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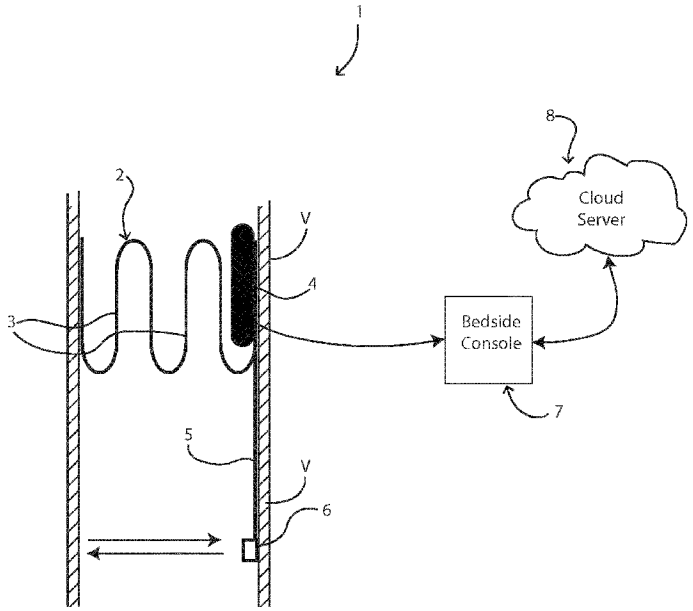

Fig.1

(57) Abstract: An implantable ultrasonic vascular sensor for implantation at a fixed location within a vessel, comprising at least one ultrasound transducer, a transducer drive circuit, and means for wirelessly transmitting ultrasound data from the at least one ultrasound transducer.

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IMPLANTABLE ULTRASONIC VASCULAR SENSOR

RELATED APPLICATIONS

WO2016/131020 and WO2017024051 are filed by the present Assignee and are incorporated by reference herein in their entirety.

FIELD OF THE DISCLOSURE

The present disclosure generally relates to the field of medical devices and methods for monitoring patient blood vessels (or "vascular lumen"), such as the inferior vena cava ("IVC").

INTRODUCTION

Conditions which may be monitored by IVC or other blood vessel monitoring

Heart failure is one of the most significant chronic conditions afflicting adult populations. In the United States, 5.7 million Americans have heart failure, with 870,000 new cases annually. As the population ages, this number is growing, as approximately 10% of the population over 80 suffers from heart failure.

In patients with chronic heart failure, significant costs are due to hospitalization to manage acutely decompensated heart failure (ADHF). Each re-hospitalization can last up to a week. ADHF is very often a result of some combination of a downturn in the heart's performance, a downturn in the kidney's removal of fluid from the bloodstream, and/or excessive intake of fluids and/or salt. This leads to a buildup of fluid in the vascular system, resulting in increased blood volume in the left atrium at higher pressure. This eventually leads to fluid filling the lungs and an inability to breathe. Managing these patients to prevent the need for re-hospitalization is extremely challenging. Non-invasive approaches to monitoring patients have been tried, such as weighing patients daily to detect fluid weight gain, or having a nurse call them daily to assess their health status, but these approaches have only modest effectiveness.

Although measurement of left atrial pressure, typically by measuring pulmonary artery wedge pressure, is commonly considered the most direct way to measure congestion in heart failure, there are other areas where congestion can be detected. When additional blood volume is added to the circulatory system, the IVC is one of the first places for that added volume to have an effect. The diameter of the IVC has demonstrated correlation with central venous pressure and right atrial pressure (as a proxy for left atrial pressure) as it flows directly into the right atrium

(and by extension left atrial pressure through the connection through the pulmonary circulation), and it may correlate with renal function and renal sodium retention, which are also very important prognostic factors of heart failure. Therefore, increasing IVC volume and/or pressure may be a very effective early indicator of worsening heart condition.

In addition to heart failure patients, hemodialysis patients have a chronic need for careful volume management. Since their kidneys aren't excreting fluid, they are constantly becoming overloaded with fluid. Furthermore, large volumes of fluid are involved in the hemodialysis process, and managing patients so that they don't end up hypovolemic or overloaded with fluid requires careful management.

There are other groups of patients who might benefit from such a monitor. For example, patients in septic shock or acute shock due to trauma are subject to hypoperfusion.

Current approaches to monitoring the IVC or other blood vessels

Prior studies of IVC dimensions have been conducted using external ultrasound imaging. This typically requires a highly trained physician or ultrasound technician to manage the ultrasound machine, ensure an appropriate connection of the transducer to the skin, position the ultrasound transducer in the appropriate location, identify the IVC, and take accurate measurements. This is not something that heart failure patients or their caregivers could typically be trained to do predictably and accurately with existing equipment. Moreover, these systems typically include large, complex, and expensive pieces of equipment which are not suitable for use outside of a specialized medical facility and are therefore not designed for serial measurements for chronic monitoring purposes.

Recent studies have indicated that the variation in IVC diameter over the respiratory cycle may be a more sensitive measurement of fluid overload and/or heart failure than simple measurement of average IVC diameter, volume, or pressure. During inspiration, intrathoracic pressure decreases, thereby increasing venous return and causing collapse of the IVC. During expiration, intrathoracic pressure increases, decreasing venous return and causing an increase in the diameter of the IVC.

While vessel dimensions may be measurable using external ultrasound, magnetic resonance imaging, computerized axial tomography, or other technologies, these imaging procedures must be administered in a hospital or other specialized facility. Furthermore, such procedures do not

permit continuous monitoring, and do not allow for monitoring of the patient at their home or other remote location. As a result, the condition of a heart failure patient can worsen into a critical state before care providers become aware of it, dramatically increasing the mortality risk and cost of treatment for the patient.

PCT publication numbers WO2016/131020 and WO2017/024051, assigned to the assignee of the present disclosure, describe approaches involving implanted and catheter-based devices for real time monitoring of IVC dimensions for the diagnosis and treatment of heart failure and other conditions.

The present disclosure is directed towards providing improved apparatus for blood vessel dimension monitoring.

SUMMARY OF THE DISCLOSURE

According to the present invention there is provided an implantable ultrasonic vascular sensor for implantation at a fixed location within a vessel, comprising:

at least one ultrasound transducer;

a transducer drive circuit; and

means for wirelessly transmitting ultrasound data from the at least one ultrasound transducer.

The at least one ultrasound transducer may comprise a first transducer for transmitting an ultrasound wave and a second transducer for receiving an ultrasound echo.

The implantable ultrasonic vascular sensor may be configured for untethered retention in a vessel. In other words, there is no catheter attached to the implant after implantation. By "implantation at a fixed location" it is meant that the sensor is an implant, not a catheter. The implantable ultrasonic vascular sensor is intended for retention in a vessel following withdrawal of a deployment catheter.

The at least one ultrasound transducer may comprise means for supporting the first transducer and the second transducer opposite one another.

The at least one ultrasound transducer may comprise means for supporting the first transducer and the second transducer adjacent each other.

The implantable ultrasonic vascular sensor may comprise means for supporting the first transducer and the second transducer back to back.

The implantable ultrasonic vascular sensor may further comprise a passive reflector attachable to a vessel wall.

The implantable ultrasonic vascular sensor may comprise a plurality of pairs of first and second transducers.

The implantable ultrasonic vascular sensor may further comprise means for supporting the plurality of pairs of first and second transducers for measuring across different chords of a vessel.

The or each transducer may be configured to transmit an ultrasound wave and receive an ultrasound echo.

The at least one transducer may be configured to provide an ultrasound wave having a beam width of between 5° and 14°.

The implantable ultrasonic vascular sensor may be configured to operate in real time for real time vessel monitoring.

The transducer drive circuit and at least one transducer may be configured to operate at a frequency in the range of 4MHz to 20 MHz.

The transducer drive circuit and at least one transducer may be configured to operate at a frequency in the range of 7 MHz to 15 MHz.

The implantable ultrasonic vascular sensor may comprise a plurality of transducers. The drive circuit may configured to time multiplex operation of the transducers.

The implantable ultrasonic vascular sensor may further comprise a support structure for supporting the or each transducer within a vessel.

The support structure may have a stent-like configuration for engaging a vessel wall around its periphery.

At least one transducer may be longitudinally separated from a main portion of the support structure.

At least one transducer may be mounted on a strut extending longitudinally from the support structure main portion.

The strut may be mechanically biased to lie against a vessel wall.

Preferably the support structure has little impact on physiological expansion or contraction of the vessel at a sensing site. In other words, in use, the support structure and the transducer(s) move with the vessel wall. A movement of the vessel wall in a radial direction would impart a corresponding movement of the transducer(s) in a radial direction.

The strut may comprise an anchor for direct anchoring to a vessel wall.

The anchor may extend from a tip of the strut.

The strut may comprise a coating to promote adhesion to a vessel wall.

The at least one transducer may include a piezoelectric element and associated electrodes.

The at least one transducer may comprise a matching layer on an ultrasonic signal path side of the piezoelectric element and having a thickness of approximately a quarter of the wavelength of operation of the piezoelectric element.

The at least one transducer may comprise an active piezoelectric layer with a thickness of approximately a half wavelength.

The at least one transducer may have a backing material for attenuation of emitted ultrasonic waves in a direction opposed to a preferred signal direction.

The backing material may comprise a carrier material with embedded particles.

The at least one ultrasound transducer may comprise:

a piezoelectric layer and first and second opposed electrodes on said piezoelectric layer;

a backing material configured to attenuate ultrasound waves and minimize reflection thereof in a direction away from a vessel volume; and

a matching layer having acoustic properties for optimizing ultrasound waves between said matching layer and blood in contact therewith;

wherein the transducer is configured to be positioned along a wall of the vessel with the matching layer exposed to blood and facing an opposing wall of the vessel.

The implantable ultrasonic vascular sensor may further comprise means for measuring an acoustic wave time of flight between an ultrasound transmitter and an ultrasound receiver.

The implantable ultrasonic vascular sensor may further comprise means for calculating the distance between the ultrasound transmitter and the ultrasound receiver based on the measured time of flight.

In accordance with the present invention there is further provided a blood vessel monitoring system comprising at least one implantable ultrasonic vascular sensor as described above, and a remote processor configured to receive the transmitted ultrasound data and calculate distance between the ultrasound transmitter and the ultrasound receiver based on the measured time of flight.

The blood vessel monitoring system may further comprise means for determining at least one blood vessel dimension from the received data.

The blood vessel monitoring system may further comprise means for recognizing a plurality of diffuse ultrasound echo wave responses and means for determining a value representing vessel diameter or diameter changes from said responses.

The blood vessel monitoring system may further comprise means for determining at least one parameter value derived from a blood vessel dimension.

The implantable ultrasonic vascular sensor may comprise a plurality of transducers arranged to transmit and receive across different chords, and the signal processing circuit may be configured to use data from said transducers to determine blood volume and/or vessel shape.

The signal processing circuit may be configured to operate according to a desired user pattern such as intermittent or continuous or a hybrid of intermittent and continuous.

The blood vessel monitoring system may comprise a component configured to be mounted internally in the patient and an external component outside the patient's body, and said components are configured to wirelessly communicate.

The blood vessel monitoring system may comprise a subcutaneous component arranged to communicate with the implantable ultrasonic vascular sensor provide the communication link to an external component.

The blood vessel monitoring system may further comprise a discrete power source arranged to be implanted subcutaneously at a remote location separated from the vascular implant.

The blood vessel monitoring system may further comprise a discrete power source arranged to be implanted subcutaneously at a location separated from the implantable ultrasonic vascular sensor.

In accordance with the present invention there is further provided a vascular monitoring method comprising:

implanting at least one ultrasound transducer within a vessel;

providing a drive signal to the at least one ultrasound transducer;

generating and transmitting an ultrasound wave;

detecting an ultrasound echo;

recording a time delay between the transmission of the ultrasound pulse and the detection of the ultrasound echo; and

wirelessly transmitting ultrasound data from the at least one ultrasound transducer.

Implanting at least one ultrasound transducer within a vessel may comprise implanting at least one ultrasound transducer within an inferior vena cava, IVC.

The ultrasound wave may have a beam width of between 5° and 14°.

The at least one transducer may be operating at a frequency in the range of 4MHz to 20 MHz.

The at least one transducer may be operating at a frequency in the range of 7 MHz to 15 MHz.

The method may further comprise calculating the distance between an ultrasound transmitter and an ultrasound receiver based on the time delay and wirelessly transmitting the distance.

The method may further comprise receiving the transmitted ultrasound data at a remote processor and calculating the distance between the ultrasound transmitter and the ultrasound receiver based on the time delay.

The method may further comprise determining at least one blood vessel dimension from the received data.

The method may further comprise recognizing a plurality of diffuse ultrasound echo wave responses and determining a value representing vessel diameter or diameter changes from said responses.

The method may further comprise determining at least one parameter value derived from a blood vessel dimension.

The method may further comprise using data from multiple transducers to determine blood volume and/or vessel shape.

The method may further comprise operating according to a desired user pattern such as intermittent or continuous or a hybrid of intermittent and continuous.

We describe a system for monitoring a blood vessel, the system comprising:

an implantable support structure configured to engage a blood vessel wall,
an ultrasonic sensor including one or more transducers mounted on or to the support structure at an orientation to direct ultrasonic waves across the vessel, and to receive ultrasonic waves,
a drive circuit for driving the transducer, and
a signal processing circuit for processing sensor outputs to monitor vessel width dimension and/or changes in dimension.

Preferably, the support structure has a stent-like configuration for engaging a vessel wall around its periphery. Preferably, at least one transducer is longitudinally separated from a main portion of the support structure, so that the structure main portion is substantially not in the path of ultrasonic waves and has little impact on physiologic expansion or contraction of the vessel at a sensing site.

Preferably, at least one transducer is mounted on a strut extending longitudinally from the support structure main portion.

In one example, the strut comprises an anchor for direct anchoring to a vessel wall in addition to being supported by the support structure. In one embodiment, the anchor extends from a tip of the strut.

In one example, the strut comprises a coating to promote adhesion to a vessel wall.

In some embodiments, the system comprises a passive reflector having an ultrasonic mismatch from blood, and being attachable to a vessel wall.

Preferably, the system comprises separate transducers for transmitting and receiving, in which at least one pair of transmit and receive transducers are arranged on the implant to be on opposite sides of the vessel. The system may comprise transmit and receive transducers which are separate or integrated, in which at least one transducer or transducer pair is arranged at approximately the same radial position in order to transmit an ultrasonic wave and receive a corresponding echo. In one embodiment, the sensor comprises a plurality of physically separate transducers mounted on a longitudinal strut extending from the support structure.

Preferably, the sensor comprises a plurality of pairs of transmit and receive transducers, arranged for measuring across different chords such as relatively orthogonal diameters of a vessel.

Preferably, at least one transducer includes a piezoelectric element and associated electrodes.

In one example, at least one transducer comprises a matching layer on an ultrasonic signal path side of the piezoelectric element and having a thickness of approximately a quarter of the wavelength of operation of the piezoelectric element.

Preferably, at least one transducer has an active piezoelectric layer with a thickness of approximately a half wavelength.

In one embodiment, at least one transducer has a backing material for attenuation of emitted ultrasonic waves in a direction opposed to a preferred signal direction.

Preferably, the backing material comprises a carrier material with embedded particles so that a wave emanating from the vibrating piezoelectric layer back surface in an unintended direction, such as away from a target and into the backing material, is absorbed and does not reflect back into a blood vessel in use.

In one example, at least one transducer comprises:

a piezoelectric layer and first and second opposed electrodes on said piezoelectric layer,

a backing material configured to attenuate ultrasound waves and minimize reflection thereof in a direction away from a vessel volume;

and

a matching layer having acoustic properties for optimizing ultrasound waves between said matching layer and blood in contact therewith;

wherein the transducer is configured to be located along a wall of the vessel with the matching layer exposed to blood and facing an opposing wall of the vessel.

Preferably, the transducer provides an ultrasound wave having a beam width of between 5° and 14°.

Preferably, the sensor and the circuit are configured to operate in real time for real time vessel monitoring.

In one example, the circuits comprise a component configured to be mounted internally in the patient and an external component outside the patient's body, and said components are configured to wirelessly communicate.

Preferably, the system comprises a subcutaneous component arranged to communicate with the sensor and provide the communication link to an external component.

Preferably, the system comprises a discrete power source arranged to be implanted subcutaneously at a location separated from the vascular implant.

Preferably, the drive circuit and at least one transducer are configured to operate at a frequency in the range of 4MHz to 20 MHz, and preferably at least 7MHz.

In one example, the drive circuit and at least one transducer are configured to operate at a frequency in the range of 7 MHz to 15 MHz.

Preferably, the sensor comprises a plurality of transducers and the drive circuit is configured to time multiplex operation of the transducers.

Preferably, the signal processing circuit is configured to recognize a plurality of diffuse ultrasound echo wave responses and to determine a value representing vessel diameter or diameter changes from said responses.

Preferably, the signal processing circuit is configured such that received waveform undergoes a Hilbert transform, whereby the timers stop when an echo waveform envelope exceeds a certain level.

In one example, the signal processing circuit is configured to determine at least one parameter value derived from a blood vessel dimension, such as blood volume.

Preferably, the sensor comprises a plurality of transducers arranged to transmit and receive across different chords, and the signal processing circuit is configured to use data from said transducers to determine blood volume and/or vessel shape.

Preferably, the signal processing circuit is configured to operate according to a desired user pattern such as intermittent or continuous or a hybrid of intermittent and continuous.

The disclosure also provides a non-transitory computer readable medium comprising software code for performing by a digital processor operations of a drive circuit and/or a signal processing circuit of a system of any embodiment.

BRIEF DESCRIPTION OF THE DRAWINGS

The disclosure will be more clearly understood from the following description of some embodiments thereof, given by way of example only with reference to the accompanying drawings in which:

Fig. 1 is a diagram showing an intravascular ultrasound measurement system having an implantable device or "implant" and a bedside console for communication with the implant, data logging, data processing, and for upload of data to local and/or remote servers;

Fig. 2 is a cross-sectional view showing the multiple layers of an ultrasound transducer of the implant;

Figs. 3 and 4 are sketches showing modes of operation of a transducer;

Fig. 5 is a diagram showing an implant having dedicated transmit and receive ultrasonic transducers mounted on diametrically opposed struts;

Fig. 6 is a diagram showing separate transmit and receive transducers mounted side-by-side on a single strut;

Fig. 7 shows an implant arrangement having two pairs of opposed transducers;

Figs. 8 and 9 are circuit block diagrams for systems of two embodiments; and

Figs. 10(a) to 10(d) are plots showing ultrasound responses which are processed by a signal processor of a system of the disclosure.

DETAILED DESCRIPTION

In various embodiments, blood vessel monitoring systems are described which include an implant with a sensor having at least one ultrasonic transducer, a data processing subsystem, a communications subsystem, and a battery power source. The transducers are supported by a stent-like support structure for both anchoring and positioning the device within a vessel such as the IVC. The support structure is flexible, elastic and highly compliant, having little influence on the normal movement and shape of the IVC.

In this specification the term "transducer" is intended to mean an ultrasound device including actively vibrating material such as a piezoelectric material and also including associated parts such as a matching layer and a backing layer. A "sensor" is an assembly of one or more transducers and all components involved for ultrasound transmitting and receiving including in some embodiments a passive reflector, as described in more detail below. The specific transducing part in which an applied voltage is transformed into mechanical vibrations is referred to as the piezoelectric material or layer.

Referring to Fig. 1, a system 1 comprises an implant 2-6 with a stent-like support structure 2 with a wave pattern 3 forming a hoop, and supporting an electronics housing 4. A longitudinal strut 5 extends from the structure 2, and is mechanically biased to be against a vessel wall, in use. An ultrasound transducer 6, comprising a piezoelectric active layer, is mounted on the strut 5, so that it is longitudinally spaced-apart from the structure 2, thereby having an unimpeded path across to the opposite side of the blood vessel and being spatially separated from the structure 2 so that the vessel is measured at a point which is not at risk of being constrained or distorted by the structure 2. The longitudinal strut 5 is configured to maintain the transducer 6 against the vessel wall while allowing the transducer 6 to move radially inwardly and outwardly with the wall during vessel contraction and expansion respectively. The transducer 6 is supported to be against the wall, and hence the strut 5 could in various embodiments be bowed, straight, angled, wavy, spring-loaded or have any other configuration to bias the transducer 6 against the vessel wall.

The system 1 also comprises a bedside console 7 wirelessly linked with the electronics housing 4 of the implant via a wireless transmitter in electronics housing and also linked with cloud servers 8, or any other data collection and processing equipment.

Support Structure 2 and Transducer Strut 5

The support structure 2 is sufficiently flexible and elastic to have little influence on the normal movement and shape of a blood vessel such as the IVC while still remaining in a fixed location in the vessel. Additionally, the longitudinal separation of the transducer 6 from support structure 2 helps to isolate it from any distortion of the vessel caused by support structure 2.

The strut 5 has a Nitinol spine alongside which are insulated electrical leads for the transducer 6.

In some embodiments, the transducer 6 and/or longitudinal strut 5 may be configured to be fixed to the vessel wall to ensure that the transducer moves with it. For example, the transducer 6 and/or the longitudinal strut, and/or the support structure 2 may have barbs, hooks, or other features on its outer side that penetrate or engage the wall tissue. The transducer 6 and/or longitudinal strut 5 may alternatively or additionally be coated with a material that adheres to tissue or encourages tissue growth around or into these components. In other embodiments the longitudinal strut 5 may have a tip extending beyond the transducer 6 and configured to penetrate into the vessel wall.

The structure 2 diameter is preferably in the range of 5 mm to 40 mm, and the length is preferably in the range of 10 mm to 40 mm. In one example the transducer 6 has a width of 4 mm, a thickness of 3 mm, and a length of 3mm, and the tubular electronics housing 4 with domed ends, has a diameter of 5 mm and a length of 10 mm.

The ultrasound transducer 6 is positioned such that it lies on the endothelium of the IVC wall, directing ultrasound pressure waves towards the diametrically opposing side of the IVC interior wall. Due to the acoustic impedance difference between the vessel wall and blood, the IVC wall is a significant reflector of ultrasound waves. Hence, the ultrasound waves are reflected from the opposing IVC wall, returning back to the ultrasound transducer where they are detected. The time delay between the transmitted ultrasound pulse and the received echo signal is recorded, allowing for the IVC diameter to be calculated.

In various embodiments, the support structure 2 may have one, two, or more rings or hoops and interconnecting longitudinal members or struts between the hoops, the hoops being resiliently biased radially outwardly in a stent-like manner to engage the vessel wall and securely anchor the device 2-6 in the vessel. The rings or hoops may have a sinusuoidal, zig-zag, or other radially collapsible configuration to facilitate delivery through the vessel to the desired location of

placement and to impart a relatively consistent radial fixation force against the vessel wall over a wide range of diameters.

Ultrasound Transducer

Referring to Fig. 2 the transducer 6 is shown diagrammatically in section. There is a piezoelectric layer 10 at its core, with electrodes 11 and 12 above and below, and a backing material 15 mounted between the active layer 10 and the transducer housing 18. There is also a matching layer 16 over the electrode 11. These layers are mounted within a sealed housing 18 of biocompatible polymeric material. The matching layer 16 is for direct contact with the blood in the vessel.

The piezoelectric material might be a piezoelectric ceramic, a piezoelectric single crystal or a piezoelectric composite material. The piezoelectric material may be diced in one direction or in orthogonal directions for reduction of lateral mode oscillations, due to lateral dimensions which approach a full wavelength.

In one embodiment, the piezoelectric layer is suitable to be driven at 4 MHz and has a thickness of 1.0 mm, and the other layers of the transducer raise this to a total thickness value in the range of 4 to 6mm. In various embodiments the piezoelectric material might need to be in excess of 3 mm in width, and might preferably be made in a composite to break up lateral modes.

Up to limits, higher drive frequencies are preferred because a sharper beam is created, increasing signal strength and decreasing the possibility of echoes from parts of the vessel other than the diametrically opposed side. Higher frequencies have their limit, however. Blood attenuation is approximately 0.15 dB/MHz/cm. So, for a 2 cm diameter vessel, at 5 MHz, the attenuation is 3 dB, while at 20 MHz it is 12 dB. In the 30 MHz range, echoes from blood begin to compete in amplitude from those of tissue, and wall determination becomes yet more difficult. Therefore the preferred range of drive frequency is 4 MHz to 20MHz, and more preferably 7 MHz to 15MHz.

In general, the piezoelectric material thickness scales inversely proportionately to the frequency of operation.

The transducer may have a single piezoelectric crystal, or a composite “pillar” structure. The pillar transducer construction may provide a lower noise signal with better signal to noise ratio, and a

relatively small aperture. A single crystal piezoelectric layer would have better amplitude conversion (voltage to displacement, and reverse) but would draw a higher current.

The matching layer 16 preferably has a thickness of a quarter wavelength.

The overall transducer may be mounted with an air gap or backing material 15 on the back side. This feature is to ensure that the waves emanating from the vibrating piezoelectric material in the unintended direction (i.e. away from the target and into the backing material), is absorbed and does not reflect back into the piezoelectric material. As shown in Fig. 2, in this embodiment there is backing material 15 of an epoxy with cork particles, chosen to have a thickness for good attenuation.

The ultrasound transducer beam profile is mainly dependent on excitation pulse frequency. For example, 4 MHz with a 3mm aperture gives a 6 dB beam width of 24°, 8 MHz gives 12°, and 10 MHz gives 9°. When targeting non planar surfaces, this can significantly affect sensor operation. There is a trade-off between beam width and angle-to-target and signal-to-noise ratio, with narrower beams providing higher signal-to-noise ratio.

Fig. 3 shows a narrow beam of 10MHz giving a 9° beam width normal to target, and therefore a good signal response. However, as shown in Fig. 4, a beam with these parameters results in the echo being missed in some circumstances. The transducer is preferably oriented such that the transmit signal is perpendicular to the opposing vessel wall to ensure that a maximum reflected signal is received by the transducer. However, perfect orientation may be challenging, and with vessel distension/contraction and other motion the angle of the vessel wall may change relative to the transducer. For this reason, a wider beam width may be more important to ensure a signal is received by the transducer.

Alternatively, as described in more detail below it may be preferred to rely on the echo structure from within the vessel wall to make measurements, as the strong specular reflection of the blood/wall interface may not always be achievable as compared to the diffuse echoes from within the vessel wall.

The following are exemplary aspects of the ultrasonic transducer for advantageous use in the application of monitoring width dimension of a blood vessel such as the IVC.

- The matching layer 16 is preferably 1/4 λ thick
- The electrodes 11 and 12 are of gold or nickle, applied with In:Ag solder
- The backing material 15 is lamination epoxy, Epotek 301
- The piezoelectric layer has a thickness of 1/2 λ, and an impedance of Zc ~ 33 M Rayles
- The backing material has a thickness and a composition to be attenuative enough to prevent reflection with an impedance to shape waveform. This may alternatively be of a rubber material, preferably embedded with particles.
- It is sub optimal if the width-to-thickness ratio of the transducer is in the range of ~ 0.7 < W/T < 5.0
- Matching layer material 16 may be Henkle Loctite Stycast 3103 epoxy, Zm ~ 4.6 M Rayls.

By way of example, for operation at 7.5 MHz, a CTS 3202HD piezoelectric ceramic with a thickness of approximately 0.3 mm (half wavelength) a surface dimension of 2.5 mm square, facing into the vessel was used. The ceramic was plated on both sides with approximately 0.2 microns of gold. The front surface matching layer material was a Henkel Loctite Stycast 3103 filled epoxy with an acoustic impedance of 4.6 MRayls, which was cast, adhesively bonded to the ceramic using EpoTek 301 epoxy, and lapped to one quarter wavelength thickness, as determined by impedance measurements. The backing material was alternatively air or a silicone rubber loaded with cork powder (acoustic impedance approximately 1.7 MRayls). 0.05 mm diameter copper leads were soldered to the opposing electrodes on the ceramic with 97:3::In:Ag solder. At approximately 30 mm from the ceramic, the leads were attached to either twisted pair wires or 50 Ohm coaxial cable for connection to the electronics.

Alternative Transducer Mounting Arrangements

Fig. 5 shows an implant 20 with a support structure 21, electronics housing 22, two longitudinal struts 25 and 23 on which are transmit and receive transducers 26 and 24, respectively. In this arrangement, the acoustic wave time of flight between transmitter and receiver is only half of that for a single combined transmitter/receiver for which the ultrasound waves traverse a round trip. Further, the signal to noise ratio is better since there is no reliance on a weak echo from a tissue/blood interface. Signal processing is required to compensate for the thickness of both the transmitter and the receiver, and it is necessary to ensure that both struts 25 and 23 keep the respective transducer parts against the vessel wall. If the transmit and receive functions are separate, at opposite sides of a vessel such as in Fig. 5, the system processors do not need to take account of the quality of reflection from the vessel wall.

A major advantage of using separate transducers for transmit and receive functions is to isolate transmit ring-down noise from the received signal. This noise would make it extremely difficult to set a meaningful threshold. Note in particular the noise on the waveforms of Figs. 10(a)-(d), immediately to the right of the transmit burst. With transmit ring-down noise, the time system would have to electronically clamp the signal to zero after transmission, and then open up sufficiently before wall echoes are anticipated.

Fig. 6 shows an implant 30 with a support structure 31, electronic housing 32, a strut 33, and separate transmit and receive transducers 34 and 35 mounted adjacent to each other or linearly spaced apart on the same strut 33 on one side of the vessel. This arrangement allows a greater signal to noise ratio for signal processing with the avoidance of interference in the received echo signal from the transmit burst. Where the transmit and receive functions are separate and on the same strut, (Fig. 6) it is preferable that they are about 0.5mm to 5mm apart.

A system with two transducers deployed at a longitudinal distance from each other, either supported by the same or different support structures, may also be implemented to measure a Doppler shift in the received signal. This would allow an estimate of volume flow.

Fig. 7 shows a further configuration 40 having two pairs of transmit/receive transducers 41, 42 oriented at 90° relative to each other. This allows determination of diameters in two orthogonal directions. Advantageously this configuration allows both the anterior-posterior dimension and medial-lateral dimension to be monitored, allowing the processor to determine IVC geometry and blood volume. Also, it allows a digital processor to perform modelling of the vessel cross-section, for example to monitor major and minor axes. Such axes may be used to model the vessel cross-section as a parallelogram and possible ellipse. The circuits may be configured to perform data correction with parallelogram edge and diagonal correction, by averaging opposed parallelogram sides. Also, the circuits may be configured to perform ellipse reconstruction to model a vessel shape, based on chordal lengths such as parallelogram side calculations, and they may be configured to apply a correction to compensate for change from a round to elliptical shape of the support structure in end view.

It is envisaged that there may be more than two transmitter/receiver transducer pairs, e.g. up to four or more pairs of transducers, and the above benefits therefore also apply, providing even further data concerning the full volume and shape of the vessel.

It is also possible to position two transducers back-to-back near the middle of the vessel lumen. Then one transducer could be used to measure the distance to one wall, and the other could be used to measure the distance to the opposite wall. The sum of those distances is the diameter of the vessel.

A passive reflector may be provided to provide a strong reflection. This may be embedded within or individually anchored to the vessel wall opposite the transmit/receive transducer. Alternatively, a passive reflector may be mounted on a longitudinal strut attached to the support structure to which the transducer is coupled. Any such passive reflector provides increased reflectivity as compared to a blood/tissue interface.

In other embodiments there may be a co-implanted passive reflector or a second receive transducer on or within the opposing wall of the vessel. This reflector would serve to ensure a strong, perpendicular reflected signal back to the transducer. This reflector would need to be mounted so as not to impact the motion of the wall but remain in contact with it. The reflector may be on a longitudinal strut extending from the opposite side of the support structure 2, 180° apart from and parallel to the strut supporting the transmitter and receiver components. Alternatively a passive reflector may be mounted to or implanted within the wall of the vessel opposite the location of transducer. The passive reflector will be composed of a material having an impedance mismatch with vessel wall tissue and/or blood, causing a strong reflection of the transmitted ultrasound signal back to the transducer. The passive reflector may comprise a staple, button, barb, or rivet configured to penetrate or fasten to the inner wall of the vessel. Alternatively the passive reflector may comprise an injectable substance such as a flowable material, pellets, or beads which can be injected into the wall tissue.

Transducer Drive and Signal Processing

Fig. 8 shows a transducer drive circuit, in which there are components as follows: P (pulser), L (limiter), P (pre-amplifier), F (band-pass filter), LA (linear amplifier), TGC (time gain compensation), and C (compression amplifier). The transducer 6 is located immediately after the pulser P, the received signals being initially handled by the limiter L, followed by the pre-

amplifier, band-pass filter, linear amplifier, time gain compensation, and the compression amplifier.

These components are within the implant electronics housing 4. The signal processor provides the wireless signals to the console 7 using Bluetooth, or an alternative local area wireless protocol. There may alternatively be a separate wireless communication interface or other wireless transceiver.

Fig. 9 shows a circuit which is suitable if integrated on a single chip, and the same annotation is used as in Fig. 8. The component C is a compression amplifier, and a digital input/output function provides time of flight and other data to the external console.

Power is provided by an implantable battery source, of a type known in the art, which is encapsulated within the housing 4. Alternatively an extra vascular power source could be used, this could be located within a subcutaneous pocket, as per implanted pacemakers, and connected to the electronics unit via a lead.

The received ultrasound signals provide data which can be processed to give a complete and accurate measurement of the IVC dimensions and further, measurements of the blood flow, blood volume, blood pressure, and possibly blood chemistry including hematocrit and oxygenation. The ultrasound echo provides data representing a diameter of the blood vessel, and from this basic data a range of derived values may be calculated as noted above.

Signal processing may involve a full waveform analysis, preferably with averaging. It may include a comparator, implemented by a System on Chip ("SOC") or a microprocessor. The wiring may be twisted pairs or shielded coax. Alternatively, the signal processor may simply have a threshold signal intensity detector, which might require less electrical processing power.

Operation of the System and Data Analysis

The IVC contracts and expands with each respiration as well as with each cardiac cycle. Periodic IVC diameter measurements may thus be taken over multiple respiratory cycles, allowing for the recording of maximum and minimum diameters, from which a measure of collapsibility can be determined. The system may measure at any other desired intervals.

The recorded data is transmitted via radio frequency (RF) communication to the external console 6. In an alternative embodiment, some or all of the data may be locally stored on the implant. In general, the data processing, memory, and storage resources may be distributed in any suitable manner between the implant and the external equipment, provided the implant electronics unit is not excessively large, physically.

In another embodiment a subcutaneous monitor device may be provided to communicate with the implant, store the data, and to then transmit it to outside the body.

In one embodiment, the drive circuit sets a threshold, starts a timer on the transmit burst, and stops the timer on the first waveform crossing of the threshold. This number is then transmitted to the external processor. Alternatively, the received waveform undergoes a Hilbert transform, whereby the timers stop when the echo waveform envelope exceeds a certain level. This type of processing has significant advantages in signal-to-noise improvements.

Monitoring may be performed continuously or for intermittent periods, depending upon the desired trade-off between data intensity and battery life. It might be most efficient and physiologically relevant to take measurements only at night, when the patient is lying down and at rest. It might be desirable to intermittently measure IVC dimensions at random, or at specific time intervals. Although measurements may start and stop at random or preconfigured points along the respiratory cycle, it is intended that the measurement period cover multiple breathing cycles to enable IVC maxima and minima be identified.

Alternatively, the device may intermittently take continuous measurements over one or more entire cardiac and/or respiratory cycles, to get an effective measurement of the maximum and minimum IVC volumes. The difference between those minimum and maximum volumes may be an important prognostic indicator. If the overall IVC diameter is large and or there is only a small variation between minimum and maximum IVC diameters, that may be an indicator of congestion.

Referring to Figs. 10(a)-(d), time moves from left to right, and it can be seen that a transmit pulse on the left is followed on the right by a number of receive echoes in some cases. Ideally one would like to see a strong well-defined received echo from the IVC wall, as seen in Fig. 10(a). However, we have found that most often ultrasound reflection from a vessel wall is in the form of multiple

reflections, each from within the vessel wall. These layers are individual tissue mis-matches within the vessel wall.

A strong, well-defined received echo as in Fig. 10(a) results from a normal reflection off the vessel wall, and is not always achievable with the dynamic variations of the vessel. More commonly, a string of diffuse echoes as in Figs. 10(b), 10(c), and 10(d) is achieved, wherein these weaker echoes result from the cellular structure of the vascular wall.

The signal processing of either the electronics on the implant, the bedside console, or the cloud server recognise such weaker sub-responses and may use for example edge detection (especially for diameter measurement) and/or averaging (especially for diameter variation tracking) to more accurately determine vessel diameter and/or collapsibility.

By way of background regarding diffuse reflection and specular reflection, IVUS images, and even echo cardiograms, rely on diffuse echoes, and where a normal reflection occurs (in cardiology, typically at the apex of the heart), a bright ring appears on the display. It would be preferable to have more specular reflections as shown in Fig. 10(a), but diffuse reflections, as shown in Figs. 10(b) to (d), are more common.

Alternatives

There are embodiments where multiple, separate transducers are used as dedicated transmit and receive transducers in order to reduce noise in the system. These could also be used to measure the vessel in multiple planes, thus generating a more complex and accurate shape of the vessel rather than a simple single diameter. These transducers could also be longitudinally disposed along the length of the device to provide more predictable send receive response by limiting the curvature and angulation of the vessel at the target location.

The disclosure is not limited to the embodiments described but may be varied in construction and detail.

CLAIMS

1. An implantable ultrasonic vascular sensor for implantation at a fixed location within a vessel, comprising:

at least one ultrasound transducer;

a transducer drive circuit; and

means for wirelessly transmitting ultrasound data from the at least one ultrasound transducer.

2. The implantable ultrasonic vascular sensor of claim 1 wherein the at least one ultrasound transducer comprises a first transducer for transmitting an ultrasound wave and a second transducer for receiving an ultrasound echo.

3. The implantable ultrasonic vascular sensor of claim 2, further comprising means for supporting the first transducer and the second transducer opposite one another.

4. The implantable ultrasonic vascular sensor of claim 1 or claim 2, further comprising means for supporting the first transducer and the second transducer adjacent each other.

5. The implantable ultrasonic vascular sensor of claim 1 or claim 2, further comprising means for supporting the first transducer and the second transducer back to back.

6. The implantable ultrasonic vascular sensor of any preceding claim, further comprising a passive reflector attachable to a vessel wall.

7. The implantable ultrasonic vascular sensor of any of claims 2 to 6, comprising a plurality of pairs of first and second transducers.

8. The implantable ultrasonic vascular sensor of claim 7, further comprising means for supporting the plurality of pairs of first and second transducers for measuring across different chords of a vessel.

9. The implantable ultrasonic vascular sensor of claim 1, wherein the or each transducer is configured to transmit an ultrasound wave and receive an ultrasound echo.

10. The implantable ultrasonic vascular sensor of any preceding claim, wherein the at least one transducer is configured to provide an ultrasound wave having a beam width of between 5° and 14°.

11. The implantable ultrasonic vascular sensor of any preceding claim configured to operate in real time for real time vessel monitoring.

12. The implantable ultrasonic vascular sensor of any preceding claim wherein the transducer drive circuit and at least one transducer are configured to operate at a frequency in the range of 4MHz to 20 MHz.

13. The implantable ultrasonic vascular sensor of any of claims 1 to 11, wherein the transducer drive circuit and at least one transducer are configured to operate at a frequency in the range of 7 MHz to 15 MHz.

14. The implantable ultrasonic vascular sensor of any preceding claim, comprising a plurality of transducers and wherein the drive circuit is configured to time multiplex operation of the transducers.

15. The implantable ultrasonic vascular sensor of any preceding claim, further comprising a support structure for supporting the or each transducer within a vessel.

16. The implantable ultrasonic vascular sensor of claim 15, wherein the support structure has a stent-like configuration for engaging a vessel wall around its periphery.

17. The implantable ultrasonic vascular sensor of claim 15 or claim 16, wherein at least one transducer is longitudinally separated from a main portion of the support structure.

18. The implantable ultrasonic vascular sensor of claim 17, wherein at least one transducer is mounted on a strut extending longitudinally from the support structure main portion.

19. The implantable ultrasonic vascular sensor of claim 18, wherein the strut is mechanically biased to lie against a vessel wall.

20. The implantable ultrasonic vascular sensor of any of claims 15 to 19, wherein the support structure has little impact on physiological expansion or contraction of the vessel at a sensing site.

21. The implantable ultrasonic vascular sensor of any of claims 18 to 20, wherein the strut comprises an anchor for direct anchoring to a vessel wall.

22. The implantable ultrasonic vascular sensor of claim 21, wherein the anchor extends from a tip of the strut.

23. The implantable ultrasonic vascular sensor of any of claims 18 to 22, wherein the strut comprises a coating to promote adhesion to a vessel wall.

24. The implantable ultrasonic vascular sensor of any preceding claim, wherein the at least one transducer includes a piezoelectric element and associated electrodes.

25. The implantable ultrasonic vascular sensor of any preceding claim, wherein the at least one transducer comprises a matching layer on an ultrasonic signal path side of the piezoelectric element and having a thickness of approximately a quarter of the wavelength of operation of the piezoelectric element.

26. The implantable ultrasonic vascular sensor of any preceding claim, wherein the at least one transducer comprises an active piezoelectric layer with a thickness of approximately a half wavelength.

27. The implantable ultrasonic vascular sensor of any preceding claim, wherein the at least one transducer has a backing material for attenuation of emitted ultrasonic waves in a direction opposed to a preferred signal direction.

28. The implantable ultrasonic vascular sensor of claim 27, wherein the backing material comprises a carrier material with embedded particles.

29. The implantable ultrasonic vascular sensor of any preceding claim, wherein the at least one ultrasound transducer comprises:

a piezoelectric layer and first and second opposed electrodes on said piezoelectric layer;

a backing material configured to attenuate ultrasound waves and minimize reflection thereof in a direction away from a vessel volume; and

a matching layer having acoustic properties for optimizing ultrasound waves between said matching layer and blood in contact therewith;

wherein the transducer is configured to be positioned along a wall of the vessel with the matching layer exposed to blood and facing an opposing wall of the vessel.

30. The implantable ultrasonic vascular sensor of any preceding claim, further comprising means for measuring an acoustic wave time of flight between an ultrasound transmitter and an ultrasound receiver.

31. The implantable ultrasonic vascular sensor of claim 30, further comprising means for calculating the distance between the ultrasound transmitter and the ultrasound receiver based on the measured time of flight.

32. A blood vessel monitoring system comprising at least one implantable ultrasonic vascular sensor of any preceding claim, and a remote processor configured to receive the transmitted ultrasound data and calculate distance between the ultrasound transmitter and the ultrasound receiver based on the measured time of flight.

33. The blood vessel monitoring system of claim 32, further comprising means for determining at least one blood vessel dimension from the received data.

34. The blood vessel monitoring system of claim 32 or claim 33, further comprising means for recognizing a plurality of diffuse ultrasound echo wave responses and means for determining a value representing vessel diameter or diameter changes from said responses.

35. The blood vessel monitoring system of any of claims 32 to 34, further comprising means for determining at least one parameter value derived from a blood vessel dimension.

36. The blood vessel monitoring system of any of claims 32 to 35, wherein the implantable ultrasonic vascular sensor comprises a plurality of transducers arranged to transmit and receive across different chords, and the signal processing circuit is configured to use data from said transducers to determine blood volume and/or vessel shape.

37. The blood vessel monitoring system of any of claims 32 to 36, wherein the signal processing circuit is configured to operate according to a desired user pattern such as intermittent or continuous or a hybrid of intermittent and continuous.

38. The blood vessel monitoring system of any of claims 32 to 37, comprising a component configured to be mounted internally in the patient and an external component outside the patient's body, and said components are configured to wirelessly communicate.

39. The blood vessel monitoring system of any of claims 32 to 38, wherein the system comprises a subcutaneous component arranged to communicate with the implantable ultrasonic vascular sensor provide the communication link to an external component.

40. The implantable ultrasonic vascular sensor of any of claims 1 to 31 further comprising a discrete power source arranged to be implanted subcutaneously at a remote location separated from the vascular implant.

41. The blood vessel monitoring system of any of claims 32 to 39 further comprising a discrete power source arranged to be implanted subcutaneously at a location separated from the implantable ultrasonic vascular sensor.

42. A vascular monitoring method comprising:

implanting at least one ultrasound transducer within a vessel;

providing a drive signal to the at least one ultrasound transducer;

generating and transmitting an ultrasound wave;

detecting an ultrasound echo;

recording a time delay between the transmission of the ultrasound pulse and the detection of the ultrasound echo; and

wirelessly transmitting ultrasound data from the at least one ultrasound transducer.

43. The method of claim 42, wherein implanting at least one ultrasound transducer within a vessel comprises implanting at least one ultrasound transducer within an inferior vena cava, IVC.

44. The method of claim 42 or claim 43, wherein the ultrasound wave has a beam width of between 5° and 14°.

45. The method of any of claims 42 to 44, wherein the at least one transducer is operating at a frequency in the range of 4MHz to 20 MHz.

46. The method of any of claims 42 to 44, wherein the at least one transducer is operating at a frequency in the range of 7 MHz to 15 MHz.

47. The method of any of claims 42 to 46, further comprising calculating the distance between an ultrasound transmitter and an ultrasound receiver based on the time delay and wirelessly transmitting the distance.

48. The method of any of claims 42 to 46, further comprising receiving the transmitted ultrasound data at a remote processor and calculating the distance between the ultrasound transmitter and the ultrasound receiver based on the time delay.

49. The method of any of claims 42 to 48, further comprising determining at least one blood vessel dimension from the received data.

50. The method of any of claims 42 to 49, further comprising recognizing a plurality of diffuse ultrasound echo wave responses and determining a value representing vessel diameter or diameter changes from said responses.

51. The method of any of claims 42 to 50, further comprising determining at least one parameter value derived from a blood vessel dimension.

52. The method of any of claims 42 to 51, further comprising using data from multiple transducers to determine blood volume and/or vessel shape.

53. The method of any of claims 42 to 52, further comprising operating according to a desired user pattern such as intermittent or continuous or a hybrid of intermittent and continuous.

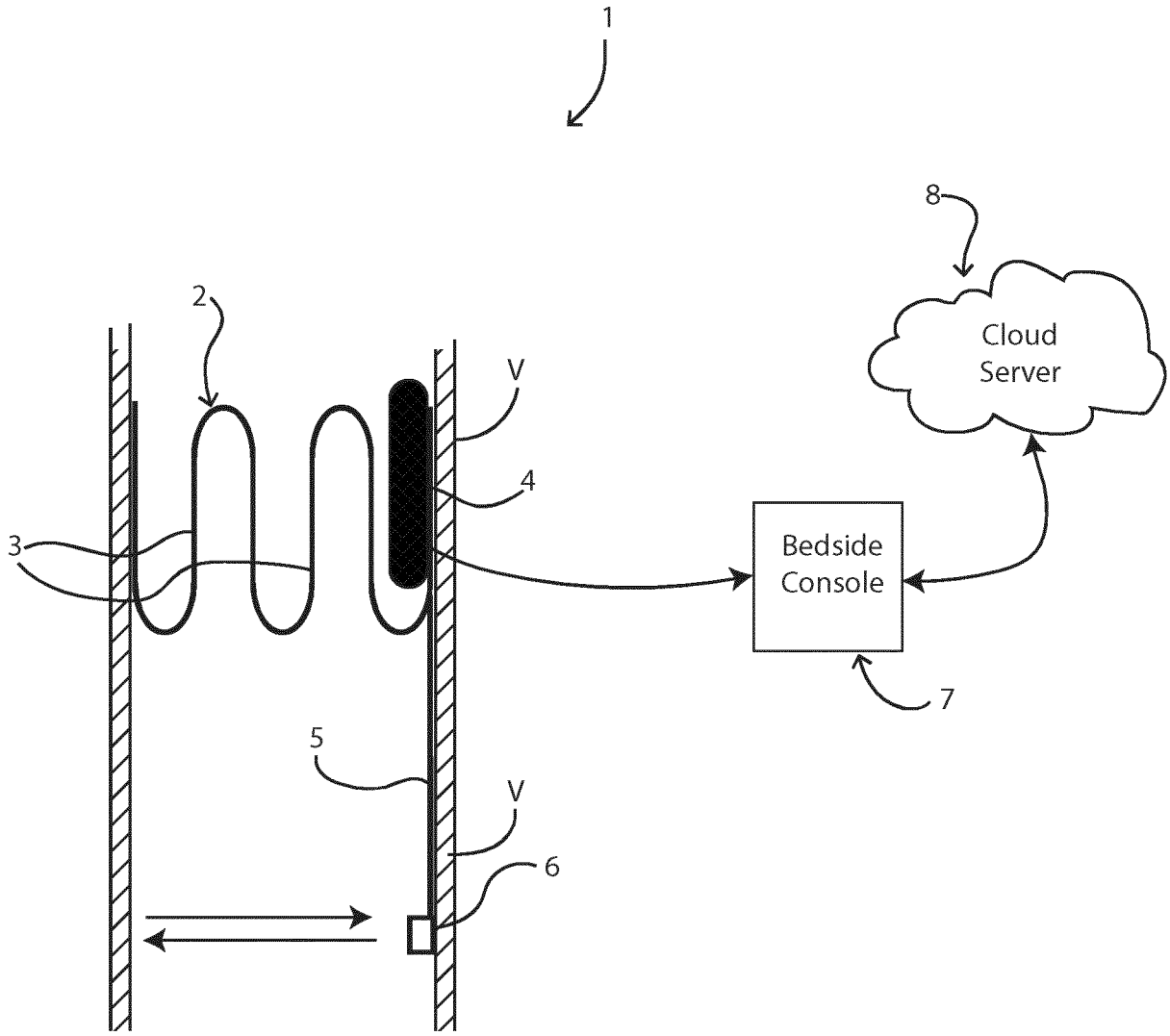


Fig.1

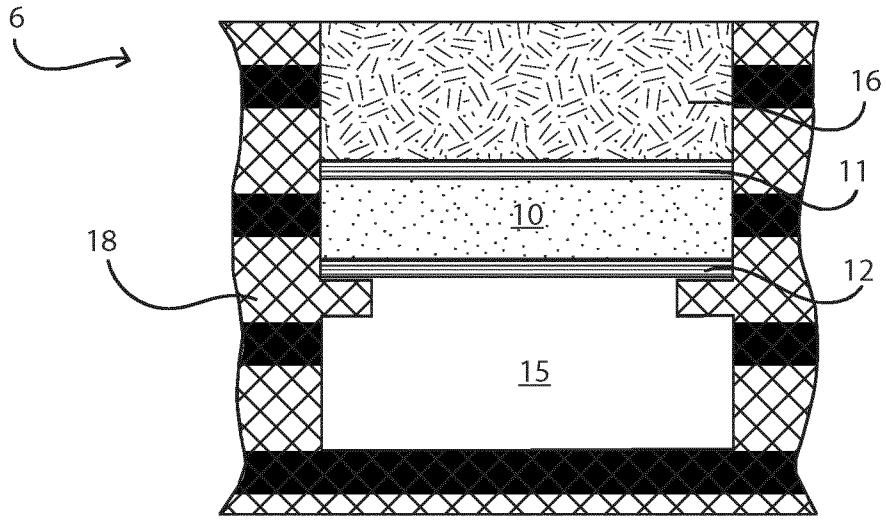


Fig.2

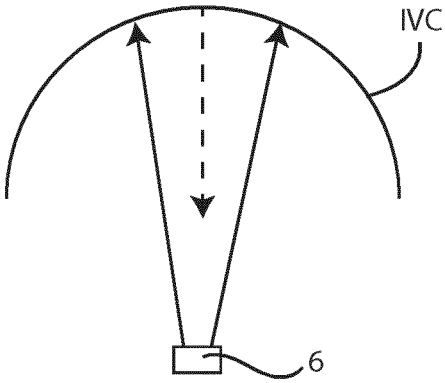


Fig.3

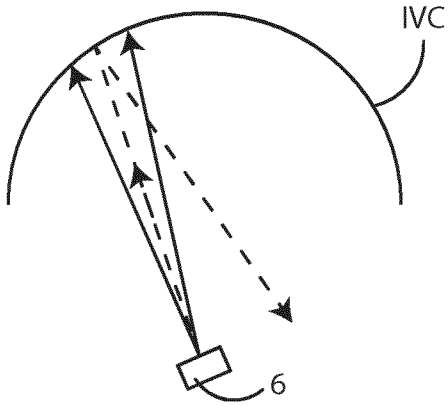


Fig.4

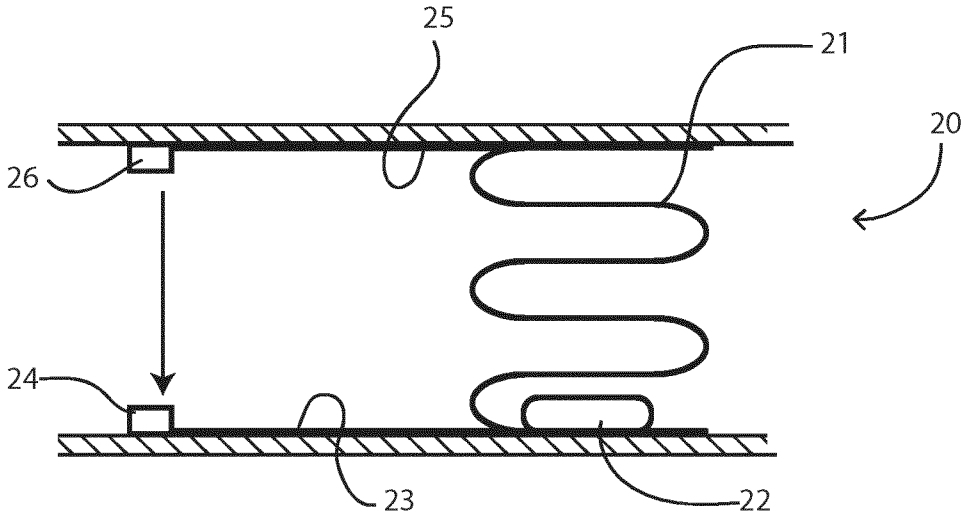


Fig.5

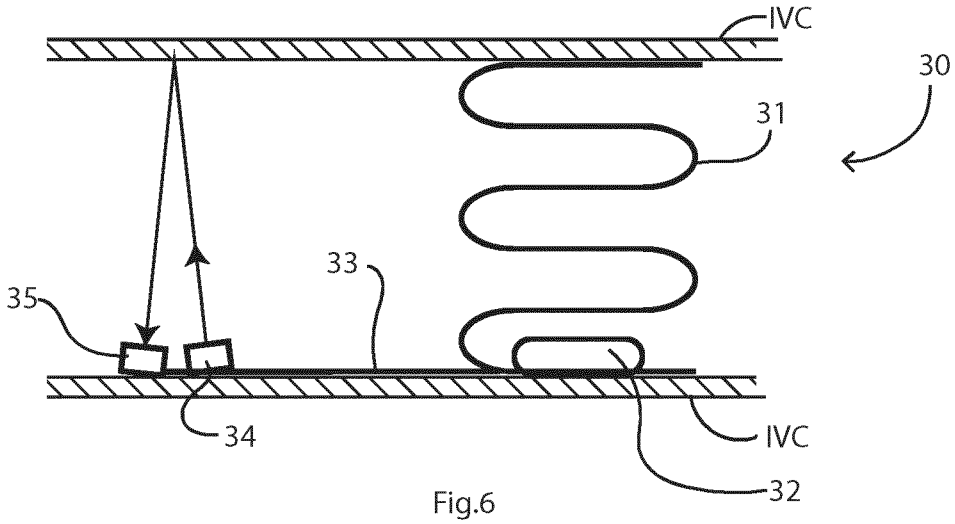


Fig.6

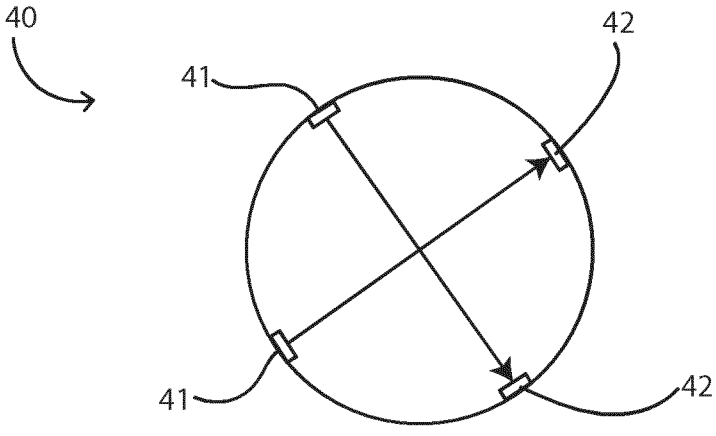
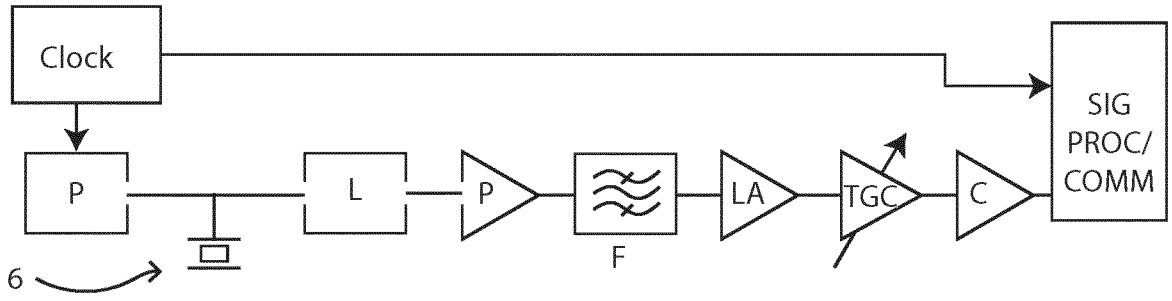


Fig.7



F= =

P=pulser, L=Limiter, P=Pre Amplifier, Band Pass filter, LA Linear Amplifer,
TGC = Time Gain compensation, C=Compression amplifer

Fig.8

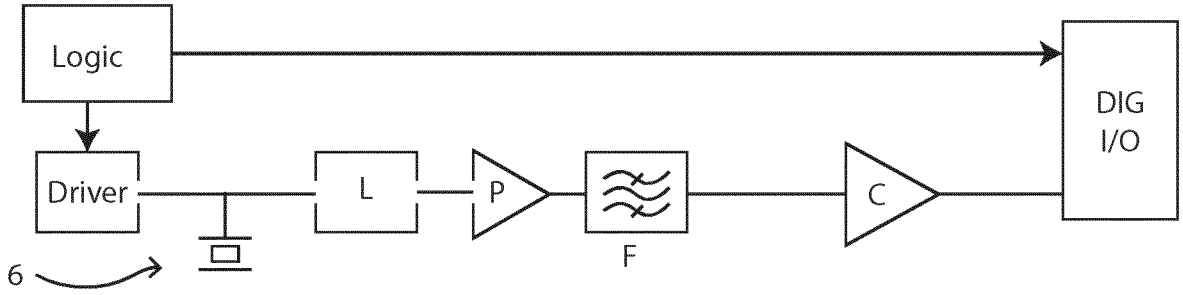


Fig.9

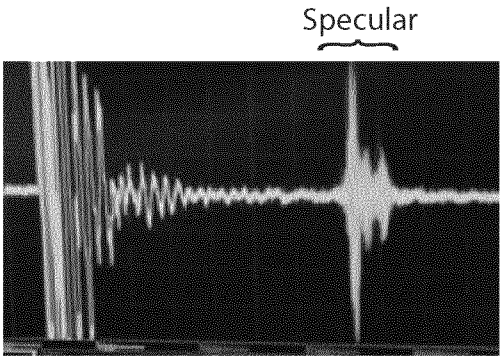


Fig.10(a)

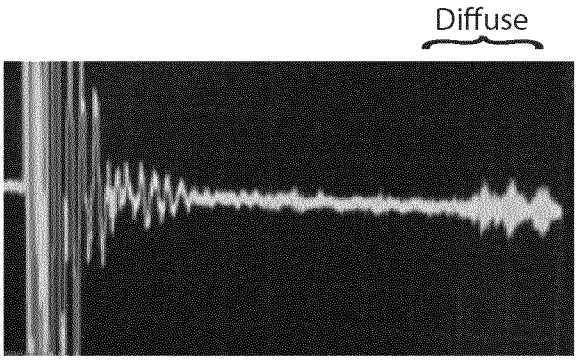


Fig.10(b)

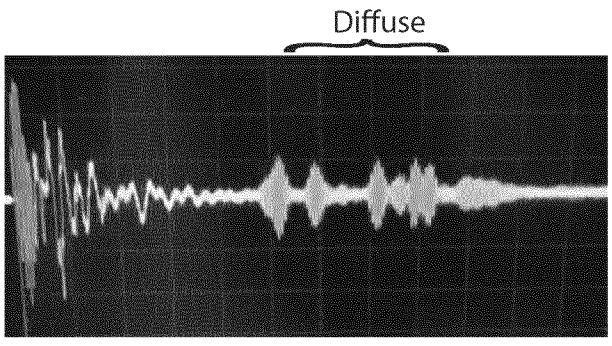


Fig.10(c)

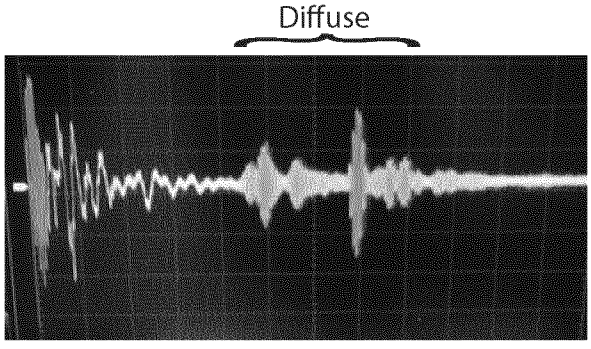


Fig.10(d)

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2018/064383

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B8/08 A61B8/00 A61B8/12
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	US 6 053 873 A (GOVARI ASSAF [IL] ET AL) 25 April 2000 (2000-04-25) column 15, line 52 - column 16, line 14 column 16, line 65 - column 17, line 1 figure 9 -----	1-5,9, 11,15, 16,20
X	WO 2016/131020 A1 (FOUNDRY INNOVATION & RES 1 LTD [IE]) 18 August 2016 (2016-08-18) cited in the application paragraphs [0047], [0049], [0051], [0052] figure 1 ----- -/--	1-41

[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
13 August 2018	21/08/2018

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	Willig, Hendrik

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

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2018/064383

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 3 568 661 A (FRANKLIN DEAN L) 9 March 1971 (1971-03-09) abstract figure 1	1-41
A	US 4 926 875 A (RABINOVITZ RAPHAEL S [US] ET AL) 22 May 1990 (1990-05-22) abstract figure 1	1-41

1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2018/064383

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

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

1. [X] Claims Nos.: 42-53
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

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

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

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

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

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

Remark on Protest

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

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

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Claims Nos.: 42-53

The method of claims 42-53 comprises the step of "implanting at least one ultrasound transducer within a vessel". This step is clearly an invasive step representing a substantial physical intervention on the body which requires professional medical expertise to be carried out and which entails a substantial health risk even when carried out with the required professional care and expertise. The method of claims 42-53 is therefore a method for treatment of the human or animal body by surgery according to Rule 39.1(iv) PCT.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2018/064383

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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专利名称(译)	植入式超声波传感器		
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摘要(译)

一种用于植入在血管内固定位置的可植入超声血管传感器，包括至少一个超声换能器，换能器驱动电路和用于无线传输来自至少一个超声换能器的超声数据的装置。