(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
19 January 2006 (19.01.2006)

PCT

(10) International Publication Number
WO 2006/006153 A1

(51) International Patent Classification[7]: A61B 5/00

(21) International Application Number:
PCT/IL2005/000720

(22) International Filing Date: 6 July 2005 (06.07.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
10/885,885 8 July 2004 (08.07.2004) US

(71) Applicant *(for all designated States except US)*: **ORSENSE LTD.** [IL/IL]; 2 Prof. Bergman Street, 76705 Rehovot (IL).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **FINAROV, Alexander** [IL/IL]; 1/10 Kovshey Ha-Hermon, 76555 Rehovot (IL). **FINE, Ilya** [IL/IL]; 59/6 Herzl Street, 76540 Rehovot (IL).

(74) Agent: **REINHOLD COHN AND PARTNERS**; P.O.B. 4060, 61040 Tel-Aviv (IL).

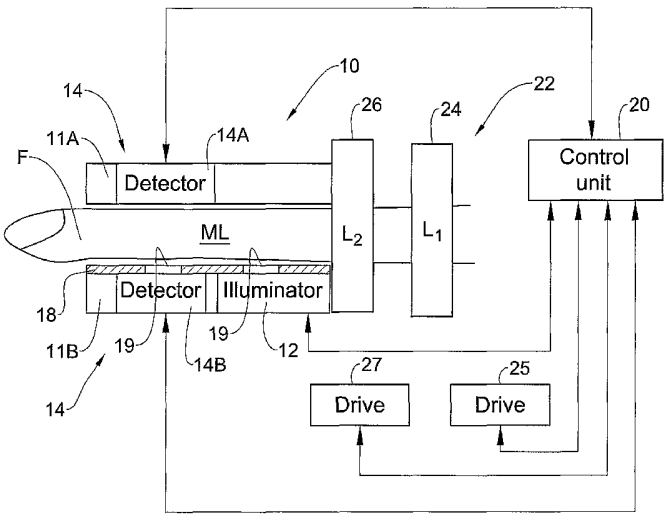
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) **Title:** DEVICE AND METHOD FOR NON-INVASIVE OPTICAL MEASUREMENTS



(57) **Abstract:** An optical measurement device (10) and method are presented for use in non-invasive measurements on a patient's body. The device comprises an illumination assembly (12) configured and operable to generate illuminating light of a predetermined wavelength range; a detection assembly (14); and a light directing assembly. The detection assembly (14) comprises a first detector (14a) unit for detecting a first light signal transmitted through an illuminated body portion and generating first measured data indicative of the detected transmitted light, and a second detector unit (14b) for detecting a second light signal reflected from the illuminated body portion. The light directing assembly comprises a light diffuser (18) for scattering back light incident thereto, to thereby direct the illuminating light or the light coming from the body portion back towards the body portion. This technique provides for increasing the amount of light reaching a region of interest inside the body portion and maximizing homogeneity of the first and second detected light signals.

WO 2006/006153 A1

DEVICE AND METHOD FOR NON-INVASIVE OPTICAL MEASUREMENTS

FIELD OF THE INVENTION

This invention relates to a device and method for non-invasive optical measurements on a human body, which is particularly useful for measuring blood-related parameters.

BACKGROUND OF THE INVENTION

Non-invasive (*in vivo*) methods for measuring various blood-related parameters have become very popular due to the fact that these measurements, in distinction to invasive ones, do not involve the physical withdrawal of a blood sample from the patient's body. Optical monitoring techniques of the kind specified 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. These methods being applied in real medicine rather than in analytical chemistry create the basis for non-invasive blood tests, which present, no doubt, one of today's most exciting challenges. To make blood tests low-cost, safe and painless means to make them non-invasive.

The two main challenges, that any non-invasive optical method has to deal with, are as follows: (1) the low signal-to-noise ratio, and, (2) the large variability of individual parameters influencing the signal of concrete patients.

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. The conventional devices of the kind specified, such as a pulse oximeter, which is the generally accepted standard of everyday clinical practice, provide for measuring enhanced optical pulsatile signals caused by the changes in the volume of a blood flowing through a fleshy medium (e.g., finger).

It is known that for blood parameters other than oxygen saturation, e.g., glucose concentration, significant difficulties have been accoutered, because their absorption spectral behavior in red and near infrared regions is not as remarkable as for the oxygenized hemoglobin. Hence, the main limitations on the way of expanding the non-invasive techniques to the measurements different from pulse oximetry are associated with the limited selectivity of the absorption based method.

A different technique is disclosed in U.S. Patent No. 6,400,972, WO 01/45553 and WO 01/96872, all assigned to the assignee of the present application. This is an occlusion-release based technique, according to which an over-systolic pressure is applied to the blood perfused fleshy medium with a normal blood flow so as to create a state of temporary blood flow cessation at the measurement location. The measurement with different wavelengths of incident radiation and/or different polarization states of detected light are carried out at timely separated sessions taken during a time period including a cessation time when the state of the blood flow cessation is maintained. This technique utilizes the condition of the "artificial blood kinetics" rather than the natural blood kinetics taking place when the state of blood cessation is not achieved. As a result of the cessation of the blood flow, a condition of the artificial kinetics is achieved with the optical characteristics of the blood associated with the light response being different from those at the natural blood kinetics. Indeed, it is known that the scattering properties of blood depend on the size and shape of scatterers (aggregates). Thus, time changes of the light response at the condition of artificial kinetics depend on the changes in the shape and average size of the

scattering centers in the medium, i.e., red blood cells (RBC) aggregation (Rouleaux effect). It was found that owing to the effect of the artificial kinetics, the optical characteristics of blood changes dramatically, such that they differ from those of the fleshy medium with a normal blood flow by about 25 to 60%, and sometimes even more. Hence, the accuracy (i.e., signal-to-noise ratio) of the technique based on the artificial kinetics as well as selectivity of the optical measurements can be substantially better when compared with those based on measurements of the blood parameters at natural kinetics.

SUMMARY OF THE INVENTION

There is a need in the art to facilitate non-invasive optical measurements of blood parameters by providing a novel device and method capable of stabilizing the optical response of an illuminated region in a patient's body.

The present invention provides for detecting the optical response formed by both light reflected from the illuminated body portion and light transmitted therethrough. It should be understood that the terms *"reflected light"* and *"transmitted light"* used herein signify light components detected at, respectively, the same side of the body portion at which the illumination is applied and the opposite side, and actually both light portions include light scattered from the illuminated region.

The present invention utilizes redirecting reflections of light on its way towards the region of interest (i.e., blood vessel) back to the region of interest. This is implemented using a diffuser accommodated in the optical path of light reflected from the body portion under measurements. Due to the provision of a diffuser, illuminating light that is reflected from the skin and bones is "collected" and directed back to the region of interest. The use of a diffuser stabilizes both the reflected and transmitted responses of the illuminated region, and causes a stable increase of the reflected signal.

Thus, according to one aspect of the invention, there is provided an optical measurement device for use in non-invasive measurements on a patient's body, the device comprising:

- an illumination assembly configured and operable to generate illuminating light of a predetermined wavelength range;
- a detection assembly comprising a first detector unit for detecting a first light signal transmitted through an illuminated body portion and generating first measured data indicative of the detected transmitted light, and a second detector unit for detecting a second light signal reflected from the illuminated body portion and generating second measured data indicative of the detected reflected light; and
- a light directing assembly comprising a light diffuser for scattering back light incident thereto, to thereby direct the illuminating light or the light coming from the body portion back towards the body portion, thereby increasing amount of light reaching a region of interest inside the body portion and thus maximizing homogeneity of the first and second detected light signals.

Preferably, the light diffuser extends along at least a part of the body portion at the illuminated side thereof. The diffuser may be formed with an optical window for allowing passage of light from the illumination assembly towards the body portion; and/or with an optical window for allowing light passage from the body portion to the second detector unit.

The diffuser may for example be, but not limited to, of dimensions of about 20x24mm, and may be made of a material such as PVC, Polyurethan.

The device may be configured for operating in the occlusion-release mode. To this end, the device includes a pressurizing assembly operable for applying an over-systolic pressure to the patient's body so as to create a condition of artificial blood kinetics in the region of interest and maintain this condition for a certain time period. The pressurizing assembly may be configured and operable for applying a secondary controllably varying under- or over-

systolic pressure to the body within the region of interest, so as to alter said condition of artificial blood kinetics over a predetermined time interval within said certain time period, to thereby modulate the amount of blood under measurements.

Preferably, the device is configured as finger holder. This may be a clip member for enclosing the body portion between its upper and lower arms, one of the upper and lower arms carrying the illumination assembly, the diffuser and the second detector unit, and the other arm carrying the first detector unit. Alternatively, this may be a ring-like device. For example, such a ring may be designed as two U-shaped semi-ring portions, one carrying the illumination assembly, the diffuser and the second detector unit, and the other carrying the first detector unit. If the occlusion-mode operation is considered, the pressurizing assembly is associated with one of the U-shaped portions being in the form of an air cushion on the inner side of said portion, in which case the air cushion is made of a light diffusing material, thereby presenting said diffuser.

According to another aspect of the invention, there is provided a method for use in non-invasive optical measurements on a patient's body utilizing illumination of a region of interest inside the body portion and detection of light response of the region of interest, the method comprising:

- collecting light coming from the body portion and directing at least a part of the collected light back to the body portion;
- detecting a first light signal transmitted through the body portion and generating first measured data indicative of the detected transmitted light, and detecting a second light signal reflected from the body portion and generating second measured data indicative of the detected reflected light;

the method providing for increasing amount of light reaching the region of interest inside the body portion, and for maximizing homogeneity of the first and second detected light signals.

BRIEF DESCRIPTION OF THE DRAWINGS

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 measurement device of the present invention utilizing a diffuser;

Fig. 2 illustrates a measurement device according to a specific example of the invention;

Figs. 3A and 3B illustrate the result of typical optical measurements without a diffuser; and

Figs. 4A and 4B illustrate the results of measurements utilizing the device of the present invention with a diffuser.

DETAILED DESCRIPTION OF THE INVENTION

Referring to **Fig. 1**, there is schematically illustrated an optical measurement device **10** of the present invention for use in non-invasive measurements on a patient's body, e.g., patient's finger **F**. The device **10** includes an illumination assembly **12**; a detection assembly **14**; and a light directing assembly **16**. A control unit **20** is provided for operating the illumination and detection assemblies and for receiving and processing measured data coming from the detection assembly.

The illumination assembly **12** is accommodated so as to direct illuminating light towards the finger **F**. The illumination assembly **12** may utilize one or more light emitting elements, e.g., LED(s). Preferably, a matrix of LEDs is used. In this specific example of measuring blood parameters, the illumination assembly **12** is designed for generating light of different wavelengths (at least two different wavelengths), which can be implemented by using different light emitting elements or a single broadband illuminator.

The light detection assembly **14** includes a first detector unit **14A** accommodated substantially opposite the illumination assembly **12** for detecting

a first light signal transmitted through the finger **F** and generating first measured data $\mathbf{MD_1}$ indicative thereof, and includes a second detector unit **14B** accommodated adjacent to the illumination assembly **12** for detecting a second light signal reflected from the inside of the finger and generating second measured data $\mathbf{MD_2}$ indicative thereof. Each of the detector units **14A** and **14B** includes one or more frequency selective detector (e.g., a matrix of detectors), such as spectrophotometer and/or photodiode typically equipped with frequency selective filter and amplifying means, which are not specifically shown.

It should be understood that generally, the light emitting element(s) as well as a detectors may be accommodated aside the finger in which case light is directed towards and away from the respective locations on the finger via fibers.

The light directing assembly **16** includes a diffuser **18** accommodated proximate the finger portion under measurements at the illuminating side, so as to collect light reflections from the finger and reflect them back towards the inside of the finger, thereby increasing the amount of light reaching the blood vessel in the finger. As shown in the present example, the diffuser **18** extends along the finger portion and is formed with an optical window **19** so as to allow passage of illuminating light towards the finger. The reflection-mode deflector **14B** may be accommodated adjacent to the diffuser slightly aside thereof to detect reflected light propagating along axes that do not intersect with the diffuser, or alternatively, may be vertically aligned with the diffuser in which case the diffuser **18** is formed with an additional optical window **19** allowing passage of light therethrough towards the detector **14B**.

The diffuser is made of a semi-transparent material, capable to diffuse visible and near-infrared light. The attenuation coefficient and spatial distribution of diffused light has to be a very weak function of wavelength in the operating spectral region. The diffuser has a certain minimal size so as to ensure that the majority of the body surface (e.g., surface of the patient's finger provides efficient return of reflected light to the examined media (e.g., about 48mm^2, e.g., dimensions of about 20x24mm).

The diffuser thus "collects" light that is typically reflected from the skin and bone while propagating towards the blood vessel and reflects this light back to the blood vessel to thereby increase the amount of light reaching the blood vessel. As a result, both the intensity of light transmitted through the blood vessel and received at the first detector unit **14A** (transmission-mode detector) and the intensity of light reflected from the blood vessel and received at the second detector unit **14B** (reflection-mode detector) are increased, and the homogeneity of the first and second light signals is thus maximized.

The device **10** may be designed as a finger holder in the form of a clip member attachable to a patient's finger so as to enclose a finger portion between upper and lower arms **11A** and **11B** of the clip member (similar to the conventionally used pulse oximeter). One of the upper and lower arms – lower arm **11B** in the present example, carries the illumination assembly **12**, the diffuser **18** and the reflection-mode detector unit **14B**, and the other arm **11A** carries the transmission-mode detector unit **14A**. The diffuser **18** extends along at least a part of the inner surface of the lower arm **11B** of the clip member.

Preferably, the measurement device **10** is configured for operating with the so-called "occlusion-release mode". To this end, the device **10** includes a pressurizing assembly **22** having an occluder arrangement (occlusion cuff) **24** associated with a drive mechanism **25** operable by the control unit **20** for applying an over-systolic pressure to the patient's finger **F** to create a state of blood flow cessation in the vicinity of a measurement location **ML** (where optical measurements are applied). The pressurizing assembly **22** may also be operable to apply a secondary controllably varying under- or over-systolic pressure to the measurement location **ML**, which in the present example of Fig. 1 is implemented using another cuff **26** associated with a drive mechanism **27**. Thus, the primary over-systolic pressure is applied to a finger location L_1 upstream of the measurement location **ML** with respect to the blood flow direction, and the variable secondary pressure is periodically applied to a location L_2 in the closest vicinity of the measurement location while in the state of

temporarily blood flow cessation, thus implementing the so-called "multiple-occlusion" mode.

The principles of the occlusion-release based measurements are disclosed in the above-indicated US Patents and the multiple-occlusion mode is described in a co-pending US patent application Ser. No. 10/452,932, all assigned to the assignee of the present application, and do not form part of the present invention.

Moreover, the principles of the present invention consisting of using a diffuser and detecting both light transmitted through and reflected from the region of interest, can advantageously be used in measurements based on detecting a pulsatile signal of a light response of the medium (such as in the conventional pulse oximeter), and in the occlusion-based measurements where a non-pulsatile signal is detected. This will be described further below with reference to Figs. 3A-3B and 4A-4B.

It should be noted that when using the simultaneous transmission- and reflection-mode measurements, the parameter of interest (e.g., glucose concentration in blood) may be calculated independently from transmission and reflection signals. When a difference between the two readings exceeds a certain predetermined value, the measurement results are defined as an outlier.

Fig. 2 illustrates a specific but not limiting example of a measurement device **100** of the present invention. In the present example, the device **100** is designed like a ring, formed by two portions **111A** and **111B** each of a substantially U-shaped cross-section arranged with respect to each other for enclosing and holding therebetween a portion of the patient's finger (not shown here). The U-shape parts **111A** and **111B** are made of a rigid or semi-rigid material, such as metal or plastic. In the cross-section, these U-shape parts can, for example, be of semi-circle or semi-oval forms. The parts **111A** and **111B** can partially overlap over a predetermined distance.

The measurement device (probe) **100** comprises an illumination assembly (not shown) mounted on a holding frame **112** associated with the semi-ring **111B**; a light detection assembly including a transmission-mode detector unit

(not shown) mounted on a holding frame **114A** associated with the semi-ring **111A** so as to be substantially opposite the illumination assembly, and a reflection-mode detector unit (not shown) mounted on the semi-ring **111B**; and a diffuser **118** located on the inner surface of the semi-ring **111B**. Similar to the previously described example, the illumination assembly can include a plurality of light sources (e.g., LEDs) associated with a suitable drive mechanism (not shown) operated by a control unit, or a single broad band illuminator. The light source (or multiple light sources) radiates the measurement location of the finger through an aperture (optical window) **119** in the diffuser **118**. In the present example, another aperture **121** is provided in the diffuser **118** to allow passage of light from the illuminated region to the reflection-mode detector. It should, however, be understood that the provision of this aperture is optional since the reflection-mode deflector may be accommodated adjacent to the diffuser slightly aside thereof to detect reflected light propagating along axes that do not intersect with the diffuser.

It should also be noted that, although in the present examples of Figs. 1 and 2, the diffuser is shown as constructional part of the illumination/detection arrangement of the measurement device (e.g., finger holder), the diffuser may be a separate element. For example, the diffuser may be configured to be put onto a finger, so as to be located between the finger and the illumination/detection arrangement of the measurement device. The diffuser may be in the form of a thin elastic cover for wrapping at least a part of the body portion (e.g., finger), and configured to enable optical measurements therethrough. For example, the diffuser may be formed with an optical windows, which when the device is put in operation is aligned with the optical path of illuminating light, and possibly also including an additional optical window aligned with the reflection mode detector.

Turning back to **Fig. 2**, the device **100** further includes a pressurizing assembly that includes an air cushion **124** associated with a drive mechanism (not shown) and operable to apply pressure to the finger portion enclosed

between the parts **111A** and **111B**. In the present example, the cushion **124** is made of a light diffusing material thus presenting the diffuser **118**.

By moving the upper and lower parts **111A** and **111B** of the probe towards each other, a position of a finger therebetween is fixed. Then, a locking device **126** further fixes the parts **111A** and **111B** to thereby apply a certain preliminary pressure to start the measurement procedure. The locking device may be implemented by any suitable known means (e.g., including a teeth arrangement and a spring assembly) and is aimed at preventing the opening of the ring-like probe. Then, the cushion **124**, which in the present example is associated with the lower semi-ring **111B**, is operated to press the finger to the upper semi-ring **111A** to thereby apply an over-systolic pressure (e.g., 220-250mmHg) and create a blood flow cessation in the finger. Then, during the measurements while in the blood flow cessation state, a variable over-systolic secondary pressure is supplied through the cushion **124**. Thus, according to this embodiment of the invention, the primary over-systolic pressure as well as the secondary pressure is applied to the same location on the finger via the same pressurizing assembly (cushion **124**).

Due to the provision of the diffuser (**18** in Fig. 1 and **118** in Fig. 2), light that while propagating from the illumination assembly towards the blood vessel in the finger is typically reflected from the skin and bone, is collected and reflected back to the blood vessel. As a result, both the intensity of light transmitted through the blood vessel and received by the transmission mode detector and the intensity of light reflected from the blood vessel and received by the reflection mode detector are increased. This maximizes the homogeneity of the detected light signals.

Reference is made to **Figs. 3A-3B and 4A-4B** showing experimental results: **Figs. 3A and 3B** illustrate the results of measurements with no diffuser and **Figs. 4A and 4B** illustrate the same with the diffuser-based device of the present invention. Each of these figures shows the time variation of a detected light response of a measurement location inside a patient's finger.

In the example of **Fig. 3A**, the finger is illuminated with 720nm light, and light reflected from the finger is measured. As shown, a graph G_1 has a pulsatile-signal part L_1 measured during a 100sec time period prior to the application of an over-systolic pressure, and a non-pulsatile part L'_1 continuously measured after the application of such pressure. Both the pulsatile and non-pulsatile reflected signals decrease during the measurements. In the example of **Fig. 3B**, the finger is illuminated with 720nm light, and time variations of light reflected from the finger G_1 and that of light transmitted through the finger G_2 are measured. Measured reflected signal G_1 has an initial pulsatile signal part L_1 and a further non-pulsatile signal part L'_1 resulting from the occlusion; and measured transmitted signal has initial pulsatile signal part L_2 and a further non-pulsatile signal part L'_2. As shown, the reflection occlusion-signal L'_1 decreases, and transmission occlusion-signal increases with time.

Figs. 4A and 4B show the measurements with the diffuser for, respectively, reflection mode, and both reflection and transmission modes. As shown, when using the diffuser, all the signal parts increase during the measurements.

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

CLAIMS:

1. An optical measurement device for use in non-invasive measurements on a patient's body, the device comprising:

- an illumination assembly configured and operable to generate illuminating light of a predetermined wavelength range;
- a detection assembly comprising a first detector unit for detecting a first light signal transmitted through an illuminated body portion and generating first measured data indicative of the detected transmitted light, and a second detector unit for detecting a second light signal reflected from the illuminated body portion and generating second measured data indicative of the detected reflected light; and
- a light directing assembly comprising a light diffuser configured for scattering back light incident thereto, to thereby direct the illuminating light or the light coming from the body portion back towards the body portion, thereby increasing amount of light reaching a region of interest inside the body portion and thus maximizing homogeneity of the first and second detected light signals.

2. The device of Claim 1, wherein the light diffuser has at least one optical window for allowing light passage therethrough.

3. The device of Claim 1 or 2, wherein the light diffuser is located adjacent to the illumination assembly and oriented such that, when the device is applied to the patient's body, the light diffuser extends along at least a part of the body portion at the illuminating side thereof.

4. The device of Claim 3, wherein the diffuser is formed with an optical window for allowing passage of light from the illumination assembly towards the body portion.

5. The device of Claim 4, wherein the diffuser has an additional optical window for allowing passage of light, reflected from the body portion, to the second detector unit.

6. The device of any one of preceding Claims, wherein the diffuser is made of a semi-transparent material, capable of diffusing visible and near-infrared light spectra.

7. The device of any one of preceding Claims, wherein the diffuser is configured such that an attenuation coefficient and spatial distribution of diffused light is a very weak function of wavelength in said predetermined spectral rage.

8. The device of any one of preceding Claims, wherein a minimal size for the diffuser is such as to ensure that majority of the body surface provides efficient return of reflected light to the region of interest in the body.

9. The device of any one of preceding Claims, wherein the diffuser has a minimal size of about $48mm^2$.

10. The device of any one of preceding Claims, wherein the detector unit includes a matrix of light detectors.

11. The device of any one of preceding Claims, wherein the diffuser is mounted on a support arrangement supporting at least one of the illumination and detection assemblies.

12. The device of any one of preceding Claims, wherein the diffuser is an elastic cover configured to wrap at least a part of the body potion under measurements.

13. The device of any one of Claims 1 to 11, wherein the diffuser is a disposable elastic cover configured to wrap at least a part of the body potion under measurements.

14. The device of any one of preceding Claims, comprising a pressurizing assembly operable for applying an over-systolic pressure to the patient's body so as to create a condition of artificial blood kinetics in the region of interest and maintain this condition for a certain time period.

15. The device of Claim 14, wherein said pressurizing assembly is configured and operable to apply a secondary controllably varying pressure to the body within the region of interest, so as to alter said condition of artificial blood

kinetics over a predetermined time interval within said certain time period, thereby to modulate scattering properties of blood.

16. The device of any one of preceding Claims, wherein the illumination assembly comprises at least one light emitting element.

17. The device of any one of preceding Claims, wherein the illumination assembly comprises a matrix of light emitting elements generating light of different wavelengths.

18. The device of any one of preceding Claims, configured as a clip member for enclosing the body portion between its upper and lower arms, one of the upper and lower arms carrying the illumination assembly, the diffuser and the second detector unit, and the other arm carrying the first detector unit.

19. The device of Claim 18, wherein the diffuser extends along at least a part of an inner surface of the respective arm of the clip member.

20. The device of Claim 19, wherein the diffuser is located between the illumination assembly and the body portion, and is formed with an optical window for allowing passage of light from the illumination assembly to the body portion.

21. The device of Claim 20, wherein the diffuser is located between the body portion and the second detector unit, and is formed with an optical window allowing light passage therethrough from the body portion to the second detector unit.

22. The device of Claim 20, wherein the diffuser is located between the body portion and the second detector unit, and is formed with an additional optical window allowing light passage therethrough from the body portion to the second detector unit.

23. The device of any one of Claims 1 to 18, comprising a clip member for enclosing the body portion between its upper and lower arms, one of the upper and lower arms carrying the illumination assembly and the second detector unit, and the other arm carrying the first detector unit, the diffuser being an elastic cover configured to wrap at least a part of the body potion under measurements,

such that when the device is put in operation, the diffuser is located between the body portion and each of said arms of the clip member.

24. The device of any one of Claims 18 to 24, configured for measuring in a patient's finger, said clip member enclosing the finger between its upper and lower arms.

25. The device of any one of Claims 1 to 17, configured for measuring in a patient's finger.

26. The device of Claim 25, having a ring-like housing for enclosing a portion of the finger therein, said housing carrying at least the illumination and detection assemblies.

27. The device of Claim 26, wherein said ring-like housing is formed by two substantially U-shaped portions configured for enclosing and holding a portion of the patient's finger therebetween.

28. The device of Claim 27, wherein one of the U-shaped portions carries the illumination assembly, the diffuser and the second detector unit, and the other of said portions carries the first detector unit.

29. The device of Claim 27, wherein one of the U-shaped portions carries the illumination assembly and the second detector unit, and the other of said portion carries the first detector unit.

30. The device of any one of Claims 26 to 29, wherein the diffuser is an elastic cover configured to wrap at least a part of the patient's finger.

31. The device of any one of Claims 26 to 29, wherein the diffuser is a disposable elastic cover configured to wrap at least a part of the patient's finger.

32. The device of Claims 14 and 27, wherein the pressurizing assembly is associated with one of the U-shaped portions.

33. The device of Claims 15 and 27, wherein said pressurizing assembly is associated with one of the U-shaped portions.

34. The device of Claims 14 and 26, wherein the pressurizing assembly comprises an air cushion extending along at least a part of an inner surface of the housing.

35. The device of Claim 34, wherein at least a part of said cushion is made of a light diffusing material, thereby presenting said diffuser.

36. A method for use in non-invasive optical measurements on a patient's body utilizing illumination of a region of interest inside the body portion and detection of a light response of the region of interest to said illumination, the method comprising:

- collecting light coming from the body portion and directing at least a part of the collected light back to the body portion;
- detecting a first light signal transmitted through the body portion and generating first measured data indicative of the detected transmitted light, and detecting a second light signal reflected from the body portion and generating second measured data indicative of the detected reflected light;

the method providing for increasing amount of light reaching the region of interest inside the body portion, and for maximizing homogeneity of the first and second detected light signals.

37. The method of Claim 36, wherein said light coming from the body portion is light reflected therefrom.

38. The method of Claim 36, wherein said collecting of the light coming from the body portion and directing at least the part of the collected light back to the body portion comprises locating a light diffuser in an optical path of the light coming from the body portion.

39. The method of Claim 37, wherein said collecting of the reflected light and directing at least the part thereof back to the body portion comprises locating a light diffuser in an optical path of the light reflected from the body portion.

40. The method of Claim 38 or 39, wherein the diffuser is made of a semi-transparent material, capable of diffusing visible and near-infrared light spectra.

41. The method of any one of Claims 38 to 40, wherein the diffuser is configured such that an attenuation coefficient and spatial distribution of diffused light is a very weak function of wavelength in an operating spectral rage.

42. The method of any one of Claims 38 to 41, comprising selecting a minimal size for the diffuser such as to ensure that majority of the body surface provides efficient return of reflected light to the region of interest in the body.

5

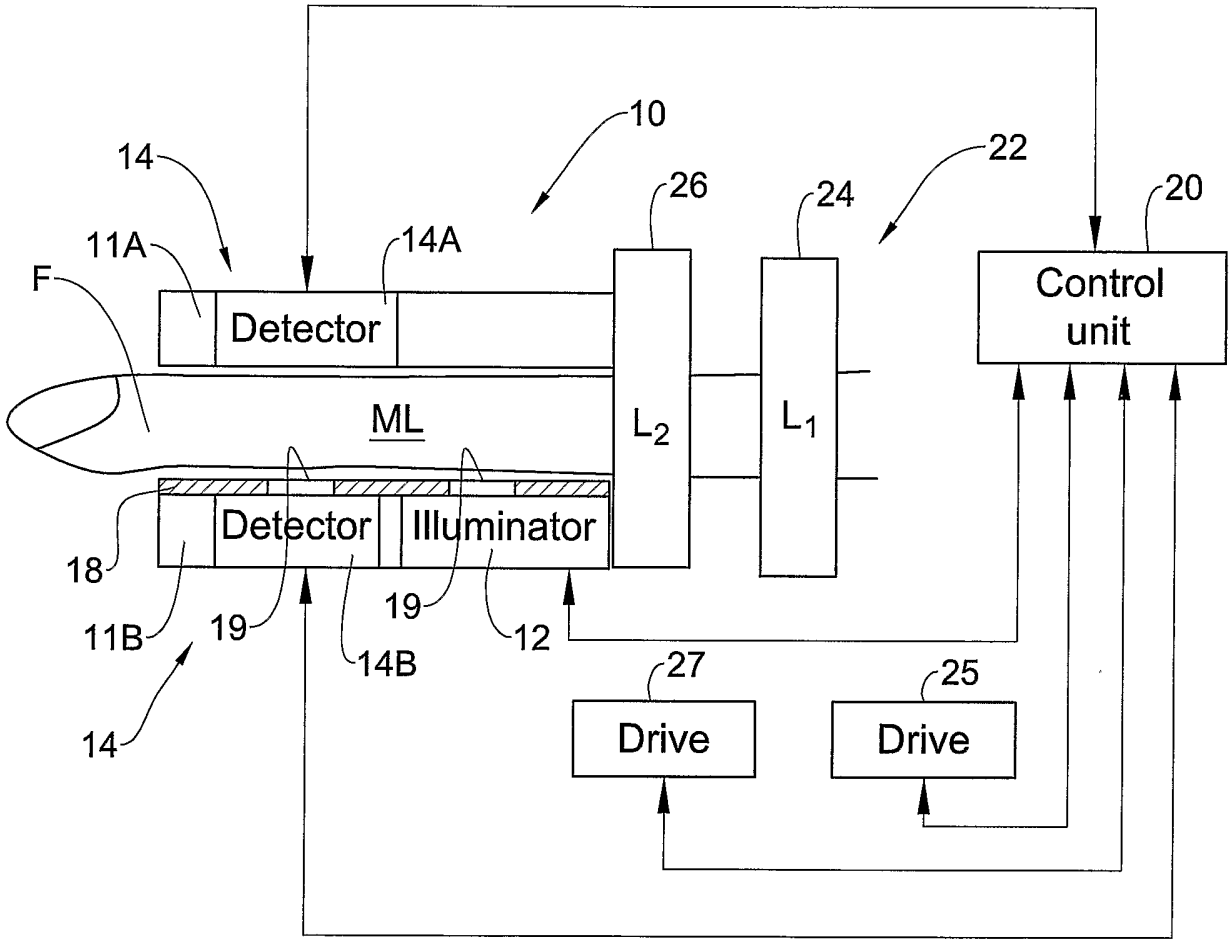

10
14
11A
14A
F
Detector
ML
Detector
Illuminator
18
11B
19
19
14B
12
14
26
24
22
20
Control unit
L_2
L_1
27
25
Drive
Drive

FIG. 1

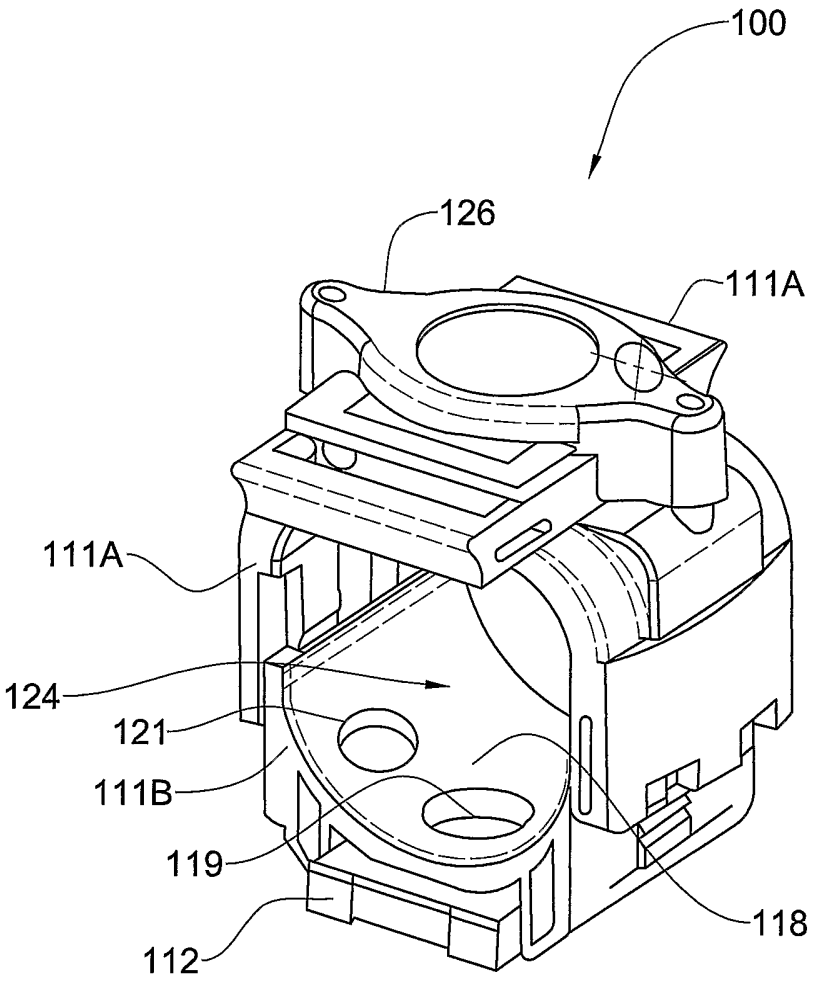


FIG. 2

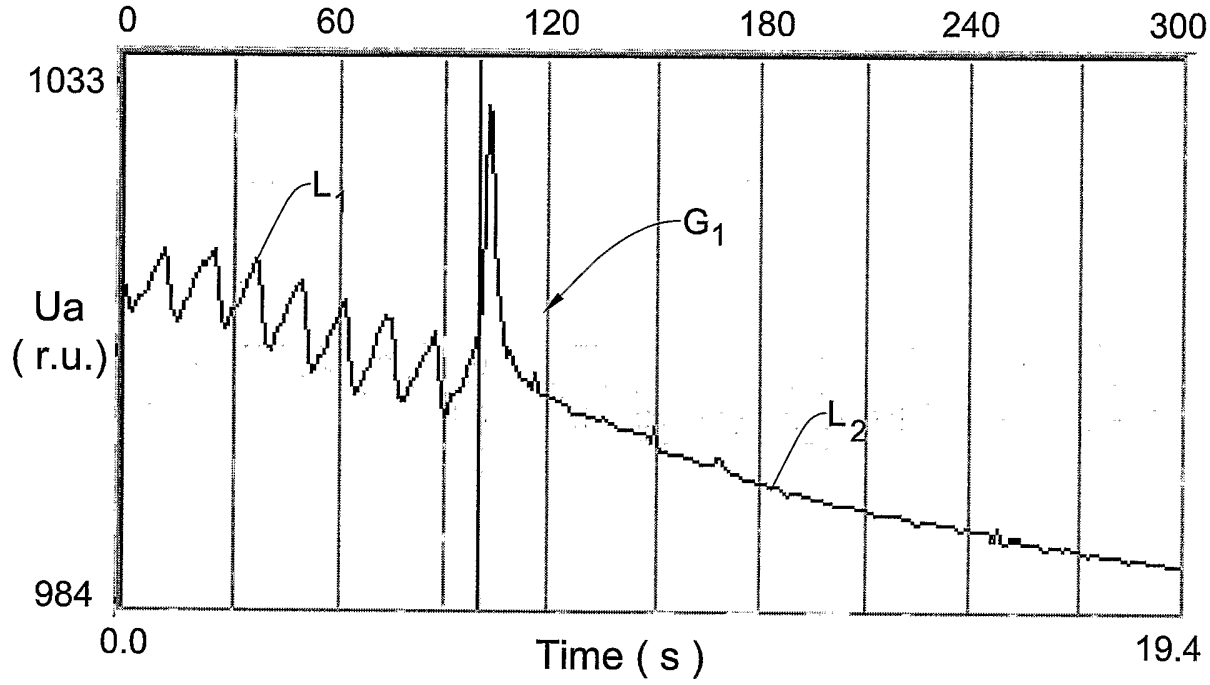

0
60
120
180
240
300
1033
Ua
(r.u.)
984
0.0
Time (s)
19.4
L1
G1
L2

FIG. 3A

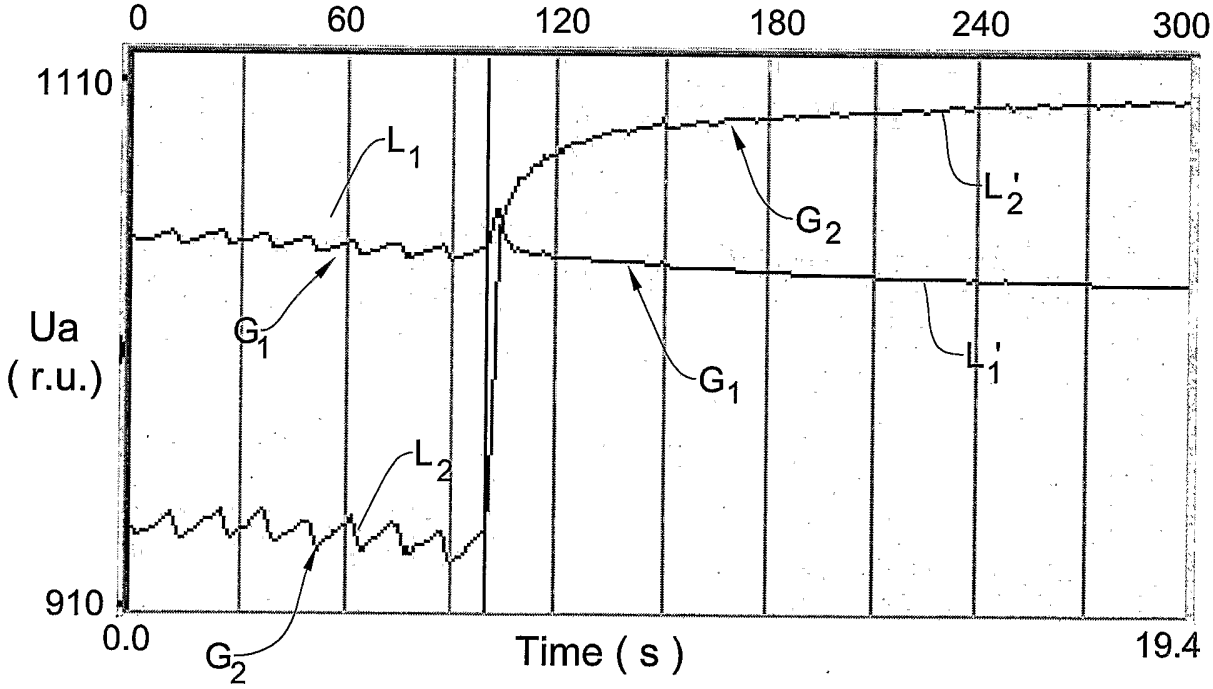

0
60
120
180
240
300
1110
Ua
(r.u.)
910
0.0
Time (s)
19.4
L1
G1
L2
G2
G1
G2
L'2
L'1

FIG. 3B

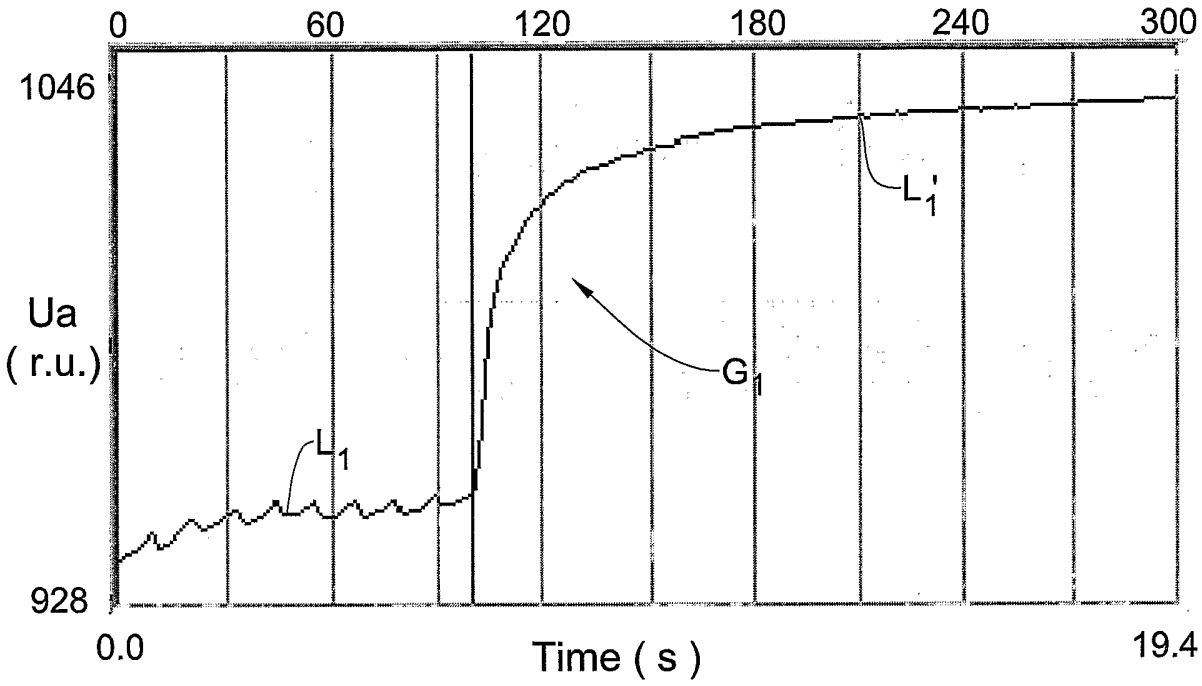

0
60
120
180
240
300
1046
Ua
(r.u.)
928
L1
G1
L'1
0.0
Time (s)
19.4

FIG. 4A

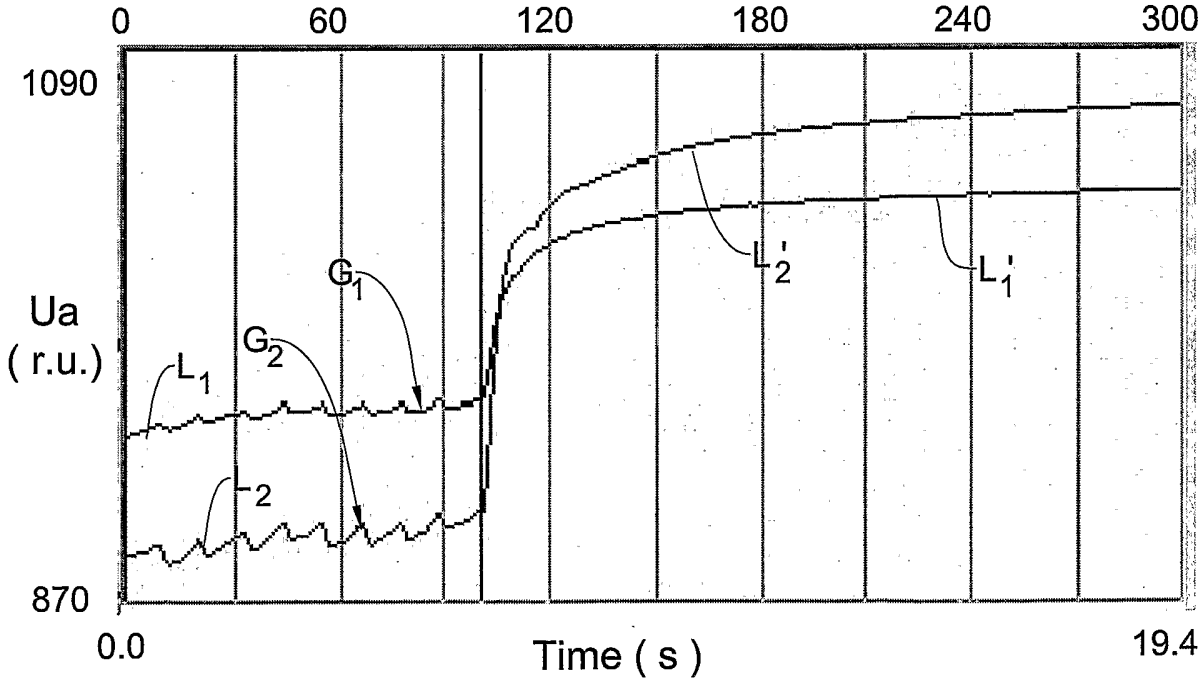

0
60
120
180
240
300
1090
Ua
(r.u.)
870
L1
G2
G1
2
L'2
L'1
0.0
Time (s)
19.4

FIG. 4B

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL2005/000720

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61B5/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 685 464 A (GOLDBERGER ET AL) 11 August 1987 (1987-08-11)	1-9,11, 12,16, 18-25, 36-42
Y	column 2, lines 51-55 column 4, lines 41-47 column 6, line 46 - column 9, line 63; figure 3 column 11, lines 1-5	13,31

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
4 October 2005	18/10/2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Kronberger, R

Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL2005/000720

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2003/036690 A1 (GEDDES LESLIE A ET AL) 20 February 2003 (2003-02-20) paragraphs '0022!, '0023!, '0030!, '0032!, '0040!; figures 1-3	1,6,11, 12, 14-16, 18,19, 23, 25-30, 32-40
X	US 2004/054290 A1 (CHANCE BRITTON) 18 March 2004 (2004-03-18) paragraphs '0008!, '0019!, '0058!, '0063!, '0064!, '0086!, '0092! - '0096!, '0099!; figures 1-4a,6	1,10,17, 36
Y	US 2002/077535 A1 (FINAROV ALEXANDER ET AL) 20 June 2002 (2002-06-20) paragraphs '0023!, '0024!	13,31
A	US 5 782 757 A (DIAB ET AL) 21 July 1998 (1998-07-21) column 7, lines 36-50; figure 3 column 8, lines 24-52 column 14, line 53 - column 15, line 7 column 17, lines 7-45 column 18, lines 36-42 column 20, lines 52-67 column 21, lines 8-10 column 21, lines 49-53	1
A	US 6 115 621 A (CHIN ET AL) 5 September 2000 (2000-09-05) column 2, line 31 - column 3, line 61	1
A	WO 01/96872 A (ORSENSE LTD; FINE, ILYA; FIKHTE, BORIS; VINOKUR, MARK) 20 December 2001 (2001-12-20) cited in the application page 2, lines 19-28 page 14, line 16 - page 15, line 20; figures 1a,2d,2e page 18, line 17 - page 19, line 17	14,15
P,X	WO 2004/105596 A (ORSENSE LTD; FINE, ILYA; FINAROV, ALEXANDER) 9 December 2004 (2004-12-09) page 22, line 8 - page 23, line 29; figure 8	1,36
P,X	WO 2004/112574 A (OPTIX LP; BLOCK, MYRON, J) 29 December 2004 (2004-12-29) page 3, line 4 - page 4, line 7; figures 1-4 page 5, line 19 - page 7, line 12	1,36

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL2005/000720

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4685464 A	11-08-1987	NONE	
US 2003036690 A1	20-02-2003	EP 1404215 A2	07-04-2004
		JP 2004532710 T	28-10-2004
		WO 03001180 A2	03-01-2003
US 2004054290 A1	18-03-2004	NONE	
US 2002077535 A1	20-06-2002	AU 1176400 A	28-09-2000
		WO 0053080 A1	14-09-2000
US 5782757 A	21-07-1998	US 6088607 A	11-07-2000
US 6115621 A	05-09-2000	NONE	
WO 0196872 A	20-12-2001	AT 303095 T	15-09-2005
		AU 7445101 A	24-12-2001
		EP 1292216 A2	19-03-2003
		US 2003137650 A1	24-07-2003
WO 2004105596 A	09-12-2004	NONE	
WO 2004112574 A	29-12-2004	US 2004257557 A1	23-12-2004