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(71) Applicant *(for all designated States except US)*: **KONINKLIJKE PHILIPS ELECTRONICS N.V.** [NL/NL]; Groenewoudseweg 1, NL-5621 BA Eindhoven (NL).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **VAN DER VOORT, Marjolein** [NL/NL]; c/o High Tech Campus, building 44, NL-5656 AE Eindhoven (NL). **BAKKER, Levinus, P.** [NL/CN]; c/o High Tech Campus, building 44, NL-5656 AE Eindhoven (NL). **LEPROUX, Anais** [FR/NL]; c/o High Tech Campus, building 44, NL-5656 AE Eindhoven (NL). **VAN DER MARK, Martinus, B.** [NL/NL]; c/o High Tech Campus, building 44, NL-5656 AE Eindhoven (NL).

(74) Agents: **VAN VELZEN, Maaike, M.** et al.; c/o High Tech Campus, building 44, NL-5656 AE Eindhoven (NL).

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(54) Title: METHOD AND DEVICE FOR VISUALIZING ACCUMULATION OR DEPLETION OF A CONTRAST AGENT IN A TURBID MEDIUM

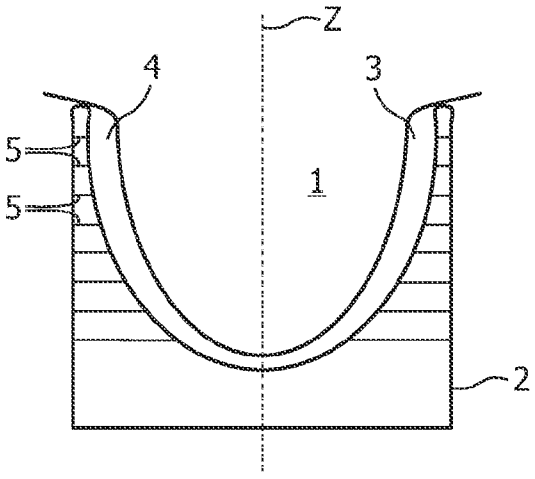

FIG. 1

(57) Abstract: A method for visualizing accumulation or depletion of a contrast agent in a turbid medium is provided. The method comprises the steps: accommodating a turbid medium (1) to which a contrast agent has been administered in a measurement volume (4); irradiating the interior of the measurement volume (4) with light from a light source unit (6) from at least one source position; for each source position, detecting light emanating from the contrast agent or detecting attenuation of the light used for irradiation caused by the contrast agent in at least one detection position as first measurement data; for each source position, detecting attenuation of the light used for irradiating in the at least one detection position as second measurement data; visualizing an accumulation or depletion of the contrast agent in the turbid medium (1) by a graphical representation of a data set obtained by manipulating the first measurement data by the second measurement data.

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Method and device for visualizing accumulation or depletion of a contrast agent in a turbid medium

FIELD OF INVENTION

The present invention relates to a method and a device for visualizing accumulation or depletion of a contrast agent in a turbid medium. More particularly, the present invention relates to an enhanced visualization of abnormal accumulation or depletion of a contrast agent in a turbid medium.

BACKGROUND OF THE INVENTION

In the context of the present application, the term turbid medium is to be understood to mean a substance consisting of a material having a high light scattering coefficient, such as for example intralipid solution or biological tissue. Further, light is to be understood to mean electromagnetic radiation, in particular electromagnetic radiation having a wavelength in the range from 180 nm to 1400 nm. The term "optical properties" covers the reduced scattering coefficient μ'_s and the absorption coefficient μ_a. Furthermore, "matching optical properties" is to be understood as having a similar reduced scattering coefficient μ'_s and a similar absorption coefficient μ_a.

A method for imaging the interior of turbid media, e.g. for breast cancer screening, which has become popular in recent years is imaging by use of light, in particular using light in the near infrared (NIR). Such methods are implemented in mammography devices and devices for examining other parts of human or animal bodies. A prominent example for such a method for imaging the interior of a turbid medium by means of light is Diffuse Optical Tomography (DOT). For example, such a DOT device for imaging the interior of a turbid medium uses a light source to irradiate the turbid medium and photodetectors for measuring a part of the light transported through the turbid medium, i.e. its intensity. A control unit is provided for controlling the scanning process. A processing unit is provided for reconstructing an image of the interior of the turbid medium on the basis of the measured intensities. Some of the known devices are particularly adapted for examining female breasts. In order to allow the examination of the turbid medium, the device is provided with a receiving portion enclosing a measurement volume and arranged to receive

the turbid medium. Light from the light source is coupled into the receiving volume and into the turbid medium. The light is chosen such that it is capable of propagating through the turbid medium. For imaging an interior of a female breast, light in the NIR (near infrared) is typically used. Scattered light emanating from the turbid medium as a result of coupling light into the receiving volume is coupled out of the receiving volume. Light coupled out of the receiving volume is used to reconstruct an image of an interior of the turbid medium. Due to different sizes of the turbid media to be examined, the size of the receiving portion may not perfectly match the size of the turbid medium, i.e. a space remains between the boundary of the receiving volume and the turbid medium. The part of the turbid medium under investigation is surrounded by a scattering medium (coupling medium) filling the space in the receiving volume. The scattering medium is chosen such that the optical parameters of the scattering medium, such as the absorption and scattering coefficients, are similar to the corresponding optical parameters of the turbid medium. The light source subsequently irradiates the turbid medium from different directions and the photodetectors measure a part of the light transmitted through the turbid medium. A plurality of such measurements are performed with the light directed to the turbid medium from different directions and, based on the results of the measurements, i.e. the obtained data set, the processing unit reconstructs the image of the examined turbid medium.

According to one development of this method, attenuation scans for light are performed in which the attenuation of light is detected for a plurality of combinations of source positions and detection positions. In these measurements the intrinsic contrast of the turbid medium is used, i.e. light at different wavelengths is attenuated by different amounts due to the presence of scatterers and chromophores such as oxy-hemoglobin, deoxy-hemoglobin, water, and lipids. From these attenuation scans, absorption images of the turbid medium can be reconstructed as well as images of physiological parameters such as e.g. the hemoglobin concentration. This technology has become known as Diffuse Optical Tomography (DOT).

According to a further development of this method, a fluorescent contrast agent which preferentially accumulates at lesions in the turbid medium under investigation, e.g. cancerous tissue in a female breast, is administered for the measurement. The turbid medium is irradiated with light from a light source, preferably a laser, and the fluorescent light which is emitted by the turbid medium is detected. From this measurement, a volumetric image of the fluorescence emission by the breast is reconstructed, i.e. exogenous contrast is used. Thus, the spatial distribution of the contrast agent in the turbid medium is

reconstructed. This method is called Diffuse Optical Fluorescence Tomography. In a typical turbid medium such as a female breast, there are several tissue structures present that may result in a non-uniform distribution of the fluorescent contrast agent. Therefore, in case of a non-targeted contrast agent, it is difficult to judge whether a structure in the fluorescence image is due to normal physiology or to an abnormality such as a malignant lesion. Methods using an absorbing contrast agent instead of a fluorescent contrast agent are also known.

SUMMARY OF THE INVENTION

It is an object of the present invention to enhance the fluorescence or absorption signal from abnormalities in the turbid medium under examination. Thus, reliable identification of the fluorescence or absorption signal from abnormal regions in the turbid medium shall be provided.

This object is solved by a method for visualizing accumulation or depletion of a contrast agent in a turbid medium according to claim 1. The method comprises the steps: accommodating a turbid medium to which a contrast agent has been administered in a measurement volume; irradiating the interior of the measurement volume with light from a light source unit from at least one source position; for each source position, detecting light emanating from the contrast agent or attenuation of the light used for irradiation caused by the contrast agent in at least one detection position as first measurement data; for each source position, detecting attenuation of the light used for irradiating in the at least one detection position as second measurement data; visualizing an accumulation or depletion of the contrast agent in the turbid medium by a graphical representation of a data set obtained by manipulating the first measurement data by the second measurement data. Since the second measurement data corresponding to the attenuation of the light used for irradiating is used for manipulating the first measurement data corresponding to the light emanating from the contrast agent or the specific attenuation caused by the contrast agent, abnormal regions in the turbid medium can be reliably visualized and distinguished from other structures providing a non-uniform distribution of the contrast agent.

According to an aspect, the light used for irradiating in the step for obtaining the first measurement data differs in wavelength from that used in the step for obtaining the second measurement data. In this case, the light source unit is capable of emitting light of at least two different wavelengths. In this case, the wavelength used for obtaining the first measurement data and the wavelength used for obtaining the second measurement data can be exactly adapted to the properties of the contrast agent and to specific physiological

parameters. Thus, the abnormal regions can be identified more reliably. Visualization by graphic representation is a very effective way of correlating the first and second measurement data.

Preferably, visualizing is performed by graphically representing the first measurement data as a function of the second measurement data or vice versa. Thus, a fast and convenient way is provided to visualize the presence of abnormal regions in the turbid medium.

If visualizing is performed by reconstructing an image of the interior of the turbid medium based on the first measurement data manipulated by the second measurement data, an image of the interior of the turbid medium is provided in which the spatial distribution of contrast agent is reliably represented and malignant abnormalities can be identified more easily.

Preferably, visualizing is performed by reconstructing images of the interior of the turbid medium based on the first measurement data and the second measurement data, as well as graphically representing the first measurement data as a function of the second measurement data or vice versa, and analyzing the interaction between the two types of representations. In this case, the two types of reconstructed images and the combined representation are provided for identifying abnormalities. Further, the interactions provide additional information.

Preferably, in the step for obtaining the second measurement data, light having a wavelength sensitive to blood concentration is used for irradiating the interior of the measurement volume. In the case that the contrast agent is injected intravenously, it will be mostly in the blood in the turbid medium, at least immediately after the injection. If it is transported through normal blood vessel structures, then part of the concentration of the contrast agent is proportional to the blood concentration. Diseased tissue often shows abnormal extravasation, i.e. a higher extravasation rate as compared to normal tissue. The part of the contrast agent concentration which is not proportional to the blood concentration may indicate the presence of an abnormality in the turbid medium. Thus, if the light having a wavelength sensitive to blood concentration is used for obtaining the second measurement data, the fluorescence signal from abnormalities in the turbid medium is improved.

If a plurality of sets of second measurement data is acquired with a plurality of different wavelengths used for irradiating the measurement volume, physiological parameters of the turbid medium such as blood volume, Hb-concentration, water concentration, lipid concentration, etc. can be determined from the sets of second measurement data. Since these

physiological parameters are different for normal healthy tissue and abnormalities, visualization of an abnormal accumulation of contrast agent is improved when the first measurement data is manipulated by the acquired second measurement data.

Preferably, at least one physiological parameter is extracted from the plurality of sets of second measurement data and the at least one physiological parameter is used for manipulating the first measurement data. In this case, a physiological parameter which is sensitive to abnormalities can be used for manipulating the first measurement data and, as a result, the fluorescence signal from abnormalities can be further enhanced.

If visualizing is performed in a graphical representation comprising more than two dimensions, features which would not become visible in a two dimensional representation become visible such that the fluorescence signal from abnormalities can be visualized more reliably. If visualizing is performed in a graphical representation using a colorscale, this is achieved in a particularly convenient way.

Preferably, the method to visualize is performed at a plurality of different points in time and the obtained visualizations are compared or manipulated by combining the datasets obtained at different points in time. In this case, the fact can be exploited that the concentration of contrast agent has a different behavior in normal healthy tissue and in lesions. Thus, visualization of the fluorescence signal from lesions is improved.

The object is further solved by a device for visualizing accumulation or depletion of a contrast agent in a turbid medium according to claim 12. The device comprises: a measurement volume for accommodating a turbid medium to which a contrast agent has been administered; a light source unit adapted to irradiate the measurement volume with light from at least one source position; a detection unit adapted to detect light emanating from the measurement volume in at least one detection position for each source position; and a control and processing unit adapted to control the device: to detect light emanating from the contrast agent or attenuation of the light used for irradiation caused by the contrast agent in of the at least one detection position for each source position as first measurement data; to detect attenuation of the light used for irradiating in the at least one detection position for each source position as second measurement data; and to visualize an accumulation or depletion of the contrast agent in the turbid medium by a graphical representation of a data set obtained by manipulating the first measurement data by the second measurement data. Since the control and processing unit is adapted such that the second measurement data corresponding to the attenuation of the light used for irradiating is used for manipulating the first measurement data corresponding to the light emanating from the contrast agent or the

specific attenuation caused by the contrast agent, abnormal regions in the turbid medium can be reliably visualized and distinguished from other structures providing a non-uniform distribution of the contrast agent.

Preferably, the device is a medical image acquisition device.

BRIEF DESCRIPTION OF THE DRAWINGS

Further features and advantages of the present invention will arise from the detailed description of embodiments with reference to the enclosed drawings.

Fig. 1 schematically shows a measurement volume of a device for visualizing accumulation of a contrast agent in a turbid medium.

Fig. 2 schematically shows an arrangement of the measurement volume, the light source unit, and the detection unit in the device of Fig. 1.

Fig. 3 shows an example for a graphical representation.

Fig. 4 shows an exemplary graphical representation comprising more than two dimensions.

DETAILED DESCRIPTION OF EMBODIMENTS

FIRST EMBODIMENT

An embodiment of the present invention will now be described with reference to Figs. 1 to 3. The device for visualizing accumulation of a contrast agent in a turbid medium according to the embodiment is a device for imaging the interior of turbid media, in particular a device for diffuse optical tomography (DOT). In particular, the device is adapted for examination of female breasts. The overall construction of such a device is known in the art. The device comprises a bed (not shown) on which the person under examination is lying in a prone position. An opening is formed in the bed below which a measurement volume 4 extends. The measurement volume 4 is shown in Fig. 1.

In the device shown in Fig. 1, the turbid medium 1 to be examined is a female human breast. The measurement volume 4 is bounded by a receiving portion 2 adapted to receive the turbid medium 1, as schematically indicated in Fig. 1. The receiving portion 2 has a cup-like shape and is provided with an opening 3. As can be seen in Fig. 1, the turbid medium 1 to be examined is placed in the measurement volume 4 such that it freely hangs in the measurement volume 4 from the side of the opening 3. The receiving portion 2 serves to position and stabilize the turbid medium 1 which is examined.

The inner surface of the receiving portion 2 facing the turbid medium 3 is provided with a plurality of ends of light guides 5 formed by optically guiding fibers connecting to a light source unit 6 and to a detection unit 7, as schematically shown in Fig. 2. The light source unit 6 comprises at least one light source preferably formed by a laser emitting light in the wavelength range between 180 nm and 1400 nm. The ends of the light guides 5 are distributed on the inner surface of the receiving portion 2. The device is adapted such that light from the light source unit 6 can be directed to the turbid medium 1 from a plurality of different directions (source positions) and light emanating from the turbid medium 1 can be detected by the detection unit 7 in a plurality of different detection positions distributed around the measurement volume 4. In the embodiment, the detection unit 7 is implemented by a plurality of detectors the corresponding light guides 5 of which are distributed on the inner surface of the receiving portion 2. The ends of the light guides 5 at the inner surface of the receiving portion 2 form a plurality of source positions and a plurality of detection positions. In the embodiment the overall number of source positions is equal to the overall number of detection positions; however, the invention is not limited to an equal number. For example, in the device according to the embodiment, 256 different source positions are provided and 256 detection positions, i.e. respective ends of light guides 5 are provided on the inner surface of the receiving portion 2. The light from the light source is subsequently directed to the turbid medium 1 from the 256 source positions and, for each source position, the light emanating from the turbid medium 1 is detected in the 256 detection positions. However, the invention is not limited to these specific numbers. For example, a device which has been implemented comprises 253 source positions and 254 detection positions.

As schematically shown in Fig. 2, the device comprises a control and processing unit 8 for controlling the acquisition of images by diffuse optical tomography. The control and processing unit 8 reconstructs an image of the interior of the turbid medium 1 based on the signals from the detection unit 7. For reconstruction, the signals sampled during a scan in which the light is directed to the turbid medium 1 from different directions are used. For reasons of simplicity, these elements of the device for imaging the interior of a turbid medium which are known in the art will not be described again.

The receiving portion 2 is further structured such that a space remains between the inner surface of the receiving portion 2 and the turbid medium 1. For examination, this space is filled with an optically matching medium. The optically matching medium is selected to provide appropriate optical coupling between the turbid medium 1 to be imaged

and the source positions and the detection positions distributed on the inner surface. For this purpose, the optically matching medium is provided with optical properties similar to the optical properties of the turbid medium 1 to be examined.

Now, operation of the device according to the embodiment will be described. The device is particularly adapted for a method in which a turbid medium 1 to which a contrast agent has been administered is examined. The turbid medium 1 to which contrast agent has been administered is placed in the measurement volume 4 and a first measurement is started in which light from the light source unit 6 is subsequently directed to the turbid medium from the plurality of source positions. The light used in this first measurement is chosen such that the contrast agent formed by a fluorescent dye preferentially accumulating in lesions in the turbid medium 1 is excited by the light to emit fluorescence light. For each of the plurality of source positions, the fluorescence light emitted by the contrast agent is detected in the plurality of detection positions as first measurement data. Detection of the fluorescence light is performed by appropriate filtering in the light paths to the detection unit 7. Based on the first measurement data, the control and processing unit 8 reconstructs a volumetric image of the fluorescence emission by the contrast agent distributed in the turbid medium 1. However, as has been described above, in case of a non-targeted contrast agent, it is difficult to judge whether a structure in the fluorescence image is due to normal physiology or to an abnormality.

Now, in order to overcome this problem, a second measurement is performed. In this second measurement again, light from the light source unit 6 is subsequently directed to the turbid medium from the plurality of source positions. However, in contrast to the first measurement, now the attenuation of the light used for irradiating is detected in the plurality of detection positions for each source position as second measurement data, i.e. the absorption of the incident light is measured. Thus, in the second measurement the intrinsic contrast of the turbid medium is used. The control and processing unit 8 reconstructs an absorption image of the interior of the turbid medium based on the second measurement data.

Preferably, the attenuation of the light used for irradiating is measured for a plurality of different wavelengths of the light from the light source unit 6. This may be accomplished by e.g. providing several different light sources in the light source unit 6, the light sources emitting light at different wavelengths. Preferably, the light sources are formed by lasers emitting monochromatic light at different wavelengths such as 690 nm, 730 nm, 780 nm, and 850 nm. If a plurality of attenuation measurements is performed with the incident light having different wavelengths, the results from the attenuation measurements

are sensitive to physiological parameters such as blood concentration, Hb concentration (oxy-hemoglobin or deoxy-hemoglobin), water concentration, lipid concentration, etc. The wavelengths mentioned above are particularly well suited in this respect.

According to the present invention, the first measurement data, i.e. the data acquired in the fluorescence measurement, is manipulated by the second measurement data, i.e. the data acquired in the attenuation measurement (or attenuation measurements), for visualizing an abnormal accumulation of the contrast agent in the turbid medium 1. For instance, the data acquired during the fluorescence measurement, and the data acquired during the absorption measurements can be reconstructed into datasets representing a 3-dimensional ('xyz') fluorescence image or absorption images of the content of the receiving volume, respectively. For example, such a fluorescence image of the interior of the turbid medium 1 is compared to the absorption image (or absorption images) of the interior of the turbid medium, and the fluorescence image is manipulated using the absorption image (or images). From the manipulated images, the fluorescence signal from abnormal regions in the turbid medium 1 can be identified. Thus, the abnormal accumulation of the contrast agent is visualized.

According to a preferred embodiment of the present invention, manipulating of the first measurement data by the second measurement data is performed in the following way: A scatter plot is made in which the signal from the first measurement data (fluorescence signal) is plotted as a function of the corresponding signal from the second measurement data (absorption signal) for every voxel in the reconstructed image. Such scatter plots are shown in Figs. 3a and 3b for a breast without a lesion (Fig. 3a) and a breast with a lesion (Fig. 3b) of the same patient measured about 8 hours after injection of a fluorescent contrast agent. The fluorescence intensity is plotted on the vertical axis and the absorption at a wavelength of 690 nm of the light used for irradiation is plotted on the horizontal axis. As can be seen in the figures, the scatter plot consists in general in a cloud of points. In this cloud, a number of distinct features can be recognized, e.g. in the example above: artifacts, the nipple, the bulk of the breast, and the lesion. In the preferred embodiment, a scatter plot is made in which the fluorescence signal is plotted as a function of the absorption of a wavelength sensitive to blood concentration as for instance 690, 730, 780, or 850 nm.

Since the contrast agent is injected intravenously, it will be mostly in the blood, at least immediately after injection. If it is transported and extravasated through normal blood vessel structures, then part of the concentration of the contrast agent is proportional to the blood concentration. In regions where the contrast agent accumulates, or

is depleted, the contrast agent concentration is not proportional to the blood concentration, and this is a sign of abnormality. The blood concentration can be derived from the absorption measurements, i.e. from the second measurement data. As a consequence, when the fluorescence signals (the first measurement data) are plotted against the absorption signals (second measurement data), the scatter plot will consist of a cloud of points with a positive slope on average. This is due to the following: the more blood is present, the higher is the absorption and the more fluorescence is generated. Regions which are correlated with structures in the fluorescence and absorption images can be identified in the cloud: artifacts in the images are usually outliers of the scatter plots, and the nipple in general has both high absorption and a strong fluorescence signal. However, for example tumors having abnormal extravasation can be found back in the cloud at regions having relatively high fluorescence signals as compared to the amount of absorption.

This can be seen in Fig. 3b in which a region (marked by the ellips) clearly "sticks out" of the scatter plot. Such a region cannot be found in the scatter plot of the healthy breast in Fig. 3a. Moreover, if the voxels corresponding to the points indicated by the ellips in Fig. 3b are marked in the corresponding fluorescence image (marked in black in Fig. 3c), it can be found that they correspond to a region having high fluorescence intensity. With respect to the example of Figs. 3b and 3c it has been verified by MRI that these points actually correspond to the location of a tumor. Thus, the accumulation of the contrast agent is visualized in a spatially resolved manner.

Thus, by manipulating the first measurement data by the second measurement data, the accumulation of abnormalities in the turbid medium 1 is visualized in an improved way.

According to a modification, apart from selecting interesting regions in the scatter plots, the data in the scatter plots can be manipulated as well, e.g. by subtracting a line which will rotate the cloud, etc., and the corrected data can be transferred into an image again. Further, the opposite, namely finding out where certain structures in an image are in a scatter plot, can help in the analysis of the measurement data as well.

According to the preferred embodiment thus two types of graphical representations of the measurement are made, namely reconstructed images or the interior of the turbid medium 1 and scatter plots (or parameter maps; see embodiments below). To achieve advantageous results, especially the interaction between two types of representation is important, since typical regions can be found in one representation (e.g. by selecting a typical part of the scatter plot) and compared to corresponding parts of the other representation (e.g. by looking back in the reconstructed images where these typical data

points are). If the selected points originate from regions with typical physiological properties, then these points are often confined to a certain region in the image as well (e.g. related to the presence of the nipple or a diseased area). In order to achieve a high amount of information, during analysis of the data several iterations can be performed in the following way: areas in the reconstructed images can be selected and it can be checked where these voxels are in the scatter plot; or regions can be selected in the scatter plot and it can be checked where these regions are located in the reconstructed images. These steps in both directions can be iteratively repeated several times to improve the results.

SECOND EMBODIMENT

According to a further embodiment, the absorption data (second measurement data) obtained for different wavelengths (as described above as a preferred modification of the first embodiment) are first translated into physiological parameters such as blood volume, Hb concentration, water concentration, lipid concentration, etc. Then, scatter plots can be made which have such a physiological parameter on one axis and the fluorescence intensity on the other axis. Here again, typical regions can be found in the scatter plots and compared to the fluorescence and absorption images and images representing concentrations of the physiological parameters.

MODIFICATIONS

In the examples described above, use is made of two-dimensional scatter plots for visualizing an accumulation of the contrast agent. However, the concept can be extended to scatter plots of three or more dimensions as well. For instance, for visualization, 3D scatter plots can be made having fluorescence intensity on one axis, absorption at a certain wavelength on a second axis, and absorption at another wavelength on a third axis. Further, 3D scatter plots can be made comprising the fluorescence intensity on one axis and physiological parameters on other axes, or fluorescence intensity on one axis, a physiological parameter on a second axis, and absorption at a certain wavelength on a third axis. Furthermore, plots can be made having fluorescence intensity on one axis, absorption at a certain wavelength or a physiological parameter on a second axis, and information on the position in the turbid medium (e.g. depth, distance from the nipple, etc.) on the third axis.

An additional dimension can be represented in the scatter plot using a color scale (or grey scale) in order to visualize additional information. An example for this is shown in Fig. 4 with respect to a phantom used as a turbid medium instead of a real female

breast. In Fig. 4, absorption at a wavelength of 690 nm is represented on one axis, fluorescence intensity is represented on a second axis, and depth in the turbid medium 1 is represented on the third axis. In Fig. 4 additionally a grey scale is used which represents the depth in the turbid medium as on the z-axis. Two main parts are visible in the 3D scatter plot of Fig. 4 the one of which at the right (part in light grey) looks like it was "sticking out" of the rest of the cloud. It corresponds to a lesion inside the measurement volume 4. It has been found that some features of the scatter plot which are not always visible in a 2D view become apparent in a 3D representation used for visualization.

A further modification will now be described. After administering of the contrast agent, the spatial distribution of the contrast agent concentration in the turbid medium 1 varies over time. Overall, the contrast agent concentration initially increases and, after a while, decreases again when the contrast agent is excreted. This results in a temporal change of both the fluorescence and (for wavelengths overlapping with the absorption spectrum of the contrast agent) the absorption signals, i.e. the first measurement data and the second measurement data. Because of the abnormal extravasation in tumors, the temporal behavior of the signals from a tumor differs from the temporal behavior of signals from normal tissue. This information can be used for visualizing tumors by comparing the scatter plots described above for different time points after administering the contrast agent. Because of the different temporal behavior of the contrast agent concentration in a tumor as compared to healthy tissue, regions in the scatter plot which correspond to a tumor will show a different temporal behavior than regions corresponding to normal tissue. Thus, such abnormal accumulations of contrast agent can be reliably visualized.

Although it has been described above that the fluorescence measurement is performed before the attenuation/absorption measurement, a skilled person will understand that the order can be reversed.

Further, although a fluorescent contrast agent has been described with respect to the embodiment above, the invention is not limited to this. Alternatively, an absorbing contrast agent could be used which has specific absorption properties. In this case, the spatial distribution of the absorbing contrast agent is reconstructed. In this case, the specific absorption of the contrast agent is detected as first measurement data. This can e.g. be realized by choosing light having a specific wavelength for irradiation in the step for acquiring the first measurement data.

The light source unit may comprise one light source emitting light having a specific wavelength or a specific range of wavelengths, or a plurality of light sources

emitting light at different specific wavelengths or at different specific wavelength ranges. Preferably each such light source is formed by a laser emitting light having a specific wavelength.

In the embodiments described above, the detection unit comprises a plurality of different detectors the respective detection positions of which are distributed around the measurement volume. This enables fast and efficient measurements. However, the detection unit may also comprise only one detector the position relative to the measurement volume of which is changed during the measurement in order to detect light in the plurality of different detection positions.

Further, although it has been described with respect to the embodiment that a plurality of source positions is used for subsequently irradiating the interior of the measurement volume and the light emanating from the measurement volume is detected in a plurality of detection positions, the embodiment is not limited to this. In principle, it would be enough if the number of source positions times the number of detection positions is a plurality. I.e. making use of either one source position and a plurality of detection positions or a plurality of source positions and one detection position would be sufficient in principle, although the arrangement comprising multiple source positions and multiple detection positions is preferred.

Further, it has been described above that the measurement volume is bounded by a receiving portion having a cup-like shape. However, the measurement volume may also have a different shape, e.g. may be bounded by two parallel plates between which the turbid medium is accommodated in a compressed state during the measurements.

CLAIMS:

1. A method for visualizing accumulation or depletion of a contrast agent in a turbid medium; the method comprising the steps:

- accommodating a turbid medium (1) to which a contrast agent has been administered in a measurement volume (4);
- irradiating the interior of the measurement volume (4) with light from a light source unit (6) from at least one source position,
- for each source position, detecting light emanating from the contrast agent or detecting attenuation of the light used for irradiation caused by the contrast agent in at least one detection position as first measurement data;
- for each source position, detecting attenuation of the light used for irradiation in the at least one detection position as second measurement data;
- visualizing an accumulation or depletion of the contrast agent in the turbid medium (1) by a graphical representation of a data set obtained by manipulating the first measurement data by the second measurement data.

2. The method according to claim 1, wherein the light used for irradiation in the step for obtaining the first measurement data differs in wavelength from that used in the step for obtaining the second measurement data.

3. The method according to any one of claims 1 or 2, wherein visualization is performed by graphically representing the first measurement data as a function of the second measurement data or vice versa.

4. The method according to any one of claims 1 or 2, wherein visualizing is performed by reconstructing an image of the interior of the turbid medium based on the first measurement data manipulated by the second measurement data.

5. The method according to any one of claims 1 or 2, wherein visualizing is performed by reconstructing images of the interior of the turbid medium (1) based on the first

measurement data and the second measurement data, as well as graphically representing the first measurement data as a function of the second measurement data or vice versa, and analyzing the interaction between the two types of representations.

6. The method according to any one of claims 1 to 5, wherein, in the step for obtaining the second measurement data, light having a wavelength sensitive to blood concentration is used for irradiating the interior of the measurement volume (4).

7. The method according to any one of claims 1 to 6, wherein a plurality of sets of second measurement data are acquired with a plurality of different wavelengths used for irradiating the measurement volume (4).

8. The method according to claim 7, wherein at least one physiological parameter is extracted from the plurality of sets of second measurement data and the at least one physiological parameter is used for manipulating the first measurement data.

9. The method according to any one of claims 1 to 8, wherein visualizing is performed in a graphical representation comprising more than two dimensions.

10. The method according to any one of claims 1 to 9, wherein visualizing is performed in a graphical representation using a colorscale.

11. The method according to any one of claims 1 to 10, wherein the method to visualize is performed at a plurality of different points in time and the obtained visualizations are compared or manipulated by combining the datasets obtained at different points in time.

12. Device for visualizing accumulation or depletion of a contrast agent in a turbid medium, the device comprising:

- a measurement volume (4) for accommodating a turbid medium (1) to which a contrast agent has been administered;
- a light source unit (6) adapted to irradiate the measurement volume (4) with light from at least one source position;
- a detection unit (7) adapted to detect light emanating from the measurement volume (4) in at least one detection position for each source position; and

- a control and processing unit (8) adapted to control the device:

to detect light emanating from the contrast agent or detect attenuation of the light used for irradiation caused by the contrast agent in the at least one detection position for each source position as first measurement data;

- to detect attenuation of the light used for irradiating in the at least one detection position for each source position as second measurement data; and
- to visualize an accumulation or depletion of the contrast agent in the turbid medium (1) by a graphical representation of a data set obtained by manipulating the first measurement data by the second measurement data.

13. The device according to claim 10, wherein the device is a medical image acquisition device.

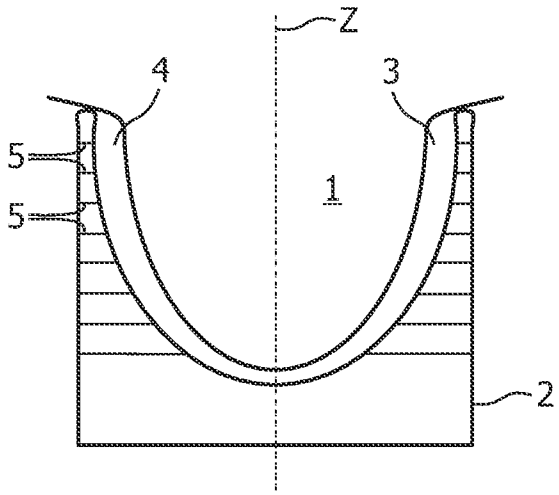

FIG. 1

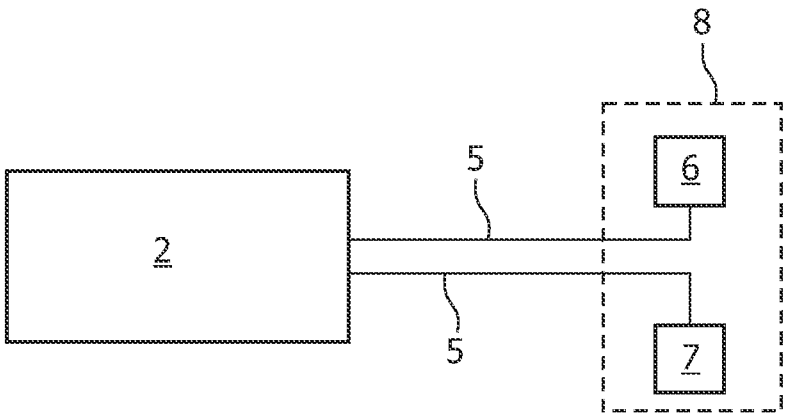

FIG. 2

FIG. 3a

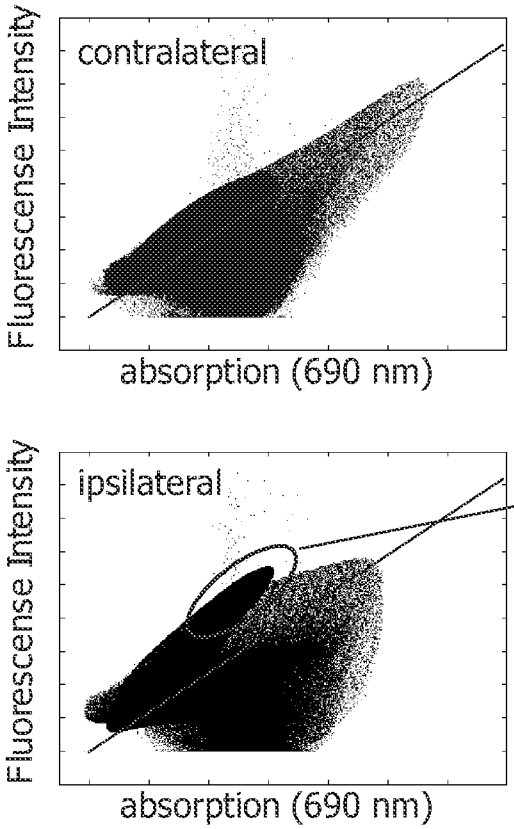

FIG. 3b

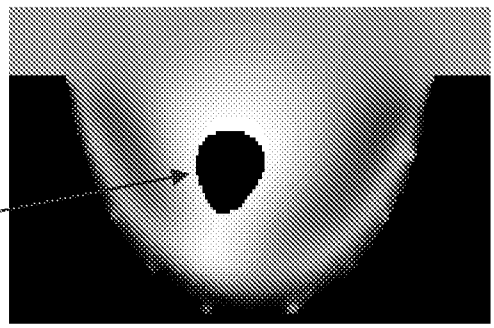

FIG. 3c

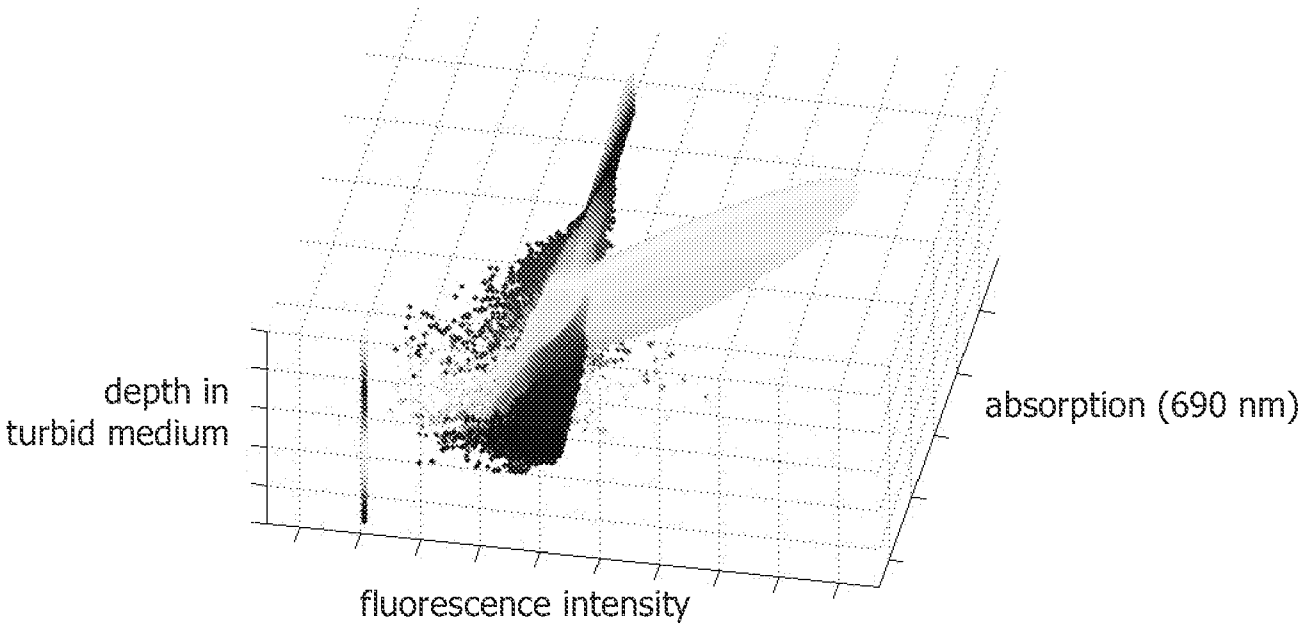
depth in
turbid medium
fluorescence intensity
absorption (690 nm)

FIG. 4

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2009/051314

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/00 G01N21/47

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)
A61B G01N

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2007/111669 A (VISEN MEDICAL INC [US]; YARED WAEL I [US]) 4 October 2007 (2007-10-04)	1-7,9, 11-13
Y	paragraphs [0019], [0090] - [0118], [0170] - [0174] figures 1,9	8
X	NTZIACHRISTOS V ET AL: "Experimental Fluorescence Tomography of Tissues With Noncontact Measurements" IEEE TRANSACTIONS ON MEDICAL IMAGING, IEEE SERVICE CENTER, PISCATAWAY, NJ, US, vol. 23, no. 4, 1 April 2004 (2004-04-01), pages 492-500, XP011110227 ISSN: 0278-0062 the whole document	1,10,12

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

[X] See patent family annex.

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 June 2009	06/07/2009

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Rapp, Alexander

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5 596 987 A (CHANCE BRITTON [US]) 28 January 1997 (1997-01-28) column 2, line 1 - column 6, line 62 -----	8
A	COLAK S B ET AL: "Clinical Optical Tomography and NIR Spectroscopy for Breast Cancer Detection" 1999, IEEE JOURNAL OF SELECTED TOPICS IN QUNTUM ELECTRONICS, PAGE(S) 1143 - 1158 5 , XP002527791 [retrieved on 1999-07-01] the whole document -----	1-13

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2009/051314

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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