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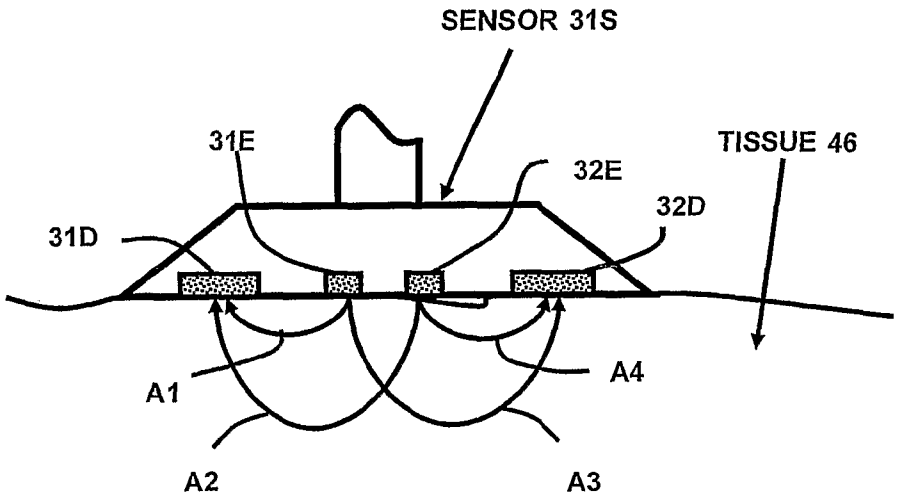
(54) **Title:** IMPROVED IN VIVO BLOOD SPECTROMETRY



(57) **Abstract:** A process and apparatus for determining the arterial and venous oxygenation of blood with improved precision. The optical properties of tissue are measured by determination of differential and total attenuations of light at a set of wavelengths . By choosing distinct wavelengths and using the measured attenuations, the influence of variables such as light scattering, absorption and other optical tissue properties is canceled out or minimized.

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TITLE: IMPROVED IN VIVO BLOOD SPECTROMETRY

BACKGROUND OF THE INVENTION

Field of the Invention

The invention relates to a process and apparatus for increasing the accuracy of optical measurements of oxygenation of blood in tissue.

Description of Related Art

A standard method to measure the arterial oxygenation of blood is known as pulse oximetry.

Pulse oximeters function on the basis that at differing wavelengths, blood attenuates light very differently depending upon the level of oxygenation. Pulse waves starting from the heart cause in the arterial blood vessel system a periodic fluctuation in the arterial blood content in the tissue. As a consequence, a periodic change in the light absorption (Fig. 1) can be registered between the light transmitter, whose radiation passes through the tissue, and the receivers, which are integrated in a pulse oximetry sensor. The evaluation of the sensor signals is normally carried out at light wavelengths of w1=660 and w2=940 nm by calculating the differential change of light absorption. It is possible to create a measured variable R which is obtained in the following manner or in a similar manner:

(1)

$$R = Rw1,w2 = \frac{\Delta(LAw1)}{\Delta(LAw2)} = \frac{\ln(Imax, w1)-\ln(Imin, w1)}{\ln(Imax, w2)-\ln(Imin, w2)}$$

The light intensities described in the formula represent the light intensities received in the receiver of the sensors used in pulse oximetry. The measured variable R serves as a measurement for the oxygen saturation. The formation of a quotient in order to form the measured variable is intended to compensate for any possible influences the haemoglobin

content of the tissue, the pigmentation of the skin or the pilosity may have on the measurement of the oxygen saturation of arterial blood. The difference of the light attenuations at a minimum and maximum value is the delta of the light attenuations for each of both wavelengths.

Measuring oxygen saturation of arterial blood in the tissue in a range of 70 to 100% using light of wavelength 940 nm and 660 nm most often produces for one single application site sufficiently accurate measured values. However, in order to measure lower oxygen saturation of arterial blood it is necessary to assume a strong influence on the measured variable R in particular caused by perfusion (i.e. blood content) (see: IEEE; Photon Diffusion Analysis of the Effects of Multiple Scattering on Pulse Oximetry by J. M. Schmitt; 1991) and other optical parameters of tissue.

Rall, US Patent No. 5,529,064, describes a fetal pulse oximetry sensor. For this kind of application, a higher measurement precision is desirable because a fetus has a physiological lower oxygenation than adult human beings and measurement error of SaO_2 increases at low oxygenations.

US Patent No. 6,226,540 to Bernreuter, incorporated by reference herein, improves the precision of pulse oximetry. However, in order to measure on different body sites with the same high resolution for the arterial oxygenation, additional precision to measure optical tissue properties is necessary. Another problem is that pulse oximetry alone does not provide sufficient diagnostic information to monitor critically ill patients (See: When Pulse Oximetry Monitoring of the Critically Ill is Not Enough by Brian F. Keogh in Anesth Analg (2002), 94:96-99).

Because of this it would be highly desirable to be able to additionally measure the mixed venous oxygenation of blood SvO_2. Methods to measure SvO_2 with NIR were described by Jöbsis in US Patent No. 4,223,680 and by Hirano et al in US Patent No. 5,057,695. A problem of those disclosed solutions

is that hair, dirt or other optically non-transparent material on the surface of tissue can influence the measured results for SvO_2.

To measure the metabolism of blood oxygenation, Anderson et al in US Patent No. 5,879,294 disclose an instrument in which the second derivative of the light spectrum used delivers information about the oxygenation. Hereby, the influence of light scattering in tissue is minimized, which can result in higher measurement precision. A disadvantage of this solution is that the calibration of the optical instruments is complicated and expensive, which makes it impractical to use such devices for sports activity applications, where light weight wearable devices would be of interest. Similar problems are known for frequency domain spectroscopy disclosed for example in Gratton, US Patent No. 4,840,485. Oximetry devices, which are described in the present specification and which simply measure light attenuations of tissue at different wavelengths, are more feasible, flexible and reliable in practice than complex time resolved methods.

SUMMARY OF THE INVENTION

Accordingly, several objects and advantages of the invention are:

a) to provide a device that measures the arterial oxygenation of blood in tissue at a certain application site with improved precision;

b) to provide a device that measures the arterial oxygenation blood in tissue at different application sites with improved precision;

c) to provide a device that measures the mixed venous or venous oxygenation blood in tissue with improved precision;

d) to provide a device that measures the mixed venous or venous and arterial oxygenation blood in tissue with improved

precision with only one sensor;

e) to provide a device that measures the mixed venous or venous oxygenation blood in tissue with improved precision without complicated empirical calibration;

f) to provide an inexpensive device that measures the mixed venous or venous oxygenation blood in tissue with improved precision;

g) to provide an inexpensive device that can directly measure oxygen extraction of tissue at the application site; and

h) to provide an inexpensive, wearable device that measures oxygenation of tissue.

There are various fields of application where the invention can be used with benefit. For example for sports activity applications, a light weight, small and inexpensive device to track the oxygen metabolism would be of interest.

Critically ill persons would benefit by continuous and more detailed diagnostic information of their physiological condition.

Newborns would benefit from better care if arterial oxygenation could be measured e.g. on the back instead on the feet where unintentional alarms more often occur due to motion effects. A higher precision of pulse oximetry could improve ventilation of newborns, and precision of fetal pulse oximetry where a high resolution of the arterial oxygenation is needed, could be improved as well (See US Patent No. 6,226,540).

In accordance with invention, a device utilizes a combination of light emitters and detectors with:

a light wavelength combination with more than two wavelengths, where the peak spectrum of a third wavelength is about the geometric mean value of the first and second wavelengths;

multiple detectors and emitters which eliminate influences on calibration by subtracting and adding measured

light attenuations;

a model-based calibration calculation, which improves precision of measured output variables.

As a result, influences on the calibration of different tissue properties can be minimized in order to measure arterial or venous or the combination of arterial and venous oxygenation. It has been discovered that by choosing one of the wavelengths as a geometric mean value of two other wavelengths, variations due to scattering can be reduced. Additional determination of light attenuation can reduce measurement errors because of variations of light absorption due to different tissue composition, i.e., variations of relative amounts of muscle, skin, fat, bone, etc.

It is noted that as used in the present specification, "venous" and "mixed venous" may be synonyms, "attenuation" may refer to absolute or differential attenuation, "tissue oxygenation" may refer to arterial, mixed venous, or venous oxygenation or a combination of thereof, and the phrase "about" in reference to wavelengths may quantify in a band of +/- 80 nm and in reference to distances quantifies in a band of +/- 2 cm.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a graph showing changes of light absorption by blood over time;

Fig. 2 is a graph illustrating the dependency of arterial oxygen saturation on the measurement variable R for different optical tissue properties;

Fig. 3 shows a reflectance oximetry sensor according to the invention in schematic cross-section;

Fig. 4 shows a finger clip sensor according to the invention in schematic cross-section;

Fig. 5 is a diagram of a multidimensional calibration of oxygenation for the two measuring variables R1, R2 vs. SaO_2;

Fig. 6 is a schematic diagram of an oximetry system in

operation;

Fig. 7 is a side view of a fetal scalp sensor according to the invention;

Fig. 8 is a bottom view of the sensor of Fig. 7;

Fig. 9 is a bottom view of the sensor of Fig. 3;

Fig. 10 is a side cross-sectional view of a variation of the sensor of Fig. 3;

Fig. 11 is a side cross-sectional view of another variation of the sensor of Fig. 3;

Fig. 12 is a bottom view of the sensor of Fig. 11;

Figs. 13-14 are side cross-sectional views of reflectance sensors fixed on the forehead;

Fig. 15 shows a system for determining cardiac output;

Fig. 16 shows person with wrist worn display and sensor applications on different sites of the body;

Fig. 17 is a schematic diagram of a hardware processing unit for an oximetry system according to the invention;

Fig. 18 is a diagram of a multidimensional calibration of oxygenation for the two measuring variables Rv1, Rv2 vs. SvO_2; and

Fig. 19 is a flow chart illustrating signal processing flow for a model-based determination of oxygen in blood.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The diagram of Fig. 1 shows the fundamental effect on which pulse oximetry and comparable methods to determine arterial blood oxygenation are based. When measuring light absorption of tissue *in vivo* light absorption changes synchronously with every heart cycle. The diagram illustrates the change of light absorption versus time, which is caused by arterial pulsations that can be measured while systole and diastole. During systole and diastole the pressure on the arterial vessel system varies from 80 mmHg to 120 mmHg. The

change of light absorption is called the AC-signal. The DC-signal, the time-invariant part of light absorption, is caused by the non-pulsating part of the arterial blood, the venous blood, bone, hair, tissue and other constant absorbing constituents versus time. The time-invariant signal is the basis for the calculation of the mixed venous oxygenation of tissue; thus, a major part of the absorption is caused by venous blood and a minor part by arterial blood.

Fig. 2 shows two calibration curves in a diagram with SaO_2 vs. R. Calibration line 42 is only valid for a first distinct set of optical properties. Calibration line 40 is only valid for a second distinct set of optical properties. The valid set of optical properties can be determined by an optical system illustrated in Figs. 3 and 6 with a sensor 31S, which is placed on tissue 46 and connected via a plug 66 to a display device 64. Additionally, Fig. 2 shows two horizontal lines at SaO_2=0.6 and at SaO_2=0.4 and one vertical line at R=1.4. If an optical system determines only R without registering the two different sets of optical properties, this would result in an error of 0.2 SaO_2 (SaO_2 at first set of optical properties - SaO_2 at second set of optical properties). An analogous relation also exists for the mixed venous saturation of blood SvO_2 and a measurement variable Rv1 and Rv2 for mixed venous oxygenation (Fig. 18).

Fig. 3 shows an oximetry sensor 31S on the upper part of the figure which is placed on tissue 46. The sensor 31S contains two light emitters 31E, 32E and two light detectors 31D, 32D. The arrows A1 through A4 show how light passes from emitters to detectors through tissue. A1 stands representative for light which is emitted in emitter 31E and received in detector 31D. A2 is light emitted in emitter 32E and detected in detector 31D. A3 is light emitted in 31E and received in 32D and A4 is light emitted in emitter 32E and detected in detector 32D.

Fig. 4 shows a finger clip sensor 54 which is fixed on a

finger 48. The finger clip sensor incorporates emitters 31E, 32E and detectors 31D, 32D. The electrical sensor signals of the finger clip sensor are transmitted via a sensor cable 60. The signals can also be conveniently transmitted wirelessly by means well known in the art (not shown).

Fig. 5 illustrates a multidimensional calibration of SaO_2 vs. R1 and R2. A certain combination of R1 and R2 corresponds to a data point on the calibration plane, which indicates the saturation level SaO_2. An analogous relation also exists in Fig. 18 for the mixed venous saturation of blood SvO_2 and two related measurement variables Rv1 and Rv2 for mixed venous oxygenation.

Figs. 7 and 8 show a fetal scalp sensor 74 with a set of emitters 31E, 32E, 33E and 34E and a set of detectors 31D, 32D, 33D and 34D from side and bottom views, respectively. The sensor can be fixed on the scalp of the fetus via a spiral needle 76 during labor. Additionally, an electrocardiogramm (ECG) of the fetus can be transmitted via the needle 76.

Fig. 9 is a bottom view of sensor 31S from Fig. 3. Detectors 35D and 36D have a concentric form to maximize reception of light emitted by the emitters 31E and 32E.

Figs. 10-12 show several modifications of sensor 31S. Fig. 10 shows sensor in side view with a flat body where detectors 31D, 32D and the emitter 32D are grouped close together and emitter 32E is positioned far from this group. The sensor can be fixed via a band 108 on tissue. A light shield 110 minimizes the influence of ambient light.

Fig. 11 shows a sensor with a sensor holder 122, while Fig. 12 is a bottom view of sensor of Fig. 11. The bottom side of sensor holder 122 can be covered with medical glue or adhesive. If sensor holder 122 is placed on sensor 31S according to Fig. 11 and applied to tissue 46, fixation is possible by glue on sensor holder 122. Sensor holder 122 can be constructed as inexpensive and disposable. Alternatively,

the bottom side of the sensor, which is applied to tissue, can be directly covered with glue. The disadvantage of this is that the sensor can not be reused. The heart rate is detected via ECG-electrode 123 which contacts the skin.

Figs. 13 and 14 show two variations of sensor 32S applied on the forehead of a person. In the first variation shown in Fig. 13, sensor 32S is fixed via a band 108 to the forehead. The arrows A32 and A42, which represent how light travels from the emitters 31E, 32E to the detectors 31 and 32D, pass through forehead tissue 152 and bone of skull 150 and pass or touch brain 148. The arrows A12 and A22 only pass through forehead tissue 152 and bone of skull 150.

The second variation of sensor 32S also applied on the forehead is shown in Fig. 14. The arrows A11, A21, A31 and A41 compared with arrows A12, A22, A32 and A42 of Fig. 13 show that by variation of the position of light detectors and emitters, oxygen content can be sensed differently without changing the outline of the sensor variation used.

Fig. 15 shows a patient lying on a bed being supplied with oxygen by an intubation tube 210, and an anesthesia machine 204. The anesthesia machine 204 is connected to the patient and has an inventive device for measuring oxygen consumption or carbon dioxide production of the patient. The sensor 32S is placed on the forehead of the patient, and is connected with oxygen extraction monitoring device 206, which calculates SaO_2 and SvO_2 and oxygen extraction. The monitoring device 206 and the anesthesia machine 204 are linked to a third device 202, which calculates cardiac output or trend of cardiac output.

Fig. 16 illustrates the use of oxygen monitoring at different application sites for sports activity, in which a wrist worn display device 220 can receive oxygenation data from a forehead-band-sensor 214, from a chest-band-sensor 224, from an arm-band-sensor 218 or from a finger-glove-sensor 222.

Fig. 17 shows the hardware for evaluating oxygenation by using two emitters 31E and 32E and two detectors 31D and 32D. The LED-drive 226 energizes the two emitters via lines 238, 248 which can incorporate coding hardware, to adjust calibration for the multidimensional calibration or to adjust calibration for varying emitter detector geometry. The amplifiers AMP1 232 and AMP2 234 are connected to detectors 31D and 32D. The demultiplexer DEMUX 320 selects each wavelength used in every emitter timed synchronously according to the switching state of the LED-DRIVE 226 and delivers the measured data via an AD-Converter AD-CONV. 236 to the CPU 228.

Fig. 19 illustrates the signal flow of a model-based calibration. An input processing circuit 260 is the first part of the signal flow. The processing circuit is connected with a circuit for calculating light attenuations 262 and a circuit calculating different measurement variables 264. The calculation for light attenuations 262 is a basis for a model-based determination circuit for mixed venous oxygenation 266 with a joint circuit to output a value for the mixed venous oxygenation SvO_2 270. A model-based determination circuit for arterial oxygenation 268 is connected to the circuit for calculating light attenuations 262 and the circuit calculating different measurement variables 264. The output value for a arterial oxygenation circuit for SaO_2 272 is linked to the model-based calculation for SaO_2 268.

By using three instead of two wavelengths to measure the arterial oxygenation, the following approximation can be derived with the help of diffusion theory. The result of this operation is:

$$R' = \frac{Rw2,w1}{Rw1,w0} * \frac{LAw2*LAw0}{LAw1*LAw1} + Q \qquad (2)$$

where Rw2,w1 and Rw1,w0 are calculated according to

equation (1) using wavelengths w0, w1, and w2 and Q is a correction parameter.

Light attenuation LAwx can be calculated in the following or similar manner:

(3) $LAwx = \ln(Iwx/Iwxo)$

LAwx corresponds to the logarithm of the ratio of light intensity Iwxo which is the emitted and light intensity Iwx the received light passing through tissue at wavelength wx. The index following suffix wx indicates the selected wavelength. Graaff et al showed that scattering in tissue decreases for higher wavelengths according to exponential functions (see: Applied Optics; Reduced Light-Scattering Properties for Mixtures of Spherical Particles: A Simple Approximation Derived from Mie Calculations by R. Graaff; 1992). LAwx corresponds to the logarithm of the ratio of light intensity Iwxo which is the emitted and light intensity Iwx the received light passing through tissue at wavelength wx. The index following suffix wx indicates the selected wavelength.

Graaff et al showed that scattering in tissue decreases for higher wavelengths according to exponential functions (see: Applied Optics; Reduced Light-Scattering Properties for Mixtures of Spherical Particles: A Simple Approximation Derived from Mie Calculations by R. Graaff; 1992). Absorption variation may also be taken from other measures or approximations such as the ac/dc ratio. The amplitude may be any measure such as peak-to-peak, RMS, average, or cross correlation coefficient. It may also be derived from other techniques such as Kalman filtering or a measure of the time derivative of the signal. Also, while calculations utilizing ratios of absorptions at different wavelengths are shown, alternate calculations may be used to give the same or approximately the same results. For instance the absorptions could be used directly, without calculating the ratios.

A preferred selection of the wavelengths combination to

reduce the influence of scattering is defined by the following equation, with wavelength w1 as the geometrical mean value of wavelength w0 and wavelength w2, defined as:

(4) $w1 = SQRT(w0 * w2)$

This combination minimizes the variation band of correction parameter Q, which has a default value of about one. The measurement variable R′ of equation (2) has minimized error related to variation of scattering and blood content of tissue.

EXAMPLES

EXAMPLE 1

The sensor 31S shown in Fig. 3 is used to determine the arterial oxygenation and the mixed venous blood oxygenation of tissue with improved precision. Equation (2) is used to provide a measurement variable R′ for the arterial oxygenation. For each of the emitters 31E and 32E, three wavelengths are defined. Initially, two measurement wavelengths w0 = 940 nm and w2 = 660 nm are selected. Using equation (4) the third wavelengths w1 is about 788 nm. Wavelength w1 = 805 nm is chosen because it is close to the calculated third wavelength and is additionally at an isobestic point of the blood absorption spectrum. The next step is to determine the resulting light attenuation LA for each of the three wavelengths w0, w1 and w3:

(5) $LAw1 = LA(A3w1) + LA(A2w1) - LA(A1w1) - LA(A4w1)$

(6) $LAw2 = LA(A3w2) + LA(A2w2) - LA(A1w2) - LA(A4w2)$

(7) $LAw3 = LA(A3w3) + LA(A2w3) - LA(A1w3) - LA(A4w3)$

where LA(Axwy) is the logarithm of received light intensity in the detector related to light arrow Ax at wavelength wy. The suffix x for light arrows Ax represents the number of the selected light arrow and y the suffix for the selected wavelength. Instead of the logarithm of light intensities, light intensity itself can be used in (5)-(7) and "+" is replaced by "*" and "-" is replaced by "/".

In the next step, Rw2,w1 and Rw1,w0 are calculated according to equation (1). As a result R' can be determined using equation (2) with Q as a correction factor which can be dependant on Rw2,w1 or Rw1,w0. The measured arterial oxygenation which is dependant on R' has minimized influence of scattering, blood content or other optical absorbing constituents in tissue.

The quotient in (8) which is part of (2) delivers a measurement variable Rv':

$$(8) \qquad Rv' = \frac{LAw2*LAw0}{LAw1*LAw1}$$

Rv' is a measure of optical absorption of tissue with decreased influence of scattering. Therefore it can be used as a signal for mixed venous oxygenation SvO_2.

A mathematically identical form of (2) is:

$$(9) \qquad R' = w2,w0 * \frac{Rv'}{Rw1,w0 * Rw1,w0} + Q$$

According to (9) the following equation can also be used to determine a measurement variable R1' for SaO2:

$$(10) \qquad R1' = Rw2,w0 * f\left(\frac{1}{Rw1,w0 * Rw1,w0}, Rv', Q\right)$$

where f is an empirical function of optical tissue parameters with variables defined above.

An empirical calibration which reduces influence of absorption and scattering of tissue on the measured variables with the variables LAw1, LAw2, LAw3, Rw1,w2 and Rw2,w3 for the whole saturation range of blood is complex. An pure empirical calibration based on these parameters additionally for different application sites is probably impossible. The proposed model-based method reduces complexity of calibration. SaO_2 can be determined with improved accuracy

being only dependent on R'.

It is also possible to use this method for other light absorbing constituents of blood like carboxyhemoglobin, methemoglobin, bilirubin or glucose dissolved in blood. Light wavelength in the range from 600 nm - 1000 nm can be used for carboxyhemoglobin and methemoglobin. Glucose shows an absorption peek dissolved in blood at 1100 nm and bilirubin in the lower wavelengths range from 300 nm - 800 nm. For every additional constituent an additional wavelengths has to be chosen. That means that to measure SaO_2 and methemoglobin at a time, four wavelength have to be selected and two different measurement variables R'1 and R'2 according equation (9) have to be defined. Accordingly, the resulting output for SaO_2 is dependent on R'1 and methemoglobin on R'2.

As a result sensor 31S is able to measure arterial and mixed venous oxygenation and other blood constituents at a time with reduced influence of measurement errors due to scattering and absorption of tissue.

EXAMPLE 2

In Fig. 4 finger clip sensor 54 is shown with the two emitters 31E, 32E and the two detectors 31D and 32D. The benefit of the finger clip sensor is that it is easy to apply. Equivalent to sensor 31S in Fig. 3, four representative light paths between the two emitters and the two detectors are possible so that all calculations according example 1 can be performed in order to calculate the output variables R' and Rv' as a measure for mixed venous and arterial oxygenation in the finger 48. The corresponding calculations can also be performed using sensor of Fig. 9. The difference here is the alternative form of detectors 35D and 36D, which are able to increase detected light intensity due to an enlarged, concentric detector area.

EXAMPLE 3

Fig. 5 shows a multidimensional calibration of SaO_2 vs. R1 and R2. R1 and R2 can be calculated according (1) by selecting two wavelengths pairs where for the first wavelengths pair the wavelengths wm1=660 nm and wm2 = 910 nm is chosen and for the second wavelengths pair wm3 = 810 nm and wm2 = 910 nm. The second wavelengths pair is less sensitive towards arterial oxygenation and is used to compensate errors due to optical tissue parameter variations. In order to guarantee that the multidimensional calibration delivers improved precision in presence of varying tissue parameters, it is important to select exactly the correspondent calibration which is specified for a distinct wavelengths set and a distinct detector emitter distance. Therefore additional information has to be coded to the selected sensor. The tissue oximeter device can read out this information and use the appropriate calibration. The coding of information can be achieved for example by a resistor implemented in the LED drive line of the sensor (see Fig. 17: 248, 238).

A variant of a multidimensional calibration (Fig. 5) can be achieved by calculating R1 according to equation (2) and R2 according to equation (8). This minimises the error of displayed arterial oxygenation SaO_2 due to varying optical tissue absorption.

EXAMPLE 4

In Fig. 7 a fetal pulse oximetry sensor 74 is shown, which punctures the skin on the head of the fetus with a spiral needle 76. The bottom view of Fig. 8 shows sensor 74 with 4 emitters 31E, 32E, 33E, 34E and four detectors 31D, 32D, 33D, 34D. Apparently, more than four different light paths per selected wavelength between emitters and detectors (is) are possible. This additional information is used to calculate a whole set of resulting light attenuations Lax.

For the different light paths it is also possible to compute a set of measurement variables Rx. Generating a weighted mean value (weight can depend on the noise of the related measurement signals) LAm and Rm of the variables LAx and Rx helps to reduce errors due to tissue inhomogenities. To achieve a stable measure for the optical tissue parameters, which are not influenced by locally varying tissue compositions, is important to minimize errors to precisely determine the inputs of model-based parameters.

EXAMPLE 5

A brain oximeter is shown in Fig. 13 which is positioned on the right side of the forehead of a patient. The cross section of the brain illustrates how four light paths travel through tissue from emitters 31E, 32E to the detectors 31D and 32D, representative for one wavelength. A resulting light attenuation LA can be achieved for each wavelength by adding light attenuations of A32 and A22 and subtracting therefrom the light attentions which are related to A42 and A12. The resulting light attenuation LA is then independent on dirt on emitters or detectors or on degeneration of those parts, which is an important feature since those sensors can be reused. Three wavelengths are chosen for each of the two emitters 31E and 32E of the sensor in Fig. 13 of the brain oxymeter: wb1 = 660 nm, wb2 = 740 nm and wb3 = 810 nm.

The ratio Rvb of the resulting light attentions LAwb2 and LAwb3 is used as a measure for the mixed venous oxygenation. The resulting light attenuation at wavelength wb3 = 810 nm can be used to eliminate the dependency of blood content in tissue of Rvb with a multidimensional calibration of SvO2 vs. Rvb and LAwb3.

A preferred emitter-detector distance between emitter 32E and detector 31D is greater than 2 cm. The longer the distance the emitter detector distance is, the deeper is the

penetration depth into the brain. In order to achieve maximum penetration depth at a minimum of sensor outline, the distance between an emitter and a detector should be the maximum distance between all emitters and detectors. Fig. 14 shows an example where within the sensor, the two detectors have the maximum distance and the detector and emitter elements are grouped symmetrically with regard to the center of the sensor. The resulting maximum penetration depth of light of A31, A21 is here less than maximum penetration depth of light of A32 of the sensor which illustrated in Fig. 13 because the maximum emitter detector distance is also less compared to sensor in Fig. 13 at the same total outline of the sensors. Positioning emitters and detectors asymmetrically is therefore the best choice to achieve oxygenation measurements in deep layers of tissue.

Fig. 12 shows a bottom view of a brain oximetry sensor, in which emitter 31E and detectors 31D and 32D are positioned in a triangle. The light paths between emitter 31E and 31D and between 31E and 32D using the wavelengths wb1 = 660 nm and wb3= 810 nm are determined to evaluate the measurement variables Rp1 and Rp2 which are calculated according to equation (1). The mean value of Rp1 and Rp2 is used as the output value for the arterial oxygenation SaO_2. Alternatively, as shown in Fig. 12a, the emitters 31E and 32E can be positioned where detectors 31D and 32D are located and detectors 31D and 32D are placed at the location of emitter 31E and 32E in Fig. 12.

EXAMPLE 6

Referring to Example 5, a brain oximetry sensor was described which is able to determine arterial and mixed venous oxygenation of tissue. These two parameters can be used to calculate the oxygen extraction of tissue. A measure therefor can be the difference of arterial and mixed venous oxygenation. Oxygen extraction reflects how well tissue is

supplied with oxygen, and can additionally be used to calculate the cardiac output or the trend of the cardiac output CaOut non-invasively. Fig. 15 shows a patient being supplied with air via an intubation tube 210. The oxygen consumption or CO_2 generation is determined within an anaesthesia machine 204. Brain oximetry sensor 32S is connected to SaO_2 and SvO_2 display device 206. The information of device 204 and device 206 is evaluated in a cardiac output monitor 202 in the following or similar manner:

$$(11) \quad CaOut = \frac{(\text{oxygen consumption per time})}{SaO2 - SvO2}$$

EXAMPLE 7

Knowledge of oxygenation of tissue of parts of the body is of high interest for sports activity monitoring. The oxygenation the muscles of the upper leg or upper arm can reflect the training level for different activities of sport. Fig. 16 shows an athlete wearing various sensors which are connected by a line or wirelessly with a wrist-worn-display 220. A sports activity sensor can have the same topology as the above mentioned brain sensor of Fig. 12. Emitter-detector distances however vary, depending on desired tissue monitoring depth. Preferred wavelengths to monitor the mixed venous oxygenation are ws1 = 700 nm, ws2 = 805 nm and ws3 = 870 nm. A resulting light attenuation LA is calculated for each wavelength: LWws1, LAws2 and LAws3 with ws1, ws2 and ws3 as index for the selected wavelengths. A measurement variable for the mixed venous oxygenation Rvs is obtained in the following or similar manner:

$$(12) \quad Rvs = \frac{LAws1 - LAws2}{LAws2 - LAws3}$$

Less influence of light scattering and absorption of tissue can be achieved for the determination of mixed venous

oxygenation in this way.

A further improvement for better measurement precision can be achieved by generating an output value for the mixed venous oxygenation which is dependant on a multidimensional calibration of SvO_2 vs. Rvs and Rv.

Although the description above contains many specificities, these should not be constructed as limiting the scope of the invention but as merely providing illustrations of some of the presently preferred embodiments of this invention. For example the shape of the emitters can be rectangular, emitters can include LEDs, detectors photodiodes; the shape of the brain sensor can be round; the proposed methods to calculate arterial and mixed venous oxygenation of tissue can be combined in different combinations, signals can be processed by Kalman filters in order to reduce influence of noise caused by motion or other unwanted sources, etc.

What is claimed is:

1. Method of measuring tissue oxygenation comprising the steps of:

(a) selecting at least one emitter with at least three wavelengths w1, w2, w3 with a defined relation of wavelengths;

(b) emitting light through the tissue with said at least one emitter at said at least three wavelengths, said light being attenuated by pulsating blood flow;

(c) detecting the attenuated light with at least one detector;

d) determining differential attenuation vs. time for w1, w1, w3;

e) calculating at least three light attenuations LAw1, LAw2 and LAw3, where each light attenuation Lawj= (light intensity received at wj); and

f) computing said tissue oxygenation depending on a calculation operation, whereby the error due to varying optical properties of said tissue is minimized.

2. The method of claim 1 wherein said wavelength w2 corresponds to the geometrical mean value of said wavelength w1 and said wavelength w3.

3. The method of claim 1 wherein a model-based calculation operation is dependent on at least a functional term Rv' or Rr', which corresponds to:

$$Rv' = \frac{LAw2*LAw0}{LAw1*LAw1}$$

$$Rr' = \frac{Rw2,w1}{Rw1,w0}$$

4. The method of claim 1, wherein the step of calculating differential attention vs. time is achieved by calculating at least two ratios of differential attenuation vs. time corresponding to:

$$Rw1,w2 = \frac{\ln(It1, w1)-\ln(It2, w1)}{\ln(It1, w2)-\ln(It2, w2)}$$

And

$$Rw2,w3 = \frac{\ln(It1, w2)-\ln(It2, w2)}{\ln(It1, w3)-\ln(It2, w3)}$$

5. The method of claim 1, wherein LAwj (j=1,2,3) is calculated by adding and subtracting the light attenuations for at least two possible light paths between at least a pair of emitters and a pair of detectors, resulting substantially in attenuation within the tissue.

6. The method of claim 1, wherein at least a measure for arterial oxygenation is produced based on detected pulsatile absorption variations or a measure which corresponds to tissue oxygenation based on a time-invariant part of light attenuation.

7. Apparatus for measuring tissue oxygenation non-invasively comprising:

(a) a sensor interface adapted to be coupled to a tissue site and including at least one light emitter with at least three different wavelengths which emits lights into tissue, and at least one light detector;

(b) means for determining at least three light attenuations LAwsj (j=1 to i) dependant on light detected at selected wavelength wsj;

(c) means for generating an output representative of tissue oxygenation selected from the group consisting of first calculation means, second calculation means and third calculation means;

wherein said first means for calculation corresponds to a calculation of at least one variable Rs which depends on said at least three light attenuations Lawsj at said selected wavelengths wsj that corresponds to:

$$Rvs = \frac{LAws1 - LAws2}{LAws2 - LAws3}$$

said second calculation means corresponds to a calculation of at least one variable Rv's which depends on said at least three light attenuations Lawsj at said selected wavelengths wsj that corresponds to:

$$Rv's = \frac{LAws2*LAws0}{LAws1*LAws1}$$

and said third calculation means corresponds to a multidimensional calibration of:

$$Rv''s = \frac{LAws1}{LAws2} \text{ and } LAws3.$$

8. The apparatus of claim 7, wherein three of said wavelengths wsj are defined by wavelengths ws1 of about 700 nm, ws2 of about 805 nm and ws3 of about 880 nm.

9. The apparatus of claim 7, wherein said means for determining at least three light attenuations LAwsj performs the calculation steps of:

calculating light attenuation LA(A1,wsj) of light emitted in a first emitter and received at a first detector;

calculating light attenuation LA(A4,wsj) of light emitted in a second emitter and received at a second detector;

calculating light attenuation LA(A2,wsj) of light emitted in said first emitter and received at said second detector;

calculating light attenuation LA(A3,wsj) of light emitted in said second emitter and received at said first detector;

detecting an optical characteristic of said tissue alone which corresponds to a resulting light attenuation LAwsj at said wavelength wsj by weighting and accumulating the light attenuations of LA(A2,wsj) and LA(A3,wsj) and subtracting therefrom the weighted and accumulated light attenuations

LA(A1,wsj) and LA(A4,wsj); and

repeating said steps for further said resulting light attenuations.

10. The apparatus of claim 7, wherein said sensor interface is coupled to tissue using a means selected from the group consisting of fixation band, sensor holder, medical glue, finger glove and finger clip.

11. The apparatus of claim 7, wherein said sensor interface delivers signals to a wrist worn display.

12. The apparatus of claim 11, wherein said apparatus is battery powered and the sensor interface includes LED emitters and photodiode detectors.

13. Apparatus for measuring tissue oxygenation comprising:

(a) a sensor interface adapted to be coupled to a tissue site and including at least two light emitters placed apart from each other on said interface with at least two different wavelengths which emit light into tissue and at least two detectors for detecting light;

(b) means for calculating at least two signals which depend on detected light for selected wavelength wsj for said two detectors and said two emitters, wherein the at least two signals are calculated by adding or subtracting light attenuations for at least two possible light paths between said at least two light emitters and said at least two detectors; and

(c) means for generating an output representative of tissue oxygenation based on the at least said two signals.

14. The apparatus of claim 13, wherein said means for calculating at least two resulting light attenuations LAwsj performs calculation steps of:

calculating light attenuation LA(A1,wsj) of light emitted in a first emitter and received at a first detector;

calculating light attenuation LA(A4,wsj) of light emitted in a second emitter and received at a second

detector;

calculating light attenuation LA(A2,wsj) of light emitted in said first emitter and received at said second detector;

calculating light attenuation LA(A3,wsj) of light emitted in said second emitter and received at said first detector;

computing the optical constitution of the tissue alone which corresponds to a resulting light attenuation LAwsj at said wavelength wsj by weighting and accumulating the light attenuations of LA(A2,wsj) and LA(A3,wsj) and subtracting therefrom the weighted and accumulated light attenuations LA(A1,wsj) and LA(A4,wsj); and

repeating the steps for further resulting light attenuations.

15. The apparatus of claim 13, wherein said sensor interface comprises a first emitter-detector pair separated with the longest emitter-detector distance as compared to another emitter-detector pair.

16. The apparatus of claim 13, wherein a first distance between one of said emitters and one of said detectors is about 3 cm, a second distance between one of said emitters and one of said detectors is about 4 cm, and a third distance between one of said emitters and one of said detectors is less than 2 cm.

17. The apparatus of claim 13, including means for generating an additional output signal indicative of arterial oxygen saturation utilizing at least one light path between one of said emitters and one of said detectors.

18. The apparatus of claim 13, wherein said emitters emit at wavelengths of about wb1 = 740 nm and wb2 = 805 nm.

19. The apparatus of claim 18, wherein at least one of said emitters is utilized to measure arterial oxygenation and emits at a third wavelengths of about wb3 = 660 nm.

20. The apparatus of claim 13, wherein said emitters

include LEDs which emit light into said tissue.

21. The apparatus of claim 13, wherein a further calculation means is included, which utilizes at least one of said means for calculating at least two resulting light attenuations LAwsj in order to minimize the dependency of said output for tissue oxygenation on Hb and blood content.

22. The apparatus of claim 13, further comprising a structure fixing said sensor interface towards tissue, said structure being selected from the group consisting of medical glue on said sensor interface, a fixation band and a disposable sensor holder.

23. Apparatus for measuring cardiac output CaOut of blood of a patient comprising:

means for determining a measure which corresponds to oxygen consumption per time by analyzing inspired and expired breath of the patient;

a patient interface means which determines arterial blood oxygenation SaO_2 according to pulse oximetry and a tissue oximeter SvO_2 non-invasively measuring light attenuations LA of tissue;

means for calculating said cardiac output CaOut which corresponds to:

$$CaOut = \frac{(\text{oxygen consumption per time}) * C}{SaO_2 - SvO_2}$$

where C is a calibration factor.

24. Apparatus for measuring tissue oxygenation comprising:

a sensor interface including at least one emitter which emits light into tissue with at least three wavelengths, and at least one detector to receive light scattered by tissue;

means for calculating said tissue oxygenation comprising means for compensating for the influence of varying optical tissue properties on said tissue oxygenation with at least three wavelengths;

means for encoding sensor information within the sensor hardware, said sensor information used to compensate for the influence of varying optical tissue properties related to said sensor interface;

whereby errors due to differences in the sensor hardware are minimized.

25. Method of measuring tissue oxygenation comprising the steps of:

(a) emitting light through tissue with an emitter radiating at least two wavelengths and detecting light related to pulsating blood flow with at least one detector;

(b) calculating differential attenuation vs. time Rd1,w1,w2 , Rd2,w1,w2 with at least two different light paths between said detectors and emitters d1, d2 with w1,w2 representing the selected wavelengths;

c) calculating at least one mean output which corresponds to a weighted mean value of at least two parameters, said Rd1,w1,w2 and said Rd2,w1,w2; and

d) determining tissue oxygenation based at least in part on said mean output.

26. Apparatus and sensor for measuring constituents of blood in tissue in vivo with a sensor connected to said apparatus determining light attenuation at a combination of light emitters and detectors comprising the following means:

(a) a light emitter and at least two detectors, said light emitter including at least three wavelengths, wherein a peak spectrum of one of said at least three wavelengths is about the geometric mean value of the two other of said three wavelengths;

(b) means for calculating at least two values of differential attenuation vs. time Rw1,w2, Rw2,w3

with w1,w2,w3 representing the selected wavelengths;

(c) means for eliminating influences on calibration by

subtracting and adding measured light attenuations to generate a signal; and

(d) means for generating a resulting output signal for a constituent of blood in vivo depending on said signal;

wherein said means for generating a resulting output minimizes the error on said resulting output.

27. The apparatus of claim 26, wherein said constituent is selected from the group consisting of carboxyhemoglobin, methemoglobin, glucose in blood, Hb, SvO_2, SaO_2 and bilirubin.

28. Apparatus for measuring tissue oxygenation comprising:

(a) a sensor interface adapted to be coupled to a tissue site of a person and including at least one light emitter with at least three different wavelengths which emits light into tissue and at least one detector;

(b)means for calculating at least three light attenuations LAwsj dependant on light detected at selected wavelength wsj;

(c) means for coupling said sensor interface on tissue selected from a group consisting of a band, a sensor holder, medical glue, finger glove and finger clip;

d) means for generating a signal representative of tissue oxygenation depending on said means for calculating at least three light attenuations; and

(e) a battery powered, wrist worn device to display signal information.

29. Apparatus of claim 28, additionally comprising means for determining heart rate.

30. Apparatus for measuring tissue oxygenation comprising:

(a) a sensor interface adapted to be coupled to a tissue site and including at least one light emitter with at least three different wavelengths which emits light into tissue and

at least one detector for detecting intensity of scattered light;

(b)means for calculating at least three light attenuations LAwsj depending on the detected light at selected wavelength wsj;

(c) means for generating an output signal representative of tissue oxygenation depending on said means for calculating at least three light attenuations;

whereby light attenuation LAwsj is calculated by adding and subtracting weighted light attenuations for at least two possible light paths between said at least one emitter and said at least one detector.

31. The apparatus of claim 13, whereby the local tissue oxygenation of brain is detected.

32. The apparatus of claim 14, whereby the local tissue oxygenation of brain is detected.

33. An apparatus for measuring tissue oxygenation comprising:

a sensor interface including at least two emitters which emits light into tissue with at least two wavelengths, and at least two detectors to receive light scattered by tissue;

means for calculating said tissue oxygenation and additionally comprising a means for compensating for influence of varying optical tissue properties on said tissue oxygenation with at least two detectors and at least two emitters operating at two or more wavelengths; and

means for encoding information about sensor hardware for said means for compensating influence of varying optical tissue properties related to said sensor interface;

whereby errors due to varying said sensor hardware are minimized.

34. The apparatus of claim 26, wherein the resulting output is SaO_2.

35. An apparatus for measuring tissue oxygenation

comprising:

(a) a sensor interface including at least two light emitters with at least two different wavelengths which emits light into tissue and at least two detector for detecting intensity of scattered light; and

(b) means for calculating tissue oxygenation for application sites and tissue types selected from the group consisting of back of body, chest, arms and tissue muscle.

36. The apparatus according to claim 35, wherein at least one emitter uses a third wavelength.

37. The apparatus according to claim 35, additionally comprising means calculating the detected signals according to a model based algorithm.

38. The apparatus according to claim 35, wherein three of said wavelengths are about 700 nm, about 805 nm and about 880 nm.

39. The apparatus according to claim 35, adapted for use on newborns.

40. The apparatus according to claim 35, additionally comprising means for calculating on an additional application site defined on the forehead, and the sensor interface is applied by the pressure of a head band, suction, medical glue or a sensor holder, and a signal selected from the group consisting of arterial oxygenation, mixed venous oxygenation and venous oxygenation is generated using said sensor interface, whereby said oxygenation is calculated by adding and subtracting measured light attenuations measured by said detectors.

41. The apparatus according to claim 35, additionally comprising means for calculating on an additional application site defined on the finger, wherein the sensor interface is applied by a finger clip including an emitter and detector at upper and lower side of said finger clip.

42. The apparatus according to claim 35, additionally comprising means for calculating oxygenation in tissue with

calibration dependent on at least one measured light attenuation for at least two different body sites, with at least one of said at least two different body sites being a forehead, back, or chest.

43. An apparatus for measuring constituents of blood in tissue, including a sensor with a combination of two light emitters and two light detectors, said apparatus comprising:

(a) means for emitting a light wavelength combination including at least two wavelengths with at least one emitter, wherein the peak spectrum of one of said at least three wavelengths is about the geometric mean value of the two others of said three wavelengths to generate a first output signal;

(b) means for calculating differential attenuation vs. time Rw1,w2, Rw2,w3;

(c) means for eliminating influences on calibration by an operation which corresponds to subtracting and adding measured light attenuations to generate an output signal for optical properties;

(d) means for encoding information about the sensor for compensating influences of varying optical tissue properties related to said sensor interface;

(e) means for generating a resulting output signal for at least one of said constituents of blood in vivo depending on said means measured on the forehead or back or chest or arm of the body; and

(f) means for generating an output signal for cardiac output depending on said blood constituents,

wherein said means for generating the resulting output signal for at least one of said constituents minimizes the error on said resulting output.

Fig. 1

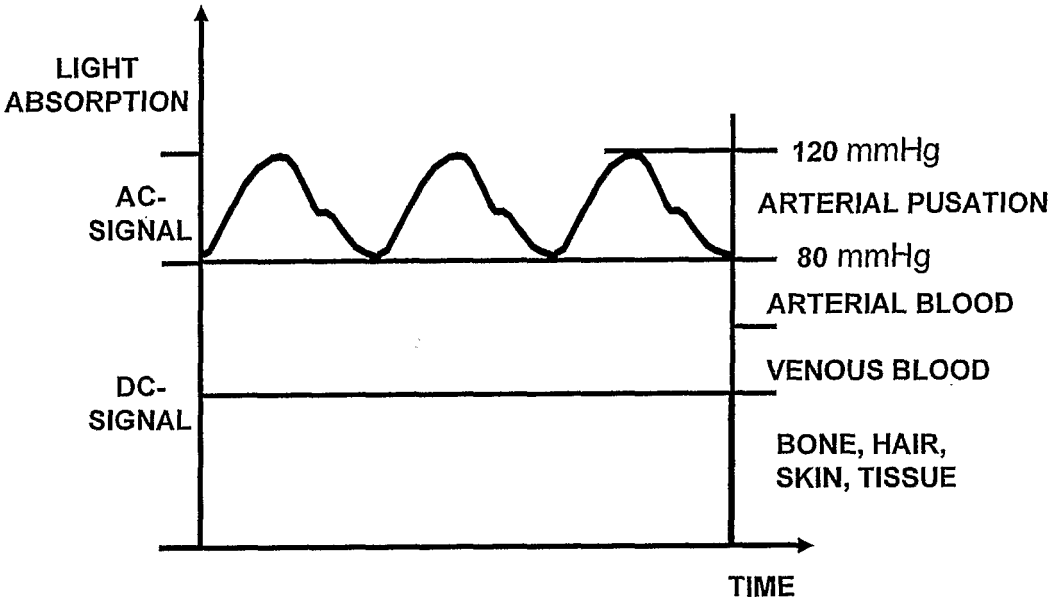

LIGHT ABSORPTION
AC-SIGNAL
DC-SIGNAL
120 mmHg
ARTERIAL PUSATION
80 mmHg
ARTERIAL BLOOD
VENOUS BLOOD
BONE, HAIR, SKIN, TISSUE
TIME

Fig. 2

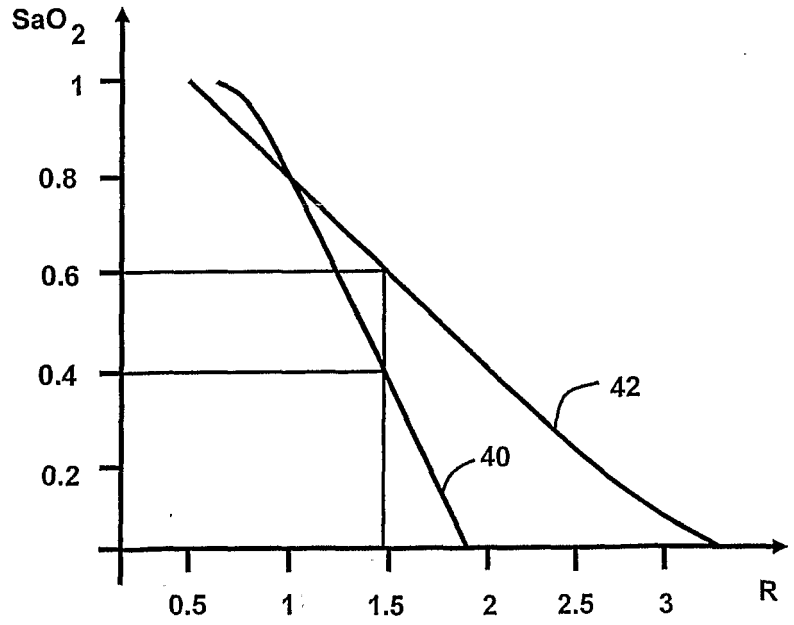

SaO2
1
0.8
0.6
0.4
0.2
42
40
0.5
1
1.5
2
2.5
3
R

Fig. 3

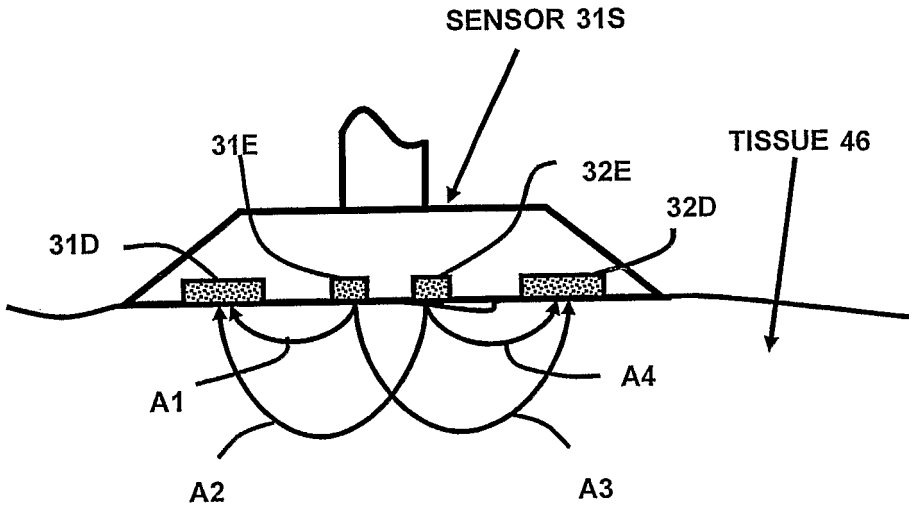

SENSOR 31S
31E
32E
TISSUE 46
32D
31D
A1
A4
A2
A3

Fig. 4

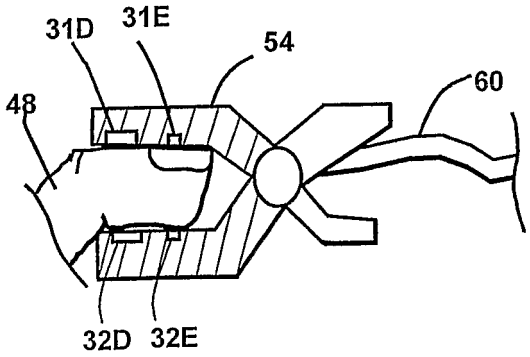

31D
31E
54
60
48
32D
32E

Fig. 5

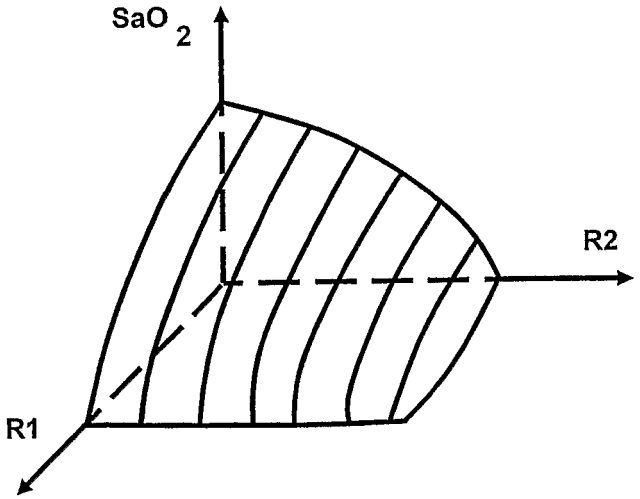


Fig. 6

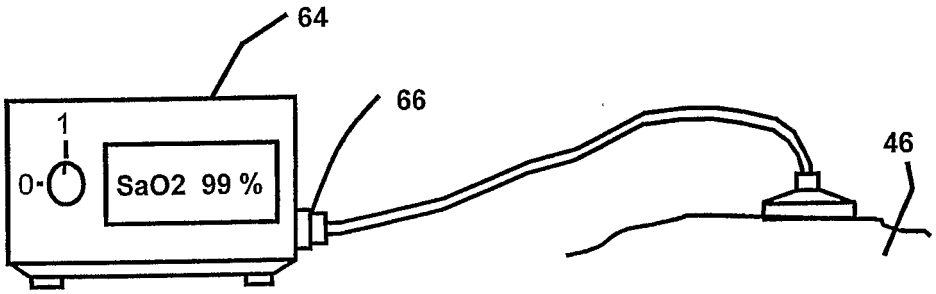


Fig. 7

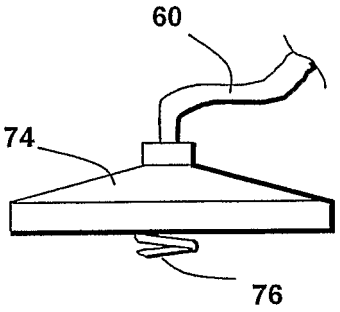


Fig. 8

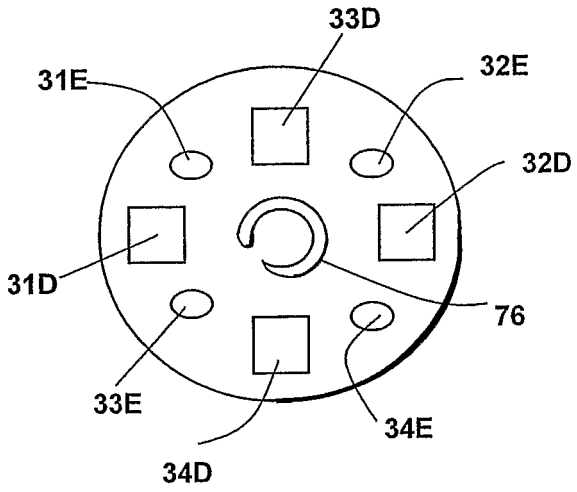


Fig. 9

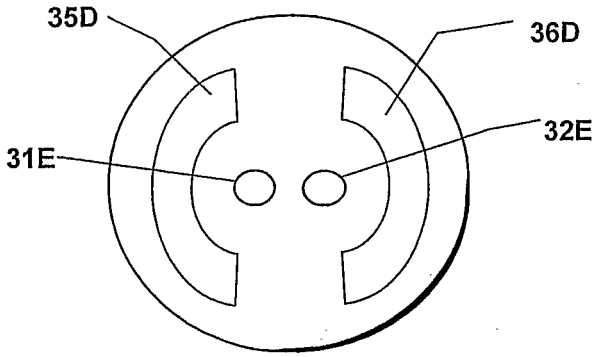


Fig. 10

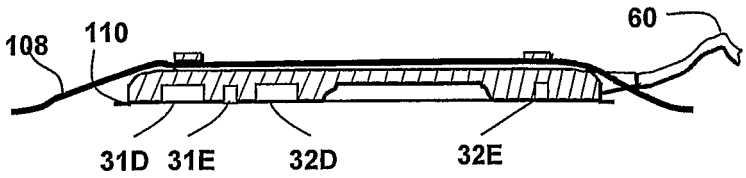


Fig. 11

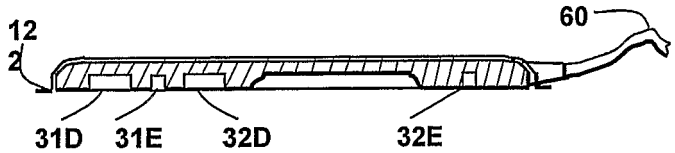


Fig. 12

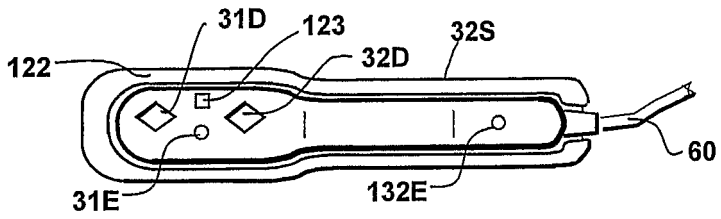


Fig. 12a

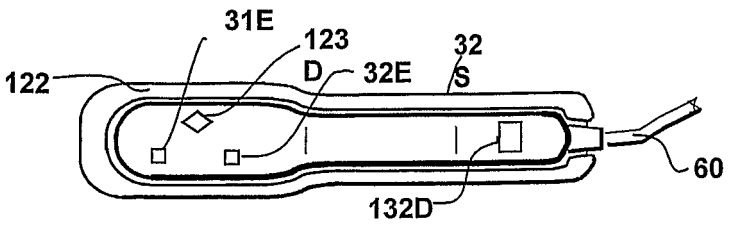


Fig. 13

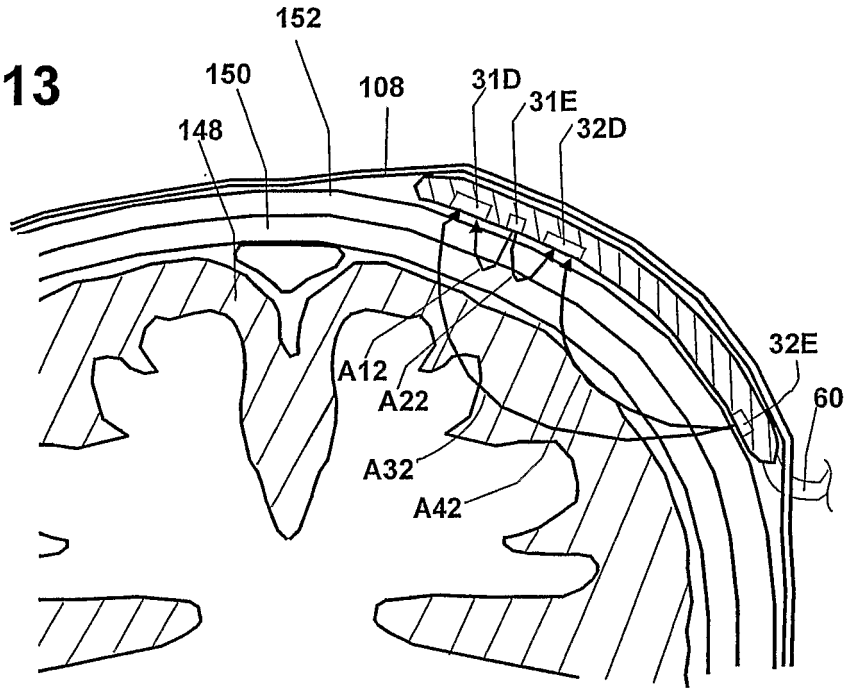

152
150
108
31D
31E
148
32D
32E
60
A12
A22
A32
A42

Fig. 14

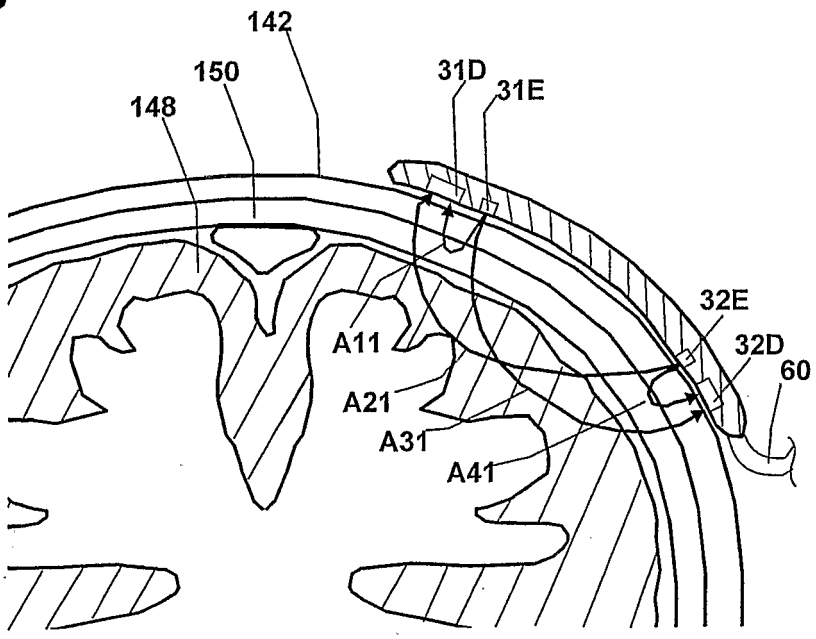

142
150
31D
31E
148
32E
32D
60
A11
A21
A31
A41

Fig. 15

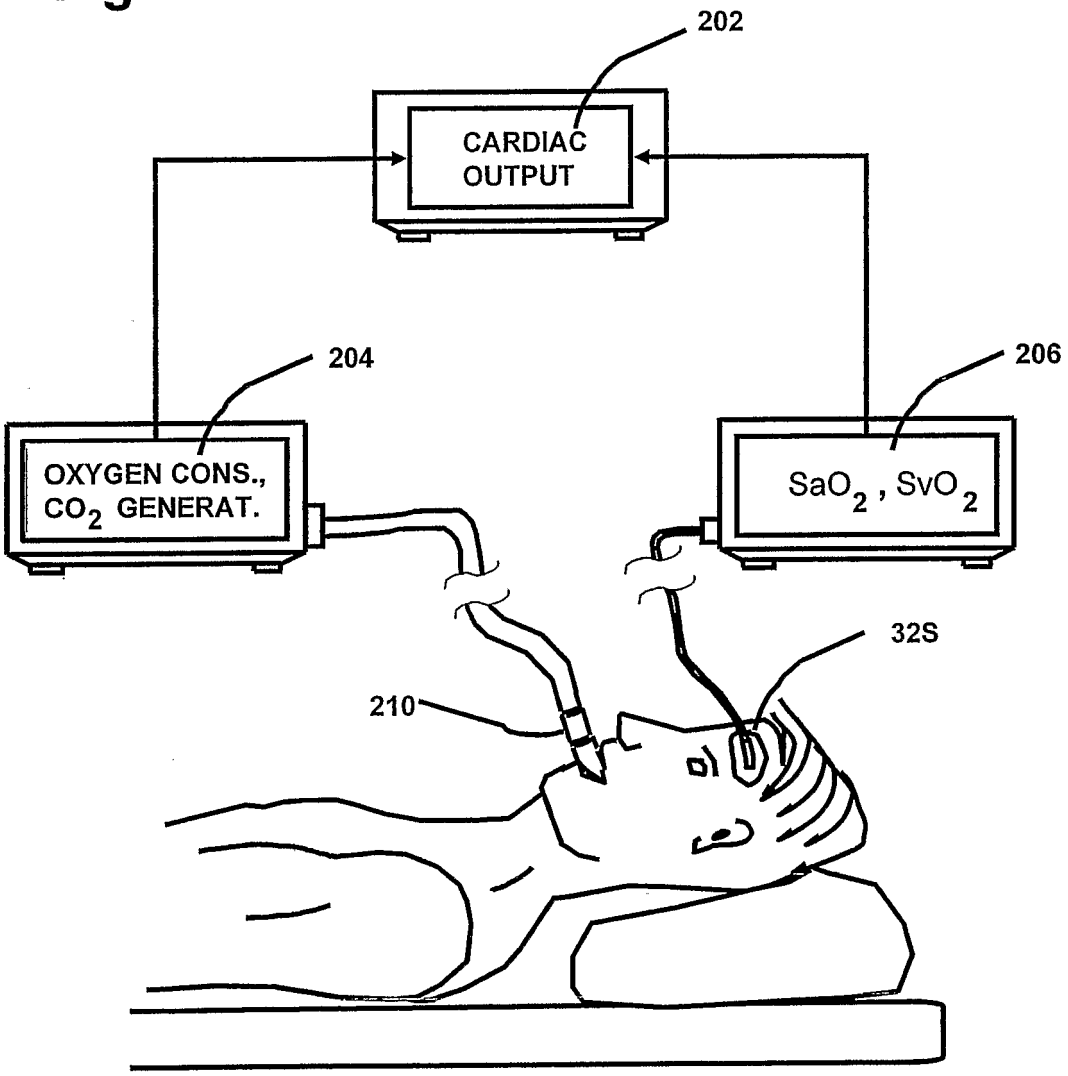

202
CARDIAC OUTPUT
204
206
OXYGEN CONS., CO_2 GENERAT.
SaO_2 , SvO_2
32S
210

Fig. 16

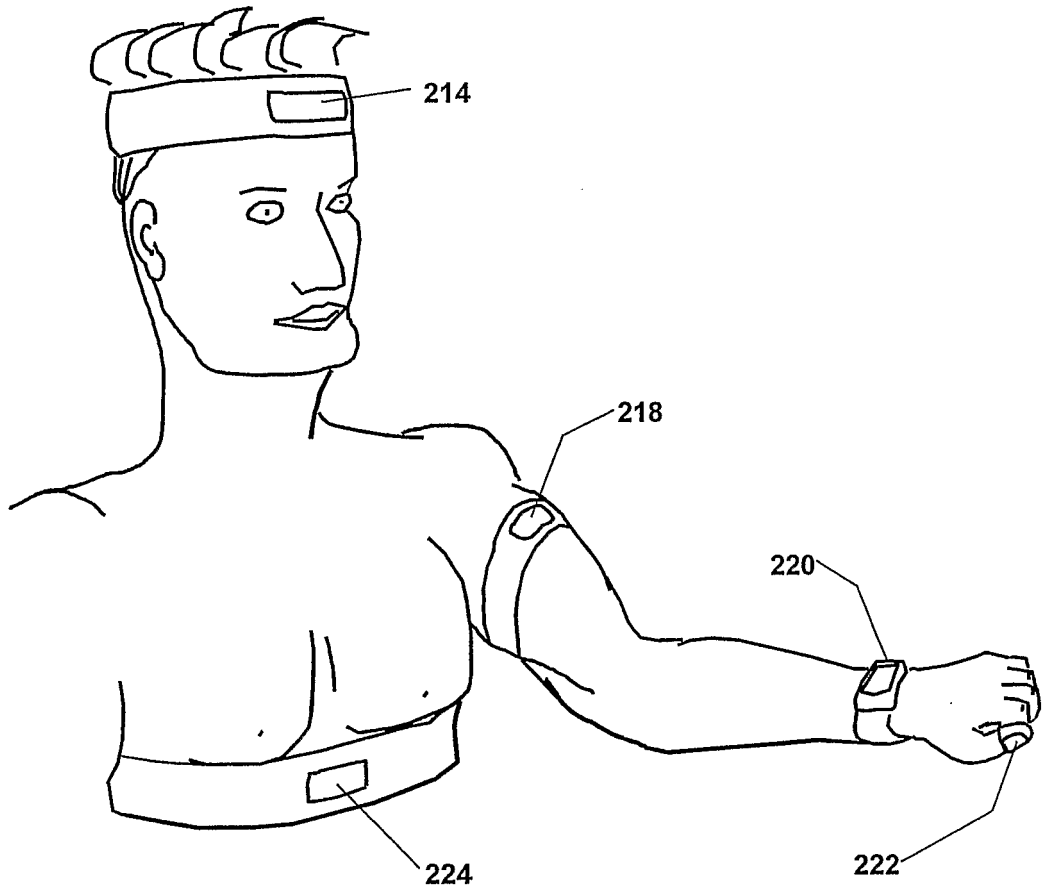


Fig. 17

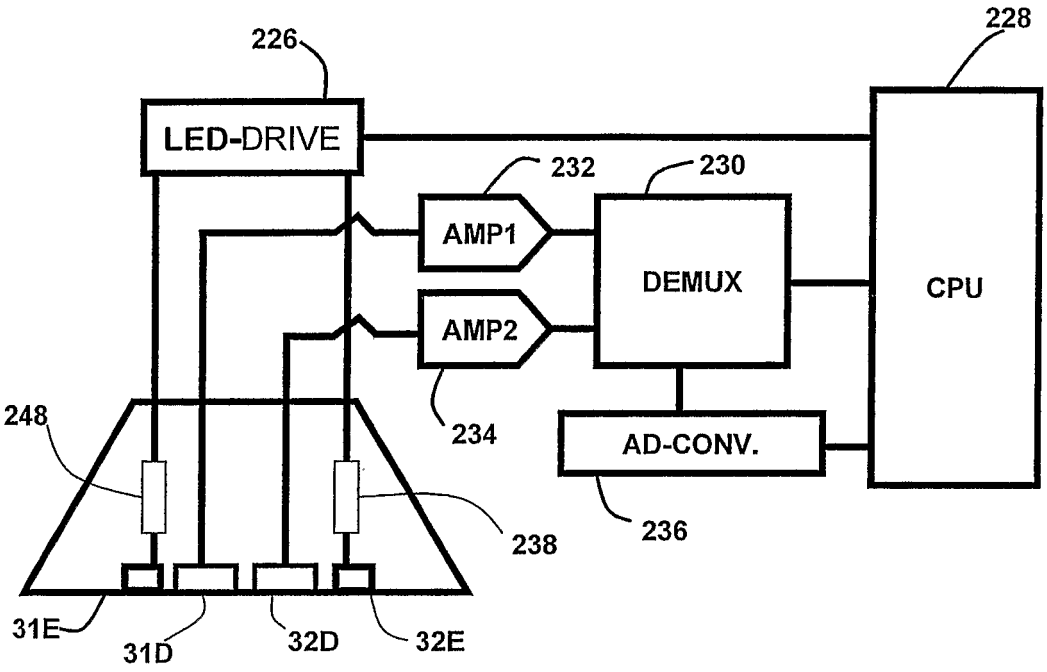

226
228
LED-DRIVE
232
230
AMP1
DEMUX
CPU
AMP2
248
234
AD-CONV.
238
236
31E
31D
32D
32E

Fig. 18

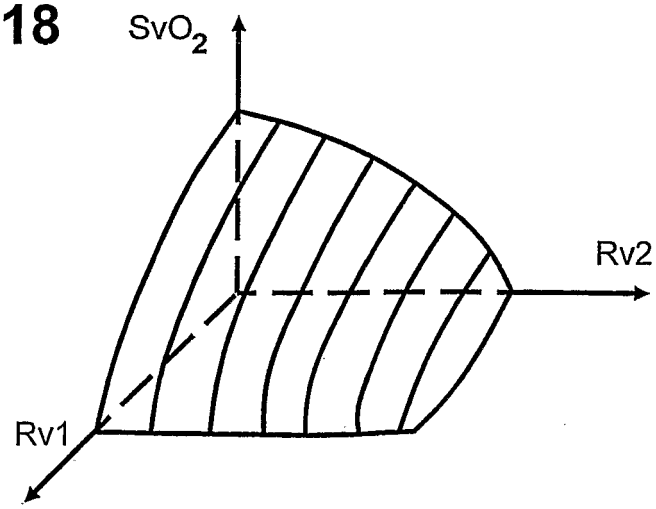
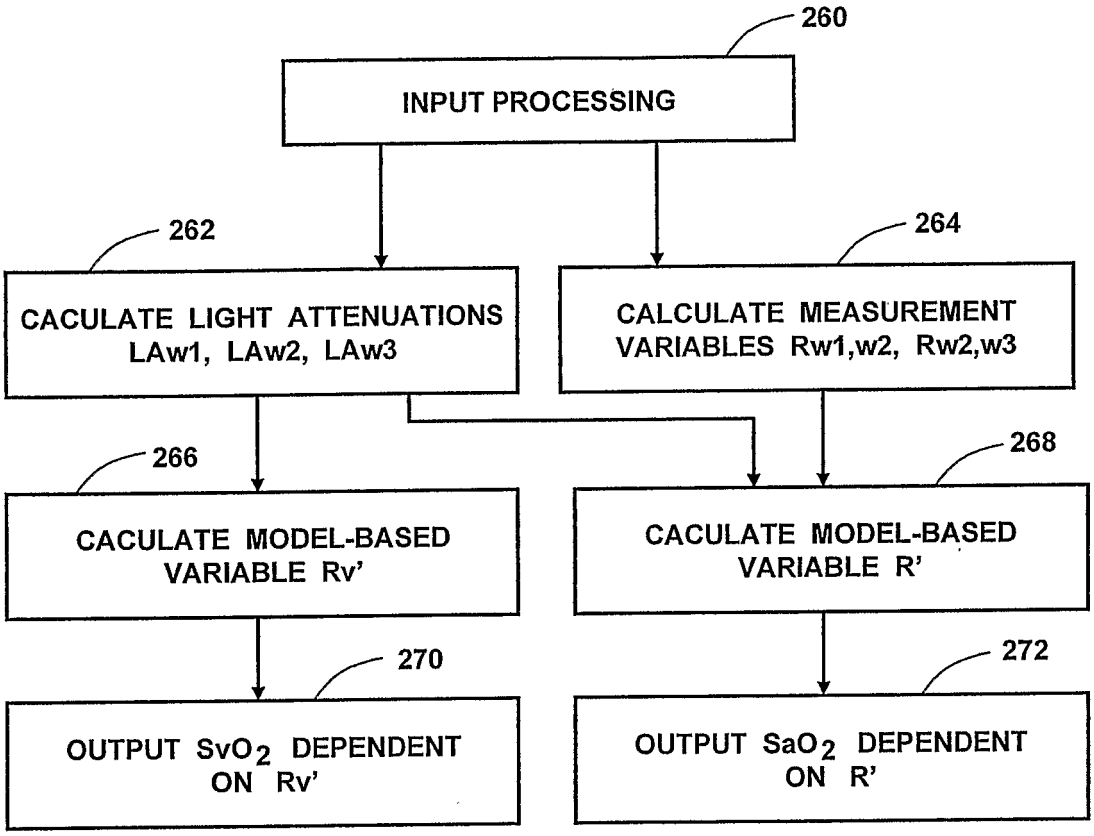

SvO2
Rv2
Rv1

Fig. 19


260
INPUT PROCESSING
262
CACULATE LIGHT ATTENUATIONS LAw1, LAw2, LAw3
264
CALCULATE MEASUREMENT VARIABLES Rw1,w2, Rw2,w3
266
CACULATE MODEL-BASED VARIABLE Rv'
268
CACULATE MODEL-BASED VARIABLE R'
270
OUTPUT SvO2 DEPENDENT ON Rv'
272
OUTPUT SaO2 DEPENDENT ON R'

专利名称(译)	改进了VIVO血液光谱法		
公开(公告)号	EP1860998A2	公开(公告)日	2007-12-05
申请号	EP2006795079	申请日	2006-03-10
[标]申请(专利权)人(译)	BERNREUTER PETER		
申请(专利权)人(译)	BERNREUTER，PETER		
当前申请(专利权)人(译)	BERNREUTER，PETER		
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发明人	BERNREUTER, PETER		
IPC分类号	A61B5/00		
CPC分类号	A61B5/1464 A61B5/14532 A61B5/14546 A61B5/14551 A61B5/14552 A61B5/14553 A61B5/6826 A61B5/6838 A61B2562/0242		
优先权	11/078399 2005-03-14 US		
外部链接	Espacenet		

摘要(译)

一种用于以提高的精度确定血液的动脉和静脉氧合的方法和设备。通过确定一组波长的光的差分和总衰减来测量组织的光学性质。通过选择不同的波长并使用测量的衰减，诸如光散射，吸收和其他光学组织特性的变量的影响被抵消或最小化。