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(54) **Method for non-invasive measurements of blood related parameters**

(57) A probe device for use in non-invasive optical measurements of at least one parameter of the patient's blood. The probe device comprises a finger holder in the form of a clip member that secures a fingertip between its clamping legs. The probe device supports a measuring unit for applying optical measurements to a measurement location on the finger and carries a pressurizing assembly operable for applying controllably variable, substantially under-systolic pressure to the finger in the vicinity of the measurement location. Several measurement sessions are performed at the measurement location with at least two different wavelength of incident light

to detect light response of the medium and generate measured data indicative thereof, and the pressure applied to the vicinity of the measurement location is simultaneously varied during measurements. The light response of the medium corresponding to different wavelength of the incident light and different pressure values during measurements. The light response of the medium corresponding to different wavelength of the incident light and different pressure values is analyzed, and an optimal pressure value is determined, so as to utilize the corresponding light response of the medium for deriving therefrom the at least on blood parameter.

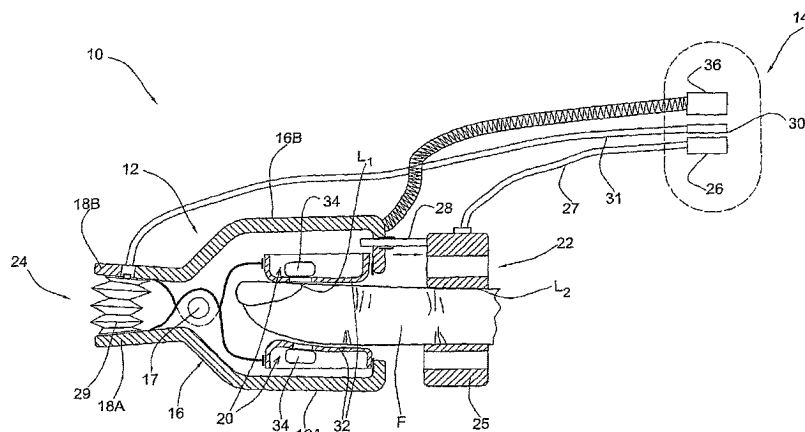


FIG. 1

Description

FIELD OF THE INVENTION

[0001] This invention is generally in the field of non-invasive optical measurement techniques for measuring blood parameters, and relates to a probe to be applied to a patient's finger.

BACKGROUND OF THE INVENTION

[0002] Non-invasive techniques for measuring various blood parameters, such as blood oxygen saturation and the concentration of substances contained in the blood (hemoglobin, glucose and other substances) have become very popular, since they do not require the withdrawal of a blood sample from a patient's body. Optical monitoring techniques of the kind specified typically utilize the detection of light transmitted or reflected from the location on the patient's body under measurement, and are based on spectrophotometric measurements enabling the indication of the presence of various blood constituents based on known spectral behaviors of these constituents. Most of these techniques utilize a measurement optical device or probe, designed in a manner to be attached to the patient's finger, which includes an optical assembly for irradiating the finger with light and detecting its light response.

[0003] US Patent No. 5,810,723 discloses an apparatus for the non-invasive monitoring of a patient's carboxyhemoglobin level. The patient breathes oxygen to saturate his blood hemoglobin prior to detection. The apparatus utilizes a clamp with arms holding the patient's finger: one arm supports a light emitting source and the other supports a detector. A microprocessor controls the measurements and processes the detected signals.

[0004] US Patent 5,638,816 and its continuation, US Patent 5,860,919, disclose an apparatus for the non-invasive monitoring of blood parameters by applying pressure to the patient's finger, thus inducing an active pulse therein. The induced change of blood volume enables a better signal-to-noise ratio to be obtained.

[0005] US 5,782,757 discloses a measuring devices in the form of disposable, folded adhesive sensors with optics embedded therein. The probe is designed so as to fit comfortably onto a patient's fingertip.

[0006] All the conventional devices of the kind specified are aimed at measuring enhanced optical pulsatile signals caused by the changes in the volume of the blood containing medium (finger). It is known that a regular optical pulsatile signal is typically 2-3% of the total transmission. The above devices are capable of obtaining the enhanced pulsatile signal that reach 8-10% of the total light transmission intensity. This enhancement of the natural pulsatile signal is a boundary of all conventional techniques of the kind specified.

[0007] A different technique is disclosed in a PCT application, International Publication No. WO 99/65384, as-

signed to the assignee of the present application. This is an occlusion based technique, where the measured signals are not pulsatile. According to this technique, the state of blood cessation is created in a medium under measurement, and measurements are taken during this state. This enables to obtain a significantly enhanced light response of the medium, as compared to that of the previously described techniques dealing with the pulsatile signals. To create such a state of blood cessation, over-systolic pressure needs to be applied to the patient's finger at a location upstream of the area under measurement, with respect to the direction of normal blood flow. Once the blood flow cessation state is established, the optical characteristics start to change dramatically, such that they differ from those of the fleshy medium with a normal blood flow by about 25 to 45%, and sometimes even by 60 %. At least two timely separated measurement sessions are performed, each including at least two measurements with different wavelengths of incident radiation. None of the conventional probes is suitable for these purposes. A probe in the form of a finger holder, suitable for applying over systolic pressure to a first location on the patient's finger and applying optical measurements to a second location downstream of the first location, is disclosed in a co-pending US application Serial No. 09/407390, assigned to the assignee of the present application.

SUMMARY OF THE INVENTION

[0008] There is a need in the art to further improve non-invasive measurements of blood parameters, by providing a novel probe device to be used in non-invasive optical measurements enabling the application of a variable controlled pressure to the patient's organ (e.g., his finger) in the vicinity of a measurement location.

[0009] It is a major object of the present invention to provide such a device that optimizes the finger tissue and blood volume, thereby providing conditions for measurements with maximum accuracy.

[0010] It was found by the inventors that the accuracy of the measured signal can be improved even more by applying certain under-systolic pressure (0-250mmHg) to a region in the vicinity of a measurement location. This pressure, required for significantly improving the accuracy of measurements, may be different for different patients, depending *inter alia* on the internal blood pressure of the specific patient, and individual peculiarity of the finger size, shape and physiological conditions. This optimal pressure value depends also on the rigidity of the construction of probe device itself. Therefore means should be provided enabling to controllably vary the magnitude of the applied pressure.

[0011] Generally speaking, the present invention provides an active sensing means that enables to select an optimal pressure for a specific patient, such that the application of this pressure provides an optimal optical measurement signal for deriving therefrom the correct

value of the parameter to be measured. In other words, the present invention enables to adjust the conditions of a measurement location on the patient's organ to the optimal signal determination.

[0012] Thus, according to one broad aspect of the present invention, there is provided a method of non-invasive optical measurement of at least one parameter of the patient's blood, the method comprising the steps of:

- (a) applying a probe device to the patient's blood perfused fleshy medium, wherein the probe device carries an optical measurement unit and a pressurizing assembly operable to apply controllably varying substantially under-systolic pressure to a measurement location on said medium;
- (b) performing several measurement sessions to a measurement location on said medium to detect light response of the medium and generate measured data indicative thereof, and simultaneously varying the pressure applied to the vicinity of said measurement location, wherein each measurement session utilizes at least two different wavelength of incident light;
- (c) analyzing the light response of the medium corresponding to different wavelengths of the incident light and different pressure values, and determining an optimal pressure value, so as to utilize the corresponding light response of the medium for deriving therefrom said at least one blood parameter.

[0013] Preferably, the method according to the invention also comprises the application of over-systolic pressure to a location upstream of the measurement location, with respect to the direction of normal blood flow in the medium, so as to create the state of blood flow cessation. In this case, the measurements are taken during this state. Several time-separated measurement sessions can be performed either during the single blood-cessation state, or during the sequential blood cessation state. The latter operational mode is actually the so-called "multiple-occlusion", obtained by sequentially applying and releasing the over-systolic pressure.

[0014] Parameters that can be measured include oxygen saturation and the concentration of substance in blood, such as hemoglobin, glucose, etc. The present invention may utilize a calibration stage, during which various patients undergo measurements, and calibration curves corresponding to different blood parameters as functions of the applied under-systolic pressure are plotted.

[0015] The wavelengths of incident light are selected in accordance with the parameter to be measured. Preferably, several different wavelengths are sequentially applied, so as to obtain data from which different blood parameters can be derived within the same measurement session.

[0016] The probe device according to the invention utilizes a finger holder carrying a measurement unit and a pressurizing assembly, all operated by a control system.

The measurement unit typically comprises illumination and detection systems, arranged so as to detect reflected or transmitted light, as the case may be. The pressurizing assembly is designed so as to apply variable controlled pressure to the tissue in the vicinity of the measurement location.

[0017] Generally, the probe device may be associated with any other suitable patient's organ, such as his hand or wrist. If the patient's hand is considered, the rigid connector engages the patient's arm to prevent its folding at the elbow joint. It is more practical, however, to apply the device to the patient's finger.

[0018] The finger holder is in the form of a clip securing the fingertip between its legs and carrying the measurement unit. The clip may be formed with one pair or two pairs of legs. The four-leg design advantageously enables to provide four-sided support for the finger, thereby preventing its folding at the distal phalanx. A pair of manipulating arms is used for opening and closing the clip when putting the device in operation. In the case of the two-legged design, the extensions of the legs serve as the manipulating arms. In the case of the four-legged design, the manipulating arms are coupled to the legs through any suitable mechanism, enabling the simultaneous pivotal movement of all the legs.

[0019] The pressurizing assembly is of a pneumatic type. According to one embodiment of the invention, the pressurizing assembly comprises a bellow-like cushion, which is interconnected between the manipulating arms by its opposite ends and is coupled to the drive operated by the control system. The expansion and squeezing of the sleeve thus operates the pivotal movement of the manipulating arms, thereby weakening or enhancing the clamping effect of the clip legs. According to another embodiment of the invention, the pressurizing assembly comprises a balloon-like flat cushion attached to the inner side of the clip between its upper leg and a flexible cushion-like member contacting the patient's finger, so as to press on the finger portion below the clip. In this case a locking device is provided to prevent the opening of the clip. According to yet another embodiment of the invention, the pressurizing assembly comprises a ring-like cushion attached to the inner side of the clip so as to wrap the finger, when putting the device into operation. The control system operates the expansion and squeezing of the cushion.

- There is thus provided according to another aspect of the invention, a probe device to be used in non-invasive optical measurements of a patient's blood parameters, the probe device comprising a finger holder having a clip member that secures a fingertip between its clamping legs, wherein the finger holder supports a measuring unit for applying optical measurements to a measurement location on the finger, and carries a pressurizing assembly operable for applying controllably variable, substantially under-systolic pressure to the finger in the vicinity of

said measurement location.

[0020] The probe device may be used with a pulse oxymeter, wherein the application of the controllably varied under-systolic pressure enables to derive more information from measured signals. This information contains the maximal amplitude of a pulsatile signal and/or AC/DC ratio.

[0021] Thus, according to yet another aspect of the present invention, there is provided a pulse-oxymeter utilizing the above probe device and a control system that operates the pressurizing assembly and the measurement unit and generates data indicative of the measured parameters.

[0022] Preferably, the probe device also comprises an additional pressurizing assembly, which may also be of a pneumatic type, and operated by the same drive means as the above-described pressurizing assembly. The additional pressurizing assembly is aimed at applying over-systolic pressure, so as to cause the state of blood flow cessation and enable the occlusion-based measurements. The over-systolic pressure is applied to a location upstream of the measurement location, with respect to a normal blood flow direction.

[0023] Preferably, the additional pressurizing assembly is coupled to the clip through a substantially rigid connector engaging the finger along its middle phalanx and proximal interphalangeal joint. This is associated with the fact that occlusion-based measurements are non-volumetric, and the changes in volume of blood in the finger portion undergoing measurement are undesirable for such measurements. However, it is a natural tendency of the finger under pressure (over-systolic pressure) to fold at the proximal interphalangeal joint, thereby causing undesirable changes in blood volume. By providing a substantially rigid support for the finger at the region of the middle phalanx during measurement, such undesirable folding can be avoided.

[0024] The present invention also provides an optical measurement device for the non-invasive measurement of patient's blood parameters, the device comprising:

- a finger holder for attaching to the patient's finger, wherein the finger holder is in the form of a clip member, which secures a fingertip between its clamping legs and supports a measuring unit in a manner allowing to apply optical measurements to a measurement location on the finger;
- a first pressurizing assembly operable for applying over-systolic pressure to a location on the patient's finger upstream of said measurement location with respect to a normal blood flow direction, so as to create a state of blood flow cessation at said measurements location;
- a second pressurizing assembly associated with the finger holder and operable for applying desired pressure to the finger in the vicinity of said measurement location; and

- a control system selectively operating the first and second pressurizing assembly, and selectively operating the measuring unit, the control system having a processor that received data indicative of measured signals coming from the measuring unit and analyzes said data.

BRIEF DESCRIPTION OF THE DRAWINGS

[0025] In order to understand the invention and to see how it may be carried out in practice, a preferred embodiment will now be described, by way of non-limiting example only, with reference to the accompanying drawings, in which:

Fig. 1 is a schematic illustration of a probe device according to one embodiment of the invention;

Fig. 2 is a schematic illustration of a probe device according to another embodiment of the invention;

Fig. 3 is a schematic illustration of a probe device according to yet another embodiment of the invention

Figs. 4a to 4d graphically illustrate experimental results obtained with different operational modes of the probe device according to the invention.

DETAILED DESCRIPTION OF A PREFERRED EMBODIMENT

[0026] Referring to Fig. 1, there is illustrated a probe device, generally designated **10**, applied to a patient's finger **F** for performing the non-invasive measurement of the patient's blood parameters, such as oxygen saturation, blood pressure or the concentration of various substances, such as hemoglobin, glucose, cholesterol and other analyte concentrations. The probe **10** is in the form of a finger holder **12** mounted on the patient's finger **F**, and is coupled to a control system **14**.

[0027] The finger holder **12** is in the form of a clip member **16** having clamping legs - two legs **16A** and **16B** in the present example, pivotal about an axis **17**, for securing the patient's finger **F** therebetween. A pair of manipulating arms **18A** and **18B** operates the pivotal movement of the clamping legs to attach the device to the patient's finger. The clip member **16** carries a measuring unit **20** mounted on its inner side so as to apply optical measurements to a measurement location **L₁** on the patient's finger. Further provided in the probe device **10** is a pressurizing assembly **24** associated with the finger holder **12**. In the present example, the probe device **10** is used for occlusion-based measurements. To this end, an additional pressurizing assembly **22** is provided for applying over-systolic pressure to the blood perfused fleshy medium therebelow. When dealing with pulse-oxymetry based measurements, the provision of the pressurizing assembly **22** could be omitted.

[0028] The pressurizing assembly (first assembly) **22** is composed of an air cushion cuff **25** in the form of a ring

wrapping the patient's finger **F** and a pneumatic drive **26** coupled to the cuff **25** through a pipe **27**. The ring wraps the finger **F** at a location **L₂** upstream of the measurement location **L₁** with respect to the direction of the normal blood flow. The pressurizing assembly **22**, when actuated, operates to apply over-systolic pressure, e.g., 220-300mmHg (generally, adjustable for each specific patient), at the location **L₂**, thereby causing the state of blood-flow cessation at the measurement location **L₁**. The cuff **25** is coupled to the clip member **16** by a substantially rigid connector **28**. The rigid plate-like connector **28** engages the finger along its middle phalanx, preventing its folding at the proximal interphalangeal joint, thereby avoiding undesirable changes in blood volume. The connector **28** is shaped like a plate, and is designed in a manner to enable reciprocating sliding movement of the cuff **25** relative to the clip **16** along the axis of the connector **28**. This enables to adjust the length of the entire finger holder **12** to that of the finger of a specific patient. For example, although not specifically shown, the plate-like connector could be formed with an elongated slot, while the cuff-ring be formed with a projection installed in this slot for reciprocating sliding movement along its axis.

[0029] In the present example of Fig. 1, the other (second) pressurizing assembly **24** is composed of a bellows-like air cushion **29** coupled to its pneumatic drive **30** through a pipe **31**. By appropriately expanding or squeezing the cushion **29**, the clamping affect of the legs is adjusted so as to apply a desired pressure onto the patient's finger in the vicinity of the measurement location **L₁**. It should, however, be noted that a common pneumatic drive could operate both the cushions **25** and **29**.

[0030] As further shown in Fig. 1, a pair of flexible, thermoconductive pads **32** (or pads with built-in heaters), made for example of rubber or silicone, is provided at the inner surfaces of the legs **16A** and **16B**. The pads **32** are coupled to a power source (not shown) operated by a corresponding utility of the control system **14** for applying appropriate, substantially low voltages (e.g., in the range 1V-24V) to the pads **32**, enabling heating the finger portion at the measurement location up to 36-38°. The heating ability of the device increases the accuracy of the non-invasively derived blood-related parameters. The substantially low voltage supply required for heating is, on the one hand, acceptable for medical devices, and, on the other hand, allows for using batteries, thereby rendering the entire device conveniently portable.

[0031] The measuring unit **20** does not form part of the present invention, and therefore need not be specifically illustrated and described, except to note that it comprises such main constructional parts as illumination and detection assemblies, generally at **34**, and generates data indicative of the light response of the finger. Generally, the illumination and detection assemblies could be accommodated either at one side of the finger when operating in a reflection mode, or at opposite sides of the finger when operating in a transmission mode. These

reflected or transmitted signals present light response of the finger to incident radiation. According to the occlusion-based technique disclosed in the above-indicated PCT application, the measuring unit provides illumination of the finger with at least two different wavelengths, and detects light transmitted therethrough.

[0032] Preferably, the illumination unit comprises a plurality of light sources (e.g., LEDs) for illuminating the measurement location with a plurality of different wavelengths in the near infrared spectra. This enables the simultaneous determination of different blood parameters. The wavelengths are selected in accordance with the parameter to be determined. For example, if the hemoglobin concentration is to be determined, the selected wavelengths are in the ranges, where the absorption properties of the hemoglobin and plasma are more sharply expressed, namely are in the ranges 600-1000nm and 1100-1400nm. If the oxygen saturation is to be determined, the selected wavelengths lie in the range where the difference in the absorption of hemoglobin (Hb) and oxyhemoglobin (HbO₂) are more sharply expressed, namely are in the ranges 600-780nm (where the difference in the sensitivity of HbO₂ and Hb is maximal) and 820-980nm (reference range). When dealing with the glucose concentration, the spectral ranges of 1500-1600nm may be added to the above-mentioned range of 600-1300nm for selecting the operational wavelengths.

[0033] The generated data indicative of the detected light (light response of the illuminated medium) is transmitted to the control system **14** for processing and analyzing. To this end, the control system **14** includes a processor **36** operated by suitable software for analyzing the detected signals and determining the desired parameter of the patient's blood, as will be described more specifically further below with reference to Figs. **4a-4d**.

[0034] Thus, each of the drives **26** and **30** of the first and second pressurizing assemblies **22** and **24**, respectively, whilst being actuated by a corresponding utility of the control system **14**, operates to apply required pressure to the finger portion at locations **L₂** and **L₁**. The pressurizing assembly **24** is first actuated, and when a certain under-systolic pressure is applied to the vicinity of the measurement location **L₁**, the control system **14** actuates the pressurizing assembly **22** to apply the over-systolic pressure to the location **L₂**. When the blood flow cessation state is created, the control system **14** operates the measurement unit **20** to illuminate the measurement location with different wavelengths and detect the light response. The application of over-systolic pressure (location **L₂**) is maintained for a period of time, so as not to cause irreversible changes in the finger, and then, the control system operates the drive **26** to release this pressure. The pressurizing assembly **24** applies a different value of the under-systolic pressure, the pressurizing assembly **22** is operated to perform a further occlusion-release session. During each such occlusion-release session, the light response of the measurement location as a function of time is determined. The effective measure-

ments, i.e., the results that have to be analyzed, are those taken at the state of blood flow cessation.

[0035] The operational mode of the device **10** may be such that the control system **14** actuates the measuring unit **20** for performing continuous measurements starting prior to the application of over-systolic pressure. In this case, only those signals, which are associated with the state of blood cessation, are taken into consideration. Measurements taken during the time period prior to the establishment of this state should be disregarded, due to the unavoidable influence of motional and/or other artifacts causing non-monotonic fluctuations of the light transmission. According to an alternative operational mode of the device **10**, the control system **14** actuates the measuring unit **20** a small period of time after the application of the over-systolic pressure. During the time period corresponding to the existence of the state of blood cessation, relative light transmission of blood is observed, which reaches its maximum and may last generally from one second to several minutes.

[0036] To obtain meaningful results, either at least two timely separated measurement sessions should be considered, at least one of them being that taken during the state of blood cessation, or a single long continuous measurement session should be considered starting after the establishment of the state of blood cessation. During the first measurement session, the control system **14** operates to maintain the cuff **25** and the cushion **29** in their squeezed position, and operates the heating element **32** to heat the finger in the vicinity of the measurement location. The control system **14** then operates the pneumatic drives **26** and **30** to release the pressure. The squeezing action of the cuff **25** is ceased, and after a short delay preset by the respective software in the control unit, the blood flow sharply increases until it reaches new steady state. Then, the control system **14** actuates the second measurement session at a state of the transitional blood flow. The illumination assembly continues to illuminate the finger, but squeezing is halted. The detection assembly, being synchronized by the control system **14**, detects the light response of the finger. In other words, the control system **14** selectively operates the measuring unit **20** and the pressurizing assemblies **22** and **24**, and analyzes data coming from the measuring unit, as will be described further below.

[0037] Reference is made to Fig. 2, illustrating a probe device **100** according to another embodiment of the invention. To facilitate understanding, the same reference numbers are used for identifying those components which are common in the devices **10** and **100**. The device **100** is constructed generally similar to the device **10**, but has a somewhat different design of a finger holder **112**. Here, a pressurizing assembly **124** utilizes a cuff-like cushion **129** coupled to a pneumatic drive **30** through a pipe **31**. In other words, the second pressurizing assembly **124** is constructed generally similar to the first assembly **22**, but is associated with the measurement location **L₁** for applying under-systolic pressures thereto.

The heating element **32** may be attached to the surface of the cushion **129** contacting the finger skin. The operation of the device **100** is similar to that of the device **10**. It should, however, be noted, that the pressurizing assembly **124** can be used in combination with the assembly **24** (Fig. 1), rather than replacing it.

[0038] Fig. 3 illustrates a probe device **200** having a somewhat different design as compared to the previously described examples. Here, a pressurizing assembly **224**, that applies under-systolic pressures to the measurement location **L₁**, includes a balloon-like flat cushion **229**, which is accommodated either between the flexible pad **32** and the inner surface of the clamping leg **16B**, or inside the pad **32**, and is coupled to the drive **30** through the pipe **31**. To prevent the opening of the clip member, when in the expanded position of the cushion **229**, a lock mechanism **230** is appropriately provided.

[0039] It should be noted, although not specifically shown, that the clip member may have a four-legged design, in which case one pair of legs engages the finger at its top and bottom thereof, and the other pair of legs engages the opposite sides of the finger. Such four-sided support of the fingertip prevents its folding at the distal phalanx, thereby avoiding undesirable blood volume changes.

[0040] It should also be noted that the rigid connector **28** may be located at either side of the patient's finger. Alternatively, a pair of such connectors can be used located at opposite sides of the finger. Additionally, the processor may be accommodated within the cuff **25**, and wires, if any, connecting the processor to the output circuit of the measuring unit **20**, may pass through the rigid connector.

[0041] Turning now to Figs. 4a-4d, the advantageous features of the present invention are graphically illustrated. Figs. 4a and 4b illustrate, respectively, graphs **G₁** and **G₂** presenting experimental results obtained with two different modes of the probe device **10**, namely, when the pressurizing assembly **24** is in its active (operational) and passive (non-operational) modes. Each of the graphs **G₁** and **G₂** corresponds to the concentration of hemoglobin derived from measurement data obtained with the measurement unit **20** as the function of the hemoglobin concentration obtained with one of the conventional techniques (invasive). To plot each of the graphs, ten measurement points were used. The results show that with the active mode of the pressurizing assembly, when a desired, optimal under-systolic pressure is applied to the measurement location, the measured correlation between the concentration values obtained with different techniques is about 0.91, and the standard deviation is 0.9. While with the passive mode of the pressurizing assembly, these parameters are, respectively, 0.79 and 1.3.

[0042] Figs. 4c and 4d illustrate examples of the technique of the present invention enabling the determination of the desired, optimal pressure to be applied by the pressurizing assembly **24** to a specific patient. Fig. 4c illus-

trates four graphs **H₁**, **H₂**, **H₃** and **H₄**. Graphs **H₁** and **H₂** correspond to the parametric slopes as functions of the pressure applied by the assembly **24**, wherein the parametric slopes were obtained for two different pairs of wavelengths: (1) $\lambda_1=660$ and $\lambda_2=940\text{nm}$, and (2) $\lambda_1=1300$ and $\lambda_2=940\text{nm}$, respectively.

[0043] The slope-based technique of determining the blood substance concentration is disclosed in the above-indicated PCT application assigned to the assignee of the present application. A parametric slope is determined as the transmission logarithm at the wavelength λ_2 , i.e., $\text{Log}(\lambda_2)$, versus the transmission logarithm at the wavelength λ_1 , i.e., $\text{Log}(\lambda_1)$, over a certain time interval (e.g., long occlusion) or at timely separated occlusion stages (i.e., multiple occlusion-release sessions). It should be understood that the slope-based technique may be applied with the pulse-oxymetry as well. In this case such a slope correspond to AC/DC ratio that enables the determination of blood-related parameters. In other words, the parametric slope is a linear function of $\text{Log}(\lambda_2)$ versus $\text{Log}(\lambda_1)$, whose slope can be determined, for example, by a known linear regression algorithm.

[0044] Graphs **H₃** and **H₄** correspond to the slope-error (i.e., standard deviation) as the function of pressure, for the above parametric slopes, respectively. To determine the slope-error, several measurement sessions were taken with the same pairs of wavelengths, corresponding parametric slopes were calculated, and standard deviation values were determined. As clearly seen in the figure, the maximum value (0.55) of the slope in graph **H₁**, which represents certain results criteria for the determination of the oxygen saturation, corresponds to the minimum value (0.04) of the respective slope-error in graph **H₃** at the pressure value of about 100mmHg. Similarly, the minimum value (0.35) of the slope in graph **H₂**, which represents another results criteria, corresponds to the minimum value (0.04) of the respective slope-error in graph **H₄** at the pressure value of about 100mmHg. Thus, this pressure is the optimal pressure for this specific patient, and should be applied to the vicinity of the measurement location on his finger during the optical measurements.

[0045] Fig. 4d illustrates the amplitude of the measured signal as the function of the applied pressure. As shown, at a certain pressure value (about 120mmHg), the amplitude reaches its maximal value.

[0046] Hence, the experimental results show that optical parameters of the patient's blood, such as slope and amplitude of the light response, changes with the pressure variations. This enables to select the optimal pressure value (or range) to increase the accuracy of measurements, and obtain better results. Generally speaking, the determination of the optimal pressure value is based on a certain optical criteria, such as minimum of the standard deviation, maximum amplitude of the measured optical signal, AC/DC ratio, parametric slope, etc. It should be understood that the pressure values in the above examples are relevant only for the specific design of the probe used in the experiments, and may be different

for different patients and different probe configurations. As indicated above, the rigidity of the constructional elements of the probe also affects the optimal pressure value to be used for optimizing the measurement results.

[0047] Those skilled in the art will readily appreciate that various modifications and changes can be applied to the preferred embodiments of the invention as hereinbefore exemplified without departing from its scope defined in and by the appended claims.

Claims

1. A method of non-invasive optical measurements on a human body, the method comprising:
 - (a) performing several optical measurement sessions on a measurement location on the patient's blood perfused fleshy medium while simultaneously controllably varying pressure applied to the vicinity of said measurement location, each measurement session utilizing at least two different wavelength of incident light, detecting light response of the medium and generating measured data indicative thereof;
 - (b) analyzing the measured data to determine the light response of the medium as a function of the wavelength of incident light and the pressure value, and determining an optimal pressure value for this specific patient, so as to utilize at least two light responses of the medium for said at least two different wavelengths, respectively, detected under the application of said optimal pressure, for deriving therefrom at least one parameter of the patient's blood.
2. The method according to Claim 1, wherein the varying pressure is substantially under-systolic pressure.
3. The method according to Claim 1, wherein said optimal pressure value is determined as the pressure value corresponding to certain optical criteria results.
4. The method according to Claim 3, wherein the criteria results utilize at least one of the following parameters: minimum of standard deviation, maximum of the amplitude of the light response, AC/DC ratio, parametric slope.
5. The method according to Claim 1, comprising applying over-systolic pressure to the medium so as to create a state of blood flow cessation at the measurement location, the measured data being indicative of time variation of the light response for each of said at least two wavelengths.
6. The method according to Claim 5, wherein the

over-systolic pressure is applied to a location on the medium upstream of the measurement location with respect to a normal blood flow direction.

7. The method according to Claim 2, comprising applying over-systolic pressure to the medium so as to create a state of blood flow cessation at the measurement location, and applying said optimal pressure to the vicinity of the measurement location, the measured data being indicative of time variation of the light response for each of said at least two wavelengths. 5
8. The method according to Claim 7, wherein the over-systolic pressure is applied to a location on the medium upstream of the measurement location with respect to a normal blood flow direction. 10
9. The method according to Claim 5, comprising performing the preliminary measurements under the application of the controllably variable under-systolic pressure and no over-systolic pressure to select the optimal value of the under-systolic pressure specific for the patient; and then performing the optical measurements while at the optimal under-systolic pressure at the measurement location and the state of blood flow cessation at the measurement location, to thereby increase accuracy of the measurements. 15
10. The method according to Claim 9, wherein the measurement sessions are performed during the single blood-cessation state. 20
11. The method according to Claim 9, wherein the measurement sessions are performed during the sequential blood cessation state, obtained by sequentially applying and releasing the over-systolic pressure. 25
12. The method according to Claim 1, wherein said at least one blood parameter includes at least one of the following: oxygen saturation, Hb, Glucose bilirubin, concentration of one or more substance in blood. 30
13. The method according to Claim 12, wherein said one or more substance includes at least one of hemoglobin and glucose. 35
14. The method according to Claim 1, wherein said analyzing of the measured data comprises utilizing calibration data indicative of different blood parameters. 40
15. The method according to Claim 14, comprising carrying out a calibration stage, during which various patients undergo the measurements, and calibration curves corresponding to different blood parameters. 45
16. The method according to Claim 1, for use in oximetry 50

measurements.

17. The method according to Claim 1, for use in pulse oximetry measurements.
18. A method for use in pulse oximetry measurements, the method comprising:
 - performing several optical measurement sessions on a measurement location on the patient's blood perfused fleshy medium while simultaneously controllably varying substantially-under-systolic pressure applied to the vicinity of said measurement location, each measurement session utilizing at least two different wavelength of incident light, detecting light response of the medium and generating measured data indicative thereof;
 - analyzing the measured data to determine the light response of the medium as a function of the wavelength of incident light and the pressure value, and determining an optimal pressure value for this specific patient, so as to utilize corresponding at least two light responses of the medium for said at least two different wavelengths, respectively, for deriving therefrom at least one parameter of the patient's blood.
19. A method for use in non-invasive measurements of blood parameters, the method comprising:
 - performing several optical measurement sessions, each with at least two different wavelength of incident light, on a measurement location on the patient's blood perfused fleshy medium, while at the state of blood flow cessation at the measurement location and application of controllably varying substantially under-systolic pressure to the vicinity of said measurement location; detecting light response of the medium; and generating measured data indicative thereof;
 - analyzing the measured data to determine the light response of the medium as a function of time, the wavelength of incident light and the under-systolic pressure value, and determining an optimal value of the under-systolic pressure for the specific patient, so as to utilize corresponding at least two time variations of the light response for said at least two different wavelengths, respectively, measured at the state of blood flow cessation in the measurement location, for deriving therefrom at least one parameter of the patient's blood.
20. A method for controlling optical measurements on a patient's blood perfused fleshy medium, the method comprising:

- operating a pressurizing assembly to apply a controllably varying pressure to a measurement location and concurrently operating an optical measuring unit to apply optical measurements to the measurement location by illuminating the measurement location with incident light of at least two different wavelengths and detecting light responses of the measurement location for said at least two different wavelengths; 5

- analyzing data indicative of the light response signals obtained with the different values of the applied pressure, and selecting an optimal pressure value for the specific patient as that corresponding to the light response signal **characterized by** at least one of the following: a maximal intensity of the light response signal, a maximal value of an AC/DC ratio in the signal from all the detected light response signals, and a predetermined range of parametric slopes, the parametric slope being indicative of a time change of the intensity of the light response to the incident light of one wavelength as a function of a time change of the intensity of the light response to the incident light of another wavelength 25

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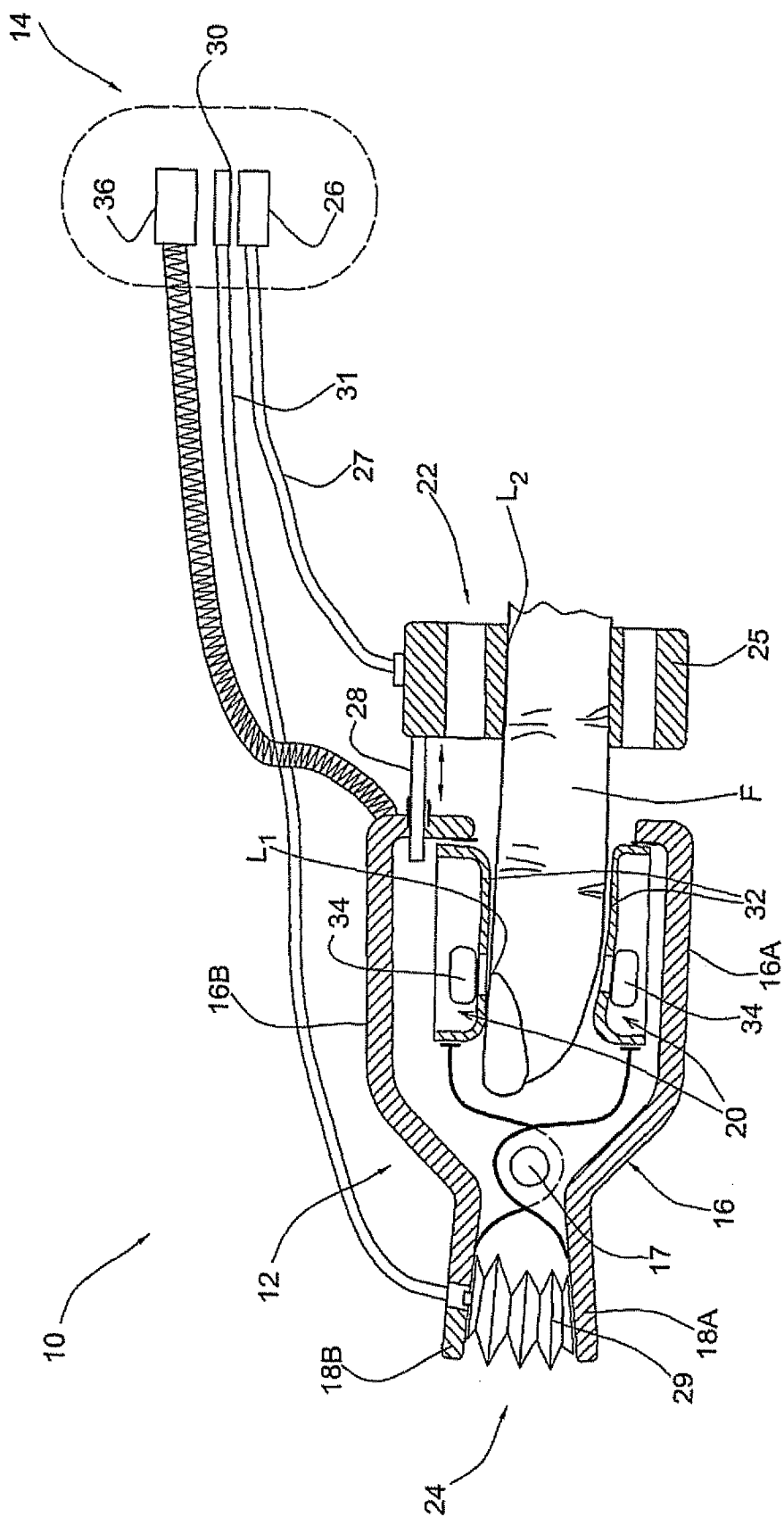


FIG. 1

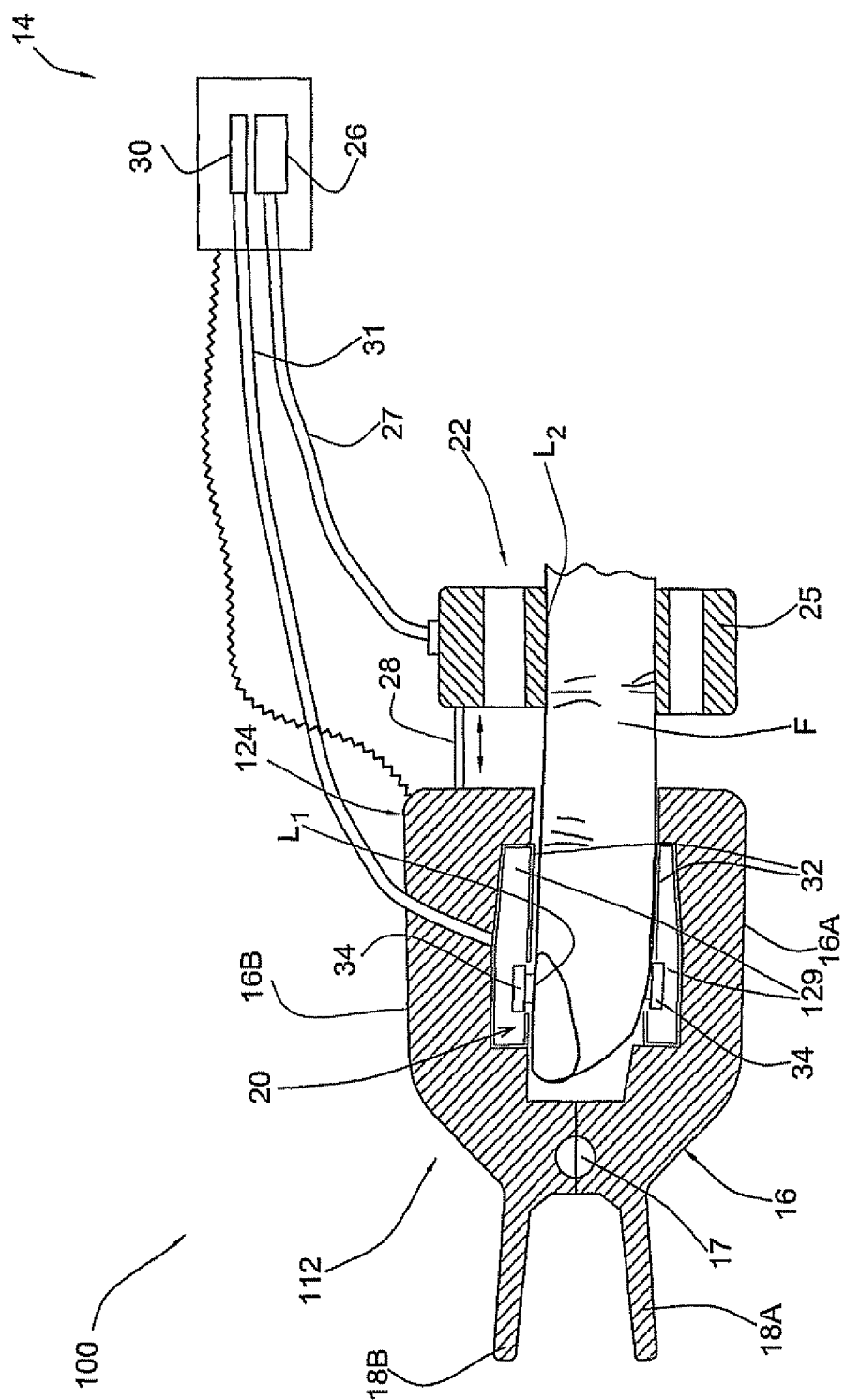
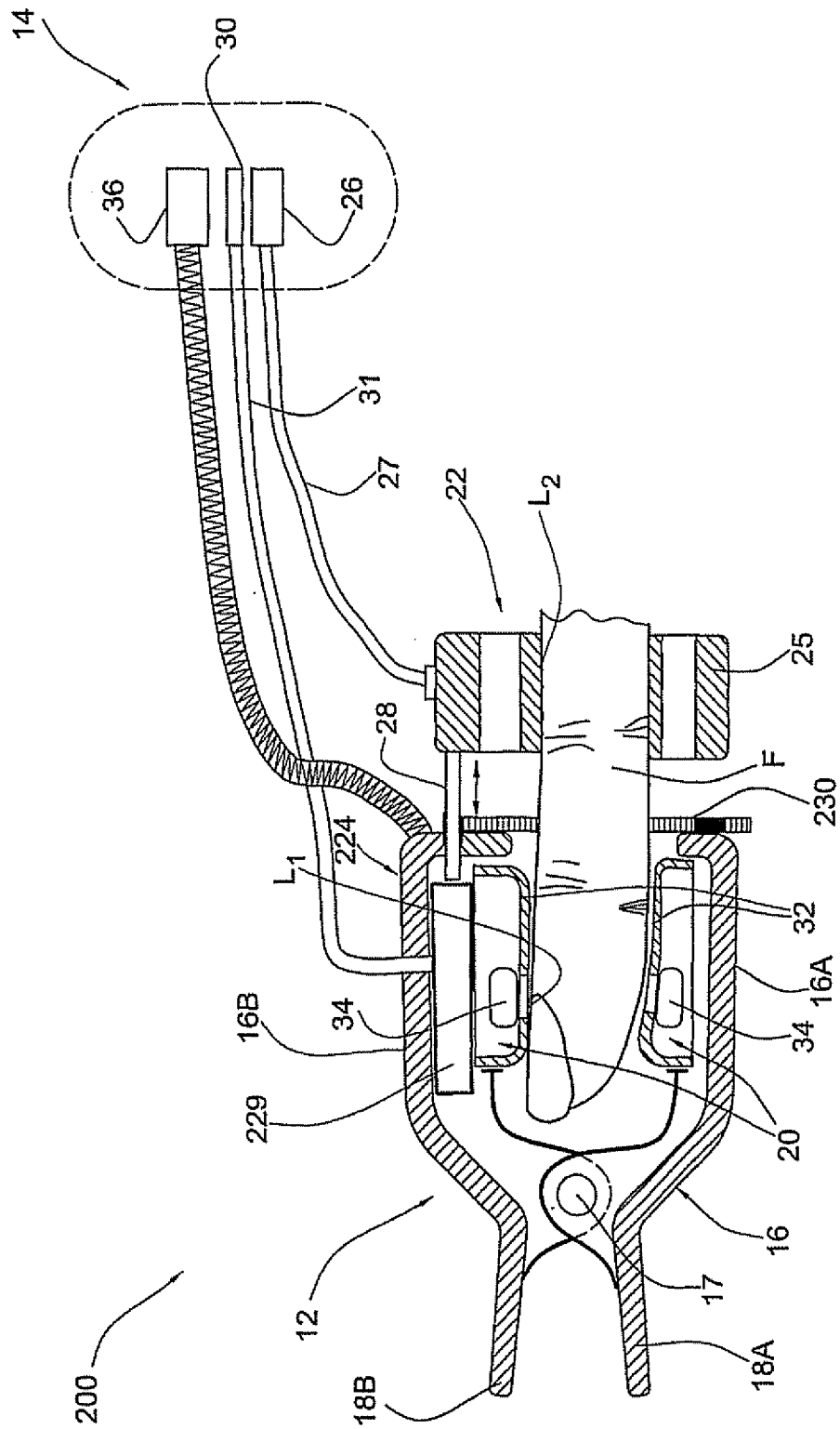


FIG. 2



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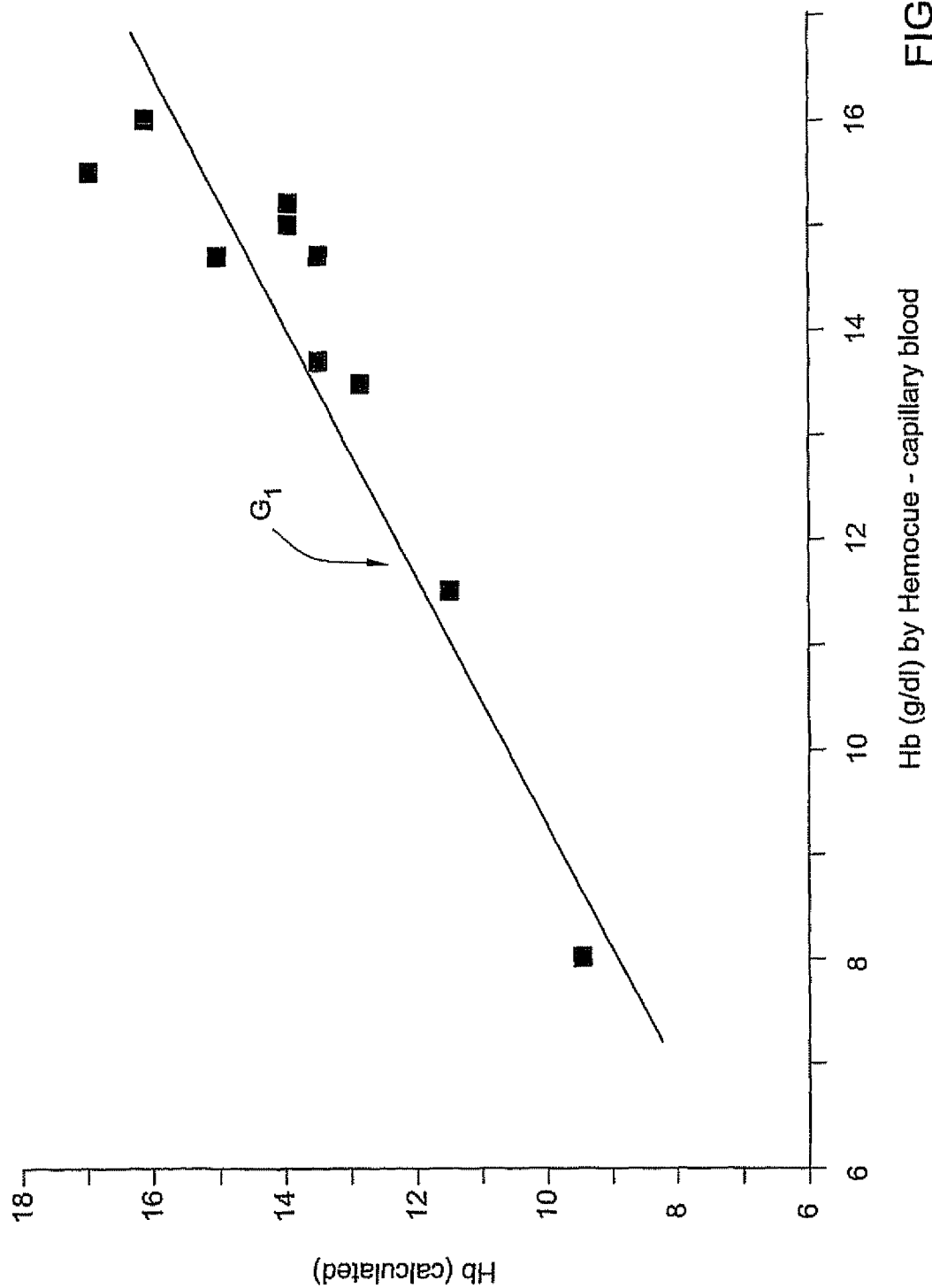
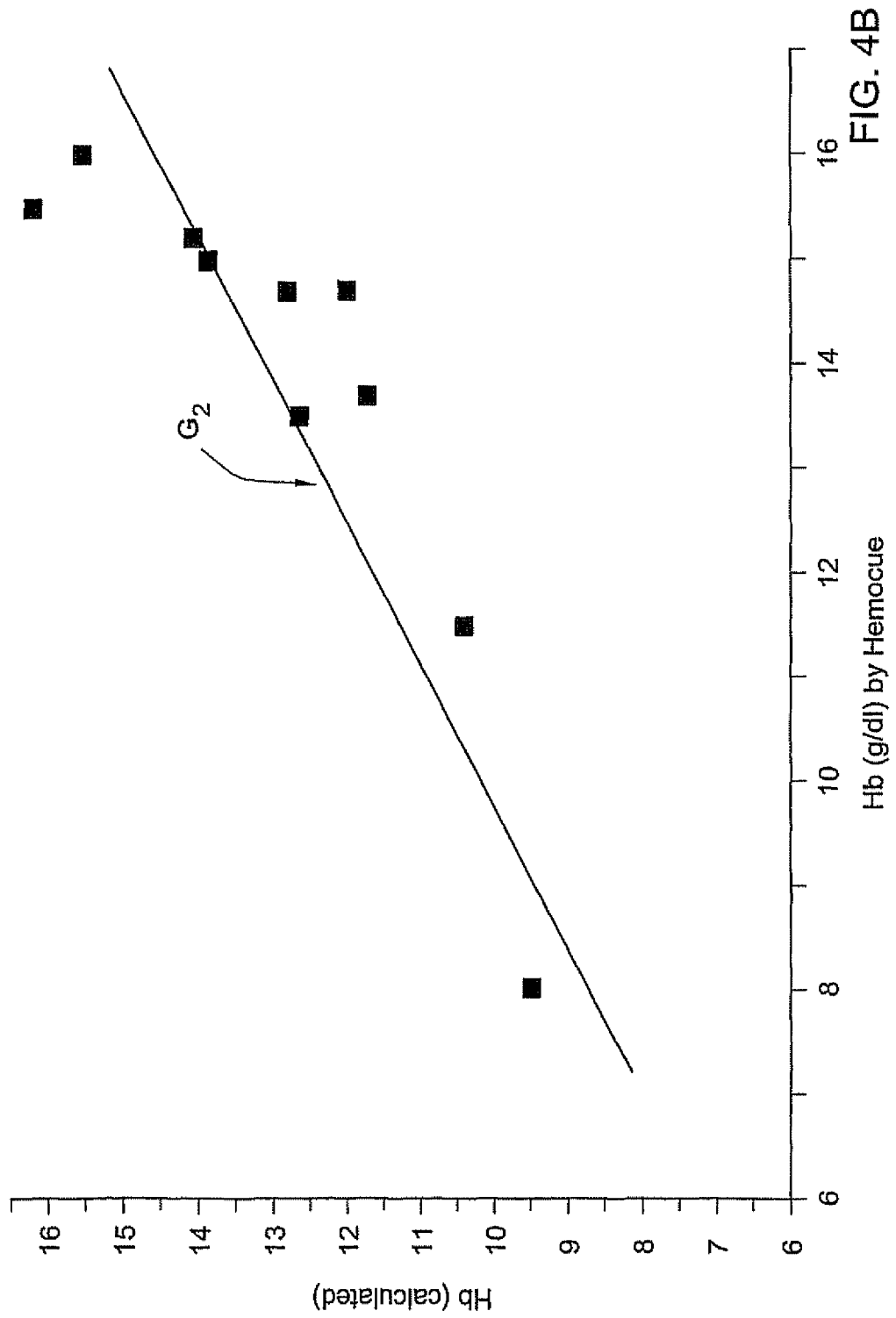


FIG. 4A



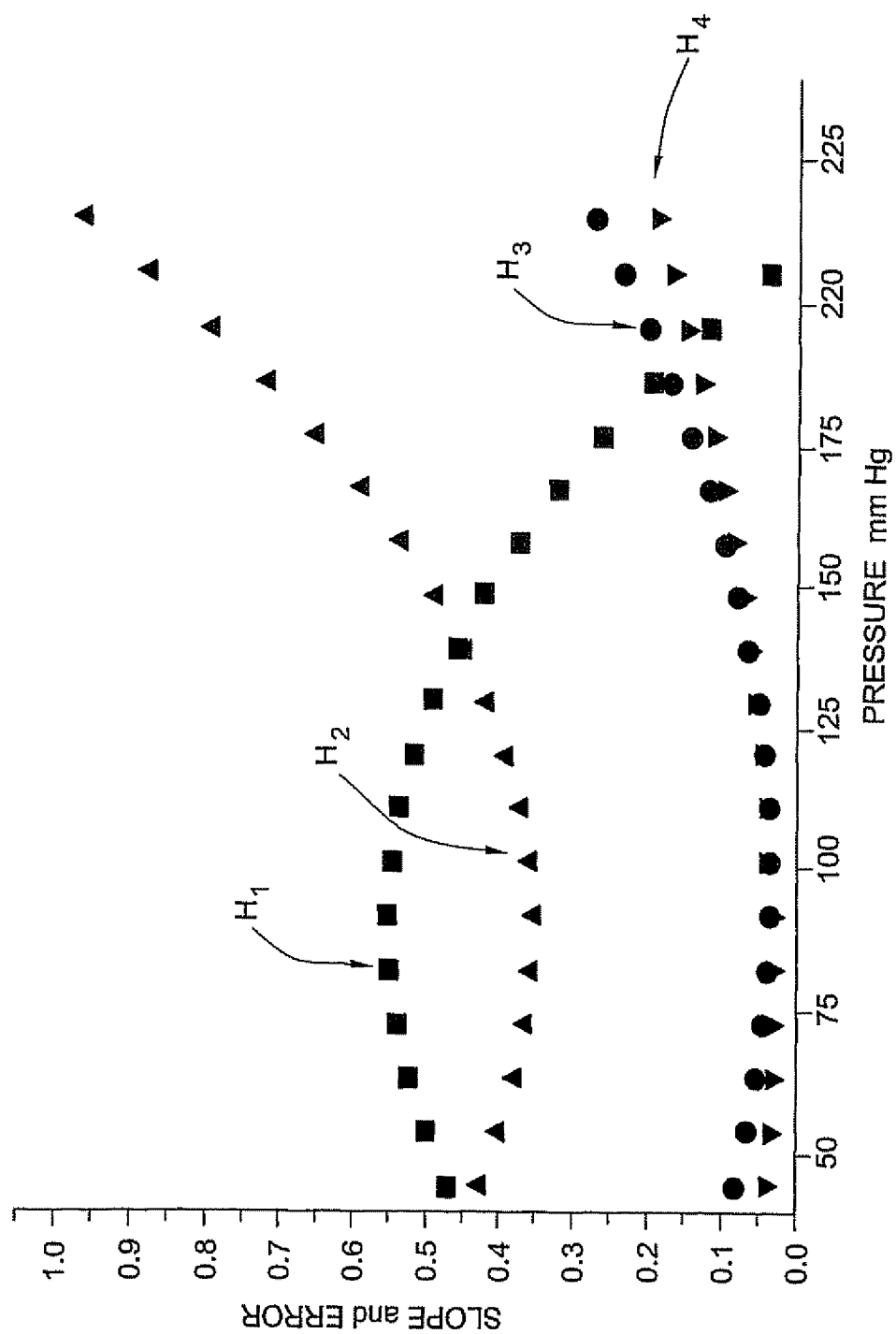


FIG. 4C

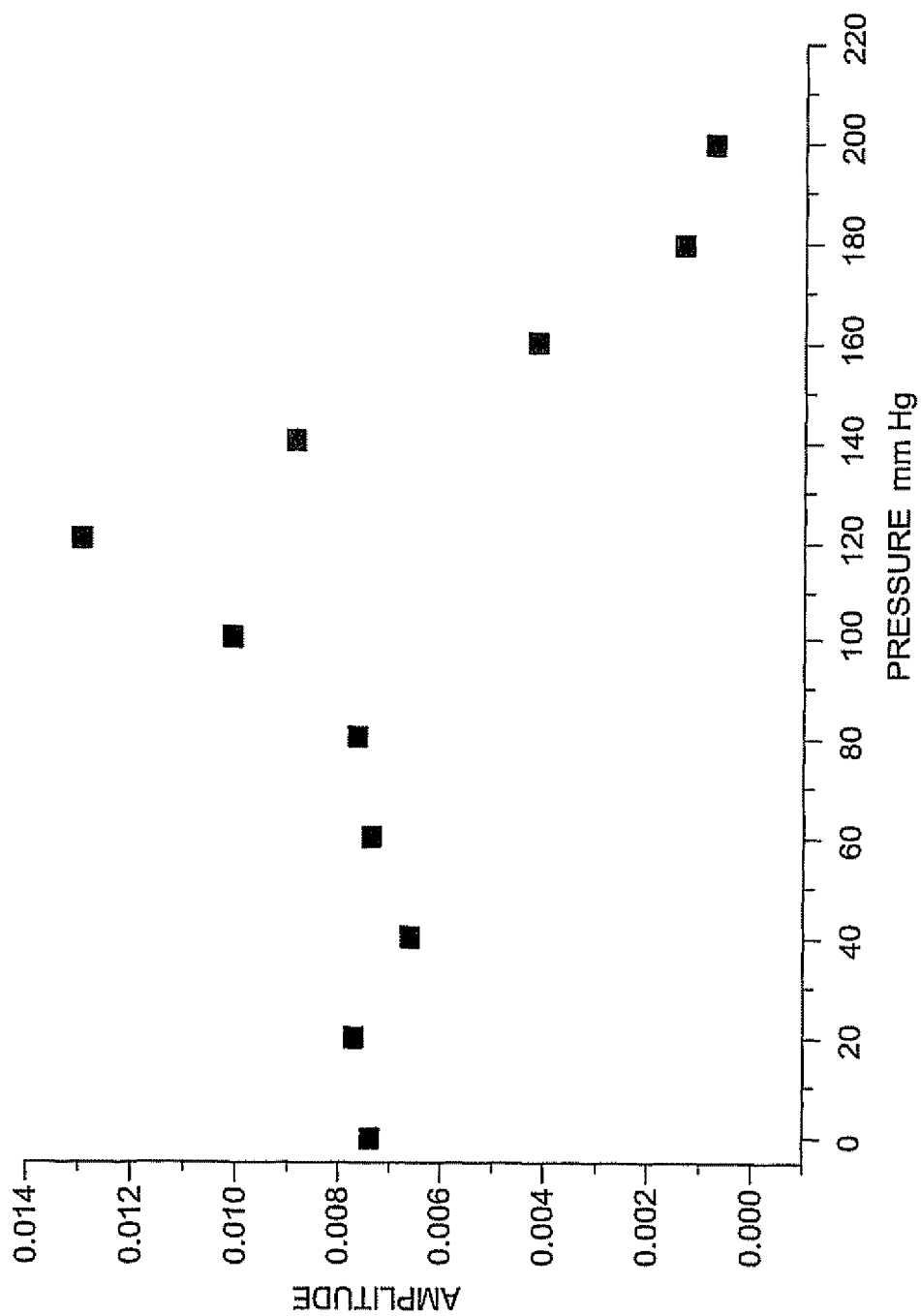


FIG. 4D



DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	US 5 111 817 A (WALLACE WILLIAM D ET AL) 12 May 1992 (1992-05-12)	1-5, 12-18,20	A61B5/00
A	* column 4, line 64 - column 6, line 27 * * column 11, line 40 - column 12, line 37; tables 1,2 *	7,9,19	A61B5/022 A61B5/0225
D,A	----- W0 99/65384 A (FINE ILYA ;ORSENSE LTD (IL)) 23 December 1999 (1999-12-23) * page 4, line 23 - page 9, line 25; tables 1-3 *	1-20	
A	----- US 5 827 181 A (DIAS J FLEMING ET AL) 27 October 1998 (1998-10-27) * column 2, line 45 - column 3, line 44 * * column 4, line 40 - column 5, line 26; tables 1,3 *	1-20	
A	----- EP 0 227 119 A (NIPPON COLIN CO LTD) 1 July 1987 (1987-07-01) * column 11, line 15 - column 14, line 5; table 2 *	1,5-12, 16-19	
	-----		TECHNICAL FIELDS SEARCHED (IPC)
			A61B
The present search report has been drawn up for all claims			
Place of search Munich		Date of completion of the search 23 November 2005	Examiner Artikis, T
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 05 11 0198

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

23-11-2005

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专利名称(译)	用于血液相关参数的非侵入式测量的方法		
公开(公告)号	EP1618839A1	公开(公告)日	2006-01-25
申请号	EP2005110198	申请日	2001-03-15
申请(专利权)人(译)	ORSENSE LTD.		
当前申请(专利权)人(译)	ORSENSE LTD.		
[标]发明人	FINE ILYA FINAROV ALEXANDER		
发明人	FINE, ILYA FINAROV, ALEXANDER		
IPC分类号	A61B5/00 A61B5/022 A61B5/0225 G01N21/27 A61B5/145 A61B5/1455 G01N21/35		
CPC分类号	A61B5/02255 A61B5/0053 A61B5/02241 A61B5/14532 A61B5/14552 A61B5/1491 A61B5/6824 A61B5/6825 A61B5/6843		
优先权	135077 2000-03-15 IL		
其他公开文献	EP1618839B1		
外部链接	Espacenet		

摘要(译)

一种探针装置，用于对患者血液的至少一个参数进行非侵入性光学测量。探针装置包括夹子构件形式的手指保持器，其将指尖固定在其夹紧腿之间。探针装置支撑测量单元，用于将光学测量值施加到手指上的测量位置，并且携带加压组件，该加压组件可操作用于将可控制地可变的，基本收缩不足的压力施加到测量位置附近的手指。在测量位置处利用至少两种不同波长的入射光执行若干测量会话以检测介质的光响应并产生指示其的测量数据，并且在测量期间同时改变施加到测量位置附近的压力。介质的光响应对应于入射光的不同波长和测量期间的不同压力值。分析对应于入射光的不同波长和不同压力值的介质的光响应，并确定最佳压力值，以利用介质的相应光响应从而得到至少一个血液参数。

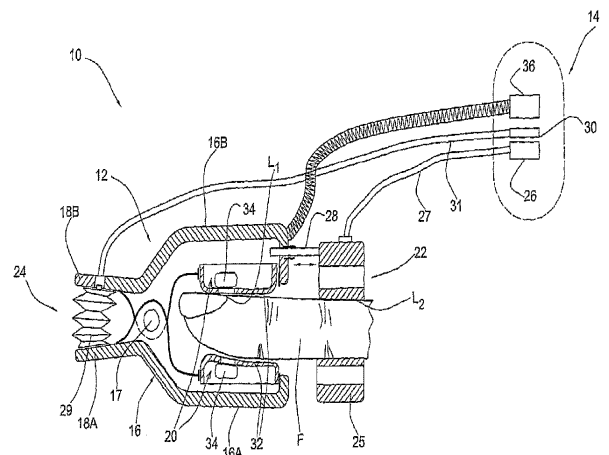


FIG. 1