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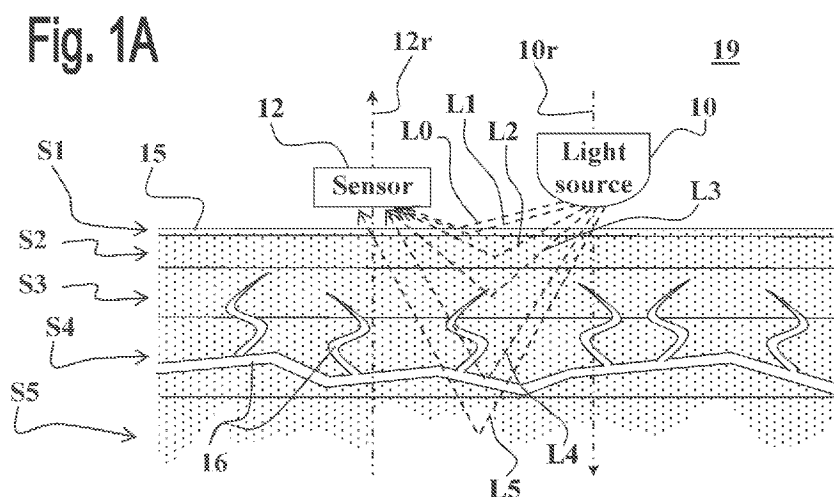
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(54) Title: METHOD AND DEVICE FOR OPTICAL MEASUREMENT OF BIOLOGICAL PROPERTIES



(57) Abstract: The subject matter discloses a device for measuring biological properties of an examined tissue, the device comprising at least one light source configured and operable to illuminate the examined tissue with light radiation of one or more wavelengths at a certain light illumination direction; and a light detector located at a same side of said examined tissue and configured and operable to receive light components of said one or more wavelengths reflected from the examined tissue in response to the illuminated light radiation at a certain light detection direction, and to generate measurement data indicative thereof, wherein at least one of said light illumination direction and detection direction is positioned at an angle of at least 2° relative to an imaginary line perpendicular to the examined tissue or form an angle of at least 2° between the light illumination direction and detection direction.

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METHOD AND DEVICE FOR OPTICAL MEASUREMENT OF BIOLOGICAL PROPERTIES

TECHNOLOGICAL FIELD

The present invention is generally in the field of optical measurement of biological properties of an examined subject, and blood related parameters and properties in particular.

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BACKGROUND

The majority of optical blood pulse measurements (*e.g.*, pulse oximetry) are carried out nowadays utilizing transmissive measurement techniques requiring sensor devices that are mountable over two opposite sides of a thin body part/organ (*e.g.*,
10 finger tip or earlobe). Particularly, transmissive measurement techniques use a light source typically placed on one side of the body part/organ for irradiating light signals thereover, and a light detector placed on the other side of the body part/organ to measure the intensity of light signals passing through it.

However, there are various advantages for reflective blood measurement
15 techniques, which are considered to be preferable in certain applications, particularly in types of wearable medical devices, such as medical watches, for example. Some of the advantages of reflective blood measurement techniques include, *inter alia*, the ability to conduct optical measurements on almost any part of the body, including thick organs. Other outstanding advantages are associated with the reduced energy consumption of
20 reflective measurement techniques stemming from the minimal energy consumption required to reflect light from tissue layers, as opposed to transmissive techniques where the light is required to pass through the entire width of the organ.

There are however various limitations associated with the reflective measurement techniques, such as low signal-to-noise ratios (SNR), the low AC/DC
25 ratios (Wherein AC is light waves reflected from (capillary) blood vessels, and DC is a combination of light waves reflected from other parts of the examine organ tissue and

light waves reflected directly from the organ surface without passing through the examine tissue. Attempts to overcome these limitations of the reflective measurement techniques by increasing the power of the irradiated light (*e.g.*, by increasing the electrical current supplied to the light source, and/or by increasing the number of light sources), typically also result in respective increase of noise components in the measured signals (due to respective increase of the baseline DC component), and thus do not provide satisfying results. There is thus a need to improve the quality of optical signals measured by reflective blood measurements techniques, to provide higher AC/DC ratios and improve the signal-to-noise ratios of the measured signals.

Some reflective measurements techniques known from the patent literature are briefly described herein below.

US Patent Publication No. 2009/082642 discloses a system and method for use in monitoring of biological parameters of a subject. The system includes an illumination unit including at least one light source of at least one pre-selected wavelength band, to be applied to a selected region in the subject; and a detection system configured for measuring reflections of the light at different angles and different spatial locations with respect to the illuminated region. The detection system is configured and operable to detect spatially separated light components corresponding to the specular dependent component of the signal and the pulsatile related diffused component of the signal coming from the subject in different directions respectively, thereby defining at least two independent channels of information, enabling identification of the reflected signal part dependent on motion effects.

US Patent Publication No. 2014/213917 describes a biofeedback device and a light sensor thereof that can be mounted on or integrated with eyewear such as swimming goggles. The biofeedback device may include a heart rate measurement apparatus comprising a reflected green light sensor, and first, second, and third green light emission elements. The biofeedback device may include a housing having a first portion and a second portion, which each of the first and second portions having a first side and a second side. At least a portion of the heart rate measurement apparatus may be disposed within the housing first portion and may be exposed through an opening in the second side of the housing first portion. The biofeedback device may also include an opening that allows the device to be removably engageable with at least a portion of the swimming goggles.

Chinese Patent publication No. 102198005 describes a reflective wrist oximeter with an electrocardiograph function, which comprises a blood oxygen acquisition module, an electrocardiosignal acquisition module, a processing module, a display module, a shell and wrist bands, wherein the blood oxygen acquisition module
5 comprises a light-emitting driver, a light-emitting tube and a photosensor; the light-emitting tube and the photosensor are arranged at the same side of a position to be detected, and an included angle having preset degrees is formed between the light-emitting tube and the photosensor; the electrocardiosignal acquisition module comprises a first electrode and a second electrode and is used for acquiring electrocardiosignals;
10 the processing module is used for processing pulse blood oxygen data acquired by the acquisition module and the electrocardiosignals acquired by the electrocardiosignal acquisition module; the display module is used for displaying information processed by the processing module to a user; the wrist bands are connected to both sides of the shell; the first electrode is arranged at one side of the shell, which is in contact with the wrist;
15 the display module is arranged at the other side of the shell, which is opposite to the first electrode; the second electrode is arranged outside the display module; and the blood oxygen acquisition module is arranged inside or outside the second electrode. The reflective wrist oximeter delicately combines the reflective blood oxygen technology and the electrocardiograph technology, and is convenient to operate.

SUMMARY OF THE INVENTION

The present invention discloses a device designed for optical measurement of biological properties of a subject employing a reflective measurement techniques. The reflective measurement techniques disclosed herein can be useful for measuring blood properties (*e.g.*, heart rate, blood parameters and/or blood analyses concentration/level) in a living tissue of the examined subject. The optical measurement device and techniques disclosed herein overcome the deficiencies associated with the conventional measurement setups by arranging one or more light sources of the reflective measurement device in certain orientations and distances relative to a light detector unit of the device's setup. Proper selection of the direction and distances of the one or more light sources relative to the light detector (or one more light detectors relative to the light source) substantially improves the magnitudes, the SNR and the AC/DC ratios, of the measured optical signals.

Optical signals measured by reflective measurement techniques can be substantially improved by properly setting a distance between a light source and a light detection unit of the device, and an angle between their light detector and light illumination directions. In this way most of the light components reaching the light detector are reflected/scattered from perfused layers of the illuminated tissue (also referred to herein as remote tissue layers), and that most of the light components reflected/scattered from non-perfused layers of the illuminated tissue (also referred to herein as near-surface tissue layers) don't reach the detector, and thus not measured.

Therefore, embodiments of the present invention provide that the majority of the light components detected by the light detection unit are scattered from tissue layers comprising blood vessels, and therefore contain more information about the blood flowing through the examined tissue (*i.e.*, the pulsating AC component). On the other hand, since many of the light components reflected/scattered from non-perfused tissue layers do not reach the detector and therefore not measured, the DC component of the measured signals is substantially reduced, which provides for substantial increase of the SNR and the AC/DC ratios of the measured signals.

In possible measurement setups of the measurement device, according to some possible embodiments at least one light source is used to emit light of one or more predetermined wavelength ranges over an examined tissue. At least one adjacently

located light detector is used to detect light radiation of said one or more predetermined wavelength ranges reflected from the illuminated tissue. The at least one light source and the at least one light detector are arranged in a spaced apart relationship to attain certain distances therebetween, and in predefined orientations one relative to the other
5 to attain a certain angle between their respective illumination and detection directions.

In some embodiments of the device configuration disclosed herein, the certain distances and predefined orientations between the light source(s) and light detector(s) of the reflective measurement device are configured such that only light components within a predetermined range of angular reflections can reach the light detector and
10 contribute to the measured optical signals. This device's configuration thereby reduces, or in some cases, substantially prevents, collection of light components directly reflected from the organ surface (*e.g.*, stratum corneum) without passing through any layer of the examine tissue, and/or reflected scattered light components from non-perfused upper layers of the examined tissue, and the like. The above two components
15 (directly surface reflection and non-perfused upper layers reflection) are the main DC components. Thereby a reduction at those components directly increase the AC/DC ratio. In some other exemplary embodiments of the present invention the reflective measurement device may be configured to increase the light emission. Such configuration can lengthen the optical path of the emitted light in a given tissue layer,
20 thereby increase the light scattering, and enhance the probability to collect light components reflected from the perfused tissue layer.

In some possible embodiments the reflective measurement device may comprise a plurality of light sources (*e.g.*, 2, 3 or 4, or more) arranged around a light detector, such that each of the light sources can direct emitted light away from the direction of
25 the light collection of the light detector. It is however noted that in some embodiments the reflective measurement device can be configured with acceptable good results using a single light source. In addition, in possible embodiments of the present invention several light detectors may be used to collect the light components reflected from examined tissue as the direction and distance of the light sources relative to the light
30 detectors of the device, may be within acceptable ranges of said certain distances and predefined directions of the measurement device.

Embodiments of the present invention may be used to implement wearable devices to be worn over a portion of body segments of a subject, such as, but not limited to, head neck, torso, or limbs (*e.g.*, over the wrist, like a watch).

The biological properties measured by the measurement device of the present invention may comprise heart rate, blood flow, arterial blood oxygen saturation, and various blood related parameters such as concentration of a substance/analyte (*e.g.*, sugar, cholesterol, hemoglobin, bilirubin) in blood, cardiac parameters, and the like. Thus, in some possible embodiment, the light source is configured to illuminate the examined tissue with multiple wavelengths selected for enabling determination of one or more biological properties of the subject.

1. It is an object of the present invention to disclose a device for measuring biological properties of an examined tissue, the device comprising, at least one light source configured and operable to illuminate the examined tissue with light radiation of one or more wavelengths at a certain light illumination direction; and a light detector located at a same side of said examined tissue and configured and operable to receive light components of said one or more wavelengths reflected from the examined tissue in response to the illuminated light radiation at a certain light detection direction, and to generate measurement data indicative thereof; at least one of said light illumination direction and detection direction is positioned at an angle of at least 2^0 relative to an imaginary line perpendicular to the examined tissue or form an angle of at least 2^0 between the light illumination direction and detection direction.

In some cases, the direction of light detector is substantially perpendicular to the surface of the examined tissue and the direction of light source is positioned at an angle of at least 2 degrees from the direction of light detector.

In some cases, the direction of light source is substantially perpendicular to the surface of the examined tissue and the direction of light detector is positioned at an angle of at least 2 degrees from the direction of light source.

In some cases, the at least one light source is oriented so as to direct the light illumination away from the light detector.

In some cases, the at least one light source is oriented so as to direct the light illumination towards the light detector.

In some cases, the at least one light source is parallel to the light detector and is positioned at an angle of at least 2^0 relative to an imaginary line perpendicular to the examined tissue.

In some cases, the at least one light source is not parallel to the light detector, wherein
5 each of the light source and the light detector forms an angle of at least 2^0 relative to an imaginary line perpendicular to the examined tissue.

In some cases, the distance between the at least one light source and the light detector is 0.1 to 30 mm.

In some cases, the angle formed between the light illumination and detection directions
10 is decreased in response to an increase in a distance between the at least one light source and the light detector.

In some cases, the device further comprises two or more light sources encircling the light detector.

In some cases, the biological properties include at least one of heart rate, oxygen
15 saturation, hemoglobin level, blood pressure, cardiac output, stroke volume, perspiration, glucose/sugar level, and bilirubin level, fat level.

In some cases, the device is a wearable device comprising a housing having bottom and upper sides and strapping means for attaching said bottom side of the housing to an examined tissue of said subject.

20 In some cases, the housing comprises at said bottom side of said housing, at least one light source configured and operable to illuminate said examined tissue with light radiation of one or more wavelengths at a certain light illumination direction, and a light detector configured and operable to receive light components of said one or more wavelengths reflected from the examined tissue responsive to the illuminated light
25 radiation at a certain light detection direction, and to generate measurement data indicative thereof, said light illumination and detection directions are selected to form an angle of at least 2^0 .

In some cases, the device further comprises a control unit configured and operable to activate said at least one light source to illuminate the examined tissue, receive and
30 process the measurement data generated by said light detector, and determined based thereon said biological properties.

In some cases, the device further comprising an output unit configured and operable to output data comprising at least one of said biological properties and said measurement data.

In some cases, the output unit comprises a display unit placed on the upper side of the
5 housing and configured and operable to receive and display said output data.

In some cases, the device further comprises an input unit configured and operable to receive input data from a user and transfer said input data to at least one of the control and display units.

BRIEF DESCRIPTION OF THE DRAWINGS

In order to understand the invention and to see how it may be carried out in practice, embodiments will now be described, by way of non-limiting example only, with reference to the accompanying drawings. Features shown in the drawings are
5 meant to be illustrative of only some embodiments of the invention, unless otherwise implicitly indicated. In the drawings like reference numerals are used to indicate corresponding parts, and in which:

Figs. 1A and 1B schematically illustrate a conventional reflective measurement device;

10 **Figs. 2A and 2B** schematically illustrate a reflective measurement setup according to some possible embodiments wherein the light source is located adjacent the light detector;

Figs. 3A and 3B schematically illustrate a reflective measurement setup according to some possible embodiments wherein the light source is relatively remote to
15 the light detector;

Fig. 4 schematically illustrates a wearable device for measuring biological properties according to some possible embodiments;

Fig. 5 exemplifies a reflective measurement device according to some possible embodiments utilizing several light sources;

20 **Fig. 6** schematically illustrate a reflective measurement setup according to possible embodiments utilizing several light detectors; and

Fig. 7 exemplifies a reflective measurement setup according to possible embodiments utilizing several light detectors.

DETAILED DESCRIPTION OF EMBODIMENTS

One or more specific embodiments of the present disclosure will be described below with reference to the drawings, which are to be considered in all aspects as illustrative only and not restrictive in any manner. In an effort to provide a concise
5 description of these embodiments, not all features of an actual implementation are described in the specification. Elements illustrated in the drawings are not necessarily to scale, emphasis instead being placed upon clearly illustrating the principles of the invention. This invention may be provided in other specific forms and embodiments without departing from the essential characteristics described herein.

10 The present invention discloses a reflective optical measurement device designed to improve the magnitudes of optical signals measured from an examined tissue, and their SNR and AC/DC ratios. It is known that a substantial portion of the optical signals measured using reflective measurement devices contain light components reflected from non-perfused tissue layers, that mainly contribute to baseline
15 DC and noise components (*i.e.*, light components that don't contain blood related information) of the measured signals. It is also known that the ratio between the perfused area to non-perfused area which influences the AC/DC ratio may vary from one body organ to another. This is demonstrated in **Figs. 1A** and **1B**, showing a typical reflective measurement setup **19** configured for measuring optical signals reflected from
20 an examined tissue **15**.

The measurement setup **19** comprises a light source **10** and a sensor unit **12**, disposed on an outer surface of the examined tissue **15**. The sensor unit **12** is also defined as a light detector **12**. Typically, the light source **10** and the light detector **12** are placed on a skin region of a subject and arranged such that the light detector **12** receives
25 components of the light emitted from the light source **10** and reflected from different layers **S1, S2, ..., S5, ...** of the examined tissue **15** towards the detector **12**. The light source **10** and the light detector **12** are substantially parallel to the surface of the examined tissue **15**, such that the direction of light illumination **10r** of the light source **10** and the direction of light detection **12r** of the light detector **12** are substantially
30 parallel.

Fig. 1A further exemplifies the scattering of light components reflected from the various layers of the examined tissue **15** in such conventional reflective measurement

5 setups **19**. As seen, the light detector **12** in the measurement setup **19** receives light components **L0** directly reflected from the outer surface **S1** of the skin, light components **L1** penetrating the outer surface **S1** and reflected from the interior of the stratum corneum, and light components **L3** reflected from the granular and spinous cell layers **S2** of the skin.

The light components **L0** reflected directly from the outer surface of the outermost skin layer **S1** do not contain any valuable information. Likewise, as the skin layers **S1** and **S2**, which form the epidermis of the skin (also referred to herein as near-surface tissue layers), don't comprise any blood vessels **16** in them, the light components **L1** and **L2** penetrating into these non-perfused tissue layers, and reflected from them towards the light detector **12**, also do not contain blood related information. Thus the light components **L0**, **L1** and **L2**, which are combined with the other light components during the optical signal measurements of the light detector **12**, do not contribute to the measured optical signals any blood related information (pulsating AC components).

The light components which contribute blood related information to the optical signals measured by the light detector **12** are **L3**, **L4** and **L5**, which penetrate into the deeper perfused tissue layers **S3**, **S4** and **S5** (also referred to herein as remote tissue layers, as they are located relatively remote from the light source). These tissue layers contain blood vessels **16**, such that the light components reflected from them towards the light detector **12** introduce pulsating components to the optical signals measured by the light detector **12**. Particularly, the light components **L3** are reflected from the dermis layer **S3**, the light components **L4** are reflected from the hypodermis (subcutaneous tissue) layer **S4**, and the light components **L5** are reflected from the tissue layers **S5** underneath the skin (*e.g.*, muscular tissue).

The light detection scheme of the measurement setup **19** is further exemplified in **Fig. 1B**, which illustrates light illumination sector **10v** of the light source **10**, and a light detection sector **12v** of the light detector **12**. The intersection **17** of the illumination sector **10v** and the detection sector **12v** represents the portion of the illuminated light that is reflected towards the light detector **12** during the measurements. The portion of sectors intersection **17** located external to the examined tissue **15** is associated with the light components **L0** reflected towards the light detector **12** directly from the outer surface **S1** of the tissue **15**. The portions of sectors intersection **17** located in the near-

surface epidermis layers **S1** and **S2** are associated with the light components from **L1** and **L2** reflected towards the detector **12** form the non-perfused tissue layers. The portions of sectors intersection **17** located in the remote tissue layers **S3**, **S4** and **S5** are associated with the light components from **L3**, **L4** and **L5**, reflected towards the
5 detector **12** form the perfused tissue layers.

The optical signals measured by the light detector **12** comprise DC components and pulsating AC components. While all the light components **L0** to **L5** measured by the light detector **12** comprise DC components, only the light components **L3** to **L5** reflected from the perfused tissue layers contribute pulsating AC components.
10 Therefore, in the optical signal measured by the light detector **12** in conventional measurement setups **19** exemplified in **Figs. 1A** and **1B**, the portion of the pulsating AC components relative to the portion of the DC components, is substantially small (*e.g.*, about 1/1000 to 1/5000 at the wrist), which thus provide poor signal quality with low SNR and AC/DC ratios.

15 In order to improve the quality of the optical signals measured by reflective measurement setups it is desired to maximize in the measured optical signals light components that interact with the perfused tissue layers **S3**, **S4** and **S5** (*i.e.*, to increase the pulsating AC components that contains blood related information), and minimize in the measured optical signals light components that interact with the non-perfused tissue
20 layers **S1** and **S2**. These objectives are achieved in some of the embodiments disclosed herein by at least one of: (i) increasing as much as possible the optical paths through which the measured light components pass through the examined tissue **15** tissue before they reach the light detector **12**, thereby causing them to interact with more of the blood vessels **16** of the examined tissue **15**; and (ii) reducing as much as possible
25 measurement of light components that are reflected from the non-perfused tissue layers (*e.g.*, external layers such as the epidermis).

In some embodiments the setup of the reflective measurement device **20** shown in **Figs. 2A** and **2B** is used, in which at least one light source **10** (only one is shown in **Figs. 2A** and **2B**) is placed spaced apart from the light detector **12**, and oriented such
30 that the angle α between the direction of light illumination **10r** and the direction of light detection **12r** is greater than 0° and smaller than 90° , optionally about 2° to 88° (*i.e.*, an angle α of 0° means that light illumination direction **10r** and the light detection direction **12r** are parallel, for example perpendicular to the examined tissue **15**, as

shown in **Fig. 1**, and an angle α of 90° is obtained when the light illumination direction **10r** is perpendicular to the light detection direction **12r**.

In this non-limiting example the angle between the light detector **12** and the examined tissue **15** results the two being substantially parallel to. Also, as seen, the light detector **12** and at least one light source **10** are located at the same side of the examined tissue **15**, wherein the same side is defined as a setup in which the light detector's position is such that the detected light is the light reflected by the body tissue

In this reflective measurement configuration **20** as the angle α between the light illumination direction **10r** and the light detection direction **12r** is increased the distance between the light source **10** and the light detector **12** are respectively reduced, and *vice versa*. For example, and without being limiting, in some embodiment the distance **T1** in the reflective measurement setup **20** is about 0.1 to 30 mm (for angles α ranging between 2° to 88° , respectively). Optionally, and in some embodiments preferably, the light detector **12** is substantially parallel to the examined tissue (*i.e.*, the light detection direction **12r** is substantially perpendicular to the surface of the examined tissue **15**), and the angle α is obtained by properly setting the orientation of the light sources **10** of the measurement setup **20**.

As shown in **Figs. 2A** and **2B**, the angle of orientation of the light source **10** permits locating the light source **10** at relative short distance **T1** in the vicinity of the light detector **12**, while guaranteeing that the light components **L0'**, **L1'** and **L2'**, are reflected from the non-perfused tissue layers **S1** and **S2** with substantially acute angles relative to the light detection direction **12r**. Thus the amount of light components **L0'**, **L1'** and **L2'** reflected from the non-perfused near-surface tissue layers **S1** and **S2** towards the light detector **12** is substantially reduced. The angle of orientation enables maintaining a small blood measurement apparatus with improved SNR and AC/DC ratio.

On the other hand, the light components **L3'**, **L4'** and **L5'**, penetrating into the remote perfused tissue layers, **S3**, **S4** and **S5**, respectively, are caused to travel greater distances until they are reflected towards the light detector **12** and therefore interact with greater amounts of perfused tissues. Due to the increased optical paths of the light components **L3'**, **L4'** and **L5'** reflected from the perfused tissue layers, **S3**, **S4** and **S5**, the amount of pulsating AC information they contain is substantially increased.

This light detection scheme of the reflective measurement setup **20** is further demonstrated in **Fig. 2B** showing the intersection **17'** of the light illumination sector **10v'** with the light detection sector **12v**. As seen, the portions of the intersection **17'** of the sectors are located only (or mainly, depending on the angle α) in the perfused tissue layers **S3**, **S4** and **S5**. Accordingly, all of the portions of the intersection **17'** are associated with the light components **L3'**, **L4'** and **L5'** reflected towards the light detector from the perfused tissue layers.

Accordingly, the baseline DC components in the optical signals measured by the light detector **12** in the reflective measurement setup **20** are substantially reduced, by reducing the amount (or altogether excluding) of light components **L0'**, **L1'** and **L2'**, reflected from the non-perfused tissue layers **S1** and **S2**. On the other hand, since the optical paths **L3'**, **L4'** and **L5'**, of the light components reflected towards the light detector **12** from the perfused tissue layers are increased, they interact more intensely with perfused tissue and thus contain significantly more blood related information and contribute greater amounts of pulsating AC components to the optical signals measured by light detector **12** (as compared to conventional measurement setup **19** of **Fig. 1**).

Experiments conducted by the inventors showed that the optical signals measured using the reflective measurement configuration **20** provide substantial improvement in the quality of the measured optical signals, and in their SNR and AC/DC ratios. For example, utilizing a reflective measurement device may increase the AC/DC ratio in a factor of 10 or more.

Figs. 3A and **3B** demonstrate another possible measurement setup **30** according to some possible embodiments. In this non-limiting example the at least one light source **10** (one light is shown in **Figs. 3A** and **3B**) is displaced from the light detector **12** to a relatively remote location over the examined tissue **15**, and respectively oriented towards the light detector **12**. As exemplified here, the light detector **12** is substantially parallel to the examined tissue **15**, and the light detector **12** and the at least one light source **10** are located at the same side of the examined tissue **15**. In possible embodiments, the distance **T2** between the light source **10** and the light detector **12** is about 0.1 to 30 mm. The angle α between the light illumination direction **10r** and the light detection direction **12r** is increased as the distance **T2** is increased.

Optionally, and in some embodiments preferably, the light detector **12** is substantially parallel to the surface of the examined tissue **15** (*i.e.*, the light detection

direction is substantially perpendicular to the tissue surface), and the orientation of the light source **10** is selected to provide suitable angle α between the light illumination and light detection directions *e.g.*, about 2° to 88° . In this arrangement, the light components **L1''** to **L5''** are reflected from the respective tissue layers **S1** to **S5** towards the light detector **12** in obtuse angles. Proper selection of the orientation of the light source **10** with respect to the distance **T2** provides that the amount of light components **L0''**, **L1''** and **L2''**, reflected from the non-perfused tissue layers **S1** and **S2** and detected by the light detector **12**, is substantially/negligibly small, while assuring substantial detection of the light components **L3''**, **L4''** and **L5''**, reflected from the perfused tissue layers, **S3**, **S4** and **S5**.

As demonstrated in **Fig. 3B**, the portions of the intersection **17''** of the light detection sector **12v** and the illumination sector **10v''** are all located in the remote perfused tissue layers **S3**, **S4** and **S5**. Accordingly, all of the portions of the intersection **17''** are associated with the light components **L3''**, **L4''** and **L5''** reflected towards the light detector **12** from the perfused tissue layers.

Accordingly, the baseline DC components in the optical signals measured by the light detector **12** in the reflective measurement setup **30** are substantially reduced, by reducing (or altogether excluding) the amount of light components **L0''**, **L1''** and **L2''**, collected by the light detector **12** from non-perfused tissue layers **S1** and **S2**. On the other hand, since the optical paths, of the light components **L3''**, **L4''** and **L5''** reflected towards the light detector **12** from the perfused tissue layers are increased, they interact more intensely with perfused tissue and thus contain significantly more blood related information and contribute greater amounts of pulsating AC components to the optical signals measured by light detector **12** (as compared to conventional measurement setup **19** of **Figs. 1A** and **1B**).

Experiments conducted by the inventors showed that the optical signals measured using the reflective measurement configuration **30** provides substantial improvement in the quality of the measured optical signals, and in their SNR and AC/DC ratios. For example, utilizing a reflective measurement device may increase the AC/DC ratio in a factor of 10 or more

Fig. 4 schematically illustrates a wearable device **40** comprising a reflective measurement setup **49** according to some possible embodiments, configured for measuring biological properties of a subject. In this non-limiting example, the wearable

device **40** comprises a housing **48** and one or more straps **47** (two straps are shown in **Fig. 4**), having respective fastening means **47f** at their ends, configured for attachment of the wearable device **40** over a body part/organ of the examined subject (*e.g.*, over the wrist, like a watch). A bottom side **48b** of the housing **48** comprises the measurement
5 setup **49**, which in this example comprises two light sources **10a** and **10c** mounted adjacent to the light detector **12**, and tilted such that their light illumination directions are directed away from the light detector **12**, *i.e.*, as in the measurement setup **20** shown in **Fig. 2**.

The measurement setup **49** is designed to place the light sources **10a** and **10c**,
10 and the light detector **12**, at the same side of the examined tissue, and to place the light detector **12** over the examined tissue substantially parallel to its surface. Although the wearable device **40** comprises only two light sources **10a** and **10c**, it should be clear that it may comprise additional light sources *e.g.*, as exemplified in **Fig. 5**.

The housing **48** comprises a control unit **43** configured and operable to operate
15 the light sources **10a** and **10c** to illuminate tissue of body part/organ on which the device **40** is worn, and receive from the light detector **12** data and/or signals indicative of the light components reflected from the examined tissue and received by the light detector **12** responsive to the light illuminated by the light sources **10a** and **10c**. The control unit **43** may further be configured to process the data/signals received from the
20 light detector.

In some embodiments the light sources **10a** and **10c** are configured and operable to illuminate the examined tissue with light of two or more wavelengths, as may be needed for determining certain blood properties/parameters. In this case the control unit **43** is further configured to operate the light sources **10a** and **10c** to illuminate the
25 examined tissue with such light radiation of one or more wavelengths, and receive from the light detector **12** corresponding data/signals indicative of the light components reflected from the examined tissue towards the light detector **12** responsive to the illuminated light.

The housing **48** may further comprise a power source **41** (*e.g.*, one or more
30 chargeable batteries), and a memory unit **42** (*e.g.*, RAM, ROM, FLASH) comprising one or more programs, and/or data, as may be needed for carrying out measurements by the measurement setup **49**. The upper side **48u** of the housing **48** may comprise a display unit **44** (*e.g.*, LCD) electrically coupled to the control unit **43** and configured

and operable to display measurement results and/or other data, thereon. The upper side **48u** of the housing **48** may further comprise an input unit **45** (*e.g.*, comprising a keypad and/or one or more press buttons) configured and operable to provide the control unit **43** with inputs from a user of the wearable device **40**.

5 The wearable device **40** may further comprise a data communication interface **46** for communicating data between the control unit **43** and an external computer system (not shown *e.g.*, a personal computer - PC). The data communication interface **46** may be configured and operable to communicate with external devices wirelessly (*e.g.*, by WiFi, Bluetooth, or Zigbee), and/or over wire lines/bus (*e.g.*, using serial
10 communication such as universal asynchronous receiver/transmitter - UART / universal serial bus – USB, or parallel bus lines such as IEEE 1284). The data communication interface **46** may be further configured to electrically couple the wearable device **40** to an external power source (not shown *e.g.*, mains power grid) for recharging the power source **41** of the wearable device **40**. The data communication interface **46** may be
15 further used to load data and/or programs into the memory unit **42** of the wearable device **40** from an external computer system, if so needed.

In some embodiment, the measured optical signals can be further improved by increasing the flux of light illuminated towards the examined tissue, for example, by using two or more light sources, as exemplified in **Fig. 4** hereinabove. The light sources
20 may be angularly spaced apart on a perimeter encircling the light detector **12**, radially spaced apart therefrom and oriented with respect to said radial distance such that the angles between the light illumination and light detection directions increases the travel paths of the detected light components through the examined tissue.

Fig. 5 exemplifies a reflective measurement device **50** according to some
25 possible embodiments comprising a single detector **12** and four light sources **10a**, **10b**, **10c** and **10d** (collectively referred to herein as light sources **10**). The light sources **10** are mounted on the support member **52** displaced and remote from the light detector **12**, and their orientations are properly set such that their light illumination directions are directed toward the light detector **12** (as in the measurement setup **30** shown in **Fig. 3**),
30 to provide a suitable angle α between the light illumination directions **10r** and the light detection direction **12r**. This arrangement allows placing the light sources **10** and the light detector **12** at the same side of the examined tissue, and the light detector **12** substantially parallel to the tissue surface.

In a similar fashion, the light sources **10** may be located on support member **52** adjacent to the light detector **12**, and tilted such that their light illumination directions are directed away from the light detector **12**, to provide a suitable angle α between the light illumination directions **10r** and light detection direction **12r** (as in the measurement setup **20** shown in **Fig. 2**).

Fig. 6 exemplifies a reflective measurement setup **69** that combines principles of the measurement setups **20** and **30** shown in **Figs. 2A-B** and **3A-B**, respectively. In this non-limiting example two light sources **62** are placed in a vicinity of a central light detector **60c** with distances **T1** there between. The two light sources **62** are oriented such that their light illumination directions are directed away from the central light detector **60c**, so as to form angles α between their light illumination direction and the light detection direction of the central detector **60c**. With this arrangement of the light sources **62** and the central light detector **60c** two intersections **17'** are formed between the detection sector **60v** of the central light detector **60c** and the illumination sectors **62v** of the light sources **62**.

The measurement setup **69** further comprises two peripheral light detectors **60r**, each associated with a respective one of the light detectors **62** and located with a distance **T2** therefrom. The tilt angle α of the light detectors **62** and the distance **T2** of their respective peripheral light detectors **60r**, are selected such that two intersections **17''** are respectively formed between the detection sectors **60v** of the peripheral light detector **60r** and the illumination sectors **62v** of their respective light sources **62**. The ranges of the distances **T1** and of the angles α are substantially as defined hereinabove with reference to **Figs. 2A-B**, and the ranges of the distances **T2** are substantially as defined hereinabove with reference to **Figs. 3A-B**, for example 0.1mm to 30mm.

Fig. 7 exemplifies a configuration of a reflective measurement device **79** comprising four light sources **70** arranged around a central light detector **70c**, and four peripheral light detectors **70r**, each associated with a respective one light source **70**. The reflective measurement device **79** is a two-dimensional implementation of the measurement setup **69** shown in **Fig. 6**. Namely, the light sources **70** are placed in the vicinity of the central light detector **70c** with distances **T1** therefrom, and tilted away therefrom such that angles are formed between the light detection direction of the light detectors **70c** and the light illumination directions of the light sources **70**. In this way, four intersections (similar to **17'** disclosed above) are defined between the light

detection sector of the central light detector **70c** and the illumination sectors of the light sources **70**, and four intersections (similar to **17''** disclosed above) are defined between the light detection sectors of the peripheral light detectors **70r** and the illumination sectors of their respective light sources **70**.

5 The reflective measurement device **79** is designed to place all light sources and detectors at the same side of the examined tissue, and place the light detectors substantially parallel to the surface of the examined tissue. The ranges of the distances **T1** and of the angles α are substantially as defined hereinabove with reference to **Figs. 2A-B**, and the ranges of the distances **T2** are substantially as defined hereinabove with
10 reference to **Figs. 3A-B**.

In some embodiments one or more optical elements are coupled to the light source **10** to provide a predefined angle of light illumination (*i.e.*, the angle of sector **10v'** and **10v''** in **Figs. 2B** and **3B**). For example, one or more lenses (not shown) may be optically coupled to the light source to provide an illumination angle of about 15° to
15 30° and reduce light dispersion of the light source **10**. Additionally, or alternatively, in possible embodiments the light source **10** may be designed to provide such the desired illumination angles without using lenses *e.g.*, by collimators. The light source **10** may be implemented using one or more light emitting diodes (LEDs). For example, and without being limiting, in some possible embodiments the light source **10** comprises
20 LEDs for emitting light radiation in at least one of the wavelengths within a range between 400nm and 1500 nm (Nanometer), which may be used for determining at least one of the biological properties, respectively: at least one of heart rate, oxygen saturation, hemoglobin level, blood pressure, cardiac output, stroke volume, perspiration, glucose/sugar level, and bilirubin level, fat level.

25 In standard devices the light source direction and light detector direction are parallel and perpendicular to the surface of the examined tissue as shown in figure 1. The present invention includes all the combinations of changing this configuration. The configurations of the present invention include:

1. The light detector in the same position and light source with inner or outer
30 angle relative to an imaginary line perpendicular of the examined tissue,
2. The light source is fixed and the light detector has the above angle,
3. Both elements have different angles, for example the light source is directed towards the light detector and the light detector is directed away from the

light source, both the detector and the source are directed towards the other or away from the other;

4. The illumination and detection directions are parallel and not perpendicular to the examine tissue surface.

5 Alternatively, the light source **10** may be implemented by a radiation source capable of simultaneously emitting light radiation in a predefined radiation spectrum range covering the one or more wavelength ranges needed for determining the biological properties. For example, and without being limiting, one or more filtering device optically coupled to the light source **10** may be used to selectively illuminate the
10 examined tissue with light radiation in a specific wavelength range at a time, as may be required for determining a specific biological property by the device.

It is note that the reflective measurement techniques disclosed herein are also very useful for portable as the improved SNR and AC/DC ratios they provide mitigates signals distortions that are induced in the measured signals due to movements of the
15 body part/organ to which the device is attached.

Fig. 8 exemplifies a method to configure the reflective measurement device, according to exemplary embodiments of the invention. In step 805 a user utilizing the reflective measurement device may configure the distances between the light detector and the light source. The light source may be configured in a certain distances relative
20 to a light detector unit of the measurement device. In step 810, the user may measure the AC/DC ratio with a specific examined tissue, in the configured distance between the light source and light detector. In some cases, the measurement process defined in step 810 may take place with number of tissue types, various wavelengths, various measured properties and additional parameters of the device. In step 815, the user may configure
25 the angle between the light source and the light detector. The angle configuration may be in accordance to the AC/DC ratio received in step 810. For example, different wavelengths may be reflected differently from the same examined tissue, the user may change the angle between the light detector and the light source, check the AC/DC ratio and in some cases, change the angle again until the received AD/DC rate reaches a
30 predefined or desired threshold or value. The angle configuration preformed in step 815 may be achieved by tilting the light detector and the light source laterally, upwards and/or downwards, or in other words closer or farther away from the examined tissue. In step 820, the user may reexamine the AC/DC ratio and preform changes in the angle

between the light source and the light detector. For example, the user may tilt the light detector upwards or downwards and thereby change the AC/DC rate received by the reflective measurement device. In some case, the user may go back to step 805 and change the distances between the light source and the light detector in order to achieve an optimal AC/DC rate. In step 825, the user may start to examine the tissue after the angle and distance are determined. Thus, the user may measure the AC/DC rate in several cases along the method described above. In some cases, different wavelengths may be emitted to the examined tissue, and then be detected by different light detectors. In some other cases, more than one tissue may be examined and the user may need to set the reflective measurement device on different organs, or limbs. The user may also be required to conduct steps 805, 810, 815, and 820 several times on various examined tissues. The techniques disclosed herein are applicable to almost any type of optical measurement of blood properties, parameters and/or analytes, employing effects of optical absorption and scattering of electromagnetic radiation in a living tissue. Particularly, the techniques disclosed herein are useful for measuring pulsating signals, as typically obtained in types of non-invasive blood measurements, such as, but not limited to, pulse oximetry, photoplethysmogram (PPG) measurements, and suchlike. For example, and without being limiting, the optical measurement techniques disclosed herein may be useful for measuring blood pulses, oxygen (O₂) saturation, hemoglobin levels, glucose/sugar levels, bilirubin levels, and suchlike.

The method of the present invention enables emission of various wavelengths and measurements of various properties. Some wavelengths are reflected differently from the same examined tissue. Hence, the present invention also disclosed selecting an optimal combination of angle between the light emitter and light detector as well as the distance between them.

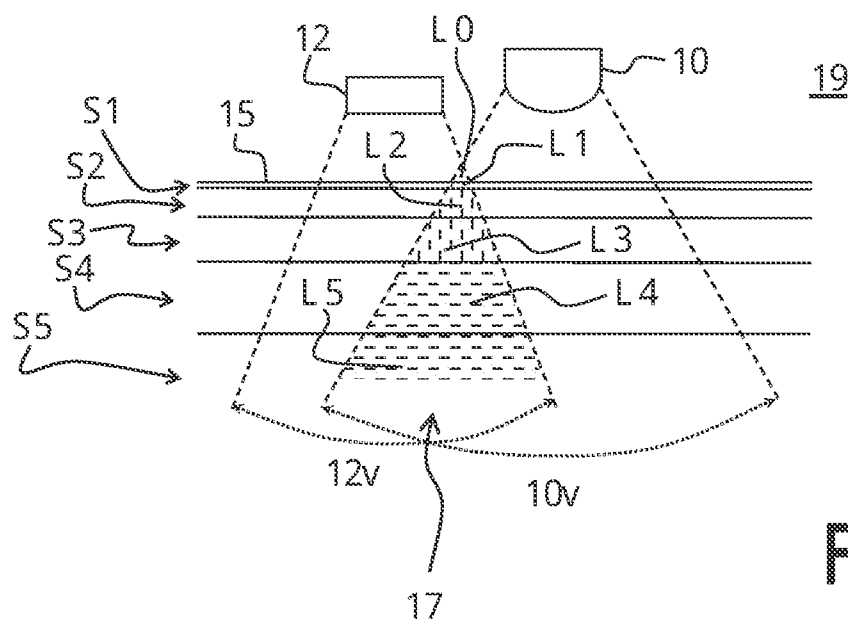
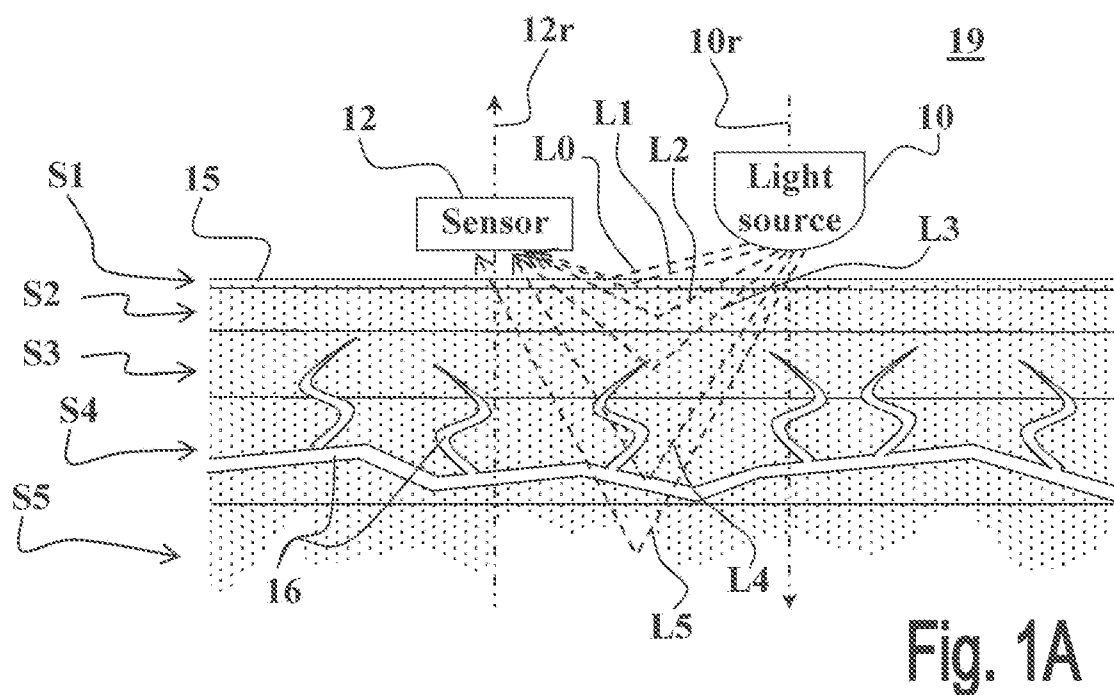
As described hereinabove and shown in the associated Figs., the present invention provides reflective measurement configurations for measuring biological properties of an examined tissue/subject with substantially improved SNR and AC/DC ratios. While particular embodiments of the invention have been described, it will be understood, however, that the invention is not limited thereto, since modifications may be made by those skilled in the art, particularly in light of the foregoing teachings. As will be appreciated by the skilled person, the invention can be carried out in a great

variety of ways, employing more than one technique from those described above, all without exceeding the scope of the invention.

CLAIMS:

1. A device for measuring biological properties of an examined tissue, the device comprising:
 - at least one light source configured and operable to illuminate the examined
 - 5 tissue with light radiation of one or more wavelengths at a certain light illumination direction; and
 - a light detector located at a same side of said examined tissue and configured and operable to receive light components of said one or more wavelengths reflected from the examined tissue in response to the illuminated light radiation at a certain light
 - 10 detection direction, and to generate measurement data indicative thereof;
 - at least one of said light illumination direction and detection direction is positioned at an angle of at least 2^0 relative to an imaginary line perpendicular to the examined tissue or form an angle of at least 2^0 between the light illumination direction and detection direction.
- 15 2. The device of claim 1 wherein the direction of light detector is substantially perpendicular to the surface of the examined tissue and the direction of light source is positioned at an angle of at least 2 degrees from the direction of light detector.
3. The device of claim 1 wherein the direction of light source is substantially perpendicular to the surface of the examined tissue and the direction of light detector is
- 20 positioned at an angle of at least 2 degrees from the direction of light source.
4. The device of claim 1, wherein the at least one light source is oriented so as to direct the light illumination away from the light detector.
5. The device of claim 1, wherein the at least one light source is oriented so as to direct the light illumination towards the light detector.
- 25 6. The device of claim 1, wherein the at least one light source is parallel to the light detector and is positioned at an angle of at least 2^0 relative to an imaginary line perpendicular to the examined tissue.
7. The device of claim 1, wherein the at least one light source is not parallel to the light detector, wherein each of the light source and the light detector forms an angle of
- 30 at least 2^0 relative to an imaginary line perpendicular to the examined tissue.
8. The device of any one of claim 1 wherein the distance between the at least one light source and the light detector is 0.1 to 30 mm.

9. The device of any one of claim 1 wherein the angle formed between the light illumination and detection directions is decreased in response to an increase in a distance between the at least one light source and the light detector.
10. The device of claim 1, further comprising two or more light sources encircling
5 the light detector.
11. The device of claim 1, wherein the biological properties include at least one of heart rate, oxygen saturation, hemoglobin level, blood pressure, cardiac output, stroke volume, perspiration, glucose/sugar level, and bilirubin level, fat level.
12. The device of claim 1, wherein the device is a wearable device comprising a
10 housing having bottom and upper sides and strapping means for attaching said bottom side of the housing to an examined tissue of said subject.
13. The device of claim 12, wherein the housing comprises:
at said bottom side of said housing, at least one light source configured and operable to illuminate said examined tissue with light radiation of one or more
15 wavelengths at a certain light illumination direction, and a light detector configured and operable to receive light components of said one or more wavelengths reflected from the examined tissue responsive to the illuminated light radiation at a certain light detection direction, and to generate measurement data indicative thereof, said light illumination and detection directions are selected to form an angle of at least 2° .
- 20 14. The device of claim 12, further comprises a control unit configured and operable to activate said at least one light source to illuminate the examined tissue, receive and process the measurement data generated by said light detector, and determined based thereon said biological properties.
15. The device of claim 12 further comprising an output unit configured and
25 operable to output data comprising at least one of said biological properties and said measurement data.
16. The device of claim 15 wherein the output unit comprises a display unit placed on the upper side of the housing and configured and operable to receive and display said output data.
- 30 17. The device of claim 12, further comprising an input unit configured and operable to receive input data from a user and transfer said input data to at least one of the control and display units.



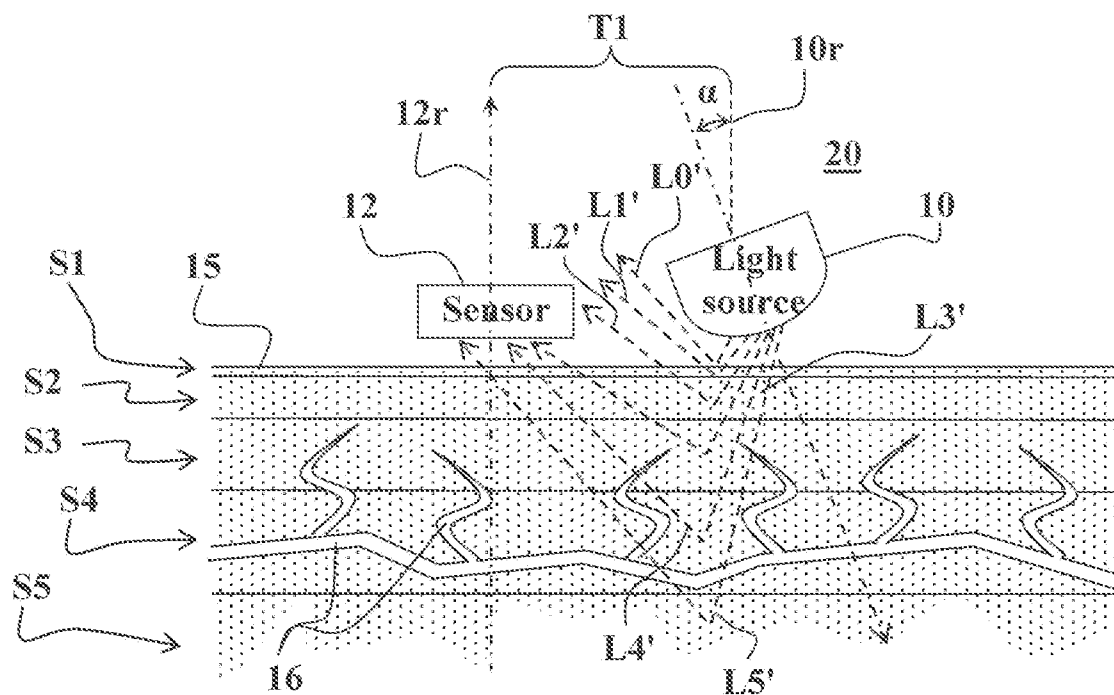


Fig. 2A

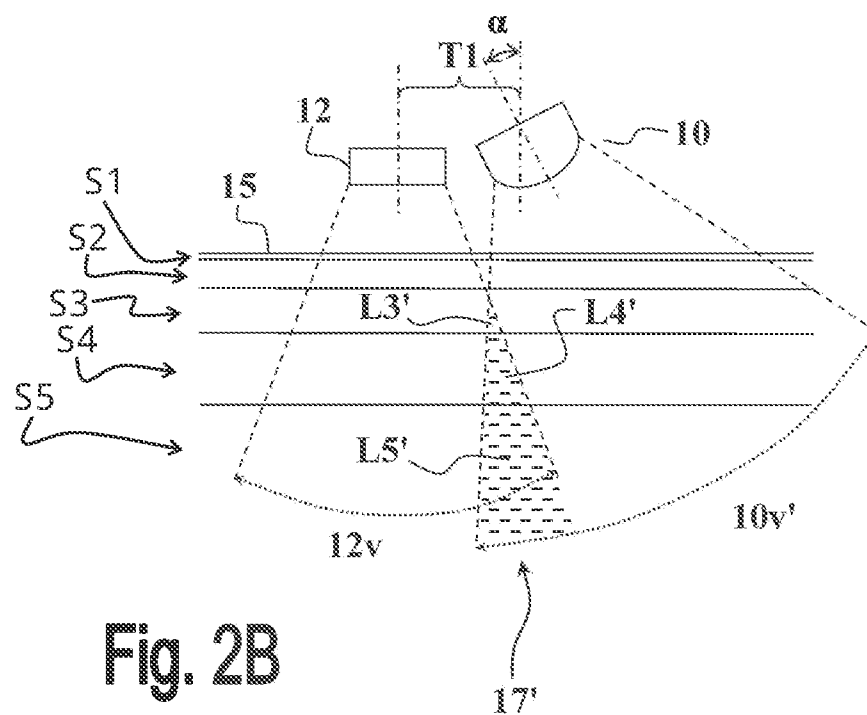
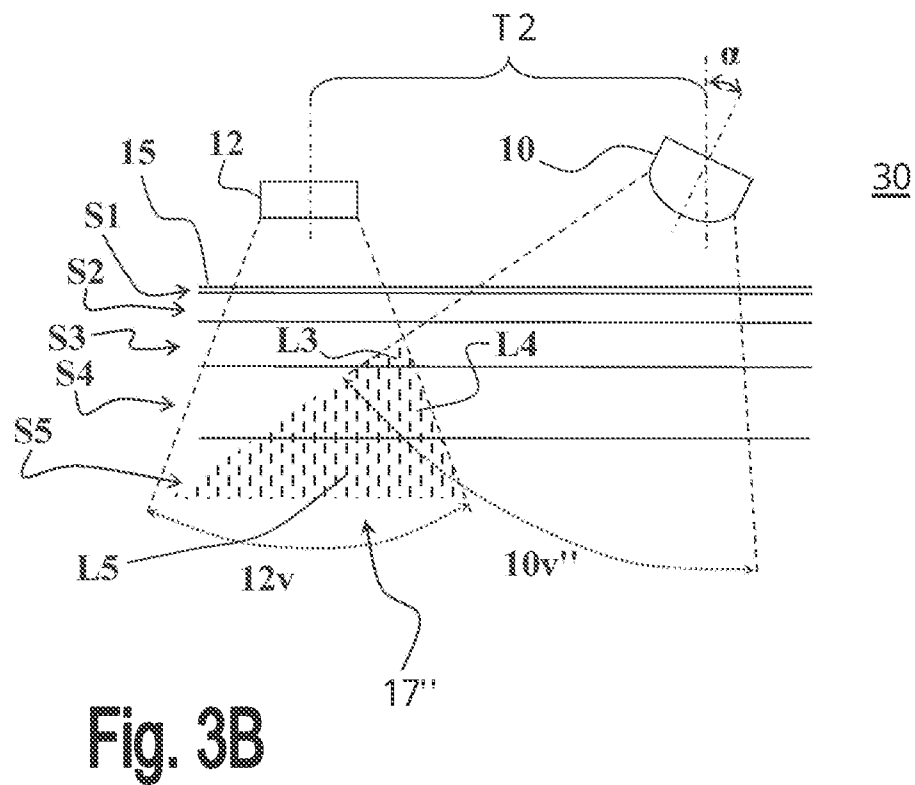
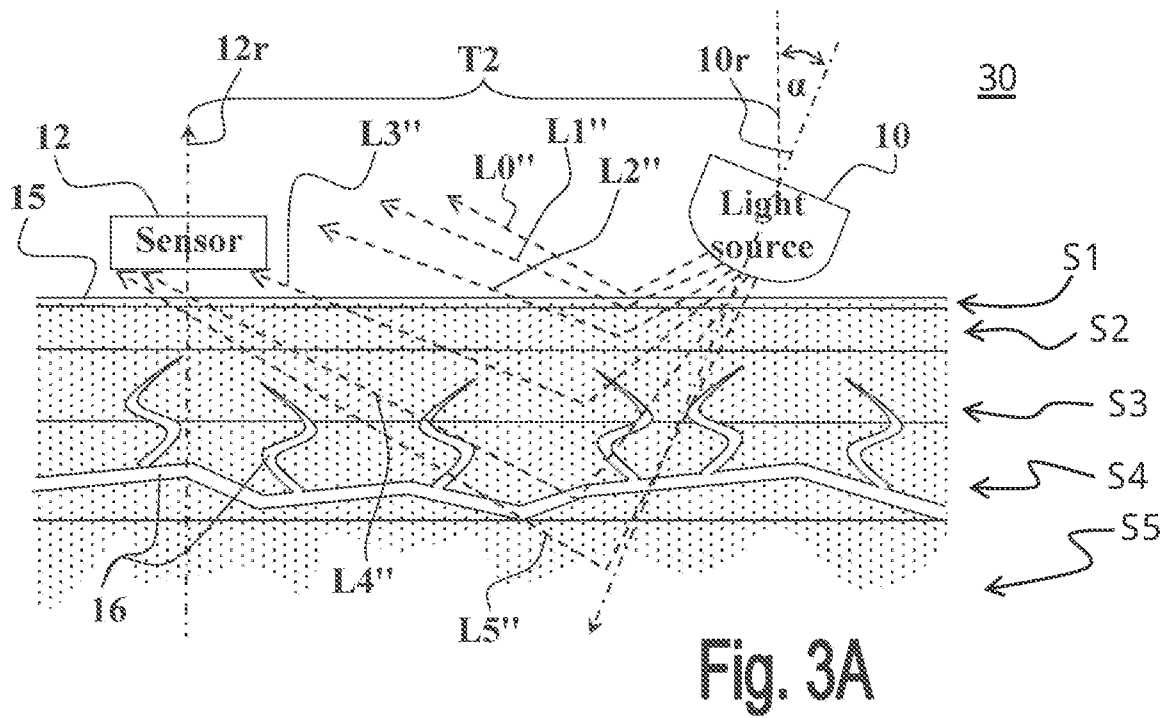


Fig. 2B



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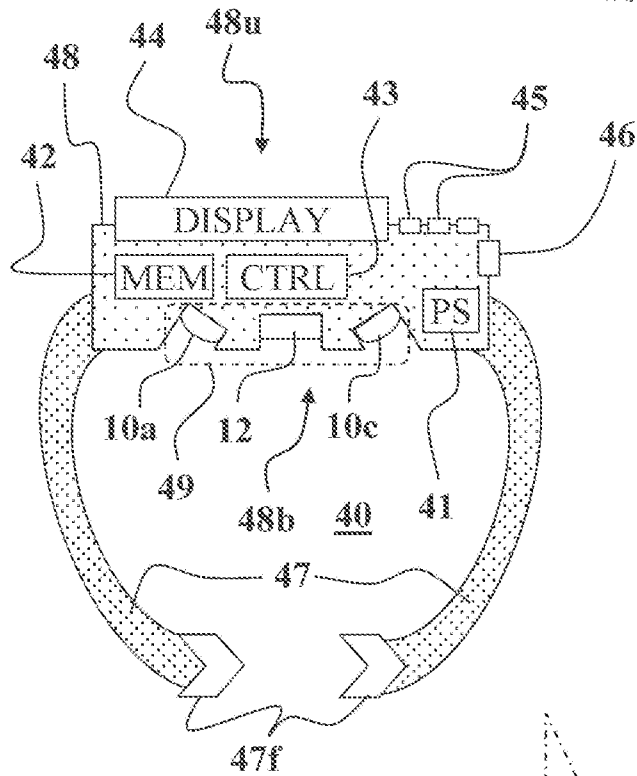


Fig. 4

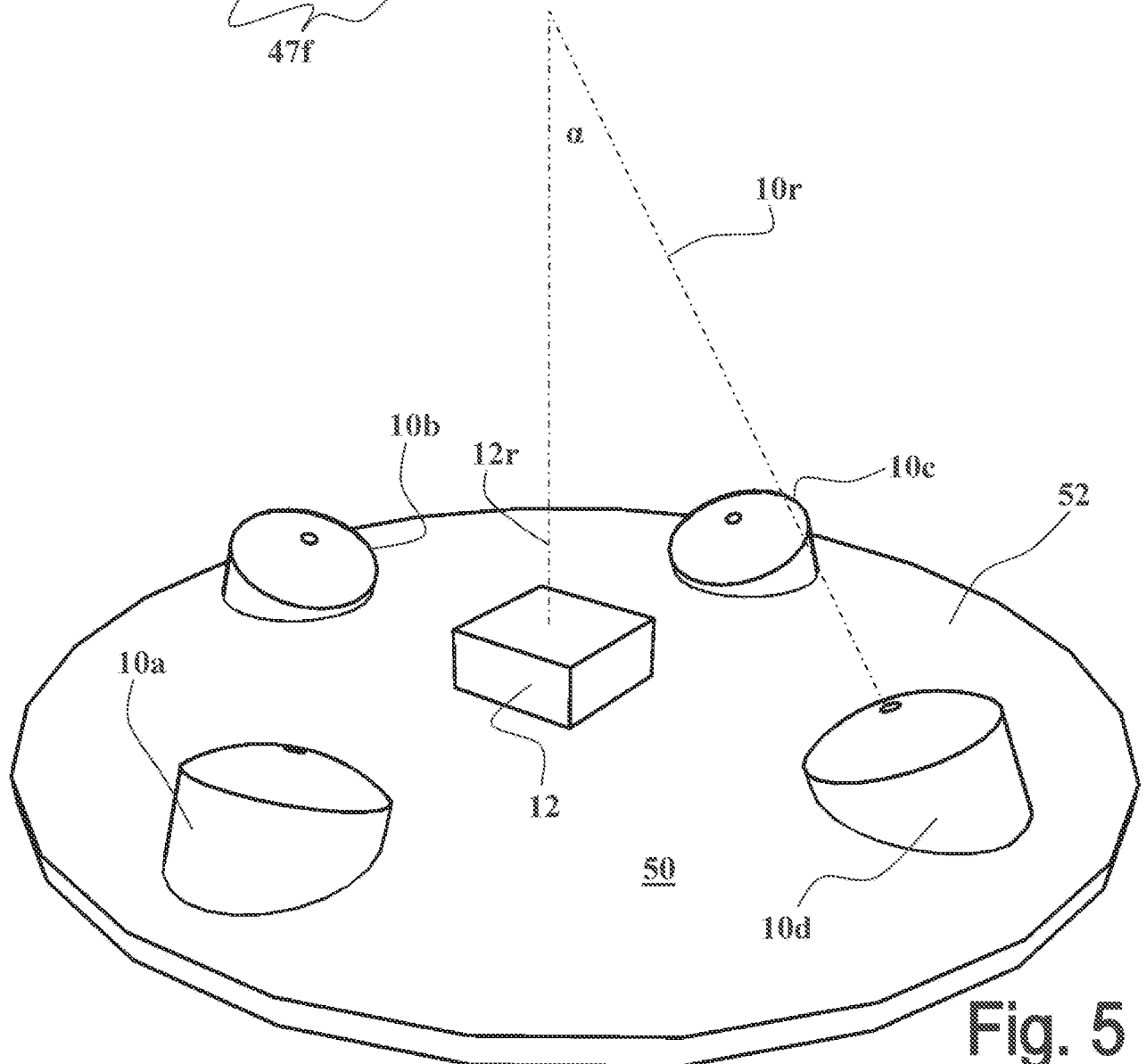
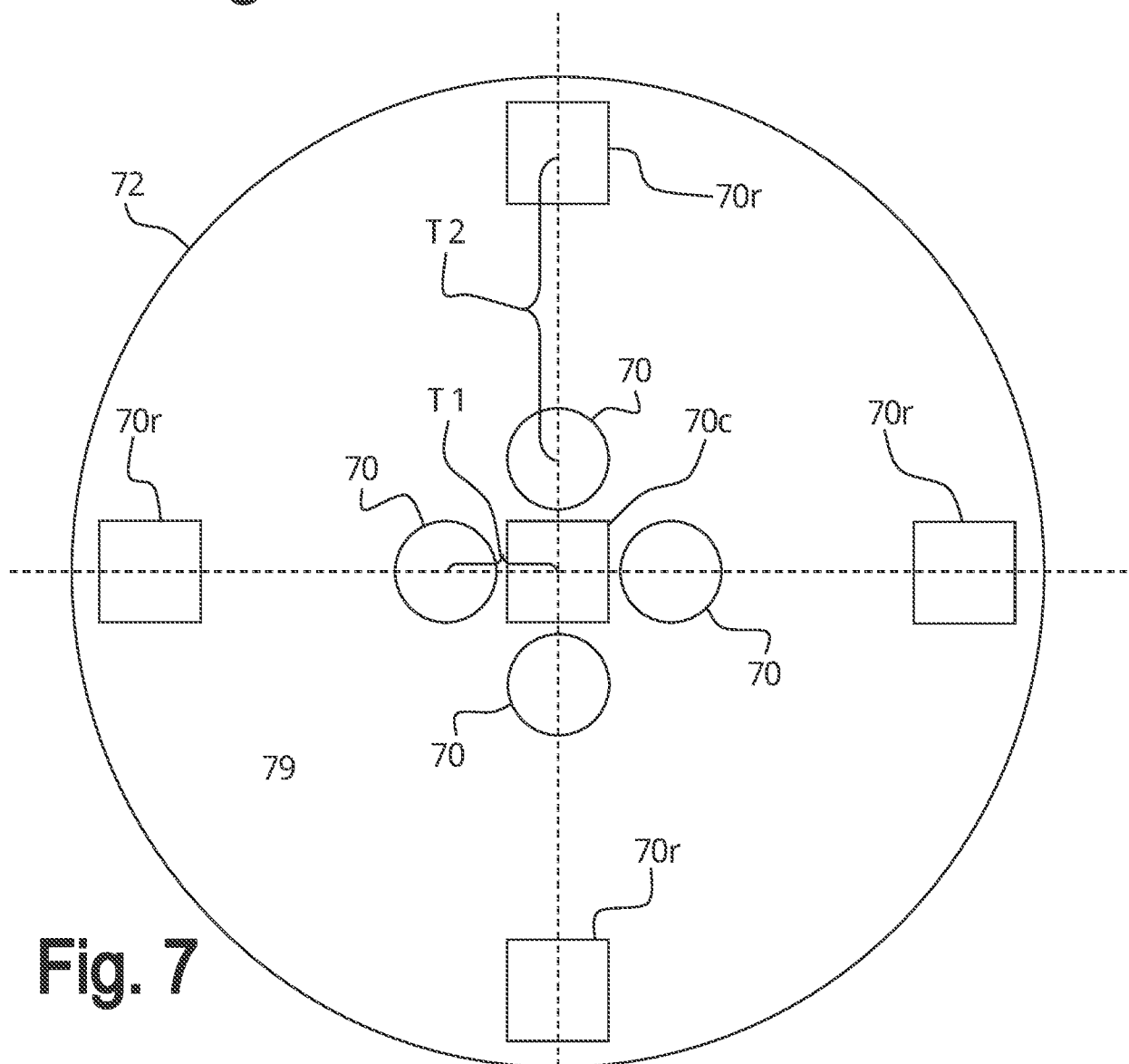
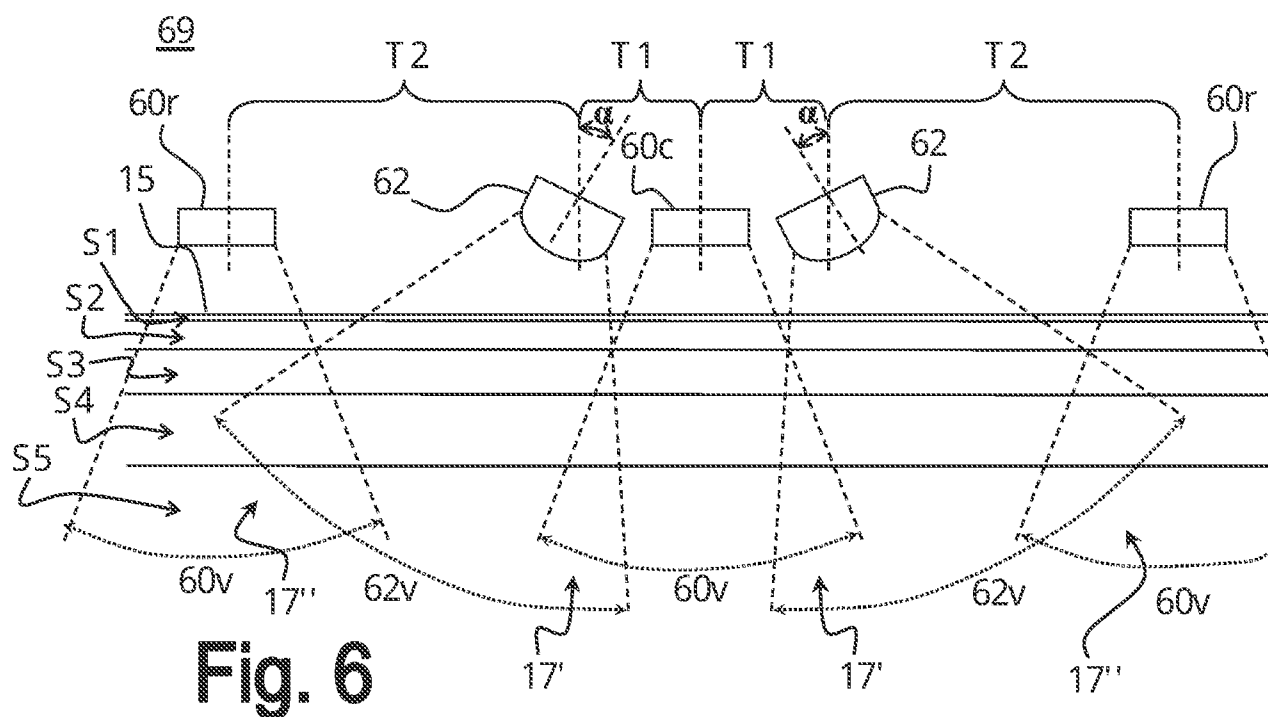


Fig. 5

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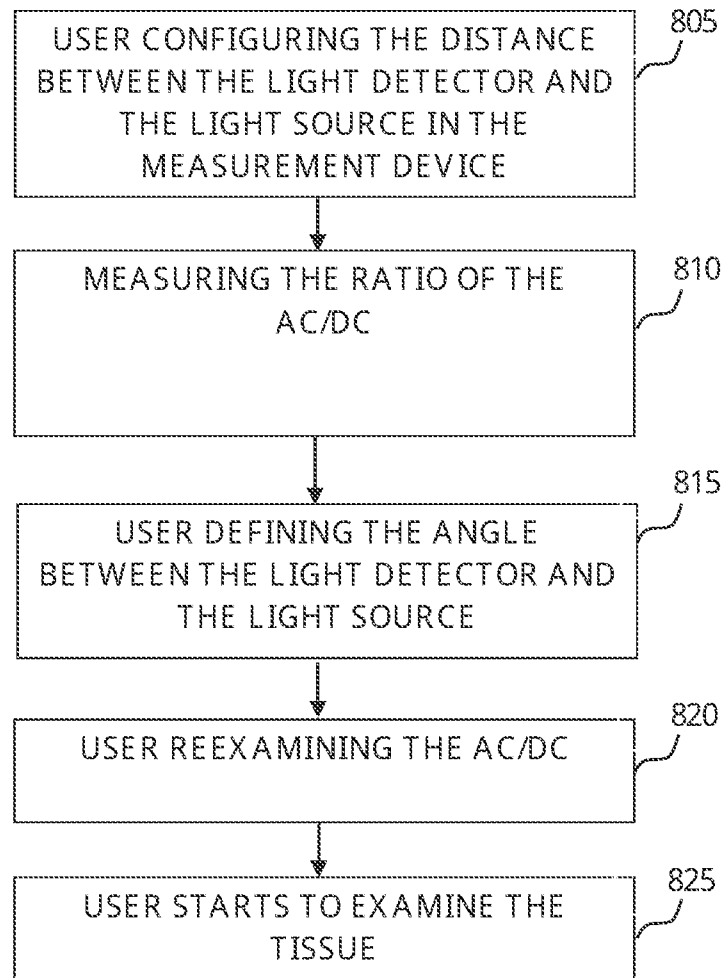


Fig. 8

INTERNATIONAL SEARCH REPORT

International application No.

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A. CLASSIFICATION OF SUBJECT MATTER IPC (2017.01) A61B 5/00 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 (2017.01) A61B 5/00 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 practicable, search terms used) Databases consulted: Esp@cenet, Google Patents, FamPat database, Orbit		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 7953474 B2 HWANG IN DUK et al. 31 May 2011 (2011/05/31) The whole document	1-17
A	US 2005002031 A1 KRAEMER UWE et al. 06 Jan 2005 (2005/01/06) The whole document	1-17
☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
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Date of the actual completion of the international search 17 Oct 2017		Date of mailing of the international search report 22 Oct 2017
Name and mailing address of the ISA: Israel Patent Office Technology Park, Bldg.5, Malcha, Jerusalem, 9695101, Israel Facsimile No. 972-2-5651616		Authorized officer DAVIDI Ariel Telephone No. 972-2-5651727

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

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Patent document cited search report			Publication date	Patent family member(s)			Publication Date
US	7953474	B2	31 May 2011	US	2008021330	A1	24 Jan 2008
				US	7953474	B2	31 May 2011
				EP	1880665	A1	23 Jan 2008
				EP	1880665	B1	07 May 2014
				KR	20080008778	A	24 Jan 2008
				KR	100813169	B1	17 Mar 2008
US	2005002031	A1	06 Jan 2005	US	2005002031	A1	06 Jan 2005
				US	7315752	B2	01 Jan 2008
				AT	401823	T	15 Aug 2008
				AU	2002361024	A1	15 Jul 2003
				AU	2002361024	A8	15 Jul 2003
				DE	10163972	A1	10 Jul 2003
				DE	10163972	B4	27 Oct 2005
				DE	50212550	D1	04 Sep 2008
				EP	1463443	A2	06 Oct 2004
				EP	1463443	B1	23 Jul 2008
				JP	2005513491	A	12 May 2005
				JP	4038179	B2	23 Jan 2008
				WO	03055382	A2	10 Jul 2003
				WO	03055382	A3	13 Nov 2003

专利名称(译)	用于光学测量生物学特性的方法和装置		
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其他公开文献	EP3487394A4		
外部链接	Espacenet		

摘要(译)

该主题公开了一种用于测量被检查组织的生物特性的装置，该装置包括至少一个光源，该光源被配置并可操作以在特定光照射方向上用一或多个波长的光辐射照射被检查组织；光检测器位于所述被检查组织的同一侧，并且被配置并可操作以响应于在特定光检测方向上的被照射光辐射接收从被检查组织反射的所述一个或多个波长的光分量，并且产生测量指示其的数据，其中所述光照射方向和检测方向中的至少一个相对于垂直于被检查组织的假想线以至少2°的角度定位或者在光照射方向之间形成至少2°的角度和检测方向。