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(54) Title: DEVICES AND METHODS FOR MONITORING CEREBRAL HEMODYNAMIC CHARACTERISTICS

(57) Abstract: Devices, and methods for receiving and comparing bioimpedance signals are disclosed. In one aspect, the devices and methods may include receiving bioimpedance signals indicative of hemodynamic characteristics within a subject's brain. Bioimpedance signals may be compared, and the comparison used to provide information for diagnosing changes in arterial occlusion. Bioimpedance signals may be associated with left and right sides of a subject's brain. Signature features within the bioimpedance signals may be detected and used to determine differences in the bioimpedance signals.

## DEVICES AND METHODS FOR MONITORING CEREBRAL HEMODYNAMIC CHARACTERISTICS

### Related Application

[001] This application claims the benefit of priority under 35 U.S.C. §119(e) of U.S. Provisional Application No. 61/441,248, filed February 9, 2011, and U.S. Provisional Application No. 61/474,739, filed April 12, 2011, both of which are incorporated herein by reference in their entirety.

### Technical Field

[002] Aspects of the present disclosure relate to detection, monitoring and/or analysis of cerebro-hemodynamic conditions, such as the existence of or change in arterial occlusion.

### Background

[003] A number of cerebro-hemodynamic characteristics may be clinically useful for diagnosing strokes, trauma, and other conditions that can affect the functioning of the cerebrovascular system. These characteristics may include cerebral blood volume, cerebral blood flow, cerebral perfusion pressure, mean transit time, time to peak, intracranial pressure, and others. Conventional methods for detecting or monitoring these parameters may include physically inserting a probe into the cerebrospinal fluid or into an artery, Angiography, computed tomography angiography(CTA), perfusion computed tomography (PCT), Transcranial Doppler Ultrasound (TCD), positron emission tomography (PET), and magnetic resonance imaging (MRI) and angiography (MRA).

[004] Some non- invasive methods for detecting or monitoring cerebro-hemodynamic parameters may require, for example, machines for carrying out CT, PCT, PET, and/or MRI procedures. In some instances, the cost of these machines, their limited mobility, and/or their significant expense per use, may limited their usefulness in situations where either regular, continuous, or frequent monitoring of cerebro-hemodynamic characteristics may be desirable.

[005] In the presently disclosed embodiments, several exemplary methods and systems are described that may be used to reliably and non-invasively detect and monitor cerebrovascular hemodynamic characteristics. These methods and systems may be practical for continuous or frequent use and may include, for example, a patient headset and cerebral perfusion monitor for monitoring

bioimpedance signals indicative of cerebrovascular hemodynamic characteristics. The patient headset and cerebral perfusion monitor may provide information for diagnosing changes in artery occlusion, such as those brought on by ischemic stroke or head trauma.

[006] The foregoing description is merely exemplary for providing general background and is not restrictive of the various embodiments of systems, methods, devices, and features as described and claimed.

### **Summary**

[007] In the presently disclosed embodiments, several exemplary methods and systems are described that may be used to detect and monitor cerebrovascular hemodynamic characteristics. In some embodiments, these methods and systems may be useful, for example, for continuous or frequent use and may involve, for example, a patient headset and cerebral perfusion monitor for synchronizing and monitoring signals indicative of cerebrovascular hemodynamic characteristics. The patient headset and cerebral perfusion monitor may provide information for diagnosing changes in arterial occlusion, such as occlusions brought on by ischemic stroke or head trauma.

[008] One exemplary disclosed embodiment may include a cerebro-hemodynamic measurement apparatus for diagnosing a change in artery occlusion over time in a brain of a subject. The apparatus may include at least one processor configured to receive at least one non-invasively-obtained bioimpedance signal associated with a first time interval, wherein the at least one bioimpedance signal is indicative of a hemodynamic characteristic of the subject's brain during the first time interval. The at least one processor may be further configured to receive at least one other non-invasively-obtained bioimpedance signal, associated with a second time interval, wherein the at least one other bioimpedance signal is indicative of a hemodynamic characteristic of the subject's brain during the second time interval. The at least one processor may be further configured to compare the at least one bioimpedance signal associated with the first time interval with the at least one other bioimpedance signal associated with the second time interval. The at least one processor may be further configured to output information for diagnosing a change in artery occlusion based on a comparison of the at least one bioimpedance signal and the at least one other bioimpedance signal.

[009] In another embodiment, the at least one received bioimpedance signal may be indicative of a comparison between bioimpedance measurements associated with right and left sides of the subject's brain during the first time interval, and the at least one other received bioimpedance signal may be indicative of a comparison between bioimpedance measurements associated with right and left sides of the subject's brain during the second time interval.

[010] In still another embodiment, the at least one received bioimpedance signal may be indicative of a bioimpedance measurement in a hemisphere of the subject's brain during the first time interval, and the at least one other received bioimpedance signal may be indicative of a bioimpedance measurement in the hemisphere of the subject's brain during the second time interval.

[011] In another embodiment, the at least one non-invasively obtained bioimpedance signal may be associated with a right side of the subject's brain, and the at least one other non-invasively obtained bioimpedance signal may be associated with a left side of the subject's brain.

[012] In yet another embodiment, the at least one processor may be further configured to receive the at least one bioimpedance signal and the at least one other bioimpedance signal via electrodes associated with a head of a subject.

[013] In a further embodiment, the electrodes may be maintained in a relatively fixed position on the head of the subject.

[014] The at least one processor may be further configured to receive a plurality of additional non-invasively-obtained signals and to compare the at least one bioimpedance signal, the at least one other bioimpedance signal, and the plurality of additional signals. The output information for diagnosing a change in artery occlusion may relate to the at least one bioimpedance signal, the at least one other bioimpedance signal, and the plurality of additional signals.

[015] In still another embodiment, some of the plurality of additional signals may be associated with a first side of a subject's brain and others of the plurality of additional signals may be associated with a second side of the subject's brain.

[016] Additionally, the at least one processor may be further configured to detect at least one signature feature within the at least one bioimpedance signal and the at least one other bioimpedance signal and to use the detected signature features to determine differences between the at least one bioimpedance signal and the at least one other bioimpedance signal.

[017] Further, the at least one processor may be further configured to detect the at least one signature feature based on a determination of one or more of inflection locations, peak locations, anticipated inflection locations, and anticipated peak locations.

[018] In still another embodiment, the at least one signature feature may be a set of signature features comprising a first peak, a second peak, a third peak, a first minimum, a second minimum, and a third minimum.

[019] In a further embodiment, the at least one bioimpedance signal may result from a measurement signal outputted via the electrodes.

[020] The foregoing summary and following description of drawings and following detailed description are exemplary and explanatory only, and are not restrictive of the invention as claimed.

#### **Brief Description of the Drawings**

[021] The accompanying drawings, which are incorporated in and constitute a part of this specification, together with the description, serve to explain the principles of the embodiments described herein.

[022] **FIG. 1** provides a diagrammatic representation of an exemplary cerebro-hemodynamic measurement apparatus consistent with exemplary embodiments of the invention.

[023] **FIG. 2** provides a diagrammatic representation of major cerebral arteries.

[024] **FIG. 3** provides a diagrammatic representation of exemplary bioimpedance signal pathways in the brain of a subject consistent with exemplary embodiments of the invention.

[025] **FIG. 4** provides a diagrammatic representation of an exemplary bioimpedance signal obtained from a cerebro-hemodynamic measurement apparatus consistent with exemplary embodiments of the invention.

[026] **FIG. 5** provides a diagrammatic representation of exemplary signature features of a single bioimpedance signal waveform period.

[027] **FIGs. 6a** and **6b** provide a diagrammatic representation of a comparison between amplitude and phase angle aspects of an exemplary bioimpedance signal waveform over multiple cardiac cycles, consistent with embodiments of the present invention.

[028] **FIG. 7** provides a diagrammatic representation of a single bioimpedance signal waveform period as decomposed by a pulse decomposition algorithm for detecting signature features in a bioimpedance signal, consistent with exemplary embodiments of the invention.

[029] **FIG. 8** provides a diagrammatic representation of a comparison between exemplary bioimpedance signals associated with different hemispheres of a subject's brain.

[030] **FIG. 9** is a flowchart showing the steps of an exemplary method for diagnosing a change in artery occlusion over time in a brain of a subject.

### **Detailed Description**

[031] Reference will now be made in detail to exemplary embodiments as illustrated in the accompanying drawings. Wherever possible, the same reference numbers will be used throughout the drawings and the following description to refer to the same or like parts. These embodiments are described in sufficient detail to enable those skilled in the art to practice the invention and it is to be understood that other embodiments may be utilized and that changes may be made without departing from the scope of the present invention. The following detailed description, therefore, is not to be interpreted in a limiting sense.

[032] Unless otherwise defined, all technical and/or scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the embodiments of the invention pertains. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of embodiments of the invention, exemplary methods and/or materials are described below. In case of conflict, the patent specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and are not intended to be necessarily limiting.

[033] Exemplary disclosed embodiments may include devices and methods for the detection and monitoring of cerebro-hemodynamic characteristics. More specifically, they may include apparatuses for obtaining and comparing bioimpedance signals and outputting information for the diagnosis of alterations in arterial occlusion.

[034] Embodiments consistent with the disclosure may include at least one processor configured to perform an action. As used herein, the term "processor"

may include an electric circuit that performs a logic operation on an input or inputs. For example, such a processor may include one or more integrated circuits, microchips, microcontrollers, microprocessors, all or part of a central processing unit (CPU), graphics processing unit (GPU), digital signal processors (DSP), field-programmable gate array (FPGA) or other circuit suitable for executing instructions or performing logic operations. The at least one processor may be configured to perform an action if it is provided with access to, is programmed with, includes, or is otherwise made capable carrying out instructions for performing the action. The at least one processor may be provided with such instructions either directly through information permanently or temporarily maintained in the processor, or through instructions accessed by or provided to the processor. Instructions provided to the processor may be provided in the form of a computer program comprising instructions tangibly embodied on an information carrier, e.g., in a machine-readable storage device, or any tangible computer-readable medium. A computer program may be written in any form of programming language, including compiled or interpreted languages, and it can be deployed in any form, including as a standalone program or as one or more modules, components, subroutines, or other unit suitable for use in a computing environment. The at least one processor may include specialized hardware, general hardware, or a combination of both to execute related instructions. The processor may also include an integrated communications interface, or a communications interface may be included separate and apart from the processor. The at least one processor may be configured to perform a specified function through a connection to a memory location or storage device in which instructions to perform that function are stored.

[035] Consistent with some embodiments of the invention, the at least one processor may be configured to receive a bioimpedance signal. As used herein, a signal may be any time-varying or spatially-varying quantity. Receiving a signal may include obtaining a signal through conductive means, such as wires or circuitry; reception of a wirelessly transmitted signal; and/or reception of a signal previously recorded, such as a signal stored in memory. Receiving a signal may further encompass other methods known in the art for signal reception. As used herein, a bioimpedance signal may include any type of signal containing information about the electrical impedance of a biological subject. The bioimpedance signal may contain information about the electrical impedance of the subject between any two portions

of a subject's body. Information about the electrical impedance of the subject may comprise information about the resistive and/or reactive components of electrical impedance.

[036] A bioimpedance signal may comprise at least one voltage signal, and/or at least one current signal. A bioimpedance signal may comprise two or more voltage and/or current signals, and may comprise a signal representative of a comparison between two or more voltage and/or current signals. A bioimpedance signal may be measured as a response to at least one measurement voltage signal, and/or at least one measurement current signal. Information about the electrical impedance of a subject's body may be contained in the amplitude, frequency, or phase angle of the signal. In a bioimpedance signal, information about the electrical impedance of a subject's body may also be contained in a comparison between the amplitudes, frequencies, or phase angles of multiple signals.

[037] In some embodiments consistent with the present disclosure, a bioimpedance signal may be non-invasively obtained. As used herein, non-invasively obtained may refer to a technique of acquiring (e.g., a signal or measurement) that does not require use of a subcutaneous or percutaneous device.

[038] In some embodiments consistent with the present disclosure, a bioimpedance signal may be associated with a first or a second time interval. A bioimpedance signal associated with a time interval may have been obtained at any time within the time interval, or may represent any type of selection or composition of bioimpedance signals measured during all or part of the time interval. For instance, a bioimpedance signal associated with a first time interval may have been obtained at the immediate start or immediate finish of a first time interval, may represent a mean bioimpedance signal measured over all or part of the time interval, may represent a mean of a sampling of bioimpedance signals measured at regular or irregular instants during the time interval, and/or any other selection or composition of bioimpedance signals measured during the first time interval. A representative bioimpedance signal may also be selected based on other signals, for example selecting a specific heart rate, such as the most common heart rate, based on an ECG signal during the time interval, and using the corresponding bioimpedance signal as representative for the time interval.

[039] In some embodiments consistent with the present disclosure, a bioimpedance signal may be indicative, of hemodynamic characteristics, for

example, cerebral perfusion pressure, cerebral blood volume, intracranial pressure, and cerebral blood flow. As used herein, such a bioimpedance signal may be indicative of a physiological characteristic when changes in the physiological characteristic result in changes to the bioimpedance signal. Thus, a bioimpedance signal indicative of hemodynamic characteristics may change when hemodynamic characteristics or conditions change. Measurement and analysis of the changing bioimpedance signal may, therefore, yield information about the changing hemodynamic characteristics or conditions. The relationship between a bioimpedance signal indicative of change in a particular hemodynamic characteristic may be direct, wherein changes in the bioimpedance signal are directly indicative of changes in the particular hemodynamic characteristic. Alternatively (or additionally) a relationship between a bioimpedance signal indicative of change in a particular hemodynamic characteristic may be indirect, requiring additional information or additional analysis in order in order to yield information about the particular hemodynamic characteristic. For instance, by way of example only, a bioimpedance signal may be directly indicative of, cerebral blood volume. A bioimpedance signal may be indirectly indicative of, for example, cerebral blood flow, intracranial pressure, or cerebral perfusion pressure, information about which may be obtained from additional analysis of information obtained about cerebral blood volume.

[040] In some embodiments consistent with the present disclosure, a first bioimpedance signal may be compared to a second bioimpedance signal. Comparing two or more bioimpedance signals may comprise any type of analysis performed on the signals. The bioimpedance signals may be compared with basic arithmetic operations, such as addition, subtraction, etc. The bioimpedance signals may be compared, for example, in a time domain or in a frequency domain, using any suitable transform. All or part of one signal may be compared to all or part of another signal. For example, the signals may be compared in their entirety, by smaller sections, and/or by discrete points. Parts of one or more signals may be compared to corresponding or non-corresponding parts of one or more other signals. Bioimpedance signals may be compared based on amplitudes, frequencies, and phase angles, as measured at time intervals of any length, and/or based on other signature features of the signals.

[041] In exemplary embodiments, a processor may be configured to detect one or more signature features within one or more bioimpedance signal waveforms.

Signature features of a bioimpedance signal may include any detectable features within the waveform. These signature features may be detectable through visual observation of a waveform, or may be detectable only through mathematical analysis of a waveform. Signature features may be defined by a single aspect of a waveform, such as maximum amplitude, or may be defined by a relationship between multiple aspects of a waveform, such as relative peak height. A bioimpedance signal waveform may be wholly or partially characterized by signature features. Examples of signature features consistent with the present disclosure may include measured or anticipated local or global maxima and minima, i.e., peaks and valleys, measured or anticipated inflection points, relative maxima height, relative minima depth, height and width ratios of maxima, depth and width ratios of minima, and ratios of any other aspects of maxima and minima. Signature features may further include frequency spectrum aspects of a waveform, including power spectrum and phase angle. Other signature features may include average waveform amplitudes over windows or ranges, or waveform slopes. Furthermore, multi-variate analysis may be used to define signature features that include aspects of several maxima, minima, and/or any other aspects of the waveforms (e.g., background amplitude, noise, amplitude over certain intervals, etc.) Signature features described herein are for exemplary purposes only, and are not intended to limit any embodiments of the disclosed methods and systems.

[042] In some embodiments consistent with the present disclosure, signature features of a bioimpedance waveform may include a first peak, a second peak, a third peak, a first minimum, a second minimum, and a third minimum. As used herein, the first, second, and third peaks may include local maxima within a bioimpedance signal waveform, and the first, second, and third minimum may include local minima within a bioimpedance signal waveform. The peaks and minima may be, for example, local maxima and minima within a single period of a cyclically repeating waveform. The peaks and minima may also include, for example, local maxima and minima within a waveform averaged over two or more signal cycles. Peaks and minima may also include, for example, local maxima and minima within a waveform determined for a specific heart rate, such as the most common heart rate in a time interval. As used herein, peaks and minima may correspond to absolute highs and lows, or may be indicative of a region where a high or low occurred.

[043] In exemplary embodiments consistent with the present disclosure, bioimpedance signals may be associated with a right or a left side of a subject's brain. A bioimpedance signal associated with a particular side of a subject's brain, as used herein, may include a bioimpedance signal indicative of hemodynamic characteristics within the side of the brain it is associated with. A bioimpedance signal associated with a particular side of a subject's brain may be obtained from the same side of the subject's head, via electrodes or the like, or may be obtained from an opposite side of the subject's head. A bioimpedance signal associated with a particular side of a subject's brain may also be obtained from other locations, such as on the neck of subject, where, for example, carotid arteries are located.

[044] In some embodiments consistent with the present disclosure, bioimpedance signals may be non-invasively obtained via electrodes associated with a head of a subject. Such electrodes may include any type of electrodes for obtaining an electrical signal from a head of a subject. These electrodes may include skin contact electrodes affixed to the skin of a subject. Alternatively, or additionally, these electrodes may include contactless electrodes.

[045] In some embodiments consistent with the present disclosure, a plurality of additional signals may be non-invasively obtained. Such additional signals may include any type of signal obtained from a subject indicative of a physiological condition. Additional signals may include, for instance, electrocardiography (ECG) signals indicative of cardiac activity, oximeter signals indicative of blood oxygen levels, sphygmomanometer signals indicative of arterial pressure, MRI signals, CT signals, and any other signals indicative of a physiological condition of a subject.

[046] In some embodiments consistent with the present disclosure, a processor may be configured to output information for diagnosing a change in artery occlusion. As used, herein, "information for diagnosing a change in artery occlusion," is any type of information that may aid a physician in detecting or diagnosing a change in artery occlusion. Such information may, for example, include a direct indication of artery occlusion, or include information that assists in diagnosis of an artery occlusion condition. Information for diagnosing a change in artery occlusion may include specific information about the location and extent of occlusion, or may include general information indicative of a change in occlusion. For example, as described later in greater detail, asymmetry in bioimpedance-related

measurements/calculations from opposite sides of a patient's head may be information that is output for diagnosis purposes. In one embodiment, the existence of asymmetry may be the only information output. In another embodiment, a measure of asymmetry might be included in the information output. In yet another embodiment, information output may include an indicator of change in asymmetry over time.

[047] **FIG. 1** provides a diagrammatic representation of an exemplary cerebro-hemodynamic measurement apparatus 100. This exemplary apparatus 100 includes electrodes 110 affixed to a subject's head via a headset 120. Electrodes 110 may be connected to cerebral perfusion monitor 130 via wires or may include a wireless connection. Cerebral perfusion monitor 130 may include a processor 160, configured to detect, monitor, and analyze physiological signals, including bioimpedance signals, associated with the subject.

[048] The exemplary headset 120 of **FIG. 1** may include one or more electrodes 110, which may be arranged singly, in pairs, or in other appropriate groupings, depending on implementation. The electrodes on exemplary headset 120 may be arranged to as to obtain bioimpedance, or impedance plethysmography (IPG), signal waveforms. Bioimpedance may be measured by two sensor sections 150, disposed on the right and left sides of the head to correspond with the right and left hemispheres of the brain, for example. While only one sensor section 150 is shown in **FIG. 1**, an opposite side of the subject's head might include a similar electrode arrangement. Each sensor section 150 may include one pair of front electrodes, front current electrode 111 and front voltage electrode 112, and one pair of rear electrodes, rear current electrode 114, and rear voltage electrode 113. The distance between the pairs may be adjusted such that a particular aspect of a cerebro-hemodynamic condition is measured, as will be discussed later in greater detail. The electrode configuration depicted in **FIG. 1** is only one example of a suitable electrode configuration. Additional embodiments may include more or few electrodes 110, additionally or alternatively arranged in different areas of exemplary headset 120. Other embodiments may include electrodes 110 configured on an alternatively shaped headset to reach different areas of the subject's head than the exemplary headset 120.

[049] Pairs of electrodes 110 arranged in a pair may include a current output electrode and a voltage input electrode. For instance, front current electrode

111 and front voltage electrode 112 may form an electrode pair. In one embodiment, an output current may be generated by cerebral perfusion monitor 130 and passed between front current electrode 111 and rear current electrode 114. The output current may include an alternating current (AC) signal of constant amplitude and stable frequency. An input voltage induced on the head due to the output current may be measured between front voltage electrode 112 and rear voltage electrode 113. An input voltage may be measured at the same frequency as the output current. A comparison between the output current signal and the input voltage signal may yield information related to the bioimpedance of the subject. More specifically, an amplitude of the bioimpedance may be computed as a ratio of the input voltage signal amplitude to the output current amplitude signal, and a phase angle of the bioimpedance may be computed as the phase difference by which the output current signal leads the input voltage signal.

[050] A bioimpedance signal may also include output current at more than a single AC frequency. The output current may include a set of predefined frequencies and amplitudes, with detection of the measured voltage at all the frequencies or a part of the frequency range.

[051] In another embodiment, a first bioimpedance signal and a second bioimpedance signal may include output AC currents at different frequencies. For example, the current outputted by electrodes located on one side of the head may be at one frequency and the current outputted by the electrodes located on the other side of the head may be at a different frequency. Detection of the voltage may be at one frequency, the other frequency, or both frequencies by proper filtering and analysis.

[052] Blood flow into and out of the head, and more specifically, the brain, during a cardiac cycle may result in a cyclic change of the bioimpedance measured by electrodes 110. Bioimpedance changes may correlate with blood content in the head and brain. In general, because blood has a relatively low impedance when compared with tissue found in the head, higher blood content results in lower impedance. Blood flow into brain tissue may also vary the frequency response of the brain impedance. Comparing bioimpedance measurements at different frequencies may provide additional information indicative of hemodynamic characteristics.

[053] The exemplary headset 120 may include further devices or elements for augmenting bioimpedance measurements or for performing measurements in

addition to bioimpedance measurements, such as additional sensor or sensors 140. In one embodiment, additional sensor 140 may include, for example, a light emitting diode 141 and a photo detector 142 for performing Photo Plethysmography (PPG) measurements either in conjunction with or in alternative to bioimpedance signal measurements. The exemplary headset 120 may further include various circuitry 170 for signal processing or other applications and may include the capability to transmit data wirelessly to cerebral perfusion monitor 130 or to other locations. In an additional embodiment, cerebral perfusion monitor 130 may be integrated with headset 120. Although illustrated in the example of Fig. 1, additional sensor 140 and circuitry 170 may be omitted.

[054] Exemplary headset 120 may include various means for connecting, encompassing, and affixing electrodes 110 to a patient's head. For example, headset 120 may include two or more separate sections that are connected to form a loop or a band that circumscribes the patient's head. Any of these aspects, including bands, fasteners, electrode holders, wiring, hook-and-loop connector strips, buckles, buttons, clasps, etc. may be adjustable in order to fit a patient's head. Portions of exemplary headset 120 may be substantially flexible and portions of the exemplary headset 120 may be substantially inflexible. For example, electrode including portions of exemplary apparatus 120 may be substantially inflexible in order to, among other things, substantially fix electrodes 110 in specific anatomical positions on the patient's head. In addition to or in the alternative, other portions, such as bands or connectors holding the exemplary headset 120 to a patient's head, may be substantially flexible, elastic and/or form fitting.

[055] Any portion of exemplary headset 120 may be specifically designed, shaped or crafted to fit a specific or particular portion of the patient's anatomy. For example, portions of exemplary headset 120 may be crafted to fit near, around or adjacent to the patient's ear. Portions of exemplary headset 120 may be specifically designed, shaped or crafted to fit the temples, forehead and/or to position electrodes 110 in specific anatomical or other positions. Portions of the exemplary headset 120 may be shaped such that electrodes 110 (or other included measurement devices) occur in specific positions for detecting characteristics of blood flow in the head or brain of the patient. Examples of such blood flow may occur in any of the blood vessels discussed herein, especially the arteries and vasculature providing blood to

the head and/or brain, regardless of whether the vessels are in the brain or feed the brain.

[056] Exemplary headset 120 may include features suitable for improving comfort of the patient and/or adherence to the patient. For example exemplary headset 120 may include holes in the device that allow ventilation for the patient's skin. Exemplary headset 120 may further include padding, cushions, stabilizers, fur, foam felt, or any other material for increasing patient comfort.

[057] Mentioned previously, exemplary headset 120 may further include one or more additional sensors 140 in addition to or as an alternative to electrical or electrode including devices for measuring bioimpedance. For example, additional sensor 140 may include one or more components configured to obtain PPG data from an area of the patient. Additional sensors 140 may include any other suitable devices, and are not limited to the single sensor illustrated in **FIG. 1**. Other examples of additional sensor 140 include devices for measuring local temperature (e.g., thermocouples, thermometers, etc.) and/or devices for performing other biomeasurements.

[058] Exemplary headset 120 may include any suitable form of communicative mechanism or apparatus. For example, headset 120 may be configured to communicate or receive data, instructions, signals or other information wirelessly to another device, analytical apparatus and/or computer. Suitable wireless communication methods may include radiofrequency, microwave, and optical communication, and may include standard protocols such as Bluetooth, WiFi, etc. In addition to, or in alternative to these configurations, exemplary headset 120 may further include wires, connectors or other conduits configured to communicate or receive data, instructions, signals or other information to another device, analytical apparatus and/or computer. Exemplary headset 120 may further include any suitable type of connector or connective capability. Such suitable types of connectors or connective capabilities may include any standard computer connection (e.g., universal serial bus connection, firewire connection, Ethernet or any other connection that permits data transmission). Such suitable types of connectors or connective capabilities may further or alternatively include specialized ports or connectors configured for the exemplary apparatus 100 or configured for other devices and applications.

[059] Cerebral perfusion monitor 130 may include at least one processor 160 configured to obtain and analyze bioimpedance signals, such as IPG signals, and/or additional signals, such as PPG, ECG, and MRI signals. Processor 160 may be configured to perform all or some of the bioimpedance signal analysis methods described herein, and may also be configured to perform any common signal processing task known to those of skill in the art, such as filtering, noise-removal, etc. Processor 160 may also be configured to perform pre-processing tasks specific to the bioimpedance signal analysis techniques described herein. Such pre-processing tasks may include, but are not limited to, removal of signal artifacts, such as motion and respiratory artifacts.

[060] **FIG. 2** provides a diagrammatic representation of major features of the cerebral vasculature 200. The cerebral vasculature in **FIG. 2** is viewed from below the brain, with the top of the page representing the front of a subject. The blood supply to the brain 201 comes from four main arteries traversing the neck. The larger two are the right and left internal carotid arteries (ICA) 210, in the front part of the neck. The vertebral arteries (VA) 220 are located in the back of the neck and join to form the basilar artery (BA) 230. The internal carotid arteries and the basilar arteries are connected by Posterior Communicating Artery (not shown) and Anterior Communicating Artery (not shown) to form the Circle of Willis (COW). In an ideal patient the COW is a network of connected arteries that allows blood supply to the brain 201 even when one or more of the feeding arteries is blocked.

[061] The main arteries that supply blood to the brain 201 are the Middle Cerebral Arteries (MCAs) 240, Anterior Cerebral Arteries (ACAs) 250, and Posterior Cerebral Arteries (PCAs) 260. The MCAs 240 may be one area of interest when diagnosing decreased blood flow to portions of the brain 201. The MCAs 240 are the sole blood supply to the largest brain region – about two thirds of each brain hemisphere.

[062] The electrodes of exemplary headset 120 may be placed such that signal pathways coincide, cross, or interact to some extent with the MCA 240 or other arteries. For example, electrodes 110 may be positioned to straddle the MCA 240, such that the MCA 240 runs between a pair of planes dissecting the head and extending through each electrode. Thus, measures of signal properties such as impedance may be indicative of and/or related to blood flow in an MCA 240 or other arteries. Specific electrode 110 placement in and around the patient's temples,

facilitated by specific configurations of headset 120, for example, may enable generation of signals including information relating to blood flow in the MCA 240, in particular. The electrodes may, for instance, be 70 mm to 90 mm apart. The electrodes may also be located at specific locations on the head. For example a first pair 111 and 112 of electrodes may be arranged on the forehead below the hair line and a second pair 113 and 114 above the ear under the upper part of the ear lobe. In these locations, the electrodes may be placed directly on bare skin and not on hair, and may achieve better electrical contact and better adhesion, than on hairy areas of the scalp, although the invention may be used in connection with electrode placement in other locations, including the scalp. The electrodes may also be placed away from external facial arteries and away from extensive muscle groups like the eye muscles.

[063] **FIG. 3** provides a diagrammatic representation of exemplary bioimpedance signal pathways 310 in the brain 201 of a subject. The exemplary configuration illustrates multiple signal pathways 310 through each of the right and left brain hemispheres. The multiple signal pathways extend between electrodes 110 affixed to the head of a subject via headset 120. The impedance of the signal pathways 310 may be influenced by the presence or absence of blood along the pathway, because blood has a relatively low impedance. At least some of the signal pathways 310 may be coincident with brain vasculature. Signal properties may thus be measured that are indicative of hemodynamic characteristics, such as blood volume, in the blood vessels of the brain 201. Changes in bioimpedance may thus be indicative of changes in blood flow in the brain 201. Signal pathways 310 depicted in **FIG. 3** are representative of only a small number of an infinite number of pathways which may exist in the general area of signal pathways 310.

[064] **FIG. 4** provides a diagrammatic representation of exemplary bioimpedance signals 401, 402 obtained from cerebro-hemodynamic measurement apparatus 100. The illustrated bioimpedance signals 401, 402 show a periodic change of impedance amplitude for right and left brain hemispheres, respectively, of a relatively healthy patient, as measured using an exemplary apparatus 100. Thus, signals 401 and 402 are examples of bioimpedance signals associated with first and/or second time intervals, and which are each indicative of a hemodynamic characteristic of the subject's brain.

[065] As shown in **FIG. 4**, bioimpedance amplitude exhibits a periodic cycle for both left and right brain hemispheres. The period of this change in amplitude is approximately the period of a cardiac cycle. In **FIG. 4**, the scale is inversely correlated with impedance. More specifically, each cardiac cycle actually begins with a decrease in impedance that corresponds to a rapid increase in blood flow, reflected in the signal peaks illustrated in **FIG. 4**. The maxima shown (i.e., the signal peaks) in each periodic cycle in **FIG. 4** are indicative of impedance minima that correspond to a maximal blood flow in response to a heartbeat.

[066] As described above, a bioimpedance signal waveform obtained from the head of a subject may be indicative of cerebral blood flow. Changes between a first time interval and a second time interval in a bioimpedance signal waveform, therefore, may be indicative of changes in cerebral blood flow. For example, if the height of the local maximum in each period, which corresponds to an impedance minimum, were reduced between a first and second time interval, that may be indicative of a reduction in cerebral blood flow. Comparing a bioimpedance signal associated with a first time interval, which may include one or more waveform periods, to a bioimpedance signal associated with a second time interval, which may include one or more waveform periods, may therefore yield information indicative of cerebro-hemodynamic characteristics.

[067] Data obtained from bioimpedance signal measurements, such as the results shown in **FIG. 4**, may be compared to and correlated with more direct measures of blood flow, such as results obtained by Magnetic Resonance Imaging (MRI), Transcranial Doppler Ultrasound (TCD), or Perfusion Computed Tomography (PCT) and Angiography (CTA). Such comparisons and correlations may then be used in the interpretation, quantification and modeling of data from bioimpedance signal measurements. At least one processor 160 in cerebral perfusion monitor 130 may use this correlation and modeling information to output information for the diagnosis of changes in cerebro-hemodynamic conditions based on non-invasively obtained bioimpedance signals.

[068] Additionally, in patients with a decreased blood flow to the brain 201, such as in patients suffering from cerebrovascular events such as strokes, often one side of the brain 201 exhibits a decrease in blood flow while the other does not. This is generally because the occlusion or blockage associated with the cerebrovascular event is local to one hemisphere. Because of this, bioimpedance signal waveforms

such as those shown in **FIG. 4** from the two hemispheres may be directly compared to one another to diagnose cerebrovascular conditions. In a patient exhibiting a cerebrovascular condition, for example, the two bioimpedance signal waveforms will generally show a greater degree of dissimilarity than exhibited in **FIG. 4** for a healthy patient. That is, in a healthy subject the blood flow in the right and left brain hemispheres is frequently similar, such as is illustrated in **FIG. 4**. Under certain conditions, asymmetry between blood flows in the two hemispheres of the brain 201 may arise that are not related to a cerebrovascular event. For example, asymmetric differences may result from head position or asymmetry in physiology of a particular subject. An example of the latter would be asymmetric narrowing of the carotid arteries. Thus, in a broad sense, an embodiment of the invention may involve a recognition that detection of asymmetry in bioimpedance measurements from opposite sides of a subject's head correlates to a cerebrovascular event, and that such information (an/or changes in asymmetry over time) can be used to diagnose a cerebrovascular event (or an improvement in a previously detected cerebrovascular event).

[069] While **FIG. 4** illustrates variations in the amplitude of a bioimpedance signal waveform, information may also be obtained from the phase angle of a bioimpedance signal waveform. The amplitude and phase of a bioimpedance signal waveform may be influenced by both resistive and reactive components of the electrical impedance of a subject. Typically, changes in the reactive components of the electrical impedance of a subject may generate changes in the phase of the measured bioimpedance signal. Both the amplitude and phase of a bioimpedance signal, therefore, analyzed separately or in combination, may be indicative of cerebro-hemodynamic characteristics.

[070] **FIG. 5** provides a diagrammatic representation of exemplary signature features of a single bioimpedance signal amplitude waveform period 510. The waveform period 510 corresponds to a cardiac cycle, and signature features in the waveform may correspond to individual events in a cardiac cycle. For instance, a first peak, P1 511 may correspond to an initial rise in blood flow following aortic valve opening, which may correspond to minimum M0 521. A second peak, P2 512, may correspond to a secondary rise in blood flow during the end of a systolic phase of the cardiac cycle, which may correspond to minimum M1 522. A minimum, M2 523, may correspond to a decrease in blood flow as the aortic valve closes. A final peak, P3

513, may correspond to a final increase in blood flow before a continuous decline during a diastolic phase at the end of a cardiac cycle.

[071] For discussion purposes only, the signature features illustrated in **FIG. 5** are only some examples of signature features that may be detected in a bioimpedance waveform. Furthermore, detected signature features need not be confined to a single waveform period. A signature feature of a bioimpedance signal may, for example, be monitored by analyzing the average amplitude of multiple corresponding maxima from different periods.

[072] Furthermore, although **FIG. 5** illustrates a bioimpedance signal waveform characterized by amplitude, methods and structures described herein may be used for the determination of signature features in other aspects of a bioimpedance signal waveform, for example, those characterized by a phase angle waveform. The phase angle aspects of a bioimpedance signal may respond differently than amplitude aspects of a bioimpedance signal since the phase angle corresponds to the reactive component of a bioimpedance signal. Analysis of phase angle aspects of bioimpedance signal waveforms may provide additional or different information about hemodynamic characteristics. Phase angle waveforms may be analyzed using any methods described herein with respect to amplitude waveforms, and by any additional methods known in the art. Phase angle waveforms of bioimpedance signals may be analyzed by themselves, and/or may be analyzed in comparison to or in conjunction with other bioimpedance signal aspects.

[073] **FIGs. 6a** and **6b** provide a diagrammatic representation of a comparison between exemplary amplitude and phase angle aspects of a bioimpedance signal waveform over multiple cardiac cycles. Under some conditions, as illustrated in **FIG. 6a**, phase angle waveforms may demonstrate similar characteristics as concurrently obtained amplitude waveforms. For example, in **FIG. 6a**, the delay between phase angle waveforms 613, 614 obtained from left (shown in black) and right (shown in gray) sides of the head, respectively, is similar to the delay in amplitude waveforms 611, 612 obtained from left (shown in black) and right (shown in gray) sides of the head, respectively. Such similarities in signature features between phase angle and amplitude aspects of a bioimpedance signal waveform may provide additional information for diagnosing a change in artery occlusion.

Phase angle waveforms may also demonstrate different characteristics than concurrently obtained amplitude waveforms, as illustrated in **FIG. 6b** for example. In **FIG. 6b**, the phase angle waveforms 623, 624 obtained from left (shown in black) and right (shown in gray) sides of the head, respectively, show a much larger asymmetry between left and right sides of the head than do the amplitude waveforms 621, 622 obtained from left (shown in black) and right (shown in gray) sides of the head, respectively. The peak of phase angle waveform 624, associated with a right side of the head is reduced compared to the peak of phase angle waveform 623, associated with the right side of the head. Furthermore, phase angle waveform 623 demonstrates a steeper decay from its peak. These differences do not appear in amplitude waveforms 621 and 622. Thus, differences in signature features of phase angle and amplitude waveforms of a bioimpedance signal may provide additional information for diagnosing a change in arterial occlusion.

[074] Signature features as illustrated in **FIG. 5** may be detected through any type of analysis. In one embodiment, signature features may be detected by finding inflection points in a measured waveform. In another embodiment, illustrated in **FIG. 7**, a pulse decomposition analysis may be conducted. Such detection analyses may be performed using at least one processor, such as at least one processor 160, described in connection with Fig. 1

[075] **FIG. 7** provides a diagrammatic representation of a bioimpedance signal waveform period 710 as decomposed by a pulse decomposition algorithm for detecting signature features in a bioimpedance signal. As discussed with respect to **FIG. 5**, a set of signature features may include first, second and third peaks P1 511, P2 512, and P3 513, and minimums M0 521, M1 522 and M2 523, which may be computed, as shown in **FIG. 5**, based on inflection points in the bioimpedance signal waveform 511. A pulse decomposition algorithm represents one alternative method of computing signature features. A pulse decomposition algorithm may parameterize a bioimpedance signal by using a combination of basic functions to approximate the bioimpedance signal.

[076] A base function used for a best fit may be related to physiological pulse waveform functions or may have a general shape that resembles a physiological pulse and provides stable fit parameters. One example of a suitable base function is a Gaussian function. A Gaussian base function may provide a clear definition of pulse width and curvature, a stable fit algorithm, and full determination of

higher derivatives. A pulse decomposition algorithm utilizing Gaussian base functions may be performed as described below, with reference to **FIG. 7**.

[077] **FIG. 7** provides a diagrammatic representation of three Gaussian base functions, first Gaussian 721, second Gaussian 722, and third Gaussian 723 computed as best fits to the second, first and third peak, P2 512, P1 511, and P3 513, respectively. Using ECG signals, a bioimpedance signal may be divided into individual waveforms 710, each corresponding to a cardiac cycle. A waveform minimum following the ECG R wave pulse may then be determined. Next, a waveform global maximum point following the minimum may be determined. It may then be determined whether the waveform global maximum point represents a first, second or third peak, P1 511, P2 512, or P3 513, based on a correspondence between the timing of the global maximum and previously obtained statistics. Next, a standard base function, such as a Gaussian, may be used to provide a best fit to the individual waveform near the determined global maximum, using timing and width limitations from previously obtained statistics. In **FIG. 7**, first Gaussian 721 is fitted to the highest peak P2 512. A best fit of the remaining two peaks, using second Gaussian 722 and third Gaussian 723 may then be determined using the same base function to the waveform remainder

[078] When combined, the Gaussian base functions form signature feature fit curve 720, which approximates the bioimpedance signal waveform. The parameters that define the component base functions of signature feature fit curve 720, as derived from the exemplary pulse decomposition algorithm may serve to characterize each cardiac cycle in the measured signals.

[079] The measured signal may then be replaced by a smooth waveform comprising the signature feature fit curves 720 of each cardiac cycle. This may permit the robust calculation of various points of interest such as minimum M0 521, minimum M1 522, minimum M2 523, and local curvatures at interest points. The computer parameters, relative amplitude, timing vs. ECG, and width may serve to characterize the waveform. Methods such as the disclosed exemplary pulse decomposition algorithm may be useful for detecting signature features that are difficult or impossible to detect through the use of other techniques, such as inflection point determination. As illustrated in **FIG. 7**, peaks P1 511, P2 512, and P3 513 do not coincide with local maxima of the bioimpedance signal waveform 710, but

with the peaks of the bioimpedance signal waveform's 710 component waveforms, Gaussians 721, 722 and 723.

[080] Additional exemplary base functions may include a Generalized Extreme Value (GEV) distribution function. A GEV function may be used in conjunction with other base functions (such as Gaussians) or as the sole base function. For example, when decomposing a periodic bioimpedance signal, Gaussian base functions may be used for fitting the first P1 511 and second P2 512 peaks in the systolic part of the waveform, and a GEV function for P3 513 on the diastolic part. This choice may give a better fit for the diastolic part than using a Gaussian base function for P3 513, because GEV functions may be asymmetric while the Gaussian function is symmetric.

[081] The parameterization of the bioimpedance signal waveform also permits the collection and comparison of additional signature features, including distribution statistics of the initial parameters. For example, the distribution of P2 512 pulse width measured on one hemisphere of a stroke patient may represent a signature feature, and may be compared with a signature feature represented by the distribution of P2 512 pulse width derived from the second hemisphere.

[082] These short term statistical comparisons (over a few hundred heart cycles, or, for example, 5-10 minutes or less) may convey physiological differences between hemispheres or changes of physiological conditions in the same hemisphere over time. For example, the width of the distribution of P2 512 timing may be larger in a hemisphere affected by stroke than in a healthier hemisphere. The larger variation may be a manifestation of blood flow instability as a result of the stroke.

[083] Signature features of a bioimpedance signal, as illustrated in **FIG. 5**, may be analyzed to provide information for diagnosing changes in cerebral blood flow, including changes in artery occlusion. Signature features may be continuously monitored and compared over a period of time to provide diagnosis information. For example, bioimpedance signal waveform data may be continuously sampled to compute signature features for every cardiac cycle within an uninterrupted time interval. The results from monitoring one portion of the uninterrupted time interval may be compared to the results from monitoring another portion of the uninterrupted time interval. For example, signature features may be continuously monitored throughout an uninterrupted time interval during a surgery performed on a patient to

diagnose any cerebral blood flow changes that occur during the surgery. The signature features detected during any one time interval of arbitrary length during the surgery may be compared to signature features detected at any later time interval of arbitrary length during the surgery.

[084] Alternatively or additionally, signature features may also be monitored and compared over non-continuous time periods to provide diagnosis information. For example, bioimpedance signal waveform data may be monitored during one time interval for comparison with bioimpedance signal waveform data monitored during a second time interval that does not overlap or adjoin the first time interval. For example, a signature feature baseline for a patient may be measured at a first time, e.g. prior to a surgery, upon admittance to a hospital, at a routine office visit, or at any other time when a baseline measurement is possible. The signature feature baseline may then be compared to signature features monitored at any later time, e.g. during a surgery, upon release from a hospital, at another routine office visit, etc.

[085] **FIG. 8** provides a diagrammatic representation of a comparison between bioimpedance signals obtained from right and left hemisphere's of a subject's brain 201. Bioimpedance signals derived from opposite sides of the head reflect the blood flow in opposite brain hemispheres. Because stroke is typically an asymmetric phenomena, comparing the characteristics of the two hemispheres may give information regarding the side of the brain affected by stroke. For instance, an occlusion in a major cerebral blood vessel, such as the Middle Cerebral Artery (MCA), has been shown through MRI and CTA techniques to result in delayed or reduced blood flow in this part of the brain 201.

[086] Similarly, stroke effects may result in measureable delays between the timing of bioimpedance signals measured in opposite hemispheres of a subject's brain 201. These delays may be manifested in aspects of signature features in the bioimpedance signals from opposite hemispheres. For example, the timing or amplitude of a maximum, such as peak P2 512, may be altered. By synchronizing bioimpedance signals with a cardiac cycle ECG signal, timing delays in the bioimpedance signals may be detected.

[087] In the signals illustrated in **FIG. 8**, a left hemisphere bioimpedance signal 812, illustrated by the dashed line, shows significantly reduced variations in impedance amplitudes as compared to a right hemisphere bioimpedance signal 811. Additionally, in the left hemisphere bioimpedance signal 812, peak P2 512 appears

to have disappeared entirely, and the remaining peak, P1 511 exhibits a timing delay with respect to the corresponding peak of right hemisphere bioimpedance signal 812. Both reduced impedance amplitudes and timing delays may be indicative of stroke. Thus, signals 811 and 812 (or corresponding sub-portions thereof) are examples of bioimpedance signals associated with first and/or second time intervals, and which are each indicative of a hemodynamic characteristic of the subject's brain. These bioimpedance signals may be processed, for example, in the at least one processor 160, described in connection with Fig. 1. These bioimpedance signals may be compared, for example, to yield information for diagnosing changes in cerebral artery occlusion.

[088] At least one processor may then output information for diagnosing changes in cerebral artery occlusion. For example, at least one processor 160 may be used to diagnose, model, and/or track changes in a patient's cerebrovascular condition based on a comparison between two or more bioimpedance signals. The output information may be as simple as an indicator to a medical professional that a significant variance exists. Alternatively, or additionally, it may include information output characterizing, for example, one or more of a magnitude of variance, a change in magnitude of variance over time, and any other data that might indicate an existence of blockage, an extent of blockage, or a change in extent of blockage.

[089] An embodiment consistent with the present disclosure includes a method for diagnosing a change in artery occlusion over time in a brain of a subject. **FIG. 9** is a flowchart showing the steps of an exemplary method for diagnosing a change in artery occlusion over time in a brain of a subject. At step 901, at least one bioimpedance signal indicative of a hemodynamic characteristic of a subject's brain at a first time may be received non-invasively. At step 902, at least one other bioimpedance signal indicative of a hemodynamic characteristic of a subject's brain at a second time may be received non-invasively. The bioimpedance signals may be received, for instance, by a suitably configured processor 160.

[090] At step 903, the at least one and the at least one other bioimpedance signal may be compared. The bioimpedance signals may be compared by a suitably configured processor 160, based on, for example, signature features of the bioimpedance signals. At step 904, results of the comparison of step 903 may be used to obtain information for use in diagnosing a change in cerebral artery

occlusion. At least one processor 160 may, for example, be configured to obtain the information.

[091] From the foregoing description, it will be appreciated that the present disclosure provides a method and apparatus for the diagnosis of changes in artery occlusion in the brain of a subject. The provided apparatus may obtain bioimpedance signals and additional physiological signals for analysis and monitoring. Using various methods and algorithms, the provided apparatus may compare bioimpedance signals and output information for the diagnosis of changes in arterial occlusion.

[092] While many of the foregoing examples were described with reference to a comparison of right and left hemispheres, it should be appreciated that measurements may be taken and compared from various locations of a subject's head, and the invention in its broadest sense does not require that comparative signals be limited only to opposing hemispheres. Similarly, while this disclosure provides examples of the analysis of bioimpedance signals, any signal that is reflective of a hemodynamic condition may be assessed consistent with broad principles of this disclosure.

[093] Further, the disclosure of uses of embodiments of the invention for detection, diagnosis, and monitoring of strokes and occlusions is exemplary only. In its broadest sense, the invention may be used in connection with the detection, diagnosis, and/or treatment of any neurological condition detectable using the principles described herein. Further, it should be appreciated that the methods and apparatus described herein to diagnose changes in artery occlusion in the brain of a subject may be generalized to diagnose changes in artery occlusion of any genesis, including stroke, vascular degeneration, etc. Alternative embodiments will become apparent to those skilled in the art to which the present invention pertains without departing from its spirit and scope. Accordingly, the scope of the present invention is defined by the appended claims rather than the foregoing description.

**What is claimed is:**

1. A cerebro-hemodynamic measurement apparatus for diagnosing a change in artery occlusion over time in a brain of a subject, the apparatus comprising:

at least one processor configured to:

receive at least one non-invasively-obtained bioimpedance signal associated with a first time interval, wherein the at least one bioimpedance signal is indicative of a hemodynamic characteristic of the subject's brain during the first time interval;

receive at least one other non-invasively-obtained bioimpedance signal, associated with a second time interval, wherein the at least one other bioimpedance signal is indicative of a hemodynamic characteristic of the subject's brain during the second time interval;

compare the at least one bioimpedance signal associated with the first time interval with the at least one other bioimpedance signal associated with the second time interval; and

output information for diagnosing a change in artery occlusion based on a comparison of the at least one bioimpedance signal and the at least one other bioimpedance signal.

2. The cerebro-hemodynamic measurement apparatus of claim 1, wherein the at least one received bioimpedance signal is indicative of a comparison between bioimpedance measurements associated with right and left sides of the subject's brain during the first time interval, and wherein the at least one other received bioimpedance signal is indicative of a comparison between bioimpedance measurements associated with right and left sides of the subject's brain during the second time interval.

3. The cerebro-hemodynamic measurement apparatus of claim 1, wherein the at least one received bioimpedance signal is indicative of a bioimpedance measurement in a hemisphere of the subject's brain during the first time interval, and wherein the at least one other received bioimpedance signal is indicative of a bioimpedance measurement in the hemisphere of the subject's brain during the second time interval.

4. The cerebro-hemodynamic measurement apparatus of claim 1, wherein the at

least one non-invasively obtained bioimpedance signal is associated with a right side of the subject's brain, and wherein the at least one other non-invasively obtained bioimpedance signal is associated with a left side of the subject's brain.

5. The cerebro-hemodynamic measurement apparatus of claim 1, wherein the at least one processor is further configured to receive the at least one bioimpedance signal and the at least one other bioimpedance signal via electrodes associated with a head of a subject.

6. The cerebro-hemodynamic measurement apparatus of claim 5, wherein the at least one processor is further configured to receive the at least one bioimpedance signal and the at least one other bioimpedance signal from electrodes that are maintained in a relatively fixed position on the head of the subject.

7. The cerebro-hemodynamic measurement apparatus of claim 1, wherein the at least one processor is further configured to receive a plurality of additional non-invasively-obtained signals; compare the at least one bioimpedance signal, the at least one other bioimpedance signal, and the plurality of additional signals; and wherein the output information for diagnosing a change in artery occlusion relates to the at least one bioimpedance signal, the at least one other bioimpedance signal, and the plurality of additional signals.

8. The cerebro-hemodynamic measurement apparatus of claim 7, wherein some of the plurality of additional signals are associated with a first side of a subject's brain and others of the plurality of additional signals are associated with a second side of the subject's brain.

9. The cerebro-hemodynamic measurement apparatus of claim 1, wherein the at least one processor is further configured to detect at least one signature feature within the at least one bioimpedance signal and the at least one other bioimpedance signal; and to use detected signature features to determine differences between the at least one bioimpedance signal and the at least one other bioimpedance signal.

10. The cerebro-hemodynamic measurement apparatus of claim 9, wherein the at

least one processor is further configured to detect the at least one signature feature based on a determination of one or more of inflection locations, peak locations, anticipated inflection locations, and anticipated peak locations.

11. The cerebro-hemodynamic measurement apparatus of claim 9, wherein the at least one signature feature is a set of signature features comprising a first peak, a second peak, a third peak, a first minimum, a second minimum, and a third minimum.

12. The cerebro-hemodynamic measurement apparatus of claim 9, wherein the at least one signature feature comprises a statistical distribution of waveform parameters.

13. The cerebro-hemodynamic measurement apparatus of claim 5, wherein the at least one bioimpedance signal results from a measurement signal outputted via the electrodes.

14. A method for diagnosing a change in artery occlusion over time in a brain of a subject comprising:

receiving at least one bioimpedance signal measured non-invasively, wherein the at least one bioimpedance signal is indicative of a hemodynamic characteristic of the subject's brain at a first time;

receiving at least one other bioimpedance signal measured non-invasively, wherein the at least one other bioimpedance signal is indicative of a hemodynamic characteristic of the subject's brain at a second time;

comparing the at least one bioimpedance signal with the at least one other bioimpedance signal; and

obtaining information as a result of the comparing for use in diagnosing a change in cerebral artery occlusion.

15. The method of claim 14, wherein the at least one bioimpedance signal is associated with a right side of a subject's brain and the at least one other bioimpedance signal is associated with a left side of the subject's brain.

16. The method of claim 15, wherein the at least one bioimpedance signal and the at least one other bioimpedance signal are received from electrodes associated with a head of a subject, wherein the at least one bioimpedance signal and the at least one other bioimpedance signal is received by a processor via the electrodes.

17. The method of claim 14, further comprising receiving a plurality of additional signals measured non-invasively; and wherein comparing includes determining differences between bioimpedance signals chosen from the group consisting of the at least one bioimpedance signal, the at least one other bioimpedance signal, and the plurality of additional signals; and diagnosing a change in artery occlusion based on the comparing.

18. The method of claim 17, wherein some of the plurality of additional signals are associated with a first side of a subject's brain and others of the plurality of additional signals are associated with a second side of the subject's brain.

19. The method of claim 14, wherein comparing includes detecting at least one signature feature within the at least one bioimpedance signal and the at least one other bioimpedance signal; and determining differences between the at least one bioimpedance signal and the at least one other bioimpedance signal using the detected signature features.

20. The method of claim 19, wherein comparing includes detecting the at least one signature feature based on a determination of one or more of inflection locations, peak locations, anticipated inflection locations, and anticipated peak locations.

21. The method of claim 19, wherein the at least one signature feature is a set of signature features including a first peak, a second peak, a third peak, a first minimum, a second minimum, and a third minimum.

22. The method of claim 19, wherein the at least one signature feature comprises a statistical distribution of waveform parameters.

23. The method of claim 16, further comprising outputting, via the electrodes, a measurement signal to generate the at least one bioimpedance signal.

24. The method of claim 14, wherein comparing occurs using at least one processor.

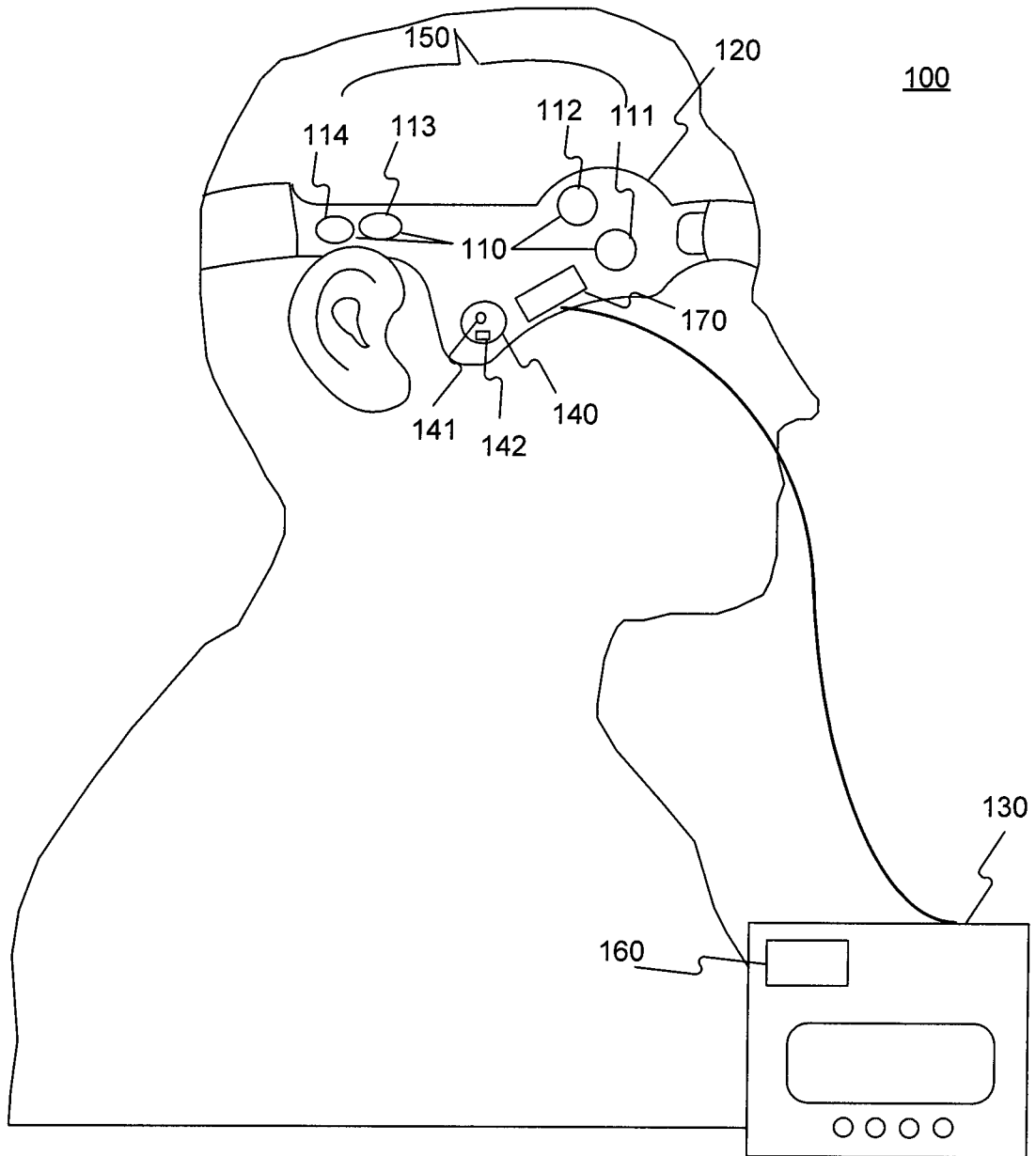


Figure 1

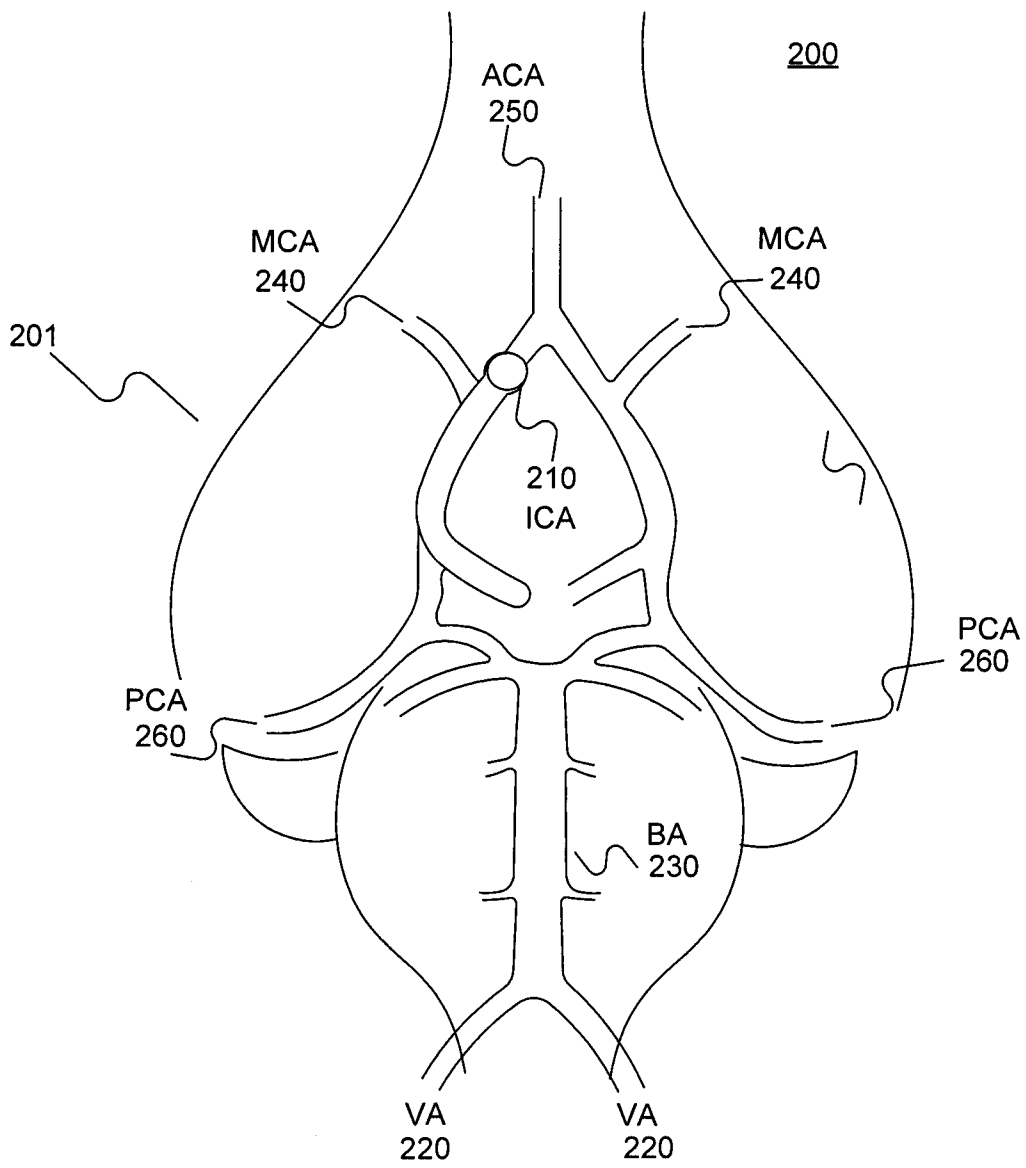
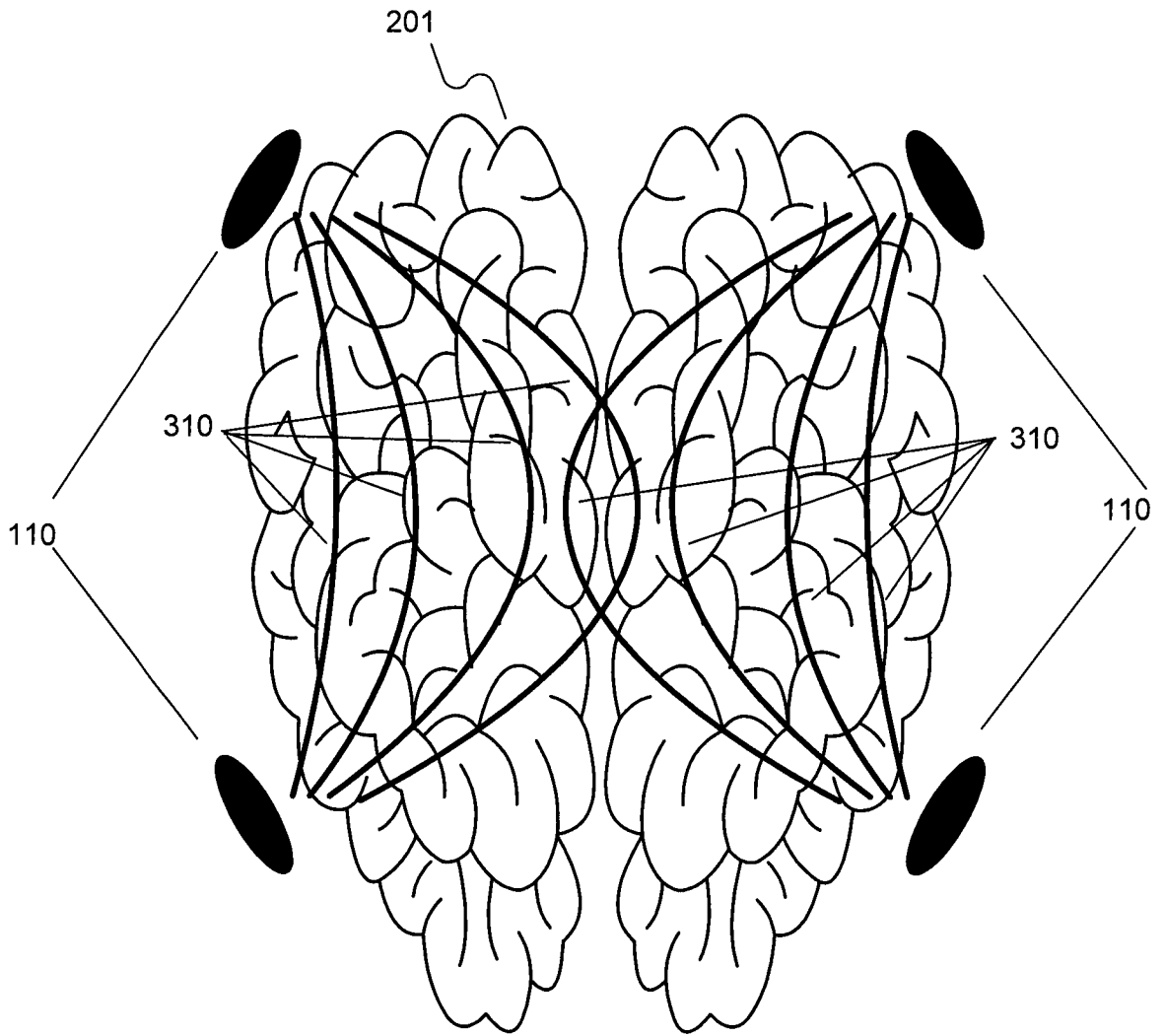


Figure 2



**Figure 3**

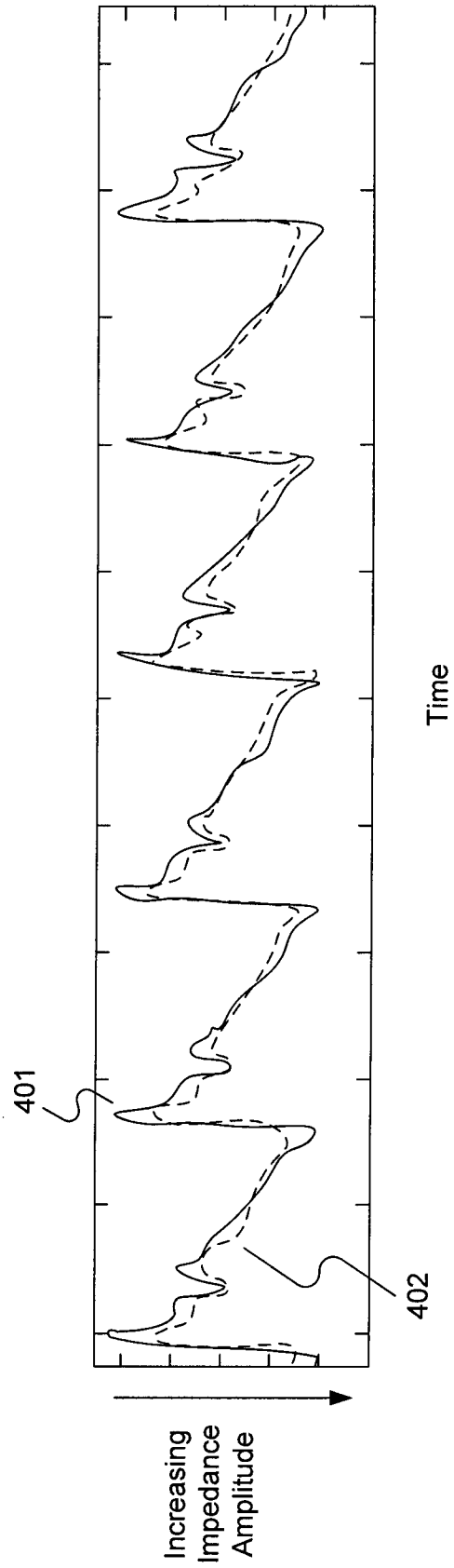
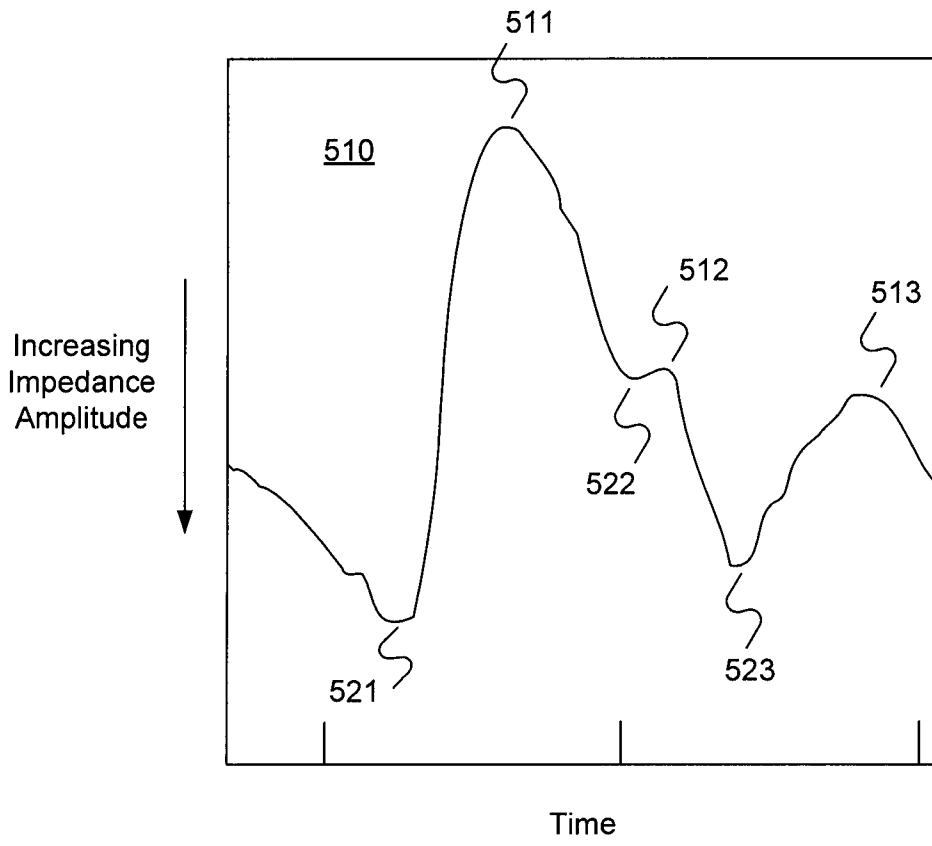
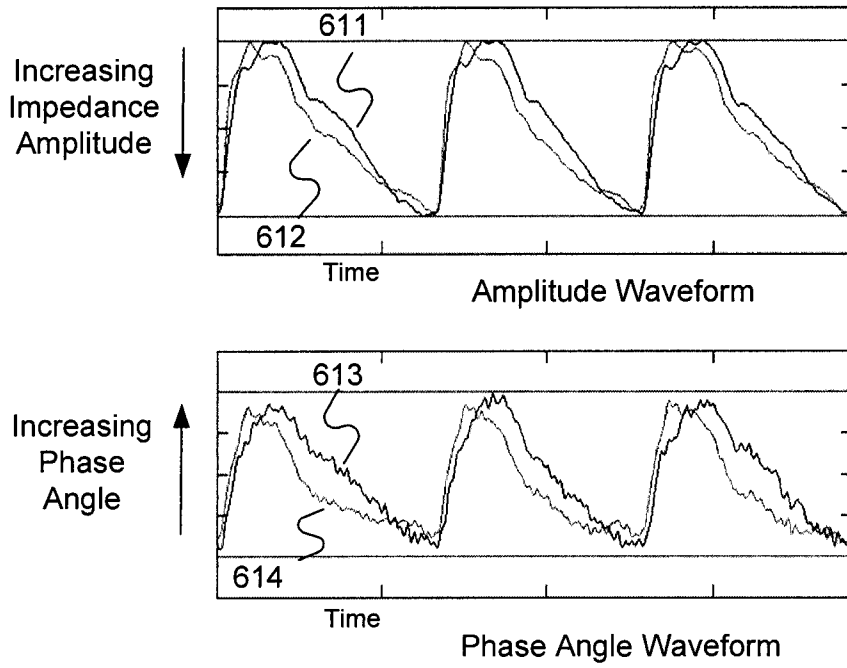


Figure 4

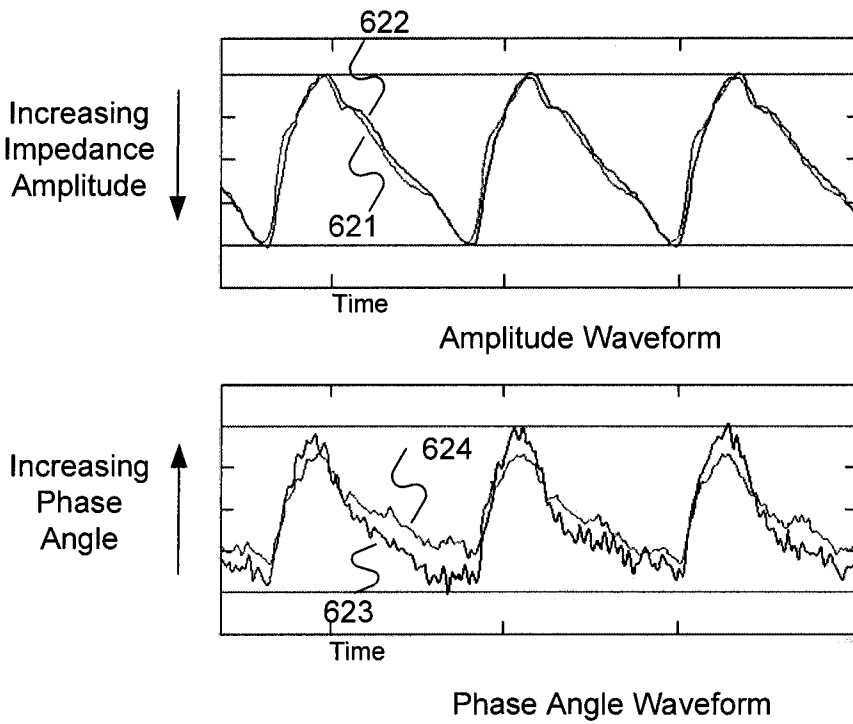


**Figure 5**

**Figure 6a**



**Figure 6b**



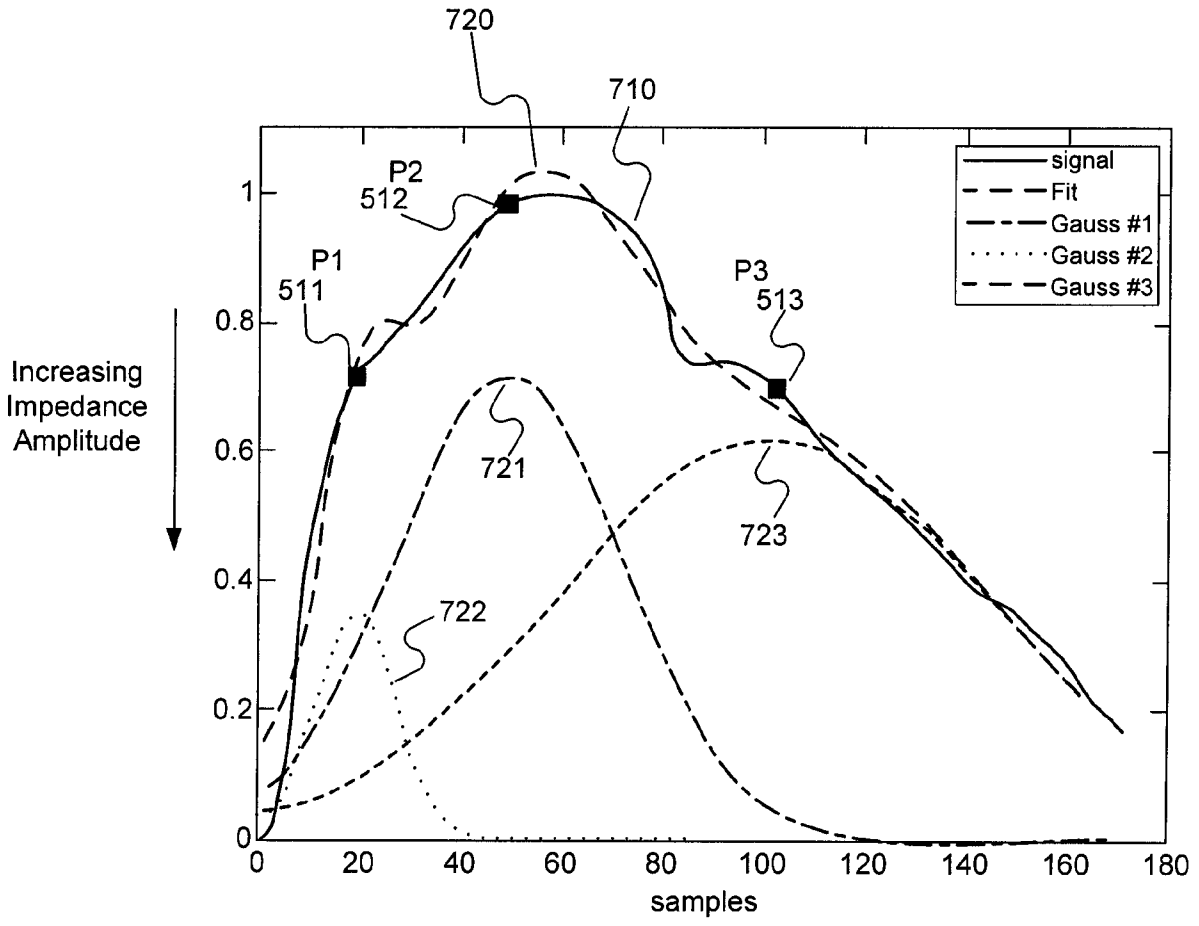


Figure 7

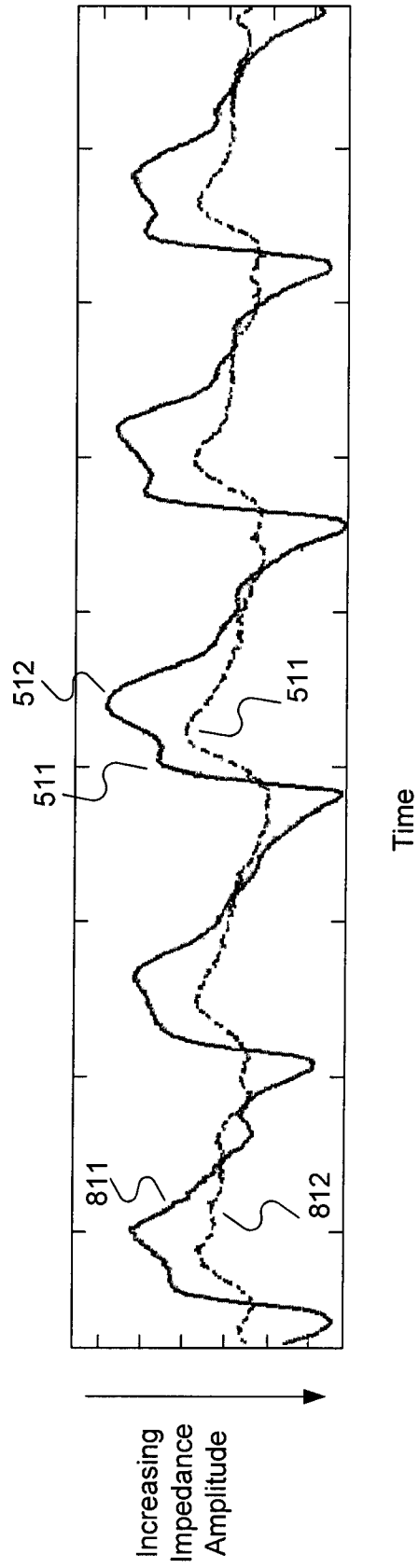
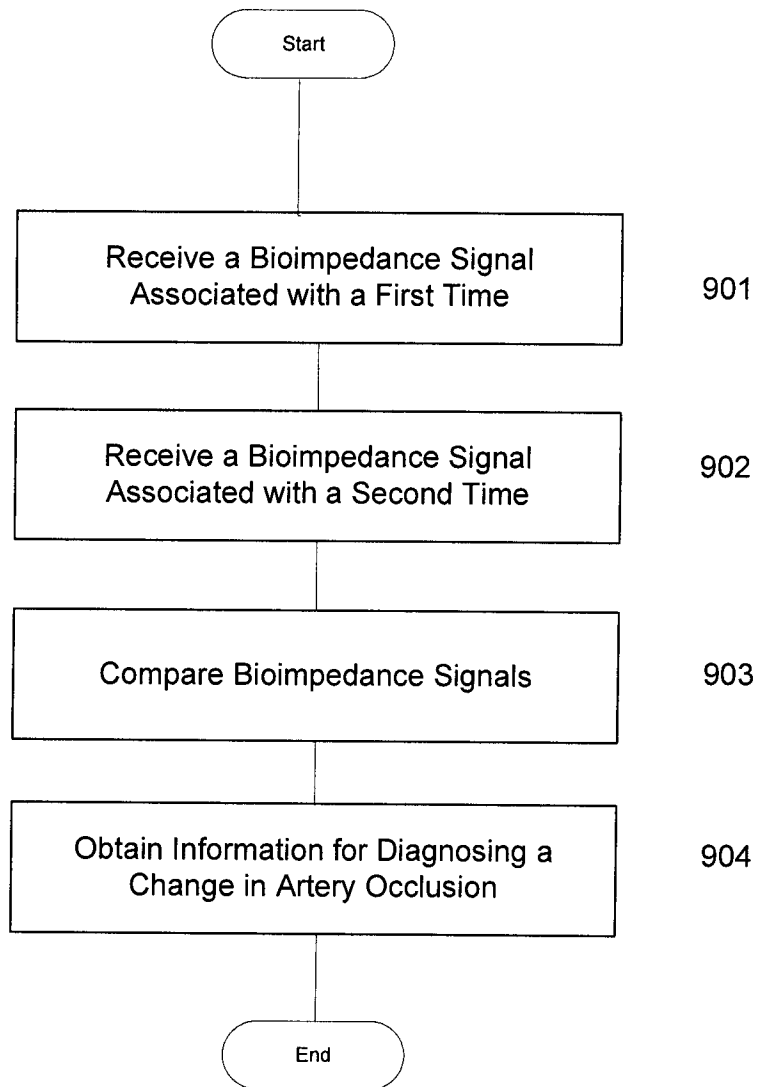


Figure 8



**Figure 9**