US006944488B2

(12) **United States Patent**
Roberts

(10) **Patent No.: US 6,944,488 B2**
(45) **Date of Patent: Sep. 13, 2005**

(54) **NORMALIZATION METHOD FOR A CHRONICALLY IMPLANTED OPTICAL SENSOR**

(75) Inventor: **Jonathan P. Roberts**, Shoreview, MN (US)

(73) Assignee: **Medtronic, Inc.**, Minneapolis, MN (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 168 days.

(21) Appl. No.: **10/426,496**

(22) Filed: **Apr. 30, 2003**

(65) **Prior Publication Data**

US 2004/0220460 A1 Nov. 4, 2004

(51) **Int. Cl.**[7] **A61B 5/00**
(52) **U.S. Cl.** **600/339**; 600/332; 600/310
(58) **Field of Search** 600/310, 322, 600/323, 331–333, 339, 342; 607/17, 22

(56) **References Cited**

U.S. PATENT DOCUMENTS

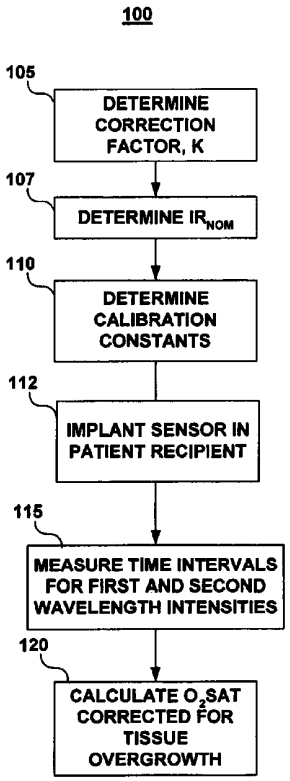
3,847,483 A 11/1974 Shaw et al.
4,202,339 A 5/1980 Wirtzfeld et al.
4,467,807 A 8/1984 Bornzin
6,125,290 A 9/2000 Miesel
6,198,952 B1 3/2001 Miesel

Primary Examiner—Eric F. Winakur
(74) *Attorney, Agent, or Firm*—Girma Wolde-Michael; Paul H. McDowall

(57) **ABSTRACT**

A system and method are provided for accurately estimating blood oxygen saturation independent of tissue encapsulation of the optical sensor. The method includes determining a tissue overgrowth correction factor that accounts for the optical properties of the tissue that cause scattering of the emitted light to a light detector and the relative amplitudes of the emitted light wavelengths. A corrected time interval measured for infrared light is based on an infrared signal returned from fluid with no tissue overgrowth. A corrected time interval for red light is determined by subtracting a red light signal attributed to the presence of tissue overgrowth. The amount of red light signal attributed to the presence of tissue overgrowth is proportional to the total infrared signal less the nominal infrared signal. Oxygen saturation is estimated based on standard calibration factors and the ratio of the corrected infrared time interval and the corrected red time interval.

26 Claims, 5 Drawing Sheets



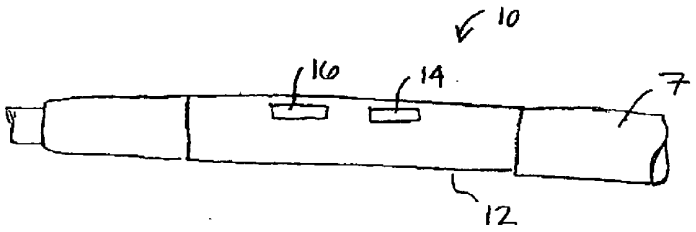


FIG. 1

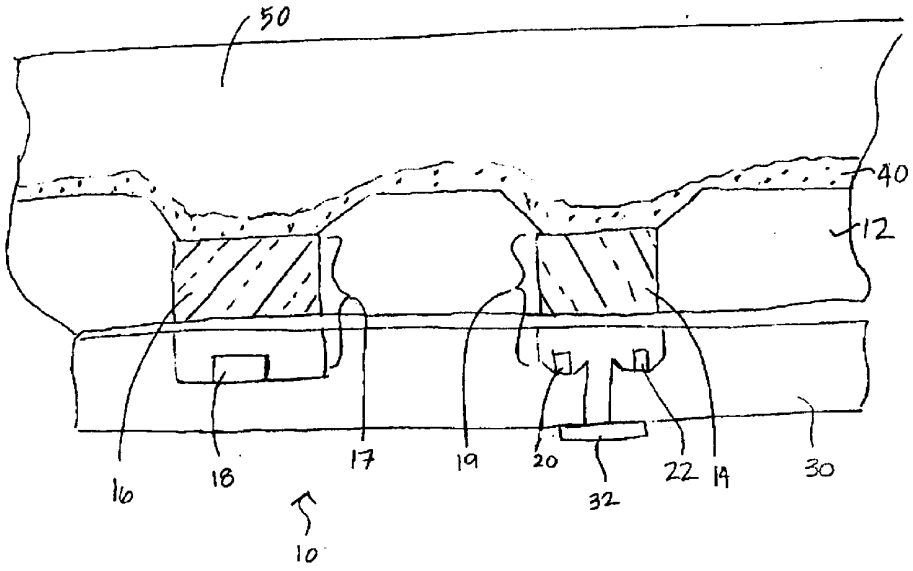


FIG. 2

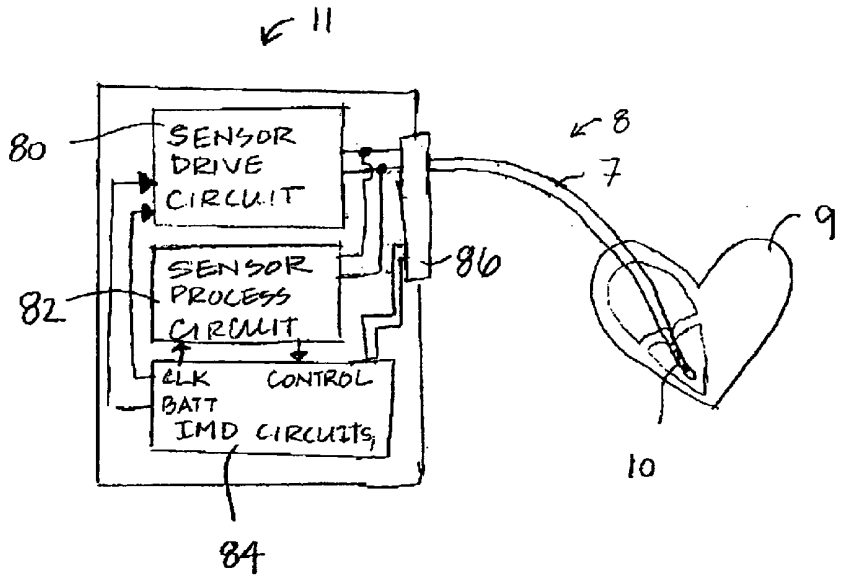

11
80
SENSOR DRIVE CIRCUIT
82
SENSOR PROCESS CIRCUIT
CLK
CONTROL
BATT
IMD CIRCUITS
84
86
8
7
9
10

FIG. 3

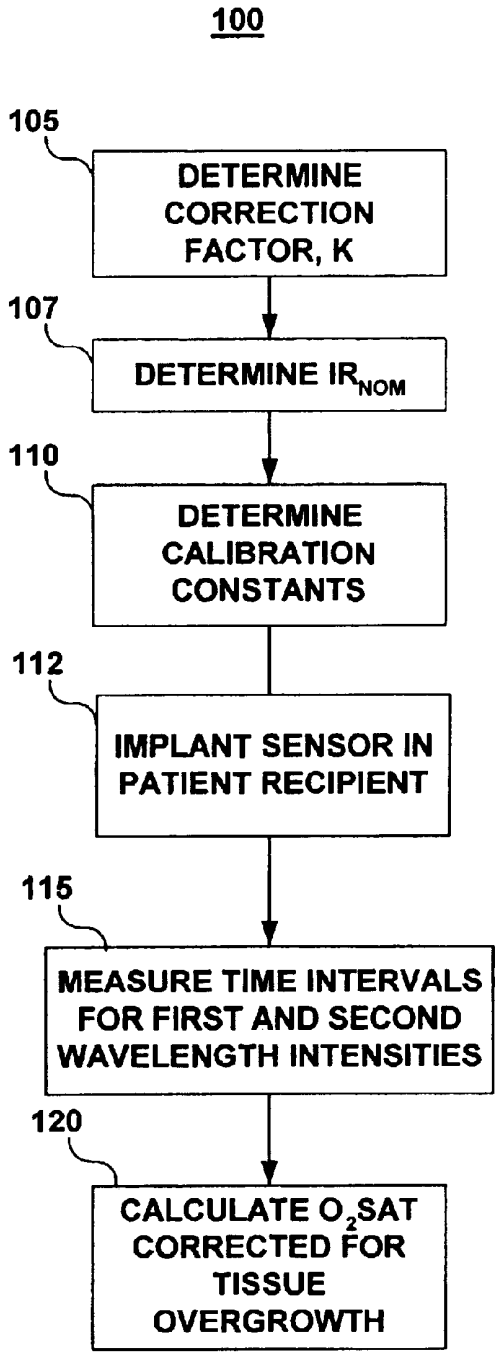

100
105
DETERMINE CORRECTION FACTOR, K
107
DETERMINE IR_{NOM}
110
DETERMINE CALIBRATION CONSTANTS
112
IMPLANT SENSOR IN PATIENT RECIPIENT
115
MEASURE TIME INTERVALS FOR FIRST AND SECOND WAVELENGTH INTENSITIES
120
CALCULATE O_2SAT CORRECTED FOR TISSUE OVERGROWTH

FIG. 4A

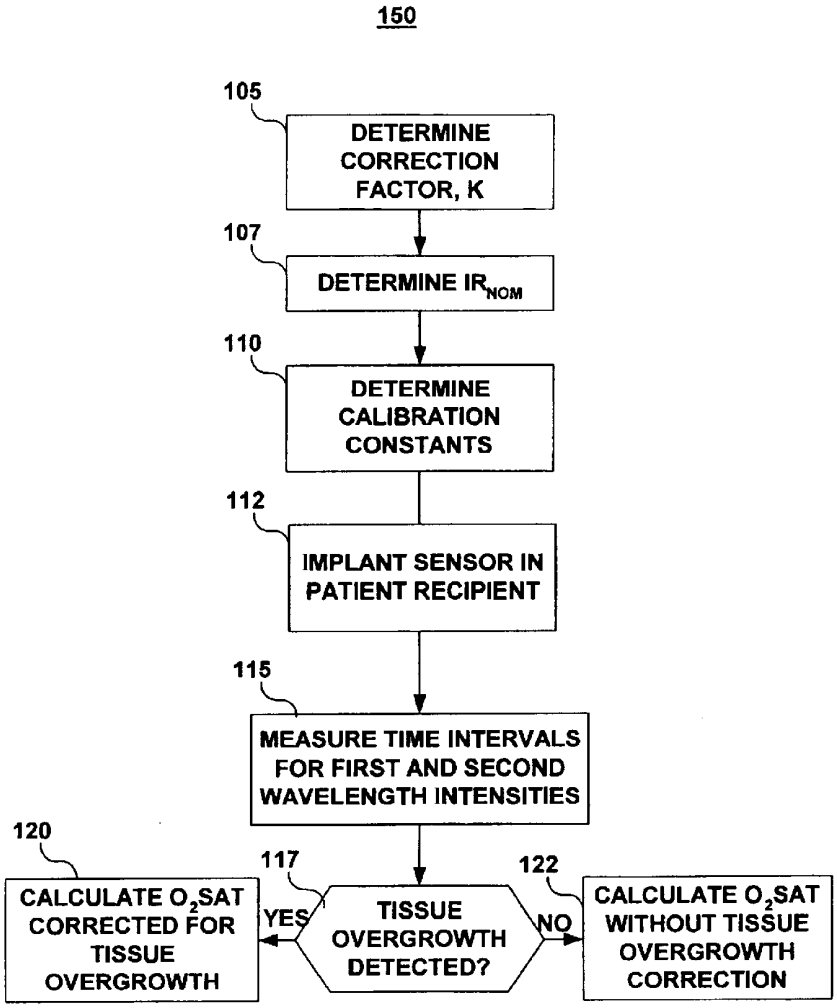

150
105
DETERMINE CORRECTION FACTOR, K
107
DETERMINE IR_{NOM}
110
DETERMINE CALIBRATION CONSTANTS
112
IMPLANT SENSOR IN PATIENT RECIPIENT
115
MEASURE TIME INTERVALS FOR FIRST AND SECOND WAVELENGTH INTENSITIES
117
TISSUE OVERGROWTH DETECTED?
YES
NO
120
CALCULATE O_2SAT CORRECTED FOR TISSUE OVERGROWTH
122
CALCULATE O_2SAT WITHOUT TISSUE OVERGROWTH CORRECTION

FIG. 4B

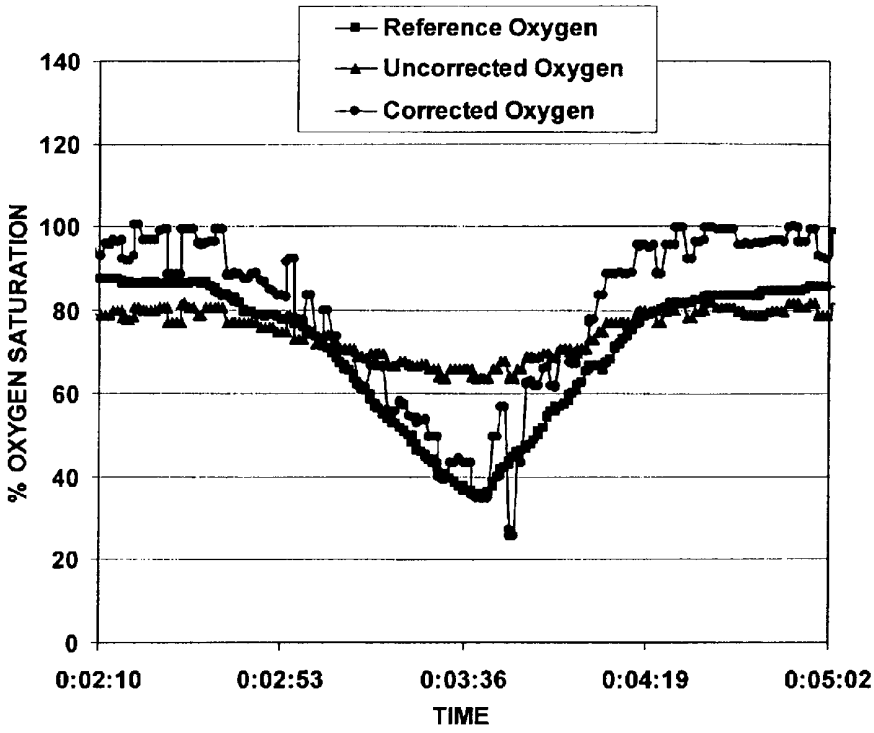

Reference Oxygen
Uncorrected Oxygen
Corrected Oxygen
% OXYGEN SATURATION
140
120
100
80
60
40
20
0
0:02:10
0:02:53
0:03:36
0:04:19
0:05:02
TIME

FIG. 5

NORMALIZATION METHOD FOR A CHRONICALLY IMPLANTED OPTICAL SENSOR

FIELD OF THE INVENTION

The present invention relates generally to the field of implantable optical sensors and more specifically to a method for providing accurate optical sensing of blood oxygen saturation in the presence of tissue overgrowth on the optical sensor.

BACKGROUND OF THE INVENTION

Implantable medical devices (IMDs) for monitoring a physiological condition or delivering a therapy typically rely on one or more sensors positioned in a patient's blood vessel, heart chamber, or other portion of the body. Examples of IMDS include heart monitors, pacemakers, implantable cardioverter-defibrillators (ICDs), myostimulators, nerve stimulators, drug delivery devices, and other IMDs where such sensors are desirable. Implantable sensors used in conjunction with an IMD generally provide a signal related to a physiological condition from which a patient condition or the need for a therapy can be assessed.

Measurement of blood oxygen saturation levels are of interest in determining the metabolic state of the patient. Generally, a decrease in blood oxygen saturation is associated with an increase in physical activity or may reflect insufficient cardiac output or respiratory activity. Thus monitoring blood oxygen saturation allows an implantable medical device to respond to a decrease in oxygen saturation, for example by pacing the heart at a higher rate. An implantable oxygen sensor for use with an implantable medical device is generally disclosed in commonly assigned U.S. Pat. No. 6,198,952 issued to Miesel, hereby incorporated herein by reference in its entirety. Cardiac pacemakers that respond to changes in blood oxygen saturation as measured by an optical sensor are generally disclosed in U.S. Pat. No. 4,202,339 issued to Wirtzfeld and in U.S. Pat. No. 4,467,807 issued to Bornzin.

One limitation encountered with the use of implantable optical sensors can arise as the result of tissue encapsulation of the sensor that occurs as a result of the body's normal response to a foreign object. If an optical blood oxygen sensor is positioned in an area of relatively high blood flow, tissue encapsulation of the sensor may not occur or may at least be minimized to a thin collagenous sheath. If a blood oxygen sensor resides in an area of relatively low blood flow or a stagnant area, tissue encapsulation is likely to occur and the capsule may become relatively thick. Such tissue overgrowth interferes with the performance of the sensor in accurately measuring blood oxygen or other metabolites by reducing the (light) signal to noise ratio. For example, the light signal associated with blood oxygen saturation is reduced due to attenuation of emitted light from the optical that reaches the blood volume and attenuation of the reflected light from the blood volume reaching a light detector included in the optical sensor. Noise due to extraneous light reaching the light detector is increased by the scattering of emitted light by the tissue overgrowth.

The time course and degree of tissue encapsulation of an optical sensor, or any other medical device implanted within the blood volume, is uncertain. Thrombus formation in the vicinity of the sensor due to blood stasis or endothelial injury can occur at unpredictable times after device implant. If the thrombus is in contact with the endocardium or endothelium, macrophages can invade the clot, phagocytose the blood cells and orchestrate collagenous encapsulation by fibroblasts. Because the time course and occurrence of these events is unpredictable, the reliability of blood oxygen saturation measurements at any point in time may be uncertain.

One approach to solving the problem of tissue overgrowth is generally disclosed in U.S. Pat. No. 6,125,290 issued to Miesel, incorporated herein by reference in its entirety. A self-test light detector is provided for estimating the amount of light reflected back into a light emitter portion instead of being transmitted through a lens for reflection from a blood volume. An output signal from self-test light detector may be employed to calibrate or adjust the output signal provided by a light detector in a manner that the estimate of blood oxygen saturation is compensated or adjusted to account for the degree or amount of tissue overgrowth of the sensor.

A need remains, however, for a method for adjusting a blood oxygen saturation (or other metabolite) measurement to account for extra light intensity associated with light scattering tissue or thrombus over the oxygen sensor, and the like. The method preferably provides accurate blood oxygen saturation measurement independent of the presence of tissue overgrowth.

SUMMARY OF THE INVENTION

In an exemplary embodiment, an implantable optical sensor system and method are provided for accurately estimating blood oxygen saturation independent of the presence of tissue encapsulation of the optical sensor. According to the present invention, dual wavelength radiation is used to beneficially provide a first wavelength signal substantially independent of the presence of a metabolite and a second wavelength signal is substantially dependent upon the presence of said metabolite.

Thus, in the exemplary embodiment, a two wavelength optical sensor is employed wherein the amount of reflected light from one wavelength, typically red, is dependent on oxygen saturation, and the second wavelength, typically infrared light, is independent of oxygen saturation. A time interval is measured for each light wavelength as the current induced on a sensor (e.g., a photodetector) in response to the intensity of the reflected light integrated over a capacitor included in the photodetector. The time interval measured for the red light signal is normalized by the time interval measured for the infrared light signal to account for differences in hematocrit and blood flow velocity.

The method includes calculating a corrected time interval measured for the red light signal and a corrected time interval measured for the infrared light signal to account for the presence of tissue overgrowth. A tissue overgrowth correction factor is used in calculating a corrected red light time interval which accounts for: 1) the optical properties of the tissue that cause scattering of the emitted light to a light detector determined experimentally, and 2) the relative amplitudes of the emitted light wavelengths from the optical sensor (e.g., as determined at the time of device manufacture). A corrected time interval measured for infrared light is determined based on the nominal infrared signal returned from an inspected volume of blood in the absence of tissue overgrowth (e.g., as determined at the time of device manufacture). A corrected time interval measured for red light is determined by subtracting the amount of red light signal attributed to the presence of tissue overgrowth from the total red light signal. The amount of red light signal

attributed to the presence of tissue overgrowth is calculated by multiplying the total infrared signal (less the nominal infrared signal) by the tissue correction factor. Oxygen saturation is estimated based on standard calibration factors and the ratio of the corrected infrared time interval and the corrected red time interval.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is an enlarged view of an exemplary oxygen sensor assembly that may be included in an implantable medical lead and with which the present invention may be usefully practiced.

FIG. **2** is a sectional view of the oxygen sensor assembly of FIG. **1**.

FIG. **3** shows a block diagram of an implantable medical device system including an implantable medical device (IMD) and medical electrical lead **8** having an optical sensor assembly for use in sensing blood oxygen saturation.

FIG. **4** is a flow chart summarizing steps included in a method for accurately estimating blood oxygen saturation using an implantable optical sensor independent of tissue overgrowth on the sensor.

FIG. **4**B is a flow chart summarizing steps included in an alternative method for accurately estimating blood oxygen saturation using an implantable optical sensor independent of tissue overgrowth on the sensor.

FIG. **5** is a graph of oxygen saturation measurements made from a chronically implanted oxygen sensor having tissue overgrowth based on prior art methods and based on the tissue overgrowth correction method provided by the present invention plotted in comparison to a reference oxygen saturation measurement.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed at providing a method for accurately measuring changes in blood oxygen saturation using a chronically implantable optical sensor. In particular, the present invention provides a method for compensating for extra light intensity detected by the optical sensor due to light scattering matter, typically collagenous tissue or thrombus, which may be present over the sensor. The methods included in the present invention employ a two-wavelength system and a correction method that allows the extra light intensity due to light scattering tissue over the sensor to be compensated for in calculating oxygen saturation.

Two-wavelength optical sensing systems are known for use in the field of blood oximetry. See for example, U.S. Pat. No. 3,847,483 issued to Shaw et al. In a two-wavelength system, the reflected light signal of one wavelength that changes in intensity with blood oxygen saturation is normalized by a second wavelength of which the reflected intensity is independent of blood oxygen saturation but dependent on other physiological changes in the measured blood volume, such as blood flow velocity and hematocrit concentration. The methods included in the present invention provide an additional correction method to account for additional light signal detected due to tissue overgrowth. The intensity of both wavelengths in a two-wavelength system will be changed in the presence of light scattering matter over the sensor. The presence of light scattering matter over the sensor is expected to affect the intensity of both wavelengths used in sensing oxygen. Hence, as will come to be understood in the description herein, the extra intensity of detected light due to the presence of light scattering matter proximate the sensor can be determined based on the intensity of the wavelength that is not affected by changes in blood oxygen saturation.

FIG. **1** is an enlarged view of an exemplary oxygen sensor assembly **10** that may be included in a medical lead and with which the present invention may be usefully practiced. An elongated sensor housing **12** is provided for housing oxygen sensor components. Lenses **14** and **16** are provided for passing emitted and reflected light from a light emitter and to a light detector, respectively, both of which reside within housing **12**. Although a single lens may be used in lieu of two lenses. Lead body **7** is provided for carrying insulated conductors from the circuitry included in sensor assembly **10** to a connector assembly (not shown) located at a proximal end of the medical lead used for mechanically and electrically connecting the lead to an implantable medical device. A lead carrying oxygen sensor assembly **10** may additionally include other types of sensors and/or electrodes according to the intended use of the lead.

FIG. **2** is a sectional view of oxygen sensor assembly **10** of FIG. **1**. Light emitters **20** and **22** are mounted on an oxygen sensor hybrid **30** in a light emitting portion **19** of oxygen sensor **10**. Each light emitter **20** and **22** emits a different wavelength. Typically one of emitters **20** and **22** emits red light and the other of emitters **20** and **22** emits infrared light. Emitted light passes through lens **14** and must also pass through any tissue overgrowth **40** that is present on all or a portion of lens **14** before it enters blood volume **50**. An optional self-test light detector **32** is shown in the light emitter portion **19** of oxygen sensor assembly **10**. In one embodiment of the present invention, self-test light detector **32** is included for detecting the presence of tissue overgrowth as disclosed in the above-cited '290 patent issued to Miesel.

Light that is reflected from the blood volume **50** must pass through any tissue overgrowth **40** present over all or a portion of lens **16** before it reaches light detector **18**. Light detector **18** is mounted on oxygen sensor hybrid **30** in a light detector portion **17** of oxygen sensor **10**. Time intervals that are inversely proportional to the intensity of the received light signals associated with each of the two measured wavelengths, red and infrared, are measured as an electrical current induced in light detector **18** (which is preferably integrated over a capacitor included in the light detector **18**). The presence of tissue overgrowth **40** generally reduces the light signal to noise ratio, as described previously, by both attenuating the reflected light signal associated with blood oxygen saturation and increasing noise due to extraneous light scattered by tissue overgrowth **40** reaching detector **18**. The methods of the present invention address the latter problem of increased extraneous light received by detector **18**, resulting in shortened time intervals, by correcting the measured time intervals for the amount of light signal attributed to noise.

FIG. **3** shows a block diagram of an implantable medical device system including an implantable medical device (IMD) **11** and medical electrical lead **8** having an optical sensor assembly **10**, for use in sensing blood oxygen saturation. Optical sensor **10** is typically mechanically and electrically coupled to the distal ends of lead conductors disposed within the body **7** of lead **8**. Connector elements disposed at the proximal end of lead **8** are connected to the proximal ends of lead conductors and provide connection to sensor drive circuit **80** and sensor processor circuit **82** via a connector block **86**. Sensor drive circuit **80** provides the operational power for optical sensor **10** and controls the

timing of optical sensor operation. Sensor process circuit **82** receives optical sensor signal output and processes the signal output to estimate a measurement of blood oxygen saturation. In accordance with the present invention, the methods used by sensor process circuit **82** for estimating blood oxygen saturation includes calculations made to correct for the presence of tissue overgrowth covering a portion of or all of the lenses **14**, **16** of optical sensor **10**.

When IMD **11** includes cardiac pacing capabilities, lead **8** may additionally include pacing, sensing and/or defibrillation electrodes generally disposed at the distal end of lead **8** in operative relation to one or more heart chambers. Alternatively, additional pacing and sensing leads are included in the IMD system. Cardiac pacing and sensing control circuitry, a clock, and a battery for powering IMD operations are included in IMD circuits **84**. Detailed descriptions of such circuitry included in an implantable medical device and its operation are provided in the above-incorporated '952 patent to Miesel.

Preferably, the reflection of red light (wavelength ~660 nm) and the reflection of infrared light (wavelength ~880 nm) are used for measuring blood oxygen saturation. The absorption of red light is a function of oxygen saturation and therefore the intensity of the reflected red light signal received by a light detector is inversely proportional to oxygen saturation. The absorption of infrared light is a function of non-oxygenated hemoglobin and hematocrit concentration. The ratio of the red light intensity to the infrared light intensity of the reflected light is used to normalize a measured light signal for changes in hematocrit and blood flow velocity. Prior art oxygen sensors therefore determine the blood oxygen saturation (SAO_2) according to the inverse relation to the reflected red light intensity normalized by the reflected infrared light intensity as shown by Equation (1):

$$SAO_2=A+B(1/(R/IR)) \quad (1))$$

wherein A and B are calibration constants defined by the intercept and slope of a calibration curve, respectively; IR is the intensity of reflected infrared light, and R is the intensity of reflected red light.

An alternative and commonly used form of Equation (1) takes the logarithm of the term including the ratio of the red to infrared light signal in order to linearize the function as shown in Equation (1'):

$$SAO_2=A+B\ \log(1/(R/IR)). \quad (1')$$

For the sake of simplicity, the methods described herein will be elaborated on with regard to Equation (1), but substitutions to be described in detail below to be made in Equation (1) for correcting for the presence of tissue overgrowth may be equivalently made in Equation (1').

Equation (1) may be re-written as:

$$SAO_2=A+B(IR/R).$$

In accordance with the present invention, the terms R and IR in Equations (1) and (2) are corrected to account for increased light signal due to tissue overgrowth by subtracting the amount of red light and infrared light signal attributed to tissue overgrowth.

In correcting for the presence of tissue overgrowth, an assumption is made that the optical properties of the tissue overgrowth will affect both red and infrared light wavelengths and that the amount of red light reflected by tissue overgrowth will be proportional to the amount of infrared light reflected by tissue overgrowth. Another assumption made is that tissue overgrowth on the optical sensor has the same effect on sensor measurements as a shortened "dark interval." Herein, the term "dark interval" refers to the time interval measured from a photodetector in the absence of any true light signal reflected from the blood. The dark interval therefore is the time interval measured due to stray current or extraneous light reaching the photodector such as light leakage from the emitter to the detector portion of the oxygen sensor. Hence, the presence of tissue overgrowth will increase extraneous light reaching the photodetector, causing a shortened dark interval. Another underlying assumption is that enough light is passed through the tissue to be reflected by the passing blood volume.

Based on the above assumptions, the "dark interval" measured in the presence of tissue overgrowth will include an infrared signal component and a red signal component. The infrared time interval contributing to the dark interval, T_{IRdark}, is given by Equation (3):

$$T_{IRdark}=1/(IR-IR_{nominal}), \quad (3)$$

wherein IR is the total infrared light signal received from all sources and $IR_{nominal}$ is the expected infrared light signal to be reflected from a blood pool when no tissue overgrowth is present.

The terms representing the IR and $IR_{nominal}$ light signals in Equation 3 can be replaced by the inverse of the time interval measured for each light signal. Hence, Equation (3) can be rewritten as:

$$T_{IRdark}=1/((1/T_{IR})-(1/T_{IRnom}) \quad (4)$$

wherein T_{IR} is the time interval measured from the photodetector due to the total infrared light signal and T_{IRnom} is the time interval measured from the photodetector due to the expected infrared light signal reflected from a blood pool in the absence of any tissue overgrowth.

As stated above, an assumption is made that the optical properties of the tissue cause red light to be reflected proportionally to infrared light. The time interval contribution to the dark interval from red light reflected from the tissue overgrowth, T_{Rdark}, can therefore be expressed as:

$$T_{Rdark}=K(T_{IRdark}), \quad (5)$$

wherein K is a correction factor that takes into account: 1) the ratio of red to infrared light intensities reflected from tissue overgrowth when red and infrared light sources emit equal intensities of red and infrared light, and 2) a scaling factor that represents the relative amplitudes of red and infrared light output power from the light emitters of the oxygen sensor. $T_{IRdark}$is given by Equation (4) above.

A corrected red time interval, $T_{Rcorrected}$, for estimating oxygen saturation can be obtained from the inverse of the total red light signal received, R, less the red light signal attributed to the tissue overgrowth, R_{dark}:

$$T_{Rcorrected}=1/(R-R_{dark}). \quad (6)$$

The terms R and R_{dark} in Equation 6 may be substituted for by the inverse of the corresponding time intervals measured by the photodetector:

$$T_{Rcorrected}=1/((1/T_R)-(1/T_{Rdark})), \quad (7)$$

wherein T_R is the time interval measured due to the total amount of reflected red light at the photodetector and T_{Rdark} is given by Equation (5) above.

The corrected infrared time interval, $T_{IRcorrected}$, is simply equal to the time interval measured for infrared light reflected from a volume of blood in the absence of any tissue overgrowth:

$$T_{IRcorrected}=T_{IRnom} \quad (8)$$

Thus, in accordance with the present invention, Equation (2) above can be rewritten as:

$$SAO_2=A+B(IR_{corrected}/R_{corrected}), \quad (9)$$

which can be rewritten in terms of measured time intervals as:

$$SAO_2=A+B(T_{Rcorrected}/T_{IRcorrected}) \quad (10)$$

By using Equations 4, 5, 7, and 8, to substitute for $T_{Rcorrected}$ and $T_{IRcorrected}$, and after mathematical simplification and reduction, Equation 10 can be equivalently rewritten as Equation 11 below in terms that are either measured or known quantities:

$$SAO_2=A+B\{(K*T_R*T_{IRnom})/((K*T_{IR}*T_{IRnom})-(T_R(T_{IRnom}-T_{IR})))\} \quad (11)$$

As indicated previously, constants A and B are standard calibration constants; K is determined by experimentally measuring the ratio of red to infrared light reflected by tissue overgrowth upon exposure to equal intensities of emitted red and infrared light for a given sensor geometry and by knowing the relative output of the red and infrared light emitters of the oxygen sensor at the time of manufacture; $T_{IRnominal}$ is determined experimentally by measuring the infrared time interval due to infrared light reflected from a volume of blood in the absence of any tissue overgrowth; and T_R and T_{IR} are the time intervals measured from the photodetector associated with the intensity of red and infrared light reflected into the detector portion of the oxygen sensor during oxygen sensing operations.

FIG. **4A** is a flow chart summarizing steps included in a method for accurately estimating blood oxygen saturation using an implantable optical sensor independent of tissue overgrowth on the sensor. Method **100** introduces the use of two new constants, K and T_{IRnom}, as defined above, in an equation for calculating oxygen saturation from optical sensor measurements. At step **105**, the value for the tissue overgrowth correction factor, K, is obtained by experimentally quantifying the ratio of equally applied intensities of red light to infrared light reflected from tissue overgrowth for a given sensor geometry and multiplying this ratio by a scaling factor that represents the relative amplitudes of red and infrared light output power from the light emitters of the oxygen sensor as determined at the time of manufacture of the sensor. The ratio of reflected red to infrared light represents the light scattering and reflecting properties of tissue encapsulating a chronically implanted oxygen sensor. The scaling factor is known at the time of sensor manufacture.

At step **107**, T_{IRnom} is determined. T_{IRnom} is also determined at the time of sensor manufacture and can be determined by measuring the reflected infrared light from a sample of material with known scattering and reflecting properties of IR light. T_{IRnom} represents the return infrared light from a volume of blood at any known level of oxygen saturation.

At step **110** the calibration constants A and B are determined as the slope and offset of an oxygen saturation curve. These constants are also determined at the time of device manufacture, based upon experimental data to determine the response of a given sensor geometry, and the red and infrared output power of the emitters for an individual sensor. The determination and use of these calibration constants is known in the prior art.

Steps **105** through **110** are performed experimentally or at the time of sensor manufacture such that the constants, K, T_{IRnom}, A and B, may be programmed into firmware or software used by an implanted medical device in calculating oxygen saturation using signals received from the optical sensor. At step **112**, the optical sensor is deployed with an associated IMD system by implanting the sensor at a desired location in the blood volume of a patient. Step **115** represents the normal operation of the optical sensor in which the intensities of red and infrared reflected light received at the light detector portion of the oxygen sensor are measured. At step **120**, oxygen saturation is calculated according to Equation 11 above, based on the tissue overgrowth correction methodology provided by the present invention.

FIG. **4B** is a flow chart summarizing steps included in an alternative method for accurately estimating blood oxygen saturation using an implantable optical sensor independent of tissue overgrowth on the sensor. Identically labeled steps included in method **150** correspond to the same steps included in method **100**, described above. However, method **150** includes a decision step **117** for determining if tissue overgrowth is present. Tissue overgrowth may be detected by the use of a self-test light detector in the emitter portion of the oxygen sensor, as generally disclosed in the above-cited '290 patent to Miesel. When tissue overgrowth is detected, Equation 11 is used by sensor processing circuitry of the implantable medical device for calculating oxygen saturation corrected for the presence of tissue overgrowth at step **120**. If tissue overgrowth is not detected at decision step **117**, Equation 2 may be used by sensor processing circuitry for calculating oxygen saturation without correcting for the presence of tissue overgrowth at step **122**.

FIG. **5** is a graph of experimental oxygen saturation measurements made from a chronically implanted oxygen sensor having tissue overgrowth based on prior art methods and based on the tissue overgrowth correction method provided by the present invention plotted compared to a reference oxygen saturation measurement. The graph is exemplary of the operation of an oxygen sensor with and without the tissue overgrowth correction method. The graph shows the results of oxygen saturation measurements obtained from a chronically implanted oxygen sensor and an acutely implanted reference oxygen saturation sensor during an oxygen desaturation experiment. Oxygen desaturation was accomplished in a sedated canine by temporarily introducing helium into the respirator, causing reduction in the uptake of oxygen.

Reference oxygen sensor measurements (square symbols) show a decrease in oxygen saturation followed by a return to normal oxygen saturation levels after respirator oxygen levels had been restored. The chronically implanted oxygen sensor in this canine has been overgrown with fibrin, causing a lack of response in the oxygen values determined without correcting for tissue overgrowth (triangle symbol) compared to the reference oxygen sensor measurements.

The tissue overgrowth correction in this example was determined using red and infrared time intervals recorded at the time of implant, rather than at the time of manufacture, since tissue response had not been determined for the sensor before manufacture. The correction was performed using time intervals extracted from the oxygen saturation and the measured infrared time intervals, since the red time intervals were not recorded as part of the original study. This causes

a decrease in resolution in the corrected oxygen saturation measurement that would not be present in a system that either compensates the signals before recording, or with a system that records the red time interval along with the IR time interval as described above.

However, it can be seen from the graph of FIG. **5** that the response of the corrected oxygen saturation measurements made from the chronically implanted, tissue overgrown sensor (circle symbols), responds to the desaturation event similarly to the reference oxygen sensor measurements, while the uncorrected oxygen saturation measurements show an attenuated response to the desaturation event.

Thus, a system and method are provided for accurately estimating blood oxygen saturation from optical sensor measurements independent of the presence of encapsulating tissue over all or a portion of the optical sensor. Methods included in the present invention have been described with regard to an optical oxygen sensor application. However, it is contemplated that tissue overgrowth correction methodologies provided by the present invention may be applied in the use of other types of implantable optical sensors employing a two-wavelength system, such as glucose sensors. Depending on the wavelengths employed, the tissue overgrowth correction factor, K, may not be a constant if the optical properties of the tissue overgrowth affect the normalizing wavelength differently than the targeted measurement wavelength. Therefore, while the present invention has been described according to specific embodiments presented herein, aspects of the present invention may be applied in alternative embodiments including implantable, two-wavelength optical sensor systems. As such the disclosed embodiments are intended to be exemplary, not limiting, with regard to the following claims.

What is claimed is:

1. A method for accurately estimating a saturation metric for a metabolite of interest in a volume of fluid by an optical sensor measurement substantially independent of the presence of encapsulating tissue over all or a portion of a lens of the optical sensor, comprising:

determining a tissue overgrowth correction factor (K) for a first and a second wavelength of optical radiation in a dual wavelength optical sensor, wherein said first wavelength of optical radiation is substantially proportional to an amount of a metabolite of interest present in a volume of fluid and said second wavelength of radiation is substantially independent to the amount of the metabolite present in the volume of fluid;

determining a nominal time interval for detecting the second wavelength of optical radiation (T2) after it is directed to a volume of fluid containing a material having known optical properties;

determining a pair of calibration constants (A,B) for said first and said second wavelength of optical radiation;

placing the dual wavelength optical sensor in a volume of fluid may contain an amount of the metabolite;

measuring a first time interval for the first wavelength of radiation and a second time interval for the second wavelength of radiation when said first and second wavelengths of radiation are directed to the volume of fluid; and

calculating a saturation metric for the metabolite of interest based upon the tissue overgrowth correction factor (K), the pair of calibration constants (A,B), the nominal time interval, the first time interval and the second time interval.

2. A method according to claim **1**, wherein the metabolite of interest is oxygen saturation and the calculating step further comprises,

calculating according to the following mathematical expression:

$$SAO_2 = A + B\{(K * T_R * T_{IRnom})/((K * T_{IR} * T_{IRnom}) - (T_R(T_{IRnom} - T_{IR})))\}$$

where T_R is the first time interval,

T_{IR} is the second time interval, and

T_{IRnom} is the nominal time interval.

3. A method according to claim **1**, further comprising providing a saturation metric output signal.

4. A method according to claim **1**, wherein after measuring the first time interval and the second time interval performing the step of:

detecting a tissue overgrowth condition, and if the tissue overgrowth condition is positive then: calculating a corrected saturation metric for the metabolite of interest; and

if the tissue overgrowth condition is negative then: calculating an uncorrected saturation metric for the metabolite of interest.

5. A method according to claim **1**, wherein the metabolite of interest is one of: an oxygen saturation, a glucose concentration, a lactate concentration, a pH concentration, a carbon dioxide concentration.

6. A method according to claim **1**, wherein the first wavelength of optical radiation is approximately 660 nm and the second wavelength of radiation is approximately 880 nm.

7. A method according to claim **1**, wherein the dual wavelength optical sensor is disposed in a volume of blood.

8. A method according to claim **1**, wherein said dual wavelength optical sensor mechanically couples to an implantable medical device.

9. A method according to claim **1**, wherein the metabolite of interest is oxygen saturation and the calculating step further comprises:

calculating according to the following mathematical expression which corrects for nonlinearity in the red response to oxygen saturation:

$$SAO_2 = A + B * \log(\{(K * T_R * T_{IRnom})/((K * T_{IR} * T_{IRnom}) - (T_R(T_{IRnom} - T_{IR})))\})$$

where T_R is the first time interval,

T_{IR} is the second time interval, and

T_{IRnom} is the nominal time interval.

10. A system for accurately estimating blood oxygen saturation in a volume of fluid by optical sensor measurement independent of the presence of encapsulating tissue over all or a portion of a lens of an optical sensor, comprising:

means for determining a tissue overgrowth correction factor (K) for a first and a second wavelength of optical radiation in a dual wavelength optical sensor, wherein said first wavelength of optical radiation is substantially proportional to an amount of a metabolite of interest present in a volume of fluid and said second wavelength of radiation is substantially independent to the amount of the metabolite present in the volume of fluid;

means for determining a nominal time interval for detecting the second wavelength of optical radiation (T2) after it is directed to a volume of fluid containing a material having known optical properties;

means for determining a pair of calibration constants (A,B) for said first and said second wavelength of optical radiation;

means for placing the dual wavelength optical sensor in a volume of fluid that may contain an amount of the metabolite;

means for measuring a first time interval for the first wavelength of radiation and a second time interval for the second wavelength of radiation when said first and second wavelengths of radiation are directed to the volume of fluid; and

means for calculating a saturation metric for the metabolite of interest based upon the tissue overgrowth correction factor (K), the pair of calibration constants (A,B), the nominal time interval, the first time interval and the second time interval.

11. A system according to claim **10**, wherein the metabolite of interest is oxygen saturation and the means for calculating the saturation metric further comprise:

means for calculating according to the following mathematical expression:

$$SAO_2=A+B\{(K*T_R*T_{IRnom})/((K*T_{IR}*T_{IRnom})-(T_R(T_{IRnom}-T_{IR})))\}$$

where T_R is the first time interval,

T_{IR} is the second time interval, and

T_{IRnom} is the nominal time interval.

12. A system according to claim **10**, further comprising means for providing a saturation metric output signal.

13. A system according to claim **10**, further comprising:

means for detecting a tissue overgrowth condition, and wherein if the tissue overgrowth condition is positive then calculating a corrected saturation metric for the metabolite of interest; and

wherein if the tissue overgrowth condition is negative then calculating an uncorrected saturation metric for the metabolite of interest.

14. A system according to claim **10**, wherein the metabolite of interest is one of: a glucose concentration, a lactate concentration, a pH concentration, a carbon dioxide concentration.

15. A system according to claim **10**, wherein the first wavelength of optical radiation is approximately 660 nm and the second wavelength of radiation is approximately 880 nm.

16. A system according to claim **10**, wherein the dual wavelength optical sensor is adapted to be disposed in a volume of blood.

17. A system according to claim **10**, wherein said dual wavelength optical sensor mechanically couples to an implantable medical device.

18. A system according to claim **10**, wherein the metabolite of interest is oxygen saturation and the means for calculating further comprises:

means for calculating according to the following mathematical expression that corrects for nonlinearity in a response to oxygen saturation by said first wavelength of optical radiation:

$$SAO_2=A+B*\log(\{(K*T_R*T_{IRnom})/((K*T_{IR}*T_{IRnom})-(T_R(T_{IRnom}-T_{IR})))\})$$

where T_R is the first time interval,

T_{IR} is the second time interval, and

T_{IRnom} is the nominal time interval.

19. A computer readable medium for storing instructions to cause a programmable processor to perform a method for accurately estimating blood oxygen saturation in a volume of fluid by optical sensor measurement independent of the presence of encapsulating tissue over all or a portion of a lens of an optical sensor, comprising:

instructions for determining a tissue overgrowth correction factor (K) for a first and a second wavelength of optical radiation in a dual wavelength optical sensor, wherein said first wavelength of optical radiation is substantially proportional to an amount of a metabolite of interest present in a volume of fluid and said second wavelength of radiation is substantially independent to the amount of the metabolite present in the volume of fluid;

instructions for determining a nominal time interval for detecting the second wavelength of optical radiation (T2) after it is directed to a volume of fluid containing a material having known optical properties;

instructions for determining a pair of calibration constants (A,B) for said first and said second wavelength of optical radiation;

instructions for measuring a first time interval for the first wavelength of radiation and a second time interval for the second wavelength of radiation when said first and second wavelengths of radiation are directed to a volume of fluid that may contain an amount of analyte; and

instructions for calculating a saturation metric for the metabolite of interest based upon the tissue overgrowth correction factor (K), the pair of calibration constants (A,B), the nominal time interval, the first time interval and the second time interval.

20. A medium according to claim **19**, wherein the metabolite of interest is oxygen saturation and the instructions for calculating further comprise:

instructions for calculating according to the following mathematical expression:

$$SAO_2=A+B\{(K*T_R*T_{IRnom})/((K*T_{IR}T_{IRnom})-(T_R(T_{IRnom}-T_{IRnom})))\}$$

where T_R is the first time interval,

T_{IR} is the second time interval, and

T_{IRnom} is the nominal time interval.

21. A medium according to claim **19**, further comprising instruction for providing a saturation metric output signal.

22. A medium according to claim **19**, wherein the medium includes further instructions executed after executing the instructions for measuring the first time interval and the second time interval comprising:

instructions for detecting a tissue overgrowth condition, and if the tissue overgrowth condition is positive then calculating a corrected saturation metric for the metabolite of interest; and if the tissue overgrowth condition is negative then calculating an uncorrected saturation metric for the metabolite of interest.

23. A medium according to claim **19**, wherein the metabolite of interest is a one of: an oxygen, a glucose concentration, a lactate concentration, a pH concentration, a carbon dioxide concentration.

24. A medium according to claim **19**, wherein the first wavelength of optical radiation is approximately 660 nm and the second wavelength of radiation is approximately 880 nm.

25. A medium according to claim **19**, wherein the fluid comprises a volume of blood.

26. A medium according to claim **19**, wherein the metabolite of interest is oxygen saturation and the instructions for calculating further comprises calculating according to the following mathematical expression that corrects for nonlin-

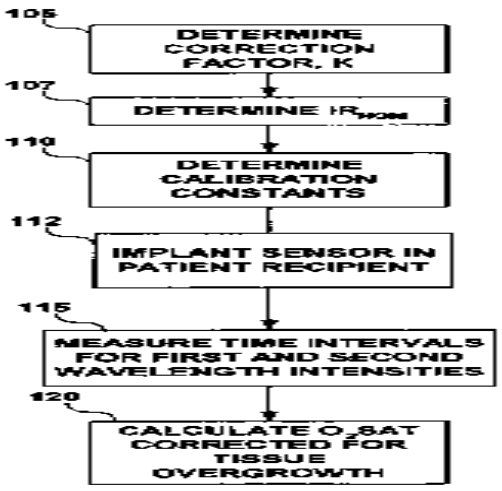
earity in a response to oxygen saturation by the first wavelength of optical radiation:

$$SAO_2 = A + B * \log(\{(K * T_R * T_{IRnom}) / ((K * T_{IR} * T_{IRnom}) - (T_R (T_{IRnom} - T_{IR})))\})$$

where T_R is the first time interval, T_{IR} is the second time interval, and T_{IRnom} is the nominal time interval.

* * * * *

专利名称(译)	用于长期植入的光学传感器的归一化方法		
公开(公告)号	US6944488	公开(公告)日	2005-09-13
申请号	US10/426496	申请日	2003-04-30
[标]申请(专利权)人(译)	美敦力公司		
申请(专利权)人(译)	美敦力公司，INC.		
当前申请(专利权)人(译)	美敦力公司，INC.		
[标]发明人	ROBERTS JONATHAN P		
发明人	ROBERTS, JONATHAN P.		
IPC分类号	A61B5/00		
CPC分类号	A61B5/1459 A61B5/1495 A61B5/14532		
其他公开文献	US20040220460A1		
外部链接	Espacenet USPTO		

摘要(译)

提供了一种系统和方法，用于精确地估计血氧饱和度，而与光学传感器的组织封装无关。该方法包括确定组织过度生长校正因子，该组织过度生长校正因子考虑了导致发射光散射到光检测器的组织的光学性质以及发射的光波长的相对幅度。针对红外光测量的校正时间间隔基于从流体返回的红外信号，没有组织过度生长。通过减去归因于组织过度生长的红光信号来确定红光的校正时间间隔。归因于组织过度生长的红光信号的量与总红外信号减去标称红外信号成比例。基于标准校准因子和校正的红外时间间隔与校正的红色时间间隔的比率来估计氧饱和度。