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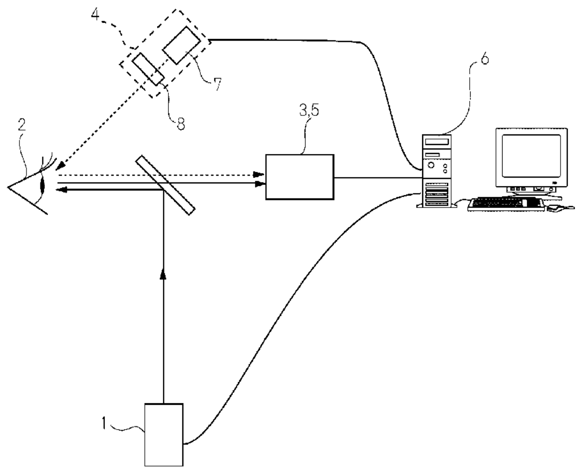
(54) Title: OXYGEN CONSUMPTION MEASUREMENT SYSTEM AND DIAGNOSTIC SYSTEM

[Fig. 1]



(57) Abstract: A system capable of obtaining oxygen consumption and the like by irradiating light on a retina is developed. An oxygen consumption measurement system is provided with a laser light source (1); a first optical detecting means (3) ; a multiple wavelength light source (4); a second optical detecting means (5); and a controller (6) connected to the first optical detecting means (3) and the second optical detecting means (5), which obtains a blood flow in a retina using a detected signal detected by the first optical detecting means (3), obtains an oxygen saturation using a detected signal detected by the second optical detecting means (5), and obtains a variation in oxygen consumption in the retina using the blood flow in the retina and the oxygen saturation.

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Description

OXYGEN CONSUMPTION MEASUREMENT SYSTEM AND DIAGNOSTIC SYSTEM

Technical Field

[0001] The present invention relates to an oxygen consumption measurement system, diagnostic system, and the like.

Background Art

[0002] In Japanese patent application laid-open No. 7-171139 and Japanese patent application laid-open No. 7-155312, a pulse oximeter that is an apparatus for measuring the blood oxygen saturation is disclosed. A pulse oximeter is a medical instrument for noninvasively monitoring pulse rate and percutaneous arterial oxygen saturation by attaching a probe to a fingertip or an ear. A pulse oximeter takes advantage of the difference in absorbance between oxygenated hemoglobin and reduced hemoglobin. Namely, since most of pulsatings in peripheral tissues are attributable to arterial blood, and quantity of transmitted light is also pulsative in accordance with quantity of arterial blood, the pulse oximeter adopts a method of taking out only the pulsative portion thereof, and measures the absorbance for a plurality of lights having different wavelengths, thereby measuring arterial blood oxygen saturation from a ratio of measurements of absorbance.

[0003] However, since measurement through the skin is performed, this method is disadvantageous in that, for example, accuracy is lacking.

[0004] Upon providing medical treatment for heart failure or the like, it is important to control blood oxygen saturation. While the blood oxygen saturation in a peripheral portion is measurable by using the prior art, it is disadvantageous that the blood oxygen saturation in a central portion cannot be accurately evaluated.

[0005] Also, in order to examine whether or not a subject is affected by an intraocular disease such as glaucoma, age related macular degeneration, or diabetic retinopathy, a technology capable of measuring localization of blood flow status and oxygen metabolic status in a retina is required.

Patent Citation 1: Japanese patent application laid-open No. 7-171139

Patent Citation 2: Japanese patent application laid-open No. 7-155312

Disclosure of the Invention

[0006] It is an object of the present invention to provide an oxygen consumption measurement system capable of obtaining oxygen consumption in each position of a retina.

[0007] It is an object of the present invention to provide an oxygen consumption measurement system capable of easily and accurately monitoring general circulatory state during medical treatment for heart failure or the like.

[0008] It is an object of the present invention to provide a diagnostic system capable of evaluating whether the subject is affected or is at a risk of being affected by an ophthalmic disease.

[0009] The present invention is based on a knowledge that a variation in oxygen consumption in the retina can be obtained basically by measuring blood flow of the retina and by obtaining oxygen saturation within the retina.

[0010] Namely the first aspect of the present invention is related to an oxygen consumption measurement system provided with: a laser light source (1); a first optical detecting means (3) detecting a light outputted from the laser light source (1) having entered an eye (2) of a subject and having been reflected thereby; a multiple wavelength light source (4); a second optical detecting means (5) detecting a light emitted from the multiple wavelength light source (4) having entered the eye (2) of the subject and having been reflected thereby; and a controller (6) connected to the first optical detecting means (3) and the second optical detecting means (5), which obtains a blood flow in a retina using a detected signal detected by the first optical detecting means (3), obtains an oxygen saturation using a detected signal detected by the second optical detecting means (5), and obtains a variation in oxygen consumption in the retina using the blood flow in the retina and the oxygen saturation

[0011] Namely, a preferred embodiment of the first aspect of the present invention is related to the above-mentioned oxygen consumption measurement system, further provided with a scanning portion for scanning the laser light source (1).

[0012] Namely, a preferred embodiment of the first aspect of the present invention is related to any one of the above-mentioned oxygen consumption measurement systems, further provided with a positioning means for displacing an irradiating position of the laser light source (1) or the multiple wavelength light source (4) in accordance with a displacement of the eye (2) of the subject.

[0013] Namely, a preferred embodiment of the first aspect of the present invention is related to any one of the above-mentioned oxygen consumption measurement systems, wherein: the multiple wavelength light source (4) comprises a single light source (7), and a filtering portion (8) through which a light from the optical source (7) is transmitted; and the filtering portion (8) comprises a plurality of optical filters having mutually different transmission characteristics.

[0014] Namely, a preferred embodiment of the first aspect of the present invention is related to any one of the above-mentioned oxygen consumption measurement systems, wherein the controller (6) outputs an indication signal for indicating at least one of the blood flow in the retina, a distribution of the oxygen saturation, and a distribution of the variation in oxygen consumption.

[0015] Namely, a preferred embodiment of the first aspect of the present invention is related to any one of the above-mentioned oxygen consumption measurement system, wherein a single CCD camera is the first optical detecting means (3) and the second optical detecting means (5).

[0016] Namely, a preferred embodiment of the first aspect of the present invention is related to any one of the above-mentioned oxygen consumption measurement systems, wherein a variation in arterial oxygen consumption is obtained.

[0017] Namely, a preferred embodiment of the first aspect of the present invention is related to any one of the above-mentioned oxygen consumption measurement systems, wherein a variation in venous oxygen consumption is obtained.

[0018] Namely, a preferred embodiment of the first aspect of the present invention is related to any one of the above-mentioned oxygen consumption measurement systems, which is used for monitoring a variation in blood oxygen consumption.

[0019] Namely the second aspect of the present invention is related to a diagnostic system provided with any one of the above-mentioned oxygen consumption measurement systems, which obtains the variation in oxygen consumption in the retina with the oxygen consumption measurement system, and evaluates whether the subject is affected or is at a risk of being affected by an ophthalmic disease by the variation in oxygen consumption obtained.

[0020] Namely, a preferred embodiment of the second aspect of the present invention is related to a diagnostic system provided with any one of the above-mentioned oxygen consumption measurement systems, which obtains the variation in oxygen consumption in the retina as well as a variation in blood vessel diameter in the retina with the oxygen consumption measurement system, and indicates the variation in oxygen consumption and the variation in blood vessel diameter obtained

[0021] Namely, a preferred embodiment of the second aspect of the present invention is related to a diagnostic system provided with any one of the above-mentioned oxygen consumption measurement systems, which obtains the variation in oxygen consumption in the retina as well as a variation in blood vessel diameter in the retina with the oxygen consumption measurement system, and measures a blood pressure with the sphygmomanometer, in order to control a cardiovascular system from the variation in oxygen consumption, the variation in blood vessel diameter, and the blood pressure obtained.

[0022] Namely the third aspect of the present invention is related to a method of diagnosing an ophthalmic disease by: using an oxygen consumption measurement system comprising: a laser light source (1); a first optical detecting means (3) detecting a light outputted from the laser light source (1) having entered an eye (2) of a subject and having been reflected thereby; a multiple wavelength light source (4); a second optical detecting means (5) detecting a light emitted from the multiple wavelength light source (4) after having entered the eye (2) of the subject and having been reflected thereby; and a controller (6) connected to the first optical detecting means (3) and the second optical detecting means (5), which obtains a blood flow in a retina using a detected signal detected by the first optical detecting means (3), obtains an oxygen saturation using a detected signal detected by the second optical detecting means (5), and obtains a variation in oxygen consumption in the retina using the blood flow in the retina and the oxygen saturation; obtaining a distribution of the variation in oxygen consumption in the retina with the oxygen consumption measurement system; and evaluating whether the subject is affected or is at a risk of being affected by an ophthalmic disease by the distribution of the variation in oxygen consumption obtained.

[0023] Namely, a preferred embodiment of the third aspect of the present invention is related to a method of diagnosing a situation of a cardiovascular system by: using an oxygen consumption measurement system comprising: a laser light source (1); a first optical detecting means (3) detecting a light outputted from the laser light source (1) having entered an eye (2) of a subject and having been reflected thereby; a multiple wavelength light source (4); a second optical detecting means (5) detecting a light emitted from the multiple wavelength light source (4) having entered the eye (2) of the subject and having been reflected thereby; and a controller (6) connected to the first optical detecting means (3) and the second optical detecting means (5), which obtains a blood flow in a retina using a detected signal detected by the first optical detecting means (3), obtains an oxygen saturation using a detected signal detected by the second optical detecting means (5), and obtains a variation in oxygen consumption in the retina using the blood flow in the retina and the oxygen saturation; obtaining a distribution of the variation in oxygen consumption in the retina as well as a variation in blood vessel diameter in the retina with the oxygen consumption measurement system; and evaluating whether the subject is affected or is at a risk of being affected by an ophthalmic disease by the distribution of the variation in oxygen consumption and the variation in blood vessel diameter obtained.

[0024] Namely, a preferred embodiment of the third aspect of the present invention is related to the above-mentioned method of diagnosing, further measuring a blood pressure with a sphygmomanometer, wherein the situation of the cardiovascular system is diagnosed by using the variation in oxygen consumption in the retina, the variation in blood vessel diameter, and the blood pressure.

[0025] According to the present invention, it is made possible to provide an oxygen consumption measurement system capable of obtaining a variation in oxygen consumption in each position of a retina by obtaining blood flow and oxygen saturation in the retina.

[0026] According to the present invention, since a variation in oxygen saturation can be continuously observed, it is made possible to provide an oxygen consumption measurement system capable of easily monitoring a variation in blood oxygen saturation of a central blood vessel during medical treatment.

[0027] According to the present invention, it is made possible to provide a diagnostic system capable of evaluating whether the subject is affected or is at a risk of being affected by an ophthalmic disease.

Brief Description of the Drawings

[0028] [fig.1]Fig.1 is a conceptual diagram showing a basic arrangement of an oxygen consumption measurement system of the present invention.
[fig.2]Fig.2 is a schematic diagram showing a laser speckle apparatus.
[fig.3]Fig.3 is a schematic diagram of a portion in an apparatus related to oximetry.
[fig.4]Fig.4 is a conceptual diagram showing how a blood flow measurement and an oximetry imaging are simultaneously performed, whereby oxygen consumption is obtained.

Explanation of Reference

[0029] 1 laser light source
2 eye
3 first optical detecting means
4 multiple wavelength light source
5 second optical detecting means
6 controller

Best Mode for Carrying Out the Invention

[0030] Hereinafter, the present invention will be specifically described based on drawings. Fig. 1 is a conceptual diagram showing a basic arrangement of an oxygen consumption measurement system of the present invention. As shown in Fig. 1, the oxygen consumption measurement system of the present invention is basically provided with a laser light source (1), a first optical detecting means (3) detecting a light outputted from the laser light source (1) having entered an eye (2) of a subject and having been reflected thereby, a multiple wavelength light source (4), a second optical detecting means (5) detecting a light emitted from the multiple wavelength light source (4) having entered the eye (2) of the subject and having been reflected thereby; and a controller (6) connected to the first optical detecting means (3) and the second optical detecting means (5), which obtains a blood flow in a retina using a detected signal detected by the first optical detecting means (3), obtains an oxygen saturation using a detected signal detected by the second optical detecting means (5), and obtains a variation in oxygen consumption in the retina using the blood flow in the retina and the oxygen saturation.

[0031] It is to be noted that an apparatus, a method, and a principle for measuring blood flow using a laser light source are publicly known as described, for example, in Japanese patent application laid-open No. 1-249722. Use of a LSFG or a Laser-Doppler technology can be mentioned for measuring blood flow with a laser light source.

[0032] Since the surface of the retina is outwardly indented, by taking this fact into consideration, a more accurate measurement is made possible. Namely, a preferred aspect of the present invention preliminarily obtains concavity and convexity of the surface of the retina by using the laser light source, and adjusts the focal position of the laser light source along the concavity and convexity of the surface. In order to adjust the focal position of the laser light source, for example, information related to the surface of the retina may be received by a controlling apparatus, whereby positions of lens system such as a condenser are adjusted as appropriate.

[0033] Moreover, since the light reaches the retina through the cornea and the vitreous body, it is desirable to take into account influences of the cornea and the vitreous body. On one hand, the eye may be displaced or traced during the measurement. Accordingly, the variation in blood oxygen consumption may be obtained by widely measuring the retina area to obtain an average. On the other hand, one provided with a positioning means for displacing an irradiating position of the laser light source (1) or the multiple wavelength light source (4) in accordance with the displacement of the eye (2) of the subject is a preferred aspect of the present invention. For example, a servomechanism may be provided for displacing laser light source, a multiple wavelength light source, or a light source for tracing the eyeball for observing a specific position (e.g. macula) in the eyeball, monitoring a variation of the specific position, and for displacing the laser light source or the multiple wavelength light source. It is to be noted that in order to observe the specific position, the laser light source and the like may be scanned, or an image of a CCD or the like may be scanned, whereby an area where a variation in color or the like is within a predetermined range or where a width of the area thus found is within a predetermined range is observed.

[0034] To displace or to trace retinal motion, we could use scanning laser ophthalmoscope as disclosed in Zhiheng Xu, et al., Tracking retinal motion with a scanning laser ophthalmoscope J. Rehabilitation Research and Development, Vol. 42, Number 3, pages 373-380. As disclosed in the document, using scanning laser ophthalmoscope make us be able to determine the location of images of visual target. Tracking the movement of the eye could be attained by using software, e.g., Block matching. Using such software, the calculation can be done in real time so that the image of blood flow and/or oxygen consumption displayed on the computer screen is stable.

[0035] As a laser light source, what is publicly known to be used for the LSFG may be used as appropriate. As a specific laser wavelength, an infrared wavelength can be mentioned. As the specific wavelength, a wavelength from 750nm to 850nm inclusive can be mentioned. As an optical system, one having a semiconductor laser such as a diode laser with a temperature controller, a projector lens for focusing the light from the semiconductor laser, and an aperture thought which the light outputted from the projector lens is transmitted can be mentioned. As a laser light, one that passes through the projector lens and the aperture, and focuses on the surface of the cornea is preferable. By thus focusing, the laser light after having passed through tissues (e.g. vitreous body) within the eyeball is irradiated on an extensive area of the retina. A preferable laser light source has a scanning portion for scanning the laser light source (1). In the presence of a scanning portion, the laser light source can be scanned within the eyeball to observe blood flow ate the predetermined region.

[0036] The first optical detecting means is not specifically limited as long as being capable of detecting light and a publicly known optical detecting means may be used as appropriate. Specifically, a publicly known optical detector such as a publicly known photo diode and CCD can be mentioned.

[0037] When the laser reaches the surface of the retina, the laser scatters and reflects various structures in the tissue. Some light reaches the choroids by reaching lower portions of the retina without being reflected. This backscattered light forms a speckle image on the graphics in the observation optical system. A light intensity at a given point can be determined by the sum of the intensities of the backscattered light. If a resultant intensity is zero, a dark speckle image can be obtained at the point, while a maximum intensity is observed if all images arrive. Thus, a speckle image can be obtained.

[0038] The speckle image is fluctuated by particles within the tissue. Since a backscatter by static particles forms a speckle pattern, by observing the speckle image, two components, a static component and a dynamic component can be obtained.

[0039] By observing a time variation of the speckle image, flow rate of a blood flow can be obtained. A largely blurred speckle pattern indicates that the speckle pattern changes rapidly, thereby indicating a part where an object is moving fast. By statically observing the speckle pattern, an absolute value of the blood flow can be obtained.

[0040] As described earlier, a technology for obtaining the blood flow using a reflected light is publicly known as the LSFG, so that the controller of the present invention may be mounted on a computer or the like having a program for obtaining the blood flow from the reflected light based on the LSFG technology stored in a main memory or the like. For the present invention, one capable of observing a variation in blood vessel diameter is preferable. In order to observe the blood vessel diameter, the laser light source or the like may be scanned, or an image of a CCD or the like may be scanned, whereby an area where a variation in color or the like is within a predetermined range or where a width of the area found is within a predetermined range is measured. Then a variation in blood vessel diameter at a certain point can be observed by using in combination with the tracing means described above as appropriate. As a marking method of the blood vessel location, for example, a location where the blood vessel branches is confirmed, the pattern of the branching is stored, and a branching location is recognized by checking whether or not it matches the stored branching pattern, so that the blood vessel diameter at the branching point may be measured, or the blood vessel diameter at a location shifted from the branching point by a predetermined location may be measured.

[0041] A multiple wavelength light source is not specifically limited as long as being capable of generating plural kinds of light including at least a light with the wavelength at the vicinity of 600nm, and a publicly known multiple wavelength light source can be adopted. A plurality of single optical lasers of different wavelengths may be used as well. Also, a multiple wavelength light source may be provided with a single light source (7), and a filtering portion (8) through which a light from the optical source (7) is transmitted, and the filtering portion (8) may be provided with a plurality of optical filters having mutually different transmission characteristics. Specifically, for example, one provided with six filters at locations that are 60 degrees shifted from each other on a circular filter board, which is sequentially switched over to one with preferable transmission characteristics.

[0042] Also, a technology for obtaining oxygen saturation from a difference in absorbance for a plurality of lights having different wavelengths is publicly known as an oximeter. Therefore, the controller of the present invention may be mounted on a computer or the like having a program for obtaining the oxygen saturation from the information of the reflected light based on the oximetry technology stored in a main program or the like. Specifically, the controller is provided with a an input device, output device, storage device such as a memory, arithmetic device such as the CPU, and a controller, the devices are mutually connected with busses or the like, so that information can be transmitted and received. Also, the input device is connected to a detecting system such as various types of photodetectors so that to be able to input information to the controller.

[0043] However in the present invention, since the light reaches the retina through the cornea and the vitreous body, it is desirable to take into account influences of the cornea and the vitreous body. Namely, in order to obtain the absorbance with a good accuracy, one having deleted therefrom the absorbance by the cornea and the vitreous body must be obtained. Therefore, a preferred embodiment of the present invention presets the amounts of absorbance by the cornea and the vitreous body, whereby the absorbance is obtained by adjusting the portion of the preset absorbance. Specifically, this can be implemented, for example, as follows: Firstly, the absorbance of the light having passed through the retina is obtained. By prestoring constants corresponding to the absorbance of the cornea and the vitreous body, the constants corresponding to absorbance of the cornea and the vitreous body are retrieved upon calculating the absorbance of the light having passed through the retina. A difference is obtained by subtracting the retrieved constants corresponding to absorbance of the cornea and the vitreous body from the absorbance obtained by using a difference circuit or by using a difference operation program. Thus, by subtracting the absorbance of the cornea and the vitreous body from the actual measurement value, the absorbance in the retina may be obtained. It is to be noted that a thickness of the vitreous body may be measured, whereby the absorbance of the vitreous body is given by a value that is the thickness multiplied by the absorbance (constant) for the unit thickness. Thus, the absorbance can be measured more accurately. For example, it is possible to consider only the absorbance of the vitreous body. Specifically, an absorbance constant of the vitreous body that is general or measured per test body is stored. Also, the thickness of the vitreous body is measured by a publicly known method, and the thickness of the vitreous body per test body is stored. The stored absorbance constant of the vitreous body and the thickness of the vitreous body are retrieved, and a multiplication operation by using a multiplication circuit or a multiplication operation program is performed, whereby the absorbance in the vitreous body is obtained to be stored in the memory. Then, the absorbance of light having passed through the retina is obtained. The absorbance of the vitreous body stored in the memory is retrieved. A difference is obtained by subtracting the retrieved absorbance of the vitreous body from the absorbance obtained by using a difference circuit or by using a difference operation program. Thus, by subtracting the absorbance of the vitreous body from the actual measurement value, the absorbance in the retina may be obtained. Also, by similarly storing a constant or the absorbance of the cornea corresponding to the thickness of the cornea, the absorbance in the retina may be obtained by subtracting the absorbance of the cornea and the retina from the actual measurement value.

[0044] On the other hand, the controller of the present invention can obtain the variation in oxygen consumption in the retina by using the blood flow in the retina and the oxygen saturation. "The variation in oxygen consumption in the retina" can be indicated by taking a certain constant value as a reference, and the amount of multiples of the reference value may be regarded as "the variation in oxygen consumption in the retina". In case "the variation in oxygen consumption in the retina" is thus obtained, this can be implemented, for example, as follows: Specifically, the reference value is prestored. Alternatively, by using the system of the present invention, the light may be

irradiated on a portion other than the blood vessel in the retina. Then, the oxygen consumption in the portion other than the blood vessel is obtained. The obtained oxygen consumption is stored in the memory as a reference value. Then, the oxygen consumption at each point in the retina is obtained. The reference value stored in the memory is retrieved, and the obtained oxygen consumption at each portion is divided by the retrieved reference value. In order to perform the division, the a divider circuit or a division operation program may be used. "The variation in oxygen consumption in the retina" can be thus obtained. Also, taking the oxygen consumption in the retina measured at a certain point of time as a reference, an amount indicating the level of variation from the reverence value can be mentioned. Alternatively, by measuring the oxygen consumption for a plurality of times, the maximum value and the minimum value thereof may be obtained, and the value obtained by dividing the maximum value by the minimum value may be regarded as "the variation in oxygen consumption in the retina". The smallest area for obtaining "the variation in oxygen consumption in the retina" varies according to the accuracy of the optical system and the optical detecting means. As a specific area for obtaining "the variation in oxygen consumption in the retina", an area between 0.1mm x 0.1mm and 2mm x 2mm inclusive can be mentioned, while between 0.5mm x 0.5mm and 1.5mm x 1.5mm inclusive is preferable.
Also, it is preferable that the controller (6) outputs an indication signal indicating at least one of the blood flow in the retina, the distribution of the oxygen saturation, and the variation in oxygen consumption. The output devices such as a monitor can create a two-dimensional picture of the variation in oxygen consumption and the like, so that by continuously monitoring the picture, the variation in the oxygen consumption and the like can be monitored. Accordingly, a variation in living body during treatment of diseases such as cardiac disease, pulmonary disease, or ophthalmic disease, or the like can be monitored.

[0045] To describe more specifically, a variation in oxygen consumption (metabolic rate of oxygen) can be obtained by using a blood flow volume, a total amount of hemoglobin, and an amount of deoxyhemoglobin. The blood flow volume can be obtained by using the LSFG and the like, while the total amount of hemoglobin and the amount of deoxyhemoglobin can be obtained by using a technology developed by the oximetry for obtaining the oxygen saturation. Also, the oxygen consumption (metabolic rate of oxygen: MRO_2) can be obtained by using a blood flow volume and an fluctuation of oxygen extraction. Specifically, assuming the blood flow to be BF and the fluctuation of oxygen extraction to be OEF, MRO_2 can be obtained by BF x OEF. On the other hand, OEF can be obtained as $(S_A\text{-}S_V)/S_A$ where arterial oxygen saturation is expressed as S_A, and venous oxygen saturation is expressed as S_V. Thus, the oxygen consumption can be obtained. Therefore, the measured values of S_A and S_V are stored in the memory to be retrieved as appropriate. $(S_A-S_V)/S_A$ is obtained by using the retrieved values of S_A and S_V with a circuit for four arithmetic operations. Alternatively, by performing a table from which a value of $(S_A-S_V)/S_A$ can be retrieved corresponding to the values of S_A and S_V may be prepared, the value of $(S_A-S_V)/S_A$ may be retrieved by using the retrieved values of S_A and S_V. Also, $(S_A-S_V)/S_A$ may be obtained by having an operating portion operate the value of $(S_A-S_V)/S_A$ by using the retrieved values of S_A and S_V. Meanwhile, the value of the BF obtained is stored in the memory. Then, the value of MRO_2 may be obtained by using the value of BF and the value of $(S_A-S_V)/S_A$ with a multiplying circuit or by having the operating portion perform the multiplication calculation.

[0046] A preferred embodiment of the present invention has a single CCD camera serves as both of the first optical detecting means (3) and the second optical detecting means (5). By using a single light receiving element, downsizing can be achieved. It is to be noted that since the oxygen saturation is obtained after measuring the blood flow in the system of the present invention, not only the variation in arterial oxygen consumption but also the variation in venous oxygen consumption are obtained. Namely, since the arterial blood and the venous blood have different colors and the like, in the preferred aspect of the present invention a CCD camera and the like recognizes the difference to obtain the oxygen consumption in the blood vessel where the desired blood flows. It is to be noted that the preferred embodiment of the present invention obtains variations in oxygen consumption in portions of the retina, classifies the variations into multiple stages, and shows the variations by the classified ranges in different colors.

[0047] Namely, the second aspect of the present invention is provided with the above-mentioned oxygen consumption measurement system, which obtains a variation in oxygen consumption in the retina with the oxygen consumption measurement system, and evaluates whether the subject is affected or is at a risk of being affected by an ophthalmic disease (specifically, diseases involving cytopathy and the like in new blood vessel or retinal blood vessel such as glaucoma, age related macular degeneration, diabetic retinopathy, retinal artery obstruction, retinal venous obstruction, central serous chorioretinopathy, central exudative chorioretinitis, retinal detachment, pigmentary degeneration of retina, neovascular maculopathy, macular hole, or proliferative vitreoretinopathy) by the variation in oxygen consumption obtained. Specifically, the preferred embodiment of the present invention relates to a diagnostic system evaluating whether or not the subject is affected or at a risk of being affected by an ophthalmic disease.

[0048] For example, when retinal cells become extinct or become less active due to glaucoma, there will be no oxygen consumption or the oxygen consumption will be significantly reduced. Accordingly, by monitoring the variation in relative value of the oxygen consumption, it is made possible to evaluate whether the subject is affected or how much is the level of risk that the subject will be affected the ophthalmic disease. Namely, when no variation in oxygen consumption is found due to death of the retina cells, possibility that the subject is affected by these diseases is high. Also, when the variation in oxygen consumption is scarce, possibility that the subject is affected by these diseases is high, so that by having variations in oxygen consumption in the retina divided into multiple stages for numerical conversion, and by comparing the measured value with the numerically converted values, the risk of being affected by these diseases can be evaluated. It is preferable that the evaluated risk is indicated on a monitor or the like. On the other hand, by observing the variation in oxygen consumption in the retina, when the variation in oxygen consumption is small in a certain portion, it is presumed that the function of the portion is declined or the portion is disordered, so that diagnosis of whether or not the subject is affected by age related macular degeneration or diabetic retinopathy is made possible.

[0049] As a matter of course, whether the subject is affected or how much is the level of risk that the subject will be affected by glaucoma, age related macular degeneration, diabetic retinopathy, and the like may be evaluated by using the above-mentioned oxygen consumption measurement system and visually observing the variation in oxygen consumption and the aspect of how the oxygen consumption is localized in a certain portion of the retina.

[0050] Namely a preferred aspect of the present invention is a method of diagnosing glaucoma, age related macular degeneration, or diabetic retinopathy by using an oxygen consumption measurement system provided with: a laser light source (1); a first optical detecting means (3) detecting a light outputted from the laser light source (1) having entered an eye (2) of a subject and having been reflected thereby; a multiple wavelength light source (4); a second optical detecting means (5) detecting a light emitted from the multiple wavelength light source (4) after having entered the eye (2) of the subject and having been reflected thereby; and a controller (6) connected to the first optical detecting means (3) and the second optical detecting means (5), which obtains a blood flow in a retina using a detected signal detected by the first optical detecting means (3), obtains an oxygen saturation using a detected signal detected by the second optical detecting means (5), and obtains a relative value of oxygen consumption in the retina using the blood flow in the retina and the oxygen saturation; obtaining a distribution of variation in oxygen consumption in the retina with the oxygen consumption measurement system; and evaluating whether the subject is affected or is at a risk of being affected by glaucoma, age related macular degeneration, or diabetic retinopathy by the distribution of variation in oxygen consumption obtained.

[0051] A preferred embodiment of the present invention is a diagnostic system which is provided with an oxygen consumption measurement system, obtains the variation in oxygen consumption in the retina as well as a variation in blood vessel diameter in the retina with oxygen consumption measurement system, and indicates the variation in oxygen consumption and the variation in blood vessel diameter obtained. At the time of surgery or the like, a situation may occur where peripheral blood vessels contract when a significant problem occurs in the cardiovascular system. Specifically, an angiospasm may cause heart failure and myocardial infarction. Also, an angiospasm in brain may cause subarachnoid bleeding and subsequent occurrence or brain ischemia. Such an angiospasm can be caused by some sort of factor upon surgical operation. Therefore, it is desirable to perform monitoring of the cardiovascular system especially during an operation. On the other hand, it is difficult to directly monitor how the blood vessels contract in the heart or how the blood vessels in the brain contract. Therefore, in the preferred embodiment of the present invention, by observing the blood vessel diameter in the retina, the situation in the cardiovascular system is recognized. Namely, in the preferred embodiment of the present invention, not only the variation in oxygen consumption is monitored but also the blood vessel diameter in the retina is monitored, so that a sudden change in the cardiovascular system can be easily recognized and can be dealt with promptly.

[0052] Namely the present invention also provides a method of diagnosing a situation of a cardiovascular system by using an oxygen consumption measurement system provided with: a laser light source (1); a first optical detecting means (3) detecting a light outputted from the laser light source (1) having entered an eye (2) of a subject and having been reflected thereby; a multiple wavelength light source (4); a second optical detecting means (5) detecting a light emitted from the multiple wavelength light source (4) having entered the eye (2) of the subject and having been reflected thereby; and a controller (6) connected to the first optical detecting means (3) and the second optical detecting means (5), which obtains a blood flow in a retina using a detected signal detected by the first optical detecting means (3), obtains an oxygen saturation using a detected signal detected by the second optical detecting means (5), and obtains a variation in oxygen consumption in the retina using the blood flow in the retina and the oxygen saturation; obtaining a distribution in the variation in oxygen consumption in the retina as well as a variation in blood vessel diameter in the retina with the oxygen consumption measurement system; and evaluating whether the subject is affected or is at a risk of being affected by an ophthalmic disease by the distribution in the variation in oxygen consumption and the variation in blood vessel diameter.

[0053] A preferred embodiment of the present invention is a diagnostic system provided with the above-mentioned oxygen consumption measurement system and a sphygmomanometer, which obtains the variation in oxygen consumption in the retina as well as a variation in blood vessel diameter in the retina with the oxygen consumption measurement system, and measures a blood pressure with the sphygmomanometer, in order to control a cardiovascular system from the variation in oxygen consumption, the variation in blood vessel diameter, and the blood pressure obtained. Since the blood pressure is important information on the cardiovascular system, an appropriate diagnosis can be performed by additionally obtaining information on the blood pressure.

[0054] The present invention also provides a method of diagnosing by measuring a blood pressure with a sphygmomanometer, wherein the situation of the cardiovascular system is diagnosed by using the variation in oxygen consumption, the variation in blood vessel diameter, and the blood pressure.

Mode for the Invention 1

[0055] Hereinafter, the present invention will bee specifically described using examples.

Since the system used in this example is basically provided with an apparatus for obtaining blood flow with a laser speckle, a part of apparatus obtaining oxygen saturation and the like with oximetry, and a controller for controlling various types of information, each of the apparatuses will be described. Fig. 2 is a schematic diagram of a laser speckle apparatus. In Fig. 2, the optical system includes, for example, a semi-conductor laser such as a diode laser including a temperature controller, a projector lens for focusing light from the semiconductor laser, and an aperture through which the light outputted from the projector lens is transmitted. After passing through the projector lens and the aperture, the laser light is focused on the corneal surface. By such a focusing, the laser is irradiated on a wide area of the retina after passing through tissues within the eyeball.

[0056] When the laser reaches the surface of the retina, the laser scatters and reflects various structures of the tissue. Some light reaches the choroids by reaching lower portions of the retina without being reflected. This backscattered light forms a speckle image on the graphics in the observation optical system. A light intensity at a given point can be determined by the sum of the intensities of the backscattered light. If a resultant intensity is zero, a dark speckle image can be obtained at the point, while a maximum intensity is observed if all images arrive. Thus, a speckle image can be obtained.

[0057] The speckle image is fluctuated by particles within the tissue. Since a backscatter by static particles forms a speckle pattern, by observing the speckle image, two components, a static component and a dynamic component can be obtained.

[0058] By observing a time variation of the speckle image, flow rate of a blood flow can be obtained. A largely blurred speckle pattern indicates that the speckle pattern changes rapidly, thereby indicating a part where an object is moving fast. By statically observing the speckle pattern, an absolute value of the blood flow can be obtained.

[0059] Fig. 3 is a schematic diagram showing a potion of an apparatus related to oximetry. In this apparatus, a wheel-like filtering apparatus having 6 filters for changing the wavelength of light that reaches the retina and other tissues through liquid light guide. The wheel-like filter is rotated by a stepping motor which is synchronized with a light receiving camera for observation using photodiodes. By irradiating lights of different wavelength bands, reflection images for 6 different wavelengths can be obtained. Each of the 6 images is converted into oxyhemoglobin, deoxyhemoglobin and total hemoglobin based on a formula conforming to a modified Beer-Lambert law.

Math.1

[0060]

$$\Delta A(\lambda, t) = (\varepsilon_{\mathrm{HbO}}(\lambda)\Delta C_{\mathrm{HbO}}(t) + \varepsilon_{\mathrm{HbR}}(\lambda)\Delta C_{\mathrm{HbR}}(t))D(\lambda)$$

[0061] In the above-mentioned formula, Delta A(lambda,t) indicates an attenuation in of the wavelengths obtained by $Log(R_0/R(t))$, R_0 and R(t) indicate reflectance intensities at baseline and at a time t, respectively. Delta C_{HbO} and Delta C_{HbR} indicate variations in oxygen consumption for oxyhemoglobin and deoxyhemoglobin, respectively. Ipusiron $_{HbO}$ and Ipusiron $_{Hb}$ indicate respective molar extinction coefficients. The above formula is obtained for each of the cells of the CCD camera.

[0062] Da(lambda) that is a coefficient of difference in optical path length is an important factor when obtaining the variation in oxygen consumption. Da is accounts for the fact that optical characteristics of the tissues depend on wavelength. As a matter of fact, the detected light travels through slightly different distances to be detected. In order to accurately obtain the hemoglobin consumption, this dependency on wavelength must be considered, whereby such a dependency of wavelength can be achieved by considering a Monte Carlo model.

[0063] Fig. 4 is a conceptual diagram showing how a blood flow measurement and an oximetry imaging are simultaneously performed, whereby oxygen consumption is obtained. In this example, two cameras were used for speckle measurements and multi-spectrum measurements. In this example, the wavelength of the speckle laser has a longer wavelength than the wavelength of the multiple wavelength light source, so that lights originated by the respective light sources can be effectively separated by using a dichroic beam splitter and band pass filters, and also can be guided to the appropriate mirrors.

Industrial Applicability

[0064] The oxygen consumption measurement system and diagnostic system of the present invention can be used in the fields of medical instruments, and the like

Claims

[1] An oxygen consumption measurement system comprising:
a laser light source (1);
a first optical detecting means (3) detecting a light outputted from the laser light source (1) having entered an eye (2) of a subject and having been reflected thereby;
a multiple wavelength light source (4);
a second optical detecting means (5) detecting a light emitted from the multiple wavelength light source (4) having entered the eye (2) of the subject and having been reflected thereby; and
a controller (6) connected to the first optical detecting means (3) and the second optical detecting means (5), which obtains a blood flow in a retina using a detected signal detected by the first optical detecting means (3), obtains an oxygen saturation using a detected signal detected by the second optical detecting means (5), and obtains a variation in oxygen consumption in the retina using the blood flow in the retina and the oxygen saturation.

[2] The oxygen consumption measurement system as claimed in claim 1, further comprising a scanning portion for scanning the laser light source (1).

[3] The oxygen consumption measurement system as claimed in claim 1, further comprising a positioning means for displacing an irradiating position of the laser light source (1) or the multiple wavelength light source (4) in accordance with a displacement of the eye (2) of the subject.

[4] The oxygen consumption measurement system as claimed in claim 1, wherein:
the multiple wavelength light source (4) comprises a single light source (7), and a filtering portion (8) through which a light from the optical source (7) is transmitted; and
the filtering portion (8) comprises a plurality of optical filters having mutually different transmission characteristics.

[5] The oxygen consumption measurement system as claimed in claim 1, wherein the controller (6) outputs an indication signal for indicating at least one of the blood flow in the retina, a distribution of the oxygen saturation, and a distribution of the variation in oxygen consumption.

[6] The oxygen consumption measurement system as claimed in claim 1, wherein a single CCD camera is the first optical detecting means (3) and the second optical detecting means (5).

[7] The oxygen consumption measurement system as claimed in claim 1, wherein a variation in arterial oxygen consumption is obtained.

[8] The oxygen consumption measurement system as claimed in claim 1, wherein a variation in venous oxygen consumption is obtained.

[9] The oxygen consumption measurement system as claimed in claim 1, which is used for monitoring a variation in blood oxygen consumption.

[10] A diagnostic system comprising the oxygen consumption measurement system as claimed in claim 1, which obtains the variation in oxygen consumption in the retina with the oxygen consumption measurement system, and evaluates whether the subject is affected or is at a risk of being affected by an ophthalmic disease by the variation in oxygen consumption obtained.

[11] A diagnostic system comprising the oxygen consumption measurement system as claimed in claim 1, which obtains the variation in oxygen consumption in the retina as well as a variation in blood vessel diameter in the retina with the oxygen consumption measurement system, and indicates the variation in oxygen consumption and the variation in blood vessel diameter obtained.

[12] A diagnostic system comprising the oxygen consumption measurement system as claimed in claim 1 and a sphygmomanometer, which obtains the variation in oxygen consumption in the retina as well as a variation in blood vessel diameter in the retina with the oxygen consumption measurement system, and measures a blood pressure with the sphygmomanometer, in order to control a cardiovascular system from the variation in oxygen consumption, the variation in blood vessel diameter, and the blood pressure obtained.

[13] A method of diagnosing an ophthalmic disease comprising the steps of:
using an oxygen consumption measurement system comprising: a laser light source (1); a first optical detecting means (3) detecting a light outputted from the laser light source (1) having entered an eye (2) of a subject and having been reflected thereby; a multiple wavelength light source (4); a second optical detecting means (5) detecting a light emitted from the multiple wavelength light source (4) after having entered the eye (2) of the subject and having been reflected thereby; and a controller (6) connected to the first optical detecting means (3) and the second optical detecting means (5), which obtains a blood flow in a retina using a detected signal detected by the first optical detecting means (3), obtains an oxygen saturation using a detected signal detected by the second optical detecting means (5), and obtains a variation in oxygen consumption in the retina using the blood flow in the retina and the oxygen saturation;
obtaining a distribution of the variation in oxygen consumption in the retina with the oxygen consumption measurement system; and
evaluating whether the subject is affected or is at a risk of being affected by an

ophthalmic disease by the distribution of the variation in oxygen consumption obtained.

[14] A method of diagnosing a situation of a cardiovascular system comprising the steps of:

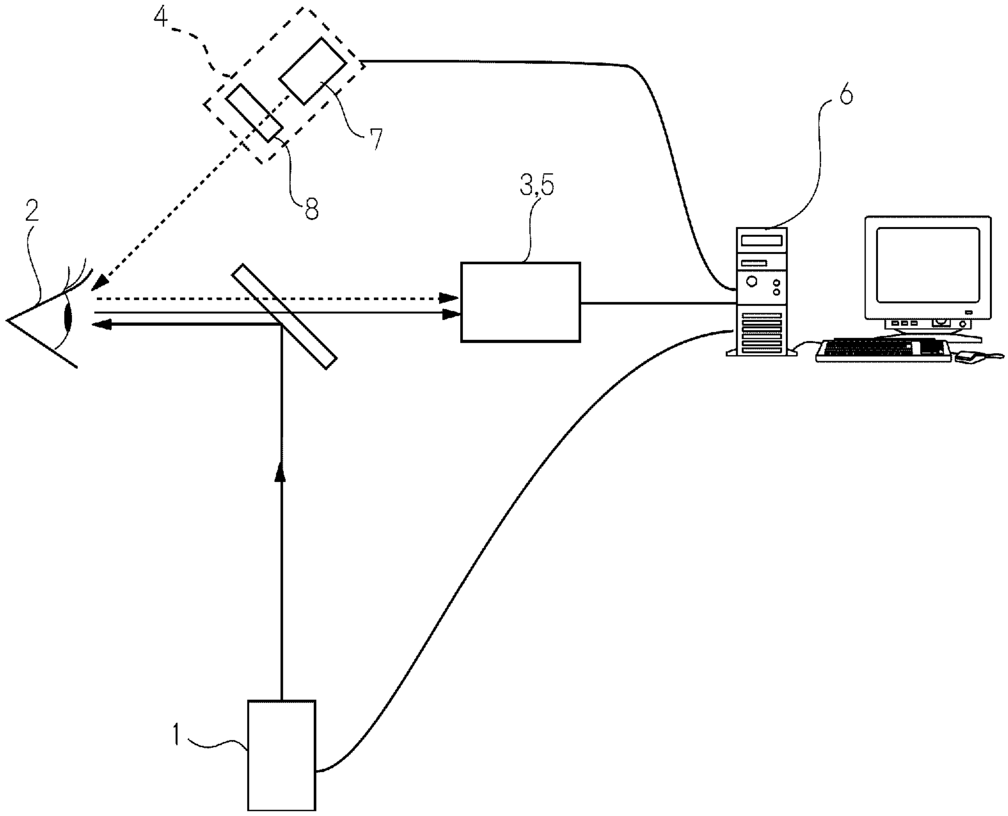
using an oxygen consumption measurement system comprising: a laser light source (1); a first optical detecting means (3) detecting a light outputted from the laser light source (1) having entered an eye (2) of a subject and having been reflected thereby; a multiple wavelength light source (4); a second optical detecting means (5) detecting a light emitted from the multiple wavelength light source (4) having entered the eye (2) of the subject and having been reflected thereby; and a controller (6) connected to the first optical detecting means (3) and the second optical detecting means (5), which obtains a blood flow in a retina using a detected signal detected by the first optical detecting means (3), obtains an oxygen saturation using a detected signal detected by the second optical detecting means (5), and obtains a variation in oxygen consumption in the retina using the blood flow in the retina and the oxygen saturation;

obtaining a distribution of the variation in oxygen consumption in the retina as well as a variation in blood vessel diameter in the retina with the oxygen consumption measurement system; and

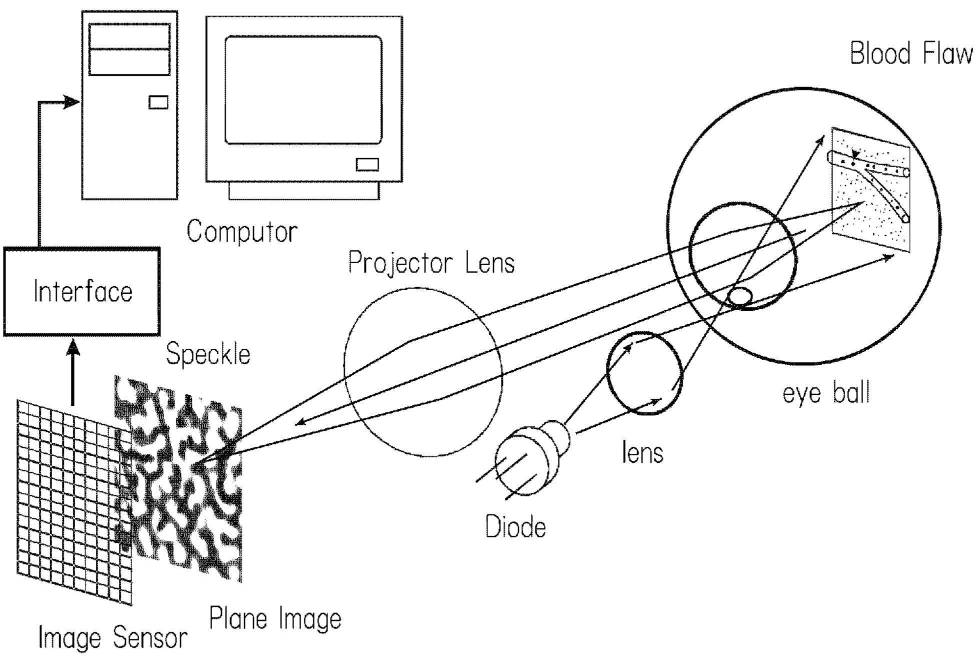
evaluating whether the subject is affected or is at a risk of being affected by an ophthalmic disease by the distribution of the variation in oxygen consumption and the variation in blood vessel diameter obtained.

[15] The method of diagnosing as claimed in claim 14, further comprising the step of measuring a blood pressure with a sphygmomanometer, wherein the situation of the cardiovascular system is diagnosed by using the variation in oxygen consumption in the retina, the variation in blood vessel diameter, and the blood pressure.

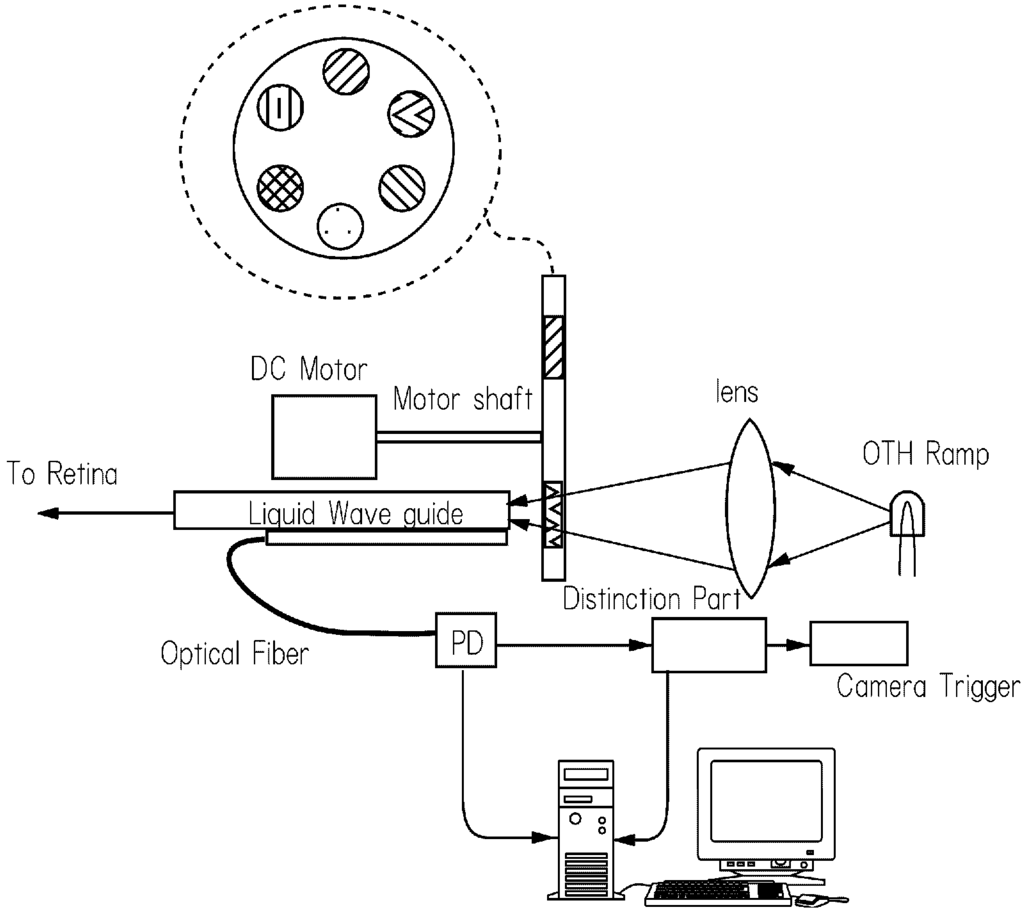
[Fig. 1]
Fig.1



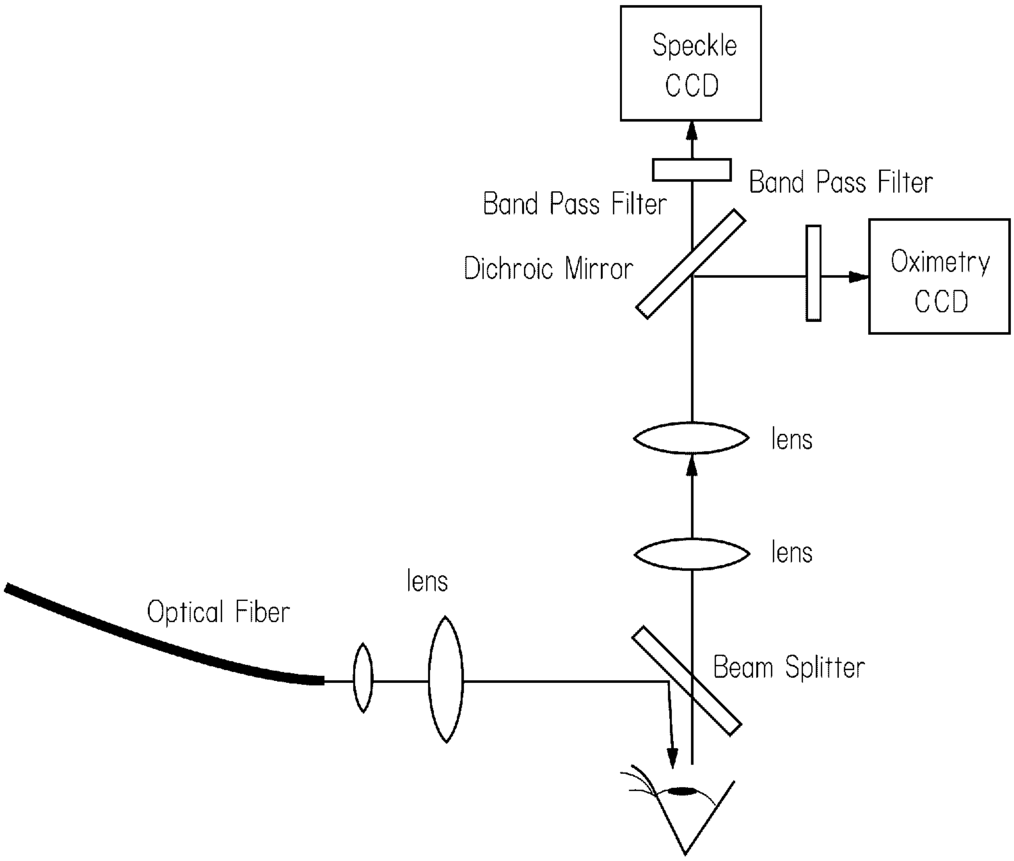
[Fig. 2]
Fig.2



[Fig. 3]
Fig.3



[Fig. 4]
Fig.4



INTERNATIONALSEARCHREPORT

International application No.
PCT/JP2007/000308

A. CLASSIFICATION OF SUBJECT MATTER

Int.Cl. A61B5/1455(2006.01)i, A61B3/10(2006.01)i, A61B3/12(2006.01)i, A61B5/026(2006.01)i

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)

Int.Cl. A61B5/1455, A61B3/10, A61B3/12, A61B5/026

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

Published examined utility model applications of Japan 1922-1996
Published unexamined utility model applications of Japan 1971-2007
Registered utility model specifications of Japan 1996-2007
Published registered utility model applications of Japan 1994-2007

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JP 2002-238850 A (CANON K.K.) 2002.08.27 Paragraph【0010】-【0043】, Fig.1-3	1-12
A	JP 2006-158547 A (TOPCON Corp.) 2006.06.22 Paragraph【0063】-【0073】, Fig.1	1-12
A	JP 2002-291711 A (HONDA Sadako) 2002.10.08 Paragraph【0005】-【0025】, Fig.1	1-12
A	Jim BEACH et al. "Spectral Reflectance Technique for Retinal Blood Oxygen Evaluation in Humans" Proceedings of the 31st Applied Imagery Pattern Recognition Workshop 2002 IEEE 2002.02.16 P.117-123	1-12

☐ Further documents are listed in the continuation of Box C. ☑ See patent family 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 application or patent 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
20.04.2007	01.05.2007

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INTERNATIONALSEARCHREPORT

International application No.
PCT/JP2007/000308

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☑ Claims Nos.: 13-15
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

The subject matter of claim 13-15 relates to diagnosis methods, which does not require an intentional search by the International Searching Authority in accordance with PCT Article 17(2)(a)(i) and [Rule 39.1(iv)].

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

JP 2002-238850 A	2002.08.27	US 6757555 B2	2004.06.29
		US 2002/0118338 A1	2002.08.29
JP 2006-158546 A	2006.06.22	JP 2006-158547 A	2006.06.22
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JP 2002-291711 A	2002.10.08	(No Families)	