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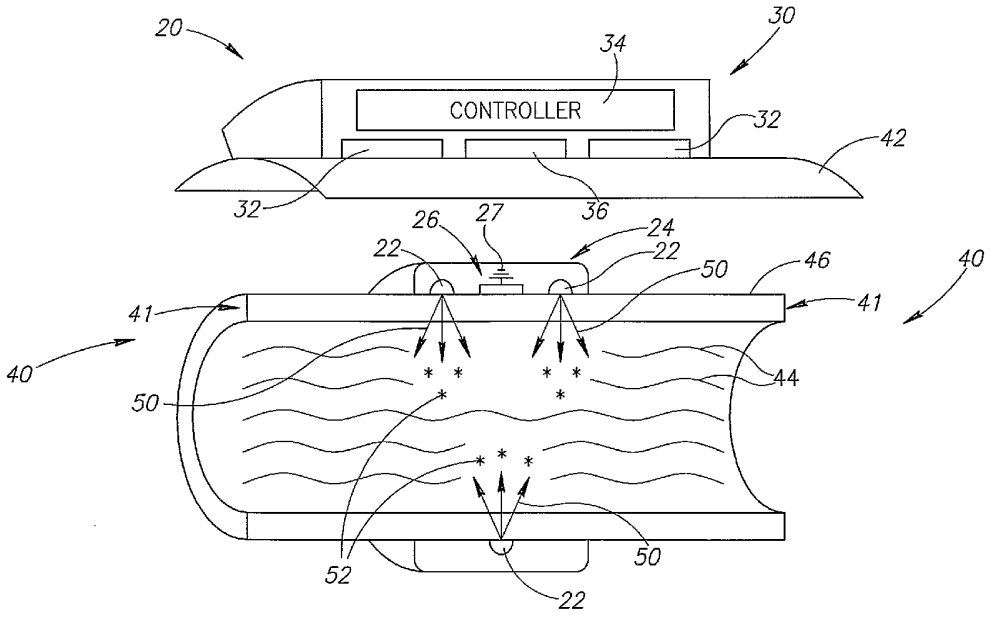
(54) Title: ASSAY APPARATUS COMPRISING AN IMPLANTED LIGHT SOURCE



(57) Abstract: Apparatus for assaying an analyte in a patient's blood comprising: at least one light source implanted in the patient's body controllable to illuminate blood in a blood vessel in the body with light at at least one wavelength that is absorbed and/or scattered by the analyte and as a result generates photoacoustic waves in the blood; at least one acoustic transducer coupled to the body that receives acoustic energy from the photoacoustic waves and generates signals responsive thereto; and a processor that receives the signals and processes them to determine a concentration of the analyte in the illuminated tissue region.

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ASSAY APPARATUS COMPRISING AN IMPLANTED LIGHT SOURCE

RELATED APPLICATIONS

The present application claims benefit under 35 U.S.C. 119(e) of provisional application 60/577,182 filed on June 7, 2004, the disclosure of which is incorporated herein by reference.

FIELD OF THE INVENTION

The invention relates to apparatus for assaying a substance in a body that can be implanted in the body and in particular, to apparatus that can be inserted into or mounted on a blood vessel in the body.

BACKGROUND OF THE INVENTION

Methods and apparatus for determining blood glucose levels for use in the home, for example by a diabetic who must monitor blood glucose levels frequently, are available. These methods and associated devices are generally invasive and usually involve taking blood samples by finger pricking. Often, a diabetic must determine blood glucose levels many times daily and finger pricking is perceived as inconvenient and unpleasant. To avoid finger pricking diabetics tend to monitor their glucose levels less frequently than is advisable.

In addition, prior art glucose assaying methods and devices, such as those based on finger pricking, are generally not suitable or cannot provide substantially continuous monitoring of a patient's glucose level. Continuous monitoring is advantageous for reducing delay from a time at which a change in blood glucose level occurs that demands patient intervention to a time at which the patient is alerted to the change. Continuous monitoring would also be particularly advantageous for use with drug delivery devices for automatic delivery of drugs to a patient to control the patient's glucose levels.

US Patent Application Publication 2003/0023317, the disclosure of which is incorporated herein by reference, describes a device, hereinafter a "glucometer", for assaying glucose that does not require finger pricking and may provide continuous monitoring of a patient's glucose levels. The glucometer is implantable and comprises a sensing membrane that includes an enzyme for detecting and assaying the patient's glucose. The glucometer comprises a bio-interface membrane overlaying the sensing membrane that promotes vascularization of tissue in a layer of the bio-interface membrane and enables glucose in the patient's body to reach and contact the enzyme in the sensing membrane. However, enzymes used in glucometers generally require periodic renewal to maintain their efficacy and therefore limit a period of time for which the implanted glucometer may be unattended.

Optical methods and devices based on optical methods for assaying glucose appear to be advantageous for long term, convenient, *in vivo* monitoring of a patient's glucose levels. Glucometers that use optical assay methods, such as for example near infrared (NIR) or mid infrared (MIR) absorption and/or scattering spectroscopy methods, do not generally require chemical interaction of glucose with another substance in order to determine concentration of a patient's glucose. Optical methods are therefore usually minimally or non-interactive with the patient's metabolism and generally do not require that a reagent, which might have to be periodically renewed, be introduced into the patient's body to assay his or her glucose.

However, light at any given wavelength in the NIR and MIR wavelength bands, is generally not "specific" to glucose (or any other particular analyte in the body), *i.e.* interacting substantially only with glucose and at most a very few additional analytes. Light at an NIR or MIR wavelength generally interacts with water and many other substances in the body besides glucose, such as urea, albumin, hemoglobin and uric acid, which in general absorb and/or scatter the light. Water in particular is a very strong absorber of light in the NIR and MIR wavelength bands and in general dominates absorption of light in these wavelength bands. As a result, determining a patient's glucose concentration from optical absorption and/or scattering processes generally requires acquiring measurements at a relatively large number of different wavelengths of light and relatively complicated multivariate analysis of the measurements. In addition, optical path lengths over which light at the different wavelengths used to perform an "absorption assay" is absorbed, in general have to be relatively accurately controlled so that the path lengths are substantially the same for all the wavelengths of light used.

Wavelengths, hereinafter "signatory wavelengths", of light do exist in the NIR and MIR bands for which light is "highly specific" to glucose and has, for a given tissue type, substantial interaction cross-sections only for glucose and water and, if at all, only a small number of other components in the tissue. Such wavelengths are potentially useable to assay glucose without requiring complicated procedures for acquiring and analyzing a relatively large number of absorption and/or scattering measurements at a plurality of different wavelengths. However, absorption of light by water at signatory wavelengths is generally so strong, that light at these wavelengths attenuates rapidly in living tissue. When a region of a person's skin is illuminated by light at the wavelengths, the light does not generally have a useful penetration depth below the skin greater than about 30 to about 50 microns for

acquiring absorption measurements. For these penetration depths, glucose measurements are generally inaccurate as indicators of a patient's glucose concentration.

An article by Martin, W. B., et al entitled "Using two discrete frequencies within the middle infrared to quantitatively determine glucose in serum"; Journal of Biomedical Optics; October 2002; Vol. 7, No. 4, pp 613-617, notes that light at wavelengths 9.66 microns (wave number 1035 cm^{-1}) and 9.02 microns (wave number 1109 cm^{-1}) can be advantageous for assaying glucose. Light at "signatory wavelength" 9.66 microns is strongly absorbed substantially only by glucose and water in living tissue and may be advantageous for assaying glucose in blood. Light at signatory wavelength 9.02 microns is strongly absorbed substantially only by glucose, hemoglobin and water in living tissue and may be advantageous for assaying glucose in interstitial fluid, which does not in general comprise hemoglobin, and for which therefore 9.02 microns is a signatory wavelength in blood. The effect of absorption of light by water at these wavelengths may generally be removed relatively straightforwardly from absorption measurements of light at the wavelengths. The article suggests that light at a wavelength of 9.66 microns may be advantageous for use in an implantable glucometer comprising both a light source and a photodetector for the light. The article does not provide details or describe a configuration of the proposed implantable glucometer.

US patent 6,049,727 the disclosure of which is incorporated herein by reference, describes an in vivo sensor for determining concentration of a constituent of a patient's body fluid comprising an optical source and a photodetector that are implanted in the patient's body with the optical source and photodetector straddling a vein. The patent describes the vein as being between 0.3 and 1.0 mm in diameter. The source and photodetector are controllable to acquire absorption measurements at a plurality of wavelengths of light, at least one of which is in the IR band. The absorption path lengths over which light at the different wavelengths is absorbed are controlled so that the path lengths are substantially collinear. For determining glucose concentration, the diameter of the vein and distances between the vein wall and the light source and photodetector appear to preclude use of light at a signatory wavelength of glucose. The patent suggests that for assaying glucose, absorption measurements at a relatively large number of about 13 different wavelengths of light should be acquired. Whereas the light source and photodetector are implanted in the body, the patent notes that components of the sensor, such as a processor, may be located external to the body.

US Provisional Patent Application 60/476,623 filed on June 9, 2003 by some of the same inventors as the present invention, the disclosure of which is incorporated herein by

reference, describes a wearable glucometer that provides real time in-vivo assays of glucose in blood in a patient's blood vessel. The glucometer transmits light through the patient's skin at an intensity and wavelength for which light penetrates body tissue and illuminates blood in the blood vessel with an amount of light that stimulates photoacoustic waves in the blood vessel having sufficient intensity so that they are useable by the glucometer to assay glucose.

US Provisional Patent Application 60/532,573 filed on December 29, 2003 by some of the same inventors of the present application, the disclosure of which is incorporated herein by reference, describes a glucometer that comprises a light source implanted into a patient's body. In an embodiment of the invention, the implanted light source is sealed in a capsule having an optical aperture substantially transparent to light provided by the light source. Optionally, the light source provides light at a signatory wavelength of glucose. Optionally, the aperture is covered with a membrane that tends to prevent formation of a barrier cell layer of inflammatory response cells (*e.g.* macrophages) over the aperture and promotes vascularization and presence of interstitial fluid comprising glucose close to the aperture. Optionally, the at least one bio-membrane promotes vascularization at distances from the aperture that are less than a small number (for example less than one, two or three) of extinction lengths of light provided by the light source in the patient's body tissue. Light provided by the light source is therefore not substantially attenuated before it interacts with the patient's interstitial fluid and/or blood and generates photoacoustic waves therein that are a function of the patient's glucose concentration. The patient's glucose is assayed responsive to the photoacoustic waves.

SUMMARY OF THE INVENTION

An aspect of some embodiments of the present invention relates to providing a glucometer that can provide relatively long term monitoring of a patient's blood glucose level without requiring substantial user attention or intervention.

An aspect of some embodiments of the present invention relates to providing a glucometer comprising at least one light source implanted in a patient's body that assays the patient's glucose responsive to interaction of light provided by the at least one light source with blood in a blood vessel of the patient.

According to an aspect of some embodiments of the invention, the assay is determined responsive to photoacoustic waves that the light generates in the blood. The at least one light source is controllable to provide light that illuminates blood in the blood vessel with light at at least one wavelength that is absorbed or scattered by glucose in the blood and stimulates

thereby photoacoustic waves responsive to concentration of glucose in the blood. Optionally, the glucometer comprises at least one acoustic transducer and a controller mounted externally to the body. The transducer generates signals responsive to the photoacoustic waves stimulated by the light and transmits the signals to the controller, which processes the signals to assay the patient's blood glucose.

According to an aspect of some embodiments of the invention, the at least one light source is mounted on an external surface region of the wall of the blood vessel. Light provided by the at least one light source propagates through the blood vessel wall to illuminate blood in the blood vessel and generate photoacoustic waves in the blood therein. Optionally, the at least one light source is comprised in an annular collar which surrounds the blood vessel and maintains the at least one light source substantially in contact with the exterior wall of the blood vessel.

According to an aspect of some embodiments of the invention, the at least one light source is positioned inside the blood vessel. Positioning the at least one light source inside the blood vessel is optionally accomplished by mounting the light source to a stent or other support structure suitable for insertion into a blood vessel, and inserting the stent or support into the blood vessel. Hereinafter, a stent or other support structure suitable for insertion into a blood vessel, to which the at least one light source is mounted is referred to generically as a stent.

In some embodiments of the invention, the collar or stent comprises an antenna for receiving electromagnetic energy and an external transmitter transmits electromagnetic waves to the antenna to power the light source. In some embodiments of the invention, the collar or stent or a portion thereof functions as the electromagnetic antenna.

In some embodiments of the invention, the collar or stent comprises an acoustic transducer and an external transmitter transmits acoustic waves to the transducer to power the light source.

According to an aspect of some embodiments of the invention, the assay is determined responsive to a degree of attenuated total reflection (ATR) of the light at an interface between blood in the blood vessel and a material in which the light propagates.

In an embodiment of the invention, the glucometer comprises a stent comprising at least one light source and at least one light detector, which is inserted into the blood vessel. At least one optic fiber or waveguide, hereinafter referred to generically as an optic fiber, optically couples the at least one light source to the at least one optical detector. At least a

portion of the surface of the optic fiber interfaces with the blood so that along the interface an evanescent field of light propagating along the fiber interacts with glucose in the blood. The interaction causes the light to suffer attenuated total reflection at the interface and affects an amount by which the light is attenuated in propagating from the at least one light source to the at least one optical detector. Signals generated by the at least one optical detector responsive to light that it receives from the at least one light source are transmitted to a controller. The controller processes the signals to determine glucose concentration in the blood responsive to an amount of attenuated total reflection suffered by the light.

There is therefore provided in accordance with an embodiment of the invention apparatus for assaying an analyte in a patient's blood comprising: at least one light source implanted in the patient's body controllable to illuminate blood in a blood vessel in the body with light at at least one wavelength that is absorbed and/or scattered by the analyte and as a result generates photoacoustic waves in the blood; at least one acoustic transducer coupled to the body that receives acoustic energy from the photoacoustic waves and generates signals responsive thereto; and a processor that receives the signals and processes them to determine a concentration of the analyte in the illuminated tissue region.

Optionally, the at least one acoustic transducer comprises at least one acoustic transducer coupled to a region of the skin.. Additionally or alternatively, the at least one acoustic transducer optionally comprises at least one acoustic transducer located inside the body.

In some embodiments of the invention, the at least one light source comprises at least one light source mounted to a collar that surrounds the blood vessel.

Optionally, the collar comprises circuitry for controlling the at least one light source. Optionally, the collar comprises a receiver for receiving transmitted energy to power the at least one light source.

In some embodiments of the invention, the apparatus comprises a transmitter that transmits energy to power the at least one light source.

In some embodiments of the invention, the at least one light source comprises at least one light source mounted to a stent that is inserted into the blood vessel. Optionally, the at least one transducer comprises at least one transducer mounted to the stent.

There is further provided, in accordance with an embodiment of the invention, apparatus for assaying an analyte in a patient's blood comprising: a stent adapted to be inserted into a blood vessel in the patient's body; at least one light source and at least one

optical detector mounted to the stent that are optically coupled by a light pipe, wherein light transmitted by the light source to the detector undergoes attenuated total reflection along the light pipe responsive to concentration of the analyte in the blood; and a processor; wherein the at least one detector generates signals responsive to light that it receives from the at least one light source and the processor processes the signals to assay the analyte responsive to a degree of ATR that the signals indicate.

Optionally, the light pipe extends through the lumen of a blood vessel into which the stent is inserted. Additionally or alternatively, the light pipe optionally extends along the wall of a blood vessel into which the stent is inserted.

In some embodiments of the invention, the light pipe comprises an optic fiber.

In some embodiments of the invention, the stent comprises circuitry for controlling the at least one light source. In some embodiments of the invention, the apparatus comprises a transmitter that transmits energy to power the at least one light source. In some embodiments of the invention, the stent comprises a receiver for receiving the transmitted energy.

In some embodiments of the invention, the energy comprises electromagnetic energy. Optionally, the electromagnetic energy comprises RF energy. Additionally or alternatively the electromagnetic energy optionally comprises optical energy. In some embodiments of the invention, the energy comprises acoustic energy.

In some embodiments of the invention, the analyte is glucose.

BRIEF DESCRIPTION OF FIGURES

Non-limiting examples of embodiments of the present invention are described below with reference to figures attached hereto, which are listed following this paragraph. In the figures, identical structures, elements or parts that appear in more than one figure are generally labeled with a same numeral in all the figures in which they appear. Dimensions of components and features shown in the figures are chosen for convenience and clarity of presentation and are not necessarily shown to scale.

Fig. 1 schematically shows a glucometer comprising an implanted light source comprised in a collar coupled to a blood vessel of a patient, in accordance with an embodiment of the present invention;

Fig. 2 schematically shows a glucometer comprising a stent having a light source that is inserted into a blood vessel of a patient, in accordance with an embodiment of the present invention;

Fig. 3 schematically shows a glucometer that is a variation of the glucometer shown in Fig. 2, in accordance with an embodiment of the present invention;

Fig. 4 schematically shows an ATR glucometer, in accordance with an embodiment of the present invention; and

Fig. 5 schematically shows an ATR glucometer, which is a variation of the ATR glucometer shown in Fig. 4, in accordance with an embodiment of the present invention..

DETAILED DESCRIPTION OF EXEMPLARY EMBODIMENTS

Fig. 1 schematically shows a perspective, cutaway image of a glucometer 20, being used to assay glucose in the blood of a patient, in accordance with an embodiment of the invention.

Glucometer 20 comprises at least one light source 22, such as an LED or laser, coupled to a blood vessel 40 having a wall 41 in the patient's body and a control unit 30 optionally mounted externally to the patient's body on a region of the patient's skin 42. At least one light source 22 is controllable to provide light at at least one wavelength that is absorbed or scattered by glucose and stimulates thereby photoacoustic waves in blood, schematically represented by wavy lines 44, in blood vessel 40.

Control unit 30 optionally comprises at least one acoustic transducer 32 that generates signals responsive to photoacoustic waves stimulated by light provided by at least one light source 22 and a controller 34 that receives the signals and processes them to assay glucose in the patient's blood. At least one acoustic transducer 32 may comprise a configuration having a plurality of transducers, in accordance with any methods and devices known in the art. By way of example, control unit 30 is shown comprising two acoustic transducers 32. Control unit 30 is optionally equipped with a suitable input and output device or devices (not shown) known in the art for displaying, transmitting and/or storing glucose assays and receiving instructions from a user and responding to received instructions. In some embodiments of the invention, assays provided by glucometer 20 are transmitted to a controller that controls a device, such as an insulin pump, for delivering medication to the patient.

At least one light source 22 is optionally comprised in a collar 24 formed from a suitable biocompatible material that is coupled to and surrounds blood vessel 40. The collar optionally maintains at least one light source 22 contiguous with the external surface 46 of blood vessel 40. By way of example, at least one light source 22 comprises a plurality of light sources 22. Whereas, only three light sources 22 are shown in Fig. 1, collar 24 optionally comprises a number of light sources 22 other than three. Furthermore, whereas light sources

22 are shown as substantially coplanar, light sources 22 are optionally positioned at different azimuth angles around the circumference of collar 24. Optionally, collar 24 and surfaces of light sources 22 that contact wall 41 of blood vessel 40 are covered with a suitable bio-sealing material known in the art, such as parylene, that retards formation of a barrier cell layer of inflammatory response cells (*e.g.* macrophages, fibroblasts and giant cells) on the collar and surfaces of the light sources.

Collar 24 optionally comprises at least two parts (not shown) and is coupled to blood vessel 40 in a procedure in which the plurality of parts are positioned around blood vessel 40 and locked together to form the complete collar 24, which surrounds and is stably positioned on the blood vessel. Any of various methods known in the art may be used to form collar 24 and mount the collar to blood vessel 40. For example, collar 24 may be a collar similar to that which is described in US patent 6,049,727 referenced above.

Collar 24 optionally comprises circuitry 26 for controlling light sources 22 and providing energy to operate the light sources. Optionally, circuitry 26 is powered by energy that it receives from a transmitter 36, optionally located in control unit 30, and comprises a receiver 27 for receiving the energy. Optionally, circuitry 26 comprises a device (not shown) for storing energy, such as a capacitor or rechargeable battery for storing energy that it receives from transmitter 36.

In some embodiments of the invention, transmitter 36 transmits electromagnetic energy to circuitry 26 and receiver 27 comprises a suitable antenna for receiving the electromagnetic energy. For such embodiments, collar 24 is formed from a material or materials and configured so that it does not prevent receiver 27 from receiving electromagnetic energy. For example, collar 24 may be formed at least partially from a non-conducting material or may comprise a portion formed from a conducting material that functions as an antenna. Methods and devices similar to those described in US Patent 5,571,152, the disclosure of which is incorporated herein by reference, may be used for transmitting energy to collar 24 to power light sources 22 and controlling the light source. Optionally, transmitter 36 transmits RF energy to circuitry 26 and transmitter 36 and receiver 27 comprise appropriate RF antenna for transmitting and receiving RF energy.

Optionally, electromagnetic energy is transmitted to collar 24 at optical frequencies. For such embodiments of the invention, transmitter 36 comprises a suitable light source for illuminating collar 24 and receiver 27 comprises a suitable photosensitive receiver, such as a photodiode, for receiving energy transmitted at optical frequencies. In some embodiments of

the invention, transmitter 36 comprises an acoustic transmitter for transmitting acoustic energy to collar 24, and receiver 27 comprises an acoustic transducer for receiving the transmitted acoustic energy. Optionally, at least one acoustic transducer 32 is controllable to transmit acoustic waves and functions as the acoustic transmitter. Methods and devices for powering and controlling a light source implanted in a body using acoustic energy transmitted to the light source from a source external to the body are described in US Patent 6,622,049, the disclosure of which is incorporated herein by reference, and similar methods and devices may be used in the practice of the present invention.

Control unit 30 and circuitry 26 cooperate to power and control light sources 22 to transmit pulses of light at a plurality wavelengths that penetrates wall 41 of blood vessel 40 and illuminates blood 44 in the blood vessel, to excite photoacoustic waves in the blood. Wavy arrows 50 represent pulses of light provided by light sources 22. Asterisks 52 represent photoacoustic waves stimulated at locations in blood 44 by light 50. Light 50 at at least one of the wavelengths of light provided by light sources 22 is absorbed and/or scattered by glucose. Optionally, at least one of the wavelengths is a signatory wavelength for glucose in blood. At least one acoustic transducer 32 receives energy in photoacoustic waves 52 and generates signals responsive thereto that it transmits to controller 34. Controller 34 processes the signals using any of various methods known in the art, such as a suitable multivariate algorithm, to determine glucose concentration of blood 44. Since, optionally, at least one of the wavelengths is a signatory wavelength of light for glucose, the plurality of wavelengths used to assay glucose in blood 44 may be a relatively small plurality.

For example, light 50 may comprise light at first and second wavelengths 9.02 and 9.66 microns. Light at 9.02 microns is a signatory wavelength of glucose that stimulates photoacoustic waves in blood due to interaction of the light with, substantially, only glucose, water and hemoglobin. At 9.66 microns, absorption of light in blood 44 and therefore generation of photoacoustic waves 52 in the region is due substantially only to concentrations of glucose and water in the blood. In accordance with an embodiment of the invention, blood 44 is also illuminated with light at a third wavelength, for example 0.810 microns, that is a signatory wavelength of hemoglobin. Light at 0.810 microns generates photoacoustic waves in blood 44 substantially only as a result of interaction of the light with hemoglobin in the blood. In accordance with an embodiment of the invention, photoacoustic waves stimulated by light at the three wavelengths is used to assay the patient's glucose.

It is noted that practice of the present invention is not limited to the use of two or three wavelengths and/or signatory wavelengths. Light sources 22 may be controllable by glucometer 20 to provide light at a suitable plurality of different signatory and/or non-signatory wavelengths to stimulate photoacoustic waves in blood 44 from which to determine glucose concentration. Any of various multivariate methods known in the art may be used to process signals generated responsive to the photoacoustic waves to determine glucose concentration.

Optionally, each light source 22 provides light at a different wavelength of light useable to assay glucose in blood 44. Optionally, control unit 30 and circuitry 26 control light sources 22 to sequentially illuminate blood 44 in blood vessel 40 at different times so that controller 34 can associate signals received from transducers 32 responsive to photoacoustic waves 52 with a particular wavelength of light that stimulates the photoacoustic waves. In some embodiments of the invention, controller 34 uses signals provided by transducers 32 to determine the locations of origins of photoacoustic waves 52. Since light 50 provided by a given light source 22 optionally has a relatively short range in blood 44, photoacoustic waves 52 stimulated by light from the given light source have their origins located in a relatively small neighborhood in the vicinity of the light source. Photoacoustic waves stimulated by light from the given light source can therefore be identified as being stimulated by the light from the light source by the locations of their origins. In some embodiments of the invention, controller 34 uses the determined locations of the origins of photoacoustic waves 52 to associate the waves with the wavelength of light that stimulates the photoacoustic waves.

Fig. 2 schematically shows another glucometer 60, in accordance with an embodiment of the invention.

Glucometer 60 comprises a controller 30 similar to controller 30 comprised in glucometer 20 shown in Fig. 1, however, glucometer 60 comprises light sources 72 that are not coupled to outer surface 46 of blood vessel 40 but are mounted to a stent 70 that is inserted into the blood vessel. Light sources 72 are optionally arrayed in a circular configuration inside stent 70.

Control circuitry 74 for controlling light sources 72 and providing energy to operate the light sources is also mounted to stent 70. Similarly to control circuitry 26 comprised in collar 24 of glucometer 20 (Fig. 1), optionally, circuitry 74 is powered by energy that it receives from a transmitter 36, optionally located in control unit 30, and comprises a receiver (not shown) for receiving the energy, which may for example be electromagnetic energy, *e.g.*

RF or optical energy, or acoustic energy. For reception of RF energy, circuitry 74 comprises an RF antenna. Optionally stent 70 or a portion thereof functions as the RF antenna. Optionally, circuitry 74 comprises a device (not shown) for storing energy, such as a capacitor or rechargeable battery for storing energy that it receives from transmitter 36. Light sources 72 and components of circuitry 74 are optionally formed using methods known in the art, such as thin film technology, on a thin flexible substrate such as a thin sheet of a suitable polymer, which is attached to stent 70.

Stent 70 is inserted into blood vessel 40 using any of various devices and methods known in the art. For example, stent 70 may be inserted into blood vessel 40 using a balloon catheter similarly to the manner in which a balloon catheter is used to insert a stent in an artery to maintain the artery open. Optionally, stent 70 is inserted into blood vessel 40 using a suitable syringe. Using a syringe to insert stent 70 into blood vessel 40 can be advantageous for inserting the stent into the blood vessel for situations in which the blood is a peripheral blood vessel. Once stent 70 is in place in blood vessel 40, control unit 30 and circuitry 74 power and control light sources 72 to illuminate blood 44 in the blood vessel and stimulate photoacoustic waves in the blood similarly to the manner in which controller 30 and circuitry 26 operate to control light sources 22 comprised in glucometer 20. Signals generated by at least one acoustic transducer 32 responsive to the photoacoustic waves stimulated by light from light sources 72 are processed, as in glucometer 20 to assay glucose in blood 44.

Whereas light sources 72 are, optionally, arrayed in a circle, other configurations of light sources in a stent, in accordance with an embodiment of the invention, are possible and can be advantageous. For example, each of light sources 72 illuminates regions of blood 44 that are relatively close to each other or are substantially overlapping. It may therefore be difficult to distinguish photoacoustic waves generated by light from different light sources 72 by the locations of the origins in the blood of the photoacoustic waves.

Fig. 3 schematically shows a glucometer 75 comprising, optionally, three light sources 77 and control circuitry 78 mounted to a stent 76 inserted in blood vessel 40, in accordance with an embodiment of the invention. Glucometer 75 is similar to and operates similarly to glucometer 60 (Fig. 2), however light sources 77 are, optionally, arrayed along a line substantially parallel to the length of stent 76. The linear array of light sources 77 in general makes it relatively easier to distinguish photoacoustic waves generated by light from different light sources 77 by the locations of their origins. By way of another example, it may be advantageous, in order to facilitate mechanical collapse of a stent comprising light sources for

insertion into a blood vessel, to have the light sources arrayed in a configuration, which when the stent is expanded is helical.

It is noted that whereas in glucometers 20, 60 and 75, photoacoustic waves are sensed by sensors located outside of the body, in some embodiments of the invention at least one sensor (*e.g.* transducers 32) for sensing photoacoustic waves is positioned inside the body. For example, an acoustic sensor for sensing photoacoustic waves is optionally mounted to collar 24 or to stent 76. The sensor may transmit signals responsive to photoacoustic waves that it senses to a controller outside of the body using any suitable transmission medium, such as electromagnetic waves and/or sound waves. Optionally, control of and power for the at least one sensor is provided by the same circuitry that controls and powers the light sources.

Fig. 4 schematically shows an "ATR" (attenuated total reflection) glucometer 80 that uses attenuated total reflection of light, in order to assay glucose in a patient's blood, in accordance with an embodiment of the invention.

Glucometer 80 comprises a control unit 90, optionally mounted externally to the patient's body on a region of the patient's skin 42 and a stent 82, which is inserted into a blood vessel 40 of the patient, in accordance with an embodiment of the invention. Stent 82 has at least one light source 84 optically coupled to at least one optical detector 86 by an optic fiber 85 and circuitry 88 for controlling and powering the light source and detector. Control unit 90 optionally comprises a controller 92, an energy transmitter 36 for transmitting energy to control circuitry 88 and communication circuitry 94 for transmitting and receiving data and control signals between communication circuitry 92 and control circuitry 88 comprised in stent 82.

Light source 84 and detector 86 are located so that when stent 82 is expanded inside blood vessel 40, optical fiber 85 optionally extends through the lumen of the blood vessel between opposite sides of wall 41. Fiber 85, light source 84 and detector 86 are optionally coated with a suitable biocompatible material that mitigates encapsulation of the fiber, the light source and the detector by a barrier cell layer of inflammatory response cells. However, the biocompatible coating at least over a portion of the surface, hereinafter an "ATR surface", of fiber 85 is sufficiently thin so that along the ATR surface an evanescent field of light provided by light source 84 that propagates along the fiber to detector 86 extends into blood 44 in blood vessel 40.

At least one light source 84 is powered and controlled by control unit 90 and control circuitry 88 to transmit light to detector 86 at a plurality of wavelengths at which the

evanescent fields of the light interact with components of blood 44, at least one of which interacting components is glucose. The interaction between the evanescent fields and the glucose in the blood modulates the internal total reflection of the transmitted light along the ATR active surface of fiber 85 and thereby an amount by which the light is attenuated. Signals generated by detector 86 responsive to the light that it receives from light source 84 are transmitted, optionally via control circuitry 88, to communication circuitry 94 in control unit 90. Controller 92 receives and processes the signals to assay glucose in blood 44.

Optionally, at least one light source 84 provides light at wavelengths in an IR range of wavelengths from 1-40 micrometers noted in US patent 5,452,716, which describes ATR methods and apparatus for performing in vivo and in vitro assays of blood glucose, the disclosure of which is incorporated herein by reference. Optionally, controller 92 processes signals from at least one detector 86 to assay glucose in blood 44 using methods similar to those described in the 5,452,716 patent.

Fig. 5 schematically shows another ATR glucometer 100, in accordance with an embodiment of the invention. ATR glucometer 100 operates similarly to ATR glucometer 80 shown in Fig. 4 and is optionally identical to ATR glucometer 80 except for the orientation of optic fiber 85. In glucometer 100, fiber 85 lies along the wall of stent 82 rather than extending across the lumen of the stent. The orientation of optic fiber 85 in glucometer 100 can be advantageous in that a tendency of the fiber to interfere with flow of blood 44 in glucometer 100 is less than its tendency to interfere with blood flow in glucometer 80.

In some embodiments of the invention, optic fiber 85 is replaced by a suitably formed light pipe. For example, in glucometer 100 optic fiber 85 may be replaced by a suitably formed light pipe that lies along the wall of stent 82 after the stent is inserted into blood vessel 41. The light pipe may, for example, be formed from a light conducting polymer in the shape of a thin ribbon having an elliptical or rectangular cross section.

It is noted that whereas in the above description of exemplary embodiments, blood glucose is assayed, the present invention is not limited to assaying blood glucose. Methods and implanted devices similar to those used for assaying blood glucose, in accordance with an embodiment of the invention may, with appropriate choice of wavelengths of light provided by a light source or light sources in the devices, can be used for assaying other analytes present in blood. For example, a patient's blood albumin or lactate may be assayed, in accordance with embodiments of the invention. Albumin has a signatory wavelength at about 6.25 microns and lactate has a signatory wavelength at about 8.81 microns.

In the description and claims of the present application, each of the verbs, "comprise" "include" and "have", and conjugates thereof, are used to indicate that the object or objects of the verb are not necessarily a complete listing of members, components, elements or parts of the subject or subjects of the verb.

The present invention has been described using detailed descriptions of embodiments thereof that are provided by way of example and are not intended to limit the scope of the invention. The described embodiments comprise different features, not all of which are required in all embodiments of the invention. Some embodiments of the present invention utilize only some of the features or possible combinations of the features. Variations of embodiments of the present invention that are described and embodiments of the present invention comprising different combinations of features noted in the described embodiments will occur to persons of the art. The scope of the invention is limited only by the following claims.

CLAIMS

1. Apparatus for assaying an analyte in a patient's blood comprising:

at least one light source implanted in the patient's body controllable to illuminate blood in a blood vessel in the body with light at at least one wavelength that is absorbed and/or scattered by the analyte and as a result generates photoacoustic waves in the blood;

at least one acoustic transducer coupled to the body that receives acoustic energy from the photoacoustic waves and generates signals responsive thereto; and

a processor that receives the signals and processes them to determine a concentration of the analyte in the illuminated tissue region.

2. Apparatus according to claim 1 wherein the at least one acoustic transducer comprises at least one acoustic transducer coupled to a region of the skin.

3. Apparatus according to claim 1 or claim 2 wherein the at least one acoustic transducer comprises at least one acoustic transducer located inside the body.

4. Apparatus according to any of claims 1-3 wherein the at least one light source comprises at least one light source mounted to a collar that surrounds the blood vessel.

5. Apparatus according to claim 4 wherein the collar comprises circuitry for controlling the at least one light source.

6. Apparatus according to claim 5 wherein the collar comprises a receiver for receiving transmitted energy to power the at least one light source.

7. Apparatus according to any of claims 1-6 and comprising a transmitter that transmits energy to power the at least one light source.

8. Apparatus according to any of claims 1-7 wherein the at least one light source comprises at least one light source mounted to a stent that is inserted into the blood vessel.

9. Apparatus according to claim 8 wherein the at least one transducer comprises at least one transducer mounted to the stent.

10. Apparatus for assaying an analyte in a patient's blood comprising:

a stent adapted to be inserted into a blood vessel in the patient's body;

at least one light source and at least one optical detector mounted to the stent that are optically coupled by a light pipe, wherein light transmitted by the light source to the detector undergoes attenuated total reflection along the light pipe responsive to concentration of the analyte in the blood; and

a processor;

wherein the at least one detector generates signals responsive to light that it receives from the at least one light source and the processor processes the signals to assay the analyte responsive to a degree of ATR that the signals indicate.

11. Apparatus according to claim 10 wherein the light pipe extends through the lumen of a blood vessel into which the stent is inserted.

12. Apparatus according to claim 10 or claim 11 wherein the light pipe extends along the wall of a blood vessel into which the stent is inserted.

13. Apparatus according to any of claims 10-12 wherein the light pipe comprises an optic fiber.

14. Apparatus according to any of claims 8-12 wherein the stent comprises circuitry for controlling the at least one light source.

15. Apparatus according to any of claims 8-14 and comprising a transmitter that transmits energy to power the at least one light source.

16. Apparatus according to any of claims 8-15 wherein the stent comprises a receiver for receiving the transmitted energy.

17. Apparatus according to any of claims 6, 7, 15 or 16 wherein the energy comprises electromagnetic energy.

18. Apparatus according to claim 17 wherein the electromagnetic energy comprises RF energy.

19. Apparatus according to claim 17 or claim 18 wherein the electromagnetic energy comprises optical energy.

20. Apparatus according to any of claims 6, 7 or 15 -19 wherein the energy comprises acoustic energy.

21. Apparatus according to any of the preceding claims wherein the analyte is glucose.

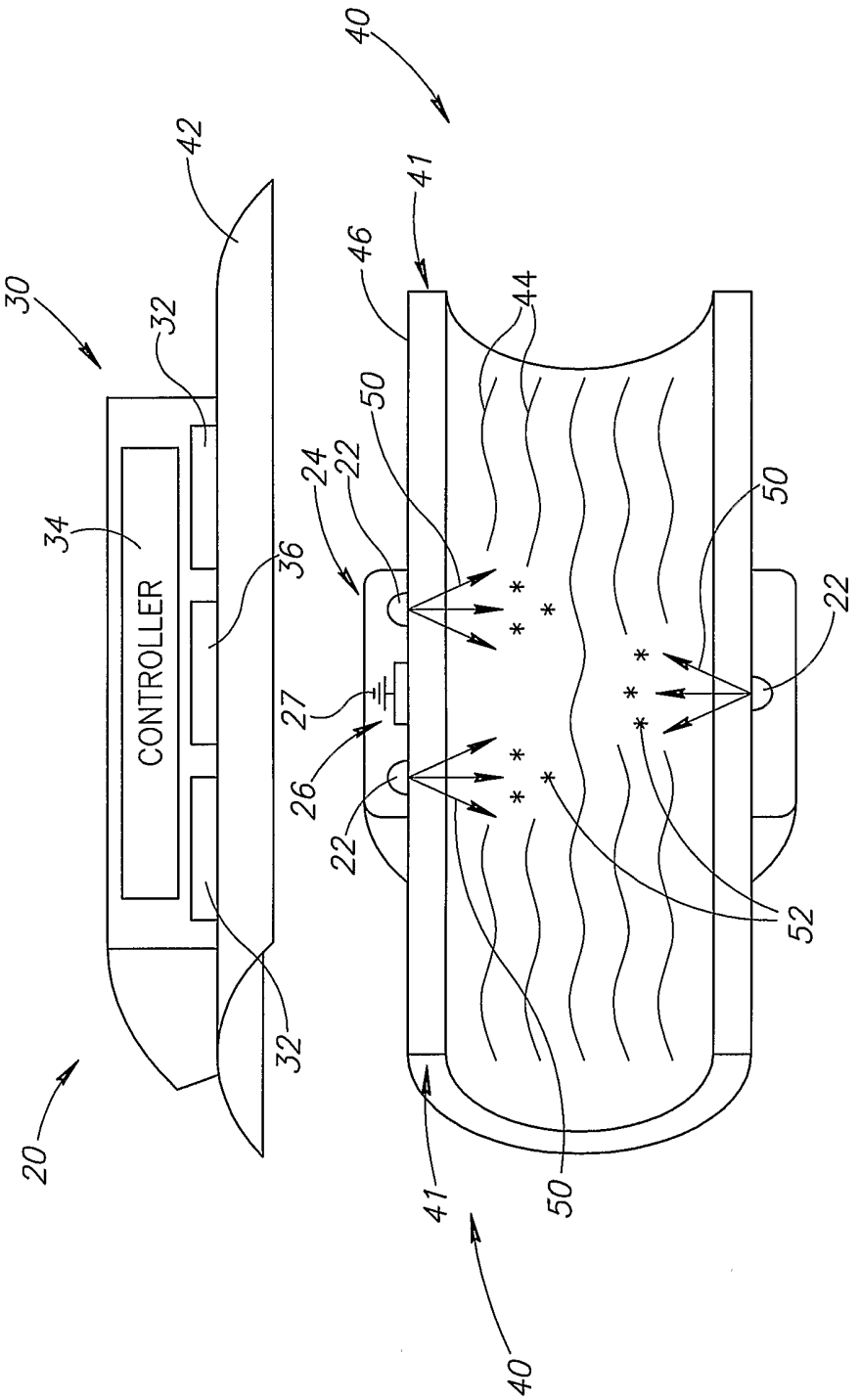
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FIG.1

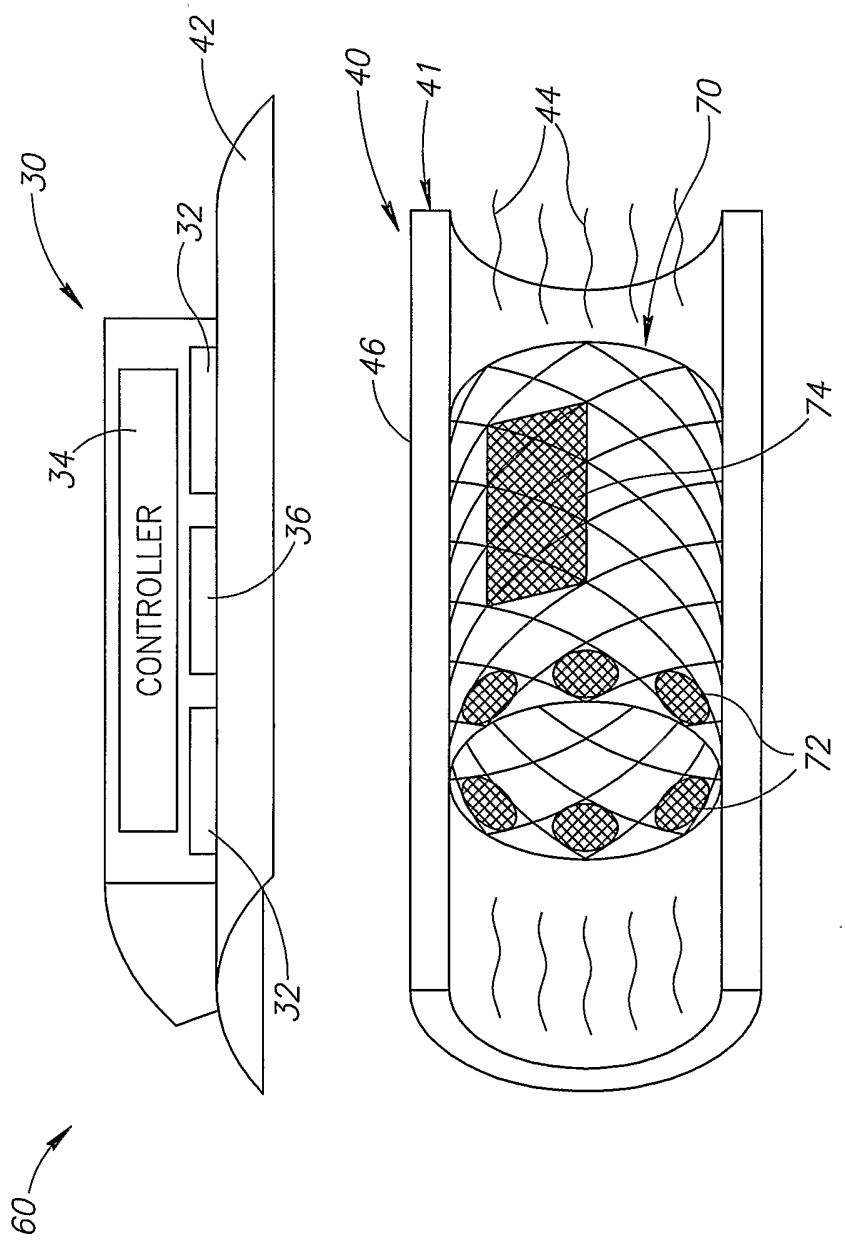

FIG.2

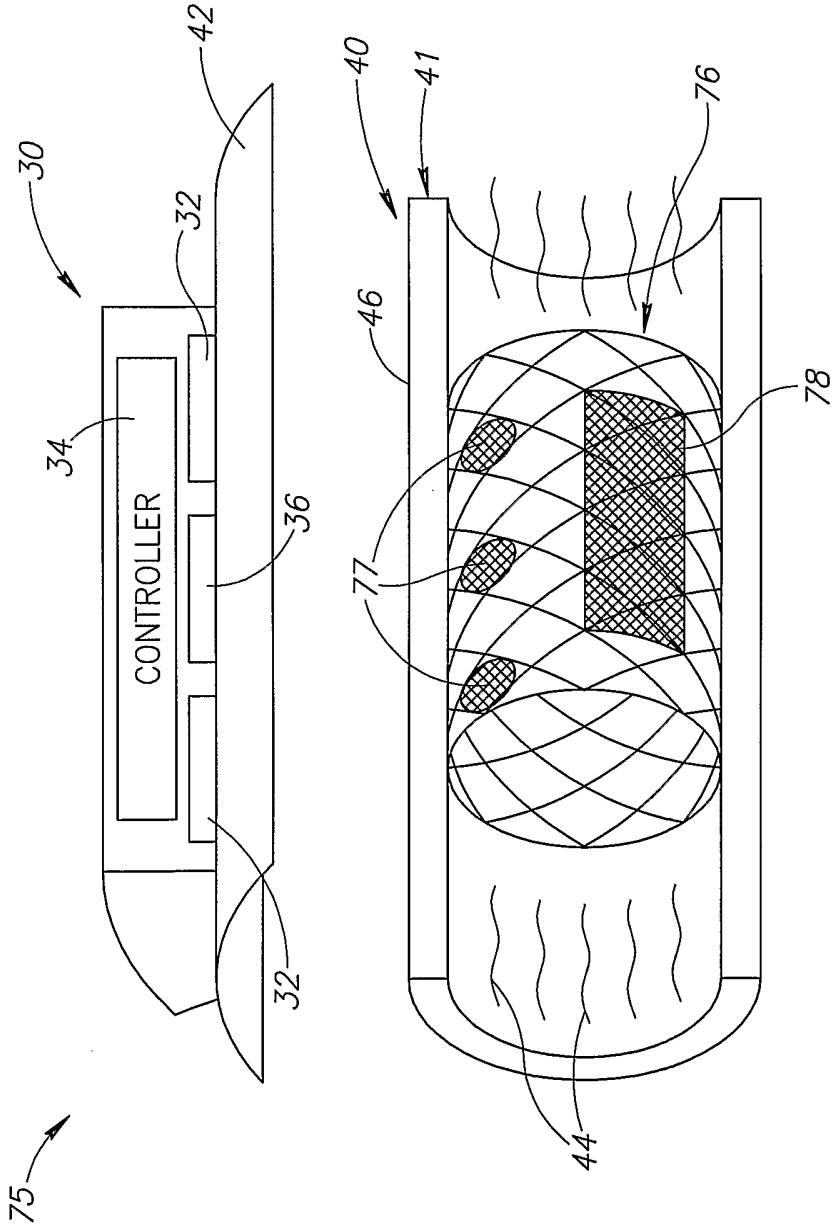

FIG.3

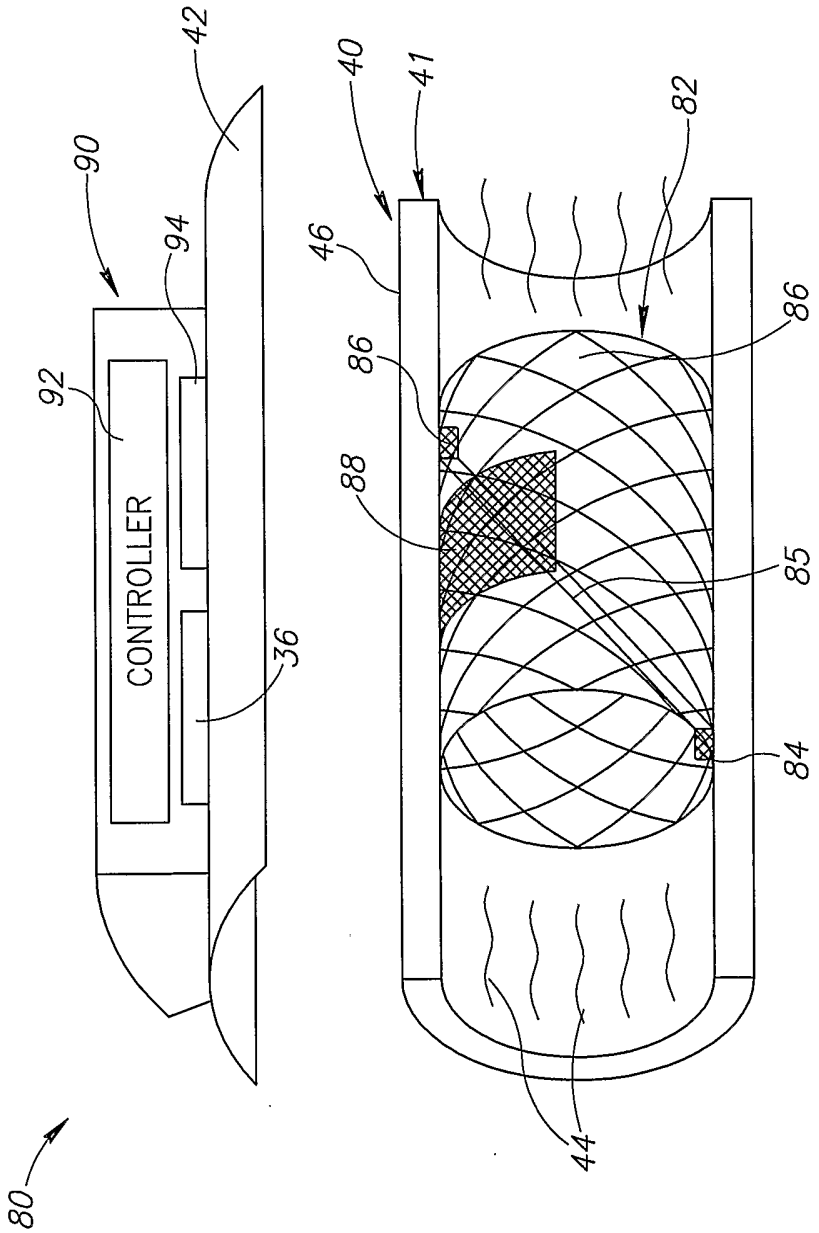

FIG.4

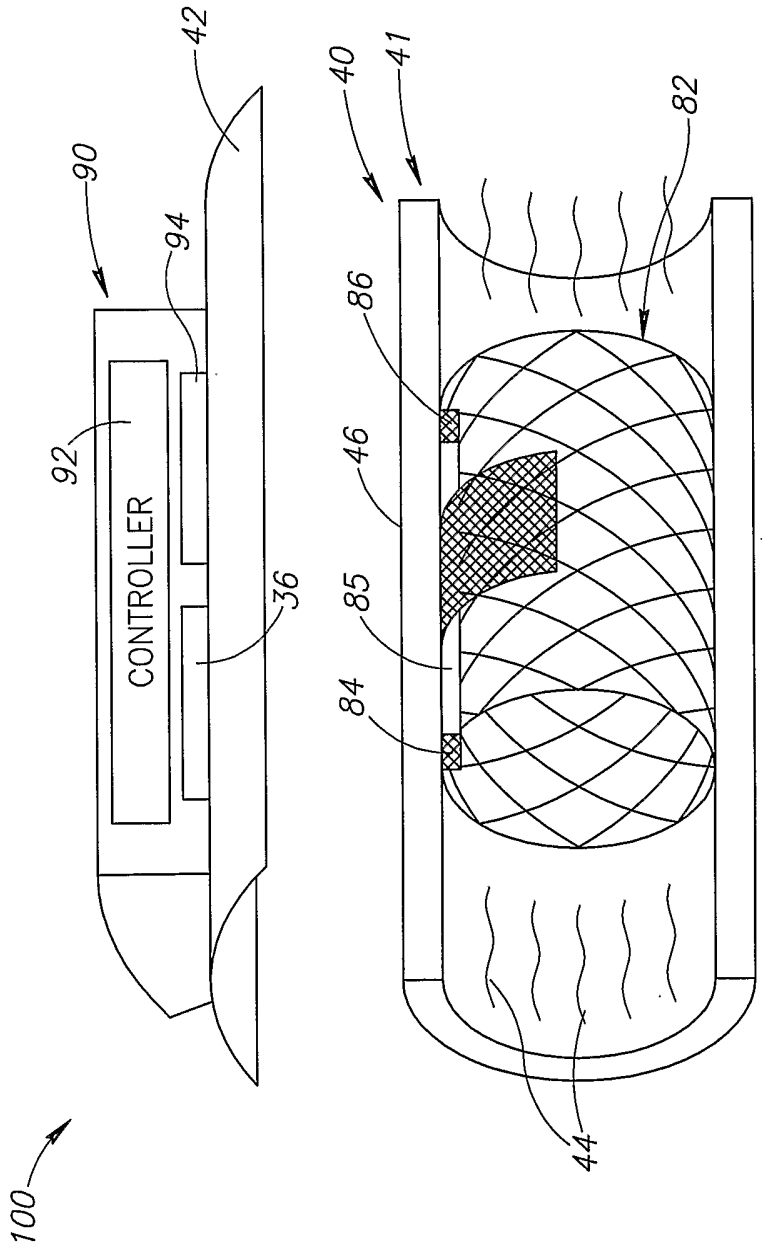

FIG.5