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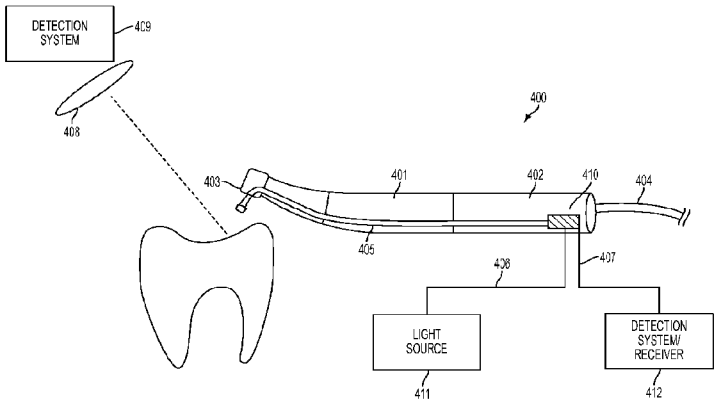


FIG. 4

(57) Abstract: A system and method for using near-infrared or short-wave infrared (SWIR) sources such as lamps, thermal sources, LED's, laser diodes, super-luminescent laser diodes, and super-continuum light sources for early detection of dental caries measure transmission and/or reflectance. In the SWIR wavelength range, solid, intact teeth may have a low reflectance or high transmission with very few spectral features while a carious region exhibits more scattering, so the reflectance increases in amplitude. The spectral dependence of the transmitted or reflected light from the tooth may be used to detect and quantify the degree of caries. Instruments for applying SWIR light to one or more teeth may include a C-clamp design, a mouth guard design, or hand-held devices that may augment other dental tools. The measurement device may communicate with a smart phone or tablet, which may transmit a related signal to the cloud, where additional value-added services are performed.

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SHORT-WAVE INFRARED SUPER-CONTINUUM LASERS FOR EARLY DETECTION OF DENTAL CARIES

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. provisional application Serial No. 61/747,477 filed December 31, 2012 and U.S. provisional application Serial No. 61/754,698 filed January 21, 2013, the disclosures of which are hereby incorporated by reference in their entirety.

[0002] This application is related to U.S. provisional application Serial No. 61/747,472 filed December 31, 2012; Serial No. 61/747,481 filed December 31, 2012; Serial No. 61/747,485 filed December 31, 2012; Serial No. 61/747,487 filed December 31, 2012; Serial No. 61/747,492 filed December 31, 2012; and Serial No. 61/747,553 filed December 31, 2012, the disclosures of which are hereby incorporated in their entirety by reference herein.

[0003] This application is being filed concurrently with International Application _____ entitled Near-Infrared Lasers For Non-Invasive Monitoring Of Glucose, Ketones, HBA1C, And Other Blood Constituents (Attorney Docket No. OMNI0101PCT); U.S. Application _____ entitled Focused Near-Infrared Lasers For Non-Invasive Vasectomy And Other Thermal Coagulation Or Occlusion Procedures (Attorney Docket No. OMNI0103PUSP); International Application _____ entitled Short-Wave Infrared Super-Continuum Lasers For Natural Gas Leak Detection, Exploration, And Other Active Remote Sensing Applications (Attorney Docket No. OMNI0104PCT); U.S. Application _____ entitled Short-Wave Infrared Super-Continuum Lasers For Detecting Counterfeit Or Illicit Drugs And Pharmaceutical Process Control (Attorney Docket No. OMNI0105PUSP); U.S. Application _____ entitled Non-Invasive Treatment Of Varicose Veins (Attorney Docket No. OMNI0106PUSP); and U.S. Application _____ entitled Near-Infrared Super-Continuum Lasers For Early Detection Of Breast And Other Cancers (Attorney Docket No. OMNI0107PUSP), the disclosures of which are hereby incorporated in their entirety by reference herein.

TECHNICAL FIELD

[0004] This disclosure relates to lasers and light sources for healthcare, medical, dental, or bio-technology applications, including systems and methods for using near-infrared or short-wave infrared light sources for early detection of dental caries, often called cavities.

BACKGROUND AND SUMMARY

[0005] Dental care and the prevention of dental decay or dental caries has changed in the United States over the past several decades, due to the introduction of fluoride to drinking water, the use of fluoride dentifrices and rinses, application of topical fluoride in the dental office, and improved dental hygiene. Despite these advances, dental decay continues to be the leading cause of tooth loss. With the improvements over the past several decades, the majority of newly discovered carious lesions tend to be localized to the occlusal pits and fissures of the posterior dentition and the proximal contact sites. These early carious lesions may be often obscured in the complex and convoluted topography of the pits and fissures or may be concealed by debris that frequently accumulates in those regions of the posterior teeth. Moreover, such lesions are difficult to detect in the early stages of development.

[0006] Dental caries may be a dynamic disease that is characterized by tooth demineralization leading to an increase in the porosity of the enamel surface. Leaving these lesions untreated may potentially lead to cavities reaching the dentine and pulp and perhaps eventually causing tooth loss. Occlusal surfaces (bite surfaces) and approximal surfaces (between the teeth) are among the most susceptible sites of demineralization due to acid attack from bacterial by-products in the biofilm. Therefore, there is a need for detection of lesions at an early stage, so that preventive agents may be used to inhibit or reverse the demineralization.

[0007] Traditional methods for caries detection include visual examination and tactile probing with a sharp dental exploration tool, often assisted by radiographic (x-ray) imaging. However, detection using these methods may be somewhat subjective; and, by the time that caries are evident under visual and tactile examination, the disease may have already progressed to an

advanced stage. Also, because of the ionizing nature of x-rays, they are dangerous to use (limited use with adults, and even less used with children). Although x-ray methods are suitable for approximal surface lesion detection, they offer reduced utility for screening early caries in occlusal surfaces due to their lack of sensitivity at very early stages of the disease.

[0008] Some of the current imaging methods are based on the observation of the changes of the light transport within the tooth, namely absorption, scattering, transmission, reflection and/or fluorescence of light. Porous media may scatter light more than uniform media. Taking advantage of this effect, the Fiber-optic trans-illumination is a qualitative method used to highlight the lesions within teeth by observing the patterns formed when white light, pumped from one side of the tooth, is scattered away and/or absorbed by the lesion. This technique may be difficult to quantify due to an uneven light distribution inside the tooth.

[0009] Another method called quantitative light-induced fluorescence – QLF – relies on different fluorescence from solid teeth and caries regions when excited with bright light in the visible. For example, when excited by relatively high intensity blue light, healthy tooth enamel yields a higher intensity of fluorescence than does demineralized enamel that has been damaged by caries infection or any other cause. On the other hand, for excitation by relatively high intensity of red light, the opposite magnitude change occurs, since this is the region of the spectrum for which bacteria and bacterial by-products in carious regions absorb and fluoresce more pronouncedly than do healthy areas. However, the image provided by QLF may be difficult to assess due to relatively poor contrast between healthy and infected areas. Moreover, QLF may have difficulty discriminating between white spots and stains because both produce similar effects. Stains on teeth are commonly observed in the occlusal sites of teeth, and this obscures the detection of caries using visible light.

[0010] As described in this disclosure, the near-infrared region of the spectrum offers a novel approach to imaging carious regions because scattering is reduced and absorption by stains is low. For example, it has been demonstrated that the scattering by enamel tissues reduces in the form of $1/(\text{wavelength})^3$, e.g., inversely as the cube of wavelength. By using a broadband light source in the short-wave infrared (SWIR) part of the spectrum, which corresponds approximately to 1400nm to

2500nm, lesions in the enamel and dentine may be observed. In one embodiment, intact teeth have low reflection over the SWIR wavelength range. In the presence of caries, the scattering increases, and the scattering is a function of wavelength; hence, the reflected signal decreases with increasing wavelength. Moreover, particularly when caries exist in the dentine region, water build up may occur, and dips in the SWIR spectrum corresponding to the water absorption lines may be observed. The scattering and water absorption as a function of wavelength may thus be used for early detection of caries and for quantifying the degree of demineralization.

[0011] SWIR light may be generated by light sources such as lamps, light emitting diodes, one or more laser diodes, super-luminescent laser diodes, and fiber-based super-continuum sources. The SWIR super-continuum light sources advantageously may produce high intensity and power, as well as being a nearly transform-limited beam that may also be modulated. Also, apparatuses for caries detection may include C-clamps over teeth, a handheld device with light input and light detection, which may also be attached to other dental equipment such as drills. Alternatively, a mouth-guard type apparatus may be used to simultaneously illuminate one or more teeth. Fiber optics may be conveniently used to guide the light to the patient as well as to transport the signal back to one or more detectors and receivers.

[0012] In one embodiment, a diagnostic system includes a light source configured to generate an output optical beam comprising one or more semiconductor sources configured to generate an input beam, one or more optical amplifiers configured to receive at least a portion of the input beam and to deliver an intermediate beam to an output end of the one or more optical amplifiers, and one or more optical fibers configured to receive at least a portion of the intermediate beam and to deliver at least the portion of the intermediate beam to a distal end of the one or more optical fibers to form a first optical beam. A nonlinear element is configured to receive at least a portion of the first optical beam and to broaden a spectrum associated with the at least a portion of the first optical beam to at least 10 nanometers through a nonlinear effect in the nonlinear element to form the output optical beam with an output beam broadened spectrum, wherein at least a portion of the output beam broadened spectrum comprises a short-wave infrared wavelength between approximately 1400 nanometers and approximately 2500 nanometers, and wherein at least a portion of the one of more fibers is a fused silica fiber with a core diameter less than approximately 400

microns. An interface device is configured to receive a received portion of the output optical beam and to deliver a delivered portion of the output optical beam to a sample comprising enamel and dentine, wherein the delivered portion of the output optical beam is configured to generate a spectroscopy output beam from the sample. A receiver is configured to receive at least a portion of the spectroscopy output beam having a bandwidth of at least 10 nanometers and to process the portion of the spectroscopy output beam to generate an output signal based on a wavelength dependence of the spectroscopy output beam over the bandwidth of at least 10 nanometers.

[0013] In another embodiment, a measurement system includes a light source configured to generate an output optical beam comprising a plurality of semiconductor sources configured to generate an input optical beam, a multiplexer configured to receive at least a portion of the input optical beam and to form an intermediate optical beam, and one or more fibers configured to receive at least a portion of the intermediate optical beam and to form the output optical beam, wherein the output optical beam comprises one or more optical wavelengths. An interface device is configured to receive a received portion of the output optical beam and to deliver a delivered portion of the output optical beam to a sample comprising enamel and dentine, wherein the delivered portion of the output optical beam is configured to generate a spectroscopy output beam from the sample. A receiver is configured to receive at least a portion of the spectroscopy output beam having a bandwidth of at least 10 nanometers and to process the portion of the spectroscopy output beam to generate an output signal based on a wavelength dependence of the spectroscopy output beam over the bandwidth of at least 10 nanometers.

[0014] In yet another embodiment, a method of measuring includes generating an output optical beam comprising generating an input optical beam from a plurality of semiconductor sources, multiplexing at least a portion of the input optical beam and forming an intermediate optical beam, and guiding at least a portion of the intermediate optical beam and forming the output optical beam, wherein the output optical beam comprises one or more optical wavelengths. The method may also include receiving a received portion of the output optical beam and delivering a delivered portion of the output optical beam to a sample, wherein the sample comprises enamel and dentine. The method may further include generating a spectroscopy output beam having a bandwidth of at least 10 nanometers from the sample, receiving at least a portion of the spectroscopy output beam, and

processing the portion of the spectroscopy output beam and generating an output signal based on a wavelength dependence of the spectroscopy output beam over the bandwidth of at least 10 nanometers.

BRIEF DESCRIPTION OF THE DRAWINGS

[0015] For a more complete understanding of the present disclosure, and for further features and advantages thereof, reference is now made to the following description taken in conjunction with the accompanying drawings, in which:

[0016] FIGURE 1 illustrates the structure of a tooth.

[0017] FIGURE 2A shows the attenuation coefficient for dental enamel and water versus wavelength from approximately 600nm to 2600nm.

[0018] FIGURE 2B illustrates the absorption spectrum of intact enamel and dentine in the wavelength range of approximately 1.2 to 2.4 microns.

[0019] FIGURE 3 shows the near infrared spectral reflectance over the wavelength range of approximately 800nm to 2500nm from an occlusal tooth surface. The black diamonds correspond to the reflectance from a sound, intact tooth section. The asterisks correspond to a tooth section with an enamel lesion. The circles correspond to a tooth section with a dentine lesion.

[0020] FIGURE 4 illustrates a hand-held dental tool design of a human interface that may also be coupled with other dental tools.

[0021] FIGURE 5 illustrates a clamp design of a human interface to cap over one or more teeth and perform a non-invasive measurement for dental caries.

[0022] FIGURE 6 shows a mouth guard design of a human interface to perform a non-invasive measurement for dental caries.

[0023] FIGURE 7 illustrates a block diagram or building blocks for constructing high power laser diode assemblies.

[0024] FIGURE 8 shows a platform architecture for different wavelength ranges for an all-fiber-integrated, high powered, super-continuum light source.

[0025] FIGURE 9 illustrates one embodiment for a short-wave infrared super-continuum light source.

[0026] FIGURE 10 shows the output spectrum from the SWIR SC laser of FIGURE 9 when about 10m length of fiber for SC generation is used. This fiber is a single-mode, non-dispersion shifted fiber that is optimized for operation near 1550nm.

[0027] FIGURE 11A illustrates a schematic of the experimental set-up for measuring the diffuse reflectance spectroscopy using the SWIR-SC light source of FIGURES 9 and 10.

[0028] FIGURE 11B shows exemplary reflectance from a sound enamel region, an enamel lesion region, and a dentine lesion region. The spectra are normalized to have equal value near 2050nm.

[0029] FIGURE 12 illustrates high power SWIR-SC lasers that may generate light between approximately 1.4-1.8 microns (top) or approximately 2-2.5 microns (bottom).

[0030] FIGURE 13 schematically shows that the medical measurement device can be part of a personal or body area network that communicates with another device (e.g., smart phone or tablet) that communicates with the cloud. The cloud may in turn communicate information with the user, dental or healthcare providers, or other designated recipients.

DETAILED DESCRIPTION OF EXAMPLE EMBODIMENTS

[0031] As required, detailed embodiments of the present disclosure are disclosed herein; however, it is to be understood that the disclosed embodiments are merely exemplary of the disclosure that may be embodied in various and alternative forms. The figures are not necessarily to

scale; some features may be exaggerated or minimized to show details of particular components. Therefore, specific structural and functional details disclosed herein are not to be interpreted as limiting, but merely as a representative basis for teaching one skilled in the art to variously employ the present disclosure.

[0032] Near-infrared (NIR) and SWIR light may be preferred for caries detection compared to visible light imaging because the NIR/SWIR wavelengths generally have lower absorption by stains and deeper penetration into teeth. Hence, NIR/SWIR light may provide a caries detection method that can be non-invasive, non-contact and relatively stain insensitive. Broadband light may provide further advantages because carious regions may demonstrate spectral signatures from water absorption and the wavelength dependence of porosity in the scattering of light.

[0033] In general, the near-infrared region of the electromagnetic spectrum covers between approximately 0.7 microns (700nm) to about 2.5 microns (2500nm). However, it may also be advantageous to use just the short-wave infrared between approximately 1.4 microns (1400nm) and about 2.5 microns (2500nm). One reason for preferring the SWIR over the entire NIR may be to operate in the so-called "eye safe" window, which corresponds to wavelengths longer than about 1400nm. Therefore, for the remainder of the disclosure the SWIR will be used for illustrative purposes. However, it should be clear that the discussion that follows could also apply to using the NIR wavelength range, or other wavelength bands.

[0034] In particular, wavelengths in the eye safe window may not transmit down to the retina of the eye, and therefore, these wavelengths may be less likely to create permanent eye damage from inadvertent exposure. The near-infrared wavelengths have the potential to be dangerous, because the eye cannot see the wavelengths (as it can in the visible), yet they can penetrate and cause damage to the eye. Even if a practitioner is not looking directly at the laser beam, the practitioner's eyes may receive stray light from a reflection or scattering from some surface. Hence, it can always be a good practice to use eye protection when working around lasers. Since wavelengths longer than about 1400nm are substantially not transmitted to the retina or substantially absorbed in the retina, this wavelength range is known as the eye safe window. For wavelengths longer than 1400nm, in general only the cornea of the eye may receive or absorb the light radiation.

[0035] FIGURE 1 illustrates the structure of an exemplary cross-section of a tooth 100. The tooth 100 has a top layer called the crown 101 and below that a root 102 that reaches well into the gum 106 and bone 108 of the mouth. The exterior of the crown 101 is an enamel layer 103, and below the enamel is a layer of dentine 104 that sits atop a layer of cementum 107. Below the dentine 104 is a pulp region 105, which comprises within it blood vessels 109 and nerves 110. If the light can penetrate the enamel 103 and dentine 104, then the blood flow and blood constituents may be measured through the blood vessels in the dental pulp 105. While the amount of blood flow in the capillaries of the dental pulp 105 may be less than an artery or vein, the smaller blood flow could still be advantageous for detecting or measuring blood constituents as compared to detection through the skin if there is less interfering spectral features from the tooth. Although the structure of a molar tooth is illustrated in FIGURE 1, other types of teeth also have similar structure. For example, different types of teeth include molars, pre-molars, canine and incisor teeth.

[0036] As used throughout this document, the term "couple" and or "coupled" refers to any direct or indirect communication between two or more elements, whether or not those elements are physically connected to one another. As used throughout this disclosure, the term "spectroscopy" means that a tissue or sample is inspected by comparing different features, such as wavelength (or frequency), spatial location, transmission, absorption, reflectivity, scattering, refractive index, or opacity. In one embodiment, "spectroscopy" may mean that the wavelength of the light source is varied, and the transmission, absorption, or reflectivity of the tissue or sample is measured as a function of wavelength. In another embodiment, "spectroscopy" may mean that the wavelength dependence of the transmission, absorption or reflectivity is compared between different spatial locations on a tissue or sample. As an illustration, the "spectroscopy" may be performed by varying the wavelength of the light source, or by using a broadband light source and analyzing the signal using a spectrometer, wavemeter, or optical spectrum analyzer.

[0037] As used throughout this disclosure, the term "fiber laser" refers to a laser or oscillator that has as an output light or an optical beam, wherein at least a part of the laser comprises an optical fiber. For instance, the fiber in the "fiber laser" may comprise one of or a combination of a single mode fiber, a multi-mode fiber, a mid-infrared fiber, a photonic crystal fiber, a doped fiber, a gain fiber, or, more generally, an approximately cylindrically shaped waveguide or light-pipe. In one

embodiment, the gain fiber may be doped with rare earth material, such as ytterbium, erbium, and/or thulium, for example. In another embodiment, the mid-infrared fiber may comprise one or a combination of fluoride fiber, ZBLAN fiber, chalcogenide fiber, tellurite fiber, or germanium doped fiber. In yet another embodiment, the single mode fiber may include standard single-mode fiber, dispersion shifted fiber, non-zero dispersion shifted fiber, high-nonlinearity fiber, and small core size fibers.

[0038] As used throughout this disclosure, the term "pump laser" refers to a laser or oscillator that has as an output light or an optical beam, wherein the output light or optical beam is coupled to a gain medium to excite the gain medium, which in turn may amplify another input optical signal or beam. In one particular example, the gain medium may be a doped fiber, such as a fiber doped with ytterbium, erbium, and/or thulium. In one embodiment, the "pump laser" may be a fiber laser, a solid state laser, a laser involving a nonlinear crystal, an optical parametric oscillator, a semiconductor laser, or a plurality of semiconductor lasers that may be multiplexed together. In another embodiment, the "pump laser" may be coupled to the gain medium by using a fiber coupler, a dichroic mirror, a multiplexer, a wavelength division multiplexer, a grating, or a fused fiber coupler.

[0039] As used throughout this document, the term "super-continuum" and or "supercontinuum" and or "SC" refers to a broadband light beam or output that comprises a plurality of wavelengths. In a particular example, the plurality of wavelengths may be adjacent to one-another, so that the spectrum of the light beam or output appears as a continuous band when measured with a spectrometer. In one embodiment, the broadband light beam may have a bandwidth or at least 10nm. In another embodiment, the "super-continuum" may be generated through nonlinear optical interactions in a medium, such as an optical fiber or nonlinear crystal. For example, the "super-continuum" may be generated through one or a combination of nonlinear activities such as four-wave mixing, the Raman effect, modulational instability, and self-phase modulation.

[0040] As used throughout this disclosure, the terms "optical light" and or "optical beam" and or "light beam" refer to photons or light transmitted to a particular location in space. The

"optical light" and or "optical beam" and or "light beam" may be modulated or unmodulated, which also means that they may or may not contain information. In one embodiment, the "optical light" and or "optical beam" and or "light beam" may originate from a fiber, a fiber laser, a laser, a light emitting diode, a lamp, a pump laser, or a light source.

TRANSMISSION OR REFLECTION THROUGH TEETH

[0041] The transmission, absorption and reflection from teeth has been studied in the near infrared, and, although there are some features, the enamel and dentine appear to be fairly transparent in the near infrared (particularly SWIR wavelengths between about 1400 and 2500nm). For example, the absorption or extinction ratio for light transmission has been studied. FIGURE 2A illustrates the attenuation coefficient 200 for dental enamel 201 (filled circles) and the absorption coefficient of water 202 (open circles) versus wavelength. Near-infrared light may penetrate much further without scattering through all the tooth enamel, due to the reduced scattering coefficient in normal enamel. Scattering in enamel may be fairly strong in the visible, but decreases as approximately $1/(\text{wavelength})^3$ [i.e., inverse of the cube of the wavelength] with increasing wavelength to a value of only 2-3 cm-1 at 1310nm and 1550nm in the near infrared. Therefore, enamel may be virtually transparent in the near infrared with optical attenuation 1-2 orders of magnitude less than in the visible range.

[0042] As another example, FIGURE 2B illustrates the absorption spectrum 250 of intact enamel 251 (dashed line) and dentine 252 (solid line) in the wavelength range of approximately 1.2 to 2.4 microns. In the near infrared there are two absorption bands in the areas of about 1.5 and 2 microns. The band with a peak around 1.57 microns may be attributed to the overtone of valent vibration of water present in both enamel and dentine. In this band, the absorption is greater for dentine than for enamel, which may be related to the large water content in this tissue. In the region of 2 microns, dentine may have two absorption bands, and enamel one. The band with a maximum near 2.1 microns may belong to the overtone of vibration of PO hydroxyapatite groups, which is the main substance of both enamel and dentine. Moreover, the band with a peak near 1.96 microns in

dentine may correspond to water absorption (dentine may contain substantially higher water than enamel).

[0043] In addition to the absorption coefficient, the reflectance from intact teeth and teeth with dental caries (e.g., cavities) has been studied. In one embodiment, FIGURE 3 shows the near infrared spectral reflectance 300 over the wavelength range of approximately 800nm to 2500nm from an occlusal (e.g., top) tooth surface 304. The curve with black diamonds 301 corresponds to the reflectance from a sound, intact tooth section. The curve with asterisks (*) 302 corresponds to a tooth section with an enamel lesion. The curve with circles 303 corresponds to a tooth section with a dentine lesion. Thus, when there is a lesion, more scattering occurs and there may be an increase in the reflected light.

[0044] For wavelengths shorter than approximately 1400nm, the shapes of the spectra remain similar, but the amplitude of the reflection changes with lesions. Between approximately 1400nm and 2500nm, an intact tooth 301 has low reflectance (e.g., high transmission), and the reflectance appears to be more or less independent of wavelength. On the other hand, in the presence of lesions 302 and 303, there is increased scattering, and the scattering loss may be wavelength dependent. For example, the scattering loss may decrease as the inverse of some power of wavelength, such as $1/(\text{wavelength})^3$ -- so, the scattering loss decreases with longer wavelengths. When there is a lesion in the dentine 303, more water can accumulate in the area, so there is also increased water absorption. For example, the dips near 1450nm and 1900nm may correspond to water absorption, and the reflectance dips are particularly pronounced in the dentine lesion 303.

[0045] FIGURE 3 may point to several novel techniques for early detection and quantification of carious regions. One method may be to use a relatively narrow wavelength range (for example, from a laser diode or super-luminescent laser diode) in the wavelength window below 1400nm. In one embodiment, wavelengths in the vicinity of 1310nm may be used, which is a standard telecommunications wavelength where appropriate light sources are available. Also, it may be advantageous to use a super-luminescent laser diode rather than a laser diode, because the broader bandwidth may avoid the production of laser speckle that can produce interference patterns due to light's scattering after striking irregular surfaces. As FIGURE 3 shows, the amplitude of the

reflected light (which may also be proportional to the inverse of the transmission) may increase with dental caries. Hence, comparing the reflected light from a known intact region with a suspect region may help identify carious regions. However, one difficulty with using a relatively narrow wavelength range and relying on amplitude changes may be the calibration of the measurement. For example, the amplitude of the reflected light may depend on many factors, such as irregularities in the dental surface, placement of the light source and detector, distance of the measurement instrument from the tooth, etc.

[0046] In one embodiment, use of a plurality of wavelengths can help to better calibrate the dental caries measurement. For example, a plurality of laser diodes or super-luminescent laser diodes may be used at different center wavelengths. Alternately, a lamp or alternate broadband light source may be used followed by appropriate filters, which may be placed after the light source or before the detectors. In one example, wavelengths near 1090nm, 1440nm and 1610nm may be employed. The reflection from the tooth 305 appears to reach a local maximum near 1090nm in the representative embodiment illustrated. Also, the reflectance near 1440nm 306 is higher for dental caries, with a distinct dip particularly for dentine caries 303. Near 1610nm 307, the reflection is also higher for carious regions. By using a plurality of wavelengths, the values at different wavelengths may help quantify a caries score. In one embodiment, the degree of enamel lesions may be proportional to the ratio of the reflectance near 1610nm divided by the reflectance near 1090nm. Also, the degree of dentine lesion may be proportional to the difference between the reflectance near 1610nm and 1440nm, with the difference then divided by the reflectance near 1090nm. Although one set of wavelengths has been described, other wavelengths may also be used and are intended to be covered by this disclosure.

[0047] In yet another embodiment, it may be further advantageous to use all of some fraction of the SWIR between approximately 1400 and 2500nm. For example, a SWIR super-continuum light source could be used, or a lamp source could be used. On the receiver side, a spectrometer and/or dispersive element could be used to discriminate the various wavelengths. As FIGURE 3 shows, an intact tooth 301 has a relatively low and featureless reflectance over the SWIR. On the other hand, with a carious region there is more scattering, so the reflectance 302,303 increases in amplitude. Since the scattering is inversely proportional to wavelength or some power of

wavelength, the carious region reflectance 302, 303 also decreases with increasing wavelength. Moreover, the carious region may contain more water, so there are dips in the reflectance near the water absorption lines 306 and 308. The degree of caries or caries score may be quantified by the shape of the spectrum over the SWIR, taking ratios of different parts of the spectrum, or some combination of this and other spectral processing methods.

[0048] Although several methods of early caries detection using spectral reflectance have been described, other techniques could also be used and are intended to be covered by this disclosure. For example, transmittance may be used rather than reflectance, or a combination of the two could be used. Moreover, the transmittance, reflectance and/or absorbance could also be combined with other techniques, such as quantitative light-induced fluorescence or fiber-optic trans-illumination. Also, the SWIR could be advantageous, but other parts of the infrared, near-infrared or visible wavelengths may also be used consistent with this disclosure.

[0049] One other benefit of the absorption, transmission or reflectance in the near infrared and SWIR may be that stains and non-calcified plaque are not visible in this wavelength range, enabling better discrimination of defects, cracks, and demineralized areas. For example, dental calculus, accumulated plaque, and organic stains and debris may interfere significantly with visual diagnosis and fluorescence-based caries detection schemes in occlusal surfaces. In the case of using quantitative light-induced fluorescence, such confounding factors typically may need to be removed by prophylaxis (abrasive cleaning) before reliable measurements can be taken. Surface staining at visible wavelengths may further complicate the problem, and it may be difficult to determine whether pits and fissures are simply stained or demineralized. On the other hand, staining and pigmentation generally interfere less with NIR or SWIR imaging. For example, NIR and SWIR light may not be absorbed by melanin and porphyrins produced by bacteria and those found in food dyes that accumulate in dental plaque and are responsible for the pigmentation.

HUMAN INTERFACE FOR MEASUREMENT SYSTEM

[0050] A number of different types of measurements may be used to image for dental caries, particularly early detection of dental caries. A basic feature of the measurements may be that the

optical properties are measured as a function of wavelength at a plurality of wavelengths. As further described below, the light source may output a plurality of wavelengths, or a continuous spectrum over a range of wavelengths. In one embodiment, the light source may cover some or all of the wavelength range between approximately 1400nm and 2500nm. The signal may be received at a receiver, which may also comprise a spectrometer or filters to discriminate between different wavelengths. The signal may also be received at a camera, which may also comprise filters or a spectrometer. In one embodiment, the spectral discrimination using filters or a spectrometer may be placed after the light source rather than at the receiver. The receiver usually comprises one or more detectors (optical-to-electrical conversion element) and electrical circuitry. The receiver may also be coupled to analog to digital converters, particularly if the signal is to be fed to a digital device.

[0051] Referring to FIGURE 1, one or more light sources 111 may be used for illumination. In one embodiment, a transmission measurement may be performed by directing the light source output 111 to the region near the interface between the gum 106 and dentine 104. In one embodiment, the light may be directed using a light guide or a fiber optic. The light may then propagate through the dental pulp 105 to the other side, where the light may be incident on one or more detectors or another light guide to transport the signal to 112 a spectrometer, receiver, and/or camera, for example. In one embodiment, the light source may be directed to one or more locations near the interface between the gum 106 and dentine 104 (in one example, could be from the two sides of the tooth). The transmitted light may then be detected in the occlusal surface above the tooth using a 112 spectrometer, receiver, or camera, for example. In another embodiment, a reflectance measurement may be conducted by directing the light source output 111 to, for example, the occlusal surface of the tooth, and then detecting the reflectance at a 113 spectrometer, receiver or camera. Although a few embodiments for imaging the tooth are described, other embodiments and techniques may also be used and are intended to be covered by this disclosure. These optical techniques may measure optical properties such as reflectance, transmittance, absorption, or luminescence.

[0052] In one embodiment, FIGURE 4 shows that the light source and/or detection system may be integrated with a dental hand-piece 400. The hand-piece 400 may also include other dental equipment, such as a drill, pick, air spray or water cooling stream. The dental hand-piece 400 may

include a housing 401 and a motor housing 402 (in some embodiments such as with a drill, a motor may be placed in this section). The end of hand-piece 403 that interfaces with the tooth may be detachable, and it may also have the light input and output end. The dental hand-piece 400 may also have an umbilical cord 404 for connecting to power supplies, diagnostics, or other equipment, for example.

[0053] A light guide 405 may be integrated with the hand-piece 400, either inside the housing 401, 402 or adjacent to the housing. In one embodiment, a light source 410 may be contained within the housing 401, 402. In an alternative embodiment, the hand-piece 400 may have a coupler 410 to couple to an external light source 411 and/or detection system or receiver 412. The light source 411 may be coupled to the hand-piece 400 using a light guide or fiber optic cable 406. In addition, the detection system or receiver 412 may be coupled to the hand-piece 400 using one or more light guides, fiber optic cable or a bundle of fibers 407.

[0054] The light incident on the tooth may exit the hand-piece 400 through the end 403. The end 403 may also have a lens system or curved mirror system to collimate or focus the light. In one embodiment, if the light source is integrated with a tool such as a drill, then the light may reach the tooth at the same point as the tip of the drill. The reflected or transmitted light from the tooth may then be observed externally and/or guided back through the light guide 405 in the hand-piece 400. If observed externally, there may be a lens system 408 for collecting the light and a detection system 409 that may have one or more detectors and electronics. If the light is to be guided back through the hand-piece 400, then the reflected light may transmit through the light guide 405 back to the detection system or receiver 412. In one embodiment, the incident light may be guided by a fiber optic through the light guide 405, and the reflected light may be captured by a series of fibers forming a bundle adjacent to or surrounding the incident light fiber.

[0055] In another embodiment, a "clamp" design 500 may be used as a cap over one or more teeth, as illustrated in FIGURE 5. The clamp design may be different for different types of teeth, or it may be flexible enough to fit over different types of teeth. For example, different types of teeth include the molars (toward the back of the mouth), the premolars, the canine, and the incisors (toward the front of the mouth). One embodiment of the clamp-type design is illustrated in FIGURE

5 for a molar tooth 508. The C-clamp 501 may be made of a plastic or rubber material, and it may comprise a light source input 502 and a detector output 503 on the front or back of the tooth, for example.

[0056] The light source input 502 may comprise a light source directly, or it may have light guided to it from an external light source. Also, the light source input 502 may comprise a lens system to collimate or focus the light across the tooth. The detector output 503 may comprise a detector directly, or it may have a light guide to transport the signal to an external detector element. The light source input 502 may be coupled electrically or optically through 504 to a light input 506. For example, if the light source is external in 506, then the coupling element 504 may be a light guide, such as a fiber optic. Alternately, if the light source is contained in 502, then the coupling element 504 may be electrical wires connecting to a power supply in 506. Similarly, the detector output 503 may be coupled to a detector output unit 507 with a coupling element 505, which may be one or more electrical wires or a light guide, such as a fiber optic. This is just one example of a clamp over one or more teeth, but other embodiments may also be used and are intended to be covered by this disclosure. For example, if reflectance from the teeth is to be used in the measurement, then the light input 502 and detected light input 503 may be on the same side of the tooth.

[0057] In yet another embodiment, one or more light source ports and sensor ports may be used in a mouth-guard type design. For example, one embodiment of a dental mouth guard 600 is illustrated in FIGURE 6. The structure of the mouth guard 601 may be similar to mouth guards used in sports (e.g., when playing football or boxing) or in dental trays used for applying fluoride treatment, and the mouth guard may be made from plastic, rubber, or any other suitable materials. As an example, the mouth guard may have one or more light source input ports 602, 603 and one or more detector output ports 604, 605. Although six input and output ports are illustrated, any number of ports may be used.

[0058] Similar to the clamp design described above, the light source inputs 602, 603 may comprise one or more light sources directly, or they may have light guided to them from an external light source. Also, the light source inputs 602, 603 may comprise lens systems to collimate or focus

the light across the teeth. The detector outputs 604, 605 may comprise one or more detectors directly, or they may have one or more light guides to transport the signals to an external detector element. The light source inputs 602, 603 may be coupled electrically or optically through 606 to a light input 607. For example, if the light source is external in 607, then the one or more coupling elements 606 may be one or more light guides, such as a fiber optic. Alternately, if the light sources are contained in 602, 603, then the coupling element 606 may be one or more electrical wires connecting to a power supply in 607. Similarly, the detector outputs 604, 605 may be coupled to a detector output unit 609 with one or more coupling elements 608, which may be one or more electrical wires or one or more light guides, such as a fiber optic. This is just one example of a mouth guard design covering a plurality of teeth, but other embodiments may also be used and are intended to be covered by this disclosure. For instance, the position of the light source inputs and detector output ports could be exchanged, or some mixture of locations of light source inputs and detector output ports could be used. Also, if reflectance from the teeth is to be measured, then the light sources and detectors may be on the same side of the tooth. Moreover, it may be advantageous to pulse the light source with a particular pulse width and pulse repetition rate, and then the detection system can measure the pulsed light returned from or transmitted through the tooth. Using a lock-in type technique (e.g., detecting at the same frequency as the pulsed light source and also possibly phase locked to the same signal), the detection system may be able to reject background or spurious signals and increase the signal-to-noise ratio of the measurement.

[0059] Other elements may be added to the human interface designs of FIGURES 4-6 and are also intended to be covered by this disclosure. For instance, in one embodiment it may be desirable to have replaceable inserts that may be disposable. Particularly in a dentist's or doctor's office or hospital setting, the same instrument may be used with a plurality of patients. Rather than disinfecting the human interface after each use, it may be preferable to have disposable inserts that can be thrown away after each use. In one embodiment, a thin plastic coating material may enclose the clamp design of FIGURE 5 or mouth guard design of FIGURE 6. The coating material may be inserted before each use, and then after the measurement is exercised the coating material may be peeled off and replaced. The coating or covering material may be selected based on suitable optical properties that do not affect the measurement, or known optical properties that can be calibrated or

compensated for during measurement. Such a design may save the dentist or physician or user considerable time, while at the same time provide the business venture with a recurring cost revenue source.

LIGHT SOURCES FOR NEAR INFRARED

[0060] There are a number of light sources that may be used in the near infrared. To be more specific, the discussion below will consider light sources operating in the short wave infrared (SWIR), which may cover the wavelength range of approximately 1400nm to 2500nm. Other wavelength ranges may also be used for the applications described in this disclosure, so the discussion below is merely provided as exemplary types of light sources. The SWIR wavelength range may be valuable for a number of reasons. First, the SWIR corresponds to a transmission window through water and the atmosphere. Second, the so-called "eye-safe" wavelengths are wavelengths longer than approximately 1400nm. Third, the SWIR covers the wavelength range for nonlinear combinations of stretching and bending modes as well as the first overtone of C-H stretching modes. Thus, for example, glucose and ketones among other substances may have unique signatures in the SWIR. Moreover, many solids have distinct spectral signatures in the SWIR, so particular solids may be identified using stand-off detection or remote sensing. For instance, many explosives have unique signatures in the SWIR.

[0061] Different light sources may be selected for the SWIR based on the needs of the application. Some of the features for selecting a particular light source include power or intensity, wavelength range or bandwidth, spatial or temporal coherence, spatial beam quality for focusing or transmission over long distance, and pulse width or pulse repetition rate. Depending on the application, lamps, light emitting diodes (LEDs), laser diodes (LD's), tunable LD's, super-luminescent laser diodes (SLDs), fiber lasers or super-continuum sources (SC) may be advantageously used. Also, different fibers may be used for transporting the light, such as fused silica fibers, plastic fibers, mid-infrared fibers (e.g., tellurite, chalcogenides, fluorides, ZBLAN, etc), or a hybrid of these fibers.

[0062] Lamps may be used if low power or intensity of light is required in the SWIR, and if an incoherent beam is suitable. In one embodiment, in the SWIR an incandescent lamp that can be used is based on tungsten and halogen, which have an emission wavelength between approximately 500nm to 2500nm. For low intensity applications, it may also be possible to use thermal sources, where the SWIR radiation is based on the black body radiation from the hot object. Although the thermal and lamp based sources are broadband and have low intensity fluctuations, it may be difficult to achieve a high signal-to-noise ratio due to the low power levels. Also, the lamp based sources tend to be energy inefficient.

[0063] In another embodiment, LED's can be used that have a higher power level in the SWIR wavelength range. LED's also produce an incoherent beam, but the power level can be higher than a lamp and with higher energy efficiency. Also, the LED output may more easily be modulated, and the LED provides the option of continuous wave or pulsed mode of operation. LED's are solid state components that emit a wavelength band that is of moderate width, typically between about 20nm to 40nm. There are also so-called super-luminescent LEDs that may even emit over a much wider wavelength range. In another embodiment, a wide band light source may be constructed by combining different LEDs that emit in different wavelength bands, some of which could preferably overlap in spectrum. One advantage of LEDs as well as other solid state components is the compact size that they may be packaged into.

[0064] In yet another embodiment, various types of laser diodes may be used in the SWIR wavelength range. Just as LEDs may be higher in power but narrower in wavelength emission than lamps and thermal sources, the LDs may be yet higher in power but yet narrower in wavelength emission than LEDs. Different kinds of LDs may be used, including Fabry-Perot LDs, distributed feedback (DFB) LDs, distributed Bragg reflector (DBR) LDs. Since the LDs have relatively narrow wavelength range (typically under 10nm), in one embodiment a plurality of LDs may be used that are at different wavelengths in the SWIR. The various LDs may be spatially multiplexed, polarization multiplexed, wavelength multiplexed, or a combination of these multiplexing methods. Also, the LDs may be fiber pig-tailed or have one or more lenses on the output to collimate or focus the light. Another advantage of LDs is that they may be packaged compactly and may have a spatially coherent beam output. Moreover, tunable LDs that can tune over a range of wavelengths

are also available. The tuning may be done by varying the temperature, or electrical current may be used in particular structures such as distributed Bragg reflector (DBR) LDs, for example. In another embodiment, external cavity LDs may be used that have a tuning element, such as a fiber grating or a bulk grating, in the external cavity.

[0065] In another embodiment, super-luminescent laser diodes may provide higher power as well as broad bandwidth. An SLD is typically an edge emitting semiconductor light source based on super-luminescence (e.g., this could be amplified spontaneous emission). SLDs combine the higher power and brightness of LDs with the low coherence of conventional LEDs, and the emission band for SLD's may be 5 to 100nm wide, preferably in the 60 to 100nm range. Although currently SLDs are commercially available in the wavelength range of approximately 400nm to 1700nm, SLDs could and may in the future be made to cover a broader region of the SWIR.

[0066] In yet another embodiment, high power LDs for either direct excitation or to pump fiber lasers and SC light sources may be constructed using one or more laser diode bar stacks. FIGURE 7 shows an example of a block diagram 700 or building blocks for constructing the high power LDs. In this embodiment, one or more diode bar stacks 701 may be used, where the diode bar stack may be an array of several single emitter LDs. Since the fast axis (e.g., vertical direction) may be nearly diffraction limited while the slow-axis (e.g., horizontal axis) may be far from diffraction limited, different collimators 702 may be used for the two axes.

[0067] Then, the brightness may be increased by spatially combining the beams from multiple stacks 703. The combiner may include spatial interleaving, it may include wavelength multiplexing, or it may involve a combination of the two. Different spatial interleaving schemes may be used, such as using an array of prisms or mirrors with spacers to bend one array of beams into the beam path of the other. In another embodiment, segmented mirrors with alternate high-reflection and anti-reflection coatings may be used. Moreover, the brightness may be increased by polarization beam combining 704 the two orthogonal polarizations, such as by using a polarization beam splitter. In a particular embodiment, the output may then be focused or coupled into a large diameter core fiber. As an example, typical dimensions for the large diameter core fiber range from diameters of approximately 100 microns to 400 microns or more. Alternatively or in addition, a

custom beam shaping module 705 may be used, depending on the particular application. For example, the output of the high power LD may be used directly 706, or it may be fiber coupled 707 to combine, integrate, or transport the high power LD energy. These high power LDs may grow in importance because the LD powers can rapidly scale up. For example, instead of the power being limited by the power available from a single emitter, the power may increase in multiples depending on the number of diodes multiplexed and the size of the large diameter fiber. Although FIGURE 7 is shown as one embodiment, some or all of the elements may be used in a high power LD, or additional elements may also be used.

SWIR SUPER-CONTINUUM LASERS

[0068] Each of the light sources described above have particular strengths, but they also may have limitations. For example, there is typically a trade-off between wavelength range and power output. Also, sources such as lamps, thermal sources, and LEDs produce incoherent beams that may be difficult to focus to a small area and may have difficulty propagating for long distances. An alternative source that may overcome some of these limitations is an SC light source. Some of the advantages of the SC source may include high power and intensity, wide bandwidth, spatially coherent beam that can propagate nearly transform limited over long distances, and easy compatibility with fiber delivery.

[0069] Supercontinuum lasers may combine the broadband attributes of lamps with the spatial coherence and high brightness of lasers. By exploiting a modulational instability initiated supercontinuum (SC) mechanism, an all-fiber-integrated SC laser with no moving parts may be built using commercial-off-the-shelf (COTS) components. Moreover, the fiber laser architecture may be a platform where SC in the visible, near-infrared / SWIR, or mid-IR can be generated by appropriate selection of the amplifier technology and the SC generation fiber. But until recently, SC lasers were used primarily in laboratory settings since typically large, table-top, mode-locked lasers were used to pump nonlinear media such as optical fibers to generate SC light. However, those large pump lasers may now be replaced with diode lasers and fiber amplifiers that gained maturity in the telecommunications industry.

[0070] In one embodiment, an all-fiber-integrated, high-powered SC light source 800 may be elegant for its simplicity (FIGURE 8). The light may be first generated from a seed laser diode 801. For example, the seed LD 801 may be a distributed feedback (DFB) laser diode with a wavelength near 1542 or 1550 nm, with approximately 0.5–2.0 ns pulsed output, and with a pulse repetition rate between about one kilohertz to about 100MHz or more. The output from the seed laser diode may then be amplified in a multiple-stage fiber amplifier 802 comprising one or more gain fiber segments. In one embodiment, the first stage pre-amplifier 803 may be designed for optimal noise performance. For example, the pre-amplifier 803 may be a standard erbium-doped fiber amplifier or an erbium/ytterbium doped cladding pumped fiber amplifier. Between amplifier stages 803 and 806, it may be advantageous to use band-pass filters 804 to block amplified spontaneous emission and isolators 805 to prevent spurious reflections. Then, the power amplifier stage 806 may use a cladding-pumped fiber amplifier that may be optimized to minimize nonlinear distortion. The power amplifier fiber 806 may also be an erbium-doped fiber amplifier, if only low or moderate power levels are to be generated.

[0071] The SC generation 807 may occur in the relatively short lengths of fiber that follow the pump laser. The SC fiber length may range from around a few millimeters to 100m or more. In one embodiment, the SC generation may occur in a first fiber 808 where the modulational-instability initiated pulse break-up occurs primarily, followed by a second fiber 809 where the SC generation and spectral broadening occurs primarily.

[0072] In one embodiment, one or two meters of standard single-mode fiber (SMF) after the power amplifier stage may be followed by several meters of SC generation fiber. For this example, in the SMF the peak power may be several kilowatts and the pump light may fall in the anomalous group-velocity dispersion regime—often called the soliton regime. For high peak powers in the anomalous dispersion regime, the nanosecond pulses may be unstable due to a phenomenon known as modulational instability, which is basically parametric amplification in which the fiber nonlinearity helps to phase match the pulses. As a consequence, the nanosecond pump pulses may be broken into many shorter pulses as the modulational instability tries to form soliton pulses from the quasi-continuous-wave background. Although the laser diode and amplification process starts with approximately nanosecond-long pulses, modulational instability in the short length of SMF

fiber may form approximately 0.5 ps to several-picosecond-long pulses with high intensity. Thus, the few meters of SMF fiber may result in an output similar to that produced by mode-locked lasers, except in a much simpler and cost-effective manner.

[0073] The short pulses created through modulational instability may then be coupled into a nonlinear fiber for SC generation. The nonlinear mechanisms leading to broadband SC may include four-wave mixing or self-phase modulation along with the optical Raman effect. Since the Raman effect is self-phase-matched and shifts light to longer wavelengths by emission of optical photons, the SC may spread to longer wavelengths very efficiently. The short-wavelength edge may arise from four-wave mixing, and often times the short wavelength edge may be limited by increasing group-velocity dispersion in the fiber. In many instances, if the particular fiber used has sufficient peak power and SC fiber length, the SC generation process may fill the long-wavelength edge up to the transmission window.

[0074] Mature fiber amplifiers for the power amplifier stage 806 include ytterbium-doped fibers (near 1060 nm), erbium-doped fibers (near 1550nm), erbium/ytterbium-doped fibers (near 1550 nm), or thulium-doped fibers (near 2000nm). In various embodiments, candidates for SC fiber 809 include fused silica fibers (for generating SC between 0.8–2.7 μm), mid-IR fibers such as fluorides, chalcogenides, or tellurites (for generating SC out to 4.5 μm or longer), photonic crystal fibers (for generating SC between 0.4 and 1.7 μm), or combinations of these fibers. Therefore, by selecting the appropriate fiber-amplifier doping for 806 and nonlinear fiber 809, SC may be generated in the visible, near-IR / SWIR, or mid-IR wavelength region.

[0075] The configuration 800 of FIGURE 8 is just one particular example, and other configurations can be used and are intended to be covered by this disclosure. For example, further gain stages may be used, and different types of lossy elements or fiber taps may be used between the amplifier stages. In another embodiment, the SC generation may occur partially in the amplifier fiber and in the pig-tails from the pump combiner or other elements. In yet another embodiment, polarization maintaining fibers may be used, and a polarizer may also be used to enhance the polarization contrast between amplifier stages. Also, not discussed in detail are many accessories

that may accompany this set-up, such as driver electronics, pump laser diodes, safety shut-offs, and thermal management and packaging.

[0076] In one embodiment, one example of the SC laser that operates in the SWIR is illustrated in FIGURE 9. This SWIR SC source 900 produces an output of up to approximately 5W over a spectral range of about 1.5 to 2.4 microns, and this particular laser is made out of polarization maintaining components. The seed laser 901 is a distributed feedback (DFB) laser operating near 1542nm producing approximately 0.5nsec pulses at an about 8MHz repetition rate. The pre-amplifier 902 is forward pumped and uses about 2m length of erbium/ytterbium cladding pumped fiber 903 (often also called dual-core fiber)with an inner core diameter of 12 microns and outer core diameter of 130 microns. The pre-amplifier gain fiber 903 is pumped using a 10W laser diode near 940nm 905 that is coupled in using a fiber combiner 904.

[0077] In this particular 5W unit, the mid-stage between amplifier stages 902 and 906 comprises an isolator 907, a band-pass filter 908, a polarizer 909 and a fiber tap 910. The power amplifier 906 uses an approximately 4m length of the 12/130 micron erbium/ytterbium doped fiber 911 that is counter-propagating pumped using one or more 30W laser diodes near 940nm 912 coupled in through a combiner 913. An approximately 1-2 meter length of the combiner pig-tail helps to initiate the SC process, and then a length of PM-1550 fiber 915 (polarization maintaining, single-mode, fused silica fiber optimized for 1550nm) is spliced 914 to the combiner output.

[0078] If an output fiber of about 10m in length is used, then the resulting output spectrum 1000 is shown in FIGURE 10. The details of the output spectrum 1000 depend on the peak power into the fiber, the fiber length, and properties of the fiber such as length and core size, as well as the zero dispersion wavelength and the dispersion properties. For example, if a shorter length of fiber is used, then the spectrum actually reaches to longer wavelengths (e.g., a 2m length of SC fiber broadens the spectrum to about 2500nm). Also, if extra-dry fibers are used with less O-H content, then the wavelength edge may also reach to a longer wavelength. To generate more spectra toward the shorter wavelengths, the pump wavelength (in this case ~1542nm) should be close to the zero dispersion wavelength in the fiber. For example, by using a dispersion shifted fiber or so-called non-zero dispersion shifted fiber, the short wavelength edge may shift to shorter wavelengths.

[0079] In one particular embodiment, the SWIR-SC light source of FIGURE 9 with output spectrum in FIGURE 10 was used in preliminary experiments for examining the reflectance from different dental samples. A schematic of the experimental set-up 1100 for measuring the diffuse reflectance spectroscopy is illustrated in FIGURE 11A. The SC source 1101 in this embodiment was based on the design of FIGURE 9 and delivered approximately 1.6W of light over the wavelength range from about 1500-2400nm. The output beam 1102 was collimated, and then passed through a chopper 1103 (for lock-in detection at the receiver after the spectrometer 1106) and an aperture 1104 for localizing the beam on the tooth location. Different teeth 1105 with different lesions and caries were placed in front of the aperture 1104, and the scattered light was passed through a spectrometer 1106 and collected on a detector, whose signal was sent to a receiver. The tooth samples 1105 were mounted in clay or putty for standing upright. Different types of teeth could be used, including molars, premolars, canine and incisor teeth.

[0080] FIGURE 11B shows exemplary reflectance spectra 1150 from a sound enamel region 1151 (e.g., without dental caries), an enamel lesion region 1152, and a dentine lesion region 1153 of various teeth. The spectra are normalized to have equal value near 2050nm. In this particular embodiment, the slope from the sound enamel 1151 is steepest between about 1500 and 1950nm, with a lesser slope in the presence of an enamel lesion 1152. When there is a sample with dentine lesion 1153, more features appear in the spectrum from the presence of water absorption lines from water that collects in the dentine. For this experiment, the spectra 1151, 1152, and 1153 are flatter in the wavelength region between about 1950nm and 2350nm. These are preliminary results, but they show the benefit of using broadband sources such as the SWIR-SC source for diagnosing dental caries. Although the explanation behind the different spectra 1150 of FIGURE 11B may not be understood as yet, it is clear that the spectra 1151, 1152 and 1153 are distinguishable. Therefore, the broadband reflectance may be used for detection of dental caries and analyzing the region of the caries. Although diffuse reflectance has been used in this experiment, other signals, such as transmission, reflectance or a combination, may also be used and are covered by this disclosure.

[0081] Although one particular example of a 5W SWIR-SC has been described, different components, different fibers, and different configurations may also be used consistent with this disclosure. For instance, another embodiment of the similar configuration 900 in FIGURE 9 may be

used to generate high powered SC between approximately 1060 and 1800nm. For this embodiment, the seed laser 901 may be a distributed feedback laser diode of about 1064nm, the pre-amplifier gain fiber 903 may be a ytterbium-doped fiber amplifier with 10/125 microns dimensions, and the pump laser 905 may be a 10W laser diode near 915nm. A mode field adapter may be including in the mid-stage, in addition to the isolator 907, band pass filter 908, polarizer 909 and tap 910. The gain fiber 911 in the power amplifier may be an about 20m length of ytterbium-doped fiber with 25/400 microns dimension. The pump 912 for the power amplifier may be up to six pump diodes providing 30W each near 915nm. For this much pump power, the output power in the SC may be as high as 50W or more.

[0082] In an alternate embodiment, it may be desirous to generate high power SWIR SC over 1.4-1.8 microns and separately 2-2.5 microns (the window between 1.8 and 2 microns may be less important due to the strong water and atmospheric absorption). For example, the top SC source of FIGURE 12 can lead to bandwidths ranging from about 1400nm to 1800nm or broader, while the lower SC source of FIGURE 12 can lead to bandwidths ranging from about 1900nm to 2500nm or broader. Since these wavelength ranges are shorter than about 2500nm, the SC fiber can be based on fused silica fiber. Exemplary SC fibers include standard single-mode fiber (SMF), high-nonlinearity fiber, high-NA fiber, dispersion shifted fiber, dispersion compensating fiber, and photonic crystal fibers. Non-fused-silica fibers can also be used for SC generation, including chalcogenides, fluorides, ZBLAN, tellurites, and germanium oxide fibers.

[0083] In one embodiment, the top of FIGURE 12 illustrates a block diagram for an SC source 1200 capable of generating light between approximately 1400 and 1800nm or broader. As an example, a pump fiber laser similar to FIGURE 9 can be used as the input to a SC fiber 1209. The seed laser diode 1201 can comprise a DFB laser that generates, for example, several milliwatts of power around 1542nm or 1553nm. The fiber pre-amplifier 1202 can comprise an erbium-doped fiber amplifier or an erbium/ytterbium doped double clad fiber. In this example a mid-stage amplifier 1203 can be used, which can comprise an erbium/ytterbium doped double-clad fiber. A bandpass filter 1205 and isolator 1206 may be used between the pre-amplifier 1202 and mid-stage amplifier 1203. The power amplifier stage 1204 can comprise a larger core size erbium/ytterbium doped double-clad fiber, and another bandpass filter 1207 and isolator 1208 can be used before the

power amplifier 1204. The output of the power amplifier can be coupled to the SC fiber 1209 to generate the SC output 1210. This is just one exemplary configuration for an SC source, and other configurations or elements may be used consistent with this disclosure.

[0084] In yet another embodiment, the bottom of FIGURE 12 illustrates a block diagram for an SC source 1250 capable of generating light between approximately 1900 and 2500nm or broader. As an example, the seed laser diode 1251 can comprise a DFB or DBR laser that generates, for example, several milliwatts of power around 1542nm or 1553nm. The fiber pre-amplifier 1252 can comprise an erbium-doped fiber amplifier or an erbium/ytterbium doped double-clad fiber. In this example a mid-stage amplifier 1253 can be used, which can comprise an erbium/ytterbium doped double-clad fiber. A bandpass filter 1255 and isolator 1256 may be used between the pre-amplifier 1252 and mid-stage amplifier 1253. The power amplifier stage 1254 can comprise a thulium doped double-clad fiber, and another isolator 1257 can be used before the power amplifier 1254. Note that the output of the mid-stage amplifier 1253 can be approximately near 1542nm, while the thulium-doped fiber amplifier 1254 can amplify wavelengths longer than approximately 1900nm and out to about 2100nm. Therefore, for this configuration wavelength shifting may be required between 1253 and 1254. In one embodiment, the wavelength shifting can be accomplished using a length of standard single-mode fiber 1258, which can have a length between approximately 5 and 50 meters, for example. The output of the power amplifier 1254 can be coupled to the SC fiber 1259 to generate the SC output 1260. This is just one exemplary configuration for an SC source, and other configurations or elements can be used consistent with this disclosure. For example, the various amplifier stages can comprise different amplifier types, such as erbium doped fibers, ytterbium doped fibers, erbium/ytterbium co-doped fibers and thulium doped fibers. One advantage of the SC lasers illustrated in FIGURES 8, 9, and 12 is that they may use all-fiber components, so that the SC laser can be all-fiber, monolithically integrated with no moving parts. The all-integrated configuration can consequently be robust and reliable.

[0085] FIGURES 8, 9, and 12 are examples of SC light sources that may advantageously be used for SWIR light generation in various medical and dental diagnostic and therapeutic applications. However, many other versions of the SC light sources may also be made that are intended to also be covered by this disclosure. For example, the SC generation fiber could be

pumped by a mode-locked laser, a gain-switched semiconductor laser, an optically pumped semiconductor laser, a solid state laser, other fiber lasers, or a combination of these types of lasers. Also, rather than using a fiber for SC generation, either a liquid or a gas cell might be used as the nonlinear medium in which the spectrum is to be broadened.

[0086] Even within the all-fiber versions illustrated such as in FIGURE 9, different configurations could be used consistent with the disclosure. In an alternate embodiment, it may be desirous to have a lower cost version of the SWIR SC laser of FIGURE 9. One way to lower the cost could be to use a single stage of optical amplification, rather than two stages, which may be feasible if lower output power is required or the gain fiber is optimized. For example, the pre-amplifier stage 902 might be removed, along with at least some of the mid-stage elements. In yet another embodiment, the gain fiber could be double passed to emulate a two stage amplifier. In this example, the pre-amplifier stage 902 might be removed, and perhaps also some of the mid-stage elements. A mirror or fiber grating reflector could be placed after the power amplifier stage 906 that may preferentially reflect light near the wavelength of the seed laser 901. If the mirror or fiber grating reflector can transmit the pump light near 940nm, then this could also be used instead of the pump combiner 913 to bring in the pump light 912. The SC fiber 915 could be placed between the seed laser 901 and the power amplifier stage 906 (SC is only generated after the second pass through the amplifier, since the power level may be sufficiently high at that time). In addition, an output coupler may be placed between the seed laser diode 901 and the SC fiber, which now may be in front of the power amplifier 906. In a particular embodiment, the output coupler could be a power coupler or divider, a dichroic coupler (e.g., passing seed laser wavelength but outputting the SC wavelengths), or a wavelength division multiplexer coupler. This is just one further example, but a myriad of other combinations of components and architectures could also be used for SC light sources to generate SWIR light that are intended to be covered by this disclosure.

WIRELESS LINK TO THE CLOUD

[0087] The non-invasive dental caries measurement device may also benefit from communicating the data output to the "cloud" (e.g., data servers and processors in the web remotely

connected) via wireless means. The non-invasive devices may be part of a series of biosensors applied to the patient, and collectively these devices form what might be called a body area network or a personal area network. The biosensors and non-invasive devices may communicate to a smart phone, tablet, personal data assistant, computer and/or other microprocessor-based device, which may in turn wirelessly or over wire and/or fiber optic transmit some or all of the signal or processed data to the internet or cloud. The cloud or internet may in turn send the data to dentists, doctors or health care providers as well as the patients themselves. Thus, it may be possible to have a panoramic, high-definition, relatively comprehensive view of a patient that doctors and dentists can use to assess and manage disease, and that patients can use to help maintain their health and direct their own care.

[0088] In a particular embodiment 1300, the non-invasive measurement device 1301 may comprise a transmitter 1303 to communicate over a first communication link 1304 in the body area network or personal area network to a receiver in a smart phone, tablet, cell phone, PDA, and/or computer 1305, for example. For the measurement device 1301, it may also be advantageous to have a processor 1302 to process some of the measured data, since with processing the amount of data to transmit may be less (hence, more energy efficient). The first communication link 1304 may operate through the use of one of many wireless technologies such as Bluetooth, Zigbee, WiFi, IrDA (infrared data association), wireless USB, or Z-wave, to name a few. Alternatively, the communication link 1304 may occur in the wireless medical band between 2360MHz and 2390MHz, which the FCC allocated for medical body area network devices, or in other designated medical device or WMTS bands. These are examples of devices that can be used in the body area network and surroundings, but other devices could also be used and are included in the scope of this disclosure.

[0089] The personal device 1305 may store, process, display, and transmit some of the data from the measurement device 1301. The device 1305 may comprise a receiver, transmitter, display, voice control and speakers, and one or more control buttons or knobs and a touch screen. Examples of the device 1305 include smart phones such as the Apple iPhones® or phones operating on the Android or Microsoft systems. In one embodiment, the device 1305 may have an application, software program, or firmware to receive and process the data from the measurement device 1301.

The device 1305 may then transmit some or all of the data or the processed data over a second communication link 1306 to the internet or "cloud" 1307. The second communication link 1306 may advantageously comprise at least one segment of a wireless transmission link, which may operate using WiFi or the cellular network. The second communication link 1306 may additionally comprise lengths of fiber optic and/or communication over copper wires or cables.

[0090] The internet or cloud 1307 may add value to the measurement device 1301 by providing services that augment the measured data collected. In a particular embodiment, some of the functions performed by the cloud include: (a) receive at least a fraction of the data from the device 1305; (b) buffer or store the data received; (c) process the data using software stored on the cloud; (d) store the resulting processed data; and (e) transmit some or all of the data either upon request or based on an alarm. As an example, the data or processed data may be transmitted 1308 back to the originator (e.g., patient or user), it may be transmitted 1309 to a health care provider or doctor or dentist, or it may be transmitted 1310 to other designated recipients.

[0091] Service providers coupled to the cloud 1307 may provide a number of value-add services. For example, the cloud application may store and process the dental data for future reference or during a visit with the dentist or healthcare provider. If a patient has some sort of medical mishap or emergency, the physician can obtain the history of the dental or physiological parameters over a specified period of time. In another embodiment, alarms, warnings or reminders may be delivered to the user 1308, the healthcare provider 1309, or other designated recipients 1310. These are just some of the features that may be offered, but many others may be possible and are intended to be covered by this disclosure. As an example, the device 1305 may also have a GPS sensor, so the cloud 1307 may be able to provide time, date, and position along with the dental or physiological parameters. Thus, if there is a medical or dental emergency, the cloud 1307 could provide the location of the patient to the dental or healthcare provider 1309 or other designated recipients 1310. Moreover, the digitized data in the cloud 1307 may help to move toward what is often called "personalized medicine." Based on the dental or physiological parameter data history, medication or medical/dental therapies may be prescribed that are customized to the particular patient. Another advantage for commercial entities may be that by leveraging the advances in wireless connectivity and the widespread use of handheld devices such as smart phones that can

wirelessly connect to the cloud, businesses can build a recurring cost business model even using non-invasive measurement devices.

[0092] Described herein are just some examples of the beneficial use of near-infrared or SWIR lasers for non-invasive measurements of dental caries and early detection of carious regions. However, many other dental or medical procedures can use the near-infrared or SWIR light consistent with this disclosure and are intended to be covered by the disclosure.

[0093] Although the present disclosure has been described in several embodiments, a myriad of changes, variations, alterations, transformations, and modifications may be suggested to one skilled in the art, and it is intended that the present disclosure encompass such changes, variations, alterations, transformations, and modifications as falling within the spirit and scope of the appended claims.

[0094] While exemplary embodiments are described above, it is not intended that these embodiments describe all possible forms of the disclosure. Rather, the words used in the specification are words of description rather than limitation, and it is understood that various changes may be made without departing from the spirit and scope of the disclosure. Additionally, the features of various implementing embodiments may be combined to form further embodiments of the disclosure. While various embodiments may have been described as providing advantages or being preferred over other embodiments with respect to one or more desired characteristics, as one skilled in the art is aware, one or more characteristics may be compromised to achieve desired system attributes, which depend on the specific application and implementation. These attributes include, but are not limited to: cost, strength, durability, life cycle cost, marketability, appearance, packaging, size, serviceability, weight, manufacturability, ease of assembly, etc. The embodiments described herein that are described as less desirable than other embodiments or prior art implementations with respect to one or more characteristics are not outside the scope of the disclosure and may be desirable for particular applications. .

WHAT IS CLAIMED IS:

1. A diagnostic system comprising:

a light source configured to generate an output optical beam, comprising:

one or more semiconductor sources configured to generate an input beam;

one or more optical amplifiers configured to receive at least a portion of the input beam and to deliver an intermediate beam to an output end of the one or more optical amplifiers;

one or more optical fibers configured to receive at least a portion of the intermediate beam and to deliver at least the portion of the intermediate beam to a distal end of the one or more optical fibers to form a first optical beam;

a nonlinear element configured to receive at least a portion of the first optical beam and to broaden a spectrum associated with the at least a portion of the first optical beam to at least 10 nanometers through a nonlinear effect in the nonlinear element to form the output optical beam with an output beam broadened spectrum; and

wherein at least a portion of the output beam broadened spectrum comprises a short-wave infrared wavelength between approximately 1400 nanometers and approximately 2500 nanometers, and wherein at least a portion of the one of more fibers is a fused silica fiber with a core diameter less than approximately 400 microns;

an interface device configured to receive a received portion of the output optical beam and to deliver a delivered portion of the output optical beam to a sample comprising enamel and dentine, wherein the delivered portion of the output optical beam is configured to generate a spectroscopy output beam from the sample; and

a receiver configured to receive at least a portion of the spectroscopy output beam having a bandwidth of at least 10 nanometers and to process the portion of the spectroscopy output beam to generate an output signal based on a wavelength dependence of the spectroscopy output beam over the bandwidth of at least 10 nanometers.

2. The system of Claim 1, wherein the wavelength dependence of the spectroscopy output beam is based at least in part on wavelength dependent scattering and water absorption characteristics of the sample.

3. The system of Claim 1, wherein the bandwidth of the spectroscopy output beam is at least 100 nanometers, and the output signal is based on the wavelength dependence of the spectroscopy output beam over the bandwidth of at least 100 nanometers.

4. The system of Claim 1, wherein the interface device further comprises a replaceable insert, and wherein the spectroscopy output beam is based on transmission, reflection or absorption of the sample.

5. The system of Claim 1, wherein the receiver further comprises a wireless transmitter configured to communicate a wireless signal associated with the output signal to a network.

6. A measurement system comprising:

a light source configured to generate an output optical beam, comprising:

a plurality of semiconductor sources configured to generate an input optical beam;

a multiplexer configured to receive at least a portion of the input optical beam and to form an intermediate optical beam; and

one or more fibers configured to receive at least a portion of the intermediate optical beam and to form the output optical beam, wherein the output optical beam comprises one or more optical wavelengths;

an interface device configured to receive a received portion of the output optical beam and to deliver a delivered portion of the output optical beam to a sample comprising enamel and dentine, wherein the delivered portion of the output optical beam is configured to generate a spectroscopy output beam from the sample; and

a receiver configured to receive at least a portion of the spectroscopy output beam having a bandwidth of at least 10 nanometers and to process the portion of the spectroscopy output beam to generate an output signal based on a wavelength dependence of the spectroscopy output beam over the bandwidth of at least 10 nanometers.

7. The system of Claim 6, wherein the light source comprises a super-continuum laser.

8. The system of Claim 6, wherein the light source comprises a super-luminescent diode.

9. The system of Claim 6, wherein the light source comprises a light emitting diode.

10. The system of Claim 6, wherein at least a portion of the one of more optical wavelengths comprises a short-wave infrared wavelength between approximately 1400 nanometers and approximately 2500 nanometers.

11. The system of Claim 6, wherein the output signal is based at least in part on wavelength dependent scattering from the sample.

12. The system of Claim 6, wherein the output signal is based at least in part on water absorption characteristics of the sample.

13. The system of Claim 6, wherein the bandwidth of the spectroscopy output beam is at least 100 nanometers, and the output signal is based on the wavelength dependence of the spectroscopy output beam over the bandwidth of at least 100 nanometers.

14. The system of Claim 6, wherein the spectroscopy output beam is based on transmission, reflection, or absorption of the sample.

15. The system of Claim 6, wherein the interface device further comprises a replaceable insert.

16. The system of Claim 6, wherein the output signal is configured to identify dental caries.

17. A method of measuring, comprising:

generating an output optical beam, comprising:

generating an input optical beam from a plurality of semiconductor sources;

multiplexing at least a portion of the input optical beam and forming an intermediate optical beam; and

guiding at least a portion of the intermediate optical beam and forming the output optical beam, wherein the output optical beam comprises one or more optical wavelengths;

receiving a received portion of the output optical beam and delivering a delivered portion of the output optical beam to a sample, wherein the sample comprises enamel and dentine;

generating a spectroscopy output beam having a bandwidth of at least 10 nanometers from the sample;

receiving at least a portion of the spectroscopy output beam; and

processing the portion of the spectroscopy output beam and generating an output signal based on a wavelength dependence of the spectroscopy output beam over the bandwidth of at least 10 nanometers.

18. The method of claim 17, wherein the one or more optical wavelengths comprises a short-wave infrared wavelength between approximately 1400 nanometers and approximately 2500 nanometers.

19. The method of claim 17, wherein the wavelength dependence of the spectroscopy output beam is based at least in part on wavelength dependent transmission, reflection, or absorption of the sample.

20. The method of claim 17, further comprising communicating a wireless signal associated with the output signal to a network.

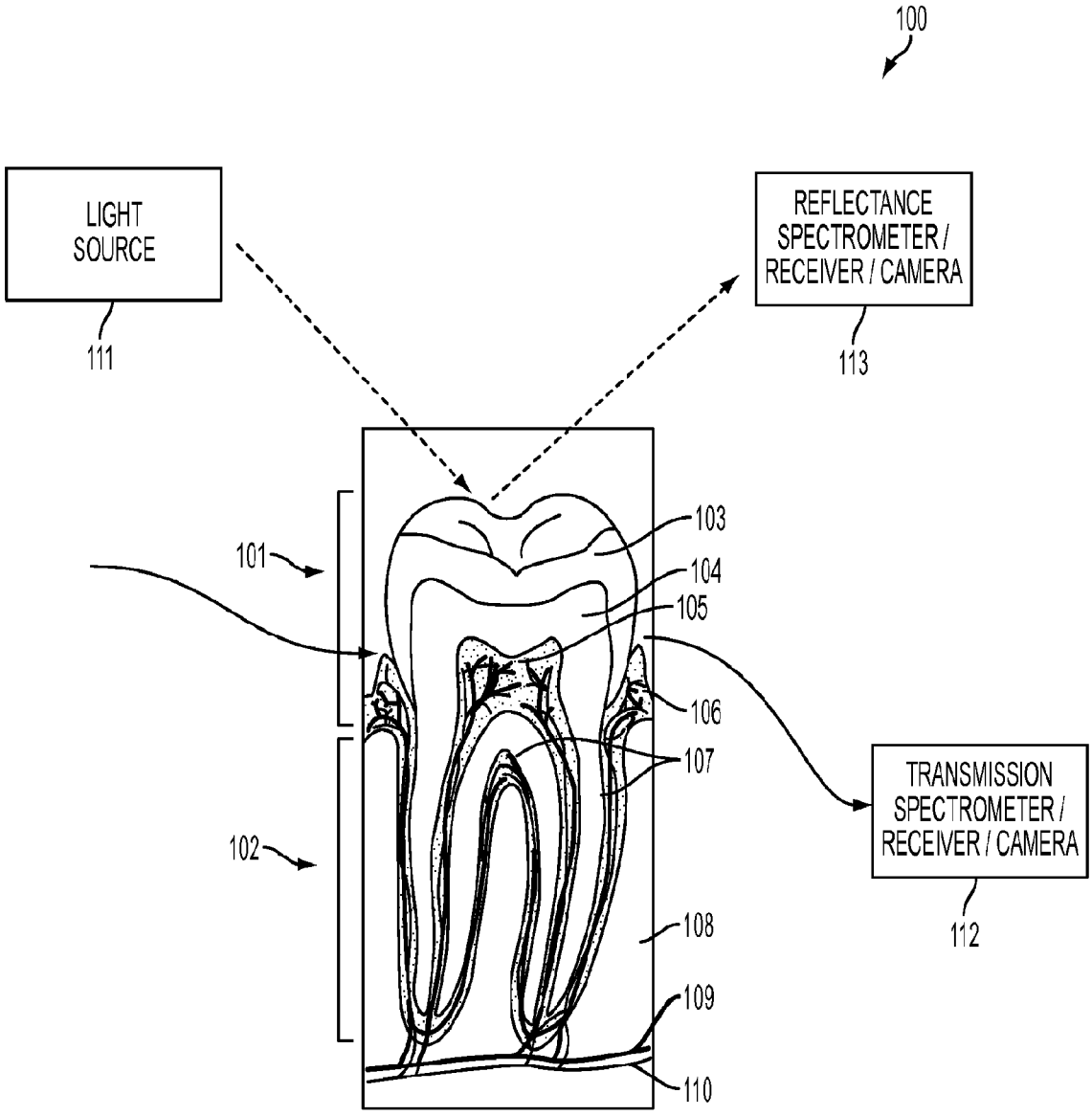

100
LIGHT SOURCE
111
REFLECTANCE SPECTROMETER / RECEIVER / CAMERA
113
101
102
103
104
105
106
107
108
109
110
TRANSMISSION SPECTROMETER / RECEIVER / CAMERA
112

FIG. 1

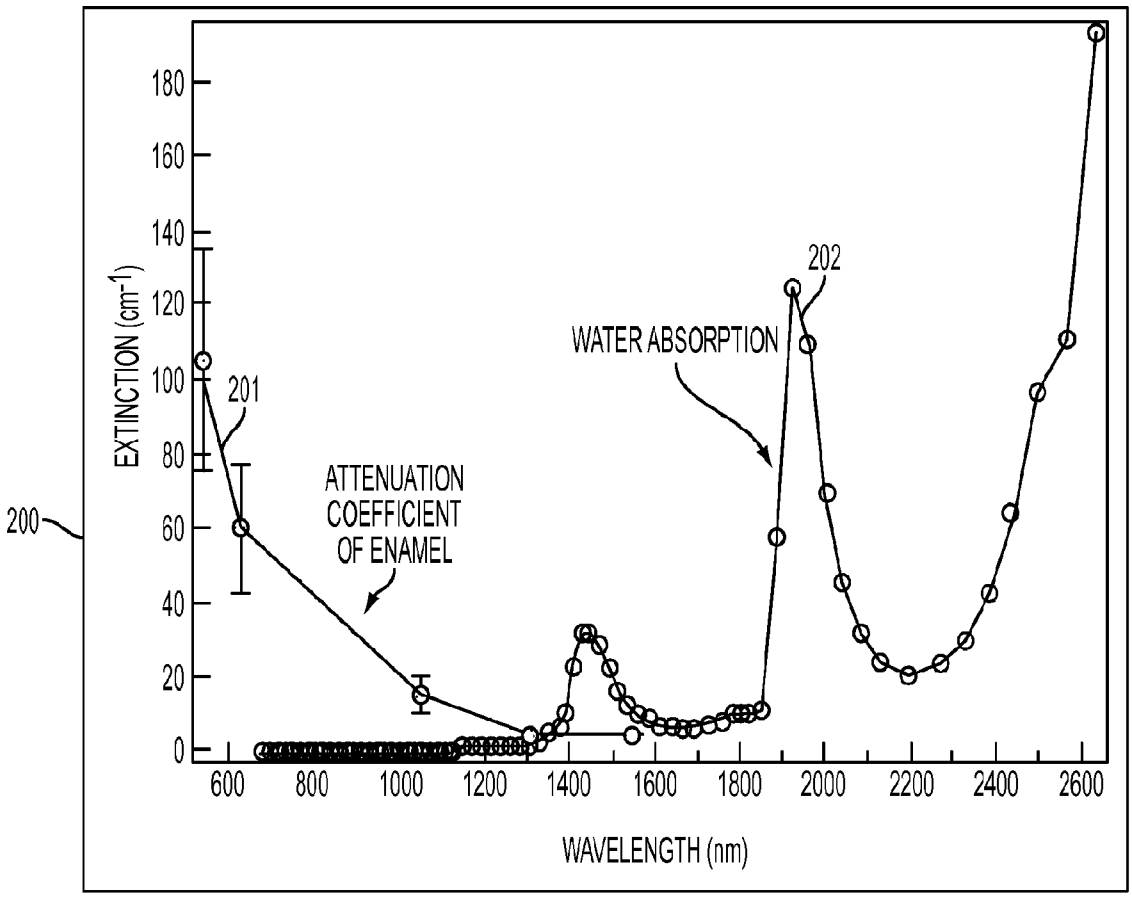

200
EXTINCTION (cm-1)
180
160
140
120
100
80
60
40
20
0
600
800
1000
1200
1400
1600
1800
2000
2200
2400
2600
WAVELENGTH (nm)
201
202
WATER ABSORPTION
ATTENUATION
COEFFICIENT
OF ENAMEL

FIG. 2A

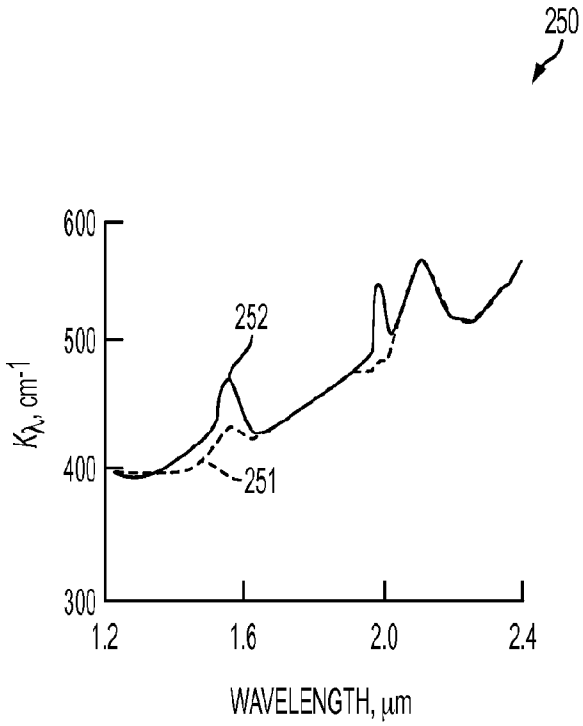

250
600
500
400
300
252
251
K_λ, cm^{-1}
1.2
1.6
2.0
2.4
WAVELENGTH, μm

FIG. 2B

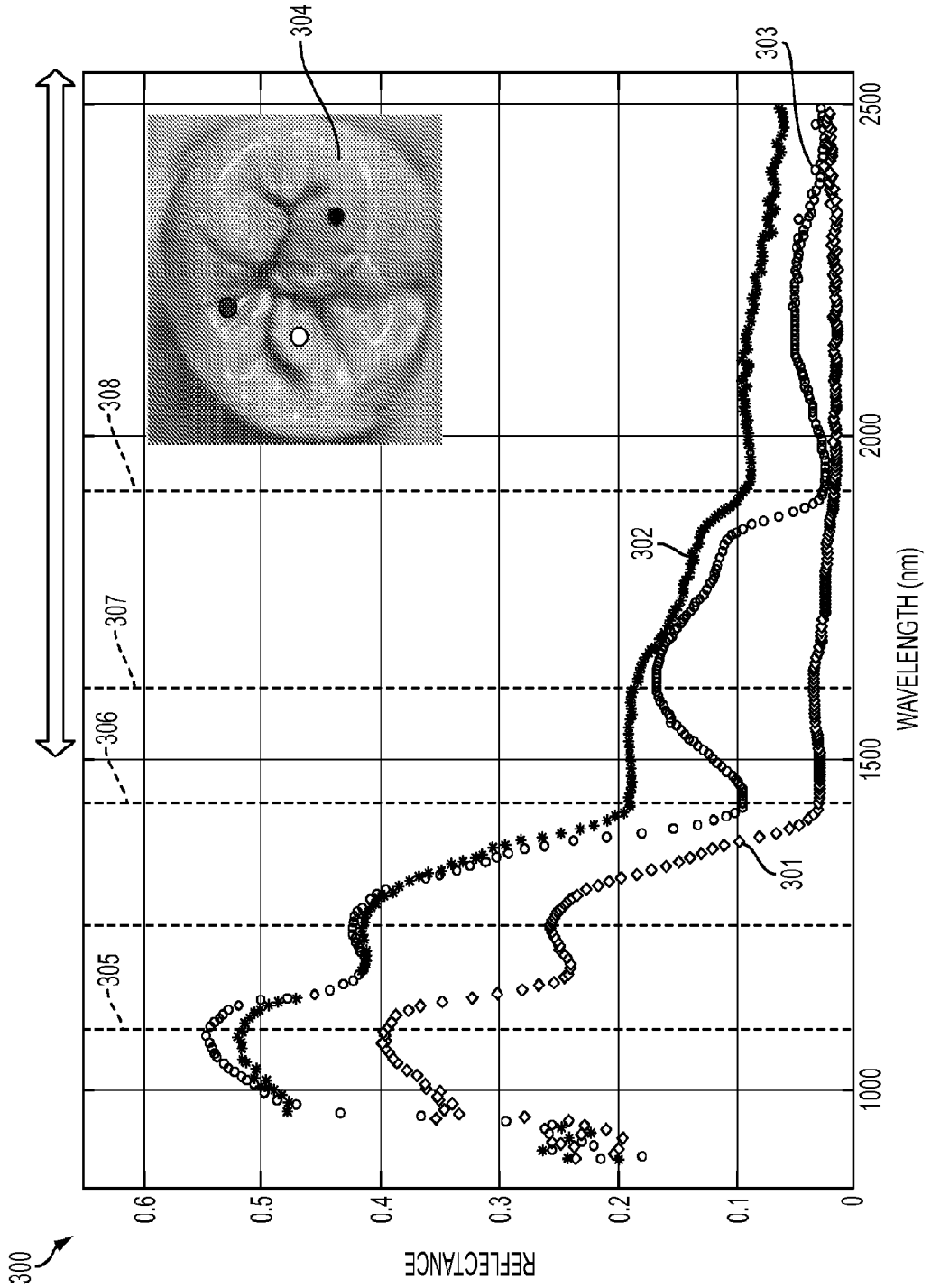

300
304
303
308
307
306
305
302
301
REFLECTANCE
0.6
0.5
0.4
0.3
0.2
0.1
0
1000
1500
2000
2500
WAVELENGTH (nm)

FIG. 3

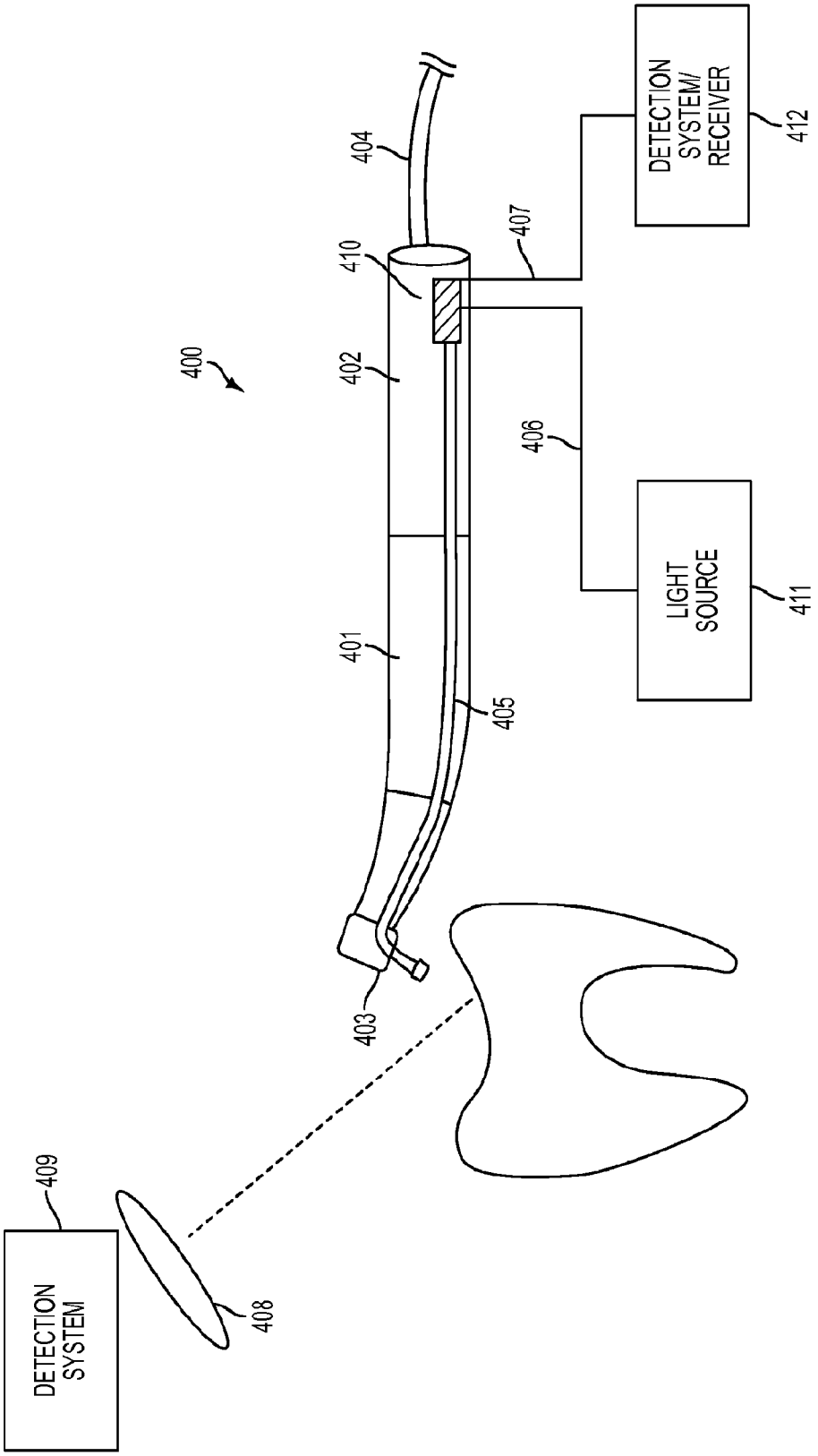

400
401
402
403
404
405
406
407
408
409
410
411
412
DETECTION SYSTEM
DETECTION SYSTEM/ RECEIVER
LIGHT SOURCE

FIG. 4

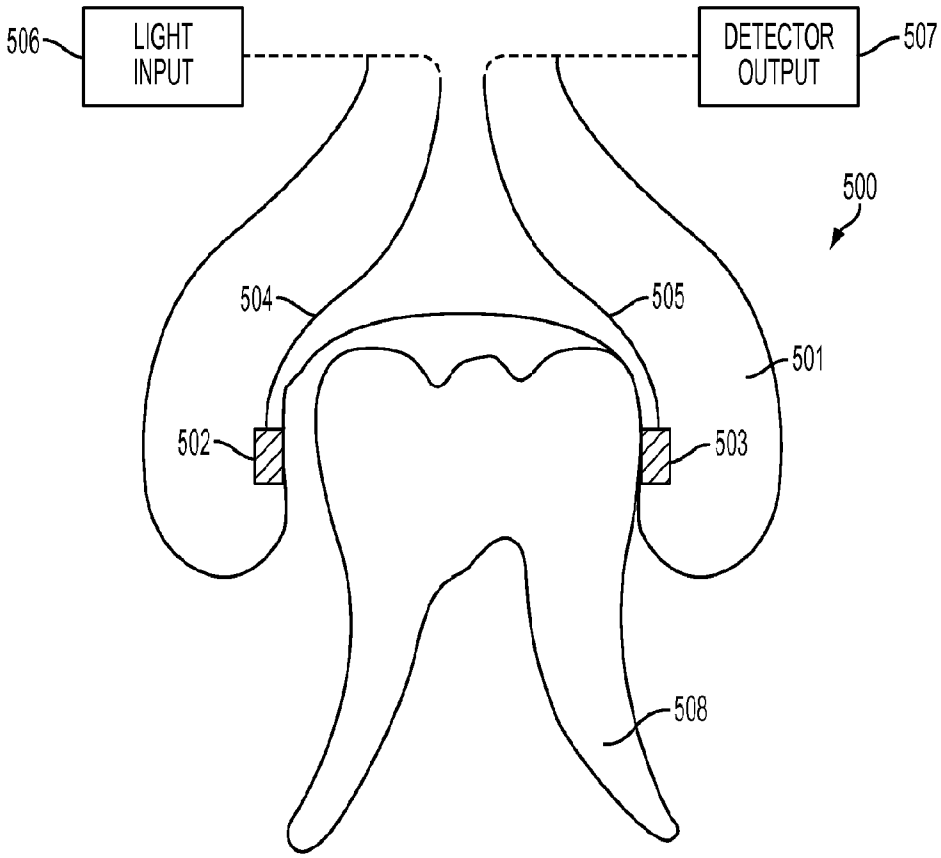

506
LIGHT INPUT
DETECTOR OUTPUT
507
500
504
505
501
502
503
508

FIG. 5

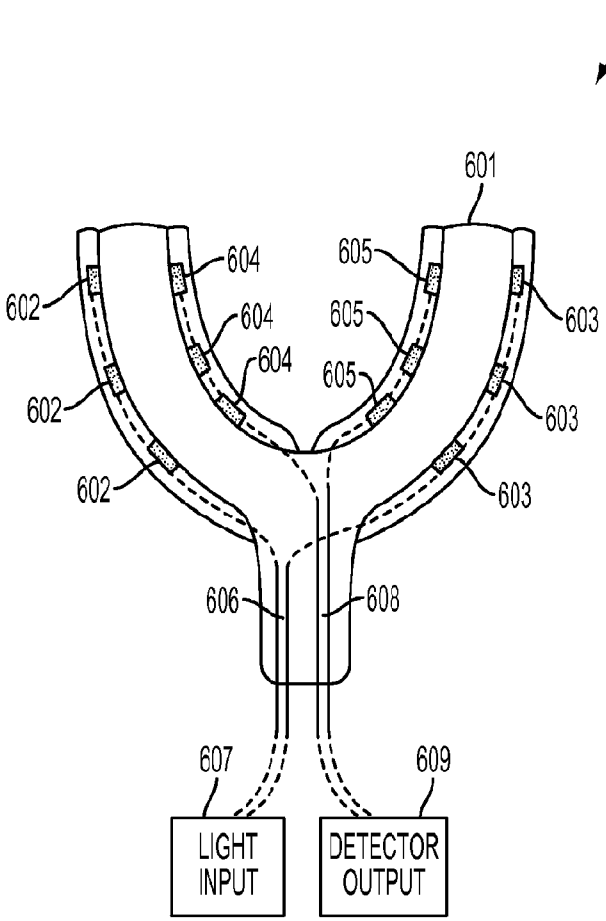

600
601
602
602
602
603
603
603
604
604
604
605
605
605
606
608
607
609
LIGHT INPUT
DETECTOR OUTPUT

FIG. 6

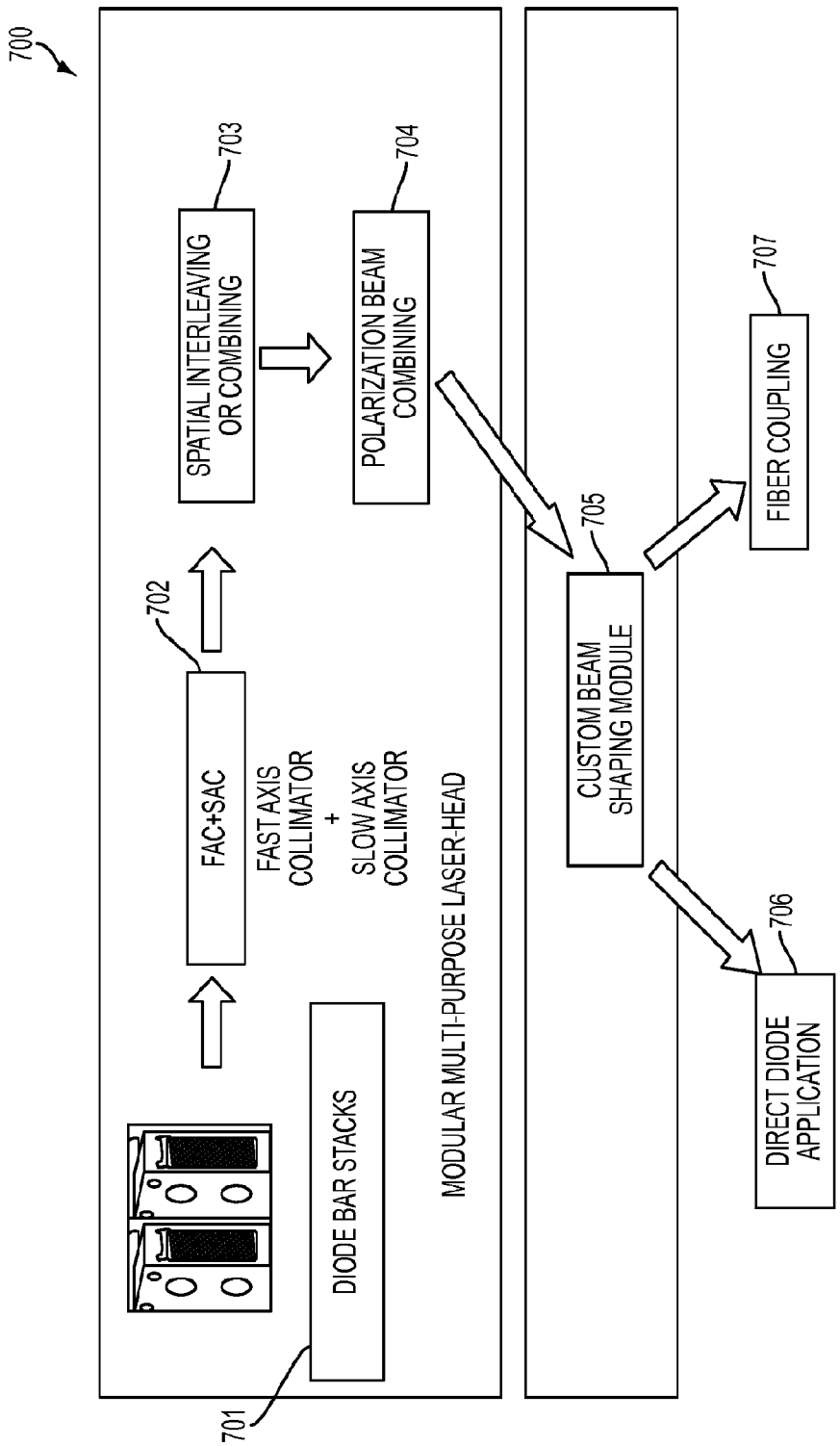

700
703
SPATIAL INTERLEAVING OR COMBINING
704
POLARIZATION BEAM COMBINING
707
FIBER COUPLING
705
CUSTOM BEAM SHAPING MODULE
702
FAC+SAC
FAST AXIS COLLIMATOR
+
SLOW AXIS COLLIMATOR
MODULAR MULTI-PURPOSE LASER-HEAD
706
DIRECT DIODE APPLICATION
DIODE BAR STACKS
701

FIG. 7

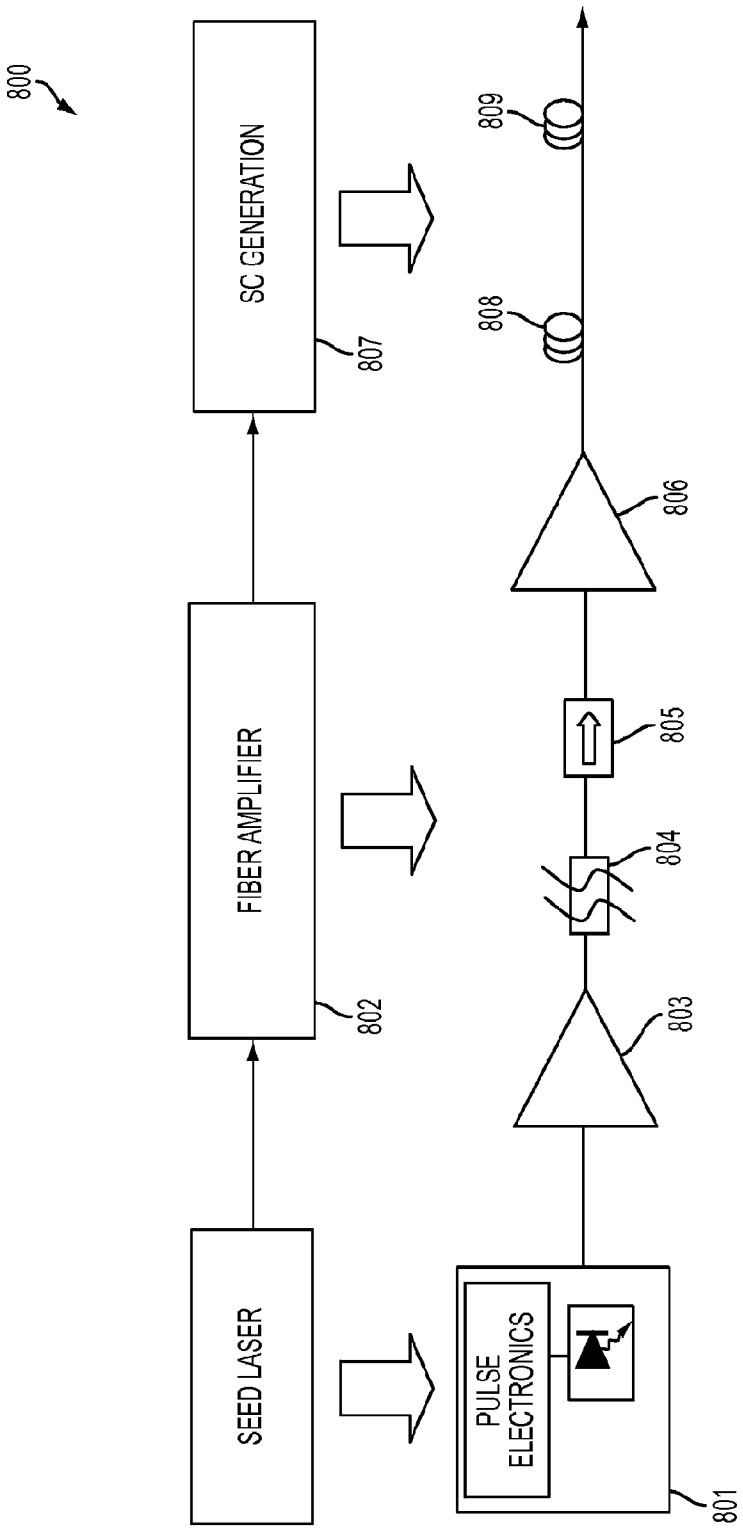

800
SEED LASER
FIBER AMPLIFIER
SC GENERATION
PULSE ELECTRONICS
801
802
803
804
805
806
807
808
809

FIG. 8

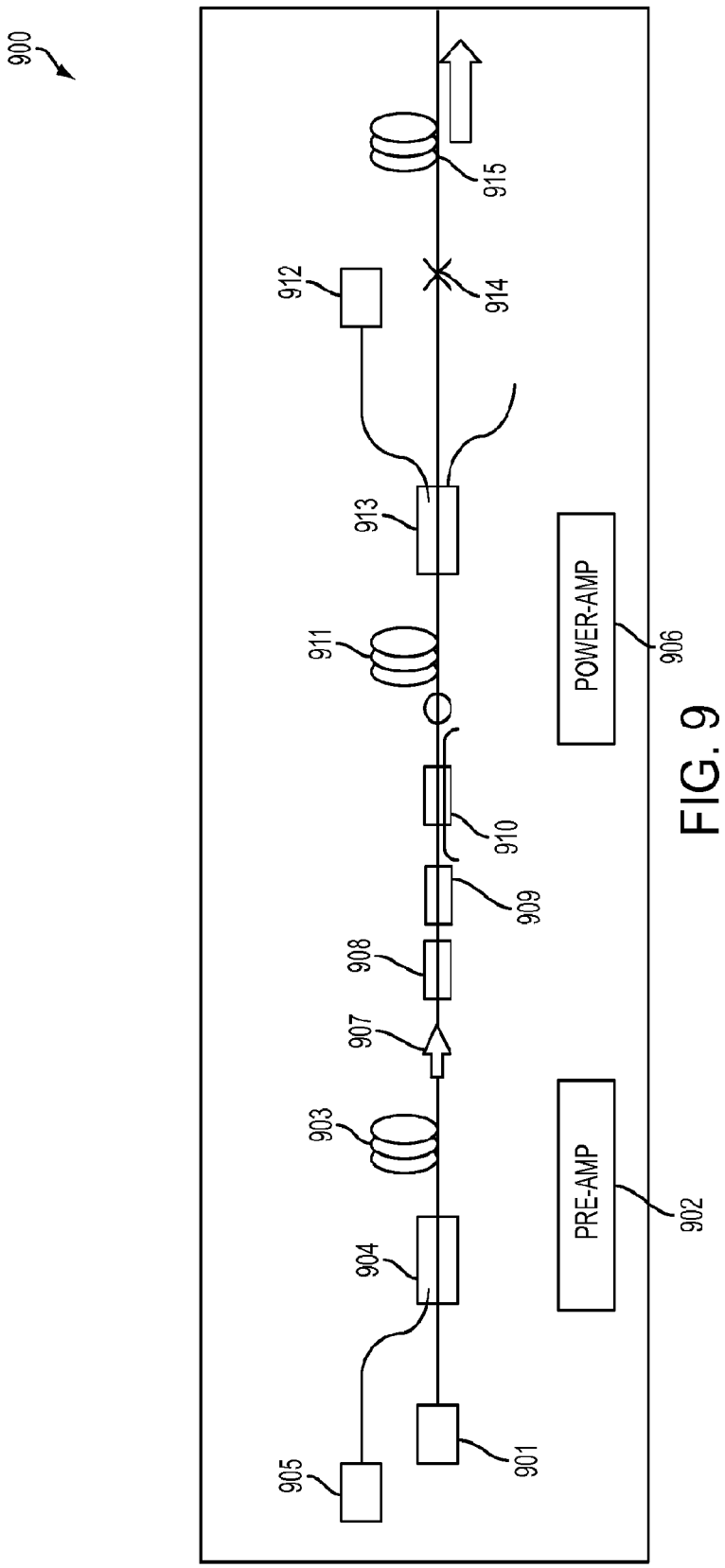

900
915
912
914
913
911
POWER-AMP
906
910
909
908
907
903
PRE-AMP
902
904
905
901

FIG. 9

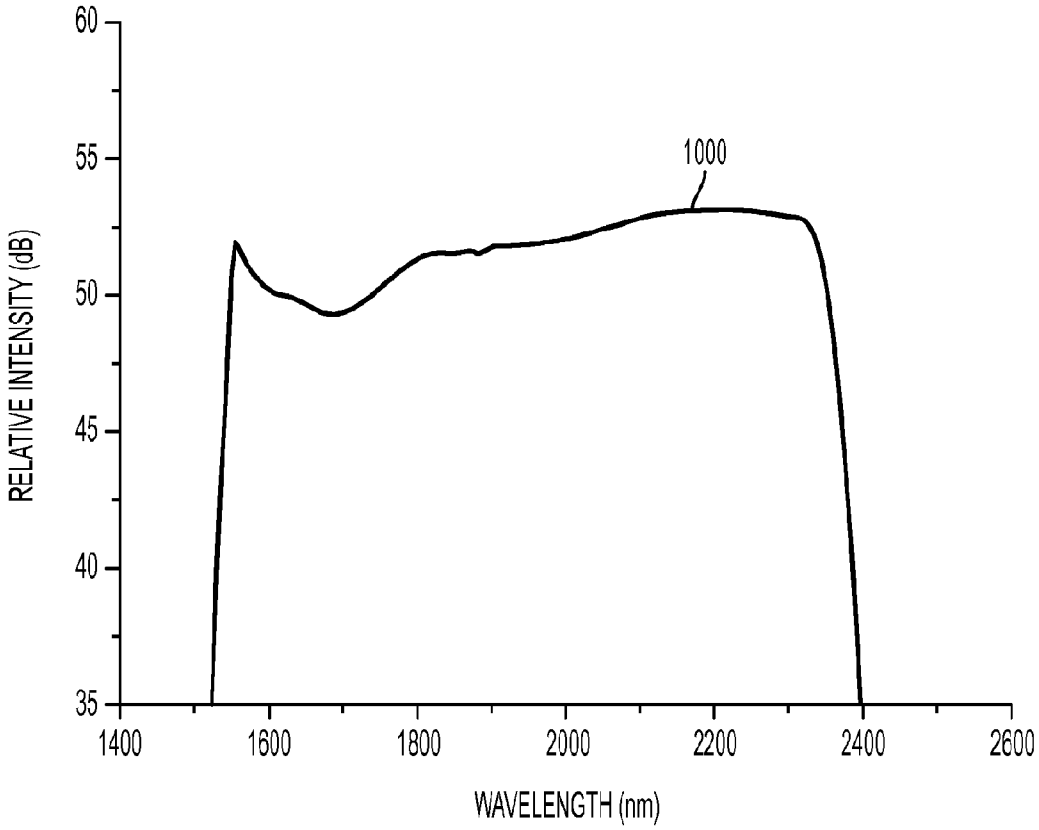

60
55
50
45
40
35
RELATIVE INTENSITY (dB)
1000
1400
1600
1800
2000
2200
2400
2600
WAVELENGTH (nm)

FIG. 10

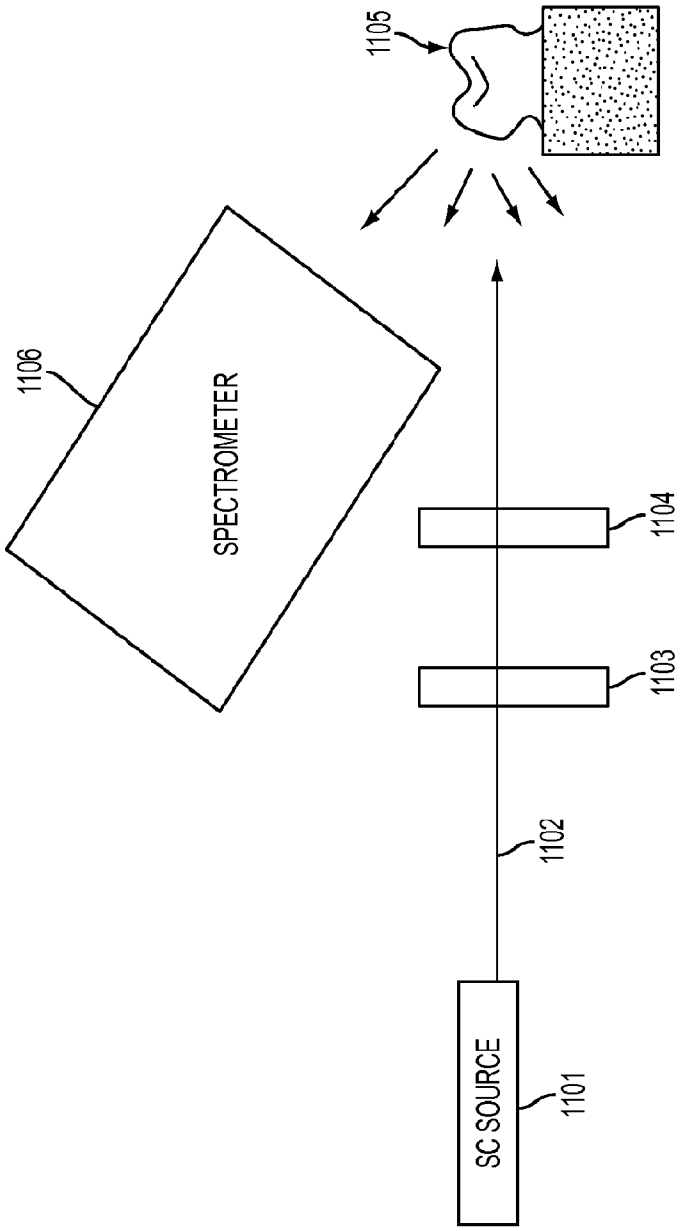


FIG. 11A

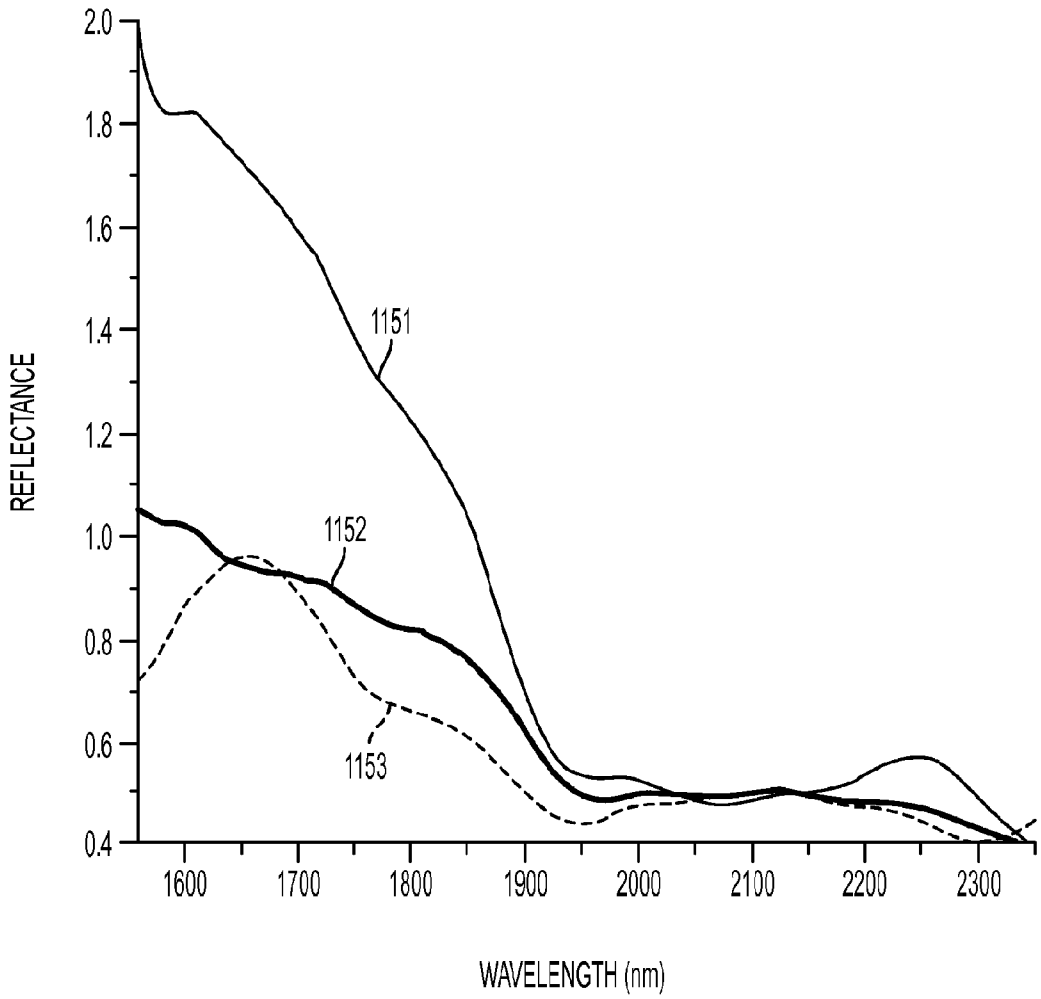

2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
REFLECTANCE
1151
1152
1153
1600
1700
1800
1900
2000
2100
2200
2300
WAVELENGTH (nm)

FIG. 11B

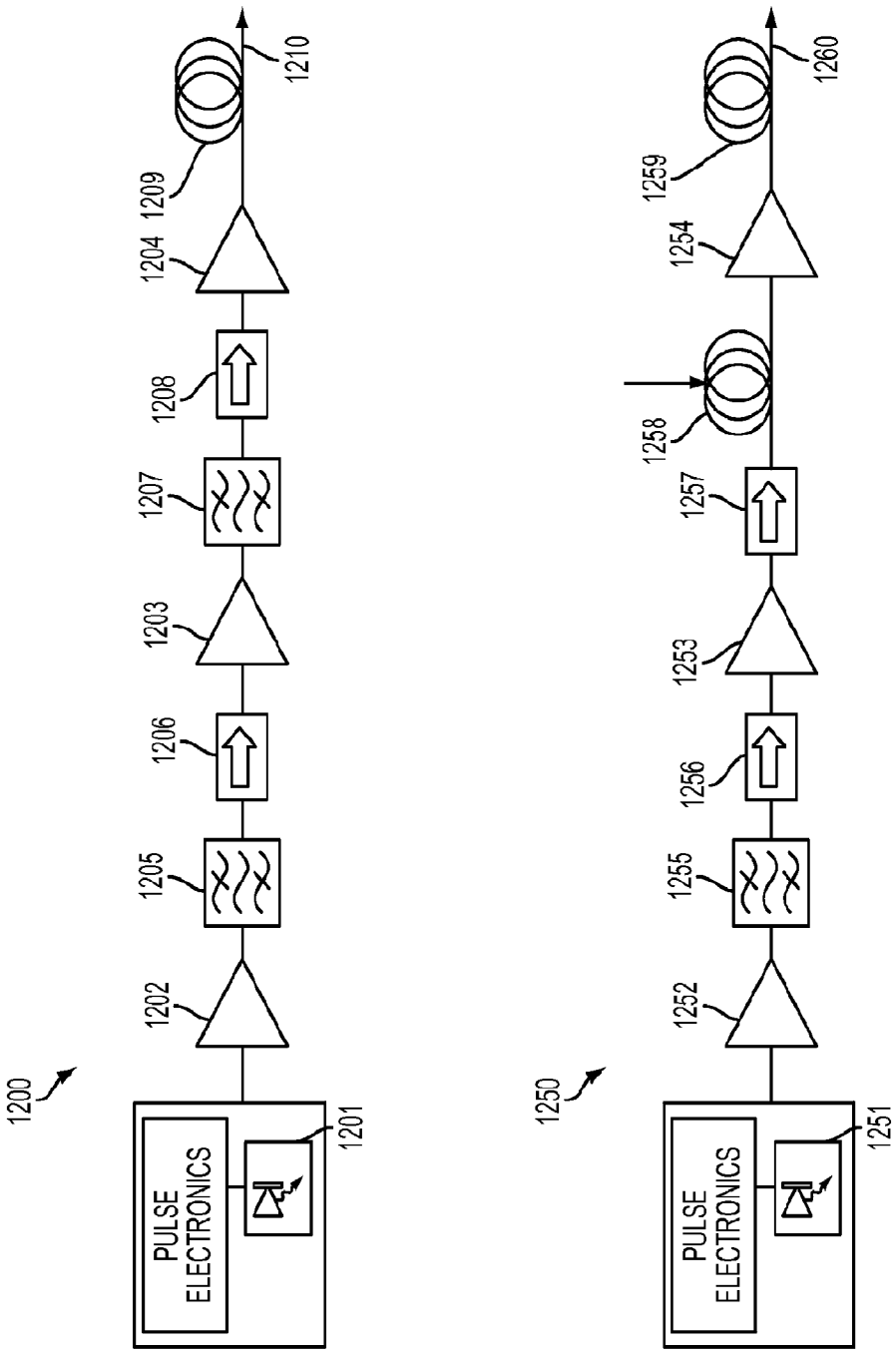

1200
PULSE ELECTRONICS
1201
1202
1205
1206
1203
1207
1208
1204
1209
1210
1250
PULSE ELECTRONICS
1251
1252
1255
1256
1253
1257
1258
1254
1259
1260

FIG. 12

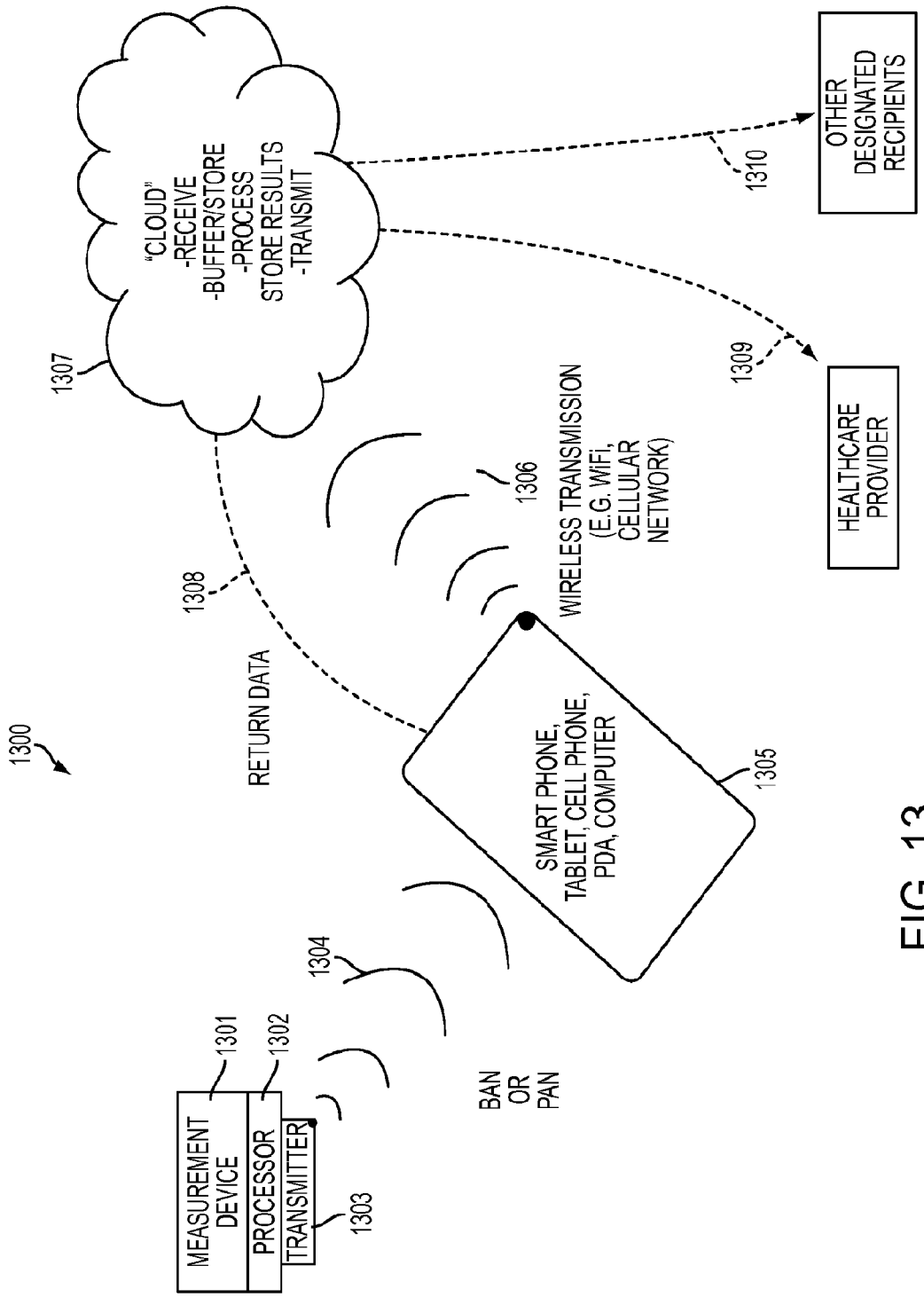

1300
MEASUREMENT DEVICE
PROCESSOR
TRANSMITTER
1301
1302
1303
1304
BAN OR PAN
SMART PHONE, TABLET, CELL PHONE, PDA, COMPUTER
1305
RETURN DATA
1308
WIRELESS TRANSMISSION (E.G. WiFi, CELLULAR NETWORK)
1306
"CLOUD" -RECEIVE -BUFFER/STORE -PROCESS STORE RESULTS -TRANSMIT
1307
HEALTHCARE PROVIDER
1309
OTHER DESIGNATED RECIPIENTS
1310

FIG. 13

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/075736

A. CLASSIFICATION OF SUBJECT MATTER

A61B 6/14(2006.01)i, A61C 19/04(2006.01)i

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61B 6/14; G06F 15/42; A61B 18/22; A61B 6/00; A61B 5/1455; A61B 5/00; A61C 19/04

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(KIPO internal) & Keywords: near-infrared, laser, diagnosis, non-invasive, tooth, glucose and blood

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2012-0239013 A1 (ISLAM, MOHAMMED N.) 20 September 2012 See abstract, paragraphs [0007], [0011], [0059], [0136]-[0139], claims 30-40, and figures 7, 19-20.	1-20
Y	US 2007-0021670 A1 (MANDELIS, ANDREAS et al.) 25 January 2007 See abstract, claims 1-26, and figure 1.	1-20
A	US 2011-0282167 A1 (RIDDER, TRENT et al.) 17 November 2011 See abstract, and claims 1-18.	1-20
A	US 5267152 A (YANG, WON S. et al.) 30 November 1993 See abstract, claim 1-3, and figure 1.	1-20
A	US 7356364 B1 (BULLOCK, AUDRA M. et al.) 08 April 2008 See abstract, and claims 14-20.	1-20

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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Date of the actual completion of the international search	Date of mailing of the international search report
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