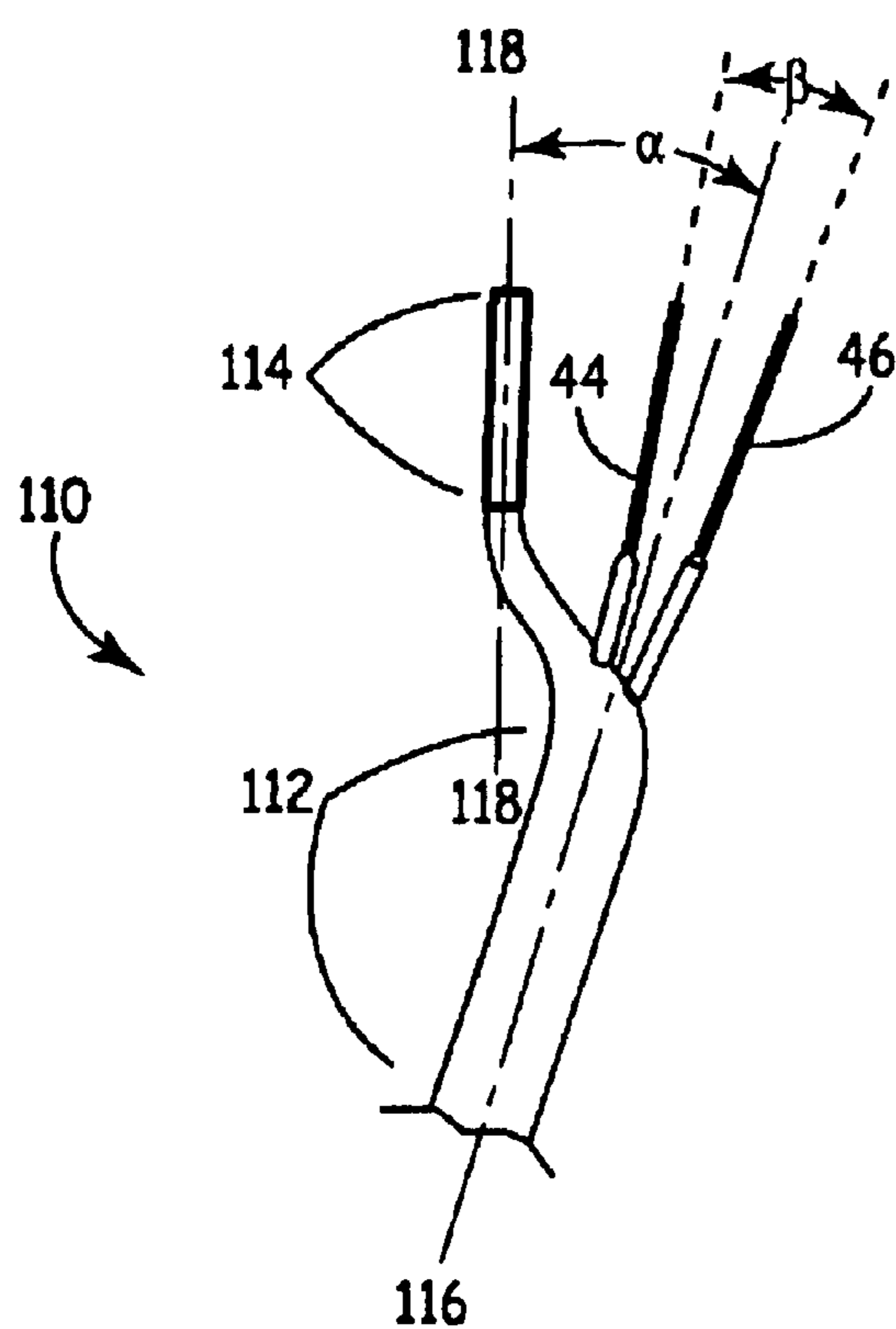


FIG. 4

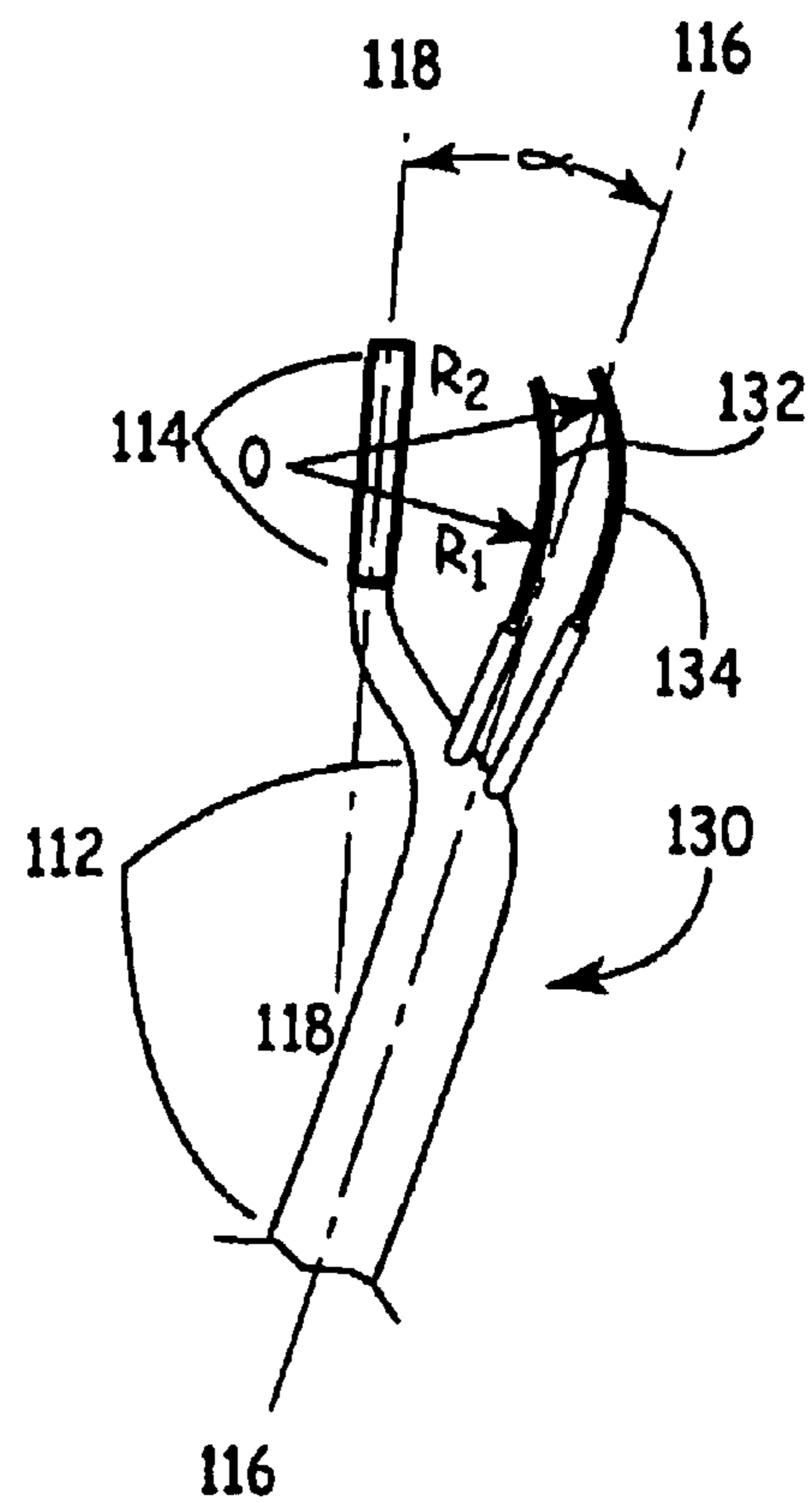


FIG. 5

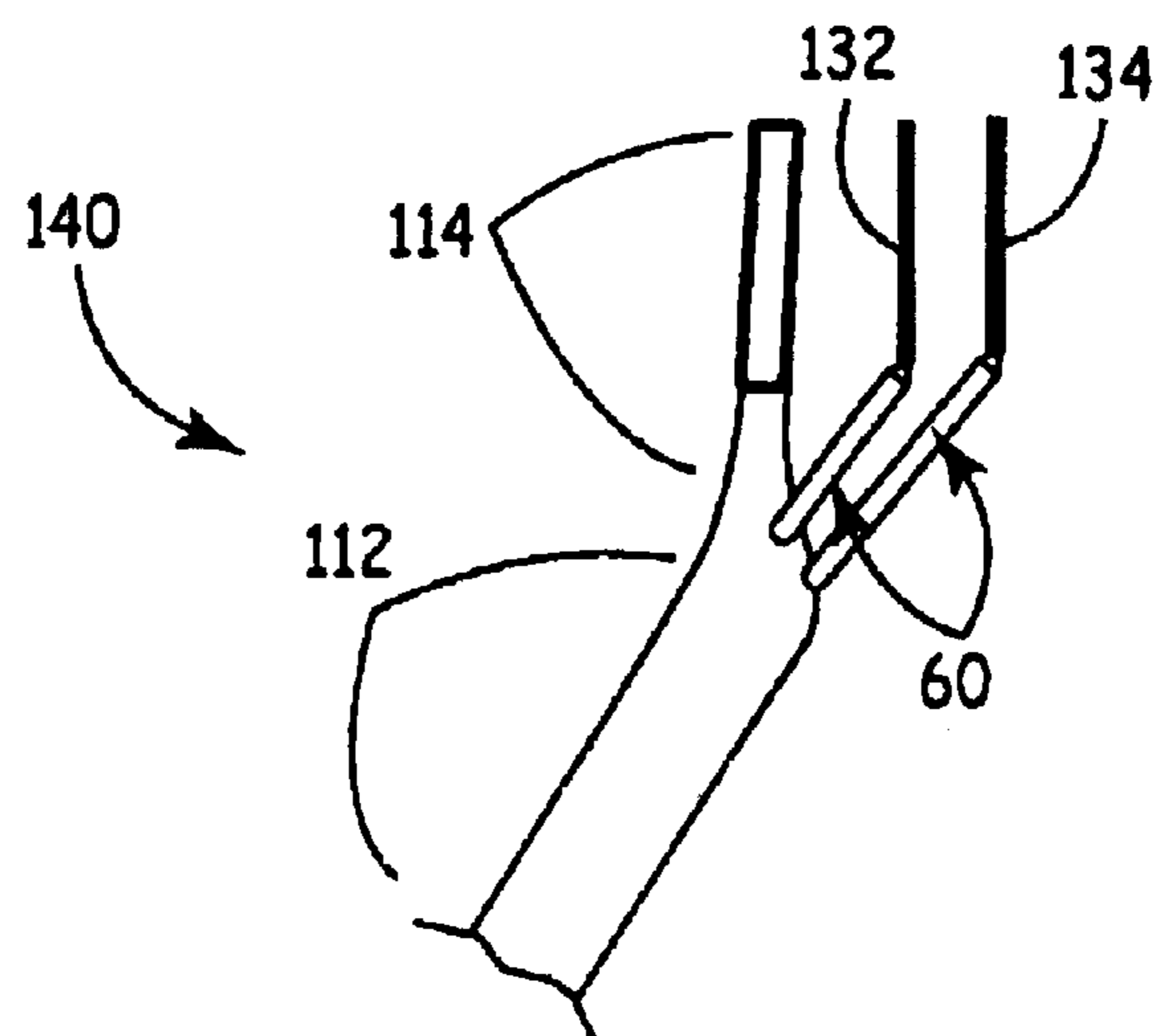


FIG. 6

## APPARATUS AND METHOD FOR THE TREATMENT OF BENIGN PROSTATIC HYPERPLASIA

**Matter enclosed in heavy brackets [ ] appears in the original patent but forms no part of this reissue specification; matter printed in italics indicates the additions made by reissue.**

### CROSS-REFERENCE TO RELATED APPLICATIONS

The present application claims priority to U.S. Provisional Application No. 60/412,705 entitled "Apparatus and method for treatment of benign prostatic hyperplasia by electroporation", which was filed Sep. 23, 2002. This application is a continuation-in-part of U.S. patent application Ser. No. 10/217,749 entitled "Apparatus and method for treatment of benign prostatic hyperplasia by electroporation", which was filed Aug. 13, 2002 (U.S. Patent Application Publication 2003/0060856, published Mar. 27, 2003) now U.S. Pat. No. 6,994,706, *which claims the benefit of U.S. Provisional Application Ser. No. 60/325,994 filed Oct. 1, 2001 and U.S. Provisional Application Ser. No. 60/311,792, filed Aug. 13, 2001.*

### BACKGROUND OF THE INVENTION

#### 1. Field of the Invention

The present invention relates generally to methods and apparatus for the electroporation of tissues and more specifically to such methods and apparatus for the treatment of benign prostatic hyperplasia.

#### 2. Description of the Related Art

Though greater detail will follow in the discussion below, succinctly stated, the present invention provides apparatus and methods of providing treatment for the undesirable proliferation of cells in the prostate by killing the cells with electric field pulses of selected duration and strength to take advantage of a cellular event known as "electroporation."

#### Electroporation

The biophysical phenomenon known as electroporation refers to the use of electric field pulses to induce microscopic pores—"electropores"—in the lipid cell membranes. Depending on the parameters of the electric pulses, an electroporated cell can survive the pulsing or die. The cause of death of an electroporated cell is believed to be a chemical imbalance in the cell, resulting from the fluid communication with the extra-cellular environment through the pores. For a given cell size, geometry, and orientation, the number of electropores—and their size created in the cell by the applied electric field pulses depends on both the amplitude  $E$  of the electric field pulses and the duration  $t$  of the pulses. That is, for a given pulse duration  $t$ , no pores will be induced in the cell until the amplitude  $E$  reaches a certain lower limit. This limit is different for different cells, particularly, for cells of different sizes. The smaller the size of a cell, the higher the electric field required to induce pores and thus the higher the lower limit is. Above the lower amplitude  $E$  limit the number of pores and their effective diameter increases proportionally with both increasing field amplitude  $E$  and pulse duration  $t$ . Electroporation is observed for pulse durations in the range from tens of microseconds to hundreds of milliseconds.

Until the upper limit of electroporation is achieved, an electroporated cell can survive the pulsing and restore its viability thereafter. Above the upper limit the pore diameters

and number of induced pores become too large for a cell to survive. The irreversibly chemically imbalanced cell cannot repair itself by any spontaneous or biological process and dies. To kill a cell a potential in the range of 2 to 4 V should be applied along the cell. The cell killing by electroporation is a probabilistic process. That is, increasing the number of applied pulses of duration  $t$  leads to an increased probability of cell killing, a probability increase that is approximately equal to the percentage increase in the total time duration of the applied electric pulses.

The survivability of electroporated cells depends significantly on their temperature. At higher temperature cells are more vulnerable to cell death by electroporation. Thus, the amplitude and duration of the electric pulses required for cell killing are lower. It is believed that this observation is explained by two underlying phenomena: at higher temperatures cells are less stable biochemically because of more intense metabolic activity; and, secondly, at elevated temperatures the strength of lipid membranes decreases, which facilitates creating larger pores or irreversible rupture of the cell membrane. At lower temperatures (about 10 to about 20 degrees Celsius) cells are more resistant to electroporation and can survive two to three times higher voltages than they can at body temperature.

#### The Prostate Gland and Benign Prostatic Hyperplasia

The prostate gland forms part of the male reproductive system. The prostate gland is located between the bladder and the rectum and wraps around the urethra, the tube that carries urine out from the bladder through the penis. The gland consists a dense fibrous capsule enclosing several lobes or regions. The prostate gland is generally composed of smooth muscles and glandular epithelial tissue. The glandular epithelial tissue produces prostatic fluid. The smooth muscles contract during sexual climax and squeeze the prostatic fluid into the urethra as the sperm passes through the ejaculatory ducts and urethra. Prostatic fluid secreted by the prostate gland provides nutrition for ejaculated spermatozooids increasing their mobility and improves the spermatozooids chances for survival after ejaculation by making the environment in the vaginal canal less acidic.

Anatomically, the prostate gland is usually described as including three glandular zones: the central, peripheral and transitional zones. The transitional zone is located right behind the place where the seminal vesicles merge with the urethra. This transitional zone tends to be predisposed to benign enlargement in later life.

The prostate reaches its normal size and weight (about 20 grams) soon after puberty. The size and weight of the prostate typically remain stable until the individual reaches his mid-forties. At this age, the prostate gland—typically in the transitional zone—begins to enlarge through a process of excessive cell proliferation known as benign prostatic hyperplasia (BPH). This overgrowth can occur in both smooth muscle and glandular epithelial tissues and has been attributed to a number of different causes, including hormones and growth factors as well as generally to the aging process.

Benign prostate hyperplasia can cause distressing urination symptoms. As the disease progresses the dense capsule surrounding the enlarging prostate prevents it from further expansion outward and forces the prostate to press against the urethra, partially obstructing the urine flow. The tension in the smooth muscles of the prostate also increases which causes further compression of the urethra and reduction of the urine flow. Some symptoms of BPH stem from the gradual loss of bladder function leading to an incomplete emptying of the bladder. The symptoms can include strain-

ing to urinate, a weak or intermittent stream, an increased frequency of urination, pain during urination, and incontinence—the involuntary loss of urine following an uncontrollable sense of urgency. These symptoms alone can negatively affect the quality of life of affected men. Left untreated, BPH can cause even more severe complications, such as urinary tract infection, acute urinary retention, and uremia.

Before age 40, only 10% of men have benign prostatic hyperplasia; but by age 80, about 80% have signs of this condition. Benign prostatic hyperplasia is the most common non-cancerous form of cell growth in men. About 14 million men in US have BPH, and about 375,000 new patients are diagnosed every year.

For many years, researchers have tried to find medications to shrink the prostate or at least stop its growth. Between 1992 and 1997, the FDA approved four drugs for treatment of BPH: finasteride, terazosin, tamsulosin, and doxazosin.

Finasteride inhibits production of hormone DHT. DHT is one of the hormones that have been found to be involved in prostate enlargement. Treatment with Finasteride has been shown to shrink the prostate in some men.

Terazosin, doxazosin, and tamsulosin belong to the class of drugs known as alpha-blockers. Alpha-blockers act by relaxing the smooth muscle of the prostate and bladder to improve urine flow and reduce bladder outlet obstruction. In men with severe symptoms, though, these medications are palliative only. They can delay but not prevent the eventual need for surgery.

Regardless of the efficacy of any drug treatment, the long term exposure to xenobiotic compounds may produce additional unwanted side effects that are not realized until years after treatment. Accordingly, a need exists for an apparatus and method for the treatment of BPH that does not require the introduction of xenobiotic compounds.

For men with the most severe symptoms, surgery is generally considered to be the best long-term solution. There are several surgical procedures that have been developed for relieving symptoms of BPH. Each of these procedures, however, suffers from one or more of the following deficiencies: high morbidity, long hospital stays, the use of general anesthesia, significant side effects such as impotence, and possible complications such as infection and inflammation.

In recent years, a number of procedures have been introduced that are less invasive than surgery. One such procedure is transurethral microwave thermal therapy. In transurethral microwave thermal therapy, a Foley-type catheter containing a microwave antenna is placed within the urethra. The microwave antenna is positioned adjacent to the transitional zone of the prostate, where BPH occurs, and allows selective heating of the prostate. Maintaining the temperature of the BPH tissue above 45 degrees C. during about a one hour session leads to necrosis of the tissues and subsequent reabsorption of necrotic tissue by the body.

Another recently developed non-invasive technique is transurethral needle ablation (TUNA). TUNA uses low level radio frequency (RF) energy to heat the prostate. Using TUNA, two separate needles are inserted into prostate through the urethra. Several watts of RF energy is applied to each needle to cause thermal necrosis of the prostate cells around the needles. Application of this treatment to several sites of the prostate typically results in sufficient necrosis to relieve symptoms of the BPH.

While generally successful, the microwave and RF therapies are relatively long procedures. Also, because of the poor temperature control of the heated volume, the volume of

removed tissue is often not sufficient for the long term relief of the symptoms and/or the healthy tissue of the urethra is damaged. A damaged urethra is capable of restoring itself, but the healing is a long morbid process accompanied by sloughing of the necrotic tissue into urethra and excretion of it during urination.

Therefore, a need exists for a minimally invasive therapy for treatment of BPH that requires shorter treatment times and is less morbid than existing therapies.

#### BRIEF DESCRIPTION OF THE INVENTION

The present invention provides apparatus and methods for the treatment of benign prostate hyperplasia and the alleviation of the symptoms associated therewith. An apparatus in accord with the present invention has a probe portion and a handle portion. The probe portion is preferably entirely or partially hollow.

In an embodiment of the present invention, the probe is a hollow body having proximal, transitional, and distal probe portions. The proximal probe portion is a substantially straight, hollow, elongate tube attached at its proximal end to the handle portion. The proximal probe section is configured to be received within the penile section of the urethra and extend to the urogenital diaphragm, an anatomical structure separating the distal end of the penis from the prostate gland. The distal probe portion is a substantially straight, hollow, elongate tube configured to be received within the prostatic segment of the urethra. The transitional probe portion is a curved, hollow, tube extending between the proximal and distal probe portions to form therewith a continuous, hollow probe capable of being received by the urethra and extending from the penile opening to within the prostate.

The hollow probe portion provides access for a plurality of electrodes and other desirable instrumentation to the prostate gland. For example, a pair of needle electrodes and an flexible fiber optic endoscope can be housed within the probe portion. If desired, separate passages or channels can be provided for the electrodes and the endoscope. The endoscope will preferably extend the length of the probe, from the probe proximal end to the probe distal end. The endoscope may be provided to enable the visualization of the urethra distally to the probe to enable safe placement and manipulation of the inventive apparatus during therapy procedures.

The needle electrodes are slidably disposed within the probe to enable their extension and retraction relative to the probe and into and out of the BPH tissue. The aforementioned channels or passages will facilitate their extension and retraction. In their retracted position, the distal ends of the needles will be positioned within and near or at the distal end of the proximal probe portion. When the probe is properly positioned relative to the prostate gland, advancing the needles will advance them into the BPH tissue of the prostate gland. Only the distal needle ends should be exposed; that is, the proximal portions of the needle electrodes should be insulated to insulate the needle electrodes from the probe body as well as each other. The proximal ends of the needles may be secured to a finger activated lever forming part of the handle portion. The lever is positioned and adapted to advance the needles relative to the probe to pierce the urethra and thus position them in the body of the prostate gland; more specifically, advancing the needles during a procedure will result in the placement of the uninsulated needle ends being disposed substantially within the transition zone where BPH occurs.

The curved probe portion serves to displace the proximal and distal portions from each other. In turn, this displace-

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ment displaces the prostatic urethral segment and the penile urethral segments from each other. The electrode needles can thus be advanced substantially parallel to the longitudinal axis of the proximal portion, and thus the penile urethral segment, into the prostate gland. Thus, this displacement facilitates ready and proper positioning of the needle electrodes into the prostate gland without the necessity of bending needles about 90 into the prostate gland and without the associated complicated structures found in the prior art. This probe geometry enables the needles to be placed into the prostate gland substantially parallel to the urethra, which in turn enables the use of fewer treatment positions and shorter treatments.

Preferably, the entirety of the inventive apparatus, save that portion of the distal probe portion that will be disposed within the prostatic urethra, is covered with a insulating biocompatible material. That uninsulated distal probe portion may serve as a third, urethral electrode. All of the electrodes will be electrically insulated from each other and will be electrically connected to a generator producing the electroporation pulses. The amplitude and duration of the pulses will be selected to provide an electric field in the prostatic tissue that exceeds the upper electroporation limit of the BPH fibromuscular and nerve tissues. The duration of the pulses may be selected to range from about 10 microseconds to about 500 milliseconds. As stated, the amplitude, duration, and number of pulses will be preselected to cause necrosis of the fibromuscular and nerve cells constituting the benign prostatic hyperplasia tissues.

In another embodiment of the present invention, the entire probe will be insulated and only the needle electrodes will be utilized for providing electroporation therapy. In this embodiment, no electric pulses will be applied to the probe itself. It is anticipated that this embodiment of the present invention will be used for cases of moderate enlargement of the prostate gland.

Stated alternatively, according to one aspect of the present invention, the probe portion may have at least three sections, wherein the first and third sections take on a substantially tubular form with differing sizes, each of the first and third sections defining a substantially longitudinal axis, with the first and third sections' longitudinal axes lying parallel but not coaxial, and the second section is a transition section between the first and third sections. The third section is desirably sized to be safely, comfortably, and appropriately received within the prostatic segment of the urethra. The first section is desirably sized to be safely, comfortably, and appropriately configured to be received within the urethra and extend from urethral opening through the penis approximately to the urogenital diaphragm. The second or transitional section is desirably sized to be safely, comfortably, and appropriately extend through the urogenital diaphragm. The probe can be manufactured as integral unit or in separate sections that are joined using known manufacturing processes.

In another aspect of the present invention, the first and third probe sections each define a longitudinal axis, with the two axes being non-parallel.

In yet another aspect of the present invention, the needle electrodes may be curved.

In still yet another aspect of the present invention, the needle electrodes may be bent in one location.

In a method in accord with the present invention, a probe having at least first and second probe portions, with the first and second probe portions each defining an axis and the first and second probe portion axes not being collinear, is inserted

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into the urethra and maneuvered until the distal end of the probe lies within the prostatic urethral segment. The distal or second probe portion displaces the prostate gland sideways relative to the axis of the proximal or first probe portion. Needle electrodes electrically connected to a power source are extended from the first probe portion and inserted into the BPH tissue of the prostate. Electric field pulses of selected amplitude and duration are applied to the BPH tissue. In a preferred embodiment, the electric field is directed radially and thus along the longer dimension of the fibromuscular cells forming benign prostate hyperplasia as well as the nerve cells contained therein.

The present invention, while described below with respect to electroporation, can also be utilized with radio frequency energies alone or in conjunction with electroporation.

The present invention, as well as its various features and advantages, will become evident to those skilled in the art when the following description of the invention is read in conjunction with the accompanying drawings as briefly described below and the appended claims. Throughout the drawings, like numerals refer to similar or identical parts.

#### BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 illustrates an embodiment of the present invention in a partial cross sectional view disposed in an operating position within a human penis and prostate gland.

FIG. 2 shows a cross-sectional view of the present invention taken along viewing plane 2—2 of FIG. 1.

FIG. 3 shows a cross-sectional view of the present invention taken along viewing plane 3—3 of FIG. 1.

FIG. 4 depicts an alternative embodiment of an apparatus in accord with the present invention.

FIG. 5 illustrates an alternative embodiment of an apparatus in accord with the present invention.

FIG. 6 shows an alternative embodiment of an apparatus in accord with the present invention.

#### DETAILED DESCRIPTION OF THE INVENTION

Cells are not, generally speaking, spherical bodies. Rather, they come in a variety of sizes and geometries. For example, for cells similar to muscle fiber cells the length to width ratio of the cell can be as great as 20–30 to 1. Nerve cells can have even greater length to width ratios. Cell vulnerability to electroporation, as noted earlier, is different for different directions of the applied electric field. That vulnerability depends on the size of the cell in the direction of the applied field. Thus, the effect of electroporation on tissue can be modulated by selecting a field direction relative to a cell's geometry. Stated otherwise, an elongated cell can be killed with significantly lower electric field strength if the field is applied along the cell. If the field is applied across such a cell, the cell is capable of surviving much higher amplitudes of the electric field.

The current invention provides relief of the symptoms of BPH by providing electroporation treatment to the BPH treatment to create a necrotic zone in the BPH tissue around the urethra. Control of the volume of the necrotic zone, its shape, and its location relative to healthy prostate tissue is provided by the present invention, including a system of electrodes that generate an electric field in the area of benign enlargement of the prostate gland. Application of multiple pulses of the electric field having the appropriate voltage and duration leads to necrosis of the prostatic tissue around the urethra.

Anatomically, the predominant direction of fibers in the fibro-muscular glandular tissue of BPH is radial to the ure-

thra. In the present invention, the preferred direction of the applied electric field is also radial to the urethra, coinciding with the predominant direction of the BPH tissue. Application of the electroporating pulses along the muscular fibers and nerves that anatomically follow them selectively kills both types of fibers. Thus, two intermediate benefits of the present therapy are achieved with selective application of electroporation pulses to BPH tissue. First, a significant volume of necrotic BPH tissue around the urethra is created by the therapy. Second, the nerves that cause elevation in tension of the muscle fibers are destroyed. Subsequently, the necrotic tissue, including both the killed BPH tissue and nerves, are removed by macrophages. Removal of the necrotic BPH tissue reduces the total volume of BPH and pressure on the urethra while removal of the destroyed nerves results in relaxation of the prostate. Both effects contribute to the improvement of the urethra and bladder functions after treatment.

While the aforementioned therapy alleviates the symptoms of BPH, care must be taken to avoid damaging or destroying other tissue in the vicinity of the applied electroporation pulses. For example, sphincters, located on the urethra anterior and posterior to the prostate gland, consist of smooth muscle cells wrapped circumferentially around the urethra. These urethral sphincters control shutting down the flow of urine from the bladder and should be preserved during a therapy treatment. An electroporation field applied radially to the prostate—that is, coincident with the elongate fibromuscular and nerve cells of the BPH—results in the field being transverse to the sphincter muscle cells, thus making them relatively resistant to the electroporation pulsing. Thus, by selectively directing the electric field, damage to these muscles, whose health and function are important to quality of life for affected individuals, can be reduced or avoided. Nevertheless, to reduce the potential of damage to the sphincter muscles further, the electrodes disposed within the urethra during therapy should not be positioned too closely to them. Additionally, the amplitude of the electric field during treatment applied to the urethra area should be selected not to exceed the upper electroporation limit of the sphincter muscles in the transverse direction.

The foregoing therapeutic benefits are obtained by providing electroporation treatment to BPH by apparatus and methods in accord with the present invention.

A BPH therapy applicator and methods of providing BPT treatment in accord with the present invention are described below with reference to FIGS. 1–3. Referring specifically to FIG. 1, this Figure illustrates a BPH therapy applicator 10 comprising a handle 12 and a probe 14. Probe 14 includes at least first and second, or proximal and distal sections, 16 and 18, respectively. In the embodiment shown, probe 14 also includes a third or transitional section 20. The applicator 10 is shown relative to a penis 22 in position for the application of an electroporation treatment to a patient experiencing BPH. Thus, the probe 10 is shown inserted into the urethra 24 through the urethral opening 26 at the proximal end of the penis 22. As shown in its operational position, probe proximal portion 16 is disposed within the penile urethral segment 30, probe distal portion 18 is disposed within the prostatic urethral segment 32, and probe transitional portion 20 extends between the proximal and distal probe portions 16 and 18 and is disposed substantially through the urogenital diaphragm 34.

Probe 14 has a substantially hollow configuration, to provide an interior passage 40. Passage 40 provides access for a flexible fiber optic endoscope 42 and at least one needle 44. In the embodiment shown in FIG. 1, two needles, 44 and 46,

are shown. One or more of the endoscope 42 and needles 44 and 46 may be enclosed within their own individual channels if desired. The endoscope 42 extends to an eye piece 48 at its proximal end 50. A light source 52, which is connected to the endoscope 42 by a fiber optic cable 54, enables visualization of the urethra during placement and manipulation of the applicator 10 in operation position and during a BPH electroporation treatment.

Needles 44 and 46 have insulating sheathes 60 on their surfaces that electrically separate or isolate them from the handle 12 and probe 14 as well as each other. Needles 44 and 46 are attached to a finger-activated lever 62 at their proximal ends in any known, appropriate manner. As seen in the Figure, lever 62 has been moved from its non-operational position seen in phantom to an operational position as indicated by the double-headed arrow 64. Movement of the lever 62 between the two positions will cause the needles to extend from their non-operational position to an operational position as seen in the Figure and to retract into their non-operational position as desired by the lever operator. Thus, movement of the lever to the operational position shown will cause the needles to extend or advance through holes 66 and 68 in the distal end 70 of the first or proximal probe section 16. The advancement of the needles 66 and 68 out of the probe 14 causes the needles to pierce the urethra 24 and the urogenital diaphragm 36 and disposes the uninsulated needle ends 74 and 76 of needles 44 and 46, respectively, which form a pair of electrodes, in the body of the prostate gland 78. Preferably, both the lengths and the operating positions of the distal end of the distal end 80 of the probe 14 and the needle electrodes 44 and 46 are selected to avoid reaching the bladder 82 to reduce the likelihood of damage thereto during a procedure. In particular, the sharp tips 84 and 86 of needles 44 and 46, respectively, should not penetrate the bladder 82.

The entirety of the surface of the applicator 10, save for a small portion 88 of the distal probe section 18 is covered with an insulating, biocompatible layer of any known or hereafter discovered, appropriate material. Uninsulated distal probe section portion 88 is therefore exposed to the surrounding tissue and can comprise a third, urethral electrode of the applicator 10. Electrodes 74, 76, and 88 are electrically insulated from each other and are connected via an appropriate connector 90 to a generator 92 that produces high voltage electrical pulses. As noted previously, the amplitude and duration of the electric pulses applied between the electrodes will be selected to provide an electric field in the prostatic tissue exceeding the upper electroporation limit of the BPH tissue, including the nerve cells contained therein. The pulse duration may be selected to be within the range of about 10 microseconds to about 500 milliseconds. The amplitude and number of applied pulses are selected to cause necrosis of the BPH tissue, including the nerves and muscle cells.

It will be observed that the proximal and distal probe sections 16 and 18 define longitudinal axes 96 and 98 respectively. As shown, axes 96 and 98 are not co-linear. They may, if desired, lie parallel to each other, however. Proximal section 16 has a larger cross-sectional area than the distal section 18, which does not need to carry the needles 44 and 46 therein, thus aiding to increase patient comfort during a procedure. Probe section 20 transitions between the larger cross-sectional area proximal section 16 and smaller cross-sectional area section 18. Additionally, the angled or curved nature of the section 20 serves to offset the proximal and distal sections 16 and 18, respectively, from each other. In doing so, the prostate gland 78 is displaced sideways relative

to the axis **96** of the proximal section **16**. This sideways displacement facilitates proper positioning of the needle electrodes in the BPH tissue.

Referring now specifically to FIG. 2, a cross-section of the prostate gland **78** is shown taken along viewing plane **2—2** of FIG. 1 with the applicator **10** in its operating position. When electric pulses are applied between the urethral electrode **88** and needle electrodes **74** and **79**, the electric field generated between the electrodes, indicated generally by field lines **100**, causes necrosis of the BPH tissue. After an electroporation treatment in one site of the prostate gland is completed, the needles can be retracted within probe **14** and the probe can be rotated a selected angle to a new position for treatment. The needles will be advanced into the operating position and the electric pulses applied once again. A plurality of such needle advancements and treatments are indicated in the Figure by the open circles **102**.

Referring now specifically to FIG. 3, a cross-section of the prostate gland **78** is shown taken along viewing plane **3—3** of FIG. 1 with the applicator **10** in its operating position. As shown, the proximal probe section **16** preferably has a substantially elliptical configuration with a ratio of the axes in the range of about 1:3 to about 1:4. The maximal diameter of the ellipse should generally not exceed about 12 to about 16 mm and minimal diameter should generally not be less than about 3 to about 4 mm. The fiber bundle **42** of the endoscope and the two needles **44** and **46** are positioned in line along the longer axis of the probe section **16**. As seen in the Figure, needles **44** and **46** are disposed, if desired, within channels or tubes **104**.

FIGS. 4–6 show alternative embodiments of the present invention. In FIG. 4, probe **110** includes proximal and distal segments **112** and **114**, respectively. Segments **112** and **114** each define an axis **116** and **118**, respectively. As indicated, axes **116** and **118** do not lie parallel to each other, but are separated by an angle  $\alpha$  lying in the range of about  $10^\circ$  to about  $45^\circ$ . Also as shown, the needles **44** and **46** can, if desired, be angularly disposed relative to each other. As seen in the Figure, needles **44** and **46** diverge by an angle  $\beta$  lying in the range of about  $0^\circ$  to about  $30^\circ$ . In this embodiment, the proximal segment **112** can be made smaller, thus increasing patient comfort.

FIG. 5 illustrates an embodiment **130** of the present invention wherein curved needles **132** and **134** having radii of curvature  $R_1$  and  $R_2$ , respectively, are used rather than the straight needles **44** and **46** previously illustrated and discussed. Where such curved needles are utilized, the radius of curvature of the needles are in the range of about 2 cm to about 5 cm.

FIG. 6 depicts another embodiment of the present invention. In this embodiment, probe **140** includes needles **142** and **142** that are bent at one location; as shown, the needles **142** and **144** are bent at the end of the insulating sheath **60**.

Operatively, the probe of the present invention will be introduced into a patient's urethra under endoscopic guidance until the distal end is positioned in the prostatic segment of the patient's urethra. The needle electrodes will then be advanced into the BPH tissue surrounding the urethra and a plurality of electric pulses will be applied. The electroporation therapy will terminate when a significant and stable drop in the electrical resistance of the treated tissue occurs. The resistance drop indicates a profound electroporation damage to the fibromuscular cells, which later leads to their necrosis and dissolution by macrophages. Overall treatment of one site may take about ten pulses and several seconds to several tens of seconds in time depending on the repetition

rate of the high voltage pulse generator. After each treatment the needle electrodes will be withdrawn and repositioned in another treatment site. Consecutive treatments are performed in light of patient comfort and safety and until the operator determines that a sufficient volume of BPH tissue has been treated.

It will be obvious to those skilled in the art that many modifications may be made within the scope of the present invention without departing from the spirit of thereof, and the invention includes all such modifications.

What is claimed is:

1. An apparatus for providing electroporation therapy for benign prostatic hyperplasia, said apparatus comprising:

a urethral applicator configured for insertion into a urethra, said applicator including:

a substantially hollow probe, said probe portion including first, second and third probe portions, said first probe portion being configured for insertion into the penile urethral segment and said third probe portion being configured for insertion into the prostatic urethral segment, said first and third probe portions defining first and second probe portion longitudinal axes, wherein said axes are not collinear with each other and wherein said second probe portion lies between said first and third probe portion;

a handle, said handle being attached to said probe;

a plurality of needle electrodes, said electrodes being mounted within said first probe portion for reciprocal movement into and out of said first probe portion substantially parallel to the urethra, said electrodes being provided for connection to an electric pulse generator; wherein when said applicator is disposed in operating position, said needle electrodes may be advanced into benign prostatic hyperplasia tissue for electroporation therapy.

2. The apparatus of claim 1 wherein said first and second probe portion longitudinal axes are parallel.

3. The apparatus of claim 1 wherein said first and second probe portion longitudinal axes are non-parallel.

4. The apparatus of claim 1 wherein said third probe portion is uninsulated and is provided for electrical connection to a pulse generator.

5. The apparatus of claim 1 wherein said first probe portion has a greater cross-sectional area than said third probe portion.

6. The apparatus of claim 1 wherein said needle electrodes are curved.

7. The apparatus of claim 1 wherein said needle electrodes are bent.

8. The apparatus of claim 1 and further including a flexible fiber optic endoscope.

9. The apparatus of claim 1 and further including an electric pulse generator.

10. The apparatus of claim 9 wherein said third probe portion is uninsulated and is electrically connected to a said electric pulse generator.

11. The apparatus of claim 1 wherein said first and third probe portions are longitudinally offset relative to each other.

12. The apparatus of claim 1 wherein said first and third probe portions are angularly off-set relative to each other.

13. The apparatus of claim 1 wherein said needle electrodes are electrically insulated from each other and said applicator.

14. The apparatus of claim 1 wherein said handle includes a lever engaged with said needle electrodes to enable the operator to selectively advance and retract said needle electrodes.

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**15.** A method of providing electroporation therapy for benign prostatic hyperplasia comprising:

providing an applicator including a probe having a proximal probe portion and a distal probe electrode portion, said portions each defining non-collinear longitudinal axes, said probe including at least one electrode for electroporation therapy;

inserting the applicator into a patient's urethra to dispose the distal probe portion in the prostatic urethral segment and the proximal probe portion in the penile urethral segment and to displace the patient's prostate gland sideways relative to the proximal probe portion;

advancing at least a first electrode into the benign prostatic hyperplasia tissue; and

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applying electric pulses to the distal probe electrode portion and the at least first electrode to generate electroporating electric fields.

**16.** The method of claim **15** and further including:

retracting the at least first electrode following the completion of electroporation therapy at a first site

rotating the probe a preselected amount;

advancing the at least first electrode into the benign prostatic hyperplasia tissue at a new location in the tissue; and

applying electric pulses to the distal probe electrode portion and the at least first electrode to generate electroporating electric fields.

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