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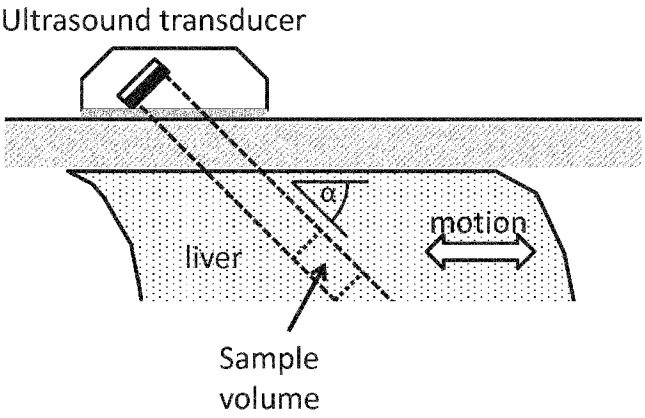

Figure 2

(57) Abstract: A method of non-invasively monitoring the respiration of a patient comprises: transmitting ultrasound into the body toward an internal structure of the patient's body, the internal structure being one of the liver, the spleen or a kidney; selecting a depth range; measuring the phase of ultrasound echo signals from the internal structure at multiple points along the depth range for at least a first and a second echo signal, the first and second echo signals being received at different times; detecting the motion of the internal structure within the patient's abdomen by reference to differences in the measured phase between the first and the second echo signals; and thereby monitoring the respiration of the patient by associating movement of the internal structure with movement caused by respiration

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ULTRASONIC METHOD AND APPARATUS FOR RESPIRATION MONITORING

The present invention relates to a non-invasive method and apparatus for monitoring the respiration of a medical or surgical patient, in particularly using ultrasound.

Measurement and monitoring of respiration is essential to treatment of a wide range of medical conditions where mistakes have grave consequences for the patients and are associated with considerable economic cost for the society. The thoracic diaphragm is the main breathing muscle, and its dysfunction can be symptomatic of many respiratory disorders and conditions.

WO 2004/049951 discloses a respiration monitor comprising an ultrasound transducer array having a plurality of individual transducer elements positioned in an intercostal space so as to span at least part of the region of thoracic diaphragm movement of a patient. Because air has a much lower acoustic impedance than tissue, the reflection of the ultrasound beam is much more pronounced when the lung is insonated. By measuring the strength of the receiving signal, it is possible to determine the presence of the patient's lung, and hence the degree of inspiration by using several transducers located along the direction of the motion of the lower lung border.

In accordance with another existing technique, the motion of the diaphragm can instead be measured by conventional ultrasound imaging techniques. A beam of ultrasound pulses is aimed from a transducer onto the skin surface towards the diaphragm from below, via the liver. A distinct, strong echo can then be detected from the diaphragm since it is a smooth, specular surface. The variations in the distance between the ultrasound transducer and this echo can then be used for measuring the magnitude of the excursions. Instead of using only a narrow beam (M-mode), a real-time two-dimensional ultrasound image (B-mode) might also be used, with the additional advantage of securing a better anatomical orientation.

It is desirable to provide further methods for monitoring of respiration.

The present invention provides a method of non-invasively monitoring the respiration of a patient comprising: transmitting ultrasound into the body toward an internal structure of the patient's body, the internal structure being one of the liver, the spleen or a kidney; selecting a depth range; measuring the phase of ultrasound echo signals from the internal structure at multiple points along the depth range for at least a first and a second echo signal, the first and second echo signals being received at different times; detecting the motion of the internal structure within the patient's

abdomen by reference to differences in the measured phase between the first and the second echo signals; and thereby monitoring the respiration of the patient by associating movement of the internal structure with movement caused by respiration.

It has been found that movement of the internal structures closely mirrors movement caused by respiration, such as movements of the thoracic diaphragm, which in turn can be used to monitor the respiration of a patient. The diaphragm is the major muscle of inspiration, and continuous monitoring may support and add information to decision makers in a variety of settings therefore making it a "technology platform" for applications in respiratory diseases, and operating room to emergency room settings. Surprisingly, the movement of internal structures as in the first aspect can be reliably mapped to the patient's respiration. The depth range may be selected based on the internal structure of interest and/or based on prior assessment of the patient, including earlier non-invasive imaging, for example. For the liver a depth range of 2-5 cm may be selected. The depth range is selected to cover a sufficient section of the internal structure so that if for some reason the signal from a part of the range is weak, as might happen if the beam is aimed through a low echo region such as a blood vessel or a bile duct, then there will always be neighbouring tissue regions within the range with adequate echo intensity that can be used instead.

The internal structures of interest are composed of generally solid tissue and move generally as a solid body. They are not liquid or gas filled such as blood vessels, the gallbladder or intestines. They are further of a sufficient size that movement caused by respiration does not cause the tissue to move entirely out of a field of view. Ultrasound is non-invasive, effective and can be used for prolonged periods of time without harm to the patient. Thus, for example, a transducer could remain on the patient for hours, days or even weeks if necessary, while continuously monitoring respiration.

The size of the ultrasound sample volume along the beam direction is preferably in the range from 2 to 5 cm. This will improve the amplitude stability of the signal and avoid drop-outs where a smaller sample volume might happen to be completely inside a vessel or a bile duct.

The method may use an unfocused, or only slightly focused, ultrasound beam. Doing so increases the time of observation of individual scatter elements in the tissue when motion is in a direction that deviates from the direction of the sound beam, and will improve the accuracy of the estimated motion and velocity.

The motion of the internal structure is calculated based on the measured phase at the multiple points along the depth range and the differences in phase for at least

two echo signals received at different times. This may be implemented by calculating the displacement of the tissue as an average along the ultrasound sound beam, where the observations of displacement at the multiple points along the depth range are weighted by their signal intensities before the averaged displacement is calculated. Note that in this situation the displacement is directly related to the phase and hence the phase difference can be considered as analogous to a displacement difference. The measured phases are monitored over time in order to identify the difference in phase with time between at least the first and second echo signal at different points on the depth range. The first and second echo signals may be consecutive signals or they may be spaced apart by other echo signals. The difference in phase with time may be determined over more than two echo signals. The multiple points along the depth range include at least two points providing an echo signal of sufficient strength, for example a strength over a given threshold. Three or more points may be used. The method may comprise using interferometry to determine a phase of a returned ultrasound echo and cumulatively summing the phase shift between ultrasound measurements at different depths to determine a displacement of the structure.

The method may comprise determining a phase shift caused by motion at two or more locations along the depth range within the tissue and determining an average phase shift to determine the motion. Doing so will determine the motion with improved accuracy. The multiple locations may be independently measured using two or more transducers, or may be measured at different depths of an ultrasound beam from a single transducer. The average is preferably an intensity-weighted average of the multiple measurements as explained above. Solid tissue, such as the liver, has structural irregularities that scatter ultrasound and the echo received from the tissue will be a sum of individual contributions from such scattering elements. Since the sum is made up from individual vectors each with a phase and amplitude, the sum might occasionally become close to zero, creating a singularity characterised by loss of echo signal. When measuring tissue motion by analysis of phase variations, this becomes a problem. When the signal becomes close to zero, quite unpredictable phase variations might occur, causing lasting errors in the estimate of tissue position. This can be overcome by making multiple observations of phase variations from a range of locations, and computing an average phase difference weighted by the intensity of the signal.

The ultrasound beam from the transducer should be at a non-perpendicular angle (α) to the motion vector of the internal structure, i.e. the cranio-caudal direction of the patient. Preferably the angle is below 60° and more preferably below 45°.

The method may further comprise determining one or more derived respiration properties from the motion include a respiratory pattern, a breathing rate, and a tidal volume.

The technique above may be particularly applicable to patients receiving support from a mechanical ventilator. Thus, in various embodiments, the patient may be receiving support from a mechanical ventilator or is undergoing a spontaneous breathing trial for removal of support from a mechanical ventilator.

The method may comprise setting initial or on-going operational parameters of the mechanical ventilator, based on the monitored respiration.

The method may comprise synchronising the operation of the mechanical ventilator with the breathing of the patient, for example a frequency or phase of pressure assistance provided by the mechanical ventilator, based on the monitored respiration. In one embodiment, the operation of the mechanical ventilator may be controlled so as to provide pressure assistance responsive to detecting patient contribution.

Where the patient is undergoing a spontaneous breathing trial, the method may comprise reducing or removing mechanical ventilation support for a period of time, such as 5 to 30 minutes, and monitoring respiration during this time to determine a likelihood of a successful spontaneous breathing trial. The method may further comprise determining, in preferably less than the duration of the trial, e.g. less than 25 minutes, that a likelihood of the patient successfully completing the spontaneous breathing trial is below a predetermined threshold and returning mechanical ventilation support before unnecessary complication of the patient's condition.

In further embodiments, the patient may be a trauma patient, a cardiac arrest patient, a spinal cord injury patient, a pulmonary patient, such as a COPD patient, or a post-operative patient.

The present invention also provides an ultrasound apparatus for non-invasively monitoring respiration of a patient, the apparatus comprising: at least one ultrasound transducer element for placing on the patient to aim at an internal structure of the patient's body; and a controller for controlling the ultrasound transducer element and processing ultrasound signals; wherein the controller is arranged to transmit ultrasound into the body toward the internal structure of the patient's body; measure the phase of ultrasound echo signals received from the internal structure at multiple points along a depth range selectable by a user; the phase being measured for at least a first and a second echo signal, the first and second echo signals being received at different times; detect the motion of the internal structure within the patient's abdomen by reference to

differences in the measured phase between the first and the second echo signals; and thereby monitor the respiration of the patient.

The apparatus is for use with internal structures including the liver, spleen and kidneys and thus is arranged to process ultrasound echo signals from those internal organs in order to monitor the respiration of the patient by associating movement of those organs with movement resulting from respiration. There may be a single ultrasound transducer element acting to both transmit and receive the ultrasound, or alternatively multiple ultrasound transducer elements may be used. The apparatus can include an input device allowing a user to select a depth range.

The controller may be arranged to carry out method steps as discussed above. For example, the motion of the internal structure may be calculated based on the measured phase at the multiple points along the depth range and the differences in phase for at least two echo signals received at different times by calculating the displacement of the tissue as an average along the ultrasound sound beam, where the observations of displacement at the multiple points along the depth range are weighted by their signal intensities before the averaged displacement is calculated.

The apparatus may comprise a contact layer to be positioned between the transducer and the skin. The contact layer might be made from an adhesive material. The contact layer comprise an ultrasound contact gel, a glue, or an adhesive tape material that allows transmission of ultrasound, such as the sonolucent silicone tape described in WO2011/135288. Gel, glue and tape might also be used in various combinations. The contact layer may comprise removing protective covers that may be removed to expose the adhesive before the surface is brought in contact with the body.

The surfaces of the apparatus adapted to be in contact with the patient's body are configured to provide conformal contact with the surface of the body.

The apparatus may include at least one power source for powering the parts of the apparatus.

The transducer may be connected either by wire or by (short-range) digital or analogue radio communication to the processing circuitry, which may provide signals from the target tissue. The processing circuitry may be partly or fully digital.

The apparatus may comprise a monitor that provides information about the measured motion of the tissue (or a respiratory property derived from the motion) to an observer (e.g. a physician or the patient). The processing circuitry and/or the monitor may provide for control of the measurements performed.

Preferably, the apparatus is a portable device adapted such that a patient can wear the device during normal life. This allows continuous monitoring outside of a hospital environment and with a non-invasive and safe technology.

As above, the apparatus (and preferably the processing circuitry of the apparatus) may determine a displacement of the internal structure obtained by any one of: integrating a velocity of the internal structure detected using the Doppler Effect; interferometry analysis of the phase of the reflected wave; mapping of ultrasound speckles within the internal structure; and determining displacement of one or more anatomical landmark.

The apparatus can advantageously be used in a mechanical ventilation system along with a mechanical ventilator, and thus the invention extends to such a system, wherein the mechanical ventilator is for providing support to a patient and the apparatus is for non-invasively monitoring the respiration of the patient during support via the mechanical ventilator.

The mechanical ventilation system may be arranged to synchronise the operation of the mechanical ventilator with the breathing of the patient based on the monitored respiration and/or to control the operation of the mechanical ventilator so as to provide pressure assistance responsive to detecting patient contribution. The system may be arranged to carry out a spontaneous breathing trial by reducing or removing mechanical ventilation support for a period of time and monitoring respiration during this time to determine a likelihood of a successful spontaneous breathing trial.

Certain preferred embodiments of the present invention will now be described in greater detail, by way of example only and with reference to the drawings, in which:

Figure 1 shows a patient connected to a system for monitoring respiration;

Figure 2 shows a partial, vertical cross section through the patient illustrating an ultrasound transducer of the system;

Figure 3 shows exemplary input and output data for the ultrasound transducer; and

Figures 4 and 5 shows a schematic illustration of processing circuitry and signal processing of the system;

A system and a method are disclosed for performing ultrasonic interferometry to produce at least one measurement of tissue structures in a living body, for acquisition of physiological signals; the data from these signals may be utilized for monitoring and diagnostic purposes. Further embodiments may also allow for the monitoring of derived signals such as respiratory patterns, breathing rate, and a tidal volume.

Since several internal organs, particularly those in the upper abdomen such as the liver, the spleen and the kidneys, move with respiration, their motions can be used to indirectly monitor respiration, i.e. without directly monitoring the lung or diaphragm. The liver, in particular, is a useful target. The liver is a large piece of tissue, allowing for placement of an ultrasound transducer on the skin surface without any need for precise anatomical guidance, and is easily accessible by ultrasound from the exterior of the body. The spleen is smaller than the liver, and can be hidden by gas pockets, but still presents a viable target. The kidneys again are smaller than the liver and are harder to access, but also move significantly with respiration.

The apparatus is illustrated in Figures 1 and 2, and is composed of several parts, including processing circuitry, at least one ultrasound transducer, and a contact layer to be positioned between the transducer and the skin. The contact layer might be made from an adhesive material. The apparatus also includes at least one power source (not shown) for powering the parts of the device, according to their requirements. Several of these parts may be integrated in a single unit.

The transducer is coupled to the patient's body by the contact layer, which may be an ultrasound contact gel, a glue or an adhesive tape material that allows transmission of ultrasound, such as the sonolucent silicone tape described in WO2011/135288. Gel, glue and tape might also be used in various combinations. The surfaces in contact with the patient's body are configured to provide conformal contact with the surface of the body. A method of applying the transducer to a living body using an adhesive tape might include removing protective covers to expose the adhesive before the surface is brought in contact with the body.

The transducer is connected either by wire or by short-range, digital or analogue radio communication to the processing circuitry, which provides signals from the target tissue. The processing circuitry is configured to process signals from the transducer so as to derive a measurement of a motion of a target tissue. The processing can be partly or fully digital.

The apparatus can be made portable so that the patient can live normally while still being continuously monitored with a non-invasive and safe technology. That is to say, a system including at least the transducer and processing circuitry is of a suitable size and weight that it can be carried on the patient's body without impeding routine activates, and the contact layer comprises an adhesive that is sufficiently strong such that the transducer remains in contact with the skin during such activities.

The system can also comprise a monitor that provides information about the measured motion parameters from the tissue to a human observer (e.g. a physician or

the patient). The processing circuitry and/or the monitor may provide for control of the measurements performed.

As shown in Figure 2, ultrasonic pulsed waves from the at least one ultrasound transducer are transmitted into the body, and the reflected echo signals are used to estimate a property of the target region, based on response (e.g. phase shift between successive ultrasound pulses).

The processing circuitry calculates tissue motion parameters, such as velocity, or other derived parameters, based on the motion pattern of the target internal structure.

The motion of the liver has been shown to closely follow the motion of the thoracic diaphragm muscle, and measurements of liver motion will, for this reason, be a good surrogate for direct measurements of diaphragm motion.

Doppler-based techniques can be used for estimating the motion of tissue and fluids. Pulses of ultrasound are emitted into the tissue, and the echoes that are received from a pre-set depth, which is determined by an adjustable delay between emission of each pulse and a corresponding reception gate (see Figure 3), are processed in order to detect and measure a shift in frequency related to tissue velocity. Integration of velocity over time will then give the displacement of the tissue. Since the phase of a signal at a given point in time is determined by the temporal integral of frequency in the past, we can instead directly use phase variations of an echo signal as a measure of tissue displacement. This technique (interferometry) is commonly used for accurate measurements of distances by counting of light wave cycles.

When a piece of tissue move a distance (s), then the change in phase ($\Delta\varphi$) of an ultrasound echo received from the tissue will be:

$$\Delta\phi = 4\pi \frac{s}{\lambda}\cos(\alpha)$$

where λ is the wavelength of the ultrasound, and α is the angle between the direction of the ultrasound beam and the motion vector, i.e. the cranio-caudal direction of the patient.

Since the wavelength depends on frequency (f_0) and speed of sound (c) we may also write:

$$\lambda = \frac{c}{f_0} \text{ and } \Delta\phi = 4\pi \frac{f_0 \, s}{c}\cos(\alpha)$$

With reference to Figure 3, each ultrasound wavetrain that is emitted and received by the transducer will give one value for the echo signal phase. In order to keep track of phase changes, the maximum phase angle between two successive ultrasound echoes must be inside the interval from $-\pi$ to π in order to be uniquely defined. The maximum distance of tissue motion between successive ultrasound pulses will then be:

$$d_{max} = \frac{\lambda}{4\cos(\alpha)} = \frac{c}{4 f_0 \cos(\alpha)}$$

This establishes a relation between ultrasound frequency, the repetition frequency of pulse emissions (f_{prf}), speed of sound, sound beam angle and the maximum displacement of the tissue between pulses, and thus also the maximum tissue velocity that can be observed. The limitation is equal to the velocity limitations of pulsed Doppler techniques.

$$V_{max} = \frac{c \cdot f_{prf}}{4 f_0 \cos(\alpha)}$$

The processing circuitry is schematically illustrated in Figures 4 and 5, and is based on a signal processing scheme that is somewhat similar to the pulsed Doppler technique that is used for blood velocity measurements. The main differences are:

- *Lower operating frequency*: Scattering and reflection of ultrasound from red blood cells is very frequency dependent, and shows a strong increase at higher frequencies. The scattering properties of solid tissue do not have such pronounced frequency dependence. Thus, a lower frequency of operation might be preferred for recording of motion in solid tissues. A typical frequency range is from 0.5 to 5 MHz.
- *Lower overall gain*: The echoes from solid tissues are about 40 – 60 dB stronger then the echo from blood, and so the amplification of the returned echo and / or the emitted ultrasound intensity can be reduced correspondingly.
- *Different filter settings*: The "wall" filter used in blood velocity measurements to remove echo components from slowly moving solid tissue elements must be set to a far lower value in order to allow the echo signals from slowly moving tissue to be processed. The preferred filter setting for recording of respiratory motion is in the range 0.01 – 0.1 Hz, dependent on the operating frequency of the system. The main purpose of this filter is to compensate for drift in electronic circuits and signal leakages between ultrasound transmit and receive circuits.

- *Larger sample volume*: During blood velocity measurements, a narrow ultrasound beam is used, and the emitted ultrasound wavetrains are short, typically 1 – 10 µs, corresponding to an axial resolution of some 0.75 to 7.5 mm. A larger volume along the beam direction is preferred for recording of respiratory motion, preferably with a size in the range from 1 to 5 cm, corresponding to a reception gate duration of 13 to 65 µs. This will improve the amplitude stability of the signal and avoid drop-outs if the sample volume happens to be completely inside a vessel or a bile duct. A typical distance from the transducer to the centre of the sample volume will be in the range from 5 to 15 cm, depending on transducer position on the body surface, and on the body and internal structure size. It might also be advantageous to use an unfocused, or only slightly focused ultrasound beam in order to increase the time of observation of individual scatter element in the tissue when motion is in a direction that deviates from the direction of the sound beam, and will improve the accuracy of the estimated motion and velocity.
- *Phase tracking and summation instead of Fourier analysis*: Instead of repetitive calculations of Fourier spectra representing velocity distributions, the phase of the returned echo signal from the selected depth range is calculated. This calculation might be based on the Hilbert transform of the signal, or on synchronous demodulation of the signal giving a composite signal that represents both the real and imaginary part of the phase vector, as shown in Figure 4 and 5.

From a series of phase vectors obtained as described above, the tissue displacement is calculated as a cumulative sum of phase differences. If P is a series of phase vectors obtained from successive ultrasound pulse emissions and receptions, then the cumulated phase shift (Φ_{cum}) caused by the total displacement at sample number n becomes:

$$\phi_{cum} = \sum_{p=1}^{n} \Delta\phi = \sum_{p=1}^{n} \arg\left(P_p \, \overline{P_{p-1}}\right)$$

The tissue displacement (S) can then be calculated as:

$$S = \frac{\lambda \phi_{cum}}{4\pi \cos(\alpha)}$$

Cumulated phase and tissue displacement can also be calculated from the pattern of sign variations of the complex vector describing the phase of the echo. This might be implemented as an up/down counter circuit controlled by two bits of information derived from the sign of the real and imaginary parts of the phase vector.

The counter should be incremented each time the vector enters a new quadrant in counter clockwise order, and decremented when a new quadrant is entered in clockwise order. This scheme can be implemented by only requiring a slow two-bit digital interface between analogue and digital circuits, leading itself to a simple low-power implementation. From the count number (N), tissue displacement can be calculated as:

$$S = \frac{N\lambda}{8\cos(\alpha)}$$

The liver and the spleen move quite uniformly and linear with respiration. Thus, as discussed above, when an ultrasonic beam is aimed towards one of these tissues, about the same velocities will be observed over a wide range of distances into the tissue along the ultrasound beam direction. This is in contrast to measurements of blood flow with Doppler techniques, where a considerable variation in fluid velocity is expected along the direction of the beam.

It is reasonable to assume that the robustness and accuracy of estimates of phase shifts in the ultrasound echo caused by solid tissue motion can be improved by averaging of observations of phase from several locations along the ultrasound beam.

Solid tissues, such as the liver, have structural irregularities that scatter ultrasound. The echo received from the tissue will be a sum of individual contributions from such scattering elements. Since the sum is made up from individual vectors each with a phase and amplitude, the sum might occasionally become close to zero, creating a singularity characterised by loss of echo signal. When measuring tissue motion by analysis of phase variations, this becomes a problem. When the signal becomes close to zero, quite unpredictable phase variations might occur, causing lasting errors in the estimate of tissue position.

This can be overcome by making multiple or continuous observations of phase variations from a range of locations (depths) along the sound beam, and computing an average phase difference ($\Delta\varphi$) weighted by the intensity of the signal, and then processing these phase values further to give tissue velocity and displacement as described above. Since the intensity at a given location along the beam might change from one pulse of ultrasound to the next due to tissue motion, the intensity of both the current and the previous ultrasound echo from that location must be considered when performing the calculation of the intensity-weighted phase.

This can be done as follows:

The received echo from two successive pulses of ultrasound (numbered as n and n+1) is complex-demodulated to give two sampled time series of the complex echo signal ($P_n(t)$ and $P_{n+1}(t)$) as a function of time or depth into the tissue. The range of (t) is set to cover the distance along the sound beam that will be used for the calculations. In order to calculate the phase difference, the product of P_{n+1} and the complex conjugate of P_n is calculated:

$$Q(t) = \overline{P_n(t)}\, P_{n+1}(t)$$

The phase contained in Q will now be the phase difference between P_{n+1} and P_n as a function of time (and distance) and the absolute value of Q will be the product of the echo amplitudes from P_{n+1} and P_n which is a suitable factor for weighting in the process of calculation of an average phase value. Calculation of the weighted phase difference between P_{n+1} and P_n can now be done by simple summation of the elements in Q and calculating the phase angle of the sum:

$$\Delta\phi = \arg\left(\sum Q\right)$$

This is repeated for successive pairs of received echo signals (P_{n+1} and P_{n+2}, P_{n+2} and P_{n+3}, P_{n+3} and P_{n+4}, etc.) to calculate the cumulated phase shift and motion of the tissue over a longer time period.

Several parameters (with suggested ranges shown in parentheses) that determine the performance of the method can be optimised, such as the emitted frequency (e.g. 1 – 10 MHz), the duration of the emitted wavetrain (e.g. 0.5 – 100 µs), the bandwidth of the synchronous demodulator (e.g. 10 kHz – 2 MHz) and the length of the depth range within the liver or spleen to use for the calculations (e.g. 0.5 – 10 cm).

The method increases the robustness in situations where the beam accidentally traverses regions within the liver that are fluid filled, such as vessels, bile ducts or cysts. The fluid within these structures gives echoes that are far weaker than echoes from the surrounding solid tissue (by some -40 dB or more), and might cause an apparent loss of signal if the measurement site happens to be located inside such a structure. As the tissue moves back and forth at an angle with respect to the sound beam, this is quite likely to occur. With the intensity-weighted phase calculation method described above, this problem will be eliminated since data is collected over a larger distance along the beam, always assuring that some part of solid tissue contributes to the signal.

As will be appreciated, the apparatus above provides a measurement of the motion of an internal structure within the patient's abdomen, such as solid tissue like the liver or spleen, which closely follows movement of the diaphragm. This can in turn

be used for any application where monitoring respiration is necessary, and may replace, or be used in combination with known devices such as respiratory belts, flowmeters, spirometers, nasal temperature sensors, pressure transducers and radar systems.

The technique may, however, also be used to monitor breathing of a patient for other applications. For example, characterization of pulmonary function might be performed by extracting information and patterns of respiratory motion that might be interpreted as a substitute for spirometry values.

Another medical application for this invention is to monitor patients on mechanical ventilation and help in the synchronization between the ventilator and the patient. A further use is to monitor the motion when the patients is decoupled from the ventilator to characterize the thoracic diaphragm movements and to determine as early as possible whether the patient can be successfully weaned from mechanical ventilation or not. It can also be used in follow up of the patients.

During or when initiating mechanical ventilation, the technique for monitoring of respiration can be used to guide the mechanical ventilation pressure and/or CPAP (continuous positive airway pressure) settings. When inhalation pressure is increased, the lungs will initially expand, and then their volume will reach a plateau where further pressure increase will not improve ventilation, and possibly cause harm. This might be avoided by monitoring the gradual downwards displacement of the organs in the upper abdomen.

The method might also be used for monitoring patients that are on mechanical ventilation support, with the purpose of detecting the patient's own breathing efforts. Such efforts might indicate that the ventilator settings are incorrect, or that the patient is insufficiently sedated.

This technique may also be used to synchronize the operation of the mechanical ventilator with the breathing efforts of the patient, for example by adjusting the frequency or phase of the mechanical ventilator's pressure assistance in order to match the patients' needs and to increase patient's comfort. This can reduce asynchrony between mechanical ventilator action and the patient's own breathing action, i.e. where the patient's effort (i.e. diaphragm movement) is out of sync with the mechanical ventilator, or where the patient's effort starts before the mechanical ventilator initiates pressure support resulting in the patient receiving no air.

The method might detect the initial contraction of the diaphragm, and use this for triggering and synchronizing the ventilator. This will enable normal chemoreceptor control of ventilation, while at the same time reducing the efforts and fatigue associated

with work of breathing. For example, when the patient makes an effort to breathe (i.e. diaphragm movement is detected) the mechanical ventilator will provide pressure support in response.

In order to determine whether a patient is ready to be removed from ventilator support, a spontaneous breathing trial (SBT) is carried out. During an STB, the mechanical ventilator is disabled for 30 minutes. If the patient is able to successfully breathe for 30 minutes, then they are taken off of the ventilator. If not, then ventilator support is returned. Ventilators are expensive to operate, and so it is desirable to remove ventilator support from patients as soon as possible. However, removing support too early can be detrimental to a patient's recovery, resulting in a prolonged need for ventilation support. It is now well known that diaphragm weakness is associated with a poorer prognosis.

The technique for monitoring respiration can be used to aid in assessing readiness for a spontaneous breathing trial (SBT). To assess SBT readiness the mechanical ventilator may be removed for a short period of time, such as 10 cycles, and diaphragm displacement can be monitored (amplitude, slope and regularity) to predict the success or failure of a 30 minutes SBT.

The technique can also be used to monitor respiration during the SBT. The development of diaphragm displacement (amplitude, slope and regularity) can be monitored during the trial to predict success or failure before the end of the trial, helping to reduce the risk of harm being caused in patients who are unlikely to succeed.

A further use will be for patients requiring respiratory rehabilitation where the movement of the diaphragm is crucial. The patients may be trauma patients, cardiac arrest patients, spinal cord injury patients or pulmonary patients such as COPD patients. The technique may also be used in post-operative patient monitoring. The respiration can be monitored to see development of diaphragm displacement (amplitude, slope and regularity) to give early warning if respiration halts.

In another embodiment, the technique above may be used during a CT guided puncture operation. However, it will be understood that, as discussed above, embodiments of the invention can also be used in any other area requiring respiration monitoring, such as the fields of radiation therapy or mechanical ventilation.

The ultrasound transducer is positioned on the patient and directed towards the liver prior to the patient being given a CT or MRI scan. The transducer emits a series of ultrasound pulses and detects their echoes in the known manner. Based on the

detected echoes, movement of the liver can be detected, and hence the position of the diaphragm can be determined.

After the patient has been fitted with the transducer, a CT or an MRI scan is performed on the patient to determine the precise location of the target (e.g. a lesion to be punctured). During the scan, the patient is required to hold his breath so that a clear image is produced with the lungs in one position. While the scan is being performed and while the patient is holding his or her breath, the exact position of the diaphragm is presented on the monitor and the position-value is noted.

The image from the scan is used to calculate the depth and angle at which a needle must be inserted for the lesion to be punctured. When the operator is ready to perform the puncture, the patient is asked to inhale until the display indicates that the diaphragm is in the same position as it was when the scan was performed. If the patient inhales too much and the transducer indicates that the level of inspiration is greater than that held during the scan, the operator can instruct the patient to exhale a little. If necessary, the patient can relax and inhale again until the operator is happy with the position of the diaphragm.

In this way, the operator can be sure that the lesion is at the same position within the patient as it is shown in the CT or MR image while he or she performs the puncture. In the case of CT, the location of the needle may, however, still be checked by means of a further scan.

As described above, the apparatus of the present invention can also be used to improve radiotherapy treatments by reducing the area that needs to be irradiated. The basic procedure described above is employed, however, the embodiment is modified to provide a control output from the processor for controlling a source of radiation.

After the location of the tumour within the patient has been determined from the scan image, a radiation source is aimed at that location. This is connected to the control output such that the radiation source only emits when triggered to do so by the output signal from the processor.

The patient is allowed to breathe continuously throughout the radiation treatment. Meanwhile, the processor uses the outputs from the transducer array to continuously monitor the position of the diaphragm. When its position corresponds to the position that was determined during the scan, the processor sends a signal to trigger the radiation source to irradiate the target area of the patient. Thus, the area of the patient that needs to be irradiated can be significantly reduced because the location of the target can be determined to a much greater accuracy.

The output of the apparatus may be in form of diaphragm position, amplitude of breathing motion, frequency (respiratory rate) and/or velocity. Successive measurements performed on a single patient or a population may yield a historical trend allowing progress or deterioration of lung function to be monitored.

Whilst a preferred embodiment of the present invention has been described, it will be appreciated that numerous variations of the system are within the scope of the invention. For example, in various embodiments, the apparatus may be composed of several transducers placed at different locations on the patient's body. The apparatus may also include additional sensors of different types, such as pulse oximeters, electrocardiographic electrodes, electromyographic electrodes, electrodermal activity sensors, or accelerometers, for simultaneous or complementary measurements.

Claims:

1. A method of non-invasively monitoring the respiration of a patient comprising:

transmitting ultrasound into the body toward an internal structure of the patient's body, the internal structure being one of the liver, the spleen or a kidney;

selecting a depth range;

measuring the phase of ultrasound echo signals from the internal structure at multiple points along the depth range for at least a first and a second echo signal, the first and second echo signals being received at different times;

detecting the motion of the internal structure within the patient's abdomen by reference to differences in the measured phase between the first and the second echo signals; and

thereby monitoring the respiration of the patient by associating movement of the internal structure with movement caused by respiration.

2. A method as claimed in claim 1, wherein the depth range is selected based on the internal structure of interest and/or based on prior assessment of the patient, and wherein the depth range is selected to cover a sufficient section of the internal structure so that if for some reason the signal from a part of the range is weak then there will always be neighbouring tissue regions within the range with adequate echo intensity that can be used instead.

3. A method as claimed in claim 1 or 2, wherein the internal structure is the liver and the selected depth range is 2-5 cm.

4. A method as claimed in claim 1, 2 or 3, wherein the size of the ultrasound sample volume along the beam direction is in the range from 2 to 5 cm.

5. A method as claimed in any preceding claim, comprising using an unfocused, or only slightly focused, ultrasound beam for transmitting ultrasound into the body.

6. A method as claimed in any preceding claim, wherein the motion of the internal structure is calculated based on the measured phase at the multiple points along the depth range and the differences in phase for at least two echo signals received at different times, and the method includes calculating the displacement of the tissue as an average along the ultrasound sound beam, where the observations of displacement

at the multiple points along the depth range are weighted by their signal intensities before the averaged displacement is calculated.

7. A method as claimed in any preceding claim, wherein the measured phases are monitored over time in order to identify the difference in phase with time between at least the first and second echo signal at different points on the depth range.

8. A method as claimed in any preceding claim, wherein the multiple points along the depth range include at least two points providing an echo signal over a given threshold.

9. A method as claimed in any preceding claim, comprising using interferometry to determine a phase of a returned ultrasound echo and cumulatively summing the phase shift between ultrasound measurements at different depths to determine a displacement of the structure.

10. A method as claimed in any preceding claim, comprising determining a phase shift caused by motion at two or more locations along the depth range within the tissue and determining an average phase shift to determine the motion.

11. A method as claimed in claim 10, wherein the average phase shift is an intensity-weighted average of the multiple phase shift measurements.

12. A method as claimed in any preceding claim, wherein the ultrasound beam is transmitted at a non-perpendicular angle (α) to the motion vector of the internal structure.

13. A method as claimed in claim 12, wherein the non-perpendicular angle is below 60° and preferably below 45°.

14. A method as claimed in any preceding claim, comprising determining one or more derived respiration properties from the motion such as a respiratory pattern, a breathing rate, and/or a tidal volume.

15. A method for supporting a patient with a mechanical ventilator comprising non-invasively monitoring the respiration of a patient as claimed in any preceding claim.

16. A method as claimed in claim 15, comprising synchronising the operation of the mechanical ventilator with the breathing of the patient based on the monitored respiration and/or controlling the operation of the mechanical ventilator so as to provide pressure assistance responsive to detecting patient contribution.

17. A method as claimed in claim 15, or 16, wherein the patient is undergoing a spontaneous breathing trial and the method comprises reducing or removing mechanical ventilation support for a period of time and monitoring respiration during this time to determine a likelihood of a successful spontaneous breathing trial.

18. An ultrasound apparatus for non-invasively monitoring respiration of a patient, the apparatus comprising:

at least one ultrasound transducer element for placing on the patient to aim at an internal structure of the patient's body; and

a controller for controlling the ultrasound transducer element and processing ultrasound signals;

wherein the controller is arranged to: transmit ultrasound into the body toward the internal structure of the patient's body; measure the phase of ultrasound echo signals received from the internal structure at multiple points along a depth range selectable by a user; the phase being measured for at least a first and a second echo signal, the first and second echo signals being received at different times; detect the motion of the internal structure within the patient's abdomen by reference to differences in the measured phase between the first and the second echo signals; and thereby monitor the respiration of the patient.

19. An apparatus as claimed in claim 18, wherein the controller is arranged to carry out the method of any of claims 1 to 17.

20. An apparatus as claimed in claim 18 or 19, comprising a monitor that provides information about the measured motion of the tissue and/or a respiratory property derived from the motion to an observer.

21. A mechanical ventilation system comprising a mechanical ventilator for providing support to a patient and an apparatus as claimed in claim 18, 19 or 20 for non-invasively monitoring the respiration of the patient.

22. A mechanical ventilation system as claimed in claim 21, wherein the system is arranged to synchronise the operation of the mechanical ventilator with the breathing of the patient based on the monitored respiration and/or to control the operation of the mechanical ventilator so as to provide pressure assistance responsive to detecting patient contribution.

23. A mechanical ventilation system as claimed in claim 21 or 22, wherein the system is arranged to carry out a spontaneous breathing trial by reducing or removing mechanical ventilation support for a period of time and monitoring respiration during this time to determine a likelihood of a successful spontaneous breathing trial.

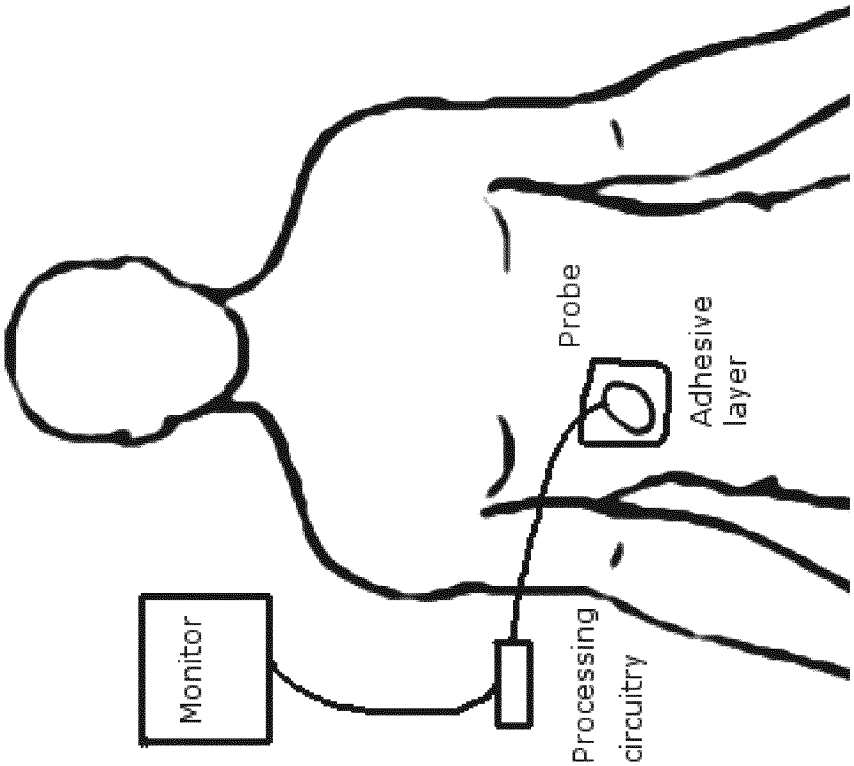


Figure 1

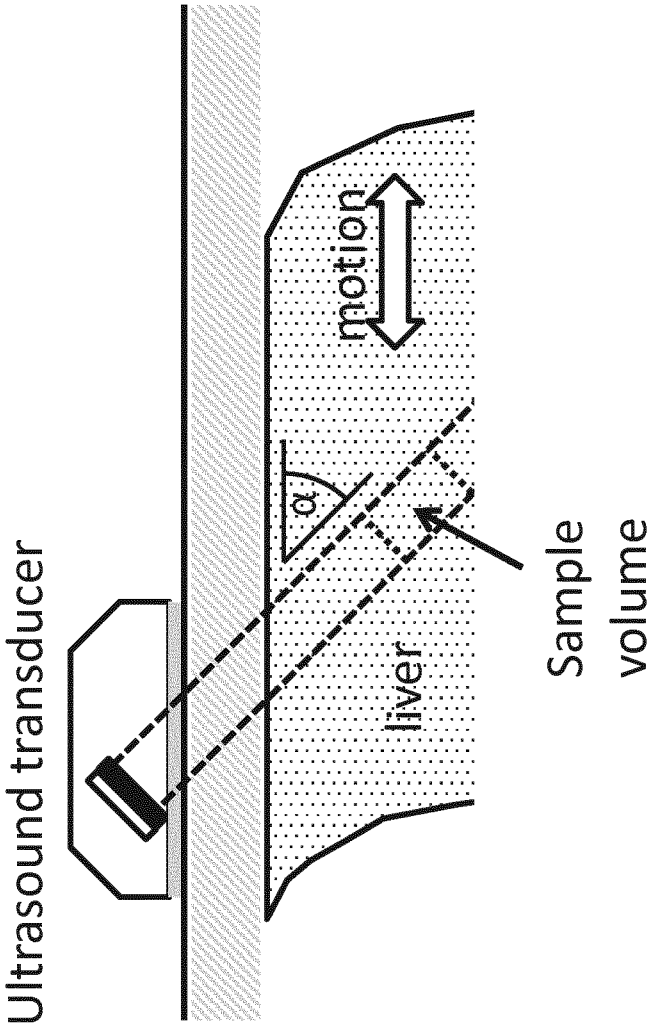
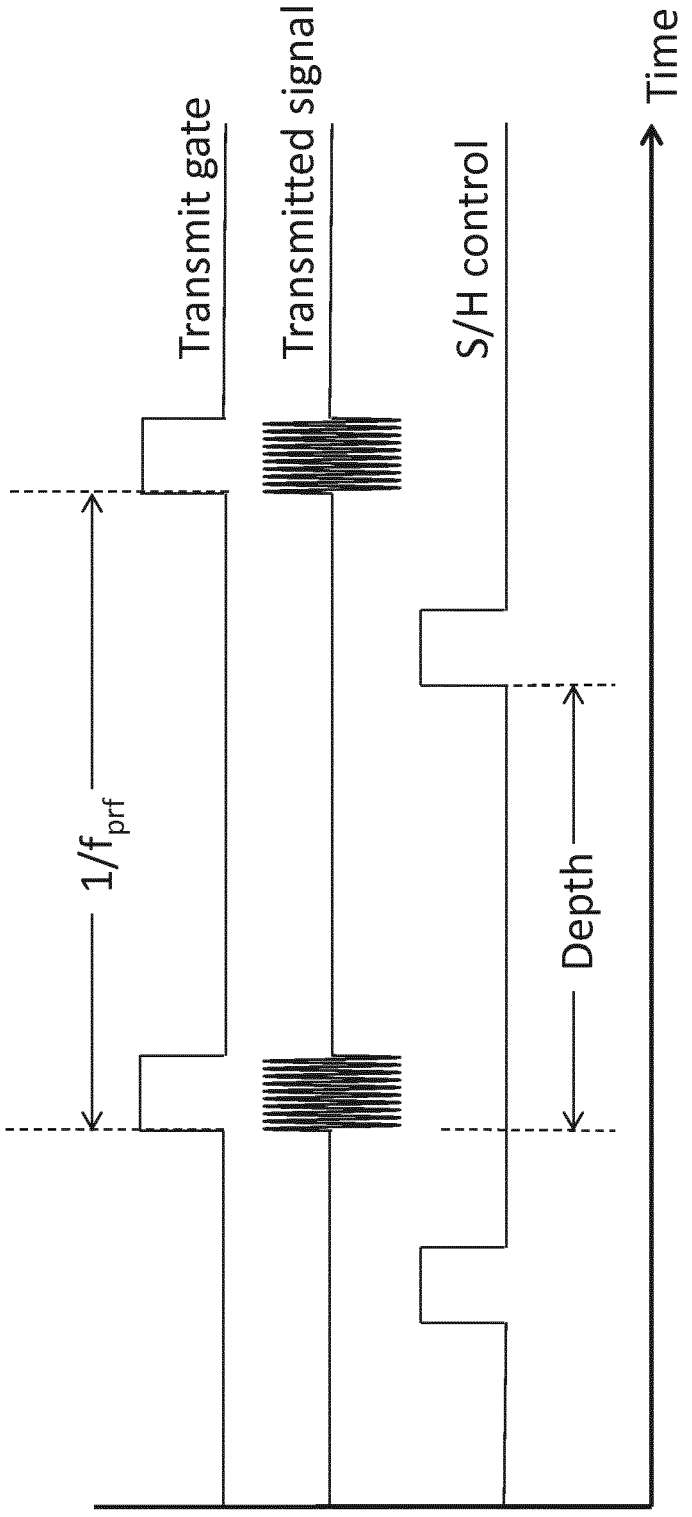


Figure 2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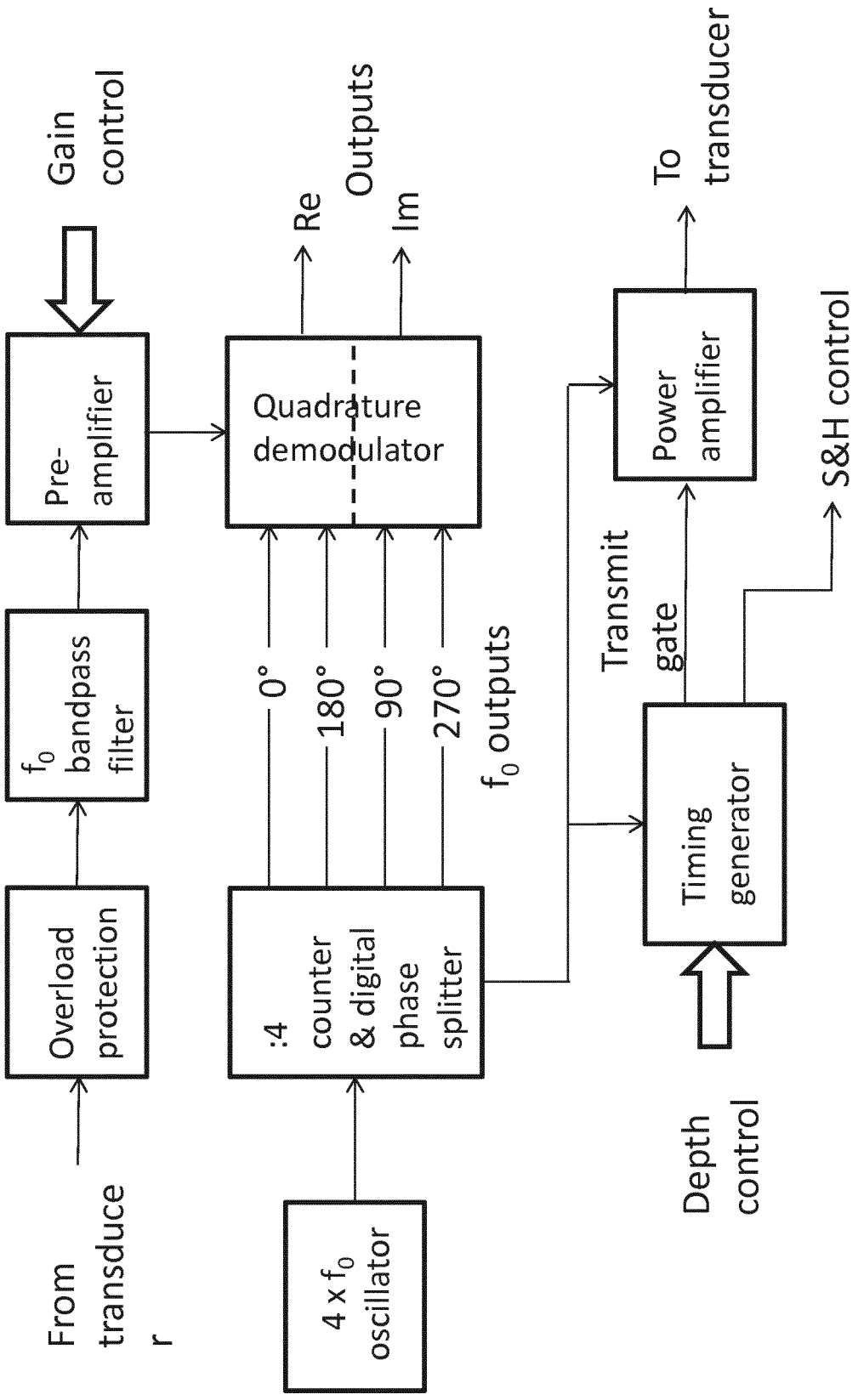
Transmitted signal
S/H control
Time
1/f_prf
Depth

Figure 3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Overload protection
f_0 bandpass filter
Pre-amplifier
Gain control
4 x f_0 oscillator
:4 counter & digital phase splitter
0°
180°
90°
270°
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Quadrature demodulator
Re
Im
Outputs
Transmit gate
Timing generator
Depth control
Power amplifier
To transducer
S&H control

Figure 4

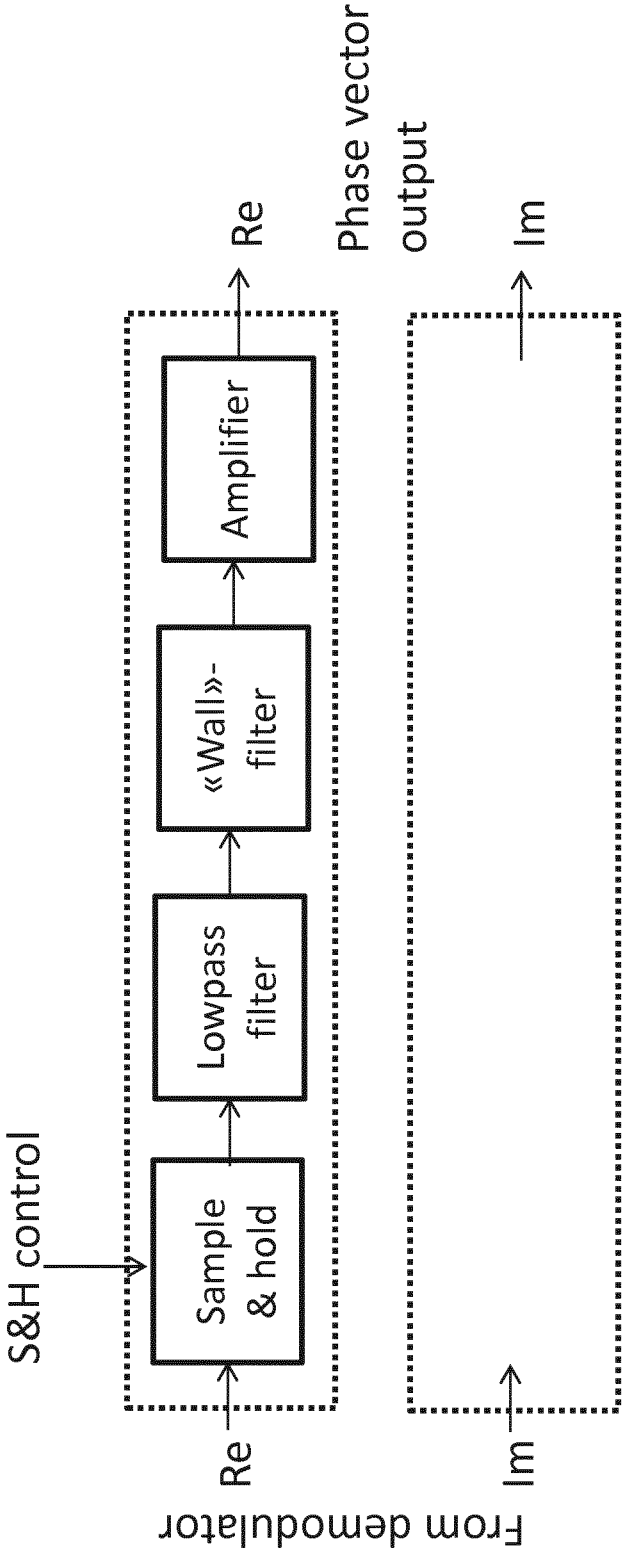
From demodulator
Re
Im
S&H control
Sample & hold
Lowpass filter
«Wall»-filter
Amplifier
Re
Im
Phase vector output

Figure 5

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2016/077426

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B8/08 A61B8/00 A61B5/113
ADD.

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

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 94/20021 A2 (ADVANCED MONITORS HOLDINGS LTD [GB]; SUMMERS JOHN BRIAN [GB]) 15 September 1994 (1994-09-15) page 1, lines 1-11; claims; figures page 1, line 23 - page 7, line 8 page 7, line 19 - page 15, line 5	1-23
X	US 2004/242997 A1 (GRIFFIN DENNIS P [US] ET AL) 2 December 2004 (2004-12-02) claims; figures paragraph [0003] - paragraph [0005] paragraph [0013] paragraph [0021] paragraph [0044] - paragraph [0046]	1-23

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[X] 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 January 2017	03/02/2017

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	Mundakapadam, S

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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.
X	US 4 122 427 A (KARSH HERBERT) 24 October 1978 (1978-10-24) column 1, lines 1-6,49 - column 2, line 49; claims; figures column 3, line 1 - column 5, line 35	1-23
A	US 2011/121996 A1 (GRIFFIN DENNIS P [US] ET AL) 26 May 2011 (2011-05-26) the whole document	1-23
A	US 2011/208060 A1 (HAASE WAYNE C [US] ET AL) 25 August 2011 (2011-08-25) paragraph [0045] - paragraph [0046]	1-23
A	CN 104 840 218 A (LENOVO BEIJING CO LTD) 19 August 2015 (2015-08-19) the whole document	1-23

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2016/077426

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9420021 A2	15-09-1994	AU 6041394 A	26-09-1994
		EP 0720443 A1	10-07-1996
		JP H08507706 A	20-08-1996
		US 5638824 A	17-06-1997
		WO 9420021 A2	15-09-1994
US 2004242997 A1	02-12-2004	NONE	
US 4122427 A	24-10-1978	NONE	
US 2011121996 A1	26-05-2011	NONE	
US 2011208060 A1	25-08-2011	NONE	
CN 104840218 A	19-08-2015	NONE	

专利名称(译)	用于呼吸监测的超声方法和装置		
公开(公告)号	EP3373821A1	公开(公告)日	2018-09-19
申请号	EP2016794355	申请日	2016-11-11
[标]申请(专利权)人(译)	拒绝		
申请(专利权)人(译)	RESPINOR AS		
当前申请(专利权)人(译)	RESPINOR AS		
[标]发明人	SOUZY NICOLAS ERIKSEN MORTEN BERARD ANDERSEN NICOLAY		
发明人	SOUZY, NICOLAS ERIKSEN, MORTEN BERARD-ANDERSEN, NICOLAY		
IPC分类号	A61B8/08 A61B8/00 A61B5/113		
CPC分类号	A61B5/113 A61B5/6823 A61B5/6832 A61B8/085 A61B8/4236 A61B8/4281 A61B8/4427 A61B8/488 A61B8/5207 A61B5/08 A61B8/08		
优先权	2015019985 2015-11-12 GB 2016014633 2016-08-30 GB		
外部链接	Espacenet		

摘要(译)

一种非侵入性地监测患者呼吸的方法包括：将超声波发射到身体内朝向患者身体的内部结构，内部结构是肝脏，脾脏或肾脏之一;选择深度范围;在深度范围的多个点处测量来自内部结构的超声回波信号的相位，用于至少第一和第二回波信号，在不同时间接收第一和第二回波信号;通过参考第一和第二回波信号之间的测量相位的差异来检测患者腹部内部结构的运动;从而通过将内部结构的运动与呼吸引起的运动相关联来监测患者的呼吸