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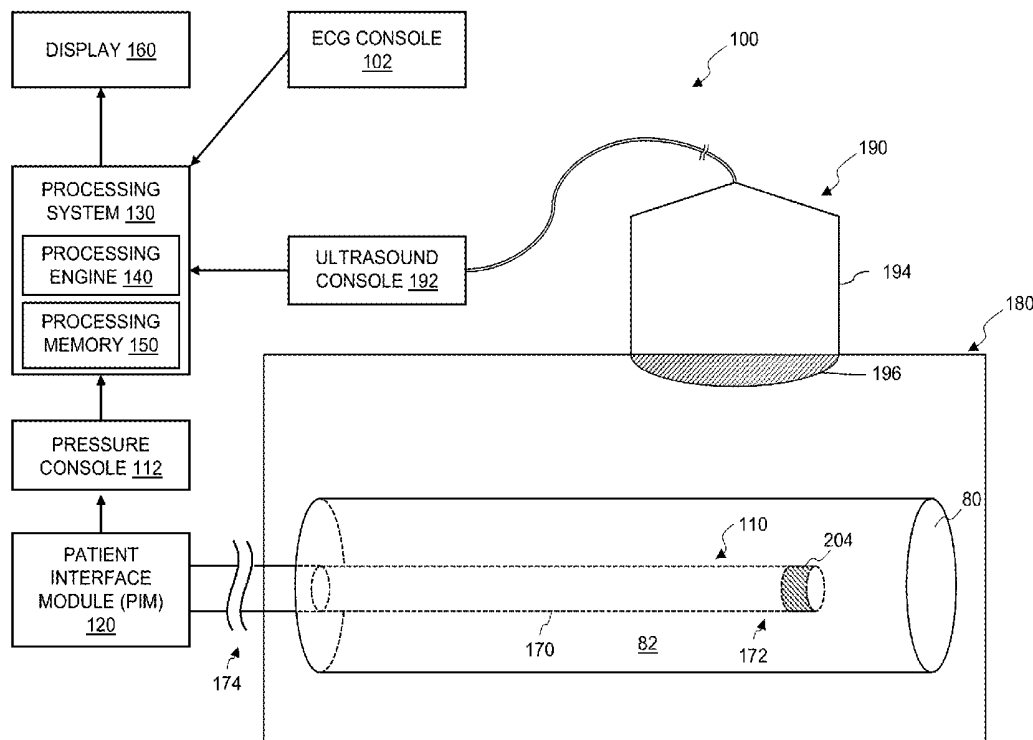
(19) **United States**(12) **Patent Application Publication**
VAN DER HORST et al.(10) **Pub. No.: US 2019/0082978 A1**(43) **Pub. Date: Mar. 21, 2019**(54) **DETERMINING PULSE WAVE VELOCITY
USING INTRAVASCULAR PRESSURE
MEASUREMENT AND EXTERNAL
ULTRASOUND IMAGING, AND
ASSOCIATED DEVICES, SYSTEMS, AND
METHODS***A61B 5/021* (2006.01)*A61B 8/04* (2006.01)(52) **U.S. Cl.**CPC *A61B 5/0285* (2013.01); *A61B 5/0215*
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(2013.01); *A61B 5/02108* (2013.01)(71) Applicant: **KONINKLIJKE PHILIPS N.V.**,
Eindhoven (NL)(72) Inventors: **Arjen VAN DER HORST**, Tilburg
(NL); **Charles Frederik SIO**,
Eindhoven (NL); **Maarten Petrus**
Joseph KUENEN, Veldhoven (NL)(21) Appl. No.: **16/194,872**(22) Filed: **Nov. 19, 2018****Related U.S. Application Data**(63) Continuation-in-part of application No. PCT/EP2017/
062230, filed on May 22, 2017.(30) **Foreign Application Priority Data**

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Jun. 29, 2016 (EP) 16176863.5

Publication Classification(51) **Int. Cl.***A61B 5/0285* (2006.01)*A61B 5/0215* (2006.01)(57) **ABSTRACT**

Devices, systems and methods for pulse wave velocity determination using intravascular pressure measurement and external ultrasound imaging are disclosed. An apparatus for pulse wave velocity (PWV) determination includes an intravascular device sized and shaped for positioning within the vessel, the intravascular device including a flexible elongate member and a pressure sensor, the pressure sensor configured to monitor a pressure of a fluid within the vessel; an imaging device configured to monitor a velocity of the fluid within the vessel, the imaging device including an external ultrasound transducer configured for positioning proximate to a body portion including the vessel; and a processing system in communication with the intravascular device and the imaging device, the processing system configured to: synchronize the monitoring of the pressure within the vessel by the pressure sensor with the monitoring of the velocity within the vessel by the imaging device; and determine the pulse wave velocity of the fluid within the vessel based on the pressure and the velocity within the vessel.



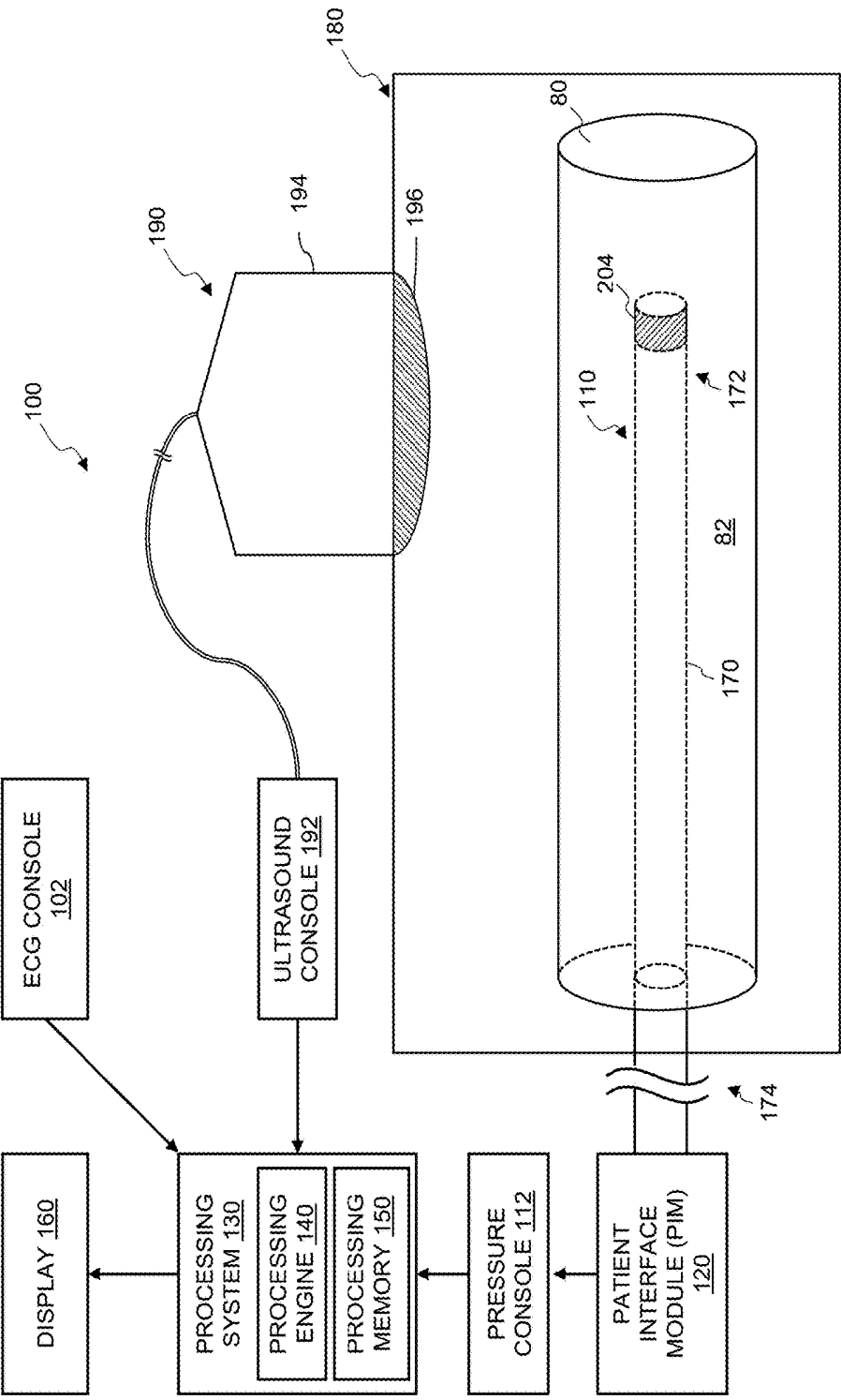


Fig. 1A

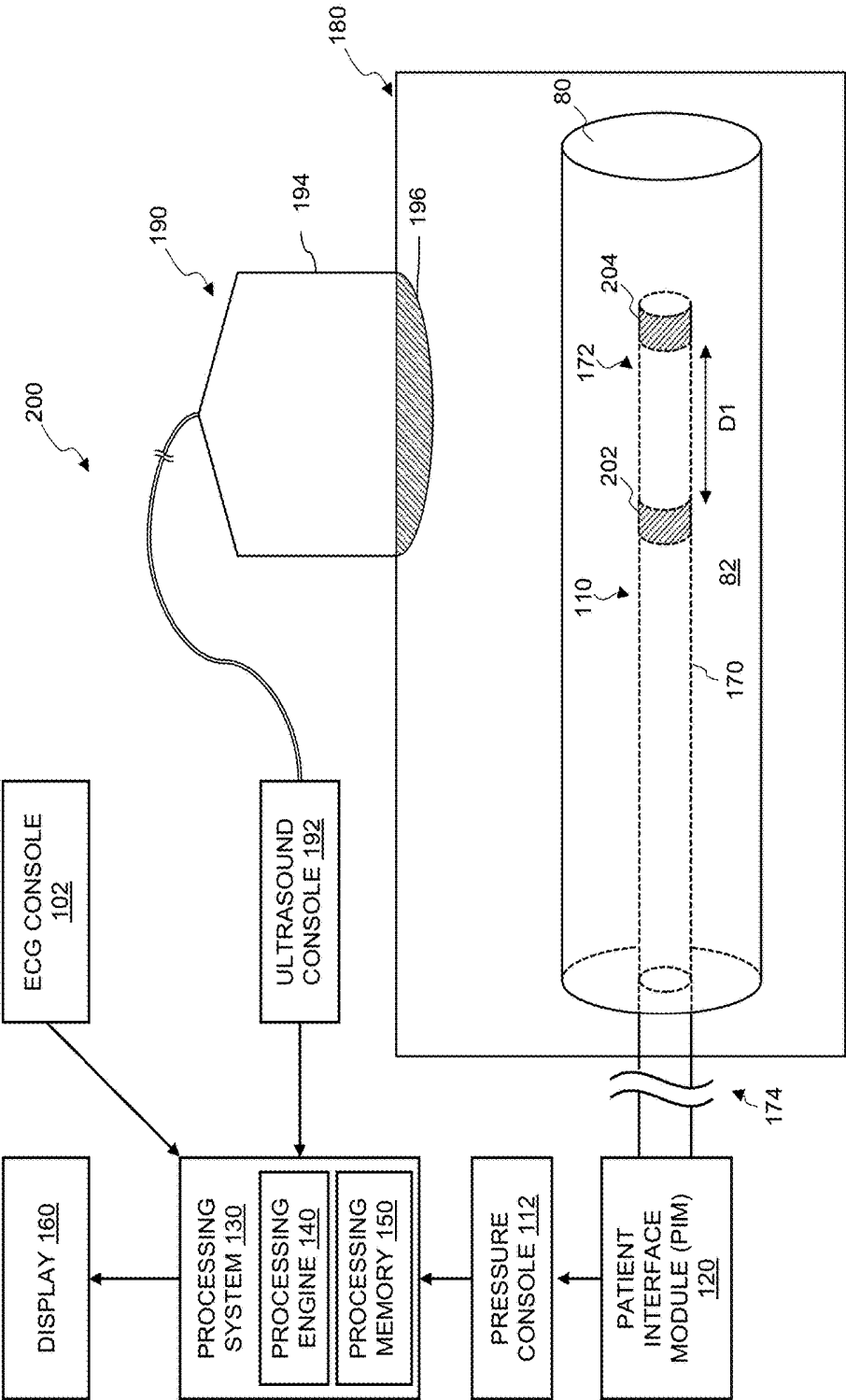


Fig. 1B

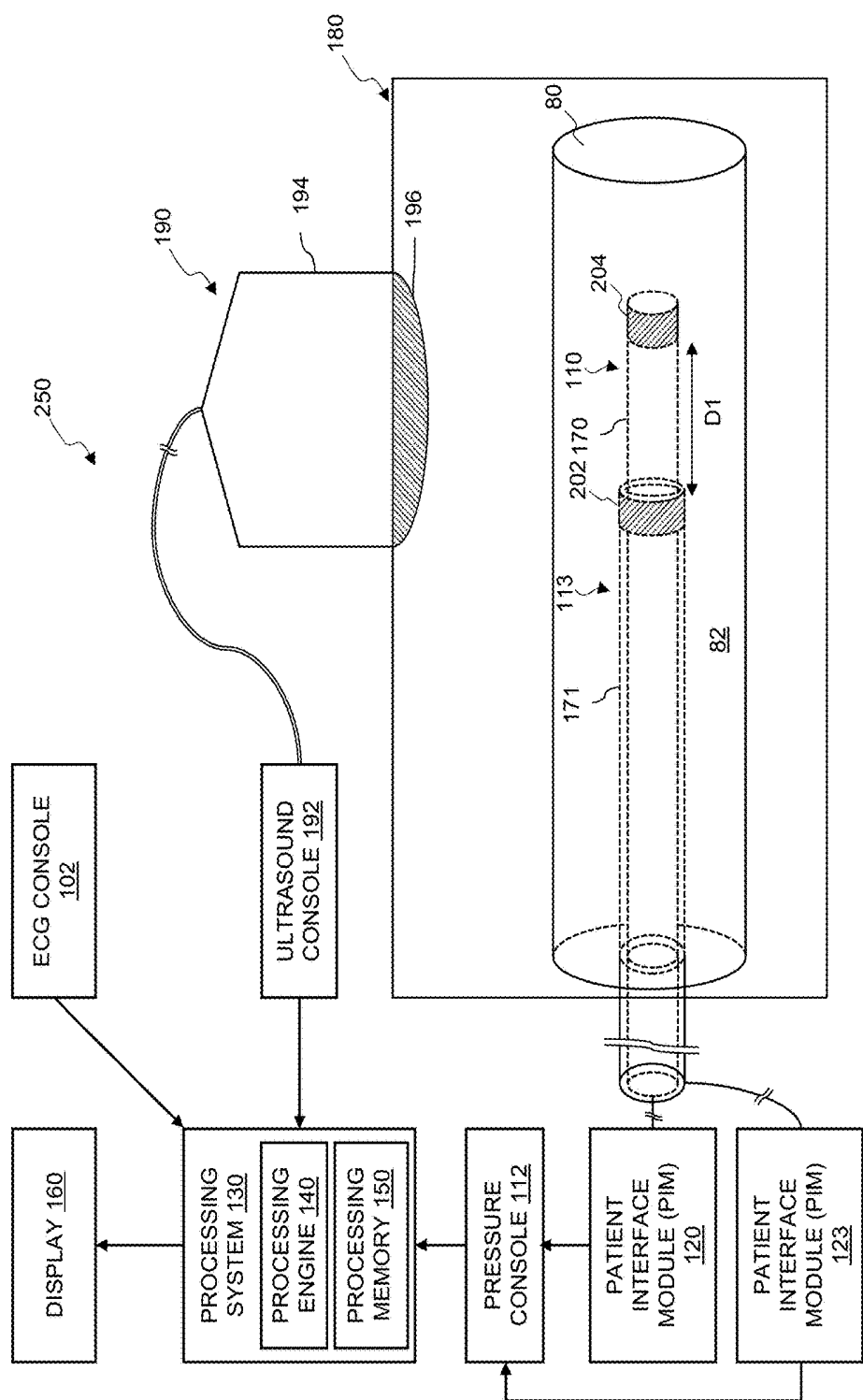


Fig. 1C

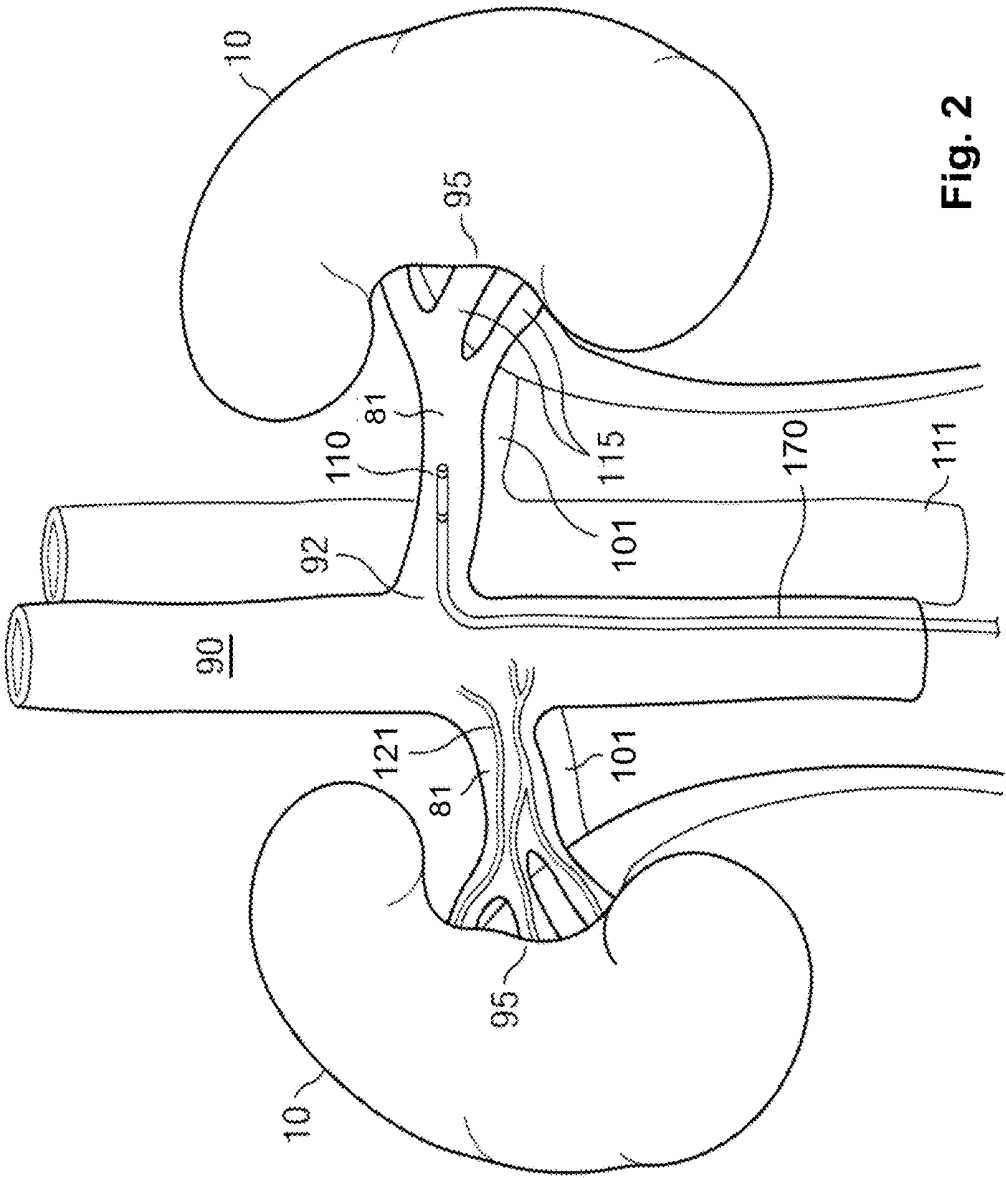


Fig. 2

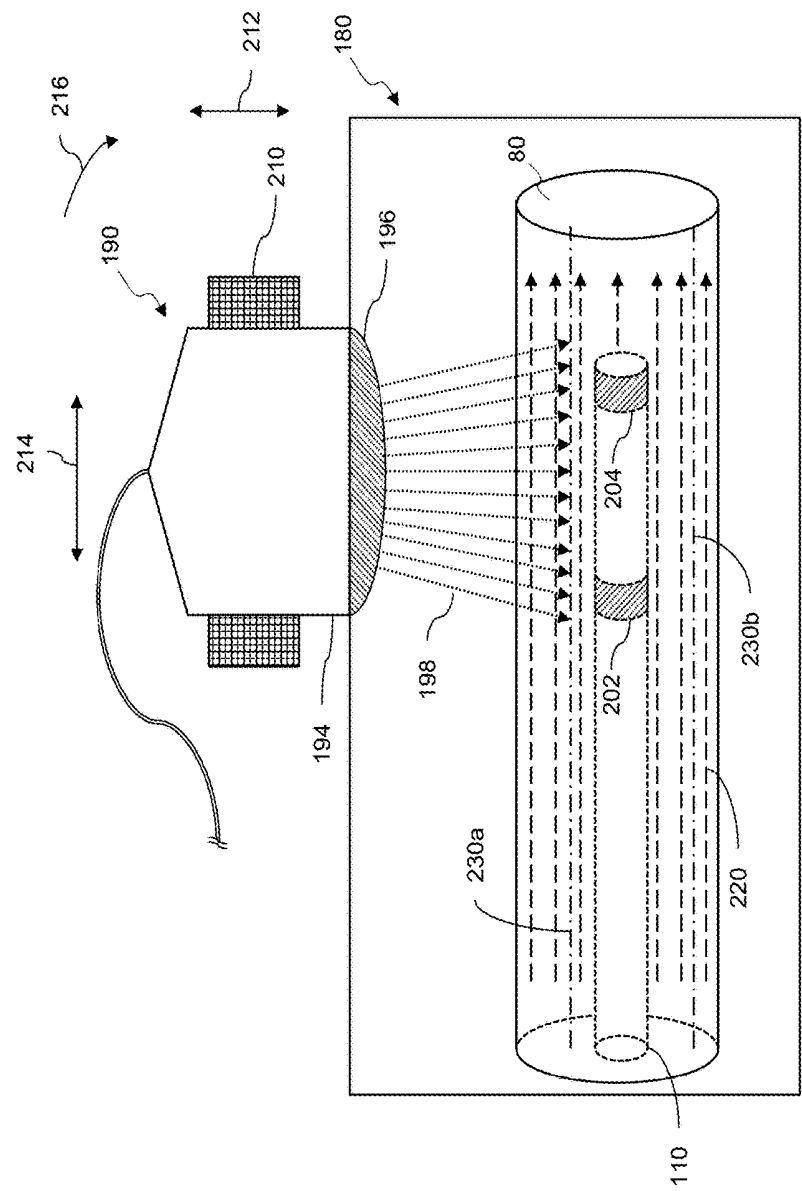


Fig. 3A

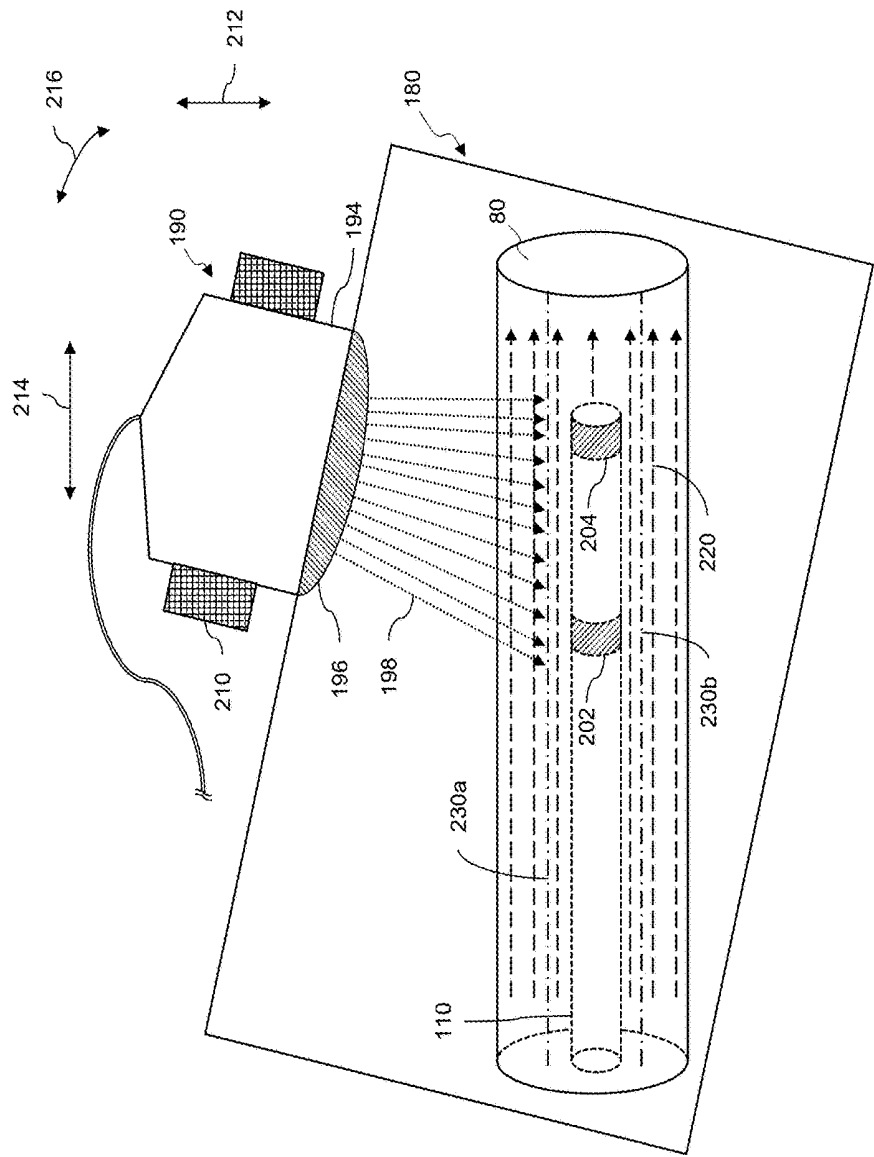


Fig. 3B

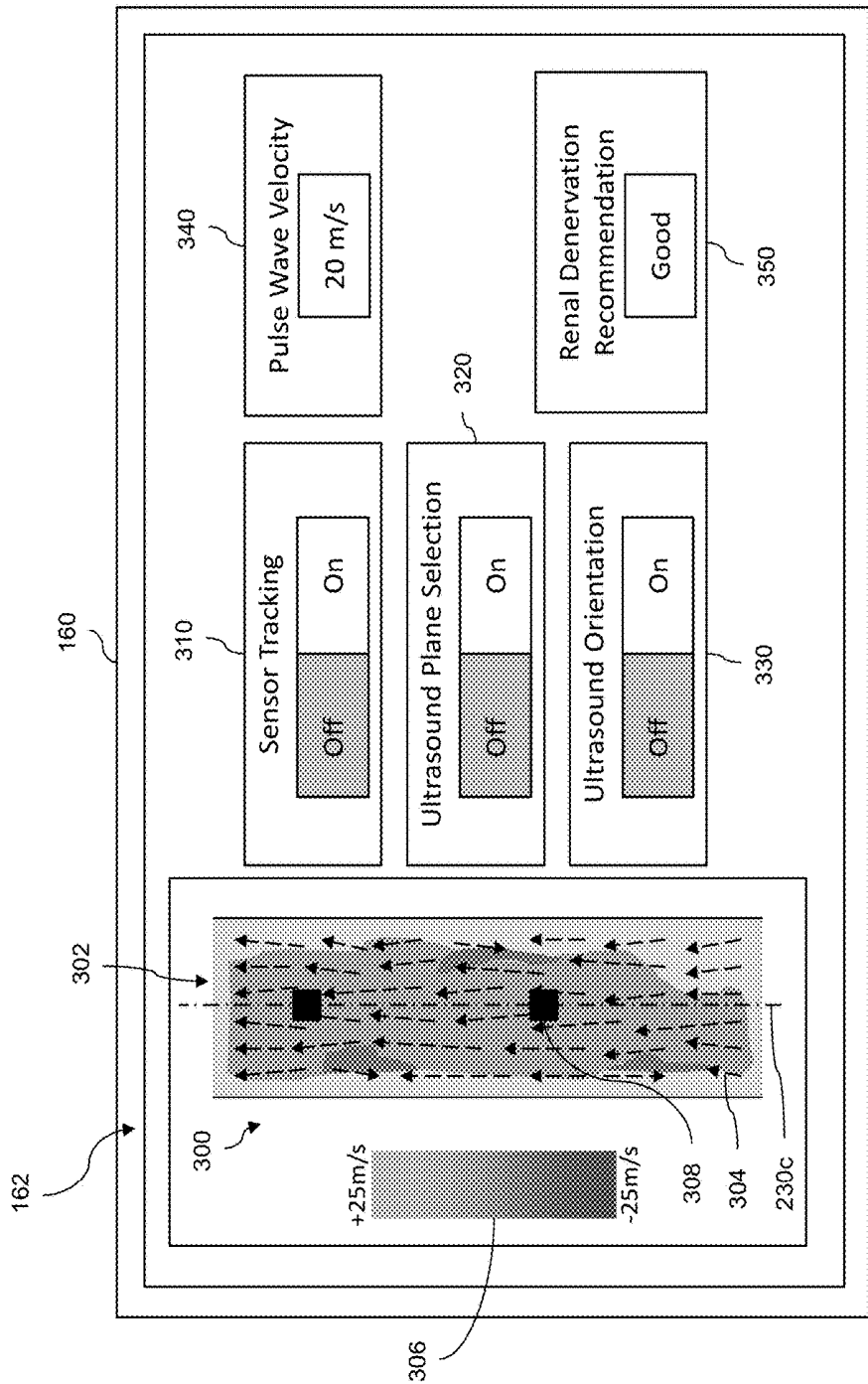


Fig. 4

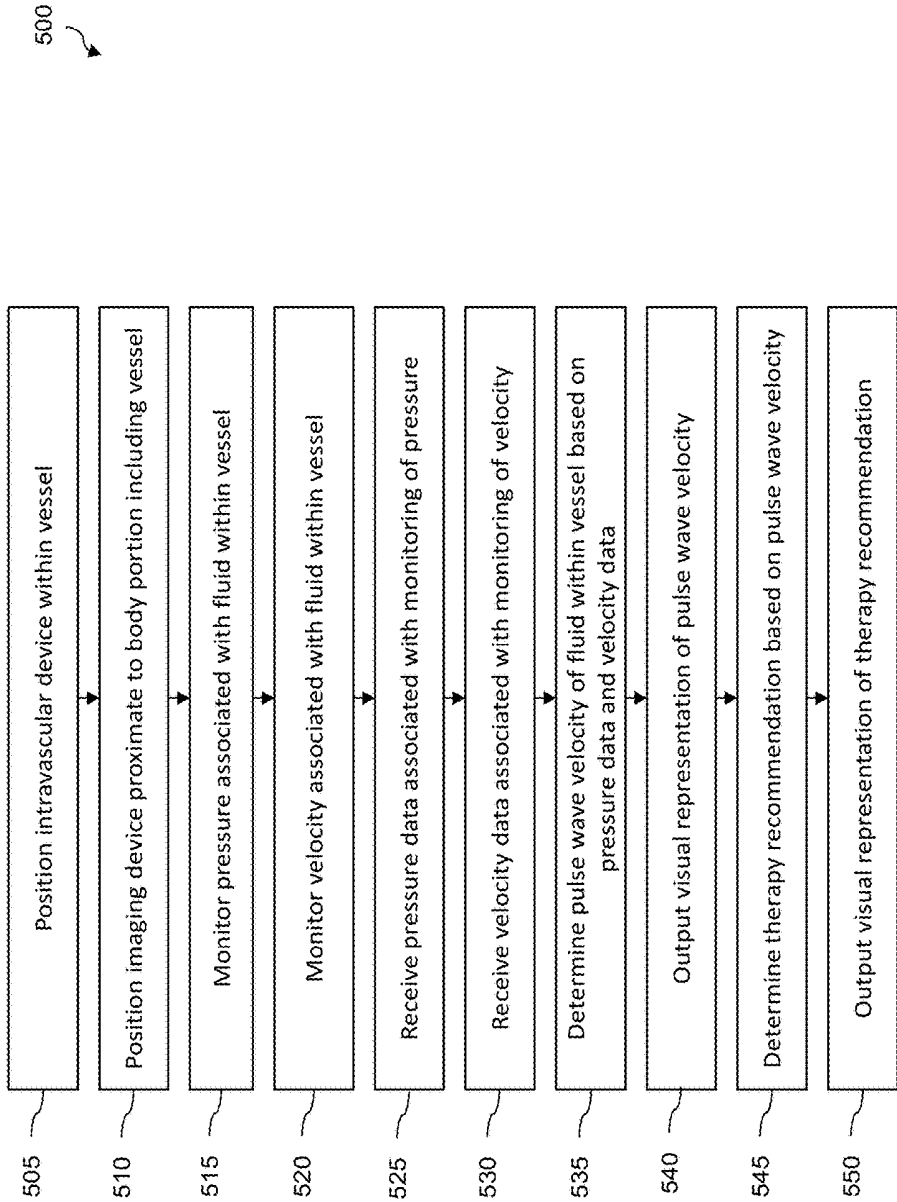


Fig. 5

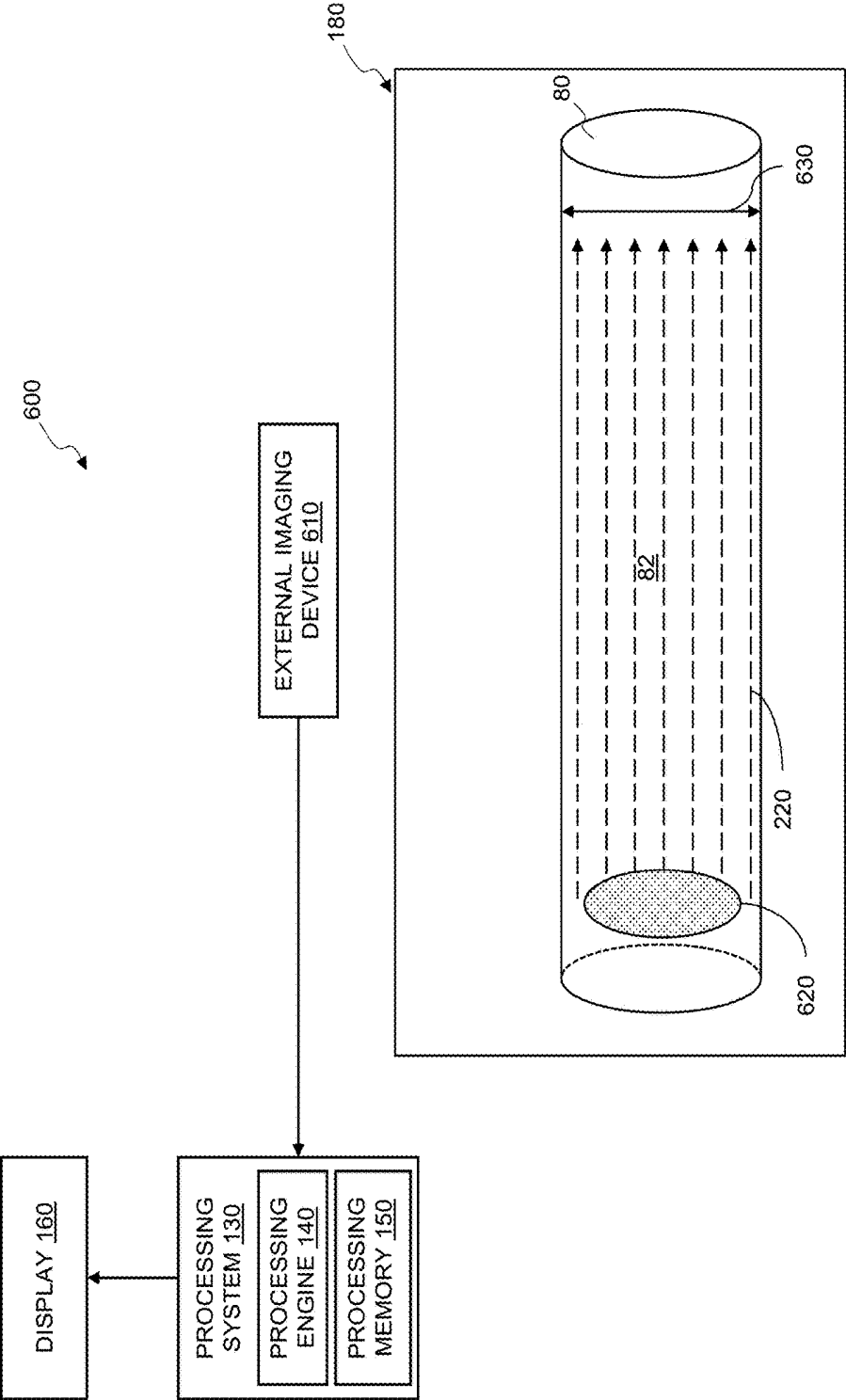


Fig. 6

**DETERMINING PULSE WAVE VELOCITY
USING INTRAVASCULAR PRESSURE
MEASUREMENT AND EXTERNAL
ULTRASOUND IMAGING, AND
ASSOCIATED DEVICES, SYSTEMS, AND
METHODS**

**CROSS REFERENCE TO RELATED
APPLICATIONS**

[0001] The present application is a continuation-in-part of International Application No. PCT/EP2017/062230, filed May 22, 2017, which claims priority to and the benefit of European Application No. EP 16176863.5, filed Jun. 29, 2016, and European Application No. EP 16170635.3, filed May 20, 2016, each of which is herein incorporated by reference in its entirety.

TECHNICAL FIELD OF THE INVENTION

[0002] Embodiments of the present disclosure relate generally to the field of medical devices and, more particularly, to apparatuses, systems, and methods for determining pulse wave velocity.

BACKGROUND OF THE INVENTION

[0003] Hypertension and its associated conditions, chronic heart failure (CHF) and chronic renal failure (CRF), constitute a significant and growing global health concern. Current therapies for these conditions span the gamut covering non-pharmacological, pharmacological, surgical, and implanted device-based approaches. Despite the vast array of therapeutic options, the control of blood pressure and the efforts to prevent the progression of heart failure and chronic kidney disease remain unsatisfactory.

[0004] Blood pressure is controlled by a complex interaction of electrical, mechanical, and hormonal forces in the body. The main electrical component of blood pressure control is the sympathetic nervous system (SNS), a part of the body's autonomic nervous system, which operates without conscious control. The sympathetic nervous system connects the brain, the heart, the kidneys, and the peripheral blood vessels, each of which plays an important role in the regulation of the body's blood pressure. The brain plays primarily an electrical role, processing inputs and sending signals to the rest of the SNS. The heart plays a largely mechanical role, raising blood pressure by beating faster and harder, and lowering blood pressure by beating slower and less forcefully. The blood vessels also play a mechanical role, influencing blood pressure by either dilating (to lower blood pressure) or constricting (to raise blood pressure).

[0005] The importance of blood pressure in the kidneys is amplified because of the central electrical, mechanical, and hormonal role of the kidneys play. For example, the kidneys affect blood pressure by signaling the need for increased or lowered pressure through the SNS (electrical), by filtering blood and controlling the amount of fluid in the body (mechanical), and by releasing key hormones that influence the activities of the heart and blood vessels to maintain cardiovascular homeostasis (hormonal). The kidneys send and receive electrical signals from the SNS and thereby affect the other organs related to blood pressure control. They receive SNS signals primarily from the brain, which partially control the mechanical and hormonal functions of the kidneys. At the same time, the kidneys also send signals

to the rest of the SNS, which may boost the level of sympathetic activation of all the other organs in the system, effectively amplifying electrical signals in the system and the corresponding blood pressure effects. From the mechanical perspective, the kidneys are responsible for controlling the amount of water and sodium in the blood, directly affecting the amount of fluid within the circulatory system. If the kidneys allow the body to retain too much fluid, the added fluid volume raises blood pressure. Lastly, the kidneys produce blood pressure regulating hormones including renin, an enzyme that activates a cascade of events through the renin-angiotensin-aldosterone system (RAAS). This cascade, which includes vasoconstriction, elevated heart rate, and fluid retention, may be triggered by sympathetic stimulation. The RAAS operates normally in non-hypertensive patients but may become overactive among hypertensive patients. The kidney also produces cytokines and other neurohormones in response to elevated sympathetic activation that may be toxic to other tissues, particularly the blood vessels, heart, and kidney. As such, overactive sympathetic stimulation of the kidneys may be responsible for much of the organ damage caused by chronic high blood pressure.

[0006] Thus, overactive sympathetic stimulation of the kidneys plays a significant role in the progression of hypertension, CHF, CRF, and other cardio-renal diseases. Heart failure and hypertensive conditions often result in abnormally high sympathetic activation of the kidneys, creating a vicious cycle of cardiovascular injury. An increase in renal sympathetic nerve activity leads to the decreased removal of water and sodium from the body, as well as increased secretion of renin, which leads to vasoconstriction of blood vessels supplying the kidneys. Vasoconstriction of the renal vasculature causes decreased renal blood flow, which causes the kidneys to send afferent SNS signals to the brain, triggering peripheral vasoconstriction and increasing a patient's hypertension. Reduction of sympathetic renal nerve activity, e.g., via renal neuromodulation or denervation of the renal nerve plexus, may reverse these processes.

[0007] Efforts to control the consequences of renal sympathetic activity have included the administration of medications such as centrally acting sympatholytic drugs, angiotensin converting enzyme inhibitors and receptor blockers (intended to block the RAAS), diuretics (intended to counter the renal sympathetic mediated retention of sodium and water), and beta-blockers (intended to reduce renin release). The current pharmacological strategies have significant limitations, including limited efficacy, compliance issues, and side effects.

[0008] As an example, thermal neuromodulation by either intravascular heating or cooling may decrease renal sympathetic activity by disabling the efferent and/or afferent sympathetic nerve fibers that surround the renal arteries and innervate the kidneys through renal denervation, which involves selectively disabling renal nerves within the sympathetic nervous system (SNS) to create at least a partial conduction block within the SNS.

[0009] Also, several forms of renal injury or stress may induce activation of the renal afferent signals (e.g., from the kidney to the brain or the other kidney). For example, renal ischemia, a reduction in stroke volume or renal blood flow, may trigger activation of renal afferent nerve activity. Increased renal afferent nerve activity results in increased systemic sympathetic activation and peripheral vasoconstriction (narrowing) of blood vessels. Increased vasocon-

striction results in increased resistance of blood vessels, which results in hypertension. Increased renal efferent nerve activity (e.g., from the brain to the kidney) results in further increased afferent renal nerve activity and activation of the RAAS cascade, inducing increased secretion of renin, sodium retention, fluid retention, and reduced renal blood flow through vasoconstriction. The RAAS cascade also contributes to systemic vasoconstriction of blood vessel, thereby exacerbating hypertension. In addition, hypertension often leads to vasoconstriction and atherosclerotic narrowing of blood vessels supplying the kidneys, which causes renal hypoperfusion and triggers increased renal afferent nerve activity. In combination this cycle of factors results in fluid retention and increased workload on the heart, thus contributing to the further cardiovascular and cardio-renal deterioration of the patient.

[0010] Furthermore, because renal denervation reduces overactive SNS activity, it may be valuable in the treatment of several other medical conditions related to hypertension. These conditions, which are characterized by increased SNS activity, include left ventricular hypertrophy, chronic renal disease, chronic heart failure, insulin resistance (diabetes and metabolic syndrome), cardio-renal syndrome, osteoporosis, and sudden cardiac death. For example, other benefits of renal denervation may theoretically include: reduction of insulin resistance, reduction of central sleep apnea, improvements in perfusion to exercising muscle in heart failure, reduction of left ventricular hypertrophy, reduction of ventricular rates in patients with atrial fibrillation, abrogation of lethal arrhythmias, and slowing of the deterioration of renal function in chronic kidney disease. Moreover, chronic elevation of renal sympathetic tone in various disease states that exist with or without hypertension may play a role in the development of overt renal failure and end-stage renal disease. Because the reduction of afferent renal sympathetic signals contributes to the reduction of systemic sympathetic stimulation, renal denervation may also benefit other organs innervated by sympathetic nerves. Thus, renal denervation may also alleviate various medical conditions, even those not directly associated with hypertension.

[0011] As noted, renal denervation is a treatment option for resistant hypertension. However, the efficacy of renal denervation may be very variable between patients. Recent studies indicate that the velocity of the pressure/flow pulse (pulse wave velocity or PWV) inside the main renal artery may be indicative of the outcome of renal denervation. Additionally, the PWV in patients with resistant hypertension may be very high (e.g., more than 20 m/s), which may make it difficult to determine the PWV in the relatively short renal arteries (e.g., 5-8 cm in length).

[0012] While existing diagnostic and/or treatment methods have been generally adequate for their intended purposes, they have not been entirely satisfactory in all respects. The devices, systems, and associated methods of the present disclosure overcome one or more of the shortcomings of the prior art.

[0013] WO 00/55579 A2 discloses a method and devices for determining volume flow, blood velocity profile, artery wall properties of a tubular conduit system and stenosis identification and localization by introducing an artificial pressure or flow excitation signal (a single signal or multiple signals) into the blood vessel (or in any other tubular flowing

fluid conduits), and or using natural heart beat signals measurement and analysis of the vessel wall displacements or vessel diameter changes.

[0014] US 2009/0270695 A1 discloses an apparatus and methods for continuous intravascular measurement of whole blood concentration, blood pressure, and pulse pressure. The intravascular catheter incorporates a sensor to measure whole blood sound velocity, attenuation, backscatter amplitude, and blood flow velocity and also incorporates existing technologies for multiple physiologic measurements of whole blood. Pulse wave velocity and wave intensity are derived mathematically for purposes of estimating degree of local vascular tone.

SUMMARY OF THE INVENTION

[0015] The present disclosure describes calculation of a physiological quantity known as a pulse wave velocity (PWV). The PWV represents the velocity of the pressure and flow waves that propagate through blood vessels of a patient as a result of the heart pumping. Recent studies indicate that the PWV within the renal artery, which is an artery that supplies blood to the kidney, is indicative of whether a therapeutic procedure known as renal denervation will be successful in the patient. Renal denervation is used to treat hypertension. As described in more detail herein, PWV can be calculated using measurements of velocity and pressure within the vessel. The velocity data can be obtained by an ultrasound imaging device positioned outside of the body. The pressure data can be obtained by an intravascular pressure-sensing device that is positioned within the vessel. By obtaining the velocity data and the pressure data simultaneously and from the same area within the vessel, a mathematical relationship between velocity and pressure is used to calculate the PWV. The calculated PWV for the patient can then be used to determine whether the patient is good candidate for treatment. For example, the PWV measurement result can be used to perform patient stratification for the renal denervation, before performing the treatment, by predicting the efficacy of renal denervation based on PWV.

[0016] In one embodiment, an apparatus for pulse wave velocity (PWV) determination in a vessel is provided. The apparatus includes an intravascular device sized and shaped for positioning within the vessel, the intravascular device including a flexible elongate member having a proximal portion and a distal portion; and a pressure sensor coupled to the distal portion of the flexible elongate member, the pressure sensor configured to monitor a pressure of a fluid within the vessel; an imaging device configured to monitor a velocity of the fluid within the vessel, the imaging device including an external ultrasound transducer configured for positioning proximate to a body portion including the vessel; and a processing system in communication with the intravascular device and the imaging device, the processing system configured to: synchronize the monitoring of the pressure within the vessel by the pressure sensor with the monitoring of the velocity within the vessel by the imaging device; and determine the pulse wave velocity of the fluid within the vessel based on the pressure and the velocity within the vessel.

[0017] In one embodiment, a method of determining pulse wave velocity (PWV) in a vessel is provided. The method includes monitoring pressure associated with a fluid within the vessel, the monitoring pressure being performed using

an intravascular device including a pressure sensor and positioned within the vessel; monitoring velocity associated with the fluid within the vessel, the monitoring velocity being performed using an imaging device positioned outside of a body portion including the vessel; receiving pressure data associated with the monitoring of the pressure; receiving velocity data associated with the monitoring of the velocity; and determining the pulse wave velocity of the fluid within the vessel based on the pressure data and the velocity data wherein the monitoring of the pressure within the vessel by the pressure sensor is synchronized by a processing system with the monitoring of the velocity within the vessel by the imaging device.

[0018] It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory in nature and are intended to provide an understanding of the present disclosure without limiting the scope of the present disclosure. In that regard, additional aspects, features, and advantages of the present disclosure will be apparent to one skilled in the art from the following detailed description.

BRIEF DESCRIPTION OF THE DRAWINGS

[0019] The accompanying drawings illustrate embodiments of the devices and methods disclosed herein and together with the description, serve to explain the principles of the present disclosure.

[0020] FIG. 1A is a diagrammatic schematic view of an exemplary intravascular system.

[0021] FIG. 1B is a diagrammatic schematic view of an exemplary intravascular system.

[0022] FIG. 1C is a diagrammatic schematic view of an exemplary intravascular system.

[0023] FIG. 2 is a schematic diagram illustrating an intravascular device positioned within renal anatomy.

[0024] FIG. 3A is a diagrammatic illustration of obtaining pressure data and velocity data within a vessel using an exemplary intravascular system.

[0025] FIG. 3B is a diagrammatic illustration of obtaining pressure data and velocity data within a vessel using an exemplary intravascular system.

[0026] FIG. 4 is an illustration of an exemplary screen display of an intravascular system.

[0027] FIG. 5 is a flowchart illustrating a method of calculating a pulse wave velocity.

[0028] FIG. 6 is a diagrammatic schematic view of an exemplary PWV determination system.

DETAILED DESCRIPTION OF THE EMBODIMENTS

[0029] For the purposes of promoting an understanding of the principles of the present disclosure, reference will now be made to the embodiments illustrated in the drawings, and specific language will be used to describe the same. It is nevertheless understood that no limitation to the scope of the disclosure is intended. Any alterations and further modifications to the described devices, systems, and methods, and any further application of the principles of the present disclosure are fully contemplated and included within the present disclosure as would normally occur to one skilled in the art to which the disclosure relates. In particular, it is fully contemplated that the features, components, and/or steps described with respect to one embodiment may be combined

with the features, components, and/or steps described with respect to other embodiments of the present disclosure. For the sake of brevity, however, the numerous iterations of these combinations will not be described separately.

[0030] The present disclosure relates generally to devices, systems, and methods for determining and measuring pulse wave velocity (PWV) in a main renal artery. An apparatus for PWV determination includes an intravascular device having a pressure sensor. The intravascular device is sized and shaped for positioning within a vessel, such as the main renal artery. While positioned within the vessel, the intravascular device obtains pressure measurements of the fluid, such as blood, flowing within the vessel. The apparatus also includes an imaging device, such as an external ultrasound device. The imaging device can be positioned outside of the body, such as in contact with and/or adjacent to a body portion including the vessel. The imaging device can obtain velocity data, including a magnitude and direction, associated with the fluid flow within the vessel. The apparatus may further include a computing device, such as a controller or computing device, in communication with intravascular device and the imaging device. The computing device calculates the PWV based on the obtained pressure data and velocity data.

[0031] The PWV may be predictive of the outcome of renal denervation in treating resistive hypertension. As described herein, the computing device can output the calculated PWV to a display. A clinician may make therapeutic and/or diagnostic decisions, taking the PWV into consideration, such as whether to recommend the patient for a renal denervation procedure. In some instances, the computer system can determine and output a therapy recommendation or a likelihood-of-success prediction to the display, based on the PWV and/or other patient data. That is, the computer system may utilize the PWV to identify which patients are more likely and/or less likely to benefit from renal denervation.

[0032] FIG. 1A is a diagrammatic schematic view of an exemplary intravascular system **100** according to some embodiments of the present disclosure. The system **100** may include an intravascular device **110**, an imaging device **190**, a processing system **130**, and a display **160**. The system **100** may also include an interface module **120**, a pressure console **112**, an ultrasound console **192**, and an electrocardiograph (ECG) console **102**. The system **100** may be configured to perform pulse wave velocity (PWV) determination in a vessel **80** within a body portion. The intravascular system **100** may be referred to as a stratification system in that the PWV may be used for patient stratification for treatment purposes. For example, the PWV determination in the renal arteries may be utilized to determine whether a patient is suitable for and/or likely to benefit from renal artery denervation. Based on the PWV determination, the intravascular system **100** may be used to classify one or more patients into groups respectively associated with varying degrees of predicted therapeutic benefit of renal denervation. Any suitable number of groups or categories are contemplated. For example, the groups may include groups respectively for those patients with low, moderate, and/or high likelihood of therapeutic benefit from renal denervation, based on the PWV. Based on the stratification or classification, the system **100** can recommend the degree to which one or more patients are suitable candidates for renal denervation.

[0033] The vessel **80** may represent fluid-filled or surrounded structures, both natural and man-made. The vessel **80** may be within a body of a patient. The vessel **80** may be a blood vessel, as an artery or a vein of a patient's vascular system, including cardiac vasculature, peripheral vasculature, neural vasculature, renal vasculature, and/or any other suitable lumen inside the body. For example, the device **110** may be used to examine any number of anatomical locations and tissue types, including without limitation, organs including the liver, heart, kidneys, gall bladder, pancreas, lungs; ducts; intestines; nervous system structures including the brain, dural sac, spinal cord and peripheral nerves; the urinary tract; as well as valves within the heart, chambers or other parts of the heart, and/or other systems of the body. In addition to natural structures, the device **110** may be used to examine man-made structures such as, but without limitation, heart valves, stents, shunts, filters and other devices. Walls of the vessel **80** define a lumen **82** through which fluid flows within the vessel **80**.

[0034] The vessel **80** may be located within the body portion **180**. When the vessel **80** is the renal artery, the patient body portion **180** may include the abdomen, lumbar region, and/or thoracic region. Generally, vessel **80** may be located within any portion **180** of the patient body, including the head, neck, chest, abdomen, arms, groin, legs, etc.

[0035] The intravascular device **110** may be a catheter, guide wire, or guide catheter, and/or other long, thin, long, flexible structure that is sized and shaped to be inserted into the lumen **82** of the vessel **80**. In that regard, the intravascular device **110** includes a flexible elongate member **170** having a distal portion **172** and a proximal portion **174**. The illustrated embodiments of the intravascular device **110** may have a cylindrical profile with a circular cross-sectional profile, which defines an outer diameter of the intravascular device **110**. In other instances, all or a portion of the intravascular device may have other geometric cross-sectional profiles (e.g., oval, rectangular, square, elliptical, etc.) or non-geometric cross-sectional profiles. In some embodiments, the intravascular device **110** may or may not include a lumen extending along all or a portion of its length for receiving and/or guiding other instruments. If the intravascular device **110** includes a lumen, the lumen may be centered or offset with respect to the cross-sectional profile of the device **110**.

[0036] The intravascular device **110**, or the various components thereof, may be manufactured from a variety of materials, including, by way of non-limiting example, plastics, polytetrafluoroethylene (PTFE), polyether block amide (PEBAX), thermoplastic, polyimide, silicone, elastomer, metals, such as stainless steel, titanium, shape-memory alloys such as Nitinol, and/or other biologically compatible materials. In addition, the intravascular device may be manufactured in a variety of lengths, diameters, dimensions, and shapes, including a catheter, guide wire, a combination of catheter and guide wire, etc. For example, in some embodiments the flexible elongate member **170** may be manufactured to have length ranging from approximately 115 cm-155 cm. In one particular embodiment, the flexible elongate member **170** may be manufactured to have length of approximately 135 cm. In some embodiments, the flexible elongate member **170** may be manufactured to have an outer transverse dimension or diameter ranging from about 0.35 mm-2.67 mm (1 Fr-8 Fr). In one embodiment, the flexible

elongate member **170** may be manufactured to have a transverse dimension of 2 mm (6 Fr) or less, thereby permitting the intravascular device **110** to be configured for insertion into the renal vasculature of a patient. These examples are provided for illustrative purposes only, and are not intended to be limiting. Generally, the intravascular device **110** is sized and shaped such that it may be moved inside the vasculature (or other internal lumen(s)) of a patient such that the pressure of a vessel **80** may be monitored from within the vessel **80**.

[0037] In the embodiment of FIG. 1A, the intravascular device **110** includes a single sensor **204** disposed at a distal portion **172** of the flexible elongate member **170**. In other embodiments, such as an intravascular system **200** of FIG. 1B, the intravascular device **110** includes two sensors **202**, **204** disposed at the distal portion **172** of the flexible elongate member **170**. The sensors **202**, **204** may be disposed a known distance **D1** apart from one another along the length of the flexible elongate member **170**. In some embodiments, the distance **D1** is fixed distance between approximately 0.5 and approximately 10 cm. In some embodiments, the distance **D1** is between approximately 0.5 cm and approximately 2 cm. In some embodiments, blood pressure measurements may be used to identify pulse waves passing through the vessel.

[0038] The sensors **202**, **204** may be configured to collect data about conditions within the vessel **80**, and in particular, monitor a pressure within the vessel **80**. Furthermore, the sensors **202**, **204** may periodically measure the pressure of fluid (e.g., blood) at the location of the sensors **202**, **204** inside the vessel **80**. In an example, the sensors **202**, **204** are capacitive pressure sensors, or in particular, capacitive MEMS pressure sensors. In another example, the sensors **202**, **204** are piezo-resistive pressure sensors. In yet another example, the sensors **202**, **204** are optical pressure sensors. In some instances, the sensors **202**, **204** include components similar or identical to those found in commercially available pressure monitoring elements such as the PrimeWire PRES-TIGE® pressure guide wire, the PrimeWire® pressure guide wire, and the ComboWire® XT pressure and flow guide wire, each available from Volcano Corporation. The intravascular device **110** is in communication with the interface module **120**, the pressure console **112**, and/or the processing system **130** such that the intravascular data obtained by the sensors **202**, **204** is transmitted by the intravascular device **110** and received at the processing system **130**.

[0039] In one embodiment, the sensors **202**, **204** are disposed circumferentially around a distal portion of the intravascular device **110**. In another embodiment, the sensors **202**, **204** are contained within the body of the intravascular device **110**. In other embodiments, the sensors **202**, **204** are disposed longitudinally and/or radially across the intravascular device **110** in a manner that permits the fluid within the vessel **80** to exert pressure on the sensors **202**, **204**. The sensors **202**, **204** may include one or more transducer elements. The sensor **202** and/or the sensor **204** may be movable along a length of the intravascular device **110** and/or fixed in a stationary position along the length of the intravascular device **110**. The sensors **202**, **204** may be part of a planar or otherwise suitably-shaped array of sensors of the intravascular device **110**. In some embodiments, the outer diameter of the flexible elongate member **170** is equal to or larger than the outer diameter of the sensors **202**, **204**. In some embodiments, the outer diameter of the flexible

elongate member 170 and sensors 202, 204 are equal to or less than about 1 mm, which may help to minimize the effect of the intravascular device 110 on pressure measurements within the vessel 80. In particular, since a renal artery generally has a diameter of approximately 5 mm, a 1 mm outer diameter of the intravascular device 110 may obstruct less than 4% of the vessel.

[0040] In some embodiments, one or both of the sensors 202, 204 may not be part of the same intravascular device 110. For example, as shown the intravascular system 250 of FIG. 1C, the sensors 202, 204 may be coupled to separate intravascular devices 110, 113. In that regard, the intravascular device 113 includes a flexible elongate member 171. The sensor 202 is coupled to a distal portion of the flexible elongate member 171. The sensor 204 may be coupled to a distal portion of the flexible elongate member 170 of the intravascular device 110. In some embodiments, the intravascular device 113 may be a catheter and the intravascular device 110 may be a guide wire extending through a lumen of the catheter such that the sensor 204 is positioned distally of the sensor 202 within the vessel 80. In such an arrangement, sensor 202 may be configured to obtain a proximal pressure measurement and the sensor 204 may be configured to obtain a distal pressure measurement. The intravascular device 113 may be in communication with the processing system 130 via the pressure console 112 and/or the interface module 123.

[0041] Referring to FIGS. 1A, 1B, and 1C, the imaging device 190 is configured to obtain imaging data associated with the vessel 80. The imaging device 190 may be an ultrasound imaging device in some embodiments. In that regard, the imaging device 190 can include a probe 194 having an ultrasound transducer 196. The transducer 196 may be a single transducer element, an array of transducer elements, and/or other suitable arrangement of transducer elements. In some instances, the probe 194 is sized and shaped for handheld grasping by a user, such as the clinician. In some embodiments, such as those illustrated in FIGS. 3A and 3B, the probe 194 is coupled to and/or disposed within a holder 210. As described herein, the holder 210 is configured to move the probe 194 into a position and/or orientation for the transducer 196 to obtain imaging data in a desired manner from the vessel 80.

[0042] Generally, as shown in FIGS. 3A and 3B, the transducer 196 is configured to emit ultrasonic energy 198 in order to create an image of the vessel 80 and/or surrounding anatomy within the body portion 180. Ultrasonic waves 198 are partially reflected by discontinuities arising from tissue structures (such as the various layers of the vessel wall), red blood cells, and other features of interest. Echoes from the reflected waves are received by the transducer and passed along to the ultrasound console 192 and/or the processing system 130. The ultrasound console 192 and/or the processing system 130 processes the received ultrasound echoes to produce an image of the vessel 80 and/or the body portion 180 based on the acoustic impedance associated with the ultrasound echoes. The image may be a two-dimensional cross-sectional image or a three-dimensional image of the vessel. The imaging device 190 and/or the ultrasound console 192 may include features similar or identical to those found in commercially available ultrasound imaging elements such as the EPIQ, Affiniti, and/or CX50 ultrasound systems, each available from Koninklijke Philips N.V.

[0043] The probe 194 and/or the transducer 196 are positioned outside of the body portion 180. However, the probe 194 and/or the transducer 196 may be positioned proximate to and/or in contact with the body portion 180 including the vessel 80. The clinician and/or the holder 210 may contact the transducer 196 to the body portion 180 such that the anatomy is compressed in a resilient manner. The view of the anatomy shown in the ultrasound image depends on the position and orientation of the probe 194. To obtain imaging data of the vessel 80, including the sensors 202, 204, the probe 194 can be suitably positioned either manually by a clinician and/or automatically by the holder 210 so that the transducers 196 emits ultrasound waves and receives ultrasound echoes from the appropriate portion of the vessel 80.

[0044] Imaging data obtained by the imaging device 190 can include velocity data and/or lumen data. In this regard, the vessel 80 includes anatomical structure, such as vessel walls that define the lumen 82, as well as fluid within the 80. Fluid within the vessel 80 is moving relative to the imaging device 190. Lumen data obtained by the imaging device 190 may be representative of relatively stationary anatomy, including the vessel walls. The ultrasound console 192 and/or the processing system 130 generate a B-mode (brightness mode) imaging of anatomy corresponding to the varying acoustic impedance of the received ultrasound echoes. The lumen data can be used to evaluate the diameter, cross-sectional area, volume, and/or other geometric data associated with the vessel 80. The velocity data obtained by the imaging device 190 is representative of the magnitude and/or the direction of fluid flow within the vessel 80. In that regard, the velocity data may be indicative of localized magnitude/direction of fluid flow (e.g., for each pixel in the image of the vessel 80). Various techniques exist for determining velocity data, including Doppler flow and vector flow. In Doppler flow imaging, the frequency shift associated with ultrasound energy obtained by the transducer 196 is calculated and used to determine the speed and direction of the fluid flow. Doppler flow imaging may depend on angle of the transducer 196 relative to the fluid flow and be limited to one-dimensional flow information. Vector flow imaging derives three-dimensional flow information from the ultrasound data obtained by the transducer 196 so that angle-independent visualization of fluid flow is provided.

[0045] The lumen data and the velocity data are often combined for display on the display 160, as shown for example in FIG. 4. Doppler flow data 302 may be illustrated as different colors indicative of varying magnitudes and direction of fluid flow, as provided in the key or legend 306. Vector flow data may be illustrated symbolically such as with arrows 304 having varying magnitudes and directions. The Doppler flow and/or vector flow data may be referenced as a velocity map that is overlaid on the B-mode image of the vessel 80 illustrating the vessel geometry.

[0046] Referring again to FIGS. 1A, 1B, and 1C, the systems 100, 200, and 250 can include an electrocardiograph (ECG) console configured to obtain ECG data from electrodes positioned on the patient. ECG signals are representative of electrical activity of the heart and can be used to identify the patient's cardiac cycle and/or portions thereof. As described in greater detail herein, the processing system 130 can utilize different formula to calculate PWV based on whether the velocity data obtained by the imaging device 190 and/or the pressure data obtained by the intravascular device 110 is obtained over an entire cardiac cycle and/or a

portion thereof. The ECG data can be used to identify the beginning and ending of the previous, current, and next cardiac cycle(s), the beginning and ending of systole, the beginning and ending of diastole, among other portions of the cardiac cycle. Generally, one or more identifiable feature of the ECG signal (including without limitation, the start of a P-wave, the peak of a P-wave, the end of a P-wave, a PR interval, a PR segment, the beginning of a QRS complex, the start of an R-wave, the peak of an R-wave, the end of an R-wave, the end of a QRS complex (J-point), an ST segment, the start of a T-wave, the peak of a T-wave, and the end of a T-wave) can be utilized to select relevant portions of the cardiac cycle. The ECG console 102 may include features similar or identical to those found in commercially available ECG elements such as the PageWriter cardiograph system available from Koninklijke Philips N.V.

[0047] In other embodiments, the pressure data obtained by the intravascular device 110 is used to identify relevant portions of the cardiac cycle. In that regard, the pressure data may be used in lieu of or in addition to the ECG data. For example, the minimum value, the maximum value, slope, and/or other values of a pressure waveform representative of the obtained pressure data may be indicative of cardiac cycle(s) and/or portions thereof, including systole and diastole.

[0048] The processing system 130 may be in communication with the intravascular device 110. For example, the processing system 130 may communicate with the intravascular device 110, including the sensor 202 and/or the sensor 204, through an interface module 120 and/or pressure console 112. The processor 140 may send commands and receive responses from the intravascular device 110. In some implementations, the processor 140 controls the monitoring of the pressure within the vessel 80 by the sensors 202, 204. In particular, the processor 140 may be configured to trigger the activation of the sensors 202, 204 to measure pressure at specific times. Data from the sensors 202, 204 may be received by the processing engine 140 of the processing system 130. In other embodiments, the processing engine 140 is physically separated from the intravascular device 110 but in communication with the intravascular device 110 (e.g., via wireless communications). In some embodiments, the processing engine 140 is configured to control the sensors 202, 204. Similarly, in embodiments including two intravascular devices (FIG. 1C), the processing system 130 may communicate with the intravascular device 113 through the interface module 123 and/or pressure console 112.

[0049] Similarly, the processing system 130 may be in communication with the imaging device 190. For example, the processing system 130 may communicate with the imaging device 190, including the transducer 196. The processor 140 may send commands and receive responses from the imaging device 190. In some implementations, the processor 140 controls the monitoring of the velocity and/or vessel geometry within the vessel 80 by the transducer 196. In particular, the processor 140 may be configured to trigger the activation of the transducer 196 to obtain velocity data and/or lumen data at specific times. Data from the transducer 196 may be received by a processing engine 140 of the processing system 130. In other embodiments, the processing engine 140 is physically separated from the intravascular device 110 but in communication with the imaging device

190 (e.g., via wireless communications). In some embodiments, the processing engine 140 is configured to control the transducer 196.

[0050] The processor 140 may include an integrated circuit with power, input, and output pins capable of performing logic functions such as commanding the sensors and receiving and processing data. The processor 140 may include any one or more of a microprocessor, a controller, a digital signal processor (DSP), an application specific integrated circuit (ASIC), a field-programmable gate array (FPGA), or equivalent discrete or integrated logic circuitry. In some examples, processor 140 may include multiple components, such as any combination of one or more microprocessors, one or more controllers, one or more DSPs, one or more ASICs, or one or more FPGAs, as well as other discrete or integrated logic circuitry. The functions attributed to processor 140 herein may be embodied as software, firmware, hardware or any combination thereof.

[0051] The processing system 130 may include one or more processors 140 or programmable processor units running programmable code instructions for implementing the pulse wave velocity determination methods described herein, among other functions. The processing system 130 may be integrated within a computer and/or other types of processor-based devices. For example, the processing system 130 may be part of a console, tablet, laptop, handheld device, or other controller used to generate control signals to control or direct the operation of the intravascular device 110. In some embodiments, a user may program or direct the operation of the intravascular device 110 and/or the imaging device 190, and/or control aspects of the display 160. In some embodiments, the processing system 130 may be in direct communication with the intravascular device 110 (e.g., without an interface module 120) and/or the imaging device 190, including via wired and/or wireless communication techniques.

[0052] The processing system 130 may be in communication with the intravascular device 110 via the interface module 120 and/or the pressure console 112. The interface module 120 can include circuitry configured to facilitate transmission of control signals from the processing system 130 to the intravascular device 110, as well as the transmission of pressure data from the intravascular device 110 to the processing system 130. In some embodiments, the interface module 120 can provide power to the sensors 202, 204. In some embodiments, the interface module can perform signal conditioning and/or pre-processing of the pressure data prior to transmission to the processing system 130.

[0053] The pressure console 112 may be representative of processing system associated specifically with the intravascular device 110. In that regard, the pressure console 112 may include a processing engine and processing memory similar to the processing engine 140 and the processing memory 150 of the processing system 130. In some instances, the pressure console 112 processes the pressure data obtained by the sensors 202, 204 to measure pressure associate with the fluid flow within the vessel 80. The processed data may be transmitted by the pressure console 112 to the processing system 130 for further processing in combination with the imaging data obtained by the imaging device 190, including calculation of the PWV based on the pressure data and the imaging data. In some instances, the pressure console 112 and/or the interface module 120 may

be omitted, and the intravascular device 110 may be directly in communication with the processing system 130.

[0054] The processing system 130 may be in communication with the imaging device 190 via the ultrasound console 192. As similarly described with respect to the pressure console 112, the ultrasound console 192 may be representative of processing system associated specifically with the imaging device 190. In that regard, the ultrasound console 192 may include a processing engine and processing memory similar to the processing engine 140 and the processing memory 150 of the processing system 130. In some instances, the ultrasound console 192 processes the imaging data, including the velocity data and/or lumen data, obtained by the transducer 196 to generate images representative of the vessel geometry and/or fluid flow velocity within the vessel 80. The processed data may be transmitted by the ultrasound console 192 to the processing system 130 for further processing in combination with the pressure data obtained by the intravascular device 110, including calculation of the PWV based on the pressure data and the imaging data. In some instances, the ultrasound console 192 may be omitted, and the imaging device 190 may be directly in communication with the processing system 130.

[0055] Moreover, in some embodiments, the pressure console 112, the interface module 120, the ultrasound console 192, and/or the processing system 130 are collocated and/or part of the same system, unit, chassis, or module. Together the pressure console 112, the interface module 120, the ultrasound console 192, and/or the processing system 130 assemble, process, and render the imaging data obtained by the imaging device 190 and the pressure data obtained by the intravascular device 110 for display as an image on a display 160. For example, in various embodiments, the interface module 120 and/or processing system 130 generate control signals to configure the sensors 202, 204, generate signals to activate the sensors 202, 204, perform calculations of pressure data, perform amplification, filtering, and/or aggregating of pressure data, and format the pressure data as an image for display. Similarly, in various embodiments, the processing system 130 generates control signals to configure the transducer 196, generate signals to activate the transducer 196, perform calculations of imaging data, perform amplification, filtering, and/or aggregating of imaging data, and format the imaging data as an image for display. The allocation of these tasks and others may be distributed in various ways between the pressure console 112, the interface module 120, the ultrasound console 192, and/or the processing system 130.

[0056] The processing system 130 is configured to synchronize the collection of the pressure data by the intravascular device 110 and the ultrasound data by the imaging device 190. In some instances, the interface module 120, the pressure console 112, and/or ultrasound console 192, as well as the processing system 130 can include a timer. By communicating to the interface module 120, the pressure console 112, and/or ultrasound console 192, the processing system 130 can synchronize the timer of the interface module 120, the pressure console 112, and/or ultrasound console 192 with the processor timer. Additionally, the interface module 120, the pressure console 112, and/or ultrasound console 192 can do the sampling of the signals received from sensors 202, 204 and the imaging device 190 and can include a time stamp to the sampled data and then send the time-stamped sampled data to the processing sys-

tem 130 such that the pressure data associated with the monitoring of the pressure within the vessel and the velocity data associated monitoring the velocity within the vessel, received by processing system 130, is time-stamped and processing system 130 can synchronize the data based on the received time stamps.

[0057] Alternatively, instead of the interface module 120, the pressure console 112, and/or ultrasound console 192, the sensors 202, 204, and the imaging device 190 can perform the sampling and send the sampled data to the processing system 130. The intravascular device 110 can include one or more timers for the sensors 202, 204, and the imaging device 190 can include a timer. The processing system 130, by communicating to intravascular device 110 and the imaging device 190, can synchronize data collection by the sensors 202, 204 and the transducer 196 with the processor timer. Thus, the data obtained by the imaging device 190 and the sensors 202, 204 can include a time stamp. The interface module 120, the pressure console 112, and/or ultrasound console 192 can use the time stamps to synchronize the obtained data and then send the data to the processing system 130. In another example, the interface module 120, the pressure console 112, and/or ultrasound console 192 can send the time-stamped data obtained by sensors 202, 204 and the imaging device 190 to the processing system 130. The processing system 130 can synchronize the data based on the received time stamps.

[0058] In some instances, ECG data obtained by the ECG console 102 can be used to synchronize collection of the pressure data by the sensors 202, 204 and the imaging data by the imaging device 190. For example, the processing system 130 can provide controls signals to the sensors 202, 204 and the imaging device 190 to simultaneously sample data at the same time in the cardiac cycle. One or more features of the ECG data may be used to determine the point during the cardiac cycle at which to simultaneously sample data.

[0059] In some instances, the sensors 202, 204 and the imaging device 190 obtain data at different rates. Accordingly, the processing system 130 is configured to align acquisition of pressure data and imaging data by offsetting the control signal transmission to sample data. For example, if the sensors 202, 204 sample data at a higher frequency than the imaging device 190, then the processing system 130 can transmit the control signal to the imaging device 190 before transmitting the control signal to the sensors 202, 204. In this manner, because the imaging device 190 has relatively more time to obtain the imaging data than the sensors 202, 204 have time to obtain pressure data, the imaging data and the pressure data can be obtained at the same time. The processing system 130 may implement a calibration procedure to determine any necessary offset in the activation signals to the imaging device 190 and the sensors 202, 204.

[0060] In some embodiments, the processing system 130 is configured to determine PWV based on the pressure data obtained by the sensors and the velocity/imaging data obtained by the imaging device 190. Generally, the PWV refers to the propagation of the pressure/flow waves within the vessel 80 that is determined by its distensibility. As described herein, the velocity data obtained by the imaging device 190 is a localized, instantaneous measurement of the velocity of blood within the vessel. Accordingly, the velocity data obtained by the imaging device 190 together with the

pressure data obtained by intravascular device **110** is used to calculate the PWV. This method of determining PWV is particularly advantageous for relatively short vessels, such as the renal artery.

[0061] As described herein, the pressure data and the velocity data can be both simultaneously obtained and obtained in the same area of the vessel **80**. The processing system **130** can utilize various mathematical relationships between the pressure and velocity within the vessel, as well as other factors, to compute the PWV. One method to determine the PWV is by utilizing the “water hammer” equation during a reflection free period of the cardiac cycle (e.g., early systole):

$$PWV = \frac{1}{\rho} \frac{dP}{dU}, \quad (1)$$

where dP is a change in the pressure over a time interval, dU is a change in the velocity over the time interval, and ρ is a density of the fluid within the vessel. Alternatively, the following relation may be used to calculate the PWV by summation over the whole cardiac cycle:

$$PWV = \frac{1}{\rho} \sqrt{\frac{\sum dP^2}{\sum dU^2}} \quad (2)$$

where dP is a change in the pressure over a time interval, dU is a change in the velocity over the time interval, and ρ is a density of the fluid within the vessel.

[0062] The processing system **130** can select an appropriate mathematical relationship based on whether the pressure data and/or the velocity data are obtained over an entire cardiac cycle or a portion thereof. In that regard, the pressure data and/or the velocity data may be gated based on the ECG data. Thus, the PWV may be calculated using equation (1) above with only the portion of pressure data and velocity data obtained during early systole, determined using the identifiable features of the ECG signal. Similarly, the relevant portion of the pressure data and the velocity data during one or more cardiac cycle(s) can be identified using the ECG signal and used to calculate the PWV with equation (2). In some instances, the features of the pressure waveform (e.g., maximum, minimum, slope, etc.) may be utilized in addition to or in lieu of the ECG data to gate the pressure data and the velocity data. In some instances, the user provides a user input to select the desired mathematical relationship to calculate the PWV, and the processing system **130** can direct collection of the pressure data and the velocity data accordingly.

[0063] The processing system **130** is additionally configured to monitor motion of intravascular device **110**, the sensors **202**, **204**, and/or the imaging device **190**. In that regard, the sensors **202**, **204** and/or the imaging device **190** may move beyond a threshold amount, which renders the data collected during the movement unreliable for PWV calculation. For example, the patient may unexpectedly move, or the clinician may unintentionally move the intravascular device **110** and/or the imaging device **190**. In such instances, the processing system **130** withholds determination of the PWV. In this manner, only reliable PWV calcu-

lations are displayed for the clinician and/or utilized by the processing system **130** to make therapy recommendations.

[0064] Various peripheral devices may enable or improve input and output functionality of the processing system **130**. Such peripheral devices may include, but are not necessarily limited to, standard input devices (such as a mouse, joystick, keyboard, etc.), standard output devices (such as a printer, speakers, a projector, graphical display screens, etc.), a CD-ROM drive, a flash drive, a network connection, and electrical connections between the processing system **130** and other components of the system **100**, system **200** and/or system **250**. By way of non-limiting example, the processing system **130** may manipulate signals from the intravascular device **110** and/or the imaging device **190** to generate an image on the display **160** representative of the acquired pressure data, imaging data, PWV calculations, and/or combinations thereof. In some instances, the display **160** may be a touch-screen display. Such peripheral devices may also be used for downloading software containing processor instructions to enable general operation of the intravascular device **110**, the imaging device **190**, and/or the processing system **130**, and for downloading software implemented programs to perform operations to control, for example, the operation of any auxiliary devices coupled to the intravascular device **110** and/or the imaging device **190**. In some embodiments, the processing system **130** may include a plurality of processing units employed in a wide range of centralized or remotely distributed data processing schemes.

[0065] The memory **150** may be a semiconductor memory such as, for example, read-only memory, a random access memory, a FRAM, or a NAND flash memory. The memory **150** may interface with the processor **140** such that the processor **140** may write to and read from the memory **150**. For example, the processor **140** may be configured to receive data from the intravascular device **110**, the interface module **120**, the pressure console **112**, the imaging device **190**, and/or the ultrasound console **192** and write that data to the memory **150**. In this manner, a series of data readings may be stored in the memory **150**. The processor **140** may be capable of performing other basic memory functions, such as erasing or overwriting the memory **150**, detecting when the memory **150** is full, and other common functions associated with managing semiconductor memory.

[0066] FIG. 2 illustrates the intravascular device **110** of FIG. 1 disposed within the human renal anatomy. The human renal anatomy includes kidneys **10** that are supplied with oxygenated blood by right and left renal arteries **81**, which branch off an abdominal aorta **90** at the renal ostia **92** to enter the hilum **95** of the kidney **10**. The abdominal aorta **90** connects the renal arteries **81** to the heart (not shown). Deoxygenated blood flows from the kidneys **10** to the heart via renal veins **101** and an inferior vena cava **111**. Specifically, the flexible elongate member **170** of the intravascular device **110** is shown extending through the abdominal aorta and into the left renal artery **81**. In alternate embodiments, intravascular device **110** may be sized and configured to travel through the inferior renal vessels **115** as well. Specifically, the intravascular device **110** is shown extending through the abdominal aorta and into the left renal artery **81**. In alternate embodiments, the catheter may be sized and configured to travel through the inferior renal vessels **115** as well. In some examples, the right or left renal artery **81** may be the vessel **80** described with respect to FIG. 1a, FIG. 1b, and FIG. 1c.

[0067] Left and right renal plexi or nerves **121** surround the left and right renal arteries **81**, respectively. Anatomically, the renal nerve **121** forms one or more plexi within the adventitial tissue surrounding the renal artery **81**. For the purpose of this disclosure, the renal nerve is defined as any individual nerve or plexus of nerves and ganglia that conducts a nerve signal to and/or from the kidney **10** and is anatomically located on the surface of the renal artery **81**, parts of the abdominal aorta **90** where the renal artery **81** branches off the aorta **90**, and/or on inferior branches of the renal artery **81**. Nerve fibers contributing to the plexi **121** arise from the celiac ganglion, the lowest splanchnic nerve, the corticorenal ganglion, and the aortic plexus. The renal nerves **121** extend in intimate association with the respective renal arteries into the substance of the respective kidneys **10**. The nerves are distributed with branches of the renal artery to vessels of the kidney **10**, the glomeruli, and the tubules. Each renal nerve **121** generally enters each respective kidney **10** in the area of the hilum **95** of the kidney, but may enter the kidney **10** in any location, including the location where the renal artery **81**, or a branch of the renal artery **81**, enters the kidney **10**.

[0068] Proper renal function is essential to maintenance of cardiovascular homeostasis so as to avoid hypertensive conditions. Excretion of sodium is key to maintaining appropriate extracellular fluid volume and blood volume, and ultimately controlling the effects of these volumes on arterial pressure. Under steady-state conditions, arterial pressure rises to that pressure level which results in a balance between urinary output and water and sodium intake. If abnormal kidney function causes excessive renal sodium and water retention, as occurs with sympathetic overstimulation of the kidneys through the renal nerves **121**, arterial pressure will increase to a level to maintain sodium output equal to intake. In hypertensive patients, the balance between sodium intake and output is achieved at the expense of an elevated arterial pressure in part as a result of the sympathetic stimulation of the kidneys through the renal nerves **121**. Renal denervation may help alleviate the symptoms and sequelae of hypertension by blocking or suppressing the efferent and afferent sympathetic activity of the kidneys **10**.

[0069] FIGS. 3A and 3B illustrate aspects of operation of the intravascular system **200** (FIG. 1B) to obtain imaging data via the imaging device **190** and pressure data via the intravascular device **110**. While FIGS. 3A and 3B are described using components of the intravascular system **200**, it is understood that imaging data and pressure data can be similarly obtained using the components of the intravascular systems **100** and **250** (FIGS. 1A and 1C).

[0070] Fluid, such as blood, flows within the vessel **80** in the exemplary direction indicated by the arrows **220**. The intravascular device **110** is positioned within the vessel such that the fluid surrounds and exerts pressure on the pressure sensors **202**, **204**. Electrical signals representative of the pressure measured by the sensors **202**, **204** are transmitted to the pressure console **112** and/or the processing system **130** for use generating a graphical representation of the pressure data and/or in calculating PWV. The graphical representation of the pressure data can include pressure waveform, numerical values of pressure, etc.

[0071] The transducer **196** of the imaging device **190** emits ultrasonic energy **198**, which is reflected by vessel **80**, the fluid within the vessel **80**, and/or other anatomy within

the patient body **180**. The ultrasound echoes from the reflected ultrasound waves are received by the transducer. Electrical signals representative of the imaging data or ultrasound data are transmitted to the ultrasound console and/or the processing system **130** for use in generating a graphical representation of the ultrasound data and/or in calculating PWV. The graphical representation of the ultrasound data can include a B-mode image and velocity map, numerical values of velocity, etc.

[0072] The transducer **196** may be configured to obtain ultrasound data while aligned with the vessel **80**. In that regard, the transducer **196** may be aligned with the vessel **80** such that the ultrasound data includes components of the intravascular device **110**, including the pressure sensors **202**, **204**. That is, the B-mode/flow image generated from the ultrasound data includes the portion of the vessel **80** in which the sensors **202**, **204** are positioned. In this manner, the velocity data obtained by the imaging device **190** is associated with fluid within the same area of the vessel **80** where the sensors **202**, **204** are located. Accordingly, the velocity data and the pressure data are obtained at the same time and from the same location within the vessel.

[0073] FIGS. 3A and 3B illustrate that the imaging device **190** is positioned within a holder **210** that is configured to move the imaging device **190**. The holder **210** may be any suitable mechanical structure that is sized and shaped to accommodate the probe **194**. The holder **210** is configured to mechanically position and/or orient the probe **194** relative to the vessel **80** such that the desired imaging data, including imaging data within portions of the vessel **80** containing the pressure sensors **202**, **204**, is obtained. The holder **210** may include one or more actuators that, in response to a control signal, translate, rotate, and/or otherwise move the probe **194** with, e.g., six degrees of freedom (three rotational degrees of freedom and three translation degrees of freedom). Three degrees of freedom are illustrated in FIGS. 3A and 3B. For example, the imaging device **190** can be translated in directions **212**, **214** and rotated in a direction **216**. Other translational/rotational degrees of freedom are not shown in FIGS. 3A and 3B.

[0074] Relative to FIG. 3A, the imaging device **190** is rotated clockwise in the direction **216** in FIG. 3B. The holder **210** may be in communication with the processing system **130**, which is configured to transmit control signals to the holder **210** to move the imaging device **190**. For example, the processing system **130** transmits a control signal to the holder **210** to move the imaging device **190** to obtain imaging data while aligned with the vessel **80** and/or the sensors **202**, **204**. In some instances, the processing system **130** utilizes a feedback loop to ensure that the imaging device **190** is properly oriented. For example, the processing system **130** may periodically evaluate the imaging data being obtained by the imaging device **190** to ensure that the vessel **80** and the sensors **202**, **204** are properly being interrogated by the transducer **196**. The holder **210** moves the imaging device **190** when the vessel **80** and the sensors **202**, **204** are not properly within view. The holder **210** may automatically adjust the imaging device **190** into alignment with the vessel **80** and/or the sensors **202**, **204** in response to a user input. As shown in the exemplary screen display of FIG. 4, the user can select the input option **330** to toggle on/off the automatic position/orientation correction provided by the holder **210** and the processing system **130**.

[0075] Referring again to FIGS. 3A and 3B, the sensors 202, 204 can be sensitive to ultrasonic waves such that the sensors are visible in the B-mode/flow image. In the regard, the sensors 202, 204 may be associated with ultrasound echoes with relatively higher amplitude, compared to surrounding regions of fluid within the vessel 80. Thus, the processing system 130 can be configured to determine and track locations of the sensors 202, 204 within the vessel 80 using the imaging data obtained by the imaging device 190. Examples of tracking sensors of an interventional tool, e.g., the intravascular device 110, are described in PCT Patent Application Publication No. WO2011138698A1, which is hereby incorporated by reference in its entirety. Additionally, as shown in FIG. 4, in some instances, the processing system 130 highlights the locations of the sensors 202, 204 in the ultrasound image 300. Indicators 308 are overlaid on the image 300 in positions corresponding to the locations of the sensors 202, 204 in the vessel 80. The user may toggle the sensor tracking on/off by selecting the input option 310 in the exemplary screen display.

[0076] Referring again to FIGS. 3A and 3B, the transducer 196 is configured to obtain ultrasound data along a plane within the anatomy. That is, the transducer 196 can focus the emitted energy 198 along the plane so that a cross-sectional image along the plane can be generated using the ultrasound data. As described herein, the processing system 130 and/or the ultrasound console 192 can determine velocity of blood flow and produce an associated velocity map along the imaging plane. Two exemplary planes 230a, 230b are illustrated in FIGS. 3A and 3B. In some instances, the processing system 130 is configured to automatically select a suitable plane such that transducer 196 obtains the ultrasound data, including the velocity data, while aligned with the sensors 202, 204. In the illustrated embodiment, the emitted energy 198 is focused along the plane 230a, which is relatively close to the sensors 202, 204. Thus, the pressure data obtained by the sensor 202, 204, and the ultrasound data obtained by the transducer 196 are from the same area of the vessel 80.

[0077] The processing system 130 can rely on various factors to select imaging/velocity plane associated with the transducer 196. For example, the processing system 130 can utilize one or more of the geometry of the vessel 80, the location of the intravascular device 110 within the B-mode/flow image of the vessel 80, and/or the tracked location of the sensors 202, 204. The geometry of the vessel 80 can include the shape, diameter, area, volume, and/or other quantities based on the obtained imaging data. The vessel geometry can be utilized to ensure that the chosen imaging/velocity plane that does not include the vessel walls, for example. The location of the sensors 202, 204 may be extrapolated from the location of the intravascular device 110 within the B-mode/flow image of the vessel. Advantageously, by tracking the location of both sensors 202, 204, the imaging device 190 can visualize a full segment (e.g., distance D1) of the intravascular device 110 such that orientation of the transducer and/or the imaging plane is selected to ensure alignment with the fluid flow in the vessel 80. Furthermore, the sensors 202, 204 may be used to automatically estimate the Doppler angle in order to estimate the flow velocity in a more reliable fashion. The tracked location of the sensors 202, 204 provides a relatively more precise guidance allowing the velocity plane to be aligned in a desired manner. As shown in FIG. 4, the user

may toggle automatic ultrasound plane selection on/off by selecting the input option 320 in the exemplary screen display. In some instances, as shown, the processing system 130 highlights the location of the selected imaging plane 230c in the ultrasound image 300.

[0078] In some embodiments, the vessel 80 in FIG. 1a, FIG. 1b, FIG. 1c, FIG. 3a, and FIG. 3b is a renal vessel consistent with the vessels 81 of FIG. 2. The processing system 130 may determine the pulse wave velocity (PWV) in the renal artery. The processing system 130 may determine a renal denervation therapy recommendation based on the pulse wave velocity in a renal artery. For example, patients that are more likely or less likely to benefit therapeutically from renal denervation may be selected based on the PWV. In that regard, based at least on the PWV of blood in the renal vessel, the processing system 130 can perform patient stratification for renal denervation.

[0079] FIG. 4 illustrates an exemplary screen display 162 that is output by the processing system 130 to the display 160. The screen display 162 can include the ultrasound or B-mode image 300 depicting the vessel geometry. The velocity map 302 and/or the arrows 304 indicative the vector flow data can be overlaid on the image 300. The key or legend 306 correlates colors illustrated in the velocity map 302 with the corresponding velocities. The imaging plane 230c and/or the sensor indicators 308 may be selectively overlaid on the image 300. The screen display additionally includes input options 310, 320, 330 for selectively activating/deactivating sensor tracking, automatic ultrasound plane selection, and automatic ultrasound orientation, respectively. In an exemplary embodiment, the display 160 is touch-sensitive monitor such that the user input can be provided by touching and/or dragging the input options 310, 320, 330.

[0080] The screen display 162 also includes a region 340 illustrating the calculated pulse wave velocity. In the illustrated embodiment, the numerical value of the PWV is shown. In other instances, color coding and/or other graphics can be displayed together with the numerical value. For example, green, yellow, red, and/or other suitable colors and patterns may be used indicate the severity of the PWV.

[0081] A region 350 of the screen display 162 includes therapy recommendation determined by the processing system 130. As described herein the processing system 130 can use the calculated PWV within the renal artery to determine which patients are likely to benefit from renal denervation treatment. In the illustrated embodiment, the therapy recommendation is a textual indication. For example, "Poor," "Fair," "Good," and/or other suitable words may communicate the predicted benefit associated with therapy for the particular patient. In other instances, a numerical score, color coding, and/or other graphics representative of the therapy recommendation can be output to the display 160.

[0082] FIG. 5 is a flow diagram of a method 500 of determining pulse wave velocity. It is understood that the steps of method 500 may be performed in a different order than shown in FIG. 5, additional steps can be provided before, during, and after the steps, and/or some of the steps described can be replaced or eliminated in other embodiments. The steps of the method 500 can be performed by components of the intravascular system 100, 200, and 250 (FIGS. 1A, 1B, and 1C).

[0083] At step 505, the method 500 includes positioning an intravascular device within the vessel. The intravascular

device may include a pressure sensor. The vessel may be the renal artery. At step 510, the method 500 includes positioning an imaging device proximate to a body portion including the vessel. The imaging device may include an external ultrasound transducer. The steps 505 and 510 may be carried out by a clinician performing the diagnostic/therapeutic procedure and/or other user.

[0084] At step 515, the method 500 includes monitoring pressure associated with fluid within vessel. Step 515 may be performed using the intravascular device positioned within the vessel. At step 520, the method 500 includes monitoring velocity associated with the fluid within the vessel. Step 520 may be performed using the imaging device the imaging device positioned outside of a body portion including the vessel.

[0085] At step 525, the method 500 includes receiving pressure data associated with monitoring of pressure. For example, a processing system may receive the pressure data directly or indirectly from the intravascular device. In some instances, the method 500 includes processing the pressure data to obtain pressure measurements from within the vessel.

[0086] At step 530, the method 500 includes receiving velocity data associated with monitoring of velocity. For example, a processing system may receive the velocity data directly or indirectly from the imaging device. In some instances, the method 500 includes processing the imaging data obtained by the imaging device to extract the velocity data.

[0087] The method 500 can also include receiving lumen data associated with the vessel and obtained by the imaging device. In that regard, the imaging data can be processed to extract the lumen data. In some instances, the method 500 includes the processing system generating and outputting, to a display, a visual representation of the vessel and/or the velocity data. For example, an ultrasound or B-mode image including a velocity map may be displayed.

[0088] The method 500 can include synchronizing the collection of the pressure data and/or the velocity data. The method 500 can also include position the imaging device such that the velocity data and pressure data are obtained from the same area within the vessel.

[0089] In some embodiments, the ultrasound transducer of the imaging device obtains ultrasound data, including the velocity data, along a plane within the vessel. The method 500 may include the processing system determining the plane using vessel geometry and/or a location of the intravascular device. The processing system can determine the vessel geometry and/or the location of the intravascular device within the vessel based on the lumen data and/or the velocity data obtained by the imaging device. In other instances, the method 500 includes determining a location of the pressure sensor within the vessel. In such instances, the plane is determined using the vessel geometry and/or the location of the pressure sensor.

[0090] In some embodiments, the intravascular device includes the pressure sensor and a further pressure sensor. The method 500 may include determining locations of the pressure sensor and the further pressure sensor within the vessel. Additionally, the method 500 may include including obtaining velocity data while the imaging device is aligned with a direction of fluid flow based on the locations of the pressure sensor and the further pressure sensor. In that regard, the processing system may determine the direction

of fluid flow based on the locations of the pressure sensors. Additionally, the angle of the direction of fluid flow with the imaging device may be used to automatically correct the determined velocity data. In some embodiments, the intravascular device is coupled to an imaging device holder. The method 500 may include outputting a control signal to an imaging device holder coupled to the imaging device to move the imaging device into alignment with the vessel. The processing system may generate and output the control signal based on identifying the location of the intravascular device and/or the pressure sensor within the vessel using the imaging data.

[0091] At step 535, the method 500 includes determine PWV of fluid within vessel based on pressure data and velocity data. In some embodiments, the PWV is determined as

$$\frac{1}{\rho} \frac{dP}{dU},$$

where dP is a change in the pressure over a time interval, dU is a change in the velocity over the time interval, and ρ is a density of the fluid within the vessel. In some embodiments, the PWV is determined by summation over the cardiac cycle as

[0092] where dP is a change in the pressure over a time interval, dU is a change in the velocity over the time interval, and ρ is a density of the fluid within the vessel. At step 540, the method 500 includes outputting a visual representation of the PWV. For example, the processing system can output display data associated with the visual representation to a display device.

[0093] At step 545, the method 500 includes determining a therapy recommendation based on the PWV. In that regard, the PWV within the renal artery may predict the effect of renal denervation in a patient. Accordingly, calculating the PWV facilitates selection of patients for whom this therapeutic procedure is likely beneficial. In some instances, the clinician determines the therapy recommendation based on the computed PWV and/or other patient data. In some embodiments, the processing system evaluates the PWV and/or other patient data to determine the therapy recommendation. In such instances, at step 550, the method 500 includes outputting a visual representation of the therapy recommendation. For example, the processing system can output display data associated with the graphical representation to a display device. The method 500 can additionally include classifying, based on the PWV, one or more patients into groups corresponding to respective degrees of predicted therapeutic benefit as a result of the renal denervation. The method 500 can also include the processing system outputting a graphical representation of the classifying step to the display device.

[0094] In some embodiments, the method 500 may be performed prior to performing a therapeutic procedure, e.g., prior to performing renal denervation. The method can determine the pulse wave velocity of a renal vessel that can be used for patient stratification and determining a renal denervation therapy recommendation. The method can be beneficial for patients with resistant hypertension. Renal sympathetic activity may worsen symptoms of hypertension, heart failure, and/or chronic renal failure. In particular, hypertension has been linked to increased sympathetic ner-

vous system activity stimulated through any of four mechanisms, namely (1) increased vascular resistance, (2) increased cardiac rate, stroke volume and output, (3) vascular muscle defects, and/or (4) sodium retention and renin release by the kidney. As to this fourth mechanism in particular, stimulation of the renal sympathetic nervous system may affect renal function and maintenance of homeostasis. For example, an increase in efferent renal sympathetic nerve activity may cause increased renal vascular resistance, renin release, and sodium retention, all of which exacerbate hypertension.

[0095] Renal denervation, which affects both the electrical signals going into the kidneys (efferent sympathetic activity) and the electrical signals emanating from them (afferent sympathetic activity) may impact the mechanical and hormonal activities of the kidneys themselves, as well as the electrical activation of the rest of the SNS. Blocking efferent sympathetic activity to the kidney may alleviate hypertension and related cardiovascular diseases by reversing fluid and salt retention (augmenting natriuresis and diuresis), thereby lowering the fluid volume and mechanical load on the heart, and reducing inappropriate renin release, thereby halting the deleterious hormonal RAAS cascade before it starts.

[0096] By blocking afferent sympathetic activity from the kidney to the brain, renal denervation may lower the level of activation of the whole SNS. Thus, renal denervation may also decrease the electrical stimulation of other members of the sympathetic nervous system, such as the heart and blood vessels, thereby causing additional anti-hypertensive effects. In addition, blocking renal nerves may also have beneficial effects on organs damaged by chronic sympathetic over-activity, because it may lower the level of cytokines and hormones that may be harmful to the blood vessels, kidney, and heart.

[0097] Use of the external ultrasound transducer can advantageously allow for highly localized pressure data and velocity data to be collected. For example, by obtaining ultrasound data along an imaging plane that is aligned with the pressure sensor in the vessel, velocity data can be derived, from the ultrasound data, at the same location of the pressure data is being obtained. Use of such highly localized pressure data and velocity data can improve the calculation of pulse wave velocity. In that regard, pulse wave velocity is a measure of vessel stiffness, which can be a local property of the vessel. The external ultrasound transducer also allows for velocity data to be obtained throughout the entire imaging plane. For example, the velocity data used from the pulse wave velocity calculation can be selected based on the location of pressure sensor within imaging plane.

[0098] In some embodiments, a flow-sensing device or a flow sensor determines the velocity data associated with fluid within the vessel **80**. The flow sensor is in communication with the processor **140** of the processing system **130**. In some embodiments, the flow sensor directly measures the speed and/or the direction of the fluid flow within the vessel **80**. In some embodiments, the flow sensors obtains flow data from which the processor **140** derives the speed and/or the direction of the fluid flow. The flow sensor may be any suitable type(s) and/or combinations thereof. The flow sensor may be an ultrasound transducer, such as a single ultrasound transducer element or an array of ultrasound transducer elements. In some embodiments, the flow sensor is configured only to obtain flow data (e.g., Doppler flow

and/or vector flow). The flow sensor may be an imaging device, such as an ultrasound imaging device. In some embodiments, the imaging device obtains by flow data and imaging data. For example, the imaging device can be an intraluminal device structurally arranged, sized and shaped, and/or otherwise configured to be positioned within a body lumen. For example, the intraluminal device can be an intravascular ultrasound (IVUS) component (e.g., a transducer or transducer array), a forward-looking IVUS (FL-IVUS) component (e.g., a transducer or transducer array), transesophageal echocardiography (TEE) component (e.g., a transducer or transducer array), an intravascular photoacoustic (IVPA) component, an optical coherence tomography (OCT) component, etc. In some embodiments, beamforming or beamsteering of a transducer array can be used to focus ultrasound signals in order to obtain velocity data. The flow sensor may be a thermal flow sensor, an anemometer (e.g., a hot-wire or hot-film anemometer), an optical flow sensor, an electromagnetic flow sensor, a micromachined flow sensor, a microelectromechanical systems (MEMS) flow sensor, a thermoelectric flow sensor, and/or a helical diffraction-grating transducer, for example.

[0099] In embodiments utilizing an ultrasound transducer to obtain velocity data and/or imaging data, the transducer may include any suitable number of transducer elements. For example, the transducer or transducer array can include between 1 acoustic element and 10000 acoustic elements, including values such as 2 acoustic elements, 4 acoustic elements, 16 acoustic elements, 64 acoustic elements, 128 acoustic elements, 500 acoustic elements, 812 acoustic elements, 3000 acoustic elements, 9000 acoustic elements, and/or other values both larger and smaller. The transducer elements of the transducer array may be arranged in any suitable configuration, such as a linear array, a planar array, a curved array, a curvilinear array, a circumferential array, an annular array, a phased array, a matrix array, a one-dimensional (1D) array, a 1.x dimensional array (e.g., a 1.5D array), or a two-dimensional (2D) array. The array of transducer elements (e.g., one or more rows, one or more columns, and/or one or more orientations) can be uniformly or independently controlled and activated. The array can be configured to obtain one-dimensional, two-dimensional, and/or three-dimensional images of patient anatomy. The ultrasound transducer elements may be piezoelectric/piezoresistive elements, piezoelectric micromachined ultrasound transducer (PMUT) elements, capacitive micromachined ultrasound transducer (CMUT) elements, and/or any other suitable type of ultrasound transducer elements.

[0100] The flow sensor may monitor the velocity of the fluid while the flow sensor is positioned within the vessel **80**, outside of the vessel **80** (e.g., within the body portion **180** and proximate to the vessel **80**), and/or outside of the body portion **180**. For example, the flow sensor can be coupled to an intravascular device (e.g., a catheter or a guidewire) structurally arranged, sized and shaped, and/or otherwise configured to be positioned within the vessel **80**. The flow sensor can be coupled to the distal portion of the flexible elongate member of the intravascular device. For example, the sensor **202** and/or the sensor **204** (FIGS. 1A-1C) can be a flow sensor. In some embodiments, one of the sensors **202**, **204** is a flow sensor and the other of the sensors **202**, **204** is a pressure sensor. For example, in FIGS. 1B and 1C, the sensor **202** can be a pressure sensor and the sensor **204** can be a flow sensor, or the sensor **202** can be a flow sensor and the

sensor **204** can be a pressure sensor. The sensors **202**, **204** can be adjacent to one another or longitudinally offset (e.g., by the distance **D1**). In some embodiments, the distance **D1** can be spaced by 0.5 cm, 1 cm, 1.5 cm, 2 cm, and/or other values both larger and smaller. In some embodiments, the flow sensor and the pressure sensor are coupled to the same intravascular device. In such embodiments, both the velocity data and the pressure data can be obtained using a single device. In some embodiments, the flow sensor is coupled to one intravascular device (e.g., a flow-sensing guidewire or a flow-sensing catheter), and the pressure sensor is coupled to another intravascular device (e.g., a pressure-sensing guidewire or a pressure-sensing catheter). One intravascular device can be received within a lumen of the other intravascular device (e.g., as shown in FIG. 1C). In some embodiments, the two intravascular devices can extend side-by-side within the vessel.

[0101] The pressure sensor can be in wired or wireless communication with the processor **140** of the processing system **130** directly or indirectly (e.g., via a PIM and/or console). The flow sensor can be in wired or wireless communication with the processor **140** of the processing system **130** directly or indirectly (e.g., a PIM and/or console). The PIM and/or console for the flow sensor can be the same or different as the PIM and/or console for the pressure sensor.

[0102] The flow sensor and/or the pressure sensor can be coupled to the flexible elongate member of the intravascular device such that the flow sensor and/or the pressure sensor is forward-looking, side-looking, backward-looking, and/or combinations thereof. The flow sensor and/or the pressure sensor can be oriented to face directly in the direction of blood flow or the opposite direction of blood flow. The flow sensor can be oriented generally towards a vessel wall, e.g., while tilted backwards or forwards. The flow sensor can be oriented perpendicular to a longitudinal axis of the intravascular device or at an oblique angle with respect to the longitudinal axis. The pressure sensor can be oriented along, parallel to, perpendicular to, or at an oblique angle with respect to the longitudinal axis.

[0103] The flow sensor and the pressure sensor can be configured to obtain the velocity data and the pressure data, respectively, during the same cardiac cycle(s) and/or over the same time interval. The velocity data and the pressure data can be obtained over complete cardiac cycle(s) or partial cardiac cycle(s). For example, the flow sensor and the pressure sensor can obtain multiple velocity measurements and pressure measurements, respectively, during the heart beat cycle(s). The flow sensor and the pressure sensor can operate at any suitable frequency such that, e.g., tens, hundreds, or thousands of pressure measurements are obtained during a cardiac cycle. In that regard, the velocity data and the pressure data are obtained at different time points in the cardiac cycle (e.g., different time points during systole and/or different time points during diastole) when the velocity data and pressure data are different. By obtaining many measurements of pressure and velocity during the cardiac cycle and at different time points thereof, the dP and dU terms in the PWV formulas can be advantageously calculated in a manner that accounts for pressure and velocity changes.

[0104] The flow sensor and the pressure sensor can be configured to obtain the velocity data and the pressure data, respectively, from the same area of the vessel. For example,

in the embodiments of FIGS. 1B and 1C, the sensors **202**, **204** can obtain velocity data and pressure data, respectively, while adjacent to one another or longitudinally spaced by the distance **D1**. In embodiments in which the flow sensor and the pressure sensor are coupled to the same intravascular device (e.g., FIG. 1B), both sensors are positioned within the same area of the vessel and obtain respective data during the same cardiac cycles and/or over the same time interval. In embodiments in which the flow sensor and the pressure sensor are coupled to different intravascular devices (e.g., FIG. 1C), both intravascular devices inserted into the vessel such that the flow sensor and the pressure sensor are positioned within the same area of the vessel and obtain respective data during the same cardiac cycles and/or over the same time interval. For example, the flow sensor and the pressure sensor are configured to operate concurrently.

[0105] Obtaining the velocity data and the pressure data during the same cardiac cycles and/or over the same time interval advantageously ensures that the velocity data and the pressure data are collected under the same blood flow conditions (e.g., heart rate, blood pressure). The blood flow conditions affect both the velocity data and the pressure data. In that regard, the calculated PWV is based on the changes in pressure and flow occurring during the same cardiac cycles and/or over the same time interval.

[0106] As discussed herein, in some embodiments, the PWV is determined using a slope method (e.g., slope of the pressure-velocity curve), by calculating

$$\frac{1}{\rho} \frac{dP}{dU},$$

where dP is a change in the pressure over a time interval, dU is a change in the velocity over the time interval, and ρ is a density of the fluid within the vessel. The processor **140** of the processing system **130** can advantageously synchronize collection of the pressure data and the velocity data (e.g., using ECG signals) when the PWV is calculated using the slope method. Synchronization can refer to collection of the pressure data the velocity data in phase with one another (e.g., at the same time points within the same cardiac cycle(s) or the same time interval). In that regard, collecting the pressure data and velocity data out of phase can introduce difficulties in calculating the PWV using the slope method.

[0107] In some embodiments, the PWV is determined by using a sum of squares method, by calculating

$$\frac{1}{\rho} \sqrt{\frac{\sum dP^2}{\sum dU^2}},$$

where dP is a change in the pressure over a time interval, dU is a change in the velocity over the time interval, ρ is a density of the fluid within the vessel, and the summations are performed over the same one or more cardiac cycle(s). Synchronization can be advantageously omitted when PWV is calculated using the sum of squares method. In that regard, the summations of dP^2 term and the dU^2 term in the formula minimize the effect of collecting on the pressure data and

velocity data out of phase with one another (e.g., at different time points within the same cardiac cycle(s) or the same time interval).

[0108] The temporal resolution of the obtained pressure data and velocity data can advantageously be same or substantially similar when calculating PWV. In that regard, the frequency at which pressure sensor operates to obtain the pressure data can be equal to or approximate the frequency at which the flow sensor operates to obtain the velocity data.

[0109] Temporal resolution can refer to the difference between the time points at which the pressure/velocity data is obtained. The processor 140 of the processing system 130 determines the change in the pressure/velocity between these time points. The temporal resolution of the obtained pressure data and velocity data is the same or substantially similar when the differences between the pressure time points and the velocity time points are the same or substantially similar. For example, the time interval over which dP and dU is calculated can be the same or substantially similar.

[0110] The pressure data used to calculate PWV can be obtained by pressure-sensing device. For example, the pressure-sensing device can be an intravascular device, such as an intravascular catheter or guidewire that includes a pressure transducer, pressure sensor, and/or other suitable pressure-monitoring element coupled to a distal portion of a flexible elongate member. The pressure sensor may be a piezoelectric sensor, an optical sensor, a micro-electro-mechanical system (MEMS), a thin-film pressure transducer, a strain sensor and/or other suitable types. The pressure-sensing device can be an external imaging device configured to obtain imaging data of the vessel 80 from which pressure data is derived.

[0111] FIG. 6 is a diagrammatic schematic view of an exemplary PWV determination system 600 according to some embodiments of the present disclosure. The components of the system 600 can be similar to components described with respect to FIGS. 1A-4. The system 600 can additionally include other components shown in FIGS. 1A-4. The system 600 includes an external imaging device 610 configured to obtain imaging data of the vessel 80, while the imaging device 610 is positioned outside of the body portion 180. The external imaging device 610 can be an x-ray imaging device, an angiographic imaging device, a fluoroscopic imaging device, a computed tomography (CT) imaging device, and/or a magnetic resonance imaging (MRI) device, for example. The imaging device 610 can be configured to obtain imaging data. The processor 140 of the processing system 130 is in communication with the external imaging device 610. From the obtained imaging data, the processor 140 is configured to extract velocity data, pressure data, and/or lumen data associated with the vessel 80. The processor 140 utilizes the velocity data, pressure data, and/or lumen data to calculate the PWV. In some embodiments, the system 600 can advantageously provides a non-invasive calculation of PWV.

[0112] For example, lumen data of the vessel 80 can include geometrical information about the vessel 80 and/or the lumen of the vessel 80, including a vessel or lumen diameter 630, cross-sectional area, volume, and/or other geometric information describe the structure of the vessel 80 and the lumen of the vessel 80. The diameter 630, cross-sectional area, and/or other measurements can be obtained at different locations along the vessel (e.g., a location proximal of a stenosis, in the aorta, in the ostium of the vessel, a

location distal of a stenosis, at the stenosis, etc.) The velocity data can include a flow rate, flow direction, flow velocity, flow volume, and/or other data. The velocity data can be based on the movement of a contrast agent 620 through the vessel (e.g., through multiple frames of the imaging data). The pressure data can include an imaging-based measurement of pressure ratio (e.g., angio FFR, CT FFR, etc.). The velocity data and/or the pressure data can be based on the geometry of the vessel, the movement of the contrast agent 620, historical imaging data of the vessel 80, current imaging data of the vessel 80, blood velocity at multiple locations in the vessel, the imaging data, Doppler or vector flow processing, an upstream pressure measurement, and/or combinations thereof.

[0113] Persons of ordinary skill in the art will appreciate that the embodiments encompassed by the present disclosure are not limited to the particular exemplary embodiments described above. In that regard, although illustrative embodiments have been shown and described, a wide range of modification, change, and substitution is contemplated in the foregoing disclosure. It is understood that such variations may be made to the foregoing without departing from the scope of the present disclosure. Accordingly, it is appropriate that the appended claims be construed broadly and in a manner consistent with the present disclosure.

1. An apparatus for pulse wave velocity determination in a blood vessel, the apparatus comprising:

- a flow-sensing device configured to monitor a velocity of blood within the blood vessel during a time interval;
- a pressure-sensing device configured to monitor a pressure of the blood within the blood vessel during the time interval;
- a processor in communication with the pressure-sensing device and the flow-sensing device, wherein the processor is configured to:
 - determine a change in the velocity of the blood over the time interval;
 - determine a change in the pressure of the blood over the time interval;
 - determine a pulse wave velocity of the blood based on the change in the pressure and the change in the velocity; and
 - output, to a display in communication with the processor, a visual representation based on the pulse wave velocity.

2. The apparatus of claim 1, wherein the pulse wave velocity is determined as

$$\frac{1}{\rho} \frac{dP}{dU}, \text{ or } \frac{1}{\rho} \sqrt{\frac{\Sigma dP^2}{\Sigma dU^2}},$$

where dP is the change in the pressure over the time interval, dU is the change in the velocity over the time interval, and ρ is a density of the blood within the blood vessel.

3. The apparatus of claim 1, wherein the processor is further configured to synchronize the monitoring of the pressure by the pressure-sensing device with the monitoring of the velocity by the flow-sensing device.

4. The apparatus of claim 1, further comprising:

- at least one intravascular catheter or guidewire sized and shaped for positioning within a blood vessel, the at least one intravascular catheter or guidewire comprising:

a flexible elongate member comprising a proximal portion and a distal portion; and
the flow-sensing device coupled to the distal portion of the flexible elongate member.

5. The apparatus of claim 4, wherein the pressure-sensing device is coupled to the distal portion of the flexible elongate member.

6. The apparatus of claim 1, wherein the flow-sensing device comprises an ultrasound transducer.

7. The apparatus of claim 6, further comprising:

an external imaging probe comprising the ultrasound transducer, wherein the external imaging probe is configured for positioning proximate to a body portion including the blood vessel.

8. The apparatus of claim 6,

wherein the ultrasound transducer is configured to obtain ultrasound data along a plane within the blood vessel to monitor the velocity of the blood within the blood vessel,

wherein the processor is further configured to:

determine lumen data of the blood vessel based on the ultrasound data, and

determine the plane using at least one of a vessel geometry or a location of the at least one intravascular catheter or guidewire within the blood vessel, based on the lumen data and/or the monitoring the velocity of the blood within the blood vessel.

9. The apparatus of claim 1, wherein the visual representation based on the pulse wave velocity comprises a numeral value of the pulse wave velocity.

10. The apparatus of claim 1, wherein the processor is further configured to determine a therapy recommendation based on the pulse wave velocity, and wherein the visual representation based on the pulse wave velocity comprises the therapy recommendation.

11. The apparatus of claim 10, wherein the blood vessel comprises a renal artery, and wherein the processor is further configured to determine a renal denervation therapy recommendation based on the pulse wave velocity.

12. The apparatus of claim 1, wherein the blood vessel comprises a renal artery, and wherein the processor is further configured to classify a patient based on a predicted therapeutic benefit of renal denervation using the pulse wave velocity.

13. The apparatus of claim 1, further comprising:

at least one intravascular catheter or guidewire sized and shaped for positioning within a blood vessel, the at least one intravascular catheter or guidewire comprising:

a flexible elongate member comprising a proximal portion and a distal portion; and

the pressure-sensing device coupled to the distal portion of the flexible elongate member.

14. The apparatus of claim 1, wherein the pressure-sensing device comprises an external imaging device configured to obtain x-ray, computed tomography (CT), and/or magnetic resonance imaging (MRI) data of a body portion including the blood vessel.

15. A method of determining pulse wave velocity in a blood vessel, comprising:

monitoring pressure associated with blood within the blood vessel during a time interval, wherein the monitoring pressure is performed using a pressure-sensing device;

monitoring velocity associated with the blood within the blood vessel during the time interval, wherein the monitoring velocity is performed using a flow-sensing device;

determining, using a processor in communication with the pressure-sensing device and the flow-sensing device, a change in the pressure during the time interval;

determining, using the processor, a change in the velocity during the time interval;

determining, using the processor, a pulse wave velocity of the blood within the blood vessel based on the change in the pressure and the change in the velocity; and
outputting, to a display in communication with the processor, a visual representation based on the pulse wave velocity.

16. The method of claim 15, wherein the pulse wave velocity is determined as

$$\frac{1}{\rho} \frac{dP}{dU}, \text{ or } \frac{1}{\rho} \sqrt{\frac{\Sigma dP^2}{\Sigma dU^2}},$$

where dP is the change in the pressure over the time interval, dU is the change in the velocity over the time interval, and ρ is a density of the blood within the blood vessel.

17. The method of claim 15, wherein the pressure-sensing device comprises at least one intravascular catheter or guidewire such that the monitoring pressure is performed while the pressure-sensing device is positioned within the blood vessel.

18. The method of claim 15, wherein the flow-sensing device comprises at least one intravascular catheter or guidewire such that the monitoring velocity is performed while the flow-sensing device is positioned within the blood vessel.

19. The method of claim 15, wherein the flow-sensing device comprises an external ultrasound transducer configured for positioning proximate to a body portion including the blood vessel, wherein the monitoring velocity comprises receiving ultrasound data obtained by the external ultrasound transducer along a plane within the blood vessel, and further comprising:

determining, using the processor, lumen data of the blood vessel based on the ultrasound data; and

determining, using the processor, the plane using at least one of a vessel geometry or a location of the at least one intravascular catheter or guidewire within the blood vessel based on the lumen data and/or the velocity data.

20. The method of claim 15, wherein the vessel comprises a renal artery, and further comprising:

determining, using the processor, a renal denervation therapy recommendation based on the pulse wave velocity, wherein the outputting comprises displaying the renal denervation therapy recommendation.

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专利名称(译)	使用血管内压力测量和外部超声成像确定脉搏波速度，以及相关的装置，系统和方法		
公开(公告)号	US20190082978A1	公开(公告)日	2019-03-21
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[标]申请(专利权)人(译)	皇家飞利浦电子股份有限公司		
申请(专利权)人(译)	皇家飞利浦N.V.		
当前申请(专利权)人(译)	皇家飞利浦N.V.		
[标]发明人	VAN DER HORST ARJEN SIO CHARLES FREDERIK KUENEN MAARTEN PETRUS JOSEPH		
发明人	VAN DER HORST, ARJEN SIO, CHARLES FREDERIK KUENEN, MAARTEN PETRUS JOSEPH		
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CPC分类号	A61B5/0285 A61B5/0215 A61B5/02108 A61B8/04 A61B5/022 A61B8/485 A61B5/489 A61B5/02007 A61B5/201 A61B5/4836 A61B5/7239 A61B5/7264 A61B5/742 A61B8/06 A61B8/0891 G16H50/20		
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外部链接	Espacenet USPTO		

摘要(译)

公开了使用血管内压力测量和外部超声成像进行脉搏波速度确定的装置，系统和方法。用于脉搏波速度（PWV）确定的装置包括血管内装置，其尺寸和形状适于定位在血管内，血管内装置包括柔性细长构件和压力传感器，压力传感器构造造成监测血管内的流体压力；成像装置，被配置为监测血管内的流体的速度，所述成像装置包括外部超声换能器，所述外部超声换能器被配置为靠近包括所述血管的身体部分定位；以及与血管内装置和成像装置通信的处理系统，该处理系统被配置为：通过压力传感器监测容器内的压力与成像装置监测容器内的速度；并根据容器内的压力和速度确定容器内流体的脉冲波速度。

