Abstract

The invention provides methods and systems for imaging vessels in a subject. In certain embodiments the vessels may be associated with a solid organ transplant.
FIG. 1A
FIG. 1B
REAL TIME VASCULAR IMAGING DURING SOLID ORGAN TRANSPLANT

FIELD OF THE INVENTION

[0001] The invention relates generally to the field of medical imaging. Certain embodiments of the invention provide methods for imaging of vasculature in a subject. Certain other embodiments provide systems which are useful for imaging vasculature in a subject.

BACKGROUND OF THE INVENTION

[0002] Imaging of biological tissues and organs assists doctors in both diagnosis and treatment. A variety of medical techniques which are suitable for imaging biological tissues and organs are known. These include traditional x-rays, ultra-sound, as well as magnetic resonance imaging (MRI), and computerized tomography (CT). A variety of dyes used in medical imaging have also been described including radio opaque dyes, fluorescent dyes, as well as, colormetric dyes (see e.g., U.S. Pat. Nos. 5,699,798; 5,279,298; 6,351,663; and U.S. patent application Ser. No. 10/365,028). Imaging techniques and systems using fluorescent dyes have been described for the heart and eye (see, U.S. Pat. No. 5,279,298; U.S. patent application Ser. Nos. 09/744,034 and 10/619,548, all of which are incorporated by reference in their entirety). Some dyes can serve both an imaging function, as well as a therapeutic function (see, e.g. U.S. Pat. No. 6,840,933).

[0003] Organ transplant is one area in which imaging methods and systems would prove useful. The demand for organ transplant continues to grow. The combined number of solid organ transplants in the US alone, is approximately 18,000 per year. Specifically the combined numbers for years 1997 and 1998 were: 1,692 lung transplants, 4,409 heart, 7,502 liver, 326 pancreas, 1,803 pancreas and kidney, and 20,956 kidney transplants (see, e.g., The U.S. Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients Annual Report, 2004).

[0004] Transplant procedures involve anastomosis. These anastomoses may be between, for example, two vessels, vessels and duct(s), two ducts, or vessels and ureter(s), two parts of a ureter, or the ureter and bladder. As such, solid organ transplant procedures would benefit from the pre-operative assessment of the patency of vessels, ducts, and ureters of the donor organs, and intra-operative and post-operative verification of anastomoses and the patency of blood vessels, ducts, and ureters of the transplanted organs, as well as other recipient blood vessels, ducts, and ureters. It would be particularly useful to provide real time, i.e. intra-operative visual confirmation regarding the verification of anastomoses and patency of vessels, e.g. vasculature. Traditional intra-operative imaging techniques, are frequently ineffective, expensive and inconvenient. The need therefore exists for methods and systems for imaging vessels associated with solid organ transplants which are safe, effective, convenient and cost effective.

SUMMARY OF THE INVENTION

[0005] In certain embodiments the invention provides a method of intra-operatively determining the patency of at least one vessel which is surgically joined to a transplanted organ in a recipient subject comprising: a) administering a fluorescent dye to the recipient subject; b) applying a sufficient amount of energy to the vessel such that the fluorescent dye fluoresces; c) obtaining a fluorescent image of the vessel surgically joined to a transplanted organ; and d) observing the image to determine if a fluorescent signal is continuous through the vessel wherein a continuous fluorescent signal in the vessel indicates the vessel is patent.

[0006] In certain embodiments the invention provides a portable system useful for imaging at least one vessel which is surgically joined to a transplanted organ in a recipient subject comprising: a) a fluorescent dye; b) an energy source capable of emitting sufficient energy such that the fluorescent dye fluoresces; and c) an imaging head.

[0007] In certain embodiments the invention provides a portable system useful for imaging at least one vessel which is surgically joined to a transplanted organ in a recipient subject comprising: a) a fluorescent dye; b) an energy source capable of emitting sufficient energy such that the fluorescent dye fluoresces; c) an imaging head; d) an articulating arm; e) a computer and monitor; f) image processing software; g) an electrical power source; and h) a housing for containing a-f, wherein the housing comprises at least 2 wheels. In some embodiments the system may also comprise at least one of the following: a motion sensor; a distance sensor; a sterile drape; and a printer.

[0008] In certain embodiments the invention provides a portable apparatus comprising a) an energy source capable of emitting sufficient energy such that a fluorescent dye fluoresces; b) an imaging head; c) an articulating arm; d) a computer and monitor; e) image processing software; f) an electrical power source; and g) a housing for containing a-f, wherein the housing comprises at least 2 wheels. In some embodiments the device may also comprise at least one of the following: a motion sensor; a distance sensor; a sterile drape; and a printer.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009] The above and further advantages of the invention may be better understood by referring to the following description in conjunction with the accompanying drawings in which:

[0010] FIG. 1 is a schematic diagram showing one embodiment of the system of the invention. FIG. 1A shows an example of an electrical configuration. FIG. 1B shows an example of an optical configuration.

DETAILED DESCRIPTION

[0011] Organ transplants of various types are performed routinely. Solid organ transplants of all types require the joining of vessels, e.g., blood vessels in order to attach the donor organ. Some organ transplants, such as a pancreas transplant also require the joining of a duct to a lumen, e.g. the pancreatic duct to the digestive tract. Occlusion, due to, thrombosis, plaque, or free floating endothelial material, for example, is a risk associated with transplant surgery. The invention described herein, in certain embodiments, provides a method and a system which a surgeon can use intra-operatively to determine if an anastomosis created during transplant surgery is patent. The invention also provides a method and system to determine, pre-surgery, if a donor organ, or a vessel attached to a donor organ, is patent.
Subject as used herein, refers to any animal. The animal may be a mammal. Examples of suitable mammals include, but are not limited to, humans, non-human primates, dogs, cats, sheep, cows, pigs, horses, mice, rats, rabbits, and guinea pigs.

Recipient subject, as used herein, refers to a subject that is receiving a solid organ transplant.

Donor subject, as used herein, refers to a subject that is donating a solid organ for transplant.

Duct, as used herein, refers to a vessel having a lumen in which a liquid is carried or transported. In some living organisms ducts are found for example in liver and in glands, such as sweat glands, or the pancreas. The pancreas secretes digestive enzymes via a duct, however, it also secretes insulin from the Islets of Langerhans directly into the blood without any duct.

Arterial graft, as used herein, refers to a natural or synthetic vessel, which delivers blood to a transplanted solid organ. It can be derived from the donor subject, the recipient subject, or a different subject. It can include a vessel made from a synthetic material, or a naturally derived material (i.e. from a living organism) or a combination of a natural and synthetic material.

Venous graft, as used herein, refers to a natural or synthetic vessel, which drains blood from a transplanted solid organ. It can be derived from the donor subject, the recipient subject, or a different subject. It can include a vessel made from a synthetic material, or a naturally derived material (i.e. from a living organism) or a combination of a natural and synthetic material.

Vessel as used herein includes any tube having a lumen capable of transporting a fluid within a subject e.g., veins, arteries and ducts.

Methods of the Invention

In certain embodiments the invention provides a method of intra-operatively determining the patency of at least one vessel, or at least one anastomosis between two vessels, or at least one anastomosis between a vessel and an intervening duct or vessel of an organ, or at least one anastomosis between a vessel and an organ, where the vessel is surgically joined to a transplanted organ in a recipient subject. The method comprises comprises administering a fluorescent dye to the subject and exposing at least one of the transplanted organ, the vessel, and the anastomosis, to a form of radiant energy, such that the fluorescent dye fluoresces and obtaining an image of at least one of the vessel, the anastomosis, and the transplanted solid organ. The image may be obtained intra-operatively. Thus, in some embodiments, the vessel may be a surgically exposed vessel which communicates with the transplanted organ.

The invention also contemplates, in some embodiments, obtaining a plurality of images. The plurality of images may be compared to each other to determine the effectiveness of a therapy, e.g., an administered pharmaceutical compound, a surgical procedure.

In certain embodiments the invention provides a method for determining the patency of a vessel attached to a donor organ, or determining the patency of a donor organ itself. The method comprises a) administering a fluorescent dye to the donor subject or donor organ; b) applying a sufficient amount of energy to the donor organ and attached vessel such that the fluorescent dye fluoresces; c) obtaining a fluorescent image of the donor organ, or a fluorescent image of the vessel attached to the donor organ; and d) observing the image to determine if a fluorescent signal is continuous through the donor organ or the vessel attached to the donor organ, wherein a continuous fluorescent signal in the vessel, or the organ indicates the vessel is patent.

In certain embodiments the invention provides a method of determining the patency of a vessel comprising a lumen. In some embodiments patency may be determined by visually inspecting an image of the vessel. As an example, but not as a limitation, a continuous signal from a dye that is uniform in thickness may indicate patency. As another non-limiting example an image displaying jagged edges, or a change in thickness may indicate stenosis. Similarly a discontinuous signal may indicate occlusion.

Solid Organs

The method of the invention may be used in any organ transplant surgery provided at least one vessel from the recipient communicates either directly, or indirectly, e.g., via an intervening vessel, with the transplanted organ, or a vessel attached to the transplanted organ. The organ may be a natural organ obtained from a donor subject or man-made synthetic organ, or a combination of the two, i.e., part naturally derived and part synthetic. Transplants involving more than one organ are also contemplated by the invention. The vessel may be synthetic, i.e., man-made or natural, i.e. derived from a biological source, including an allograft, an autograft and a xenograft, or a combination of a biological and synthetic source.

As an example, but not as a limitation, the solid organ transplant may be chosen from a heart, a lung, a liver, a kidney, a pancreas, any combination of heart, lung, pancreas, liver and kidney. The organ may be obtained from a living donor or a deceased donor. The organ may be a whole organ or a part of an organ. For example liver transplants can involve the transplant of a whole liver, or a part of the liver.

Where the transplanted solid organ is a heart the method of the invention may be used to determine the patency of any vessel anastomosed to the heart, e.g., inferior vena cava, superior vena cava, atrial cuffs, aortic root, aorta and its branches (e.g., descending aorta, common carotid, subclavian), pulmonary trunk, pulmonary artery, pulmonary vein, or their combined anastomosis to the atrium. Where the transplanted solid organ is a lung the method of the invention may be used to determine the patency of any vessel anastomosed to the lung, e.g., pulmonary vein, pulmonary artery. Where the transplanted solid organ is a liver the method of the invention may be used to determine the patency of any vessel anastomosed to the liver, e.g., the hepatic artery, the hepatic vein, and branches of either, the portal vein, as well as, the bile duct and its branches. Where the transplanted solid organ is a kidney the method of the invention may be used to determine the patency of any vessel anastomosed to the kidney, e.g., the renal artery, the renal vein, the ureter. Where the transplanted solid organ is a pancreas the method of the invention may be used to determine the patency of any vessel anastomosed to the pancreas, e.g., the splenic artery and its branches, the pancreaticoduodenal arteries and their branches, the pancreatic
duct. The vessel may be an arterial graft or venous graft in any of the solid organ transplants described herein.

Dyes

[0026] Suitable fluorescent dyes include any non-toxic dye which fluoresces when exposed to radiant energy, e.g. light. In certain embodiments the dye is a fluorescent dye that emits light in the infrared spectrum. In certain embodiments the dye is a tricarbocyanine dye such as indocyanine green (ICG). In other embodiments the dye is selected from fluorescein isothiocyanate, rhodamine, phycoerythrin, phycoerycin, allophycocyanin, o-phthalaldehyde, fluoresceamine, rose Bengal, trypan blue, and fluoro-gold. The aforementioned dyes may be mixed or combined in certain embodiments. In some embodiments dye analogs may be used. A dye analog includes a dye that has been chemically modified, but still retains its ability to fluoresce when exposed to radiant energy of an appropriate wavelength.

[0027] In some embodiments the dye may be administered intravenously, e.g., as a bolus injection. In some embodiments the bolus injection may comprise a volume of about 0.5 ml. In other embodiments the bolus injection may comprise a volume in the range of about 0.1 ml to about 10 ml. In some embodiments the dye may be injected into a vein or artery. In yet other embodiments the dye may be injected directly into the transplanted organ. In still other embodiments, the dye is injected within about a 15 cm radius of the transplanted organ. In yet other embodiments the dye may be administered parenterally. Where multiple dyes are used they may be administered simultaneously, e.g., in a single bolus, or sequentially, e.g., in separate boluses. In some embodiments the dye may be administered by a catheter, e.g., during a minimally invasive procedure.

[0028] The dye may be administered at a suitable concentration such that the fluorescence may be detected when the appropriate wavelength of radiant energy is applied. In some embodiments where the dye is ICG a suitable concentration is about 0.03 mg/ml at the site of detection. In other embodiments a suitable concentration of ICG is in the range of about 0.003 mg/ml to about 75 mg/ml. In some embodiments the ICG is administered in the range of about 1 mg/kg body weight to about 6 mg/kg body weight. In yet other embodiments the dye is administered at a concentration of about 0.5 mg/kg body weight. In still other embodiments the dye is administered in a range of about 0.01 mg/kg body weight to about 3 mg/kg body weight. In certain embodiments a suitable maximum daily dose of ICG may be administered to a subject. The maximum daily dose may be in the range of about 70 mg-about 140 mg.

[0029] The dye may be provided as a lyophilized powder or solid. In certain embodiments it may be provided in a vial, e.g. a sterile vial which may permit reconstitution with a sterile syringe. It may be reconstituted using any appropriate carrier or diluent. Examples of carriers and diluents are provided below. In certain embodiments the dye may be reconstituted at a concentration in the range of about 0.001 mg/ml-100 mg/ml. In other embodiments the dye is reconstituted to a concentration of about 10 mg/ml, about 20 mg/ml, about 30 mg/ml, about 40 mg/ml, about 50 mg/ml. The dye may be reconstituted, e.g., with water, immediately before administration.

[0030] In certain embodiments the dye may be administered to the subject less than an hour in advance of obtaining an image. In some embodiments the dye may be administered to the subject less than 30 minutes in advance of obtaining an image. In yet other embodiments the dye may be administered at least 30 seconds in advance of obtaining an image. In still other embodiments the dye is administered contemporaneously with obtaining an image.

Diluents and Carriers

[0031] Any diluent or carrier which will maintain the dye in solution may be used. As an example, in certain embodiments where the dye is ICG the dye may be reconstituted with water. In other embodiments where the dye is ICG, the dye may be reconstituted with an alcohol, e.g. ethyl alcohol. In some embodiments once the dye is reconstituted it may be mixed with additional diluents and carriers. In some embodiments the dye may be conjugated to another molecule, e.g., a protein, a peptide, an amino acid, a synthetic polymer, or a sugar e.g., to enhance solubility or to enhance stability.

[0032] Additional examples of diluents and carriers which may be used in the invention include glycerin, polyethylene glycol, propylene glycol, polysorbate 80, Tween, liposomes, amino acids, lecithin, dodecyl sulfate, phospholipids, deoxycholate, soybean oil, vegetable oil, safflower oil, sesame oil, peanut oil, cottonseed oil, sorbitol, acacia, aluminum monostearate, polyoxyethylated fatty acids, and mixtures thereof. Additional buffering agents may optionally be added including Tris, HCl, NaOH, phosphate buffer, HEPES.

Radiant Energy

[0033] In certain embodiments of the invention radiant energy is applied to the transplanted solid organ, or a vessel communicating directly, or indirectly with the transplanted organ, in an amount sufficient to cause a fluorescent dye to fluoresce thereby permitting at least one of the transplanted solid organ, or a vessel communicating directly, or indirectly with the transplanted organ to be imaged. In some embodiments the energy is light energy. In some embodiments the source of the light energy is a laser. An example of a suitable laser is the Magnum 3000 (Lasiris St-Laurent, Quebec, Canada), however, the skilled artisan will appreciate many other suitable lasers are commercially available. The laser may be comprised of a driver and diode. The laser may optionally include a filter, e.g. a bandpass filter, to ensure that the emitted radiation is of a substantially uniform wavelength. The laser may comprise optics for diverging the laser. The optics may be adjustable permitting variation in the field of illumination. The adjustable optics may also be used to provide even illumination over a given area.

[0034] In some embodiments the laser output is continuous. In other embodiments the laser output is pulsed. The pulsed output may be synchronized with image acquisition by using a pulse generator. In some embodiments the laser pulse may last for at least 3 femtoseconds. In some embodiments the laser output lasts for about 30 seconds. In other embodiments the laser output lasts about 0.5 seconds-about 60 seconds. A suitable repetition rate for the pulsed laser may be in the range of e.g., 1 Hz-80 MHz, 10 Hz-100 Hz, 100 Hz-1 kHz, 1 kHz-100 kHz, 100 kHz-80 MHz. In some embodiments the laser may be operated at power output of 2.2 watts. In other embodiments the laser may be operated
at power output in the range of 1-4 watts. In still other embodiments the average power is less than 5 watts.

In certain embodiments the source of the light energy is an incandescent light with an appropriate filter so as to provide a suitable wavelength of light to induce the fluorescent dye to fluoresce. In yet other embodiments the light source is light emitting diode (LED).

In some embodiments the light energy may have a wavelength in the range of 150 nm-1500 nm. In other embodiments the light energy may be comprised of infra red light. In some embodiments the administered light has a wavelength of about 805 nm. In other embodiments the administered light has a wavelength in the range of about 805 nm-850 nm. The light energy may be administered at a wavelength which is shorter than the collection wavelength, i.e. detection wavelength. The light energy may be administered diffusely so as not to damage the irradiated tissue. In some embodiments the light is administered over an area of about 7.5 cm x 7.5 cm. In other embodiments the light is administered over an area in the range of about 1 cm x 1 cm. to about 20 cm x 20 cm.

Image Acquisition

Image acquisition may be achieved using any sensor capable of detecting a fluorescent signal. Examples include silicon based sensors, composite metal oxide semi oxide (CMOS) sensors and photographic film. In one embodiment the sensor comprises a camera, e.g. charge coupled device (CCD). Examples of a CCD include the Hitachi KP-M2; KP-M3 (Hitachi, Tokyo, Japan).

In certain embodiments an endoscope comprising a sensor may be used. The endoscope may additionally comprise a source of radiant energy. The endoscope may be comprised of optical fibers. In certain other embodiments a microscope comprising a sensor may be used, e.g., a surgical microscope. In another embodiment the sensor comprises a video camera. In certain embodiments the sensor may capture images at the rate of at least 10 per second, at least 15 per second, at least 20 per second, at least 30 per second, at least 50 per second. Thus in certain embodiments the invention contemplates a plurality of images. In other embodiments the invention contemplates one image.

The camera may be comprised of a means for focusing the image. In certain embodiments the invention contemplates a manual means for focusing an image. In other embodiments the invention contemplates an automated means for focusing an image. The camera may further be comprised of a lens system that permits magnification of an image field.

In one embodiment the relative positioning of the camera and laser is fixed so as to enhance clarity and minimize background noise. In this embodiment the laser is located at an angle of less than about 85° with respect to the axes of the laser and the camera. In another embodiment the laser is located at an angle from about 200 to about 70° with respect to the axes of the laser and the camera.

In certain embodiments the camera relays the captured image to an analog to digital converter and then through image capture and processing software running on a computer. The digital image of the fluorescing agent, corresponding to the transplanted organ and/or communicating vessel, may then be displayed on a monitor and recorded by the computer or a peripheral device. The image may be stored in any suitable medium, e.g., a hard drive, an optical disk, magnetic tape. The camera may also direct images to a television/VCR system such that the images may be displayed in real time, recorded and played back at a later time.

Systems of the Invention

In certain embodiments the invention provides a system for imaging at least one vessel joined to a transplanted solid organ, see, e.g., FIG. 1. The system may be used intra-operatively during transplant surgery to visualize at least one surgically exposed vessel which is joined to the transplanted organ.

In certain embodiments, the system comprises: a) a fluorescent dye; b) an energy source capable of emitting sufficient energy such that the fluorescent dye fluoresces; c) an imaging head; d) an articulating arm; e) a computer and monitor; f) image processing software; g) an electrical power source; and h) a housing for containing a-g, wherein the housing is portable and comprises at least 2 wheels. In some embodiments the system may also comprise at least one of the following: a motion sensor; a distance sensor; a sterile drape; and a printer. The system may further comprise an instruction booklet. The system may be portable and thus may be transported in and out of the operating room. The system may be self standing and thus does not require to be held by a physician or a technician.

The imaging head may be comprised of a sensor, e.g., a camera. The imaging head, may in some embodiments also contain the energy source, e.g., the laser. In some embodiments the laser contained within the imaging head provides a nominal ocular hazard distance (NOHD) of about 27 cm. The NOHD is the distance at which the beam irradiance or radiant exposure equals the corneal maximum permissible exposure. In certain embodiments the imaging head is joined to the housing by virtue of the articulating arm.

The articulated arm provides six degrees of freedom for the imaging head. The imaging head can be translated and positioned in three linear movements (X, Y and Z), and three angular movements (pitch, yaw and roll). Pitch is the rotation of the SPY HEAD about the Y axis. Roll is the rotation of the SPY HEAD about the X axis and Yaw is the rotation of the SPY HEAD about the Z axis.

The articulated arm is comprised of three sections, the horizontal section, the articulated section and the yoke. The horizontal section attaches to the cart, or housing, and provides movement along the horizontal axis (X axis and also roll) and can move in 270 degrees of freedom. The articulated section is hinged in the middle of its length forming two segments. Each segment can rotate with 90 degrees of freedom in one axis. The articulated section provides movement in the vertical axis (Z and also X and Y). The yoke section is a curved section that attaches to the distal end of the articulated section. The yoke has two rotational attachment points. One point attaches to the articulated arm and the other to the imaging head. The yoke provides the imaging head two rotational degrees of freedom (pitch and roll). The articulating arm thus provides a means for positioning the imaging head directly over the subject.
In certain embodiments the imaging head is positioned above the patient and the appropriate field of view is obtained with the aid of real time images on a computer monitor. The physician may adjust the range of focus, e.g., by intermittently observing images on the computer monitor. In another embodiment two laser pointers are provided, e.g., one at each end of the imaging head. The laser beams may radiate green light. The laser beams from the pointers point down toward the patient and provide a means of focusing the camera, without the need to look away from the patient, e.g., at a computer screen. When the two dots from the laser beams converge to the centre of the image is determined. The device may be provided with buttons that allow for manually turning the laser pointers on and off. The buttons may be covered by the sterile drape, but may protrude enough to facilitate ease in switching the laser pointers on and off.

In certain embodiments the computer is a personal computer comprising at least 512 Megabytes of random access memory (RAM) and at least 10 Gigabytes of storage. In some embodiments the computer may contain a Pentium IV processor (Intel, Santa Clara, Calif.). In some embodiments the computer may also have a CD and DVD drive. The drive may have read and write functionality. The system also provides image processing software. In one embodiment the image processing software is FloVision™.

In certain embodiments the image processing software permits selection of the optimal image for analysis. In some embodiments the image processing software may permit manipulation of contrast. In some embodiments the image processing software can permit manipulation of resolution. In another embodiment the image processing software can permit manipulation of the number of pixels in a field. In another embodiment the image processing software may permit control of the rate at which images are acquired. The software may be able to determine the relative contrast of one image with another, and then select the images having the greatest contrast for analysis, e.g., images of transplanted organs emitting detectable fluorescence.

In certain embodiments the software may be used to compare images of pre and post treatment vessels to determine flow within the vessel, e.g., blood flow. The comparison may be performed by calculating and comparing the area of fluorescence (e.g., the number of pixels associated with the fluorescing dye) in pre and post treatment images corresponding to a selected area of interest in the vessel. In other embodiments the relative maximum fluorescent intensity may be calculated, e.g., pre and post treatment. A greater number of pixels or a greater fluorescent intensity in a post treatment vessel, as compared to a pre-treatment vessel, may be indicative of potency.

The system also provides, in certain embodiments, a housing to contain the computer, the monitor, the electrical supply, the printer, and the imaging head. The housing may be portable to permit movement within the operating room, or alternatively to permit movement of the system in and out of the operating room. In some embodiments the housing is comprised of at least two wheels. In other embodiments the housing is comprised of four wheels. The wheels may have locks to prevent unwanted movement.

In certain embodiments the housing has a width of about 30 inches, a depth of about 35 inches and height of about 82 inches. In certain embodiments the housing width is less than 45 inches. In certain embodiments the depth is less than 45 inches. In certain embodiments the height is less than 102 inches. The housing is not hand held, and thus the system is not required to be hand held.

The electrical power supply may be comprised of a lock in some embodiments. The lock serves as a safety device to prevent inadvertent activation of the system, in particular activation of the laser.

In some embodiments the system may be comprised of a motion detector. The motion detector determines if the imaging head moves. In certain embodiments the system comprises a distance sensor. The distance sensor determines the distance between the imaging head and another object, e.g., the subject. In some embodiments it incorporates a visual display which provides feedback to a physician so that the laser and camera may be located at a distance from the tissue of interest that is optimal for capturing high quality images, thereby minimizing the need for focusing the camera during the procedure.

In some embodiments the system comprises a sterile drape. The sterile drape covers the articulating arm to prevent or minimize the risk of contamination of the subject. The sterile drape may have an aperture in it. The aperture may be covered with a material which is capable of transmitting radiant energy, e.g., infrared light generated by a laser.

Apparatus

Certain embodiments of the invention provide an apparatus which may be used for intra-operative imaging, e.g., in a surgical suite. The apparatus may be portable so that it may be conveniently transported into and out of an operating room. The apparatus may be free standing and thus not require a physician, nurse or technician to hold it. The apparatus may comprise a) an energy source capable of emitting sufficient energy such that a fluorescent dye fluoresces; b) an imaging head; c) an articulating arm; d) a computer and monitor; e) image processing software; f) an electrical power source; and g) a housing for containing a-f, wherein the housing comprises at least 2 wheels. In some embodiments the apparatus may also comprise at least one of the following: a motion sensor; a distance sensor; a sterile drape; and a printer. In some embodiments the housing is comprised of at least two wheels. In other embodiments the housing is comprised of four wheels. The wheels may have locks to prevent unwanted movement. The apparatus may also comprise a focusing device, e.g., at least one focusing laser, e.g., a first and a second laser pointer, the first laser pointer positioned at a first end of the imaging head, and a second laser pointer positioned at a second end of the imaging head. The two laser pointers may be provide radiant light in the green wavelength range and may provide a means of focusing the camera.

The apparatus may be of a suitable size so that it is free standing, but is small enough so as not to provide a significant obstruction in an operating room. In certain embodiments the apparatus has a width of about 30 inches, a depth of about 35 inches and height of about 82 inches. In certain embodiments the apparatus width is less than 45 inches. In certain embodiments the apparatus depth is less than 45 inches. In certain embodiments the apparatus height is less than 102 inches.
Many modifications and variations of this invention can be made without departing from its spirit and scope, as will be apparent to those skilled in the art. The specific embodiments described herein are offered by way of example only and are not meant to be limiting in any way. It is intended that the specification and examples be considered as exemplary only, with a true scope and spirit of the invention being indicated by the following claims.

What is claimed is:

1. A method of intra-operatively determining the patency of at least one vessel which is surgically joined to a transplanted organ in a recipient subject comprising:
   a. administering a fluorescent dye to the recipient subject;
   b. applying a sufficient amount of energy to the vessel such that the fluorescent dye fluoresces;
   c. obtaining a fluorescent image of the vessel surgically joined to a transplanted organ; and
   d. observing the image to determine if a fluorescent signal is continuous through the vessel, wherein a continuous fluorescent signal in the vessel indicates the vessel is patent.
2. The method of claim 1, wherein the recipient subject is a human.
3. The method of claim 1, wherein the fluorescent dye is a tricarbocyanine dye or an analog thereof.
4. The method of claim 3, wherein the tricarbocyanine dye is indocyanine green.
5. The method of claim 1, wherein the dye is administered intravenously.
6. The method of claim 1, wherein the dye is administered as a bolus injection.
7. The method of claim 1, wherein the dye is administered less than an hour before determining patency.
8. The method of claim 1, wherein the dye is administered more than 30 seconds before determining patency.
9. The method of claim 1, wherein the energy is light energy.
10. The method of claim 9, wherein the light energy is provided by a laser.
11. The method of claim 9, wherein the light energy is provided by an incandescent light and a filter.
12. The method of claim 9, wherein the wavelength of the light energy is in the infra-red spectrum.
13. The method of claim 9, wherein the wavelength of the light energy is about 805 nanometers.
14. The method of claim 1, wherein the image is obtained by a camera.
15. The method of claim 14, wherein the camera is a charge coupled device.
16. The method of claim 14, wherein the camera is a video recorder.
17. The method of claim 10, wherein the laser power output is about 2.5 watts.
18. The method of claim 17, wherein the laser power output lasts for about 30 seconds.
19. The method of claim 17, wherein the output is a continuous wave.
20. The method of claim 1, wherein the vessel is a blood vessel.
21. The method of claim 1, wherein the vessel is an artery.
22. The method of claim 1, wherein the vessel is a vein.
23. The method of claim 1, wherein the vessel is a ureter.
24. The method of claim 1, wherein the vessel is comprised of a duct.
25. The method of claim 1, wherein the organ is chosen from a heart, a liver, a pancreas, a kidney and a lung.
26. The method of claim 1, wherein the organ is a heart and a lung.
27. The method of claim 1, wherein the organ is a pancreas and a kidney.
28. The method of claim 1, wherein the vessel is chosen from an inferior vena cava, superior vena cava, an atrial cuff, an aortic root, an aorta, a pulmonary trunk, a pulmonary vein, a pulmonary artery, a hepatic artery, a hepatic vein, a portal vein, a bile duct, a renal artery, a renal vein, a pancreatic duct, a pancreatic artery, a pancreatic vein, an arterial graft, a venous graft.
29. The method of claim 1, wherein the vessel comprises an anastomosis.
30. The method of claim 1, further comprising a method of determining the patency of at least one vessel which is attached to a donor organ in a donor subject comprising:
   a. administering a fluorescent dye to the donor subject;
   b. applying a sufficient amount of energy to the vessel such that the fluorescent dye fluoresces;
   c. obtaining a fluorescent image of the vessel attached to a donor organ; and
   d. observing the image to determine if a fluorescent signal is continuous through the vessel, wherein a continuous fluorescent signal in the vessel indicates the vessel is patent.
31. The method of claim 1, further comprising a method of determining the patency of at least one vessel which is attached to a donor organ comprising:
   a. administering a fluorescent dye to the vessel attached to the donor organ;
   b. applying a sufficient amount of energy to the vessel such that the fluorescent dye fluoresces;
   c. obtaining a fluorescent image of the vessel attached to a donor organ; and
   d. observing the image to determine if a fluorescent signal is continuous through the vessel, wherein a continuous fluorescent signal in the vessel indicates the vessel is patent.
32. The method of claim 30, wherein the method is performed ex vivo.
33. A portable system useful for imaging at least one vessel which is surgically joined to a transplanted organ in a recipient subject comprising: a) a fluorescent dye; b) an energy source capable of emitting sufficient energy such that the fluorescent dye fluoresces; c) an imaging head.
34. The system of claim 33, wherein the fluorescent dye is a tricarbocyanine dye or an analog thereof.
35. The system of claim 34, wherein the tricarbocyanine dye is indocyanine green.
36. The system of claim 33, wherein the energy source is a laser.
37. The system of claim 36, wherein the laser emits infra red light.
38. The system of claim 33, wherein the imaging head comprises a camera.
39. The system of 38, wherein the camera is a charge coupled device.
40. A portable system useful for imaging at least one vessel which is surgically joined to a transplanted organ in a recipient subject comprising:
   a. a fluorescent dye;
   b. an energy source capable of emitting sufficient energy such that the fluorescent dye fluoresces;
   c. an imaging head;
   d. an articulating arm;
   e. a computer and monitor;
   f. image processing software;
   g. an electrical power source; and
   h. a housing for containing a-g, wherein the housing comprises at least 2 wheels.
41. The system of claim 40 further comprising a motion sensor.
42. The system of claim 40 further comprising a distance sensor.
43. The system of claim 40 further comprising a sterile drape.
44. The system of claim 40 further comprising a printer.
45. The system of claim 40, wherein the articulating arm comprises a horizontal section.
46. The system of claim 40, wherein the housing is a mobile cart.
47. The system of claim 46, wherein the mobile cart comprises four wheels.
48. The system of claim 40, wherein the imaging head comprises a camera.
49. The system of claim 48, wherein the camera is a charge coupled device.
50. The system of claim 40, wherein the imaging head, the motion sensor, and the distance sensor are attached to the articulating arm.
51. The system of claim 40, wherein the mobile cart houses the electrical power source, the printer, the computer, and the energy source.
52. The system of claim 40, wherein the energy source is a laser.
53. The system of claim 40, further comprising a syringe to administer the fluorescent dye to a subject.
54. The system of claim 45, wherein the articulating arm provides six degrees of freedom for the imaging head.
55. The system of claim 40, wherein the energy is light energy.
56. The system of claim 55, wherein the light energy has a wavelength in the infra-red spectrum.
57. The system of claim 56, wherein the light energy has a wavelength of about 805 nanometers.
58. The system of claim 40, wherein the sterile drape is comprised of a transparent aperture such that the energy passes through the sterile drape.
59. The system of claim 40, wherein the fluorescent dye is a tricarbocyanine dye or an analog thereof.
60. The system of claim 40, wherein the tricarbocyanine dye is indocyanine green.
61. The system of claim 40 further comprising an instruction booklet.
62. The system of claim 40, wherein the system is free standing.
63. The system of claim 40, wherein the system is not required to be hand held.
64. The system of claim 40, wherein the imaging head is contained in an endoscope.
65. The method of claim 1, wherein the imaging head is from a biological source.
66. The method of claim 65, wherein the graft is chosen from an allograft, an autograft and a xenograft.
67. The method of claim 1, wherein the vessel is from a synthetic source.

* * * * *