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(54) **DEVICES AND METHODS FOR DETECTING AND MEASURING SYMPATHETIC VASOMOTION**

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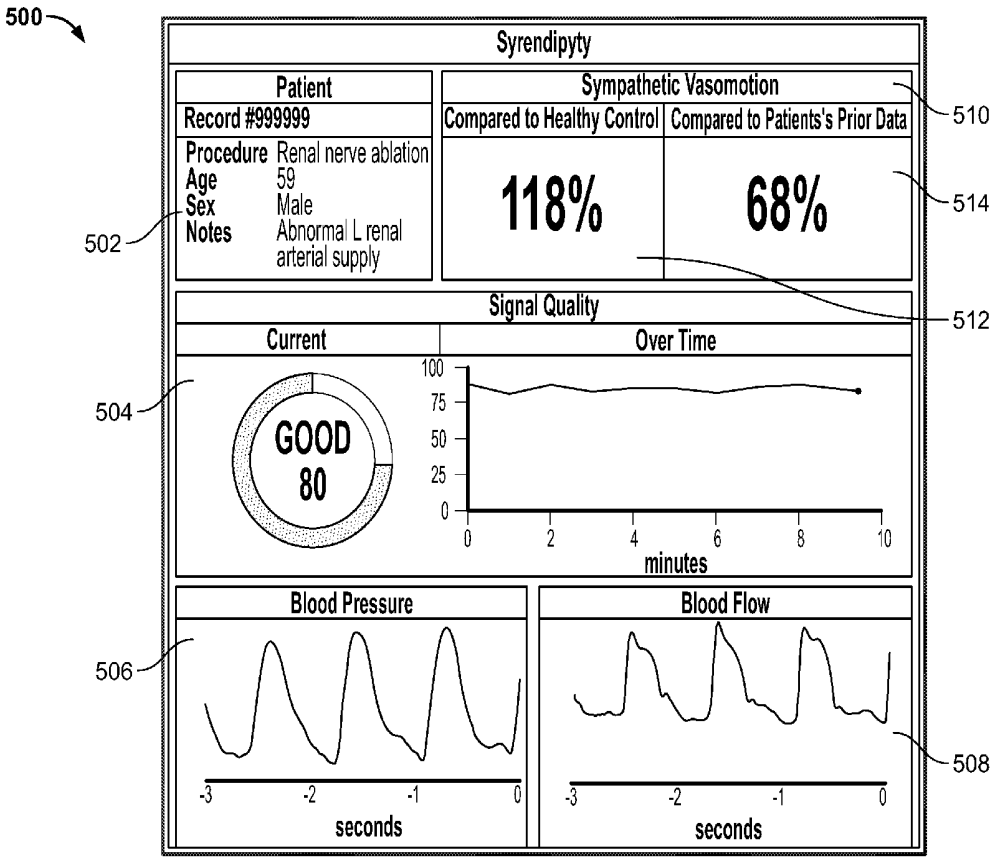
(57) **ABSTRACT**

Sympathetic vasomotor identification and quantification systems that provide ways to assess therapies, diseases, and conditions which affect sympathetic innervation and function are described. Because sympathetic vasomotion relies on intact, functional sympathetic nerves, some embodiments of the sympathetic vasomotor identification and quantification systems described herein include a signal processing functionality that establishes sympathetic vasomotor signatures through the collection of arterial blood pressure and blood flow signals.



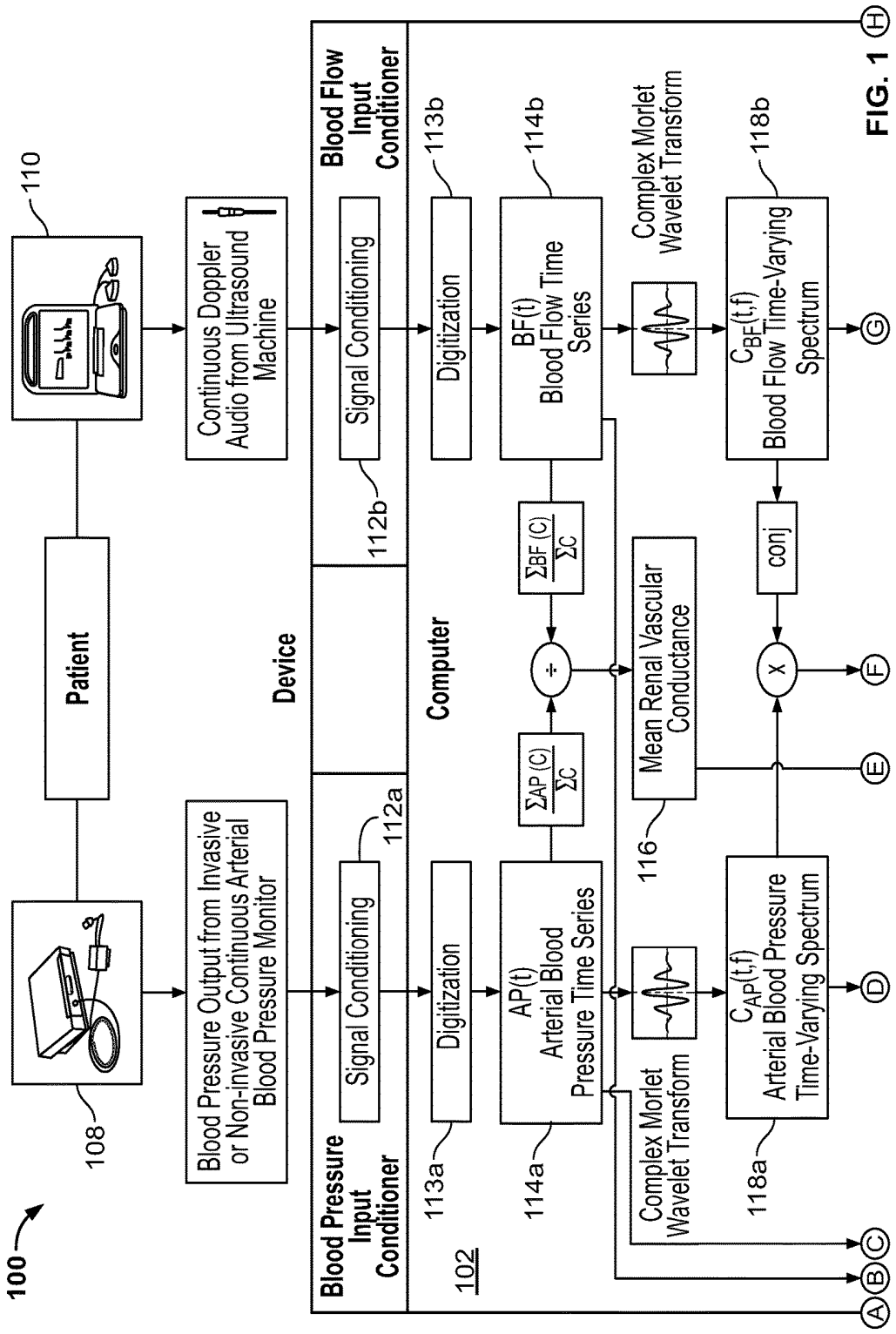

100
108
110
Patient
Blood Pressure Output from Invasive or Non-invasive Continuous Arterial Blood Pressure Monitor
Continuous Doppler Audio from Ultrasound Machine
Device
Blood Pressure Input Conditioner
Signal Conditioning
112a
Digitization
113a
AP(t) Arterial Blood Pressure Time Series
114a
Blood Flow Input Conditioner
Signal Conditioning
112b
Digitization
113b
BF(t) Blood Flow Time Series
114b
Computer
102
ΣAP (C) / ΣC
ΣBF (C) / ΣC
÷
Mean Renal Vascular Conductance
116
Complex Morlet Wavelet Transform
Complex Morlet Wavelet Transform
conj
×
CAP(t,f) Arterial Blood Pressure Time-Varying Spectrum
118a
CBF(t,f) Blood Flow Time-Varying Spectrum
118b
A
B
C
D
E
F
G
H

FIG. 1

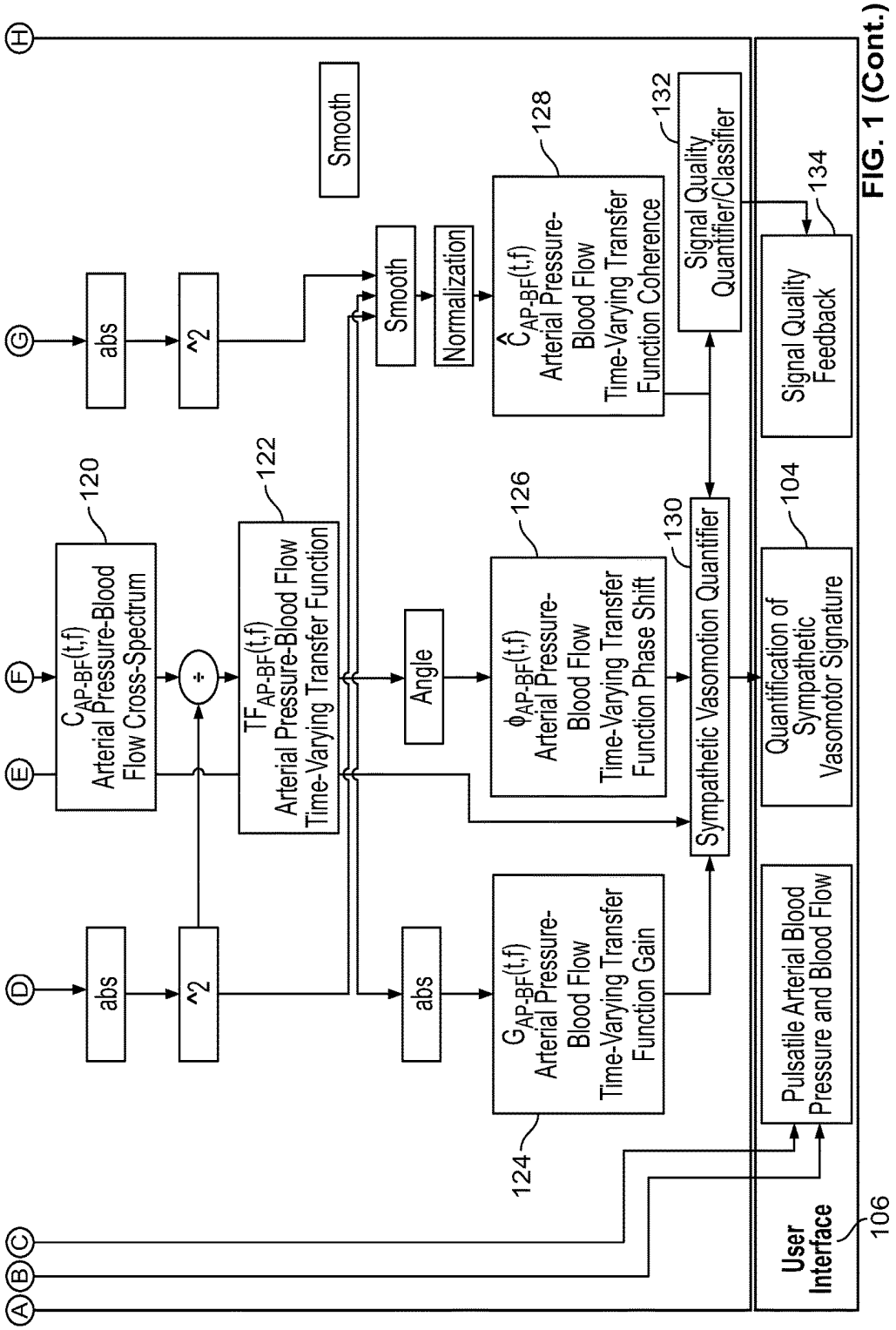

A
B
C
D
E
F
G
H
abs
^2
÷
Smooth
Normalization
Angle
abs
^2
Smooth
$C_{AP\text{-}BF}(t,f)$ Arterial Pressure-Blood Flow Cross-Spectrum
120
$TF_{AP\text{-}BF}(t,f)$ Arterial Pressure-Blood Flow Time-Varying Transfer Function
122
$G_{AP\text{-}BF}(t,f)$ Arterial Pressure-Blood Flow Time-Varying Transfer Function Gain
124
$\phi_{AP\text{-}BF}(t,f)$ Arterial Pressure-Blood Flow Time-Varying Transfer Function Phase Shift
126
$\hat{C}_{AP\text{-}BF}(t,f)$ Arterial Pressure-Blood Flow Time-Varying Transfer Function Coherence
128
Sympathetic Vasomotion Quantifier
130
Signal Quality Quantifier/Classifier
132
Signal Quality Feedback
134
Quantification of Sympathetic Vasomotor Signature
104
Pulsatile Arterial Blood Pressure and Blood Flow
User Interface
106

FIG. 1 (Cont.)

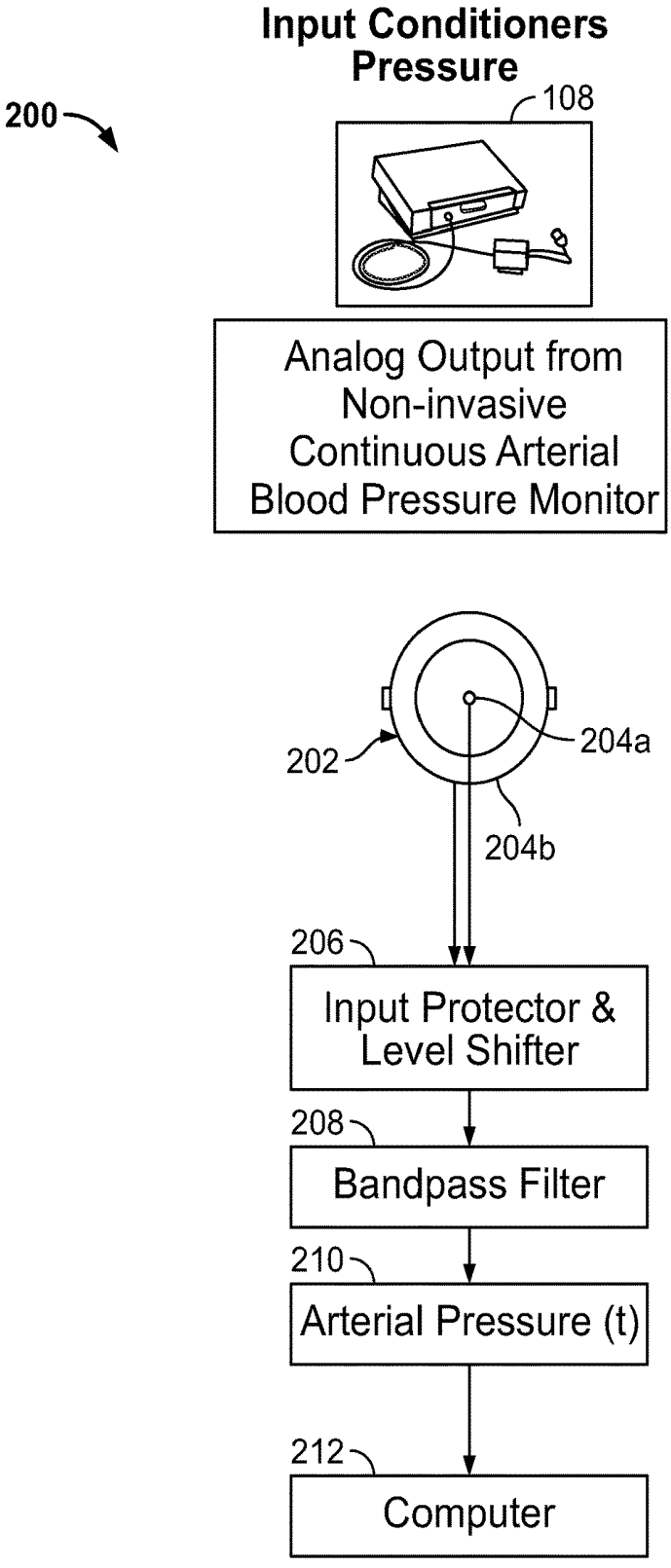

Input Conditioners
Pressure
200
108
Analog Output from Non-invasive Continuous Arterial Blood Pressure Monitor
202
204a
204b
206
Input Protector & Level Shifter
208
Bandpass Filter
210
Arterial Pressure (t)
212
Computer

FIG. 2A

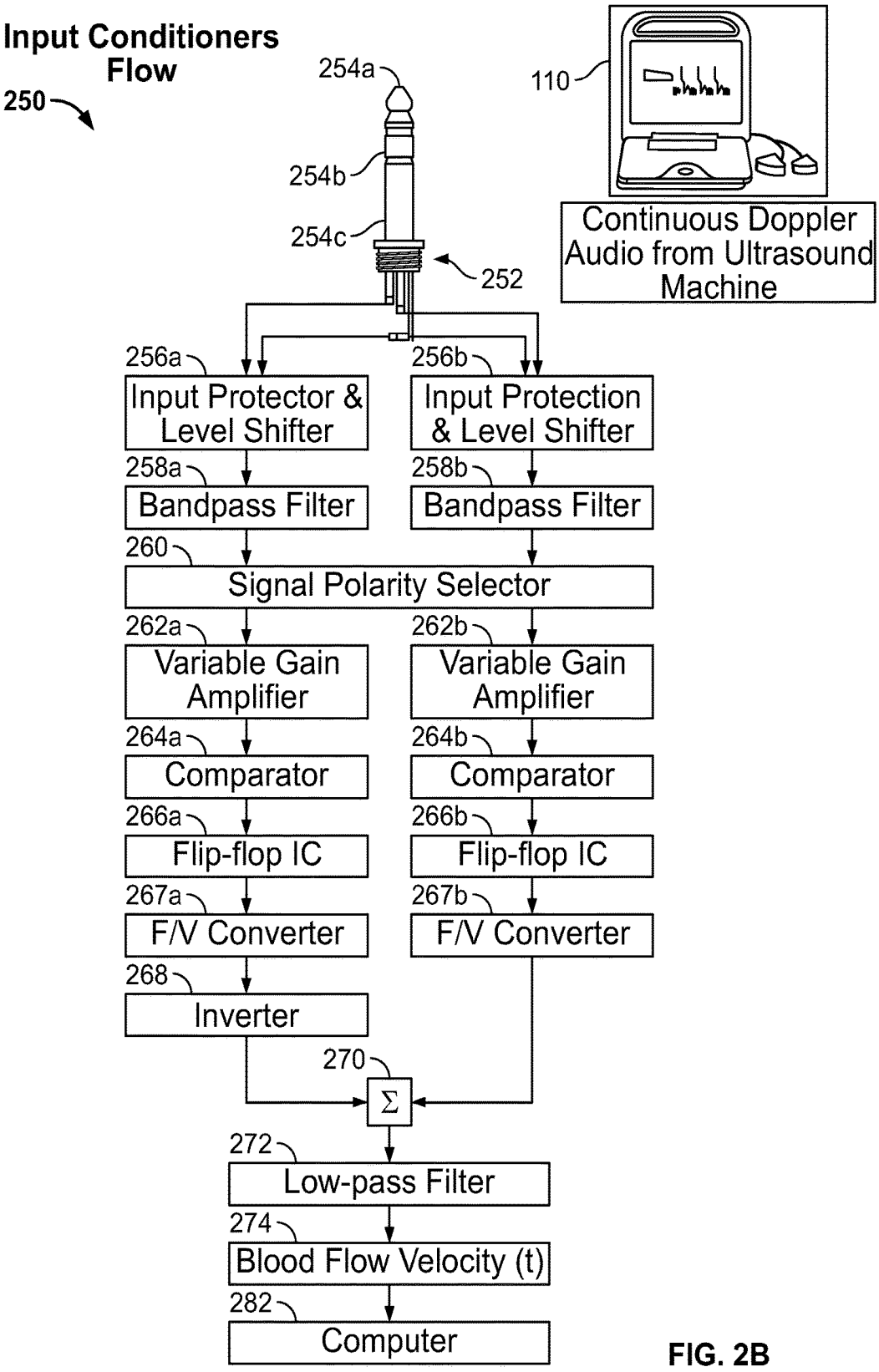

Input Conditioners
Flow
250
254a
254b
254c
252
110
Continuous Doppler Audio from Ultrasound Machine
256a
256b
Input Protector & Level Shifter
Input Protection & Level Shifter
258a
258b
Bandpass Filter
Bandpass Filter
260
Signal Polarity Selector
262a
262b
Variable Gain Amplifier
Variable Gain Amplifier
264a
264b
Comparator
Comparator
266a
266b
Flip-flop IC
Flip-flop IC
267a
267b
F/V Converter
F/V Converter
268
Inverter
270
Σ
272
Low-pass Filter
274
Blood Flow Velocity (t)
282
Computer

FIG. 2B

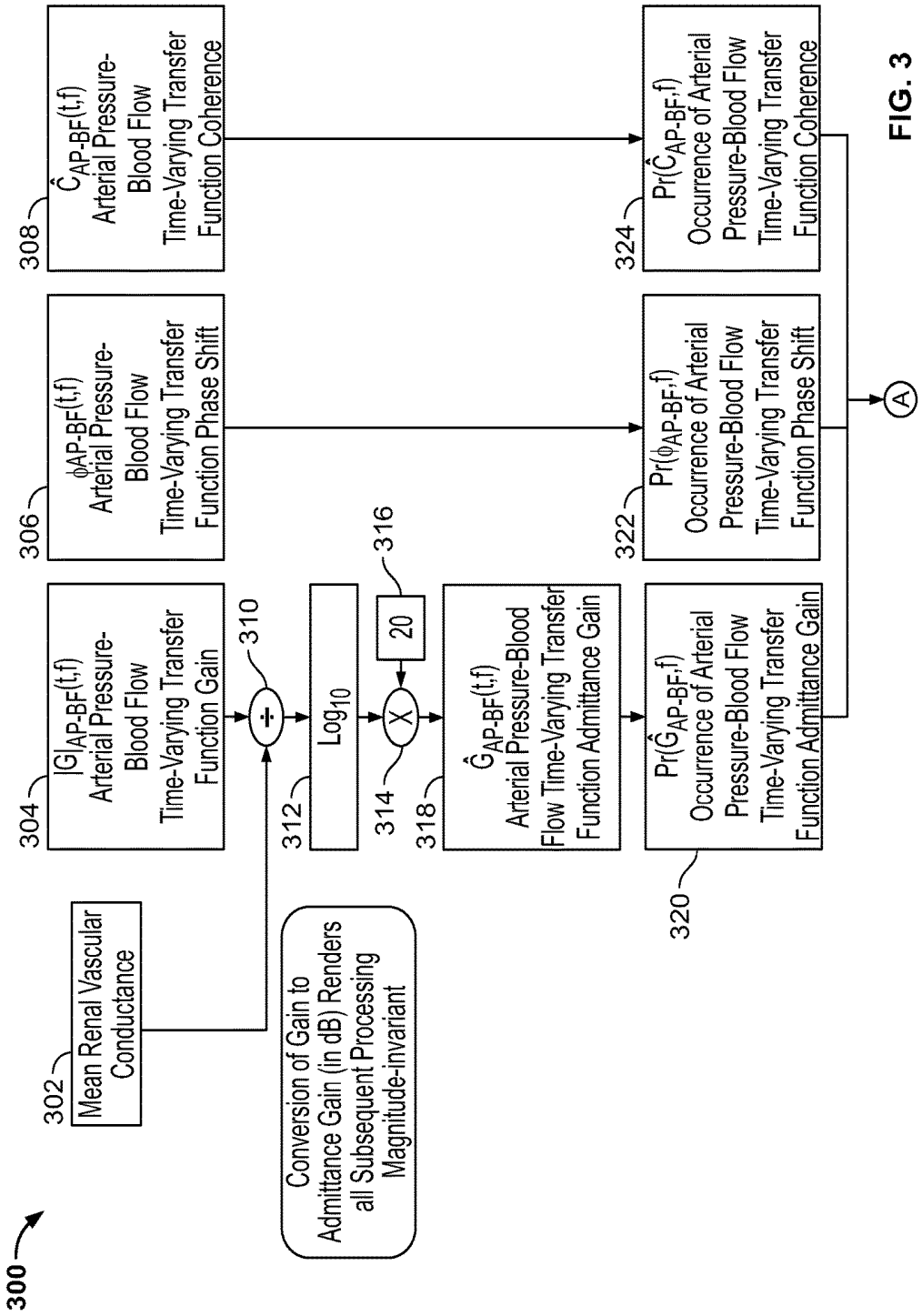

300
302
Mean Renal Vascular Conductance
Conversion of Gain to Admittance Gain (in dB) Renders all Subsequent Processing Magnitude-invariant
304
$|G|_{AP\text{-}BF}(t,f)$ Arterial Pressure-Blood Flow Time-Varying Transfer Function Gain
306
$\phi_{AP\text{-}BF}(t,f)$ Arterial Pressure-Blood Flow Time-Varying Transfer Function Phase Shift
308
$\hat{C}_{AP\text{-}BF}(t,f)$ Arterial Pressure-Blood Flow Time-Varying Transfer Function Coherence
310
÷
312
Log_{10}
314
X
316
20
318
$\hat{G}_{AP\text{-}BF}(t,f)$ Arterial Pressure-Blood Flow Time-Varying Transfer Function Admittance Gain
320
$Pr(\hat{G}_{AP\text{-}BF},f)$ Occurrence of Arterial Pressure-Blood Flow Time-Varying Transfer Function Admittance Gain
322
$Pr(\phi_{AP\text{-}BF},f)$ Occurrence of Arterial Pressure-Blood Flow Time-Varying Transfer Function Phase Shift
324
$Pr(\hat{C}_{AP\text{-}BF},f)$ Occurrence of Arterial Pressure-Blood Flow Time-Varying Transfer Function Coherence
A

FIG. 3

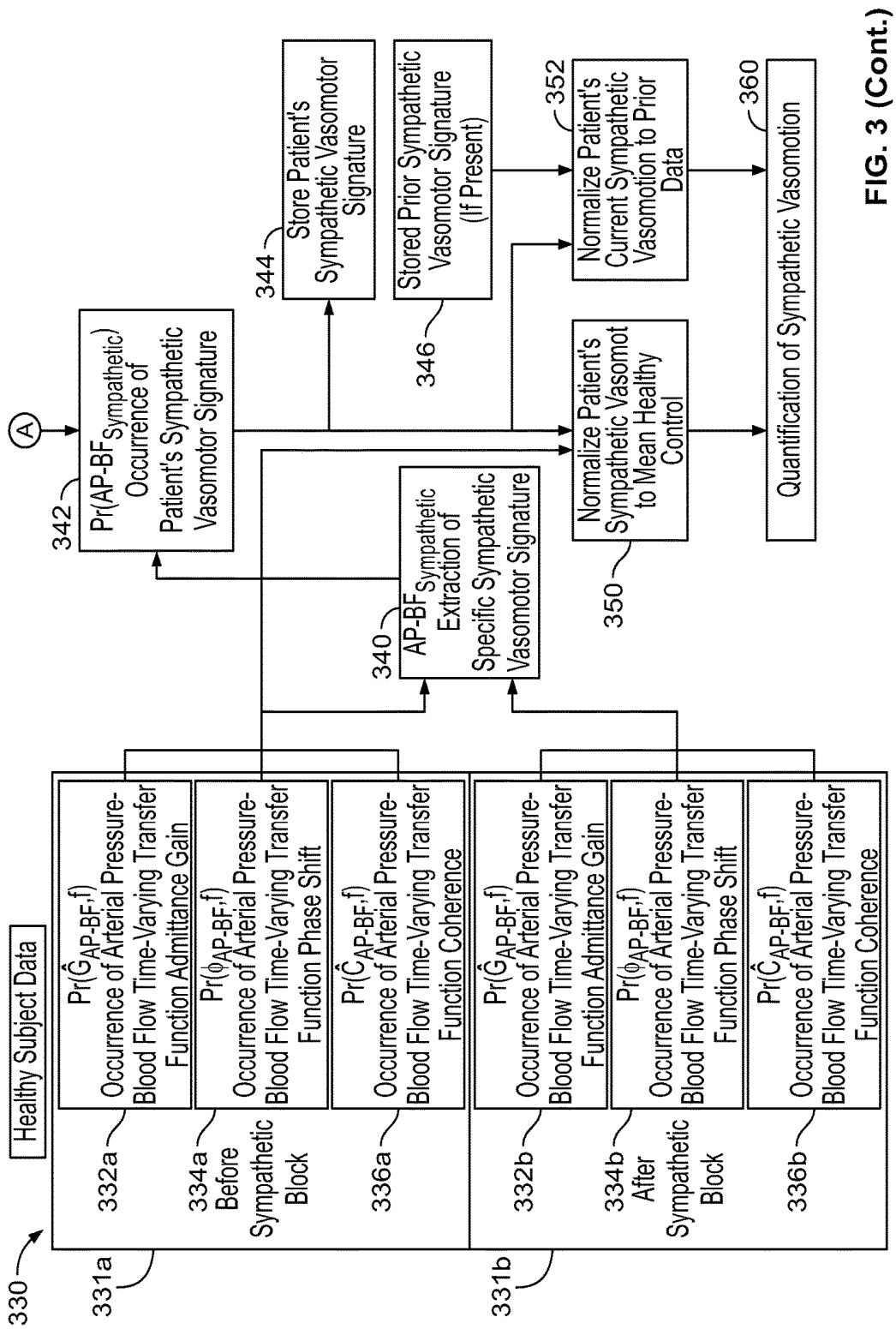

330
Healthy Subject Data
331a
331b
332a
$Pr(\hat{G}_{AP\text{-}BF},f)$ Occurrence of Arterial Pressure-Blood Flow Time-Varying Transfer Function Admittance Gain
334a Before Sympathetic Block
$Pr(\phi_{AP\text{-}BF},f)$ Occurrence of Arterial Pressure-Blood Flow Time-Varying Transfer Function Phase Shift
336a
$Pr(\hat{C}_{AP\text{-}BF},f)$ Occurrence of Arterial Pressure-Blood Flow Time-Varying Transfer Function Coherence
332b
$Pr(\hat{G}_{AP\text{-}BF},f)$ Occurrence of Arterial Pressure-Blood Flow Time-Varying Transfer Function Admittance Gain
334b After Sympathetic Block
$Pr(\phi_{AP\text{-}BF},f)$ Occurrence of Arterial Pressure-Blood Flow Time-Varying Transfer Function Phase Shift
336b
$Pr(\hat{C}_{AP\text{-}BF},f)$ Occurrence of Arterial Pressure-Blood Flow Time-Varying Transfer Function Coherence
340
$AP\text{-}BF_{Sympathetic}$ Extraction of Specific Sympathetic Vasomotor Signature
342
$Pr(AP\text{-}BF_{Sympathetic})$ Occurrence of Patient's Sympathetic Vasomotor Signature
344
Store Patient's Sympathetic Vasomotor Signature
346
Stored Prior Sympathetic Vasomotor Signature (If Present)
350
Normalize Patient's Sympathetic Vasomot to Mean Healthy Control
352
Normalize Patient's Current Sympathetic Vasomotion to Prior Data
360
Quantification of Sympathetic Vasomotion
A

FIG. 3 (Cont.)

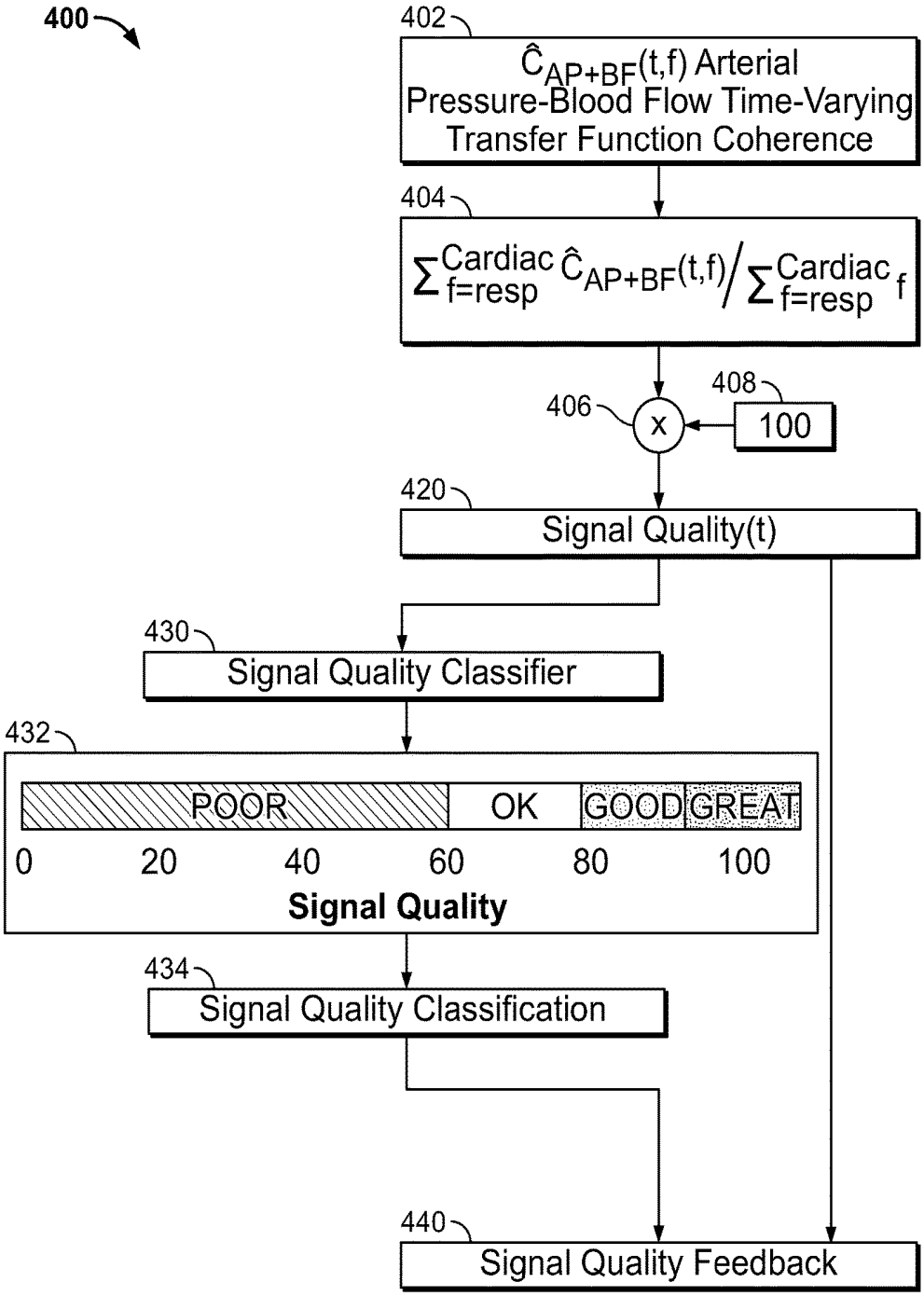

400
402
$\hat{C}_{AP+BF}(t,f)$ Arterial Pressure-Blood Flow Time-Varying Transfer Function Coherence
404
$\sum_{f=resp}^{Cardiac} \hat{C}_{AP+BF}(t,f) / \sum_{f=resp}^{Cardiac} f$
406
x
408
100
420
Signal Quality(t)
430
Signal Quality Classifier
432
POOR
OK
GOOD
GREAT
0
20
40
60
80
100
Signal Quality
434
Signal Quality Classification
440
Signal Quality Feedback

FIG. 4

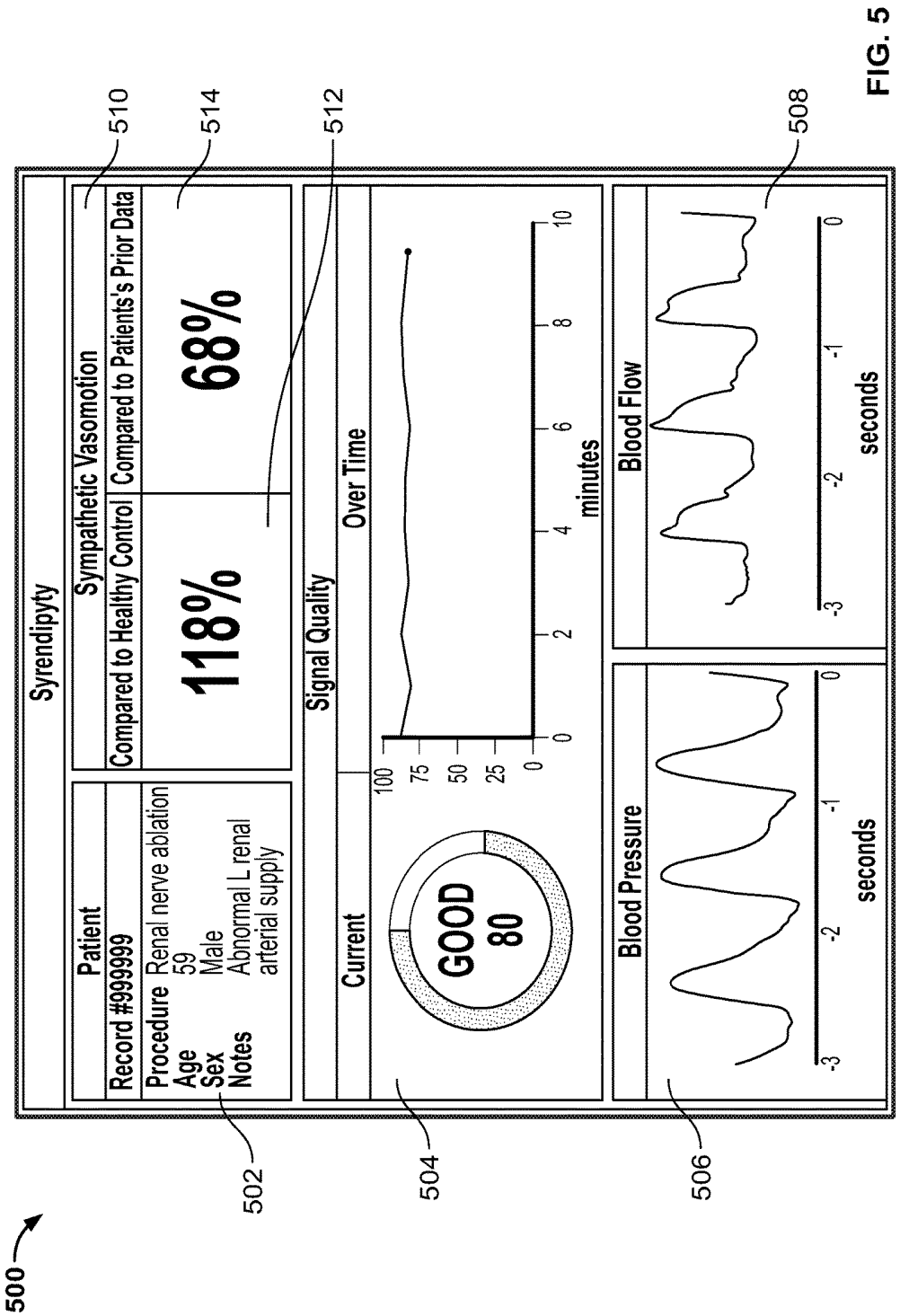

500
Syrendipyty
Patient
Record #999999
Procedure Renal nerve ablation
Age 59
Sex Male
Notes Abnormal L renal arterial supply
502
Sympathetic Vasomotion
Compared to Healthy Control
118%
Compared to Patients's Prior Data
68%
510
514
512
Signal Quality
Current
GOOD
80
Over Time
100
75
50
25
0
0
2
4
6
8
10
minutes
504
Blood Pressure
-3
-2
-1
0
seconds
506
Blood Flow
-3
-2
-1
0
seconds
508

FIG. 5

DEVICES AND METHODS FOR DETECTING AND MEASURING SYMPATHETIC VASOMOTION

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 62/312,513, filed Mar. 24, 2016. The disclosure of the prior application is considered part of and is incorporated by reference in the disclosure of this application.

STATEMENT AS TO FEDERALLY SPONSORED RESEARCH

[0002] This invention was made with government support under Grant No. P01 HL062222 and Grant No. F30 HL118974 awarded by the National Institutes of Health. The government has certain rights in the invention.

TECHNICAL FIELD

[0003] The present disclosure relates to sympathetic vasomotor identification and quantification systems. The systems provide ways to assess therapies, diseases, and conditions which affect sympathetic innervation and function.

BACKGROUND

[0004] The sympathetic nervous system is an important guardian of body homeostasis that innervates arteries and veins releasing norepinephrine and causing these blood vessels to constrict. This norepinephrine release is rhythmic and leads to a rhythmic constriction and relaxation of the vessels that is known as sympathetic vasomotion.

SUMMARY

[0005] The present disclosure describes sympathetic vasomotor identification and quantification systems that provide ways to assess therapies, diseases, and conditions which affect sympathetic innervation and function. Because sympathetic vasomotion relies on intact, functional sympathetic nerves, systems described herein include a signal processing functionality that establishes sympathetic vasomotor signatures through the collection of arterial blood pressure and blood flow signals.

[0006] In one aspect, this disclosure is directed to a sympathetic vasomotion monitoring system that includes a user interface comprising a display, and a sympathetic vasomotion monitoring device comprising a sympathetic vasomotion quantifier. The sympathetic vasomotion monitoring device is configured to: (1) receive one or more blood pressure signals corresponding to a time-based series of blood pressure readings from a blood pressure monitoring device; (2) receive one or more blood flow signals corresponding to a time-based series of blood flow readings from a blood flow monitoring device; (3) calculate, by the sympathetic vasomotion quantifier, one or more quantifications of a sympathetic vasomotion signature based on: (a) the time-based series of blood pressure readings, (b) the time-based series of blood flow readings, and (c) a set of sympathetic vasomotion quantifier parameters comprising one or more types of physiological data; and (4) output to the display: (i) the one or more quantifications of the sympathetic vasomotion signature, (ii) the time-based series of blood pressure readings, (iii) the time-based series of blood flow readings, and (iv) a signal quality metric indicative of a quality of at least the one or more blood flow signals corresponding to the time-based series of blood flow readings.

[0007] Such a sympathetic vasomotion monitoring system may optionally include one or more of the following features. The set of sympathetic vasomotion quantifier parameters comprises blood pressure data and blood flow data may correspond to a specific vascular bed. The specific vascular bed may be a renal vascular bed. The set of sympathetic vasomotion quantifier parameters may include blood pressure data and blood flow data associated with a disease or condition. The disease or condition may be selected from a group consisting of: epilepsy, spinal-cord injuries, drug-induced autonomic dysfunction, pheochromocytoma, migraine, sleep apnea, adrenal insufficiency, mastocytosis, complex regional pain syndrome, chronic fatigue syndrome, alcoholism, carcinoid tumors, cancer, cyclic vomiting, neuroleptic malignant syndrome, hypertension, heart failure, cardiomyopathy, Takotsubo syndrome, chronic kidney failure, metabolic syndrome, insulin resistance, obesity, panic disorder, hemodynamic instability, hemorrhage, shock, and cerebrovascular accident. The set of sympathetic vasomotion quantifier parameters may include blood pressure data and blood flow data associated with a treatment. The treatment may be a renal denervation treatment. The one or more quantifications of the sympathetic vasomotion signature output to the display may include a sympathetic vasomotion quantifier comparing current sympathetic vasomotion to a healthy control. The one or more quantifications of the sympathetic vasomotion signature output to the display may include a sympathetic vasomotion quantifier comparing current sympathetic vasomotion to a patient's prior data.

[0008] In another aspect, this disclosure is directed to a method for monitoring sympathetic vasomotion. The method includes: (a) receiving at a sympathetic vasomotion monitoring device (i) one or more blood pressure signals corresponding to a time-based series of blood pressure readings from a blood pressure monitoring device and (ii) one or more blood flow signals corresponding to a time-based series of blood flow readings from a blood flow monitoring device; (b) calculating, by a processor of the sympathetic vasomotion monitoring device, an arterial pressure-blood flow time-varying transfer function; (c) calculating, by a sympathetic vasomotion quantifier of the sympathetic vasomotion monitoring device, one or more quantifications of a sympathetic vasomotion signature based on the arterial pressure-blood flow time-varying transfer function and a set of sympathetic vasomotion quantifier parameters comprising one or more types of physiological data; (d) outputting, to a display, the one or more quantifications of the sympathetic vasomotion signature; and (e) displaying, at the display, the one or more quantifications of the sympathetic vasomotion signature.

[0009] Such a method for monitoring sympathetic vasomotion may optionally include one or more of the following features. The set of sympathetic vasomotion quantifier parameters may include blood pressure data and blood flow data corresponding to a specific vascular bed. The specific vascular bed may be a renal vascular bed. The set of sympathetic vasomotion quantifier parameters may include blood pressure data and blood flow data associated with a disease or condition. The disease or condition may be

selected from a group consisting of: epilepsy, spinal-cord injuries, drug-induced autonomic dysfunction, pheochromocytoma, migraine, sleep apnea, adrenal insufficiency, mastocytosis, complex regional pain syndrome, chronic fatigue syndrome, alcoholism, carcinoid tumors, cancer, cyclic vomiting, neuroleptic malignant syndrome, hypertension, heart failure, cardiomyopathy, Takotsubo syndrome, chronic kidney failure, metabolic syndrome, insulin resistance, obesity, panic disorder, hemodynamic instability, hemorrhage, shock, and cerebrovascular accident. The set of sympathetic vasomotion quantifier parameters may include blood pressure data and blood flow data associated with a treatment. The treatment may be a renal denervation treatment. The displaying the one or more quantifications of the sympathetic vasomotion signature may include displaying a comparison between current sympathetic vasomotion and a healthy control. The displaying the one or more quantifications of the sympathetic vasomotion signature may include displaying a comparison between current sympathetic vasomotion and a patient's prior data. The method may also include determining a treatment protocol based on the displayed one or more quantifications of the sympathetic vasomotion signature. The treatment protocol may include a treatment time for a renal denervation procedure.

[0010] In another aspect, this disclosure is directed to a sympathetic vasomotion monitoring system that includes a user interface comprising a display, and a sympathetic vasomotion monitoring device comprising a sympathetic vasomotion quantifier. The sympathetic vasomotion monitoring device may be configured to: (i) receive one or more blood pressure signals corresponding to a time-based series of blood pressure readings; (ii) receive one or more blood flow signals corresponding to a time-based series of blood flow readings; (iii) calculate, by the sympathetic vasomotion quantifier, one or more quantifications of a sympathetic vasomotion signature based on: (a) the time-based series of blood pressure readings, (b) the time-based series of blood flow readings, and (c) a set of sympathetic vasomotion quantifier parameters comprising physiological data; and (iv) output to the display the one or more quantifications of the sympathetic vasomotion signature.

[0011] Certain embodiments described herein may have particular advantages. For example, some embodiments of the sympathetic vasomotor identification and quantification systems can provide real-time, reliable, and quantitative indications of sympathetic vasomotion. Accordingly, in some embodiments the technology can help diagnose the presence of sympathetic failure and sympathetically-mediated pain, characterize the extent of sympathetic failure, differentiate between types of sympathetic failure, and/or stratify patients within one disease type to personalize treatment options and assess the response to therapy. The systems also allow for sympathetic vasomotion to be measured regionally and/or locally, such as in a particular vascular bed.

[0012] Additionally, in some embodiments the sympathetic vasomotor identification and quantification systems described herein are advantageously non-invasive, using arterial blood flow and blood pressure signals to calculate the quantitative sympathetic vasomotion readout.

[0013] Furthermore, in some embodiments the sympathetic vasomotor identification and quantification systems described herein enable continuous, real-time monitoring of sympathetic vasomotion. As such, the sympathetic vasomotor identification and quantification systems can be advantageously used in parallel with many treatments (such as, but not limited to, renal denervation), while providing a real-time readout as to whether the treatment is effective.

[0014] Other features and advantages of the invention will be apparent from the following detailed description and figures, and from the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0015] FIG. **1** is a block diagram that depicts the structure of an example sympathetic vasomotion identification and quantification system, in accordance with some embodiments.

[0016] FIG. **2**A is a block diagram of an example blood pressure input conditioner.

[0017] FIG. **2**B is a block diagram of an example blood flow input conditioner.

[0018] FIG. **3** is a flowchart depicting an example process for quantifying sympathetic vasomotion.

[0019] FIG. **4** is a flowchart depicting an example signal quality monitoring process.

[0020] FIG. **5** is a screen shot of an example user interface of the sympathetic vasomotion identification and quantification systems in accordance with some embodiments.

DETAILED DESCRIPTION

[0021] Turning to the figures, FIG. **1** is a block diagram depicting the structure of an example sympathetic vasomotion identification and quantification system **100** in accordance with some embodiments provided herein. In the depicted embodiment, the sympathetic vasomotion identification and quantification system **100** includes a sympathetic vasomotion monitoring device **102** for quantifying sympathetic vasomotion. The sympathetic vasomotion monitoring device **102** outputs a quantification of a sympathetic vasomotion signature **104** to be displayed via a user interface **106**.

[0022] In the depicted embodiment, the sympathetic vasomotion identification and quantification system **100** also includes an arterial blood pressure monitor **108** and an arterial blood flow monitor **110**. The arterial blood pressure monitor **108** and the arterial blood flow monitor **110** provide signals corresponding to a patient's arterial blood pressure and arterial blood flow, respectively, to the sympathetic vasomotion monitoring device **102**.

[0023] In some cases, the arterial blood pressure signal may be acquired using non-invasive methods such as, but not limited to, oscillometry, tonometry, volume-clamp, pulse wave velocity, and pulse transit time method. In some cases, the arterial blood pressure signal may be acquired more invasively using methods such as, but not limited to, by placement of an arterial pressure transducer directly in a subject's artery. In some cases, the blood flow signal may be acquired as blood flow velocity using techniques such as, but not limited to, ultrasound or laser Doppler technology, or by transit-time ultrasound.

[0024] While in the depicted embodiment the arterial blood pressure monitor **108** and the arterial blood flow monitor **110** are depicted as separate monitoring systems, in some embodiments the arterial blood pressure and the blood flow signals are obtained from a combined system. For example, in some embodiments signals corresponding to a patient's arterial blood pressure and blood flow can be

obtained from an intravascular device that includes a pressure sensor and a flow sensor that are combined on the same wire or catheter. In some embodiments, such a combined pressure/flow measuring device can be steerable and may include additional advantageous functionalities. Some non-limiting examples of such combination pressure/flow measuring devices are the COMBOWIRE® XT pressure/flow guide wires marketed by Volcano Corporation of San Diego, Calif., USA.

[0025] In the depicted embodiment of sympathetic vasomotion identification and quantification system **100**, the signals output from the arterial blood pressure monitor **108** and the arterial blood flow monitor **110** are conditioned by signal conditioners represented here by signal conditioning **112***a* and **112***b*, which are described further below in reference to FIG. **2**. After signal conditioning **112***a* and **112***b*, the resulting signals are digitized at signal digitization **113***a* and **113***b*. Thereafter, the digitized signals are turned into an arterial blood pressure time series **114***a* and an arterial blood flow time series **114***b* respectively.

[0026] In the depicted embodiment, the arterial blood pressure time series **114***a* and the arterial blood flow time series **114***b* are used to calculate a mean vascular conductance **116**. The mean vascular conductance **116** gives a snapshot of the static vascular behavior of the patient. In some embodiments, the arterial blood pressure time series **114***a* and the arterial blood flow time series **114***b* are transformed into an arterial blood pressure time-varying spectrum **118***a* and an arterial blood flow time-varying spectrum **118***b*, respectively, using complex Morlet Wavelet transforms or other time-frequency (e.g., Gabor transform) or time-scale (complex Gaussian wavelet) transforms.

[0027] Still referring to FIG. **1**, in the depicted embodiment the arterial blood pressure time-varying spectrum **118***a* and the arterial blood flow time-varying spectrum **118***b* are used to calculate an arterial pressure-blood flow cross-spectrum **120** and an arterial pressure-blood flow time-varying transfer function **122**. The gain **124**, phase shift **126**, and coherence **128** of the arterial pressure-blood flow time-varying transfer function **122** are calculated and input to a sympathetic vasomotion quantifier **130** alongside the mean renal vascular coherence **116**. The coherence **128** of the arterial pressure-blood flow time-varying transfer function **122** is also provided to a signal quality quantifier **132**.

[0028] In some embodiments, the signal quality quantifier **132** processes the coherence **128** to quantify and/or classify the quality of one or more of the signal(s). For example, in some embodiments the signal quality quantifier **132** can output a value such as a percentage or other scaled numeric value (e.g., zero to ten) as an expression of the quality of the signal. In another example, the quantifier can output one or more indicia such as a rating (e.g., an "A" to "F" letter grade, a zero to five-star rating, and the like), a class (e.g., "great," "good," "OK," "poor," etc.), or any other appropriate form of classification of a signal's quality. In some embodiments, the output of the quantifier **132** is output as a signal quality feedback value **134** to the user interface **106**.

[0029] The sympathetic vasomotion quantifier **130** is application specific, meaning that sympathetic vasomotion quantifier parameters (i.e., one or more types of physiological data) of the sympathetic vasomotion quantifier **130** differ depending on which vascular bed is being monitored and/or which disease or treatment is being monitored. The particular sympathetic vasomotion quantifier **130** that is used in the sympathetic vasomotion monitoring device **102** for a particular monitoring period may be selected by a clinician or other user of the sympathetic vasomotion identification and quantification system **100**.

[0030] In the depicted embodiment, the sympathetic vasomotion quantifier **130** leverages both the frequency and the magnitude of the gain and phase time-frequency distributions to identify that the vasomotion is of sympathetic origin. Ohm's Law assures a constant, linear relationship between blood pressure and blood flow for passive blood vessels, and thus active, time-varying vasomotion can be identified and quantified by the time variability in the pressure-flow relationship. This time variability manifests directly as low coherence as well as elevated measures of variability (standard deviation, interquartile range) of the pressure-flow relationship over time.

[0031] In frequency, sympathetic vasomotion can affect the pressure-flow relationship at higher frequencies than other sources of vasomotion. For example, in rabbit studies, the pressure-flow relationship is affected at high frequencies of between 0.2 and 0.75 Hz. In humans, this high frequency is approximately 0.1 Hz. Other sources of vasomotion, for example auto-regulatory mechanisms in the kidney, occur at lower frequencies, allowing them to be filtered out. For example, the auto-regulator mechanisms in a rabbit kidney produce affects to the pressure-flow relationship at frequencies of 0.02-0.2 Hz. In gain, sympathetic vasomotion, as a vasoconstrictor, decreases the magnitude of the pressure-flow admittance. In phase, sympathetic vasomotion is readily distinguishable from autoregulatory mechanisms, as autoregulatory mechanisms lag changes in renal blood flow (i.e., give rise to time-frequency distributions with positive phase) whereas sympathetic vasomotion gives rise to pressure-flow variability centered either at zero or at a negative phase lag, depending on the vascular bed and hemodynamic state. The occurrence of high-frequency, low-gain, negative-phase, low-coherence occurrences of the pressure-flow relationship can be used to sensitively and specifically identify as well as quantify sympathetic vasomotion in a vascular bed of interest.

[0032] In some embodiments, the sympathetic vasomotion quantifier **130** may look at a particular portion of the time-varying data (for example a one, two, three, four, five, six, seven, eight, nine, or ten-minute period, or longer), and compare the gain, phase shift, and coherence across that portion to a control data set or a previously-taken data set from the same patient. Depending on the disease, condition, or treatment being monitored, the sympathetic vasomotion quantifier **130** may be provided with and/or utilize a different control data set. For example, if a renal denervation treatment is being monitored, the sympathetic vasomotion quantifier **130** may compare the time-varying data with a data from a denervated kidney and provide a quantification of a sympathetic vasomotor signature **104** to the user interface **106** based on the comparison performed by the sympathetic vasomotion quantifier **130**.

[0033] In some embodiments, the sympathetic vasomotion identification and quantification system **100** can assess sympathetic activity in diseases where excessive sympathetic activity contributes to disease progression and mortality. For example, such diseases can include, but are not limited to, cardiovascular diseases like hypertension, heart failure, cardiomyopathy, Takotsubo syndrome, renal diseases like

chronic kidney failure, metabolic diseases like metabolic syndrome, insulin resistance, and obesity, and psychiatric diseases like panic disorder.

[0034] In some embodiments, the sympathetic vasomotion identification and quantification system **100** can help diagnose the presence of sympathetic failure and sympathetically-mediated pain, characterize the extent of sympathetic failure, differentiate between types of sympathetic failure, and stratify patients within one disease to personalize treatment options and assess the response to therapy. In some embodiments, the system **100** and method can be used for patients with primary disorders of the autonomic nervous system, including, but not limited to, postural tachycardia syndrome (POTS), neurogenic orthostatic hypotension, vasovagal syncope, pure autonomic failure, autonomic epilepsy, neutrally-mediated syncope (NMS, formerly called neurocardiogenic syncope or neutrally-mediated hypotension), multiple system atrophy (Shy-Drager Syndrome), cerebral salt-wasting syndrome, deficiencies of tetrahydrobioperterin, tyrosine hydroxylase oraromatic L-amino acid decarboxylase, dopamine beta-hydroxylase deficiency, Menkes disease and other ATP7A-related disorders, norepinephrine transporter deficiency, monoamine oxidase deficiency, and congenital central hypoventilation syndrome and other PHOX2B-related disorders.

[0035] In some embodiments, the sympathetic vasomotion identification and quantification system **100** can be used for peripheral autonomic disorders including, but not limited to, diabetic autonomic dysfunction, amyloidotic autonomic failure, autoimmune autonomic ganglionopathy, Guillain-Barre' syndrome, hereditary autonomic neuropathies, familial dysautonomia (i.e. Riley-Day Syndrome), and vitamin B12 deficiency. In some embodiments, the sympathetic vasomotion identification and quantification system **100** can be used for patients with other chronic, progressive diseases involving the sympathetic nervous system including, but not limited to, Parkinson's disease, dementia with Lewy Bodies, and pure autonomic failure that result in sympathetic failure. Further, in some embodiments the sympathetic vasomotion identification and quantification system **100** can be used in the evaluation of patients presenting with complaints that frequently have autonomic components, including, but not limited to, syncope, orthostatic intolerance, impotence (male erectile dysfunction), hyper- and hypo-hydrosis, sleep apnea, and fecal incontinence. Moreover, in some embodiments the sympathetic vasomotion identification and quantification system **100** can be used for patients diagnosed with conditions which may have autonomic involvement, such as epilepsy, spinal-cord injuries, drug-induced autonomic dysfunction, pheochromocytoma, migraine, sleep apnea, adrenal insufficiency, mastocytosis, complex regional pain syndrome, chronic fatigue syndrome, alcoholism, carcinoid tumors, cancer (which can cause paraneoplastic autonomic dysfunction), cyclic vomiting, and neuroleptic malignant syndrome.

[0036] FIG. **2**A is a block diagram of an example blood pressure input signal conditioner **200**. In general, in some embodiments the blood pressure input signal conditioner **200** accepts an analog electrical output signal from a non-invasive, continuous arterial blood pressure monitor, and prepares the signal for digitization. In some embodiments, the blood pressure input signal conditioner **200** can perform the signal conditioning **112***a* of FIG. **1**. For example, the blood pressure input signal conditioner **200** can be used to interface the example arterial blood pressure monitor **108** in preparation for the digitization **113***a* of FIG. **1**.

[0037] A connector **202** includes a blood pressure signal contact **204***a* and a ground contact **204***b*. In some embodiments, the connector **202** can be configured to electrically interface with a blood pressure monitor. For example, the connector **202** can be formed as part of jack that plugs into the arterial blood pressure monitor **108** to receive analog electrical waveforms that are representative of blood pressure readings.

[0038] In the depicted embodiment, the blood pressure signal contact **204***a* and the ground contact **204***b* are in electrical communication with an input protector and level shifter **206**. The input protector and level shifter **206**, as the name suggests, performs at least two functions. First, the input protector and level shifter **206** includes circuitry that can resist the effects of voltages and/or currents present at the blood pressure signal contact **204***a* and the ground contact **204***b*. For example, the input protector and level shifter **206** can include circuitry that resists reverse polarities (e.g., a ground applied to the blood pressure signal contact **204***a* and/or a voltage applied to the ground contact **204***b*), resists electrical spikes (e.g., static shock), resists or snubs over-voltages (e.g., due to plugging the connector **202** into an incompatible device), or can help protect the device **100** from combinations of these and/or other non-blood pressure signal related electrical conditions. Second, the input protector and level shifter **206** includes circuitry that can provide electrical signal level shifting. For example, the input protector and level shifter **206** can be configured to amplify, attenuate, compress, expand, offset (e.g., combine a positive or negative DC voltage onto the blood pressure signal), or perform combinations of these and other appropriate forms of electrical signal modifications. The output of the input protector and level shifter **206** is a protected and modified signal based the analog electrical waveforms received by the input protector and level shifter **206**.

[0039] In the depicted embodiment, the input protector and level shifter **206** is in electrical contact with a signal filter **208**, and passes the modified signal to the signal filter **208**. The signal filter **208** performs frequency-based filtering of the modified signal and provides a filtered signal as an output. For example, the signal filter **208** may attenuate signal components in the modified signal that are above a predetermined frequency (e.g., low-pass filtering), below a predetermined frequency (e.g., high-pass filtering), between two predetermined frequencies (e.g., bandpass filtering), or are outside the range of two predetermined frequencies (e.g., notch filtering).

[0040] The output of the signal filter **208** is a filtered form of the blood pressure signal as modified by the input protector and level shifter **206**. This resulting signal is provided as an arterial pressure signal **210**. In some implementations, the arterial pressure signal **210** can be an analog waveform representative of the time-domain, protected, shifted, and filtered blood pressure signal received from the arterial blood pressure monitor **108**.

[0041] In the depicted embodiment, the arterial pressure signal **210** is then provided to a computer **212**. In some embodiments, the computer **212** can be or can comprise a portion of the sympathetic vasomotion monitoring device **102** (FIG. **1**). For example, in some embodiments the arterial pressure signal **210** can be provided for digitization by the example digitization step **113***a*.

[0042] In some embodiments, the arterial blood pressure monitor **108** (FIG. **1**) may be configured to provide digital signals that are representative of blood pressure readings, and the input protector and level shifter **206** and the filter **208** can include circuitry and/or software modules that when executed by a processor can protect, limit, and/or shift digital waveforms in order to provide a digital version of the arterial pressure signal **210**. In some embodiments, such a digital version of the arterial pressure signal **210** may be provided directly to the sympathetic vasomotion monitoring device **102** as the example arterial blood pressure time series **114***a*.

[0043] FIG. **2**B is a block diagram of an example blood flow input signal conditioner **250**. In general, in the depicted embodiment the blood flow input signal conditioner **202** accepts an analog electrical output signal that represents the continuous Doppler audio from a non-invasive, ultrasound machine, and prepares the signal for digitization. In some embodiments, the blood flow input signal conditioner **250** can perform the signal conditioning **112***b* of FIG. **1**. For example, the blood flow input signal conditioner **250** can be used to interface the example arterial blood flow monitor **110** in preparation for the digitization **113***b* of FIG. **1**.

[0044] A connector **252** includes a blood flow signal contact **254***a*, a blood flow signal contact **254***b*, and a ground contact **254***c*. In some embodiments, the connector **202** can be configured to electrically interface with a blood pressure monitor. For example, the connector **252** can be formed as part of jack that plugs into the arterial blood flow monitor **110** to receive analog electrical waveforms that are representative of blood flow readings.

[0045] In the depicted embodiment, the blood pressure signal contact **254***a* and the ground contact **254***c* are in electrical communication with an input protector and level shifter **256***a*. In some embodiments, the input protector and level shifter **256***a*, as the name suggests, performs at least two functions. First, the input protector and level shifter **256***a* includes circuitry that can resist the effects of voltages and/or currents present at the blood pressure signal contact **254***a* and the ground contact **254***c*. For example, the input protector and level shifter **256***a* can include circuitry that resists reverse polarities (e.g., a ground applied to the blood flow signal contact **254***a* and/or a voltage applied to the ground contact **254***c*), resists electrical spikes (e.g., static shock), resists or snubs over-voltages (e.g., due to plugging the connector **252** into an incompatible device), or can help protect the device **100** from combinations of these or other non-blood pressure signal related electrical conditions. Second, the input protector and level shifter **256***a* includes circuitry that can provide electrical signal level shifting. For example, the input protector and level shifter **256***a* can be configured to amplify, attenuate, compress, expand, offset (e.g., combine a positive or negative DC voltage onto the blood pressure signal), or perform combinations of these and other appropriate forms of electrical signal modifications. The output of the input protector and level shifter **256***a* is a protected and modified signal based the analog electrical waveforms received by the input protector and level shifter **256***a*.

[0046] In the depicted embodiment, the blood pressure signal contact **254***b* and the ground contact **254***c* are in electrical communication with an input protector and level shifter **256***b*. The input protector and level shifter **256***b* performs substantially the same functions for the signals provided at the blood pressure signal contact **254***b* and the ground contact **254***c* as the input protector and level shifter **256***a* performs for the signals provided at the blood pressure signal contact **254***a* and the ground contact **254***c*. The output of the input protector and level shifter **256***b* is a protected and modified signal based the analog electrical waveforms received by the input protector and level shifter **256***b*.

[0047] In the depicted embodiment, the input protector and level shifter **256***a* is in electrical contact with a signal filter **258***a*, and passes the modified signal to the signal filter **258***a*. The signal filter **258***a* performs frequency-based filtering of the modified signal and provides a filtered signal as an output. For example, the signal filter **258***a* may attenuate signal components in the modified signal that are above a predetermined frequency (e.g., low-pass filtering), below a predetermined frequency (e.g., high-pass filtering), between two predetermined frequencies (e.g., bandpass filtering), or are outside the range of two predetermined frequencies (e.g., notch filtering).

[0048] In the depicted embodiment, the input protector and level shifter **256***b* is in electrical contact with a signal filter **258***b*, and passes modified signal to the signal filter **258***b*. The signal filter **258***b* performs substantially the same function for the modified signal of the input protector and level shifter **256***b* as the signal filter **258***a* performs for the for the modified signal of the input protector and level shifter **256***a*.

[0049] The output of the signal filters **258***a* and **258***b* are filtered forms of the blood flow signals as modified by the input protector and level shifters **256***a* and **256***b*. These resulting signals are provided to a signal polarity selector **260**.

[0050] In general, one of the blood flow signals will be a positive signal, and the other will be a negative signal. However, in some implementations these signals may be received with reversed polarity (e.g., the connector **252** was plugged in backwards, the ultrasound machine was misconfigured or used in error). As such, in some such implementations, the polarity of the signals may need to be reversed before they can be properly conditioned and/or processed further.

[0051] In some embodiments, the signal polarity selector **260** includes circuitry that identifies the polarity of the blood flow signals as provided by the signal filters **258***a* and **258***b* and a switching network that can direct the blood flow signals to a pair out outputs based on the identified polarity (e.g., reverse the polarity of the signals). For example, the signal polarity selector **260** can determine if the output of the signal filter **258***a* should be provided to a variable gain amplifier **262***a* and the output of the signal filter **258***b* should be provided to a variable gain amplifier **262***b*, or if the polarity should be reversed by providing the output of the signal filter **258***a* the variable gain amplifier **262***b* and by providing the output of the signal filter **258***b* to the variable gain amplifier **262***a*.

[0052] In the depicted embodiment, the variable gain amplifiers **262***a* and **262***b* are configured to provide a predetermined amount of gain or attenuation to the signals provided by the signal polarity selector **260**. In some implementations, the variable gain amplifiers **262***a* and **262***b* may amplify or attenuate the two received signals differently (e.g., to increase the balance between waveforms).

[0053] In the depicted embodiment, the variable gain amplifier **262***a* provides an amplified signal to a comparator

264*a*. The comparator **264***a* compares the amplified signal to a predetermined comparison voltage, and provides one or more digital signals that indicate which of the amplified signal or the comparison voltage is higher. The one or more digital signals is/are provided to a flip-flop **266***a*. The variable gain amplifier **262***b* provides an amplified signal to a comparator **264***b* that performs a substantially similar function as the comparator **264***a*, and the resulting digital signal is provided to a flip-flop **266***b*.

[0054] In the depicted embodiment, the flip-flop **266***a* provides a toggled digital output that is in one of two stable states. The state of the toggled digital output is changed based on the digital signal received from the comparator **264***a*. The flip-flop **266***a* is configured to change its toggled digital output on and off in response to the received digital signal changing to a selected one of "off" or "on." For example, when the flip-flop **266***a* receives an "on" signal, the state of the toggled digital output can be toggled "on" or "off." The flip-flop **266***b* performs a substantially similar function as the flip-flop **266***a*, and provides a toggled digital output based on the digital signal received from the comparator **264***b*.

[0055] In the depicted embodiment, the toggled digital output of the flip-flop **266***a* is provided to a frequency-to-voltage converter **267***a*. The toggled digital output of the flip-flop **266***b* is provided to a frequency-to-voltage converter **267***b*. The voltage output of the frequency-to-voltage converter **267***a*, the blood flow velocity toward the ultrasound transducer, is passed to an inverter **268**. The inverter **268** inverts this directional blood flow velocity so that it may be passed along with the output of the frequency-to-voltage converter **267***b* to a summing amplifier **270**. The output of the summing amplifier **270** then represents the net blood arterial blood flow at a given point in time.

[0056] In the depicted embodiment, the combined digital output signal of the combiner **270** is provided to a signal filter **272**. The signal filter **278** performs frequency-based filtering of the modified signal and provides a filtered signal as an output. For example, the signal filter **278** may attenuate signal components in the modified signal that are above a predetermined frequency (e.g., low-pass filtering), below a predetermined frequency (e.g., high-pass filtering), between two predetermined frequencies (e.g., bandpass filtering), or are outside the range of two predetermined frequencies (e.g., notch filtering).

[0057] The output of the signal filter **278** is a filtered form of the combined digital output signal provided by the combiner **270**. This resulting signal is provided as blood flow velocity signal **274**. In some implementations, the blood flow velocity signal **274** can be a digital waveform representative of the time-domain, protected, filtered, digitized, and combined blood flow signals received from the arterial blood flow monitor **110**. In other embodiments, the arterial blood flow monitor could use a different method to measure blood flow, including, but not limited to, transit-time volumetric flow (e.g., from a pen-arterial probe) or intravascular Doppler flow velocity (e.g., from an intra-arterial catheter).

[0058] The blood flow velocity signal **274** is then provided to a computer **282**. In some embodiments, the computer **212** can be or can comprise a portion of the sympathetic vasomotion monitoring device **102** (FIG. **1**). For example, the blood flow velocity signal **274** can be provided for digitization by the example digitization step **113***b*.

[0059] In some embodiments, the arterial blood flow monitor **110** may be configured to provide digital signals that are representative of blood flow readings, and the input protector and components of the blood flow input signal conditioner **250** can include circuitry and/or software modules that when executed by a processor can protect, limit, shift, filter, repolarize, amplify, compare, toggle, and/or combine digital waveforms in order to provide a digital version of the blood flow velocity signal **274**, which may be provided directly to the sympathetic vasomotion monitoring device **102** (FIG. **1**) as the example arterial blood flow time series **114***b*.

[0060] FIG. **3** is a flowchart depicting an example process **300** for quantifying the amount of renal sympathetic vasomotion occurring over time. In some implementations, the process **300** can be performed by the example sympathetic vasomotion quantifier **130** of FIG. **1**.

[0061] In the process **300**, a value **302** representative of a mean renal vascular conductance (e.g., the mean renal vascular conductance **116**), a value **304** representative of an arterial pressure blood flow time-varying transfer function gain (e.g., gain **124**), a value **306** representative of an arterial pressure blood flow time varying transfer function phase shift (e.g., phase shift **126**), and a value **308** representative of an arterial pressure blood flow time-varying transfer function (e.g., coherence **128**) are received.

[0062] The value **304** is divided (i.e., normalized) by value **302** in process **310** and converted **312** to a log **10** scale and multiplied **314** by a factor of twenty **316** to yield value **318**, the admittance gain in dB. The conversion of gain to the admittance gain (in dB) can cause subsequent processing to be substantially magnitude-invariant. These admittance gain values **318** are calculated for the duration of the sympathetic vasomotion assessment, and this is then binned (e.g., into bins of 5 dB width) to yield the occurrence of admittance gain over the time course of the renal sympathetic vasomotion assessment, value **320**.

[0063] The value **306** is calculated for the duration of the sympathetic vasomotion assessment, and these values are then binned (e.g., into bins of $\pi/10$ width) to yield the occurrence of phase shift over the time course of the renal sympathetic vasomotion assessment, value **322**. The value **308** is calculated for the duration of the renal sympathetic vasomotion assessment, and these values are then binned (e.g., into bins of 0.05 width) to yield the occurrence of coherence over the time course of the renal sympathetic vasomotion assessment, value **322**. The value **308** is applied to an occurrence of arterial pressure blood flow time-varying coherence transfer function to determine a value **324**.

[0064] At this point in the example process **300**, the blood pressure-blood flow relationship over time has been characterized in terms of the occurrence of admittance gain, phase shift, and coherence, and now the sympathetic vasomotion component of this relationship must be extracted and quantified. Identifying the sympathetic vasomotion signature is depicted in this example process **300** by using normative data from healthy subjects before and after sympathetic block. A collection **330** of healthy subject (e.g., patent) data is obtained in accordance with some embodiments of process **300**. The collection can include a block of data **331***a* and a block of data **331***b*. The block of data **331***a* includes an occurrence of arterial pressure blood flow time-varying transfer function admittance gain value **332***a*, an occurrence of arterial pressure blood flow time-varying

phase shift value **334***a*, and an occurrence of arterial pressure blood flow time-varying coherence value **336***a*. The values **332***a*, **334***a*, and **336***a* are values obtained before a sympathetic block has been performed (e.g., baseline "before" readings). The block of data **331***b* includes an occurrence of arterial pressure blood flow time-varying transfer function admittance gain value **332***b*, an occurrence of arterial pressure blood flow time-varying phase shift value **334***b*, and an occurrence of arterial pressure blood flow time-varying coherence value **336***b*. The values **332***b*, **334***b*, and **336***b* are values obtained after a sympathetic block has been performed (e.g., "after" readings).

[0065] The blood pressure-blood flow admittance gain, phase shift, and coherence occurrence that is significantly reduced by sympathetic blockade is sympathetic vasomotion. The occurrence bins that are affected in this manner from the block **331** are the extraction of the specific sympathetic vasomotor signature, value **340**.

[0066] This extracted sympathetic vasomotor signature can be used to quantify sympathetic vasomotion in ways that are useful to the clinician or patient. In the simplest manifestation, the patient's sympathetic vasomotor signature is obtained by extracting the bins identified as the specific sympathetic vasomotor signature **340** from the patient's data in the values **320**, **322**, and **324** to obtain the occurrence of the patient's sympathetic vasomotor signature as value **342**. The value **342** is stored **344**, for example, in a computer memory or data storage device such as a hard disk drive or FLASH memory, from where the value can be retrieved **346** later.

[0067] The value **342** and the data from the block **331***a* are also applied by normalizing the patient's sympathetic vasomotion to the mean sympathetic vasomotion from the healthy control data in **331** to determine a value **350**. In the example process, the corresponding values of **342** are divided by the mean occurrence of each of the bins identified as part of the sympathetic signature in value **340** using the data from block **331***a*. The median across all bins is then used to express the patient's renal sympathetic vasomotion during the most recent time interval compared to healthy subjects. This can be useful in diagnosing pathology (e.g., patients with cardiovascular disease have increased renal sympathetic outflow) or identifying patients that might respond well to therapy (e.g., increased renal sympathetic drive may indicate a greater therapeutic response to renal nerve ablation).

[0068] The value **342**, along with a stored prior sympathetic vasomotor signature value that is retrieved **346**, if such a value is present, are applied by normalizing the patient's current sympathetic vasomotion to prior data to determine a value **352**. In the example process, the corresponding values of **342** are divided by the occurrence of each of the bins identified as part of the sympathetic signature in value **340** using the data from block **331***a*. The median across all bins is then used to express the patient's renal sympathetic vasomotion during the most recent time interval compared to this prior level of renal sympathetic vasomotion. This allows for longitudinal assessment of this patient's sympathetic vasomotion over time. In this process, this could be used to assess response to a treatment (e.g., efficacy of renal nerve ablation in a hypertensive patient) or assess disease progression (e.g., increased renal sympathetic outflow portends a poor prognosis in heart failure patients).

[0069] The value **350** and the value **352** are then applied in a transfer function that quantifies the patient's sympathetic vasomotion to determine a value **360**. In some implementations, the value **360** can be the example quantification of a sympathetic vasomotion signature **104** of FIG. **1**.

[0070] FIG. **4** is a flowchart depicting an example signal quality monitoring process **400**. In some implementations, the signal quality monitoring process **400** can be performed by the example signal quality quantifier **132** of FIG. **1**.

[0071] Because blood flow passively follows blood pressure very closely at frequencies above those associated with the vascular control mechanisms, the coherence at these very high frequencies (i.e., ranging from the respiratory frequency to the cardiac frequency, approximately 0.4 Hz to 1 Hz in humans) can be used to assess the signal quality. The average coherence **402** of an arterial pressure-blood flow time-varying transfer function for frequencies ranging from the respiratory frequency to the cardiac frequency provides a value between 0 and 1. For example, the coherence **402** may be the example coherence **128** of FIG. **1**.

[0072] The transformed **404** value is multiplied **406** by a factor **408** of one hundred to determine a signal quality value **420**. For example, the coherence **402** may be a fractional value in a range of zero to one, and the signal quality value may be a value in a range of zero to one hundred.

[0073] The signal quality value **420** is received by a signal quality classifier **430**. The classifier compares the signal quality value **420** to a collection of ranges **432** that represent a collection of signal quality classifications. In the illustrated example, signal quality values **402** ranging from zero to about sixty are classified as being "poor", values ranging from about sixty to about eighty are classified as being "OK", values ranging from about eighty to about ninety are classified as being "good", and values above about ninety are classified as being "great." The output of the signal quality classifier **430** is provided as a signal quality classification value **434**.

[0074] The signal quality value **420** and the signal quality classification value **434** are then provided as signal quality feedback data **440**. In some implementations, the signal quality feedback data **440** is the information that is output as the example signal quality feedback value **134** to the example user interface **106**. The user interface **106** can update its display based on the signal quality feedback data **440**. For example, for a signal quality value of "0.95", the user interface **160** may indicate a signal quality of "95" and "great." The display of signal quality will be discussed further in the description of FIG. **5**.

[0075] FIG. **5** is an example screen capture of an embodiment of a user interface **500** of the sympathetic vasomotion identification and quantification systems provided herein. Other variations of user interface data displays are also envisioned.

[0076] In the depicted embodiment, the user interface **500** is configured to display patient data **502**, which includes a patient identification number, a procedure description, patient age and sex, and notes. The user interface **500** is also configured to display a signal quality metric **504** (e.g., from the signal quality quantifier **132** as described in reference to FIG. **1**). The user interface **500** is also configured to display a time-based blood pressure readout **506**, and a time-based blood flow readout **508**.

[0077] In the depicted embodiment, the user interface **502** is also configured to display one or more quantifications of

sympathetic vasomotion **510**. Here, the quantifications of sympathetic vasomotion include a percentage of sympathetic vasomotion compared to a healthy control **512** and a percentage of sympathetic vasomotion compared to the patient's prior data **514**. For example, in some cases (without limitation) the embodiment of the user interface **502** shown in this figure may be displayed during a renal denervation procedure where the sympathetic vasomotion identification and quantification system **100** is employed to monitor treatment progress. In the depicted example, the one or more quantifications of sympathetic vasomotion **510** shows that the patient has 118% sympathetic vasomotion compared to a healthy control measured at a similar vascular bed, yet the patient's sympathetic vasomotion is 68% of the sympathetic vasomotion from the patient's prior data. A clinician performing a renal denervation procedure, for example, may use the one or more quantifications of sympathetic vasomotion **510** to decide when to end a procedure, or to determine a procedure's effectiveness. Additionally or alternatively, the user interface **500** may display an effectiveness quantification or a treatment recommendation based on the one or more quantifications sympathetic vasomotion **510**.

[0078] While this specification contains many specific implementation details, these should not be construed as limitations on the scope of any invention or of what may be claimed, but rather as descriptions of features that may be specific to particular embodiments of particular inventions. Certain features that are described in this specification in the context of separate embodiments can also be implemented in combination in a single embodiment. Conversely, various features that are described in the context of a single embodiment can also be implemented in multiple embodiments separately or in any suitable subcombination. Moreover, although features may be described herein as acting in certain combinations and even initially claimed as such, one or more features from a claimed combination can in some cases be excised from the combination, and the claimed combination may be directed to a subcombination or variation of a subcombination.

[0079] Similarly, while operations are depicted in the drawings in a particular order, this should not be understood as requiring that such operations be performed in the particular order shown or in sequential order, or that all illustrated operations be performed, to achieve desirable results. In certain circumstances, multitasking and parallel processing may be advantageous. Moreover, the separation of various system modules and components in the embodiments described herein should not be understood as requiring such separation in all embodiments, and it should be understood that the described program components and systems can generally be integrated together in a single product or packaged into multiple products.

[0080] Particular embodiments of the subject matter have been described. Other embodiments are within the scope of the following claims. For example, the actions recited in the claims can be performed in a different order and still achieve desirable results. As one example, the processes depicted in the accompanying figures do not necessarily require the particular order shown, or sequential order, to achieve desirable results. In certain implementations, multitasking and parallel processing may be advantageous.

What is claimed is:

1. A sympathetic vasomotion monitoring system, comprising:

a user interface comprising a display; and

a sympathetic vasomotion monitoring device comprising a sympathetic vasomotion quantifier, the sympathetic vasomotion monitoring device configured to:

receive one or more blood pressure signals corresponding to a time-based series of blood pressure readings from a blood pressure monitoring device;

receive one or more blood flow signals corresponding to a time-based series of blood flow readings from a blood flow monitoring device;

calculate, by the sympathetic vasomotion quantifier, one or more quantifications of a sympathetic vasomotion signature based on: (a) the time-based series of blood pressure readings, (b) the time-based series of blood flow readings, and (c) a set of sympathetic vasomotion quantifier parameters comprising one or more types of physiological data; and

output to the display: (i) the one or more quantifications of the sympathetic vasomotion signature, (ii) the time-based series of blood pressure readings, (iii) the time-based series of blood flow readings, and (iv) a signal quality metric indicative of a quality of at least the one or more blood flow signals corresponding to the time-based series of blood flow readings.

2. The sympathetic vasomotion monitoring system of claim **1**, wherein the set of sympathetic vasomotion quantifier parameters comprises blood pressure data and blood flow data corresponding to a specific vascular bed.

3. The sympathetic vasomotion monitoring system of claim **2**, wherein the specific vascular bed is a renal vascular bed.

4. The system of claim **1**, wherein the set of sympathetic vasomotion quantifier parameters comprises blood pressure data and blood flow data associated with a disease or condition.

5. The system of claim **4**, wherein the disease or condition is selected from a group consisting of: epilepsy, spinal-cord injuries, drug-induced autonomic dysfunction, pheochromocytoma, migraine, sleep apnea, adrenal insufficiency, mastocytosis, complex regional pain syndrome, chronic fatigue syndrome, alcoholism, carcinoid tumors, cancer, cyclic vomiting, neuroleptic malignant syndrome, hypertension, heart failure, cardiomyopathy, Takotsubo syndrome, chronic kidney failure, metabolic syndrome, insulin resistance, obesity, panic disorder, hemodynamic instability, hemorrhage, shock, and cerebrovascular accident.

6. The system of claim **1**, wherein the set of sympathetic vasomotion quantifier parameters comprises blood pressure data and blood flow data associated with a treatment.

7. The system of claim **6**, wherein the treatment is a renal denervation treatment.

8. The system of claim **1**, wherein the one or more quantifications of the sympathetic vasomotion signature output to the display comprises a sympathetic vasomotion quantifier comparing current sympathetic vasomotion to a healthy control.

9. The system of claim **1**, wherein the one or more quantifications of the sympathetic vasomotion signature output to the display comprises a sympathetic vasomotion quantifier comparing current sympathetic vasomotion to a patient's prior data.

10. A method for monitoring sympathetic vasomotion, comprising:

receiving at a sympathetic vasomotion monitoring device: (i) one or more blood pressure signals corresponding to a time-based series of blood pressure readings from a blood pressure monitoring device and (ii) one or more blood flow signals corresponding to a time-based series of blood flow readings from a blood flow monitoring device;

calculating, by a processor of the sympathetic vasomotion monitoring device, an arterial pressure-blood flow time-varying transfer function;

calculating, by a sympathetic vasomotion quantifier of the sympathetic vasomotion monitoring device, one or more quantifications of a sympathetic vasomotion signature based on the arterial pressure-blood flow time-varying transfer function and a set of sympathetic vasomotion quantifier parameters comprising one or more types of physiological data;

outputting, to a display, the one or more quantifications of the sympathetic vasomotion signature; and

displaying, at the display, the one or more quantifications of the sympathetic vasomotion signature.

11. The method of claim **10**, wherein the set of sympathetic vasomotion quantifier parameters comprises blood pressure data and blood flow data corresponding to a specific vascular bed.

12. The method of claim **11**, the specific vascular bed is a renal vascular bed.

13. The method of claim **10**, wherein the set of sympathetic vasomotion quantifier parameters comprises blood pressure data and blood flow data associated with a disease or condition.

14. The method of claim **13**, wherein the disease or condition is selected from a group consisting of: epilepsy, spinal-cord injuries, drug-induced autonomic dysfunction, pheochromocytoma, migraine, sleep apnea, adrenal insufficiency, mastocytosis, complex regional pain syndrome, chronic fatigue syndrome, alcoholism, carcinoid tumors, cancer, cyclic vomiting, neuroleptic malignant syndrome, hypertension, heart failure, cardiomyopathy, Takotsubo syndrome, chronic kidney failure, metabolic syndrome, insulin resistance, obesity, panic disorder, hemodynamic instability, hemorrhage, shock, and cerebrovascular accident.

15. The method of claim **10**, wherein the set of sympathetic vasomotion quantifier parameters comprises blood pressure data and blood flow data associated with a treatment.

16. The method of claim **15**, wherein the treatment is a renal denervation treatment.

17. The method of claim **10**, wherein the displaying the one or more quantifications of the sympathetic vasomotion signature comprises displaying a comparison between current sympathetic vasomotion and a healthy control.

18. The method of claim **10**, wherein the displaying the one or more quantifications of the sympathetic vasomotion signature comprises displaying a comparison between current sympathetic vasomotion and a patient's prior data.

19. The method of claim **10**, further comprising determining a treatment protocol based on the displayed one or more quantifications of the sympathetic vasomotion signature.

20. The method of claim **19**, wherein the treatment protocol comprises a treatment time for a renal denervation procedure.

21. A sympathetic vasomotion monitoring system, comprising:

a user interface comprising a display; and

a sympathetic vasomotion monitoring device comprising a sympathetic vasomotion quantifier, the sympathetic vasomotion monitoring device configured to:

receive one or more blood pressure signals corresponding to a time-based series of blood pressure readings;

receive one or more blood flow signals corresponding to a time-based series of blood flow readings;

calculate, by the sympathetic vasomotion quantifier, one or more quantifications of a sympathetic vasomotion signature based on: (a) the time-based series of blood pressure readings, (b) the time-based series of blood flow readings, and (c) a set of sympathetic vasomotion quantifier parameters comprising physiological data; and

output to the display the one or more quantifications of the sympathetic vasomotion signature.

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专利名称(译)	用于检测和测量交感神经血管舒缩的装置和方法		
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摘要(译)

描述了交感神经血管舒缩识别和定量系统，其提供了评估影响交感神经支配和功能的治疗，疾病和病症的方法。因为交感神经血管舒动依赖于完整的功能性交感神经，所以本文所述的交感神经血管舒缩识别和定量系统的一些实施方案包括通过收集动脉血压和血流信号建立交感神经血管舒缩特征的信号处理功能。