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(54) **IMAGING SYSTEM FOR GENERATING A RENDERED IMAGE**

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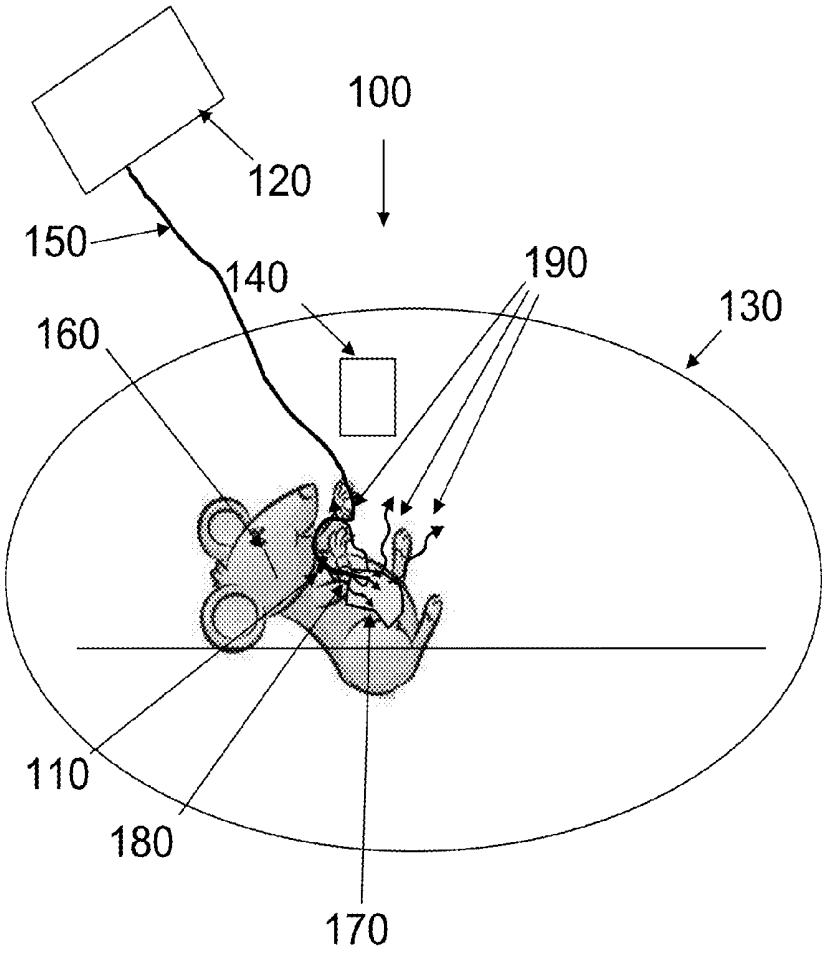
(57) **ABSTRACT**

The present invention provides an imaging system having an imaging device for imaging at least a portion of an animal; said imaging device selected from a group consisting of X-ray computed tomography (CT), positron emission tomography (PET), single-photon emission computed tomography (SPECT), fluorescence and phosphorescence microscopy (FPM) and any combination thereof; consisting of CT, computer-assisted tomography; IR, rendered images comprising infrared light spectroscopy; PET, positron emission tomography; fluorescence and phosphorescence microscopy, a Raman spectroscopic imaging system, ultrasound and any combination thereof.



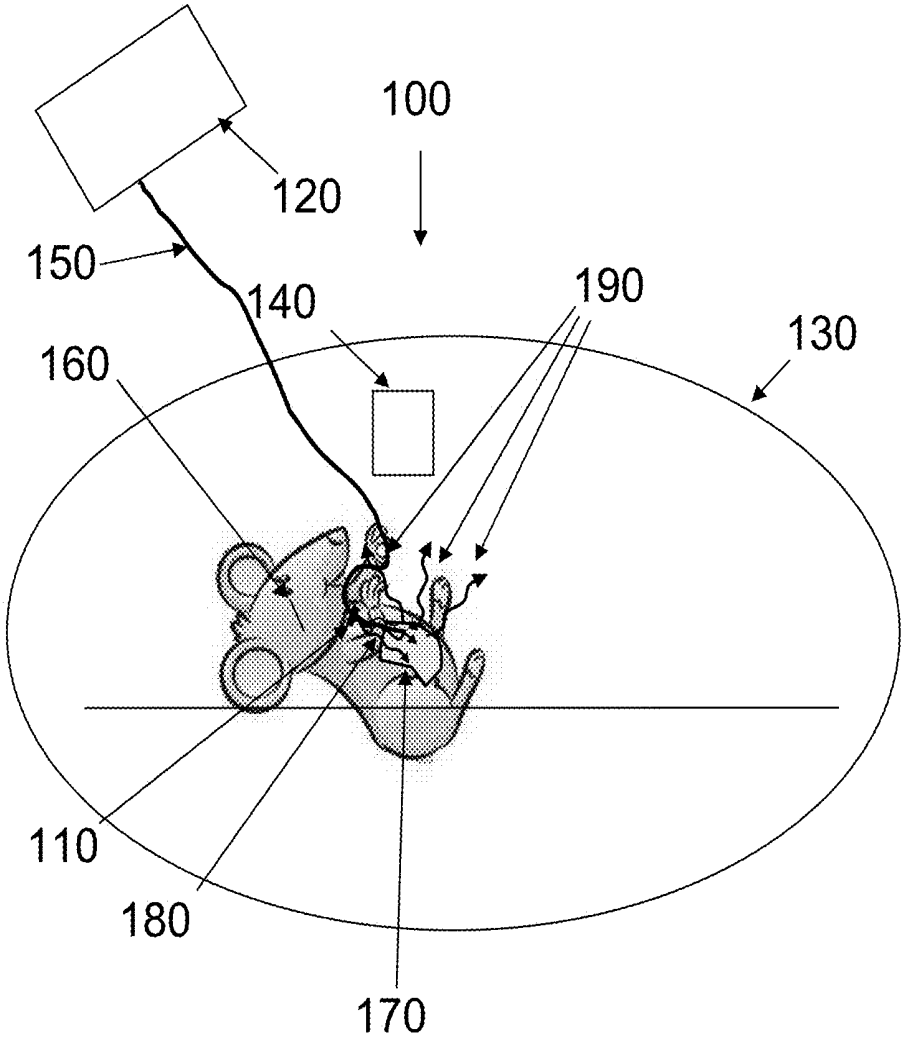


Fig. 1

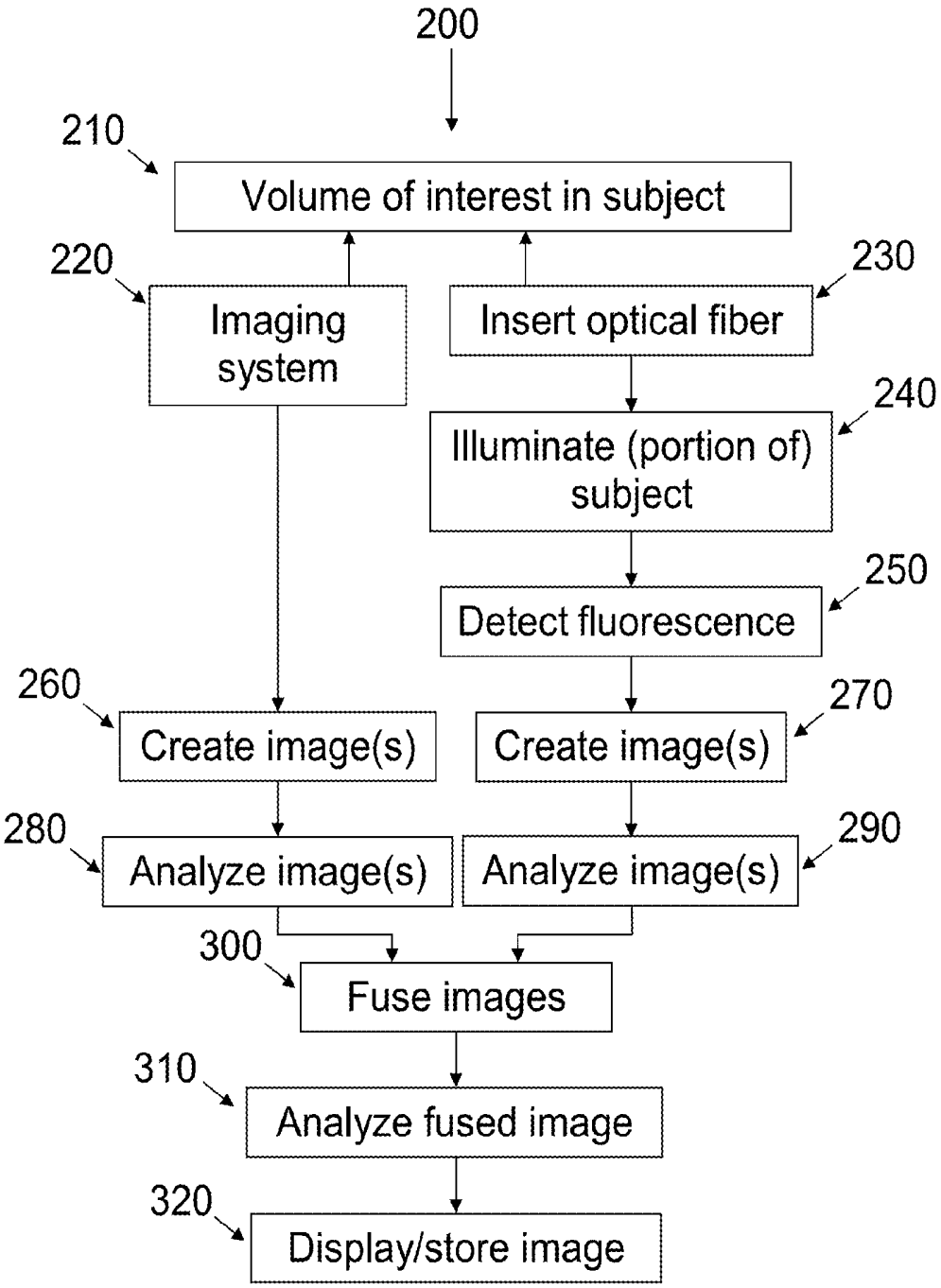

200
210
Volume of interest in subject
220
Imaging system
230
Insert optical fiber
240
Illuminate (portion of) subject
250
Detect fluorescence
260
Create image(s)
270
Create image(s)
280
Analyze image(s)
290
Analyze image(s)
300
Fuse images
310
Analyze fused image
320
Display/store image

Fig. 2

IMAGING SYSTEM FOR GENERATING A RENDERED IMAGE

FIELD OF THE INVENTION

[0001] The present invention generally pertains to a system and method for an imaging system for generating a rendered image of an interior portion of an animal by superimposing two images from different imaging systems, one being a fluorescence image, where the fluorescence is excited by light emitted by a photon emitter located within the animal.

BACKGROUND OF THE INVENTION

[0002] In vivo fluorescence imaging uses a sensitive camera to detect fluorescence emission from fluorophores in whole-body living small animals. To overcome the photon attenuation in living tissue, fluorophores with long emission at the near-infrared (NIR) region are generally preferred, including widely used small indocarbocyanine dyes.

[0003] Molecules that absorb in the near infrared (NIR) region, 700-1000 nm, can be efficiently used to visualize and investigate in vivo molecular targets because most tissues generate little NIR fluorescence. The most common organic NIR fluorophores are polymethines Among them, pentamethine and heptamethine cyanines comprising benzoxazole, benzothaizole, indolyl, 2-quinoline or 4-quinoline have been found to be the most useful.

[0004] Fluorescence images enable determination of cells types, cell activity and protein activity, but provide little information on the structure of the body or body part under investigation. Combination of in vivo fluorescence imaging with other techniques, such as CAT scans, ultrasound imaging, infrared imaging, X-radiography, Raman spectroscopy, single photon emission computed tomography or microwave imaging will enable synergies between the types of information provided by the different probes, allowing, for example, precise knowledge of the location of cell types and cell activities within organs and structures of the body.

[0005] Patent application US 2005/0028482 discloses systems and methods for multi-modal imaging with light and a second form of imaging. Light imaging involves the capture of low intensity light from a light-emitting object. A camera obtains a two-dimensional spatial distribution of the light emitted from the surface of the subject. Software operated by a computer in communication with the camera may then convert two-dimensional spatial distribution data from one or more images into a three-dimensional spatial representation. The second imaging mode may include any imaging technique that compliments light imaging. Examples include magnetic resonance imaging (MRI) and computer topography (CT). An object handling system moves the object to be imaged between the light imaging system and the second imaging system, and is configured to interface with each system. However, the energy inducing the fluorescence within the animal is supplied from a source external to the animal.

[0006] It is therefore a long felt need to provide a multimodal system combining structural imaging systems such as CAT or ultrasound scans with fluorescence imaging for preclinical and clinical investigations of tumors where the source of energy used to induce fluorescence is not located outside the body.

SUMMARY OF THE INVENTION

[0007] It is an object of the present invention to disclose a system and method for an imaging system for generating a rendered image of an interior portion of an animal by superimposing two images from different imaging systems, one being a fluorescence image, where the fluorescence is excited by light emitted by a photon emitter located within the animal

[0008] It is an object of the present invention to disclose an imaging system having an imaging device for imaging at least a portion of an animal; said imaging device selected from a group consisting of X-ray computed tomography (CT), positron emission tomography (PET), single-photon emission computed tomography (SPECT), fluorescence and phosphorescence microscopy (FPM) and any combination thereof; consisting of CT, computer-assisted tomography; IR, rendered images comprising infrared light spectroscopy; PET, positron emission tomography; fluorescence and phosphorescence microscopy, a Raman spectroscopic imaging system, ultrasound and any combination thereof; said system characterized by (a) a photon transmitter of photons, introducible within the body of an animal; (b) at least one imaging photon detector located either within or outside said animal, for detecting fluorescence excited within said animal by said transmitted photons; and (c) an image processor adapted to superimpose said imaging device image and said photon detector image generating a rendered image of said at least a portion of said animal.

[0009] It is another object of the present invention to disclose the imaging system, wherein the transmitter of photons is selected from the group consisting of an optical fiber, a cannula, a light pipe, a light tube, and any combination thereof.

[0010] It is another object of the present invention to disclose the imaging system, wherein the optical fiber is selected from the group consisting of silica glass fiber, fluorozirconate glass fiber, fluoroaluminate glass fiber, chalcogenide glass fiber, sapphire fiber, and polymer optical fiber.

[0011] It is another object of the present invention to disclose the imaging system, wherein the transmitter of photons enters the body through an orifice selected from the group consisting of a cannula inserted in the animal, a trocar inserted in the animal, a laparoscopy system inserted in the animal, the nose, the mouth, the anus, the vagina, the urethra, the ear, and any combination thereof.

[0012] It is another object of the present invention to disclose the imaging system, wherein the photons are in at least one range selected from the group consisting of X-rays, far ultraviolet, near ultraviolet, visible light, near infrared and far infrared.

[0013] It is another object of the present invention to disclose the imaging system, wherein the at least one photon detector is selected from the group consisting of a CCD array, a camera, a photoconductive detector array, a photovoltaic detector array, a quantum dot array, a superconducting single-photon detector array, a photovoltaic cell array, a phototube array, and any combination thereof.

[0014] It is another object of the present invention to disclose the imaging system, wherein the image processor is adapted to render the superimposed image by a Boolean method of correlating or combining at least a portion of the imaging system image and at least a portion of the photon detector image.

[0015] It is another object of the present invention to disclose the imaging system, wherein the Boolean method uses

Boolean operators selected from the group consisting of OR, AND, NOT, EXCLUSIVE OR and any combination thereof.

[0016] It is another object of the present invention to disclose a method for imaging at least a portion of an animal, comprising steps of: (a) providing an imaging system, having an imaging device for imaging at least a portion of an animal; and selecting said device from a group consisting of X-ray computed tomography (CT), positron emission tomography (PET), single-photon emission computed tomography (SPECT), fluorescence and phosphorescence microscopy (FPM) and any combination thereof; said imaging device selected from a group consisting of CT, computer-assisted tomography; IR, rendered images comprising infrared light spectroscopy; PET, positron emission tomography; fluorescence and phosphorescence microscopy, a Raman spectroscopic imaging system, ultrasound and any combination thereof; said system characterized by (i) a photon transmitter, introducible within the body of an animal; (ii) at least one imaging photon detector located either within or outside said animal, for detecting fluorescence excited within said animal by said transmitted photons; and (iii) an image processor adapted to superimpose said imaging system image and said photon detector image, generating a rendered IMAGING SYSTEM image of said at least a portion of said animal; (b) introducing said photon transmitter within the body of an animal; (c) imaging said at least a portion of said animal with said imaging device; (d) creating a photon detector image of said at least a portion of said animal; and (e) superimposing said imaging device image and said at least one optical image of said object, thereby generating said rendered image of said at least a portion of said animal.

[0017] It is another object of the present invention to disclose the method, additionally comprising a step of selecting the transmitter of photons from the group consisting of an optical fiber, a cannula, a light pipe, a light tube, and any combination thereof.

[0018] It is another object of the present invention to disclose the method, additionally comprising a step of selecting the optical fiber from the group consisting of silica glass fiber, fluorozirconate glass fiber, fluoroaluminate glass fiber, chalcogenide glass fiber, sapphire fiber, and polymer optical fiber.

[0019] It is another object of the present invention to disclose the method, additionally comprising a step of emplacing the fiber within the body through an orifice selected from the group consisting of a cannula inserted in the animal, a trocar inserted in the animal, a laparoscopy system inserted in the animal, the nose, the mouth, the anus, the vagina, the urethra, the ear, and any combination thereof.

[0020] It is another object of the present invention to disclose the method, additionally comprising a step of selecting the range of the photons to be at least one of the group consisting of X-rays, far ultraviolet, near ultraviolet, visible light, near infrared and far infrared.

[0021] It is another object of the present invention to disclose the method, additionally comprising a step of selecting the at least one photon detector from the group consisting of a CCD array, a camera, a photoconductive detector array, a photovoltaic detector array, a quantum dot array, a superconducting single-photon detector array, a photovoltaic cell array, a phototube array, and any combination thereof.

[0022] It is another object of the present invention to disclose the method, additionally comprising a step of rendering the superimposed image by a Boolean method of correlating or combining at least a portion of the imaging device image and at least a portion of the photon detector image.

[0023] It is still another object of the present invention to disclose the method, additionally comprising a step of selecting the Boolean operators in the Boolean method from the group consisting of OR, AND, NOT, EXCLUSIVE OR and any combination thereof.

BRIEF DESCRIPTION OF THE FIGURES

[0024] In order to better understand the invention and its implementation in practice, a plurality of embodiments will now be described, by way of non-limiting example only, with reference to the accompanying drawings, wherein

[0025] FIG. **1** schematically illustrates an embodiment of the system of the present invention; and

[0026] FIG. **2** depicts a block diagram of an embodiment of a method of using the present invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0027] The following description is provided, alongside all chapters of the present invention, so as to enable any person skilled in the art to make use of the invention and sets forth the best modes contemplated by the inventor of carrying out this invention. Various modifications, however, will remain apparent to those skilled in the art, since the generic principles of the present invention have been defined specifically to provide a means and method for method for providing a rendered image of a living subject.

[0028] In vivo fluorescence imaging uses a sensitive camera to detect fluorescence emission from fluorophores in whole-body living small animals. To overcome the photon attenuation in living tissue, fluorophores with long emission at the near-infrared (NIR) region, 700-1000 nm, are generally preferred because they can be efficiently used to visualize and investigate in vivo molecular targets, since most tissues generate little NIR fluorescence.

[0029] One widely used class of fluorophores is small indocarbocyanine dyes. In addition, fluorescent organic, inorganic and biological nanoparticles are used. Another class of probes for in vivo fluorescence imaging is semiconductor nanocrystals or quantum dots. QDs that emit at several different wavelengths can be excited with a single wavelength, and thus are suitable for multiplex detection of multiple targets in a single experiment.

[0030] Fluorescence images of the tumors enable determination of cells types (senescent, aggressive, etc.) and protein activity, while, especially, CAT scans, ultrasound imaging and microwave imaging provide information on the locations of the structures, such as organs, blood vessels, nerves and tumors, within the body. Other methods of acquiring structural information include infrared imaging, X-radiography, and Raman spectroscopy.

[0031] The system of the present invention provides a system of simultaneously acquiring structural images and fluorescence images in living subjects of organs, tumors, blood vessels, nerves, or any other objects in the living subject that can be made to fluoresce.

[0032] In reference to FIG. **1**, which shows one embodiment (**100**) of the system, the subject (**110**), or the portion of the subject containing the volume of interest, is placed within the imaging device (**130**). An optical fiber (**150**) connectable to an appropriate light source (**120**) is passed into the subject

through incision **160** to a position in proximity with the volume of interest (**170**), where the provided light (**180**) causes fluorescence (**190**) of fluorescent material in the volume of interest. This fluorescent light is detected with sensors (**140**) outside the body of the subject.

[0033] The optical fiber (**150**) can be introduced into the body through a cannula or a trocar, either an independent cannula or trocar or one forming part of a laparoscopy system, or it can lie within an incision without trocar or cannula. It can also be introduced via a body orifice, such as the nose, mouth, anus, vagina, or urethra, or via a body orifice, as given above, and through a body tissue, either via an incision or through a cannula. One example of the last would be positioning the optical fiber within the skull by passing it via the nasal passages to the ethmoid bone and through the ethmoid bone to the interior of the skull.

[0034] In the system of the present invention, the scanner images provide structural information about body parts, such as organs, blood vessels, or tumors, in the volume of interest, while the fluorescence images, provide functional information about the body part or parts. For non-limiting example, CAT scan images show the shape and size of a tumor, while fluorescence image shows the locations of apoptopic cells and aggressively dividing cells within it.

[0035] In reference to FIG. **2**, a block diagram (**200**) of an embodiment of a method of using the system is shown. At least a volume of interest within the subject is placed within the system. The volume of interest can be the entire subject or a portion thereof, such as an organ or a tumor within the subject, a set of blood vessels or a set of nerves. An optical fiber is emplaced within the subject (**230**) in such a position that light from the fiber will activate fluorescent material within the volume of interest inside the subject. The fluorescent material can be material introduced into the subject by any of the means well known in the art, or it can be fluorescent material produced by the subject. The volume of interest is illuminated (**240**) via the optical fiber and the resulting fluorescence is detected by a detector outside the body of the subject (**250**). An image or images are created (**270**) of the volume of interest, using the detected fluorescence, and the image or images are analyzed (**290**).

[0036] A scan or scans of the volume of interest in the subject is made (**220**), using a structural scanning method such as CAT scans, ultrasound imaging and microwave imaging, infrared imaging, X-radiography, or an independent scanning technique such as Raman spectroscopy. An image or images is created (**260**) of the volume of interest from the structural or Raman scan, and the image or images are analyzed (**280**).

[0037] The structural (or Raman) and fluorescence images are then fused (**300**), using techniques well known in the art, and the combined image is analyzed (**310**) and displayed or stored for later use (**320**).

[0038] Fusing techniques include rendering the images using Boolean methods of correlating and combining the images. Combining binary images using Boolean logic makes it possible to select structures or objects based on multiple criteria, such as, but not limited to, masking and threshholding. The Boolean operators commonly used are OR, AND, NOT, EXCLUSIVE OR and combinations thereof.

[0039] Optical fibers are most commonly silica glass, but can also be made from fluorozirconate glass, fluoroaluminate glass, chalcogenide glass, sapphire, and polymers. The most common polymer optical fibers (POF) are (1) polymethylmethacrilate (PMMA) core with fluorinated polymer cladding, although other POF include: PMMA or Polystyrene core with silicone resin cladding, perfluorinated polymer (mainly polyperfluorobutenylvinylether) POFs, and microstructured polymer optical fibers (mPOF), which are a type of photonic crystal fiber.

1. An imaging system having an imaging device for imaging at least a portion of an animal; said imaging device selected from a group consisting of X-ray computed tomography (CT), positron emission tomography (PET), single-photon emission computed tomography (SPECT), fluorescence and phosphorescence microscopy (FPM) and any combination thereof; consisting of CT, computer-assisted tomography; IR, rendered images comprising infrared light spectroscopy; PET, positron emission tomography; fluorescence and phosphorescence microscopy, a Raman spectroscopic imaging system, ultrasound and any combination thereof; said system characterized by

a. a photon transmitter of photons, introducible within the body of an animal;

b. at least one imaging photon detector located either within or outside said animal, for detecting fluorescence excited within said animal by said transmitted photons; and

c. an image processor adapted to superimpose said imaging device image and said photon detector image generating a rendered image of said at least a portion of said animal.

2. The imaging system of claim **1**, wherein the transmitter of photons is selected from the group consisting of an optical fiber, a cannula, a light pipe, a light tube, and any combination thereof.

3. The imaging system of claim **2**, wherein the optical fiber is selected from the group consisting of silica glass fiber, fluorozirconate glass fiber, fluoroaluminate glass fiber, chalcogenide glass fiber, sapphire fiber, and polymer optical fiber.

4. The imaging system of claim **1**, wherein said transmitter of photons enters the body through an orifice selected from the group consisting of a cannula inserted in the animal, a trocar inserted in the animal, a laparoscopy system inserted in the animal, the nose, the mouth, the anus, the vagina, the urethra, the ear, and any combination thereof.

5. The imaging system of claim **1**, wherein said photons are in at least one range selected from the group consisting of X-rays, far ultraviolet, near ultraviolet, visible light, near infrared and far infrared.

6. The imaging system of claim **1**, wherein said at least one photon detector is selected from the group consisting of a CCD array, a camera, a photoconductive detector array, a photovoltaic detector array, a quantum dot array, a superconducting single-photon detector array, a photovoltaic cell array, a phototube array, and any combination thereof.

7. The imaging system of claim **1**, wherein said image processor is adapted to render said superimposed image by a Boolean method of correlating or combining at least a portion of said imaging system image and at least a portion of said photon detector image.

8. The imaging system of claim **7**, wherein said Boolean method uses Boolean operators selected from the group consisting of OR, AND, NOT, EXCLUSIVE OR and any combination thereof.

9. A method for imaging at least a portion of an animal, comprising steps of:

a. providing an imaging system, having an imaging device for imaging at least a portion of an animal; and selecting said device from a group consisting of X-ray computed tomography (CT), positron emission tomography (PET), single-photon emission computed tomography (SPECT), fluorescence and phosphorescence microscopy (FPM) and any combination thereof; said imaging device selected from a group consisting of CT, computer-assisted tomography; IR, rendered images comprising infrared light spectroscopy; PET, positron emission tomography; fluorescence and phosphorescence microscopy, a Raman spectroscopic imaging system, ultrasound and any combination thereof; said system characterized by

i. a photon transmitter, introducible within the body of an animal;

ii. at least one imaging photon detector located either within or outside said animal, for detecting fluorescence excited within said animal by said transmitted photons; and

iii. an image processor adapted to superimpose said imaging system image and said photon detector image, generating a rendered IMAGING SYSTEM image of said at least a portion of said animal;

b. introducing said photon transmitter within the body of an animal;

c. imaging said at least a portion of said animal with said imaging device;

d. creating a photon detector image of said at least a portion of said animal; and

e. superimposing said imaging device image and said at least one optical image of said object, thereby generating said rendered image of said at least a portion of said animal.

10. The method of claim **9**, additionally comprising a step of selecting the transmitter of photons from the group consisting of an optical fiber, a cannula, a light pipe, a light tube, and any combination thereof.

11. The method of claim **10**, additionally comprising a step of selecting said optical fiber from the group consisting of silica glass fiber, fluorozirconate glass fiber, fluoroaluminate glass fiber, chalcogenide glass fiber, sapphire fiber, and polymer optical fiber.

12. The method of claim **9**, additionally comprising a step of emplacing said fiber within said body through an orifice selected from the group consisting of a cannula inserted in the animal, a trocar inserted in the animal, a laparoscopy system inserted in the animal, the nose, the mouth, the anus, the vagina, the urethra, the ear, and any combination thereof.

13. The method of claim **9**, additionally comprising a step of selecting the range of said photons to be at least one of the group consisting of X-rays, far ultraviolet, near ultraviolet, visible light, near infrared and far infrared.

14. The method of claim **9**, additionally comprising a step of selecting said at least one photon detector from the group consisting of a CCD array, a camera, a photoconductive detector array, a photovoltaic detector array, a quantum dot array, a superconducting single-photon detector array, a photovoltaic cell array, a phototube array, and any combination thereof.

15. The method of claim **9**, additionally comprising a step of rendering said superimposed image by a Boolean method of correlating or combining at least a portion of said imaging device image and at least a portion of said photon detector image.

16. The method of claim **13**, additionally comprising a step of selecting said Boolean operators in said Boolean method from the group consisting of OR, AND, NOT, EXCLUSIVE OR and any combination thereof.

* * * * *

专利名称(译)	用于生成渲染图像的成像系统		
公开(公告)号	US20160166353A1	公开(公告)日	2016-06-16
申请号	US15/041274	申请日	2016-02-11
[标]申请(专利权)人(译)	阿斯派克影像有限公司		
申请(专利权)人(译)	方位成像LTD.		
当前申请(专利权)人(译)	方位成像LTD.		
[标]发明人	RAPOPORT URI BATT ARYEH		
发明人	RAPOPORT, URI BATT, ARYEH		
IPC分类号	A61B90/30 A61B90/00 A61B90/20		
CPC分类号	A61B90/30 A61B90/20 A61B90/361 A61B2090/306 A61B2576/00 A61B2090/3762 A61B2090/378 A61B2503/40 A61B2090/373 A61B5/0035 A61B5/0071 A61B5/0084 A61B6/508 A61B6/5247 A61B8/5261		
优先权	221489 2012-08-15 IL		
外部链接	Espacenet USPTO		

摘要(译)

本发明提供一种成像系统，其具有用于对动物的至少一部分成像的成像装置;所述成像装置选自X射线计算机断层扫描（CT），正电子发射断层扫描（PET），单光子发射计算机断层扫描（SPECT），荧光和磷光显微镜（FPM）及其任何组合;由CT，计算机辅助断层扫描组成; IR，渲染图像包括红外光谱; PET，正电子发射断层扫描;荧光和磷光显微镜，拉曼光谱成像系统，超声波及其任何组合。