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(54) METHOD AND APPARATUS FOR SPECTROPHOTOMETRIC BLOOD OXYGENATION MONITORING

VERFAHREN UND VORRICHTUNG FÜR DIE SPEKTROPHOTOMETRISCHE ÜBERWACHUNG DER OXYGENIERUNG VON BLUT

PROCEDE ET APPAREIL DE SURVEILLANCE SPECTROPHOTOMETRIQUE DE L'OXYGENATION SANGUINE

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Description

BACKGROUND OF THE INVENTION

1. Technical Field.

[0001] This invention relates to methods for non-invasively determining biological tissue oxygenation in general, and to non-invasive methods utilizing near infrared spectroscopy (NIRS) techniques in particular.

2. Background Information.

[0002] The molecule that carries the oxygen in the blood is hemoglobin. Oxygenated hemoglobin is called oxyhemoglobin (HbO_2) and deoxygenated hemoglobin is deoxyhemoglobin (Hb). Total hemoglobin is the summation of the two states of hemoglobin (Total Hb = HbO_2+ Hb), and is proportional to relative blood volume changes, provided that the hematocrit or hemoglobin concentration of the blood is unchanged. The mammalian cardiovascular system consists of a blood pumping mechanism (the heart), a blood transportation system (blood vessels), and a blood oxygenation system (the lungs). Blood oxygenated by the lungs passes through the heart and is pumped into the arterial vascular system. Under normal conditions, oxygenated arterial blood consists predominately of HbO_2. Large arterial blood vessels branch off into smaller branches called arterioles, which profuse throughout biological tissue. The arterioles branch off into capillaries, the smallest blood vessels. In the capillaries, oxygen carried by hemoglobin is transported to the cells in the tissue, resulting in the release of oxygen molecules ($HbO_2 \Rightarrow$ Hb). Under normal conditions, only a fraction of the HbO_2 molecules give up oxygen to the tissue, depending on the cellular metabolic need. The capillaries then combine together into venuoles, the beginning of the venous circulatory system. Venuoles then combine into larger blood vessels called veins. The veins further combine and return to the heart, and then venous blood is pumped to the lungs. In the lungs, deoxygenated hemoglobin Hb collects oxygen becoming HbO_2 again and the circulatory process is repeated.

[0003] Oxygen saturation is defined as:

$$O_2\ saturation\ \% = \frac{HbO_2}{\left(HbO_2 + Hb\right)} * 100\% \qquad \text{(Eqn.1)}$$

In the arterial circulatory system under normal conditions, there is a high proportion of HbO_2 to Hb, resulting in an arterial oxygen saturation (defined as SaO_2 %) of 95-100%. After delivery of oxygen to tissue via the capillaries, the proportion of HbO_2 to Hb decreases. Therefore, the measured oxygen saturation of venous blood (defined as SvO_2 %) is lower and may be about 70%.

[0004] One spectrophotometric method, called pulse oximetry, determines arterial oxygen saturation (SaO_2) of peripheral tissue (i.e. finger, ear, nose) by monitoring pulsatile optical attenuation changes of detected light induced by pulsatile arterial blood volume changes in the arteriolar vascular system. The method of pulse oximetry requires pulsatile blood volume changes in order to make a measurement. Since venous blood is not pulsatile, pulse oximetry cannot provide any information about venous blood.

[0005] Near-infrared spectroscopy (NIRS) is an optical spectrophotometric method of continually monitoring tissue oxygenation that does not require pulsatile blood volume to calculate parameters of clinical value. The NIRS method is based on the principle that light in the near-infrared range (700 to 1,000 nm) can pass easily through skin, bone and other tissues where it encounters hemoglobin located mainly within micro-circulation passages; e.g., capillaries, arterioles, and venuoles. Hemoglobin exposed to light in the near infra-red range has specific absorption spectra that varies depending on its oxidation state; i.e., oxyhemoglobin (HbO_2) and deoxyhemoglobin (Hb) each act as a distinct chromophore. By using light sources that transmit near-infrared light at specific different wavelengths, and measuring changes in transmitted or reflected light attenuation, concentration changes of the oxyhemoglobin (HbO_2) and deoxyhemoglobin (Hb) can be monitored. The ability to continually monitor cerebral oxygenation levels is particularly valuable for those patients subject to a condition in which oxygenation levels in the brain may be compromised, leading to brain damage or death.

[0006] The apparatus used in NIRS analysis typically includes a plurality of light sources, one or more light detectors for detecting reflected or transmitted light, and a processor for processing signals that represent the light emanating from the light source and the light detected by the light detector. Light sources such as light emitting diodes (LEDs) or laser diodes that produce light emissions in the wavelength range of 700-lOOOnm at an intensity below that which would damage the biological tissue being examined are typically used. A photodiode or other light source detector is used to detect light reflected from or passed through the tissue being examined. The processor takes the signals from the light

sources and the light detector and analyzes those signals in terms of their intensity and wave properties. In a time-resolved measurement, as disclosed in EP-0710832-A1, the absorption coefficient is measured based on waveform analysis rather than the Beer-Lambert Law.

[0007] It is known that relative changes of the concentrations of $Hb0_2$ and Hb can be evaluated using apparatus similar to that described above, including a processor programmed to utilize a variant of the Beer-Lambert Law, which accounts for optical attenuation in a highly scattering medium like biological tissue. The modified Beer-Lambert Law can be expressed as:

$$A_\lambda = -\log(I/I_o)_\lambda = \alpha * C * d * B_\lambda + G \quad \text{(Eqn.2)}$$

wherein "A_λ" represents the optical attenuation in tissue at a particular wavelength λ (units: optical density or OD); "I_o" represents the incident light intensity (units: W/cm^2); "I" represents the detected light intensity; "α_λ" represents the wavelength dependent absorption coefficient of the chromophore (units: $OD * cm^{-1} * \mu M^{-1}$); "C" represents the concentration of chromophore (units: μM); "d" represents the light source to detector (optode) separation distance (units: cm); "B_λ" represents the wavelength dependent light scattering differential pathlength factor (unitless); and "G" represents light attenuation due to scattering within tissue (units: OD). The product of "$d*B_\lambda$" represents the effective pathlength of photon traveling through the tissue.

[0008] Absolute measurement of chromophore concentration (C) is very difficult because G is unknown or difficult to ascertain. However, over a reasonable measuring period of several hours to days, G can be considered to remain constant, thereby allowing for the measurement of relative changes of chromophore from a zero reference baseline. Thus, if time t_1 marks the start of an optical measurement (i.e., a base line) and time t_2 is an arbitrary point in time after t_2, a change in attenuation (ΔA) between t_1 and t_2 can be calculated, and variables G and I_o will cancel out providing that they remain constant.

[0009] The change in chromophore concentration ($\Delta C = C(t_2) - C(t_1)$) can be determined from the change in attenuation ΔA, for example using the following equation derived from the modified Beer-Lambert Law:

$$\Delta A_\lambda = -\log(I_{t2}/I_{t1})_\lambda = \alpha_\lambda * \Delta C * d * B_\lambda \quad \text{(Eqn.3)}$$

Presently known NIRS algorithms that are designed to calculate the relative change in concentration of more than one chromophore use a multivariate form of Equation 2 or 3. To distinguish between, and to compute relative concentration changes in, oxyhemoglobin (ΔHbO_2) and deoxyhemoglobin (ΔHb), a minimum of two different wavelengths are typically used. The concentration of the HbO_2 and Hb within the examined tissue is determined in μmoles per liter of tissue (μM).

[0010] The above-described NIRS approach to determining oxygenation levels is useful, but it is limited in that it only provides information regarding a change in the level of oxygenation within the tissue. It does not provide a means for determining the absolute value of oxygen saturation within the biological tissue.

[0011] At present, information regarding the relative contributions of venous and arterial blood within tissue examined by NIRS is either arbitrarily chosen or is determined by invasive sampling of the blood as a process independent from the NIRS examination. For example, It has been estimated that NIRS examined brain tissue comprising about 60 to 80% blood venous and about 20 to 40% arterial blood. Blood samples from catheters placed in venous drainage sites such as the internal jugular vein, jugular bulb, or sagittal sinus have been used to evaluate NIRS measurements. Results from animal studies have shown that NIRS interrogated tissue consists of a mixed vascular bed with a venous-to-arterial ratio of about 2:1 as determined from multiple linear regression analysis of sagittal sinus oxygen saturation ($SssO_2$) and arterial oxygen saturation (SaO_2). An expression representing the mixed venous / arterial oxygen saturation ($SmvO_2$) in NIRS examined tissue is shown by the equation:

$$SmvO_2 = Kv * SvO_2 + Ka * SaO_2 \quad \text{(Eqn.4)}$$

where "SvO_2" represents venous oxygen saturation; "SaO_2" represents arterial oxygen saturation; and Kv and Ka are the weighted venous and arterial contributions respectively, with Kv + Ka = 1. The parameters Kv and Ka may have constant values, or they may be a function of SvO_2 and SaO_2. Determined oxygen saturation from the internal jugular vein ($Sijv0_2$), jugular bulb ($SjbO_z$), or sagittal sinus ($Sss0_2$) can be used to represent $Sv0_2$. Therefore, the value of each term in Equation 4 is empirically determined, typically by discretely sampling or continuously monitoring and subsequently

evaluating patient arterial and venous blood from tissue that the NIRS sensor is examining, and using regression analysis to determine the relative contributions of venous and arterial blood independent of the NIRS examination. US 2001/0047128 relates to a method for determining blood oxygen saturation level within tissue by determining differential attenuation as a function of wavelength. Attenuation attributable to background scattering and other factors is therefore cancelled out. US 2002/0016536 describes a non-invasive NIRS monitoring transducer assembly in which optical attenuation due to scattering may be cancelled out.

[0012] To non-invasively determine oxygen saturation within tissue at certain depth, it is necessary to limit the influence from the superficial tissues. For example, to determine brain oxygen saturation of adult human with NIRS technology, the contamination from extracraninal tissue (scalp and skull) must be eliminated or limited.

[0013] What is needed, therefore, is a method for non-invasively determining the level of oxygen saturation within biological tissue that can determine the absolute oxygen saturation value rather than a change in level; a method that provides calibration means to account for energy losses (i.e. light attenuation) due to light scattering within tissue, other background absorption losses from biological compounds, and other unknown losses including measuring apparatus variability; and a method that can non-invasively determine oxygen saturation within tissue at certain depth by limiting the influence from the superficial tissues.

DISCLOSURE OF THE INVENTION

[0014] According to the present invention, a method and apparatus for non- invasively determining the blood oxygen saturation level within a subject's tissue is provided as defined by claims 1 and 22. The invention utilizes a near infrared spectrophotometric (NIRS) sensor capable of transmitting a light signal into the tissue of a subject and sensing the light signal once it has passed through the tissue via transmittance or reflectance. The method includes the steps of: (1) transmitting a light signal into the subject's tissue, wherein the transmitted light signal includes a first wavelength, a second wavelength, and a third wavelength; (2) sensing a first intensity and a second intensity of the light signal, along the first, second, and third wavelengths after the light signal travels through the subject at a first and second predetermined distance; (3) determining an attenuation of the light signal for each of the first, second, and third wavelengths using the sensed first intensity and sensed second intensity of the first, second, and third wavelengths; (4) determining a difference in attenuation of the light signal between the first wavelength and the second wavelength, and between the first wavelength and the third wavelength; and (5) determining the blood oxygen saturation level within the subject's tissue using the difference in attenuation between the first wavelength and the second wavelength, and the difference in attenuation between the first wavelength and the third wavelength.

[0015] The present method makes it possible to account for energy losses (i.e. light attenuation) due to light scattering within tissue, other background absorption losses from biological compounds, and other unknown losses including measuring apparatus variability. By determining differential attenuation as a function of wavelength, the energy losses due to scattering as well as other background absorption from biological compounds are cancelled out or minimized relative to the attenuation attributable to deoxyhemoglobin, and attenuation attributable to oxyhemoglobin.

[0016] In order to account for the resulting minimized differential attenuation attributable to tissue light scattering characteristics, fixed light absorbing components, and measuring apparatus characteristics, each of the parameters must be measured or calibrated out. Since direct measurement is difficult, calibration to empirically determined data combined with data developed using the NIRS sensor is performed by using regression techniques. The empirically determined data is collected at or about the same time the data is developed with the NIRS sensor. Once the calibration parameters associated with attenuation attributable to tissue light scattering characteristics, fixed light absorbing components, and measuring apparatus characteristics have been determined, the NIRS sensor can be calibrated.

[0017] The calibrated sensor can then be used to accurately and non-invasively determine the total oxygen saturation level in the original subject tissue or other subject tissue. In addition, if effective pathlength of photon traveling through the tissue is known, for example, the separation distance ("d") between the light source to the light detector is known or is determinable, and the value of "B_λ", which represents the wavelength dependent light scattering differential pathlength factor, then the total amount of concentrations of deoxyhemoglobin (Hb) and oxyhemoglobin (HbO_2) within the examined tissue can be determined using the present method and apparatus.

[0018] The calibrated sensor can be used subsequently to calibrate similar sensors without having to invasively produce a blood sample. Hence, the present method and apparatus enables a non-invasive determination of the blood oxygen saturation level within tissue. For example, an operator can create reference values by sensing a light signal or other reference medium using the calibrated sensor. The operator can then calibrate an uncalibrated sensor by sensing the same light signal or reference medium, and subsequently adjusting the uncalibrated sensor into agreement with the calibrated sensor. Hence, once a reference sensor is created, other similar sensors can be calibrated without the need for invasive procedure.

[0019] There are, therefore, several advantages provided by the present method and apparatus. Those advantages include: 1) a practical non-invasive method and apparatus for determining oxygen saturation within tissue that can be

used to determine the total blood oxygen saturation within tissue as opposed to a change in blood oxygen saturation; 2) a calibration method that accounts for energy losses (e.g., light attenuation) due to light scattering within tissue, other background absorption losses from biological compounds, and other unknown losses including measuring apparatus variability; and 3) a practical non-invasive method and apparatus for determining oxygen saturation within tissue that can distinguish between the contribution of oxygen saturation attributable to venous blood and that saturation attributable to arterial blood; 4) a practical non-invasive method and apparatus for determining oxygen saturation within tissue at certain depth that limits the influence from the superficial tissues.

[0020] In an alternative embodiment, aspects of the above-described methodology are combined with pulse oximetry techniques to provide a non-invasive method of distinguishing between blood oxygen saturation within tissue that is attributable to venous blood and that which is attributable to arterial blood. Pulse oximetry is used to determine arterial oxygen saturation, and the arterial oxygen saturation is, in turn, used to determine the venous oxygen saturation.

[0021] These and other objects, features, and advantages of the present invention method and apparatus will become apparent in light of the detailed description of the invention provided below and the accompanying drawings. The methodology and apparatus described below constitute a preferred embodiment of the underlying invention and do not, therefore, constitute all aspects of the invention that will or may become apparent by one of skill in the art after consideration of the invention disclosed overall herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0022]

FIG.1 is a diagrammatic representation of a NIRS sensor.
FIG.2 is a diagrammatic representation of a NIRS sensor placed on a subject's head.
FIG.3 is a diagrammatic view of a NIRS sensor.
FIG.4 is a block diagram of the present methodology for calibrating a NIRS sensor.
FIG.5 is a graph showing an exemplary plot of absorption coefficient vs. wavelength.

DETAILED DESCRIPTION THE INVENTION

[0023] The present method of and apparatus for non-invasively determining the blood oxygen saturation level within a subject's tissue is provided that utilizes a near infrared spectrophotometric (NIRS) sensor that includes a transducer capable of transmitting a light signal into the tissue of a subject and sensing the light signal once it has passed through the tissue via transmittance or reflectance. The present method and apparatus can be used with a variety of NIRS sensors. The present method is not limited to use with this preferred NIRS sensor, however.

[0024] Referring to FIGS. 1-5, the preferred NIRS sensor includes a transducer portion 10 and processor portion 12. The transducer portion 10 includes an assembly housing 14 and a connector housing 16. The assembly housing 14, which is a flexible structure that can be attached directly to a subject's body, includes one or more light sources 18 and light detectors 19, 20. A disposable adhesive envelope or pad is used for mounting the assembly housing 14 easily and securely to the subject's skin. Light signals of known but different wavelengths from the light sources 18 emit through a prism assembly 22. The light sources 18 are preferably laser diodes that emit light at a narrow spectral bandwidth at predetermined wavelengths. In one embodiment, the laser diodes are mounted within the connector housing 16. The laser diodes are optically interfaced with a fiber optic light guide to the prism assembly 22 that is disposed within the assembly housing 14. In a second embodiment, the light sources 18 are mounted within the assembly housing 14. A first connector cable 26 connects the assembly housing 14 to the connector housing 16 and a second connector cable 28 connects the connector housing 16 to the processor portion 12. The light detector 20 includes one or more photodiodes. The photodiodes are also operably connected to the processor portion 12 via the first and second connector cables 26, 28. The processor portion 12 includes a processor for processing light intensity signals from the light sources 18 and the light detectors 19, 20.

[0025] The processor utilizes an algorithm that characterizes a change in attenuation as a function of the difference in attenuation between different wavelengths. The present method advantageously accounts for but minimizes the effects of pathlength and parameter "E", which represent energy losses (i.e. light attenuation) due to light scattering within tissue (G), other background absorption losses from biological compounds (F), and other unknown losses including measuring apparatus variability (N). $E = G + F + N$.

[0026] Refer to Figure 1, the absorption $A_{b\lambda}$ detected from the deep light detector 20 comprises of attenuation and energy loss from both the deep and shallow tissue, while the absorption $A_{x\lambda}$ detected from the shallow light detector 19 comprises of attenuation and energy loss from shallow tissue only. Absorptions $A_{b\lambda}$ and $A_{x\lambda}$ can be expressed in the form of Equation 5 and Equation 6 below which is a modified version of Equation 2 that accounts for energy losses due to "E":

$$A_{b\lambda} = -\log\left(I_b / I_o\right)_\lambda = \alpha_\lambda * C_b * L_b + \alpha_\lambda * C_x * L_x + E_\lambda \text{ (Eqn.5)}$$

$$A_{x\lambda} = -\log\left(I_x / I_o\right)_\lambda = \alpha_\lambda * C_x * L_x + E_{x\lambda} \quad \text{(Eqn.6)}$$

Substituting Equation 6, into Equation 5 yields A'_λ, which represents attenuation and energy loss from deep tissue only:

$$A'_\lambda = A_{b\lambda} - A_{x\lambda} = \alpha_\lambda * C_b * L_b + \left(E_\lambda - E_{x\lambda}\right) = -\log\left(\frac{I_b}{I_x}\right)_\lambda$$

(Eqn.7)

Where L is the effective pathlength of the photon traveling through the deep tissue and A'_1, and A'_2 are the absorptions of two different wavelengths. Let $E'_\lambda = E_\lambda - E_{x\lambda}$, therefore:

$$A'_1 - A'_2 = \Delta A'_{12} \quad \text{(Eqn.8)}$$

Substituting Equation 7 into Equation 8 for A'_1 and A'_2, $\Delta A'_{12}$ can be expressed as:

$$\Delta A'_{12} = \alpha_{\lambda 12} * C_b * L_b + \Delta E'_{12} \quad \text{(Eqn.9)}$$

and rewritten Equation 9 in expanded form:

$$\Delta A'_{12} = \left\langle (\alpha_{r1} - \alpha_{r2})[Hb]_b + (\alpha_{o1} - \alpha_{o2})[HbO_2]_b \right\rangle L_b + (E'_1 - E'_2)$$
$$= \left(\Delta\alpha_{r12} * [Hb]_b * L_b \right) + \left(\Delta\alpha_{o12} * [HbO_2]_b * L_b \right) + \Delta E'_{12}$$

(Eqn.10)

where:

($\Delta\alpha_{r12} * [Hb]_b * L_b$) represents the attenuation attributable to Hb;
($\Delta\alpha_{o12} * [HbO_2]_b * L_b$) represents the attenuation attributable to HbO_2; and
$\Delta E'_{12}$ represents energy losses (i.e. light attenuation) due to light scattering within tissue, other background absorption losses from biological compounds, and other unknown losses including measuring apparatus variability.

[0027] The multivariate form of Equation 10 is used to determine $[HbO_2]_b$ and $[Hb]_b$ with three different wavelengths:

$$\begin{bmatrix} \Delta A'_{12} - \Delta E'_{12} \\ \Delta A'_{13} - \Delta E'_{13} \end{bmatrix} (L_b)^{-1} = \begin{bmatrix} \Delta\alpha_{r12} & \Delta\alpha_{o12} \\ \Delta\alpha_{r13} & \Delta\alpha_{o13} \end{bmatrix} \begin{bmatrix} [Hb]_b \\ [HbO_2]_b \end{bmatrix}$$

(Eqn. 11)

Rearranging and solving for $[HbO_2]_b$ and $[Hb]_b$, simplifying the $\Delta\alpha$ matrix into $[\Delta\alpha']$:

$$\begin{bmatrix} \Delta A'_{12} \\ \Delta A'_{13} \end{bmatrix} [\Delta\alpha']^{-1} (L_b)^{-1} - \begin{bmatrix} \Delta E'_{12} \\ \Delta E'_{13} \end{bmatrix} [\Delta\alpha']^{-1} (L_b)^{-1} = \begin{bmatrix} [Hb]_b \\ [HbO_2]_b \end{bmatrix}$$

(Eqn. 12)

Then combined matrices $[\Delta A'] [\Delta\alpha']^{-1} = [A_c]$ and $[\Delta E] [\Delta\alpha']^{-1} = [\Psi_c]$:

$$\begin{bmatrix} A_{Hb} \\ A_{HbO_2} \end{bmatrix} (L_b)^{-1} - \begin{bmatrix} \Psi_{Hb} \\ \Psi_{HbO_2} \end{bmatrix} (L_b)^{-1} = \begin{bmatrix} [Hb]_b \\ [HbO_2]_b \end{bmatrix} \qquad \text{(Eqn. 13)}$$

The parameters A_{Hb} and A_{HbO2} represent the product of the matrices $[\Delta A_\lambda]$ and $[\Delta\alpha']^{-1}$ and the parameters Ψ_{Hb} and Ψ_{HbO2} represent the product of the matrices $[\Delta E'_\lambda]$ and $[\Delta\alpha']^{-1}$. To determine the level of cerebral blood oxygen saturation (SnO_2), Equation 13 is rearranged using the form of Equation 1 and is expressed as follows:

$$SnO_2\% = \frac{\left(A_{HbO_2} - \Psi_{HbO_2}\right)}{\left(A_{HbO_2} - \Psi_{HbO_2} + A_{Hb} - \Psi_{Hb}\right)} * 100\% \qquad \text{(Eqn.14)}$$

Note that the effective pathlength L_b cancels out in the manipulation from Equation 13 to Equation 14.

[0028] The value for SnO_2 is initially determined from $SmvO_2$ using Equation 4 and the empirically determined values for SvO_2 and SaO_2. The empirically determined values for SvO_2 and SaO_2 are based on data developed by discrete sampling or continuous monitoring of the subject's blood performed at or about the same time as the sensing of the tissue with the sensor. The temporal and physical proximity of the NIRS sensing and the development of the empirical data helps assure accuracy. The initial values for Kv and Ka within Equation 4 are clinically reasonable values for the circumstances at hand. The values for A_{HbO2} and A_{Hb} are determined mathematically using the values for $I_{b\lambda}$ and $I_{x\lambda}$ for each wavelength sensed with the NIRS sensor (e.g., using Equation 5 and 6). The calibration parameters Ψ_{Hb} and Ψ_{HbO2}, which account for energy losses due to scattering as well as other background absorption from biological compounds, are then determined using Equation 14 and non-linear regression techniques by correlation to different weighted values of SvO_2 and SaO_2; i.e., different values of Ka and Kv. Statistically acceptable values of Kv and Ka and Ψ_{Hb} and Ψ_{HbO2} are converged upon using the non-linear regression techniques. Experimental findings show that after proper selection of Ka and Kv, the calibration parameters Ψ_{Hb} and Ψ_{HbO2} are constant within a statistically acceptable margin of error for an individual NIRS sensor used to monitor brain oxygenation on different human subjects. In other words, once the sensor is calibrated it can be used on various human subjects and produce accurate information for each human subject. The same is true for animal subjects.

[0029] In an alternative method of determining the absolute oxygen saturation value Equation 7 is rewritten:

$$A'_\lambda - E'_\lambda = -\log(I_b / I_x)_\lambda - E'_\lambda$$
$$= \alpha_\lambda * C * L_b = (\alpha_{r\lambda}[Hb]_b + \alpha_{o\lambda}[HbO_2]_b)L_b \quad \text{(Eqn.15)}$$

For a two wavelength system, let "R" be a calibration index parameter:

$$R = \frac{A'_1 - E'_1}{A'_2 - E'_2} = \frac{(\alpha_{r1}[Hb]_b + \alpha_{o1}[HbO_2]_b)L_b}{(\alpha_{r2}[Hb]_b + \alpha_{o2}[HbO_2]_b)L_b}$$
$$= \frac{\alpha_{r1} + \alpha_{o1}\dfrac{[HbO_2]_b}{[Hb]_b}}{\alpha_{r2} + \alpha_{o2}\dfrac{[HbO_2]_b}{[Hb]_b}} = \frac{\alpha_{r1} + \alpha_{o1}\dfrac{SnO_2}{1 - SnO_2}}{\alpha_{r2} + \alpha_{o2}\dfrac{SnO_2}{1 - SnO_2}} \quad \text{(Eqn.16)}$$

Canceling out L_b and substituting:

$$\frac{[HbO_2]_b}{[Hb]_b} = \frac{SnO_2}{1 - SnO_2} \quad \text{from} \quad SnO_2 = \frac{[HbO_2]_b}{[HbO_2]_b + [Hb]_b}$$

the following expression for SnO_2 is obtained:

$$SnO_2 = \frac{\alpha_{r1} - \alpha_{r2}R}{(\alpha_{r1} - \alpha_{o1}) + (\alpha_{o2} - \alpha_{r2})R} \quad \text{(Eqn.17)}$$

[0030] The value of A_1' and A_2' are determined by measuring I_b and I_x for each wavelength. The parameters E'_1 and E'_2 can be considered as empirically determined calibration coefficients derived from the "best-fit" combinations of the weighted ratios of venous and arterial blood-oxygen saturation of the brain. By using non-linear regression techniques, the values of E'_1 and E'_2 are determined by correlating to different combinations of venous and arterial oxygen saturation weighted values to find the "best-fit" relationship of "R" as a function of A_1', A_2', E'_1 and E'_2 (Equation 17) to a specific ratio of venous and arterial saturation weighted values.

[0031] In the determination of the SnO_2 percentage, the effective photon pathlength L_b cancels out. If, however, the photon pathlength is known or estimated, then the determination of the total value of Hb and/or HbO_2 is possible. For example, if a value for pathlength L_b is input into Equation 13 along with the calibration values Ψ_{Hb} and Ψ_{HbO2}, then the total value of Hb and/or HbO_2 can be calculated. According to Equation 2, pathlength L can be estimated from the product of "B*d". The light source to detector separation (optode) distance parameter "d" in the pathlength calculation is a measurable value and can be made constant by setting a fixed distance between light source to detector in the NIRS sensor design. Alternatively, the parameter "d" can be measured once the optodes are placed on the subject by use of calipers, ruler, or other distance measurement means. The pathlength differential factor "B" is more difficult to measure and requires more sophisticated equipment. From a large data set of measured neonatal and adult head differential pathlength factor values, an estimation of the value of "B" can be determined within a statistically acceptable margin of error. Substitution of these predetermined values of "B" into Equation 13 results in the determination of the total values of Hb and HbO_2.

[0032] An alternative method of determining total values of Hb and HbO_2 combines Equation 3 and Equation 13 together. The multivariate form of Equation 3 is shown below:

$$\begin{bmatrix} -\log(I_{t2}/I_{t1})_{\lambda 1}/L_{\lambda 1} \\ -\log(I_{t2}/I_{t1})_{\lambda 2}/L_{\lambda 2} \\ -\log(I_{t2}/I_{t1})_{\lambda 3}/L_{\lambda 3} \end{bmatrix} = \begin{bmatrix} \alpha_{Hb\lambda 1} & \alpha_{HbO_2\lambda 1} \\ \alpha_{Hb\lambda 2} & \alpha_{HbO_2\lambda 2} \\ \alpha_{Hb\lambda 3} & \alpha_{HbO_2\lambda 3} \end{bmatrix} * \begin{bmatrix} \Delta Hb \\ \Delta HbO_2 \end{bmatrix} \qquad \text{(Eqn.18)}$$

At time t = t_1, the values of ΔHb and ΔHbO_2 are zero. Applying Equation 13, and knowing the calibration values of Ψ_{Hb} and Ψ_{HbO2} at a predetermined differential pathlength factor "B" and optode separation "d", the total absolute values of Hb and HbO_2 are determined at time t = t_1, which are represented by $[Hb]_{t1}$ and $[HbO_2]_{t1}$ respectively. At time t=t_2, the values of ΔHb and ΔHbO_2 are then determined using Equation 18. The total values of Hb and HbO_2 are then determined at time t = t_2 using the following equations:

$$[Hb]_{t_2} = \Delta Hb(t_2) + [Hb]_{t_1} \qquad \text{(Eqn.19)}$$

$$[HbO_2]_{t_2} = \Delta HbO_2(t_2) + [HbO_2]_{t_1} \qquad \text{(Eqn.20)}$$

Equations 19 and 20 are valid only if all the shared parameters in Equations 13 and 18 are exact. Reduced to practice, the advantage of combining Equations 13 and 18 result in improved signal to noise ratio (SNR) in the calculation of the total values for Hb and HbO_2. Conversely, improved SNR in the calculation of SnO_2 is also obtained from the following expression:

$$SnO_2\ \% = \frac{HbO_2}{(HbO_2 + Hb)} * 100\% \qquad \text{(Eqn.21)}$$

[0033] After the calibration parameters Ψ_{Hb} and Ψ_{HbO2} are determined using the above-described methodology for an individual NIRS sensor, this particular sensor is said to be calibrated. A calibrated NIRS sensor affords accurate measurement of total tissue oxygen saturation, SnO_2, by non-invasive means. The calibrated sensor can be used thereafter on any human patient, including adults and neonates. The same is true for animal subject if the sensor was calibrated on animals. Although the present method is described above in terms of sensing blood oxygenation within cerebral tissue, the present method and apparatus are not limited to cerebral applications and can be used to determine blood oxygenation within tissue found elsewhere within the subject's body.

[0034] According to an additional aspect of the present invention, the above-described method can also be used to establish a calibrated "reference" sensor that can be used to calibrate similar sensors through the use of a phantom sample (also referred to as a "reference sample"). The phantom sample has optical characteristics that are similar to the tissue being examined by the NIRS sensor. The calibrated reference NIRS sensor is used to sense the phantom sample and produce reference values. Similar, but uncalibrated, NIRS sensors can thereafter be calibrated by sensing the same phantom sample and adjusting either the hardware of the uncalibrated sensor or the output of the uncalibrated sensor until the output of the uncalibrated sensor agrees with the reference values produced by the calibrated reference sensor. Therefore, the calibration parameters Ψ_{Hb} and Ψ_{HbO2} for the uncalibrated sensor would be determined from the phantom sample. This technique makes it unnecessary to calibrate each new sensor in the manner described above, and thereby provides a relatively quick and cost effective way to calibrate NIRS sensors.

[0035] Besides Hb and HbO_2, other biological constituents of interest (e.g., cytochrome aa_3, etc.) could be determined using the multivariate forms of equations 2, 3, 6 or 7. For each additional constituent to be determined, an additional measuring wavelength will be needed.

[0036] In an alternative embodiment, the above-described methodology can be combined with pulse oximetry techniques to provide an alternative non-invasive method of distinguishing between oxygen saturation attributable to venous blood and that attributable to arterial blood. As demonstrated by Equation 4, $SmvO_2$ is determined by the ratio of venous oxygen saturation SvO_2 and arterial oxygen saturation SaO_2. A calibrated NIRS sensor affords accurate measurement of total tissue oxygen saturation, SnO_2, by using regression techniques by correlation to mixed venous oxygen saturation

$SmvO_2$. Therefore, the following expression will result:

$$SnO_2 = SmvO_2 = K_v * SvO_2 + Ka * SaO_2 \qquad \text{(Eqn. 22)}$$

Non-invasive pulse oximetry techniques can be used to determine the arterial oxygen saturation (SaO_2) of peripheral tissue (i.e. finger, ear, nose) by monitoring pulsatile optical attenuation changes of detected light induced by pulsatile arterial blood volume changes in the arteriolar vascular system. Arterial blood oxygen saturation determined by pulse oximetry is clinically denoted as SpO_2. If NIRS monitoring and pulse oximetry monitoring are done simultaneously and SpO_2 is set equal to SaO_2 in Equation 23, then venous oxygen saturation can be determined from the following expression:

$$SvO_2 = \frac{SnO_2 - (Ka * SpO_2)}{Kv} \qquad \text{(Eqn. 23)}$$

For the brain, venous oxygen saturation SvO_2 would be determined from internal jugular vein ($SijvO_2$), jugular bulb ($SjbO_2$), or sagittal sinus ($SssO_2$) and the parameters Ka and Kv would be empirically determined during the calibration of the NIRS sensor. Under most physiological conditions, SpO_2 is representative of brain arterial oxygen saturation SaO_2. Therefore, depending on which venous saturation parameter was used to calibrate the NIRS sensor, this clinically important parameter (i.e., $SijvO_2$, $SjbO_2$, or $SssO_2$) can be determined by Equation 24 by non-invasive means.

[0037] Since many changes and variations of the disclosed embodiment of the invention may be made without departing from the inventive concept, it is not intended to limit the invention otherwise than as required by the appended claims.

Claims

1. A method for non-invasively determining a blood oxygen saturation level within a subject's tissue using a near infrared spectrophotometric sensor capable of transmitting a light signal into the tissue of a subject and sensing the light signal at a predetermined distance once it has passed through the tissue via transmittance or reflectance, said method comprising the steps of:

   transmitting a light signal into the subject's tissue using a light source (18) of the sensor, wherein the transmitted light signal includes a first wavelength, a second wavelength, and a third wavelength;
   sensing a first intensity of the light signal using a first light detector (20) of the sensor at a first predetermined distance and sensing a second intensity of the light signal using a second light detector (19) of the sensor at a second predetermined distance from the light source (18), comprising sensing at the first, second, and third wavelengths after the light signal travels through the subject, wherein the first intensity sensed at the first predetermined distance after the light signal travels through the subject comprises of attenuation and energy loss from both deep and shallow tissue and wherein the second intensity sensed at the second predetermined distance after the light signal travels through the subject comprises of attenuation and energy loss from shallow tissue;
   and, with a processor:

      determining an attenuation of the light signal for each of the first, second, and third wavelengths using the sensed first intensity and sensed second intensity at the first, second, and third wavelengths;
      determining a difference in the attenuation of the light signal between the first wavelength and the second wavelength, and between the first wavelength and the third wavelength;
      cancelling out or minimizing the energy losses (E) due to: light scattering within the tissue (G); other background absorption losses from biological compounds (F); and other losses including measuring apparatus variability (N), by determining differential attenuation as a function of wavelength; and
      determining the blood oxygen saturation level within the subject's tissue using the difference in attenuation between the first wavelength and the second wavelength, and the difference in attenuation between the first wavelength and the third wavelength.

2. The method of claim 1, wherein the sensor is calibrated using equation:

$$SmvO_2 = Kv*SvO_2 + Ka*SaO_2$$

where $SmvO_2$ is mixed venous oxygen saturation;
SVO_2 is venous oxygen saturation;
SaO_2 is arterial oxygen saturation; and
Kv and Ka are calibration parameters.

3. The method of claim 2, wherein the sensor is calibrated by using empirical data to determine a first calibration constant and a second calibration constant.

4. The method of claim 1, wherein the sensor is calibrated using empirical data that relates to the subject's tissue that is sensed by the sensor to account for light signal attenuation resulting from light signal scattering within the subject's tissue.

5. The method of any preceding claim, further comprising:

determining a first calibration constant and a second calibration constant using empirical data developed from the subject at or about the same time as when the sensing occurs; and
determining the blood oxygen saturation level within the subject's tissue using the first calibration constant and the second calibration constant.

6. The method of any preceding claim, further comprising:

determining a first calibration constant and a second calibration constant using empirical data developed from the subject at or about the same time as when the sensing occurs; and
calibrating the sensor using the first calibration constant and the second calibration constant.

7. The method of any of claims 3 to 6, wherein the empirical data is collected by discretely sampling a venous blood source and an arterial blood source from the subject.

8. The method of any of claims 3 to 6, wherein the empirical data is collected by continuously monitoring a venous blood source and an arterial blood source from the subject.

9. The method of any preceding claim, wherein the step of determining the blood oxygen saturation level within the subject's tissue utilizes the equation:

$$SnO_2\% = \frac{(A_{HbO_2} - \Psi_{HbO_2})}{(A_{HbO_2} - \Psi_{HbO_2} + A_{Hb} - \Psi_{Hb})} * 100\%$$

where Ψ_{HbO_2} represents a or the first calibration constant, Ψ_{Hb} represents a or the second calibration constant, A_{HbO_2} represents a difference in attenuation of light signal attributable to oxyhemoglobin, and A_{Hb} represents a difference in attenuation of light signal attributable to deoxyhemoglobin.

10. The method of claim 9, further comprising the steps of:

determining a photon pathlength L_b; and
determining a concentration of oxyhemoglobin and a concentration of deoxyhemoglobin within the subject's tissue using the first and second calibration constants.

11. The method of claim 10, wherein the concentration of oxyhemoglobin (HbO_2) and the concentration of deoxyhemoglobin (Hb) within the subject's tissue are determined using the equation:

$$\begin{bmatrix} A_{Hb} \\ A_{HbO_2} \end{bmatrix} (L_b)^{-1} - \begin{bmatrix} \Psi_{Hb} \\ \Psi_{HbO_2} \end{bmatrix} (L_b)^{-1} = \begin{bmatrix} [Hb]_b \\ [HbO_2]_b \end{bmatrix}.$$

12. The method of any preceding claim, wherein the step of determining a difference in attenuation of the light signal between the first wavelength and the second wavelength utilizes the equation:

$$\begin{aligned} \Delta A'_{12} &= A'_1 - A'_2 = -\log(I_b/I_x)_1 + \log(I_b/I_x)_2 \\ &= \{(\alpha_{r1} - \alpha_{r2})[Hb]_b + (\alpha_{o1} - \alpha_{o2})[HbO_2]_b\} L_b + (E'_1 - E'_2) \\ &= (\Delta\alpha_{r12}[Hb]_b + \Delta\alpha_{o12}[HbO_2]_b) L_b + \Delta E_{12} \end{aligned}.$$

and the step of determining a difference in attenuation of the light signal between the first wavelength and the third wavelength utilizes the equation:

$$\begin{aligned} \Delta A'_{13} &= A'_1 - A'_3 = -\log(I_b/I_x)_1 + \log(I_b/I_x)_3 \\ &= \{(\alpha_{r1} - \alpha_{r3})[Hb]_b + (\alpha_{o1} - \alpha_{o3})[HbO_2]_b\} L_b + (E'_1 - E'_3) \\ &= (\Delta\alpha_{r13}[Hb]_b + \Delta\alpha_{o13}[HbO_2]_b) L_b + \Delta E_{13} \end{aligned}.$$

13. The method of claim 12, wherein the step of determining an attenuation of the light signal of a wavelength λ utilizes the equation:

$$\begin{aligned} A'_\lambda &= -\log(I_b/I_x)_\lambda = (\alpha_{r\lambda}[Hb]_b + \alpha_{o\lambda}[HbO_2]_b) L'_b + E'_\lambda \\ &= (\alpha_{r\lambda}[Hb]_b + \alpha_{o\lambda}[HbO_2]_b) L_b + (E - E_x)_\lambda \end{aligned}$$

for one or more of the first, second, and third wavelengths.

14. The method of any preceding claim, further comprising determining a concentration of oxyhemoglobin and a concentration of deoxyhemoglobin within a subject's tissue at an initial time *t1* and a subsequent time *t2,* said method comprising the steps of:

(a) determining a first calibration constant and a second calibration constant using empirical data developed from the subject at or about the same time as when the sensing occurs;
(b) determining a photon pathlength L_b;
(c) determining the concentration of oxyhemoglobin and the concentration of deoxyhemoglobin within the subject's tissue at the initial time t1 using the equation:

$$\begin{bmatrix} A_{Hb} \\ A_{HbO_2} \end{bmatrix} (L_b)^{-1} - \begin{bmatrix} \Psi_{Hb} \\ \Psi_{HbO_2} \end{bmatrix} (L_b)^{-1} = \begin{bmatrix} Hb \\ HbO_2 \end{bmatrix}$$

where Ψ_{HbO2} represents the first calibration constant, Ψ_{Hb} represents the second calibration constant, A_{HbO2} represents a difference in attenuation of light signal attributable to oxyhemoglobin, and A_{Hb} represents a difference in attenuation of light signal attributable to deoxyhemoglobin;

(d) determining a change in the concentration of oxyhemoglobin and a change in the concentration of deoxyhemoglobin from the initial time *t1* to a subsequent second time *t2*, determined using the equation:

$$\begin{bmatrix} -\log(I_{t2}/I_{t1})_{\lambda 1}/L_{\lambda 1} \\ -\log(I_{t2}/I_{t1})_{\lambda 2}/L_{\lambda 2} \\ -\log(I_{t2}/I_{t1})_{\lambda 3}/L_{\lambda 3} \end{bmatrix} = \begin{bmatrix} \alpha_{Hb\lambda 1} & \alpha_{HbO_2\lambda 1} \\ \alpha_{Hb\lambda 2} & \alpha_{HbO_2\lambda 2} \\ \alpha_{Hb\lambda 3} & \alpha_{HbO_2\lambda 3} \end{bmatrix} * \begin{bmatrix} \Delta Hb \\ \Delta HbO_2 \end{bmatrix};$$

and

(e) determining the concentration of oxyhemoglobin and the concentration of deoxyhemoglobin within the subject's tissue at the subsequent time *t2* using the equations:

$$[Hb]_{t_2} = \Delta Hb(t_2) + [Hb]_{t_1}$$

and

$$[HbO_2]_{t_2} = \Delta HbO_2(t_2) + [HbO_2]_{t_1}.$$

15. The method of any preceding claim, further comprising:

sensing a third intensity and a fourth intensity of the light signal, using a light detector (19, 20) of the sensor at said first and said second predetermined distances, comprising sensing at the second wavelength, after the light signal travels through the subject;

determining a first attenuation of the light signal for the first wavelength using said first intensity and said second intensity;

determining a second attenuation of the light signal for the second wavelength using said third intensity and said fourth intensity;

determining a ratio of said first and said second attenuations of the light signal for the first, and second wavelengths;

determining the blood oxygen saturation level within the subject's tissue using said ratio.

16. The method of claim 15, wherein the step of determining the blood oxygen saturation level within the subject's tissue utilizes the equation:

$$SnO_2\% = \frac{\alpha_{r1} - \alpha_{r2}R}{(\alpha_{r1} - \alpha_{o1}) + (\alpha_{o2} - \alpha_{r2})R} 100\%$$

where R represents the ratio of attenuations of the light signal for each of the first, and second wavelengths.

17. The method of claim 16, wherein the step of determining the ratio R of attenuations of the light signal for the first, and second wavelengths utilizes the equation:

$$R = \frac{A_1' - E_1'}{A_2' - E_2'}$$

where E'_1 represents the first calibration constant, E'_2 represents the second calibration constant, A'_1 represents the first attenuation of light signal of the first wavelength, and A'_2 represents the second attenuation of light signal of the second wavelength.

18. The method of claim 17, wherein the step of determining the first attenuation of the first wavelength utilizes the equation:

$$-\log(I_b / I_x)_1 = (\alpha_{r1}[Hb]_b + \alpha_{o1}[HbO_2]_b)L_b + (E - E_x)_1 .$$

and the step of determining the second attenuation of the second wavelength utilizes the equation:

$$-\log(I_b / I_x)_2 = (\alpha_{r2}[Hb]_b + \alpha_{o2}[HbO_2]_b)L_b + (E - E_x)_2 .$$

19. The method of claim 15, wherein the step of determining the blood oxygen saturation level within the subject's tissue comprising the steps of:

determining the attenuation ratio R of the light signal for each of the first, and second wavelengths;
determining the blood oxygen saturation level utilizing an empirical obtained calibration curve defining the relationship between the said attenuation ratio *R* with blood oxygen saturation.

20. The method of claim 15, further comprising the steps of:

determining a photon pathlength L_b; and
determining a concentration of oxyhemoglobin and a concentration of deoxyhemoglobin within the subject's tissue using first and second calibration constants.

21. The method of claim 20, wherein the concentration of oxyhemoglobin (HbO_2) and the concentration of deoxyhemoglobin (Hb) within the subject's tissue are determined using the equation:

$$\begin{bmatrix} A_1' \\ A_2' \end{bmatrix} \begin{bmatrix} \alpha_{r1} & \alpha_{o1} \\ \alpha_{r2} & \alpha_{o2} \end{bmatrix}^{-1} (L_b)^{-1} - \begin{bmatrix} E_1' \\ E_2' \end{bmatrix} \begin{bmatrix} \alpha_{r1} & \alpha_{o1} \\ \alpha_{r2} & \alpha_{o2} \end{bmatrix}^{-1} (L_b)^{-1} = \begin{bmatrix} [Hb]_b \\ [HbO_2]_b \end{bmatrix}$$

where E'_1 represents the first calibration constant, E'_2 represents the second calibration constant, A'_1 represents the first attenuation of light signal of the first wavelength, and A'_2 represents the second attenuation of light signal of the second wavelength.

22. An apparatus for non-invasively determining a blood oxygen saturation level within a subject's tissue using a near infrared spectrophotometric sensor capable of transmitting a light signal into the tissue of a subject and sensing the light signal at a predetermined distance once it has passed through the tissue via transmittance or reflectance, wherein:

a light source (18) of the sensor is arranged to transmit a light signal into the subject's tissue, wherein the transmitted light signal includes a first wavelength, a second wavelength, and a third wavelength;
a first light detector (20) of the sensor is arranged at a first predetermined distance from the light source (18) to sense a first intensity of the light signal at the first, second, and third wavelengths after the light signal travels through the subject, and a second light detector (19) of the sensor is arranged at a second predetermined distance from the light source (18), to sense a second intensity of the light signal at the first, second, and third wavelengths after the light signal travels through the subject, wherein the first intensity sensed at the first predetermined distance after the light signal travels through the subject comprises of attenuation and energy loss from both deep and shallow tissue and wherein the second intensity sensed at the second predetermined distance after the light signal travels through the subject comprises of attenuation and energy loss from shallow tissue;
wherein the sensor is arranged to cancel out or minimize the energy losses (E) due to: light scattering within the tissue (G); other background absorption losses from biological compounds (F); and other losses including measuring apparatus variability (N), by determining differential attenuation as a function of wavelength;
wherein said apparatus further comprises:

means for determining an attenuation of the light signal for each of the first, second, and third wavelengths using the sensed first intensity and sensed second intensity of the first, second, and third wavelengths;
means for determining a difference in the attenuation of the light signal between the first wavelength and the second wavelength, and between the first wavelength and the third wavelength; and
means for determining the blood oxygen saturation level within the subject's tissue using the difference in attenuation between the first wavelength and the second wavelength, and the difference in attenuation between the first wavelength and the third wavelength.

Patentansprüche

1. Verfahren zum nicht-invasiven Bestimmen eines Blutsauerstoffsättigungsgrads im Gewebe eines Probanden unter Verwendung eines spektrophotometrischen Nahinfrarot-Sensors, der in der Lage ist, ein Lichtsignal in das Gewebe eines Probanden zu übertragen und das Lichtsignal in einem vorbestimmten Abstand zu erfassen, sobald es das Gewebe per Transmission oder Reflexion durchdrungen hat, wobei das Verfahren die Schritte umfasst des:

Übertragens eines Lichtsignals in das Gewebe des Probanden unter Verwendung einer Lichtquelle (18) des Sensors, wobei das übertragene Lichtsignal eine erste Wellenlänge, eine zweite Wellenlänge und eine dritte Wellenlänge beinhaltet;
Erfassens einer ersten Intensität des Lichtsignals unter Verwendung eines ersten Lichtdetektors (20) des Sensors in einem ersten vorbestimmen Abstand, und Erfassens einer zweiten Intensität des Lichtsignals unter Verwendung eines zweiten Lichtdetektors (19) des Sensors in einem zweiten vorbestimmten Abstand von der Lichtquelle (18), umfassend das Erfassen bei der ersten, zweiten und dritten Wellenlänge, nachdem das Lichtsignal den Probanden durchläuft, wobei die erste Intensität, die im ersten vorbestimmten Abstand erfasst wird, nachdem das Lichtsignal den Probanden durchläuft, aus Dämpfung und Energieverlust von sowohl tiefem als auch oberflächlichem Gewebe besteht, und wobei die zweite Intensität, die im zweiten vorbestimmten Abstand erfasst wird, nachdem das Lichtsignal den Probanden durchläuft, aus Dämpfung und Energieverlust von oberflächlichem Gewebe besteht;
und, mit einem Prozessor:

Bestimmens einer Dämpfung des Lichtsignals für jede der ersten, zweiten und dritten Wellenlänge unter Verwendung der erfassten ersten Intensität und erfassten zweiten Intensität bei der ersten, zweiten und dritten Wellenlänge;
Bestimmens einer Differenz in der Dämpfung des Lichtsignals zwischen der ersten Wellenlänge und der zweiten Wellenlänge, und zwischen der ersten Wellenlänge und der dritten Wellenlänge;
Aufhebens oder Minimierens der Energieverluste (E), die bedingt sind durch: Lichtstreuung im Gewebe (G); andere Hintergrundabsorptionsverluste wegen biologischer Verbindungen (F); und andere Verluste, einschließlich Messvorrichtungsvariabilität (N), durch Bestimmen von differentieller Dämpfung als eine Funktion der Wellenlänge; und
Bestimmens des Blutsauerstoffsättigungsgrads im Gewebe des Probanden unter Verwendung der Differenz in der Dämpfung zwischen der ersten Wellenlänge und der zweiten Wellenlänge, und der Differenz in der Dämpfung zwischen der ersten Wellenlänge und der dritten Wellenlänge.

2. Verfahren nach Anspruch 1, wobei der Sensor kalibriert wird unter Verwendung von Gleichung:

$$SmvO_2 = Kv*SvO_2 + Ka*SaO_2$$

wobei $SmvO_2$ gemischtvenöse Sauerstoffsättigung ist;
SvO_2 venöse Sauerstoffsättigung ist;
SaO_2 arterielle Sauerstoffsättigung ist; und
Kv und Ka Kalibrierungsparameter sind.

3. Verfahren nach Anspruch 2, wobei der Sensor unter Verwendung von empirischen Daten kalibriert wird, um eine erste Kalibrierungskonstante und eine zweite Kalibrierungskonstante zu bestimmen.

4. Verfahren nach Anspruch 1, wobei der Sensor unter Verwendung von sich auf das Gewebe des Probanden beziehenden empirischen Daten kalibriert wird, die vom Sensor erfasst werden, um Lichtsignaldämpfung zu berücksichtigen, die aus Lichtsignalstreuung im Gewebe des Probanden resultiert.

5. Verfahren nach einem der vorstehenden Ansprüche, weiter umfassend:

Bestimmen einer ersten Kalibrierungskonstante und einer zweiten Kalibrierungskonstante unter Verwendung von empirischen Daten, die von dem Probanden zu dem gleichen oder etwa dem gleichen Zeitpunkt entwickelt werden, zu dem das Erfassen stattfindet; und
Bestimmen des Blutsauerstoffsättigungsgrads im Gewebe des Probanden unter Verwendung der ersten Kalibrierungskonstante und der zweiten Kalibrierungskonstante.

6. Verfahren nach einem der vorstehenden Ansprüche, weiter umfassend:

Bestimmen einer ersten Kalibrierungskonstante und einer zweiten Kalibrierungskonstante unter Verwendung von empirischen Daten, die von dem Probanden zu dem gleichen oder etwa dem gleichen Zeitpunkt entwickelt werden, zu dem das Erfassen stattfindet; und
Kalibrieren des Sensors unter Verwendung der ersten Kalibrierungskonstante und der zweiten Kalibrierungskonstante.

7. Verfahren nach einem der Ansprüche 3 bis 6, wobei die empirischen Daten durch diskretes Abtasten einer venösen Blutquelle und einer arteriellen Blutquelle von dem Probanden gesammelt werden.

8. Verfahren nach einem der Ansprüche 3 bis 6, wobei die empirischen Daten durch kontinuierliches Überwachen einer venösen Blutquelle und einer arteriellen Blutquelle von dem Probanden gesammelt werden.

9. Verfahren nach einem vorstehenden Anspruch, wobei der Schritt des Bestimmens des Blutsauerstoffsättigungsgrads im Gewebe des Probanden die Gleichung:

$$SnO_2\% = \frac{(A_{HbO_2} - \Psi_{HbO_2})}{(A_{HbO_2} - \Psi_{HbO_2} + A_{Hb} - \Psi_{Hb})} * 100\%$$

nutzt, wobei ψ_{HbO_2} eine oder die erste Kalibrierungskonstante darstellt, ψ_{Hb} eine oder die zweite Kalibrierungskonstante darstellt, A_{HbO_2} eine Differenz in der Dämpfung des Lichtsignals darstellt, die auf Oxyhämoglobin zurückzuführen ist, und A_{Hb} eine Differenz in der Dämpfung des Lichtsignals darstellt, die auf Desoxyhämoglobin zurückzuführen ist.

10. Verfahren nach Anspruch 9, weiter umfassend die Schritte des:

Bestimmens einer Photonenweglänge L_b; und
Bestimmens einer Konzentration von Oxyhämoglobin und einer Konzentration von Desoxyhämoglobin im Gewebe des Probanden unter Verwendung der ersten und zweiten Kalibrierungskonstante.

11. Verfahren nach Anspruch 10, wobei die Konzentration von Oxyhämoglobin (HbO_2) und die Konzentration von Desoxyhämoglobin (Hb) im Gewebe des Probanden unter Verwendung der Gleichung:

$$\begin{bmatrix} A_{Hb} \\ A_{HbO_2} \end{bmatrix} (L_b)^{-1} - \begin{bmatrix} \Psi_{Hb} \\ \Psi_{HbO_2} \end{bmatrix} (L_b)^{-1} = \begin{bmatrix} [Hb]_b \\ [HbO_2]_b \end{bmatrix}$$

bestimmt werden.

12. Verfahren nach einem vorstehenden Anspruch, wobei der Schritt des Bestimmens einer Differenz in der Dämpfung des Lichtsignals zwischen der ersten Wellenlänge und der zweiten Wellenlänge die Gleichung:

$$\begin{aligned} \Delta A'_{12} &= A'_1 - A'_2 = -\log(I_b/I_x)_1 + \log(I_b/I_x)_2 \\ &= \{(\alpha_{r1} - \alpha_{r2})[Hb]_b + (\alpha_{o1} - \alpha_{o2})[HbO_2]_b\} L_b + (E'_1 - E'_2) \\ &= (\Delta\alpha_{r12}[Hb]_b + \Delta\alpha_{o12}[HbO_2]_b) L_b + \Delta E_{12} \end{aligned}$$

nutzt, und der Schritt des Bestimmens einer Differenz in der Dämpfung des Lichtsignals zwischen der ersten Wellenlänge und der dritten Wellenlänge die Gleichung:

$$\begin{aligned} \Delta A'_{13} &= A'_1 - A'_3 = -\log(I_b/I_x)_1 + \log(I_b/I_x)_3 \\ &= \{(\alpha_{r1} - \alpha_{r3})[Hb]_b + (\alpha_{o1} - \alpha_{o3})[HbO_2]_b\} L_b + (E'_1 - E'_3) \\ &= (\Delta\alpha_{r13}[Hb]_b + \Delta\alpha_{o13}[HbO_2]_b) L_b + \Delta E_{13} \end{aligned}$$

nutzt.

13. Verfahren nach Anspruch 12, wobei der Schritt des Bestimmens einer Dämpfung des Lichtsignals einer Wellenlänge A die Gleichung:

$$\begin{aligned} A'_\lambda &= -\log(I_b/I_x)_\lambda = (\alpha_{r\lambda}[Hb]_b + \alpha_{o\lambda}[HbO_2]_b) L'_b + E'_\lambda \\ &= (\alpha_{r\lambda}[Hb]_b + \alpha_{o\lambda}[HbO_2]_b) L_b + (E - E_x)_\lambda \end{aligned}$$

für eine oder mehrere der ersten, zweiten und dritten Wellenlänge nutzt.

14. Verfahren nach einem der vorstehenden Ansprüche, weiter umfassend das Bestimmen einer Konzentration von Oxyhämoglobin und einer Konzentration von Desoxyhämoglobin im Gewebe eines Probanden zu einem anfänglichen Zeitpunkt *t1* und einem nachfolgenden Zeitpunkt *t2*, wobei das Verfahren die Schritte umfasst des:

(a) Bestimmens einer ersten Kalibrierungskonstante und einer zweiten Kalibrierungskonstante unter Verwendung von empirischen Daten, die von dem Probanden zu dem gleichen oder etwa dem gleichen Zeitpunkt entwickelt werden, zu dem das Erfassen stattfindet;
(b) Bestimmens einer Photonenweglänge L_b;
(c) Bestimmens der Konzentration von Oxyhämoglobin und der Konzentration von Desoxyhämoglobin im Gewebe des Probanden zum anfänglichen Zeitpunkt t1 unter Verwendung der Gleichung:

$$\begin{bmatrix} A_{Hb} \\ A_{HbO_2} \end{bmatrix} (L_b)^{-1} - \begin{bmatrix} \Psi_{Hb} \\ \Psi_{HbO_2} \end{bmatrix} (L_b)^{-1} = \begin{bmatrix} Hb \\ HbO_2 \end{bmatrix}$$

wobei ψ_{HbO_2} die erste Kalibrierungskonstante darstellt, ψ_{Hb} die zweite Kalibrierungskonstante darstellt, A_{HbO_2} eine Differenz in der Dämpfung des Lichtsignals darstellt, die auf Oxyhämoglobin zurückzuführen ist, und A_{Hb} eine Differenz in der Dämpfung des Lichtsignals darstellt, die auf Desoxyhämoglobin zurückzuführen ist;
(d) Bestimmens einer Veränderung in der Konzentration von Oxyhämoglobin und einer Veränderung in der Konzentration von Desoxyhämoglobin vom anfänglichen Zeitpunkt *t1* zu einem nachfolgenden zweiten Zeitpunkt *t2*, die unter Verwendung der Gleichung:

$$\begin{bmatrix} -\log(I_{t2}/I_{t1})_{\lambda 1}/L_{\lambda 1} \\ -\log(I_{t2}/I_{t1})_{\lambda 2}/L_{\lambda 2} \\ -\log(I_{t2}/I_{t1})_{\lambda 3}/L_{\lambda 3} \end{bmatrix} = \begin{bmatrix} \alpha_{Hb\lambda 1} & \alpha_{HbO_2\lambda 1} \\ \alpha_{Hb\lambda 2} & \alpha_{HbO_2\lambda 2} \\ \alpha_{Hb\lambda 3} & \alpha_{HbO_2\lambda 3} \end{bmatrix} * \begin{bmatrix} \Delta Hb \\ \Delta HbO_2 \end{bmatrix}$$

bestimmt wird; und
(e) Bestimmens der Konzentration von Oxyhämoglobin und der Konzentration von Desoxyhämoglobin im Gewebe des Probanden zum nachfolgenden Zeitpunkt *t2* unter Verwendung der Gleichungen:

$$[Hb]_{t_2} = \Delta Hb(t_2) + [Hb]_{t_1}$$

und

$$[HbO_2]_{t_2} = \Delta HbO_2(t_2) + [HbO_2]_{t_1}.$$

15. Verfahren nach einem der vorstehenden Ansprüche, weiter umfassend:

Erfassen einer dritten Intensität und einer vierten Intensität des Lichtsignals unter Verwendung eines Lichtdetektors (19, 20) des Sensors im ersten und dem zweiten vorbestimmten Abstand, umfassend das Erfassen bei der zweiten Wellenlänge, nachdem das Lichtsignal den Probanden durchläuft;
Bestimmen einer ersten Dämpfung des Lichtsignals für die erste Wellenlänge unter Verwendung der ersten Intensität und der zweiten Intensität;
Bestimmen einer zweiten Dämpfung des Lichtsignals für die zweite Wellenlänge unter Verwendung der dritten Intensität und der vierten Intensität;
Bestimmen eines Verhältnisses der ersten und der zweiten Dämpfung des Lichtsignals für die erste und zweite Wellenlänge;
Bestimmen des Blutsauerstoffsättigungsgrads im Gewebe des Probanden unter Verwendung des Verhältnisses.

16. Verfahren nach Anspruch 15, wobei der Schritt des Bestimmens des Blutsauerstoffsättigungsgrads im Gewebe des Probanden die Gleichung:

$$SnO_2\% = \frac{\alpha_{r1} - \alpha_{r2}R}{(\alpha_{r1} - \alpha_{o1}) + (\alpha_{o2} - \alpha_{r2})R} 100\%$$

nutzt, wobei R das Verhältnis von Dämpfungen des Lichtsignals für jede der ersten und zweiten Wellenlänge darstellt.

17. Verfahren nach Anspruch 16, wobei der Schritt des Bestimmens des Verhältnisses R von Dämpfungen des Lichtsignals für die erste und zweite Wellenlänge die Gleichung:

$$R = \frac{A_1' - E_1'}{A_2' - E_2'}$$

nutzt, wobei E'_1 die erste Kalibrierungskonstante darstellt, E'_2 die zweite Kalibrierungskonstante darstellt, A'_1 die erste Dämpfung von Lichtsignal der ersten Wellenlänge darstellt, und A'_2 die zweite Dämpfung von Lichtsignal der zweiten Wellenlänge darstellt.

18. Verfahren nach Anspruch 17, wobei der Schritt des Bestimmens der ersten Dämpfung der ersten Wellenlänge die Gleichung:

$$-\log(I_b/I_x)_1 = (\alpha_{r1}[Hb]_b + \alpha_{o1}[HbO_2]_b)L_b + (E - E_x)_1$$

nutzt und der Schritt des Bestimmens der zweiten Dämpfung der zweiten Wellenlänge die Gleichung:

$$-\log(I_b/I_x)_2 = (\alpha_{r2}[Hb]_b + \alpha_{o2}[HbO_2]_b)L_b + (E - E_x)_2$$

nutzt.

19. Verfahren nach Anspruch 15, wobei der Schritt des Bestimmens des Blutsauerstoffsättigungsgrads im Gewebe des Probanden die Schritte umfasst des:

Bestimmens des Dämpfungsverhältnisses *R* des Lichtsignals für jede der ersten und zweiten Wellenlänge;
Bestimmens des Blutsauerstoffsättigungsgrads unter Nutzung einer empirisch erhaltenen Kalibrierungskurve, die die Beziehung zwischen dem Dämpfungsverhältnis *R* zu der Blutsauerstoffsättigung definiert.

20. Verfahren nach Anspruch 15, weiter die Schritte umfassend des:

Bestimmens einer Photonenweglänge L_b; und
Bestimmens einer Konzentration von Oxyhämoglobin und einer Konzentration von Desoxyhämoglobin im Gewebe des Probanden unter Verwendung der ersten und zweiten Kalibrierungskonstante.

21. Verfahren nach Anspruch 20, wobei die Konzentration von Oxyhämoglobin (HbO_2) und die Konzentration von Desoxyhämoglobin (Hb) im Gewebe des Probanden unter Verwendung der Gleichung:

$$\begin{bmatrix} A'_1 \\ A'_2 \end{bmatrix} \begin{bmatrix} \alpha_{r1} & \alpha_{o1} \\ \alpha_{r2} & \alpha_{o2} \end{bmatrix}^{-1} (L_b)^{-1} - \begin{bmatrix} E'_1 \\ E'_2 \end{bmatrix} \begin{bmatrix} \alpha_{r1} & \alpha_{o1} \\ \alpha_{r2} & \alpha_{o2} \end{bmatrix}^{-1} (L_b)^{-1} = \begin{bmatrix} [Hb]_b \\ [HbO_2]_b \end{bmatrix}$$

bestimmt werden, wobei E'_1 die erste Kalibrierungskonstante darstellt, E'_2 die zweite Kalibrierungskonstante darstellt, A'_1 die erste Dämpfung des Lichtsignals der ersten Wellenlänge darstellt, und A'_2 die zweite Dämpfung des Lichtsignals der zweiten Wellenlänge darstellt.

22. Vorrichtung zum nicht-invasiven Bestimmen eines Blutsauerstoffsättigungsgrads im Gewebe eines Probanden unter Verwendung eines spektrophotometrischen Nahinfrarot-Sensors, der in der Lage ist, ein Lichtsignal in das Gewebe eines Probanden zu übertragen und das Lichtsignal in einem vorbestimmten Abstand zu erfassen, sobald es das Gewebe per Transmission oder Reflexion durchdrungen hat, wobei:

eine Lichtquelle (18) des Sensors angeordnet ist, um ein Lichtsignal in das Gewebe des Probanden zu übertragen, wobei das übertragene Lichtsignal eine erste Wellenlänge, eine zweite Wellenlänge und eine dritte Wellenlänge beinhaltet;
ein erster Lichtdetektor (20) des Sensors in einem ersten vorbestimmten Abstand von der Lichtquelle (18) angeordnet ist, um eine erste Intensität des Lichtsignals bei der ersten, zweiten und dritten Wellenlänge zu erfassen, nachdem das Lichtsignal den Probanden durchläuft, und ein zweiter Lichtdetektor (19) des Sensors in einem zweiten vorbestimmten Abstand von der Lichtquelle (18) angeordnet ist, um eine zweite Intensität des Lichtsignals bei der ersten, zweiten und dritten Wellenlänge zu erfassen, nachdem das Lichtsignal den Probanden durchläuft, wobei die erste Intensität, die im ersten vorbestimmten Abstand erfasst wird, nachdem das

Lichtsignal den Probanden durchläuft, aus Dämpfung und Energieverlust von sowohl tiefem als auch oberflächlichem Gewebe besteht, und wobei die zweite Intensität, die im zweiten vorbestimmten Abstand erfasst wird, nachdem das Lichtsignal den Probanden durchläuft, aus Dämpfung und Energieverlust von oberflächlichem Gewebe besteht;
wobei der Sensor angeordnet ist, um die Energieverluste (E) aufzuheben oder zu minimieren, die bedingt sind durch: Lichtstreuung im Gewebe (G); andere Hintergrundabsorptionsverluste wegen biologischen Verbindungen (F); und andere Verluste, einschließlich Messvorrichtungsvariabilität (N), durch Bestimmen von differentieller Dämpfung als eine Funktion der Wellenlänge;
wobei die Vorrichtung weiter umfasst:

Mittel zum Bestimmen einer Dämpfung des Lichtsignals für jede der ersten, zweiten und dritten Wellenlänge unter Verwendung der erfassten ersten Intensität und erfassten zweiten Intensität der ersten, zweiten und dritten Wellenlänge;
Mittel zum Bestimmen einer Differenz in der Dämpfung des Lichtsignals zwischen der ersten Wellenlänge und der zweiten Wellenlänge, und zwischen der ersten Wellenlänge und der dritten Wellenlänge; und
Mittel zum Bestimmen des Blutsauerstoffsättigungsgrads im Gewebe des Probanden unter Verwendung der Differenz in der Dämpfung zwischen der ersten Wellenlänge und der zweiten Wellenlänge, und der Differenz in der Dämpfung zwischen der ersten Wellenlänge und der dritten Wellenlänge.

Revendications

1. Procédé pour déterminer de manière non invasive un niveau de saturation du sang en oxygène à l'intérieur d'un tissu d'un sujet au moyen d'un capteur spectrophotométrique proche-infrarouge capable de transmettre un signal lumineux dans le tissu d'un sujet et de détecter le signal lumineux à une distance prédéterminée dès qu'il est passé à travers le tissu par transmittance ou réflectance, ledit procédé comprenant les étapes suivantes :

la transmission d'un signal lumineux dans le tissu du sujet au moyen d'une source de lumière (18) du capteur, dans lequel le signal lumineux transmis inclut une première longueur d'onde, une deuxième longueur d'onde, et une troisième longueur d'onde ;
la détection d'une première intensité du signal lumineux au moyen d'un premier détecteur de lumière (20) du capteur à une première distance prédéterminée et la détection d'une deuxième intensité du signal lumineux au moyen d'un second détecteur de lumière (19) du capteur à une seconde distance prédéterminée par rapport à la source de lumière (18), comprenant une détection aux première, deuxième, et troisième longueurs d'onde après le passage du signal lumineux à travers le sujet, dans lequel la première intensité détectée à la première distance prédéterminée après le passage du signal lumineux à travers le sujet comprend une atténuation et une perte d'énergie provenant à la fois d'un tissu profond et peu profond et dans lequel la deuxième intensité détectée à la seconde distance prédéterminée après le passage du signal lumineux à travers le sujet comprend une atténuation et une perte d'énergie provenant d'un tissu peu profond ;
et, avec un processeur :

la détermination d'une atténuation du signal lumineux pour chacune des première, deuxième, et troisième longueurs d'onde au moyen de la première intensité détectée et de la deuxième intensité détectée aux première, deuxième, et troisième longueurs d'onde ;
la détermination d'une différence dans l'atténuation du signal lumineux entre la première longueur d'onde et la deuxième longueur d'onde, et entre la première longueur d'onde et la troisième longueur d'onde ;
l'annulation ou la minimisation des pertes d'énergie (E) dues à : la diffusion de la lumière à l'intérieur du tissu (G) ; d'autres pertes par absorption de fond à partir de composés biologiques (F) ; et d'autres pertes incluant la variabilité de l'appareil de mesure (N), en déterminant une atténuation différentielle en fonction de la longueur d'onde ; et
la détermination du niveau de saturation du sang en oxygène à l'intérieur du tissu du sujet en utilisant la différence d'atténuation entre la première longueur d'onde et la deuxième longueur d'onde, et la différence d'atténuation entre la première longueur d'onde et la troisième longueur d'onde.

2. Procédé selon la revendication 1, dans lequel le capteur est étalonné en utilisant l'équation :

$$SmvO_2 = Kv*SvO_2 + Ka*SaO_2$$

où $SmvO_2$ est la saturation en oxygène du sang veineux mêlé ;
SvO_2 est la saturation en oxygène du sang veineux ;
SaO_2 est la saturation en oxygène du sang artériel ; et
Kv et Ka sont des paramètres d'étalonnage.

3. Procédé selon la revendication 2, dans lequel le capteur est étalonné en utilisant des données empiriques pour déterminer une première constante d'étalonnage et une seconde constante d'étalonnage.

4. Procédé selon la revendication 1, dans lequel le capteur est étalonné en utilisant des données empiriques qui concernent le tissu du sujet qui est détecté par le capteur pour prendre en compte l'atténuation du signal lumineux résultant de la diffusion du signal lumineux à l'intérieur du tissu du sujet.

5. Procédé selon l'une quelconque des revendications précédentes, comprenant en outre :

la détermination d'une première constante d'étalonnage et d'une seconde constante d'étalonnage en utilisant des données empiriques développées à partir du sujet au même moment ou à peu près au même moment où la détection a lieu ; et
la détermination du niveau de saturation du sang en oxygène à l'intérieur du tissu du sujet en utilisant la première constante d'étalonnage et la seconde constante d'étalonnage.

6. Procédé selon l'une quelconque des revendications précédentes, comprenant en outre :

la détermination d'une première constante d'étalonnage et d'une seconde constante d'étalonnage en utilisant des données empiriques développées à partir du sujet au même moment ou à peu près au même moment où la détection a lieu ; et
l'étalonnage du capteur en utilisant la première constante d'étalonnage et la seconde constante d'étalonnage.

7. Procédé selon l'une quelconque des revendications 3 à 6, dans lequel les données empiriques sont collectées par l'échantillonnage discret d'une source de sang veineux et d'une source de sang artériel provenant du sujet.

8. Procédé selon l'une quelconque des revendications 3 à 6, dans lequel les données empiriques sont collectées en surveillant de manière continue une source de sang veineux et une source de sang artériel provenant du sujet.

9. Procédé selon l'une quelconque des revendications précédentes, dans lequel l'étape de détermination du niveau de saturation du sang en oxygène à l'intérieur du tissu du sujet utilise l'équation :

$$SnO_2\% = \frac{(A_{HbO_2} - \Psi_{HbO_2})}{(A_{HbO_2} - \Psi_{HbO_2} + A_{Hb} - \Psi_{Hb})} * 100\%$$

où ψ_{HbO2} représente un ou la première constante d'étalonnage, ψ_{Hb} représente une ou la seconde constante d'étalonnage, A_{HbO_2} représente une différence d'atténuation de signal lumineux attribuable à l'oxyhémoglobine, et A_{Hb} représente une différence d'atténuation de signal lumineux attribuable à la désoxyhémoglobine.

10. Procédé selon la revendication 9, comprenant en outre les étapes suivantes :

la détermination d'une longueur de parcours de photon L_b ; et
la détermination d'une concentration en oxyhémoglobine et d'une concentration en désoxyhémoglobine à l'intérieur du tissu du sujet en utilisant les première et seconde constantes d'étalonnage.

11. Procédé selon la revendication 10, dans lequel la concentration en oxyhémoglobine (HbO_2) et la concentration en désoxyhémoglobine (Hb) à l'intérieur du tissu du sujet sont déterminées en utilisant l'équation :

$$\begin{bmatrix} A_{Hb} \\ A_{HbO_2} \end{bmatrix} (L_b)^{-1} - \begin{bmatrix} \Psi_{Hb} \\ \Psi_{HbO_2} \end{bmatrix} (L_b)^{-1} = \begin{bmatrix} [Hb]_b \\ [HbO_2]_b \end{bmatrix}.$$

12. Procédé selon l'une quelconque des revendications précédentes, dans lequel l'étape de détermination d'une différence d'atténuation du signal lumineux entre la première longueur d'onde et la deuxième longueur d'onde utilise l'équation :

$$\begin{aligned} \Delta A'_{12} &= A'_1 - A'_2 = -\log(I_b/I_x)_1 + \log(I_b/I_x)_2 \\ &= \{(\alpha_{r1} - \alpha_{r2})[Hb]_b + (\alpha_{o1} - \alpha_{o2})[HbO_2]_b\} L_b + (E'_1 - E'_2) \\ &= (\Delta\alpha_{r12}[Hb]_b + \Delta\alpha_{o12}[HbO_2]_b) L_b + \Delta E_{12} \end{aligned}$$

et l'étape de détermination d'une différence d'atténuation du signal lumineux entre la première longueur d'onde et la troisième longueur d'onde utilise l'équation :

$$\begin{aligned} \Delta A'_{13} &= A'_1 - A'_3 = -\log(I_b/I_x)_1 + \log(I_b/I_x)_3 \\ &= \{(\alpha_{r1} - \alpha_{r3})[Hb]_b + (\alpha_{o1} - \alpha_{o3})[HbO_2]_b\} L_b + (E'_1 - E'_3) \\ &= (\Delta\alpha_{r13}[Hb]_b + \Delta\alpha_{o13}[HbO_2]_b) L_b + \Delta E_{13} \end{aligned}$$

13. Procédé selon la revendication 12, dans lequel l'étape de détermination d'une atténuation du signal lumineux d'une longueur d'onde A utilise l'équation :

$$\begin{aligned} A'_\lambda &= -\log(I_b/I_x)_\lambda = (\alpha_{r\lambda}[Hb]_b + \alpha_{o\lambda}[HbO_2]_b) L'_b + E'_\lambda \\ &= (\alpha_{r\lambda}[Hb]_b + \alpha_{o\lambda}[HbO_2]_b) L_b + (E - E_x)_\lambda \end{aligned}$$

pour une ou plusieurs des première, deuxième, et troisième longueurs d'onde.

14. Procédé selon l'une quelconque des revendications précédentes, comprenant en outre la détermination d'une concentration en oxyhémoglobine et d'une concentration en désoxyhémoglobine à l'intérieur d'un tissu d'un sujet à un temps initial *t1* et un temps ultérieur *t2*, ledit procédé comprenant les étapes suivantes :

(a) la détermination d'une première constante d'étalonnage et d'une seconde constante d'étalonnage en utilisant des données empiriques développées à partir du sujet au même moment ou à peu près au même moment où la détection a lieu ;
(b) la détermination d'une longueur de parcours de photon L_b ;
(c) la détermination de la concentration en oxyhémoglobine et de la concentration en désoxyhémoglobine à

l'intérieur du tissu du sujet au temps initial *t1* en utilisant l'équation :

$$\begin{bmatrix} A_{Hb} \\ A_{HbO_2} \end{bmatrix} (L_b)^{-1} - \begin{bmatrix} \Psi_{Hb} \\ \Psi_{HbO_2} \end{bmatrix} (L_b)^{-1} = \begin{bmatrix} Hb \\ HbO_2 \end{bmatrix}$$

où ψ_{HbO_2} représente la première constante d'étalonnage, ψ_{Hb} représente la seconde constante d'étalonnage, A_{HbO_2} représente une différence d'atténuation de signal lumineux attribuable à l'oxyhémoglobine, et A_{Hb} représente une différence d'atténuation de signal lumineux attribuable à la désoxyhémoglobine ;

(d) la détermination d'un changement de la concentration en oxyhémoglobine et d'un changement de la concentration en désoxyhémoglobine à partir du temps initial *t1* jusqu'à un second temps *t2* ultérieur, déterminés en utilisant l'équation :

$$\begin{bmatrix} -\log(I_{t2}/I_{t1})_{\lambda 1}/L_{\lambda 1} \\ -\log(I_{t2}/I_{t1})_{\lambda 2}/L_{\lambda 2} \\ -\log(I_{t2}/I_{t1})_{\lambda 3}/L_{\lambda 3} \end{bmatrix} = \begin{bmatrix} \alpha_{Hb\lambda 1} & \alpha_{HbO_2\lambda 1} \\ \alpha_{Hb\lambda 2} & \alpha_{HbO_2\lambda 2} \\ \alpha_{Hb\lambda 3} & \alpha_{HbO_2\lambda 3} \end{bmatrix} * \begin{bmatrix} \Delta Hb \\ \Delta HbO_2 \end{bmatrix} ;$$

et

(e) la détermination de la concentration en oxyhémoglobine et de la concentration en désoxyhémoglobine à l'intérieur du tissu du sujet au temps ultérieur *t2* en utilisant les équations :

$$[Hb]_{t_2} = \Delta Hb(t_2) + [Hb]_{t_1}$$

et

$$[HbO_2]_{t_2} = \Delta HbO_2(t_2) + [HbO_2]_{t_1} .$$

15. Procédé selon l'une quelconque des revendications précédentes, comprenant en outre :

la détection d'une troisième intensité et d'une quatrième intensité du signal lumineux, en utilisant un détecteur de lumière (19, 20) du capteur à ladite première et à ladite seconde distance prédéterminée, comprenant une détection à la deuxième longueur d'onde, après le passage du signal lumineux à travers le sujet ;

la détermination d'une première atténuation du signal lumineux pour la première longueur d'onde en utilisant ladite première intensité et ladite deuxième intensité ;

la détermination d'une seconde atténuation du signal lumineux pour la deuxième longueur d'onde en utilisant ladite troisième intensité et ladite quatrième intensité ;

la détermination d'un rapport entre ladite première et ladite seconde atténuation du signal lumineux pour les première et deuxième longueurs d'onde ;

la détermination d'un niveau de saturation du sang en oxygène à l'intérieur du tissu du sujet en utilisant ledit rapport.

16. Procédé selon la revendication 15, dans lequel l'étape de détermination du niveau de saturation du sang en oxygène à l'intérieur du tissu du sujet utilise l'équation :

$$SnO_2\% = \frac{\alpha_{r1} - \alpha_{r2} R}{(\alpha_{r1} - \alpha_{o1}) + (\alpha_{o2} - \alpha_{r2}) R} 100\%$$

où *R* représente le rapport d'atténuations du signal lumineux pour chacune des première et deuxième longueurs d'onde.

17. Procédé selon la revendication 16, dans lequel l'étape de détermination du rapport *R* des atténuations du signal lumineux pour les première et deuxième longueurs d'onde utilise l'équation :

$$R = \frac{A_1' - E_1'}{A_2' - E_2'}$$

où E'_1 représente la première constante d'étalonnage, E'_2 représente la seconde constante d'étalonnage, A'_1 représente la première atténuation du signal lumineux de la première longueur d'onde, et A'_2 représente la seconde atténuation du signal lumineux de la deuxième longueur d'onde.

18. Procédé selon la revendication 17, dans lequel l'étape de détermination de la première atténuation de la première longueur d'onde utilise l'équation :

$$-\log(I_b / I_x)_1 = (\alpha_{r1}[Hb]_b + \alpha_{o1}[HbO_2]_b) L_b + (E - E_x)_1$$

et l'étape de détermination de la seconde atténuation de la deuxième longueur d'onde utilise l'équation :

$$-\log(I_b / I_x)_2 = (\alpha_{r2}[Hb]_b + \alpha_{o2}[HbO_2]_b) L_b + (E - E_x)_2 .$$

19. Procédé selon la revendication 15, dans lequel l'étape de détermination du niveau de saturation du sang en oxygène à l'intérieur du tissu du sujet comprend les étapes suivantes :

la détermination du rapport d'atténuation *R* du signal lumineux pour chacune des première et deuxième longueurs d'onde ;
la détermination du niveau de saturation du sang en oxygène en utilisant une courbe d'étalonnage obtenue de manière empirique définissant la relation entre ledit rapport d'atténuation *R* avec la saturation du sang en oxygène.

20. Procédé selon la revendication 15, comprenant en outre les étapes suivantes :

la détermination d'une longueur de parcours de photon L_b ; et
la détermination d'une concentration en oxyhémoglobine et d'une concentration en désoxyhémoglobine à l'intérieur du tissu du sujet en utilisant les première et seconde constantes d'étalonnage.

21. Procédé selon la revendication 20, dans lequel la concentration en oxyhémoglobine (HbO_2) et la concentration en désoxyhémoglobine (Hb) à l'intérieur du tissu du sujet sont déterminées en utilisant l'équation :

$$\begin{bmatrix} A_1' \\ A_2' \end{bmatrix} \begin{bmatrix} \alpha_{r1} & \alpha_{o1} \\ \alpha_{r2} & \alpha_{o2} \end{bmatrix}^{-1} (L_b)^{-1} - \begin{bmatrix} E_1' \\ E_2' \end{bmatrix} \begin{bmatrix} \alpha_{r1} & \alpha_{o1} \\ \alpha_{r2} & \alpha_{o2} \end{bmatrix}^{-1} (L_b)^{-1} = \begin{bmatrix} [Hb]_b \\ [HbO_2]_b \end{bmatrix}$$

où E'_1 représente la première constante d'étalonnage, E'_2 représente la seconde constante d'étalonnage, A'_1 représente la première atténuation du signal lumineux de la première longueur d'onde, et A'_2 représente la seconde atténuation du signal lumineux de la deuxième longueur d'onde.

22. Appareil pour déterminer de manière non invasive un niveau de saturation du sang en oxygène à l'intérieur d'un tissu d'un sujet au moyen d'un capteur spectrophotométrique proche-infrarouge capable de transmettre un signal lumineux dans le tissu d'un sujet et de détecter le signal lumineux à une distance prédéterminée dès qu'il est passé à travers le tissu par transmittance ou réflectance, dans lequel :

une source de lumière (18) du capteur est agencée pour transmettre un signal lumineux dans le tissu du sujet, dans lequel le signal lumineux transmis inclut une première longueur d'onde, une deuxième longueur d'onde, et une troisième longueur d'onde ;
un premier détecteur de lumière (20) du capteur est agencé à une première distance prédéterminée par rapport à la source de lumière (18) pour détecter une première intensité du signal lumineux aux première, deuxième, et troisième longueurs d'onde après le passage du signal lumineux à travers le sujet, et un second détecteur de lumière (19) du capteur est agencé à une seconde distance prédéterminée par rapport à la source de lumière (18), pour détecter une deuxième intensité du signal lumineux aux première, deuxième, et troisième longueurs d'onde après le passage du signal lumineux à travers le sujet, dans lequel la première intensité détectée à la première distance prédéterminée après le passage du signal lumineux à travers le sujet comprend une atténuation et une perte d'énergie provenant à la fois d'un tissu profond et peu profond et dans lequel la deuxième intensité détectée à la seconde distance prédéterminée après le passage du signal lumineux à travers le sujet comprend une atténuation et une perte d'énergie provenant d'un tissu peu profond ;
dans lequel le capteur est agencé pour annuler ou minimiser les pertes d'énergie (E) dues à : la diffusion de la lumière à l'intérieur du tissu (G) ; d'autres pertes par absorption de fond à partir de composés biologiques (F) ; et d'autres pertes incluant la variabilité de l'appareil de mesure (N), en déterminant une atténuation différentielle en fonction de la longueur d'onde ;
dans lequel ledit appareil comprend en outre :

des moyens pour déterminer une atténuation du signal lumineux pour chacune des première, deuxième, et troisième longueurs d'onde en utilisant la première intensité détectée et la deuxième intensité détectée des première, deuxième, et troisième longueurs d'onde ;
des moyens pour déterminer une différence dans l'atténuation du signal lumineux entre la première longueur d'onde et la deuxième longueur d'onde, et entre la première longueur d'onde et la troisième longueur d'onde ; et
des moyens pour déterminer le niveau de saturation du sang en oxygène à l'intérieur du tissu du sujet en utilisant la différence d'atténuation entre la première longueur d'onde et la deuxième longueur d'onde, et la différence d'atténuation entre la première longueur d'onde et la troisième longueur d'onde.

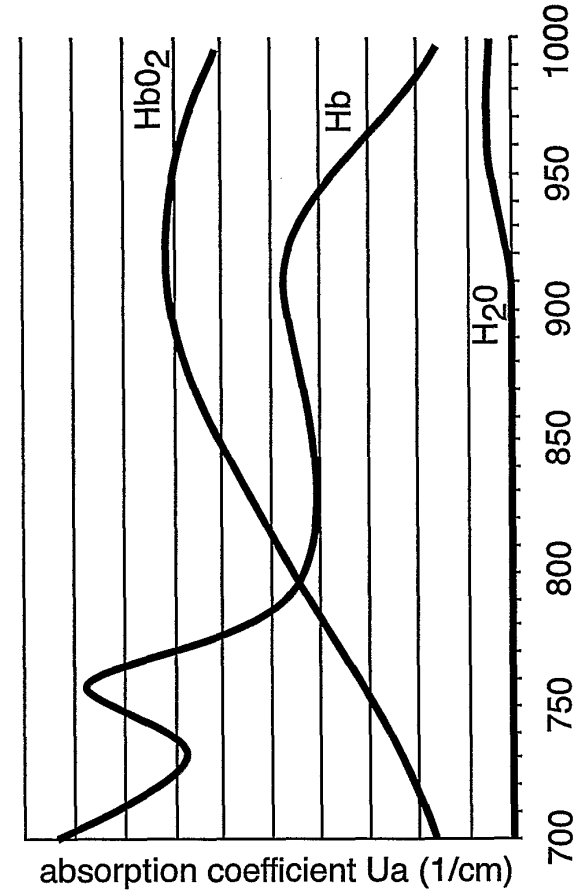

FIG. 5

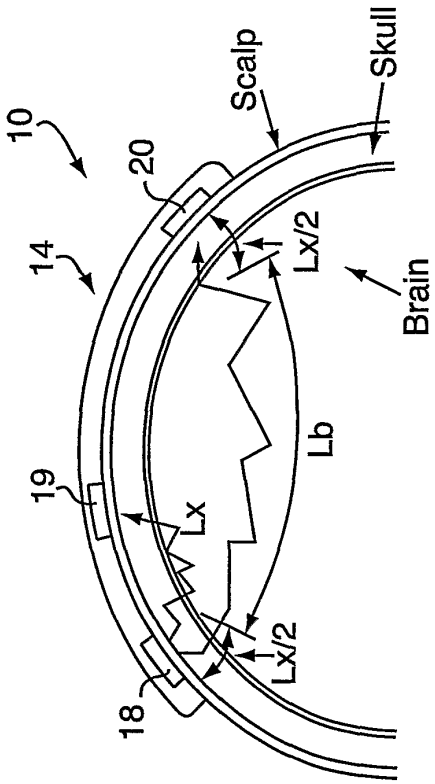

FIG. 1

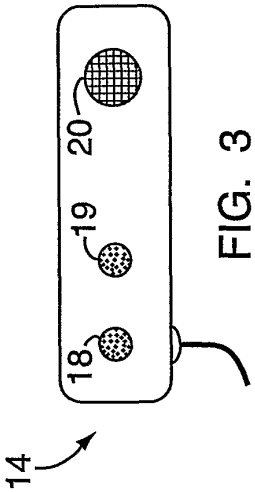

FIG. 3

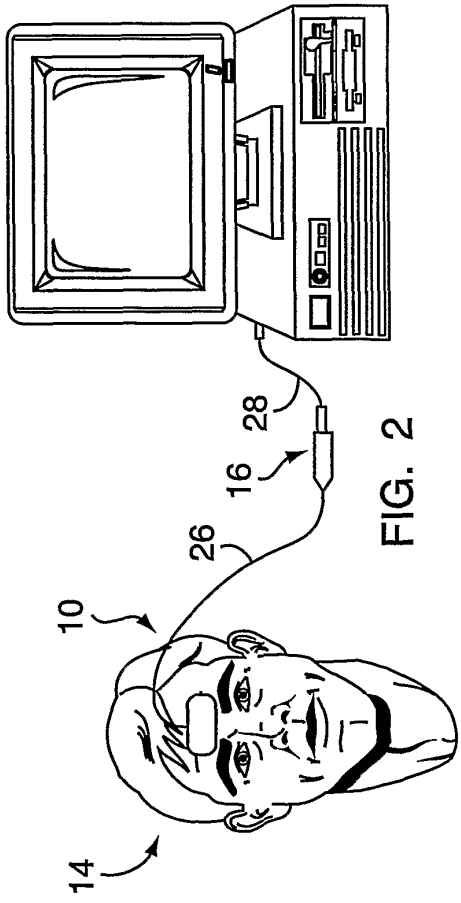

FIG. 2

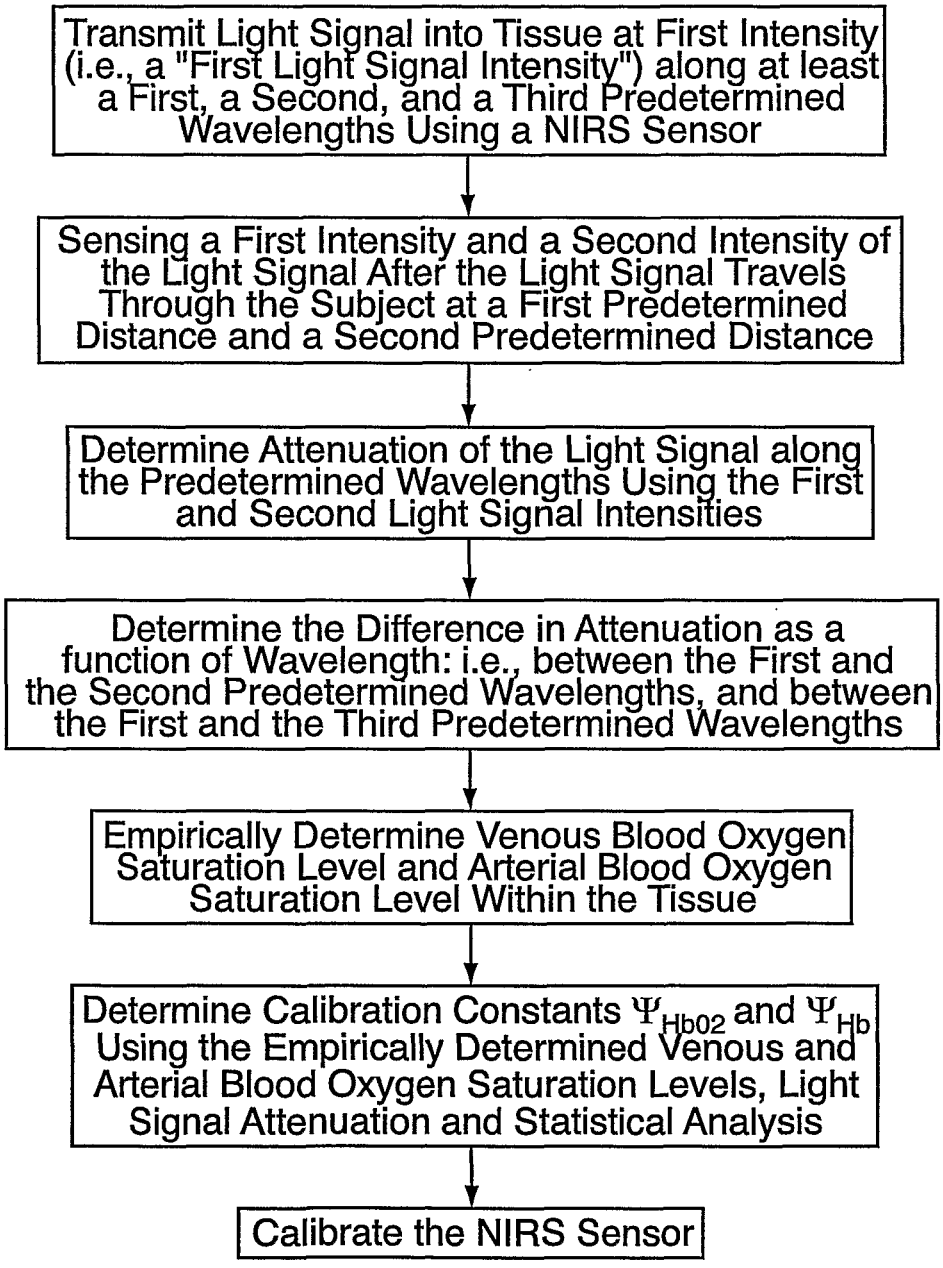
Transmit Light Signal into Tissue at First Intensity (i.e., a "First Light Signal Intensity") along at least a First, a Second, and a Third Predetermined Wavelengths Using a NIRS Sensor
Sensing a First Intensity and a Second Intensity of the Light Signal After the Light Signal Travels Through the Subject at a First Predetermined Distance and a Second Predetermined Distance
Determine Attenuation of the Light Signal along the Predetermined Wavelengths Using the First and Second Light Signal Intensities
Determine the Difference in Attenuation as a function of Wavelength: i.e., between the First and the Second Predetermined Wavelengths, and between the First and the Third Predetermined Wavelengths
Empirically Determine Venous Blood Oxygen Saturation Level and Arterial Blood Oxygen Saturation Level Within the Tissue
Determine Calibration Constants Ψ_{Hb02} and Ψ_{Hb} Using the Empirically Determined Venous and Arterial Blood Oxygen Saturation Levels, Light Signal Attenuation and Statistical Analysis
Calibrate the NIRS Sensor

FIG. 4

REFERENCES CITED IN THE DESCRIPTION

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Patent documents cited in the description

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- US 20020016536 A **[0011]**

专利名称(译)	分光光度法血氧监测方法		
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当前申请(专利权)人(译)	CAS医疗系统，INC.		
[标]发明人	CHEN BO BENNI PAUL B		
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其他公开文献	EP1545298A4 EP1545298B1		
外部链接	Espacenet		

摘要(译)

提供了一种用于非侵入性地确定对象组织内的血液氧合作用的方法和设备，其利用近红外分光光度法（NIRS）传感器，该传感器能够将光信号传输到对象的组织中并且一旦其穿过就感测该光信号。通过透射率或反射率组织。