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(54) **Title:** METHOD AND DEVICE FOR MEASURING PARAMETERS OF CARDIAC FUNCTION

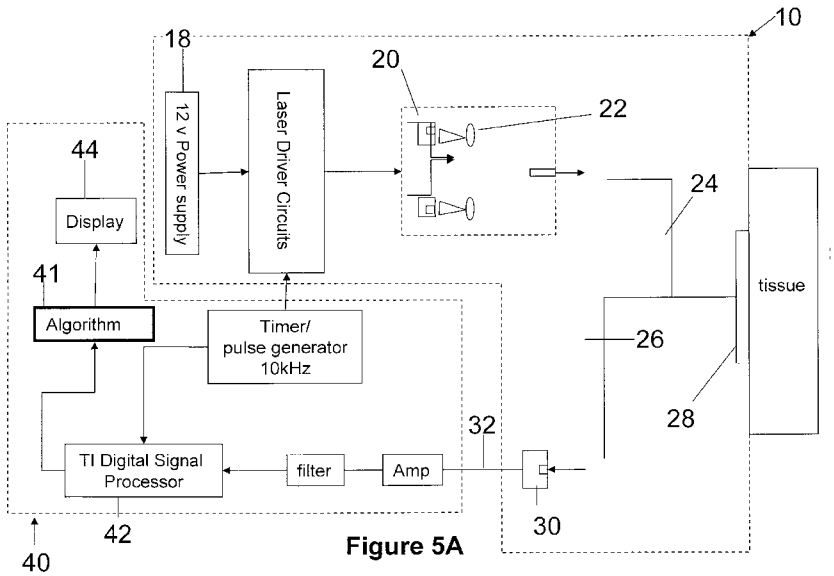

Figure 5A

(57) **Abstract:** A device for non-invasively measuring at least one parameter of a cardiac blood vessel in a patient is provided. The device comprises at least one light source that emits light in the 400 nm to 1000 nm wavelength range; at least one photodetector adapted to receive light emitted by the light source and generate an output based on the received light, wherein said light is reflected from or transmitted through tissue of the patient, the output of said photodetector being correlated with a parameter of the blood vessel; and at least one probe for facilitating delivery of light from the light source to an external tissue site on the patient in the proximity of the cardiac blood vessel and receipt of light by the photodetector. A system and methods of monitoring/measuring cardiac parameters utilizing the device and/or system are also provided.

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METHOD AND DEVICE FOR MEASURING PARAMETERS OF CARDIAC FUNCTION

FIELD OF THE INVENTION

[0001]The present invention is related to techniques for monitoring vital functions of the human body, including cardiac functions such as cardiac output and central venous blood oxygenation. It relates, in particular, to an optical method and device for the non-invasive and continuous monitoring of cardiac parameters such as blood flow, blood volume and blood oxygen saturation.

BACKGROUND OF THE INVENTION

[0002]The evaluation of jugular venous pulse has been an integral part of cardiovascular examination and has important clinical diagnostic values [1-2]. Jugular venous pulse is produced by the changes in blood flow and pressure in central veins caused by right atrial and ventricular filling and contraction. The two main objectives of the bedside examination of jugular vein pulse include the estimation of central venous pressure and the inspection of the waveform. Because of its more direct route to the right atrium, the right internal jugular vein is superior for the purpose. Based upon these measurements, physicians can access hemodynamic events in the right atrium and thus diagnose heart diseases and abnormalities. For example, the most common cause of elevated jugular venous pressure is an increase in right ventricular pressure such as occurs in patients with pulmonary stenosis, pulmonary hypertension, or right ventricular failure secondary to right ventricular infarction. The venous pressure also is elevated when obstruction to right ventricular inflow occurs, such as with tricuspid stenosis or right atrial myxoma, or when constructive pericardial disease impedes right ventricular inflow. It may also result from vena caval obstruction and, at times, an increased blood volume. Patients with obstructive pulmonary disease may have an elevated venous pressure only during expiration.

[0003]The conventional technique for measuring venous pulse and waveform has been described in the literature [3]. The patient is examined at the optimum degree of trunk elevation for visualization of venous pulsations. The venous pressure is measured by a ruler as the vertical distance from the top of the oscillating venous column, to the level of the sternal angle plus vertical distance to the right atrium Due

to the fact that the venous pulse is in generally very small, and due to complications with patients, this method is challenging for physicians to use and provides approximate values only.

[0004]Cardiac output is defined as the volume of blood circulated per minute. It is equal to the heart rate multiplied by the stroke volume (the amount ejected by the heart with each contraction). Cardiac output is of central importance in the monitoring of cardiovascular health [4]. Accurate clinical assessment of circulatory status is particularly desirable in critically ill patients in the ICU and patients undergoing cardiac, thoracic, or vascular interventions, and has proven valuable in long term follow-up of outpatient therapies. As a patient's hemodynamic status may change rapidly, continuous monitoring of cardiac output will provide information that allows rapid adjustment of therapy. Measurements of cardiac output and blood pressure can also be used to calculate peripheral resistance.

[0005]Jansen (J.R.C. Jansen, "Novel methods of invasive/non-invasive cardiac output monitoring", Abstracts of the 7th annual meeting of the European Society for Intravenous Anesthesia, Lisbon 2004) describes eight desirable characteristics for cardiac output monitoring techniques; accuracy, reproducibility or precision, fast response time, operator independency, ease of use, continuous use, cost effectiveness, and no increased mortality and morbidity.

[0006]***Pulmonary artery catheter (PAC) thermodilution*** method is generally accepted as the clinical standard for monitoring cardiac output, to which all other methods are compared as discussed by Conway and Lund-Johansen [6]. As this technology is highly invasive, complicated, and expensive, many new methods have been developed in an attempt to replace it, but none have so far gained acceptance. A recent review of the various techniques for measuring cardiac output is given in Linton and Gilon [5]. This article lists both non/minimally invasive and invasive methods and compares the advantages and disadvantages of each. A brief description of some of these techniques follows.

[0007]***Indicator dilution techniques.*** There are several indicator dilution techniques including transpulmonary thermodilution (also known as PiCCO technology, Pulsion Medical Technologies of Munich, Germany), transpulmonary lithium dilution method

(LiDCO Group plc of London, UK), PAC based thermo-dilution and other methods (Vigilance, Baxter; Opti-Q, Abbott; and TruCCOMS, AorTech). Application of such techniques assumes three major conditions, namely, complete mixing of blood and indicator, no loss of indicator between place of injection and place of detection, and constant blood flow. The errors associated with indicator dilution techniques are primarily related to the violation of these conditions, as discussed by Lund-Johansen [7 - 8].

[0008]***Fick principle.*** The direct oxygen Fick approach is currently the standard reference technique for cardiac output measurement as discussed by Keinanen et al [9-10]. It is generally considered the most accurate method currently available. The NICO (Novametrix) system is a non-invasive device that applies Fick's principle and relies solely on airway gas measurement as described by Botero et al [11]. This method shows a lack of agreement between thermodilution and CO_2-rebreathing cardiac output as described in Nielsson et al [12], due to unknown ventilation/perfusion inequality in patients.

[0009]***Bio-Impedance and conduction techniques.*** The bio-impedance method was developed as a simple, low-cost method that gives information about the cardiovascular system and/or (de)-hydration status of the body in a non-invasive way. Over the years, a diversity of thoracic impedance measurement systems have also been developed. These systems determine CO on a beat-to-beat time basis. Studies have been reported with mostly poor results, but in some exceptional cases, there was good correlation with a reference method. Many of these studies refer to the poor physical principles of the thoracic impedance method as described in Patterson "Fundamentals of impedance cardiography", IEEE Engineering in Medicine and Biology 1989; 35 to explain the discrepancies.

[0010]***Echo-Doppler ultrasound.*** This technique uses ultrasound and the Doppler Effect to measure cardiac output. The blood velocity through the aorta causes a 'Doppler shift' in the frequency of the returning ultrasound waves. Echo-Doppler probes positioned inside the esophagus with their echo window on the thoracic aorta may be used for measuring aortic flow velocity, as discussed by Schmidlin et al [13]. Aortic cross sectional area is assumed in devices such as the CardioQ, made by Deltex Medical PLC, Chichester, UK, or measured simultaneously as, for example, in

the HemoSonic device made by Arrow International. With these minimally invasive techniques what is measured is aortic blood flow, not cardiac output. A fixed relationship between aortic blood flow and cardiac output is assumed. Echo-Doppler ultrasound requires an above average level of skill on the part of the operator of the ultrasound machine to get accurate reliable results.

[0011]***Arterial pulse contour analysis***. The estimation of cardiac output based on pulse contour analysis is an indirect method, since cardiac output is not measured directly but is computed from a pressure pulsation on the basis of a criterion or model [14- 17]. Three pulse contour methods are currently available; PiCCO (Pulsion), PulseCO (LiDCO) and Modelflow (TNO/BMI). All three of these pulse contour methods use an invasively measured arterial blood pressure and they need to be calibrated. PiCCO is calibrated by transpulmonary thermodilution, LiDCO by transpulmonary lithium dilution and Modelflow by the mean of 3 or 4 conventional thermodilution measurements equally spread over the ventilatory cycle.

[0012]Near infrared spectroscopy has been used to non-invasively measure various physiological properties in animal and human subjects. The basic principle underlying near infrared spectroscopy is that a physiological medium such as tissues includes a variety of light-absorbing (chromophores) and light-scattering substances which can interact with transmitted low energy near infrared photons. For example, deoxygenated and oxygenated hemoglobins in human blood are the most dominant chromophores in the spectrum range of 400 nm to 1000 nm. Therefore, diffuse optical spectroscopy has been applied to non-invasively measure oxygen levels in the physiological medium in terms of tissue hemoglobin oxygen saturation. Technical background for diffuse optical spectroscopy has been discussed in, e.g., Neuman, M. R., Pulse Oximetry: Physical Principles, Technical Realization and Present Limitations,@ Adv. Exp. Med. Biol., vol. 220, p.135-144, 1987 and Severinghaus, J. W., History and Recent Developments in Pulse Oximetry,@ Scan. J. Clin. and Lab. Investigations, vol. 53, p.105-111, 1993.

[0013]Because of the highly scattering nature of tissue to the visible and near infrared light (400nm – 1000nm), it is difficult to apply diffuse optical spectroscopy non-invasively to select blood vessels within a tissue to calculate blood oxygenation. Thus, diffuse optical spectroscopy has only been used to measure the combined or

average oxygenation of blood from arteries, veins, and capillaries within a tissue medium. However, in many clinical applications, it is desirable to know the blood oxygenation of particular blood vessels. To do so, various invasive methods have been developed which involve the use of catheters that must be inserted into a targeted blood vessel to make the measurement.

[0014]None of the above-mentioned techniques of measuring cardiac output combines all of the eight "Jansen" criteria mentioned above and, thus, none can displace the conventional thermodilution technique as described by Jansen et al [18]. Although highly invasive, complicated and expensive, the conventional thermodilution method remains the method of choice for measuring cardiac output. Given the foregoing, it would be highly desirable to develop a non-invasive method for real-time monitoring of cardiac output in a clinical setting which is accurate, reliable, cost effective and easy to use.

SUMMARY OF THE INVENTION

[0015]The present invention provides a device, system and method by which cardiac parameters can be continuously monitored in a non-invasive manner by the optical measure of venous blood flow, venous blood pressure and blood content including oxygenation.

[0016]Thus, in one aspect of the invention, a device for non-invasively measuring at least one parameter of a cardiac blood vessel in a patient is provided comprising:

at least one light source that emits light in the 400 nm to 1000 nm wavelength range;

at least one photodetector adapted to receive light emitted by the light source and generate an output based on the received light, wherein said light is reflected from or transmitted through tissue of the patient, the output of said photodetector being correlated with a parameter of the blood vessel; and

at least one probe for facilitating delivery of light from the light source to an external tissue site on the patient in the proximity of the cardiac blood vessel and receipt of light by the photodetector.

[0017]In another aspect of the invention, a device useful to monitor a parameter of a cardiac blood vessel in a patient is provided comprising:

at least one light-emitting component adapted to emit light in the 400 nm to 1000 nm wavelength range;

at least one light-receiving component adapted to receive light emitted by the light-emitting component and translate said light into a recordable output, wherein said light is reflected from or transmitted through tissue of the patient; and

at least one probe which facilitates delivery of light from the light-emitting component to an external tissue site on the patient in the proximity of a cardiac blood vessel and receipt of light reflected from or transmitted through said patient site by the light-receiving component.

[0018]In another aspect of the invention, a system useful to monitor a parameter of a cardiac blood vessel in a patient is provided comprising:

at least one light-emitting component adapted to emit light in the 400 nm to 1000 nm wavelength range;

at least one light-receiving component adapted to receive light emitted by the light-emitting component and translate said light into a recordable output, wherein said light is reflected from or transmitted through tissue of the patient; and

at least one probe which facilitates delivery of light from the light-emitting component to an external tissue site on the patient in the proximity of a cardiac blood vessel and receipt of light reflected from or transmitted through said patient site by the light-receiving component; and

a signal-processing device adapted to translate the output from said light-receiving component to a visual form.

[0019]In another aspect of the invention, a method for determining a parameter of a cardiac blood vessel in a patient is provided comprising the steps of:

directing a beam of light having a wavelength in the range of 400 nm to 1000 nm to an external tissue site on the patient that is in the proximity of the blood vessel;

detecting light reflected from the tissue site or transmitted through the tissue site;

translating the detected light into an output signal against time; and

calculating the parameter of the blood vessel using the output signal.

[0020]In another aspect of the invention, a method for measuring the blood content of a chromophore in a patient is provided comprising:

directing a light beam having at least first and second selected wavelengths at an external tissue site on the patient that is in the proximity of a cardiac blood vessel, wherein said selected wavelengths are based on the absorption characteristics of the chromophore;

detecting light reflected from the tissue or transmitted through the tissue at the selected wavelengths; and

translating the detected light into an output current in order to determine the blood content of said chromophore according to modified Beer Lambert's law.

[0021]In a further aspect, a method of determining blood oxygenation of a cardiac vessel in a patient is provided comprising:

directing a first light beam having a first wavelength of 780 nm and a second light beam having a second wavelength of 850 nm at an external tissue site on the patient that is in the proximity of a cardiac blood vessel;

detecting light reflected from the tissue or transmitted through the tissue at the first and second wavelengths; and

translating the detected light into an output current for the first and second wavelengths in order to calculate the blood oxygenation of the cardiac vessel according to modified Beer Lambert's law.

[0022]In another aspect of the invention, s method of determining central venous pressure in a patient is provided comprising:

directing a beam of light having a wavelength in the range of 400 nm to 1000 nm at a series of external tissue sites on the patient along the jugular vein starting from the sternal angle;

detecting light reflected from the tissue site or transmitted through each tissue site;

translating the detected light into an output signal against time to determine the highest position along the vein to yield a signal (d); and

calculating the central venous pressure (P) according to the equation P = (d +5) sin 9, wherein 9 is the inclined body angle from horizontal of the patient.

[0023]These and other aspects of the present invention will become apparent by reference to the detailed description that follows, and the drawings in which:

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 illustrates a top view of a device (A) for monitoring cardiac output in accordance with an aspect of the invention and placement of the device relative to cardiac vessels (B);

Figure 2 illustrates a side view of a device as in Fig. 1;

Figure 3 illustrates a system incorporating the device of Fig. 1;

Figure 4 illustrates a signal or waveform produced using a device as in Fig. 1;

Figure 5 (A and B) is a block diagram of a system incorporating a device as in Fig. 1;

Figure 6 (A-C) illustrates probes for use in the device;

Figure 7 illustrates a top view of embodiments of the invention (A, B) comprising multiple light sources and photodetectors;

Figure 8 is a block diagram of a system incorporating a device as in Fig. 7;

Figure 9 (A-C) illustrates a top view of embodiments of the invention comprising multiple photodetectors per light source;

Figure 10 illustrates a dual signal (waveform) generated by an embodiment of Fig. 9;

Figure 11 illustrates a top view of a cardiac monitoring device according to an embodiment of the invention comprising multiple sensor patches;

Figure 12 illustrates a waveform obtained using a device in accordance with the invention;

Figure 13 illustrates a top view of a device in accordance with a further aspect of the invention;

Figure 14 illustrates different source-detector configurations (A, B and C) of a device useful to measure blood pressure;

Figure 15 illustrates a waveform obtained using a device according to Fig. 13 (B) in three different positions (A); and

Figure 16 is a block diagram illustrating a system according to an aspect of the invention.

DETAILED DESCRIPTION OF THE INVENTION

[0024]A device 10 for measuring a parameter of cardiac function in a patient is provided as shown in Fig. 1A, comprising a light source 20 that emits light in the 400 nm to 1000 nm wavelength range, e.g. visible and infra-red light, a photodetector 30 adapted to receive light from the light source 20(as shown in Fig. 2) and translate the received light into an output signal and a patch probe 28 for placement on a patient at an external site in the vicinity of a cardiac blood vessel (as shown in Fig. 1B) which functions as the interface of the device between light source 20/photodetector 30 and a selected external patient site. Thus, the probe 28 permits/facilitates delivery of light emitted by the light source 20 to the selected patient site and transfer of light reflected from or transmitted through the patient site to the photodetector 30. To generate a visual signal, the device 10 may additionally comprise a signal-processing component 40 (Fig. 3) which communicates with the photodetector 30 to translate light received by the photodetector 30 into a recordable visual signal or waveform of the cardiac vessel (e.g. representative of a time course plot of a measurable characteristic or parameter of the blood vessel such as a pressure waveform or central venous pulse).

[0025] The light source 20 may be any suitable light source such as a laser diode (e.g. RLT7605G, 760 nm, 5 mW, sm, 9.0 mmh, or RLT8510MG, 850 nm, 10 mW, sm, 5.6 mm), a light emitting diode (LED) or a broadband light source emitting a selected wavelength in the range of 400nm to 1000nm, for example, a wavelength in the range of 780nm and 850nm. In an embodiment, the light source is adapted to emit light in two or more wavelengths, e.g. by association with a frequency oscillator. The light source 20 is powered by an appropriate power supply 18 such as a 12V DC power supply. Light from the light source 20 is directed to at least one external tissue site on the patient that is within close proximity to a cardiac blood vessel, such as the internal jugular vein, the external jugular vein and the carotid artery, while the internal jugular vein is preferred. The neck, for example, represents a suitable site for monitoring a cardiac parameter.

[0026]As shown in Fig. 5A/5B, in one embodiment, light from the light source 20 may be directed or focussed by an optical lens 22 into a transmitting means 24, such as transmitting optical fibre bundles, for transmission to the selected patient site. Receiving means 26, such as optical fibre bundles, may also be used to receive light that is reflected/transmitted from the patient site and convey this light to photodetector 30 (Fig. 5A). As one of skill in the art will appreciate, each fibre optic bundle will incorporate fibres manufactured of material appropriate for the transmission of the wavelength of the light emitted from the light source 20. For example, if the light source 20 emits in the visible wavelength range, both multiple mode plastic and glass optical fibres may be used. The number and diameter of the fibres in the fibre optic bundle is optimized empirically to provide the highest signal to noise ratio in a given application. In the embodiments shown in Fig. 5A/5B, the transmitting and receiving optical fibre bundles 24, 26 are set in the patch probe 28, either at distinct spaced sites or they may be combined together at a single site.

[0027]As shown in Fig. 6A/6C, optical mirrors 29 may be utilized to direct or reflect light from the transmitting fibre bundle 24 into the tissue at the selected patient site, and to direct reflected or transmitted light from the patient site into the receiving fibre bundle 26 (Fig.6A). Alternatively, the light source 20 and photodetector 30 may be set directly in the patch probe 28 obviating the need for optical fibres as shown in Fig. 6B. In yet another embodiment, a combination of the foregoing embodiments may be

utilized in which the light source 20 is set directly in the probe 28 to deliver light to the patient site, while the reflected/transmitted light is received by optical fibres 26 for delivery to the photodetector 30. A converse embodiment may also be used in which the probe 28 comprises transmitting optical fibres 24 to deliver light from the light source to the patient site, and a photodetector 30 set directly in the probe 28 to receive the reflected/transmitted light (Fig. 6C). Accordingly, the light source 20 and photodetector 30 are each coupled to the probe 28 (e.g. attached to, integrally formed with or set directly in the probe 28).

[0028]The light source 20 or transmitting optical fibres 24 may be set in the same patch probe 28 as the photodetector 30 or receiving optical fibres 26, or in a separate patch probe 28 for placement at a distinct site on the patient that is within a suitable distance from the photodetector 30 or receiving optical fibres 26 to permit detection of reflected/transmitted light. The distance between the component delivering light to the patient site (light source or transmitting optical fibres) and the component receiving light from the patient site (photodetector or receiving optical fibres) may vary depending on the nature of each of the components, while a typical distance is generally between 2 and 4 cm, for example, 3 cm.

[0029]The patch probe 28 may be made out of any material suitable to support the electronic/optical components it houses, e.g. light source, photodetector, optical fibres or mirrors, and which is compatible for placement on the skin. An example of one such suitable material is medical rubber. The patch 28 may be held in position manually, may be held in position by adhesives (one side of the patch may be coated with a material that is adhesive to skin such as a hydro gel adhesive) or may be adapted to be held in place with straps that can be tied or otherwise secured. Opposing ends of the band may also include an adhesive material such as Velcro to facilitate their attachment and to hold the device in place.

[0030]The photodetector 30 translates received reflected/transmitted light into a recordable output such as current or voltage. An example of a suitable photodetector 30 for use in the present device is a silicon photo diode (e.g. Hamamatsu S8553). Condensor lenses may be incorporated, if required, to refocus the reflected or transmitted beam of light to be received by the photodetector 30. As will be understood by a person skilled in the art, silicon photodiodes are semiconductor light

sensors that generate a current or voltage when the P-N junction in the semiconductor is illuminated by light. Accordingly, the photodetector 30 provides a current/voltage signal in response to the received light signal. Thus, the current/voltage signal output generated by the photodetector 30 is proportional to the instantaneous light intensity of the light signal received at the photodetector 30. Accordingly, the photodetector 30 provides a time-varying output (e.g. current/voltage as a function of time) which is dependent upon the received light and its characteristics.

[0031]In an aspect of the invention, a system is provided, for example as shown in Figures 5, 8 or 16 , in which the photodetector 30 of device 10 is connected to a signal processing device 40. The signal processing device 40 is operable to receive the signal provided by the photodetector 30 (e.g. the time varying current/voltage signal) and translate the signal into a visual output such as a waveform. Thus, the signal processing device 40 is operable to digitize the output provided by the photodetector 30 into a recordable output for presenting on a display (e.g. 44).

[0032]Referring to Figure 5 or 8, a system is provided comprising at least one light source 20 for emitting light, a probe 28 for facilitating the delivery of light to an external tissue site on the patient, at least one photodetector 30 configured for receiving light emitted by the light source 20 (which is either reflected from or transmitted through the tissue site) and translating the light to a current/voltage signal in response thereto, a signal processing device 40 for translating the signal from the photodetector 30 into a visual output such as a time-varying waveform. As will be described below, the signal processing device 40 may include a microprocessor (e.g. digital signal processor, Texas Instruments) or digital acquisition board 42 to digitize the signal (e.g. current/voltage) from the photodetector 30, and a display unit 44, such as a monitor, which is in communication with or connected to the microprocessor 42 (Fig. 5), and functions to display the signal as a waveform.

[0033]Alternatively, as will be understood by a person of skill in the art and as shown in Fig. 5B, the signal processing device 40 may be separate from the display unit 44, and in communication with an external display unit 44 for presenting the output of the signal processing device 40 thereon. For convenience, the monitor may be portable, and battery operated. According to another embodiment, the signal processing device 40 may further comprise an algorithm processing module 41 (e.g. illustrated in Figure

8) for receiving an indication of the desired cardiac parameter output (e.g. via a user interface or predefined selection of the desired cardiac parameter). The algorithm processing module 41 is operable to translate the signal received from the photodetector 30 into the desired cardiac parameter output (e.g. blood pressure waveform).

[0034]Referring to Figure 16, the signal processing device 40 can be implemented on one or more respective computing device(s) 101. The devices 101 in general can include a network connection interface 200, such as a network interface card or a modem, coupled via connection 218 to a device infrastructure 204. The connection interface 200 is connectable during operation of the device(s) 101 to a network 11 (e.g. an intranet and/or an extranet such as the Internet) which enables the device(s) 101 to communicate with each other as appropriate. The network 11 can, for example, support the communication of the output signal (e.g. current/voltage signal) provided by the photodetector 30 to the signal processing device 40.

[0035]The device(s) 101 may also have a user interface 202, as also shown in Fig. 16, coupled to the device infrastructure 204 by connection 222 to interact with a user. The user interface 202 can include one or more user input devices such as, but not limited to, a QWERTY keyboard, a keypad, a trackwheel, a stylus, a mouse, a microphone and a user output device such as an LCD screen display and/or a speaker. If the screen is touch sensitive, then the display can also be used as the user input device as controlled by the device infrastructure 204.

[0036]Operation of the device(s) 101 is facilitated by the device infrastructure 204. The device infrastructure 204 includes one or more computer processors 208 (e.g. a Digital Signal Processor) and can include an associated memory 210 (e.g. a random access memory). The computer processor 208 facilitates performance of the computing device 101 configured for the intended task through operation of the network interface 200, the user interface 202 and other application programs/hardware 207 of the computing device 101 by executing task-related instructions. These task-related instructions may be provided by an operating system and/or software applications 207 located in the memory 210, and/or by operability that is configured into the electronic/digital circuitry of the processor(s) 208 designed to perform the specific task(s). Further, it is recognized that the device infrastructure

204 may include a computer readable storage medium 212 coupled to the processor 208 for providing instructions to the processor 208. The computer readable medium 212 can include hardware and/or software such as, by way of example only, magnetic disks, magnetic tape, optically readable medium such as CD/DVD ROMS, and memory cards. In each case, the computer readable medium 212 may take the form of a small disk, floppy diskette, cassette, hard disk drive, solid-state memory card or RAM provided in the memory module 210. It should be noted that the above listed examples of computer readable media 212 may be used either alone or in combination. The device memory 210 and/or computer readable medium 212 may be used to store, for example, the desired output (e.g. pressure waveform) for use in processing of the signal received from the photodetector 30.

[0037]Further, it is recognized that the computing device(s) 101 may include executable applications 207 comprising code or machine readable instructions for implementing predetermined functions/operations including those of an operating system. The processor 208 as used herein is a configured device and/or set of machine-readable instructions for performing operations as described by example above. As used herein, the processor 208 may comprise any one or combination of, hardware, firmware, and/or software. The processor 208 acts upon information by manipulating, analyzing, modifying, converting or transmitting information for use by an executable procedure or an information device, and/or by routing the information with respect to an output device. The processor 208 may use or comprise the capabilities of a controller or microprocessor, for example. Accordingly, the functionality of the signal processing device 40 and/or the photodetector 30 may be implemented in hardware, software or a combination of both. Accordingly, the use of a processor 208 as a device and/or as a set of machine-readable instructions is hereafter referred to generically as a processor/module for the sake of simplicity.

[0038]It will be understood that the computing device(s) 101 may be, for example, personal computers, personal digital assistants, mobile phones, and content players. Further, it is recognised that each server computing device 101, although depicted as a single computer system, may be implemented as a network of computer processors, as desired.

[0039]Referring to Figure 8, the signal processing device 40 may execute an algorithm (e.g. via the algorithm processing module 41) to translate the signal received by the photodetector 30 to a waveform. The waveform is the time varying component of the optical signal associated with cardiac activities, which can be translated into dynamic information such as blood flow, flow velocity, blood volume, blood pressure and blood content such as oxygenation or physical displacement of blood within the vessel.

[0040]In one embodiment, for example, the signal is translated into a pressure waveform. Since the central venous pressure waveform is proportional to the blood volume inside the jugular vein, and the amplitude of the received signal from the photodetector (e.g. the current/voltage signal) is inversely proportional to the blood volume, the central venous pressure waveform is constructed by an algorithm that inverts the signal received by the photodetector as follows:

$P(t) \sim 1/S(t)$

where P is the pressure waveform and S is the signal from photodetector (e.g. the current/voltage signal).

[0041]The absorbance values collected at regular user-determined intervals, for example, 10 data points/mm, are stored as a spreadsheet associated with a cardiac parameter or cardiac output. The display unit 44 functions in real-time to display the selected blood vessel waveform according to an executed algorithm (via the algorithm processing module 41) against time which can be used as described below to calculate, for example, a cardiac parameter or cardiac output.

[0042]A sample display of a waveform (e.g. generated based on a signal obtained by the photodetector and processed by a signal processing device 40) obtained using the present device is shown in Fig. 4. As can be seen, there is a time course variation in the signal detected by the photodetector 30 that results from a selected blood vessel pulse, changes in the blood volume and content (such as oxygen saturation) inside the blood vessel. The blood volume and content in the selected blood vessel affects the absorption of light, thereby resulting in a signal with varying amplitude. For example, as the jugular vein pulse increases and decreases the blood volume in the jugular vein, the amplitude of the detected optical signal (e.g. as received by photodetector 30) will

decrease and increase, respectively. The time course plot of the amplitude of the recorded signal reflects the waveform of the jugular vein pulse.

[0043]In another embodiment of the present invention, a device 100, operable to measure blood content, such as the blood oxygen saturation of central venous blood, is provided. As the jugular vein, especially the right internal jugular vein, is directly connected to the superior vena cava as shown in Fig. 1, the jugular vein waveform is representative of the parameters of central venous blood.

[0044]For this utility, the device 100, as shown in Figs. 7 and 8, comprises at least two light sources 120, each emitting light of a different wavelength within the range of 400nm to 1000nm. The device also comprises a photodetector 130 for each light source 120 adapted to receive the transmitted or reflected light at a given wavelength. As set out above, each light transmitting component (e.g. light source 120 or transmitting optical fibres 124) and light receiving component (e.g. photodetector 130 or receiving optical fibres 126) is set in a patch probe 128, and may be arranged as shown in Fig. 7A or 7B; however, as one of skill in the art will appreciate, alternative arrangements of the light-transmitting components and light-receiving components exist which will not affect the function of the device 100. For example, the device 100 may comprise multiple patches probes 128, each of which includes a light-transmitting component and a light-receiving component. Alternatively, the device 100 may comprise a single patch 128 including multiple light-transmitting components and light-receiving components. In another alternative, the device 100 may comprise a first patch 128 with one or more light-transmitting components and light- receiving components, and a second patch with one or more light-transmitting components and corresponding light-receiving components. As set out above, regardless of the number of patches and arrangements thereof, the device may be incorporated within a system as described above comprising a signal receiving device 140 and to translate the output of the photodetector 130 into, for example, a desirable form.

[0045]The time course variation in the detected signal associated with a cardiac vessel pulse at different wavelengths may be used to calculate the blood content, such as blood oxygen saturation, and other parameters associated with the cardiac vessel pulse. There are various ways to calculate blood oxygen saturation as a function of

variations in the detected signal caused by cardiac vessel pulse at multiple light wavelengths, e.g. at 780 nm and 850 nm. As one of skill in the art will appreciate, the selected wavelengths for use in blood content determination will vary with the blood parameter being determined. For example, wavelengths of 690nm and 830nm, may be used to obtain deoxygenated haemoglobin and oxygenated haemoglobin content, respectively. A wavelength of 950nm may be used to obtain water content of blood. Moreover, the blood parameter of interest may be determined through photon diffusion equations, photon transportation equations or Modified Beer Lambert's Law as will be described.

Modified Beer Lambert's Law

[0046] The detected signal (e.g. current) may be expressed as:

$$I_{\lambda_1} = I_{0,\lambda_1} e^{-B[\varepsilon_{Hb,\lambda_1}\cdot(C_{Hb}+\Delta C_{Hb})+\varepsilon_{HbO,\lambda_1}\cdot(C_{HbO}+\Delta C_{HbO})]L+A} \quad (1)$$

where:

I_{λ_1} is the signal provided by the photodetector at wavelength λ_1,

I_{0,λ_1} is the signal from the light source at wavelength, λ_1,

C_{Hb}, C_{HbO} are the concentrations of deoxygenated and oxygenated hemoglobin of steady tissue medium blood;

$\Delta C_{Hb}, \Delta C_{HbO}$ are the changes in the concentrations of deoxygenated and oxygenated hemoglobin caused by the jugular vein pulse;

$\varepsilon_{Hb,\lambda_1}, \varepsilon_{HbO,\lambda_1}$ are the absorption properties of deoxygenated and oxygenated hemoglobin at wavelength λ_1 for the purposes of calculating blood oxygen

saturation. Blood saturation of other chromophores can also be calculated by substituting into the equation the appropriate extinction coefficients (ε) for the selected chromophore including, for example, water, cytochromes such as cytochrome oxides, and cholesterol; and

A. B are constants determined by boundary conditions.

[0047]The relative change in signal from the signal emitted from the light source to the signal detected by the photodetector which is caused by the jugular vein pulse is represented for a first wavelength by:

$$\Delta I_{\lambda_1} = e^{-B[\varepsilon_{Hb,\lambda_1}\cdot(\Delta C_{Hb})+\varepsilon_{HbO,\lambda_1}\cdot(\Delta C_{HbO})]L} \quad (2);$$

or as

$$OD_{\lambda_1} = \ln(\Delta I_{\lambda_1}) = -B(\varepsilon_{Hb,\lambda_1}\cdot\Delta C_{Hb} + \varepsilon_{HbO,\lambda_1}\cdot\Delta C_{HbO}) \quad (3).$$

[0048]Similarly, the change in signal between emitted and detected signal for a second light wavelength is represented by:

$$OD_{\lambda_2} = \ln(\Delta I_{\lambda_2}) = -B(\varepsilon_{Hb,\lambda_2}\cdot\Delta C_{Hb} + \varepsilon_{HbO,\lambda_2}\cdot\Delta C_{HbO}) \quad (4).$$

[0049]Blood oxygenation derived from jugular vein pulse is then determined using the following equation:

$$S_{jv}O_2 = \frac{\Delta C_{HbO}}{\Delta C_{Hb} + \Delta C_{HbO}} = \frac{\varepsilon_{Hb,\lambda_1}\cdot OD_{\lambda_2} - \varepsilon_{Hb,\lambda_2}\cdot OD_{\lambda_1}}{(\varepsilon_{Hb,\lambda_1} - \varepsilon_{HbO,\lambda_1})\cdot OD_{\lambda_2} - (\varepsilon_{Hb,\lambda_2} - \varepsilon_{HbO,\lambda_2})\cdot OD_{\lambda_1}} \quad (5).$$

[0050]In use, the patch probe 28 of device 10 comprising light source(s) 20 and photodetector(s) 30 is generally placed on the neck of the patient at a site near a

selected blood vessel, for example, the internal jugular vein. It is desirable for the patient to be lying down at about a 30 degree incline from the horizontal. The patient maintains regular breathing during the process of measuring the pulse of the blood vessel. Light from the light source 20 is either reflected off of, or transmitted through, the target site on the patient's neck, and detected by the photodetector 30. The photodetector 30 translates the detected light into an output signal (e.g. current/voltage) that may be digitized for expression as amplitude as a function of time to result in a waveform of the selected blood vessel pulse. The amplitude of signals obtained using different wavelengths may be used according to Lambert's law as above to determine blood oxygenation.

[0051] In another embodiment, illustrated in Fig. 9 (A-C) , a device 200 is provided comprising one or more light sources 220, each emitting selected wavelengths of light in the 400nm to 1000nm range. Each light source 220 is coupled with at least two photodetectors 230 each adapted to receive light emitted at a given frequency. As discussed above, the device 200 may optionally be incorporated within a system as illustrated in Fig. 5, for example.

[0052]The device 200 is useful to simultaneously measure multiple cardiac blood vessel pulses, such as jugular venous pulse as well as carotid arterial pulse, thereby generating a dual waveform as illustrated in Fig.10, and thus, has utility to simultaneously measure arterial blood oxygenation, S_aO_2, in addition to central venous oxygenation, $S_{jv}O_2$, as described above. As one of skill in the art will appreciate, in the case of multiple light sources 220, each light source is turned on in sequence, and the amplitude of light emitted from the light source(s) is modulated at a selected frequency, such as 10 kHz or 20kHz. Alternatively, light emitted by a single light source 220 can be sequentially modulated at two alternating frequencies, such as 10 kHz and 20 kHz . The output from the photodetectors (e.g. current/voltage) is filtered at a frequency selected to correlate with a given frequency emitted from a light source, for example, using a band pass filter which allows a selected frequency, such as a 10kHz or 20kHz signal, to pass through but blocks other frequency components in the signal.

[0053]In another embodiment, cardiac output may be measured or monitored. As the jugular vein pulse represents central venous blood and correlates well with mixed

venous blood, the trend of cardiac output can be calculated through Fick's Law as follows:

$$COI = \frac{OCR}{S_aO_2 - S_vO_2} \qquad (6)$$

where COI is the cardiac output index which is the cardiac output (CO) per unit body surface;

OCR is the oxygen consumption rate which is oxygen consumption (OC) per unit body surface;

S_aO_2 is the arterial blood oxygen saturation; and

$S_{jv}O_2$ is the venous blood oxygen saturation.

S_aO_2 and $S_{jv}O_2$ may be determined as outlined above using a device in accordance with the invention.

The following equation depicts cardiac output (CO) as a whole rather than per unit body surface:

Or:
$$CO = \frac{OC}{S_aO_2 - S_{jv}O_2} \qquad (7)$$

[0054]As the oxygen consumption or oxygen consumption rate are constant during many clinical procedures, the trend of cardiac output index or cardiac output can be reliably monitored.

[0055]In another embodiment, a method of measuring central venous pressure is provided. Central venous pressure is the pressure at the vena cava close to the right atrium. Abnormally high central venous pressure is an early indication of right atrial heart failure. Currently, central venous pressure is measured through invasive catheters which are inserted through the internal jugular vein to the vena cava.

[0056]A method for measuring central venous blood pressure in a patient is provided that is based on the fact that the length of blood filled inside a jugular vein directly

reflects the central venous pressure. A determination of the highest position along the jugular vein where there is a pressure wave provides information that may be used to calculate venous blood pressure. Thus, the method comprises the step of determining the highest position along the jugular vein to yield a waveform. The "highest position" is measured from the sternal angle. The sternal angle is the angle formed by the junction of the manubrium and the body of the sternum in the form of a secondary cartilaginous joint (symphysis). This is also called the manubriosternal joint or Angle of Louis.

[0057]A waveform is obtained by directing a beam of light having a wavelength in the range of 400 nm to 1000 nm at an external tissue site on the patient that is in the proximity of the jugular vein, detecting light reflected from the tissue site or transmitted through the tissue site and translating the detected light into an output signal against time to generate a waveform. The highest position along the jugular vein to yield a waveform is determined when the next highest position does not yield a waveform.

[0058]The mean central venous pressure (P) is calculated as follows:

$$P = (d + 5) \cdot \sin 9$$

wherein d is the distance from the sternal angle to the highest position that yields a waveform. The addition of 5 to d represents the distance from the sternal angle to the right atrium. The symbol, 9, is the inclined angle of the upper body relative to the horizontal position.

[0059]Having obtained a waveform from a cardiac vein, the central blood pressure may be calculated as follows:

$$P = a + b\frac{T}{t}$$

wherein **a** is a constant that relates to the position of the sensor on the neck, and **b** is a constant which relates to the distance between the source and the photodetector of the sensor; and

T is the pulse width and t is the average rise and fall time of the pulse.

[0060]In accordance with the method of measuring central venous pressure, a device 300 is provided. The device 300, as shown in Fig. 13, includes a series of light sources 320 located adjacent to one another along a length appropriate to measure the blood level in a cardiac vein, such as the internal or external jugular vein. The length will generally be about 1.5 to 10 cm. Each light source 320 emits light at a wavelength of from 600 nm to 900 nm and is associated with a corresponding photodetector 330 suitable to detect reflected or transmitted light from its corresponding light source 320. The device 300 additionally includes a patch probe 328 that functions as the interface between the light sources (320) and photodetectors (330) and is adapted for placement on a patient at a site in the vicinity of a selected cardiac blood vessel, such as a cardiac vein. The probe 328 may incorporate the light sources 320 and photodetectors 330 directly, or may instead incorporate light transmitting optical fibres and light receiving optical fibres connected to the light sources and photodetectors, respectively, or may include a combination of these, e.g. light sources and light receiving optical fibres, or light-transmitting optical fibres and photodetectors. In addition, the device 300 may be incorporated within a system as previously described including a signal-processing device to translate the output of the photodetectors into a desirable form.

[0061]In use, the device 300 is placed on the patient at an appropriate site in which a terminal light source in the series is lined up with the sternal angle. The light from each light source is detected by its corresponding photodetector. The signal (e.g. current/voltage) of each photodetector is monitored (or transmitted to a signal processing device for translation to an alternate form of output such as a visual waveform output which is monitored) to determine whether there is an output or not. The highest position (d) along the vein to yield an output, e.g. a waveform, is then determined based on the output from each photodetector in the sequence. The mean central venous pressure (P) may then be calculated as described above.

[0062]Figure 14 illustrates other embodiments of the device 300 that may also be useful to measure central venous pressure as described above. Each embodiment includes a different configuration of the light source(s) and photodetectors. For example, Fig. 14A illustrates a device including a single light source and an array of adajacent photodetectors that may be used to obtain an output, e.g. a waveform,

sequentially along a vein to determine the highest position (d). Fig. 14B illustrates a device including sequential source-detector pairs in an alternating configuration (source-detector, source-detector, etc.) for placement along a vein as shown . Fig. 14C illustrates a device similar to that of Fig. 14B including multiple rows of alternating source-detector pairs. As one of skill in the art will appreciate, a device as shown in Fig. 1 may also be used to determine the highest position (d) along the vein to yield an output signal (e.g. a waveform) by obtaining waveform readings sequentially from the sternal angle upward along the vein. Further, as previously described, the device, regardless of its configuration may be incorporated within a system comprising a signal-processing device in order to translate the output of the photodetector into a visual output such as a pressure waveform.

[0063]The central venous pressure may also be determined utilizing pressure detection e.g. determination of a pressure waveform, as described above and an externally applied pressure. In this case, a pressure waveform is obtained, as described, and monitored via a display unit 44. An external pressure is then applied to the selected venous vessel from the skin surface while monitoring the pressure waveform (representative of baseline pressure). The externally applied pressure is increased until the pressure waveform disappears as determined by monitoring the display unit. The central venous pressure P_c is then determined as follows:

$$P_c = P_{ef} - P_{ei}$$

wherein $p_{ef,}$ is the value of the externally applied pressure at which the pressure waveform disappears and $p_{ei,}$ is the value of pressure at which the pressure waveform starts to change (or the amplitude of the waveform starts to decrease).

[0064]A device comprising two light source-detector pairs, or two patches each comprising a light source-detector pair may be used in accordance with the foregoing method.

[0065]Central venous blood flow velocity may also be measured using a device in accordance with the present invention. By measuring the rise or fall time of a

pressure waveform (t), or the mean of the rise and fall time, the central venous blood flow can be calculated as follows:

$$v = \frac{d}{t}$$

wherein d is the spacing between the source and photodetector; and
t is the rise time of the pressure waveform (from the bottom to the peak).

[0066]The blood flow may be estimated according to:

F= v x S

wherein S is the cross-sectional area of the blood vessel, which can be obtained through ultrasound imaging, and velocity (v) is determined as indicated above.

[0067]In a further embodiment of the present invention, a device corresponding to the device of Fig. 1 is provided which is adapted to generate an output from a cardiac vein remotely. Accordingly, the device comprises a remote light source capable of delivering a light beam to a desired site on a patient, e.g. a site on the neck of the patient in close proximity to a cardiac vessel; and a remote photodetector, such as a CCD camera adapted to receive light from the source which is reflected off of the patient at the desired site. As described, the photodetector generates an output signal (e.g. current/voltage) that may be processed by a signal-processing device to generate a visual output (e.g. waveform) for display on a display unit.

[0068]Embodiments of the present invention are described by reference to the following specific examples which are not to be construed as limiting.

Example 1 – Measurement of venous pulse in a patient

The venous pulse of a human subject was obtained using a device as shown in Fig. 1. The patient lay on a chair at about a 30 degree recline. The sensor patch of the device was placed on the neck of the patient at a site over the internal jugular vein. While the subject maintained normal breathing, venous pulse was measured and recorded.

Fig. 12 illustrates the waveform recorded. The amplitude of the detected signal is represented along the y-axis while the x-axis represents time.

Example 2 – Measurement of central venous pressure in a patient

The central venous pressure of a human subject was obtained using a device as shown in Fig. 13. The sensor patch of the device was placed on the neck of the patient at a site over the internal jugular vein such that the terminal source/detector of the device was at the sternal angle of the subject. While the subject maintained normal breathing, venous pressure was measured and recorded as a function of body position when the patient was lying flat (0 degree incline, e.g. horizontal), at a partial rise (45 degree incline from the horizontal) and sitting upright (90 degree incline from the horizontal) as shown in Fig. 15A. The measured pressure as depicted by the waveform illustrated in Fig. 15B is consistent with the expected central venous pressure in a healthy subject which decreases as body position rises from the horizontal position.

References

1. Naveen Greg et al, "Jugular Venous Pulse: An Appraisal", Journal, Indian Academy of Clinical Medicine, Vol 1, No. 3, Oct. – Dec.,2000

2. Reference:O'Rourke,R.A.and Others,General Examination of the Patient,Hurst's, The Heart,Eighth Edition,Pp.238-242

3. http://depts.washington.edu/physdx/neck/tech2.html

4. Conway "Clinical assessment of cardiac output", Eur. Heart J. 11, 148 – 150 (1990).

5. "Advances in non-invasive cardiac output monitoring", Annals of Cardiac Anaesthesia, 2002, volume 5, p 141 – 148.

6. "Thermodilution method for measuring cardiac output", Europ. Heart J. 11(Suppl 1), 17 – 20, 1990.

7. "The dye dilution method for measurement of cardiac output", Europ. Heart J. 11 (Suppl 1), 6 – 12 (1990))

8. de Leeuw and Birkenhager ("Some comments of the usefulness of measuring cardiac output by dye dilution", Europ. Heart J. 11 (Suppl 1), 13 – 16 (1990)).

9. "Continuous measurement of cardiac output by the Fick principle: Clinical validation in intensive care", Crit Care Med 20(3), 360 – 365 (1992)

10. Doi et al., "Frequently repeated Fick cardiac output measurements during anesthesia", J. Clin. Monit. 6, 107 – 112 (1990).

11. "Measurement of cardiac output before and after cardiopulmonary bypass: Comparison among aortic transit-time ultrasound, thermodilution, and noninvasive partial CO2 rebreathing", J. Cardiothoracic. Vasc. Anesth. 18(5) 563 – 572 (2004).

12. Nielsson et al. al "Lack of agreement between thermodilution and CO2-rebreathing cardiac output" Acta Anaesthesiol Scand 2001; 45:680.

13. Schmidlin et al, "Transoesophageal echocardiography in cardiac and vascular surgery: implications and observer variability", Brit. J. Anaesth. 86(4), 497 – 505 (2001).

14. Manning et al. "Validity and reliability of diastolic pulse contour analysis (Windkessel model) in humans", Hypertension. 2002 May; 39(5):963-8.

15. "Pulse contour analysis versus thermodilution in cardiac surgery", Acta Anaesthesiol Scand 2002; 46:424, Linton et al.

16. "Estimation of changes in cardiac output from arterial blood pressure waveform in the upper limb", Br J Anaesth 2001; 86:486 and Jansen et al.

17. "A comparison of cardiac output derived from the arterial pressure wave against thermodilution in cardiac surgery patients" Br J Anaesth 2001; 87:212.

18. Jansen et al. "An adequate strategy for the thermodilution technique in patients during mechanical ventilation", Intensive Care Med 1990; 16:422.

CLAIMS

We Claim:

1. A device for non-invasively measuring at least one parameter of a cardiac blood vessel in a patient comprising:

at least one light source that emits light in the 400 nm to 1000 nm wavelength range;

at least one photodetector adapted to receive light emitted by the light source and generate an output based on the received light, wherein said light is reflected from or transmitted through tissue of the patient, the output of said photodetector being correlated with a parameter of the blood vessel; and

at least one probe for facilitating delivery of light from the light source to an external tissue site on the patient in the proximity of the cardiac blood vessel and receipt of light by the photodetector.

2. A device as defined in claim 1, additionally comprising a signal-processing device in communication with the photodetector, said signal-processing device adapted to translate light received from the photodetector into a visual output.

3. A device as defined in claim 2, wherein said visual output is a time-varying waveform.

4. A device as defined in claim 1, adapted to emit and receive light of at least two different wavelengths in the 400nm to 1000nm wavelength range.

5. A device as defined in claim 1, comprising at least two photodetectors, each of said photodetectors adapted to receive light at a distinct wavelength.

6. A device as defined in claim 1, wherein said light source and said photodetector are embedded in said probe.

7. A device as defined in claim 1, wherein transmitting optical fibres transmit light from said light source to said probe.

8. A device as defined in claim 1, wherein receiving optical fibres receive reflected light from said probe.

9. A device as defined in claim 1, comprising a plurality of light sources and a plurality of-photodetectors, wherein each light source emits light that is received by a corresponding photodetector.

10. A device as defined in claim 4, wherein said light source is adapted to emit light at more than one wavelength.

11. A device as defined in claim 4, comprising at least a first and second light source each of which emit light at a different wavelength, and at least a first and second photodetector, wherein said first photodetector is adapted to receive light from said first light source and said second photodetector is adapted to receive light from said second light source.

12. A device as defined in claim 1, comprising a plurality of probes, wherein each probe comprises at least one light source and at least one photodetector.

13. A device useful to monitor a parameter of a cardiac blood vessel in a patient comprising:

at least one light-emitting component adapted to emit light in the 400 nm to 1000 nm wavelength range;

at least one light-receiving component adapted to receive light emitted by the light-emitting component and translate said light into a recordable output, wherein said light is reflected from or transmitted through tissue of the patient; and

at least one probe which facilitates delivery of light from the light-emitting component to an external tissue site on the patient in the proximity of a cardiac blood vessel and receipt of light reflected from or transmitted through said patient site by the light-receiving component.

14. A device as defined in claim 13, wherein the output from said light-receiving component is current.

15. A device as defined in claim 13, wherein said light-emitting component is a light source that is set in the probe.

16. A device as defined in claim 13, wherein said light-receiving component is a photodetector that is set in the probe.

17. A device as defined in claim 13, wherein said light-emitting component comprises a light source and light-transmitting optical fibres, wherein said fibres are set in the probe.

18. A device as defined in claim 13, wherein said light-receiving component comprises a photodetector and light-receiving optical fibres, wherein said fibres are set in the probe.

19. A system useful to monitor a parameter of a cardiac blood vessel in a patient comprising:

at least one light-emitting component adapted to emit light in the 400 nm to 1000 nm wavelength range;

at least one light-receiving component adapted to receive light emitted by the light-emitting component and translate said light into a recordable output, wherein said light is reflected from or transmitted through tissue of the patient; and

at least one probe which facilitates delivery of light from the light-emitting component to an external tissue site on the patient in the proximity of a cardiac blood vessel and receipt of light reflected from or transmitted through said patient site by the light-receiving component; and

a signal-processing device adapted to translate the output from said light-receiving component to a visual form.

20. A system as define in claim 19, wherein said signal-processing device comprises a microprocessor and a display unit.

21. A method for determining a parameter of a cardiac blood vessel in a patient comprising the steps of:

directing a beam of light having a wavelength in the range of 400 nm to 1000 nm to an external tissue site on the patient that is in the proximity of the blood vessel;

detecting light reflected from the tissue site or transmitted through the tissue site;

translating the detected light into an output signal against time; and

calculating the parameter of the blood vessel using the output signal.

22. A method as defined in claim 21, wherein the parameter is selected from the group consisting of blood vessel pulse, blood vessel volume, blood vessel oxygenation, blood vessel flow, blood vessel pressure and blood vessel content.

23. A method as defined in claim 21, wherein the cardiac blood vessel is selected from the group consisting of the internal jugular vein, the external jugular vein and the carotid artery.

24. A method as defined in claim 21, wherein the output signal is current or voltage.

25. A method as defined in claim 21, wherein the output signal is translated into a time-varying visual output .

26. A method as defined in claim 25, wherein the time-varying visual output is a waveform.

27. A method as defined in claim 21, comprising directing more than one beam of light at the same or different tissue site on a patient, each beam having a different wavelength in the range of 400nm to 1000nm.

28. A method as defined in claim 27, wherein the parameter is blood content calculated according to modified Beer Lambert's law.

29. A method as define in claim 27, wherein the parameter is blood oxygenation calculated according to modified Beer Lambert's law.

30. A method as defined in claim 27, wherein the light of each wavelength is detected to generate an output signal for two different blood vessels.

31. A method for measuring the blood content of a chromophore in a patient comprising:

directing a light beam having at least first and second selected wavelengths at an external tissue site on the patient that is in the proximity of a cardiac blood vessel, wherein said selected wavelengths are based on the absorption characteristics of the chromophore;

detecting light reflected from the tissue or transmitted through the tissue at the selected wavelengths; and

translating the detected light into an output current in order to determine the blood content of said chromophore according to modified Beer Lambert's law.

32. A method of determining blood oxygenation of a cardiac vessel in a patient comprising:

directing a first light beam having a first wavelength of 780 nm and a second light beam having a second wavelength of 850 nm at an external tissue site on the patient that is in the proximity of a cardiac blood vessel;

detecting light reflected from the tissue or transmitted through the tissue at the first and second wavelengths; and

translating the detected light into an output current for the first and second wavelengths in order to calculate the blood oxygenation of the cardiac vessel according to modified Beer Lambert's law.

33. A method of determining cardiac output in a patient comprising;

calculating the blood oxygenation of the internal jugular vein as defined in claim 32;

calculating the blood oxygenation of the carotid artery as defined in claim 32; and

calculating the cardiac output according to Fick's law using the calculated blood oxygenation of the internal jugular vein blood and the carotid artery.

34. A method of determining central venous pressure in a patient comprising:

directing a beam of light having a wavelength in the range of 400 nm to 1000 nm at a series of external tissue sites on the patient along the jugular vein starting from the sternal angle;

detecting light reflected from the tissue site or transmitted through each tissue site;

translating the detected light into an output signal against time to determine the highest position along the vein to yield a signal (d); and

calculating the central venous pressure (P) according to the equation P = (d +5) sin 9, wherein 9 is the inclined body angle from horizontal of the patient.

AMENDED CLAIMS
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1. A system useful to monitor a parameter of a cardiac blood vessel **selected from the group consisting of the internal jugular vein, the external jugular vein, the carotid artery and the superior vena cava,** in a patient comprising:

at least one light-emitting component adapted to emit light in the 400 nm to 1000 nm wavelength range;

at least one light-receiving component adapted to receive light emitted by the light-emitting component and translate said light into a recordable output wherein said light is reflected from or transmitted through tissue of the patient; and

at least one probe which facilitates delivery of light from the light-emitting component to an external tissue site on the patient in the proximity of the cardiac blood vessel and receipt of light reflected from or transmitted through said patient site by the light-receiving component;

a signal-processing device **in communication with the light-receiving component** adapted to translate the output from said light-receiving component **to reflect variations in blood volume or blood flow in the selected cardiac blood vessel and calculate therefrom a jugular or a central venous parameter selected from the group of blood flow velocity, blood pressure, blood content and blood oxygenation.**

2. **A system as defined in claim 1, wherein the signal-processing device executes an algorithm that inverts the output from the light-receiving component in order to reflect variations in blood volume or blood flow in the selected cardiac blood vessel and thereby yield a pressure waveform.**

3. A system as defined in claim 3, wherein the light-emitting component comprises at least one light source and the light-receiving component comprises at least one photodetector.

4. A system as defined in claim 1, wherein said light source and said photodetector are embedded in said probe.

5. A system as defined in claim 1, adapted to emit and receive light of at least two different wavelengths in the 400nm to 1000nm wavelength range.

6. A system as defined in claim 1, comprising a plurality of light sources and a plurality of photodetectors, wherein each light source emits light that is received by a corresponding photodetector.

7. A system as defined in claim 3, wherein said light source is adapted to emit light at more than one wavelength.

8. A system as defined in claim 5, comprising at least a first and second light source each of which emit light at a different wavelength, and at least a first and second photodetector, wherein said first photodetector is adapted to receive light from said first light source and said second photodetector is adapted to receive light from said second light source.

9. A system as defined in claim 1, comprising a plurality of probes, wherein each probe comprises at least one light source and at least one photodetector.

10. A system as defined in claim 1, wherein said probe is compatible for placement on the skin of a patient.

11. A device as defined in claim 1, wherein said light-emitting component comprises a light source and light-transmitting optical fibres, wherein said fibres are set in the probe.

12. A device as defined in claim 1, wherein said light-receiving component comprises a photodetector and light-receiving optical fibres, wherein said fibres are set in the probe.

13. A system as defined in claim 1, wherein said signal-processing device comprises a microprocessor and a display unit.

14. A method for determining a parameter of a cardiac blood vessel, **selected from the group consisting of the internal jugular vein, the external jugular vein, the carotid artery and the superior vena cava,** in a patient comprising the steps of:

directing a beam of light having a wavelength in the range of 400 nm to 1000 nm to an external tissue site on the patient that is in the proximity of the selected blood vessel;

detecting light reflected from the tissue site or transmitted through the tissue site and translating the detected light into an output signal against time **to reflect variations in blood volume or blood flow in the selected cardiac blood vessel; and**

calculating a jugular or central venous parameter selected from the group of blood flow velocity, blood pressure, blood oxygenation and blood content, based on the output signal.

15. A method as defined in claim 14, wherein the output signal is current or voltage.

16. A method as defined in claim 14, wherein the output signal is translated into a time-varying visual output .

17. A method as defined in claim 16, wherein the time-varying visual output is a waveform.

18. A method as defined in claim 14, comprising directing more than one beam of light at the same or different tissue site on a patient, each beam having a different wavelength in the range of 400nm to 1000nm.

19. A method as defined in claim 18, wherein the light of each wavelength is detected to generate an output signal for two different blood vessels.

20. A method for measuring the blood content of a chromophore in a patient comprising:

directing a light beam having at least first and second selected wavelengths at an external tissue site on the patient that is in the proximity of a cardiac blood vessel **selected from the group consisting of the internal jugular vein, the external jugular vein, the carotid artery and the superior vena cava,**, wherein said selected wavelengths are based on the absorption characteristics of the chromophore;

detecting light reflected from the tissue or transmitted through the tissue at the selected wavelengths; and

translating the detected light into an output current in order to determine the blood content of said chromophore according to modified Beer Lambert's law.

21. A method of determining blood oxygenation of a cardiac vessel **selected from the group consisting of the internal jugular vein, the external jugular vein, the carotid artery and the superior vena cava** in a patient comprising:

directing a first light beam having a first wavelength of 780 nm and a second light beam having a second wavelength of 850 nm at an external tissue site on the patient that is in the proximity of the cardiac blood vessel;

detecting light reflected from the tissue or transmitted through the tissue at the first and second wavelengths; and

translating the detected light into an output current for the first and second wavelengths in order to calculate the blood oxygenation of the cardiac vessel according to modified Beer Lambert's law.

22. A method of determining cardiac output in a patient comprising;

calculating the blood oxygenation of the internal jugular vein as defined in claim 21;

calculating the blood oxygenation of the carotid artery as defined in claim 21; and

calculating the cardiac output according to Fick's law using the calculated blood oxygenation of the internal jugular vein blood and the carotid artery.

23. A method of determining central venous pressure in a patient comprising:

directing a beam of light having a wavelength in the range of 400 nm to 1000 nm at a series of external tissue sites on the patient along the jugular vein starting from the sternal angle;

detecting light reflected from the tissue site or transmitted through each tissue site;

translating the detected light into an output signal against time to determine the highest position along the vein to yield a signal (d); and

calculating the central venous pressure (P) according to the equation $P = 5+d^* \sin 9$, wherein 9 is the inclined body angle from horizontal of the patient.

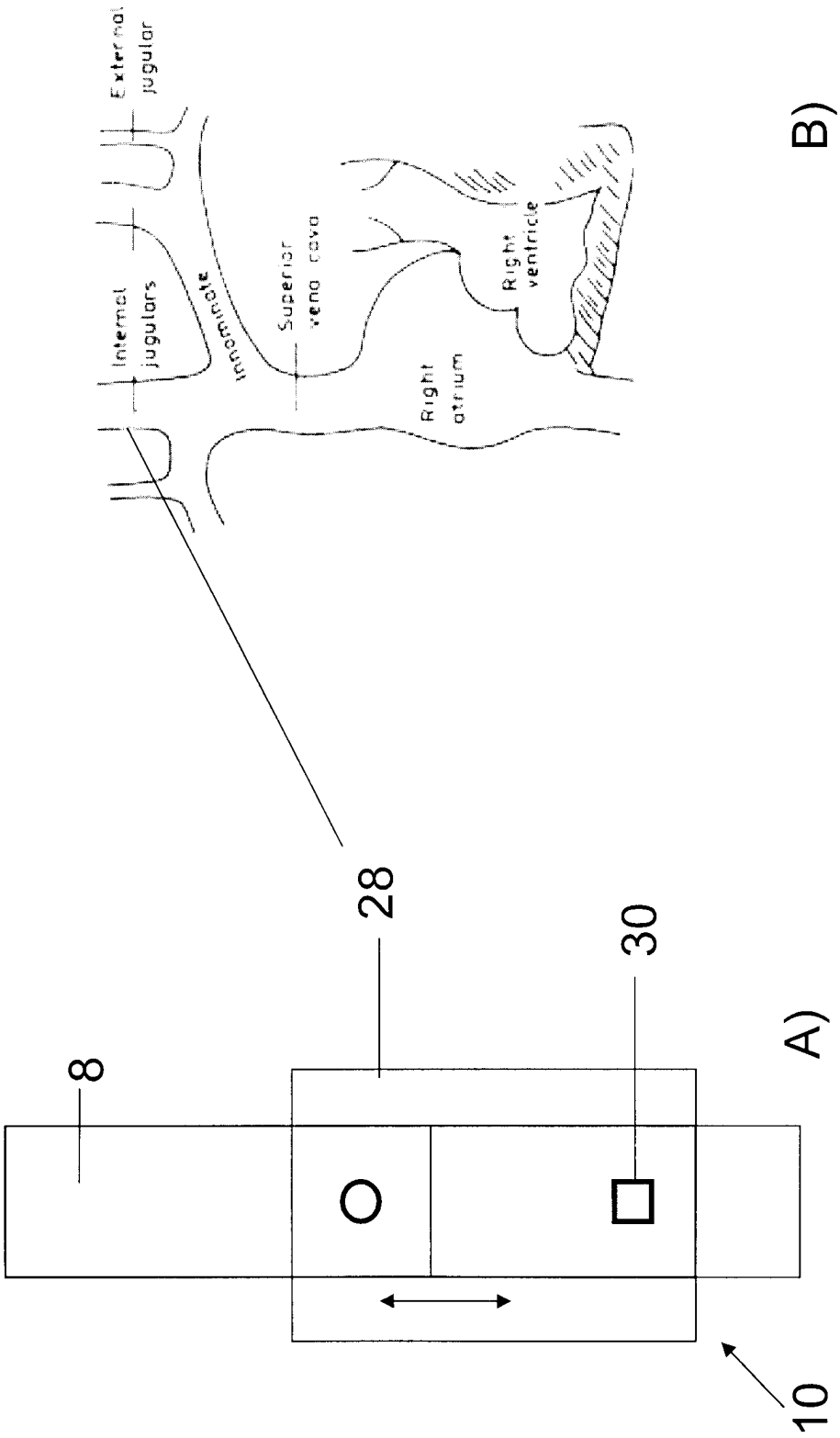

External jugular
Internal jugulars
Innominate
Superior vena cava
Right atrium
Right ventricle
B)
28
30
8
A)
10

Figure 1

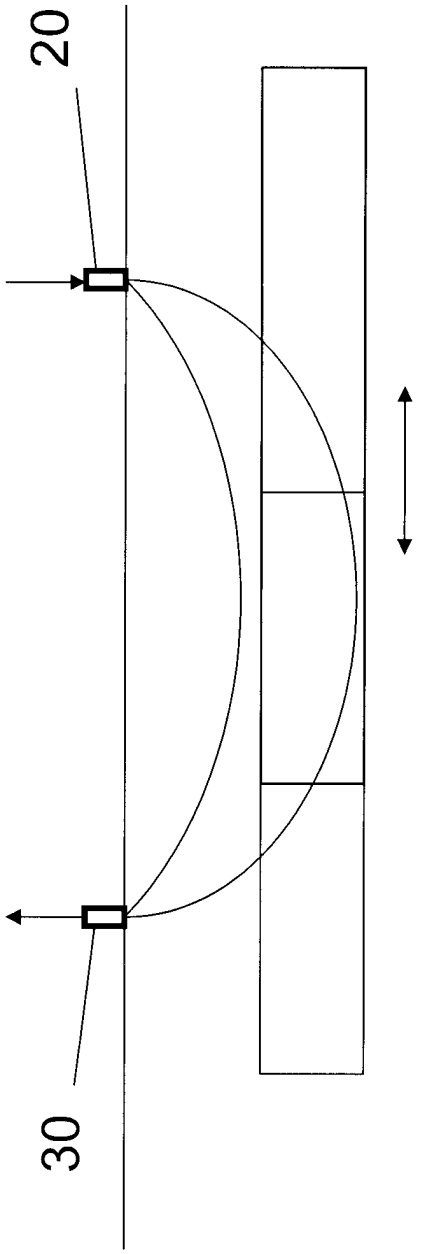


Figure 2

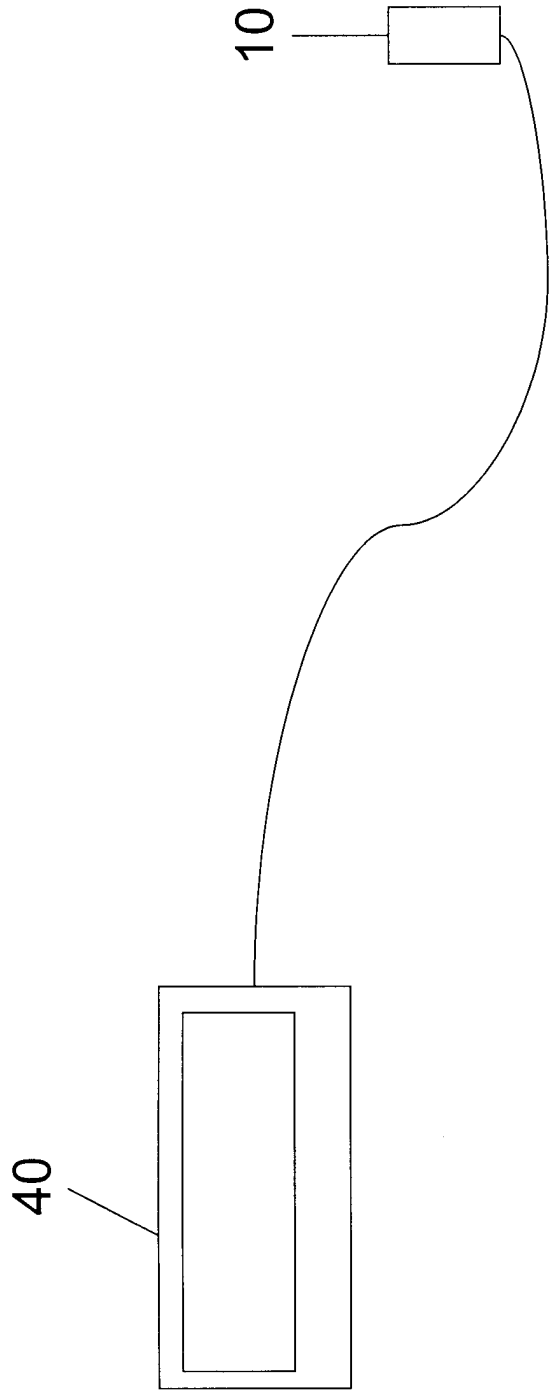


Figure 3

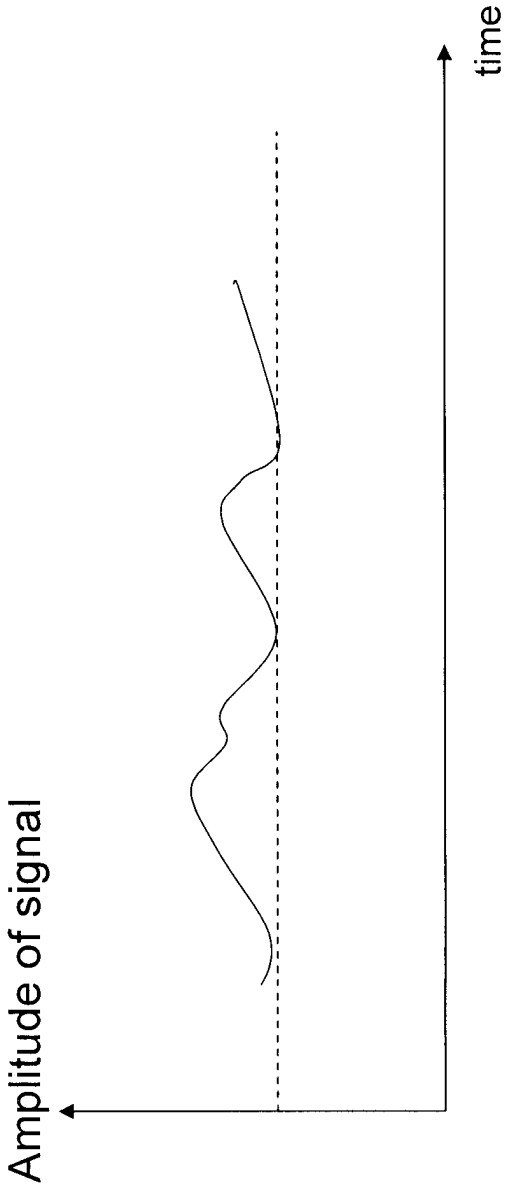


Figure 4

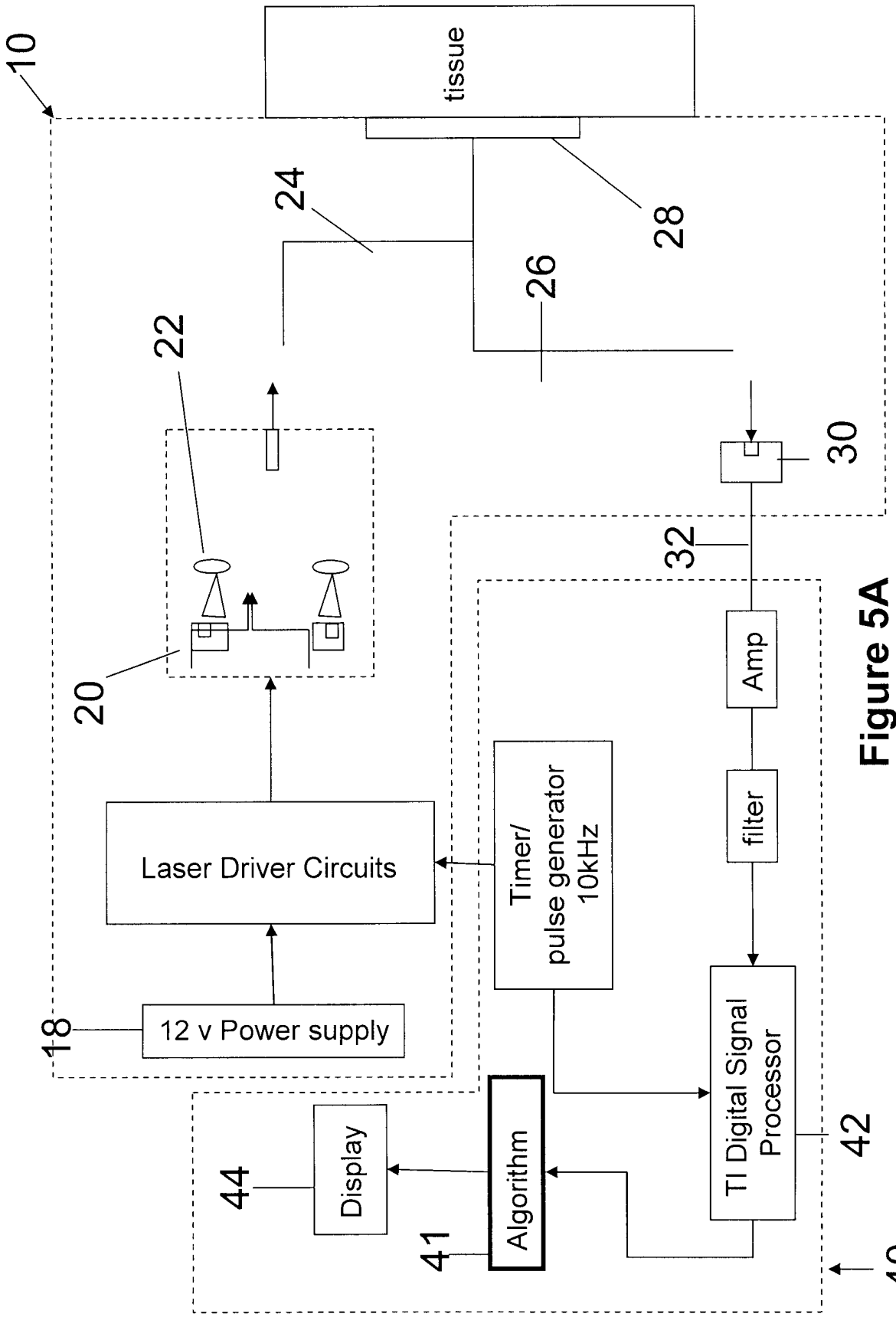

10
tissue
24
28
26
22
30
32
Amp
filter
20
Laser Driver Circuits
Timer/
pulse generator
10kHz
18
12 v Power supply
TI Digital Signal
Processor
42
Display
44
Algorithm
41
40

Figure 5A

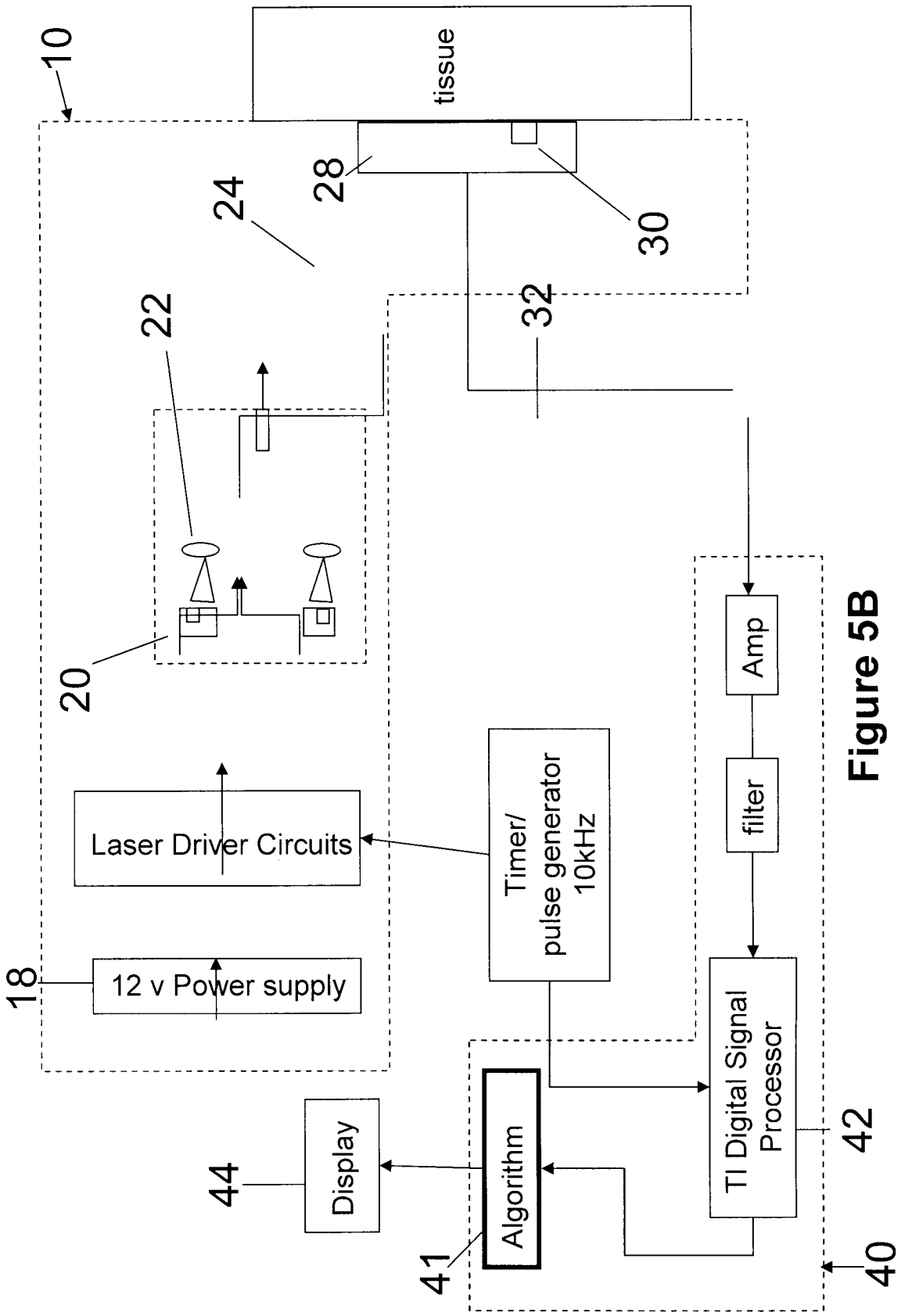

10
tissue
28
30
24
32
22
20
Amp
filter
Timer/
pulse generator
10kHz
Laser Driver Circuits
18
12 v Power supply
TI Digital Signal
Processor
42
Algorithm
41
Display
44
40

Figure 5B

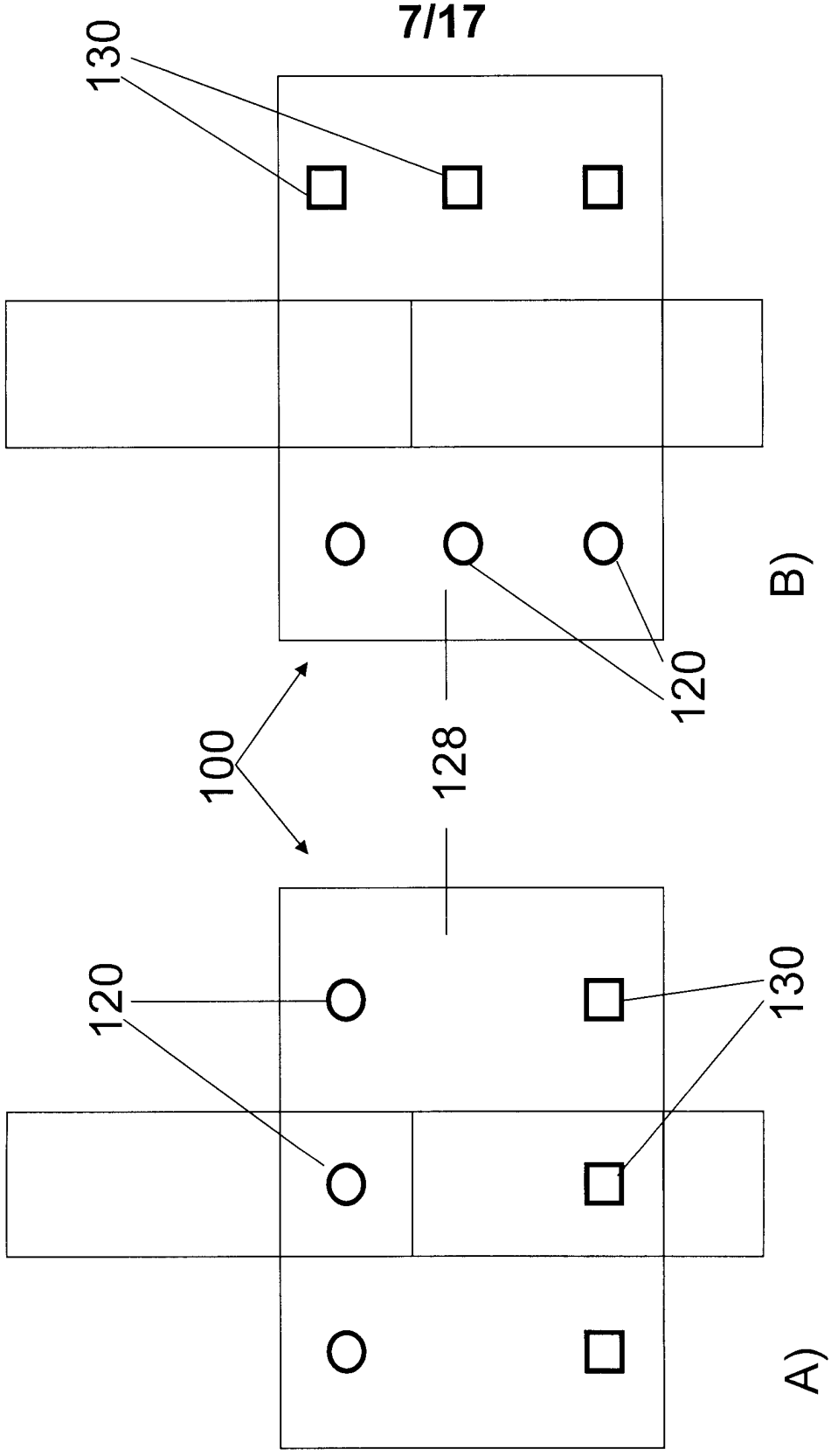


Figure 7

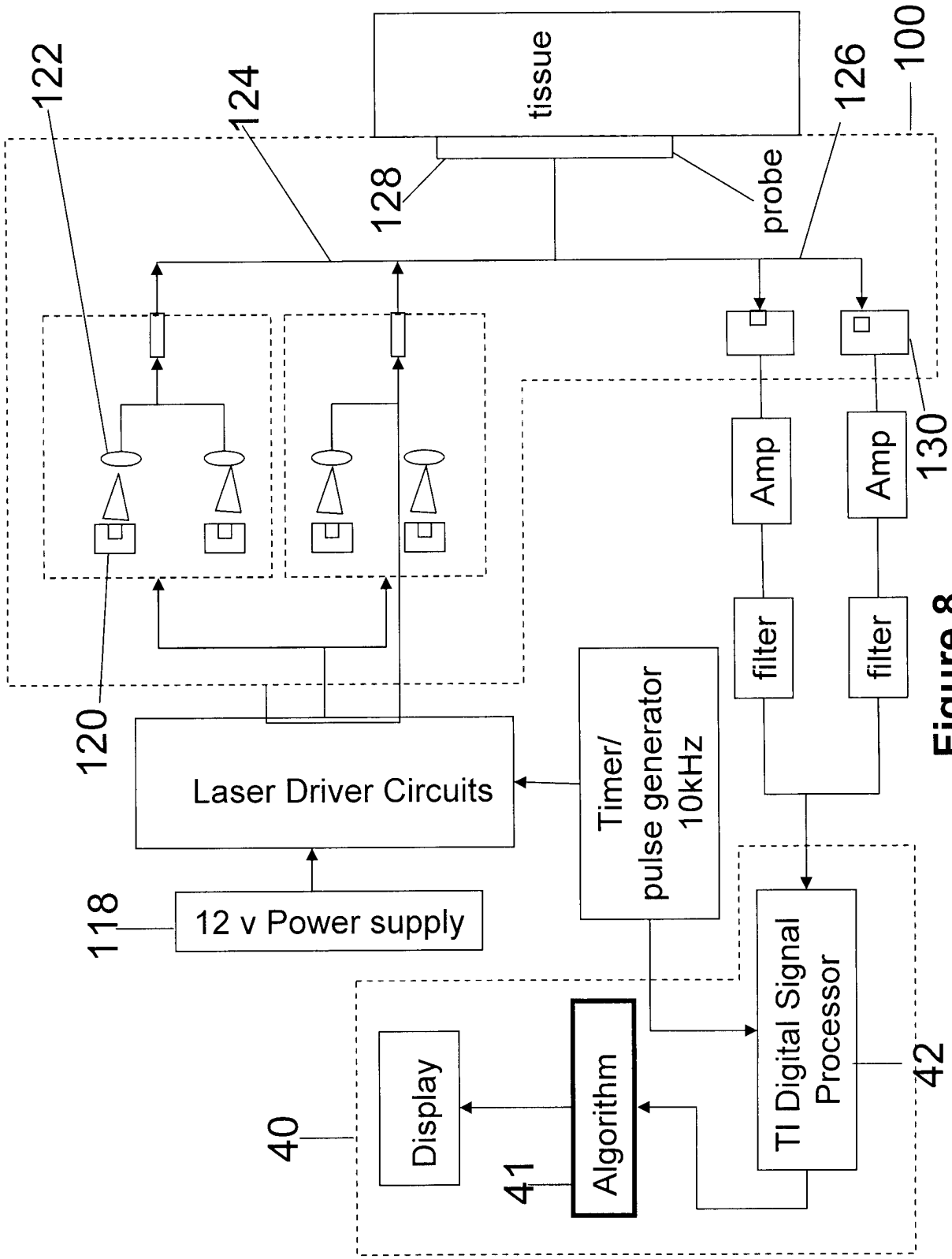
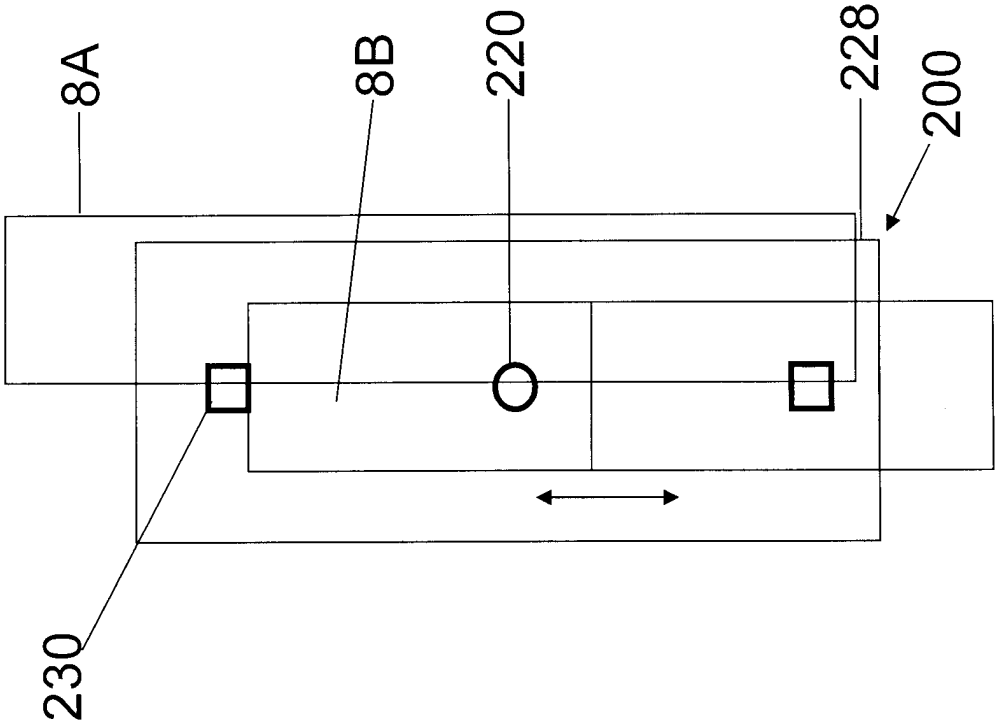

tissue
probe
100
122
124
126
128
130
Amp
Amp
filter
filter
120
Laser Driver Circuits
Timer/
pulse generator
10kHz
118
12 v Power supply
TI Digital Signal
Processor
42
Display
Algorithm
40
41

Figure 8



A)

Figure 9

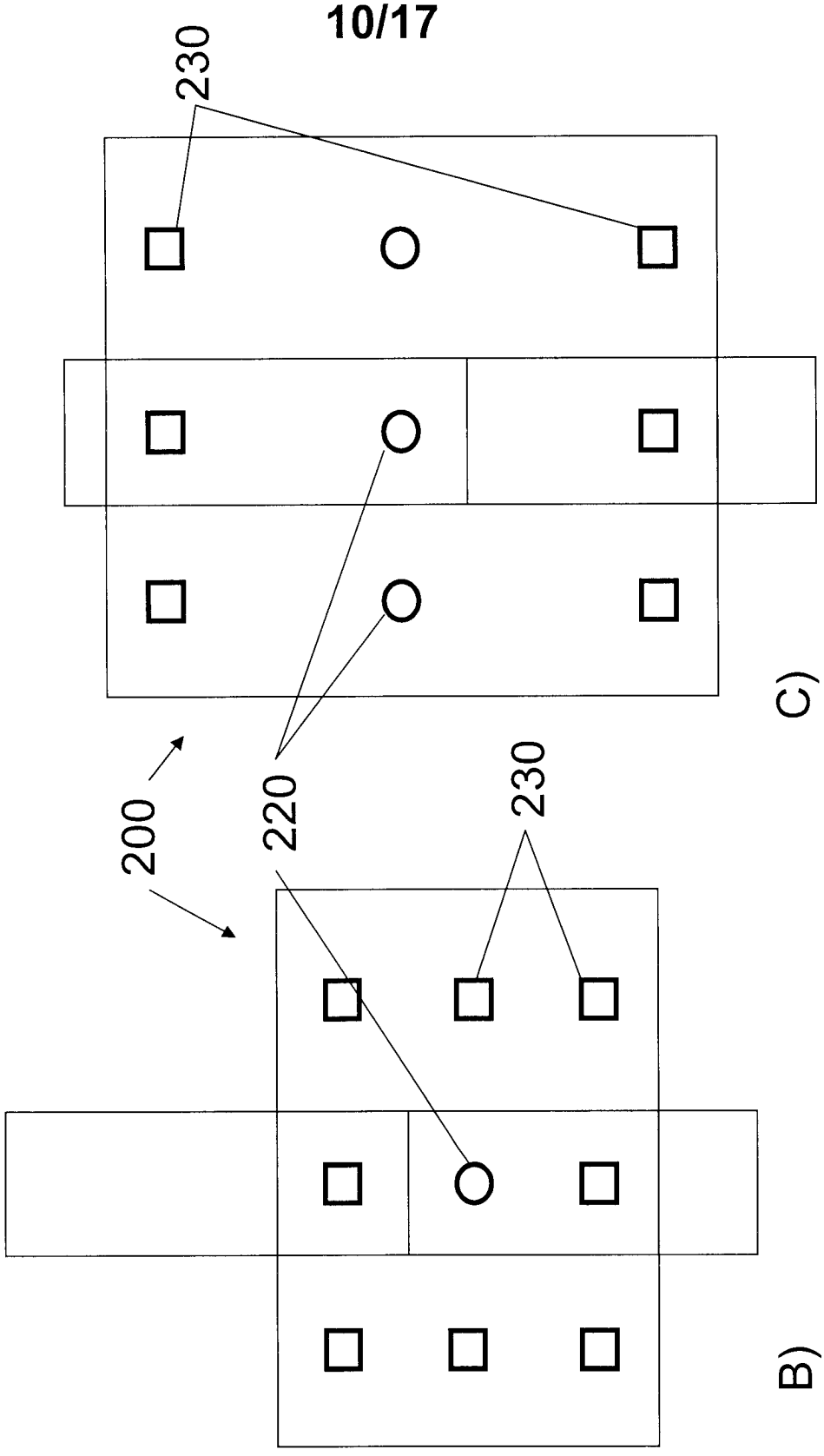


Figure 9

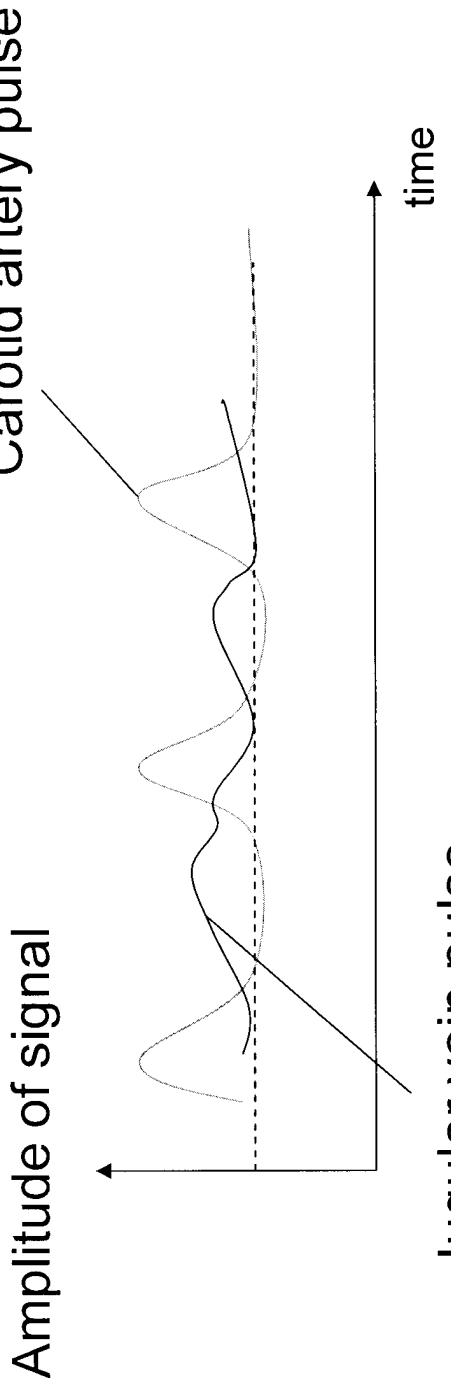

Carotid artery pulse
time
Amplitude of signal
Jugular vein pulse

Figure 10

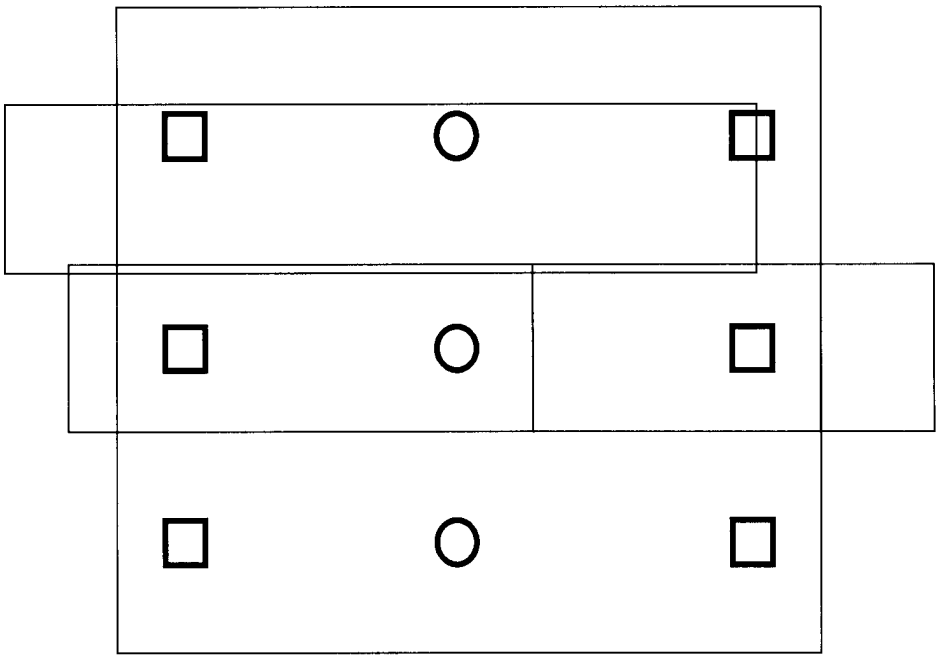


Figure 11

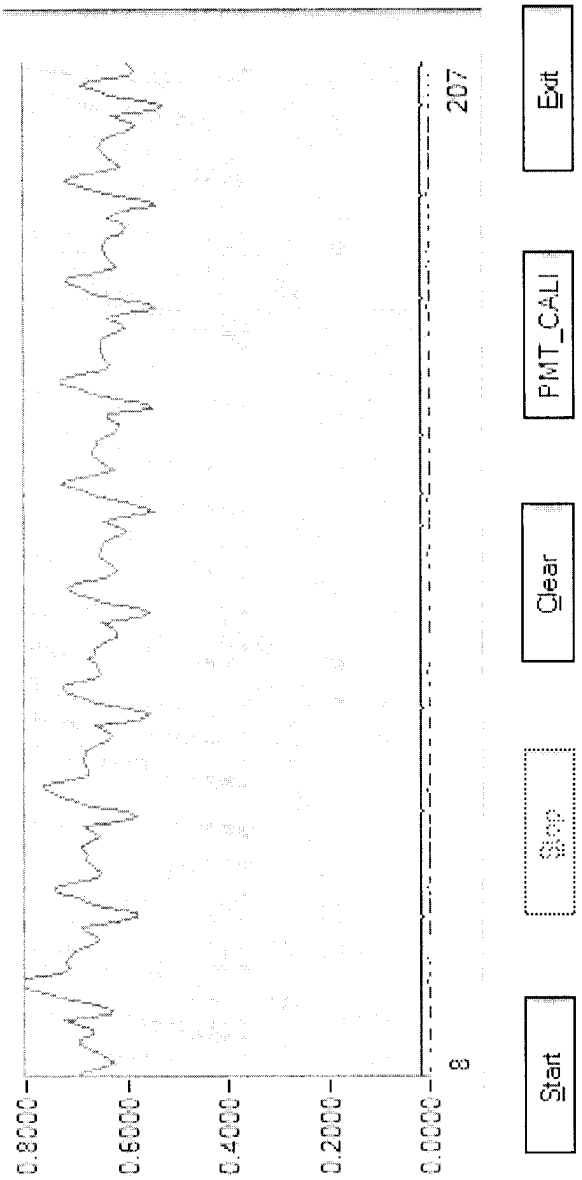

0.8000
0.6000
0.4000
0.2000
0.0000
0
207
Start
Stop
Clear
PMT_CALI
Exit

Figure 12

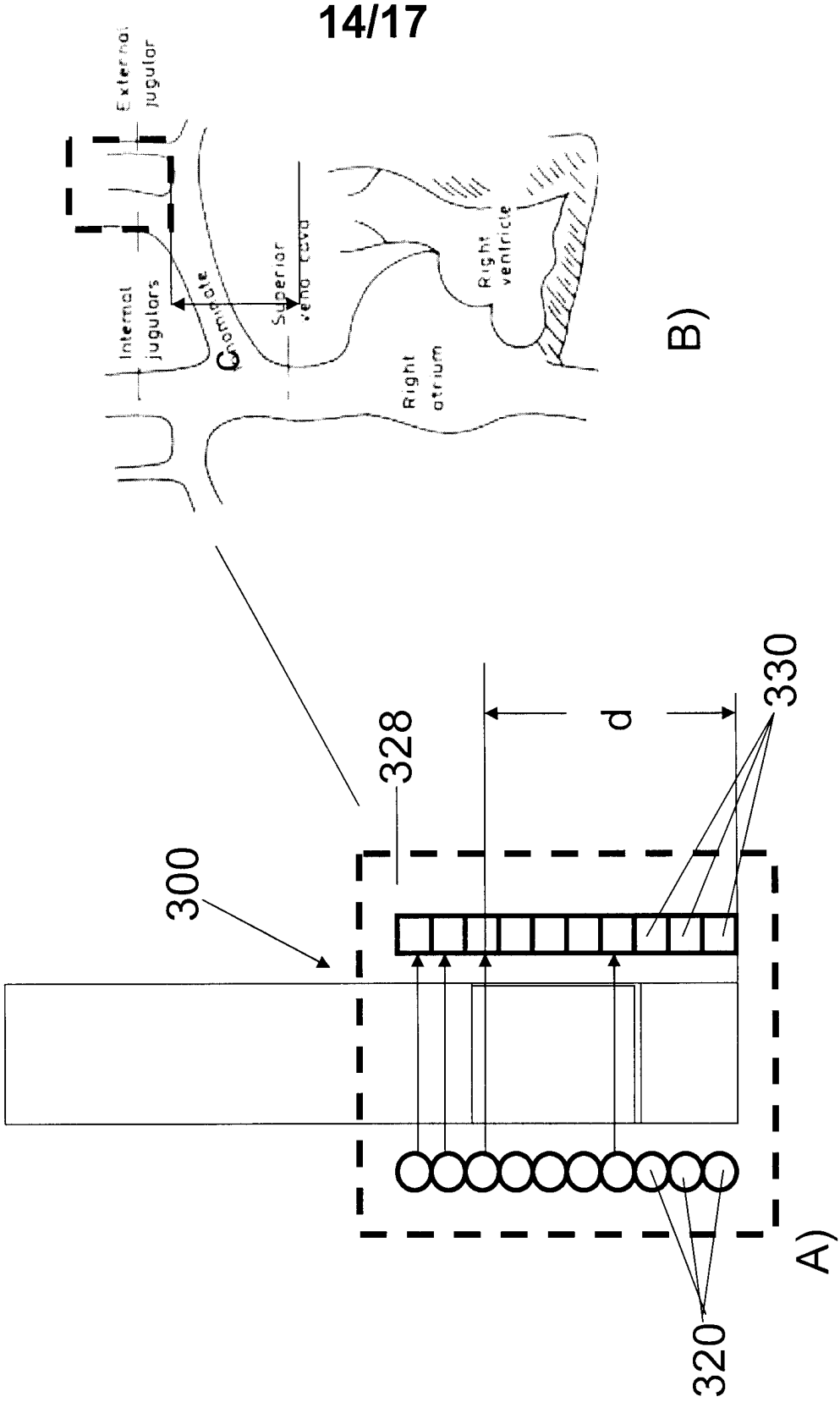

External jugular
Internal jugulars
Superior vena cava
Right ventricle
Right atrium
B)
300
328
d
330
320
A)

Figure 13

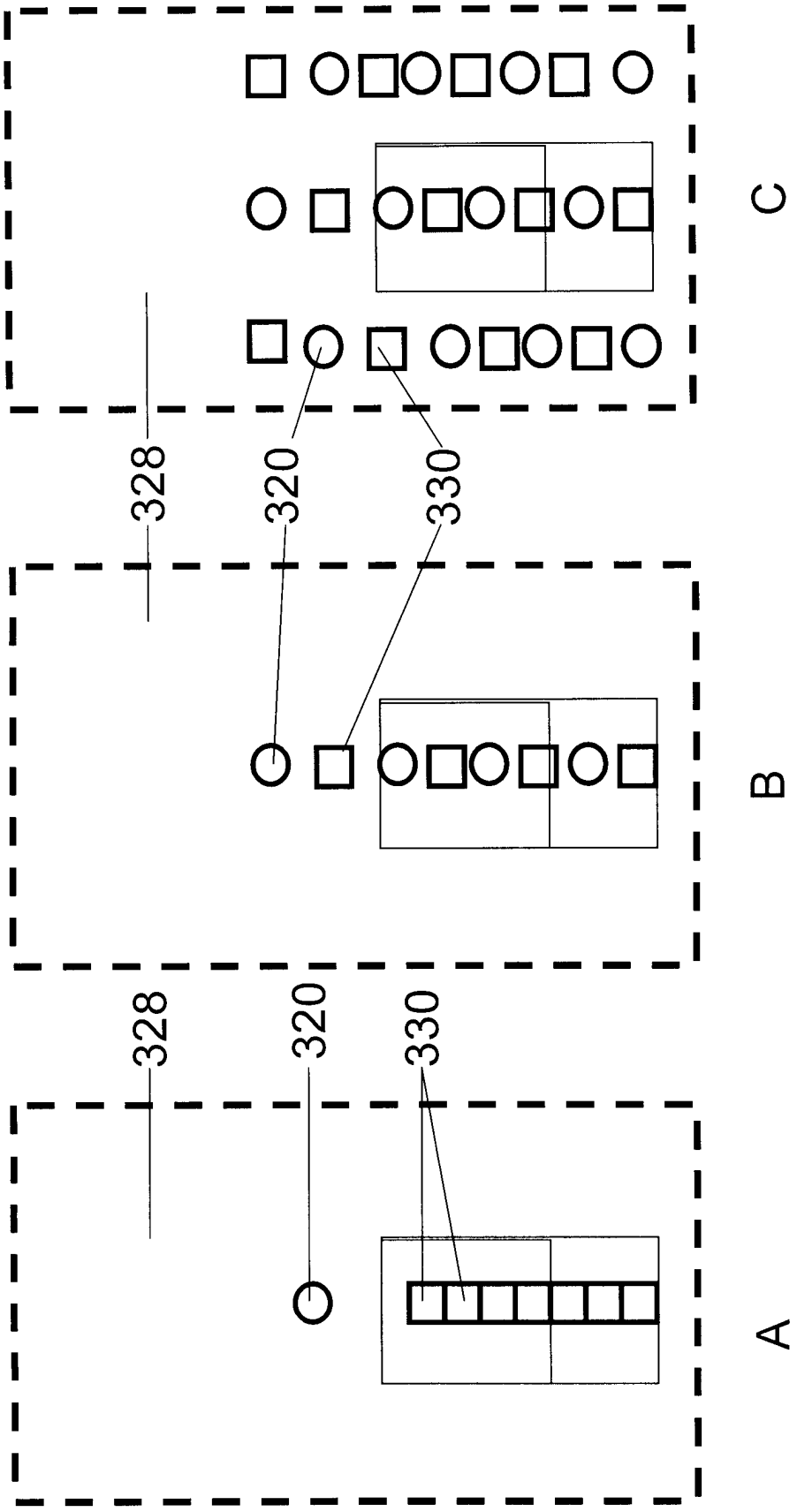


Figure 14

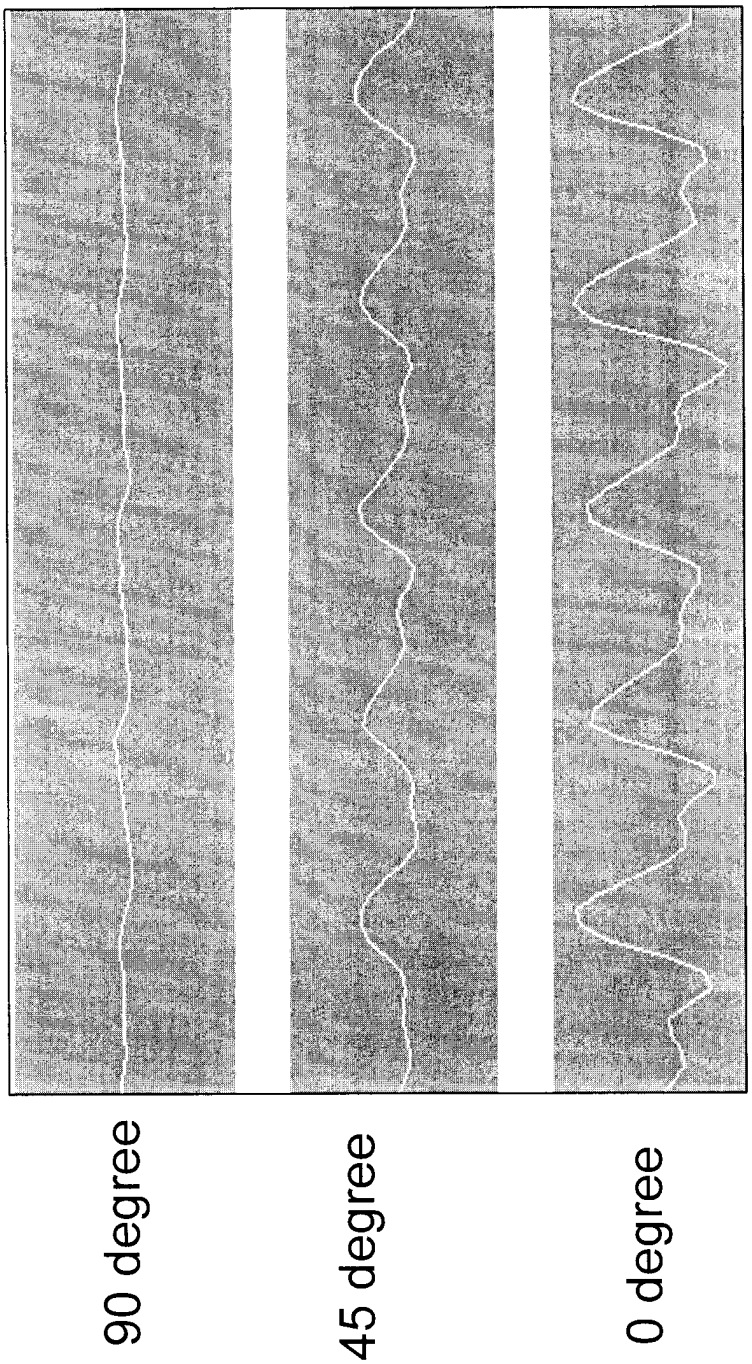


Figure 15

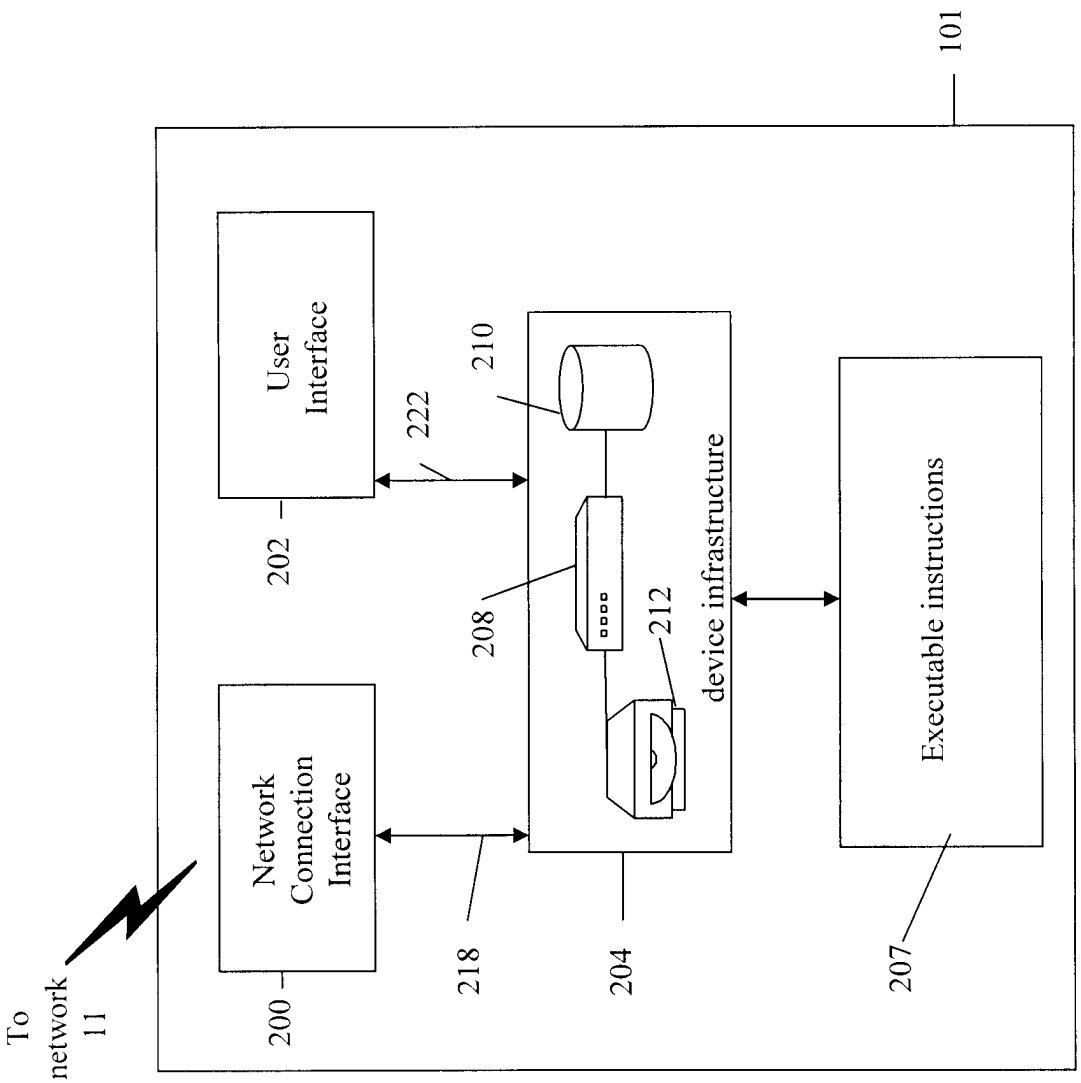

101
User Interface
202
222
210
208
212
device infrastructure
Executable instructions
207
Network Connection Interface
200
218
204
To network 11

Figure 16

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2008/000262

A. CLASSIFICATION OF SUBJECT MATTER
IPC: ***A61B 5/02*** (2006.01) , ***A61B 5/021*** (2006.01) , ***A61B 5/024*** (2006.01) , ***A61B 5/026*** (2006.01) , ***A61B 5/1455*** (2006.01) , ***A61B 6/00*** (2006.01)
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

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

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

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)
Databases: Delphion, CPD (Canadian Patent Database), Pluspat, IEEE Xplore, Google
Keywords: cardiac, blood vessel, blood oxygenation, infrared, probe, light source

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 078 833 20 Jun.2000 (20-06-2000) by Hueber et al. ** see entire document, Fig.4**	1,4-18
Y	US 6 801 648 (B2) 2 Oct. 2004 (5-10-2004) by Cheng et al. ** see abstract, entire document**	1-30,34
Y	US 6 587 703 1 Jun. 2003 (01-06-2003) by Cheng ** see abstract, entire document**	1-30,34
Y	US 6 151 518 21 Nov. 2000 (21-11-2000) by Hayashi ** see abstract, entire document**	1-30,34

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

[X] 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 May 2008 (20-05-2008)	23 May 2008 (23-05-2008)

Name and mailing address of the ISA/CA	Authorized officer
Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001-819-953-2476	Karen Oprea 819- 934-2668

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2008/000262

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the 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. [ ] Claim Nos. :
because they relate to subject matter not required to be searched by this Authority, namely :

2. [ ] Claim Nos. :
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 :

3. [ ] Claim Nos. :
because they are dependant 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 :

Group A: Claims 1-30,34 are directed to a device and method which non invasively measure at least one parameter of a cardiac blood vessel in a patient wherein said device and method is adapted to emit and receive light of at least two wavelenghts in the 400-1000nm range, said device comprising a light source, photodetector and at least one probe.

Gruop B: Claims 31-33 are directed to a method of measuring the blood content of a chromophore in a patient wherein a light beam is directed to an external tissue site on the patient and the light is reflected from and to the tissue at selected wavelengths, 780 and 850nm respectively, according to the modified Beer Lambert's law.

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 claim Nos. :

4. [X] 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 claim Nos. : 1-30,34

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.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/CA2008/000262

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
US6078833	20-06-2000	CA2266284 A1	25-09-1999
		EP0945100 A1	29-09-1999
		JP11344442 A	14-12-1999
US6801648	05-10-2004	AU8100501 A	18-02-2002
		CA2417917 A1	14-02-2002
		EP1307135 A2	07-05-2003
		JP2004534934T T	18-11-2004
		TW588158B B	21-05-2004
		US6516209 B2	04-02-2003
		US6587703 B2	01-07-2003
		US6597931 B1	22-07-2003
		US6735458 B2	11-05-2004
		US2002033454 A1	21-03-2002
		US2002035317 A1	21-03-2002
		US2004162468 A1	19-08-2004
		WO0212854 A2	14-02-2002
US6587703	01-06-2003	US6801648 B2	05-10-2004
US6151518	21-11-2000	JP11244267 A	14-09-1999

专利名称(译)	测量心脏功能参数的方法和装置		
公开(公告)号	EP2120689A1	公开(公告)日	2009-11-25
申请号	EP2008714585	申请日	2008-02-13
[标]申请(专利权)人(译)	米斯比尔生命科学公司		
[标]发明人	CHENG XUEFENG		
发明人	CHENG, XUEFENG		
IPC分类号	A61B5/02 A61B5/021 A61B5/024 A61B5/026 A61B5/1455 A61B6/00 A61B5/0215 A61B5/00 A61B5/0205 A61B5/029		
CPC分类号	A61B5/021 A61B5/0205 A61B5/02116 A61B5/029 A61B5/1455 A61B5/14552 A61B5/4884 A61B5/6833 A61B2562/0233 A61B2562/043 A61B2562/046		
优先权	11/707095 2007-02-16 US		
其他公开文献	EP2120689A4 EP2120689B1		
外部链接	Espacenet		

摘要(译)

提供了一种用于非侵入性地测量患者中的心脏血管的至少一个参数的装置。该装置包括发射在400nm至1000nm波长范围内的光的至少一个光源;至少一个光电检测器，其适于接收由所述光源发射的光并基于所接收的光产生输出，其中所述光从所述患者的组织反射或透射通过所述患者的组织，所述光电检测器的输出与所述血液的参数船只;以及至少一个探针，用于促进将光从所述光源递送到所述患者上在所述心脏血管附近的外部组织部位以及由所述光电检测器接收光。还提供了利用该装置和/或系统监测/测量心脏参数的系统和方法。