US 20120184827A1

(19) **United States**

(12) **Patent Application Publication**

Shwartz et al.

(10) **Pub. No.: US 2012/0184827 A1**

(43) **Pub. Date: Jul. 19, 2012**

(54) **MINIATURE DISEASE OPTICAL SPECTROSCOPY DIAGNOSTIC SYSTEM**

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(21) Appl. No.: **13/378,916**

(22) PCT Filed: **Jun. 16, 2010**

(86) PCT No.: **PCT/IL2010/000477**

§ 371 (c)(1),
(2), (4) Date: **Mar. 5, 2012**

Related U.S. Application Data

(60) Provisional application No. 61/187,280, filed on Jun. 16, 2009.

Publication Classification

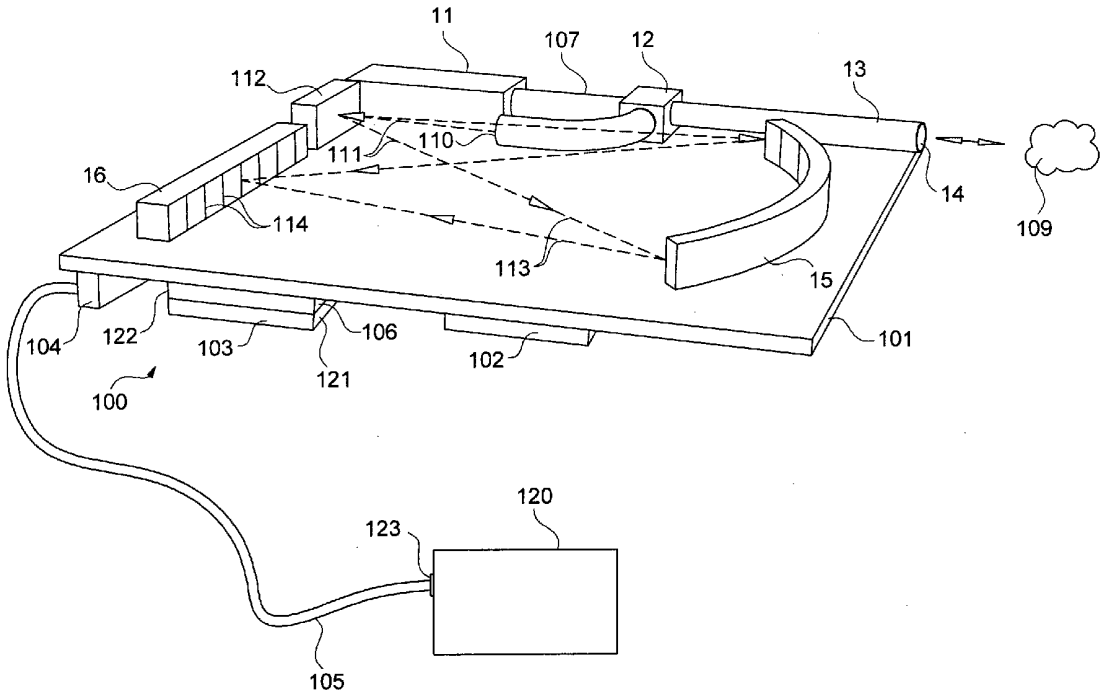
(51) **Int. Cl.**

G01J 3/42	(2006.01)
A61B 5/07	(2006.01)
A61B 10/02	(2006.01)
A61B 5/00	(2006.01)
A61B 1/06	(2006.01)
A61B 5/02	(2006.01)

(52) **U.S. Cl.** **600/302**; 356/402; 250/339.07; 356/326; 250/341.8; 600/178; 600/479; 600/562; 600/583

(57) **ABSTRACT**

A miniature medical spectrometer is provided, the spectrometer comprises: a room temperature, electrically excited, solid state two photon laser generating high intensity broad wavelength; a light projection optics, projecting said generated light on biological subject; a light collection optics, collecting reflected light from said biological subject; a wavelength selector spectrally analyzing said collected light; a detector, detecting said analyzed light; and a controller analyzing the reflected spectra and calculating result indicative of the medical state of the biological subject based on said spectrum.



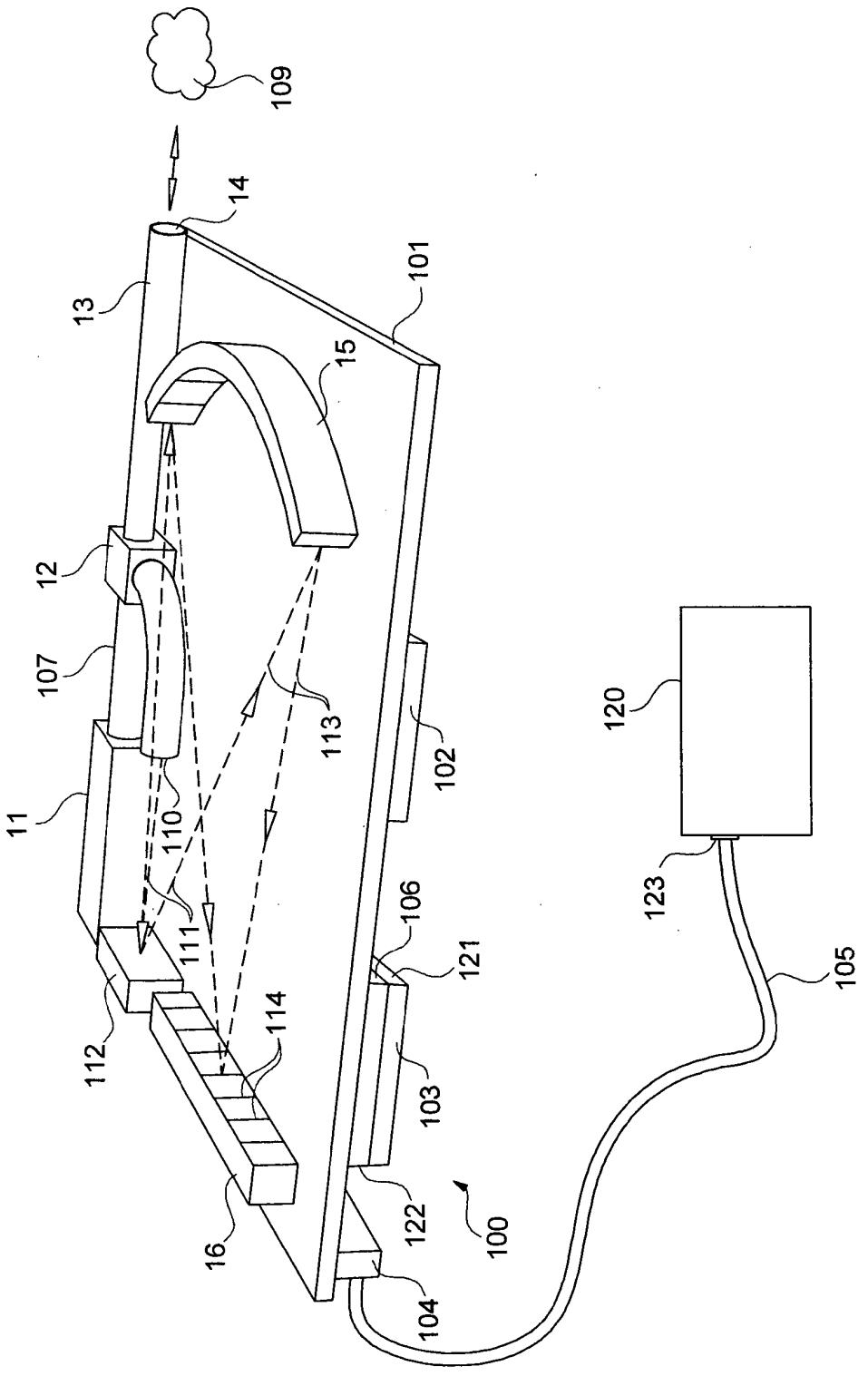

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Fig. 1

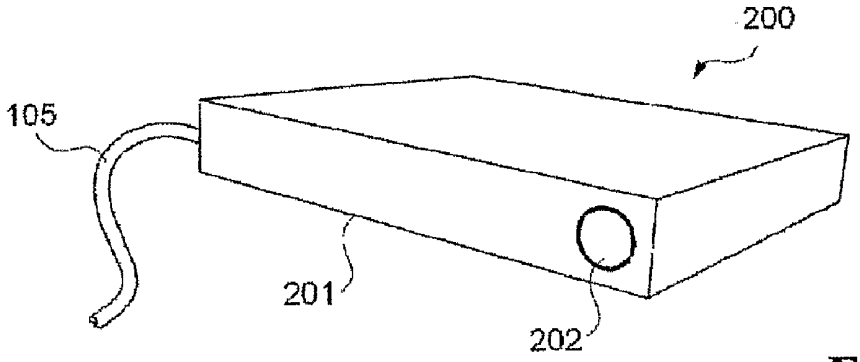
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Fig. 2a

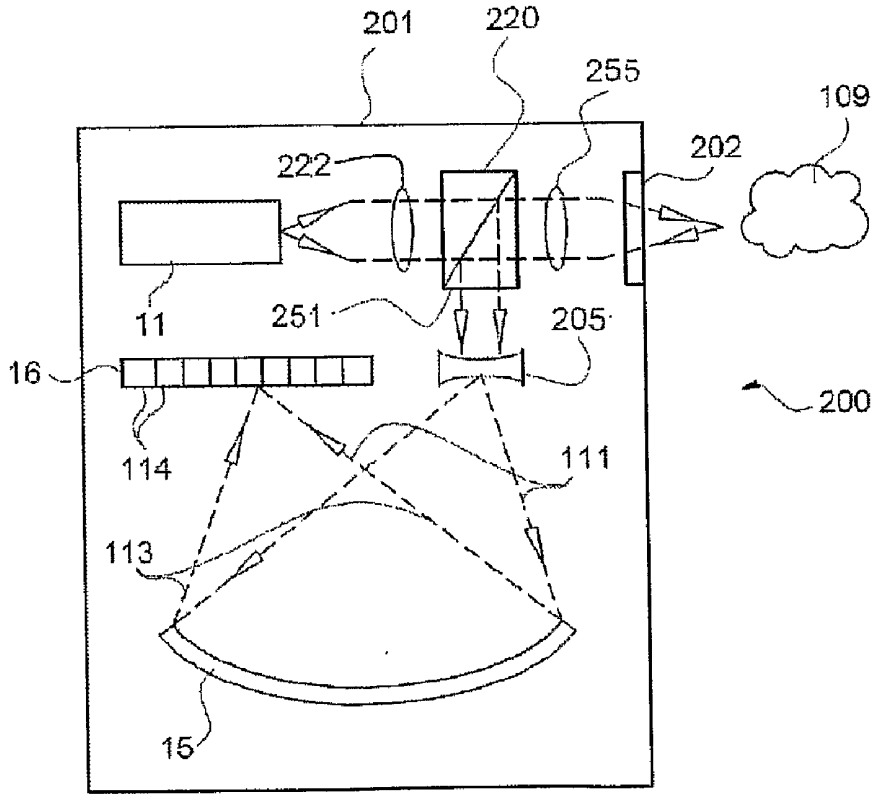
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Fig 2b.

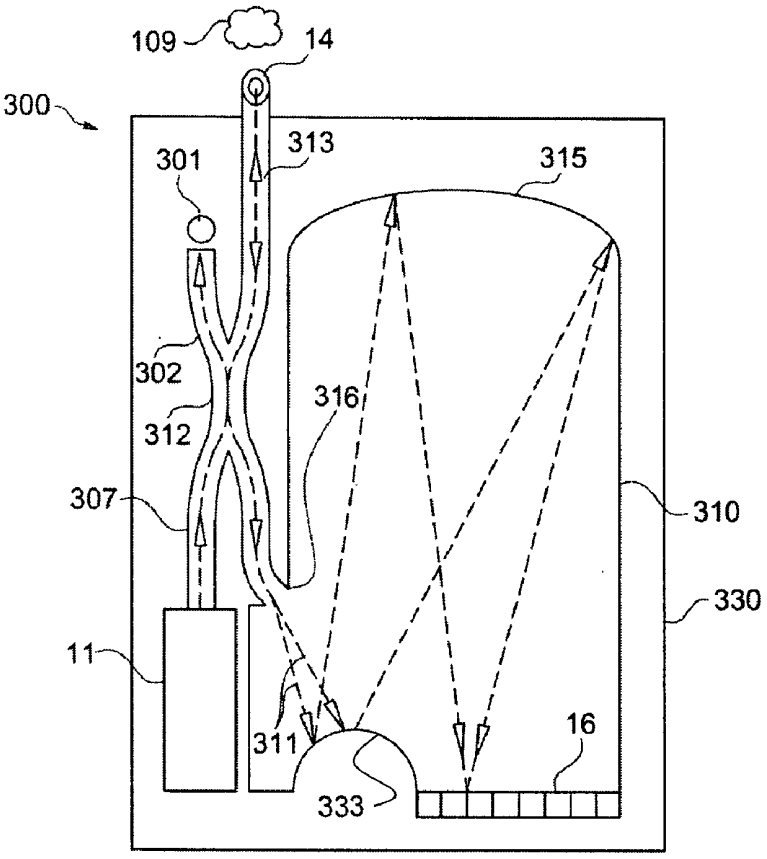
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Fig. 3

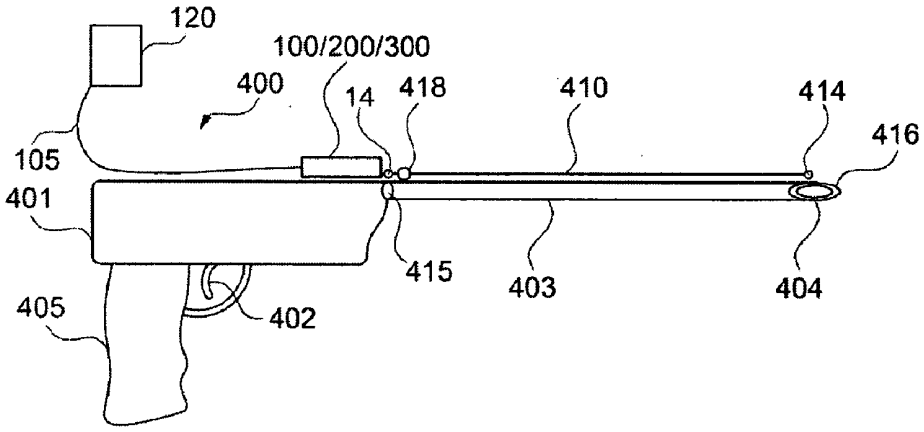
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Fig. 4a

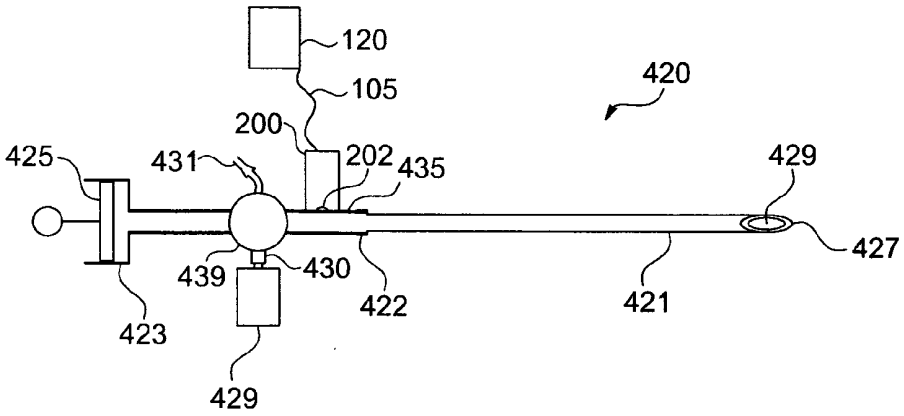
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Fig. 4b

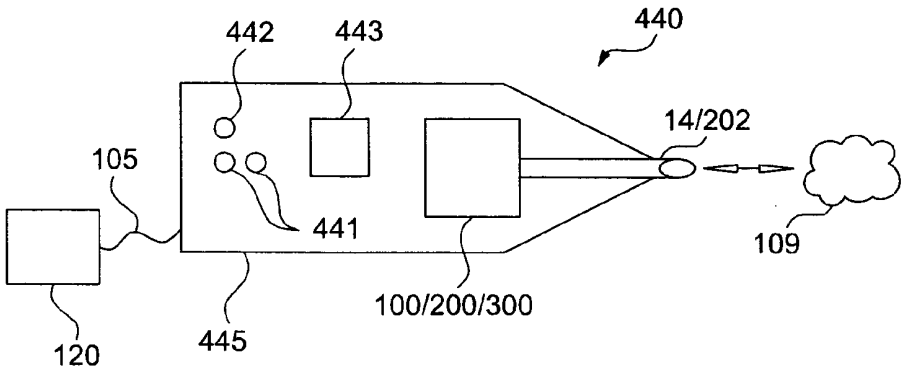
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Fig. 4c

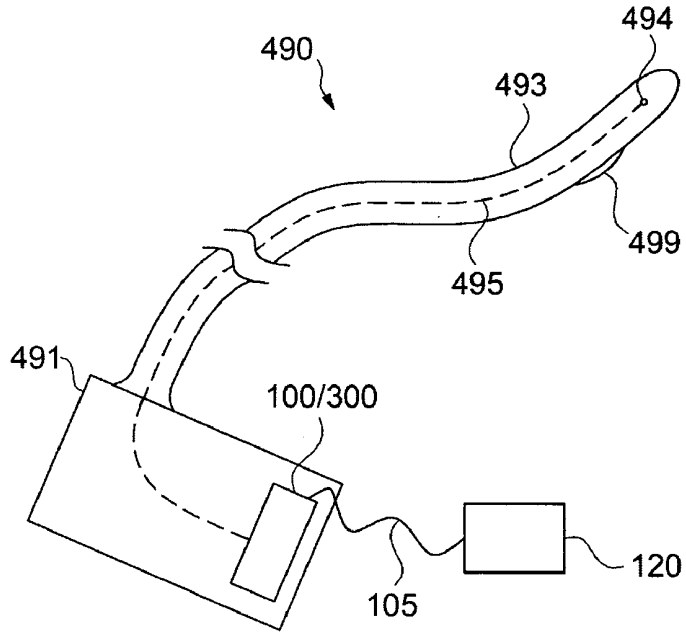
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Fig. 4f

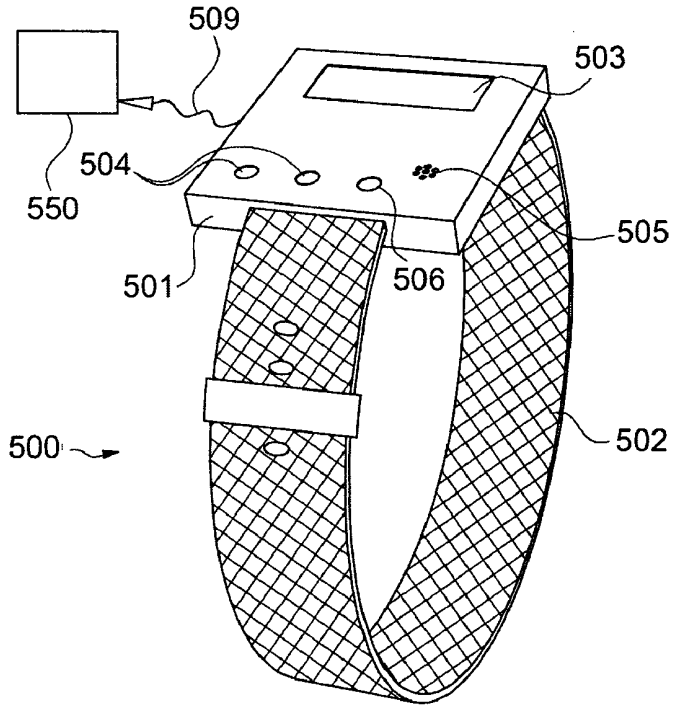
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Fig. 5a

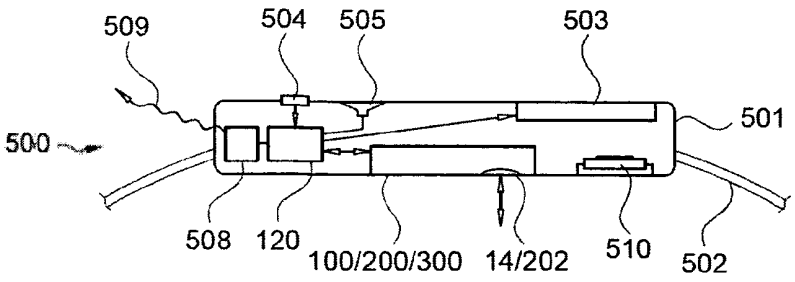
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Fig. 5b

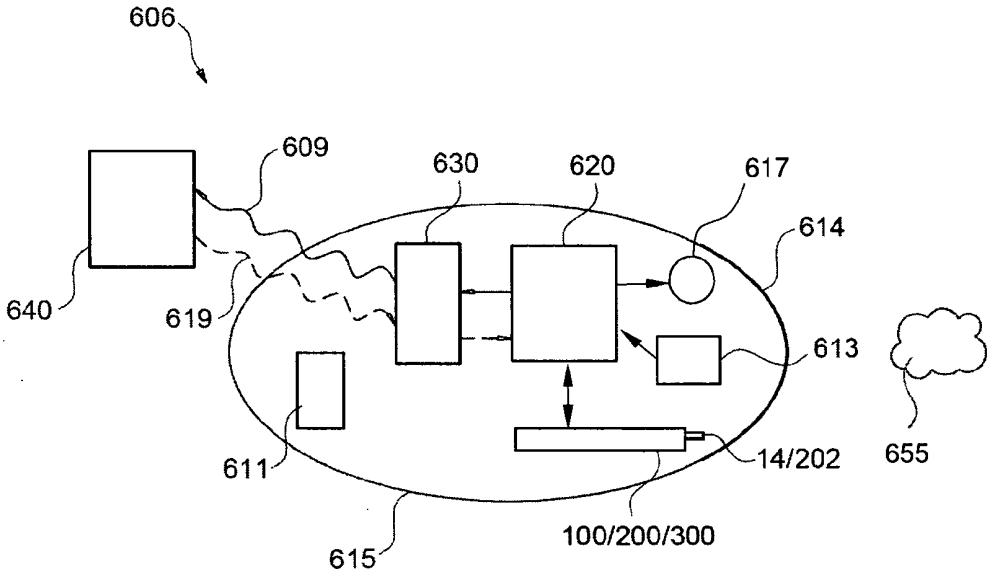
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Fig. 6

MINIATURE DISEASE OPTICAL SPECTROSCOPY DIAGNOSTIC SYSTEM

FIELD OF THE INVENTION

[0001] The present invention generally relates to disease diagnostic system. In particular, the invention relates to "optical pathology" using a miniature to semiconductor based devices for infrared spectroscopic diagnostics of cancer and other maladies.

BACKGROUND OF THE INVENTION

[0002] One of the problems that the present invention is solving is the identification of human cancer cells in real time, in-vivo or ex-vivo.

[0003] The limitations of the current practice of therapeutic excision are the inability to provide an answer, before the completion of the surgery, whether there are residual malignant cells whether the excised tumor's margins are clear or the inaccuracy of current practice (frozen section-when used) which may result in an additional surgery due to discovery of residual cancerous cells after the surgery.

[0004] In some endoscopic procedures, inability to assess-in real time, the nature of the tissue may result in missing the target tissue.

[0005] Current core needle biopsy practice is limited because the physician is not certain that the sample drawn is from the target tissue or its vicinity. Therefore multiple samples are taken.

[0006] The limitations of the current PAPS practice are: inability to have an accurate diagnostic result in real time and at point of care (gynecologist's office). In addition PAPS sensitivity and specificity, as reported in the literature, are 50% and 70-95%, respectively.

[0007] US application 20100069720A1; titled "spectroscopically enhanced imaging"; Fulghum, Stephen; et. al.; discloses systems and methods for the spectroscopic determination of the physical characteristics of the tissue under observation by an autofluorescence or other endoscope without the requirement of contacting the tissue directly. The optical probe contained in the endoscope itself is passive and may be either built into the endoscope or positioned in a biopsy channel of same. The spectroscopic information, combined with other information provided by the endoscope such as total fluorescence, improves the sensitivity and specificity of the identification of to precancerous or cancerous lesions.

[0008] US application 20090135870A1; titled "Light source based on simultaneous Two-Photon emission"; to Hayat, Alex, et. al.; discloses a semiconductor device for, e.g. target material analyzing system, produces at least 1 W/m2 two photon emission power per area, when operating at one or more temperatures greater than 20 K.

[0009] U.S. Pat. No. 5,522,870; titled "Fast changing heating-cooling device and method"; to Ben-Zion Maytal, and references therein; discloses a miniature cryogenic cooler for surgical instrument treating human skin, brain or eye—uses gas which liquefies when expanded.

[0010] The scientific literature provides a plurality of references for usefulness of optical spectroscopy for tissue diagnostics. Among these references are:

[0011] DIEM, M. X., E, S. S., & A, L. I. (1999). "Infrared Spectroscopy of Cells and Tissues: Shining Light onto a Novel Subject."; Applied Spectroscopy. Vol 3, no 4, 1999

[0012] Haka, A. S., Shafer-peltier, K. E., Fitzmaurice, M., Crowe, J., Dasari, R. R., Feld, M. S., et al. (2005). "Diagnosing breast cancer by using Raman spectroscopy", PNAS, vol. 102, no. 35, 12371-12376

[0013] Haka, A. S. (2006). "In vivo Margin Assessment during Partial Mastectomy Breast Surgery Using Raman Spectroscopy.", Cancer Research, (6), 3317-3322.

[0014] Haka, A. S., Volynskaya, Z., Gardecki, J. A., Nazemi, J., Shenk, R., Wang, N., et al. (2009). "Diagnosing breast cancer using Raman spectroscopy: prospective analysis.", Journal of Biomedical Optics, 14 (October).

[0015] Lyng, F. M., Conroy, J., Meade, A. D., Knief, P., Duffy, B., Hunter, M. B., et al. (2007). "Vibrational spectroscopy for cervical cancer pathology, from biochemical analysis to diagnostic tool." Experimental and Molecular Pathology, 82, 121-129.

SUMMARY OF THE INVENTION

[0016] A system according to the present invention is based on a semiconductor infrared emission source (e.g. based on **2**-photons as is disclosed in U.S. patent application Ser. No. 11/987,071 Hayat et al. titled "Light Source Based on Simultaneous Two-Photon Emission" filed on Nov. 27, 2007). A hand held device or an integrated device with the semiconductor emission source and detector(s) integrated inside it is placed in proximity or in contact with the tissue and illuminates the examined site (in the examples above: excised tumor margin, margins in the excised area, target tissue in endoscopy, the target tissue of the core needle biopsy, cervix, blood vessels, internal tissues such as intestines, skin etc). The device may operate at room temperature and in the environment of surgery room. The light reflected from the tissue is collected, detected and analyzed by an adjoint processing unit, using special algorithms to determine the "finger-prints" and their classification, with the potential of accurate, possibly non-invasive, in-vivo or ex-vivo and immediate diagnosis of the presence or absence of malignant tissue or of other maladies. The device is designed for easy use in the surgery room, the Ob/Gyn practitioner, dermatologist office etc.

[0017] The present invention may be used in numerous applications, including but not limited to:

[0018] Therapeutic Excisions.

[0019] Diagnosing tumor margins during surgical oncology for residual cancerous cells. The current practice is to inspect a specimen (be it part of the removed tumor or tissue from the margins) ex-vivo or post-surgery, by a pathologist, to assess whether all cancer cells have been completely removed. Currently, "frozen section" studies are occasionally used for obtaining pathology results during surgery. However, this procedure of the art, when done during surgery, is time consuming and requires a pathologist on site. In contrast, using the current invention, results may be available during the surgery or immediately post-surgery.

[0020] Micro-Surgery and Endoscopic Procedures:

[0021] During endoscopic or minimally invasive procedures, there is a need to diagnose tissue inside the body (e.g., identify cancerous cells). The current practice in oncological micro-surgery, is to inspect a specimen ex-vivo to assess whether the specimen has cancer cells or is clear of them.

[0022] Core-needle biopsy: a needle is inserted into the body to take biopsy of tissue suspected of having some malignancy. The needle is guided to the target tissue by previously taken or "on-line" images of the area (such as ultrasonic

images, X-Ray and others). On the average **6** insertions are performed in a single biopsy, as reported in the literature.

[0023] Screening and Diagnosis of Cervical Cancer.

[0024] Current practice: the gynecologist takes a sample from several locations in the cervix, called PAP smear and sends it to a lab for analysis. Results are reported after a few days.

[0025] Vulnerable Plaque.

[0026] 70% of acute coronary syndromes, amongst them heart attacks are caused by "vulnerable plaque"—a hazardous type of plaque which is characterized by its lipid-rich chemical composition. These plaques are currently undetectable by the common imaging methods.

[0027] Screening and Diagnosis of Tumors and Polyps in the Digestive Tract.

[0028] Some of the diagnostics of lesions in the digestive tract, specifically in the upper part, are done using gastroendoscope. For the large intestine, a colonoscopy is utilized. Another method is by a swallowable capsule containing a camera which travels in the digestive tract.

[0029] The system according to the present invention can be used for numerous healthcare related diagnosis applications, not limited to the applications listed below:

[0030] The system according to the present invention can be used by the surgeon during lumpectomy, nephrectomy, prostatectomy, esophagus cancer surgery, pancreatic cancer surgery, lung cancer etc. to examine the margins of the tumor and get an immediate result. This result is the indication whether all cancerous cells were removed, whether the clear margins are within the required values, or there is a need to shave additional layers in order to ensure area clear of malignant cells

[0031] The system according to the present invention can be integrated in an endoscope to be used during endoscopic and minimally invasive procedures

[0032] The system according to the present invention can be further miniaturized and integrated within the needle which is used to perform the biopsy, guiding the needle to the target tissue and possibly identify the malignant tissue

[0033] The system according to the present invention can be used by the Ob/Gyn to perform PAP smear tests in the office and obtain immediate results without the need to take a sample from the cervix and send it to the lab for analysis. (Taking a sample may be optional in case it is positive because it may be required to keep a sample when it is positive for the records and future use)

[0034] The system according to the present invention can be used by the dermatologist to assess presence or absence of suspected skin cancer.

[0035] The system according to the present invention can be integrated at the tip of an intravascular catheter; it can be used to identify vulnerable plaque.

[0036] The system according to the present invention can be embedded in a capsule, for scanning internal organs such as the esophagus, small and large intestines for suspected lesions.

[0037] The system according to the present invention can be used externally to assess glucose level in diabetic patients

[0038] Use of an infrared source which emits one or two photons, operates in room temperature, emits a wide spectrum of infrared light (e.g., near infrared, mid-infrared), can provide immediate diagnostic results. The source is made of available, inexpensive materials. Another novelty is by making the spectroscopy device small enough, enabling its insertion into the body such as in endoscopic procedures, core needle biopsy, swallow-able capsule, intravascular catheter etc.

[0039] The current invention provides a small footprint, low cost and low power consumption inspection device that allows for a variety of possible configurations, for example a hand held spectral inspection tool.

[0040] It is another aspect of the invention to provide a health monitoring device, for example glucose monitor. The monitor is preferably shaped as a wrist watch. A miniature spectrometer in the monitor directs laser light to the skin of the user and determine non-invasively the glucose level and/or level of other substances in the tissue in front of its optical window.

[0041] It is yet another aspect of the invention to provide a swallowable pill comprising a power source, a communication unit, a camera and a light source and a miniature spectrometer. In operation, the pill is swallowed and travels through the digestive track of a patient. The pill transmits to a unit outside the patient's body correlated images and at least one spectra of suspected tissue in at least one location along the digestive track.

[0042] According to one aspect of the current invention a medical spectrometer is provided, the spectrometer comprises: a solid state light source generating high intensity broad wavelength; a light projection optics, projecting said generated light on biological subject; a light collection optics, collecting reflected light from said biological subject; a wavelength selector spectrally analyzing said collected light;

[0043] a detector, detecting said analyzed light; and a housing holding said light source, said optics, said wavelength selector and said detector, wherein said housing is sized to be hand held.

[0044] In some embodiments the solid state light source is a two photon emission source.

[0045] In some embodiments the two photon emission source is a room m temperature two photon emission laser.

[0046] In some embodiments the solid state light source is capable of emitting light in the range of 2 to 5 micrometers wavelength.

[0047] In some embodiments the solid state light source is electrically excited.

[0048] In some embodiments the wavelength selector is a grating.

[0049] In some embodiments the detector is a solid state detector array.

[0050] In some embodiments the detector is a room temperature detector.

[0051] In some embodiments the spectrometer further comprises at least one waveguide for delivering light from said light source to said biological subject, wherein length of said waveguide is less than 100 cm.

[0052] In some embodiments the spectrometer further comprises at least one waveguide for delivering light from said light source to said biological subject, wherein length of said waveguide is less than 10 cm.

[0053] In some embodiments at least one of: a light projection optics; light collection optics; or wavelength selector are constructed from a sheet of IR transparent material.

[0054] In some embodiments the spectrometer is integrated into a hand held probe.

[0055] In some embodiments the spectrometer is integrated into an endoscope.

[0056] In some embodiments the spectrometer is integrated into the distal end of an endoscope.

[0057] In some embodiments the spectrometer is integrated into a vascular catheter.

[0058] In some embodiments the spectrometer is capable of determining presence of plaque on walls of blood vessels.

[0059] In some embodiments the spectrometer is integrated into a biopsy apparatus, wherein spectral data collected from said spectrometer is used for guiding the biopsy apparatus.

[0060] In some embodiments the biopsy apparatus is capable of obtaining biopsy samples, and said spectrometer is capable of real time acquisition of spectra from tissue adjacent to the biopsy-obtaining-tip of said biopsy apparatus.

[0061] In some embodiments the biopsy apparatus comprises an aspiration needle, and said spectrometer is capable of real time acquisition of spectra from aspired liquid.

[0062] In some embodiments the spectrometer is integrated into a swallowable pill.

[0063] In some embodiments the spectrometer in said pill is capable of real time acquisition of spectra from walls of the digestive track.

[0064] In some embodiments the spectrometer further comprises a controller unit, wherein said controller unit is capable of receiving data from said detector, analyzing said data and calculating result indicative of medical state of said biological subject.

[0065] In some embodiments the biological subject is human tissue, and said result is indicative of the probability of said tissue being cancerous.

[0066] In some embodiments the biological subject is human tissue and said result is indicative of the glucose level in said tissue.

[0067] In some embodiments the biological subject is human blood and said result is indicative of levels of substances such as glucose, lipids and hormones in said blood.

[0068] In some embodiments the spectral acquisition is performed in vivo.

[0069] In some embodiments the spectral acquisition is performed on extracted blood sample.

[0070] In some embodiments the spectrometer is a disposable spectrometer.

[0071] In some embodiments the light projection optics is less than 10 mm from said biological subject during acquisition of spectral data.

[0072] In some embodiments the light projection optics is in contact with said biological subject during acquisition of spectral data.

[0073] According to another aspect of the invention, a method for acquiring spectra from biological tissue is provided, the method comprises: generating high intensity, broad wavelength light in the 2 to 5 micrometer wavelength range by a room temperature, electrically excited, two photon light source; projecting said generated light onto biological subject; collecting light reflected from said biological subject; spectrally analyzing said collected light; detecting said spectrally analyzed light and generating signal indicative of optical spectrum of said detected light.

[0074] According to another aspect of the invention, a method for diagnosing tissue is provided, the method comprising: generating high intensity, broad wavelength light in the 2 to 5 micrometer wavelength range by a room temperature, electrically excited, two photon light source; projecting said generated light onto biological subject; collecting light reflected from said biological subject; spectrally analyzing said collected light; detecting said spectrally analyzed light and generating signal indicative of optical spectrum of said detected light; and calculating result indicative of medical state of said biological subject based of said signal indicative of optical spectrum of said detected light.

[0075] In some embodiments the biological subject comprises tissue cells, and calculating result indicative of medical state of said biological subject is based on differences in light reflection between cell's nucleuses and cell's cytoplasm.

[0076] In other embodiments, calculating result indicative of medical state of said biological subject is based on differences in light reflection caused by difference in fat content of said tissue.

[0077] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable methods and materials are described below. In case of conflict, the patent specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

BRIEF DESCRIPTION OF THE DRAWINGS

[0078] Some embodiments of the invention are herein described, by way of example only, with reference to the accompanying drawings. With specific reference now to the drawings in detail, it is stressed that the particulars shown are by way of example and for purposes of illustrative discussion of the preferred embodiments of the present invention only, and are presented in the cause of providing what is believed to be the most useful and readily understood description of the principles and conceptual aspects of the invention. In this regard, no attempt is made to show structural details of the invention in more detail than is necessary for a fundamental understanding of the invention, the description taken with the drawings making apparent to those skilled in the art how the several forms of the invention may be embodied in practice.

[0079] In the drawings:

[0080] FIG. **1** illustrates a miniature spectrometer-on-a-chip device in accordance with a preferred embodiment of the present invention.

[0081] FIG. **2***a* schematically depicts a miniature spectrometer device according to another exemplary embodiment of the invention.

[0082] FIG. **2***b* schematically depicts the main components of device according to an exemplary embodiment of the current invention.

[0083] FIG. **3** schematically depicts a miniature spectrometer device having its optical system primarily etched from a thin sheet of transparent material.

[0084] FIG. **4***a* schematically depicts a core biopsy device capable of removing a biopsy sample from tissue.

[0085] FIG. **4***b* schematically depicts a guided aspiration biopsy apparatus **420** according to another embodiment of the current invention.

[0086] FIG. **4***c* schematically depicts an optical spectroscopy probe according to an exemplary embodiment of the current invention.

[0087] FIG. **4***d* schematically depicts a diagnostic endoscope having a miniature spectrometer at its distal end according to an exemplary embodiment of the current invention.

[0088] FIG. **4***e* schematically a diagnostic endoscope according to an exemplary embodiment o the current invention.

[0089] FIG. **4***f* schematically depicts a vascular diagnostic catheter according to an exemplary embodiment of the current invention.

[0090] FIG. **5***a* shows an external view of glucose monitor according to an exemplary embodiment of the current invention.

[0091] FIG. **5***b* shows a cross section view of glucose monitor according to an exemplary embodiment of the current invention.

[0092] FIG. **6** schematically depicts a swallow-able spectroscopy pill according to yet another exemplary embodiment of the current invention.

DESCRIPTION OF PREFERRED EMBODIMENTS

[0093] Before explaining at least one embodiment of the invention in detail, it is to be understood that the invention is not necessarily limited in its application to the details set forth in the following description or exemplified by the

[0094] Examples. The invention is capable of other embodiments or of being practiced or carried out in various ways.

[0095] The terms "comprises", "comprising", "includes", "including", and "having" together with their conjugates mean "including but not limited to".

[0096] The term "consisting of has the same meaning as "including and limited to".

[0097] The term "consisting essentially of" means that the composition, method or structure may include additional ingredients, steps and/or parts, but only if the additional ingredients, steps and/or parts do not materially alter the basic and novel characteristics of the claimed composition, method or structure.

[0098] As used herein, the singular form "a", "an" and "the" include plural references unless the context clearly dictates otherwise. For example, the term "a compound" or "at least one compound" may include a plurality of compounds, including mixtures thereof.

[0099] Throughout this application, various embodiments of this invention may be presented in a range format. It should be understood that the description in range format is merely for convenience and brevity and should not be construed as an inflexible limitation on the scope of the invention. Accordingly, the description of a range should be considered to have specifically disclosed all the possible sub-ranges as well as individual numerical values within that range.

[0100] It is appreciated that certain features of the invention, which are, for clarity, described in the context of separate embodiments, may also be provided in combination in a single embodiment. Conversely, various features of the invention, which are, for brevity, described in the context of a single embodiment, may also be provided separately or in any suitable sub-combination or as suitable in any other described embodiment of the invention. Certain features described in the context of various embodiments are not to be considered essential features of those embodiments, unless the embodiment is inoperative without those elements.

[0101] In discussion of the various figures described herein below, like numbers refer to like parts. The drawings are generally not to scale. For clarity, non-essential elements were omitted from some of the drawing.

[0102] The system according to the claimed invention provides results in real is time easy to use, operates at point-of-care, operates at room temperature, provides full infrared spectrum, emits streams of simultaneous photon groups, provides higher signal to noise ratio, gives more accurate results, can be very small, can provide results in noisy environment, is cheap to manufacture, can be sterile and can include disposable parts, such as the emission source.

[0103] Reference is now made to FIG. **1** schematically illustrating a miniature spectrometer on a chip device **100** in accordance with a preferred embodiment of the present invention.

[0104] Miniature spectrometer device **100** comprises a carrier **101** on which electro-optical components are integrated.

[0105] Broad band light is produced by a Miniature solid-state Infrared light source **11** which emits broad spectral light. Preferably light source **11** is a two photon laser **11** capable of producing Infra Red (IR) light. Preferably, light produced by laser **11** is in the wavelength range of 2 to 5 micrometer, however different range of wavelengths may be used. For example, wavelength range of 3 to 5 micrometer may be preferred as it may probe rich spectral features of biological molecules. Optionally, wavelength range may extend to shorter wavelength such as to 1 or even 0.5 micrometer using a solid state two photon laser. In contrast to other sources of broad band light such as black body, source **11** produces high light intensity per area, and collimated light capable of being efficiently coupled into input waveguide **107**. Source **11** may emit a single stream of photons, or two streams of correlated photons. For example, two streams may be chosen for improved signal to noise ratio by correlations measurements. The source may be composed of a single or a few electrically excited solid state sources.

[0106] Input light in input waveguide **107** arrives at coupler **12** and continues towards the tissue to be examined via waveguide **13** that directs the light towards the tissue, and collect the reflected light back to coupler **12**.

[0107] Optical output probe tip **14** is a tip, delivering the light to and from the tested tissue **109**. Tip **14** may be in contact with the tested tissue or in proximity to said tissue **109**. In some applications, tip **14** is a one-use consumable element designed to provide sterility, while miniature spectrometer on a chip device **100** is capable of being reused. In other application the entire miniature spectrometer on a chip device **100** is a one-use device.

[0108] Light reflected from tested tissue **109** is collected by tip **14** and arrives at coupler **12** via waveguide **13**. Coupler **12** is designed to separate the source light from the back reflected light and directs the reflected light to its output port **110**. From output port **110** of coupler **12**, light is spread **111** on grating **15** by a dispersing optical element such as mirror **112**. Mirror **112** may be a flat or convex mirror, a lens, a lens system or combination of some of these elements. In some embodiments, spreading of light is due to the small aperture of the output port **110** of coupler **12**. In some embodiments, optical element **112** is astigmatic to provide spreading of the light on grating **15**, while preventing the spread of light in the direction normal to carrier **101**.

[0109] Grating **15** is preferably a curved grating acting to disperse the different wavelengths of light, and focusing each range of wavelength of the wavelength dispersed light **113** on a separate element **114** of detector array **16**. In some embodi-

ments, grating **15** may be replaced with other spectral dispersing of filtering elements such as prisms, filter array or tunable spectral filter.

[0110] Detector array **16** is preferably a One Dimensional (**1** D) array of detectors. Typically, each element **114** detects the reflected light in a specific range within the spectrum of interest. Detector array **16** may be composed for example of 64 elements, optionally with some separation between their detected spectrums. Alternatively, detector array **16** comprises a plurality of discrete detector elements, positioned at locations where relevant wavelengths are focused, with gaps where wavelengths irrelevant to the desired diagnosis are focused. This reduces the number of detection elements and reduces cost and power consumption. Detector array **16** preferably does not require to cryogenic temperature for its operation. Detector array may comprise indium antimonide (InSb) semiconductor detector array or a miniature bolometer array.

[0111] Preferably, integrated onto carrier **101** is electronics module **102**, coupled to detector array **16** and to electric cable **105**. Electronics module **102** is preferably an integrated circuit (IC) such as an Application Specific Integrated Circuit (ASIC) comprising amplifiers for the signals from elements **114** of detector **16**. Electronics module **102** may provide other signal conditioning and signal processing functions such as filtering, smoothing, lock-in-amplifier function, and Amplitude to Digital Conversion (ADC) function.

[0112] Optionally, electronics module **102** comprises a plurality of ICs and/or discrete electronic elements. Electronics module **102** may also be used to control the light source **11**, for example providing intensity modulation of light source **11**. Modulation of light source **11** may be achieved by modulating the current powering source **11**. Modulation of light source **11** may be in the form of pulses or sinusoidal. Modulation of light source **11**, in combination with synchronous detection improves the Signal to Noise Ration (SNR) and allows operation of the miniature spectrometer device **100** in the presence of background light. This allows operation of the device, for example, during surgery without diming or turning off the lights.

[0113] In some embodiments, integrated to carrier **101** is a heat removal unit **121**. Heat removal **121** may be a liquid or gas cooling unit, for example a miniature Joule-Thompson cooler. Preferably heat removal unit **121** comprises a Thermo Electric Cooler (TEC) **122** coupled with heat sink **103**. Optional heat removal unit **121** removes heat generated by light source **11** and optionally maintain it at proper operational temperature. Additionally or alternatively heat removal unit **121** cools detector array **16** for example to maintain it at proper operational temperature. Additionally or alternatively heat removal unit **121** removes heat generated by electrical module **102**. Same heat removal device may be used for cooling more than one unit of the miniature spectrometer such as electronics, light source and detector, or separate heat removal devices may be used, or some or all the units are not cooled.

[0114] Miniature spectrometer device **100** is connected to a controller unit **120**, preferably using cable **105**. Preferably cable **105** is connected to miniature spectrometer device **100** via connector **104**, which allows replacing miniature spectrometer device **100** and reusing controller unit **120**. Alternatively, cable **105** is connected to controller unit **120** at connector **123**. Controller unit **120** may be powered by a battery or a rechargeable battery or may be connected to main power outlet. Controller **120** may comprise input and output devices and connectors for programming, controlling and interfacing with the controller such as display, mouse, keyboard and communication devices such as wired or wireless communication such as LAN, USB, Wi-Fi, and other public or proprietary communication protocols. Controller **120** may optionally be split to several sub units. For example, controller **120** may comprise a front end unit supplying power to, receiving data from, and controlling the spectrometer; and data processing unit for analyzing the collected data and determine the type of data. Optionally, the data processing unit may be a laptop computer, a PC, a notebook computer, a PDA, a smart phone or other computing device known in the art.

[0115] In some embodiments, for example when device **100** is part of a laboratory apparatus, miniature spectrometer device **100** and controller unit **120** are integrated into one apparatus.

[0116] In some embodiments, cable **105** allows inserting miniature spectrometer device **100** into natural or made cavity in the human body, for example using a catheter or an endoscope or a probe such as vascular catheter, urological catheter, vaginal probe or a colonoscope.

[0117] Not seen in FIG. **1** is a cover, a housing or encapsulation of device **100**. For use near of within the body, said encapsulation is made of bio-compatible material and optionally can be sterilized.

[0118] FIG. **2***a* schematically depicts a miniature spectrometer device **200** according to another exemplary embodiment of the invention.

[0119] Devices **100** and **200** primarily differ by their optical system used for interfacing with tissue **109**. Similar components and structures are marked with like numbers and their function already disclosed.

[0120] Device **200** is seen enclosed in enclosure **201**, having an optical port **202**. Light exits housing **201** through optical port **202**, and interacts with tissue or sample outside the housing. Light reflected from the tissue or sample enters the housing through the optical port **202**, where it is analyzed and detected. Cable **105** provides electrical power to device **200**, transmits data indicative of the detected light, provides control signals, and optionally carry cooling fluids.

[0121] FIG. **2***b* schematically depicts the main components of device **200** according to an exemplary embodiment of the current invention.

[0122] Light from source **11** is optionally collimated by optional light collimator **222** and enters coupler **220**. Collimator **222** may be a lens or other optical element such as concave mirror, etc. Optionally, collimator **222** in integrated into source **11**, for example as convex front face.

[0123] Coupler **220** is preferably a beam splitter directing at least some of the source light to a focusing optical element such as lens **255**. In some embodiments, coupler **220** comprises a polarizer and phase retarding wave plate (not seen for drawing clarity) for efficient coupling of collimated polarized source light from source **11** to tissue **109**, and efficient coupling of reflected light to output port **251** of coupler **220**.

[0124] Output light **111** is spreads over grating **15** by defocusing optical element **205**. Defocusing element **205** may be for example a concave lens. Alternatively, a system of lenses, or mirrors or combination thereof may be used.

[0125] Optical port **202** may be a flat optical window, transparent at the relevant wavelength. Optionally, optical port **202** is integrated with other optical components such as focusing lens **255**.

[0126] In some embodiments of the invention at least some of the optical path is confined to a two dimensional (2D) waveguide in the form of thin sheet of transparent material. For example, spreading light **111**, and wavelength dispersed light **113** may travel in a 2D waveguide having grating **15** etched onto it, and detector array **16** coupled to it, preferably using index matching or antireflection coating, interface or gel. In this case, defocusing elements **205** (or **112**) may also be parts of the 2D waveguide. 1D waveguides **107** and **13** may also be etched in the transparent sheet. Other elements such as couplers may also be integrated or created as part of a waveguiding sheet.

[0127] FIG. **3** schematically depicts a miniature spectrometer device **300** having its optical system primarily etched from a thin sheet of transparent material **310**.

[0128] In the embodiment depicted in FIG. **3**, some or all of the optical components of device **300** are integrated into one or few thin sheet of optically transparent material **300**. The thickness of sheet **310** is preferably such that it confines the light in the plane of the sheet creating a 2D optical system. Confinement into 2D surface may be achieved by total internal reflection, or by reflective coating. Optionally thickness of sheet **310** is such that the confined light is limited essentially to first optical mode in the direction normal to sheet **310**. Shape of sheet **310**, and optical components shaped into it may be created by etching, for example lithography or laser etching or other etching methods known in the art. Preferably, sheet **310** is made of material transparent to the wavelength range used. For the preferred range of 2 to 5 micrometers, such material may be ZnSe or Si.

[0129] Sheet **310** is preferably carried on mechanical support **330**. Input waveguide **307** may be etched as 1D waveguide, leading to coupler **312** and splitting to sample waveguide **313** that directs the light towards the tissue, and collect the reflected light back to coupler **312**. A second port **302** of coupler **312** may be terminated by a monitoring detector **301** used for monitoring and adjusting the output power of source **11** for calibration

[0130] From output port **316** of coupler **312**, light is spread **311** on grating **315** by a dispersing optical element such as mirror **333**. Mirror **333** is preferably a convex etch in sheet **310**. Similarly, grating **315** may also be created by etching a pattern in sheet **310**.

[0131] Optionally, surface of mirror **333** and/or grating **315** are coated with highly reflecting material such as gold, Aluminum or other reflecting structure such as dielectric coating.

[0132] Sheet **310** is preferably thin enough to provide light confinement in the direction normal to its plane. For example, sheet **310** may have a thickness compatible to the light wavelength.

[0133] In some embodiments, coupler **312** is a three terminals ("Y") coupler having no port **302**. Preferably, detector array **16** is abutted to sheet **310**, optionally using some index matching means such as gel, glue or coating.

[0134] Generally, coupler **12**, **220** or **312** may be missing and replaced with an illumination optical path for illuminating the sample **109** with light from laser **11** and reflection optical path for collecting reflected light from sample **109** and directing it to the light spreading element such as **112** **205** or **333** which spreads it on the grating.

[0135] In some embodiments, the construction of spectrometers **100**, **200** or **300** is three dimensional such that optical paths may be in different layers or heights respect to carrier **101** or **330**, and grating **15** may be concave or spherical.

[0136] Alternatively, to a detector array, a single detector is used in combination with a tunable filter. The filter may be situated on the optical path between laser **11** and tissue, or on the path between the tissue and said single detector.

[0137] In some embodiments light from light source is projected onto the tissue by light projection optics, and reflected light is collected by a light collection optics that is used as an input to the spectrometer, wherein light projection optics collection optics uses separate optical paths.

[0138] In some embodiments the inventive miniature spectrometer may be to small enough to be integrated into a hand held probe or to an endoscope. For example, spectrometer **100** may be as small as 50 mm by 30 mm by 15 mm. Optionally, spectrometer **100** may be as small as 20 mm by 15 mm by 5 mm or smaller.

[0139] FIGS. **4***a* to **4***e* schematically depicts medical applications for miniature spectroscopy devices such as device **100**, **200** or **300**.

[0140] FIG. **4***a* schematically depicts a core biopsy device **400** capable of removing a biopsy sample from tissue. Core biopsy device **400** comprises a body **401** equipped with handle **405** and trigger **402** to trigger sample extraction from opening **404** by biopsy needle **403** having a sharp penetrating end **416** and connector **415** to connect to body **401**.

[0141] Guided core biopsy device **400** further comprises a miniature spectroscopy device such as device **100**, **200** or **300**. The miniature spectroscopy device is attached to or integrated within body **401** of guided core biopsy apparatus **400**. The miniature spectrometer is optically interfaced with the tissue to be sampled using a needle waveguide **410** ending with optical tip **414** for illuminating the tissue and collecting reflected light. Needle waveguide **410** interfaces with miniature spectrometer **100**, **200** or **300** using interface **418** which interfaces the spectrometer optical port **14** (or **202**) with waveguide **410**.

[0142] Optionally, needle **403** and waveguide **410** with their parts are integrated into one consumable guided biopsy needle configured as one-use device. The one-use device is preferably configured for fast connection to body **401** of guided core biopsy **400**. Waveguide **410** may be a hollow optical fiber or a waveguide made of IR transparent material. It should be noted that the short length of waveguide **410** reduces optical loss. Short waveguide is possible by placing spectrometer **100**, **200** or **300** near the proximal end of needle **403**. This is impossible to do if large size spectrometer is used, for example a Fourier Transform InfraRed spectrometer (FTIR) or large size light source such as a hot black body are used.

[0143] Spectrometer **100**, **200** or **300** interfaces with controller **120** which may be integrated into body **401** or may be remotely situated, connected by cable **105**.

[0144] In operation, user advances the needle **403** into the tissue while the miniature spectrometer analyzes in real time the light reflected from the tissue in location of or proximate to the location where biopsy sample may be taken.

[0145] Controller **120** report to the user about the probability of the tissue to be sampled being a target tissue. For example, controller **120** may emit an acoustic signal having volume or pitch indicative of the location of tip **414** in contact to target tissue such as cancerous tumor. Additionally or alternatively, controller **120** may comprise a display or other

visual indicator for informing the user of properties of tissue near opening **404** of needle **403**.

[0146] When the user discovers that opening **404** is near or at target tissue type, he may release the trigger **402** to obtain a tissue sample.

[0147] The guided biopsy apparatus according to the current invention increases the probability of obtaining the correct sample, reducing the number of needle insertions to collect specimen, reducing false negative sample, reducing cost and patient discomfort.

[0148] Needle waveguide **410** is preferably as short as needed for reducing light loss from the source to the tissue and back to the spectrometer.

[0149] Optionally, when coupler is missing from the spectrometer, needle waveguide **410** is replaced with two waveguides: one for delivering laser light, and the other for returning reflected light.

[0150] Similar configuration may apply to forceps biopsy taking apparatus where optical tip **414** is situated in proximity or within the tissue removing forceps.

[0151] FIG. **4***b* schematically depicts a guided aspiration biopsy apparatus **420** according to another embodiment of the current invention.

[0152] Guided aspiration biopsy **420** comprises a hollow aspiration needle **421** ending in a sharp penetrating tip **427** and connecting to the apparatus in connector **422**. Needle **421** has a channel opened at orifice **429** at or near sharp **427** and leading to measurement chamber **435** in the body of guided aspiration biopsy apparatus **420**.

[0153] A valve **439** connected to a suction device **423**, for example a cylinder with a piston **425** allows the user to suck a fluid sample from tissue near orifice **429** into chamber **435**. Sample in chamber **435** is optically probed by miniature spectroscope device **200** having optical port **202** in optical communication with fluid sample in chamber **435**. Alternatively, spectrometer **200** is replaced with spectrometer **100** or **300** having its tip **14** in optical communication with fluid sample in chamber **435**.

[0154] Valve **439** allows transferring the collected fluid into sample bottle **429**, preferably having fast connection **430** allowing collecting a plurality of samples from plurality of locations in the tissue. Additionally and optionally, valve **439** may be set to discard the collected sample to waste **431**.

[0155] In operation, the user advances the needle while drawing liquid at slow rate or intermittently. Spectrometer **200** analyzes the fluid in chamber **435** in real time. When the user determine that orifice **429** is near the target tissue, valve **439** is activated manually or automatically to collect a sample for further analysis, for example at a pathology lab.

[0156] FIG. **4***c* schematically depicts an optical spectroscopy probe **440** according to an exemplary embodiment of the current invention.

[0157] Probe **440** may be used for example during surgery to examine excision site after removal of a tumor for identification of cancerous tissue due to incomplete removal. Similarly, margins of removed tumor may be examined to ensure that a safety layer of healthy tissue exists around the removed tumor. Probe may be used for example for testing lymph nodes for presence of cancerous cells. The probe may also be used non-invasively for identification and classification of exposed tissue, for example testing skin lesions for cancer such as melanoma.

[0158] Probe **440** comprises a housing **445**, for housing miniature spectrometer **100**, **200** or **300**. Tip **14** extends beyond housing **445**, or window **202** on surface of housing **445** is brought to contact with or to proximity of the tissue **109** to be examined.

[0159] Control unit **120** may be integrated into housing **445** or situated remotely and connected by cable **105** to housing **445**.

[0160] In some embodiments probe **440** is a self contained probe having controller **120** integrated into its body **445**. In this embodiment, housing **445** may also comprise a power source such as a battery or a rechargeable battery, controlling buttons and other user inputs **441** for example such as on/off switch, activate measurement button and tissue type selector. Probe **440** may also comprise outputs such as a display **443**, visual and/or audio indicator **442** and the likes.

[0161] Preferably, probe **440** is sized to be hand held. Optionally, probe **440** may be sterilized or covered with a sterile cover having a light transparent window or tip such that it may be used in an operation room. However, for external use, or to be used on removed tissue, sterilization may not be needed.

[0162] It should be noted that in the probe **440**, optical path to the tissue and back is short, thus optical loss may be minimized.

[0163] Hand held probe may be made as small as few cm in size so it can be manipulated in the operation room. For example, the probe may be sized as a mobile phone.

[0164] FIG. **4***d* schematically depicts a diagnostic endoscope **460** having a miniature spectrometer **100**, **200** or **300** at its distal end.

[0165] Endoscope **460** may be shaped and function as an endoscope of the art with an addition of optical tip **14** extending from, or window **202** exposed on its surface near its distal end.

[0166] In the depicted exemplary embodiment, distal end of shaft **460** of diagnostic endoscope **460** shown with working channel **463**, illumination light source **464**, camera **462** and spectroscopy tip or window **14** or **202**.

[0167] It should be noted that endoscope **460** may further comprise other channels and means such as irrigation channel, optical surfaces cleaning jets, and tissue manipulation or treatment means.

[0168] Endoscope **460** may be flexible or rigid and may comprise means for navigation and positioning. Preferably, spectroscopic tip **14** or window **202** is so situates such that the part of tissue that is spectroscopically examined is within the field of view of camera **462**. Optionally, tip **14** or window **202** is situated on the side wall of shaft **461**. Optionally endoscope **460** comprises a plurality of tips **14** or windows **202** connected to one or to plurality of spectrometers **100**, **200** or **300**.

[0169] In some embodiments, controller **120** is integrated into endoscope **460**. In other embodiments, parts or the entire controller **120** is remotely positioned, optionally wirelessly communicating with the endoscope.

[0170] Having miniature spectrometer **100**, **200** or **300** in proximity to distal end of endoscope **460** is advantageous as it reduces loss of light in transferring light to the tissue and transferring reflected light from the tissue to the spectrometer.

[0171] FIG. **4***e* schematically depicts a diagnostic endoscope **480** according to an exemplary embodiment of the current invention.

[0172] In contrast to endoscope **460**, miniature spectrometer **100** or **200** is located in the base **481** of endoscope **480**, and connected to tip **14** with elongated waveguide **483**. This

embodiment is advantageous for endoscopes having thin shaft **484** such as endoscopes used in the uterus.

[0173] FIG. **4***f* schematically depicts a vascular diagnostic catheter **490** according to an exemplary embodiment of the current invention.

[0174] Catheter **490** comprises a flexible shaft **493** having an exposed optical port **494**, preferably located on the side of the shaft close to the distal end of shaft **493**. Flexible waveguide **495** communicates illumination light to port **494** and returns scattered light to spectrometer **100** or **300** in base **491** of catheter **490**.

[0175] Optionally, radio-opaque mark enables locating the position, and optionally the orientation of distal end of catheter **499** using standard X-Ray fluoroscopy equipment. Other localization and orientation finding methods may be used.

[0176] In operation, shaft of catheter **490** is advanced for example in an artery to a desired location where existence or type of plaque in front of optical port **494** is determined using spectrometer **100** or **300**.

[0177] FIGS. **5***a* and **5***b* schematically depict personal spectroscopic glucose monitoring device **500** according to an exemplary embodiment of the current invention.

[0178] FIG. **5***a* shows an external view of monitor **500**, and FIG. **5***b* shows a cross section of said monitor.

[0179] Monitor **500** is preferably shaped like a wrist watch having a body **501** and a wrist band **502**.

[0180] Body **501** of monitor **500** comprises an optical port (not seen in this figure) on its bottom side that faces and in contact with the skin of the monitored person.

[0181] On the upper face of body **501** is a display **503** and control switches **504** for controlling the operation of monitor **500**. Optional audible alarm **505** may provide acoustic alarm to alert the user of abnormal readings. Optionally, additionally or alternatively, vibration may be used as alarm.

[0182] Optionally, monitor **500** may act as a normal watch showing time, date, etc.

[0183] Optionally, monitor **500** is attached to the body at location other than the wrist, for example on the abdomen or the arm or leg. In some embodiments strap is missing and adhesive is used.

[0184] Preferably, monitor **500** comprises a wireless communication unit **508** for wirelessly communicating **509** with external unit **550**. In these cases monitor **500** may not comprise display or controls except for example an optional on/off switch and/or optional indicator **506** such as on/off indicator and/or low battery indicator. In some embodiments, external unit **550** may comprise an insulin pump, for example external or implanted insulin pump. Using an insulin pump with an optical glucose monitor according to the current invention enables for example a continues and optionally fully automatic control of glucose levels in diabetic patients.

[0185] External unit **550** may be an insulin pump, internally implanted or external to the user.

[0186] External unit **550** may provide some of the functions of controller **120**, for example analyzing spectra obtained by spectrometer **100**, **200** or **300** to determine and log glucose level. External unit **550** may be in constant communication with monitor **500** or communicate periodically or on demand. External unit **550** may be a smart phone, a computer or a specifically made device made for communicating with monitor **500**.

[0187] Monitor **500** is powered by a replaceable or rechargeable battery **510**.

[0188] Monitor **500** may optionally, additionally or alternatively monitor other bodily functions and levels of chemicals other than glucose, for example oxygenation level, hormonal levels.

[0189] FIG. **6** schematically depicts a swallow-able spectroscopy pill **606** according to yet another exemplary embodiment of the current invention.

[0190] Pill **606** comprises a body **615** sized to be swallowed by a human patient and pass through his digestive track.

[0191] Body **615** comprises a transparent dome **614**. Camera **613** and illumination light source **617** are positioned behind dome **614** for providing images of digestive track tissue **655** in front of said dome. Light source **617** illuminates the tissue **655** and camera **613** images the light reflected from the tissue **655**.

[0192] Controller **620** receives image data from camera **613** and transmits said image data using wireless communication unit **630** to control unit **640** over RF link **609**.

[0193] Control unit **640** preferably comprises a computer such as a PC, laptop, or a notebook computer or other computer having a display and user interface such as a keyboard or a mouse.

[0194] Once a user identifies a suspected tissue **655** from said camera's image, he uses user input on control unit **640** to communicate via optional link **619** and wireless communication unit **630** a command, commanding controller **620** to activate miniature spectrometer **100**, **200** or **300** within body **615** to acquire a spectra of said suspected tissue **655**.

[0195] Alternatively, spectroscopic data is acquired and transmitted automatically or periodically. Optical port **14** or **202** of miniature spectrometer **100**, **200** or **300** is preferably oriented such that IR source light is directed towards tissue **655** and reflected IR light is reflected at least in part to said optical port **14** or **202**.

[0196] Additionally or alternatively, acquiring spectra may be triggered automatically, for example by an image processing unit, identifying that suspected tissue is in front of the spectrometer.

[0197] Acquired spectra from tissue **655** may be analyzed by unit **640** to determine the probability of said tissue being cancerous or inflamed.

[0198] Although the invention has been described in conjunction with specific embodiments thereof, it is evident that many alternatives, modifications and variations will be apparent to those skilled in the art. Accordingly, it is intended to embrace all such alternatives, modifications and variations that fall within the spirit and broad scope of the appended claims. All publications, patents and patent applications mentioned in this specification are herein incorporated in their entirety by reference into the specification, to the same extent as if each individual publication, patent or patent application was specifically and individually indicated to be incorporated herein by reference. In addition, citation or identification of any reference in this application shall not be construed as an admission that such reference is available as prior art to the present invention.

1. A medical spectrometer comprising:

a solid state, electrically excited, two photon emission light source generating high intensity broad wavelength infrared light;

a light projection optics, projecting said generated light on biological subject;

a light collection optics, collecting reflected light from said biological subject;

a wavelength selector spectrally analyzing said collected light;

a detector, detecting said analyzed light; and

a housing holding said light source, said optics, said wavelength selector and said detector, wherein said housing is sized to be hand held.

2. (canceled)

3. The spectrometer of claim **1**, wherein said two photon emission source is a room temperature two photon emission source.

4. The spectrometer of claim **1** wherein said solid state light source is capable of emitting light in the range of 2 to 5 micrometers wavelength.

5. (canceled)

6. The spectrometer of claim **1** wherein said wavelength selector is a grating.

7. The spectrometer of claim **1** wherein said detector is a room temperature solid state detector array.

8. (canceled)

9. The spectrometer of claim **1** and further comprising at least one waveguide for delivering light from said light source to said biological subject, wherein length of said waveguide is less than 100 cm.

10. (canceled)

11. (canceled)

12. The spectrometer of claim **6**, wherein at least one of: a light projection optics; light collection optics; or wavelength selector are constructed from a sheet of IR transparent material.

13. The spectrometer of claim **1** wherein said spectrometer is integrated into a hand held probe.

14. The spectrometer of claim **1** wherein said spectrometer is integrated into an endoscope.

15. The spectrometer of claim **10**, wherein said spectrometer is integrated into the distal end of an endoscope.

16. The spectrometer of claim **1** wherein said spectrometer is integrated into a vascular catheter, and wherein said spectrometer is capable of determining presence of plaque on walls of blood vessels.

17. (canceled)

18. The spectrometer of claim **1** wherein said spectrometer is integrated into a biopsy apparatus capable of obtaining biopsy samples, wherein spectral data collected from said spectrometer is used for guiding the biopsy apparatus and said spectrometer is capable of real time acquisition of spectra from tissue adjacent to the biopsy-obtaining-tip of said biopsy apparatus.

19. (canceled)

20. The spectrometer of claim **1** wherein said spectrometer is integrated into an aspiration needle biopsy apparatus capable of obtaining liquid samples, wherein spectral data collected from said spectrometer is used for guiding the biopsy apparatus, and said spectrometer is capable of real time acquisition of spectra from aspired liquid.

21. The spectrometer of claim **1** wherein said spectrometer is integrated into a swallowable pill and wherein said spectrometer is capable of real time acquisition of spectra from walls of the digestive track.

22. (canceled)

23. The spectrometer of claim **1** and further comprising a controller unit, wherein said controller unit is capable of receiving data from said detector, analyzing said data and calculating result indicative of medical state of said biological subject.

24. The spectrometer of claim **16** wherein said biological subject is human tissue, and said result is indicative of the probability of said tissue being cancerous.

25. (canceled)

26. The spectrometer of claim **16** wherein said biological subject is human blood and said result is indicative of levels of substances such as glucose, lipids and hormones in said blood.

27. The spectrometer of claim **1** wherein said spectral acquisition is performed in vivo.

28. The spectrometer of claim **26** claim **1** wherein said spectral acquisition is performed on extracted blood sample.

29. The spectrometer of claim **1** wherein said spectrometer is a disposable spectrometer.

30. (canceled)

31. The spectrometer of claim **1** wherein said light projection optics is in contact with said biological subject during acquisition of spectral data.

32. A method for acquiring spectra from biological tissue comprising:

generating high intensity, broad wavelength light in the 2 to 5 micrometer wavelength range by a room temperature, electrically excited, two photon light source;

projecting said generated light onto biological subject;

collecting light reflected from said biological subject;

spectrally analyzing said collected light;

detecting said spectrally analyzed light and generating signal indicative of optical spectrum of said detected light.

33. A method for diagnosing tissue comprising:

generating high intensity, broad wavelength light in the 2 to 5 micrometer wavelength range by a room temperature, electrically excited, two photon light source;

projecting said generated light onto biological subject;

collecting light reflected from said biological subject;

spectrally analyzing said collected light;

detecting said spectrally analyzed light and generating signal indicative of optical spectrum of said detected light; and

calculating result indicative of medical state of said biological subject based of said signal indicative of optical spectrum of said detected light.

34. The method of claim **27** wherein said biological subject comprises tissue cells, and calculating result indicative of medical state of said biological subject is based on differences in light reflection between cell's nucleuses and cell's cytoplasm.

* * * * *

专利名称(译)	微型疾病光谱诊断系统		
公开(公告)号	US20120184827A1	公开(公告)日	2012-07-19
申请号	US13/378916	申请日	2010-06-16
[标]申请(专利权)人(译)	SHWARTZ SHOULAMIT COHEN 奥伦斯坦MEIR		
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IPC分类号	G01J3/42 A61B5/07 A61B10/02 A61B5/00 A61B1/06 A61B5/02		
CPC分类号	A61B5/0075 G01N2201/0612 A61B5/0086 A61B5/02007 A61B5/14532 A61B5/1455 A61B5/415 A61B5/418 A61B5/4331 A61B5/444 A61B5/445 A61B5/681 A61B5/6849 A61B5/6861 A61B10/0283 A61B2562/028 G01N21/35 G01N2201/0221 A61B5/0084		
优先权	61/187280 2009-06-16 US		
外部链接	Espacenet USPTO		

摘要(译)

本发明提供一种微型医用光谱仪，该光谱仪包括：室温，电激发，固态双光子激光器，产生高强度宽波长;光投射光学系统，将所产生的光投射到生物体上;光收集光学器件，收集来自所述生物体的反射光;波长选择器，对所收集的光进行光谱分析;检测器，检测所分析的光;控制器根据所述光谱分析反射光谱并计算指示生物体的医疗状态的结果。