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(54) **CONTINUOUS OPTOACOUSTIC MONITORING OF HEMOGLOBIN CONCENTRATION AND HEMATOCRIT**

KONTINUIERLICHE OPTOAKUSTISCHE ÜBERWACHUNG VON HÄMOGLOBINKONZENTRATION UND HÄMATOKRIT

SUIVI OPTO-ACOUSTIQUE CONTINU DU TAUX D'HEMOGLOBINE ET D'HEMATOCRITE

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Description

BACKGROUND OF THE INVENTION

1. Field of the Invention

[0001] The present invention relates to an apparatus for non-invasive, real-time, accurate, continuous monitoring of hemoglobin concentration and hematocrit and a method for continuously or discretely monitoring hemoglobin concentration and hematocrit.

[0002] More particularly, the present invention relates to an optoacoustic apparatus including a nanosecond pulsed laser, a fiber-optic delivery system and a probe including a sensitive acoustic transducer and hardware and software for converting a received acoustic signal into a measurement of hemoglobin concentration and hematocrit and to methods for monitoring hemoglobin concentration and hematocrit using the apparatus and methods for making the apparatus.

2. Description of the Related Art

[0003] Continuous noninvasive monitoring of blood hemoglobin concentration and hematocrit offers great promise in the diagnosis and management of many diseases and life-threatening conditions, such as emergency department stabilization of hemorrhaging patients, management of critically ill patients in Intensive Care Units, and performance of extensive surgical procedures. Current techniques are invasive, requiring blood sampling and analysis, and cannot be performed continuously, in real time for extended intervals. Presently, there is no system for accurate, non-invasive, and continuous monitoring of hemoglobin concentration and hematocrit.

[0004] Because of the importance of hemoglobin concentration in oxygen delivery, hematocrit and hemoglobin are among the most frequently obtained blood tests in both outpatients and inpatients. Current techniques for measuring hemoglobin concentration and hematocrit require withdrawal of a blood sample from a vein or artery. Subsequently, the sample can be centrifuged, separating the fraction of red cells from plasma or chemically analyzed. These techniques are accurate but invasive and can result in iatrogenic anemia in patients who require frequent blood sampling [3-7]. Continuous invasive techniques are available for monitoring hemoglobin concentration, but these require access to an extracorporeal loop containing circulating blood (as is present, for example, during hemodialysis) [8-12]. Although non-invasive techniques such as pulse oximetry are available to monitor arterial oxygen saturation, no noninvasive technique is available to monitor hemoglobin concentration or hematocrit.

[0005] One additional major problem with intermittent measurement of hemoglobin concentration or hematocrit is the inevitable delay associated with withdrawal of a blood sample, transport to a measuring device, and processing. If the laboratory is remote from the site of care, the delay can be considerable. Even if the laboratory is in close proximity to the site of care, frequent sampling in a critically ill patient may occupy a substantial proportion of a technician's time, thereby increasing the cost of care and limiting the availability of that technician for other duties.

[0006] Thus, there is a need in the art for a non-invasive, real-time, accurate, continuous apparatus and a method using the apparatus for monitoring hemoglobin concentration and hematocrit.

[0007] WO 01/10295 discloses an optoacoustic apparatus which includes a radiation source of pulsed radiation and a probe having a front face to be placed in close proximity to or in contact with a tissue site of an animal body. The probe further includes a plurality of optical fibers terminating at the surface of the front face of the probe and connected at their other end to a pulsed laser. The front face of the probe also has mounted therein or thereon a transducer for detecting an acoustic response from blood in the tissue site to the radiation pulses connected to a processing unit which converts the transducer signal into a measure of venous blood oxygenation.

SUMMARY OF THE INVENTION

[0008] According to the present invention there is provided an optoacoustic apparatus comprising:

a pulsed radiation source;
an optical system including an optical fiber, where the system is connected to an output of the radiation source at its proximal end;
a probe including a housing, a tip, a ring-shaped piezoelectric element, a backing element and an isolating layer, where the optical system enters the housing at its proximal end passes through a center of the piezoelectric element and terminates flush with the housing at the probe's tip;
a cable connected to the transducer at its proximal end and exiting the probe out of the back portion of the probe; and
a processing unit connected to the distal end of the cable; characterized in that:-

1) said apparatus is for monitoring hemoglobin concentration in a blood vessel of an animal
2) said optical system includes an optical screen (114; 214) and an acoustic screen (116; 216); and
3) said processing unit is for converting the transducer output into a measure of blood hemoglobin concentration and/or hematocrit.

[0009] The blood vessel may be the aorta of an animal.

[0010] The apparatus may be one in which the radiation source generates short optical pulses.

[0011] The radiation source may be laser and the pulses are of a nanosecond duration.

[0012] The hemoglobin may be associated with blood in a blood vessel or tissue site.

[0013] The piezoelectric element may be one which detects pressure waves resulting from pulsed irradiation of the vessel and has sufficient sensitivity, temporal resolution, and bandwidth to collect data from which a hemoglobin concentration is derived.

[0014] The processing unit may be one which calculate a hemoglobin concentration from the recorded optoacoustic pressure profiles and amplitudes.

[0015] The pulsed radiation source may be one which produces light pulses in the spectral range from about 400 to about 2500 nm.

[0016] The pulsed radiation source may be one which comprises two sources producing light pulses of different wavelengths. The two sources may comprise lasers.

[0017] The blood vessel may comprise an aorta and the probe may be inserted into an esophagus and pulses travel to the aorta through the esophagus wall adjacent the aorta.

[0018] The blood vessel may comprise an artery, e.g. a radial artery, a carotid artery, a brachial artery, or a femoral artery or a vein, e.g. a vein under the skin or in a hollow organ.

[0019] The pulsed radiation source may comprise a Nd:YAG laser or a tunable laser or an optical parametric generator or mixtures or combinations thereof, in which case the light pulses have a wavelength of about 548, 568, 587, 805 nm or mixture or combinations thereof where an absorption coefficient of oxy- and deoxygenated blood are similar so that the hemoglobin concentration can be derived from both oxygenated and deoxygenated blood. The tunable lasers may comprise a Ti:Sapphire laser or a dye laser or mixtures or combinations thereof. The light pulses may have a wavelength in spectral ranges from about 400 to about 640 or above about 1120nm where an absorption coefficient of oxy- and deoxygenated blood are similar so that the hemoglobin concentration is derived from oxygenated and deoxygenated blood.

[0020] The apparatus may be used for hematocrit measurements in the spectral range from 400 to 2500 nm, and preferably in the spectral range above 1350 nm, where optoacoustic signal characteristics are more sensitive to the changes in blood scattering and, therefore, to changes in hematocrit.

[0021] The apparatus may also be used for blood volume measurements.

[0022] The apparatus may further be used for ultrasound-guided optoacoustic monitoring of fetal anemia during pregnancy, or for measuring hematocrit and a hemoglobin concentration in cord blood, or for hemoglobin concentration monitoring in patients with kidney failure or patients on dialysis.

[0023] The probe may include a front face having mounted thereon a piezoelectric transducer connected to an output cable that exits a back portion of the probe, a plurality of optical fibers entering the probe from the back portion of the probe and terminating at or in the front face of the probe, where light from a laser is sent through the fibers and exit the probe at its front face causing an acoustic response which is measured by the transducer mount in the probe.

[0024] The apparatus of the invention may be used in a method for continuously measuring optoacoustic monitoring of hemoglobin concentration and hematocrit including the step of directing radiation pulse from a laser via optical fibers into a probe of present invention having its front face in contact with a tissue site (blood vessel) of an animal including human. The light pulse leaves the probe face and enters the tissue site causing the production of an acoustic signal. The acoustic signal is received by a transducer mounted on the front face of the probe. The signal is then transmitted to a processing unit which converts the signal into a measure of hemoglobin concentration and hematocrit. The method can also include displaying the measurement on a display device. Preferably, the radiation is pulsed and particularly, the radiation is pulsed in a nanosecond time frame.

DESCRIPTION OF THE DRAWINGS

[0025] The invention can be better understood with reference to the following detailed description together with the appended illustrative drawings in which like elements are numbered the same:

Figure 1 depicts a graph of optoacoustic signals induced in blood at different volumes;
Figure 2 depicts a graph of blood absorption coefficient calculated from optoacoustic slopes at different volumes;
Figure 3 depicts a graph of blood absorption coefficient calculated from optoacoustic slopes at different hemoglobin

concentrations;

Figure 4 depicts a graph of optoacoustic signals induced in blood irradiated through 1-cm turbid gelatin slab at different volumes;

Figure 5 depicts a graph of blood absorption coefficient calculated from optoacoustic slopes at different blood volumes where the blood was irradiated through 1-cm turbid gelatin slab;

Figure 6 depicts a graph of blood absorption coefficient calculated from the optoacoustic slopes as a function of hemoglobin concentration where the blood was irradiated through 1-cm turbid gelatin slab;

Figure 7 depicts a graph of optoacoustic signals induced in naphthol green solution irradiated through 1-cm turbid gelatin slab at different volume;

Figure 8 depicts a graph of absorption coefficient of naphthol green solution calculated from the optoacoustic slopes at different volume. The solution was irradiated through 1-cm turbid gelatin slab;

Figure 9 depicts a graph of absorption coefficient of naphthol green solution calculated from the optoacoustic slopes as a function of concentration. The solution was irradiated through 1-cm turbid gelatin slab;

Figures 10A-C depict three preferred embodiment of an optoacoustic probe used in the apparatus of this invention;

Figures 10D-E depict two preferred embodiment of an optoacoustic probe used in the apparatus of this invention for use in the esophagus for monitoring hemoglobin concentration in aorta blood;

Figure 11 depicts a graph of optoacoustic signals from aorta phantom with blood at different Hb concentrations;

Figure 12 depicts a graph of slope of optoacoustic signal recorded from aorta phantom as a function of Hb concentration;

Figure 13 depicts a graph of optoacoustic signals recorded from 2.2-mm tube with solution at different absorption coefficient;

Figure 14 depicts a graph of amplitude ofoptoacoustic signal recorded from the 2.2-mm tube as a function ofHb concentration;

Figure 15 depicts a graph of slope of optoacoustic signal recorded from the 2.2-mm tube as a function of Hb concentration;

Figure 16 depicts a graph of optoacoustic signal recorded from the tube at different axial distance between the tube and the probe;

Figure 17 depicts a graph of amplitude of optoacoustic signal recorded from the tube as a function axial distance between the tube and the probe;

Figure 18 depicts a graph of optoacoustic signal recorded from the tube at different lateral distance between the tube and the probe; and

Figure 19 depicts a graph of amplitude of optoacoustic signal recorded from the tube as a function of lateral displacement of the probe with respect to the tube.

DETAILED DESCRIPTION OF THE INVENTION

[0026] The inventors have found that a new and efficient monitor can be constructed for monitoring hemoglobin concentration and hematocrit using an optoacoustic monitoring apparatus. The monitor may be used in a method which can be implemented manually or automatically
(computer) controlled and supervised for monitoring on a continuous or discrete basis hemoglobin concentration and hematocrit. The present invention can be used in animals, where an animal is any member of the animal kingdom, including, without limitation, mammals and especially humans.

[0027] The inventors have found a novel technique that accurately monitors and quantifies blood hemoglobin concentration and hematocrit. This technique is based on generation of ultrasonic (optoacoustic) waves in blood circulating in vessels via short optical pulses and detection of these waves by a sensitive acoustic transducer. The temporal characteristics and amplitude of these waves are dependent on hemoglobin concentration and hematocrit. Since the optoacoustic waves can propagate in tissues with low attenuation and distortion, this technique has high resolution and permits localization of vessels of interest with high accuracy. This localization permits direct detection and measurement of signals induced in blood circulating in vessels without signal contamination from tissues between the transducer and blood. The present invention is ideally-suited for non-invasive, continuous monitoring of hemoglobin concentration in blood by measuring induced acoustic signals in tissues and vessels such as the aorta, radial, femoral, carotid arteries or other blood vessels.

[0028] The apparatus of the present invention may be used in a method of hemoglobin concentration monitoring that comprises the steps of: irradiating a blood vessel with at least one optical pulse resulting in an optoacoustic pressure wave in the vessel; time-resolved detecting of the optoacoustic wave with an acoustic detector; analyzing a temporal profile and/or amplitude of the optoacoustic wave with a processing unit including computer software adapted to convert the wave data into digital data; and calculating a hemoglobin concentration in blood in the vessel.

[0029] Preferably, the radiation source emits light in the spectral range from about 400 to about 2500 nm. The apparatus

can include one or more radiation sources as described in U.S. Pat. No. 5,840,023 and co-pending application Serial Nos. 09/179,791 and 09/633,597. Although the optical and transducer part of the probe can be housed in separate probes, it is preferably to have the optical and acoustic part of the apparatus in the same probe.

[0030] One preferred application of this invention is to measure a hemoglobin concentration in blood in the aorta or other artery that is not skin accessible. Another preferred application of this invention is to measure hemoglobin concentration in arteries that can be measure by situating the probe on the skin of the patient near the artery such as a radial artery, a carotid artery, a brachial artery, femoral artery or other artery.

[0031] The method using the apparatus of the invention can be applied to any vessel including arteries or veins. The veins can be under the skin or in a hollow organ. For veins the radiation is preferably of wavelengths of about 548, 568, 587, and 805 nm or the isobestic points and in the spectral ranges from about 400 to about 640 and above 1120 nm where absorption coefficients of oxy- and deoxygenated blood are close to each other.

[0032] The preferred radiation sources include light derived from the fist harmonic (1064 nm) or the second harmonic (532 nm) of Nd:YAG laser or tunable lasers such as a Ti:Sapphire laser or a dye laser or an optical parametric generators or mixtures or combinations thereof.

[0033] The method may also be used for hematocrit measurements in the spectral range from 400 to 2500 nm and preferably in the spectral range above 1350 nm where optoacoustic signal characteristics are more sensitive to the changes in blood scattering and, therefore, to changes in hematocrit. The method can be used for blood volume measurements, for ultrasound-guided optoacoustic monitoring of fetal anemia during pregnancy, for measurements of hematocrit and hemoglobin in cord blood, for hemoglobin concentration monitoring in patients with kidney failure and dialysis.

[0034] The apparatus of this invention will generally include between 1 and 144 optical fibers, preferably, between about 6 to about 60 optical fibers, particularly, between about 12 and about 48 and especially between about 18 and 36, with 24 optical fibers being most preferred for probes designed to contact the skin. For probes designed to contact the wall of the esophagus so the Hb concentration in the aorta can be monitored, such probes will include between 1 and about 20 optical fibers, with between about 1 and about 10 being preferred, and between about 1 and about 5 being particularly preferred. The optical fibers have diameters between about 10 μm to about 5 mm, preferably, between about 0.1 mm and 2 mm, particularly between about 0.2 mm and 1.5 mm. For esophagus probes (needle probes), the smaller diameter fiber are preferred. These needle probes can also be used to monitor Hb concentration in various regions of the heart during bypass surgery or other myocardial surgical procedures.

[0035] The probes also include a sensitive acoustic transducer having a size controlled by the application and by design criteria. The optical fiber and transducer are preferably contained in a single housing to provide stable irradiation and detection conditions. For skin applications, the fibers can be mounted around the transducer, adjacent to the transducer or in the center of a ring shaped transducer. For aorta monitor via the esophagus wall, the fiber(s) can mounted within a center of a ring shaped piezoelectric element, surrounding a disk shaped transducer or adj acent to the transducer.

[0036] A sensitive wide-band transducer is designedto detect optoacoustic waves from blood circulating in a target vessel or tissue such as the aorta or other blood vessels. The choice of optimal designs of and materials for the piezoelectric element and the acoustic transducer depend on a number ofparameters: bandwidth, sensitivity, acoustic impedance matching to tissues, etc. For example, polyvinylidene fluoride (PVDF) slabs are suitable transducers for sensitive detection of optoacoustic waves from vessels and/or tissues. The inventors have found that a PVDF slab having a thickness between about 10 μm to about 1 mm thick is preferred. Other suitable piezoelectric materials include, without limitation, PZT, lithium niobide or other similar piezoelectric materials. The present invention can also use other pressure sensing devices such as optical devices that measure the acoustic waves optically such as interferometric devices or other similar devices.

Importance and Significance

[0037] In this invention the inventors disclose a novel technique for noninvasive continuous monitoring of hemoglobin concentration and hematocrit in blood. The monitor can be used for (1) noninvasive measurement of hemoglobin concentration without blood sampling and standard blood testing and (2) continuous measurement of hemoglobin concentrations during surgical procedures, saline or drug infusions, blood infusions, and infusions of stroma-free hemoglobin.

[0038] The apparatuses of this invention are ideally-suited for monitoring hemoglobin concentration in several large patient populations, including, without limitation, normal subjects, patients with blood diseases, and patients with a variety of other conditions. For example, patients who suffer hemorrhage secondary to multisystem trauma being treated in an emergency department, typically have a nearly normal hemoglobin concentration because both blood and plasma have been lost. However, as resuscitation begins with red cell -free fluids, the patient's hemoglobin concentration can and often does decrease rapidly.

[0039] A continuous measurement ofhemoglobin concentration would permit prompt recognition of the need to include red cell containing fluids during resuscitation and would also provide early evidence of continued hemorrhaging. Patients in Intensive Care Units often suffer from blood loss through gastrointestinal hemorrhage and blood loss from other sites,

including blood sampling for diagnostic purposes.

[0040] A continuous, noninvasive measurement of hemoglobin concentration would permit prompt diagnostic and therapeutic interventions and would also reduce iatrogenic blood loss necessitated by the need to obtain blood samples for current hemoglobin measurements. During major surgery, particularly surgery involving major blood vessels, the availability of a continuous measurement of hemoglobin concentration would permit not only prompt administration of needed red cells, but also would facilitate avoidance of unnecessary transfusion by demonstrating that hemoglobin exceeded an acceptable concentration.

[0041] Maintenance of adequate systemic oxygen delivery (cardiac output multiplied by arterial oxygen content) is one of the principal clinical goals in caring for acutely traumatized patients, patients undergoing intensive care, and patients undergoing extensive surgery. However, many chronic diseases, such as chronic renal failure, also are associated with anemia and require intermittent measurement of hemoglobin concentration or hematocrit. Because virtually all blood oxygen content consists of oxygen combined with hemoglobin, oxygen content bears a linear relation to hemoglobin concentration and reduction of hemoglobin concentration requires physiologic compensation, such as increased cardiac output.

[0042] Although the normal hemoglobin concentration is between about 13 and about 15 grams/dL, otherwise healthy individuals tolerate reductions ofhemoglobin to levels as low as 7 g/dL or less, as long as their total blood volume is adequate. However, some patients, such as those with coronary artery disease, may develop severe symptoms, such as angina pectoris, at hemoglobin concentrations below about 10 g/dL. Because there are risks (*e.g.*, transmission of viral diseases [1,2]) associated with transfusion of blood, accurate monitoring of hemoglobin concentration or hematocrit facilitates both necessary transfusions and avoidance of unnecessary transfusions.

[0043] Noninvasive monitoring of fetal anemia during pregnancy is also an ideal use for the apparatuses and methods of this invention as well as measuring hematocrit and hemoglobin concentration in cord blood during pregnancy and delivery.

[0044] Additionally, continuous measurement ofhemoglobin concentration using the apparatuses and methods are useful in monitoring blood volume. In this case, a known small volume of saline, ΔV, is injected via i.v. and a decrease of hemoglobin concentration in blood due to the injection , ΔC, is used to calculate the volume of circulating blood, V as shown in equation (1):

$$V = C\frac{\Delta V}{\Delta C} \qquad (1)$$

where C represents the hemoglobin concentration in the blood.

[0045] Laser optoacoustics, is a novel technique for tissue characterization and diagnostic imaging [13-16], and the inventors have found that the technique is adaptable for hemoglobin concentration monitoring as set forth herein. Optoacoustics utilizes sensitive detection of laser-induced ultrasonic waves instead of the detection of scattered photons. An advantage of ultrasonic detection compared with optical detection is that propagation of acoustic waves in tissues is much less influenced by scattering than propagation of photon waves. Time-resolved detection of the pressure profiles by ultrasound transducers and analysis of the pressure signals allows reconstruction of optoacoustic images which resemble the distribution of optical absorption in the irradiated tissue.

[0046] In contrast to pure optical methods in which diagnostic information about tissue structure is integrated over the entire optical path, the laser optoacoustic imaging permits direct reconstruction of the absorbed energy distribution from the profile of laser-induced pressure [13-19]. The time-resolved detection and analysis of the laser-induced ultrasonic waves offers a unique possibility to visualize tissue structure at depths as great as six centimeters with spatial resolution exceeding 0.5 millimeters in optically turbid and opaque tissues [19-21] and to reconstruct optoacoustic images [22, 23].

[0047] Laser optoacoustic imaging combines the merits of optical tomography (high optical contrast) and ultrasound imaging (insignificant scattering of acoustic waves) to yield a noninvasive diagnostic modality with high contrast, sensitivity and resolution. The optoacoustic imaging in tissues is disclosed in U.S. Pat. No. 5,840,023 [24] and in U.S. Application Serial No. 09/179,791 filed 27 October 1998 [25].

[0048] The optoacoustic technique is also useful in blood oxygenation monitoring as described in U.S. Application Serial No. 09/633,597, filed 7 August 2000 [26]. Recently, optoacoustic technique was applied for noninvasive, real-time, continuous monitoring of tissue coagulation and temperature [27-29].

Theoretical Background

[0049] Although not intending to be bound by any theory, the magnitude of optoacoustic pressure is proportional to the temperature rise in the irradiated medium.

[0050] The temperature rise distribution, AT(r), is expressed by the following equation (2):

$$\Delta T(r) = \frac{\mu_a(r)\Phi(r)}{\rho C_V} \qquad (2)$$

where $\mu_a(r)$ is the absorption coefficient in the tissue, $\Phi(r)$ is the fluence distribution in the tissue, p is the tissue density, and C_v is the heat capacity at constant volume. The formula shown in equation (2) is valid upon irradiation condition of heat confinement, which means that insignificant heat diffusion occurs during laser pulse excitation.

[0051] If a short laser pulse irradiates the tissue, the irradiation condition of temporal stress confinement in the tissue volume of interest also can be satisfied. The laser irradiation under conditions of temporal stress confinement means insignificant stress (pressure) relaxation during the laser pulse excitation [30]. In a one dimensional case, the pressure rise distribution P(z) can be expressed as shown in equation (3):

$$P(z) = (\beta c^2 / C_p)\mu_a F = \Gamma(z)\mu_a F(z) = \Gamma(z)\mu_a F_0 e^{-\mu_a z} \qquad (3)$$

where z is tissue depth in the z direction, $\Gamma(z)$ is the efficiency of thermo-acoustic excitation often called the Grüneisen coefficients. The Grüneisen coefficient is a function of three physical parameters of the irradiated sample: the thermal expansion coefficient, β, the speed of sound, c_s, and the heat capacity at constant pressure, C_p as given by equation (4):

$$\Gamma = \frac{\beta c_s^2}{C_p} \qquad (4)$$

[0052] Irradiation conditions of temporal pressure confinement can usually be achieved by irradiating the sample with laser pulses having a pulse width having a nanosecond duration. The exponential factor $\exp(-\mu_a z)$ represents the exponential attenuation of the optical radiation in the medium due to absorption. According to equation (3) optoacoustic pressure is proportional to the Grüneisen parameter, fluence, and absorption coefficient of the medium. Equation (3) is valid for blood when the blood is irradiated with laser light in the visible and near-infrared spectra because the absorption coefficient of blood is greater than or close to the reduced scattering coefficient, $\mu's = \mu_s(1-g)$, where μ_s is the scattering coefficient and g is the anisotropy factor [31]. The apparatus and methods of this invention are based on the fact that the absorption coefficient of blood is proportional to hemoglobin concentration. Therefore, both the amplitude and slope of the generated optoacoustic pressure induced in blood are dependent on hemoglobin concentration.

[0053] Since z and t are related by the simple equation:

$$z = c_s t \qquad (5)$$

and the spatial distribution of laser-induced pressure P(z) is detected by an acoustic transducer as its corresponding temporal profile P(t) as shown in equation (6):

$$P(t) = \Gamma \mu_a F_0 e^{-\mu_a c_s t} \qquad (6)$$

[0054] Therefore, by recording and analyzing the temporal profile of optoacoustic pressure induced in blood, one can measure the absolute value of hemoglobin concentration with high accuracy. The high z-axial resolution of the optoacoustic technique permits direct measurement of hemoglobin concentration in blood vessels, because the signal from the blood arrives at the acoustic transducer at the time defined by equation (5).

[0055] Tissues are strongly scattering media. Three major optical parameters are responsible for the distribution of light in tissues: absorption, scattering, and the tissues effective attenuation, μ_{eff}, coefficients. The effective attenuation coefficient is related to μ_a and μ_s as shown in equation (7):

$$\mu_{eff} = (\mu_a(\mu_a + \mu_s(1-g)))^{1/2} \qquad (7)$$

and characterizes light penetration in tissue [31]. Light penetration depth is defined as $1/\mu_{eff}$. Absorption and scattering coefficients of tissues are low in the near-infrared spectral range (from about 600 to about 1300 nm) resulting in deeper penetration of near-infrared radiation compared with light in other parts of the electromagnetic spectrum. Near-infrared radiation is the preferred spectral range for the apparatuses and methods of this invention because near-infrared light allows sufficient light penetration into a tissue for effective optoacoustic monitoring of hemoglobin concentration within the tissue including a blood vessel.

[0056] Another feature of near-infrared light as the excitation radiation is that near-infrared light induces insignificant temperature and pressure rises in the tissue being monitored resulting in little and probably no thermal or mechanical damage to the irradiated tissue.

[0057] The signal process apparatus of the present invention can comprise any analog or digital processing unit or computer capable of converting a signal into an output. Such devices include, without limitation, any digital processing unit comprising a processing unit, memory, peripherals, an operating systems and communication hardware and software. Illustrative examples include personal computers, minimainframe computers, or the like.

Sites and Spectral Ranges for Monitoring Hemoglobin Concentration and Hematocrit

[0058] The present invention is ideally suited for measuring hemoglobin (Hb) concentrations and hematocrit in oxygenated blood or tissues having oxygenated blood. Oxygenated blood and especially highly oxygenated blood is ideal for optoacoustic monitoring because the optical properties of blood are dependent on hemoglobin concentration and oxygen saturation.

[0059] Since arterial blood is 95 to 98 % oxygenated, the use of the optoacoustic signals induced in arterial blood provides highly accurate hemoglobin concentration measurements. The most preferable arteries include, but are not limited to, the aorta, radial, carotid, and femoral arteries.

[0060] Hb concentration measurements in blood or tissue can be performed with high accuracy at any wavelength within the visible and near infrared spectral range. Monitoring of hemoglobin concentration in the aorta can be performed by using a small optoacoustic probe inserted in the esophagus.

[0061] The aorta is the largest artery having a diameter between about 20 and about 25 mm and located in close proximity to the esophagus. Part of the aorta (approximately one to two inches) is in direct contact with esophagus wall. The thickness of aorta and esophagus is about 1 and 2-3 mm, respectively. This means that blood circulating in aorta represents a large optoacoustic source closely located to the optoacoustic probe, if the latter is inserted in the esophagus adjacent the part of the aorta in direct contact with the esophagus wall. The large diameter of the aorta and the short distance between the inner wall of the esophagus and blood circulating in the aorta allows substantially precise measurements of hemoglobin concentration to be obtained using the apparatuses and methods of this invention.

[0062] Detection of optoacoustic signals induced in the radial, carotid, and femoral arteries also provides a highly accurate measurement of Hb in the blood circulating through these arteries. In this case, the optoacoustic probe can be larger and can be placed on the skin surface simplifying design and use of the probe. Moreover, these latter probes can be applied to a wider patient population.

[0063] The inventors have also found that optoacoustic signals induced in veins can be used to monitor hemoglobin concentration in deoxygenated blood provided the wavelengths at isobestic points (*e.g.*, 548, 568, 587, and 805 nm) are applied. At these wavelengths oxy- and deoxyhemoglobin have equal absorption coefficients providing accurate measurements of hemoglobin concentration even at variation of oxygen saturation in venous blood. High accuracy can also be obtained in the spectral ranges from about 400 to about 640 nm and above about 1120 nm because absorption coefficients of oxy- and deoxygenated blood are close to each other. Suitable lasers for measuring hemoglobin concentrations in veins, include, without limitation, the second harmonic of a Nd:YAG laser (532 nm), a Ti: Sapphire, dye laser, an Alexandrite laser; a ruby laser, an optical parametric generator, or any other source of short optical pulses in these spectral ranges.

[0064] The inventors have found that attenuation of light with a wavelength above about 1300 to about 1350 nm in blood is dependent mostly on hematocrit, but not on hemoglobin concentration. Optoacoustic signal characteristics in this spectral range will be sensitive to the changes in blood scattering and therefore, to changes in hematocrit. Measurement ofhematocrit is especially important when hematocrit does not follow hemoglobin concentration (*e.g.*, during blood transfusions, etc.).

Design of Optoacoustic Probes

[0065] The inventors have found that a preferred optoacoustic monitoring system of this invention includes an optoacoustic probe that will provide both irradiation ofblood and detection of optoacoustic waves by an acoustic transducer. Such optoacoustic probe include a light delivery system (usually fiber-optic system) and a sensitive piezoelectric element to detect the optoacoustic waves. Different configurations of the probes are possible, depending on the site of monitoring and depth of the blood vessels. The optoacoustic probe can be placed on the skin surface, when monitoring blood in radial, femoral, carotid or other arteries or veins located relatively close to the skin surface, where relatively close means less than about 5 cm from the skin surface and preferably about 2 cm from the skin surface.

[0066] For hemoglobin monitoring in the aorta due to limitation in space in the esophagus, small needle hydrophones are incorporated into optoacoustic probes to minimize the dimensions of the probe. The thickness of the needle hydrophones is generally about 1 mm which are incorporated into small optoacoustic probes with the transverse dimensions of about 2 to about 3 mm. The length of such optoacoustic probe is generally from about 1 to about 2 meters or more to provide delivery of light and signal recording by a distant optoacoustic system.

[0067] The optoacoustic probes of this invention can have an acoustic transducer(s) surrounded by optical fiber(s) or vice versa. Moreover, the optical fiber(s) and the acoustic transducer(s) can be arranged in an adjacent configuration or can be housed in two different probes, an excitation probe and an receiving probe.

EXPERIMENTAL RESULTS

[0068] The inventors performed experiments with blood *in vitro* and in phantoms to test the capability of the optoacoustic technique to monitor hemoglobin concentration. Heparinized sheep arterial blood in a plastic cuvette was irradiated by nanosecond Nd:YAG laser pulses (wavelength = 1064 nm). The blood was under a layer of mineral oil to avoid contact with air. Ultrasonic gel was used to provide acoustic contact between the acoustic transducer and the cuvette. Pulsed laser irradiation of blood and detection ofoptoacoustic waves were performed from two opposite surfaces of the cuvette. Optoacoustic pressure waves induced in blood propagated to the transducer and were recorded by a scope. The initial volume of whole blood with a hemoglobin concentration of 12.4 g/dL was 30 mL. Blood dilutions were performed with 1-mL saline injections into the blood sample with a syringe. The influence on optoacoustic pressure signals due to the change in blood volume is displayed in Figures 1 for four (4) different volumes. As shown in Figure 1, saline injections dramatically changed the amplitude and slope of the pressure signal.

[0069] Blood absorption coefficient calculated from the pressure slopes decreased with increasing blood volume as shown in Figure 2 due to blood dilution. Since the initial blood volume and volume of injected saline are known, one can calculate a hemoglobin concentration in blood after each saline injection. The optoacoustic signal slope was found to be linearly dependent on hemoglobin concentration as shown in Figures.

[0070] Similar experiments and calculations were performed when blood was irradiated through a turbid gelatin slab with the thickness of 1 cm. The gelatin slab had optical properties similar to that oftissues in the near infrared spectral range (μ_a= 0.6 cm^{-1} and μ_s = 2.9 cm^{-1}) and can be used to simulate a tissue layer *in vivo.* The results presented in Figures 4, 5, and 6 indicate that the addition of the turbid slab did not decrease the accuracy of the blood Hb concentration measurements. The amplitude of the signals is close to that recorded from blood irradiated without the gelatin slab despite attenuation, because scattering in the slab resulted in an increase of irradiated blood area and, therefore, an increase in optoacoustic signal amplitude.

[0071] Experiments were also performed with an aqueous solution colored with an absorbing dye (naphthol green) simulating blood. The experiment demonstrated similar results to the previous experiments as shown in Figures 7, 8, 9.

[0072] To monitor hemoglobin concentration and hematocrit *in vivo,* irradiation of tissue by laser light and detection the laser-induced optoacoustic waves should generally be performed from the same side of the tissue. The inventors designed, built, and, tested different optoacoustic probes: (1) with a ring shape piezoelectric element and optical fiber in the center of the ring (see Figure 10A); (2) with optical fibers surrounding a disc shaped piezoelectric element (see Figure 10B); and (3) with optical fibers adjacent to a disc shaped piezoelectric element (see Figure 10C). Each of these configurations has advantages and each used a PVDF based transducer. The most preferable probe configuration for hemoglobin monitoring includes a ring shaped piezoelectric element with optical fibers in the center of the ring as shown in Figure 10A. The results of tests of the probe of Figure 10A are presented below. Looking at Figures 10A-C, a probe generally **100** is shown to include a housing **102** which can be composed of metal or other structural material such as plastic, an optical system **104,** a backing element **106,** a piezoelectric element **108** and an isolating layer **110.** The optical system **104** includes an optical fiber **112,** an optical screen **114** and an acoustic screen **116.** The system **104** would connect at its proximal end to a pulsed light source such as a laser (not shown), while its distal end **118** terminates flush with the housing **102** at the probe's distal end **120.** The probe of Figure 10A has the optical system **104** passing through a center **122** of a ring-shaped piezoelectric element **108.** The probe of Figure 10B has the optical system **104** distributed around a disk shaped piezoelectric element **108.** And, the probe of Figure 10C has the optical system **104** positions

next to (a side-by-side arrangement) the piezoelectric element **108** which can be of any desired shape.

[0073] Referring now to Figure 10D and E, two preferred embodiments of esophagus probes **200** is shown to includes a housing **202** which can be composed of metal or other structural material such as plastic, an optical system **204,** a backing element **206**, a piezoelectric element **208** and an isolating layer **210.** The optical system **204** includes an optical fiber **212,** an optical screen **214** and an acoustic screen **216.** The system **204** would connect at its proximal end to a pulsed light source such as a laser (not shown), while its distal end **218** terminates flush with the housing **202** at the probe's distal end or tip **220.** The probe of Figure 10D has the optical system **204** passing through a center **222** of a ring-shaped piezoelectric element **208.** The probe of Figure 10B also has the optical system **204** passing through the center **220** of a ring-shaped piezoelectric element **208,** but the distal end **218** of the optical system **204,** the transducer **208** and the isolating layer **210** so that the tip **220** is oriented at a right angle to the main body **224** of the probe **200.** Of course, the tip **220** can be oriented at any angle relative to the main body **224** provided that the tip **220** can contact the esophagus wall adjacent the aorta.

Results Obtained with the Optoacoustic Probe of Figure 10A

[0074] The inventors performed experiments with whole sheep blood and absorbing solutions in phantoms simulating aorta and radial artery. Rubber tubes having a diameter of about 25 mm and a length of about 50 mm were filled with blood with different Hb concentrations (6.0, 6.2, 7.0, and 8.0 g/dL). The tubes were then covered with a 3-mm turbid gelatin slab to provide irradiation and detection conditions similar to ones for optoacoustic monitoring of hemoglobin concentration in aorta. The optoacoustic signals induced in blood start at about 3 to about 3.5μs depending on hemoglobin concentration as shown in Figure 11. Looking at Figure 11, the first two sharp peaks are signals induced in the thin metal housing of the probe. The flexible tubes and gelatin slabs used to simulate a real aorta and esophagus wall with different thicknesses resulted in a shift in time for the signals induced in the blood within the tubes. Despite differences in irradiation and detection conditions for the tubes, the optoacoustic slope calculated from the recorded signals increased linearly with Hb concentration as shown graphically in Figure 12. The signals were normalized before the slope calculations. Calculation of the normalized signal slope provides measurement of Hb concentration with high accuracy, *e.g.* about 0.5 g/dL.

[0075] Referring now to Figure 13, optoacoustic signals recorded from a phantom (2.2-mm plastic tube in a turbid solution) simulating radial artery are shown. The absorbing solution in the tube had an absorption coefficient of about 2 to about 24 cm^{-1}. The first peak at about 1.2 μs is a signal induced in the housing of the probe and the turbid solution. The signals induced in the tube start at about 3 μs representing time of flight of the optoacoustic waves from the upper surface of the tube to the probe. Both amplitude and temporal profile of the signals induced in the tube are dependent on the solution absorption coefficient. The optoacoustic signal amplitude increases gradually with absorption coefficient as shown in Figure 14. The signal from the solutions with high absorption coefficient values has two positive peaks, while only one positive peak is recorded from solutions with low absorption coefficient values. The optoacoustic signals were normalized and their first derivatives (slope) were calculated. The slope of the signals at, about 5 μs is the most sensitive to changes in the absorption coefficient as shown in Figure 15. It is positive for solutions with high absorptions and negative for ones with low absorptions. The measurement and calculation of the slope can be used to provide accurate measurement of blood Hb concentrations.

[0076] Referring now to Figure 16, the optoacoustic signals recorded at different axial distance between the tube and the probe for solution with an absorption coefficient of about 13 cm^1 are shown. The variation of the distance simulated different thicknesses of tissue between the probe and a simulated artery (radial, carotid, or femoral). The position of the signal changes with the distance indicating the depth of the artery in the solution, *i.e.*, its location in a tissue. The temporal profile of the signals change slightly with depth while the signal amplitude sharply decreases with increasing depth due to stronger attenuation of light and propagation of the optoacoustic signals from the cylindrical source as shown in Figure 17. Lateral displacement of the probe with respect to the tube changes both amplitude and profile of the signals as shown in Figures 18 and 19. These data indicate that lateral alignment of the probe is important for accurate measurement of Hb concentration. Thus, by laterally scanning the optoacoustic probe on the skin surface, the practitioner can obtain highly accurate Hb concentration measurements, where the scanning is used to maximize the measuring process - maximize signal amplitude.

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[0077]

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[0078] While this invention has been described fully and completely, it should be understood that, within the scope of the appended claims, the invention may be practiced otherwise than as specifically described. Although the invention has been disclosed with reference to its preferred embodiments, from reading this description those of skill in the art may appreciate changes and modification that may be made which do not depart from the scope of the invention as described above and claimed hereafter.

Claims

1. An optoacoustic apparatus comprising:

a pulsed radiation source;
an optical system (104; 204) including an optical fiber (112; 212), where the system is connected to an output of the radiation source at its proximal end;
a probe (100; 200) including a housing (102; 202), a tip, a ring-shaped piezoelectric element (108; 208), a backing element (106; 206) and an isolating layer (110; 210), where the optical system (104; 204) enters the housing (102; 202) at its proximal end passes through a center of the piezoelectric element (108; 208) and terminates flush with the housing (102; 202) at the probe's tip;
a cable connected to the transducer at its proximal end and exiting the probe out of the back portion of the probe; and
a processing unit connected to the distal end of the cable; **characterized in that**:-

1) said apparatus is for monitoring hemoglobin concentration in a blood vessel of an animal
2) said optical system includes an optical screen (114; 214) and an acoustic screen (116; 216); and
3) said processing unit is for converting the transducer output into a measure of blood hemoglobin concentration and/or hematocrit.

2. An apparatus as claimed in claim 1, wherein the radiation source generates short optical pulses.

3. An apparatus as claimed in claim 1, wherein the radiation source is a laser and the pulses are of a nanosecond duration.

4. An apparatus as claimed in claim 1, wherein the hemoglobin is associated with blood in a blood vessel or tissue site.

5. An apparatus as claimed in claim 1, wherein the piezoelectric element (108; 208) detects pressure waves resulting from pulsed irradiation of the vessel and has sufficient sensitivity, temporal resolution, and bandwidth to collect data from which a hemoglobin concentration is derived.

6. An apparatus as claimed in claim 1, wherein the processing unit calculates a hemoglobin concentration from the recorded optoacoustic pressure profiles and amplitudes.

7. An apparatus as claimed in claim 1, wherein the source produces light pulses in the spectral range from about 400 to about 2500 nm.

8. An apparatus as claimed in claim 1, wherein the source comprises two sources producing light pulses of different wavelengths.

9. An apparatus as claimed in claim 8, wherein the two sources comprises lasers.

10. An apparatus as claimed in claim 1, wherein the vessel comprises an aorta and wherein the probe (100; 200) inserted into an esophagus and pulses travel to the aorta through the esophagus wall adjacent the aorta.

11. An apparatus as claimed in claim 4, wherein the vessel comprises an artery.

12. An apparatus as claimed in claim 11, wherein the artery comprises a radial artery, a carotid artery, a brachial artery, or a femoral artery.

13. An apparatus as claimed in claim 4, wherein the vessel comprises a vein.

14. An apparatus as claimed in claim 13, wherein the vein comprises a vein under the skin or in a hollow organ.

15. An apparatus as claimed in claim 1, wherein the source comprises a Nd:YAG laser or a tunable laser or an optical parametric generator or mixtures or combinations thereof.

16. An apparatus as claimed in claim 15, wherein the tunable lasers comprises a Ti:Sapphire laser or a dye laser or mixtures or combinations thereof.

17. An apparatus as claimed in claim 15, wherein the light pulses have a wavelength of about 548, 568, 587, 805 nm or mixture or combinations thereof where an absorption coefficient of oxy- and deoxygenated blood are similar so that the hemoglobin concentration can be derived from both oxygenated and deoxygenated blood.

18. An apparatus as claimed in claim 15, wherein the light pulses have a wavelength in spectral ranges from about 400 to about 640 or above about 1120nm where an absorption coefficient of oxy- and deoxygenated blood are similar so that the hemoglobin concentration is derived from oxygenated and deoxygenated blood.

19. An apparatus as claimed in claim 1, which is used for hematocrit measurements in the spectral range from 400 to 2500 nm, and preferably in the spectral range above 1350 nm, where optoacoustic signal characteristics are more sensitive to the changes in blood scattering and, therefore, to changes in hematocrit.

20. An apparatus as claimed in claim 1, which is used for blood volume measurements.

21. An apparatus as claimed in claim 1, which is used for ultrasound-guided optoacoustic monitoring of fetal anemia during pregnancy.

22. An apparatus as claimed in claim 1, which is used for measuring hematocrit and a hemoglobin concentration in cord blood.

23. An apparatus as claimed in claim 1, which is used for hemoglobin concentration monitoring in patients with kidney failure or patients on dialysis.

Patentansprüche

1. Optoakustische Vorrichtung, die Folgendes umfasst:

eine gepulste Strahlungsquelle;
ein optisches System (104; 204) mit einem Lichtwellenleiter (112; 212), wobei das System mit einem Ausgang der Strahlungsquelle an seinem proximalen Ende verbunden ist;
eine Sonde (100; 200) mit einem Gehäuse (102; 202), einer Spitze, einem ringförmigen piezoelektrischen Element (108; 208), einem Trägerelement (106; 206) und einer Isolierschicht (110; 210), wobei das optische System (104; 204) an seinem proximalen Ende in das Gehäuse (102; 202) eintritt, durch eine Mitte des piezoelektrischen Elements (108; 208) gelangt und bündig mit dem Gehäuse (102; 202) an der Spitze der Sonde endet;
ein Kabel, das an seinem proximalen Ende mit dem Messaufnehmer verbunden ist und aus dem hinteren Abschnitt der Sonde aus der Sonde austritt; und
eine Verarbeitungseinheit, die mit dem distalen Ende des Kabels verbunden ist,

dadurch gekennzeichnet, dass:

1) die genannte Vorrichtung zum Überwachen der Hämoglobinkonzentration in einem Blutgefäß eines Tiers dient
2) das genannte optische System einen optischen Schirm (114; 214) und einen akustischen Schirm (116; 216) umfasst; und
3) die genannte Verarbeitungseinheit zum Wandeln des Messaufnehmerausgangs in ein Maß von Bluthämo-

globinkonzentration und/oder Hämatokrit dient.

2. Vorrichtung nach Anspruch 1, wobei die Strahlungsquelle kurze optische Impulse erzeugt.

3. Vorrichtung nach Anspruch 1, wobei es sich bei der Strahlungsquelle um einen Laser handelt und die Impulse von einer Dauer im Nanosekundenbereich sind.

4. Vorrichtung nach Anspruch 1, wobei das Hämoglobin mit Blut in einem Blutgefäß oder einer Gewebestelle assoziiert ist.

5. Vorrichtung nach Anspruch 1, wobei das piezoelektrische Element (108; 208) von gepulster Bestrahlung des Gefäßes resultierende Druckwellen erfasst und ausreichend Empfindlichkeit, zeitliche Auflösung und Bandbreite aufweist, um Daten zu sammeln, aus denen eine Hämoglobinkonzentration abgeleitet wird.

6. Vorrichtung nach Anspruch 1, wobei die Verarbeitungseinheit eine Hämoglobinkonzentration aus den aufgezeichneten optoakustischen Druckprofilen und

- amplituden berechnet.

7. Vorrichtung nach Anspruch 1, wobei die Quelle Lichtimpulse im Spektralbereich von ungefähr 400 bis ungefähr 2500 nm erzeugt.

8. Vorrichtung nach Anspruch 1, wobei die Quelle zwei Quellen umfasst, die Lichtimpulse unterschiedlicher Wellenlängen erzeugen.

9. Vorrichtung nach Anspruch 8, wobei die zwei Quellen Laser umfassen.

10. Vorrichtung nach Anspruch 1, wobei das Gefäß eine Aorta umfasst und wobei die Sonde (100; 200) in eine Speiseröhre eingeführt wird und sich Impulse durch die Speiseröhrenwand angrenzend an die Aorta zur Aorta bewegen.

11. Vorrichtung nach Anspruch 4, wobei das Gefäß eine Arterie umfasst.

12. Vorrichtung nach Anspruch 11, wobei die Arterie eine Speichenarterie, eine Halsarterie, eine Oberarmarterie oder eine Oberschenkelarterie umfasst.

13. Vorrichtung nach Anspruch 4, wobei das Gefäß eine Vene umfasst.

14. Vorrichtung nach Anspruch 13, wobei die Vene eine Vene unter der Haut oder in einem hohlen Organ umfasst.

15. Vorrichtung nach Anspruch 1, wobei die Quelle einen Nd:YAG Laser oder einen abstimmbaren Laser oder einen optisch parametrischen Generator oder Mischungen oder Kombinationen derselben umfasst.

16. Vorrichtung nach Anspruch 15, wobei die abstimmbaren Laser einen Ti:Saphir Laser oder einen Farbstofflaser oder Mischungen oder Kombinationen derselben umfassen.

17. Vorrichtung nach Anspruch 15, wobei die Lichtimpulse eine Wellenlänge von ungefähr 548, 568, 587, 805 nm oder Mischungen oder Kombinationen derselben haben, wo ein Absorptionskoeffizient von oxigeniertem und desoxigeniertem Blut ähnlich sind, so dass die Hämoglobinkonzentration sowohl von oxigeniertem als auch von desoxigeniertem Blut abgeleitet werden kann.

18. Vorrichtung nach Anspruch 15, wobei die Lichtimpulse eine Wellenlänge in Spektralbereichen von ungefähr 400 bis ungefähr 640 oder über ungefähr 1120 nm haben, wo ein Absorptionskoeffizient von oxigeniertem und desoxigeniertem Blut ähnlich sind, so dass die Hämoglobinkonzentration von oxigeniertem und desoxigeniertem Blut abgeleitet wird.

19. Vorrichtung nach Anspruch 1, die für Hämatokritmessungen im Spektralbereich von 400 bis 2500 nm und vorzugsweise im Spektralbereich über 1350 nm verwendet wird, wo optoakustische Signaleigenschaften auf die Änderungen in der Blutstreuung und daher auf Änderungen im Hämatokrit empfindlicher sind.

20. Vorrichtung nach Anspruch 1, die für Blutvolumenmessnngen verwendet wird.

21. Vorrichtung nach Anspruch 1, die für die ultraschallgeführte optoakustische Überwachung von fetaler Anämie während der Schwangerschaft verwendet wird.

22. Vorrichtung nach Anspruch 1, die zum Messen von Hämatokrit und einer Hämoglobinkonzentration in Nabelschnurblut verwendet wird.

23. Vorrichtung nach Anspruch 1, die für die Hämoglobinkonzentrationsüberwachung bei Patienten mit Nierenversagen oder Dialysepatienten verwendet wird.

Revendications

1. Appareil opto-acoustique comprenant :

une source de rayonnement pulsé ;
un système optique (104 ; 204) comportant une fibre optique (112 ; 212), où le système est connecté à une sortie de la source de rayonnement à son extrémité proximale ;
une sonde (100 ; 200) comportant un boîtier (102 ; 202), une pointe, un élément piézo-électrique en forme d'anneau (108 ; 208), un élément de support (106 ; 206) et une couche isolante (110 ; 210), où le système optique (104 ; 204) entre dans le boîtier (102 ; 202) à son extrémité proximale, passe par un centre de l'élément piézo-électrique (108 ; 208) et se termine à niveau avec le boîtier (102 ; 202) au niveau de la pointe de la sonde ;
un câble connecté au transducteur à son extrémité proximale et sortant de la sonde par la partie arrière de la sonde ; et
une unité de traitement connectée à l'extrémité distale du câble, **caractérisé en ce que**

1) ledit appareil sert à surveiller la concentration en hémoglobine dans un vaisseau sanguin d'un animal
2) ledit système optique comporte un écran optique (114 ; 214) et un écran acoustique (116 ; 216) ; et
3) ladite unité de traitement sert à convertir la sortie du transducteur en une mesure de la concentration en hémoglobine et/ou d'hématocrite dans le sang.

2. Appareil selon la revendication 1, dans lequel la source de rayonnement génère de courtes impulsions optiques.

3. Appareil selon la revendication 1, dans lequel la source de rayonnement est un laser et les impulsions sont d'une durée de nanosecondes.

4. Appareil selon la revendication 1, dans lequel l'hémoglobine est associée au sang dans un site de vaisseau ou de tissu sanguin.

5. Appareil selon la revendication 1, dans lequel l'élément piézoélectrique (108 ; 208) détecte des ondes de pression résultant de l'irradiation pulsée du vaisseau et a une sensibilité, résolution temporelle et bande passante suffisantes pour collecter des données à partir desquelles une concentration en hémoglobine est dérivée.

6. Appareil selon la revendication 1, dans lequel l'unité de traitement calcule une concentration en hémoglobine à partir des profils et amplitudes des pressions opto-acoustiques enregistrées.

7. Appareil selon la revendication 1, dans lequel la source produit des impulsions de lumière dans la gamme spectrale d'environ 400 à environ 2500 nm.

8. Appareil selon la revendication 1, dans lequel la source comprend deux sources produisant des impulsions de lumière de différentes longueurs d'onde.

9. Appareil selon la revendication 8, dans lequel les deux sources comprennent des lasers.

10. Appareil selon la revendication 1, dans lequel le vaisseau comprend une aorte et dans lequel la sonde (100 ; 200) insérée dans un oesophage et les impulsions se propagent jusqu'à l'aorte à travers la paroi de l'oesophage adjacente à l'aorte.

11. Appareil selon la revendication 4, dans lequel le vaisseau comprend une artère.

12. Appareil selon la revendication 11, dans lequel l'artère comprend une artère radiale, une artère carotide, une artère brachiale, ou une artère fémorale.

13. Appareil selon la revendication 4, dans lequel le vaisseau comprend une veine.

14. Appareil selon la revendication 13, dans lequel la veine comprend une veine située sous la peau ou dans un organe creux.

15. Appareil selon la revendication 1, dans lequel la source comprend un laser Nd:YAG ou un laser accordable ou un générateur paramétrique optique ou des mélanges ou combinaisons de ceux-ci.

16. Appareil selon la revendication 15, dans lequel les lasers accordables comprennent un laser Ti:saphir ou un laser à colorant ou des mélanges ou combinaisons de ceux-ci.

17. Appareil selon la revendication 15, dans lequel les impulsions de lumière ont une longueur d'onde d'environ 548, 568, 587, 805 mm ou un mélange ou des combinaisons de celles-ci où des coefficients d'absorption du sang oxygéné et désoxygéné sont semblables de telle sorte que la concentration en hémoglobine puisse être dérivée à la fois du sang oxygéné et du sang désoxygéné.

18. Appareil selon la revendication 15, dans lequel les impulsions de lumière ont une longueur d'onde comprise dans des plages spectrales d'environ 400 à environ 640 ou plus d'environ 1120 nm où des coefficients d'absorption du sang oxygéné et désoxygéné sont semblables de telle sorte que la concentration en hémoglobine soit dérivée à la fois du sang oxygéné et du sang désoxygéné.

19. Appareil selon la revendication 1, lequel est utilisé pour des mesures d'hématocrite dans la gamme spectrale de 400 à 2500 nm, et de préférence dans la gamme spectrale au-dessus de 1350 nm, où les caractéristiques de signal opto-acoustique sont plus sensibles aux changements de la diffusion dans le sang et, en conséquence, aux changements de l'hématocrite.

20. Appareil selon la revendication 1, lequel est utilisé pour des mesures de volume sanguin.

21. Appareil selon la revendication 1, lequel est utilisé pour la surveillance opto-acoustique guidée par ultrasons de l'anémie foetale durant la grossesse.

22. Appareil selon la revendication 1, lequel est utilisé pour mesurer l'hématocrite et une concentration en hémoglobine dans le sang de cordon ombilical.

23. Appareil selon la revendication 1, lequel est utilisé pour la surveillance de la concentration en hémoglobine chez les patients souffrant d'insuffisance rénale ou les patients sous dialyse.

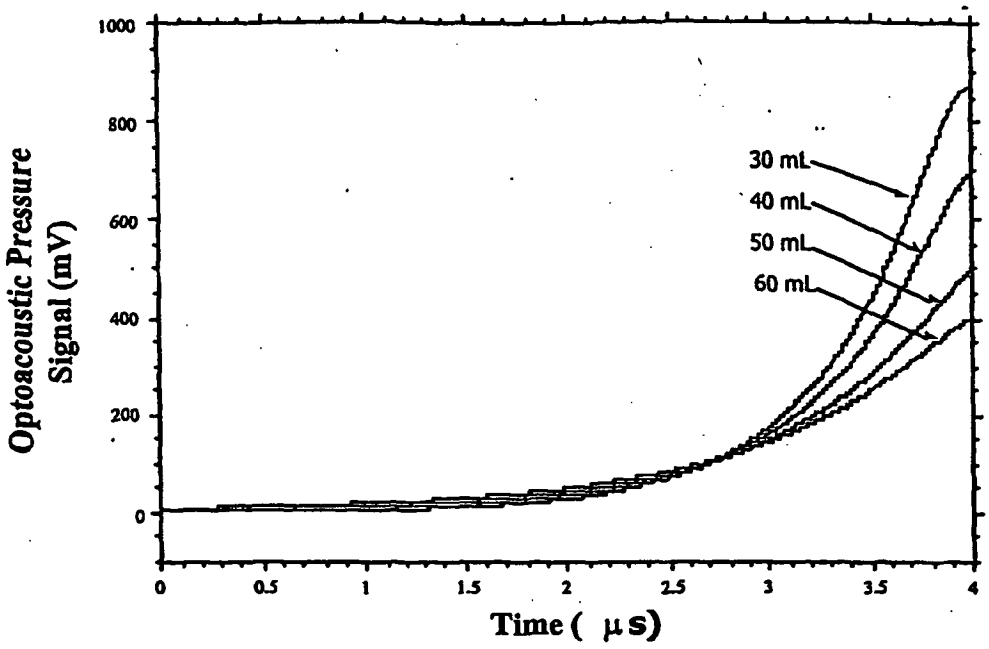
Optoacoustic Pressure Signal (mV)
1000
800
600
400
200
0
0
0.5
1
1.5
2
2.5
3
3.5
4
Time (μs)
30 mL
40 mL
50 mL
60 mL

FIG. 1

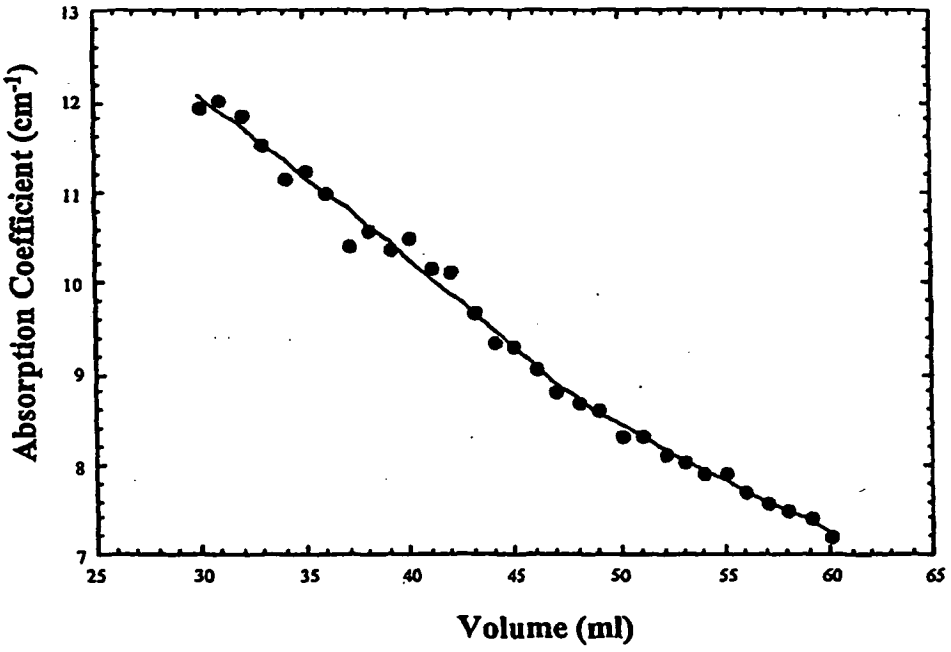
Absorption Coefficient (cm-1)
13
12
11
10
9
8
7
25
30
35
40
45
50
55
60
65
Volume (ml)

FIG. 2

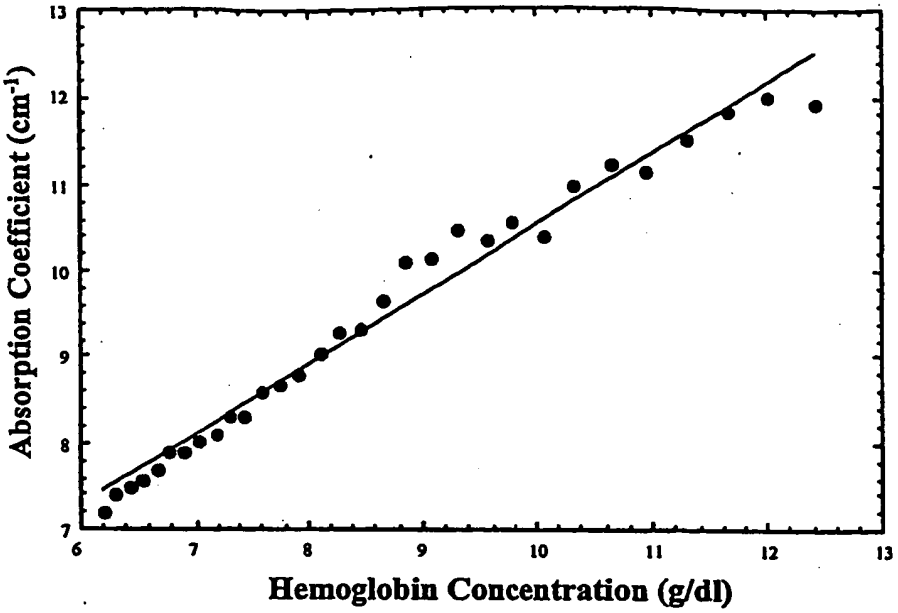
Absorption Coefficient (cm-1)
Hemoglobin Concentration (g/dl)
13
12
11
10
9
8
7
6
7
8
9
10
11
12
13

FIG. 3

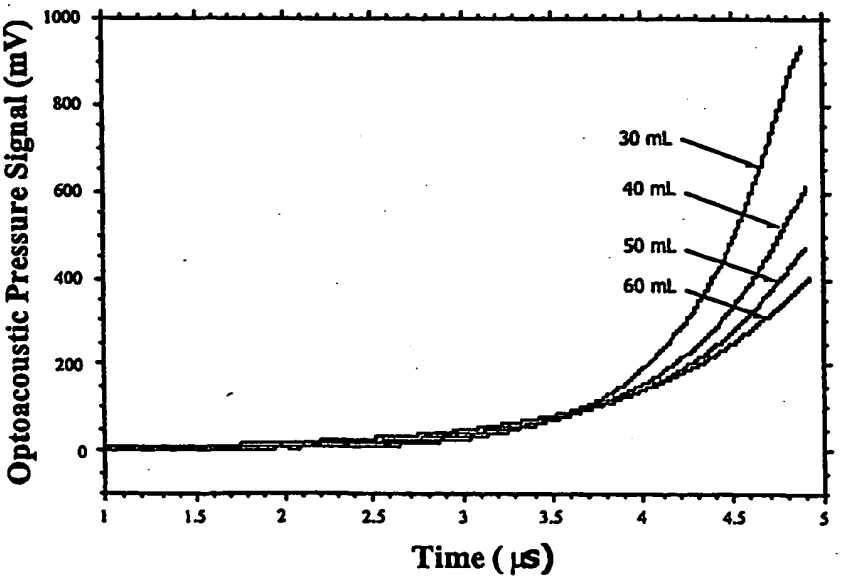
Optoacoustic Pressure Signal (mV)
Time (μs)
1000
800
600
400
200
0
1
1.5
2
2.5
3
3.5
4
4.5
5
30 mL
40 mL
50 mL
60 mL

FIG. 4

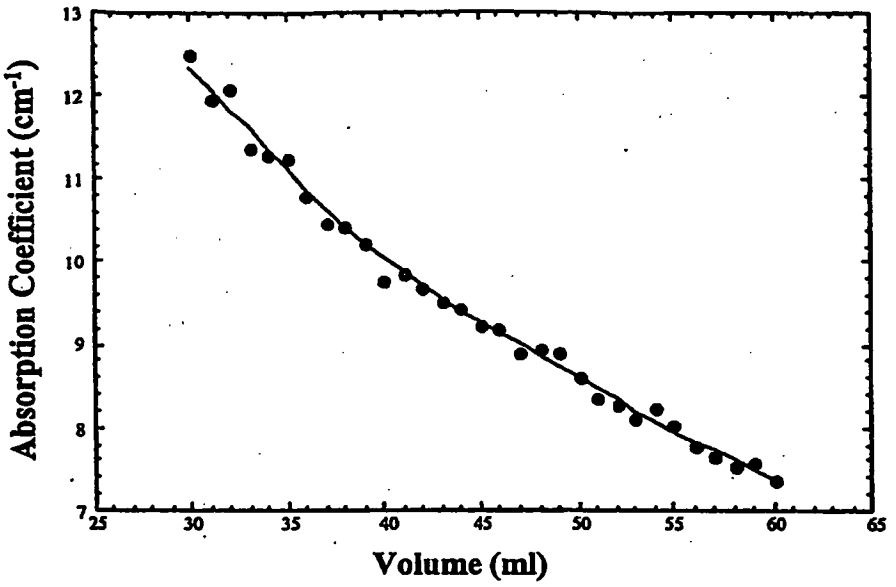
Absorption Coefficient (cm-1)
13
12
11
10
9
8
7
25
30
35
40
45
50
55
60
65
Volume (ml)

FIG. 5

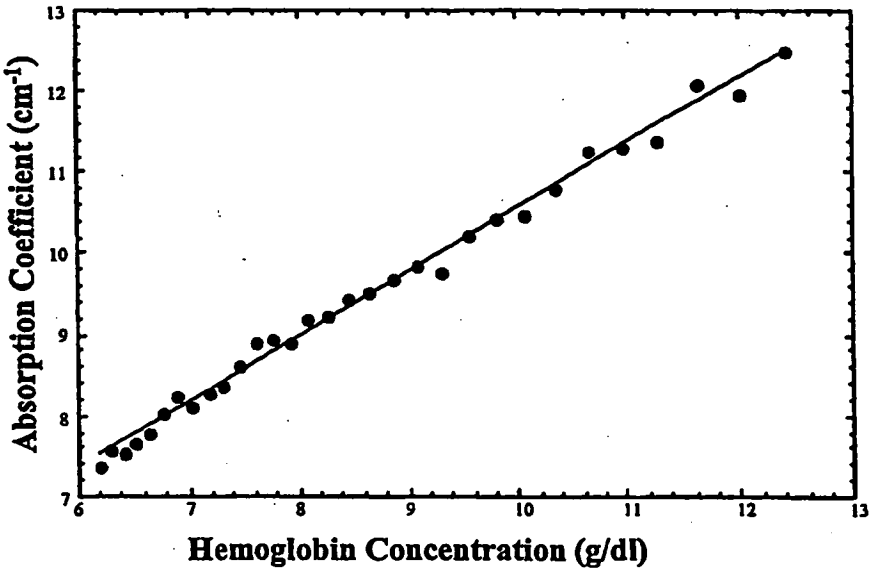
Absorption Coefficient (cm-1)
13
12
11
10
9
8
7
6
7
8
9
10
11
12
13
Hemoglobin Concentration (g/dl)

FIG. 6

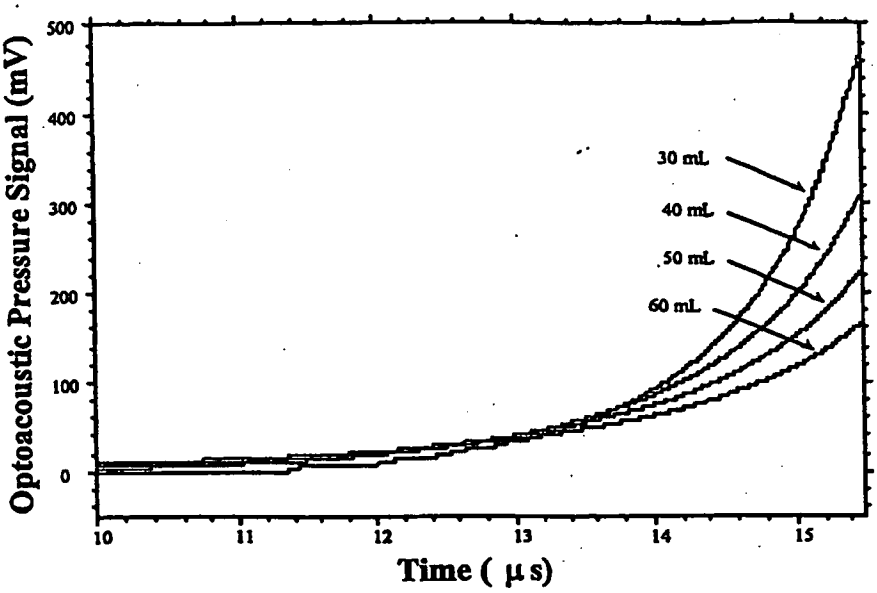
Optoacoustic Pressure Signal (mV)
500
400
300
200
100
0
10
11
12
13
14
15
Time (μs)
30 mL
40 mL
50 mL
60 mL

FIG. 7

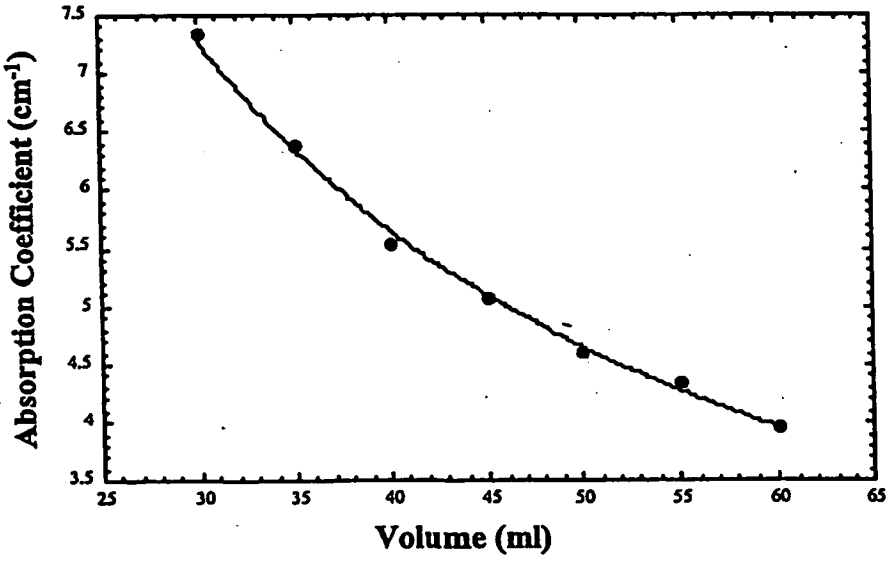
Absorption Coefficient (cm-1)
7.5
7
6.5
6
5.5
5
4.5
4
3.5
25
30
35
40
45
50
55
60
65
Volume (ml)

FIG. 8

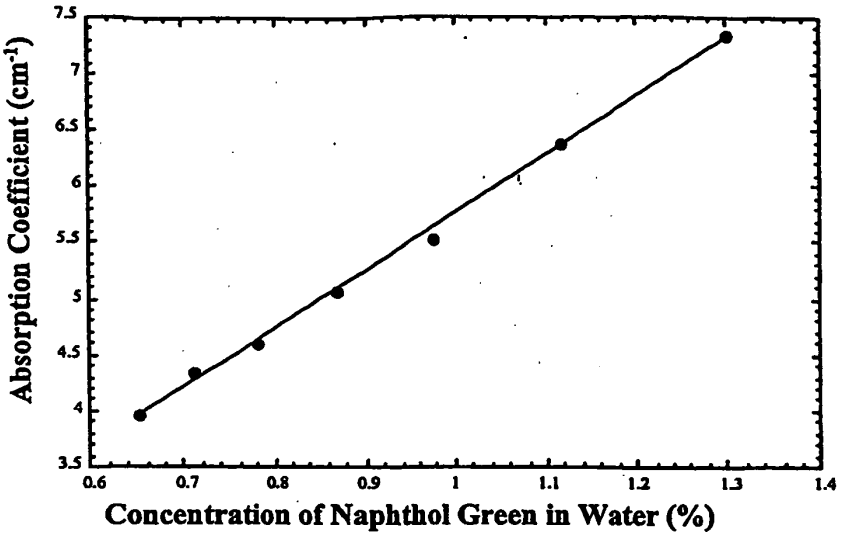

FIG. 9

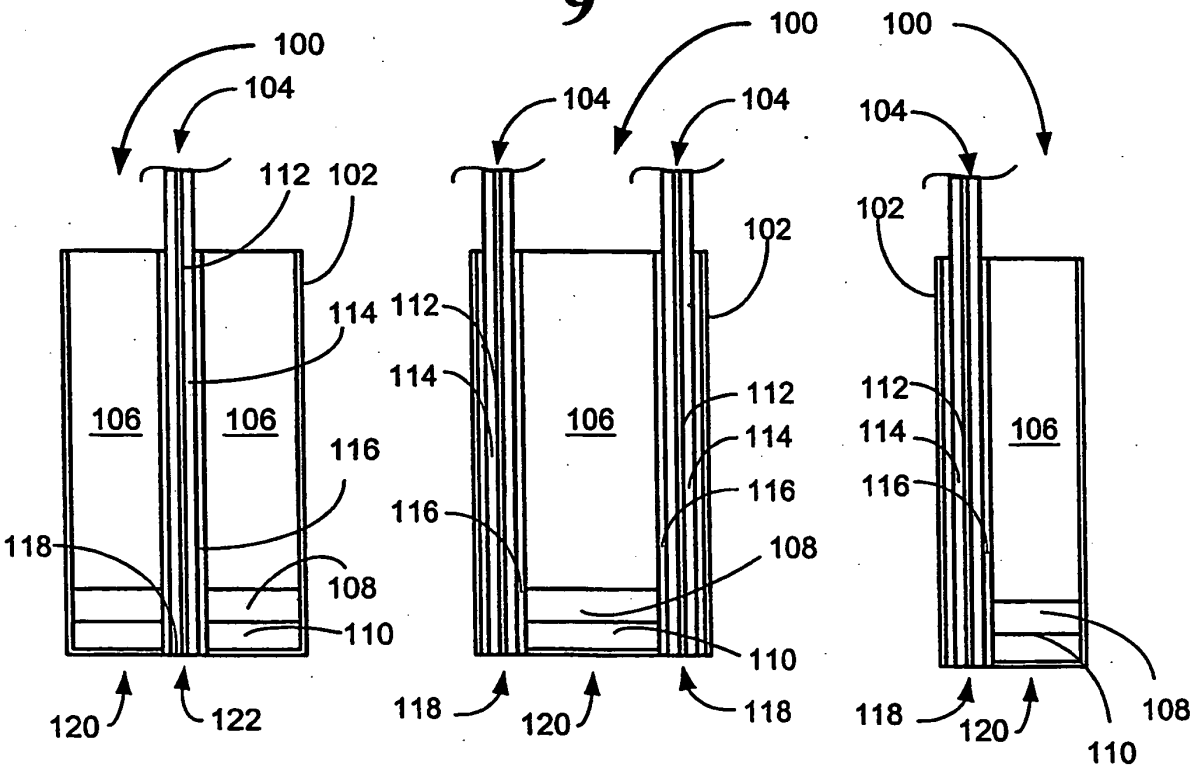

FIG. 10A FIG. 10B FIG. 10C

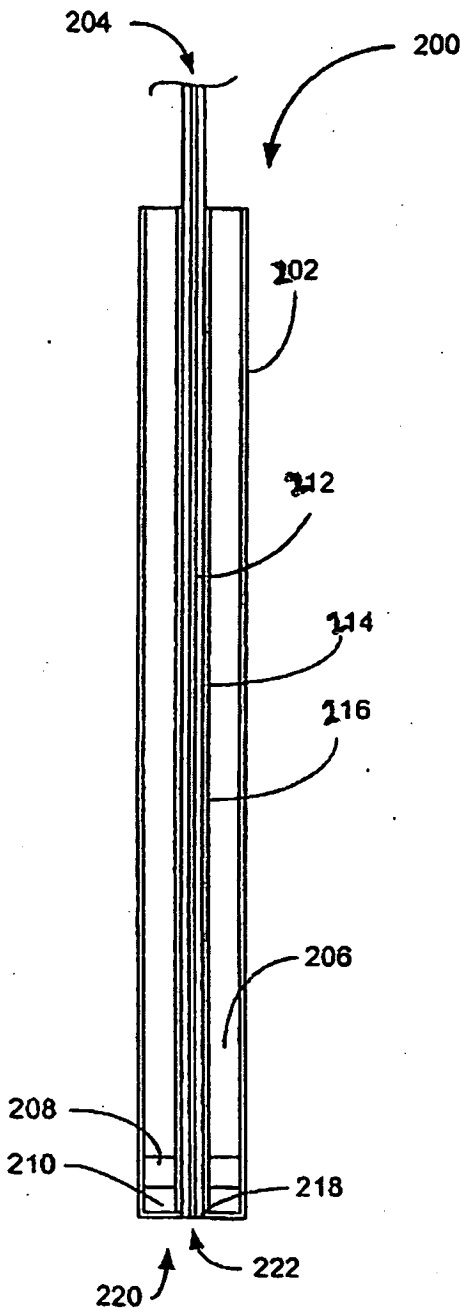

FIG. 10D

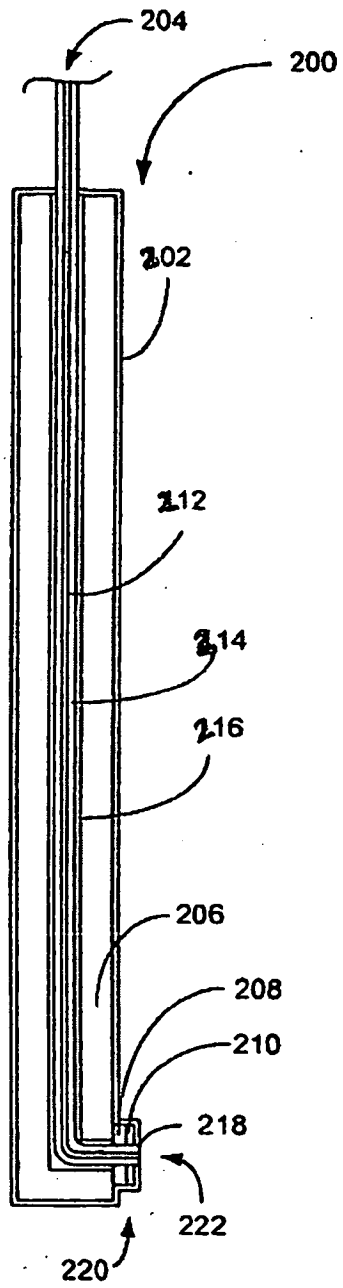

FIG. 10E

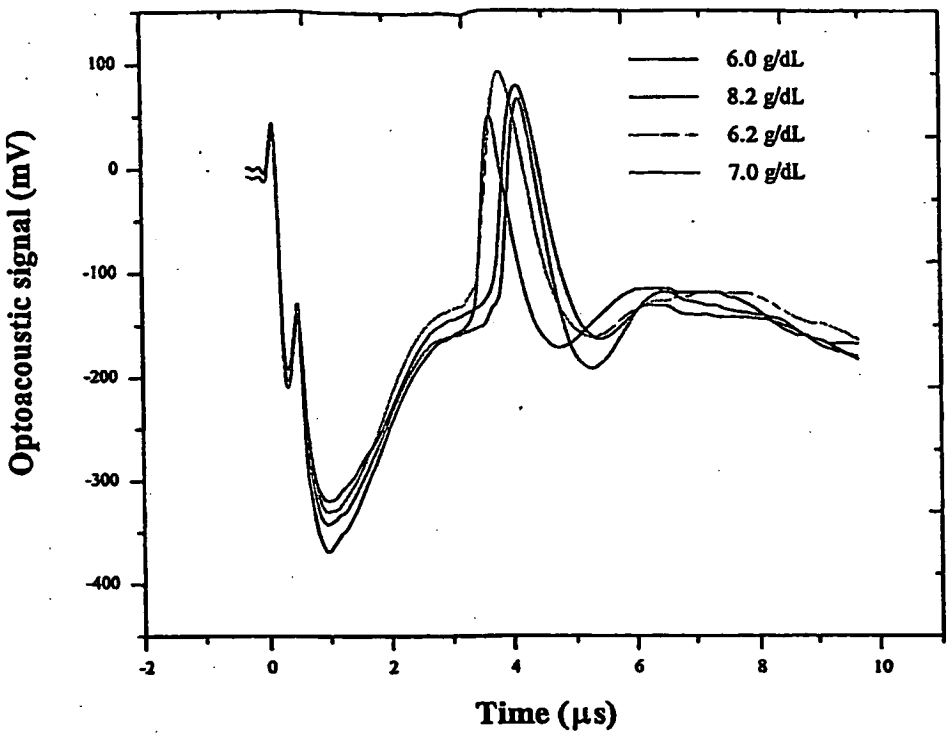
Optoacoustic signal (mV)
100
0
-100
-200
-300
-400
-2
0
2
4
6
8
10
Time (μs)
6.0 g/dL
8.2 g/dL
6.2 g/dL
7.0 g/dL

FIG. 11

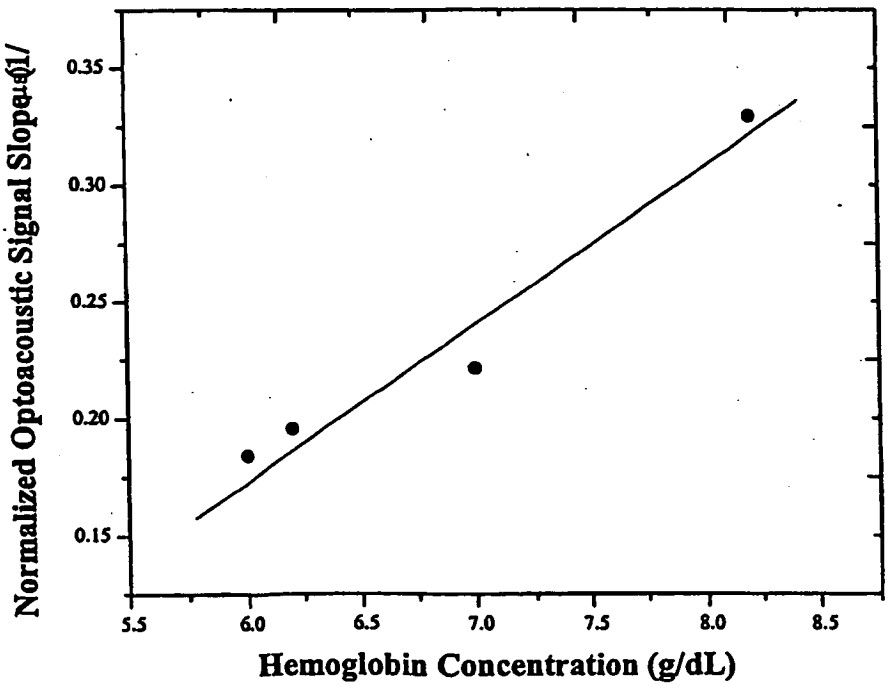
Normalized Optoacoustic Signal Slope
0.35
0.30
0.25
0.20
0.15
5.5
6.0
6.5
7.0
7.5
8.0
8.5
Hemoglobin Concentration (g/dL)

FIG. 12

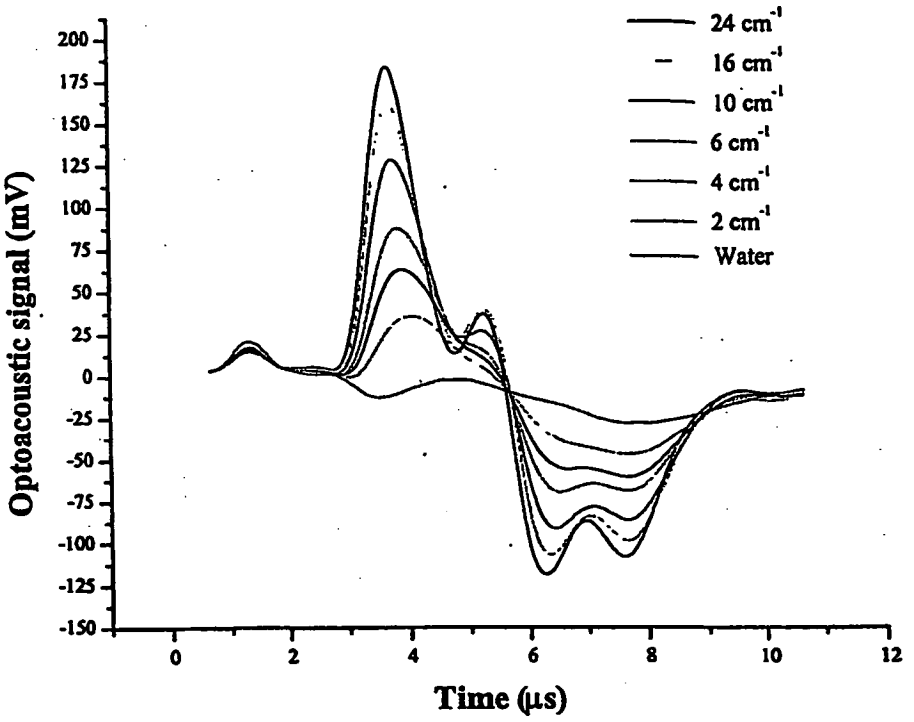
24 cm-1
16 cm-1
10 cm-1
6 cm-1
4 cm-1
2 cm-1
Water
Optoacoustic signal (mV)
Time (μs)

FIG. 13

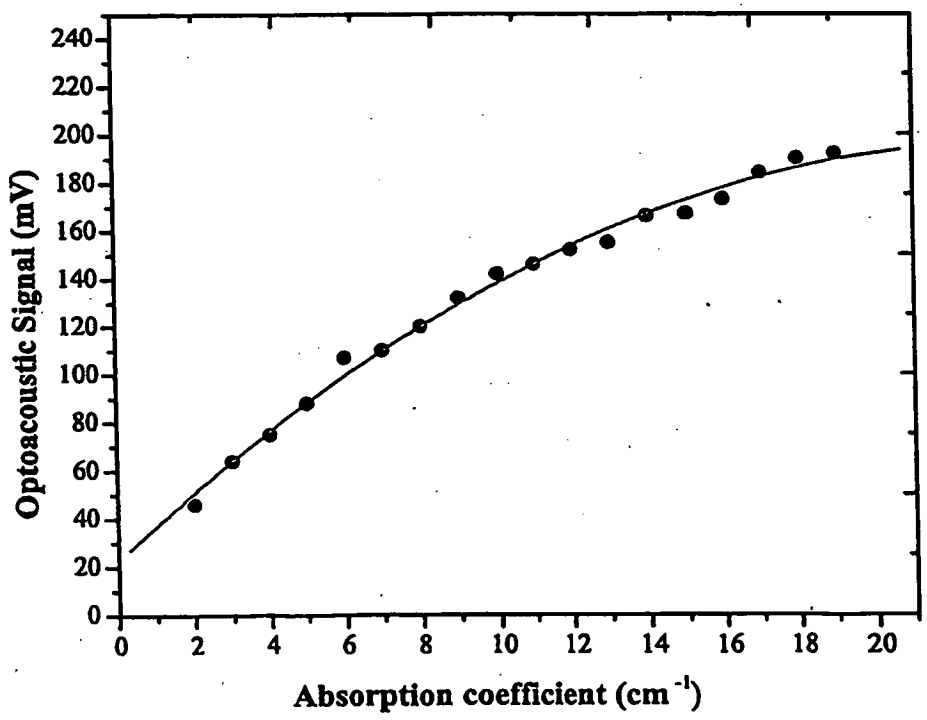
Optoacoustic Signal (mV)
Absorption coefficient (cm-1)

FIG. 14

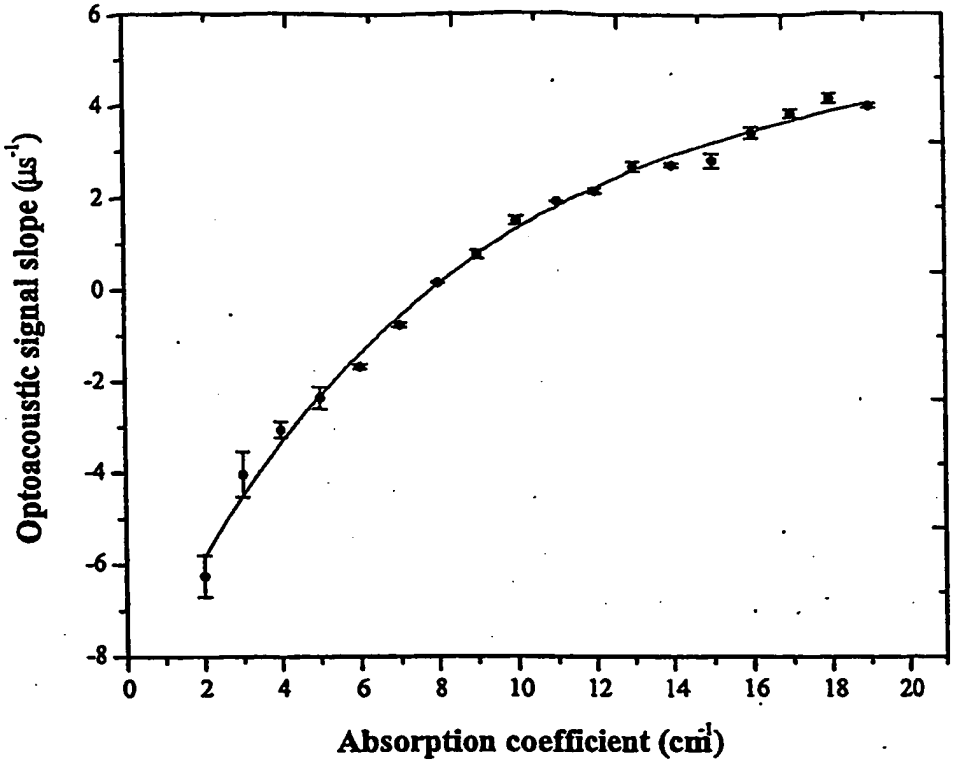
Optoacoustic signal slope (μs-1)
Absorption coefficient (cm-1)
6
4
2
0
-2
-4
-6
-8
0
2
4
6
8
10
12
14
16
18
20

FIG. 15

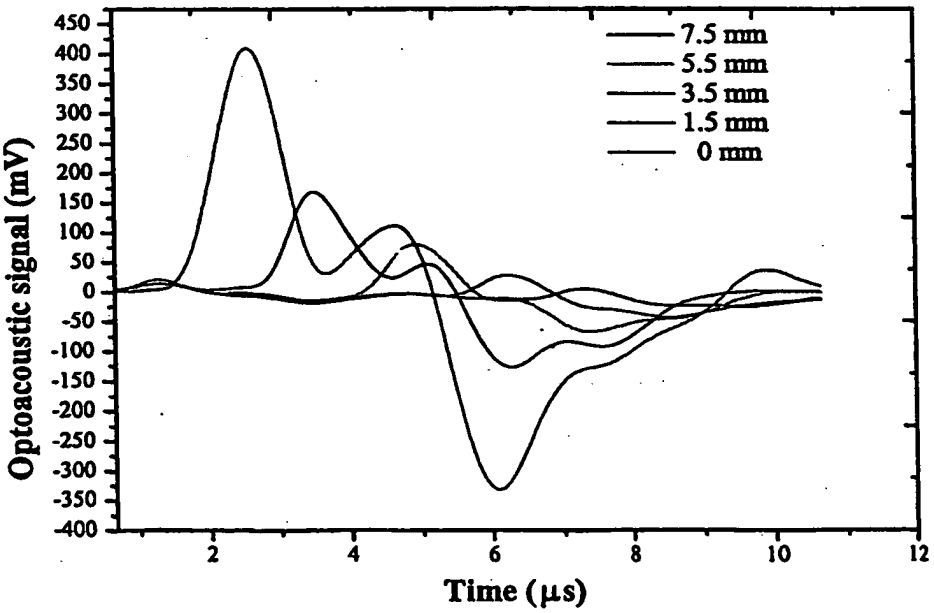
Optoacoustic signal (mV)
Time (μs)
7.5 mm
5.5 mm
3.5 mm
1.5 mm
0 mm
450
400
350
300
250
200
150
100
50
0
-50
-100
-150
-200
-250
-300
-350
-400
2
4
6
8
10
12

FIG. 16

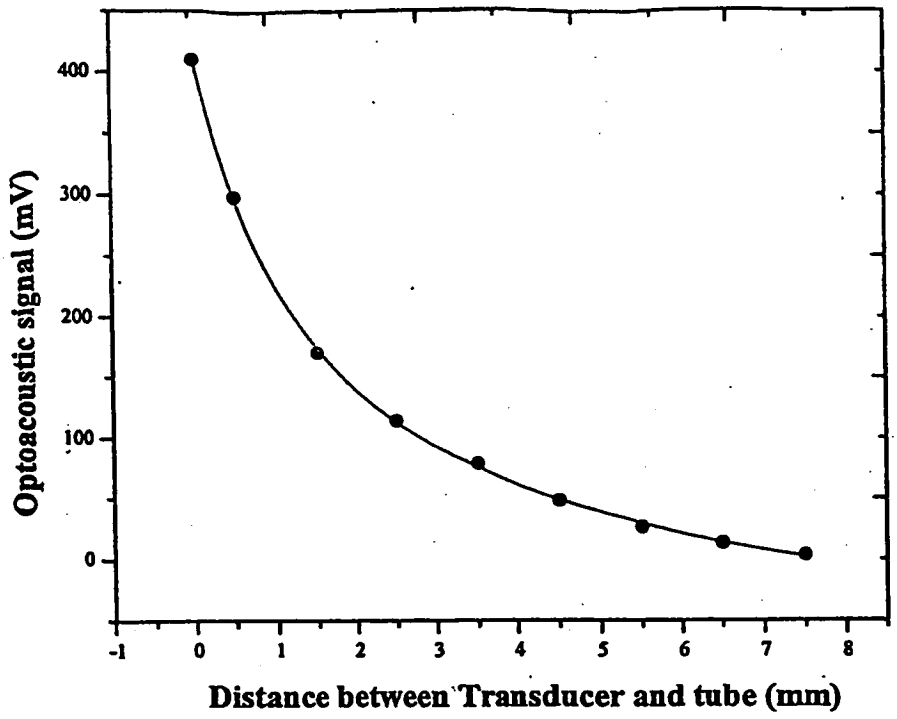
Optoacoustic signal (mV)
400
300
200
100
0
-1
0
1
2
3
4
5
6
7
8
Distance between Transducer and tube (mm)

FIG. 17

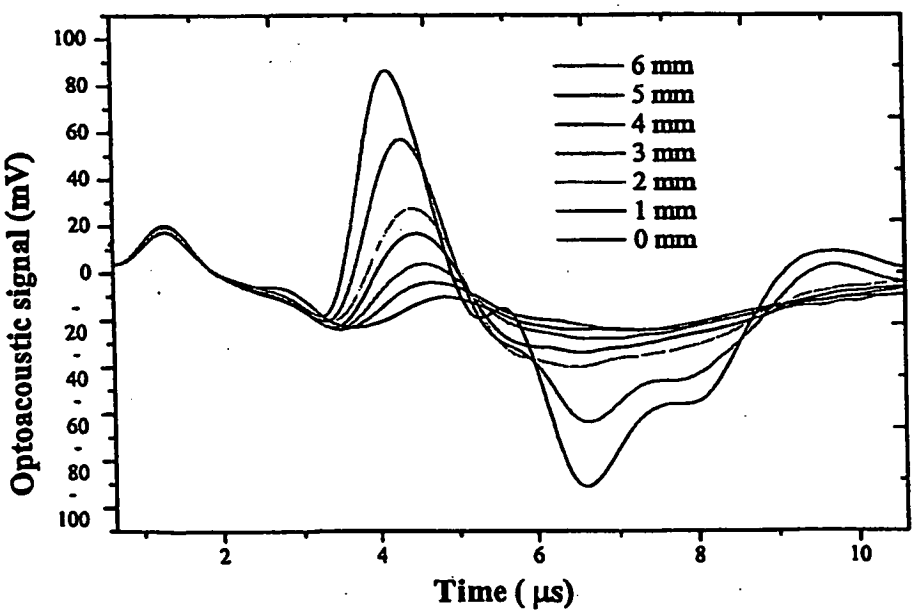
Optoacoustic signal (mV)
100
80
60
40
20
0
20
40
60
80
100
2
4
6
8
10
Time (μs)
6 mm
5 mm
4 mm
3 mm
2 mm
1 mm
0 mm

FIG. 18

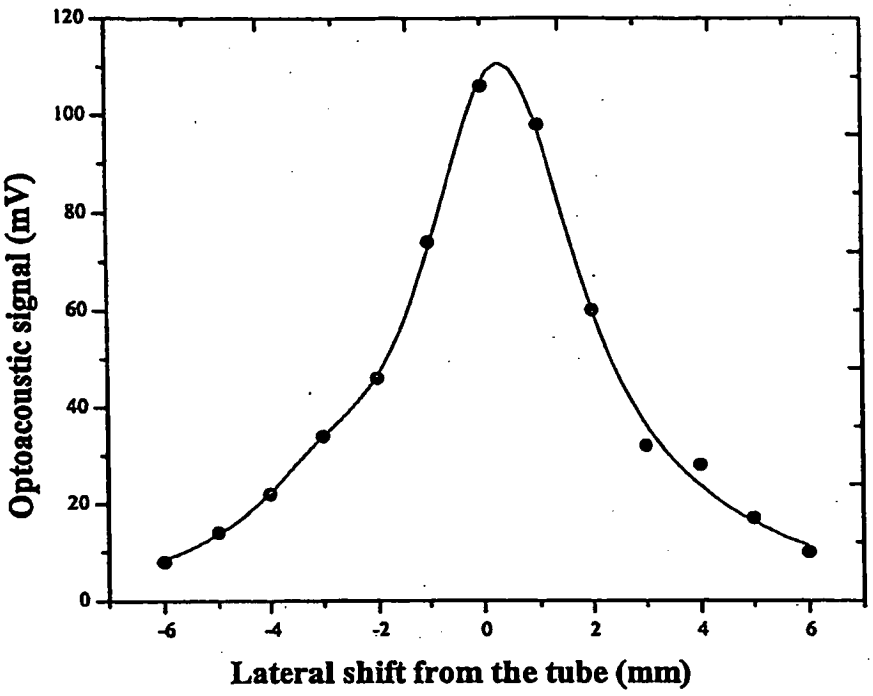
Optoacoustic signal (mV)
120
100
80
60
40
20
0
-6
-4
-2
0
2
4
6
Lateral shift from the tube (mm)

FIG. 19

REFERENCES CITED IN THE DESCRIPTION

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专利名称(译)	连续光声监测血红蛋白浓度和血细胞比容		
公开(公告)号	EP1526804B1	公开(公告)日	2009-03-11
申请号	EP2002756648	申请日	2002-07-26
申请(专利权)人(译)	校董会，得克萨斯州大学系统		
当前申请(专利权)人(译)	校董会，得克萨斯州大学系统		
[标]发明人	ESENALIEV RINAT MOTAMEDI MASSOUD PROUGH DONALD D		
发明人	ESENALIEV, RINAT MOTAMEDI, MASSOUD PROUGH, DONALD, D.		
IPC分类号	A61B5/00 A61B8/00 G01N21/17 A61B8/12		
CPC分类号	A61B5/0086 A61B5/0095 A61B5/14535 A61B8/12 G01N21/1702		
其他公开文献	EP1526804A1		
外部链接	Espacenet		

摘要(译)

本发明公开了一种光声装置，其包括脉冲辐射的辐射源和探针，探针具有与动物体的组织部位接触放置的正面。该探头还包括光纤，该光纤终止于探头前面的表面，并在其另一端连接到脉冲激光器。探头的前面还安装有压电换能器，用于检测连接到处理单元的辐射脉冲的声响应，该处理单元将换能器信号转换成血红蛋白浓度和/或血液血细胞比容的量度。

$$V = C\frac{\Delta V}{\Delta C} \qquad (1)$$