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(54) **MODIFIED PULSE OXIMETRY TECHNIQUE FOR MEASUREMENT OF OXYGEN SATURATION IN ARTERIAL AND VENOUS BLOOD**

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(57) **ABSTRACT**

A method for the measurement of oxygen saturation in arterial blood SaO_2 by means of pulse oximetry without calibration is described. Photoplethysmography (PPG) is measured in three wavelengths in the infrared and for each PPG curve the relative change in light transmission is obtained. Two equations, each relating SaO_2 to the ratio of the relative changes in light transmission for two wavelengths, using the values of the extinction coefficients of oxygenated and deoxygenated hemoglobin for the three wavelengths, enable the determination of SaO_2, assuming linear dependence of the optical path-length on the wavelength, for the three wavelengths in the infrared. Similar technique for the determination of oxygen saturation in venous blood from changes in light transmission due to changes in venous blood volume is suggested

FIG. 1

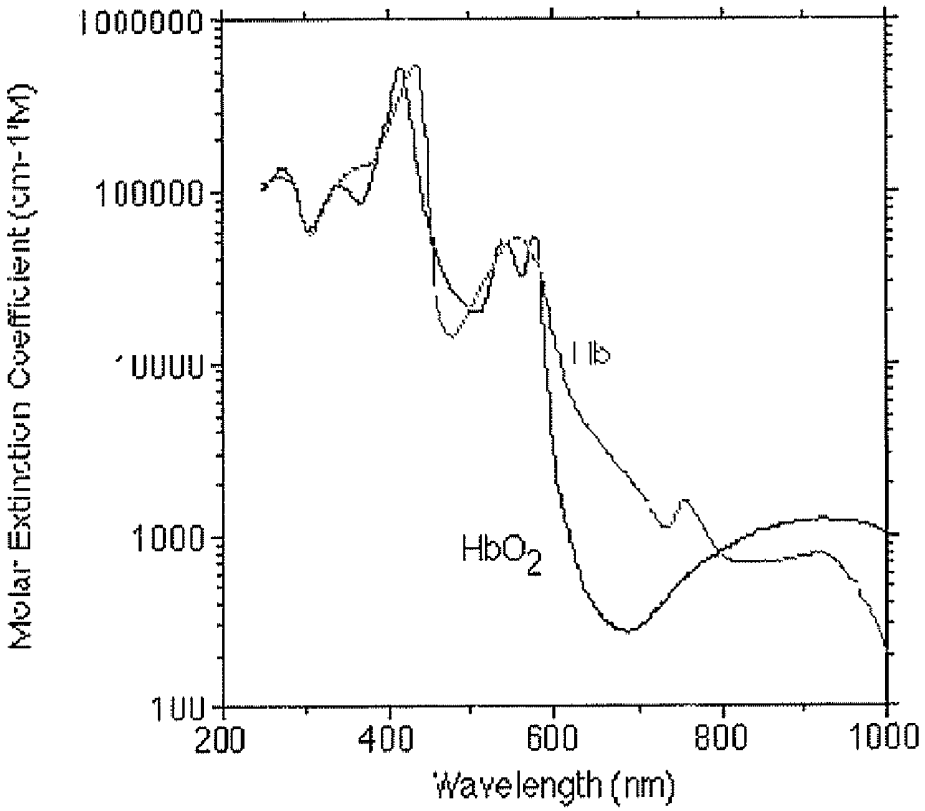

1000000
100000
1000
100
200
400
600
800
1000
Hb
HbO2
Wavelength (nm)

FIG. 2

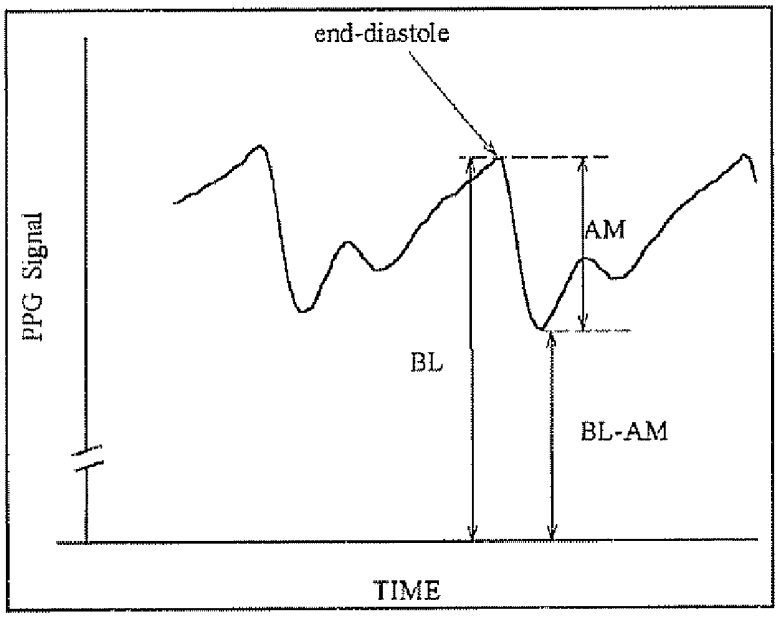
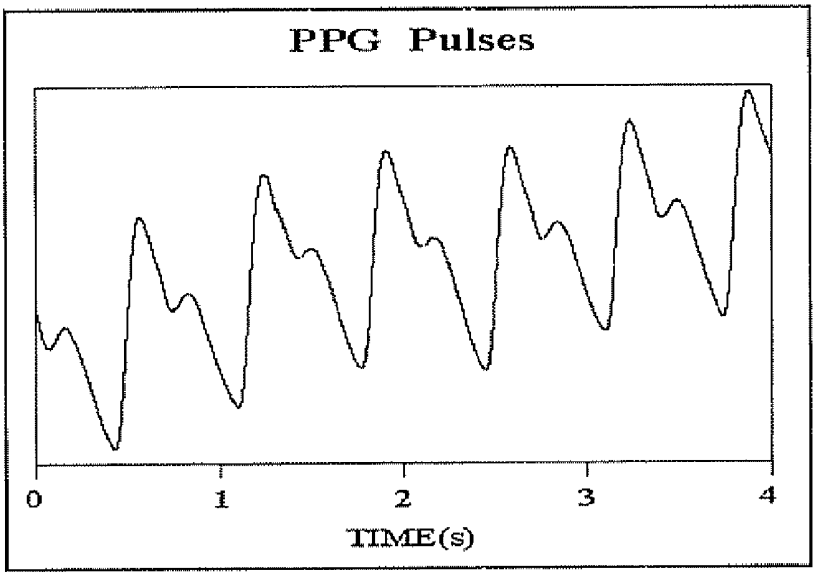

end-diastole
PPG Signal
AM
BL
BL-AM
TIME

FIG. 3



MODIFIED PULSE OXIMETRY TECHNIQUE FOR MEASUREMENT OF OXYGEN SATURATION IN ARTERIAL AND VENOUS BLOOD

FIELD AND BACKGROUND OF THE INVENTION

1.1. Arterial and Venous Oxygen Saturation

[0001] Transfer of oxygen from the lungs to the tissue cells is done mainly via the hemoglobin molecules in the red blood cells. Total oxygen content in blood includes the oxygen connected to hemoglobin and the dissolved oxygen in arterial plasma, measured by the partial pressure PaO_2 of the dissolved oxygen. Oxygen saturation SO_2 is the ratio of oxygenated hemoglobin to total hemoglobin ($SO_2=HbO_2/(HbO_2+Hb)$), and its value in the arterial blood, SaO_2, depends on the adequacy of the ventilation and respiratory function. SaO_2 is related to the partial oxygen pressure PaO_2 by S-shaped curve: SaO_2 increases steeply with PaO_2 for PaO_2 values between 10 and 50 mmHg (at PaO_2 of 50 mmHg SaO_2 is about 80%), then increases moderately. Normal values of SaO_2 are 94-99%. Assessment of SaO_2 is mainly important for clinical evaluation of proper respiratory function.

[0002] Most of the hemoglobin in venous blood is still oxygenated: normal values of the oxygen saturation in the peripheral venous blood, SvO_2 are 70-80%. SvO_2 also has physiological and clinical significance, as lower blood flow to the tissue results in higher utilization of the oxygen in the blood and lower value of SvO_2. The assessment of blood supply to the skin in limbs or other organ can provide information on the adequacy of skin blood flow. Low values of skin blood flow can also indicate the occurrence of shock or cardiac failure, in which blood flow is diverted from the peripheral circulation towards more vital organs. Note that, in contrast to the routine use of pulse oximetry for SaO_2 measurement, no accepted method for the measurement of SvO_2 is available.

1.2 Optical Measurement of Arterial Oxygen Saturation

[0003] The different light absorption spectrum for oxygenated and de-oxygenated hemoglobin enables the noninvasive assessment of oxygen saturation in the blood. The transmission of light through a given tissue depends on the light absorption and the light scattering coefficients of the various components of the tissue, including the arterial and venous blood. Transmission of light depends on the light scattering because the latter increases the path-length of the light (by a factor of 5-10). In order to isolate the contribution of the arterial blood to the light absorption, the absorption of light of several wavelengths through the ear-lobe was measured after heating the tissue to 41° C., which results in "arterialization" of the blood (Mendelson, 1988). At present the usual technique for the isolation of the contribution of the arterial blood to the light absorption is based on photoplethysmography (PPG)—the measurement of light absorption changes due to the cardiac induced blood volume changes (Yoshiya, 1980). Since the PPG signal originates from the arterial blood volume increase during systole, the measurement of the PPG signal in several wavelengths—pulse oximetry—enables the assessment of the oxygen saturation in the arterial blood, SaO_2.

1.3. The PPG Signal and its Origin

[0004] Photoplethysmography (PPG) is the recording of tissue blood volume changes by the measurement of light absorption in the tissue. The PPG probe consists of a light source emitting light into the tissue and a photodetector measuring the light transmitted through the tissue. During systole blood is ejected from the left ventricle into the peripheral vascular system, thereby increasing the arterial blood content, and consequently decreasing the light intensity transmitted through the tissue. The PPG signal is shown in FIG. **2**. The decrease in the transmitted light intensity during systole originates from the cardiac induced increase in the arterial blood volume during systole. The maximal value of the PPG signal (BL in FIG. **2**) is proportional to the light irradiance transmitted through the tissue at end-diastole, when the tissue blood volume is minimal. The amplitude AM of the PPG signal is related to the maximal arterial blood volume change during systole ΔV_a. It can be shown (Babchenko et al. 2001) that since in general AM<<BL,

$$AM/BL=\alpha_a\Delta V_a \tag{1}$$

where α_a is the effective absorption coefficient of the arterial blood, which is a function of the absorption and scattering attenuation constants. In general the PPG signal is presented in inverted form (FIG. **3**) so that increase in the PPG signal corresponds to increase in tissue blood volume.

1.4. Theory of Pulse Oximetry

[0005] The theory of deriving arterial oxygen saturation from the PPG signals at two wavelengths is described in several articles (see Wieben, 1997, Mannheimer et al, 1997, Nitzan et al, 2000). The transmitted light intensity, I_t, through a sample of hemolized blood is given by the Beer-Lambert Law:

$$I_t=I_0\exp(-\alpha d) \tag{2}$$

where I_α is the incident light intensity, α is the absorption constant of the blood, and d is the width of the tissue sample. The transmitted light intensity, I_t, through a tissue sample which includes vessels with whole blood is given by:

$$I_t=I_0\exp(-\alpha l-\epsilon cl) \tag{3}$$

where l is the effective optical path-length, which is higher than d because of scattering in the tissue, α is the absorption constant of the tissue, c is the concentration of the blood in the tissue, and ϵ is the extinction coefficient of the blood, defined as the absorption constant of the blood divided by the concentration of the blood in the tissue.

[0006] During systole the tissue blood volume increases and consequently the light transmission through the tissue decreases. Photoplethysmography (PPG) is the measurement of the oscillatory changes in light transmission through tissue due to the cardiac induced blood volume changes in the tissue. If I_S is the light transmission through the tissue during the maximal increase in tissue blood volume and I_D is the light transmitted through the tissue during end diastole (when the tissue blood volume has its minimal value), then

$$I_S=I_D\exp(-\epsilon_a\Delta c_a l)$$

$$\ln(I_D/I_S)=\epsilon_a\Delta c_a l \tag{4}$$

where ϵ_a is the extinction coefficient for the arterial blood, and Δc_a is the increase of blood concentration (in the tissue) due to the maximal systolic increase of blood volume. For small blood volume changes $\Delta I_a=I_D-I_S<<I_S$, and $\ln(I_D/I_S)$ can be approximated by $\Delta I_a/I_S$. If the light transmission is measured for two wavelengths λ_1 and λ_2, then

$$(\Delta I_a/I_S)_1=\epsilon_{a1}\Delta c_{a1}l_1;\ (\Delta I_a/I_S)_2\epsilon_{a2}\Delta c_{a2}l_2 \tag{5}$$

and the ratio R, defined by

$$R = \frac{(\Delta I_a / I_S)_1}{(\Delta I_a / I_S)_2} \quad (6)$$

satisfies the equation

$$R \approx \frac{\varepsilon_{a1} l_1}{\varepsilon_{a2} l_2} \quad (7a)$$

assuming that the difference in the blood concentration change Δc_a between the two wavelengths can be neglected ($\Delta c_{a1} \approx \Delta c_{a2}$). Note that the last assumption is not always satisfied if the penetration depth for the two wavelengths is different, which can especially occur in reflection PPG. If the two wavelengths are close to each other then the difference of the effective optical path-length is small and

$$R \approx \frac{\varepsilon_{a1}}{\varepsilon_{a2}} \quad (7b)$$

The relationship between the ratio R—the measured parameter—and the oxygen saturation SaO_2 can be derived from the decomposition of the extinction coefficient ϵ into its two components, the extinction coefficients for oxygenated blood ϵ_o and for deoxygenated blood ϵ_d:

$$\varepsilon = \varepsilon_o SaO_2 + \varepsilon_d (1 - SaO_2) = \varepsilon_d + SaO_2(\varepsilon_o - \varepsilon_d) \quad (8)$$

Then

$$R = \frac{\varepsilon_{d1} + SaO_2(\varepsilon_{o1} - \varepsilon_{d1})}{\varepsilon_{d2} + SaO_2(\varepsilon_{o2} - \varepsilon_{d2})} \quad (9)$$

and

$$SaO_2 = \frac{\varepsilon_{d1} - R\varepsilon_{d2}}{R(\varepsilon_{02} - \varepsilon_{d2}) + (\varepsilon_{d1} - \varepsilon_{01})} \quad (10)$$

In order to have a higher difference in light transmittance between the two wavelengths, commercial pulse oximeters choose one of the wavelengths in the infrared region, above the isosbestic wavelength (805 nm) and the other in the red region, where the difference in the extinction coefficient between oxygenated and deoxygenated blood is maximal. However, for this choice, the red light scattering constant significantly differs from that of the infrared light resulting in non-negligible difference in optical path-lengths for the two wavelengths. From Equation (7a)

$$R(l_1 / l_2) = \frac{\varepsilon_{o1}}{\varepsilon_{o2}} \quad (11)$$

By replacing R in Eqs. 9-10 with $R(l_2/l_1)$, Equation (10) becomes

$$SaO_2 = \frac{\varepsilon_{d1} - R(l_1 / l_2)\varepsilon_{d2}}{R(l_1 / l_2)(\varepsilon_{02} - \varepsilon_{d2}) + (\varepsilon_{d1} - \varepsilon_{01})} \quad (12)$$

Taking λ_1 as the lower wavelength, l_1 is higher than l_2 due to the higher scattering for the lower wavelength. By using the measured higher value of R instead of the lower value of $R(l_2/l_1)$, the calculated value of SaO_2 is lower than its real value.

[0007] Due to the difference between the optical properties of the red and infrared light, the clinical parameter oxygen saturation SaO_2 cannot be derived from the measured parameter R and Equation (10). The actual relationship between the measured parameter R and oxygen saturation SaO_2 is achieved for each pulse oximeter sensor by calibration (Schowalter, 1997): R is measured in several persons simultaneously with in vitro SaO_2 measurement in extracted arterial blood by means of co-oximeter which is the gold-standard for SaO_2 measurements. For each person R and SaO_2 measurements are taken for several values of SaO_2, achieved by changing the partial pressure of oxygen in the inspired air. The table of the simultaneous measurements of R and SaO_2 provides the required calibration for the derivation of the clinical parameter oxygen saturation SaO_2 from the measured parameter R. The reliability of the calibration is based on the assumption that l_2/l_1 does not change between different persons and different physiological and clinical situations. The validity of this assumption is limited and deviations from this assumption are the likely origin of the inherent inaccuracy of the pulse oximetry technique for the assessment of the oxygen saturation, SaO_2, in the arterial blood.

[0008] In the description of the pulse oximetry method presented above, R was defined as the ratio of the ratios $\Delta I_a/I_S$ for the two wavelengths R can also be defined as the ratio of two values of a parameter related to change in light transmission for the two wavelengths, and this parameter can be different than $\Delta I_a/I_S$. It can be chosen as (I_D/I_S) (as in U.S. Pat. Nos. 4,773,422 and 4,167,331) or the derivative of I divided by I (as in U.S. Pat. No. 6,505,060). As stated above, due to the higher scattering for the lower wavelength, $l_1 > l_2$ for $\lambda_1 < \lambda_2$, and by using the measured higher value of R instead of the lower value of $R(l_2/l_1)$, the calculated value of SaO_2 is lower than its real value. If the two wavelengths are close to each other, l_2/l_1 is expected to be about 1 and SpO_2 can be derived from Equation (10) without calibration. This was shown in our study (Nitzan et al 2000), in which we measured SpO_2, using pulse oximetry based on two infrared wavelengths (767 and 811 nm) and Equation (10), without calibration. The SpO_2 values were lower than that of the available pulse oximeters using red and infrared light, probably because the limitation of the assumption of $l_2/l_1=1$. The accuracy of the technique increased by using Equation (12) and assessing (l_2/l_1) value from published data (like that of Duncan et al. 2000 for the forearm, $(l_2/l_1)=0.97$) but since l_2/l_1 is not known for the specific examination the accuracy is still limited.

[0009] Oxygen saturation in the peripheral venous blood SvO_2 also has physiological and clinical significance, as described above, but in contrast to the routine use of pulse oximetry to SaO_2 measurement, no accepted method for the measurement of SvO_2 is available. Similar to pulse oximetry which utilizes the PPG changes (corresponding to arterial blood volume changes) in the heart rate for the evaluation of the arterial oxygen saturation, we measured (Nitzan et al. 2000) venous oxygen saturation in the blood accumulated in the veins after applying to the arm pressure higher than venous blood pressure. The use of two wavelengths of similar value of l_2/l_1 is essential because blood extracted from big

veins does not necessarily has the same value of oxygen saturation as that of small veins in specific skin site and therefore calibration cannot be used. SvO_2 can also be measured by using the spontaneous blood volume changes in the respiratory rate and in lower frequencies (of about 0.1 Hz and about 0.02 Hz) (Nitzan et al. 1994). We found that the blood volume changes in very-low-frequency are mainly attributed to tissue venous blood volume changes (Nitzan et al 1996).

1.5. The Accuracy of Arterial Oxygen Saturation Measurement by Pulse Oximetry

[0010] The accuracy of SaO_2 measurement by pulse oximetry (SpO_2) is obtained by comparing the SpO_2 measurement to SaO_2 measurement in extracted arterial blood by means of co-oximeter, which is the gold-standard for SaO_2 measurements. The accuracy of SpO_2 as declared by the manufacturers is 2%, say the standard deviation of the SpO_2 and co-oximeter measurements is 2%, which means that for 5% of the examinations the deviation from the gold-standard is 4%. For SaO_2 values below 80% the accuracy is even lower. Such accuracy is acceptable for the present main use of pulse oximetry; say monitoring arterial oxygen saturation during surgical operations and at intensive care units, in order to check qualitatively that no adverse change happened to the patient. In these cases detection of 3-4% decrease in SaO_2 is required, and in general this task can be properly performed by the available pulse oximeter monitors. However, in some medical units, where respiratory function assessment is required, higher accuracy of SaO_2 measurement is needed. In some studies where accurate oxygenation measurement was required invasive PaO_2 measurement was used instead of noninvasive SpO_2 measurement. As an example, Seccombe et al (2004) examined the effect of lower-than-normal oxygen pressure in breathed air on lung patients, by measuring invasively PaO_2 in their arterial blood, for assessing their potential response to flight environment.

[0011] Note that in general the range of SaO_2 values is 80-100%, so that standard deviation of 2% is not small relative to the range values. In particular the range of normal values of SaO_2 is 94-99%, so that pulse oximetry in its present configuration is not useful for assessing SaO_2 in physiological studies of the normal range and for sports medicine.

[0012] The low accuracy of SpO_2 measurement probably originates from the requirement for calibration. As stated above, the derivation of the oxygen saturation SaO_2 from the measured ratio R cannot be achieved directly from Equation (10) and together with the values of the extinction coefficients for oxygenated blood ϵ_o and for deoxygenated blood ϵ_d because l_1 and l_2 are not equal. Equation (12) cannot be used because l_1/l_2 is not known. The calibration process assumes constant value of l_1/l_2 for all persons undergoing examination, independent on the clinical variables, which is not always achieved.

[0013] Furthermore, the assumption that the difference in the blood concentration change Δc_a, between the two wavelengths can be neglected ($\Delta c_{a1} \approx \Delta c_{a2}$) is not achieved if the penetration depth for the two wavelengths is different and the tissue is not homogenous. In our studies we found (Nitzan et al. 2000) that the significance of these two phenomena can be reduced, if the two wavelengths will be chosen close to one another so that they will be of similar path-length and similar penetration depth. By using Equation (12) and assessing (l_2/l_1) value from published data (see above), the technique provides SpO_2 value with no need for calibration. The technique requires the use of the values of the extinction coefficients of oxygenated and deoxygenated hemoglobin for the three wavelengths. The accuracy of the technique is, however still limited since l_2/l_1 is not known for the specific vascular setup and blood distribution in tissue for each examination. Accordingly, there is a need for innovative improvement of pulse oximetry in order to obtain accurate non-invasive technique for the monitoring of the oxygen saturation in arterial blood, SaO_2.

[0014] Furthermore, there is a need to modify the pulse oximetry technique so that it will be appropriate to measure the oxygen saturation in venous blood, SvO_2.

SUMMARY OF THE INVENTION

[0015] The present invention is a pulse oximetry technique for measurement of oxygen saturation in arterial or venous blood.

[0016] According to the teachings of the present invention there is provided, a method for the measurement of oxygen saturation in arterial blood, the method comprising: (a) applying to the skin an apparatus including: (i) light-sources for generating light of three peak wavelengths λ_1, λ_2 and λ_3; (ii) a detector arrangement, and (iii) an electronics unit, the apparatus configured to detect, for each light-source, the transmitted light through the tissue; (b) for each light source, deriving a PPG curve; (c) deriving from the three PPG curves a parameter related to the relative change in light transmission for each of the three wavelengths, and the ratio R_{12} and R_{13} of that parameter for the two wavelengths λ_1 and λ_2 and for the two wavelengths λ_1 and λ_3, respectively; and (d) determining the oxygen saturation in arterial blood, SaO_2, from the solution of three equations including:

[0017] a. relationship between SaO_2 and R_{12}, which includes the optical path-lengths l_1 and l_2,

[0018] b. relationship between SaO_2 and R_{13}, which includes the optical path-lengths l_1 and l_3;

[0019] c. relationship between small changes in the path-length l and small changes in the wavelength λ,

where the first two equations include the values of the extinction coefficient for the three peak wavelength for oxygenated blood ϵ_o, and for decoxygenated blood ϵ_d.

[0020] There is also provided according to the teachings of the present invention, a method for the measurement of oxygen saturation in arterial blood, the method comprising: (a) applying to the skin an apparatus including: (i) light-sources for generating light of three peak wavelengths λ_1, λ_2 and λ_3; (ii) a detector arrangement; and (iii) an electronics unit, the apparatus configured to detect, for each light-source, the transmitted light through the tissue; (b) for each light-source, determining the mean extinction coefficients over the spectrum band of the light-source emitted light for oxygenated blood ϵ_o and for deoxygenated blood ϵ_d; (c) for each light-source, deriving a PPG curve; (d) deriving from the three PPG curves a parameter related to the relative change in light transmission for each of the three wavelengths, and the ratio R_{12} and R_{13} of that parameter for the two wavelengths λ_1 and λ_2 and for the two wavelengths λ_1 and λ_3, respectively; and (e) determining the oxygen saturation in arterial blood, SaO_2, from the solution of three equations including:

[0021] a. relationship between SaO_2 and R_{12}, which includes the optical path-lengths l_1 and l_2;

[0022] b. relationship between SaO_2 and R_{13}, which includes the optical path-lengths l_1 and l_3;

[0023] c. relationship between small changes in the path-length l and small changes in the wavelength λ.

where the first two equations include the values of the mean extinction coefficient for the three light sources for oxygenated blood ϵ_o and for deoxygenated blood ϵ_d.

[0024] According to a further feature of the present invention, the relationship between SaO_2 and R_{12}, which includes the optical path-lengths l_1 and l_2 is

$$SaO_2 = \frac{\varepsilon_{d1} - R_{12}(l_1/l_2)\varepsilon_{d2}}{R_{12}(l_1/l_2)(\varepsilon_{02} - \varepsilon_{d2}) + (\varepsilon_{d1} - \varepsilon_{01})}$$

[0025] According to a further feature of the present invention, the relationship between SaO_2 and R_{13}, which includes the optical path-lengths l_1 and l_3 is

$$SaO_2 = \frac{\varepsilon_{d1} - R_{13}(l_1/l_3)\varepsilon_{d3}}{R_{13}(l_1/l_3)(\varepsilon_{02} - \varepsilon_{d3}) + (\varepsilon_{d1} - \varepsilon_{01})}$$

[0026] According to a further feature of the present invention, the three peak wavelengths are in the infrared region.

[0027] According to a further feature of the present invention, the relationship between small changes in the path-length l and small changes in the wavelength λ is a linear relationship.

[0028] According to a further feature of the present invention, the parameter related to the relative change in light transmission is selected from the group comprising:

[0029] a. $(I_D-I_S)/I_S$, where I_D is the maximal light transmission and I_S is the minimal light transmission;

[0030] b. $[I(t_1)-I(t_2)]/I(t_2)$, where $I(t_1)$ and $I(t_2)$ are light transmission values at two time points, t_1 and t_2, along the rise-time of the PPG pulse;

[0031] c. $\ln(I_D/I_S)$;

[0032] d. $\ln[I(t_1)/I(t_2)]$, where t_1 and t_2 are two time points along the rise-time of the PPG pulse;

[0033] e. (dI(t)/dt)/I(t) at some point along the rise-time of the PPG pulse; and

[0034] f. mean of the values of (dI(t)/dt)/I(t) at some points along the rise-time of the PPG pulse.

[0035] According to a further feature of the present invention, the light sources are selected from the group comprising: light emitting diodes, light emitting diodes with filter and laser diodes.

[0036] There is also provided according to the teachings of the present invention, a method for the measurement of oxygen saturation in tissue venous blood, the method comprising: (a) applying to the skin an apparatus including: (i) light-sources for generating light of three peak wavelengths λ_1, λ_2 and λ_3; (ii) a detector arrangement; and (iii) an electronics unit, the apparatus configured to detect, for each light-source, the transmitted light through the tissue; (b) for each light source, deriving a curve of light transmission through the tissue while venous blood volume changes; (c) deriving from the three light transmission curves a parameter related to the relative change in light transmission for each of the three wavelengths, and the ratio R_{12} and R_{13} of that parameter for the two wavelengths λ_1 and λ_2 and for the two wavelengths λ_1 and λ_3, respectively; and (d) determining the oxygen saturation in venous blood, SvO_2, from the solution of three equations including:

[0037] a. relationship between SaO_2 and R_{12}, which includes the optical path-lengths l_1 and l_2;

[0038] b. relationship between SaO_2 and R_{13}, which includes the optical path-lengths l_1 and l_3;

[0039] c. relationship between small changes in the path-length l and small changes in the wavelength λ,

where the first two equations include the values of the extinction coefficient for the three peak wavelength for oxygenated blood ϵ_o and for deoxygenated blood ϵ_d.

[0040] There is also provided according to the teachings of the present invention, a method for the measurement of oxygen saturation in tissue venous blood, the method comprising. (a) applying to the skin an apparatus including: (i) light-sources for generating light of three peak wavelengths λ_1, λ_2 and λ_3; (ii) a detector arrangement; and (iii) an electronics unit, the apparatus configured to detect, for each light-source, the transmitted light through the tissue; (b) for each light-source, determining the mean extinction coefficients over the spectrum band of the light-source emitted light for oxygenated blood ϵ_o and for deoxygenated blood ϵ_d; (c) for each light-source, deriving a curve of light transmission through the tissue while venous blood volume changes; (d) deriving from the three light transmission curves a parameter related to the relative change in light transmission for each of the three wavelengths, and the ratio R_{12} and R_{13} of that parameter for the two wavelengths λ_1 and λ_2 and for the two wavelengths λ_1 and λ_3, respectively; and (e) determining the oxygen saturation in venous blood, SvO_2, from the solution of three equations including:

[0041] a. relationship between SaO_2 and R_{12}, which includes the optical path-lengths l_1 and l_2;

[0042] b. relationship between SaO_2 and R_{13}, which includes the optical path-lengths l_1 and l_3;

[0043] c. relationship between small changes in the path-length l and small changes in the wavelength λ.

where the first two equations include the values of the mean extinction coefficient for the three light sources for oxygenated blood ϵ_o and for deoxygenated blood ϵ_d.

[0044] According to a further feature of the present invention, the relationship between SvO_2 and R_{12}, which includes the optical path-lengths l_1 and l_2 is

$$SvO_2 = \frac{\varepsilon_{d1} - R_{12}(l_1/l_2)\varepsilon_{d2}}{R_{12}(l_1/l_2)(\varepsilon_{02} - \varepsilon_{d2}) + (\varepsilon_{d1} - \varepsilon_{01})}$$

[0045] According to a further feature of the present invention, the relationship between SvO_2 and R_{13}, which includes the optical path-lengths l_1 and l_3 is

$$SvO_2 = \frac{\varepsilon_{d1} - R_{13}(l_1/l_3)\varepsilon_{d3}}{R_{13}(l_1/l_3)(\varepsilon_{02} - \varepsilon_{d3}) + (\varepsilon_{d1} - \varepsilon_{01})}$$

[0046] According to a further feature of the present invention, the three peak wavelengths are in the infrared region.

[0047] According to a further feature of the present invention, the relationship between small changes in the path-length l and small changes in the wavelength λ is linear relationship.

[0048] According to a further feature of the present invention, the parameter related to the relative change in light transmission is selected from the group comprising:

[0049] a. $(I_D-I_S)/I_S$, where I_D is the maximal light transmission and I_S is the minimal light transmission;

[0050] b. $[I(t_1)-I(t_2)/I(t_2)$, where $I(t_1)$ and $I(t_2)$ are light transmission values at two time points, t_1 and t_2, along the rise-time of the PPG pulse;

[0051] c. $\ln (I_D/I_S)$;

[0052] d. $\ln [I(t_1)/I(t_2)]$, where t_1 and t_2 are two time points along the rise-time of the PPG pulse;

[0053] e. $(dI(t)/dt)/I(t)$ at some point along the rise-time of the PPG pulse; and

[0054] f. mean of the values of $(dI(t)/dt)/I(t)$ at some points along the rise-time of the PPG pulse.

[0055] According to a further feature of the present invention, the light sources are selected from the group comprising: light emitting diodes, light emitting diodes with filter and laser diodes.

[0056] According to a further feature of the present invention, the change in venous blood volume is achieved by closing the veins conveying blood from the tissue, by use of a pressure cuff.

[0057] According to a further feature of the present invention, the change in venous blood volume is spontaneous.

[0058] According to a further feature of the present invention, the spontaneous change in venous blood volume is at the respiratory rate.

[0059] According to a further feature of the present invention, the spontaneous change in venous blood volume is at a frequency of about 0.1 Hz.

[0060] According to a further feature of the present invention, the spontaneous change in venous blood volume is at a frequency of 0.01-0.04 Hz

BRIEF DESCRIPTION OF THE DRAWINGS

[0061] The invention is herein described, by way of example only, with reference to the accompanying drawings, wherein:

[0062] FIG. **1** is a graph showing the extinction coefficients for oxygenated blood (HbO_2) and for deoxygenated blood (Hb) as a function of the wavelength.

[0063] FIG. **2** is a plot of a PPG signal against time showing variations at the heart rate, wherein maximal intensity of transmitted light occurs at end-diastole when the tissue blood volume is minimum and the light transmitted through the tissue is at maximal intensity, and wherein. BL is the baseline, AM is the amplitude; and P is the period.

[0064] FIG. **3** is a plot showing a series of PPG pulses inverted.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0065] In the current invention, the transmission of light through the finger of three adjacent wavelengths in the infrared region, λ_1, λ_2, and λ_3, will be measured for the assessment of SaO_2. Equation (12) will be used for the two pairs λ_1, λ_2, and λ_3:

$$SaO_2 = \frac{\varepsilon_{d1} - R_{12}(l_1/l_2)\varepsilon_{d2}}{R_{12}(l_1/l_2)(\varepsilon_{02} - \varepsilon_{d2}) + (\varepsilon_{d1} - \varepsilon_{01})} \quad (13)$$

$$SaO_2 = \frac{\varepsilon_{d1} - R_{13}(l_1/l_3)\varepsilon_{d3}}{R_{13}(l_1/l_3)(\varepsilon_{02} - \varepsilon_{d3}) + (\varepsilon_{d1} - \varepsilon_{01})}$$

where R_{12} and R_{13} are the ratio of the relative changes in light transmission $\Delta I_a/I_S$ for the two wavelengths λ_1 and λ_2 and the two wavelengths λ_1 and λ_3, respectively, and l_1, l_2 and l_3 are the path-lengths of the three wavelengths, λ_1, λ_2, and λ_3, respectively.

[0066] R_{12} and R_{13} of Equation (13) can be measured and the extinction coefficients for the three wavelengths can be found for oxygenated blood ϵ_o and for deoxygenated blood ϵ_d in the literature. FIG. **1** shows a graph of the extinction coefficients for oxygenated blood (HbO_2) and for deoxygenated blood (Hb) as a function of the wavelength. However, in order to determine SaO_2, it is necessary to find l_1/l_2 and l_1/l_3. Since the dependence of scattering on the wavelength is smooth, the relationship between the path-length l and the wavelength λ is also smooth, and one can assume linear relationship between small changes in the path-length l and small changes in the wavelength λ.

$$l=l_0+\text{Const}(\lambda-\lambda_0) \quad (14)$$

which yields the following relationship between l_1/l_2 and l_1/l_3:

$$(\lambda_2-\lambda_1)/(\lambda_3-\lambda_1)=(l_2-l_1)/(l_3-l_1)=(l_2/l_1-1)/(l_3/l_1-1) \quad (15)$$

From the three equations, Equations (13) and Equation (15), SaO_2 can be determined without prior information on l_1/l_2 and l_1/l_3, since we have three equations in three unknowns.

[0067] The measurement of pulse oximetry by three wavelengths or more has been already suggested for accurate measurement of oxygen saturation in the presence of carboxyhemoglobin and methemoglobin (U.S. Pat. Nos. 5,413,100, 4,167,331). The extinction coefficient of carboxyhemoglobin and of methemoglobin differs from that of oxygenated hemoglobin and deoxygenated hemoglobin: carboxyhemoglobin is almost transparent in the infrared region and methemoglobin has higher absorption for the red light and lower absorption for the infrared region. Our technique is different since it is based on Equations (13) and (15).

[0068] U.S. Pat. No. 6,801,799 by Mendelson suggests pulse oximeter of three wavelengths, one in red and two in infrared. The latter two wavelengths are used for compensating for changes in contact pressure or site-to-site variations. The technique suggested by Mendelson includes several detectors arranged around the light sources in closed path, while our technique requires only one detector and is based on Equations (13) and (15). Mannheimer in U.S. Pat. No. 5,782,756 utilizes three wavelengths for compensating for variations caused by scattering differences at different wavelengths. This is done by deriving SaO_2 by means of two pairs of wavelengths in the regular technique (say Equation (10) or similar equation, including calibration for the determination of the relationship between SaO_2 and R). The first pair of wavelengths provides the SaO_2 initial assessment and the other SaO_2 value, derived from the other pair of wavelengths, is used for correcting the initial assessment. In our technique the two pairs of PPG measurement are utilized, together with a third equation, for the determination of SaO_2.

[0069] The technique suggested by Mannheimer in U.S. Pat. No. 5,782,756 differs from our technique in three elements.

[0070] The algorithms are different

[0071] Calibration is required for the technique suggested by Mannheimer, while our technique needs no calibration. On the other hand, in our technique the mean extinction coefficients over the spectrum band of the light-source emitted light has to be derived for the three

wavelengths both for oxygenated blood ϵ_o and for deoxygenated blood ϵ_d, while in Mannheimer's technique it is not required

[0072] The choice of the suitable three wavelengths is different. Mannheimer suggests preferred wavelength combinations based on overlap in penetration of light and sufficient difference in extinction coefficient between the wavelengths. In our technique we suggest using light of wavelengths in the infrared region, as well as small difference between the wavelengths, so that the dependence of the path-length l and the wavelength λ is linear.

[0073] The suggested technique is also suitable for SvO_2 assessment, by measuring light transmission change in infrared light of three wavelengths, originated from change in venous blood volume. As noted above, the change in venous blood volume can be a result of vein occlusion after applying to the arm pressure higher than venous blood pressure but lower than arterial blood pressure, or can be spontaneous, in respiration rate due to the respiratory effect on blood vessels or in lower frequency, due to autonomic nervous system activity.

[0074] The preferred pulse oximeter is a device, applied to the skin, which includes single LED or several LEDs of three peak wavelengths in the infrared region and a detector which can detect, for each wavelength, the transmitted light through the tissue. For each LED, the mean extinction coefficients over the spectrum band of the LED emitted light is derived for oxygenated blood ϵ_o and for deoxygenated blood ϵ_d. For each wavelength a PPG curve is obtained. From the three PPG curves a parameter related to the relative change in light transmission is obtained for each of the three wavelengths, and the ratio R_{12} and R_{13} of that parameter for the two wavelengths λ_1 and λ_2 and for the two wavelengths λ_1 and λ_3, respectively, is derived. SaO_2 is determined from the pair of equations.

$$SaO_2 = \frac{\varepsilon_{d1} - R_{12}(l_1/l_2)\varepsilon_{d2}}{R_{12}(l_1/l_2)(\varepsilon_{02} - \varepsilon_{d2}) + (\varepsilon_{d1} - \varepsilon_{01})}$$

and

$$SaO_2 = \frac{\varepsilon_{d1} - R_{13}(l_1/l_3)\varepsilon_{d3}}{R_{13}(l_1/l_3)(\varepsilon_{02} - \varepsilon_{d3}) + (\varepsilon_{d1} - \varepsilon_{01})}$$

using linear relationship between small changes in the path-length l and small changes in the wavelength λ.

[0075] In another preferred embodiment laser diodes with optic fibers are used instead of LEDs. The emission spectrum of laser diode is sharper than that of LED, so that the calculation of the mean extinction coefficients over the spectrum band of the emitted light is simpler and more accurate.

[0076] In another preferred embodiment the LEDs are used with narrow-band filter to reduce the emission spectrum of the LED, so that the calculation of the mean extinction coefficients over the spectrum band of the emitted light is simpler and more accurate.

[0077] In another preferred embodiment laser diodes or LEDs for emitting light in three wavelengths are used, together with a detector, for measuring the changes in light transmission through the tissue, originating from changes in venous blood volume. Oxygen saturation in venous blood SvO_2 is then determined from the corresponding relative changes in light transmission $\Delta I_v/I_S$ for the three wavelengths, and the ratio of the relative changes in light transmission $\Delta I_v/I_S$ for the two wavelengths λ_1 and λ_2 and for the two wavelengths λ_1 and λ_3, R_{12} and R_{13} respectively, using Equations (13) and (15).

BIBLIOGRAPHY

[0078] 1. Mendelson Y Transcutaneous blood gas measurement. In *Encyclopedia of Medical Devices and Instrumentation*, J. G. Webster, Editor in Chief, John Wiley & Sons, New York, 1988 pp 448-460.

[0079] 2. I Yoshiya, Y Shimady and K Tanake. Spectrophotometric monitoring of arterial oxygen saturation on the fingertip. *Med Biol. Eng Comput.* 18:27-32 (1980).

[0080] 3. A. Babchenko, E. Davidson, Y. Ginosar, V. Kurtz, I. Feib, D. Adler and M. Nitzan, 2001. Photoplethysmographic measurement of changes in total and pulsatile tissue blood volume following sympathetic blockade. *Physiol Meas.* 22:389-396.

[0081] 4. O. Wieben. Light absorbance in pulse oximetry In: *Design of Pulse Oximeters* J. G. Webster, editor. Institute of Physics Publishing, Bristol, pp 40-55, (1997)

[0082] 5. P. D. Mannheimer, J. R. Casciani, M. E. Fein, S. L. Nierlich. Wavelength selection for low-saturation pulse oximetry. *IEEE Trans. Biomed. Eng.* 44(3): 148-158 (1997)

[0083] 6. M. Nitzan, A. Babchenko, B. Khanokh, and H. Taitelbaum. The measurement of oxygen saturation in venous blood by dynamic near IR spectroscopy. J Biomed Optics. 5:155-162 (2000)

[0084] 7. Schowalter J S, Calibration. In. *Design of Pulse Oximeters*. J. G. Webster, editor. Institute of Physics Publishing, Bristol, pp. 159-175, (1997).

[0085] 8. A. Duncan , J. H. Meek, M. Clemence, C. E. Elwell. L. Tyszczuk, M. Cope and D. T. Delpy. Optical pathlength measurements on adult head, calf and forearm and the head of the newborn infant using phase resolved spectroscopy. *Phys. Med Biol*, 40:295-304 (1995).

[0086] 9. M. Nitzan, H. de Boer, S. Turivnenko, A. Babchenko, and D. Sapoznikov 1994. Power spectrum analysis of the spontaneous fluctuations in the photoplethysmographic signal *J Basic and Clinical Physiol and Pharmacol.* 5:269-276.

[0087] 10. M. Nitzan, S. Turivnenko, A. Milston, A. Babchenko and Y. Mahler, 1996. Low frequency variability in the blood volume and in the blood volume pulse measured by photoplethysmography. *J. Biomed Optics,* 1:223-229.

[0088] 11. L M Seccombe, P T Kelly, C K Wong, P G Rogers, Lim S and M J Peters, 2004. Effect of simulated commercial flight on oxygenation in patients with interstitial lung disease and chronic obstructive pulmonary disease Thorax 59:966-970.

1. A method for the measurement of oxygen saturation in arterial blood, the method comprising:

(a) applying to the skin an apparatus including:

(i) light-sources for generating light of three peak wavelengths λ_1, λ_2 and λ_3; (ii) a detector arrangement; and (iii) an electronics unit, the apparatus configured to detect, for each light-source, the transmitted light through the tissue;

(b) for each light source, deriving a PPG curve;

(c) deriving from the three PPG curves a parameter related to the relative change in light transmission for each of the three wavelengths, and the ratio R_{12} and R_{13} of that

parameter for the two wavelengths λ_1 and λ_2 and for the two wavelengths λ_1, and λ_3, respectively; and

(d) determining the oxygen saturation in arterial blood, SaO_2, from the solution of three equations including:

a. relationship between SaO_2 and R_{12}, which includes the optical path-lengths l_1 and l_2;

b. relationship between SaO_2 and R_{13}, which includes the optical path-lengths l_1 and l_3;

c. relationship between small changes in the path-length l and small changes in the wavelength λ,

where the first two equations include the values of the extinction coefficient for the three peak wavelength for oxygenated blood ϵ_o and for deoxygenated blood ϵ_d.

2. A method for the measurement of oxygen saturation in arterial blood, the method comprising:

(a) applying to the skin an apparatus including:

(i) light-sources for generating light of three peak wavelengths λ_1, λ_2 and λ_3; (ii) a detector arrangement; and (iii) an electronics unit, the apparatus configured to detect, for each light-source, the transmitted light through the tissue;

(b) for each light-source, determining the mean extinction coefficients over the spectrum band of the light-source emitted light for oxygenated blood ϵ_o and for deoxygenated blood ϵ_d;

(c) for each light source, deriving a PPG curve;

(d) deriving from the three PPG curves a parameter related to the relative change in light transmission for each of the three wavelengths, and the ratio R_{12} and R_{13} of that parameter for the two wavelengths λ_1 and λ_2 and for the two wavelengths λ_1 and λ_3, respectively; and

(e) determining the oxygen saturation in arterial blood, SaO_2, from the solution of three equations including:

a. relationship between SaO_2 and R_{12}, which includes the optical path-lengths l_1 and l_2;

b. relationship between SaO_2 and R_{13}, which includes the optical path-lengths l_1 and l_3;

c. relationship between small changes in the path-length l and small changes in the wavelength λ,

where the first two equations include the values of said mean extinction coefficient for the three light sources for oxygenated blood ϵ_o and for deoxygenated blood ϵ_d.

3. A method as in claim **2**, where said relationship between SaO_2 and R_{12}, which includes the optical path-lengths l_1 and l_2 is

$$SaO_2 = \frac{\varepsilon_{d1} - R_{12}(l_1/l_2)\varepsilon_{d2}}{R_{12}(l_1/l_2)(\varepsilon_{02} - \varepsilon_{d2}) + (\varepsilon_{d1} - \varepsilon_{01})}$$

4. A method as in claim **3**, where said relationship between SaO_2 and R_{13}, which includes the optical path-lengths l_1 and l_3 is

$$SaO_2 = \frac{\varepsilon_{d1} - R_{13}(l_1/l_3)\varepsilon_{d3}}{R_{13}(l_1/l_3)(\varepsilon_{02} - \varepsilon_{d3}) + (\varepsilon_{d1} - \varepsilon_{01})}$$

5. A method as in claim **1**, where said three peak wavelengths are in the infrared region.

6. A method as in claim **2**, where said three peak wavelengths are in the infrared region.

7. A method as in claim **2**, where said relationship between small changes in the path-length l and small changes in the wavelength λ is a linear relationship.

8. A method as in claim **2**, where said parameter related to the relative change in light transmission is selected from the group comprising:

a. $(I_D - I_S)/I_S$, where I_D is the maximal light transmission and I_S is the minimal light transmission;

b. $[I(t_1) - I(t_2)]/I(t_2)$, where $I(t_1)$ and $I(t_2)$ are light transmission values at two time points, t_1 and t_2, along the rise-time of the PPG pulse,

c. $\ln (I_D/I_S)$;

d. $\ln [I(t_1)/I(t_2)]$, where t_1 and t_2 are two time points along the rise-time of the PPG pulse,

e. $(dI(t)/dt)/I(t)$ at some point along the rise-time of the PPG pulse; and

f. mean of the values of $(dI(t)/dt)/I(t)$ at some points along the rise-time of the PPG pulse.

9. A method as in claim **1**, where the light sources are selected from the group comprising: light emitting diodes, light emitting diodes with filter and laser diodes.

10. A method as in claim **2**, where the light sources are selected from the group comprising: light emitting diodes, light emitting diodes with filter and laser diodes.

11. A method for the measurement of oxygen saturation in tissue venous blood, the method comprising:

(a) applying to the skin an apparatus including:

(i) light-sources for generating light of three peak wavelengths λ_1, λ_2 and λ_3; (ii) a detector arrangement; and (iii) an electronics unit, the apparatus configured to detect, for each light-source, the transmitted light through the tissue;

(b) for each light source, deriving a curve of light transmission through the tissue while venous blood volume changes;

(c) deriving from the three light transmission curves a parameter related to the relative change in light transmission for each of the three wavelengths, and the ratio R_{12} and R_{13} of that parameter for the two wavelengths λ_1 and λ_2 and for the two wavelengths λ_1 and λ_3, respectively, and

(d) determining the oxygen saturation in venous blood, SvO_2, from the solution of three equations including:

a. relationship between SaO_2 and R_{12}, which includes the optical path-lengths l_1 and l_2;

b. relationship between SaO_2 and R_{13}, which includes the optical path-lengths l_1 and l_3;

c. relationship between small changes in the path-length l and small changes in the wavelength λ,

where the first two equations include the values of the extinction coefficient for the three peak wavelength for oxygenated blood ϵ_o and for deoxygenated blood ϵ_d.

12. A method for the measurement of oxygen saturation in tissue venous blood, the method comprising:

(a) applying to the skin an apparatus including:

(i) light-sources for generating light of three peak wavelengths λ_1, λ_2 and λ_3; (ii) a detector arrangement; and (iii) an electronics unit, the apparatus configured to detect, for each light-source, the transmitted light through the tissue;

(b) for each light-source, determining the mean extinction coefficients over the spectrum band of the light-source emitted light for oxygenated blood ϵ_o and for deoxygenated blood ϵ_d;

(c) for each light source, deriving a curve of light transmission through the tissue while venous blood volume changes;

(d) deriving from the three light transmission curves a parameter related to the relative change in light transmission for each of the three wavelengths, and the ratio R_{12} and R_{13} of that parameter for the two wavelengths λ_1 and λ_2 and for the two wavelengths λ_1 and λ_3, respectively; and

(e) determining the oxygen saturation in venous blood, SvO_2, from the solution of three equations including:

a. relationship between SaO_2 and R_{12}, which includes the optical path-lengths l_1 and l_2;

b. relationship between SaO_2 and R_{13}, which includes the optical path-lengths l_1 and l_3;

c. relationship between small changes in the path-length l and small changes in the wavelength λ,

where the first two equations include the values of said mean extinction coefficient for the three light sources for oxygenated blood ϵ_o and for deoxygenated blood ϵ_d.

13. A method as in claim **12** where said relationship between SvO_2 and R_{12}, which includes the optical path-lengths l_1 and l_2 is

$$SvO_2 = \frac{\varepsilon_{d1} - R_{12}(l_1/l_2)\varepsilon_{d2}}{R_{12}(l_1/l_2)(\varepsilon_{02} - \varepsilon_{d2}) + (\varepsilon_{d1} - \varepsilon_{01})}$$

14. A method as in claim **13**, where said relationship between SvO_2 and R_{13}, which includes the optical path-lengths l_1 and l_3 is

$$SvO_2 = \frac{\varepsilon_{d1} - R_{13}(l_1/l_3)\varepsilon_{d3}}{R_{13}(l_1/l_3)(\varepsilon_{02} - \varepsilon_{d3}) + (\varepsilon_{d1} - \varepsilon_{01})}$$

15. A method as in claim **11**, where said three peak wavelengths are in the infrared region.

16. A method as in claim **12**, where said three peak wavelengths are in the infrared region.

17. A method as in claim **12**, where said relationship between small changes in the path-length l and small changes in the wavelength λ is linear relationship

18. A method as in claim **12**, where said parameter related to the relative change in light transmission is selected from the group comprising:

a. $(I_D - I_S)/I_S$, where I_D is the maximal light transmission and I_S is the minimal light transmission;

b. $[I(t_1) - I(t_2)]/I(t_2)$, where $I(t_1)$ and $I(t_2)$ are light transmission values at two time points, t_1 and t_2, along the rise-time of the PPC pulse;

c. $\ln (I_D/I_S)$;

d. $\ln [I(t_1)/I(t_2)]$, where t_1 and t_2 are two time points along the rise-time of the PPG pulse;

e. (dI(t)/dt)/I(t) at some point along the rise-time of the PPG pulse; and f mean of the values of (dI(t)/dt)/I(t) at some points along the rise-time of the PPG pulse.

19. A method as in claim **11**, where the light sources are selected from the group comprising: light emitting diodes, light emitting diodes with filter and laser diodes.

20. A method as in claim **12**, where the light sources are selected from the group comprising: light emitting diodes, light emitting diodes with filter and laser diodes.

21. A method as in claim **12**, where said change in venous blood volume is achieved by closing the veins conveying blood from said tissue, by use of a pressure cuff.

22. A method as in claim **12**, where said change in venous blood volume is spontaneous.

23. A method as in claim **22**, where said spontaneous change in venous blood volume is at the respiratory rate.

24. A method as in claim **22**, where said spontaneous change in venous blood volume is at a frequency of about 0.1 Hz

25. A method as in claim **22**, where said spontaneous change in venous blood volume is at a frequency of 0.01-0.04 Hz.

* * * * *

专利名称(译)	改良脉搏血氧仪测定动脉和静脉血氧饱和度		
公开(公告)号	US20080208019A1	公开(公告)日	2008-08-28
申请号	US11/677585	申请日	2007-02-22
申请(专利权)人(译)	耶路撒冷职业技术学院学报		
当前申请(专利权)人(译)	耶路撒冷职业技术学院学报		
[标]发明人	NITZAN MEIR		
发明人	NITZAN, MEIR		
IPC分类号	A61B5/00		
CPC分类号	A61B5/14551		
外部链接	Espacenet USPTO		

摘要(译)

描述了一种通过脉冲血氧测定法无需校准来测量动脉血SaO2中的氧饱和度的方法。光电容积脉搏波描记术（PPG）在红外线中以三个波长测量，并且对于每个PPG曲线，获得光透射的相对变化。两个方程，每个方程将SaO2与两个波长的光透射相对变化的比率相关联，使用三个波长的氧合血红蛋白和脱氧血红蛋白的消光系数的值，使得能够确定SaO2，假设光学路径的线性依赖性波长的长度，红外线中的三个波长。建议采用类似的技术来测定静脉血液中由于静脉血容量变化引起的光透射变化的血氧饱和度

FIG. 1

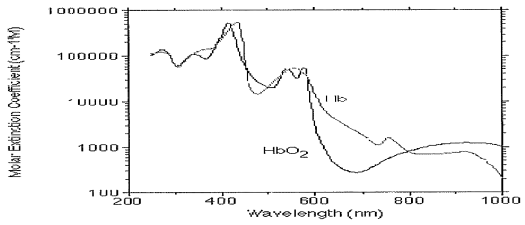


FIG. 2