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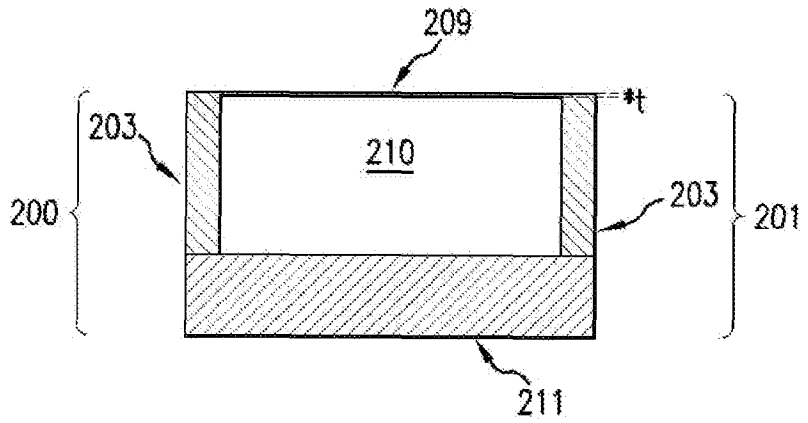
(54) **Title**: METHOD OF DETECTING PORTAL AND/OR HEPATIC PRESSURE AND A PORTAL HYPERTENSION MONITORING SYSTEM



(57) **Abstract**: The devices and methods generally relate to vibratable sensors for measuring ambient fluid pressure, in particular implantable sensors. The devices and methods are particularly well-suited to implantation within the body of a living animal or human to monitor physiological conditions, such as portal and/or hepatic venous blood pressure, and allow frequent, remote interrogation of venous pressure using the resonance frequency of an implanted sensor. The sensor devices are relatively small compared to conventional devices for measuring fluid pressure and can be implanted in the porto- hepatic venous system, whereas conventional devices are too large. The small size of the device is accomplished by using a thick sensor membrane, compared to conventional devices, and by limiting the size of additional elements of the device relative to the size of the sensor membrane. The thicker sensor member also obviates the need for multiple sensor arrays and maintains the accuracy and robustness of the sensor device. A data capture, processing, and display system provides a pressure measurement reading, and is particularly well-suited for detecting portal hypertension in patients with liver disorders.

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METHOD OF DETECTING PORTAL AND/OR HEPATIC PRESSURE AND A PORTAL HYPERTENSION MONITORING SYSTEM

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims benefit of priority to U.S. Provisional Application Ser. No. 61/530,040, filed on September 1, 2011, which is incorporated herein by reference in its entirety.

FIELD OF INVENTION

[0002] The method and apparatus generally relate to measuring ambient pressure in systems comprising incompressible fluids. More precisely, the method and apparatus relate to monitoring blood pressure, and the corresponding blood pressure gradient, between the portal and hepatic veins which together comprise the porto-hepatic venous system, via a small, passive, sensor that is deployed (implanted) in the portal vein only or in both the hepatic and portal veins. The sensor is capable of implantation in the porto-hepatic venous system due to its reduced dimensions, as compared to current sensors for measuring fluid pressure which are too large and invasive to allow frequent, accurate monitoring of porto-hepatic blood pressures. The implanted sensor measures portal vein blood pressure and/or the porto-hepatic venous pressure gradient by correlation between the blood pressure and the frequency response of the sensor, and may be used in a system which provides pressure readings via an external processing and display system.

BACKGROUND

[0003] The portal vein is a vessel in the abdominal cavity that drains deoxygenated blood to the liver for cleaning. A system of blood vessels called the hepatic veins remove the cleaned blood from the liver to the inferior vena cava, where it is returned to the heart. Portal

hypertension ("PHT") occurs when the portal vein experiences a rise in blood pressure that is not a consequence of an increase in a patient's overall systemic blood pressure. Often, PHT is defined according to a "portal pressure gradient," or, the difference in pressure between the portal vein and the hepatic veins, for example of 10 mmHg or greater. A typical portal venous pressure under normal physiological conditions is less than or equal to approximately 10 mmHg, and the hepatic venous pressure gradient (HVPG) is less than approximately 5 mmHg. Increased portal pressure leads to the formation of porto-systemic collaterals; the most serious of them being gastroesophageal varices. Once formed, varices represent a major risk for the patient due to the susceptibility for rupture and subsequent hemorrhage that in many cases leads to death. As a result, PHT is considered the most severe complication of cirrhosis of the liver and is the major cause of morbidity and mortality in cirrhosis patients.

[0004] Current procedures for monitoring portal pressure generally involve an indirect measurement of the portal venous pressure through the hepatic venous system. One such procedure is known as the hepatic venous pressure gradient or HVPG. HVPG is used to provide an indirect measurement of the portal vein pressure. The procedure is minimally invasive and involves catheterization of the hepatic venous system via femoral vein or jugular entry. A balloon tipped radiolucent catheter that is capable of measuring local blood pressure usually via a pressure transducer is placed in the Inferior Vena Cava or a large hepatic vein segment. Once in place the pressure is measured to provide the free hepatic venous pressure or FHVP. The FHVP is measured to quantify the external pressures being applied to the venous systems and to zero out the effects of systemic pressure. The catheter is then advanced into a small branch and a complete obstruction of flow is created (wedge position usually done by inflating balloon) to provide the wedged hepatic venous pressure or WHVP. The HVPG is given by HVPG = WHVP

– FHVP. While the HVPG has been shown to be a very effective diagnostic and prognostic indicator, it has been limited by the invasiveness of the procedure and the need for standardization to provide reliable results.

[0005] Other indirect procedures include, for example, measurement of variceal pressure which employs esophago-gastric approaches to advance an inflatable balloon-catheter into the abdomen of patients via the esophagus and stomach and position the balloon, adjacent to a gastroesophageal varix. The force of inflation required against the wall of the varix is used to calculate the intravariceal blood pressure. In general, non-direct portal venous pressure measurement is less precise, while still invasive and uncomfortable for a patient.

[0006] Direct measurement of the portal vein has been attempted in the past. One such procedure involves puncture catheterization, wherein a radiologist accesses the portal and/or hepatic venous systems, under fluoroscopic guidance, by puncturing the tissue of the system with a needle or catheter from outside of the system. Using puncture catheterization, the portal vein may be accessed via a transhepatic puncture using either an intracostal or subxiphoid approach, wherein a needle or catheter is inserted at a patient's 12^{th} vertebrae, between the ribs, and punctures through to the portal vein. The hepatic venous system may be accessed via a transjugular approach, wherein a needle or catheter is inserted into the jugular vein and advanced into the hepatic vein via the vena cava. The portal vein may also be accessed from the hepatic venous system, using an intrahepatic puncture from the hepatic to portal venous systems. Thus, in order to monitor a portal pressure gradient, two separate punctures (for the portal and hepatic veins) are required. Physicians are reluctant to perform frequent, direct portal vein pressure measurements, due to the invasiveness of the procedure and as a result, it is not clinically practiced.

[0007] There exists a strong clinical need for a pressure monitoring system that can provide accurate pressure measurements of portal and/or hepatic blood pressure while allowing the physician to monitor those pressures non-invasively.

[0008] Conventional devices include active electronics, sensors, and controls which require a power supply, or a connection to the outside world, and which increase the size of conventional devices thus restricting their use in the porto-hepatic venous system. In addition, conventional devices rely on components, for example sensors and/or membranes, that are large and/or needed in plurality of sensors/membranes, in order to maintain functionality, due, in part, to their tendency to rupture.

[0009] A need therefore exists for a pressure measurement system that is small in size, sensitive in function, and does not require redundancy. In addition, a need exists for a sensor system that may be operated without the need for wires or cables to transmit the pressure experienced by the sensor to an external device. The pressure measurement system should be miniature, passive, implantable and wireless to allow for non-invasive, frequent monitoring of portal venous pressure.

SUMMARY OF THE INVENTION

[0010] The present invention relates to a method and apparatus for measuring portal and/or hepatic pressures. The apparatus is a sensor device that is miniature, passive, implantable and wireless, to allow for non-invasive, frequent monitoring of portal venous pressure. The sensor device is miniature to allow for safe implantation into the target vessels. In one embodiment, the sensor device structure comprises a single sensor unit having a sensor membrane of a thickness greater than at least 1 micron and an overall sensor device size range of

0.1 mm - 1 mm in width (*w*), 0.1 mm - 1 mm in depth (*d*), and 0.1 mm - 0.75 mm in height (*h*). The overall volume of the sensor device will preferably not exceed 0.3 cubic millimeters. Other examples of volumetric ranges (in mm^3) for the sensor device are, *e.g.*, 0.005-0.008, 0.01-0.09, or 0.1-0.3. The apparatus is passive to allow the treating physician to monitor the patient as often as is desired or needed. The invention is useful for interrogating ambient conditions in systems that comprise an incompressible fluid particularly in measuring portal and/or hepatic pressures.

[0011] One object of the present invention is to provide a sensor device for measuring ambient fluid pressure in a system comprising an incompressible fluid, e.g., a liquid. The sensor device may be a naked vibratable sensor or a vibratable sensor housed in a cavity with or without a bottom film sealing the housing. In one embodiment, the sensor device comprises a vibratable sensor having a sensor membrane, which sensor membrane has a resonance frequency responsive to ambient fluid pressure conditions. The sensor membrane has a thickness in the range of 1 micron - 200 microns and forms one side of a chamber. The chamber is defined by the sensor membrane and a plurality of walls which are substantially perpendicular to the sensor membrane. The chamber may be sealed with a compressible gas of predefined pressure disposed therein. The chamber is sealed with a bonding layer using an anodic bonding process. The bonding layer may provide a means for attachment of the vibratable sensor to an anchoring device. As such, the sensor device comprising a naked vibratable sensor may be a hermetically sealed, substantially or partially non-solid component of any shape having a sensor membrane and a chamber. Alternatively, the vibratable sensor may be an acoustically-active solid, *i.e.*, a sensor membrane without a chamber. In either aspect, the vibratable sensor is biocompatible, *i.e.*, substantially non-reactive within a human body.

[0012] In another embodiment, the vibratable sensor may be disposed in a cavity defined by a housing. In this embodiment a cover plate covers the housing cavity such that the bonding layer faces the cover plate. A base plate forms the foundation for the housing. The base plate may contain an orifice exposing the sensor membrane of the vibratable sensor to the bodily environment to be measured. In one aspect of this embodiment, the housing further comprises a bottom film. The bottom film may be semi-permeable or non-permeable to external fluids and/or tissues and may enclose an incompressible fluid.

[0013] The present invention also relates to a method for measuring portal and/or hepatic pressure, wherein a sensor device has been implanted in one or both of the portal and hepatic veins, wherein each device has a resonance frequency response that is dependent upon ambient pressure and each device has a predefined, non-overlapping resonance frequency response to pressure comprising the steps of: subjecting each sensor device to ultrasonic vibrations; receiving vibrations elicited in each sensor device by the ultrasonic vibrations, each received vibration including a vibration frequency; determining the resonance frequency response of each device from each elicited vibration frequency; determining the ambient pressure surrounding each sensor device from the frequency response of each sensor device; and in certain circumstances, determining a pressure gradient between each sensor device. Where two sensors are in close proximity to one another, the method further comprises distinguishing the frequency response of each sensor.

[0014] In one embodiment, a sensor device may be implanted in the portal vein thereby providing a combination of hemostatic and intra-abdominal pressure. In another embodiment, a sensor device may be implanted in each the hepatic and portal venous systems. Implantation into the portal vein may be carried out via a transhepatic puncture using either an intracostal or

subxiphoid approach, while the hepatic vein implantation may be carried out through the transjugular approach. In this way, the system may provide information on the pressure gradient between the hepatic venous systems. In this latter embodiment, the system provides both the porto-hepatic pressure gradient and the portal venous pressure in the same session. Implanting the sensor may also include the steps of anchoring the sensor to a bodily tissue or organ, or securing the sensor to a scaffold and implanting the scaffold.

[0015] In another embodiment, a sensor device may be implanted in each of the hepatic and portal venous systems. For example, the portal implantation may be performed by a transjugular approach and then traversing a transjugular intrahepatic portosystemic (TIPS) shunt for access to the portal system. In this embodiment the measured porto-hepatic pressure gradient may provide the physician with a method of non-invasively monitoring the patency of the TIPS shunt.

[0016] A further object of the invention is to provide a method for measuring portal vein pressure, with an implanted and anchored sensor device in the portal vein comprising the steps of: applying low- and high- frequency acoustic waves to the sensor, receiving the frequencies elicited in the sensor by the low- and high- frequency waves, and processing the received frequencies as acoustic data in order to determine the frequency response, e.g., resonance frequency, of the vibratable sensor, and thereby determine the ambient fluid pressure of the environment in which the sensor is disposed.

[0017] An additional object of the invention is to provide a method for detecting and/or monitoring portal hypertension, wherein an implanted sensor device has a frequency response to ambient pressure conditions and at least one frequency response per given pressure comprising the steps of: transmitting low-frequency acoustic waves from a low-frequency acoustic

transmitter, transmitting high-frequency acoustic waves from a high-frequency acoustic transmitter, and receiving reflected high-frequency acoustic waves with a high-frequency acoustic receiver and determining a pressure gradient wherein a raised pressure gradient is indicative of an active portal hypertension condition in need of treatment. Under normal physiological conditions the gradient between the portal and hepatic venous pressures is less than about 10 mm Hg. PHT is often defined as a gradient of 10 mm Hg or more. The method may further comprise capturing, processing, and displaying the received high-frequency acoustic waves as acoustic data.

[0018] Another object of the invention is to provide a method for measuring ambient fluid pressure in a subject system, from a sensor device disposed in the subject system, where the sensor device includes a vibration sensor with a sensor membrane that has a resonance frequency response dependent on ambient pressure conditions and at least one frequency response per given pressure, comprising the steps of: subjecting the sensor to low- and high-frequency acoustic waves in order to elicit acoustic resonances, or vibrations, in the sensor, detecting the acoustic resonances as reflected signals from the sensor, and processing the detected acoustic resonances in order to determine ambient fluid pressure.

BRIEF DESCRIPTION OF THE DRAWINGS

[0019] FIG. 1 shows a device in accordance with the invention for measuring portal venous pressure.

[0020] FIGS. 2, 2A and 2B show a sensor in accordance with the invention for measuring portal venous pressure.

[0021] FIG. 3 shows a system in accordance with the invention for measuring, interpreting, and displaying portal venous pressure.

[0022] FIG. 4 shows a passive sensor manufacturing method in accordance with the invention.

[0023] FIGS. 5A-5C show various embodiments of a passive sensor anchoring device in accordance with the invention.

[0024] FIGS. 6A-6B show aspects of various embodiments of a passive sensor implantation device in accordance with the invention.

[0025] FIG. 7 illustrates exemplary resonance frequencies from a vibration sensor as a function of ambient pressure in response to three different excitation frequencies, based on pressure oscillations around the mean value to be measured.

DETAILED DESCRIPTION OF THE INVENTION

[0026] The method and apparatus of the invention generally relate to measuring ambient pressure in a system comprising an incompressible fluid. For purposes of this application, "incompressible fluid" refers generally to non-vapor, non-compressible, flowable media, such as liquids, slurries and gels. In particular, the method and apparatus relate to devices which are implanted in a body to monitor hepatic and/or portal venous pressure. The miniature size of the apparatus, compared to current conventional devices for measuring ambient fluid pressure, and relatively low invasiveness of the apparatus and method are particularly well suited to medical and physiological applications, including, but not limited to, measuring: i) blood vessel/artery/vein pressures such as, for example, in portal hypertension; ii) spinal fluid pressure

in brain ventricles; iii) intra-abdominal pressures such as in the urinary tract, bladder, kidney, and bile ducts; and the like. The method may be applicable to any disease or condition involving bodily systems through which fluids, *i.e.*, incompressible fluids, e.g., liquids, flow.

[0027] The invention is discussed and explained below with reference to the accompanying drawings. The drawings are provided as an exemplary understanding of the invention and to schematically illustrate particular embodiments and details of the invention. The skilled artisan will readily recognize other similar examples equally within the scope of the invention. The drawings are not intended to limit the scope of the invention as defined in the appended claims.

[0028] **Fig. 1** illustrates a sensor device system of the invention. Sensor device **100** measures ambient pressure of the implanted sensor device. Sensor device **100** is subjected to high frequency acoustic waves **101** and low frequency acoustic waves **102** which are generated by high frequency transmitter **103** and low frequency transmitter **104**, respectively. High frequency transmitter **103** and low frequency transmitter **104** may comprise any transducer suitable for controllably generating acoustic energy beams (such as, but not limited to sonic or ultrasonic beams) as is known in the art. Typically such transducers are called tactile transducers and are capable of converting an electrical signal into, for example, vibrations that may be felt or used for work. The transducers provide a field of view comprising a depth of penetration of 4-16 cm and a beam spot diameter of 3 cm generating a measurement ellipsoid, for example. The transducers may be implemented using suitable piezoelectric transducers, but other transducers known in the art may be used, such as, but not limited to, capacitive transducers, wideband capacitive transducers, composite piezoelectric transducers, electromagnetic transducers, various transducer array types and various suitable combinations of such transducers configured for

obtaining different frequencies and/or beam shapes. For example, acoustic transmitters manufactured by Vemco, PCB Piezoelectronics, and Hardy Instruments may be used. Acoustic waves **101**, **102** are directed at the sensor device **100**, producing modulated acoustic waves **105** that are detected by high frequency receiver **106**. Subsequent processing of waves **105** enables calculation of the ambient pressure in device **100**.

[0029] One aspect of the invention relates to an implantable sensor device comprising a miniature sensor device for measuring ambient fluid pressure. The sensor device comprises a vibratable sensor having a sensor membrane, which has a frequency response to ambient pressure conditions. The sensor membrane of the vibratable sensor forms one side of a chamber wherein resides a compressible gas of predefined pressure. The chamber is further defined by at least one wall which is preferably substantially perpendicular to the sensor membrane. In one embodiment, the vibratable sensor is made of silicon, but other suitable materials may be used, for example a metal, Pyrex® or other glass, boron nitride, or the like. Non-limiting examples of metals include, *e.g.*, Titanium, Gold, Stainless Steel, Platinum, Tantalum, or any suitable metal, alloy, shape memory alloy such as NITINOL ®. The chamber may be sealed with a bonding layer forming a side of the chamber opposite the sensor membrane. Where the vibratable sensor includes a bonding layer for sealing the chamber, the bonding layer may also be used for attachment to an anchoring means. In one embodiment, the bonding layer provides a hermetic seal for the chamber disposed in the vibratable sensor. The bonding layer may comprise Pyrex®, glass, silicon, or other suitable materials.

[0030] Generally, the vibratable sensor is manufactured by etching the appropriate shape and materials from a larger panel of the material. For example, the larger panel of material may be covered with a mask, the mask defining the shape of a plurality of the desired vibratable

sensors, and then subjected to etching, which may be, for example, chemical etching or physical etching. The mask protects those areas of the panel that must not be removed during the etching process in order to produce the desired shape. For example, a plurality of vibratable sensors is formed when a mask having a plurality of precisely measured cut-outs cover a larger panel of material during the etching process, until chambers of the desired shape are produced in the larger panel to a depth that is substantially equal to a cut-out in the mask. The depth of the chamber may be controlled by various factors, for example where chemical etching is used: the volatility, duration, and number of chemical treatments. Each vibratable sensor may then be cut from the larger panel by slicing between consecutive chambers such that the amount of material remaining on each side of the chamber will be the thickness of walls defining a chamber in the vibratable sensor. The amount of material remaining between the bottom surface of the chamber and bottom of the larger panel will be the thickness of the sensor membrane. Any material that requires joining may be connected, for example, by brazing or welding.

[0031] As noted above, the vibratable sensor may additionally include a bonding layer of, for example, Pyrex® or other suitable material, in order to hermetically seal the vibratable sensor, preferably by joining the bonding layer to the walls of the chamber such that the bonding layer and sensor membrane are substantially parallel. In one embodiment, the bonding layer and sensor membrane form opposite walls of a vibratable sensor chamber. The bonding layer may provide a surface for attachment to anchors or other components.

[0032] **Fig. 2** shows a cross sectional illustration of one embodiment of the sensor device **200**. In this embodiment, the sensor device **200** is a substantially cubic vibratable sensor **201**. As such, the sensor device **200** of **Fig. 2** comprises a sensor membrane **209** and chamber **210** which is sealed by bonding layer **211**, as described above. The sensor membrane **209** is

comparatively thick relative to other remotely operated vibratable fluid pressure sensors. The sensor membrane **209** has a thickness in the range of 1 micron – 200 microns. Some exemplary but non-limiting thicknesses include 1.5 microns, 2 microns, 2.5 microns, and 5 microns. The sensor device **200** of the invention retains its accuracy despite the comparatively thick sensor membrane **209**. The use of a single sensor (as compared to the plurality of sensors required by prior art remotely-operated vibratable sensors) reduces the overall size of sensor device **200** compared to such conventional devices, making sensor device **200** suitable for use in the porto-hepatic venous system.

[0033] The vibratable sensor **201** has a height *h*, width *w*, and depth *d*. In one embodiment, the vibratable sensor **201** measures 0.3 mm (*h*) x 0.5 mm (*w*) x 0.5 mm (*d*). The width and depth of the vibratable sensor may be equal resulting in a substantially cubic structure. However, the dimensions of the vibratable sensor **201** may generally be any dimensions that do not exceed a maximum volume of about 0.3 mm^3, preferably having a size of equal to or less than 0.125 mm^3. A minimum volume for the vibratable sensor **201** is about 0.008 mm^3. Various alternative embodiments of the vibratable sensor **201** have volumetric ranges (in mm^3) of, *e.g.*, 0.005-0.008, 0.01-0.09, or 0.1-0.3, as use requires. Vibratable sensor **201** may be solid, or may be a hermetically sealed, substantially non-solid component, of any shape, which includes sensor membrane **209** and chamber **210**, in the example illustrated by **Fig. 2**. Sensor membrane **209** in the illustrated example is a side of the chamber **210** of the vibratable sensor **201**. The depth of the chamber **210** is defined by the height (*h*) of the walls **203** of the vibratable sensor **201**. The sensor membrane **209** may have a thickness (*t*) on the order of about 2 microns in thickness (*t*), but more generally, the thickness (*t*) of the sensor membrane **209** is greater than one micron and

less than or equal to **200** microns. Thickness (*t*) is measured along the height dimension (*h*) as depicted in **Fig. 2**.

[0034] Vibratable sensor **201** may comprise the cropped rectangular overall shape illustrated in **Fig. 2**, or one or more other suitable shapes, including but not limited to a sphere, pyramid, trapezoid, or other symmetrical or non-symmetrical shape. In one embodiment, the vibratable sensor **201** comprises silicon. In another embodiment vibratable sensor **201** comprises titanium or another acoustically active material. In other embodiments, vibratable sensor **201** comprises a rubber, polymer, and/or a ceramic material. Alternatively, the vibratable sensor **201** may comprise any suitable material capable of being excited by acoustic stimulation. As used in this application, "silicon" refers to silica and silicates, glasses, cements, and ceramics; it also refers to the class of silicones for which it is a constituent element, including various synthetic plastic and rubber substances made of silicon, oxygen, carbon and hydrogen, for example.

[0035] In other embodiments of the sensor device **200**, illustrated in **Figs. 2A** and **2B**, the vibratable sensor is disposed in a cavity **208** defined by a housing **202**. The housing **202** encloses the sides of the vibratable sensor **201** but not all or part of the sensor membrane (**209** in **Fig. 2** and **2B**, unnumbered in **Fig. 2A**), and the bonding layer **211** faces a cover plate **204** which is mechanically fixed to one side of the housing and serves as a surface for attachment to an anchoring means in certain embodiments. In one aspect of the embodiment illustrated in **Fig. 2A**, the cover plate **204** may include a fill port **205**. The fill port **205** may be used to fill the cavity **208** with an incompressible fluid. As illustrated in **Figs. 2A** and **2B**, the housing **202** is disposed atop a base plate **206**, which provides a foundation for the housing **202** and holds the vibratable sensor **201** inside the cavity **208**. The base plate **206** may contain an orifice **212**, as

shown in **Fig. 2B**, which exposes the sensor membrane **209** to acoustic activity thereby allowing vibrations to reach and return from vibratable sensor **201**.

[0036] In the particular embodiment illustrated in cross-sectional view in **Fig. 2B** the vibratable sensor **201** is disposed in cavity **208** of housing **202**, wherein the orifice **212** in base plate **206** exposes all or a portion of the sensor membrane **209** of vibratable sensor **201** to an acoustically transparent bottom film **207**. Bottom film **207** is designed to allow for the transmission of acoustic waves, hydrostatic and hydrodynamic pressures from the surrounding environment. Depending upon the choice of material used for the bottom film **207**, it may also function to protect the sensor. When the bottom film **207** comprises a semi permeable material, the film protects the vibratable sensor from direct exposure to bodily tissues or other solid bodily matter. When the bottom film **207** comprises an impermeable material, the film **207** may completely protect the vibratable sensor from all bodily fluids and/or materials. In an embodiment wherein the bottom film **207** is impermeable to all fluids and solids, a fill port (not shown in **Fig. 2B**) may be used to fill the cavity **208** with an incompressible fluid. Bottom film **207** comprises any suitable bioinert material or combinations thereof, including but not limited to, titanium, gold, stainless steel, platinum, tantalum, or any suitable metal, alloy, shape memory alloy such as NITINOL ®, silicon, glass, quartz, a ceramic material, a composite material, a metallic or non-metallic nitride, boron nitride, a carbide, a metal oxide, a non-metallic oxide, a polymer based material, a gel, and combinations thereof. Alternatively, bottom film **207** may comprise titanium in one embodiment, for example diffusion-bonded Grade I titanium. In various embodiments, bottom film **207** may substantially seal vibratable sensor **201** in cavity **208**, for example when bottom film **207** comprises a substantially non-porous material, or bottom film **207** may be porous, to varying degrees, and expose vibratable sensor **201** to bodily

fluids and/or tissues. In the embodiment shown in **Fig. 2A**, described above, bottom film **207** is absent from base plate **206**. In such an embodiment, the vibratable sensor **201** would be completely exposed to the ambient environment via orifice **212**.

[0037] Cover plate **204**, housing **202**, and base plate **206** may each comprise any suitable bioinert materials or combinations thereof, including but not limited to titanium, gold, stainless steel, platinum, tantalum, or any suitable metal, alloy, shape memory alloy such as NITINOL ®, silicon, glass, quartz, a ceramic material, a composite material, a metallic or non-metallic nitride, boron nitride, a carbide, a metal oxide, a non-metallic oxide, a polymer based material, a gel, and combinations thereof. Alternatively, base plate **206** may comprise a Pyrex ® material. Base plate **206**, housing **202**, and cover plate **204** comprise titanium in one embodiment, for example Grade I titanium. These components may be formed and assembled from separate pieces or may be formed as one element or combined elements to function as described above.

[0038] In the embodiment depicted by **Fig. 2B**, the vibratable sensor **201** contained in the housing cavity **208** may be surrounded by bodily fluid, *e.g.*, blood-flow, which enters the cavity **208** via a porous or absent bottom film **207**. Alternatively, the vibratable sensor **201** may be surrounded by an incompressible fluid that is sealed in cavity **208** by a substantially solid or impermeable bottom film **207**, after the incompressible fluid is introduced to cavity **208** through fill port **205**. A substantially solid bottom film **207** also prevents the introduction of bodily fluids and/or tissues into cavity **208**.

[0039] Base plate **206** is relatively thin (in the *h* direction), generally, compared to the overall height of the device as shown in **Figs. 2A**, **2B**. In one embodiment, base plate **206** represents, for example, 100 microns of an approximately 500 micron overall device height. In

other embodiments, base plate **206** may be 5%-20% of the overall device height, but is generally less than or equal to 40% of the overall device height. The height of the base plate **206** should generally be minimized to allow for a maximum cavity **208** volume, which contributes to the accuracy of the device and therefore an overall reduced size when compared to conventional, vibratable sensors having a housing. The base plate **206** also provides a foundation for the device assembly, and absorbs mechanical stresses by providing a sink material (a material to absorb force or energy) where such stresses may dissipate.

[0040] Bottom film **207** may be bonded to all or a portion of the base plate **206** and provides further tolerance for stresses. The relatively thin bottom film is generally on the order of 1-10 microns. In one embodiment, the bottom film **207** is desirably 4 microns in thickness. The thin bottom film **207** is generally more pliable than thicker components of the device and may absorb stresses from, for example, expansion and contraction due to changing temperatures. Bottom film **207** is designed to allow for the transmission of acoustic waves, hydrostatic and hydrodynamic pressures from the surrounding environment.

[0041] As illustrated in **Fig. 2B**, cover plate **204** is substantially parallel to base plate **206**, and base plate **206** is substantially parallel to, and disposed on, bottom film **207**. **Fig. 2B** shows a cross-section of the sensor having a wafer-style stacking of the bottom film **207**, base plate **206**, vibratable sensor **201**, housing **202**, and cover plate **204**, wherein the layers may be hermetically sealed and the vibratable sensor **201** is disposed in the cavity **208** of the housing **202** in the illustrated embodiment. Techniques for hermetically sealing the layers of the sensor include but are not limited to diffusion bonding. In certain embodiments, bottom film **207** is sealed by controlled environment methods that minimize oxygenation and other impurities of the bottom film, where conventional, uncontrolled sealing techniques may damage the bottom layer

207. Remaining volume within the cavity **208** may be filled with an incompressible fluid, through the fill port **205** (**Fig. 2A**) of the cover plate **204**. After filling is complete, fill port **205** is temporarily or permanently sealed with different welding technologies such as, for example, arc, laser, resistance, ultrasonic, or torsional, or by diffusion bonding, swedging, adhesives gaskets, capillary seals, or other suitable means for sealing. The manufacturing and assembly method is detailed herein below with respect to the description of **Fig. 4**.

[0042] The overall size of the sensor device **200** depicted in **Fig. 2**, which is desirably extremely small compared to conventional wireless devices for measuring fluid pressure, may be 0.1 mm - 1 mm in width (*w*), 0.1 mm - 1 mm in depth (*d*), and 0.1 mm - 0.75 mm in height (*h*). In one embodiment, the sensor device **200** has an equal width and depth, forming a substantially cubic structure. Generally, the overall volume of the sensor device will not exceed 0.3 cubic millimeters. For the embodiment shown in **Figs. 2A**, **2B**, housing **202** has a minimum wall thickness of **300** microns. Base plate **206** has a height, *h* of approximately 100 microns. Further, base plate **206** is relatively thin compared to the overall height of the sensor device **200** depicted in **Figs. 2A**, **2B**, which may be, for example, 100 microns (base plate **206**) compared to 500 microns (for the overall sensor device). Such a configuration provides more robustness for sensor device **200**. In addition, cavity **208** desirably has a height of approximately 400 microns -- measured from the surface of base plate **206** abutting cavity **208** to the surface of cover plate **204** abutting cavity **208** -- but is at least 100 microns in height, and is relatively large compared to the overall height of the device, 400 microns (cavity) versus 500 microns (height of the overall sensor device) in the example of **Figs. 2A, 2B**.

[0043] The above principles allow for an overall reduction in size from conventional wireless devices for measuring fluid pressure, because the above principles allow for a relatively

thick (greater than 1 micron, for example, 2 microns) sensor membrane **209** which is accurate and robust enough to obviate further active components and/or sensor arrays.

[0044] Another aspect of the invention relates to a method for determining pressure in the porto-hepatic venous system. Once the sensor device **100** (**Fig. 1**) is located, data is collected using the transmitter/receiver array **103**, **104**, **106** as illustrated in **Fig. 1**. High frequency **101** and low frequency **102** acoustic beams are generated by high frequency **103** and low frequency **104** transmitters, and applied to sensor device **100**. Acoustic beams **101**, **102** are typically initiated by positioning the transmitters **103**, **104** in close but external proximity to the sensor device **100**, where "close proximity" is any distance sufficient to apply acoustic beams **101**, **102** to sensor device **100** in accordance with the devices and methods herein. Vibrations from the sensor, interrogated and excited by the high frequency **101** and low frequency **102** acoustic beams, create modulated acoustic waves **105**, due to the vibration of the vibratable sensor **201** (**Fig. 2**). Modulated acoustic waves **105** are detected by high frequency receiver **106** which is also placed in close proximity to sensor device **100**.

[0045] **Fig. 3** shows one embodiment of a processing and display system **300** of the system of the current invention and illustrates operation of the sensor device in the system. **Fig. 3** makes reference to **Fig. 1**, which illustrates a generic sensor device **100** of the system of the invention, however the processing and display system **300** of **Fig. 3** applies equally to the sensor device **200** as illustrated in **Figs. 2, 2A** and **2B**. Thus, for purposes of describing the operation of the sensor device and system with reference to **Fig. 3**, sensor device reference numbers **100** and **200** are used interchangeably.

[0046] Referring to **Fig. 3**, high frequency receiver **106** transmits data **305** to processing unit **301**. Data **305** may include radio waves, electrical signals, digital signals, waveform signals, or any other means sufficient for communicating the acoustic properties of modulated acoustic waves **105**, as received by high frequency receiver **106**. Processing unit **301** interprets data **305** using the properties of modulated acoustic waves **105** to determine a frequency response of the sensor device **100**. The frequency response of the sensor is defined herein as the frequency of vibrations, including at least one resonance frequency, emitted by the sensor in response to the transmission of ultrasonic vibrations from transmitters **103**, **104**, at a given ambient pressure. For example, the frequency response of sensor device **100** is known when sensor device **100** is subject to "normal", *i.e.*, non-symptomatic, physiological conditions. In the portal venous system, "normal" conditions are a pressure approximately 5 mmHg or less, and a pressure gradient between the portal and the hepatic vein of approximately 10 mmHg or less. The internal pressure of sensor device **100** -- *i.e.*, the pressure within cavity **208** -- is known and substantially constant. In the portal venous system, the frequency response of sensor device **100** changes in accordance with changes in the venous pressure. Low-frequency acoustic waves **102**, for example at 50 kHz, will stimulate at least one frequency response of vibrations in sensor device **100**, at a given pressure, by exciting vibrations in vibratable sensor **201** (**Fig. 2**). High frequency acoustic waves, for example 750 kHz, may be used to interrogate the excited vibratable sensor **201** (**Fig. 2**). This results in modulated acoustic waves **105** that can be detected by receiver **106**. High frequency acoustic waves are meant to interrogate, not to excite, the membrane **209** of the vibratable sensor **201**, and preferably minimally interact with the membrane **209** to maximize linearity of the system.

[0047] One type of frequency response which may be measured according to the present invention is a resonance frequency. For example, resonance frequency(-ies) of the sensor device **100** may be identified as the frequency(-ies) which exhibit peak vibration amplitudes returned from the sensor device **100**. In an alternative embodiment, the resonance frequencies are absorbed by bottom film **207**, and therefore do not materialize as vibrations generated by the sensor device **100**, and are identified as the frequencies where vibrations are not returned from the sensor device **100**, or where the minima of amplitude vibrations returned from sensor device **100** exist. The difference between the actual resonance frequency excited in the sensor device **100** and the resonance frequency of the sensor device under normal conditions is correlated to the difference in pressure between normal conditions and the actual blood pressure. Thus, actual portal venous pressure is calculated based on the measured resonance frequencies of sensor device **100**.

[0048] In one embodiment of the invention, the low frequency transmitter is an annular low frequency piezoelectric transducer having a working range of 0-100 kHz, 30-100 kHz, or 50-100 kHz, for example, depending on the precision required. It is, however, noted that any other suitable low frequency transducer known in the art may be used for implementing the invention.

[0049] In another embodiment of the invention, the high frequency transmitter **103** is an annular high frequency transmitting transducer, implemented as a low noise (*i.e.*., low-range or low-bandwidth) frequency generator unit designed to generate a high frequency acoustic wave **101** at, for example, 750 kHz. It is noted, however, that other different values of the high frequency acoustic wave may also be used in implementing the present invention.

[0050] In one embodiment of the invention high frequency receiver **106** is a disc-like high frequency receiving piezoelectric transducer. The annular high frequency transmitter **103** and the high frequency receiver **106** are, for example, a model CLI 7900 general-purpose ultrasonic probe, commercially available from, for example, Capistrano Labs, Inc., San Clemente, Calif., USA. When the acoustic waves including the high frequency acoustic waves **101** and low frequency acoustic waves **102** are directed at the sensor device **100**, the high frequency receiver **106** receives the modulated acoustic waves **105** which are excited in the sensor device **100** as well as other noise, e.g., signals that are reflected from other materials in the measurement environment or interference. The high frequency receiver **106** generates an electrical signal representative of the returning acoustic signals that it receives. The electrical signal produced by the receiver **106** is processed by the system described herein, for example as shown in **Fig. 3**.

[0051] In another embodiment, low frequency transmitter **104** has a working range of 30-90 kHz, and transmits acoustic frequencies, for example, at 50 kHz; high frequency transmitter **103** transmits, for example, at approximately 750 kHz with a narrow bandwidth (range); high frequency receiver **106**, under the example, operates in the range of 750 (high) ± 50 (low) kHz. Low frequency transmitter **104**, high frequency transmitter **103**, and high frequency receiver **106** may alternatively operate in any range suitable for use with the devices and methods disclosed herein, and as particularly required for measuring fluid pressure in particular environments.

[0052] High frequency receiver **106** is also a transducer, and is used for receiving the signals returning from the sensor when the sensor is interrogated by the high frequency acoustic waves **101**. For example, the transducer may be implemented using suitable piezoelectric transducers, but any other type of transducers known in the art may be used to implement the

transducers, such as, but not limited to, capacitive transducers, wideband capacitive transducers, composite piezoelectric transducers, electromagnetic transducers, various transducer array types, cMUTs, cymbal transducers and various suitable combinations of such transducers configured for obtaining different frequencies and/or beam shapes. For example, acoustic receivers manufactured by Vemco, PCB Piezoelectronics, and Hardy Instruments may be used.

[0053] Modulated acoustic waves **105** are the result of combining high frequency acoustic waves **101** and low frequency acoustic waves **102** in a reversible manner, in order to achieve a waveform with a desired frequency, wavelength, and/or amplitude. Unmodulated noise, for example caused by reflections of acoustic waves off of materials in the sensor device **100** environment, is thus distinguished from the modulated acoustic waves **105** that are excited by the sensor device **100**. When the received signal amplitude (in dB) is analyzed according to the frequency (in MHz), the amplitude peaks at the resonance frequency of the sensor device **100**. High frequency receiver **106** communicates the modulated acoustic waves **105** to a processing and display system, detailed in **Fig. 3**, for interpretation and use.

[0054] In one embodiment, vibrations excited in sensor device **100** are distinguished from noise by correlating pressure measurements to a heart rate or pulse measurement. In this embodiment, a plurality of pressure measurements are taken during the interrogation period, for example, at least one cycle of expansion and contraction of the heart (pulse cycle). During the pulse cycle, the pressure of the entire vascular system will change continuously as the heart draws blood in and forces blood out. Accordingly, an acoustic signal that changes in a consistent manner correlated to the pulse cycle demonstrates an excitation in the sensor. Noise reflected from, for example, surrounding tissues in the interrogation environment, does not produce such a continuously changing signal that is correlated to the pulse cycle. The above features are not

limited to a single embodiment; rather, those features and functions may be applied in place of or in conjunction with the other embodiments and concepts herein. The pulse cycle and waveform may be measured by an external device, for example using a pulse oximeter, heart rate monitor, ECG, etc. Optionally, such instruments may be connected to the pressure monitoring system of the invention to input the pulse or pulse waveform into the system for correlation with the acquired pressure waveform from the sensor to determine the validity of the acquired signal.

[0055] In operation, sensor device **100** is disposed in a measurement environment, for example, implanted in an area, vessel, artery, or the like, where pressure measurements are desired. The sensor system may be implanted by methods including, for example, portal venous catheterization procedures to position the sensor device **500** in the portal vein shown, for example, via scaffoldings **504** illustrated in **Figs. 5-6**. In such a procedure a percutaneous transhepatic approach to the portal vein may be employed, for example inserting the cannula **601** into a subject between the ribs and puncturing through to the portal vein. For the hepatic vein, the sensor device **500** may be inserted, for example, by transjugular hepatic vein access, similar to the procedure used in hepatic vein pressure-gradient measurements. In this procedure, a catheter is inserted into the jugular vein in the neck and advanced into the hepatic vein via the vena cava. The portal vein is also accessible by puncture from the hepatic vein, after a catheter has been inserted via transjugular hepatic procedures similar to the implantation of transjugular intrahepatic portosystemic shunts. Implantation into the portal vein may also involve traversing a TIPS shunt, in which case the patency of the TIPS shunt may be non-invasively monitored. Implantation is typically performed by an interventional radiologist under fluoroscopic guidance. Sensor device **500** is guided to the intended position using catheter delivery system **600**, for example, as shown in **Figs. 6A-6B**. Once deployed in the intended location, sensor device **500**

remains in the vessel or area. Other methods for deploying the sensor as are known in the art may alternatively be employed. Non-limiting examples of such deployment methods include, but are not limited to, those described in U.S. Patent No. 6,331,163 to Kaplan and U.S. Patent Publication No. 2005-0124896 to Richter, which are incorporated herein by reference.

[0056] According to one aspect of the invention, the implanted sensor device **100** is subjected to both high and low frequency acoustic waves **101**, **102**, the latter excites vibrations in the sensor device **100**, and the reflected high frequency acoustic waves are then manifested as modulated acoustic waves **105**. High frequency receiver **106** receives the modulated acoustic waves **105** and communicates the properties of the modulated acoustic waves **105** to a processing and display system, detailed in **Fig. 3**, for interpretation and use.

[0057] Returning to **Fig. 3** which shows one embodiment of a processing and display system **300** of the current invention, data **305** from high frequency receiver **106** is transmitted to a processing unit **301** which determines the pressure of the environment surrounding the sensor device **100**. Data **305** is communicated between high frequency receiver **106** and processing unit **301** via a wired **308** or wireless **309** connection. Wired connection **308** is, for example, an electronic cable or integral connection, or the like. Wireless connection **309**, for example, operates by transmitting radio waves, acoustic waves, or other known media for remotely communicating data.

[0058] Processing unit **301** may comprise a computer, workstation, or other electrical or mechanical device programmed to perform the data conversions and/or displays described herein and as needed for the method of use. By way of a non-limiting example, the invention may be practiced on a standard workstation personal computer, for example those manufactured by Dell,

IBM, Hewlett-Packard, or the like, and which typically include at least one processor, for example those manufactured by Intel, AMD, Texas Instruments, or the like. Processing unit **301** also comprises dedicated hardware and/or software, *e.g.*, a data capture system such as the National Instruments PCI-6115 data capture board or may be comprised of a custom designed device for that purpose.

[0059] The output of processing unit **301** is a pressure measurement that is converted to a usable, displayable measurement either by processing unit **301** or display unit **302**, or a combination thereof. For example, pressure measurements may be reported in numerical units of mmHg or Torr or maybe displayed with relation to a predefined arbitrary scale. Display unit **302** may comprise a monitor, numerical display, LCD, or other audio or visual device capable of displaying a numerical measurement. As shown in the embodiment of **Fig. 3**, display unit **302** is connected to or integral with processing unit **301** by connection **306**, for example in the case of a computer with processing and display units, which optionally includes as a remote element, separate wired element, or integral element to processing **301** and/or display **302** units, interface **303** and input/output elements **304**, such as a keyboard, mouse, disk drive, optical pen, or the like, to allow a user to collect, manipulate, track, and record data. Connection **306** may optionally be a remote connection **307**, operating by transmission of radio waves, acoustic waves, or other known remote transmission methods.

[0060] One aspect of the invention is directed to a method of monitoring PHT. The sensor device **100** may be implanted in either or both of the portal and/or hepatic veins according to the procedures described herein or known. Once implanted in the porto-hepatic venous system, the method comprises the steps of: subjecting the sensor device **100** to ultrasonic vibrations from high frequency **103** and low frequency **104** transmitters; receiving the frequency

response of one (or each) of the sensor devices **100**; determining a resonance frequency of the (or each) sensor device **100** from the received frequency response; determining ambient fluid pressure surrounding the (or each) sensor device **100** from the resonance frequency of the (or each) sensor device **100**; determining a pressure gradient between each sensor device **100** (in each of the portal and hepatic veins) wherein an elevated gradient (generally greater than 10 mm Hg) is indicative of an active portal hypertension condition in need of treatment; and displaying and/or recording the pressure measurements according to the system described with respect to **Fig. 3**. Thus, the pressure of the portal and/or hepatic veins may be independently interrogated, determined, and displayed. Where the pressure gradient between the portal and hepatic veins is desired, one sensor may be implanted in each of those systems, and data captured for each sensor in the manner described above. The numerical measurement of the hepatic vein pressure, for example, could then be subtracted by further processing from the numerical measurement of the portal vein pressure, providing the gradient, or difference in pressure, between the two systems.

[0061] The method of monitoring a pressure gradient between the portal and hepatic veins includes the additional step of delineating between each sensor while performing the interrogation. The mechanism for the differentiation can be one of the following or both: (i) differences in frequency responses between the sensors may be detected by changing the dimensions of the membrane while maintaining the pressure ranges and accuracy of the sensor (*i.e.*, one sensor will have a frequency response at a defined pressure between 30-50 kHz while the other may have a frequency response of 60-80 kHz at the defined pressure). Such a design entails a low frequency transmitter with a wide enough bandwidth to enable the operation of both sensors (*i.e.*, between 30-50 and 60-80 kHz), or two or more low-frequency transmitters, one for each type of sensor; (ii) a narrow high or low (or both) frequency acoustic field is applied to the

vicinity of the sensors to precisely locate each sensor during interrogation while acoustically isolating any other sensors in the vicinity.

[0062] In one embodiment, determining the pressure in the portal and/or hepatic veins comprises obtaining the mean pressure by a phase inversion method of calculation, which relies on small pressure oscillations created by the heartbeat. The small pressure oscillations exist around the mean pressure value which is to be measured. In order to determine the mean pressure value to be measured, a receiver as described for example with respect to **Fig. 3** measures the response power of the sensor device, which is the amplitude of the oscillation of the vibratable sensor and is measured in decibels (dB). As illustrated in **Fig. 7,** the small pressure oscillations occur around a particular mean value – for example 90 Torr, indicated by the solid vertical line. When the sensor device is excited by certain frequencies, for example f1 and f2, the response power is an increasing function of the pressure, whereas excitation by another frequency, f3, results in a response power that is a decreasing function of the pressure. As a direct result the response power of f1 and f2 oscillate in phase with each other (and with the pressure) and that of f3 oscillates with an opposite phase. When the small pressure oscillations occur around a different mean value – for example 100 torr, indicated in **Fig. 7** by the dashed vertical line – the response power of f1 is an increasing function of the pressure, whereas that of f2 and f3 are decreasing functions of the pressure. As a result, the response power of f1 oscillates in phase with the pressure, and that of f2 and f3 oscillated with an opposite phase. The phase inversion algorithm is based on these observations. The resonance frequency of the sensor device at the mean ambient pressure is that around which the phase inversion occurs. In this embodiment, the pulse cycle and waveform may be measured with an external device for correlation with the acquired pressure waveform from the sensor.

[0063] This technique is particularly applicable to PHT since only a mean pressure reading is necessary.

[0064] With reference now to **Fig. 4**, one example of a manufacturing method embodiment is shown for a sensor device in accordance with the devices and methods described herein. In step **401**, vibratable sensors are etched and cut from a panel of material to produce a plurality of individual vibratable sensors **402**, each of which may be hermetically sealed with a layer, such as bonding layer **211** (illustrated in **Figs. 2, 2B**) made of, for example, Pyrex®, which may be anodically bonded to one side of vibratable sensor **402**, or attached by brazing, welding (such as, for example, arc, laser, resistance, ultrasonic, or torsional), diffusion bonding, vapor deposition, adhesives, epoxies, or the like. Each vibratable sensor may then be assembled into a sensor device directly or may be further processed to be inserted into a housing cavity, as described below. Housing defining a cavity may be created in parallel steps, in which an individual housing is etched and cut **403** from larger panels of material and assembled **404** into a housing having a cavity. Cutting is accomplished by any suitable method, *e.g.*, chemical etching, laser cutting, mechanical cutting, plasma cutting, punching, or the like. In a similar fashion if a cover plate is desired, a cover plate and fill port are machined **405** from a larger panel of material. Similarly, a base plate may be machined **406** from a larger panel of material. In one embodiment, a bottom film is hermetically sealed to the face of the base plate opposite the face that will abut the stacked assembly, in step **407**, via brazing, welding (such as, for example, arc, laser, resistance, ultrasonic, or torsional), diffusion bonding, vapor deposition, adhesives, epoxies, or the like. In another embodiment, the bottom film is not used. A vibratable sensor is then inserted into the cavity in the housing and the sensor-housing assembly is disposed on a base plate in a wafer-style stacking arrangement **408** (see also **Fig. 2B**). As part of step **408**, the

cover plate is disposed on the housing and encloses the vibratable sensor in the cavity, and the base plate and housing, and housing and cover plate, are hermetically sealed via brazing, welding (such as, for example, arc, laser, resistance, ultrasonic, or torsional), diffusion bonding, vapor deposition, adhesives, epoxies, or the like. In a further, non-illustrated step, the empty space of the cavity surrounding the vibratable sensor is filled with an incompressible fluid via the fill port in the cover plate, and the fill port is subsequently hermetically sealed using brazing, welding (such as, for example, arc, laser, resistance, ultrasonic, or torsional), diffusion bonding, or the like.

[0065] In the embodiment where the sensor without a housing is desired, the sensor is further manufactured by attaching the vibratable sensor to an anchoring means. In one embodiment, a bonding layer (illustrated as **211** in **Figs. 2, 2B**) is attached to the vibratable sensor by brazing, welding, diffusion bonding, vapor deposition, adhesives, epoxies, or the like. The bonding layer provides a surface to attach the sensor to a support structure, for example an anchoring means. The bonding layer and support structure may be joined by brazing, welding, diffusion bonding, vapor deposition, adhesives, epoxies, or the like. In one embodiment, the bonding layer comprises Pyrex®.

[0066] The sensor device with or without a housing may be fixed to a desired support structure by various means known in the art. A support structure such as, for example, an annular shaped structure may be pressed against the vessel wall wherein the sensor device is attached thereto. In another embodiment, hooks, tethers, or other fixation devices may be used to fix the sensor into the desired position. **Fig. 5** shows attachment of sensor device **500** to an exemplary anchoring means; in this example, sensor device **500** may be diffusion bonded, welded, brazed, soldered, or otherwise suitably attached to an inner side **505** of scaffold **504**.

Scaffold **504** may be a stent-like structure, which is a tubular device that is typically implanted in a damaged vessel or artery to maintain the opening of the vessel or artery, as described for example in U.S. patent no. 7,763,064 to Pinchasik. Scaffold **504** comprises inner side **505**, an outer side **506**, and a longitudinal axis **507**. In some embodiments, scaffold **504** has a high degree of radial force in direction *r*, in order to hold a vessel or artery open. When a stent is used as scaffold **504** it is preferred that the stent provide sufficient radial resistance in direction *r* (*see* **Fig. 5B**) to hold the stent in a constant position in the vessel; *i.e.*, to secure the sensor in the desired position. U.S. patent no. 7,763,064 to Pinchasik describes such scaffolds and is incorporated by reference in its entirety.

[0067] The scaffold **504** may be either self-expanding or expanded by an inflatable balloon. In one embodiment the scaffold is balloon expandable, and the delivery system includes an inflation lumen. An inflation balloon may be coaxially disposed on the outside of the cannula or catheter. Scaffold **504**, including passive sensor **500**, is crimped onto the inflation balloon for insertion and placement. After scaffold **504** is in place within the body, inflation balloon is inflated under the control of the operator. Scaffold **504** expands until it reaches a desired diameter within a vessel or area. The inflation balloon is then deflated and removed, leaving scaffold **504**, including sensor device **500**, within the vessel or area. Scaffold **504** comprises, for example, nitinol, stainless steel, cobalt chromium, or other biocompatible materials with sufficient elasticity and plasticity to expand under the force of inflation balloon and remain securely in place after expansion.

[0068] In another embodiment, scaffold **504** is made from Nitinol, or another self-expandable material that will expand, for example, under higher, *in vivo*, temperatures and pressures. For certain sensor devices, it may be desirable to deploy the sensor without the need

for an inflation balloon to prevent damage to the attached sensor device. U.S. 2006/0122691 to Richter, for example, discusses such materials and their use in scaffolds and is incorporated by reference in its entirety.

[0069] Scaffold **504** comprises, for example, nitinol, stainless steel, cobalt chromium, or other biocompatible materials with sufficient elasticity and plasticity to expand under the force of inflation balloon inflating and remain securely in place after expansion. Typically, an animal body will respond to the presence of a foreign object, such as the scaffold **504**, by forming neointima, which aids in securing the scaffold **504**. U.S. patent publication no. 2006/0122691 to Richter, for example, discusses neointimal growth and securing scaffolds in place by burying the scaffold in neointima and is incorporated by reference in its entirety.

[0070] **Fig. 5B** shows an embodiment where sensor device **500** is tethered to scaffold **504** via a lead line **509**, which is a stent strut, cable, wire, or other suitable material that is capable of resisting the force of blood-flow and potential influence on the position of the device, and is bioinert as herein discussed. A lead line is attached to sensor device **500** and scaffold **504** by welding, brazing, tying, adhesives, or the like, or may be an integral part of scaffold **504**.

[0071] An alternative method of implanting a sensor device of the invention in a measurement environment involves the use of an anchoring mechanism other than a scaffold. **Fig. 5C** illustrates an embodiment for an anchoring mechanism from the prior art comprising a first support leg **590** and a second support leg **591** which are attached at a first end **595** to the sensor housing **592** of a sensor device of the invention. At a second end **593,** each support leg **590**, **591** has a protrusion **594** in the shape of a hook, or the like. The protrusions **594** of the

anchoring mechanisms attach to the tissues or walls of vessels in which the sensor housing **592** is implanted, thereby securing the assembly.

[0072] The sensor of the invention may be delivered to the target site by various methods known in the art. Implantation into the portal vein may be done via a transhepatic puncture using either an intracostal or subxiphoid approach. Implantation may also be done using a transjugular approach that would necessitate an intrahepatic puncture from the hepatic to portal venous systems. **Fig. 6** shows one embodiment of a delivery system **600** for use in delivering the sensor device **500** and attachment means to the sensing environment. As illustrated in **Fig. 6**, the delivery system **600** comprises an intravenous cannula or catheter that includes an internal tube **604** having a lumen about a longitudinal axis **605** and an external or outer tube **611**. A cut-away view of **611** in **Figs. 6A** and **6B** shows the scaffold **504** with the sensor **500** may be coaxially disposed about the internal tubular structure **604** of the delivery system, for example a cannula or catheter. In this embodiment, the scaffold **504** is self-expanding. As shown in **Fig. 6A** and **6B**, the scaffold **504** may be crimped around the internal tube **604** and held in the compressed delivery configuration by the outer tube **611**. To deploy the scaffold **504**, the outer tube **611** is removed to permit the scaffold **504** to expand and engage the vessel lumen. Once expanded the interior tube **604** may be withdrawn leaving the scaffold **504** in the vessel, with the sensor **500** exposed to the ambient fluid of the vessel. In the embodiment illustrated in **Fig. 6,** the cannula **604** or catheter has at a distal end **601** a trocar **602** having a sharp tip **609** for puncturing the bodily tissues and organs is coaxially disposed inside the lumen of the cannula **601**. Alternatively the cannula **604** or catheter on which the scaffold **504** is disposed may be threaded through a needle-based system, which is used to penetrate the tissue and into the appropriate

vessel, and advanced to the location where the sensor device **500** is to be deployed. Preferably, the tip of the catheter has a soft, rounded tip.

[0073] **Fig. 6A** shows an embodiment, wherein the scaffold **504** and sensor device **500** depicted in **Fig. 5A** are mounted on the catheter delivery system **600** coaxially. **Fig. 6B** shows a similar delivery system for a sensor **500** attached to scaffold **504** by lead line **509**. When the scaffold **504** is implanted and expanded, sensor **500** is engulfed by the bloodstream, for example.

[0074] Once in place, the sensor may be located by various methods known in the art. For example, the presence and the intensity of Doppler shifted sideband peaks in the frequency response of the sensor may be used to identify or locate the sensor in the body and to assist the centering of the interrogating ultrasound beam on the sensor(s). The sensor reflects the carrier frequency ultrasound signal (with Doppler shift) with much higher amplitude than any tissue in the human body, thus the identification and localization of the sensor and the centering of the interrogating beam may be performed by searching for a significant Doppler effect in the received signal. If the interrogating beam is scanned across the region in which the sensor is implanted or located, the beam is centered on the sensor when the sideband frequency's amplitude is maximal. When correlating a received signal to a pulse cycle measurement, the pulsatile pressure changes the signal amplitude of the Doppler sideband frequency (or frequencies) during the pulse cycle time. These pulsatile pressure induced sideband amplitude changes are present only in the signal reflected from the vibratable membranes of the sensor. Maximizing the amplitude of these pulsatile (periodic) amplitude changes may also be used by the system for sensor identification and for beam centering. Thus, the operator or user of the device may scan the interrogating beam in the region where the implanted sensor is assumed to be positioned and look for the presence of a sideband component (or components) at the

expected frequency (or frequencies) having an amplitude which periodically varies in time at a rate similar to the blood pulse rate. In accordance with an embodiment of the invention, the pulsating sideband component may be visually detected on a display device coupled to the system. The interrogating beam may then be centered by carefully changing the beam direction and/or orientation in until the amplitude of the amplitude of the periodically varying sideband is maximal.

[0075] The system's operator may then carefully scan the interrogating beam position for fine-tuning the best beam position. The beam's position may be fine-tuned or optimized by slowly changing the beam direction and/or orientation until the amplitude of the sideband peak(s) is the maximized. By maximizing the sideband amplitude the operator may ensure a good signal to noise ratio by maximizing the received energy at the sideband frequency or frequencies. Maximizing the amplitude of sideband frequency (or frequencies) may also contribute to improving the signal-to-noise ratio and therefore the measurement accuracy and/or the inter-test and/or intra-test accuracy, repeatability and sensitivity. After beam centering, the operator may use the system for determining the blood pressure by determining the resonance frequency of the sensor(s) as disclosed in detail herein and computing the blood pressure from the determined resonance frequency (or frequencies).

[0076[It will be appreciated by persons having ordinary skill in the art that many variations, additions, modifications, and other applications may be made to what has been particularly shown and described herein by way of embodiments, without departing from the spirit or scope of the invention. Therefore, it is intended that the scope of the invention, as defined by the claims below, includes all foreseeable variations, additions, modifications, or applications.

What is claimed is:

1. A sensor device for measuring fluid pressure, comprising:

a vibratable sensor comprising a sensor membrane, wherein the sensor membrane has a thickness of at least one micron, and the vibratable sensor has a total volume of less than or equal to 0.3 cubic millimeters.

2. The device of claim 1, further comprising a bonding layer which is securedly attached to the vibratable sensor.

3. The device of claim 2, further comprising an anchoring means which is securedly attached to the bonding layer.

4. The device of claim 1, wherein the sensor membrane has a thickness of two microns.

5. The device of claim 1, further comprising:

a housing enclosing the vibratable sensor, wherein the housing does not enclose all of the sensor membrane; and

a base plate having an orifice, wherein the base plate is less than or equal to 150 microns in thickness.

6. The device of claim 5, further comprising a bottom film enclosing the sensor membrane.

7. The device of claim 6, wherein the bottom film is substantially non-permeable.

8. The device of claim 6, wherein the bottom film is permeable.

9. The device of claim 6, wherein the bottom film is acoustically transparent.

10. A sensor device for measuring fluid pressure, comprising:

a vibratable sensor comprising a sensor membrane, wherein the sensor membrane is at least one micron in thickness;

a housing defining a cavity into which the vibratable sensor is disposed; and

a base plate onto which the housing is disposed, wherein the thickness of the base plate is less than or equal to one-fifth of the overall height of the device.

11. The device of claim 9, further comprising a bottom film, wherein the bottom film is disposed on the base plate.

12. The device of claim 10, wherein the cavity has a height which is greater than or equal to four-fifths of the overall height of the device.

13. The device of claim 10, wherein the bottom film is substantially non-permeable.

14. The device of claim 10, wherein the bottom film is permeable.

15. The device of claim 11, wherein the bottom film is acoustically transparent

16. The device of claim 10, wherein the cavity further encloses an incompressible fluid.

17. A system for monitoring portal hypertension comprising the device of any one of claims 1-16; the system further comprising:

a delivery system; and

a scaffold, the sensor device connected to the scaffold.

18. The system of claim 17, wherein the sensor device is connected to the scaffold via a lead line.

19. The system of claim 17, wherein the delivery system is a needle based delivery system.

20. A method for detecting portal or hepatic fluid pressure from an implanted sensor device wherein the device comprises a vibration sensor having a resonance frequency that is dependent upon ambient fluid pressure, comprising the steps of:

subjecting the implanted device to ultrasonic vibrations;

receiving vibrations generated by the device in response to the ultrasonic vibrations, the generated vibration including a vibration frequency;

determining the resonance frequency of the device from the vibration frequency;

determining the ambient pressure of fluid surrounding the device from the resonance frequency of the device.

21. The method of claim 20, wherein the resonance frequency is determined using a phase inversion algorithm.

22. A method for monitoring portal hypertension from a sensor device implanted in each of the portal and hepatic venous systems, wherein each device comprises a vibration sensor having a resonance frequency that is dependent upon ambient fluid pressure, comprising:

subjecting each device to ultrasonic vibrations;

receiving vibrations generated by each device in response to the ultrasonic vibrations, each generated vibration including a vibration frequency;

determining the resonance frequency of each device from the respective vibration frequency of each device;

determining the ambient pressure of fluid surrounding each device from the resonance frequency of each device; and

determining a pressure gradient between the devices.

23. The method of claim 22, wherein the resonance frequency is determined using a phase inversion algorithm.

24. The method of claim 22, further comprising displaying the pressure gradient.

25. The method of claim 22, wherein said method further includes monitoring the patency of a transjugular intrahepatic portosystemic shunt.

26. The method of claim 22, wherein determining the pressure gradient further comprises distinguishing each vibration frequency from noise.

27. The method of claim 26, wherein distinguishing each vibration frequency from noise comprises identifying an amplitude peak in each vibration frequency.

28. The method of claim 26, wherein distinguishing each vibration frequency from noise comprises:

identifying a pulse cycle;

receiving a plurality of vibration signals generated by each device during the pulse cycle;

comparing the pulse cycle to the received signals; and,

identifying a waveform that correlates to the pulse cycle.

29. The method of claim 22, further comprising distinguishing each sensor by a unique frequency response for each sensor at a given pressure.

30. A method for detecting portal hypertension from a sensor device implanted in the porto-hepatic venous system, wherein the device comprises a vibration sensor having a resonance frequency that is dependent upon ambient fluid pressure, comprising:

subjecting the device to ultrasonic vibrations;

receiving a vibration generated by the device, the generated vibration including a vibration frequency;

determining the resonance frequency of the device from the vibration frequency; and,

determining the ambient pressure of fluid surrounding the device from the resonance frequency of the device.

31. The method of claim 30, wherein the resonance frequency is determined using a phase inversion algorithm.

32. The method of claim 30, further comprising displaying the ambient pressure.

33. The method of claim 30, wherein determining the ambient pressure further comprises distinguishing the vibration frequency from noise.

34. The method of claim 33, wherein distinguishing the vibration frequency from noise comprises identifying an amplitude peak in the vibration frequency.

35. The method of claim 33, wherein distinguishing the vibration frequency from noise comprises:

identifying a pulse rate, and determining a pulse cycle which comprises at least one cycle of expansion and contraction of the heart;

receiving a plurality of vibration signals generated by the device during the pulse cycle;

comparing the pulse cycle to the received signals; and,

identifying a waveform that correlates to the pulse cycle.

36. The method of any one of claims 21, 23 or 31, further comprising measuring the pulse cycle and waveform with an external device and correlating with the acquired pressure waveform from the sensor.

37. A method for detecting ambient fluid pressure using a sensor device disposed in a fluid environment, wherein said device comprising a vibration sensor having a frequency response that is dependent upon ambient fluid pressure of said environment, the fluid comprising the steps of:

subjecting the device to ultrasonic vibrations;

receiving vibrations generated by the device in response to the ultrasonic vibrations, the generated vibration including a vibration frequency;

determining the resonance frequency of the device from the vibration frequency;

determining the ambient pressure of fluid surrounding the device from the resonance frequency of the device.

38. The method of claim 37, wherein the resonance frequency is determined using a phase inversion algorithm.

39. The method of claim 37, further comprising displaying the ambient pressure.

40. The method of claim 37, wherein determining the ambient pressure further comprises distinguishing the vibration frequency from noise.

41. The method of claim 40, wherein distinguishing the vibration frequency from noise comprises identifying an amplitude peak in the vibration frequency.

42. A method for detecting ambient fluid pressure from sensor devices disposed in each of two environments, wherein each device comprises a vibration sensor having a resonance frequency response that is dependent upon ambient fluid pressure, comprising:

subjecting each device to ultrasonic vibrations;

receiving vibrations generated by each device in response to the ultrasonic vibrations, each generated vibration including a vibration frequency;

determining the resonance frequency of each device from the respective vibration frequency of each device;

determining the ambient pressure of fluid surrounding each device from the resonance frequency of each device; and

determining a pressure gradient between the devices.

43. The method of claim 42, wherein the resonance frequency is determined using a phase inversion algorithm.

44. The method of claim 42, further comprising displaying the pressure gradient.

45. The method of claim 42, wherein determining the pressure gradient further comprises distinguishing each vibration frequency from noise.

46. The method of claim 45, wherein distinguishing each vibration frequency from noise comprises identifying an amplitude peak in each vibration frequency.

47. The method of claim 42, further comprising distinguishing each sensor by a unique resonance frequency for each sensor at a given pressure.

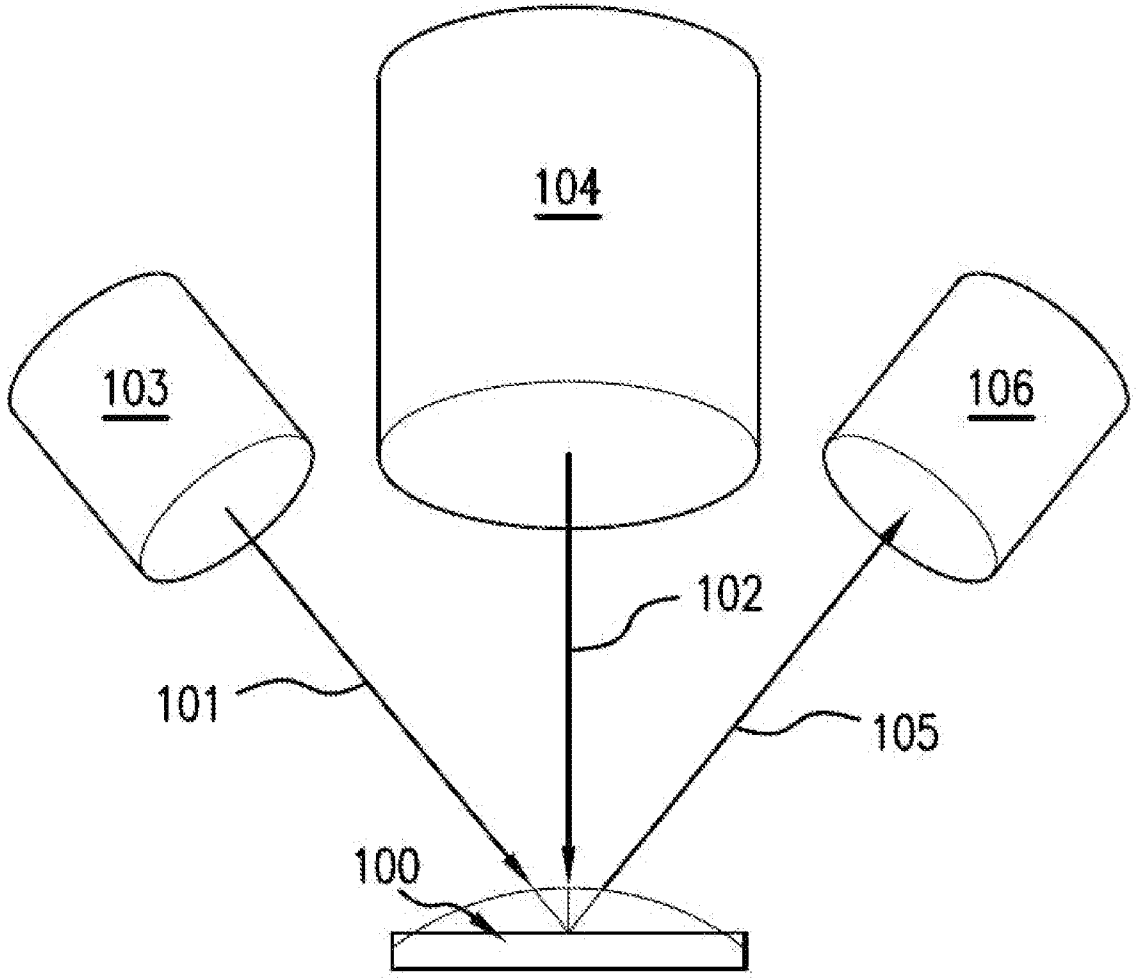

FIG. 1

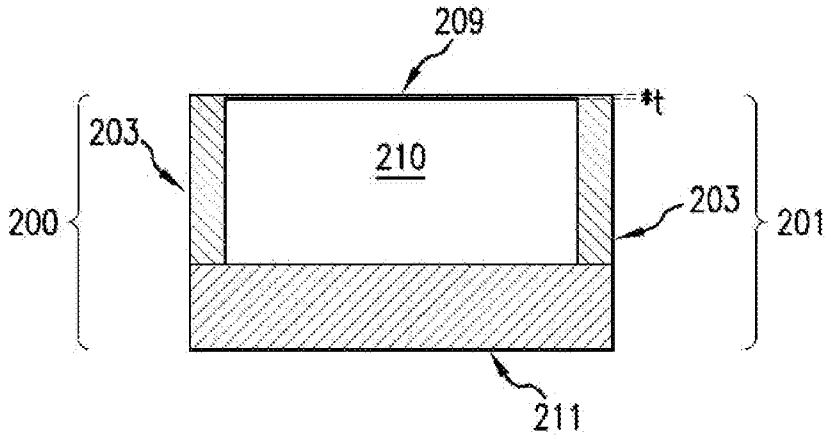

FIG.2

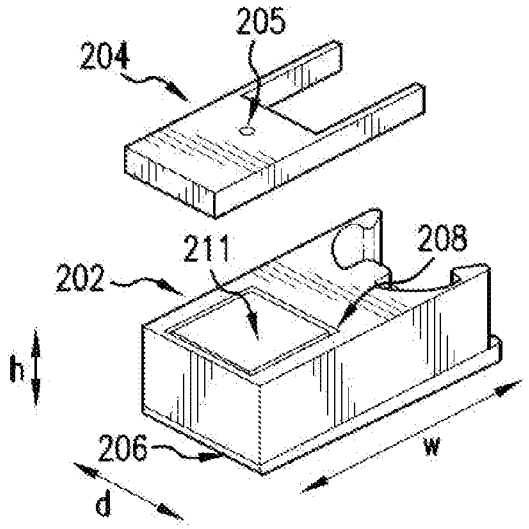

FIG.2A

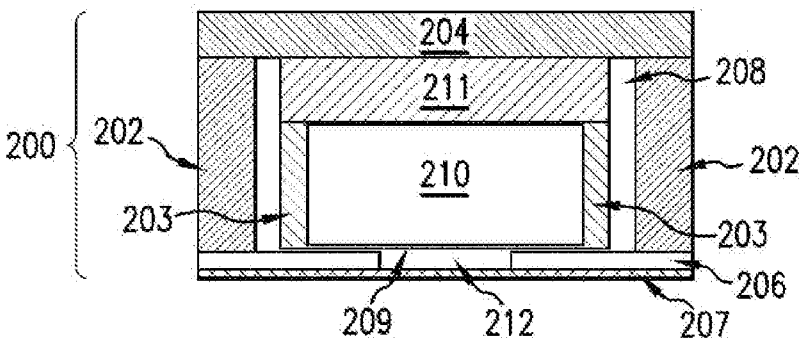

FIG.2B

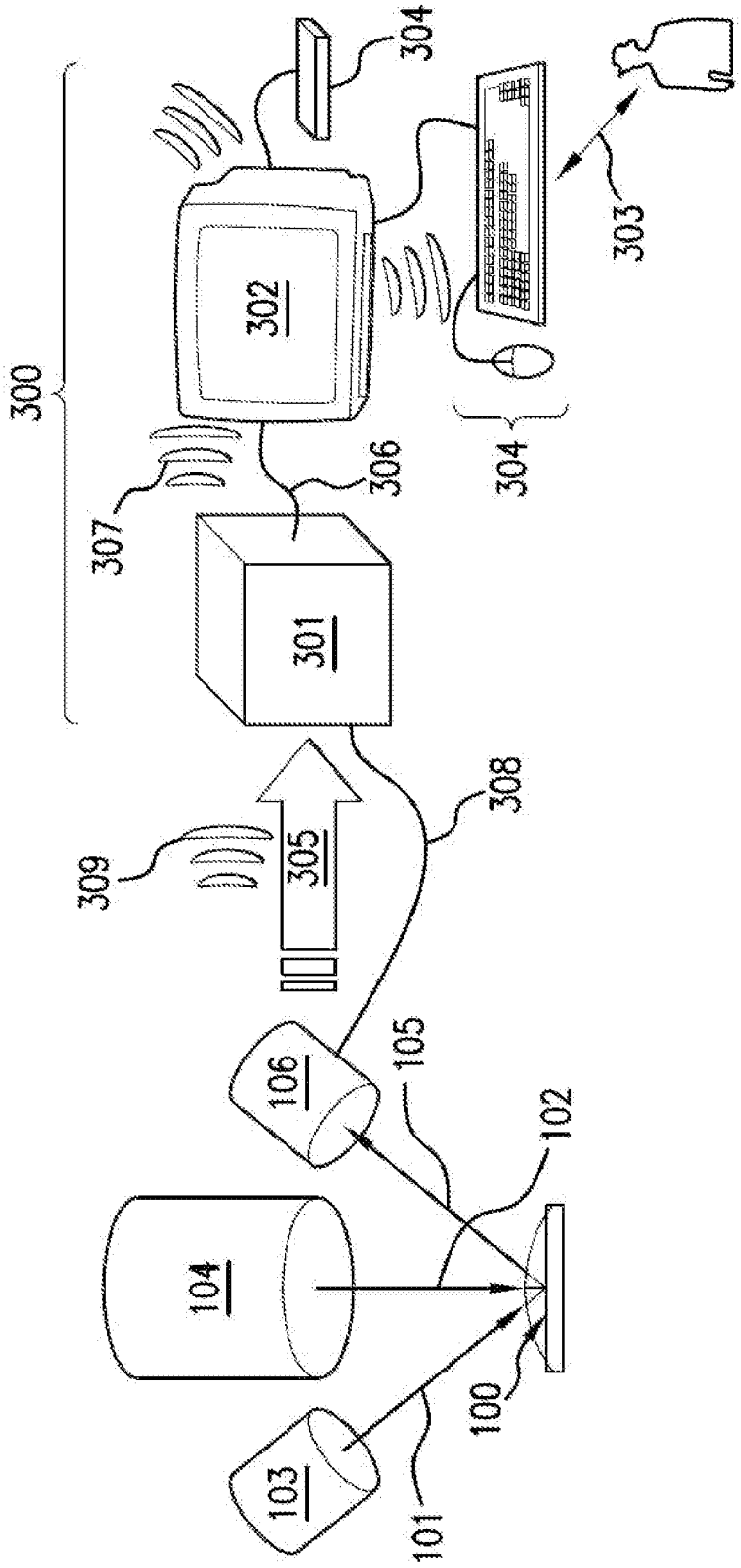
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FIG. 3

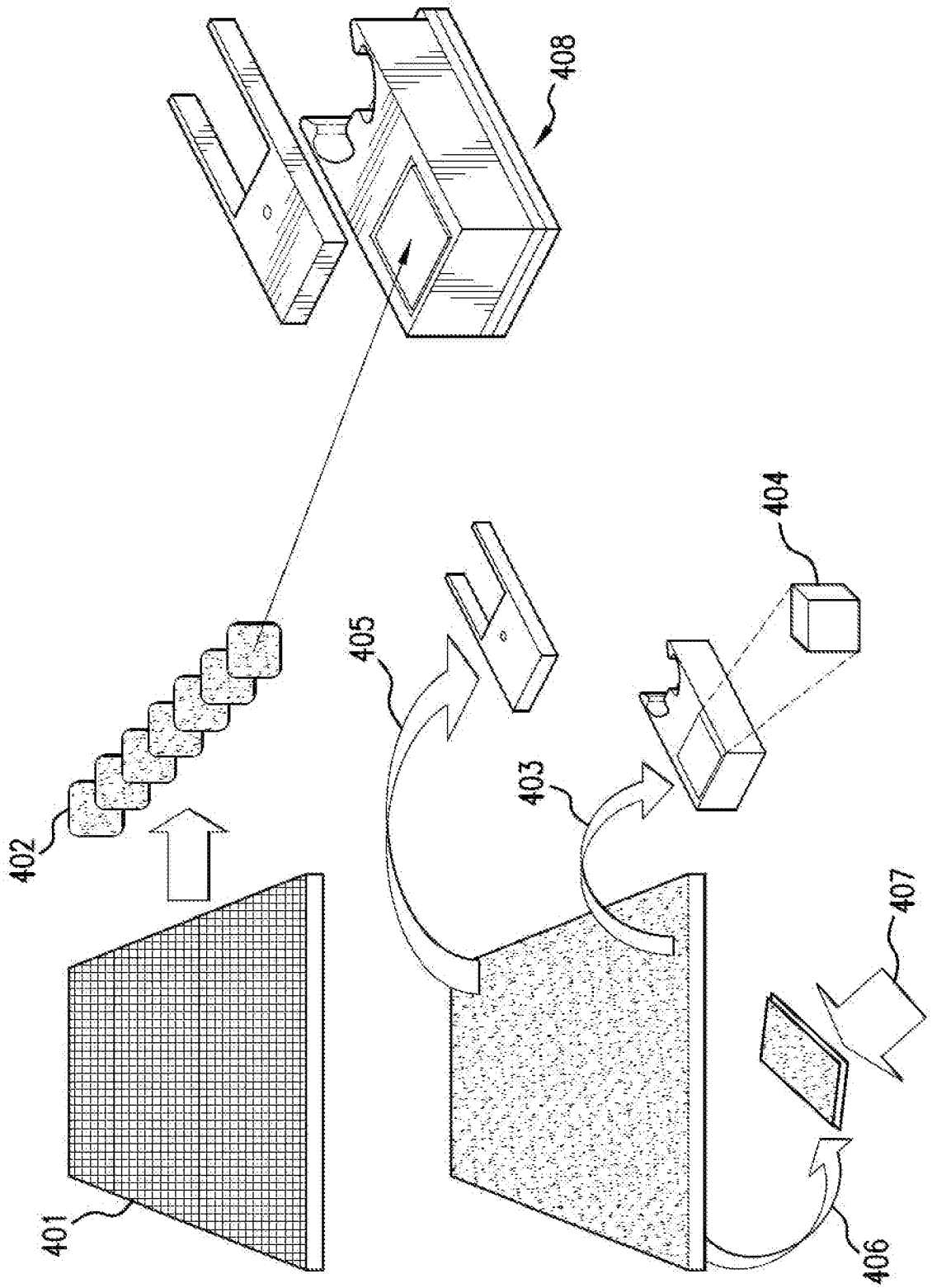

FIG. 4

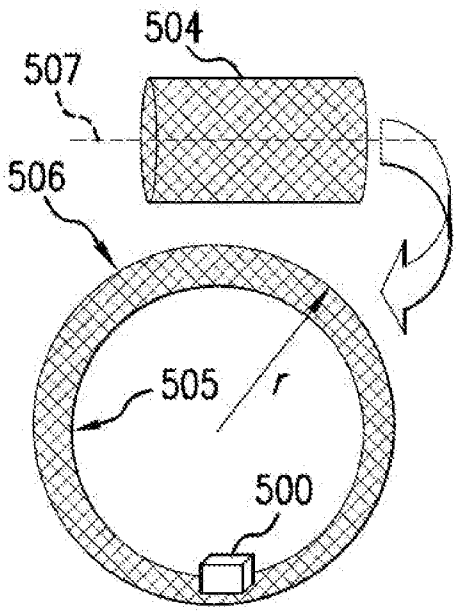

FIG.5A

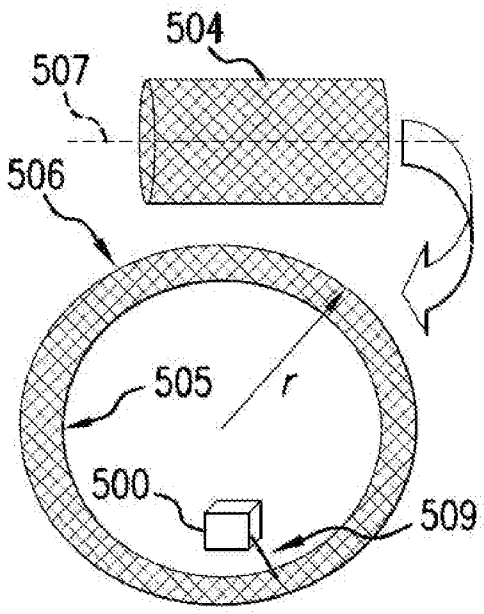

FIG.5B

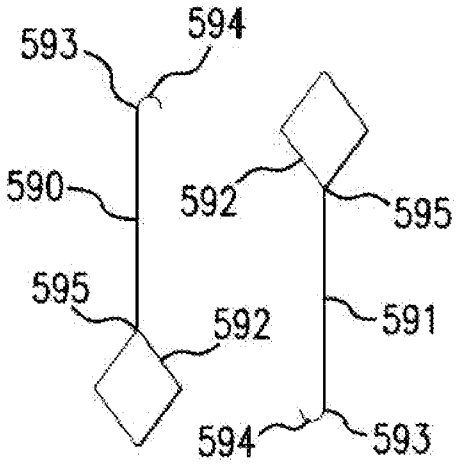

FIG.5C

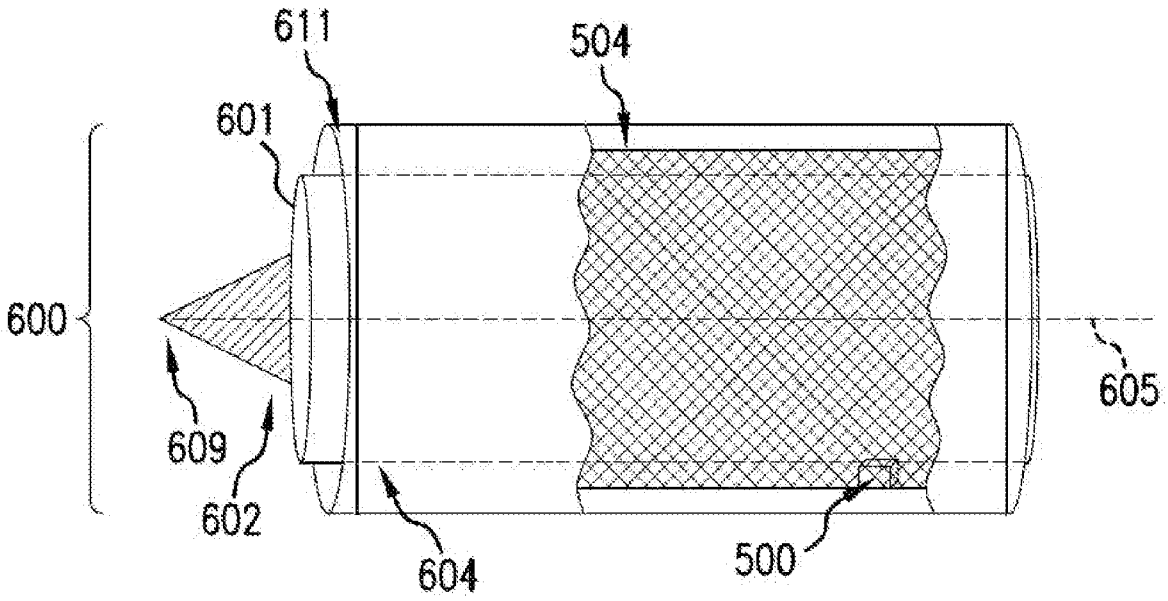
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FIG.6A

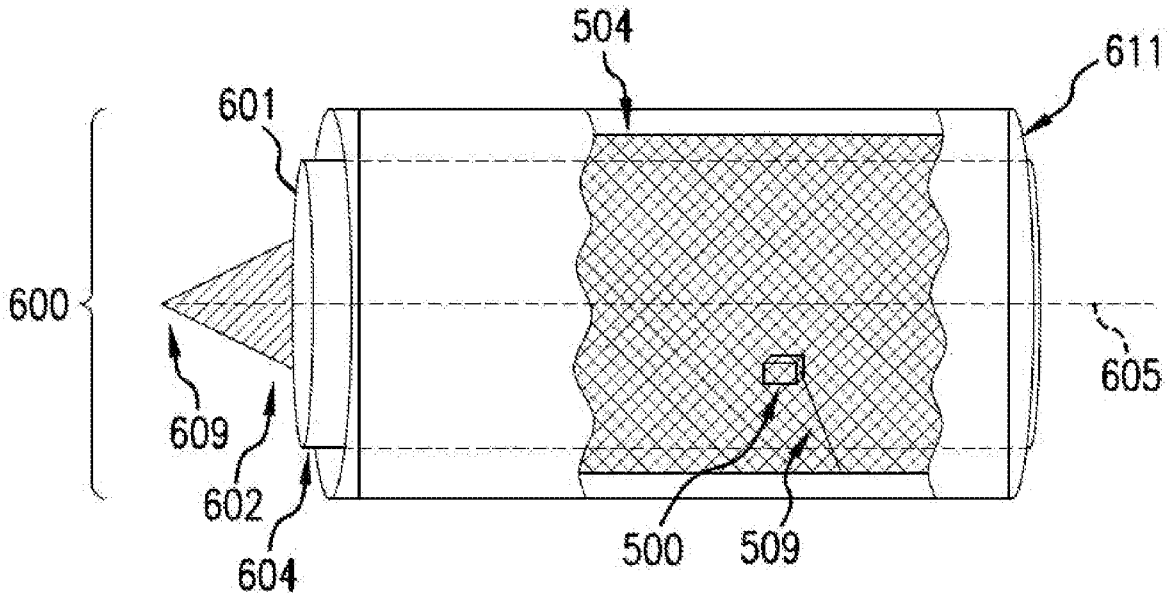
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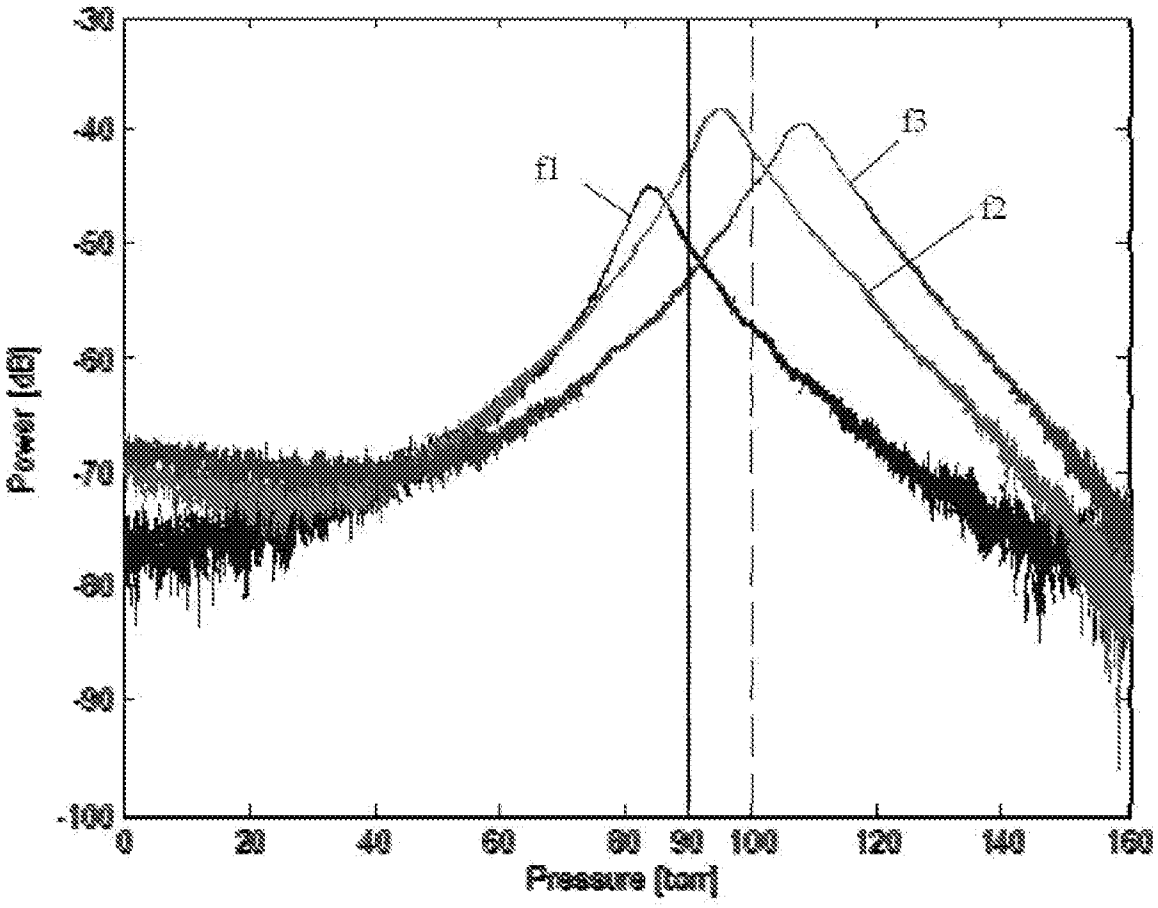
FIG.6B

FIG. 7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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2012/053298

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/0215 A61B5/00
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	EP 1 068 836 A2 (MICROSENSE CARDIOVASCULAR [IL] MICROSENSE CARDIOVASCULAR SYS [IL]) 17 January 2001 (2001-01-17) paragraphs [0001], [0007], [0009] - [0017], [0034] - [0061]; claims; figures	1-47
X	WO 2009/132396 A1 (COMMW SCIENT IND RES ORG [AU]; LIFFMAN KURT [AU]; SUTALO ILIJA DENIS [) 5 November 2009 (2009-11-05)	20,22, 30,37,42
A	the whole document	1-19,21, 23-29, 31-36, 38-41, 43-47

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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
9 January 2013	15/01/2013

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)

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2012/053298

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	US 2005/049499 A1 (KAPLAN SHAY [IL]) 3 March 2005 (2005-03-03) the whole document	20,22, 30,37,42 1-19,21, 23-29, 31-36, 38-41, 43-47

A	WO 2005/024367 A2 (MICROSENSE CARDIOVASCULAR SYS [IL]; MELAMUD ALEXANDER [IL]; LOKCHINE S) 17 March 2005 (2005-03-17) the whole document	1-47

A	WO 2004/096007 A2 (MICROSENSE CARDIOVASCULAR SYS [IL]; GIRMONSKY DORON [IL]; EISENBERG RA) 11 November 2004 (2004-11-11) the whole document	1-47

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2012/053298

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 1068836 A2	17-01-2001	AR 024750 A1	23-10-2002
		AU 779088 B2	06-01-2005
		AU 4383700 A	18-01-2001
		AU 5703700 A	05-02-2001
		BR 0002803 A	13-03-2001
		CA 2313859 A1	16-01-2001
		CN 1293348 A	02-05-2001
		DE 10033943 A1	08-02-2001
		EE 200000306 A	16-04-2001
		EP 1068836 A2	17-01-2001
		GB 2355532 A	25-04-2001
		HK 1036394 A1	15-08-2003
		JP 2001061790 A	13-03-2001
		KR 20010049758 A	15-06-2001
		MX PA00006966 A	15-10-2004
		NO 20003608 A	17-01-2001
		NZ 505711 A	31-05-2002
		PL 341197 A1	29-01-2001
		RU 2220749 C2	10-01-2004
		SG 83801 A1	16-10-2001
		SK 10302000 A3	12-03-2001
		US 6331163 B1	18-12-2001
		WO 0105301 A2	25-01-2001
WO 2009132396 A1	05-11-2009	NONE	
US 2005049499 A1	03-03-2005	AT 532455 T	15-11-2011
		AU 2004268192 A1	10-03-2005
		CA 2535732 A1	10-03-2005
		EP 1662988 A2	07-06-2006
		EP 2319402 A1	11-05-2011
		ES 2374271 T3	15-02-2012
		JP 2007503583 A	22-02-2007
		US 2005049499 A1	03-03-2005
		US 2008066550 A1	20-03-2008
		WO 2005022110 A2	10-03-2005
WO 2005024367 A2	17-03-2005	NONE	
WO 2004096007 A2	11-11-2004	CA 2564854 A1	11-11-2004
		EP 1617752 A2	25-01-2006
		US 2004211260 A1	28-10-2004
		WO 2004096007 A2	11-11-2004

专利名称(译)	检测门静脉和/或肝脏压力的方法和门静脉高压监测系统		
公开(公告)号	EP2750587A1	公开(公告)日	2014-07-09
申请号	EP2012759322	申请日	2012-08-31
[标]申请(专利权)人(译)	微创医学科技有限公司		
申请(专利权)人(译)	MICROTECH MEDICAL TECHNOLOGIES LTD.		
当前申请(专利权)人(译)	MICROTECH MEDICAL TECHNOLOGIES LTD.		
[标]发明人	RICHTER YORAM TAMMAM ERIC S MANDEL SHAHAR EVEN DAR		
发明人	RICHTER, YORAM TAMMAM, ERIC, S. MANDEL, SHAHAR, EVEN-DAR		
IPC分类号	A61B5/0215 A61B5/00		
CPC分类号	A61B5/02152 A61B5/6862 A61B5/6876 A61B5/6882 A61B2562/0247 A61B2562/12		
优先权	61/530040 2011-09-01 US		
外部链接	Espacenet		

摘要(译)

该装置和方法通常涉及用于测量环境流体压力的可振动传感器，特别是可植入传感器。所述装置和方法特别适合植入活体或人体内以监测生理状况，例如门静脉和/或肝静脉血压，并允许使用共振频率频繁地远程询问静脉压。植入传感器。与用于测量流体压力的传统装置相比，传感器装置相对较小并且可以植入肝静脉系统中，而传统装置太大。与常规装置相比，通过使用厚传感器膜并通过相对于传感器膜的尺寸限制装置的附加元件的尺寸来实现装置的小尺寸。较厚的传感器构件还消除了对多个传感器阵列的需要并且保持了传感器装置的准确性和稳健性。数据采集，处理和显示系统提供压力测量读数，特别适用于检测肝脏疾病患者的门静脉高压症。