#### (12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau





## (10) International Publication Number WO 2010/054097 A2

#### (43) International Publication Date 14 May 2010 (14.05.2010)

- (51) International Patent Classification: G01J 9/02 (2006.01) A61B 5/00 (2006.01) G02B 27/26 (2006.01)
- (21) International Application Number:

PCT/US2009/063420

(22) International Filing Date:

5 November 2009 (05.11.2009)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/111,479 5 November 2008 (05.11.2008) US

- (71) Applicant (for all designated States except US): THE GENERAL HOSPITAL CORPORATION [US/US]; 55 Fruit Street, Boston, MA 02114 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): DE BOER, Johannes, F. [NL/NL]; Baken 24, NL-1186 DC Anstelveen (NL). PARK, Boris, Hyle [US/US]; 353 Somerville Avenue #1, Somerville, MA 02143 (US). KIM, Ki Hean [KR/KR]; Gyosu Apt. 9-602, Jigok-dong, Nam-gu Pohang, Gyeongbuk 790-751 (KR).
- (74) Agents: SHRAVAH, Aasheesh et al.; Dorsey & Whitney LLP, 250 Park Avenue, New York, NY 10177 (US).

- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available); ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

#### Published:

without international search report and to be republished upon receipt of that report (Rule 48.2(g))



(54) Title: SYSTEM AND METHOD FOR PROVIDING FULL JONES MATRIX-BASED ANALYSIS TO DETERMINE NON-DEPOLARIZING POLARIZATION PARAMETERS USING OPTICAL FREQUENCY DOMAIN IMAGING

(57) Abstract: Exemplary embodiments of apparatus, methods and systems according to the present disclosure can be provided for optical frequency domain imaging (e.g., partially fiber- based) to obtain information associated with an anatomical structure or a sample. For example, it is possible to provide at least one first electro-magnetic radiation, where a frequency of radiation associated with the first electro-magnetic radiation(s) varies over time. In addition, it is possible to separate at least one portion of a radiation which is (i) the first electro-magnetic radiation(s) and/or (ii) at least one further radiation into second and third radiations having difference orthogonal states, and to apply at least one first characteristic to the second radiation and at least one second characteristic to at least one third radiation. The first and second characteristics can be different from one another.

# SYSTEM AND METHOD FOR PROVIDING FULL JONES MATRIX-BASED ANALYSIS TO DETERMINE NON-DEPOLARIZING POLARIZATION PARAMETERS USING OPTICAL FREQUENCY DOMAIN IMAGING

#### 5 CROSS-REFERENCE TO RELATED APPLICATION(S)

[0001] This application relates to and claims the benefit of priority from U.S. Patent Application Serial No. 61/111,479, filed on November 5, 2008, the entire disclosure of which is incorporated herein by reference.

#### FIELD OF THE DISCLOSURE

10 [0002] The present disclosure relates to methods, arrangements and systems for optical frequency domain imaging (e.g., partially fiber-based) to obtain information associated with an anatomical structure or a sample, and more particular wherein the evolution of the polarization state of the sample arm light is used to determine the non-depolarizing polarization parameters of the sample.

#### 15 BACKGROUND INFORMATION

20

25

[0003] Optical coherence tomography ("OCT") is an imaging technique that can measure an interference between a reference beam of light and a beam reflected back from a sample. A detailed system description of traditional time-domain OCT is described in Huang et al., "Optical Coherence Tomography," Science 254, 1178 (1991). Optical frequency domain imaging ("OFDI") techniques, which can be also known as swept source or Fourier-domain optical coherence tomography (OCT) techniques, can be OCT procedures which generally use swept laser sources. For example, an optical beam is focused into a tissue, and the echo time delay and amplitude of light reflected from tissue microstructure at different depths are determined by detecting spectrally resolved interference between the tissue sample and a reference as the source laser wavelength is rapidly and repeatedly swept. A Fourier transform of the signal generally forms an image data along the axial line (e.g., an A-line).

A-lines are continuously acquired as the imaging beam is laterally scanned across the tissue in one or two directions that are orthogonal to the axial line.

[0004] The resulting two or three-dimensional data sets can be rendered and viewed in arbitrary orientations for gross screening, and individual high-resolution cross-sections can be displayed at specific locations of interest. This exemplary procedure allows clinicians to view microscopic internal structures of tissue in a living patient, facilitating or enabling a wide range of clinical applications from disease research and diagnosis to intraoperative tissue characterization and image-guided therapy. Exemplary detailed system descriptions for spectral-domain OCT and Optical Frequency Domain Interferometry are described in International Patent Application No. PCT/US03/02349 and U.S. Patent Application Serial No. 60/514,769, respectively.

10

15

20

25

[0005] A contrast mechanism in the OFDI techniques can generally be an optical back reflection originating from spatial reflective-index variation in a sample or tissue. The result can be a so-called an "intensity image" that may indicate the anatomical structure of tissue up to a few millimeters in depth with spatial resolution ranging typically from about 2 to 20 μm. While the intensity image can provide a significant amount of morphological information, birefringence in tissues may offer another contrast useful in several applications such as quantifying the collagen content in tissue and evaluating disease involving the birefringence change in tissue. Polarization-sensitive OCT can provide an additional contrast by observing changes in the polarization state of reflected light. The first fiber-based implementation of polarization-sensitive time-domain OCT is described in Saxer et al., "High-speed fiber-based polarization-sensitive optical coherence tomography of in vivo human skin," Opt. Lett. 25, 1355 (2000).

[0006] In polarization-sensitive time-domain OCT techniques, a simultaneous detection of interference fringes in two orthogonal polarization channels can facilitate a complete

characterization of a reflected polarization state, as described in J.F. de Boer et al., "Determination of the depth-resolved Stokes parameters of light backscattered from turbid media by use of polarization-sensitive optical coherence tomography," Opt. Lett. 24, 300 (1999). There can be two non-depolarizing polarization parameters: birefringence, characterized by a degree of phase retardation and an optic axis orientation, and diattenuation, which can be related to dichroism and characterized by an amount and an optic axis orientation. Together, these optical properties may be described by, e.g., the 7 independent parameters in the complex 2x2 Jones matrix.

[0007] The polarization state reflected from the sample can be compared to the state incident on the sample quite easily in a bulk optic system, as the polarization state incident on the sample can be controlled and fixed. However, an optical fiber may have a significant disadvantage in that a propagation through optical fiber can alter the polarization state of light. In this case, the polarization state of light incident on the sample may not be easily controlled or determined. In addition, the polarization state reflected from the sample may not be necessarily the same as the polarization state received at the detectors. Assuming negligible diattenuation, or polarization-dependent loss, optical fiber changes the polarization states of light passing through such fiber in such a manner as to preserve the relative orientation between states. The overall effect of propagation through optical fiber and non-diattenuating fiber components can be similar to an overall coordinate transformation or some arbitrary rotation. In other words, the relative orientation of polarization states at all points throughout propagation can be preserved, as described in U.S. Patent No. 6,208,415.

10

15

20

[0008] There have been a number of approaches that can take advantage to determine the polarization properties of a biological sample imaged with polarization-sensitive OCT. Such approaches have suffered from some disadvantage, however.

[0009] For example, a vector-based method has been used to characterize birefringence and optic axis orientation only by analyzing rotations of polarization states reflected from the surface and from some depth for two incident polarization states perpendicular in a Poincaré sphere representation as described in the Saxer Publication, J.F. de Boer et al., "Determination of the depth-resolved Stokes parameters of light backscattered from turbid media by use of polarization-sensitive optical coherence tomography," Opt. Lett. 24, 300 (1999), and B.H. Park et al., "In vivo burn depth determination by high-speed fiber-based polarization sensitive optical coherence tomography," J. Biomed. Opt. 6, 474 (2001).

[0010] Mueller matrix based methods are capable of determining birefringence, diattenuation, and optic axis orientation as described in S.L. Jiao et al., "Two-dimensional depth-resolved Mueller matrix of biological tissue measured with double-beam polarization-sensitive optical coherence tomography," Opt. Lett. 27, 101 (2002), S. Jiao et al., "Optical-fiber-based Mueller optical coherence tomography," Opt. Lett. 28, 1206 (2003), and S.L. Jiao et al., "Depth-resolved two-dimensional Stokes vectors of backscattered light and Mueller matrices of biological tissue measured with optical coherence tomography," Appl. Opt. 39, 6318 (2000). These typically utilize a multitude of measurements using a combination of incident states and detector settings and limits their practical use for in vivo imaging.

10

15

[0011] Jones matrix based approaches have also been used to characterize the nondepolarizing polarization properties of a sample as described in S. Jiao et al., "Optical-fiberbased Mueller optical coherence tomography," Opt. Lett. 28, 1206 (2003) and S.L. Jiao and
L.V. Wang, "Jones-matrix imaging of biological tissues with quadruple-channel optical
coherence tomography," J. Biomed. Opt. 7, 350 (2002). The description of these approaches
has limited a use of optical fiber and fiber components such as circulators and fiber splitters
such that these components must be traversed in a round-trip fashion and assumes that sample

birefringence and diattenuation share a common optic axis. These approaches can use a multitude of measurements using a combination of incident states and detector settings and limits their practical use for in vivo imaging.

[0012] Generally, in nearly all of polarization sensitive time domain, Spectral Domain OCT, or OFDI systems, the polarization properties can be measured using different incident polarization states on the sample in a serial manner, i.e. the incident polarization state incident on the sample was modulated as a function of time.

[0013] Exemplary system and method for obtaining polarization sensitive information is described in U.S. Patent No. 6,208,415. Exemplary OFDI techniques and systems are described in International Application No. PCT/US04/029148. Method and system to determine polarization properties of tissue is described in International Application No. PCT/US05/039374.

[0014] Accordingly, there may be a need to address and/or overcome at least some of the deficiencies described herein above.

#### 15 SUMMARY OF EXEMPLARY EMBODIMENTS OF THE DISCLOSURE

10

[0015] To overcome at least some of the deficiencies described herein above, exemplary embodiments of method, arrangement and system according to the present invention can be provided, where two independent polarization states may be simultaneously incident on the sample.

20 [0016] For example, the two incident polarization states can be discerned by tagging the two states with different frequency shifts such that the carrier frequencies of the interference fringes are different. Moreover, in the exemplary detection system, apparatus and method, the complex field of the reflected sample arm light can be determined independently for each incident polarization state simultaneously. The simultaneous detection of the complex electrical fields and their relative phase can facilitate a determination of, e.g., all 7

independent parameters of the Jones matrix, whereas in prior methods, only, e.g., 5 independent parameters are determined. (See B.H. Park, M.C. Pierce, B. Cense and J.F. de Boer, "Jones matrix analysis for a polarization-sensitive optical coherence tomography system using fiber-optic components," Optics Letters 29(21): 2512-2514 (2004).).

[0017] Thus, according to certain exemplary embodiments of the present invention, exemplary systems, apparatus and processes can be provided for determining the non-depolarizing polarization properties (e.g., all 7 independent parameters of the complex 2x2 Jones matrix) of a sample imaged by interferometry with no restrictions on the use of optical fiber or non-diattenuating fiber components, such as circulators and splitters. The exemplary embodiments of the process, software arrangement and system according to the present invention are capable of determining, e.g., all 7 independent parameters of the complex 2x2 Jones matrix between two different locations within the sample probed simultaneously with a minimum of two unique incident polarization states imaged by interferometry. Thus, according to the exemplary embodiments of the present invention, it is possible to:

10

15

20

- determine the full polarization properties of a sample by determining all 7 independent parameters of the complex 2x2 Jones matrix between two different locations within the sample probed simultaneously with a minimum of two unique incident polarization states;
- provide an unrestricted placement of optical fiber and non-diattenuating fiber
   components throughout a polarization-sensitive interferometric imaging system;
- provide a power efficient interferometer configuration, where the number of
  optical elements in the sample arm path to the detectors is minimal, providing the
  most power to the sample, and minimal loss of reflected sample arm light reaching
  the detectors, and

determine, e.g., the full sample Jones matrix with no assumptions regarding the
 optic axes for sample birefringence and diattenuation.

[0018] For example, an exemplary embodiment of system, apparatus and procedure according to the present invention can facilitate a determination of the non-depolarizing polarization properties of a sample by comparing the light reflected from two different locations within the sample probed simultaneously with a minimum of two unique incident polarization states in such a way that, e.g., all 7 unique elements of the Jones matrix can be determined.

[0019] Further, exemplary embodiments of apparatus, methods and systems according to the present disclosure can be provided for optical frequency domain imaging (e.g., partially fiber-based) to obtain information associated with an anatomical structure or a sample. For example, it is possible to provide at least one first electro-magnetic radiation, e.g., using at least one first arrangement, where a frequency of radiation associated with the first electro-magnetic radiation(s) varies over time. In addition, using at least one second arrangement, it is possible to separate at least one portion of a radiation which is (i) the first electro-magnetic radiation(s) and/or (ii) at least one further radiation into second and third radiations having difference orthogonal states, and to apply at least one first characteristic to the second radiation and at least one second characteristic to at least one third radiation. The first and second characteristics can be different from one another.

10

15

25

20 [0020] According to another exemplary embodiment of the present disclosure, it is possible to produce at least one further electro-magnetic radiation by depolarizing the first electro-magnetic radiation(s) using at least one third arrangement, where the second and third radiations can be generated based on the at least one further radiation.

[0021] For still another exemplary embodiment of the present disclosure, it is possible, using at least one fourth arrangement, to receive and/or detect an interference between (i) at

least one fourth radiation and (ii) the second and third radiations, and determine at least some of Jones matrix elements of a sample based on a radiation reflected from the sample, or possibly, all of the Jones matrix elements of the sample. For example, the second and third radiations can be received and/or detected simultaneously. The radiation reflected from the sample can provided from at least two different locations within the sample which are received simultaneously. The fourth arrangement can be configured to separate the interference into additional radiations having respective first and second polarization states. At least one fifth arrangement can be provided to generate at least one image as a function of at least one of the Jones matrix elements.

[0022] For example, the first characteristic(s) can be a first frequency shift of the second radiation, and the second characteristic(s) can be a second frequency shift of the third radiation. Further, the first and second frequency shifts can be different from one another. The at least one first arrangement is an energy source arrangement. The energy source arrangement can be a swept source arrangement which rapidly tunes a wavelength of the first radiation(s).

10

15

20

[0023] According to a further exemplary embodiment of the present disclosure, the second arrangement(s) can include at least one acousto-optic modulator arrangement. Further, it is possible to configure the second arrangement(s) to overlap and/or combine the second and third radiations after the first and second characteristics are applied thereto. apparatus according to claim 3, wherein the at least one fourth arrangement is further configured to separate the interference into additional radiations having respective first and second polarization states.

[0024] These and other objects, features and advantages of the exemplary embodiment of the present disclosure will become apparent upon reading the following detailed description

of the exemplary embodiments of the present disclosure, when taken in conjunction with the appended claims.

### BRIEF DESCRIPTION OF THE DRAWING(S)

10

15

20

[0025] 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 disclosure, in which:

[0026] Figure 1 is a diagram of an exemplary embodiment of a polarization-sensitive interferometric imaging system/apparatus which can be used with the exemplary software arrangements and processes/methods according to the present disclosure;

[0027] Figure 2 is a diagram of an alternative exemplary embodiment of a polarization-sensitive interferometric imaging system/apparatus which can be used with the exemplary software arrangements and processes/methods according to the present disclosure; and

[0028] Figures 3(a)-3(g) are exemplary images obtained using the exemplary system/apparatus shown in Figure 1, whereas Figures 3(a) and 3(b) are exemplary images of a chicken muscle, ex-vivo, Figures 3(c) and 3(d) are exemplary images of a human hand top, in-vivo, and Figures 3(e) and 3(f) are exemplary images of a mouse cancer model, in-vivo.

[0029] 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 disclosure 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 exemplary embodiments without departing from the true scope and spirit of the subject disclosure as defined by the appended claims.

#### **DETAILED DESCRIPTION OF EXEMPLARY EMBODIMENTS**

10

15

20

25

[0030] Exemplary embodiments of systems, apparatus, arrangements, software arrangements and processes/methods according to the present disclosure can be implemented in, e.g., a variety of OCT systems. Figure 1 shows an exemplary embodiment of a polarization-sensitive interferometric arrangement that can be used for implementing the exemplary embodiments of the systems, apparatus, arrangements, software arrangements and processes/methods according to the present disclosure.

[0031] In particular, as shown in a diagram of Figure 1, the exemplary arrangement of an apparatus and/or system according to the present disclosure can include, e.g., a rapid wavelength tunable source 10 that can be configured to generate an electro-magnetic radiation or light signal. Such radiation and/or light signal can be transmitted through a static polarization controller, and then can enter a depolarizing unit/arrangement 50. Such depolarizing unit/arrangement can include an optional polarizer 20 oriented, e.g., at 45 degrees with respect to a horizontal plane. The light (e.g., or other electro-magnetic radiation) can than be split by a first polarizing beam splitter 30 into, e.g., equal intensities with orthogonal polarization states (e.g., horizontal and vertical). The horizontal and vertical polarization states can each travel along a different path length before a recombination of the beam paths in a second polarizing beam splitter 40. The path length difference between the orthogonal polarization states can preferably be larger than the instantaneous coherence length of the source light/radiation.

[0032] After exiting the second polarizing beam splitter 40, the light/radiation can be depolarized with a zero degree of polarization. The light/radiation can be separated into a sample arm component and a reference arm component. The sample arm light/radiation component can be directed to a circulator 70 and a sample arm 200. The reflected light/radiation from the sample can be directed by the circulator to an acousto-optic

modulator (AOM) crystal 160 and incident on a non-polarizing beam splitter 130. The reference arm light/radiation can be directed to a polarization tagging state unit/arrangement 210 that can split the unpolarized light/radiation in two portions by, e.g., a polarizing beam splitter 80. The two (or more) portions can receive a frequency shift by AOM Freq 1 100 and AOM Freq 2 110, where the frequency shift introduced by AOM Freq 1 100 can be different from the frequency shift introduced by AOM Freq 2 110.

[0033] As shown in the exemplary embodiment of Figure 1, the orthogonal polarizations (e.g., two or more) can be recombined by a polarizing beam splitter 90. The light/radiation can propagate optionally through a Quarter Wave Plate (QWP) 120 and/or via an optical fiber and/or through free space to a non polarizing beam splitter 130 to recombine the sample and reference arm lights/radiations to form interference fringes in beam paths 133, 137. The light/radiation in the beam paths 133, 137 can be split into orthogonal polarization states by, e.g., polarizing beam splitters 140, 150, respectively, and a first balanced receiver 170 can receive the balanced interference signal for one polarization state, and a second balanced receiver 180 can receive the balanced interference for the orthogonal polarization state.

10

15

20

25

[0034] For example, the reference arm light/radiation can be prepared by the QWP 120 and/or a fiber based polarization controller, such that the light intensity that has passed through the AOM Freq 1 100 can be split in, e.g., equal parts in the beam paths 133, 137. Subsequently, the intensity in the four beams after polarizing beam splitters 140 and 150 can all be nearly equal. In addition, the light/radiation intensity that has passed through the AOM Freq 2 110 can be split, e.g., in equal parts in the beam paths 133, 137, and subsequently the intensity in the four beams after polarizing beam splitters 140 and 150 can all be nearly equal. The signals of the balanced receivers can be processed by an image processing unit/arrangement 190 to obtain, e.g., a plurality of (e.g., 7) independent parameters of the complex 2x2 Jones matrix.

[0035] A retrieval of sample optical polarization properties and the (e.g., 7) independent parameters of the complex 2x2 Jones matrix can be described in the following manner. After the depolarizer, the light/radiation provided by the source 10 can be unpolarized (e.g., a degree of polarization can be zero).

[0036] For example, it is possible to assume the reference arm with AOM Freq 2 110 is blocked by a beam stop. Further, likely only the polarization component of the unpolarized sample arm light/radiation (which is equal to the polarization component transmitted through AOM Freq 1 100) interferes with the reference arm light/radiation. The interference fringes can be centered at the AOM frequency 1 frequency. The balanced detector units/arrangements 170, 180 can detect the orthogonal components of the interference fringes for, e.g., a single sample arm polarization state incident on the sample. A phase sensitive demodulation of the interference fringes centered at AOM frequency 1 can facilitate a determination of the complex electric field components reflected from the sample arm.

10

15

20

[0037] Further, with the assumption that the reference arm with AOM Freq 1 100 is blocked by a beam stop, the balanced detector units/arrangements 170, 180 can detect the orthogonal components of the interference fringes for the orthogonal sample arm polarization state incident on the sample, where the interference fringes can be centered at the AOM frequency 2 frequency. In addition, without the beam stops, the sample polarization information can be measured for, e.g., 2 or more sample polarization states simultaneously incident on the sample, where the information for the two polarization states can be centered at a carrier frequency determined by AOM frequency 1 and AOM frequency 2, respectively.

[0038] Preferably, the signal bandwidth for each polarization state can be smaller than the frequency difference between AOM frequency 1 and AOM frequency 2. As a result, the complex field components along orthogonal directions for two orthogonal polarization states

reflected from the sample arm can be simultaneously measured, e.g., permitting a complete determination of the complex 2x2 Jones matrix.

[0039] Referring again to the diagram of the exemplary apparatus/system of Figure 1, the source 10 can be, e.g., a polygonal-scanner based wavelength-swept source. According to one exemplary embodiment, the source 10 can operate at, e.g., 31K axial scans/s with the output of 45 mW, the bandwidth of 1300nm centered at 1295 nm, and its spectral line width of 0.23nm for the depth range of 1.6mm in the air in one side. According to a further exemplary embodiment, the light/radiation from the source 10 can first be forwarded to a depolarizer arrangement (e.g., element/arrangement) 50, where light can be equally split depending on the polarization state and recombined with a sufficient path length delay on one side which can be, e.g., much longer than the coherence length of the source 10.

10

15

20

25

[0040] Further, the recombined light/radiation can be depolarized. After the depolarizer arrangement 50, e.g., 90% of the light/radiation can be forwarded to the sample arm 200 for probing the sample(s), and the rest 10% of the light/radiation can be forwarded to the transmission reference arm. In the transmission reference arm, individual polarization states can be tagged by a polarization state tagging unit/arrangement 210, in which the states can be frequency shifted to, e.g., about 20MHz and 40MHz, respectively, by two or more acousto-optic modulators (AOMs) 100, 110 to utilize both sides of frequency bands, and to, e.g., double the imaging depth range which can become, e.g., about 3.2mm in the air. The light/radiation from the reference transmission arm can be combined with the light/radiation reflected from the sample for interference, and the interference signal can be detected at the balanced receivers 170, 180 in the exemplary polarization-diverse balanced detection configuration. A plurality (e.g., two) channel signals from the exemplary polarization diverse configuration can be acquired simultaneously at an ADC board running at, e.g., about 100MHz sampling frequency, incorporated in the image processing unit/arrangement 190.

From the exemplary available signal bandwidth of about 50 MHz, the interference signals of individual incident polarization states can occupy, e.g., two separate detection bands: e.g., one band from about 10MHz to 30MHz, and another one from about 30MHz to 50MHz.

[0041] According to a particular exemplary embodiment, the acquired exemplary spectra can contain, e.g., about 3072 pixels in 130nm bandwidth in FWHM. The spectra can be Fourier transformed into the frequency domain, and divided into the two frequency bands. Each frequency band was demodulated, and inverse Fourier transformed to the time domain. Then, the time to k-space mapping can be applied to the spectra based on pre-calibrated wavelength data and interpolation procedure, and the dispersion compensation can be applied based on the pre dispersion measurement due to the difference of dispersion between reference and sample arms. Further, the spectra in equal K-space can be Fourier transformed into reflectivity profiles in depth space. The imaging was performed with a handheld probe with an optical window at the tip. The depth range of the cross-sectional image can be, e.g., about 2.3mm, with consideration of the refractive index of tissues being about 1.4. Exemplary intensity images can be obtained by, e.g., summing intensities of both channels and bands, and polarization sensitive (PS) exemplary images can be obtained as accumulative phase retardation with respect to the surface states, and displayed as black for 0°, and white for 180° phase retardations, and then wrapped back to black for 360°.

10

20

25

[0042] Figure 2 illustrates a diagram of another exemplary embodiment of the system/apparatus according to the present disclosure which can accomplish same or similar goals and/or results as the exemplary embodiment illustrated in Figure 1. With respect to Figure 2, the depolarizing element/arrangement 50 can be excluded, and the tagging of orthogonal independent polarization states can be accomplished in the sample arm using element/arrangements 80, 90, 100, 110, where these elements/arrangement can be similar, equal to or same as those described herein above.

[0043] The exemplary embodiment of a PS analysis method according to exemplary embodiment of the present disclosure can be based on Jones matrix. The non-depolarizing polarization properties of an exemplary optical system/apparatus can be described by its complex Jones matrix, J, which transforms an incident polarization state, described by a complex electric field vector,  $E = \{H \mid V\}^T$ , to a transmitted state,  $E : \{H \mid V\}^T$ . In the PS-OCT analysis method based on the Jones matrix, the measurement of polarization states within the sample,  $[H_1' V_1']^T$ ,  $[H_2' V_2']^T$  with respect to the surface polarization states,  $[H_1 \mid V_1]^T$ ,  $[H_2 \mid V_2]^T$  is formulated as,

$$\left[H_{-1}^{-1}H_{-2}^{-1};\,V_{-1}^{-1}\,V_{-2}^{-1}\right] = \exp\left(i\Delta_{-}\psi_{-1}\right) \times \mathbf{J}_{-\infty}, \mathbf{J}_{-2}^{-1}\mathbf{J}_{-2}^{-1}\left[H_{-1}^{-1}\exp\left(i\alpha_{-}\right)H_{-2};\,V_{-1}^{-1}\exp\left(i\alpha_{-}\right)V_{-2}^{-1}\right]^{\frac{1}{2}}$$

10

15

20

where  $J_{...}$  describes the optical path from the sample surface to the detectors, and is modeled as elliptical retarders.  $J_{x}$  describes the round-trip Jones matrix of the sample, and can be decomposed into a form of  $J_{x} = J_{x}J_{z}$  where  $J_{x}$  and  $J_{z}$  describe a retarder and a polarizer respectively.  $\alpha$  is the phase difference between the measurements with two incident polarization states. Since the two measurements can be simultaneous in the exemplary configuration, there is likely no ambiguity in phase and  $\alpha$  become zero,  $\alpha = 0$ . The above-described formula become simplified as follows:

$$\mathbf{J}_{\mathrm{T}} = \exp(-i\Delta\psi_{1}) \times \left[H_{1}' H_{2}' ; V_{1}' V_{2}'\right] \times \left[H_{1} H_{2} ; V_{1} V_{2}\right]^{-1},$$

where  $J_{ij}$  is a combined Jones matrix including the output path,  $J_{ij} = J_{ij}J_{i$ 

[0044] In order to demonstrate the implementation of the exemplary embodiments of the method, apparatus and system according to the present disclosure, samples of chicken thigh muscles were imaged as ex-vivo, and the back sides of a human hand were imaged in vivo as shown in Figures 3(a)-3(f). Dimensions of cross-sectional images were 2.3mm x 8mm in the

tissue depth and lateral directions respectively. The exemplary intensity image of the chicken muscle as provided in Figure 3(a) shows its structures with slow intensity decay with the depth compared with other biological tissues, and the exemplary PS image of Figure 3(b) shows frequent horizontal black-white banding patterns down to bottom of the image. The exemplary intensity image of the hand in Figure 3(c) shows the superficial epithelium, and the underlying dermis structures, and the exemplary PS image of Figure 3(d) shows some birefringence. As shown in Figures 3(c) and 3(d), the back side of the hand showed stronger birefringence than the other side. The PS imaging is known to provide additional contrast to distinguish between normal and cancerous tissues in case the normal tissue is birefringent.

10

15

20

25

[0045] To demonstrate such exemplary procedure and implementation in the animal model, a mouse cancer model was imaged with the exemplary embodiment of a PS-OFDI system in accordance with the present disclosure. Cancer cells were injected into the back legs of mice superficially, and the exemplary PS-OFDI imaging was performed from day 1 longitudinally until day 10. Since the cancer was injected just under the skin at the location of muscle, PS-OFDI imaging showed some distinction of the cancer region from the normal muscle tissue. Dimensions of cross-sectional images were 2.3mm x 12mm in the tissue depth, and lateral directions respectively. Both the exemplary intensity and PS images of Figures 3(e) and 3(f) shows a distinction of the cancer tissue from the surrounding tissue: the cancer tissue appears as relatively homogeneous structures without banding pattern indicating no birefringence. It appears that the cancer section has clear boundaries separating from normal tissue sections without metastasis.

[0046] The foregoing merely illustrates the principles of the invention. Various modifications and alterations to the described embodiments will be apparent to those skilled in the art in view of the teachings herein. Indeed, the arrangements, systems and methods according to the exemplary embodiments of the present invention can be used with imaging

systems, and for example with those described in International Patent Publication WO 2005/047813published May 26, 2005, U.S. Patent Publication No. 2006/0093276, published May 4, 2006, and U.S. Patent Publication No. 2005/0018201, published January 27, 2005, the disclosures of which are incorporated by reference herein in their entireties. It will thus be appreciated that those skilled in the art will be able to devise numerous systems, arrangements and methods which, although not explicitly shown or described herein, embody the principles of the invention and are thus within the spirit and scope of the present invention. In addition, to the extent that the prior art knowledge has not been explicitly incorporated by reference herein above, it is explicitly being incorporated herein in its entirety. All publications referenced herein above are incorporated herein by reference in their entireties.

5

10

#### What Is Claimed Is:

5

10

15

1. An apparatus comprising:

at least one first arrangement configured to provide at least one first electro-magnetic radiation, wherein a frequency of radiation provided by the at least one first arrangement varies over time; and

at least one second arrangement configured to separate at least one portion of a radiation which is at least one of (i) the at least one first electro-magnetic radiation or (ii) at least one further radiation into second and third radiations having difference orthogonal states, and to apply at least one first characteristic to the second radiation and at least one second characteristic to at least one third radiation, the first and second characteristics being different from one another.

- 2. The apparatus according to claim 1, further comprising at least one third arrangement configured to produce the at least one further electro-magnetic radiation by depolarizing the at least one first electro-magnetic radiation, wherein the at least one second arrangement is configured to generate the second and third radiations based on the at least one further radiation.
- 3. The apparatus according to claim 1, further comprising at least one fourth
  20 arrangement configured to receive or detect an interference between (i) at least one fourth
  radiation and (ii) the second and third radiations, and determine at least some of Jones matrix
  elements of a sample based on a radiation reflected from the sample.
- 4. The apparatus according to claim 3, wherein the at least one fourth arrangementconfigured to determine all of the Jones matrix elements of the sample.

5. The apparatus according to claim 3, wherein the at least one fourth arrangement configured to receive or detect the second and third radiations simultaneously.

- 6. The apparatus according to claim 3, wherein the radiation reflected the sample is provided from at least two different locations within the sample which are received simultaneously.
- 7. The apparatus according to claim 1, wherein the at least one first characteristic is a first frequency shift of the second radiation, and the at least one second characteristic is a second frequency shift of the third radiation.
  - 8. The apparatus according to claim 7, wherein the first and second frequency shifts are different from one another.
- 15 9. The apparatus according to claim 1, wherein the at least one first arrangement is an energy source arrangement.
  - 10. The apparatus according to claim 9, wherein the energy source arrangement is a swept source arrangement which rapidly tunes a wavelength of the at least one first radiation.

20

10

11. The apparatus according to claim 1, wherein the at least one second arrangement includes at least one acousto-optic modulator arrangement.

12. The apparatus according to claim 1, wherein the at least one second arrangement is further configured to overlap or combine the second and third radiations after the first and second characteristics are applied thereto.

- 5 13. The apparatus according to claim 3, wherein the at least one fourth arrangement is further configured to separate the interference into additional radiations having respective first and second polarization states.
- 14. The apparatus according to claim 3, further comprising at least one fifth arrangement10 configured to generate at least one image as a function of at least one of the Jones matrix elements.
  - 15. A method comprising:

20

providing at least one first electro-magnetic radiation, wherein a frequency of

radiation associated with the at least one first radiation varies over time; and

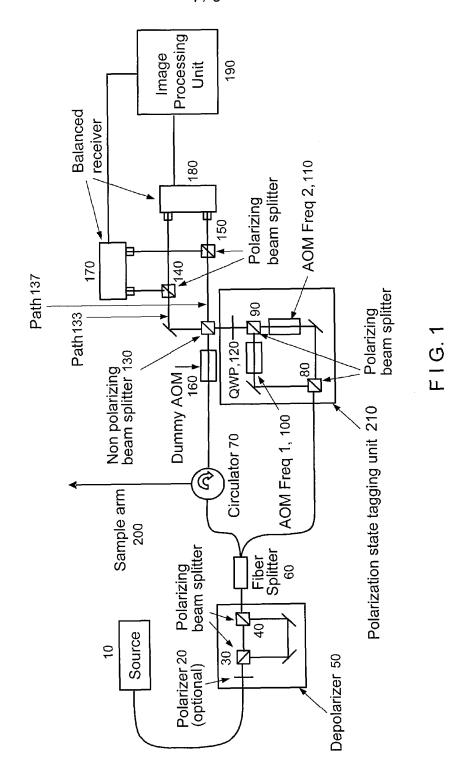
separating at least one portion of a radiation which is at least one of (i) the at least one first electro-magnetic radiation or (ii) at least one further radiation into second and third radiations having difference orthogonal states, and to apply at least one first characteristic to the second radiation and at least one second characteristic to at least one third radiation, the first and second characteristics being different from one another.

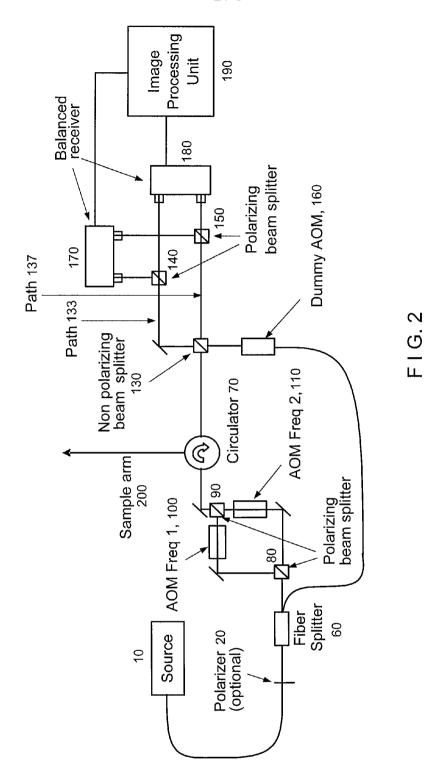
16. The method according to claim 15, further comprising producing the at least one further electro-magnetic radiation by depolarizing the at least one first electro-magnetic radiation.

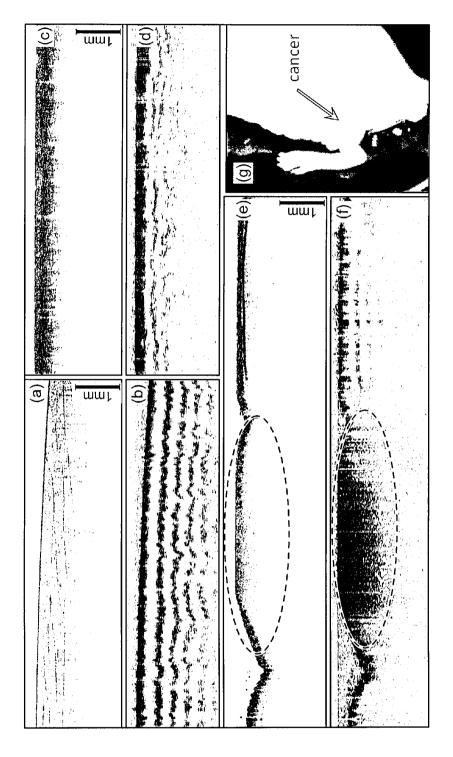
17. The method according to claim 15, further comprising receiving or detecting an interference between (i) at least one fourth radiation and (ii) the second and third radiations, and determine at least some of Jones matrix elements of a sample based on a radiation reflected from the sample.

5

- 18. The method according to claim 17, wherein the determining procedure comprising determining all of the Jones matrix elements of the sample.
- 19. The method according to claim 17, wherein the second and third radiations arereceived or detected simultaneously.







F I G. 3