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(54) **DEVICES AND METHODS FOR MONITORING CEREBRAL HEMODYNAMIC CONDITIONS**

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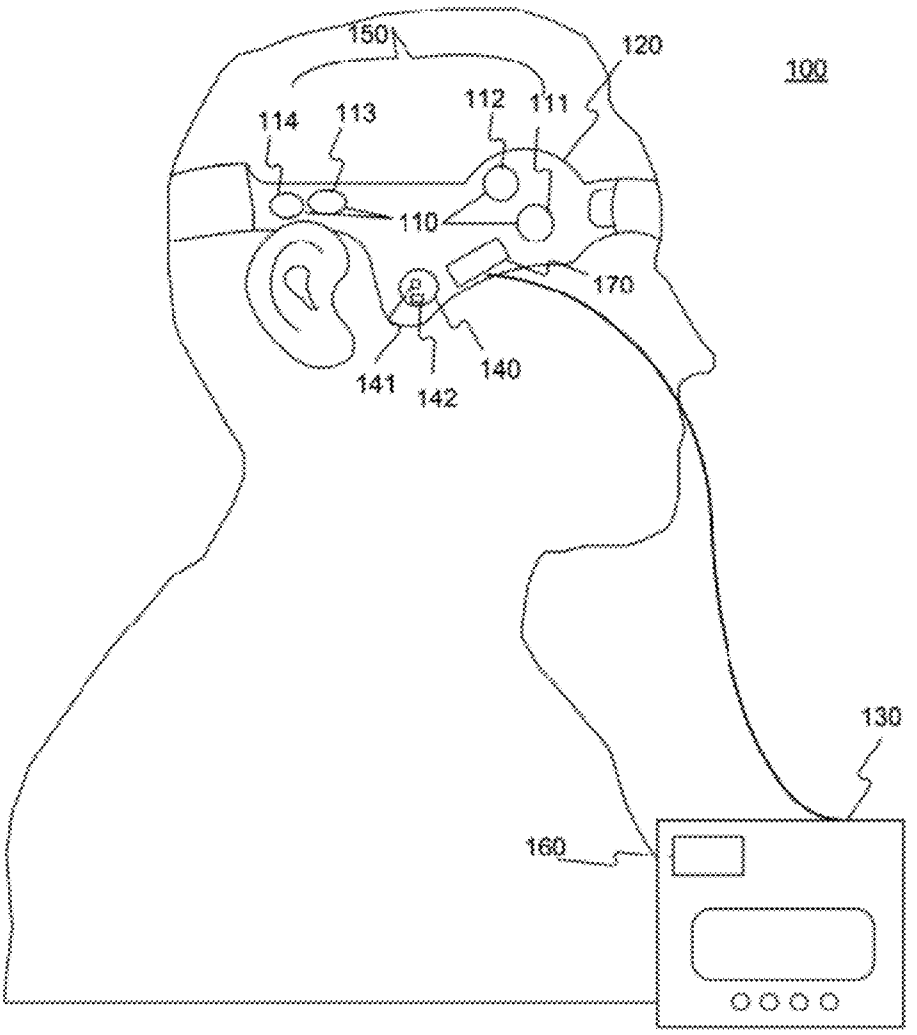
(57) **ABSTRACT**

Devices, and methods for synchronizing cerebro-hemodynamic signals are disclosed. In one aspect, the devices and methods may include synchronizing first and second signals indicative of hemodynamic characteristics within a subject's brain. Differences may be determined between the synchronized signals and used to provide information for diagnosing changes in arterial occlusion. Differences between the synchronized signals may include differences, such as timing delays, between signature features of the synchronized signals. The first and second signals may be indicative of hemodynamic characteristics in first and second hemisphere's of a subject's brain. The first and second signals may be bio-impedance signals.



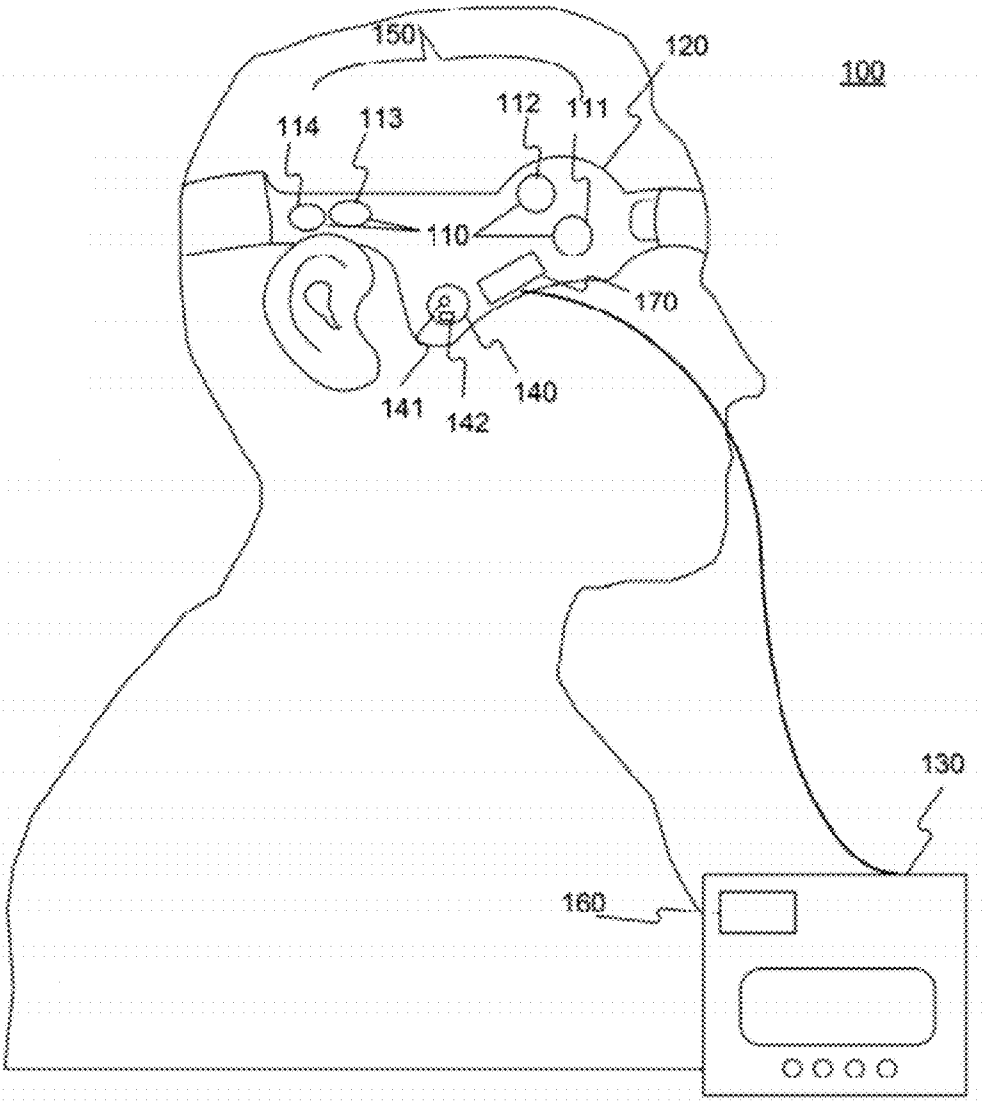


Figure 1

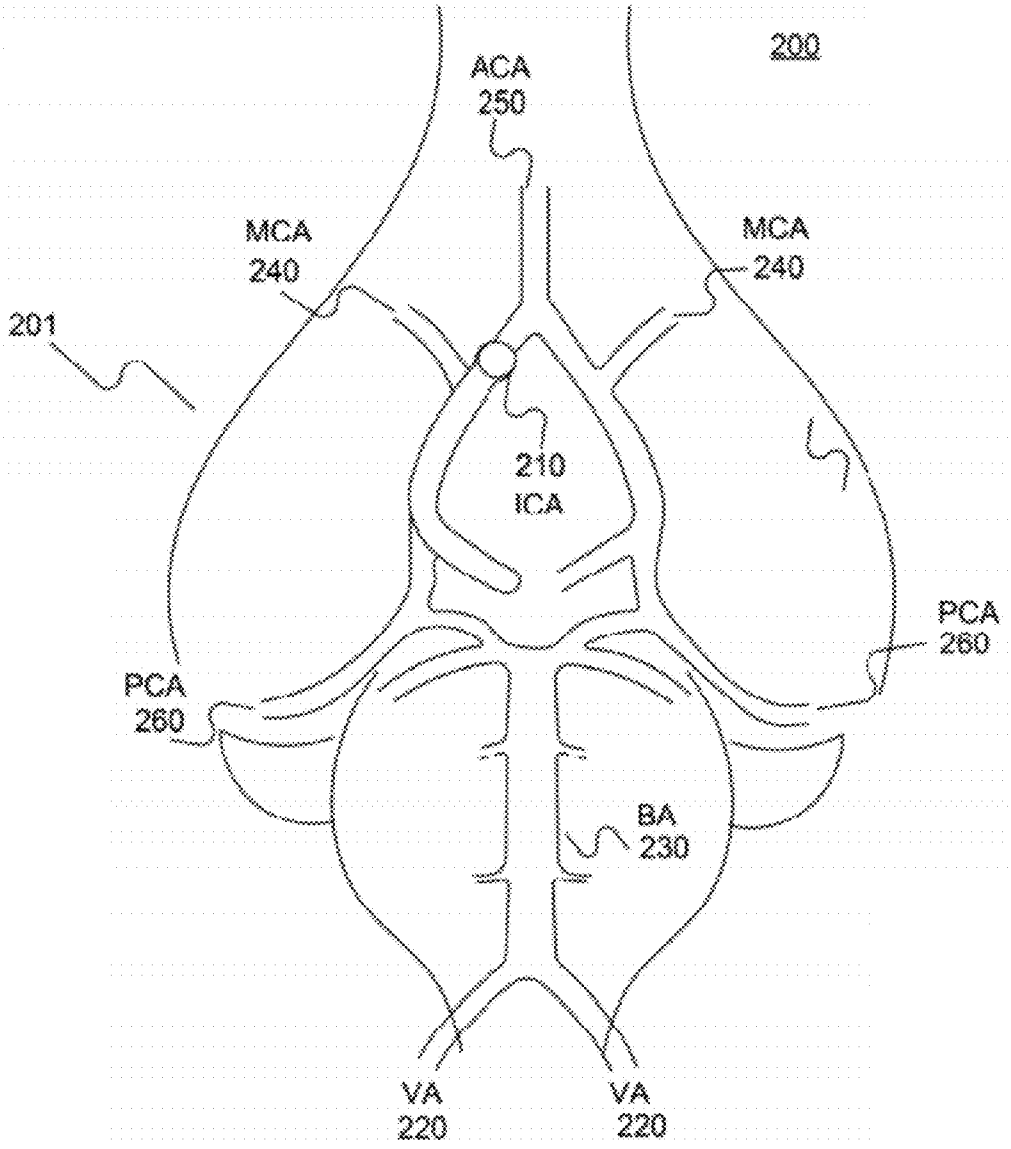

200
ACA
250
MCA
240
MCA
240
201
210
ICA
PCA
260
PCA
260
BA
230
VA
220
VA
220

Figure 2

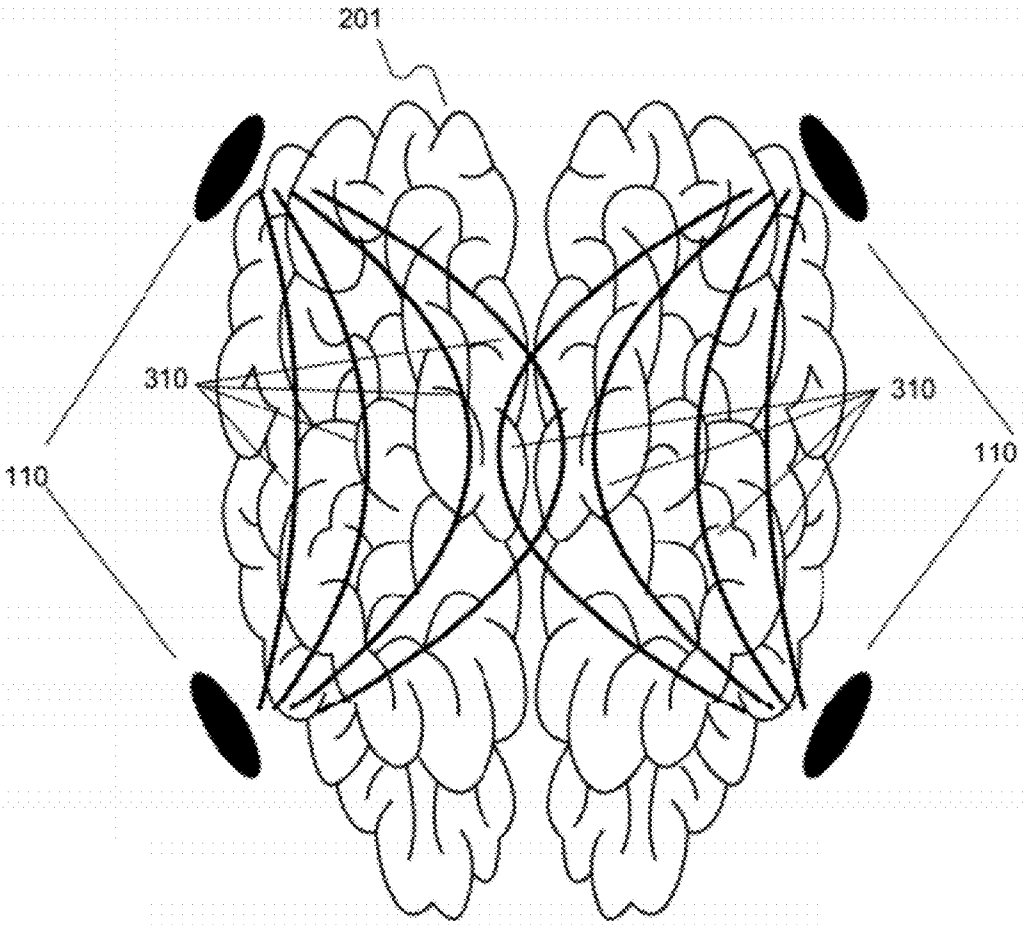


Figure 3

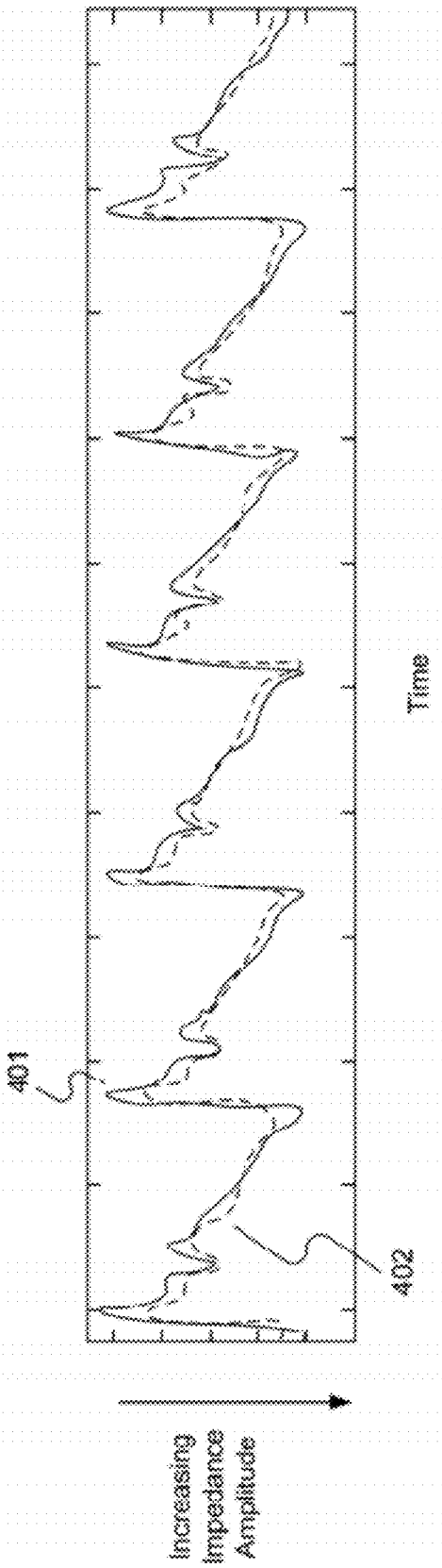


Figure 4

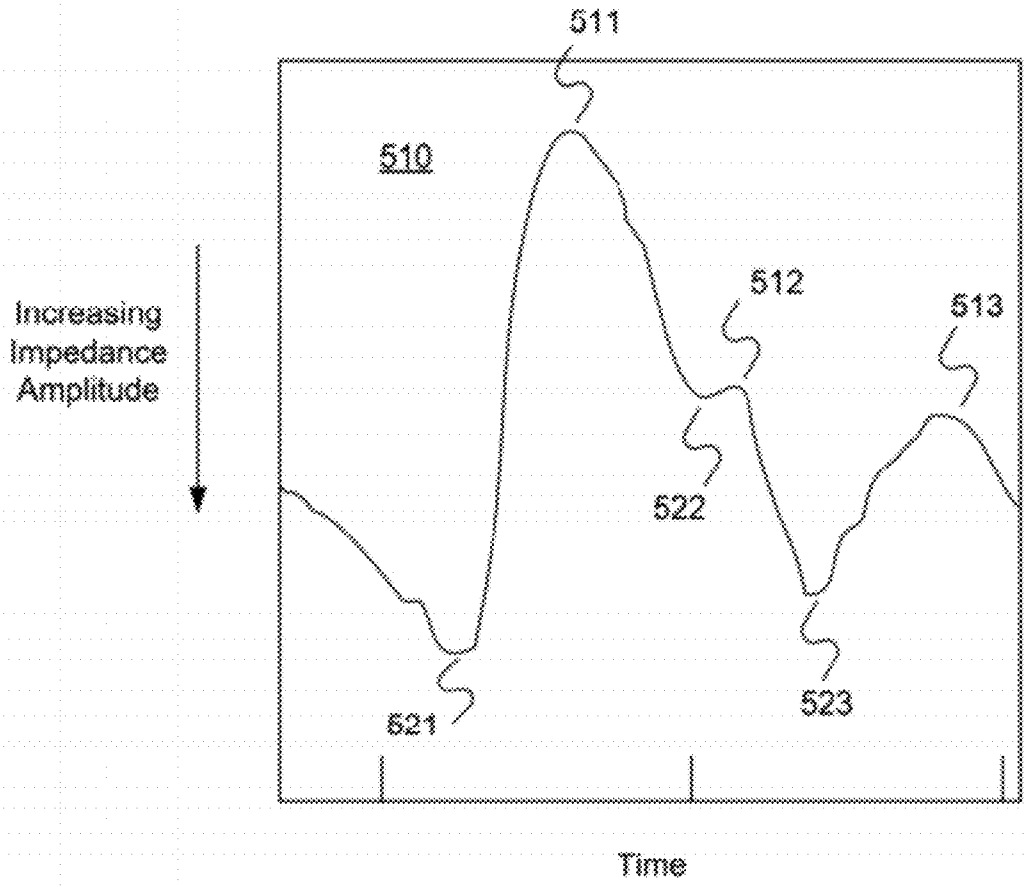

511
510
512
513
Increasing
Impedance
Amplitude
522
521
523
Time

Figure 5

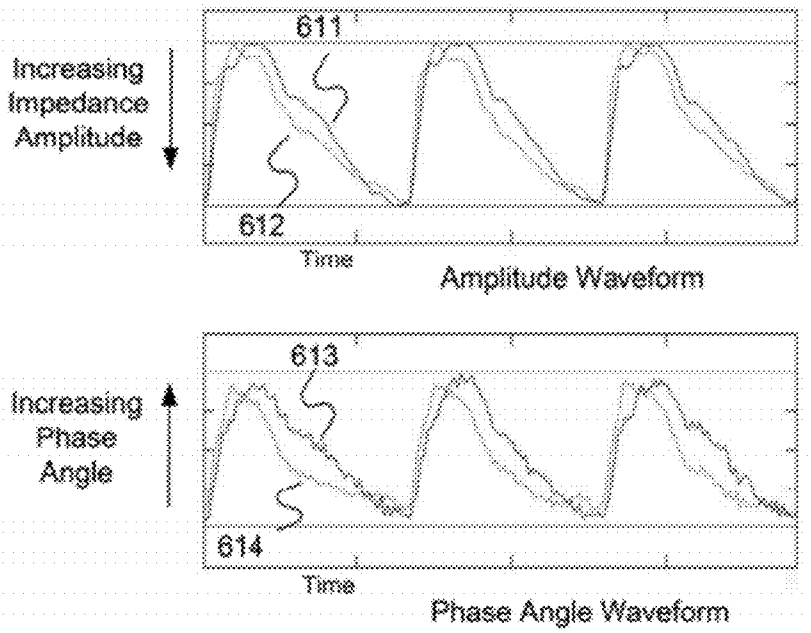


Figure 6a

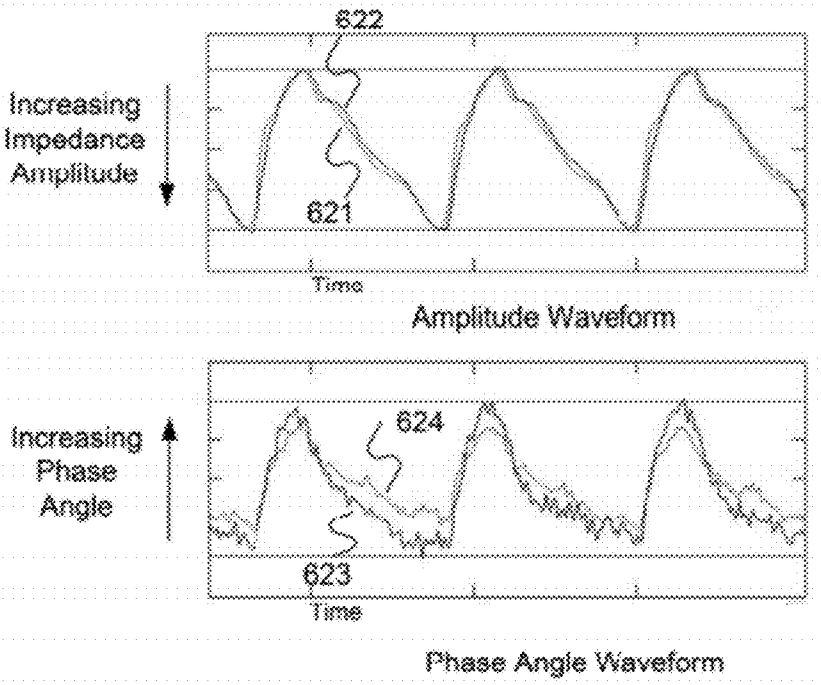


Figure 6b

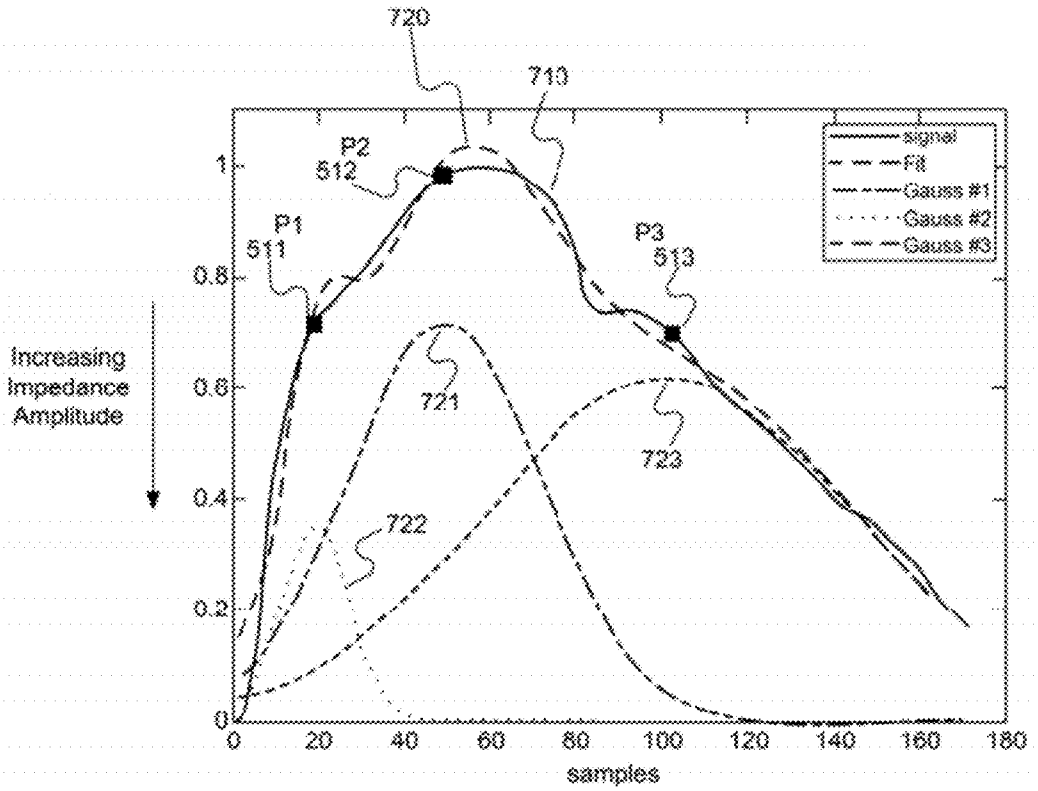

720
710
P2
512
P1
511
P3
513
721
722
723
Signal
Fit
Gauss #1
Gauss #2
Gauss #3
Increasing
Impedance
Amplitude
0
0.2
0.4
0.6
0.8
1
0
20
40
60
80
100
120
140
160
180
samples

Figure 7

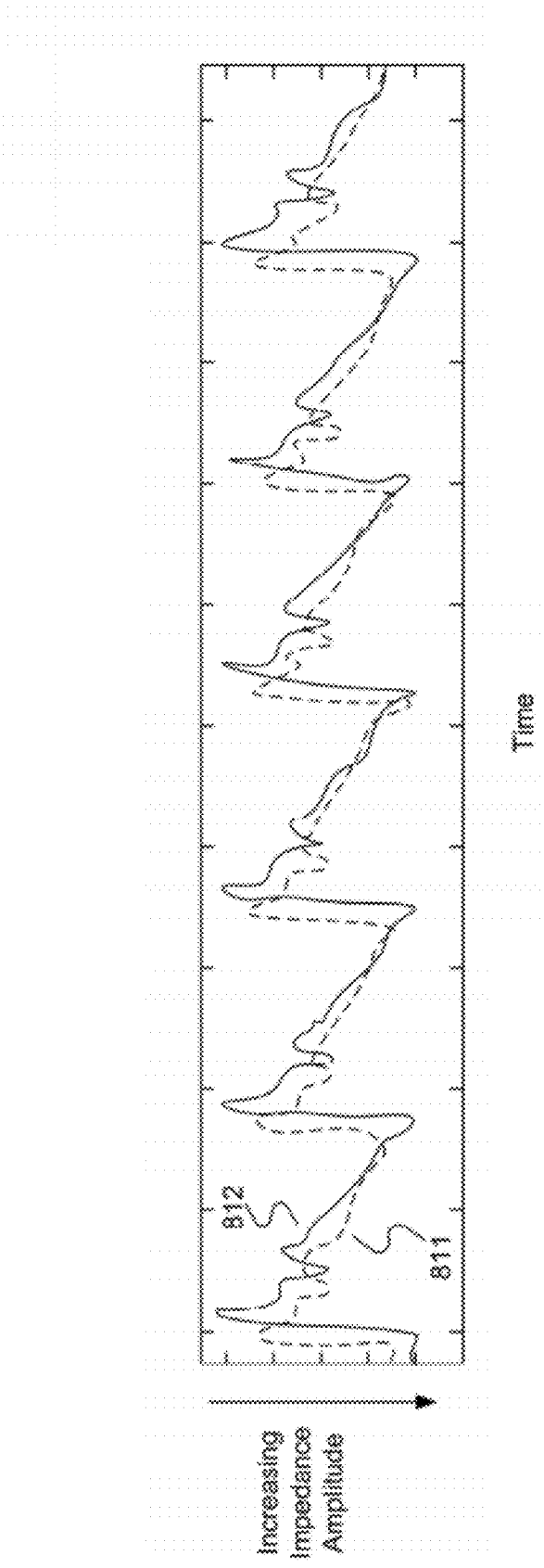


Figure 8

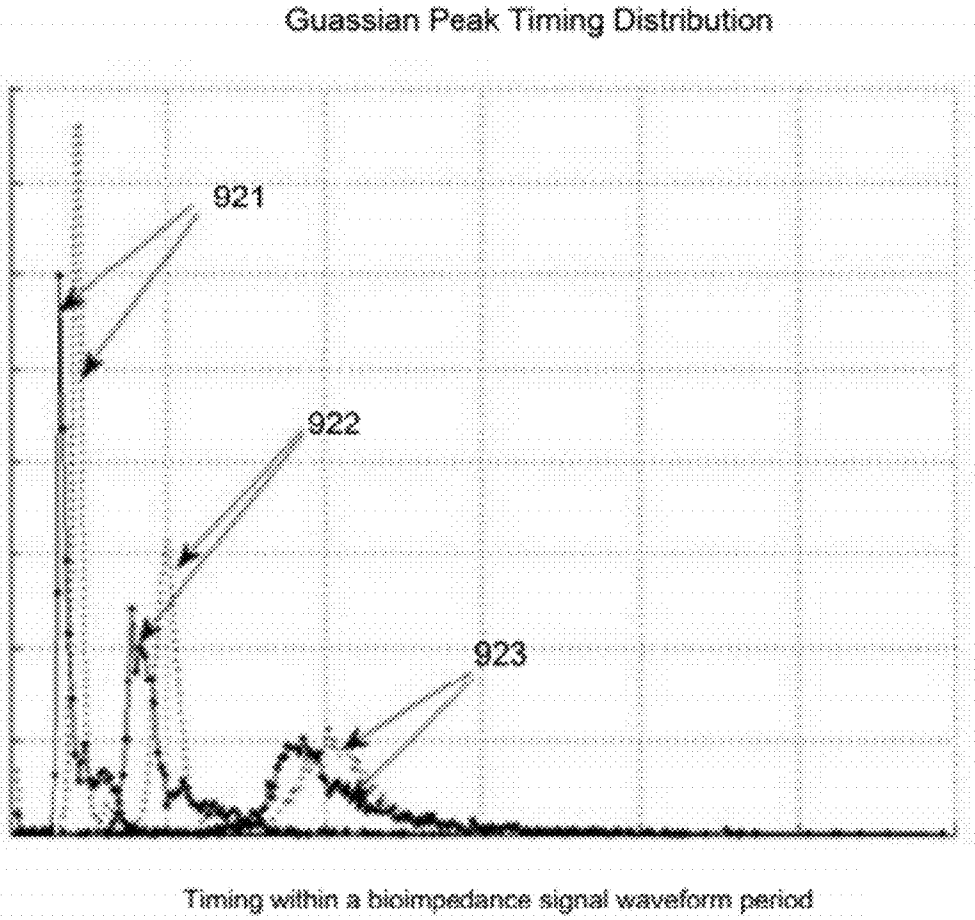

Guassian Peak Timing Distribution
921
922
923
Timing within a bioimpedance signal waveform period

Figure 9

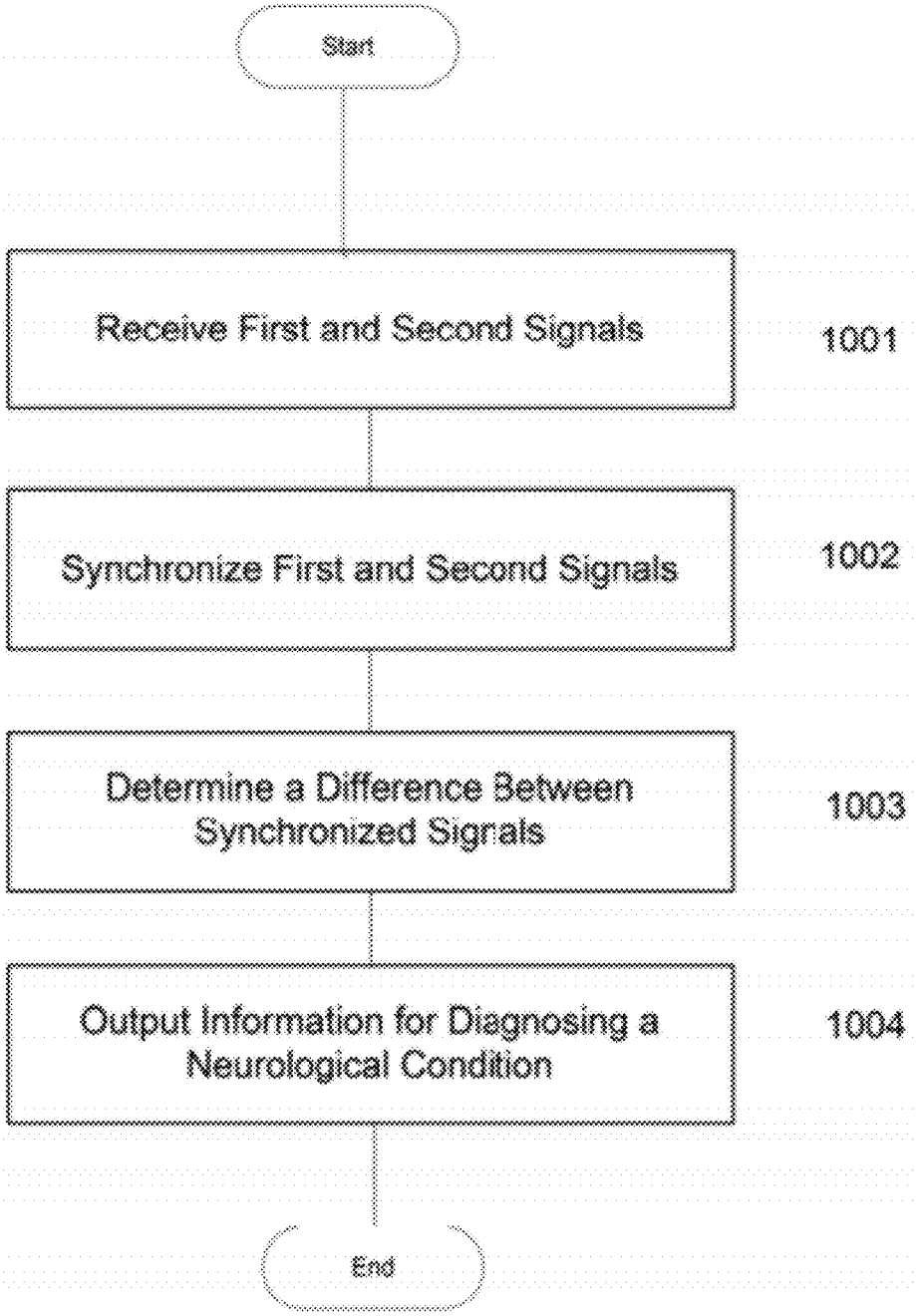

Start
Receive First and Second Signals
1001
Synchronize First and Second Signals
1002
Determine a Difference Between Synchronized Signals
1003
Output Information for Diagnosing a Neurological Condition
1004
End

Figure 10

DEVICES AND METHODS FOR MONITORING CEREBRAL HEMODYNAMIC CONDITIONS

RELATED APPLICATION

[0001] This application claims the benefit of priority under 35 U.S.C. §119(e) of U.S. Provisional Application No. 61/441,248, filed Feb. 9, 2011, and U.S. Provisional Application No. 61/474,739, filed Apr. 12, 2011, both of which are incorporated herein by reference in their entirety.

TECHNICAL FIELD

[0002] 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

[0003] 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).

[0004] 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 limit their usefulness in situations where either regular, continuous, or frequent monitoring of cerebro-hemodynamic characteristics may be desirable.

[0005] 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

[0006] 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.

[0007] One exemplary disclosed embodiment may include a cerebro-hemodynamic measurement apparatus. The apparatus may include at least one processor configured to receive a first signal associated with a brain of a subject, the first signal being indicative of a hemodynamic characteristic of the subject's brain. The at least one processor may be further configured to receive a second signal associated with the brain of the subject, the second signal being indicative of a hemodynamic characteristic of the subject's brain. The at least one processor may be further configured to synchronize to within 40 ms of each other the first signal and the second signal, determine at least one difference between the synchronized first signal and the second signal, and output information for diagnosing changes in cerebral artery occlusion.

[0008] In another embodiment, the first signal may be indicative of a hemodynamic characteristic of a first hemisphere of the subject's brain and the second signal may be indicative of a hemodynamic characteristic of a second hemisphere of the subject's brain.

[0009] In still another embodiment, the first signal and the second signal may be bioimpedance signals.

[0010] In still another embodiment, synchronizing may occur with reference to at least a portion of a cardiac cycle. In still another embodiment, synchronizing may occur with reference to a cardiac R wave.

[0011] In still other embodiments, synchronizing to within 40 ms includes synchronizing to within 10 ms, 5 ms, 1 ms, and 0.1 ms.

[0012] In still another embodiment, the processor may be further configured to detect at least one signature feature in each of the first signal and the second signal.

[0013] In another embodiment, the at least one signature feature may be a plurality of signature features including at least one peak and at least one minimum for the first signal and for the second signal

[0014] In yet another embodiment, a plurality of signature features may include a first peak, a second peak, a third peak, a first minimum, a second minimum, and a third minimum for the first signal and/or for the second signal.

[0015] In a further embodiment, the at least one difference between the synchronized first signal and the second signal may be a timing delay between the at least one signature feature in the first signal and the at least one signature feature in the second signal.

[0016] The at least one processor may be further configured to output information for diagnosing a neurological condition based on a change over time of the at least one difference between the synchronized first signal and second signal.

[0017] Additionally, the at least one processor may be further configured to synchronize the first signal and the second signal in real time, as they are received.

[0018] Further, the at least one processor may be configured to store the first signal and the second signal in memory and synchronize the first signal and the second signal in a non-real time manner.

[0019] The at least one processor may be configured to diagnose the absence of hemorrhagic stroke based on a diagnosis of the presence of ischemic stroke.

[0020] Information for diagnosing changes in cerebral artery occlusion may include, for example, information for diagnosing the presence of ischemic stroke.

[0021] 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

[0022] 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.

[0023] FIG. **1** provides a diagrammatic representation of an exemplary cerebro-hemodynamic measurement apparatus consistent with exemplary embodiments of the invention.

[0024] FIG. **2** provides a diagrammatic representation of major cerebral arteries.

[0025] FIG. **3** provides a diagrammatic representation of exemplary bioimpedance signal pathways in the brain of a subject consistent with exemplary embodiments of the invention.

[0026] 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.

[0027] FIG. **5** provides a diagrammatic representation of exemplary signature features of a single bioimpedance signal waveform period.

[0028] FIGS. **6***a* and **6***b* 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.

[0029] 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.

[0030] FIG. **8** provides a diagrammatic representation of a timing delay between exemplary bioimpedance signals associated with different hemispheres of a subject's brain.

[0031] FIG. **9** provides a diagrammatic representation of an exemplary statistical timing delay comparison between two bioimpedance signal waveforms as decomposed by a pulse decomposition algorithm.

[0032] FIG. **10** is a flowchart showing the steps of an exemplary method for diagnosing a neurological condition consistent with the invention.

DETAILED DESCRIPTION

[0033] 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.

[0034] 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.

[0035] 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, synchronizing and determining differences between signals and outputting information for the diagnosis of alterations in arterial occlusion.

[0036] 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.

[0037] Consistent with some embodiments of the invention, the at least one processor may be configured to receive a 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.

[0038] In some embodiments consistent with the present disclosure, a processor may be configured to receive signals indicative of hemodynamic characteristics of a subject's brain, for example, cerebral blood pressure, cerebral blood volume, intracranial pressure, and cerebral blood flow. As used herein, such a signal may be indicative of a physiological characteristic when changes in the physiological characteristic result in changes to the signal. Thus, a signal indicative of hemodynamic characteristics may change when hemodynamic characteristics or conditions change. Measurement and analysis of the changing signal may, therefore, yield information about the changing hemodynamic characteristics or conditions. The relationship between a signal indicative of change in a particular hemodynamic characteristic may be

direct, wherein changes in the signal are directly indicative of changes in the particular hemodynamic characteristic. Alternatively (or additionally) a relationship between a signal indicative of change in a particular hemodynamic characteristic may be indirect, requiring additional information or additional analysis in order to yield information about the particular hemodynamic characteristic. For instance, by way of example only, a signal may be directly indicative of cerebral blood volume. A 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.

[0039] In some embodiments consistent with the present disclosure, first and second signals indicative of hemodynamic characteristics in a subject's brain may be synchronized to within 40 ms of each other. As used herein, synchronization may be made, for example, with respect to a common reference timeframe, wherein the signals in the reference timeframe do not differ by more than 40 ms of each other as compared to their actual occurrence. For example, two signals obtained from different sources may simultaneously reflect an identical event. However, due to equipment, signal processing, or other limitations, the timeframes within which these signals are recorded may differ. Thus, the event may appear to have occurred at one time in a first signal and a different time in a second signal. By synchronizing the signals to within 40 ms of each other, the signals may then be viewed in a common reference timeframe. In the common reference timeframe, the occurrence of the event, simultaneously recorded by both signals, may not differ by more than 40 ms between the first signal and the second signal. In some embodiments consistent with the present disclosure, a first and second signal may alternatively be synchronized to within 10 ms, 5 ms, 1 ms, and 0.1 ms of each other (or any other time difference that permits diagnosis of a hemodynamic condition). Signals may be synchronized to each other through various means, including the use of timing equipment and reference features within the signals.

[0040] In some embodiments consistent with the present disclosure, first and second signals may be synchronized to each other with reference to at least a portion of a cardiac cycle. Such synchronization may be performed, for example, by using a portion of a cardiac cycle as a common event. In this example, a portion of a cardiac cycle may be simultaneously detected in a first and second signal. The first and second signal may then be synchronized with reference to that portion of the cardiac cycle. In some embodiments consistent with the present disclosure, signals may be synchronized, for example, with reference to a cardiac R wave. A cardiac R wave may be determined from ElectroCardioGram (ECG) measurements, and may be one of the first or second signals or serve as an additional synchronization signal. Synchronization by common clock distribution or other common timing signals may be used together or separately from ECG signal synchronization.

[0041] Signals may be indicative, for example, of hemodynamic characteristics within a first and/or a second hemisphere of a subject's brain. First and second hemispheres may refer to right and left hemispheres of a subject's brain, in any order. A signal indicative of hemodynamic characteristics within 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 signal indicative of hemodynamic characteristics within a particular side of a subject's brain may also be obtained from other locations, such as on the neck of a subject, where, for example, carotid arteries are located.

[0042] In some embodiments consistent with the present disclosure, signals indicative of hemodynamic characteristics of a subject's brain may be bioimpedance signals. As used herein, a bioimpedance signal may include any type of signal containing information about the electrical impedance of a biological subject. A 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 include information about the resistive and/or reactive components of electrical impedance.

[0043] A bioimpedance signal may include at least one voltage signal, and/or at least one current signal. A bioimpedance signal may include two or more voltage and/or current signals, and may include 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. In a bioimpedance signal, information about the electrical impedance of a subject's body may be contained in the amplitude, frequency, or phase angle of the 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.

[0044] In some embodiments consistent with the present disclosure, at least one difference between a first signal and a second signal may be determined. A difference between two or more signals may be determined through any type of analysis performed on the signals. By way of example only, a difference may be determined with basic arithmetic operations, such as addition, subtraction, or any other mathematical calculation that enables a variation to be determined. Such differences between signals may be determined, for example, in a time domain or in a frequency domain, using any suitable transform. A difference may be determined between all or part of one signal and all or part of another signal. For example, a difference may be determined between the signals in their entirety, by smaller sections, and/or by discrete points. Alternatively (or additionally), a difference may be determined between parts of one or more signals and corresponding or non-corresponding parts of one or more other signals. Further, differences may be determined between signals 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.

[0045] In exemplary embodiments, 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, multivariate 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.

[0046] 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 signal waveform, and the first, second, and third minimum may include local minima within a signal waveform. These 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.

[0047] In exemplary embodiments consistent with the present disclosure, at least one difference between the synchronized first signal and the second signal may be a timing delay between at least one signature feature in the first signal and at least one signature feature in the second signal. As used herein, a timing delay between signature features of synchronized signals may include a delay between the occurrence of a signature feature in a single waveform period of a first signal and a corresponding signature feature in a single waveform period of a second signal when the signals are analyzed in a common reference timeframe. A timing delay between signature features of synchronized signals may also include delays between non-corresponding signature features. A timing delay between signature features of synchronized signals may further include delays between the averaged, aggregated, or other statically defined occurrence timing of the signature features in their respective signals over a time period.

[0048] Consistent with the present disclosure, at least one 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," may include 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 might 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.

[0049] Information for diagnosing of a change in artery occlusion may include information for diagnosing the presence of ischemic stroke. A change in artery occlusion may lead to ischemic stroke, a cerebral condition in which a portion of the brain does not receive adequate blood supply due to arterial blockage. In some embodiments, a processor may be configured to diagnose the absence of hemorrhagic stroke based on the presence of ischemic stroke. Hemorrhagic stroke is a cerebral condition in which a portion of the brain does not receive adequate blood supply due to bleeding in the brain. Outward symptoms of ischemic and hemorrhagic stroke may be similar. The presence of ischemic stroke in a subject demonstrating outward stroke symptoms may indicate the absence of hemorrhagic stroke.

[0050] FIG. **1** provides a diagrammatic representation of an exemplary cerebro-hemodynamic measurement apparatus **100**. This exemplary apparatus **100** comprises 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 could alternatively 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.

[0051] 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 **113**, and rear voltage electrode **114**. 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 then the exemplary headset **120**.

[0052] Pairs of electrodes **110** 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 **113**. 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 **114**. 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 of the bioimpedance may be computed as the phase difference by which the output current signal leads the input voltage signal.

[0053] 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.

[0054] 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.

[0055] 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.

[0056] 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 an 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.

[0057] 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.

[0058] 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.

[0059] 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.

[0060] As mentioned previously, exemplary headset **120** may 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 comprise 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.

[0061] 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 spe-

cialized ports or connectors configured for the exemplary apparatus **100** or configured for other devices and applications.

[0062] Cerebral perfusion monitor **130** may comprise 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 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 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.

[0063] 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.

[0064] 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.

[0065] 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.

[0066] 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**.

[0067] 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 first and second signals associated with a brain of a subject, and which each are indicative of a hemodynamic characteristic of the subject's brain.

[0068] Bioimpedance signal waveforms, as illustrated in FIGS. **4-7** are shown after signal conditioning to remove noise and respiration artifacts. Signal conditioning of this type may result in a 'flat' baseline on the displayed waveforms and can be performed in multiple ways by use of filtering in the frequency or time domains. Such filtering does not change the relative timing of signals, by using either the same phase delay on all signals or using zero phase delay filtering. Maintaining identical phase delays in order to avoid distortion of timing delays is known to those of skill in the art.

[0069] 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 y-scale is inversely correlated with impedance amplitude. That is, high values of impedance amplitude are reflected by low values in the signal as illustrated in FIG. **4**. 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.

[0070] 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 comprise one or more waveform periods, to a bioimpedance signal associated with a second time interval,

which may comprise one or more waveform periods, may therefore yield information indicative of cerebro-hemodynamic characteristics.

[0071] 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.

[0072] 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 event, 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).

[0073] 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, reactive components of the electrical impedance of a subject may generate a phase difference in 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.

[0074] FIG. **5** provides a diagrammatic representation of exemplary signature features of a single bioimpedance signal 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 P**1**, **511** may correspond to an initial rise in blood flow following aortic valve opening, which may correspond to minimum M**0**, **521**. A second peak P**2**, **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 M**1**, **522**. A minimum M**2**, **523** may correspond to a decrease in blood flow as the aortic valve closes. A final peak P**3**, **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. 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.

[0075] 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. 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.

[0076] FIGS. **6***a* and **6***b* 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. **6***a*, phase angle waveforms may demonstrate similar characteristics as concurrently obtained amplitude waveforms. For example, in FIG. **6***a*, 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.

[0077] Phase angle waveforms may also demonstrate different characteristics than concurrently obtained amplitude waveforms, as illustrated in FIG. **6***b* for example. In FIG. **6***b*, 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 blood pressure.

[0078] 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**.

[0079] 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 comprise first, second and third peaks P**1** **511**, P**2** **512**, and P**3** **513**, and minimums M**0** **521**, M**1** **522** and M**2** **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.

[0080] 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**.

[0081] 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, P**2** **512**, P**1** **511**, and P**3** **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, P**1** **511**, P**2** **512**, or P**3** **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 P**2** **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

[0082] 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.

[0083] 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 M**0** **521**, minimum M**1** **522**, minimum M**2** **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 P**1** **511**, P**2** **512**, and P**3** **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**.

[0084] 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 P**1** **511** and second P**2** **512** peaks in the systolic part of the waveform, and a GEV function for P**3** **513** on the diastolic part. This choice may give a better fit for the diastolic part than using a Gaussian base function for P**3** **513**, because GEV functions may be asymmetric while the Gaussian function is symmetric.

[0085] 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 P**2** **512** pulse timing 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 P**2** **512** pulse timing derived from the second hemisphere.

[0086] 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 P**2** **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.

[0087] 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.

[0088] Alternatively or additionally, signature features may also be monitored and compared over non-continuous time periods to provide diagnosis information. For example, bio-

impedance 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 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.

[0089] FIG. **8** provides a diagrammatic representation of a timing delay between exemplary bioimpedance signals associated with different hemispheres 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**.

[0090] Similarly, ischemic stroke effects may result in measurable 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 of maximum, such as peak P**2 512**, may be altered. By synchronizing the right and left hemisphere bioimpedance signals, for instance with a cardiac cycle ECG signal, timing delays in the bioimpedance signals may be detected.

[0091] In the signals illustrated in FIG. **8**, a left hemisphere bioimpedance signal **812**, illustrated by the solid line, shows a timing delay with respect to the right hemisphere bioimpedance signal **811**. The illustrated timing delays may be indicative of ischemic stroke. Thus, signals **811** and **812** (or corresponding sub-portions thereof) are examples of first and second signals associated with a brain of a subject, and which are each indicative of a hemodynamic characteristic of the subject's brain. These signals might be processed, for example, in the at least one processor **160**, described in connection with FIG. **1**.

[0092] Embodiments of the invention may involve synchronizing to within 40 ms of each other the first signal and the second signals. Such synchronization may occur, for example, on an independent scale, for example with a common electronic clock signal], or may occur with reference to a biologic scale. One example of a biologic scale may be defined by ECG. Specifically, timing of the bioimpedance waveform signals (or portions thereof) from opposite brain hemispheres may be synchronized to a scale defined by ECG. In one embodiment, this synchronization may occur to within 40 ms. Longer synchronization schemes may be used consistent with the invention as can shorter schemes. For example, synchronization of signals may be performed to within milliseconds of each other. Non-limiting examples of timing synchronization may include synchronization to within about 40 ms, about 30 ms, about 20 ms, about 10 ms and about 5 ms. In other embodiments, the waveforms may be synchronized to within 5 ms of one another or to within fractions of a millisecond, such as, for example, to within 0.1 ms or less. Such a synchronization analysis may be performed while bioimpedance signal waveforms are being collected and may be performed on recorded bioimpedance signal waveforms stored in a memory (e.g., external or computer memory).

[0093] Embodiments of the invention may include determining at least one difference between the synchronized first signal and the second signal. Such a determination may occur, for example, using at least one processor **160**, as described earlier in connection with FIG. **1**. The at least one processor **160**, might, for example, determine a timing difference (as described earlier) between right and left hemispheres for either portions or all of a bioimpedance signal waveform. In other embodiments, processor **160** might determine other differences, such as an amplitude difference, or a difference based on a calculation derived from the bioimpedance signals.

[0094] At least one processor **160** 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 using differences between the two 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.

[0095] Waveforms for right and left brain hemispheres, for example, may be synchronized using at least one processor **160** included within precision timing equipment such that data is extracted from both hemispheres simultaneously or with a known temporal relationship. For example, waveforms may be synchronized to within several milliseconds such that features such as peak onset, for example, can be related. Alternatively, or in addition to equipment-based synchronization, signals may be synchronized based on features in the waveform or features of a cardiac electric signal. For example, a cardiac R wave, the electrical signal preceding a heartbeat, may be detected by analyzing an ECG signal measured in parallel to the bioimpedance waveform. Therefore, the waveforms from different hemispheres, for example, may be synchronized using the detection or identification of R wave onset in each waveform. The waveforms from different hemispheres, for example, may also be synchronized using the detection or identification of any other portion of a cardiac cycle. Such a synchronization analysis may be performed while bioimpedance signal waveforms are being collected (e.g., in real time) or performed on recorded bioimpedance signal waveforms stored in memory (e.g., non-real time).

[0096] By determining timing delays between signature features of signals received from the right and left hemispheres, different information about cerebral hemodynamic characteristics may be provided. Such timing delays may be between entire bioimpedence waveforms, or only portions of waveforms. For example, delays may be examined for a particular peak or valley (e.g., P**1 511**, P**2 512**, P**3 513**, M**1 521**, M**2 522**, and M**3 523**) or various combinations thereof. In some embodiments, delays may only be considered significant if they pass a particular threshold. Under some conditions, greater delays may indicate an exacerbated condition as compared to shorter delays. Furthermore, changes over time in the duration of delay may indicate either an improving or deteriorating condition. In some embodiments, changes in timing delays over time may be monitored. A decrease in

delay over a treatment period may indicate that the patient's cerebrovascular condition is improving, while an increase in delay may indicate that a patient's condition is worsening.

[0097] Synchronizing signals may also permit a reduction in effects caused by heart rate variance when determining differences between signals. Variation in heart rate results in changes in the length of cardiac cycles. As a result, timing of corresponding signature features in a signal may vary due heart rate variance. For example, peak P**1 511** may occur earlier within a signal waveform period when heart rate is elevated. Thus, analyzing the timing of signature features within unsynchronized waveforms may be affected by variations in heart rate. Determining differences between two synchronized signals may thus reduce the effects of heart rate variation.

[0098] FIG. **9** provides a diagrammatic representation of an exemplary statistical timing delay comparison between two bioimpedance signal waveforms as decomposed by a pulse decomposition algorithm. FIG. **9** illustrates pulse decompositions of two bioimpedance signal waveform, performed by a method similar to that described with respect to FIG. **6**. The solid line represents the distribution of the timing of peaks P**1**, P**2**, and P**3**, as computed by a pulse decomposition method, over multiple bioimpedance signal waveform periods obtained from a right hemisphere of a subject's brain. The dotted line represents the distribution of the timing of peaks P**1 511**, P**2 512**, and P**3 513** as computed by a pulse decomposition method, over multiple bioimpedance signal waveform periods obtained from a left hemisphere of a subject's brain. For each hemisphere, the multiple bioimpedance signal waveform periods were obtained during corresponding time intervals. Peaks **921** represents the distribution of the timing of peaks P**1 511** over multiple bioimpedance signal waveform periods. Peaks **922** represent the distribution of the timing of peaks P**2 512** over multiple bioimpedance signal waveform periods. Peaks **923** represent the distribution of the timing of peaks P**3 513** over multiple bioimpedance signal waveform periods.

[0099] As illustrated in FIG. **9**, the dotted line, representing peak distributions obtained from the left hemisphere, shows delays in all three peaks **921**, **922**, and **923** with respect to those of the right hemisphere. These timing delays may be indicative of cerebral hemodynamic abnormalities in the left hemisphere. The timing delays, as computed here, may be monitored over time, for example, to determine whether a patient's condition is improving or deteriorating.

[0100] FIG. **9** illustrates one exemplary method of determining timing delays between synchronized signal waveforms. Alternate embodiments, however, may utilize other methods of determining timing delays between synchronized signal waveforms. For example, in some embodiments signature features other than peaks P**1 511**, P**2 512**, and P**3 513** may be used. In some embodiments, alternate pulse decomposition methods for signature feature detection may be used. And in some embodiments, alternate methods of signature feature detection may be used. Thus, it will be appreciated by those of ordinary skill that various analysis techniques exist for determining differences between two or more synchronized signal waveforms, and the invention in its broadest sense is not limited to any particular technique.

[0101] In an embodiment consistent with the present disclosure, a method for diagnosing a neurological condition is provided. FIG. **10** is a flowchart showing the steps of an exemplary method for diagnosing a neurological condition. At step **1001**, first and second signals associated with a brain of subject, indicative of a hemodynamic characteristic of the subject's brain, may be received. The signals may be received, for instance, by a suitably configured processor **160**. At step **1002**, the first and second signals may be synchronized to each other. For example, the signals may be synchronized to within about 40 ms, about 30 ms, about 20 ms, about 10 ms, about 5 ms, or even less, Such synchronization may be performed, for example, by a processor **160**.

[0102] At step **1003**, at least one difference between the synchronized first and second signals may be determined. The at least one difference may be determined by a suitably configured processor **160**, based on, for example, a timing delay between the two signals. At step **1004**, results of the determination of step **1003** may be used to output information for diagnosing a neurological condition. A processor **160** may, for example, be configured to output the information. Additional methods for diagnosing a neurological condition may include any and/or all of the techniques disclosed herein.

[0103] 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.

[0104] 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, comprising:

at least one processor configured to:

receive a first signal associated with a brain of a subject, the first signal being indicative of a hemodynamic characteristic of the subject's brain;

receive a second signal associated with the brain of the subject, the second signal being indicative of a hemodynamic characteristic of the subject's brain;

synchronize to within 40 ms of each other the first signal and the second signal;

determine at least one difference between the synchronized first signal and the second signal; and

output information for diagnosing changes in cerebral artery occlusion.

2. The cerebro-hemodynamic measurement apparatus of claim **1**, wherein the first signal is indicative of a hemodynamic characteristic of a first hemisphere of the subject's

brain and wherein the second signal is indicative of a hemodynamic characteristic of a second hemisphere of the subject's brain.

3. The cerebro-hemodynamic measurement apparatus of claim **1**, wherein the first signal and the second signal are bioimpedance signals.

4. The cerebro-hemodynamic measurement apparatus of claim **1**, wherein synchronizing occurs with reference to at least a portion of a cardiac cycle.

5. The cerebro-hemodynamic measurement apparatus of claim **4**, wherein synchronizing occurs with reference to a cardiac R wave.

6. The cerebro-hemodynamic measurement apparatus of claim **1**, wherein synchronizing to within 40 ms includes synchronizing to within 10 ms.

7. The cerebro-hemodynamic measurement apparatus of claim **1**, wherein synchronizing to within 40 ms includes synchronizing to within 5 ms.

8. The cerebro-hemodynamic measurement apparatus of claim **1**, wherein synchronizing to within 40 ms includes synchronizing to within 1 ms.

9. The cerebro-hemodynamic measurement apparatus of claim **1**, wherein synchronizing to within 40 ms includes synchronizing to within 0.1 ms.

10. The cerebro-hemodynamic measurement apparatus of claim **1**, wherein the processor is further configured to detect at least one signature feature in each of the first signal and the second signal.

11. The cerebro-hemodynamic measurement apparatus of claim **10**, wherein the at least one signature feature is a plurality of signature features including at least one peak and at least one minimum for the first signal and for the second signal.

12. The cerebro-hemodynamic measurement apparatus of claim **11**, wherein the plurality of signature features includes a first peak, a second peak, a third peak, a first minimum, a second minimum, and a third minimum for the first signal and for the second signal.

13. The cerebro-hemodynamic measurement apparatus of claim **10**, wherein the at least one difference between the synchronized first signal and the second signal is a timing delay between the at least one signature feature in the first signal and the at least one signature feature in the second signal.

14. The cerebro-hemodynamic measurement apparatus of claim **1**, wherein the processor is further configured to output information for diagnosing a neurological condition based on a change over time of the at least one difference between the synchronized first signal and second signal.

15. The cerebro-hemodynamic measurement apparatus of claim **1**, wherein the processor is further configured to synchronize the first signal and the second signal in real time, as they are received.

16. The cerebro-hemodynamic measurement apparatus of claim **1**, wherein the processor is further configured to:

store the first signal and the second signal in memory;

synchronize the first signal and the second signal in a non-real time manner.

17. The cerebro-hemodynamic measurement apparatus of claim **1**, wherein information for diagnosing changes in cerebral artery occlusion includes information for diagnosing the presence of ischemic stroke.

18. The cerebro-hemodynamic measurement apparatus of claim **17**, wherein the processor is further configured to diagnose the absence of hemorrhagic stroke based on a diagnosis of the presence of ischemic stroke.

19. A method for diagnosing a neurological condition, comprising

receiving a first signal associated with a brain of a subject, the first signal being indicative of a hemodynamic characteristic of the subject's brain;

receiving a second signal associated with the brain of the subject, the second signal being indicative of a hemodynamic characteristic of the subject's brain;

synchronizing to within 40 ms of each other the first signal and the second signal;

determining at least one difference between the synchronized first signal and the second signal; and

outputting information for diagnosing a neurological condition based on the at least one difference between the synchronized first signal and the second signal.

20. The method of claim **19**, wherein the first signal is indicative of a hemodynamic characteristic of a first hemisphere of the subject's brain and wherein the second signal is indicative of a hemodynamic characteristic of a second hemisphere of the subject's brain.

21. The method of claim **19**, wherein the first signal and the second signal are bioimpedance signals.

22. The method of claim **19**, wherein synchronizing occurs with reference to at least a portion of a cardiac cycle.

23. The method of claim **22**, wherein synchronizing occurs with reference to a cardiac R wave.

24. The method of claim **19**, wherein synchronizing to within 40 ms includes synchronizing to within 10 ms.

25. The method of claim **19**, wherein synchronizing to within 40 ms includes synchronizing to within 5 ms.

26. The method of claim **19**, wherein synchronizing to within 40 ms includes synchronizing to within 1 ms.

27. The method of claim **19**, wherein synchronizing to within 40 ms includes synchronizing to within 0.1 ms.

28. The method of claim **19**, further comprising detecting at least one signature feature in the first signal and the second signal.

29. The method of claim **28**, wherein detecting the at least one signature feature in the first signal and the second signal further comprises detecting a plurality of signature features including at least one peak and at least one minimum for the first signal and for the second signal.

30. The method of claim **29**, wherein the plurality of signature features includes a first peak, a second peak, a third peak, a first minimum, a second minimum, and a third minimum for the first signal and for the second signal.

31. The method of claim **28**, wherein the at least one difference between the synchronized first signal and the second signal is a timing delay between the at least one signature feature in the first signal and the at least one signature feature in the second signal.

32. The method of claim **19**, wherein outputting information for diagnosing a neurological condition is further based on a change over time of the at least one difference between the synchronized first signal and second signal.

33. The method of claim **19**, further comprising synchronizing the first signal and the second signal in real time, as they are received.

34. The method of claim **19**, further comprising:

storing the first signal and the second signal in a computer memory;

synchronizing the first signal and the second signal in a non-real time manner.

35. The cerebro-hemodynamic measurement apparatus of claim **19**, wherein information for diagnosing changes in cerebral artery occlusion includes information for diagnosing the presence of ischemic stroke.

36. The cerebro-hemodynamic measurement apparatus of claim **35**, wherein the processor is further configured to diagnose the absence of hemorrhagic stroke based on a diagnosis of the presence of ischemic stroke.

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