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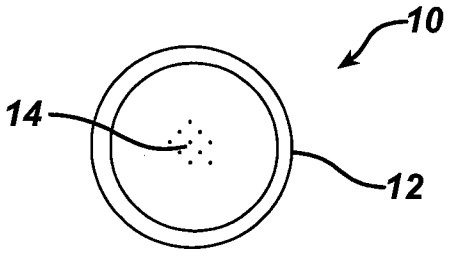

FIG. 1

(57) Abstract: Various compositions, methods, and devices are provided that use fluorescent nanoparticles, which can function as markers, indicators, and light sources. The fluorescent nanoparticles can be formed from a fluorophore core surrounded by a biocompatible shell, such as a silica shell. In one embodiment, the fluorescent nanoparticles can be delivered to tissue to mark the tissue, enable identification and location of the tissue, and/or illuminate an area surrounding the tissue. In another embodiment, the fluorescent nanoparticles can be used on a device or implant to locate the device or implant in the body, indicate an orientation of the device or implant, and/or illuminate an area surrounding the device or implant. The fluorescent nanoparticles can also be used to provide a therapeutic effect.

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FLUORESCENT NANOPARTICLE COMPOSITIONS, METHODS, AND DEVICES

FIELD OF THE INVENTION

[0001] The present invention relates to fluorescent nanoparticles, and in particular to various compositions, methods, and devices that use fluorescent nanoparticles.

BACKGROUND OF THE INVENTION

[0002] Illuminating light incident on tissue is transmitted through, scattered by, absorbed, or reflected by that tissue. At certain wavelengths, after absorbing the illuminating light, tissue can re-emit light energy at a different wavelength (autofluorescence). If a substance is introduced into the tissue or is present between tissue layers, or in lumens, it can fluoresce after absorbing incident light as well. Detecting devices can be placed in relationship to the tissue to image light that is transmitted, scattered, reflected, or fluoresced from the tissue. It is well known in the art that certain wavelengths of light tend to be preferentially absorbed, reflected, or transmitted through different types of tissue. Generally, near infrared light (600 - 1300 nm) tends to coincide with minima in the spectral absorption curve of tissue, and thus allows the deepest penetration and transmission of light. For optical analysis of surface structures or diagnosis of diseases very close to the body surface or body cavity surfaces or lumens, UV light and visible light below 600 nm can also be used, as it tends to be absorbed or reflected near the surface of the tissue.

[0003] Various modalities are currently used for imaging of tissue and organs, including visible light endoscopes, ultrasound, magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography (PET). Many anatomical spaces and tissues, however, are not easily accessible and viewable. Moreover, the use of imaging equipment can be expensive and time consuming, and their application is often limited.

[0004] Various contrast agents are also employed to effect image enhancement in a variety of fields of diagnostic imaging, the most important of these being X-ray, magnetic

resonance imaging (MRI), ultrasound imaging, and nuclear medicine. Additionally, optical labels, such as fluorescent dyes, are introduced into tissue samples to signal abnormal biological and/or chemical conditions of tissues of a living subject. Despite many successful applications, conventional optical labels have many drawbacks. For example, conventional optical labels are generally toxic to living cells and tissues comprised of living cells. Additionally, conventional optical labels such as fluorescent dyes generally suffer from short-lived fluorescence because the dyes undergo photo bleaching after minutes of exposure to an excitation light source. This renders them unsuitable for optical imaging that requires extended time period of monitoring. Moreover, conventional optical labels are sensitive to environmental changes such as pH and oxygen concentration. Another drawback of conventional optical labels is that typically the excitation spectra of such labels are quite narrow, while the emission spectra of such labels is relatively broad, resulting in overlapping emission spectra. Thus, when a combination of conventional optical labels with different emission spectra are used in optical imaging, multiple filters are need to detect the resultant emission spectra of the combination. Additionally, fluorescent labels are generally inefficient at converting the excitation light to the emission wavelength, and the resulting signal can be very weak.

[0005] Accordingly, there remains a need for improved compositions, methods, and devices for use in medical imagining, and more particularly for marking, indicating, and illuminating tissue.

SUMMARY OF THE INVENTION

[0006] The present invention generally provides various compositions, methods, and devices that use fluorescent nanoparticles, which can function as markers, indicators, and light sources. In one embodiment, a method for locating, marking, or illuminating tissue is provided and includes delivering at least one fluorescent nanoparticle to tissue. The fluorescent nanoparticle can be formed from a fluorescent core and a biocompatible shell surrounding the fluorescent core. The method can also include delivering energy to the at least one fluorescent nanoparticle to cause the at least one fluorescent nanoparticle to fluoresce in a manner that can be detected to produce an image of the nanoparticle.

Various methods can be used to deliver the nanoparticle(s) to tissue including, for example, injecting the nanoparticle(s) into tissue, delivering the nanoparticle(s) using an intravenous catheter, and coating a solution containing the nanoparticle(s) onto a tissue surface using, for example, an applicator. Where a coating is used, in one embodiment the nanoparticle(s) can be used to illuminate a body cavity when energy is delivered thereto. In another embodiment, the nanoparticle(s) can be delivered into a kidney, and the nanoparticle(s) can have a size such that the kidney filters the at least one fluorescent nanoparticle into the ureter. Similarly, the nanoparticle(s) can be delivered into a liver, and the nanoparticle(s) can have a size such that the liver filters the at least one fluorescent nanoparticle into the colon.

[0007] In yet another embodiment, a medical device is provided and includes an elongate shaft having a proximal end adapted to remain outside of a patient's body and a distal end adapted to be disposed within a patient's body. The distal end can have at least one fluorescent nanoparticle adapted to fluoresce when energy is delivered thereto. The fluorescent nanoparticle(s) can be adapted to illuminate an area surrounding the distal end of the elongate shaft when energy is delivered thereto, and/or to indicate an orientation of the distal end of the elongate shaft when energy is delivered thereto. The nanoparticle(s) can be embedded in, coated on, or contained within the distal end of the elongate shaft.

[0008] In other aspects, a surgical method is provided and includes positioning a device in a patient's body. The device can contain at least one fluorescent nanoparticle. The method can further include delivering energy to the at least one fluorescent nanoparticle to cause the at least one fluorescent nanoparticle to fluoresce. The nanoparticle(s) can illuminate an area surrounding the device when energy is delivered thereto, and/or it can be used to locate the device and/or indicate an orientation of the device. In one embodiment, the device can be an implant. When energy is delivered to the at least one fluorescent nanoparticle, the at least one fluorescent nanoparticle can indicate, for example, a location of a refill port on the implant and/or a size of the implant. In another embodiment, the device can be an elongate shaft having a distal end positioned in a body lumen of the patient while a proximal end of the elongate shaft remains external to the patient.

[0009] In other aspects, a medical composition is provided and includes a fluorescent nanoparticle having a core containing at least one dye adapted to emit visible light, and at least one dye adapted to emit non-visible light, and a biocompatible shell surrounding the core. In use, at least one fluorescent nanoparticle can be delivered to tissue, visible light can be delivered to the tissue to cause a first dye contained within the at least one fluorescent nanoparticle to emit visible light, and invisible light can be delivered to the tissue to cause a second dye contained within the at least one fluorescent nanoparticle to emit invisible light.

[0010] In yet another embodiment, a medical composition is provided and includes a fluorescent nanoparticle having a core containing at least one fluorescent dye, a biocompatible shell surrounding the core, and a magnetic material located in at least one of the core and the shell. In use, at least one fluorescent nanoparticle can be delivered to tissue, and energy can be delivered to the tissue to locate the at least one fluorescent nanoparticle and to cause a magnetic material in the at least one fluorescent nanoparticle to deliver heat to the tissue.

[0011] In yet another embodiment, a method for identifying tumor passage into the sentinel lymph node is provided and includes delivering at least one fluorescent nanoparticle to a tumor. The fluorescent nanoparticle can be formed from a fluorescent core and a biocompatible shell surrounding the fluorescent core. Energy can be delivered to tissue surrounding the tumor to locate the at least one fluorescent nanoparticle to determine whether the at least one fluorescent nanoparticle has reached a sentinel lymph node.

[0012] An endoscopic adaptor is also provided for viewing fluorescent nanoparticles. In one embodiment, the adaptor can include first and second members removably matable to one another and adapted to engage a portion of an endoscope eyepiece therebetween. The first member can have a viewing lumen formed therethrough and adapted to axially align with a viewing lumen formed in an endoscope eyepiece, and a cavity formed therein for seating a filter adapted to filter light received through the viewing lumen of the first member. In use, the adaptor can be coupled to a proximal end of an endoscope having a

light transmitting element at a distal end adapted to emit excitation light and an image obtaining element adapted to obtain an image that includes both reflected and fluoresced light. The distal end of the endoscope can be inserted into a body cavity so as to position the distal end adjacent to tissue containing a fluorescent nanoparticle, and the light transmitting element can be activated to emit excitation light onto the tissue containing the at least one fluorescent nanoparticle such that fluorescent light is then transmitted through the tissue and received by the image obtaining element. The image obtaining element can transmit the image to the adaptor. In one embodiment, the adaptor can include a filter disposed therein and configured to reject (reflect or absorb) light in the excitation waveband and transmit light in the fluorescent waveband. The transmitted fluorescent light can be imaged onto a detector array (camera) sensitive to this waveband which can then generate an image on a display.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] The invention will be more fully understood from the following detailed description taken in conjunction with the accompanying drawings, in which:

[0014] FIG. 1 is a side view of one embodiment of a fluorescent nanoparticle having a core and a shell;

[0015] FIG. 2 is a perspective view of one embodiment of an applicator for applying fluorescent nanoparticles to a tissue surface;

[0016] FIG. 3 is a top view of a drug delivery pump having fluorescent nanoparticles disposed around a bolus port for locating the bolus port once the pump is implanted;

[0017] FIG. 4 is a perspective view of a gastric restriction band having fluorescent nanoparticles disposed thereon for indicating a size of the band;

[0018] FIG. 5A is a side view of an elongate shaft having fluorescent nanoparticles disposed around a distal end thereof for illuminating a body cavity;

[0019] FIG. 5B is a side view of an elongate shaft having fluorescent nanoparticles

disposed on a distal end thereof for indicating an insertion depth of the elongate shaft into a body lumen;

[0020] FIG. 5C is a side view of an elongate shaft having fluorescent nanoparticles disposed to form an arrow indicating a direction orientation of a distal end of the elongate shaft;

[0021] FIG. 6 is a diagram illustrating one embodiment of a laparoscopic system for viewing fluorescent nanoparticles;

[0022] FIG. 7A is a diagram illustrating one embodiment of a laparscope having an image combiner for viewing visible and non-visible wavelengths emitted by fluorescent nanoparticles;

[0023] FIG. 7B is a diagram illustrating the embodiment of FIG. 7A incorporated into a hand held instrument with a self-contained monitor or display output that feeds to other displays;

[0024] FIG. 8 is a cross-sectional view of one embodiment of an adaptor mated to an endoscope eyepiece; and

[0025] FIG. 9 is a perspective view of another embodiment of a portion of an adaptor for mating to an endoscope, showing a removable filter cartridge.

DETAILED DESCRIPTION OF THE INVENTION

[0026] Certain exemplary embodiments will now be described to provide an overall understanding of the principles of the structure, function, manufacture, and use of the devices and methods disclosed herein. One or more examples of these embodiments are illustrated in the accompanying drawings. Those skilled in the art will understand that the devices and methods specifically described herein and illustrated in the accompanying drawings are non-limiting exemplary embodiments and that the scope of the present invention is defined solely by the claims. The features illustrated or described in connection with one exemplary embodiment may be combined with the features of other

embodiments. Such modifications and variations are intended to be included within the scope of the present invention.

[0027] The present invention generally provides various compositions, methods, and devices that use fluorescent nanoparticles, which can function as markers, indicators, and light sources. The particular configuration of the fluorescent nanoparticles can vary, but preferably the nanoparticles are biocompatible and non-toxic. The shape, size, and morphology of the nanoparticles can vary. In an exemplary embodiment, as shown in FIG. 1, the nanoparticles 10 can be formed from a fluorophore core 14 and a biocompatible shell 12 that surrounds the core 14. The use of a biocompatible shell is particularly advantageous as it is non-toxic when used in medical applications. The shell can also be configured to intensify the photophysical properties of the core such that, when this dye is excited by light, the observed fluorescence is brighter than the dye itself. This enables viewing through tissue having a thickness of about 2cm or less.

[0028] The particular materials used to form the core and the shell can vary depending on the intended use, but in an exemplary embodiment the core includes organic dye molecules and the shell is silica-based. Fluorescing dyes are available at various wavelengths, including both visible and non-visible wavelengths. Dyes having any wavelength can be used with the present invention, but the particular dye selected may depend on the intended use. For example, where the dye needs to be viewed through tissue, the dye preferably has a wavelength that is near or within the infrared range, i.e., from about 600nm to 1350nm. Particular dyes in the near infrared wavelength are preferred as they demonstrate the best transmissibility for passing through tissue. In an exemplary embodiment, the nanoparticles contain a dye that has an absorption and emission cross-section in the region of about 800nm. One exemplary dye is Cy 5.5 manufactured by GE Healthcare. In order to view dyes with an emission cross-section outside of the visible spectrum for medical applications, energy must be delivered to the dye to excite the molecules and the resulting emission by the molecules must be collected by specialized equipment sensitive to this non-visible waveband. Various exemplary methods and devices for delivering energy to dyes with emission cross-sections outside of the visible spectrum will be discussed in more

detail below. Where the dye does not need to be viewed through tissue, the dye can have a wavelength that is within the visible range, i.e., from about 400nm to 700nm. When used in the body, light may need to be delivered to the tissue containing the particles to enable viewing. The light source may be external to the body for delivering light internally, or an internal light source may be used for internal application.

[0029] A person skilled in the art will appreciate the fluorescent nanoparticles can be formed from a variety of materials using various methods. Exemplary fluorescent nanoparticles and methods for making the same are disclosed in detail in U.S. Publication No. 2004/0101822 of Wiesner et al. entitled "Fluorescent Silica-Based Nanoparticles," U.S. Publication No. 20046/0183246 of Wiesner et al. entitled "Fluorescent Silica-Based Nanoparticles," and U.S. Publication No. 2006/0245971 of Burns et al. entitled "Photoluminescent Silica-Based Sensors and Methods of Use," which are hereby incorporated by reference in their entireties. A person skilled in the art will also appreciate that fluorescent semiconductor nanocrystals, also referred to as quantum dots, can also be used with the various methods and devices disclosed herein.

[0030] As indicated above, the present invention provides various compositions, methods, and devices that use fluorescent nanoparticles. In one embodiment, fluorescent nanoparticles can be used to locate, mark, or illuminate tissue. A person skilled in the art will appreciate that the particular tissue or body lumen to be located, marked, or illuminated, as well as the technique for delivering the nanoparticles to the tissue, can vary and the following techniques are merely exemplary.

[0031] In one embodiment the nanoparticles can be used to locate a structure that traverses through other tissue or is otherwise visually inaccessible. Many tubular structures, such as the ureter, are not visually accessible, but rather traverse through other tissue. Various regions of the colon can also be difficult to access visually. A solution containing fluorescent nanoparticles can thus be delivered to the structure of interest to enable a surgeon to locate the structure. The method of delivery can vary. For example, the fluorescent nanoparticles can be disposed in a liquid, foam, or gel solution, such as a saline solution, and they can be delivered using an intravenous (IV) drip or they can be injected

directly into the tissue. Where the solution has a low viscosity, the structure can be isolated, e.g., clamped off or otherwise closed, to contain a finite volume of particles therein, or an open line, such as a saline drip, can be continuously fed to the structure. Alternatively, the solution can be modified to have a high viscosity and/or to contain adhesives, as will be discussed in more detail below. Exemplary solutions will be discussed in more detail below.

[0032] In yet another embodiment, the nanoparticles can have a property that enables them to be filtered into a desired structure, such as the ureter or colon. In particular, delivery to the kidney will enable filtration into the ureter, and delivery to the liver will enable filtration into the colon. For delivery to the ureter via the kidney, the particles typically have a size in the range of about 4nm to 11nm, whereas the particles typically have a size that is greater than about 12nm for delivery to the colon via the liver. Various delivery techniques can be used, including those previously discussed, such as IV delivery into the patient's circulatory system.

[0033] In yet another embodiment, the nanoparticles can be used to identify the spread of cancerous cells. With certain types of cancer, such as breast cancer, the nanoparticles can be injected into the tumor. The nanoparticles will be carried into other parts of the body by way of the blood or lymphatic vessels or membranous surfaces. Energy can thus be delivered to the body to locate the nanoparticles and thus identify whether the tumor has spread. This is particularly useful in determining whether cancerous cells have reached the sentinel lymph node. The use of nanoparticles formed from a fluorophore center core and a biocompatible shell is also advantageous as it provides a non-toxic method for locating cancerous cells, unlike prior art methods which utilize radio-isotopes and semi-conductive nanoparticles which contain toxic metals.

[0034] A person skilled in the art will appreciate that the aforementioned techniques can be used to locate any structure. By way of non-limiting example, other exemplary structures include the structures in the biliary system, the lymphatic system, and the circulatory system.

[0035] The present invention also provides methods for marking tissue. In one embodiment, the nanoparticles, or a solution containing the nanoparticles, can be applied or "painted" onto a tissue surface, or injected into tissue. The applied nanoparticles can function as a marking used to allow for subsequent identification of the tissue. For example, during a colonoscopy the nanoparticles can be applied to or near a polyp that cannot be removed during the procedure. During a subsequent procedure, the nanoparticles can be used to locate and identify the polyp, for example from the abdominal perspective. The markings can also be used to indicate orientation. For example, directional markings can be made with the nanoparticles. In another embodiment, the markings can be used to detect leaks, for example in a closed system fluid based implant, such as with gastric bands. One failure mode experienced with gastric band is that the system can leak due to punctures of the catheter with a needle during an adjustment, undetected puncturing of the balloon with a suture needle during surgery, and partially or completely disconnected catheter-to-port connections. The fluorescent particles can be delivered to the band, e.g., in a solution, and their disappearance from the band system or their location outside of the band system in the body can be used to indicate the presence of a leak.

[0036] In another embodiment, fluorescent nanoparticles can be used to illuminate tissue. For example, the nanoparticles can be applied to a tissue surface in a body cavity to illuminate the body cavity, such as the stomach or uterus. By way of non-limiting example, the nanoparticles can be disposed within a gel, such as KY® Jelly, carboxy methyl cellulose, collagen, and hydrogel, and delivered to the uterus. The nanoparticles are thus effective to illuminate the uterus during a hysterectomy or other procedures. Similarly, the nanoparticles could be applied to an area of tissue within the stomach to thereby illuminate the stomach during various procedures.

[0037] Various devices can be used to apply the particles to a tissue surface, including rigid and flexible devices, such as elongate shafts, syringes, or hand held pens with marking tips configured to coat, inject, or otherwise deliver the nanoparticles to tissue. The markings can also be applied manually using ones finger tips. FIG. 2 illustrates one

exemplary embodiment of a marking device 20. As shown, the marking device 20 has an elongate shaft with a distal tip 24 having a nozzle formed thereon for spraying the nanoparticles onto a tissue surface. The tip can, however, have a variety of other configurations. For example, the tip can include a brush for brushing the particles onto a tissue surface. The particular configuration can vary depending on the intended use. In use, as shown in FIG. 2, the marking device 20 can be inserted through a trocar 22 that extends through a tissue surface and into the abdominal cavity. Endoscopes or other access devices can also optionally be used, and/or the device can be introduced through a natural orifice or through a man-made orifice. Once positioned adjacent to a target tissue, the marking device 20 can be manipulated using, for example, controls to articulate the distal end of the device and controls to actuate the nozzle, to apply the nanoparticles to the tissue surface. A person skilled in the art will appreciate that a variety of marking devices known in the art can be used. By way of non-limiting example, U.S. Patent Appl. No. 11/533,506 of Gill et al., filed on September 20, 2006 and entitled "Dispensing Fingertip Surgical Instrument," which is incorporated herein by reference in its entirety, discloses one exemplary embodiment of a marking device that can be used to apply nanoparticles to a tissue surface.

[0038] In each of the various embodiments disclosed herein the nanoparticles can optionally be delivered in a carrier. The particular composition of the carrier can vary, and suitable carriers include any biocompatible liquid, foam, gel, or solid. The carrier and/or the nanoparticles can also include other substances, such as pharmaceutical and/or therapeutic substances. In one exemplary embodiment a more viscous liquid, foam, or gel is used to prevent the particles from being flushed from the tissue site. Exemplary high viscosity liquids include, by way of non-limiting example, KY® Jelly, carboxy methyl cellulose, collagen, and hydrogel. The solution can also optionally have adhesive properties to help retain the nanoparticles in a desired location. Exemplary adhesives are disclosed, by way of non-limiting example, in U.S. Publication No. 2004/0190975 of Goodman entitled "Applicators, Dispensers and Methods for Dispensing and Applying Adhesive Material," which is hereby incorporated by reference in its entirety. This reference also discloses various exemplary applicator devices that can be used to deliver

nanoparticles to tissue. The nanoparticles can also be combined with existing marking fluids, such as biocompatible dyes, stains, or colored adhesives. A person skilled in the art will appreciate that any carrier can be used.

[0039] The composition of the fluorescent nanoparticles can also vary to provide different functions. In one embodiment, a combination of visible and non-visible dyes can be used to form fluorescent nanoparticles for use in marking tissue. Such dual- or multi-wavelength nanoparticles can be delivered to tissue and, once delivered, the visible dyes can be used to quickly locate a tissue containing the particles and the non-visible dyes can provide more precise viewing. By way of non-limiting example, nanoparticles containing visible and non-visible dyes can be delivered to the ureter. Visible dyes located near the surface can be viewed with visible light to help locate the ureter. Once located, an infrared light can be used to see the non-visible dye locating the ureter path located deeper within tissue. Exemplary viewing methods will be discussed in more detail below. While visible fluorescent dyes are preferred, other types of visible dyes may be used in combination with non-visible fluorescent nanoparticles.

[0040] In other embodiments, the composition can be adapted to provide a therapeutic effect. For example, a magnetic material can be used with the fluorescent nanoparticles to enable therapeutic energy to be delivered to tissue. Various techniques can be used to associate a magnetic material with the nanoparticles. For example, the particles can be manufactured with a magnetic or magnetic-containing core. Alternatively, the particles can be coated with a magnetic material, or they can be disposed within a magnetic solution. In use, the magnetic nanoparticles can be applied to tissue to be treated using various methods, including those previously discussed. The location of the particles can be identified using light, and once identified an alternating current can be delivered to the particles to induce inductive heating. As a result, the magnetic nanoparticles will release heat, thereby cauterizing or otherwise treating the tissue. The use of magnetic particles in combination with fluorescent nanoparticles is particularly advantageous as the fluorescent nanoparticles enable precise identification of the tissue being treated, thereby limiting or avoiding damage to healthy tissue or minimize margins needed. In another embodiment, a

sensor can be provided for sensing the tissue temperature to enable a desired temperature range to be maintained during energy delivery. The sensor can be disposed on a distal end of a device, such as an endoscope, catheter, or other delivery device, and it can be coupled to an external apparatus that displays the measured temperature. In certain exemplary embodiments, the temperature of the tissue being treated is maintained at a range of about 150°F to 180°F. The magnetic particle property may also be used to steer the particle to a preferred location or accumulate at a preferred location.

[0041] In another embodiment, fluorescent nanoparticles can be used on medical devices to indicate the location and/or orientation of the device once introduced into a patient's body, or to illuminate a body cavity within which the device is disposed. For example, fluorescent nanoparticles can be coated onto, embedded within, or disposed within an implant to enable future location and identification of the implant. The particles, or a liquid or solid containing the particles, can also be disposed within a capsule or other structure, and that structure can in turn be disposed within an implant. By way of non-limiting example, the nanoparticles can be placed around a port, such as a bolus port in a drug pump or a fluid-refill port in a gastric band. FIG. 3A illustrates a drug delivery pump 30 having a bolus port 31 with nanoparticles 32 disposed therearound. The nanoparticles can be used to locate the port and allow easy access for introducing and removing fluids to and from the port. For example, FIG. 3B illustrates the nanoparticles radiating through the tissue to enable location of the port, thereby allowing a syringe, as shown, to be inserted into the port. A reading unit with a fluorescence meter can be used to identify and locate the particles and thus the port. The nanoparticles can also be used to indicate size and/or directional orientation. For example, the nanoparticles can be located around a gastric band, either by coating the particles onto the band, embedding the particles in the band during manufacturing, or filling the band with a nanoparticles-containing solution. FIG. 4 illustrates a gastric band 40 having a balloon containing nanoparticles or a nanoparticle solution 42. In use, the nanoparticles can be viewed to determine the size of the gastric band, thereby enabling a surgeon to easily determine whether any adjustments are necessary. In yet another embodiment, a catheter, endoscope, or other devices that are introduced into body can have nanoparticles positioned to allow the location of distal end

of the device to be identified during use, to indicate a directional orientation of the device, and/or to illuminate an area surrounding a portion of the device. By way of non-limiting example, FIG. 5A illustrates a catheter or endoscope 50 having nanoparticles 52 disposed around a distal end thereof to illuminate tissue surrounding the distal end of the device 50. The use of nanoparticles for illumination is particularly advantageous as it eliminates the need for a separate light source on the device. The particles could also be positioned to form indicia that indicate a directional orientation or physical end of the device. For example, FIG. 5B illustrates an elongate shaft 54, such as a catheter or endoscope, having particles disposed on the device so as to form a series of parallel lines 56 along a length of the distal end of a device 54. The lines 56 can thus be used to indicate the insertion depth of the distal end of the device 54 into a body lumen. The lines could also be used as a bar code. The nanoparticles could also be disposed to form one or more directional indicators, such as an arrow 58 as shown in FIG. 5C, that enables a surgeon to determine the particular directional orientation of the device within a body lumen or cavity. In yet another embodiment, the nanoparticles can be located or, disposed within, or embedded in an absorbable material, such as a suture or fastener, that would leave a the nanoparticles in the tissue after the absorbable material is absorbed.

[0042] Various exemplary methods and devices are also provided to excite the fluorescent nanoparticles to enable viewing. In an exemplary embodiment, electromagnetic energy can be delivered to fluorescent nanoparticles disposed within a patient's body using a delivery apparatus, such as an endoscope or laparoscope. The delivery apparatus can be located externally, e.g., above the tissue surface, or internally. The excitation source can include any device that can produce electromagnetic energy at wavelengths that correspond to the absorption cross section of the nanoparticles, including but not limited to, incandescent sources, light emitting diodes, lasers, arc lamps, plasma sources, etc. Various imaging technologies can also be used for detecting, recording, measuring or imaging fluorescent nanoparticles. In an exemplary embodiment, the imaging technology is adapted to reject excitation light, detect fluorescent light, form an image of the location of the nanoparticles, and transmit that image to either a storage or display medium. Exemplary devices include, for example, a flow cytometer, a laser scanning cytometer, a

fluorescence micro-plate reader, a fluorescence microscope, a confocal microscope, a bright-field microscope, a high content scanning system, fiber optic cameras, digital cameras, scanned beam imagers, analog cameras, telescopes, microscopes and like devices.

[0043] In an exemplary embodiment, the energy source is light, i.e., electromagnetic radiation, and the reading apparatus has an elongate shaft that is adapted to be inserted into a body lumen and that includes a light emitting mechanism and an image receiving apparatus. Since fluorescent nanoparticles formed from a fluorophore core and a silica shell can absorb and emit energy in the visible, infrared and near infrared frequencies, and they are illuminated at one wavelength and observed at a different shifted wavelength, it is desirable to provide an imaging apparatus that can enable visualization of such nanoparticles. FIG. 6 illustrates one exemplary embodiment of a laparoscope that has two illumination or light emitting sources. As shown, the laparoscope utilizes an optical switch to select the illumination source. One illumination source may be a standard white light source, such as a Xenon arc lamp used in standard endoscopic systems for illuminating and viewing in the visible spectrum. The second light source may be a narrow-band source associated with the absorbance cross section of the nanoparticles, such as a laser, LED, mercury source, or filtered broadband source. FIG. 6 illustrates a 780nm pigtailed laser diode. The optical switch can connect the selected source to an optical fiber bundle that extends through the laparoscope for transmitting the light through an eyepiece at the distal end of the laparoscope. When the light is transmitted, e.g., by depressing a switch, button, or foot pedal, the fluorescent nanoparticles will excite and fluoresce. The laparoscope can also include an image receiving apparatus or camera for collecting the reflected light from the fluorescent nanoparticles. As shown in FIG. 6, the device can include a filter switch to place the appropriate optical filter between the eyepiece and the camera. The filter that is used for visualization of the nanoparticles, for example, must be highly efficient at rejecting the excitation wavelength in order to avoid saturation of the camera, while still being highly transparent at the wavelength of the emission of the nanoparticles. One exemplary filter is an interferometric long-pass filter with four orders of magnitude of rejection at the excitation wavelength and over 80% transmission at the peak of the fluorescent band. As further shown in FIG. 6, the captured image can be transmitted to a

monitor for viewing. The monitor can be an on-board monitor or an external monitor, or other reading devices can be used such as a readout display, an audible device, a spectrometer, etc. A person skilled in the art will appreciate that, while a laparoscope is shown, various other elongate shafts, such as catheters and endoscopes, can be used to transmit and receive light for viewing fluorescent nanoparticles. The embodiment described illustrates real time viewing. A person skilled in the art will also appreciate that image(s) can be captured and stored for overlay transmission, such as showing a peristaltic pulse as a continuous path.

[0044] Additional utilization can also be achieved in the non-visible ranges, as previously indicated, by combining a visible light source with a non-visible light source enabling the ability to turn the non-visible image on or off. The images may be viewed either side by side or simultaneously by overlapping the images. The visible light source can vary and can be an ambient room source, an LED, a laser, a thermal source, an arc source, a fluorescent source, a gas discharge, etc., or various combinations thereof. The light source can also be integrated into the instrument or it may be an independent source that couples to the instrument.

[0045] FIG. 7A illustrates one embodiment of a laparoscope that has the ability to overlay a fluorescent image onto a visible image to enable simultaneous viewing of both images. In this embodiment, both light sources can be combined into an illumination port of the laparoscope using, for example, a bifurcated fiber. At the eyepiece of the scope, a specialized optical fiber can be used to split the light to two separate cameras. For example, a filter can reflect all visible light to a visible image camera and can transmit all other light for receipt by the fluorescent camera. A second interference filter can be placed in the transmitted path to direct only fluorescent waveband to the fluorescent camera. Both camera outputs can be combined and overlaid using techniques well known in the art to display a simultaneous image. In an exemplary embodiment, the fluorescent image can be color-shifted to stand out relative to the visible display. FIG. 7B shows yet another embodiment where the above-described capability can be incorporated into a hand held instrument with a self-contained monitor or display output that feeds to other displays such

as those noted above.

[0046] FIG. 8 illustrates one exemplary embodiment of an adaptor 80 for enabling a conventional laparoscope or endoscope to view fluorescent nanoparticles. A person skilled in the art will appreciate that while an endoscope is shown, the adaptor can be used on any type of scope, including scopes used during open, endoscopic, and laparoscopic procedures. As shown, the adaptor 80 generally includes an extension eyepiece 82, a filter 84, and a mating element 86. The extension eyepiece is adapted to extend the eyepiece on a standard scope, and has a generally cylindrical shape with a viewing window or lumen 83 formed therethrough and adapted to be aligned with the viewing window or lumen 103 formed in the eyepiece 100 of a scope. The extension eyepiece 82 can also include an enlarged region 82a having a diameter greater than a diameter of an endoscope eyepiece 100 to allow the enlarged region 82a to be disposed around at least a portion of the endoscope eyepiece 100. As further shown, the extension eyepiece 82 can include a cavity formed therein for seating a filter 84, as shown. The cavity can extend across the path of the lumen 83 such that the filter 84 will extend across the viewing path of the eyepieces 82, 100 to thereby filter light viewed through the eyepieces 82, 100. The filter can be used to block out visible light, thereby enabling clear viewing of the non-visible wavelengths. As further shown, the adaptor 80 can also include a mating element 86 for mating the extension eyepiece 82 to the endoscope eyepiece 100. While various mating elements can be used, in the illustrated embodiment the mating element 86 is in the form of a ring having a cavity formed in a distal end thereof for receiving the eyepiece 100. The mating element 86 can be loaded onto the eyepiece 100 by removing the eyepiece 100 and sliding the mating element 86 over the proximal end of the eyepiece 100. As a result, the eyepiece 100 will be positioned between the mating element 86 and the extension eyepiece 82. The mating element 86 can also include threads formed on an outer surface thereof for mating with threads formed within a cavity in a proximal end of the extension eyepiece 82. Thus, the mating element 86 can be disposed around the eyepiece 100 and threaded into the extension eyepiece 82 to engage the endoscope eyepiece 100, as well as the filter 84, therebetween.

[0047] In other embodiments, where the eyepiece on the endoscope is not removable, the mating element 82 can be formed from two halves that mate together to allow the mating element to be positioned around the eyepiece. The two halves can optionally be hingedly connected, and/or they can include other features to facilitate alignment of the halves with one another. For example, the two halves can include a pin and bore connection for aligning the two halves. An alignment mechanism is preferred in order to align the threads on the two halves to enable threading of the mating element into the extension eyepiece. A person skilled in the art will appreciate that the mating element and the extension eyepiece can be mated using a variety of other mating techniques, such as a snap-fit connection, a luer lock, an interference fit, etc.

[0048] In another embodiment, the filter can be removable. FIG. 9 illustrates another embodiment of an extension eyepiece 82' having a removable filter cartridge. As shown, the extension eyepiece 82' includes a cut-out or slot 88' extending therethrough and across the viewing lumen 83'. The slot 88' is configured to slidably and removably receive a filter cartridge 87' such that a filter 89' held within the filter cartridge 87' is aligned with the viewing lumen 83' in the extension eyepiece 82' to thereby filter light passing therethrough. The filter cartridge 87' can thus be removed and replaced with another filter cartridge 87', or alternatively the filter 89' in the filter cartridge 87' can be replaced, to enable different types of filters to be disposed within the extension eyepiece 82'. A person skilled in the art will appreciate that a variety of other techniques can be used to provide an interchangeable filter. For example, a kit containing multiple adaptors, or multiple extension eyepieces, having different filters can be provided.

[0049] One skilled in the art will appreciate further features and advantages of the invention based on the above-described embodiments. Accordingly, the invention is not to be limited by what has been particularly shown and described, except as indicated by the appended claims. All publications and references cited herein are expressly incorporated herein by reference in their entirety.

[0050] What is claimed is:

1. A method for locating, marking, or illuminating tissue, comprising:

delivering at least one fluorescent nanoparticle to tissue, the fluorescent nanoparticle being formed from a fluorescent core and a biocompatible shell surrounding the fluorescent core;

delivering energy to the at least one fluorescent nanoparticle to cause the at least one fluorescent nanoparticle to fluoresce; and

collecting light fluoresced from the at least one fluorescent nanoparticle.

2. The method of claim 1, further comprising determining a location of the at least one fluorescent nanoparticle based on the collected light.

3. The method of claim 1, wherein the at least one fluorescent nanoparticle is injected into the tissue.

4. The method of claim 1, wherein the at least one fluorescent nanoparticle is delivered into the tissue using an intravenous catheter.

5. The method of claim 1, wherein delivering at least one fluorescent nanoparticle to tissue comprises coating a solution containing at least one fluorescent nanoparticle onto a tissue surface.

6. The method of claim 5, wherein the tissue surface is in a body cavity and wherein the at least one fluorescent nanoparticle illuminates the body cavity when energy is delivered thereto.

7. The method of claim 1, wherein delivering at least one fluorescent nanoparticle to tissue comprises delivering at least one fluorescent nanoparticle into a kidney, and wherein the at least one fluorescent nanoparticle has a property such that the kidney filters the at least one fluorescent nanoparticle into the ureter.

8. The method of claim 1, wherein delivering at least one fluorescent nanoparticle to tissue comprises delivering at least one fluorescent nanoparticle into a liver, and wherein

the at least one fluorescent nanoparticle has a property such that the liver filters the at least one fluorescent nanoparticle into the colon.

9. The method of claim 1, wherein delivering at least one fluorescent nanoparticle to tissue comprises applying the at least one fluorescent nanoparticle onto a tissue surface using an applicator.

10. The method of claim 1, wherein the at least one fluorescent nanoparticle is applied to tissue to be removed.

11. A medical device, comprising:

an elongate shaft having a proximal end adapted to remain outside of a patient's body and a distal end adapted to be disposed within a patient's body, the distal end having at least one fluorescent nanoparticle adapted to fluoresce when energy is delivered thereto.

12. The device of claim 11, wherein the at least one fluorescent nanoparticle is adapted to illuminate an area surrounding the distal end of the elongate shaft when energy is delivered thereto.

13. The device of claim 11, wherein the at least one fluorescent nanoparticle is adapted to indicate an orientation of the distal end of the elongate shaft when energy is delivered thereto.

14. The device of claim 11, wherein the at least one fluorescent nanoparticle is embedded in the distal end of the elongate shaft.

15. The device of claim 11, wherein the at least one fluorescent nanoparticle is coated on the distal end of the elongate shaft.

16. The device of claim 11, wherein the at least one fluorescent nanoparticle is disposed within the distal end of the elongate shaft.

17. A surgical method, comprising:

positioning a device in a patient's body, the device containing at least one

fluorescent nanoparticle; and

delivering energy to the at least one fluorescent nanoparticle to cause the at least one fluorescent nanoparticle to fluoresce.

18. The method of claim 17, wherein the at least one nanoparticle illuminates an area surrounding the device when energy is delivered thereto.

19. The method of claim 17, further comprising viewing the at least one fluorescent nanoparticle after energy is delivered thereto to locate the device.

20. The method of claim 17, further comprising viewing the at least one fluorescent nanoparticle after energy is delivered thereto to determine an orientation of the device.

21. The method of claim 17, wherein the device comprises an implant.

22. The method of claim 21, wherein, when energy is delivered to the at least one fluorescent nanoparticle, the at least one fluorescent nanoparticle indicates a location of a port on the implant.

23. The method of claim 21, wherein, when energy is delivered to the at least one fluorescent nanoparticle, the at least one fluorescent nanoparticle indicates a size of the implant.

24. The method of claim 17, wherein the device comprises an elongate shaft having a distal end positioned in a body lumen of the patient while a proximal end of the elongate shaft remains external to the patient.

25. A medical composition, comprising:

a fluorescent nanoparticle having a core containing at least one dye adapted to emit light at a first frequency, and at least one dye adapted to emit light at a second frequency that differs from the first frequency, and a biocompatible shell surrounding the core.

26. The composition of claim 25, wherein the first frequency is within a visible wavelength, and the second frequency is within a non-visible wavelength.

27. A surgical method, comprising:

delivering at least one fluorescent nanoparticle to tissue;

delivering visible light to the tissue to cause a first dye contained within the at least one fluorescent nanoparticle to emit visible light; and

delivering invisible light to the tissue to cause a second dye contained within the at least one fluorescent nanoparticle to emit invisible light.

28. A medical composition, comprising:

a fluorescent nanoparticle having a core containing at least one fluorescent dye, a biocompatible shell surrounding the core, and a magnetic material located in at least one of the core and the shell.

29. A method for treating tissue, comprising:

delivering at least one fluorescent nanoparticle to tissue; and

delivering energy to the tissue to locate the at least one fluorescent nanoparticle and to cause a magnetic material in the at least one fluorescent nanoparticle to deliver heat to the tissue.

30. A method for identifying tumor passage into the sentinel lymph node, comprising:

delivering at least one fluorescent nanoparticle to a tumor, the fluorescent nanoparticle being formed from a fluorescent core and a biocompatible shell surrounding the fluorescent core; and

delivering energy to tissue surrounding the tumor to locate the at least one fluorescent nanoparticle to determine whether the at least one fluorescent nanoparticle has reached a sentinel lymph node.

31. An endoscopic adaptor for viewing fluorescent nanoparticles, comprising:

first and second members removably matable to one another and adapted to engage a portion of an endoscope eyepiece therebetween, the first member having a viewing lumen formed therethrough and adapted to axially align with a viewing lumen formed in an endoscope eyepiece, and a cavity formed therein for seating a filter adapted to filter light received through the viewing lumen of the first member.

32. A method for viewing fluorescent nanoparticles, comprising:

coupling an adaptor to a distal end of an endoscope, the endoscope having a light transmitting element adapted to emit fluorescent light and an image obtaining element adapted to obtain an image from reflected fluorescent light;

inserting the distal end of the endoscope into a body lumen to position the distal end adjacent to tissue containing a fluorescent nanoparticle; and

activating the light transmitting element to emit fluorescent light onto the fluorescent nanoparticle such that reflected fluorescent light is received from the fluorescent nanoparticles by the image obtaining element.

33. An endoscopic adaptor for viewing fluorescent nanoparticles, comprising:

first and second members removably matable to one another and adapted to engage a portion of an endoscope eyepiece therebetween, the first member having a viewing lumen formed therethrough and adapted to axially align with a viewing lumen formed in an endoscope eyepiece, and a cavity formed therein for seating a filter adapted to filter light received through the viewing lumen of the first member.

34. The endoscopic adaptor of claim 33, further comprising a filter disposed within the cavity in the first member.

35. The endoscopic adaptor of claim 25, wherein the filter is adapted to transmit light in the fluorescent waveband.

36. The endoscopic adaptor of claim 35, wherein the filter comprises an interferometric long-pass filter.

37. The endoscopic adaptor of claim 33, wherein the second member comprises a ring having a lumen extending therethrough with an enlarged diameter portion adapted to receive an enlarged diameter portion formed on an endoscopic eyepiece.

38. The endoscopic adaptor of claim 33, further comprising a filter cartridge removably disposed within the first member and adapted to retain a filter therein.

39. The endoscopic adaptor of claim 38, wherein the first member includes a slot formed therein and extending across the viewing lumen for receiving the filter cartridge such that a filter containing in the filter cartridge is disposed across the viewing lumen.

40. The endoscopic adaptor of claim 33, wherein the second member includes first and second hemi-cylindrical halves that are hingedly mated to one another to allow the second member to be positioned around an endoscopic eyepiece.

41. The endoscopic adaptor of claim 33, wherein the first and second members are threadably matable to one another.

42. The endoscopic adaptor of claim 33, wherein the first and second members have a substantially hollow cylindrical shape.

43. An endoscopic system, comprising:

an endoscope eyepiece having a viewing lumen formed therethrough between proximal and distal ends thereof; and

an adaptor adapted to removably mate to the endoscope eyepiece and adapted to retain a filter therein such that the filter is in alignment with the viewing lumen formed in the endoscope eyepiece to thereby filter light through the viewing lumen.

44. The endoscopic system of claim 43, wherein the adaptor includes a viewing lumen extending therethrough and adapted to be aligned with the viewing lumen in the endoscope eyepiece when the adaptor is mated to the endoscope eyepiece.

45. The endoscopic system of claim 44, wherein the adaptor comprises an eyepiece extension member having the viewing lumen formed therein, and a mating element adapted to mate to the eyepiece extension to engage a portion of the endoscope eyepiece therebetween.

46. The endoscopic system of claim 43, further comprising a filter disposed within the adaptor.

47. The endoscopic system of claim 46, wherein the filter is removable.

48. The endoscopic system of claim 46, wherein the filter is adapted to transmit light in the fluorescent waveband.

49. The endoscopic system of claim 43, further comprising a filter cartridge removably disposed within the adaptor and adapted to retain a filter therein.

50. A method for viewing fluorescent nanoparticles, comprising:

coupling an adaptor to a proximal end of an endoscope;

inserting a distal end of the endoscope into a body lumen to direct the distal end toward tissue containing at least one fluorescent nanoparticle; and

activating a light transmitting element to emit fluorescent light onto the at least one fluorescent nanoparticle such that reflected fluorescent light is transmitted through a filter contained within the adaptor and is received by an image obtaining element coupled to the endoscope.

51. The method of claim 50, wherein the light transmitting element extends through the endoscope to emit fluorescent light onto the at least one fluorescent nanoparticle.

52. The method of claim 50, wherein the filter blocks visible light.

53. The method of claim 50, wherein the adaptor engages an eyepiece on the endoscope.

54. A method for locating, marking, or illuminating tissue, comprising:

delivering at least one biocompatible fluorescent nanoparticle to tissue;

delivering energy to the at least one fluorescent nanoparticle to cause the at least one fluorescent nanoparticle to fluoresce; and

collecting light fluoresced from the at least one fluorescent nanoparticle.

55. The method of claim 54, wherein the fluorescent nanoparticle is formed from a fluorescent core and a biocompatible shell surrounding the fluorescent core.

56. The method of claim 54, wherein the light is collected through an elongate cannula.

57. The method of claim 54, wherein the at least one fluorescent nanoparticle is delivered in a carrier solution.

58. The method of claim 57, wherein the carrier solution contains an adhesive.

59. The method of claim 54, wherein the tissue comprises an organ.

60. The method of claim 54, wherein the tissue comprises a tubular structure.

61. The method of claim 54, further comprising determining a location of the at least one fluorescent nanoparticle based on the collected light.

62. The method of claim 54,wherein the at least one fluorescent nanoparticle is injected into the tissue.

63. The method of claim 54,wherein the at least one fluorescent nanoparticle is delivered into the tissue using an intravenous catheter.

64. The method of claim 54, wherein delivering at least one fluorescent nanoparticle to tissue comprises coating a solution containing at least one fluorescent nanoparticle onto a tissue surface.

65. The method of claim 58, wherein the tissue surface is in a body cavity and wherein the at least one fluorescent nanoparticle illuminates the body cavity when energy is delivered thereto.

66. The method of claim 65, wherein the body cavity is selected from the group consisting of the stomach, uterus, abdominal cavity, thoracic cavity, vaginal canal, nasal passages, and ear canal.

67. The method of claim 54, wherein delivering at least one fluorescent nanoparticle to tissue comprises delivering at least one fluorescent nanoparticle into a kidney, and wherein the at least one fluorescent nanoparticle has a property such that the kidney filters the at least one fluorescent nanoparticle into the ureter.

68. The method of claim 54,wherein delivering at least one fluorescent nanoparticle to tissue comprises delivering at least one fluorescent nanoparticle into a liver, and wherein the at least one fluorescent nanoparticle has a property such that the liver filters the at least one fluorescent nanoparticle into the colon.

69. The method of claim 54,wherein delivering at least one fluorescent nanoparticle to tissue comprises applying the at least one fluorescent nanoparticle onto a tissue surface using an applicator.

70. The method of claim 68,wherein the applicator is introduced through a cannula having a working channel extending into a body cavity containing the tissue.

71. The method of claim 54,wherein the at least one fluorescent nanoparticle is applied to tissue to be removed.

72. The method of claim 71, further comprising locating the tissue based on the collected light, and removing the tissue containing the at least one fluorescent nanoparticle.

73. The method of claim 54, wherein the at least one fluorescent nanoparticle includes visible and non-visible dyes therein, and wherein the method further includes locating the tissue by viewing light emitted from the visible dyes, and delivering energy to the tissue to view the non-visible dyes.

74. A method for identifying tumor passage into the sentinel lymph node, comprising:

delivering at least one fluorescent nanoparticle to a tumor, the fluorescent nanoparticle being formed from a fluorescent core and a biocompatible shell surrounding the fluorescent core; and

delivering energy to tissue surrounding the tumor to locate the at least one fluorescent nanoparticle to determine whether the at least one fluorescent nanoparticle has reached a sentinel lymph node.

75. The method of claim 74, wherein the at least one fluorescent nanoparticle is injected into the tumor.

76. The method of claim 74, wherein the at least one fluorescent nanoparticle is delivered in a carrier solution.

77. The method of claim 74, wherein the energy comprises electromagnetic energy.

78. The method of claim 74, wherein the energy is delivered through a delivery apparatus.

79. The method of claim 78, wherein the delivery apparatus comprises an endoscope that is disposed through a natural orifice.

80. The method of claim 78, wherein the delivery apparatus comprises a laparoscope that is inserted through a puncture hole formed in tissue.

81. The method of claim 74, wherein the at least one fluorescent nanoparticle includes visible and non-visible fluorescent dyes therein, and wherein the method further includes, prior to delivering energy, locating the tumor by viewing light emitted from the visible fluorescent dyes.

82. A method for identifying the spread of cancerous cells, comprising:

injecting a solution containing at least one fluorescent nanoparticle formed from a fluorescent core and a biocompatible shell into a tumor; and

delivering electromagnetic energy to the tumor to cause the fluorescent core to fluoresce.

83. The method of claim 82, further comprising locating the at least one fluorescent nanoparticle using an imaging apparatus adapted to view fluorescent light.

84. The method of claim 83, further determining whether the at least one fluorescent nanoparticle has reached a sentinel lymph node based on the location of the at least one fluorescent nanoparticle.

85. The method of claim 82, wherein the energy is delivered through a delivery apparatus.

86. The method of claim 82, wherein the delivery apparatus comprises an endoscope that is disposed through a natural orifice.

87. The method of claim 82,wherein the delivery apparatus comprises a laparoscope that is inserted through a puncture hole formed in tissue.

88. The method of claim 82,wherein the at least one fluorescent nanoparticle includes a magnetic material, and the method further comprises delivering an alternating current to the at least one fluorescent nanoparticle to cause the magnetic material to release heat and thereby treat the tissue.

89. The method of claim 82, wherein the at least one fluorescent nanoparticle includes visible and non-visible fluorescent dyes therein, and wherein the method further includes, prior to delivering energy, locating the tumor by viewing light emitted from the visible fluorescent dyes.

90. A medical device, comprising:

a biocompatible body adapted to be at least partially disposed within a patient's body, the body having at least one fluorescent nanoparticle adapted to fluoresce when energy is delivered thereto.

91. The device of claim 90, wherein the at least one fluorescent nanoparticle is adapted to illuminate an area surrounding the body when energy is delivered thereto.

92. The device of claim 90, wherein the at least one fluorescent nanoparticle is adapted to indicate an orientation of the body when energy is delivered thereto.

93. The device of claim 90, wherein the at least one fluorescent nanoparticle is embedded in the body.

94. The device of claim 90, wherein the at least one fluorescent nanoparticle is coated on the body.

95. The device of claim 90, wherein the at least one fluorescent nanoparticle is

disposed within a cavity formed in the body.

96. The medical device of claim 90, wherein the body comprises an elongate shaft having a proximal end adapted to remain outside of a patient's body and a distal end adapted to be disposed within a patient's body.

97. The medical device of claim 96, wherein the at least one fluorescent nanoparticle is located on the distal end of the elongate shaft.

98. The medical device of claim 90, wherein the biocompatible body comprises an implant containing the at least one fluorescent nanoparticle.

99. The medical device of claim 90, wherein the biocompatible body comprises a suture.

100. The medical device of claim 90, wherein the biocompatible body is absorbable.

101. The device of claim 100, wherein the elongate shaft includes an inner lumen extending therethrough and defining a working channel.

102. A medical device, comprising:

an elongate shaft having a proximal end adapted to remain outside of a patient's body and a distal end adapted to be disposed within a patient's body; and

at least one fluorescent nanoparticle associated with the elongate shaft and adapted to fluoresce when energy is delivered thereto.

103. The device of claim 102,wherein the at least one fluorescent nanoparticle is adapted to illuminate an area surrounding the elongate shaft when energy is delivered thereto.

104. The device of claim 102, wherein the at least one fluorescent nanoparticle is adapted to indicate an orientation of the elongate shaft when energy is delivered thereto.

105. A surgical method, comprising:

positioning a device in a patient's body, the device containing at least one fluorescent nanoparticle; and

delivering energy to the at least one fluorescent nanoparticle to cause the at least one fluorescent nanoparticle to fluoresce.

106. The method of claim 105, wherein the at least one nanoparticle illuminates an area surrounding the device when energy is delivered thereto.

107. The method of claim 105, further comprising viewing the at least one fluorescent nanoparticle after energy is delivered thereto to locate the device.

108. The method of claim 105, further comprising viewing the at least one fluorescent nanoparticle after energy is delivered thereto to determine an orientation of the device.

109. The method of claim 105,wherein the device comprises an implant.

110. The method of claim 105, wherein, when energy is delivered to the at least one fluorescent nanoparticle, the at least one fluorescent nanoparticle indicates a location of a port on the implant.

111. The method of claim 110, wherein, when energy is delivered to the at least one fluorescent nanoparticle, the at least one fluorescent nanoparticle indicates a size of the implant.

112. The method of claim 105, wherein the device comprises an elongate shaft having a distal end positioned in a body lumen of the patient while a proximal end of the elongate shaft remains external to the patient.

113. A medical composition, comprising:

a fluorescent nanoparticle having a core containing at least one dye adapted to emit light at a first frequency, and at least one dye adapted to emit light at a second frequency that differs from the first frequency, and a biocompatible shell surrounding the core.

114. The composition of claim 113, wherein the first frequency is within a visible wavelength, and the second frequency is within a non-visible wavelength.

115. The composition of claim 113, wherein the first frequency is in the range of about

600nm to 1350nm, and the second frequency is in the range of about 400nm to 700nm.

116. The composition of claim 113, wherein the biocompatible shell comprises a silica shell.

117. The composition of claim 113, wherein the fluorescent nanoparticle further includes a magnetic material.

118. A surgical method, comprising:

delivering at least one fluorescent nanoparticle to tissue;

delivering visible light to the tissue to cause a first dye contained within the at least one fluorescent nanoparticle to emit visible light; and

delivering invisible light to the tissue to cause a second dye contained within the at least one fluorescent nanoparticle to emit invisible light.

119. The method of claim 118, further comprising initially locating the tissue using the visible light, and precisely locating the tissue using the invisible light.

120. The method of claim 119, wherein initially locating the tissue using the visible light comprises delivering visible light to at least one fluorescent nanoparticle located at or adjacent to a surface of the tissue, and precisely locating the tissue using the invisible light comprises delivering the invisible light to at least one fluorescent nanoparticle located deep within the tissue.

121. The method of claim 118, wherein the fluorescent nanoparticle is formed from a fluorescent core and a biocompatible shell surrounding the fluorescent core.

122. The method of claim 118, wherein the at least one fluorescent nanoparticle is delivered in a carrier solution.

123. The method of claim 118, wherein the at least one fluorescent nanoparticle is injected into the tissue.

124. The method of claim 118, wherein the at least one fluorescent nanoparticle is

delivered into the tissue using an intravenous catheter.

125. The method of claim 118, wherein delivering at least one fluorescent nanoparticle to tissue comprises delivering at least one fluorescent nanoparticle into a kidney, and wherein the at least one fluorescent nanoparticle has a property such that the kidney filters the at least one fluorescent nanoparticle into the ureter.

126. The method of claim 118, wherein delivering at least one fluorescent nanoparticle to tissue comprises delivering at least one fluorescent nanoparticle into a liver, and wherein the at least one fluorescent nanoparticle has a property such that the liver filters the at least one fluorescent nanoparticle into the colon.

127. The method of claim 118, wherein the at least one fluorescent nanoparticle is applied to tissue to be removed.

128. The method of claim 127, further comprising locating the tissue using the visible light, and using the invisible light to remove the tissue containing the at least one fluorescent nanoparticle.

129. A medical composition, comprising:

a fluorescent nanoparticle having a core containing at least one fluorescent dye, a biocompatible shell surrounding the core, and a magnetic material located in at least one of the core and the shell.

130. The composition of claim 129, wherein the at least one fluorescent dye has a wavelength in the range of about 600nm to 1350nm.

131. The composition of claim 129, wherein the magnetic material is selected from the group consisting of $Fe(OH)_2$, Fe_2O_3, and Fe_3O_4 combinations thereof.

132. The composition of claim 129,wherein the magnetic material is contained within the core.

133. The composition of claim129,wherein the magnetic material is coated onto the

shell.

134. The composition of claim 129, wherein the shell comprises a silica shell.

135. The composition of claim 129,wherein the core includes at least one dye adapted to emit light at a first frequency, and at least one dye adapted to emit light at a second frequency that differs from the first frequency.

136. A method for treating tissue, comprising:

delivering at least one biocompatible fluorescent nanoparticle to tissue; and

delivering an alternating current to the tissue to cause a magnetic material in the at least one fluorescent nanoparticle to deliver heat to the tissue.

137. The method of claim 136, further comprising, prior to delivering alternating current, delivering energy to the tissue to locate the at least one fluorescent nanoparticle.

138. The method of claim 137, wherein the at least one fluorescent nanoparticle is located by collecting light fluoresced from the at least one fluorescent nanoparticle, and viewing the collected light on an image display apparatus.

139. The method of claim 136,wherein the heat is effective to cauterize the tissue.

140. The method of claim 136, wherein the fluorescent nanoparticle is formed from a fluorescent core and a biocompatible shell surrounding the fluorescent core.

141. The method of claim 136, wherein the at least one fluorescent nanoparticle is delivered in a carrier solution.

142. The method of claim 136, wherein the at least one fluorescent nanoparticle is injected into the tissue.

143. The method of claim 136, wherein the at least one fluorescent nanoparticle is delivered into the tissue using an intravenous catheter.

144. The method of claim 136, wherein delivering at least one fluorescent nanoparticle

to tissue comprises coating a solution containing at least one fluorescent nanoparticle onto a tissue surface.

145. The method of claim 136,wherein delivering at least one fluorescent nanoparticle to tissue comprises applying the at least one fluorescent nanoparticle onto a tissue surface using an applicator.

146. The method of claim 136,wherein the at least one fluorescent nanoparticle includes visible and non-visible dyes therein, and wherein the method further includes locating the tissue by viewing light emitted from the visible dyes, and delivering energy to the tissue to view the non-visible dyes.

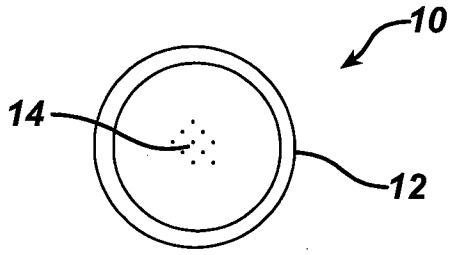


FIG. 1

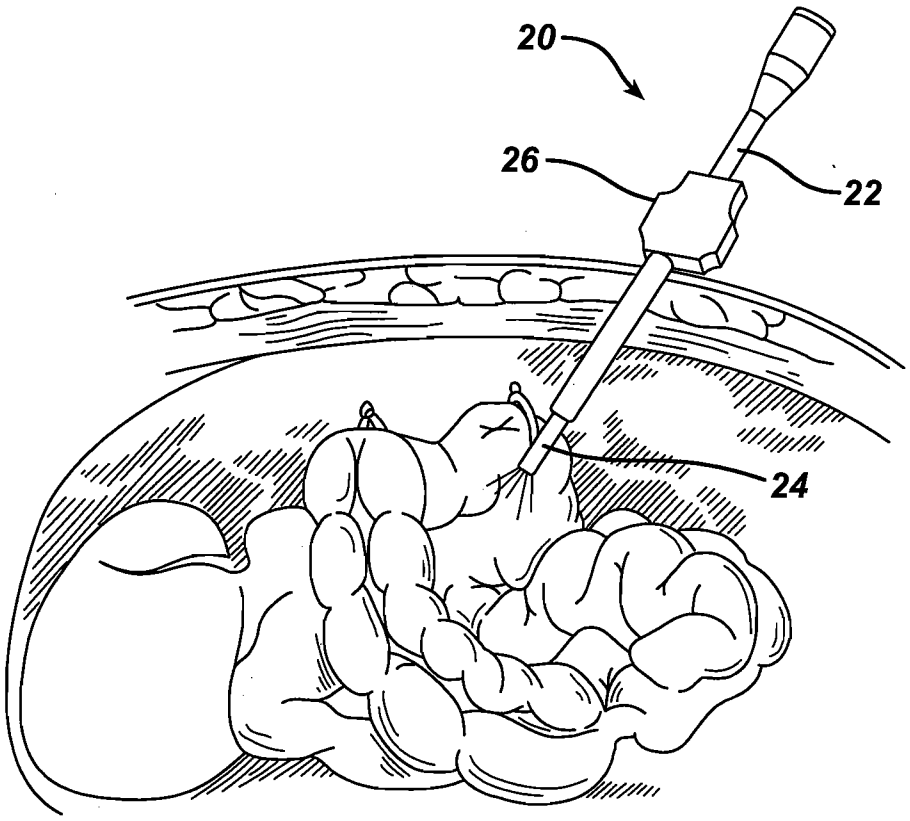


FIG. 2

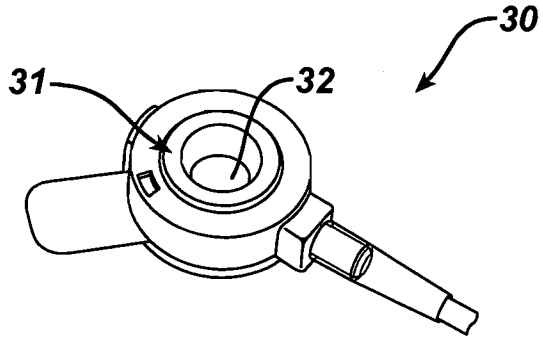


FIG. 3A

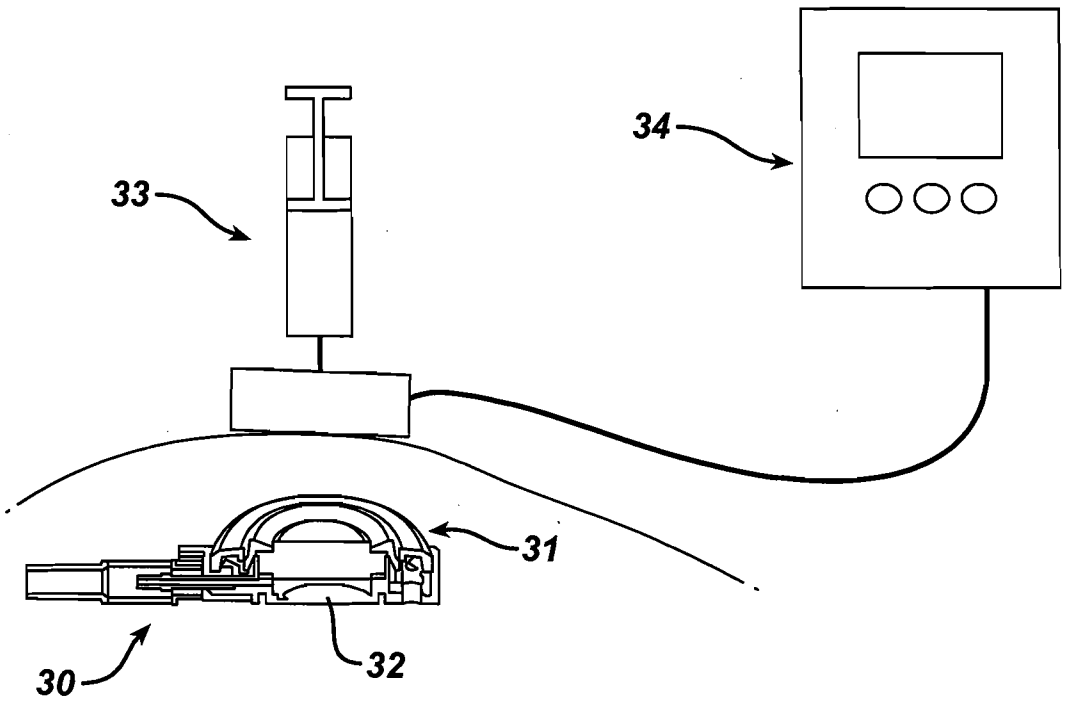
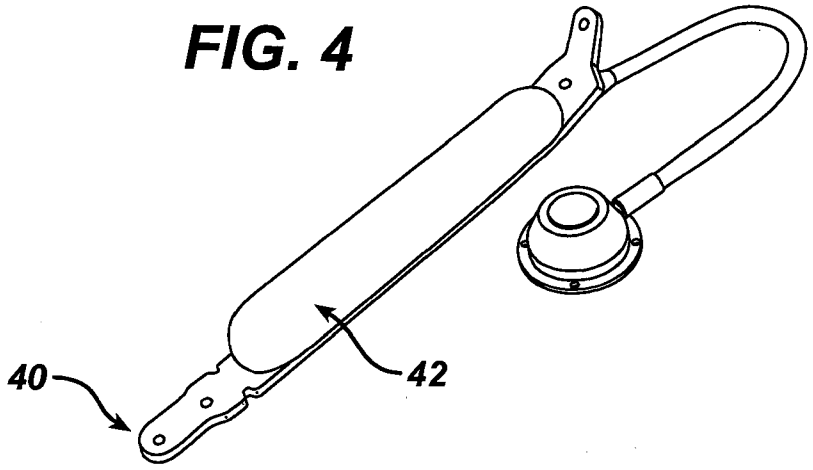


FIG. 3B

FIG. 4



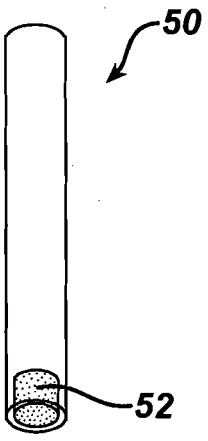


FIG. 5A

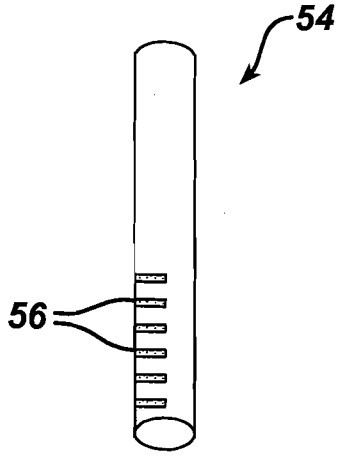


FIG. 5B

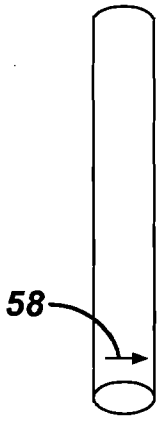


FIG. 5C

FIG. 6

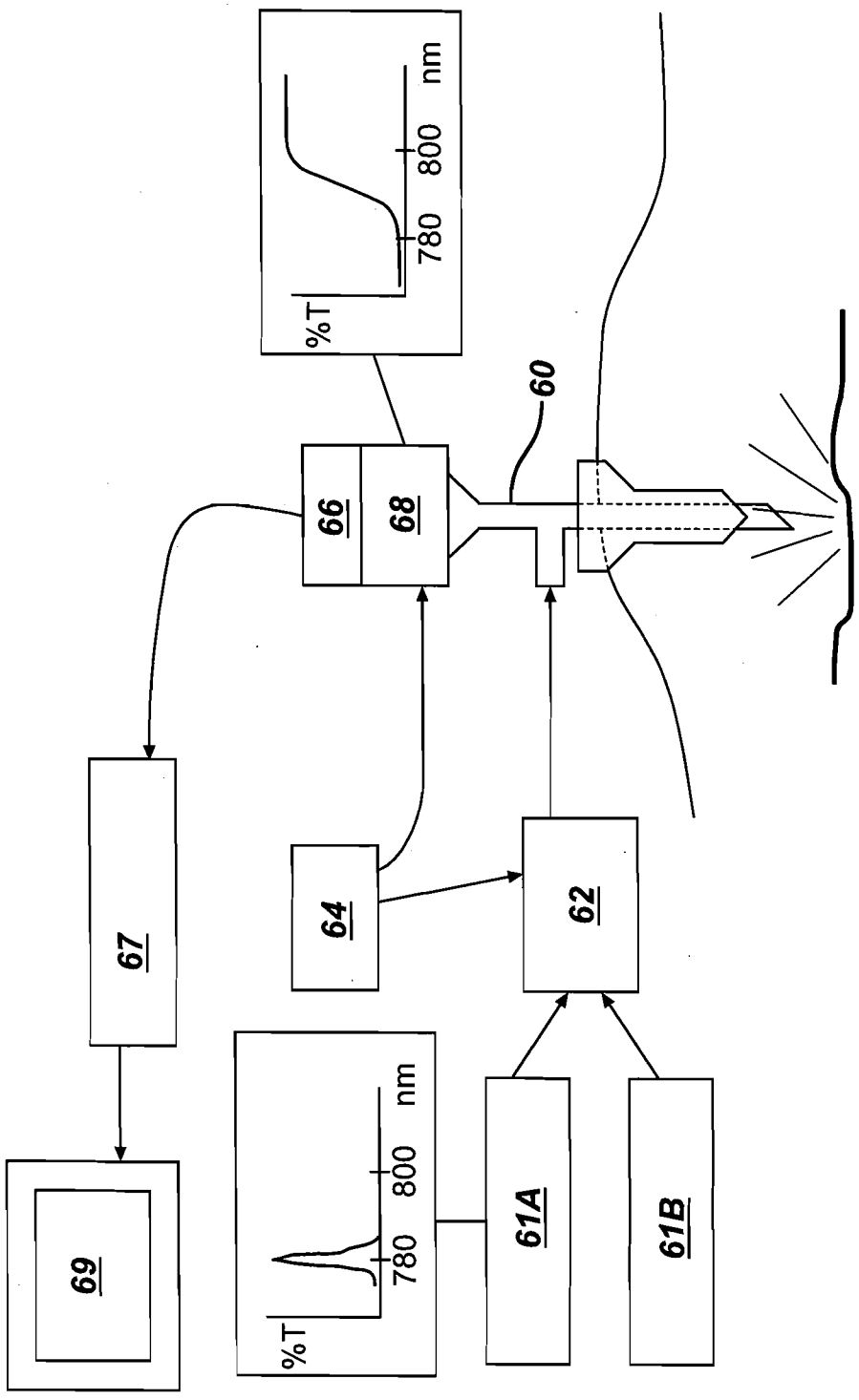
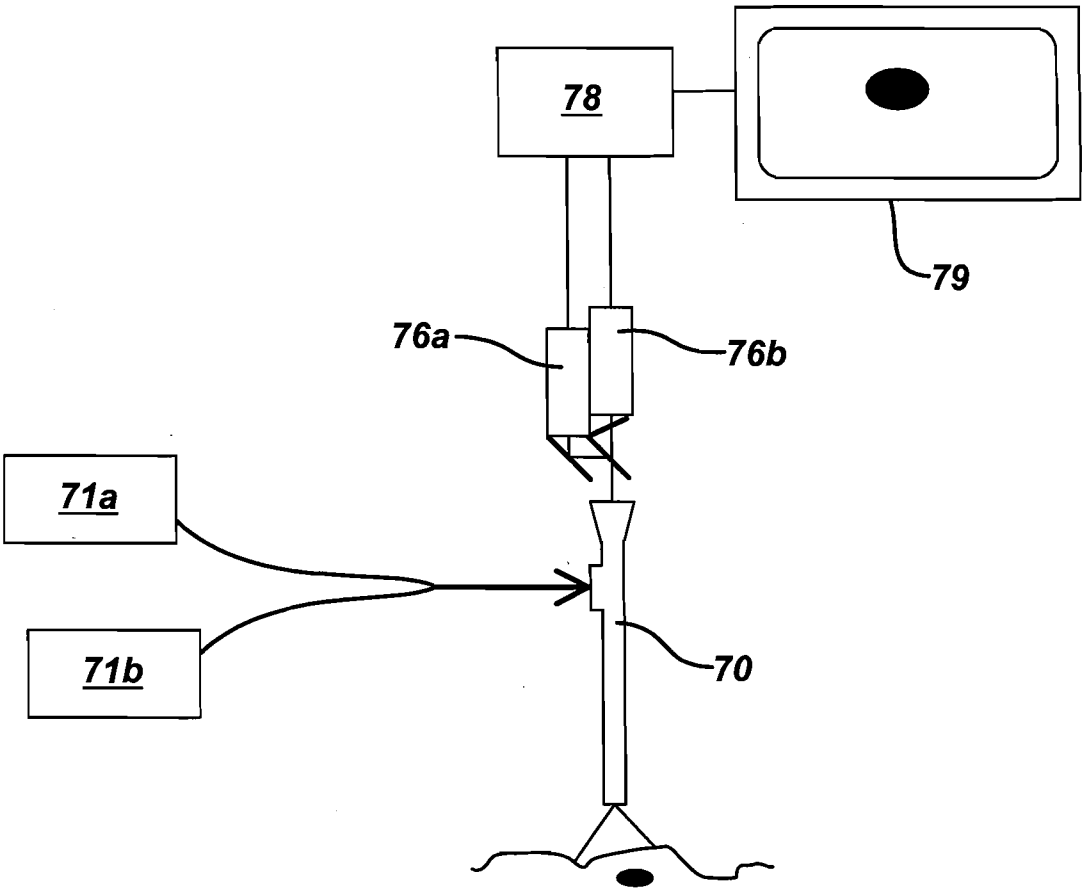


FIG. 7A



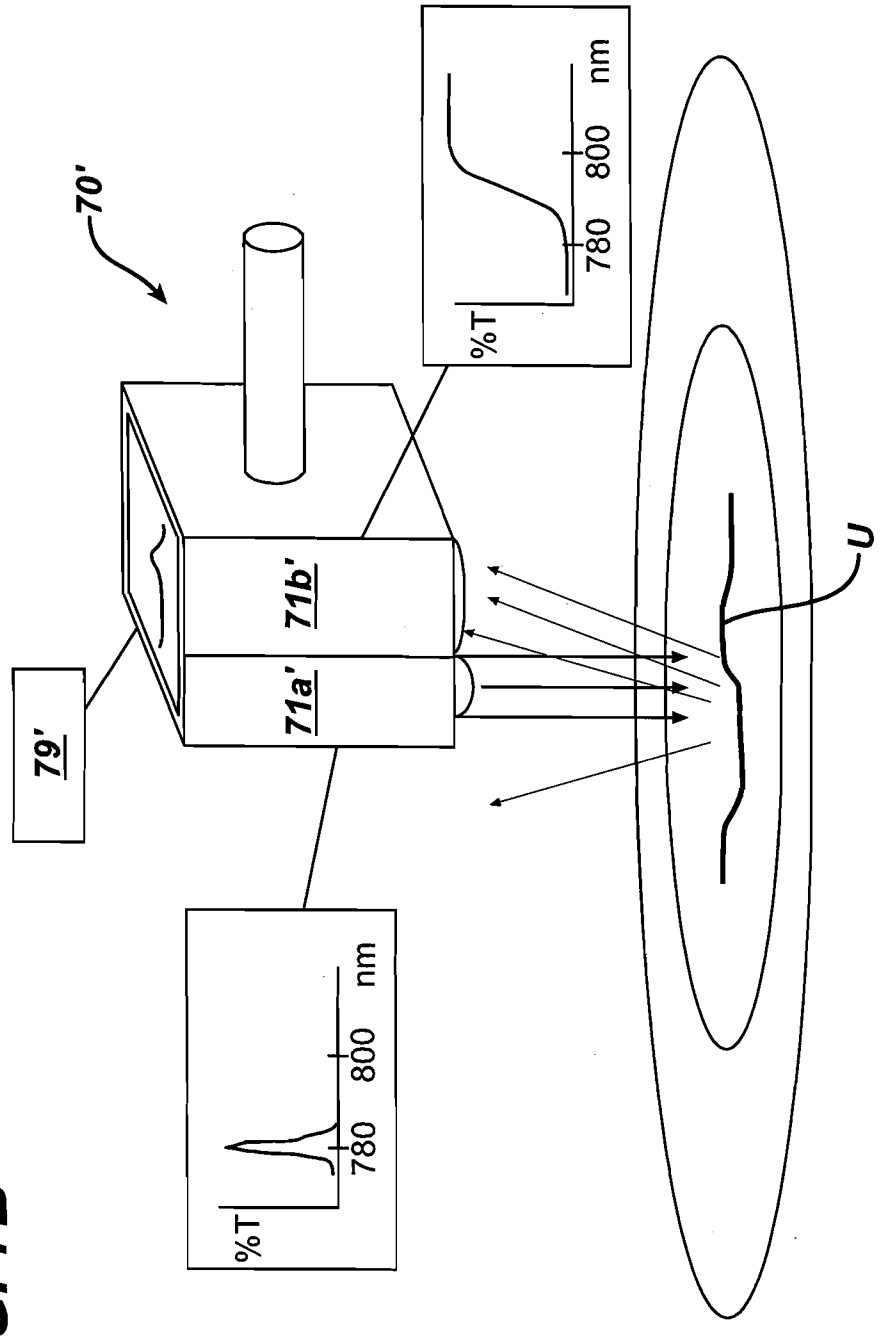


FIG. 7B

FIG. 8A

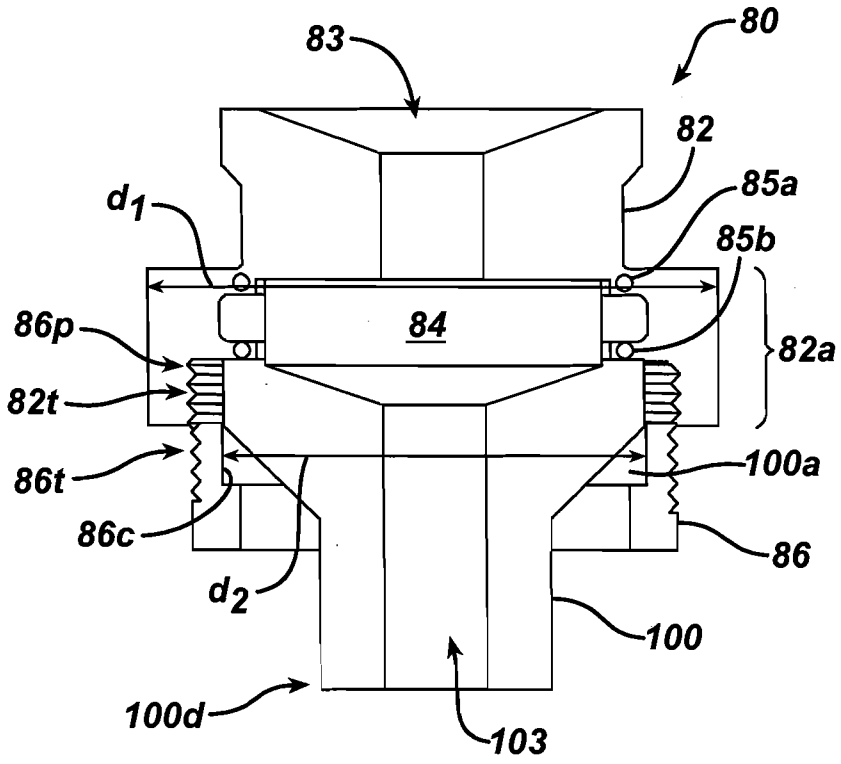

83
80
82
85a
d_1
85b
84
86p
82a
82t
86t
100a
86c
86
d_2
100
100d
103

FIG. 8B

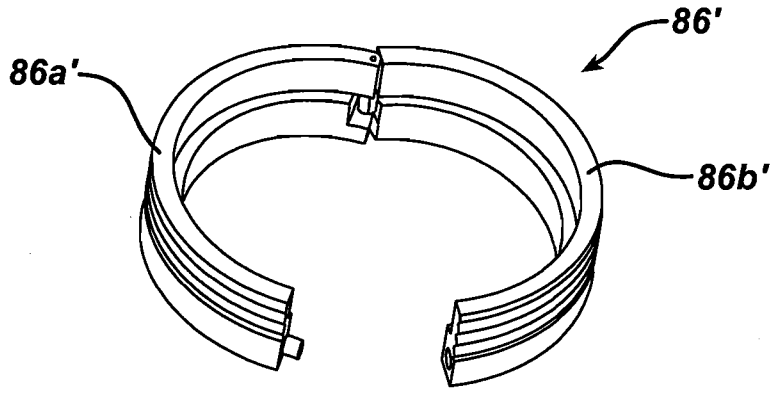
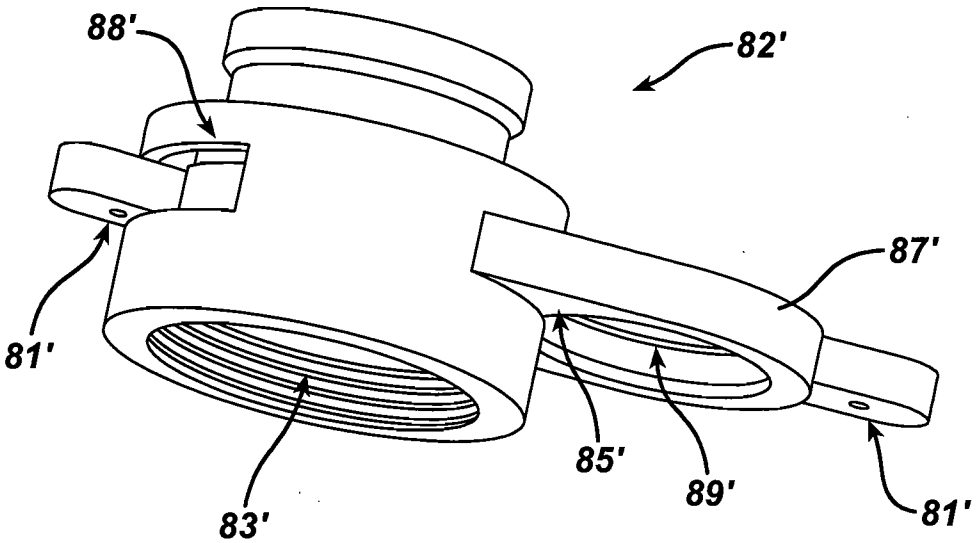

86'
86a'
86b'

FIG. 9



专利名称(译)	荧光纳米颗粒组合物和在手术期间使用的装置		
公开(公告)号	EP2146751A2	公开(公告)日	2010-01-27
申请号	EP2008745616	申请日	2008-04-11
[标]申请(专利权)人(译)	伊西康内外科公司		
申请(专利权)人(译)	爱惜康内镜手术，INC.		
当前申请(专利权)人(译)	爱惜康内镜手术，INC.		
[标]发明人	VOEGELE JAMES W TRUSTY ROBERT M GILL ROBERT M DLUGOS DANIEL F MURRAY MICHAEL A HESS CHRISTOPHER J		
发明人	VOEGELE, JAMES W. TRUSTY, ROBERT M. GILL, ROBERT M. DLUGOS, DANIEL F. MURRAY, MICHAEL A. HESS, CHRISTOPHER J.		
IPC分类号	A61K49/00 A61K41/00 A61B1/05 A61B1/313		
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优先权	11/771361 2007-06-29 US 11/771472 2007-06-29 US 11/771384 2007-06-29 US 11/771399 2007-06-29 US 60/911546 2007-04-13 US 11/771481 2007-06-29 US 11/771490 2007-06-29 US		
外部链接	Espacenet		

摘要(译)

提供了使用荧光纳米颗粒的各种组合物，方法和装置，其可以用作标记物，指示物和光源。荧光纳米颗粒可以由被生物相容性壳包围的荧光团核心形成，例如二氧化硅壳。在一个实施方案中，荧光纳米颗粒可以被递送至组织以标记组织，使得能够识别和定位组织，和/或照射组织周围的区域。在另一个实施方案中，荧光纳米颗粒可以用在装置或植入物上，以将装置或植入物定位在体内，指示装置或植入物的取向，和/或照射装置或植入物周围的区域。荧光纳米颗粒也可用于提供治疗效果。