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(54) **ARRANGEMENTS AND SYSTEMS FOR OBTAINING INFORMATION ASSOCIATED WITH AN ANATOMICAL SAMPLE USING OPTICAL MICROSCOPY**

ANORDNUNGEN UND SYSTEME ZUM ABRUFEN VON INFORMATIONEN IM ZUSAMMENHANG
MIT EINER ANATOMISCHEN PROBE MITHILFE EINES OPTISCHEN MIKROSKOPS

DISPOSITIFS ET SYSTÈMES POUR OBTENIR DES INFORMATIONS ASSOCIÉES À UN
PRÉLÈVEMENT ANATOMIQUE UTILISANT LA MICROSCOPIE OPTIQUE

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(73) Proprietor: **The General Hospital Corporation
Boston, MA 02114 (US)**

(72) Inventor: **YUN, Seok-Hyun
Cambridge, MA 02140 (US)**

(74) Representative: **Maiwald Patentanwalts GmbH
Elisenhof
Elisenstrasse 3
80335 München (DE)**

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Description**FIELD OF THE INVENTION**

[0001] The present invention relates to methods, arrangements and systems which obtain information associated with an anatomical sample using optical microscopy, and more particularly to such methods, systems and arrangements that obtain the information based on light scattering in an anatomical structure via acoustic phonons optically generated in the anatomical structure.

BACKGROUND INFORMATION

[0002] When an optical wave is propagated in a medium, a portion of its energy can be converted to the kinetic energy of the medium by exciting acoustic phonons. This process can be facilitated by various mechanisms such as thermal or electrostriction effect. The excited acoustic phonons in turn generate inelastic scattering of the optical wave, known as Brillouin scattering. The magnitude and frequency (e.g., spectrum) of the Brillouin scattered light can be determined using the acoustic phonons generated therein. Such generated photons are likely closely related to mechanical properties of the medium, such as modulus, density, and structural shape. These mechanical properties therefore can be measured by examining the Brillouin scattered light. This technique is known as Brillouin spectroscopy. Various conventional techniques to detect the Brillouin signal have been applied in physics, material science, and mechanical engineering area. In addition, the Brillouin process can be enhanced via the use of multiple optical pump waves with frequencies separated by those of the acoustic phonons in the medium.

[0003] The Brillouin microscopy generally differs from the Raman microscopy or spectroscopy in that the Brillouin microscopy involves acoustic phonons instead of vibrational phonons Raman scattering is generally based upon. Since the Brillouin shift ranges typically from 10 MHz to 10 GHz, the direct electrical detection of the acoustic wave may also be possible.

[0004] Accordingly, there is a need to overcome the deficiencies described herein above.

[0005] Document US4479449 A discloses the subject-matter of the preamble of claim 1.

OBJECTS AND SUMMARY OF THE INVENTION

[0006] To address and/or overcome the above-described problems and/or deficiencies, exemplary embodiments of microscopy systems, arrangements and processes can be provided that are capable of combining the Brillouin effects with high-resolution microscopy to probe mechanical properties of an anatomical sample, such as human tissue in vivo or artificially engineered tissue. When applied to the biological tissue, these exemplary embodiments of the microscopy systems, arrangements and processes allow the biomechanical properties to be characterized at the tissue or possibly cellular level.

[0007] In one exemplary embodiment of the present invention, a pump beam can be scanned over the biological sample through an objective lens, and the beating signal between the pump and Brillouin-shifted optical waves may be detected to characterize the Brillouin spectrum. The measured spectral features of the Brillouin signal can be converted to an image, e.g., by use of a proper lookup table or computer software which associates the spectral features to data associated with images. For example, thin cross-sectional images of a thick biological sample can be obtained by using a high numerical-aperture objective lens and confocal detection.

[0008] According to another exemplary embodiment of the present invention, a secondary pump beam with a different optical frequency can be used to facilitate a generation of acoustic phonons through stimulated or forced Brillouin scattering. In an exemplary variant of the present invention, anti-stokes Brillouin scattering technique(s) can be implemented using multiple pump beams. Various pump and probe techniques, and/or heterodyne or spectrometer-based detection techniques can be used.

[0009] Tissue biomechanical properties can be altered in a variety of disease states, and therefore may be appropriate targets for non-invasive diagnosis. A further exemplary embodiment of the systems, arrangements and processes of the present invention can make it possible to obtain the information about intrinsic tissue biomechanical properties that are not readily available by other ways, and therefore determine a wide range of applications in biology and medicine. For example, the Brillouin microscopy can become a clinical tool for the detection of early-stage cancers or intra-operative determination of tumor margins. Considering that tumors are generally stiffer than surrounding healthy tissue, the Brillouin spectrum of a tumor can possibly exhibit a stronger magnitude at high frequencies than that of normal tissues. Atherosclerosis is another medical area the Brillouin microscopy may be useful for characterizing stress and tissue compliance to identify plaques at risk for causing an acute coronary event. For example, a scanning catheter or hand-held endoscope may be used to perform the Brillouin measurement in living patients.

[0010] Thus the invention of claim 1 is provided.

[0011] According to another exemplary embodiment of the present invention, the information based on data associated with the second electro-magnetic radiation can be analyzed. The first electro-magnetic radiation may include at least one first magnitude and at least one first frequency. The second electro-magnetic radiation can include at least one second magnitude and at least one second frequency. The data may relate to a first difference between the first and second magnitudes and/or a second difference between the first and second frequencies. The second difference may be approximately between -100 GHz and 100 GHz, excluding zero.

[0012] In another example of the present disclosure, at least one fourth arrangement configured to image the portion of the anatomical sample based on data associated with the second electro-magnetic radiation can be provided. Further, at least one fifth arrangement is provided to translate the at least one electro-magnetic radiation across the anatomical sample. The fifth arrangement may include at least one lens, and the lens can focus the first electro-magnetic radiation and can collect the second electro-magnetic radiation. The second arrangement can include a spectral filter which may facilitate a determination of a spectrum of the second electro-magnetic radiation. The information can be associated with a biomechanical property of the anatomical sample. The anatomical sample may be a living subject.

[0013] According to still another exemplary embodiment of the present invention, the first electromagnetic radiation may have a center wavelength which is approximately between 0.5 - 1.8 μm . The first electromagnetic radiation can have a line width which is smaller than approximately 100 MHz. The first electromagnetic radiation can have a form of a plurality of pulses, and the duration of each of the pulses may be longer than approximately 10 ns. The first electro-magnetic radiation can also include at least two first electro-magnetic radiations, a first one of the first electro-magnetic radiations possibly having a first frequency, and a second one of the first electro-magnetic radiations possibly having a second frequency. A difference between the first and second frequencies may be between approximately zero and 100 GHz. It is possible to receive at least one third electro-magnetic radiation which has at least one third magnitude and at least one third frequency. The second frequency may be determined as a function of the first and third frequencies. The third electro-magnetic radiation can be forwarded from an electromagnetic radiation source.

[0014] These and other objects, features and advantages of the present invention will become apparent upon reading the following detailed description of embodiments of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

[0015] Further objects, features and advantages of the present invention will become apparent from the following detailed description taken in conjunction with the accompanying figures showing illustrative embodiments of the present invention, in which:

Fig. 1A is a first illustration of an exemplary embodiment of an application and a Brillouin effect of a method according to the present invention;

Fig. 1B is a second illustration of an exemplary embodiment of the application and a Brillouin effect of the method according to the present invention;

Fig. 2 is an illustration of a Brillouin scattering procedure in tissue using the exemplary embodiment of the method according to the present invention;

Fig. 3A is a first illustration of a further application of the exemplary embodiment of the method according to the present invention which produces a beam scanning Brillouin imaging;

Fig. 3B is a second enlarged illustration of the application of the exemplary embodiment of the method shown in Fig. 3A;

Fig. 4A is a first illustration of a beam focusing procedure implemented by the exemplary embodiment of the method according to the present invention in an exemplary embodiment of an arrangement according to the present invention;

Fig. 4B is a second illustration of a beam focusing procedure implemented by the exemplary embodiment of the method as shown in Fig. 4A

Fig. 4C is a third illustration of a beam focusing procedure implemented by the exemplary embodiment of the method as shown in Figs. 4A and 4B;

Fig. 5 is a block diagram of an exemplary embodiment of a scanning-beam Brillouin spectroscopy arrangement in accordance with the present invention;

Fig. 6A is a block diagram of a first exemplary embodiment of a Brillouin microscopy arrangement that can use interferometry in accordance with the present invention;

Fig. 6B is a block diagram of a second exemplary embodiment of the Brillouin microscopy arrangement that can use interferometry in accordance with the present invention;

Fig. 6C is a block diagram of a third exemplary embodiment of the Brillouin microscopy arrangement that can use interferometry in accordance with the present invention;

Fig. 7A is an illustration of a first stage in generating an exemplary two-frequency pump wave using an exemplary embodiment of a method and arrangement in accordance with the present invention;

Fig. 7B is an illustration of a second stage in generating the exemplary two-frequency pump wave in conjunction with the generation shown in Fig. 7A;

Fig. 7C is an illustration of a third stage in generating the exemplary two-frequency pump wave in conjunction with the generation shown in Figs. 7A and 7B;

Fig. 7D an illustration of is a fourth stage in generating the exemplary two-frequency pump wave in conjunction with the generation shown in Figs. 7A-7C;

Fig. 8A is a first exemplary illustration of a Brillouin signal generation using the exemplary embodiment of the method and arrangement in accordance with the present invention;

Fig. 8B is a second exemplary illustration of the Brillouin signal generation using the exemplary embodiment of the method and arrangement in accordance with the present invention;

Fig. 8C is a illustration of an image produced by the signals shown in Figs. 8A and 8B using the exemplary embodiment of the method and arrangement in accordance with the present invention;

Fig. 9A is an illustration of a medical application using an exemplary embodiment of a catheter in accordance with the present invention; and

Fig. 9B is an illustration of a medical application using an exemplary embodiment of an endoscope in accordance with the present invention.

[0016] Throughout the figures, the same reference numerals and characters, unless otherwise stated, are used to denote like features, elements, components or portions of the illustrated embodiments. Moreover, while the subject invention will now be described in detail with reference to the figures, it is done so in connection with the illustrative embodiments. It is intended that changes and modifications can be made to the described embodiments; whereas the invention is defined by the appended claims.

DETAILED DESCRIPTION OF EXEMPLARY EMBODIMENTS

[0017] Figs. 1A and 1B illustrate exemplary application of an exemplary embodiment of a method which implement a principle of Brillouin scattering according to the present invention. For example, a monochromatic pump light with a frequency $\nu = \omega/2\pi$ can be provided incident on a medium under test. An exemplary generation of an acoustic wave can be initiated by seed photons which may quantum-mechanically originate from a vacuum fluctuation. There may be one seed photon per unit frequency bandwidth.

[0018] The pump and seed photons may interfere with one another, and generate a mechanical stress modulation in the medium via thermal or electrostriction effects. When the stress modulation is phase-matched to one of the characteristic acoustic phonon modes in the medium, the corresponding acoustic phonons can develop efficiently through a coherent process. The excited acoustic phonons in turn may create a refractive-index modulation in the medium, and generate inelastic scattering of photons. The energy and momentum of the photons can be modified by an inelastic scattering procedure. The magnitude of a frequency shift in the scattered photons can be substantially or approximately equal to that of the acoustic phonons. This exemplary procedure is called "Brillouin phenomenon" or "Brillouin scattering." Although both Stokes and anti-Stokes components can be generated, typically Stokes Brillouin component (e.g., frequency down shifted) would likely be predominantly generated.

[0019] Exemplary phase matching conditions between the pump scattering light and the acoustic wave can be expressed as:

$$\omega_A = \omega_p - \omega_s \quad (1)$$

$$\vec{k}_A = \vec{k}_p - \vec{k}_s \quad (2)$$

where ω and k are angular frequency and wave number, respectively, and the subscript A, p, and s represent acoustic phonons, pump and scattering (or signal) photons, respectively. The frequency of the phase matched phonons, e.g., the difference between the pump and scattering photons, can be given by

$$\omega_A = |\vec{k}_A| V_A = 2V_A |\vec{k}_p| \sin(\theta/2) \quad (3)$$

[0020] Where V_A denotes the speed of the acoustic phonon mode (e.g., an acoustic wave) in the medium and θ is an angle between the pump and scattering photons (e.g., optical waves). The Brillouin shift, as expressed in Eq. (3), can increase with the acoustic speed. In a solid state medium, the acoustic speed is proportional to the square root of the modulus. When the two waves propagate at the opposite direction, $\theta = 180^\circ$, the magnitude of Brillouin shift can become maximum.

[0021] For example, Fig. 1A illustrates a backward Brillouin scattering effect in an exemplary implementation of an exemplary embodiment of the present invention. The pump wave 12 with frequency ν is incident on a medium 10, and generates an acoustic wave represented by the wave fronts 13 and its wave vector 14 corresponding to an acoustic frequency ν_B . The Brillouin scattered light 16 satisfying the phase matching condition may have a frequency $\nu - \nu_B$. For example, if there are a large number of acoustic modes present in a sample; then the spectrum of the Brillouin scattered light may consist of multiple lines characterized by their frequencies, magnitudes, and spectral widths, all of which may be related to the mechanical properties of the sample. If the medium 10 is optically transparent, no Anti-stokes Brillouin light 18 with a frequency higher than that of the pump wave would likely be produced. In a turbid medium such as biological tissue, and the light can experience a strong elastic Mie or Rayleigh scattering, in addition to much weaker inelastic Brillouin or Raman scattering. The elastically scattered light, diffused in random directions, may interfere with each other, and can result in a detectable Anti-stokes Brillouin light.

[0022] When the acoustic wave is initially provided, the Brillouin phenomenon can be accelerated because of the presence of the scattered light. The scattered light, coherent with the pump light, may amplify the resonant acoustic wave, which in turn may enhance the Brillouin scattering. This positive feedback can result in a strong Brillouin shifted scattered light, e.g., a procedure called "stimulated Brillouin scattering." In a long optical fiber, this exemplary procedure can arise at a very low pump power of several tens of mW, and may be characterized by the Brillouin gain provided by

$$g_B(\nu_B) = \frac{2\pi n^7 p_{12}^2}{c \lambda_p^2 \rho_0 V_A \Delta \nu_B} \omega_p - \omega_s \quad (4)$$

where n is the refractive index, p_{12} is the elasto-optic coefficient, and ρ is the density.

[0023] Fig. 1B shows another application of a Brillouin interaction according to the exemplary embodiment of the present invention in a turbid medium 22 initiated by two pump waves 20, 21 with a frequency difference of $\Delta\nu$. The exemplary elastic scattering of the pump waves can stimulate the excitation of acoustic waves (phonons) propagating multiple directions. In the exemplary illustration of Fig. 1B, only two waves propagating along the forward and backward directions 23, 24. The resulting Brillouin scattered light has multiple spectral lines including the Stokes 26 and anti-Stokes 28 components. This exemplary application according to the present invention may be used to enhance the generation of the anti-Stokes line. For example, the maximum Brillouin efficiency can be achieved when the frequency difference substantially matches the frequency of at least one of the acoustic waves (phonons) generated in this manner.

[0024] Because the efficiency of Brillouin scattering is likely proportional to an optical intensity, a higher efficiency can be obtained by focusing the pump light to the sample. By focusing, higher spatial discrimination or resolution can be

obtained. Figure 2 illustrates an exemplary use of objective lens 30 in accordance with an exemplary embodiment of the present invention for both focusing a pump beam 32 to a sample 34, and collecting a backward propagating Brillouin scattered light 36. Such exemplary detection scheme can be called the "epi configuration." For example, Fig. 2 shows an associated acoustic wave 38 propagating forward, as well as elastically scattered, diffused waves 40. A portion of the elastically scattered light within the numerical aperture of the lens may be also collected. Because the Brillouin process can produce a phase conjugation, the backward Brillouin scattering may be efficiently collected, even with a low numerical-aperture objective lens.

[0025] Brillouin spectroscopy is a technique that can measure the spectrum of the Brillouin scattered light, thereby allowing the properties of inherent acoustic phonons of a medium. The Brillouin spectrum may be closely related to the mechanical properties of the medium through the phase matching conditions represented in Equations (1) and (2) (e.g., in their simplest forms).

[0026] One of the important features of the present invention is an image generation feature. Using a predetermined or calculated conversion table, the spatial variation of the Brillouin spectra may be presented as an image. To generate images, the pump or probe beam can be scanned laterally across the sample, and/or the sample can itself be translated. Figs 3A and 3B illustrate two respective beam scanning applications in accordance with an exemplary embodiment of the present invention which can use a galvanometer and rotational catheter. As shown in Fig. 3A, the pump wave 60 may be reflected by a galvanometer-mounted mirror 62, and focused by an objective lens 64 to a medium 68. Light collected by the objective lens 64 in the epi mode can consist of a backscattered component 70 and a Brillouin shifted component 72. Other conventional scanners can be used, including but not limited to polygonal mirror scanners and MEMS mirrors. Fig. 3B depicts an exemplary beam-scanning application that uses an exemplary embodiment of an arrangement according to the present invention based on a fiber-optic catheter or endoscope for an application to, for example, luminal organ imaging. For example, a catheter can include a single mode fiber 80, a focusing lens 82, a prism 84, a drive shaft 86, and a protective sheath 88. A catheter core, rotated inside the stationary sheath 88, can scan across the tissue 92 using an optical beam 90 in a helical manner.

[0027] The beam size of the pump beam at the sample can determine the spatial resolution. When a coarse spatial resolution is sufficient, it is possible to use a collimated beam. As shown in Fig. 4A, an exemplary implementation of an objective lens 100 with a low numerical aperture ("NA") can result in a low transverse resolution. With the longitudinal interaction length likely being long and well defined (Fig. 4A); an objective lens 102 with a high NA may provide better transverse and axial resolution, as shown in Fig. 4B. With the high NA, the Brillouin interaction length is likely to be short, and the phase matching can be met over a large solid angle. In both cases, the backward-propagating Brillouin light may be detected in the epi configuration. Fig. 4C depicts another exemplary implementation an use of the exemplary embodiments of the method and arrangement according to the present invention using at least two objective lenses 104, 106. This scheme, however, may not be appropriate for thick tissue or *in vivo* applications.

[0028] Fig. 5 depicts a block diagram of an exemplary embodiment of an arrangement according to the present invention. For example, the arrangement of Fig. 5 includes a light source 110, preferably a monochromatic laser emitting visible or infrared light source, and a pump beam/wave 111 that can be illuminated to a sample 112 through a beam splitter 114, a beam scanner 116, and an objective lens 118. The light source 110 can be, but not limited to, a cw single frequency laser with a center wavelength between 0.5 and 1.8 microns and a narrow line width, typically less than 100 MHz, providing temporal coherence longer than the lifetime of phonons. Another preferred type of light source is a Q-switched single frequency laser. The pulse repetition rate may range from 1 to 100 kHz, and the pulse duration from 10 ns to 1 μ s. The Q-switched pump light can result in higher Brillouin generation efficiency because the intensity is higher than that of cw light at the same average power level. The light source 110 may utilize or include an optical arrangement to deliver more than one frequency components (illustrated in Figs. 8A and 8B). The lateral step size of the beam scan can be approximately equal to the focal spot size of the pump beam/wave 111 in the sample 112.

[0029] The scattered light 120 provided from the sample 112 and collected by the objective lens 118 may originate from both elastic and inelastic scattering. The spectrum of the scattered light may be measured using a spectrally-selective arrangement 120, such as scanning filters, etalons, virtual interferometer phase arrays, or spectrometers. Various scanning filters are known in the art, including but not limited to a Fabry-Perot interferometer. For example, the Brillouin shift can be as high as several tens of GHz. The exemplary Fabry-Perot scanning interferometer may have a free spectral range of 50 GHz, and finesse of 1000. The spectrally selected optical photons may then be converted to electrical signals at a detector 122 (e.g., a photo-multiplier tube, avalanche photodiode, or charge-coupled-device array).

[0030] Other exemplary embodiments of the present invention that use fiber-optic heterodyne interferometers are shown in the block diagrams of Figs. 6A and 6B. In Fig. 6A, a single-frequency laser 150 is shown to be coupled to a fiber-optic beam splitter 152 with an exemplary splitting ratio of approximately 90:10. One optical path, termed a sample arm 154, can be connected to a beam scanner 156 via a circulator 158, and the other path, termed a reference arm 170, may contain a frequency shifter 172 such as an acousto-optic or electro-optic modulator. Both the sample and reference arms 154, 170 may be combined at another fiber-optic beam splitter 180, with, e.g., equal splitting ratios. The interference signal between the backscattered light in the sample arm 154 and the frequency-shifted reference light in

the reference arm 170 can be measured by a dual balanced receiver 182, and processed using a computer 184. The frequency shifter 172 can be used to decrease the beat frequency between scattered and reference light, and a polarization controller 174 may also be utilized, as shown in Fig. 6A. According to another exemplary embodiment of the present invention, an electrical spectrum analyzer may replace or complement the computer 184. Alternatively, the Brillouin spectra may be determined by tuning the magnitude of frequency shift by the shifter 172 and measuring the beat signal with a low-bandwidth detector 182.

[0031] Fig. 6B depicts a block diagram of another exemplary configuration according to a further exemplary embodiment of the present invention that uses two monochromatic lasers 200, 202, with a tunable frequency difference. One laser 200 is coupled to a sample arm 210 for delivering the pump wave. The second laser 202 can serve as a local oscillator to provide the reference light with a frequency detuned from that of the pump source by a predetermined amount. The frequency of the local oscillator can be close to that of one of Brillouin signal light, and the beat frequency may be measured by a detector 220. For example, the line widths of the pump source 200 and the local oscillator 202 should be significantly narrow, and typically less than 100 kHz, to effect a temporal coherency between the scattered and reference light.

[0032] Fig. 6C illustrates a block diagram of yet another exemplary embodiment of the arrangement according to the present invention based on a frequency-swept laser 230 that can be preferably either one of a mode-hop-free extended-cavity semiconductor laser, temperature-tuned distributed feedback laser, and cavity-modulated solid-state laser. The reference arm 232 may contain a delay line 234 providing an optical delay by a fixed amount and/or a variable amount controlled by the length difference between the reference and sample arms 232, 240. The length mismatch between the two arms can be selected as follows:

$$\Delta L \approx \frac{c}{n \alpha} v_B, \quad (5)$$

where c is the speed of light, n is the refractive index of medium, α is the tuning speed, and v_B is the frequency of acoustic phonons of interest. Pursuant to such selection, the electrical beat frequency measured by a detector 244 can be significantly smaller than the acoustic frequency. On the other hand, when the path lengths of the two arms 232, 240 are substantially matched, such exemplary measurement technique may be similar to the optical frequency domain reflectometry. The interference signal measured as a function of wavelength can be processed via a Fourier transform to produce an axial profile of elastic backscattering coefficients. Similarly, with appropriate length mismatch, similar signal processing may yield an axial profile of Brillouin scattering coefficients.

[0033] Figs. 7A-7D depict various stages of two different exemplary source arrangements according to an exemplary embodiment of the present invention which are capable of producing the pump wave consisting of two different frequency components. The Brillouin spectroscopy based on such two-frequency pump wave is illustrated in Fig. 1B and described herein above. For example, in Fig. 7A, an electro-optic modulator with a proper DC bias can produce two sidebands from a monochromatic laser input. In Fig. 7B, two low-drift monochromatic lasers may be combined with a beam combiner 270. In the epi configuration, the combined pump waves may be delivered to a sample 280 through an objective lens 282, as shown in Fig. 7C. In a transmission configuration, a secondary objective lens 284 may be used to launch one of the two frequency components in the opposite direction, as shown in Fig. 7D.

[0034] Figs. 8A and 8B illustrate exemplary Brillouin spectra obtained from two different locations in a sample according to the exemplary embodiment of the present invention. For example, the difference between the two spectra, represented in these figures by the magnitude of v_B , may indicate a difference in stiffness between the two locations. An image 300 (shown in Fig. 8C) can be formed based on the measured Brillouin signal and by using a grayscale look up table 310 and/or a false color lookup table 320. The lookup table(s) 310, 320 may be based on the magnitude and/or the frequency of one or more specific Brillouin peaks.

[0035] Figs. 9A and 9B illustrates possible exemplary clinical applications of Brillouin microscopy 400 in human 410 by use of a fiber-optic catheter 420 or endoscope 430 in accordance with an exemplary embodiment of the present invention. The catheter 420 may have a similar configuration as shown in Fig. 3B. and described above. The endoscope 430 may employ a two-axis XY beam scanning actuator, such as MEMS scanners. Potential applications of Brillouin microscopy can include tissue characterization based on biomechanical properties, cancer diagnosis, tumor margin determination, wound healing monitoring, tissue ablation monitoring, and tissue engineering among many.

[0036] The foregoing merely illustrates the principles of the invention. The arrangements, systems and methods according to the exemplary embodiments of the present invention can be used with any OCT system, OFDI system, spectral domain OCT (SD-OCT) system or other imaging systems, and for example with those described in International Patent Application PCT/US2004/029148, (WO2005/047813), filed September 8, 2004, U.S. Patent Application No. 11/266,779, (US2006-0093276 A1), filed November 2, 2005, and U.S. Patent Application No. 10/501,276, filed (US2005-0018201 A1), July 9, 2004.

Claims

1. An apparatus, comprising:

at least one first arrangement which is adapted to provide at least one first electro-magnetic radiation (12) to an anatomical sample which is a living subject so as to be able to generate at least one acoustic wave in the anatomical sample, wherein at least one second electro-magnetic radiation is producible in the living subject based on the at least one acoustic wave;

at least one second arrangement which is adapted to receive at least one portion of the at least one second electro-magnetic radiation (16) which is used so as to determine information associated with at least one portion of the anatomical sample wherein the second arrangement is adapted to be able to measure a Brillouin-shifted component of the second electro-magnetic radiation (72, 26, 28);

characterised by further comprising at least one third arrangement configured to generate an image (300) of the at least one portion of the anatomical sample based on data associated with the at least one second electro-magnetic radiation, and

at least one fourth arrangement which is at least one of a catheter (420), an endoscope (430), a laparoscope, or an ophthalmic visualization device, which is configured to translate the at least one first radiation across said anatomical sample.

2. The apparatus according to claim 1, wherein the live biological sample is at least one of an organ, a tissue or cell. AO:

3. The apparatus according to claim 1, wherein the at least one fourth arrangement includes at least one lens (118), and wherein the at least one lens focuses the at least one first electro-magnetic radiation and collects the at least one second electro-magnetic radiation.

4. The apparatus according to claim 2, wherein the at least one first electro-magnetic radiation includes at least one first magnitude and at least one first frequency, wherein the at least one second electro-magnetic radiation includes at least one second magnitude and at least one second frequency, and wherein the data relates to at least one of a first difference between the first and second magnitudes or a second difference between the first and second frequencies.

5. The apparatus according to claim 4, wherein the second difference is approximately between -100 GHz and 100 GHz, excluding zero.

6. The apparatus according to claim 1, wherein the at least one second arrangement includes a spectral filter which facilitates a determination of a spectrum of the at least one second electro-magnetic radiation.

7. The apparatus according to claim 1, wherein the information is associated with a biomechanical property of the anatomical sample.

8. The apparatus according to claim 1, wherein the at least one first electromagnetic radiation has a center wavelength which is approximately between 0.5 - 1.8 μm .

9. The apparatus according to claim 8, wherein the at least one first electromagnetic radiation has a line width which is smaller than approximately 100 MHz.

10. The apparatus according to claim 8, wherein the at least one first electromagnetic radiation has a form of a plurality of pulses, and wherein the duration of each of the pulses is longer than approximately 10 ns.

11. The apparatus according to claim 1, wherein the at least one first electro-magnetic radiation includes at least two first electro-magnetic radiations, wherein a first one of the at least two first electro-magnetic radiations has a first frequency, and a second one of the at least two first electro-magnetic radiations has a second frequency, and wherein a difference between the first and second frequencies is between approximately zero and 100 GHz.

12. The apparatus according to claim 1, wherein the at least one first electro-magnetic radiation includes at least one first magnitude and at least one first frequency, wherein the at least one second electro-magnetic radiation includes at least one second magnitude and at least one second frequency, wherein at least one third electro-magnetic radiation which has at least one third magnitude and at least one third frequency is further provided to the sample,

and wherein the second frequency is determined as a function of the first and third frequencies.

13. The apparatus according to claim 12, wherein the at least one third electro-magnetic radiation is forwarded from an electromagnetic radiation source.

14. The apparatus according to claim 1, comprising:

at least one arrangement which analyzes the information based on data associated with the at least one second electro-magnetic radiation; and

wherein the at least one first electro-magnetic radiation includes at least one first magnitude and at least one first frequency, wherein the at least one second electro-magnetic radiation includes at least one second magnitude and at least one second frequency which is different from the at least one first frequency, and wherein the data relates to second magnitudes or a difference between the first and second frequencies, and wherein the difference between the first and second frequencies is approximately between -100 GHz and 100 GHz.

15. The apparatus according to claim 14, further comprising at least one arrangement which is adapted to image the at least one portion of the anatomical sample based on data associated with the at least one second electro-magnetic radiation.

16. The apparatus according to claim 14, wherein the at least one fifth arrangement includes at least one lens (118), and wherein the at least one lens focuses the at least one first electro-magnetic radiation and collects the at least one second electro-magnetic radiation.

17. The apparatus according to claim 14, wherein the at least one second arrangement includes a spectral filter which facilitates a determination of a spectrum of the at least one second electro-magnetic radiation.

18. The apparatus according to claim 14, wherein the information is associated with a biomechanical property of the anatomical sample.

19. The apparatus according to claim 14, wherein the at least one first electromagnetic radiation has a center wavelength which is approximately between 0.5 and 1.8 μm .

20. The apparatus according to claim 19, wherein the at least one first electromagnetic radiation has a line width which is smaller than approximately 100 MHz.

21. The apparatus according to claim 19, wherein the at least one first electromagnetic radiation has a form of a plurality of pulses, and wherein the duration of each of the pulses is longer than approximately 10 ns.

22. The apparatus according to claim 14, wherein the at least one first electro-magnetic radiation includes at least two first electro-magnetic radiations, wherein a first one of the at least two first electro-magnetic radiations has a first frequency, and a second one of the at least two first electro-magnetic radiations has a second frequency, and wherein a difference between the first and second frequencies is between approximately zero and 100 GHz.

23. The apparatus according to claim 14, wherein at least one third electro-magnetic radiation which has at least one third magnitude and at least one third frequency is provided to the sample, and wherein the second frequency is determined as a function of the first and third frequencies.

24. The apparatus according to claim 23, wherein the at least one third electro-magnetic radiation is forwarded from an electromagnetic radiation source.

Patentansprüche

1. Eine Vorrichtung, umfassend:

wenigstens eine erste Anordnung, welche dazu ausgebildet ist, wenigstens eine erste elektromagnetische Strahlung (12) zu einer anatomischen Probe, welche ein lebendes Subjekt ist, bereitzustellen, um es zu ermöglichen,

wenigstens eine akustische Welle in der anatomischen Probe zu erzeugen,
wobei wenigstens eine zweite elektromagnetische Strahlung in dem lebenden Subjekt basierend auf der wenigstens einen akustischen Welle erzeugbar ist;

wenigstens eine zweite Anordnung welche dazu ausgebildet ist, wenigstens einen Teil der wenigstens einen zweiten elektromagnetischen Strahlung (16) zu empfangen, welche verwendet wird um Informationen, welche wenigstens einem Teil der anatomischen Probe zugeordnet sind, zu bestimmen, wobei die zweite Anordnung dazu eingerichtet ist, um eine Brillouin-versetzte Komponente der zweiten elektromagnetischen Strahlung (72, 26, 28) zu messen;

gekennzeichnet durch

wenigstens eine dritte Anordnung welche konfiguriert ist, ein Bild (300) des wenigstens einen Teils der anatomischen Probe basierend auf Daten, welche der wenigstens einen zweiten elektromagnetischen Strahlung zugeordnet sind,

zu generieren, und

wenigstens eine vierte Anordnung welche wenigstens eines ist von einem Katheter (420), einem Endoskop (430), einem Laparoskop, oder einem ophthalmischen Visualisierungsgerät, welches konfiguriert ist um die wenigstens eine erste Strahlung über besagte anatomische Probe zu verschieben.

2. Die Vorrichtung nach Anspruch 1, wobei die lebende biologische Probe wenigstens eines ist von einem Organ, Gewebe oder Zelle.

3. Die Vorrichtung nach Anspruch 1, wobei die wenigstens eine vierte Anordnung wenigstens eine Linse (118) enthält und wobei die wenigstens eine Linse die wenigstens eine erste elektromagnetische Strahlung fokussiert und die wenigstens eine zweite elektromagnetische Strahlung sammelt.

4. Die Vorrichtung nach Anspruch 2, wobei die wenigstens eine elektromagnetische Strahlung wenigstens eine erste Stärke und wenigstens eine erste Frequenz beinhaltet, wobei die wenigstens eine zweite elektromagnetische Strahlung wenigstens eine zweite Stärke und wenigstens eine zweite Frequenz beinhaltet, und wobei die Daten sich auf wenigstens eins von einer ersten Differenz zwischen den ersten und zweiten Stärken oder einer zweiten Differenz zwischen den ersten und zweiten Frequenzen beziehen.

5. Die Vorrichtung nach Anspruch 4, wobei die zweite Differenz ungefähr zwischen -100GHz und 100 GHz ist, ausschließlich Null.

6. Die Vorrichtung nach Anspruch 1, wobei die wenigstens eine zweite Anordnung einen spektralen Filter beinhaltet, welcher eine Bestimmung eines Spektrums der wenigstens einen zweiten elektromagnetischen Strahlung ermöglicht.

7. Die Vorrichtung nach Anspruch 1, wobei die Information einer biomechanischen Eigenschaft der anatomischen Probe zugeordnet ist.

8. Die Vorrichtung nach Anspruch 1, wobei die wenigstens eine erste elektromagnetische Strahlung eine zentrale Wellenlänge hat, welche ungefähr zwischen 0.5 - 1.8 μm ist.

9. Die Vorrichtung nach Anspruch 8, wobei die wenigstens eine erste elektromagnetische Strahlung eine Linienbreite hat, welche kleiner ist als ungefähr 100 MHz.

10. Die Vorrichtung nach Anspruch 8, wobei die wenigstens eine erste elektromagnetische Strahlung eine Form einer Vielzahl vom Pulsen hat, und wobei die Dauer von jedem der Pulse länger ist als ungefähr 10 ns.

11. Die Vorrichtung nach Anspruch 1, wobei die wenigstens eine erste elektromagnetische Strahlung wenigstens zwei erste elektromagnetische Strahlungen aufweist, wobei einer erste von den wenigstens zwei elektromagnetischen Strahlungen einer ersten Frequenz hat, und eine zweite der wenigstens zwei elektromagnetischen Strahlungen eine zweite Frequenz hat, und wobei eine Differenz zwischen den ersten und zweiten Frequenzen zwischen ungefähr Null und 100 GHz ist.

12. Die Vorrichtung nach Anspruch 1, wobei die wenigstens eine erste elektromagnetische Strahlung wenigstens eine erste Stärke und wenigstens eine erste Frequenz beinhaltet, wobei die wenigstens eine zweite elektromagnetische Strahlung wenigstens eine zweite Stärke und wenigstens eine zweite Frequenz beinhaltet, wobei wenigstens eine

dritte elektromagnetische Strahlung welche wenigstens eine dritte Stärke und wenigstens eine dritte Frequenz beinhaltet zusätzlich zu der Probe bereitgestellt wird, und wobei die zweite Frequenz als eine Funktion der ersten und dritten Frequenz bestimmt wird.

- 5 **13.** Die Vorrichtung nach Anspruch 12, wobei die wenigstens eine dritte elektromagnetische Strahlung von einer elektromagnetischen Strahlungsquelle ausgesendet wird.
- 14.** Die Vorrichtung nach Anspruch 1, umfassend:
 - 10 wenigstens eine Anordnung, welche die Informationen basierend auf Daten welche der wenigstens einen zweiten elektromagnetischen Strahlung zugeordnet sind, analysiert; und
wobei die wenigstens eine erste elektromagnetische Strahlung wenigstens eine erste Stärke und wenigstens eine erste Frequenz beinhaltet, wobei die wenigstens eine zweite elektromagnetische Strahlung wenigstens eine zweite Stärke und wenigstens eine zweite Frequenz, welche unterschiedlich von der wenigstens einen ersten Frequenz ist, beinhaltet, und wobei die Daten sich auf zweite Stärken oder eine Differenz zwischen den ersten und zweiten Frequenzen beziehen, und wobei die Differenz zwischen den ersten und zweiten Frequenzen ungefähr zwischen -100 GHz und 100 GHz ist.
- 15 **15.** Die Vorrichtung nach Anspruch 14, weiter aufweisend wenigstens eine Anordnung welche dazu eingerichtet ist, den wenigstens einen Teil der anatomischen Probe basierend auf Daten, die der wenigstens einen zweiten elektromagnetischen Welle zugeordnet sind, abzubilden.
- 20 **16.** Die Vorrichtung nach Anspruch 14, wobei die wenigstens eine fünfte Anordnung wenigstens eine Linse (118) beinhaltet, und wobei die wenigstens eine Linse die wenigstens eine erste elektromagnetische Strahlung fokussiert und die wenigstens eine zweite elektromagnetische Strahlung sammelt.
- 25 **17.** Die Vorrichtung nach Anspruch 14, wobei die wenigstens eine zweite Vorrichtung einen spektralen Filter beinhaltet, welcher eine Bestimmung eines Spektrums der wenigstens einen zweiten elektromagnetischen Strahlung ermöglicht.
- 30 **18.** Die Vorrichtung nach Anspruch 14, wobei die Informationen einer biomechanischen Eigenschaft der anatomischen Probe zugeordnet sind.
- 35 **19.** Die Vorrichtung nach Anspruch 14, wobei die wenigstens eine elektromagnetische Strahlung eine zentrale Wellenlänge aufweist, welche ungefähr zwischen 0.5 und 1.8 μm ist.
- 20.** Die Vorrichtung nach Anspruch 19, wobei die wenigstens eine elektromagnetische Strahlung eine Linienbreite hat, die kleiner ist als ungefähr 100 MHz.
- 40 **21.** Die Vorrichtung nach Anspruch 19, wobei die wenigstens eine erste elektromagnetische Strahlung eine Form von einer Vielzahl von Pulsen hat, und wobei die Länge von jedem der Pulse nicht länger ist als ungefähr 10 ns.
- 45 **22.** Die Vorrichtung nach Anspruch 14, wobei die wenigstens eine erste elektromagnetische Strahlung wenigstens zwei erste elektromagnetische Strahlungen aufweist, wobei einer erste von den wenigstens zwei elektromagnetischen Strahlungen einer ersten Frequenz hat, und eine zweite der wenigstens zwei elektromagnetischen Strahlungen eine zweite Frequenz hat, und wobei eine Differenz zwischen den ersten und zweiten Frequenzen zwischen ungefähr Null und 100 GHz ist.
- 50 **23.** Die Vorrichtung nach Anspruch 14, wobei wenigstens eine dritte elektromagnetische Strahlung, welche wenigstens eine dritte Stärke und wenigstens eine dritte Frequenz beinhaltet zu der Probe bereitgestellt wird, und wobei die zweite Frequenz als eine Funktion der ersten und dritten Frequenz bestimmt wird.
- 55 **24.** Die Vorrichtung nach Anspruch 23, wobei die wenigstens eine dritte elektromagnetische Strahlung von einer elektromagnetischen Strahlungsquelle ausgesendet wird.

Revendications

1. Appareil comportant :

au moins un premier agencement qui est adapté pour fournir au moins un premier rayonnement électromagnétique (12) à un échantillon anatomique qui est un sujet vivant de manière à pouvoir générer au moins une onde acoustique dans l'échantillon anatomique, dans lequel au moins un deuxième rayonnement électromagnétique est productible dans le sujet vivant sur la base de la au moins une onde acoustique, au moins un deuxième agencement qui est adapté pour recevoir au moins une partie du au moins un deuxième rayonnement électromagnétique (16) qui est utilisé de manière à déterminer des informations associées à au moins une partie de l'échantillon anatomique, dans lequel le deuxième agencement est adapté pour pouvoir mesurer une composante décalée par effet Brillouin du deuxième rayonnement électromagnétique (72, 26, 28), **caractérisé en ce qu'il** comporte en outre au moins un troisième agencement configuré pour générer une image (300) de la au moins une partie de l'échantillon anatomique sur la base de données associées au au moins un deuxième rayonnement électromagnétique, et au moins un quatrième agencement qui est au moins un élément parmi un cathéter (420), un endoscope (430), un laparoscope ou un dispositif de visualisation ophtalmique, qui est configuré pour déplacer en translation le au moins un premier rayonnement à travers ledit échantillon anatomique.

2. Appareil selon la revendication 1, dans lequel l'échantillon biologique vivant est au moins un élément parmi un organe, un tissu ou une cellule.

3. Appareil selon la revendication 1, dans lequel le au moins un quatrième agencement comprend au moins une lentille (118), et dans lequel la au moins une lentille focalise le au moins un premier rayonnement électromagnétique et capte le au moins un deuxième rayonnement électromagnétique.

4. Appareil selon la revendication 2, dans lequel le au moins un premier rayonnement électromagnétique comprend au moins une première amplitude et au moins une première fréquence, dans lequel le au moins un deuxième rayonnement électromagnétique comprend au moins une deuxième amplitude et au moins une deuxième fréquence, et dans lequel les données se rapportent à au moins une différence parmi une première différence entre les première et deuxième amplitudes ou une seconde différence entre les première et deuxième fréquences.

5. Appareil selon la revendication 4, dans lequel la seconde différence est approximativement comprise entre - 100 GHz et 100 GHz, zéro exclu.

6. Appareil selon la revendication 1, dans lequel le au moins un deuxième agencement comprend un filtre spectral qui facilite une détermination d'un spectre du au moins un deuxième rayonnement électromagnétique.

7. Appareil selon la revendication 1, dans lequel les informations sont associées à une propriété biomécanique de l'échantillon anatomique.

8. Appareil selon la revendication 1, dans lequel le au moins un premier rayonnement électromagnétique a une longueur d'onde centrale qui est approximativement comprise entre 0,5 et 1,8 μm .

9. Appareil selon la revendication 8, dans lequel le au moins un premier rayonnement électromagnétique a une largeur de raie qui est plus petite qu'approximativement 100 MHz.

10. Appareil selon la revendication 8, dans lequel le au moins un premier rayonnement électromagnétique a la forme d'une pluralité d'impulsions, et dans lequel la durée de chacune des impulsions est plus longue qu'approximativement 10 ns.

11. Appareil selon la revendication 1, dans lequel le au moins un premier rayonnement électromagnétique comprend au moins deux premiers rayonnements électromagnétiques, dans lequel un premier des au moins deux premiers rayonnements électromagnétiques a une première fréquence, et un second des au moins deux premiers rayonnements électromagnétiques a une seconde fréquence, et dans lequel une différence entre les première et seconde fréquences est comprise entre approximativement zéro et 100 GHz.

12. Appareil selon la revendication 1, dans lequel le au moins un premier rayonnement électromagnétique comprend

au moins une première amplitude et au moins une première fréquence, dans lequel le au moins deuxième rayonnement électromagnétique comprend au moins une deuxième amplitude et au moins une deuxième fréquence, dans lequel au moins un troisième rayonnement électromagnétique qui a au moins une troisième amplitude et au moins une troisième fréquence est en outre fourni à l'échantillon, et dans lequel la deuxième fréquence est déterminée en fonction des première et troisième fréquences.

13. Appareil selon la revendication 12, dans lequel le au moins un troisième rayonnement électromagnétique est transmis à partir d'une source de rayonnement électromagnétique.

14. Appareil selon la revendication 1, comportant :

au moins un agencement qui analyse les informations sur la base de données associées au au moins un deuxième rayonnement électromagnétique, et dans lequel le au moins un premier rayonnement électromagnétique comprend au moins une première amplitude et au moins une première fréquence, dans lequel le au moins deuxième rayonnement électromagnétique comprend au moins une deuxième amplitude et au moins une deuxième fréquence qui est différente de la au moins une première fréquence, et dans lequel les données se rapportent à des deuxièmes amplitudes ou à une différence entre les première et deuxième fréquences, et dans lequel la différence entre les première et deuxième fréquences est approximativement comprise entre - 100 GHz et 100 GHz.

15. Appareil selon la revendication 14, comportant en outre au moins un agencement qui est adapté pour reproduire en image la au moins une partie de l'échantillon anatomique sur la base de données associées au au moins un deuxième rayonnement électromagnétique.

16. Appareil selon la revendication 14, dans lequel le au moins un cinquième agencement comprend au moins une lentille (118), et dans lequel la au moins une lentille focalise le au moins un premier rayonnement électromagnétique et capte le au moins un deuxième rayonnement électromagnétique.

17. Appareil selon la revendication 14, dans lequel le au moins un deuxième agencement comprend un filtre spectral qui facilite une détermination d'un spectre du au moins un deuxième rayonnement électromagnétique.

18. Appareil selon la revendication 14, dans lequel les informations sont associées à une propriété biomécanique de l'échantillon anatomique.

19. Appareil selon la revendication 14, dans lequel le au moins un premier rayonnement électromagnétique a une longueur d'onde centrale qui est approximativement comprise entre 0,5 et 1,8 μm .

20. Appareil selon la revendication 19, dans lequel le au moins un premier rayonnement électromagnétique a une largeur de raie qui est plus petite qu'approximativement 100 MHz.

21. Appareil selon la revendication 19, dans lequel le au moins un premier rayonnement électromagnétique a la forme d'une pluralité d'impulsions, et dans lequel la durée de chacune des impulsions est plus longue qu'approximativement 10 ns.

22. Appareil selon la revendication 14, dans lequel le au moins un premier rayonnement électromagnétique comprend au moins deux premiers rayonnements électromagnétiques, dans lequel un premier des au moins deux premiers rayonnements électromagnétiques a une première fréquence, et un second des au moins deux premiers rayonnements électromagnétiques a une seconde fréquence, et dans lequel une différence entre les première et seconde fréquences est comprise entre approximativement zéro et 100 GHz.

23. Appareil selon la revendication 14, dans lequel au moins un troisième rayonnement électromagnétique qui a au moins une troisième amplitude et au moins une troisième fréquence est fourni à l'échantillon, et dans lequel la deuxième fréquence est déterminée en fonction des première et troisième fréquences.

24. Appareil selon la revendication 23, dans lequel le au moins troisième rayonnement électromagnétique est transmis à partir d'une source de rayonnement électromagnétique.

Fig 1A

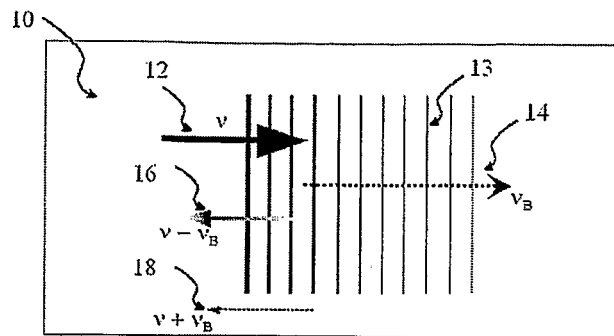


Fig 1B

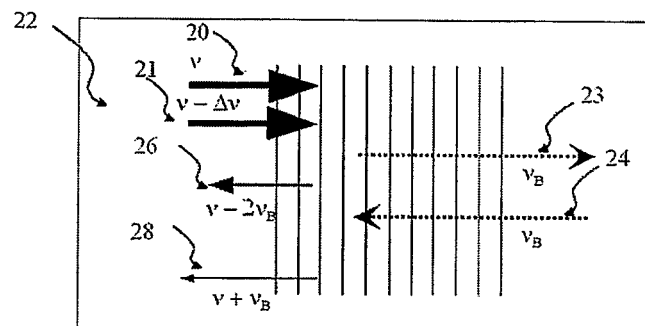


Fig 2

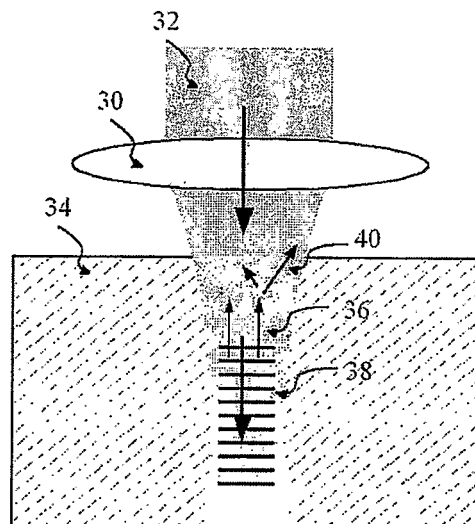


Fig 3A

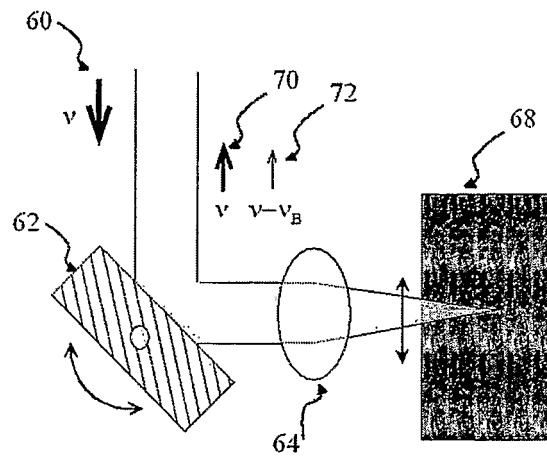
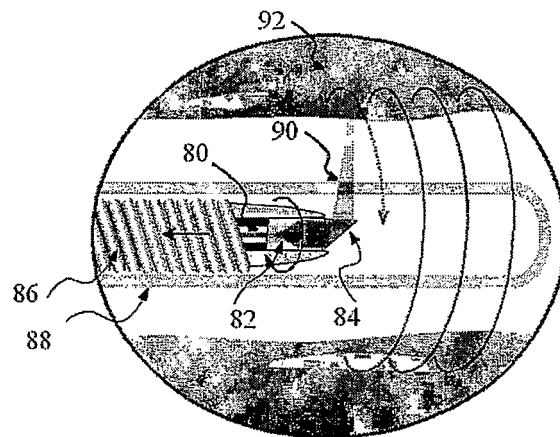


Fig 3B



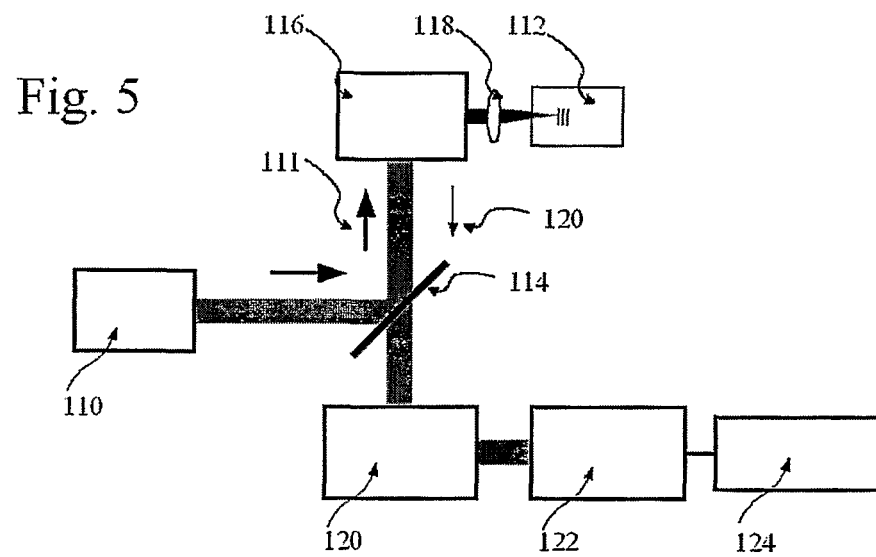
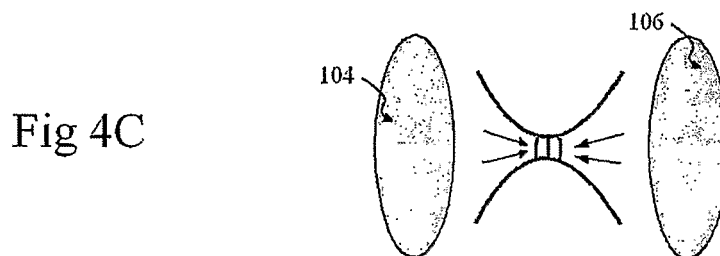
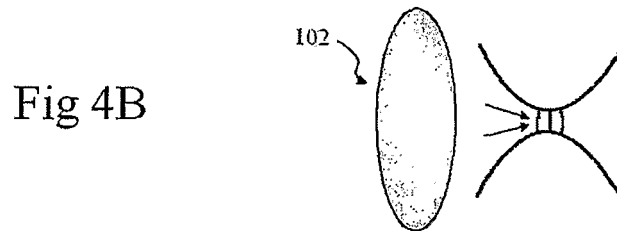
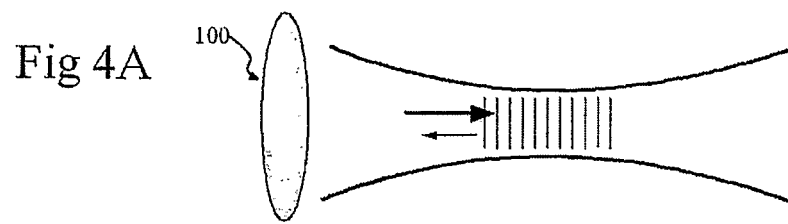


Fig 6A

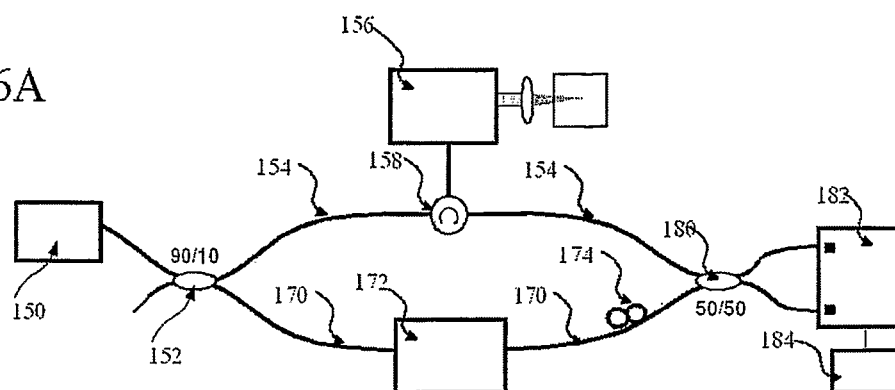


Fig 6B

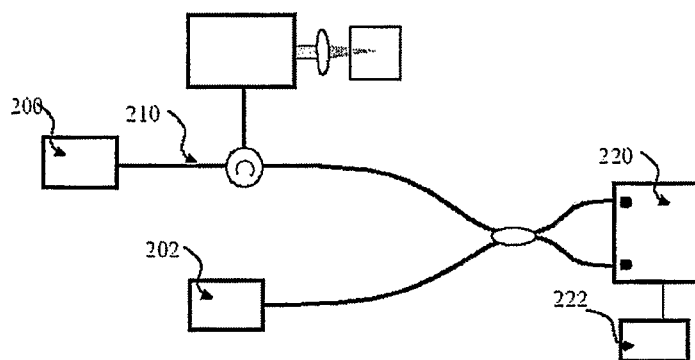


Fig. 6C

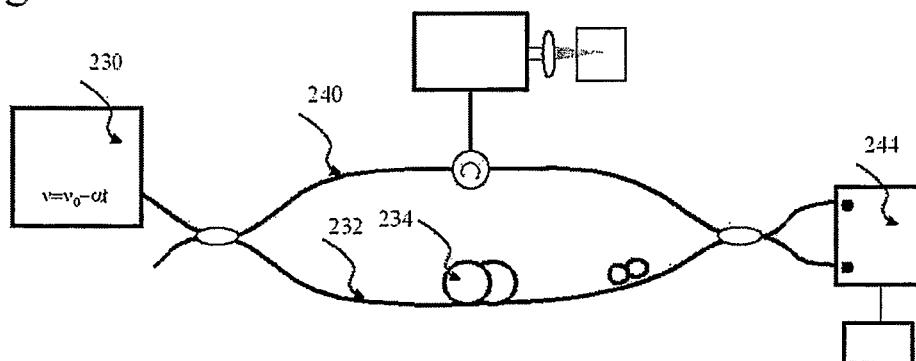


Fig 7A

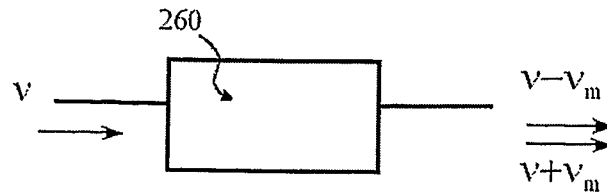


Fig 7B

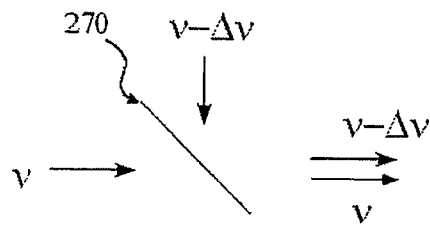


Fig 7C

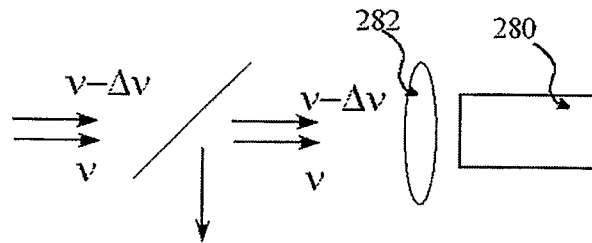


Fig 7D

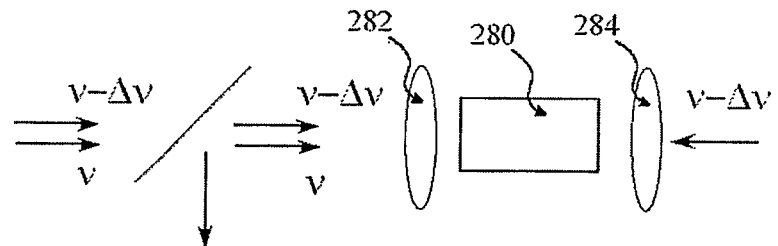


Fig 8A

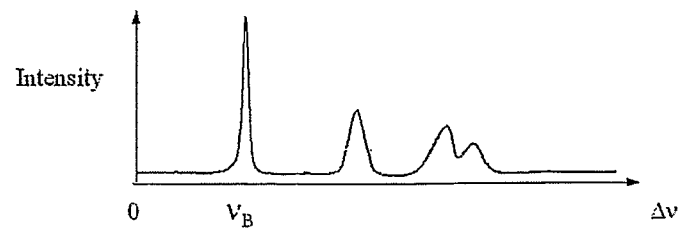


Fig 8B

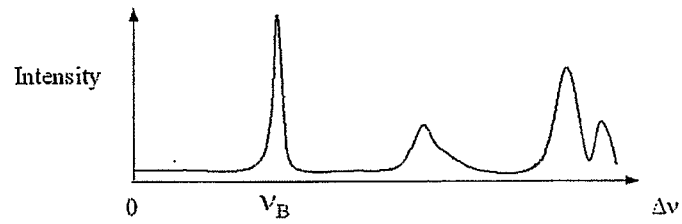


Fig 8C

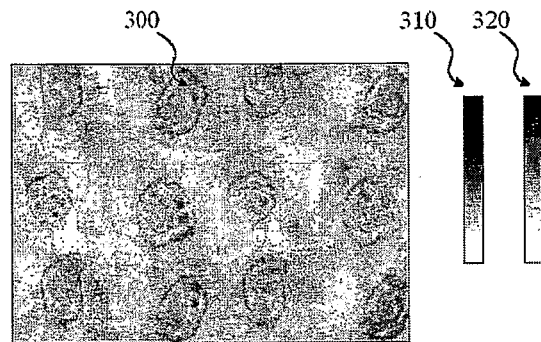


Fig 9A

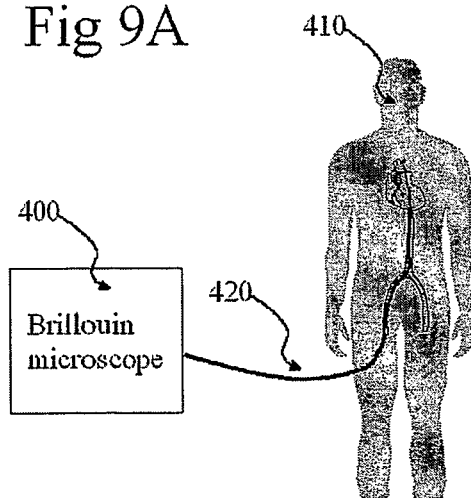
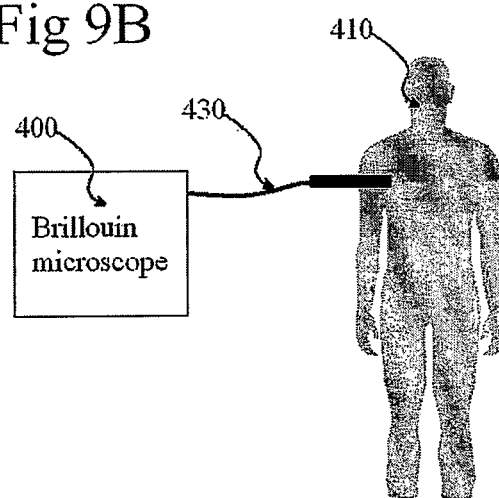


Fig 9B



REFERENCES CITED IN THE DESCRIPTION

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外部链接	Espacenet		

摘要(译)

提供了用于获得与解剖样本相关的信息的装置和方法。例如，可以向解剖学样本提供至少一个第一电磁辐射，以便在解剖学样本中产生至少一个声波。可以基于声波产生至少一个第二电磁辐射。可以提供至少一个第二电磁辐射的至少一部分，以便确定与解剖学样本的至少一部分相关的信息。另外，可以分析基于与第二电磁辐射相关联的数据的信息。第一电磁辐射可包括至少一个第一幅度和至少一个第一频率。第二电磁辐射可包括至少一个第二幅度和至少一个第二频率。该数据可以涉及第一和第二幅度之间的第一差异和/或第一和第二频率之间的第二差异。第二个差异可以大约在-100GHz和100GHz之间，不包括零。

