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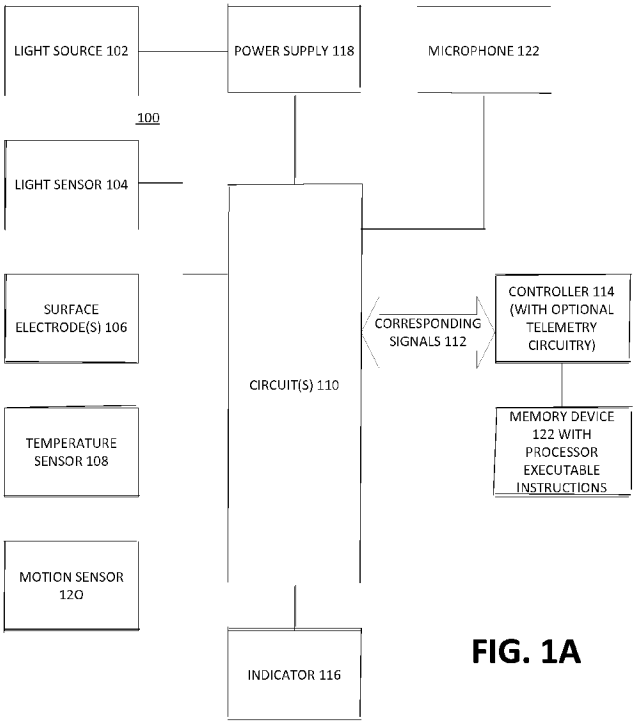

FIG. 1A

(57) Abstract: A system for measuring pain of a person, the system for use with the tissue of the person. Various sensors and detectors on the tissue provide signals to a controller for determining and indicating a pain level of the person. All components can be integrated into one unit or separated into a sensing unit that wirelessly communicates with a processing unit.

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REAL-TIME TRACKING OF CEREBRAL HEMODYNAMIC RESPONSE (RTCHR) OF A SUBJECT BASED ON HEMODYNAMIC PARAMETERS

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

[0001] Not Applicable

REFERENCE TO SEQUENCE LISTING, A TABLE, OR A COMPUTER PROGRAM LISTING COMPACT DISK APPENDIX

[0002] Not Applicable

BACKGROUND

[0003] The present invention is in the medical field of blood flow and brain activity monitoring including hemodynamic measurement. More specifically, the present invention is in the medical, person management, animals and pets management, and pharmaceutical management fields of measuring blood flow and cerebral hemodynamic changes and impacts associated with several sensory stimuli including pain, brain injury, other neurological disorders, and anesthesia as well as others.

[0004] Measurement of pain can include a subjective component when a person's mood, culture, and other sociological, psychological, and other factors contribute to sensation and reporting of pain. Some persons like neonates, infants, children, Alzheimer persons, and/or persons under anesthesia, or in an ICU, have no mechanism of self-reporting. Also, if pain progression could be measured and a threshold set, early intervention could minimize pain progression. This is also true for persons with migraine or cluster headaches and other pains.

[0005] Pain management and treatment solutions rely on subjective data. As a result, persons are either over-medicated or under treated. Stimulation devices for treatment of pain could deliver more appropriate therapy if the stimulation level was correlated to objective, independent, reliable, and repeatable pain measurement. The evaluation and treatment of persons occurs because many may not be able to self-report their health condition, and the typical behavioral signs may be subtle or absent.

SUMMARY

[0006] In one form, a system according to embodiments of the invention indicates pain or a surrogate of pain symptoms of a person and is for use with the tissue of the

person. A light source is adapted for illuminating the tissue of the person. An optical sensor is adapted for sensing light emitted or reflected by the tissue of the person. The optical sensor generates a light signal indicative of a light parameter of the sensed light. A surface electrode is adapted for sensing an electrical parameter of the tissue of the person. The surface electrode generates an electrode signal indicative of an electrical parameter of the sensed electrical parameter. A temperature sensor is adapted for sensing a temperature of the tissue of the person. The temperature sensor generates a temperature signal indicative of the sensed temperature. One or more circuits is adapted for receiving the light signal, the electrode signal, and the temperature signal and provides corresponding signals. A controller is adapted for receiving and processing the corresponding signals and is adapted for providing a pain indication signal which is a function of the corresponding signals. An indicator is adapted to be responsive to the controller for providing an indication which is indicative of the pain indication signal. A power supply supplies power to the system.

[0007] A system for cerebral monitoring of a person and a method for providing an indication of pain of a person such as measuring pain or a surrogate of pain symptoms of a person are also presented.

BRIEF DESCRIPTION OF THE DRAWINGS

[0008] Fig. 1 illustrates a sensor system according to the system and method and a plurality of exemplary locations for the placement of the sensor system on a person's forehead.

[0009] Fig. 1A is block diagram illustrating a system and method.

[0010] Fig. 2 illustrates a block diagram of the device for the real-time tracking of the cerebral hemodynamic changes on ambulatory subjects using the Real-time Tracking of Cerebral Hemodynamic Response (RTCHR) system.

[0011] Figs. 3A and 3B illustrate the physics of chirp optical modulation to track hemodynamic response changes.

[0012] Fig. 4 illustrates the period of time during which the assessments of Figs. 5-8 were taken.

[0013] FIG. 5 illustrates graphs of Objective Pain Level Assessment: hemodynamic changes in response to external severe cold pain stimuli.

[0014] FIG. 6 illustrates graphs of Objective Pain Level Assessment: hemodynamic changes in response to external severe heat pain stimuli. Hemodynamic response did not return to baseline due to continued burning sensation.

[0015] FIG. 7 illustrates graphs of Objective Pain Level Assessment: hemodynamic changes in response to external severe sharp pain stimuli.

[0016] FIG. 8 illustrates graphs of Objective Pain Level Assessment: hemodynamic changes in response to internal severe back pain stimuli. Subject with back pain was asked to twist his back to temporarily increase pain level.

[0017] FIG. 9 illustrates graphs of heart and respiration rate Estimation: The derivative of forehead pulse can be used to estimate Heart and respiration rates.

DETAILED DESCRIPTION

[0018] Vital signs should not be used as primary indicators of person health condition, but rather vital signs should be considered as a cue to begin further assessment. Other than vital signs, human brain reactivity to external/internal stimuli such as pain and anesthesia has been extensively studied with the use mainly of magnetic resonance imaging and positron-emission tomography. However, the use of these sophisticated methods may be unrealistic as an affordable and ambulatory product for everyday use. Of interest to assessing these persons in a clinical and non-clinical setting is the noninvasive measurement of regional cerebral tissue oxygenation with the pulse oximetry, EEG, and near-infrared spectroscopy (NIRS) techniques. An objective of this invention is to develop cheaper techniques of detecting the cerebral hemodynamic characteristics and changes associated with sensory stimuli, including pain and anesthesia, among others. An objective of this invention is to develop a device for real-time profiling and detection of the cerebral hemodynamic patterns and changes on an ambulatory and non-ambulatory subjects using fully automatic and advanced machine learning techniques. Also provided is a system that can communicate and provide person feedback with healthcare professionals or persons to adjust the therapy or adjust other interventions.

[0019] The present invention includes a device and method for a real-time profiling, pattern recognition, and tracking of the cerebral hemodynamic changes of persons (ambulatory and/or non-ambulatory) using automatic and advanced machine learning techniques to process biological data collected using a sensor patch or a series of sensors (e.g., red and infrared lights transmitters, and/or electroencephalography—EEG, and not limited to other sensors such as accelerometers, position sensor, impedance sensor, and the like).

[0020] In an embodiment, a device could be designed and used for neonatal persons where a baseline is created and deviation from brain hemodynamics and/or other sensor parameters could alarm the nurse of infants' discomfort which could lead to pain progression or

distress. The device could be a patch with wireless data communication capability. The device could transmit and receive data from the hospital monitor. The device could also include visual, audio, or electronic feedback such as colored LEDs, alarm, or data transmission to inform the hospital staff or parents of the pain or stress status of the person.

[0021] In another embodiment, the device could include an optional microphone (122; see Fig. 1A) to record neonates crying and distress levels. The device could also simultaneously detect and measure the hemodynamic or other sensors levels to define a pain or cry threshold. Such a device could be programmed to alarm the hospital staff and parents that the neonate is progressing toward higher levels of pain and distress. Therefore, an intervention could be applied before the neonate reached a maximal pain or distress level.

[0022] In yet another embodiment, a device could be designed and developed for persons under anesthesia undergoing surgery. These persons have no capability to report pain. Similar to the previously described device, a profile and threshold of the hemodynamic and other sensors could be established even prior to surgery when the person is awake and continue to record sensor measurements during surgery. If a device detects deviation from the anesthesia baseline that indicates pain or consciousness, the anesthesiologist could adjust the drug levels to comply with device trending and recommendation. This device could be a patch that also includes communications and person feedback, which can also be integrated with hospital monitoring systems. In yet another embodiment, a device could command the anesthesiologist or the anesthesia machine to deliver additional drugs to minimize pain or sensors information deviation measured by the device. In an embodiment, all devices could be disposable or reusable.

[0023] In another embodiment, a device could be worn by an ambulatory, non-ambulatory, or mobile person where the pain management device directly communicates with a control device. The control device could be a pager, a mobile phone with an app, or other variation. The control device could be programmed to request a measurement from the hemodynamic measurement device. This measurement could be programmed on hourly, daily, or other intervals. The person himself could request for an objective pain measurement through use of the mobile device. If the patch senses deviation from a baseline or emergence of pain is imminent, while it takes the objective measurements, it could send a signal to the mobile device and request the person to include his subjective level of pain. Such simultaneous objective and subjective pain measurement data could be matched and used for better treatment of the person. Persons could be alarmed of a baseline deviation and a potential for the emergence or an

increase in pain sensation. For example, it is understood if migraine pain is detected early before reaching debilitating levels, persons can immediately intervene with medication and or make a change in their environment to minimize pain progression. Such a device could be a non-invasive patch or an implantable device placed under the hair, in forehead, or another part of the head and neck. This device could be a very thin and invisible device. Such a device is capable of measurements on-demand, objective, and subjective pain, and other sensor data.

[0024] Given different body positions could lead to a different type of pain (i.e., low back while standing is sensed more than lying down). In an embodiment, the device includes a position sensor. The device could also include a GPS sensor as certain environments and/or movements could lead to higher level pain inducement or sensation.

[0025] Such a device could also be used to measure a person's compliance with medications of other therapies. The mobile device could remind the person of taking medications on time and, within a given interval of time, measure changes in objective pain measurements to learn if the medication was effective. Physicians can also program and/or receive information about person objective, or subjective pain levels and medication of other therapy compliance. Physicians could also command pain level measurements both objective from the patch and subjective from the mobile device app and the person. The received information could be used for treatment titration and compliance improvement.

[0026] The device and method could also include communications in the form of a Q&A with the person to better categorize pain, mood, stress, emotional, and behavioral variations in sensor measurements level. The sensors results could be matched with a person's conditions and/or environments to therefore provide improved person pain management. Thus, the objective sensor measurement may be combined, synchronized, and/or aligned with a person's subjective input in a variety of environments.

[0027] It is contemplated that at least some embodiments of the devices or methods of the invention could be implemented to aid in reducing addictions to opiates medication, i.e., narcotics and pain killers such as Oxycontin™ (onycodone HCl). Addiction to opiate drugs are increasing at alarming rates and causing significant issues to the healthcare system including rising costs, suicides, and dependencies. However, if these drugs are administered when the patient really needs it rather than at a prescribed rate, there is a possibility to reduce dependencies.

[0028] It is contemplated that at least some embodiments of the devices or methods of the invention could also help to self-discipline or discipline patients to administer/consume

the medications when there is significant pain on the horizon. The predictability of rising pain levels based on history of a patient could help with minimizing the required medication to treat the pain at an early onset. Therefore, at least some embodiments of the devices or methods of the invention could minimize required medications for the treatment of pain.

[0029] In today's subjective pain measurement, a person is asked to rate the pain level from 1-10 in a doctor's office or another location. The same format of subjective pain measurements, Q&A, or other approaches can be combined into a mobile APP and synchronized with the measurement by the system of the invention or vice versa. A person may feel more pain in one environment or position vs. another. The system may measure the same pain level but the person's perception could be different at a different environment. The system will identify these differences or changes and create different profiles related to mood, stress, environment, and/or positions to help with person management. For example, one environment may require increased pain medication to alleviate pain. Therefore, the device will be intelligent enough to provide proper information to the person. Besides measurement and monitoring of pain, this device could be used for managing a brain injury, for diagnosis of a brain injury as well as used for sleep apnea diagnosis.

[0030] The real-time tracking of cerebral hemodynamic response (RTCHR) optical technology systems, unlike pulse oximetry, uses chirp modulation in the hardware to measure the level of hemogolobin oxygenation ("oxy Hb"). The RTCHR technology is also different than spectroscopy because spectroscopy requires several wavelengths of light. The pulse oximeter uses the property that oxyhemoglobin and deoxyhemoglobin absorb light of different wavelengths in a specific way. A light source is provided to sequentially pass light of different wavelengths through a sample of oxy Hb. A detector determines the amount of light, at each wavelength, has been absorbed. Pulse oximetry uses two wavelengths (i.e., 650 and 950 nm). One is a red light, which has a wavelength of approximately 650 nm. The other is an infrared light, which has a wavelength of 950 nm. The pulse oximeter determines the oxygen saturation by comparing the amount of red light and infra-red light are absorbed by the blood. Depending on the amounts of oxy Hb and deoxy Hb present, the ratio of the amount of red light absorbed compared to the amount of infrared light absorbed changes.

[0031] Functional Near-Infra-Red Spectroscopy (INIRS) uses a similar approach, but it looks at all waveforms in a near infra-red field. Further, INIRS uses the near-infrared region of the electromagnetic spectrum (i.e., from about 800 nm to 2500 nm). Typical applications include pharmaceutical, medical diagnostics (including blood sugar and blood oxygenation),

food and agrochemical quality control, and combustion research, as well as research in functional neuroimaging, sports medicine & science, elite sports training, ergonomics, rehabilitation, neonatal research, brain computer interface, urology (bladder contraction), and neurology (neurovascular coupling). In NIRS, multiple LED senders and receivers with different wavelength/light settings are used to get light reflection at different wavelengths. To get more spectrum data at more wavelengths, more LED sensors and receivers are needed. This dramatically increases the price of the NIRS, and it increases complexity of hardware and software.

[0032] In the present invention, lights with different wavelengths are induced over time using frequency modulation (chirp profile) to fit the need of a specific person or obtain most accurate hemodynamic measurements. In this approach, multiple LEDs are not needed, and the invention only needs one pair LED transceivers and different lights are induced over time using chirp frequency excitation of LEDs (see Figure 3). This will make RTCHR technology different than current pulse oximetry and existing NIRS devices, which need multiple LED senders/receivers. This will make the technology inexpensive compared to NIRS and compatible to the cost of a pulse oximetry device.

[0033] In an embodiment, the device includes the correlation of presence and level of pain with heart rate, temperature, brain activity, blood pressure, or vice versa. The system measures all these parameters simultaneously and can analyze the data to identify patterns and intelligence. The system could also correlate pain level to certain positions, activity levels, and/or locations/environments.

[0034] The system could be used for human and animal subjects as well. Pet owners have significant interests to know if their pets are experiencing pain, and if the pain management and treatment is effective. Therefore, another variation of this device could be designed and developed to fit certain pet specifies. The system could be used for drug/pharmaceutical development purposes as well.

[0035] Referring now to the invention in more detail, FIG. 1 shows a lateral view of the face and location of a real-time tracking of cerebral hemodynamic response (RTCHR) patch system 100 for real-time tracking of cerebral hemodynamic response changes on an ambulatory subject. It records hemodynamic response changes, heart rate, respiration, and Electroencephalogram (EEG). To localize hemodynamic response and estimate stimulus type, one or more additional patch systems 100 positioned on the forehead, on the skull or other part of body can be used. In Figure 1:

1) Optical sender/receiver unit 1A, 2B.

2) Standard Surface electrode 2A, 2B.

3) Accelerometer/GPS sensor 3.

4) Temperature sensor 4.

5) Data acquisition unit 5 to fetch data from sensors, apply any necessary filtering, convert the sensor data in a form for transmission to a control 7, and transmit recorded sensor data via wired or wireless transmission to the control 7.

6) Display 6 such as LCD/LEDs on the patch system 100 to display pain level and heart/respiration rates.

7) Control 7 fetches sensor data via wired or wireless transmission line and applies necessary signal processing and machine learning techniques to estimate hemodynamic parameters in real-time while subject can do his/her normal daily activities. It then displays the hemodynamic parameters and stores raw and estimated results in a dedicated server. The control box could be stand-alone or integrated with patch.

[0036] Fig. 1A is block diagram illustrating a RTCHR system 100 and method. The system 100 measures pain of a person and is for use with the tissue (e.g., skin) of the person. A light source 102 is adapted for illuminating the tissue of the person. An optical sensor 104 is adapted for sensing light emitted or reflected by the tissue of the person. The optical sensor 104 generates a light signal indicative of a light parameter of the sensed light. The light signal is indicative of pulse oxygen levels, respirations and heart rate.

[0037] A surface electrode 106 is adapted for sensing an electrical parameter of the tissue of the person. The surface electrode 106 generates an electrode signal indicative of an electrical parameter of the sensed electrical parameter. The electrode signal is indicative of heart rate, sweat and respirations.

[0038] A temperature sensor 108 is adapted for sensing a temperature of the tissue of the person. The temperature sensor 108 generates a temperature signal indicative of the sensed temperature. The temperature signal is indicative of body temperature.

[0039] One or more circuits 110 are adapted for receiving the light signal, the electrode signal, and the temperature signal and providing corresponding signals 112. The circuits 110 apply any necessary filtering, convert the sensor data in a form for transmission to a controller 114, and transmit recorded sensor data via wired or wireless transmission to the control114. Thus, in one embodiment, the controller 114 includes optional telemetry circuitry to

communicate with other devices. For example, the controller 114 may communicate with a mobile device such as a cell phone or hospital monitor and provide information indicative of the signals to the mobile device. The controller 114 is adapted for receiving and processing the corresponding signals and is adapted for providing a pain indication signal which is a function of the corresponding signals. An indicator 116 is adapted to be responsive to the controller 114 for providing an indication which is indicative of the pain indication signal pain signal such as a signal indicative of measured pain or indicative of a surrogate of pain symptoms. [Herein, the pain indication signal is also referred to as a pain signal.] A power supply 118 supplies power to the system.

[0040] A motion sensor 120 is adapted for sensing a motion of the person. The motion sensor 120 generates a motion signal indicative of the sensed motion. The controller 114 is adapted for receiving and processing the motion signal and is adapted providing the pain signal as a function of the motion signal and as a function of the corresponding signals. The indicator 116 may be driven by the circuit(s) 110 and/or by the controller 114. In one form, the controller is a processor having a memory device 122 storing computer executable instructions for calculating the pain signal and wherein the processor is adapted to execute the instructions.

[0041] In one exemplary optional form, a method for measuring pain of a person is described. The method is for use with the tissue of the person, and comprises:

illuminating the tissue of the person;

sensing light emitted or reflected by the tissue of the person;

generating a light signal indicative of a light parameter of the sensed light;

sensing an electrical parameter of the tissue of the person;

generating an electrode signal indicative of an electrical parameter of the sensed electrical parameter;

sensing a temperature of the tissue of the person;

generating a temperature signal indicative of the sensed temperature;

processing the light signal, the electrode signal and the temperature signal and providing a pain signal which is a function of the processed signals; and

providing an indication which is indicative of the pain signal.

[0042] The phrase measuring pain as used in this document is in reference to measuring one or more parameters that are reflective of pain. As doctors will understand, the device does not measure pain per se but measures one or more parameters that are reflective of pain and directly related to a level of pain.

[0043] In one exemplary optional form, the motion sensor comprises at least one of an accelerometer; a GPS sensor; and a gyroscope.

[0044] In one exemplary optional form, the light source comprises at least one of: a light source emitting light having a frequency in the range of near infrared wavelengths (e.g., about 1014 Hz; about 1000nm in wavelength); an LED (light emitting diode); an LED emitting visible light; and an LED emitting light having a frequency in the range of infrared wavelengths (e.g., between 1011 to 1015 Hz; between 1000nm to 1 cm in wavelength).

[0045] In one exemplary optional form, the optical sensor comprises at least one of: a photodetector; and a light sensitive element and the light parameters comprise at least one of: light intensity; light frequency; light wavelength; and a light emitting pattern (chirp pattern).

[0046] In one exemplary optional form, the surface electrode comprises at least one of: an electrode (e.g., a wet electrode, an AG/AGCL Electrode (Lead), or a dry electrode such as metal probes adapted to contact the tissue); and conductive elements adapted to contact the tissue.

[0047] In one exemplary optional form, the electrical parameters comprise at least one of: voltage; current; resistance; capacitance; inductance; impedance; and charge.

[0048] In one exemplary optional form, the temperature sensor comprises at least one of: a resistive temperature sensitive element; a bi-metallic element; and a MEMS temperature sensor.

[0049] In one exemplary optional form, the one or more circuits comprise: an analog to digital circuit; a signal conditioning circuit; a filtering circuit; and hardware and drivers for optical transceivers in both normal and chirp modulation modes.

[0050] In one exemplary optional form, the light source, the optical sensor, the surface electrode, the temperature sensor and the one or more circuits comprise one unitary, integrated component and the controller is a separate, unitary, integrated component and further comprising a wireless link between the controller and the one or more circuits.

[0051] In one exemplary optional form, the light source, the optical sensor, the surface electrode, the temperature sensor, the one or more circuits, the power supply and the controller comprise one unitary, integrated component.

[0052] In one exemplary optional form, the indicator comprises at least one of: one or more LEDs; an LCD device; a screen; and a set of LEDs operating in visible wavelength as indicators of hemodynamic change rate and/or pain level.

[0053] In one exemplary optional form, the controller comprises a processor having a memory device storing computer executable instructions which estimate hemodynamic parameters and wherein the processor is adapted to execute the instructions.

[0054] In one exemplary optional form, the hemodynamic parameters comprise at least one of the following: hemoglobin oxygenation; hemoglobin deoxygenation; heart rate; respiration rate; forehead and/or body temperature; and forehead and/or body impedance.

[0055] In one exemplary optional form, the controller comprises a processor having a memory device storing computer executable instructions wherein the processor processes the received, corresponding signals according to at least one of the following: instructions for an algorithm to compute the pain signal based on hemodynamic parameters and hemodynamic response to external and/or internal stimulus in real-time or near real-time; instructions for comparing the signals to a reference (history of hemodynamic parameters and hemodynamic response; and instructions for scaling the hemodynamic response to the range of [0, 10].

[0056] In one exemplary optional form, the instructions for the algorithm executed by the processor comprises instructions for fusing over a preset time interval a plurality of samples of a magnitude of the light signal LS, the electrode signal ES, and the temperature signal TS, adjusted by preset weights a, b, and c, to compute a pain indicative signal PS corresponding to a fused signal according to the following:

$$\text{Fused Signal} = \Sigma\ (a*LS + b*ES + c*TS).$$

[0057] In another exemplary optional form, the instructions for the algorithm executed by the processor comprises instructions for using over a preset time interval a plurality of samples of a magnitude of a light pain signal LPS indicative of a pain level, an electrode pain signal EPS indicative of a pain level, and a temperature pain signal TPS indicative of a pain level, adjusted by preset weights a, b, and c, to compute an estimated pain indicative signal PS corresponding to a fused signal according to the following:

$$\text{Fused Signal} = \Sigma\ (a*LPS + b*EPS + c*TPS).$$

[0058] In one exemplary optional form, the instructions for the algorithm executed by the processor comprises instructions for summing over a preset time interval of a plurality of samples of a magnitude of the light signal LS, the electrode signal ES and the temperature signal

TS, wherein each sample is compared to preset ranges and the magnitude of the signals is adjusted according to a relationship between each signal and the preset ranges.

[0059] In one exemplary optional form, the instructions comprise instructions for inputting personal input into the controller by an input device such as a keypad or keyboard, the personal input including conditions and/or environments of the person and wherein the pain signal is coordinated with the personal input whereby improved person pain management is provided.

[0060] In one exemplary optional form, the personal input includes a level of consciousness indicator, such as:

0 Awake;

2 Light/Moderate Sedation;

4 General Anesthesia;

6 Deep Hypnotic State;

8 Burst Suppression; and

10 Fully unconscious.

[0061] In one exemplary optional form, the controller processes at least one of the corresponding signals according to chirp based optical modulation.

[0062] In one exemplary optional form, the optical sensor comprises a blood oxygenation sensor for sensing a blood oxygenation of the person and wherein the chirp based optical modulation by the processor comprises measuring the light signal in different wavelengths as indicative of blood oxygenation.

[0063] In one exemplary optional form, the chirp based optical modulation comprises varying a carrier frequency in optical modulation over time to mimic hemodynamic response in different wavelengths over time to detect hemodynamic response recursively over time in a serial (recursive) approach.

[0064] In one exemplary optional form, the controller calculates respirations and heart rate by evaluating different frequency components in raw sensor data from the optical sensor.

[0065] In one exemplary optional form, a respiratory signal has a frequency component of the raw data [2-5Hz] which can be extracted using a band pass frequency with cut off [2-5Hz], and wherein the processor evaluates frequency components of 5-100Hz to obtain heart rate.

[0066] In one exemplary optional form, the controller comprises a processor having a memory device storing computer executable instructions comprising machine learning techniques and wherein the processor is adapted to execute the instructions, wherein the machine learning techniques include at least one of: adaptive and non-adaptive noise cancelation of noise in the signals; signal Envelope Detection; low pass, band-pass, band-stop and high pass digital filters to extract different hemodynamic parameters from sensor data spectrum; and supervised or unsupervised clustering including at least one of k-means, fuzzy c-means artificial neural networks, support vector machine, fuzzy systems to characterize hemodynamic response across different persons (persons) and across days (inter and intra subject variability characterization).

[0067] In one exemplary optional form, the controller calibrates the system using a baseline wander correction algorithm based on at least one of adaptive or non-adaptive filtering.

[0068] In one exemplary optional form, data is provided to the controller indicative of feedback from a person to train the controller or set a range.

[0069] In one exemplary optional form, the data comprises subjective pain measurements from the person synchronized with pain indicator measurements by the system, wherein the subjective pain measurement comprise:

0-1 No pain;

2-3 Mild pain;

4-5 Discomforting - moderate pain;

6-7 Distressing - severe pain;

8-9 Intense - very severe pain;

10 Unbearable pain.

[0070] In one exemplary optional form, the controller synchronizes objective hemodynamic parameters of the sensor signals with subjective measurements provided by the person so that the sensor and person or a physician establishes communication and coordination between the sensors and the person or physician.

[0071] In one exemplary optional form, the controller generates commands to which the person responds to at a particular point to define a baseline. For example, the device will continuously or at programmed intervals ask the person to respond to the device by defining his subjective pain level through a mobile phone or other communication interface. As a result, the device/system is capable of calibrating/coordinating its objective measurements with the

person's subjective measurements. This process will also help with baseline creation so that the objective and subjective pain levels correlate at the moment in time.

[0072] In one exemplary optional form, the controller is responsive to a person or physician to trigger the hemodynamic monitor to make measurements and define a baseline.

[0073] In one exemplary optional form, a person indicates his/her pain status among environmental parameters to train the device for threshold definition.

[0074] In one exemplary optional form, the device communicates with the persons regarding its pain status in order to define a baseline and threshold for device training and personalization.

[0075] In one exemplary optional form, the system is configured to be implantable within a person. One device variation could be a single patch placed on the person forehead, head, or neck. Another optional variation could be multiple sensors being placed on the forehead or circumference of the head similar to a bandana. Yet another optional variation of the device and method could be an implantable device with sensors and battery and wireless operation that can be continuous or activated by mobile phone or any other activator to activate the sensor for a programmed period of time and transmit information to the receiver outside or inside the body. The implantable device could be rechargeable over the scalp. This implantable device could be implanted underneath hair in or underneath the scalp via a simple insertion like a hairpin or incision. The implantable device will be removable as well. Implantable device could have flat or other geometrical form factors to fit the person's head/scalp/skull. The receiver device could be a mobile phone, a hat, headband, or other similar form factors. The implantable device could be powered using an external power source such as an RF generator or coil-to-coil power generation where a capacitor in the device stores enough energy to perform a required measurement and transmission of the information.

[0076] In further detail, referring to FIG. 2, the Real-Time Tracking of Cerebral Hemodynamic Response (RTCHR) system 100 includes three stages. A first stage 202 employs a sensor unit for recording data. The sensor unit includes, for example, a surface electrode and optical sender/receiver LEDs, an accelerometer, a GPS, and temperature sensors. The sensor data are processed and properly conditioned in the next stage 204 and then, with a wired or wireless transmission unit, the sensor data are transferred at a third state 206 to a control for further processing (e.g., advance real-time signal processing and machine learning) to estimate hemodynamic response changes due to external/internal stimulus (anesthesia, pain, and the like), heart rate, respiration and other parameters. The advance real-time signal processing stage

includes real-time denoising, baseline wander removal, extraction of different band of sensor data related to heart pulse, respiration and/or cerebral hemodynamic response trace based on frequency domain filtering envelop detection and real-time source separations. To estimate hemodynamic response change over time some statistical and morphological features such as norm, root-mean-square, skewness, kurtosis, entropy, and the like are extracted and input to a real-time machine learning stage to compare blood oxygen consumption pattern between present and past. Also, machine learning based predictive models can be used to predict onset of pain in the close future in pain management applications.

[0077] The advantage of the current invention as compared to other digital interfaces is that in one embodiment of the invention a single forehead patch can be used to estimate hemodynamic parameters using a new optical modulation which makes it different compared to current optical sensing such as oximetry and functional near-infrared (INIR) technology devices, such as shown in FIG. 3A. FIG. 3A illustrates on the left a graph of the absorption of spectra of oxy-Hb and deoxy-Hb in the near infrared range (the three graphical lines illustrate HbO_2, Hb, and water, from left to right). FIG. 3A on the right illustrates the path of light on a human head from emitter to detector. A chirp signal such as illustrated in FIG. 3B is used to emit light with different wavelengths in red and near infra-red ranges. By use of chirp modulation according to the invention, tracking of hemodynamic response changes will be maximized and RTCHR provides a new class of optical sensing compared to oximetry and spectroscopy.

[0078] Chirp based optical modulation according to one aspect of the invention measures blood oxygenation in different wavelengths. In chirp modulation, a carrier frequency in optical modulation varies over time to mimic hemodynamic response in different wavelengths over time. In contrast, in oximetry, only two wavelengths are used and in NIR spectroscopy a set of optical senders and receivers are used to get hemodynamic responses over different wavelengths in parallel. Chirp based optical modulation according to one aspect of the invention detects hemodynamic response recursively over time. Since hemodynamic response is slow, the system detects hemodynamic responses over different wavelengths in a serial (recursive) approach. Modulation pattern and number and range of frequency (wavelength) modulation can be controlled by a person at software level, but hardware for chirp modulation may also be used to implement control. For instance, a person could take two wavelengths readings, one in red field and another in near-infra red. On this case, the device acts as a pulse oximeter. In other words, the system with its novel recursive modulation ability can induce any pattern including two wavelength readings (oximeter mode) or chirp mode (multiple wavelengths reading).

[0079] It is noteworthy that the single forehead patch could include several of the hemodynamic and other sensors for multiple measurements across different locations on the forehead or the brain.

[0080] A typical application for RTCHR system 100 and method according to the invention provide objective pain level assessment. Currently in clinics, persons are asked to score their pain level to a number between 0-10: 1-3: mild pain, 4-7 moderate pain and 8-10 sever pain. The system 100 and its method are capable of estimating pain level by tracking hemodynamic baselines and/or changes in response to internal/external pain stimulus. For example, in one embodiment, previous sensor readings from few minutes and/or hours ago are used as baseline hemodynamic response and the current sensor reading is compared with the history of data to determine level of deviation. Alternatively and in addition, a baseline could be arbitrary. If a nurse, doctor, or the person starts baseline recording at a certain point in time or under certain conditions, this also could be considered baseline. The device/system will allow a person (e.g., person, doctor, technician) to choose and set up a certain condition as "baseline". Yet, when an infant cries or is in stress due to pain, the higher level or threshold could be considered baseline, too, not necessarily the lowest measurement. Thus, a baseline is a reference, either arbitrary or defined.

[0081] In general, a baseline is a reference point. For example, a baseline may be established in several ways. 1) When the subject is in a normal state or in pain. In a normal state, any increase in pain is tracked; in a pain state, increases or decrease in pain due to therapy are tracked. 2) In a situation where there is previous data from a person, the data may be used to establish a baseline, such as body temperature or blood pressure. For example, one day data could be used to establish a normal range of body temperature.

[0082] To demonstrate the ability of RTCHR to estimate pain levels, subject data using the forehead patch as shown in FIG. 1, before, during and after an external pain stimulus (e.g., sever cold, heat and sharp pains) were recorded. FIGs. 5-8 illustrate the recorded data, showing the hemodynamic changes in response to external and internal pain stimulus. The Y-axis is an estimated pain level (1st norm scaled to 0-10) per second for first and second subplots and per 10 second for the third subplot. Fig. 4 illustrates the period of time during which the assessments of Figs. 5-8 were taken.

[0083] FIG. 5 illustrates graphs of Objective Pain Level Assessment: hemodynamic changes in response to external severe cold pain stimuli. Levels 1-10 during the first 20 seconds illustrate the baseline. Levels 11-20 during the next 20 seconds illustrate the response during

pain stimulus. Levels 21-30 during the last 20 seconds illustrate the response during recovery after pain stimulus has ended.

[0084] FIG. 6 illustrates graphs of Objective Pain Level Assessment: hemodynamic changes in response to external severe heat pain stimuli. Hemodynamic response did not return to baseline due to continued burning sensation. Levels 1-10 during the first 20 seconds illustrate the baseline. Levels 11-20 during the next 20 seconds illustrate the response during pain stimulus. Levels 21-30 during the last 20 seconds illustrate the response during recovery after pain stimulus has ended.

[0085] FIG. 7 illustrates graphs of Objective Pain Level Assessment: hemodynamic changes in response to external severe sharp pain stimuli. Levels 1-10 during the first 20 seconds illustrate the baseline. Levels 11-20 during the next 20 seconds illustrate the response during pain stimulus. Levels 21-30 during the last 20 seconds illustrate the response during recovery after pain stimulus has ended.

[0086] FIG. 8 illustrates graphs of Objective Pain Level Assessment: hemodynamic changes in response to internal severe back pain stimuli. Subject with back pain was asked to twist his back to temporarily increase pain level. Levels 1-10 during the first 20 seconds illustrate the baseline. Levels 11-20 during the next 20 seconds illustrate the response during pain stimulus. Levels 21-30 during the last 20 seconds illustrate the response during recovery after pain stimulus has ended.

[0087] The RTCHR system 100 and its method also provide heart and respiration rates. FIG. 9 illustrates graphs of heart and respiration rate Estimation: The derivative of forehead pulse can be used to estimate Heart and respiration rates. Figure 9 shows a typical forehead pulse and estimated heart and respiration rates. To calculate respiration and heart rate, the processor evaluates different frequency components in raw sensor data from the optical sensor. A respiratory signal is a frequency component of the raw data [2-5Hz] which can be extracted using a band pass frequency with cut off [2-5Hz]. To get heart rate, the processor evaluates frequency components of 5-100Hz.

[0088] Heart rate and/or respiration rate can be measured or calculated manually or automatically. In one embodiment, respiration rate and heart rate signals can be extracted from a light signal and/or surface electrode signal and for analysis according to at least some embodiments of the systems and methods of the invention.

[0089] Another application for RTCHR is in the area of sensation as associated with brain activity. Images in movies and photos can generate empathic pain. Subjects shown a

series of images or movies with injuries or other pain related events have reported definite pain to at least one image of movie. It has been determined that subjects who report pain in response to such images activate pain matrix regions in the brain, which are responsible for generating pain. Therefore, observing painful images modulates motor responses, which suggest sensorimotor involvement. For example, a person reported feeling physical pain when observing his wife experience superficial pain. Various types of pain have been measured, for instance, somatic pain (e.g., tingling, aching, sharp, shooting, throbbing, sickening, splitting, heavy, stabbing, and tender types of pain have been described) and visceral pain. Further, rCBF response to heighted unpleasantness has been recorded. Pain activates a large amount of neural tissue. However, understanding chronic pain is unresolved. Imaging studies have illustrated that chronic pain is associated with functional, structural and chemical changes in the brain; however, it is not known how neural activity is translated into a feeling. Areas of the brain that are usually active provide for pain inhibition, and a lack of pain inhibition causes chronic pain. In addition, dysfunctional psychological processing changes underlying patterns of brain activation and causes chronic pain. Typically, pain is reported by asking subjective questions of persons and not by imaging anatomic information and determining the activation of brain distress centers. RTCHR may be used to better evaluate and understand these aspects.

[0090] Studies have been made using a functional Magnetic Resonance Imaging ("fMRI") scanner to study pain. The fMRI records the variable magnetic property of tissue. For instance, fMRI scanning has been utilized during the presentation of real noxious heat stimuli, as well as during the suggestion of a real noxious heat stimuli to a set of eight subjects. All the subjects reported a sensation of at least heat during the suggestion and five reported pain. In addition, fMRI can determine the Blood Oxygen Level Dependent (BOLD) signal, which measures an "effect parameter". However, a disadvantage of using BOLD is that the signal changes are small making the analysis difficult, tedious and complicated, requiring significant subjectivity. RTCHR may be used to better evaluate and understand these aspects.

[0091] fMRI has been used to study empathetic pain. For instance, ten pain responders and ten non-responders acting as controls were give a set of pain images and a set of emotional images. Using fMRI the anterior midcingulate cortex ("aMCC") was monitored. The responders consistently activated aMCC, anterior insula, prefrontal cortex and primary (S1) and secondary (S2) somatosensory cortex for all pain images and emotional images. In contrast, the non-responders consistently activated aMCC and prefrontal cortex but failed to activate insula, S1 or S2. Therefore, regional activation is specifically and actively involved in the generation of

pain, and empathetic pain appears to involve the same mechanism. For example, using hypnosis one can direct generation of pain via the usual pain neuromatrix. Once again, RTCHR may be used to better evaluate and understand these aspects. Instead of using fMRI, applying RTCHR provides objective measurements hemodynamic response, heart and respiration rates, to determine and predict the onset of pain.

[0092] It is known that brain lesions can cause pain. In addition, it is known that newborns have an exaggerated sensitivity to touch that diminishes with maturity. Further, it has been determined that blocking descending inhibition in animals causes hyperalgesia. Thus it is possible that functional pain is caused by a disruption to descending inhibition. fMRI has also been used to study offset analgesia. Offset analgesia is the perception of profound analgesia during a slight incremental decrease of a noxious heat stimulus that is more pronounced than would be predicted by the rate of the temperature decrease. Offset analgesia is an active process probably involving descending inhibitory mechanisms to modulate pain. Using fMRI, twelve control subjects, free of neurological disorder and chronic pain, completed an offset analgesia procedure. They completed the offset procedure six times; twice at each temperature (high, medium, and low). The results indicated that: 1) during baseline, there is little pain and little activation; 2) during constant, there is pain and plenty of pain activation; and 3) during offset there is less pain and little activation. Therefore, one can conclude that normal controls can be induced to feel pain without any physically noxious stimulus. Functional pain person might generate pain in a similar fashion. Also, normal controls can be induced to feel a noxious stimulus as less painful without any physical change in the stimulus. Therefore, functional pain persons may lack endogenous analgesic mechanisms such as offset analgesia. RTCHR may be used to better evaluate and understand these aspects.

[0093] It is possible to utilize a device of the invention to measure issues with brain development in neonates. Some neonates have problems with normal development of the brain and the device is helpful to detect and report such issues despite whether the neonate feels pain or not. For example, a “normal” level of sensor measurement expected in a larger group of neonates (expected baseline data) can be used as a baseline to compare to other neonates who have severe deviation from the baseline. In addition, the device may be used for cerebral monitoring such as a particular brain function monitoring instead of the pain application. For example, the device in at least certain persons may indicate or detect early onset of epilepsy or another brain related issues (e.g., Alzheimer, Parkinson’s, brain tumors). Thus, the device may be used to capture early onset of epilepsy or another brain related issues in an inexpensive and

ambulatory way by use of a single patch on a forehead or a person or at other locations on the body. In this context, the pain signal comprises a cerebral monitoring signal.

[0094] It is also contemplated that the device may be used by athletes for performance enhancement as it relates to cerebral flow and pain perception.

FEEDBACK

[0095] In one aspect, feedback from the person may be used to train the system 100 or set a range. Also, a person may choose which days/time should be compared with current time [reference point and baseline setting]. Also, a person's subjective pain level can be compared with objective (automated) pain assessment. This is called interactive pain. Enabled with artificial intelligence and real-time learning mode, this applies self-tuning, particularly when there is a large difference between objective and subject pain levels.

OXIMETER/DEVICE COMBINATION

[0096] In one embodiment, a pulse oximeter can be modified to also provide a cerebral hemodynamic tracking system according to the invention to measure pain, trauma, epilepsy, level of consciousness, attention monitoring and other brain related applications. For example, the pulse oximeter is modified to detect a light signal, an electrical parameter electrode signal and a temperature signal. In addition, the firmware of pulse oximeter is updated to have access to raw data from LEDs and apply an algorithm for generating a pain signal which is a function of the corresponding signals and for providing an indicator indicative of the pain signal.

CALIBRATION

[0097] In one form, baseline wander correction algorithms (based on adaptive or non-adaptive filtering techniques) may be used to perform self-calibration and to account for sensor data drift coming from hardware and/or human condition changes such as sweating or motion.

[0098] Another application of at least some embodiments of the device or method of the invention is in various product configurations for the OBGYN applications. For example, a consumer patch and a smart phone app could be used to track uterus contractions prior to childbirth. In today's environment, expectant mothers have to record the frequency of the uterus contractions and keep a record with a timer in hand. Once contractions happen too closely, it will be time to attend a clinic or hospital for child delivery. So often expectant mothers miss the

true contraction frequency and associated pain level. Uterus contractions cause proportional pain. At least some embodiments of the device or method of the invention attached to the forehead could keep track of the pain associated with the uterus contractions and maintain a concise time and pain amplitude profile without a subject's intervention. As a result, at least some embodiments of the device or method of the invention could advise the subject when to attend to the clinic while simultaneously transmitting the complete contraction profile to the clinic or the attending doctors prior to arrival.

[0099] At least some embodiments of the device or method of the invention could be used for epidural pain management to measure pain and automatically administer pain medication.

[00100] At least some embodiments of the device or method of the invention could be used for post childbirth pain management in natural or C-section type childbirth where pain management is a major issue. All data collected can be integrated into a patient profile at the hospital EMR.

[00101] Yet another application could be a handheld device for tracking children pain due to teething or other painful situations to assist parents in managing children or infant pain. At least some embodiments of the device or method of the invention could be similar to a handheld thermometer with memory. Routine baseline measurements can be recorded. Once the infant is in a stressful situation and crying for no apparent reason, parents can place the device on the forehead for a period of time to measure if pain is present. At least some embodiments of the device or method of the invention could be be used on neonates at the hospitals or non-responders in ICU and nursing homes.

[00102] Yet another application is in post-surgery where a patient's pain is being managed by a PCA (patent controlled analgesia) infusion pump. Many post-surgery cases involve keeping a patient at a hospital for 3-7 days, connected to a PCA pump where the patient controls the amount of pain medication delivery. While this is very efficient compared to a preset infusion rate, in many situations when a patient falls sleep for 8-12 hours, the lack of pain management leads to adverse events such as inflammation or other causes of chronic pain. In these situations, if the acute pain is not treated properly, it can translate to chronic pain which is inconvenient to the patient and costly the healthcare system.

[00103] At least some embodiments of the device or method of the invention could be programmed to either administer a drug by instructing the infusion to deliver more medication, wake the patient up by sound or other stimulus, or send a notification to the nursing station.

Therefore, pain is managed continuously even when patients are sleep. All data from the device will be integrated into the hospital EMR.

[00104] Yet another application is in pain medication drug discovery. Pain medication drug discovery today is a cumbersome process. During clinical trials, a patient is asked for a subjective pain level in order to learn if the drug is effective. So often this type of drug discovery leads to failure due to a placebo effect or improper subjective pain level reporting. Utilizing at least some embodiments of the device or method of the invention, a majority of the ambiguity in pain drug discoveries could be resolved. Companies also can receive real-time effect of their newly developed pain medications from subjects and patients enrolled in clinical trials in real-time.

[00105] Yet another variation of At least some embodiments of the device or method of the invention could be to identify and diagnose other neurological disorders such as onset or prediction of bipolar disorder, mood change, schizophrenia, and/or depressions.

[00106] The Abstract and summary are provided to help the reader quickly ascertain the nature of the technical disclosure. They are submitted with the understanding that they will not be used to interpret or limit the scope or meaning of the claims. The summary is provided to introduce a selection of concepts in simplified form that are further described in the Detailed Description. The summary is not intended to identify key features or essential features of the claimed subject matter, nor is it intended to be used as an aid in determining the claimed subject matter.

[00107] For purposes of illustration, programs and other executable program components, such as the operating system, are illustrated herein as discrete blocks. It is recognized, however, that such programs and components reside at various times in different storage components of a computing device, and are executed by a data processor(s) of the device.

[00108] Although described in connection with an exemplary computing system environment, embodiments of the aspects of the invention are operational with numerous other general purpose or special purpose computing system environments or configurations. The computing system environment is not intended to suggest any limitation as to the scope of use or functionality of any aspect of the invention. Moreover, the computing system environment should not be interpreted as having any dependency or requirement relating to any one or combination of components illustrated in the exemplary operating environment. Examples of well known computing systems, environments, and/or configurations that may be suitable for

use with aspects of the invention include, but are not limited to, personal computers, server computers, hand-held or laptop devices, multiprocessor systems, microprocessor-based systems, set top boxes, programmable consumer electronics, mobile telephones, network PCs, minicomputers, mainframe computers, distributed computing environments that include any of the above systems or devices, and the like.

[00109] Embodiments of the aspects of the invention may be described in the general context of data and/or processor-executable instructions, such as program modules, stored one or more tangible, non-transitory storage media and executed by one or more processors or other devices. Generally, program modules include, but are not limited to, routines, programs, objects, components, and data structures that perform particular tasks or implement particular abstract data types. Aspects of the invention may also be practiced in distributed computing environments where tasks are performed by remote processing devices that are linked through a communications network. In a distributed computing environment, program modules may be located in both local and remote storage media including memory storage devices.

[00110] In operation, processors, computers and/or servers may execute the processor-executable instructions (e.g., software, firmware, and/or hardware) such as those illustrated herein to implement aspects of the invention.

[00111] Embodiments of the aspects of the invention may be implemented with processor-executable instructions. The processor-executable instructions may be organized into one or more processor-executable components or modules on a tangible processor readable storage medium. Aspects of the invention may be implemented with any number and organization of such components or modules. For example, aspects of the invention are not limited to the specific processor-executable instructions or the specific components or modules illustrated in the figures and described herein. Other embodiments of the aspects of the invention may include different processor-executable instructions or components having more or less functionality than illustrated and described herein.

[00112] The order of execution or performance of the operations in embodiments of the aspects of the invention illustrated and described herein is not essential, unless otherwise specified. That is, the operations may be performed in any order, unless otherwise specified, and embodiments of the aspects of the invention may include additional or fewer operations than those disclosed herein. For example, it is contemplated that executing or performing a particular operation before, contemporaneously with, or after another operation is within the scope of aspects of the invention.

[00113] When introducing elements of aspects of the invention or the embodiments thereof, the articles "a," "an," "the," and "said" are intended to mean that there are one or more of the elements. The terms "comprising," "including," and "having" are intended to be inclusive and mean that there may be additional elements other than the listed elements.

[00114] In view of the above, it will be seen that several advantages of the aspects of the invention are achieved and other advantageous results attained.

[00115] Not all of the depicted components illustrated or described may be required. In addition, some implementations and embodiments may include additional components. Variations in the arrangement and type of the components may be made without departing from the spirit or scope of the claims as set forth herein. Additional, different or fewer components may be provided and components may be combined. Alternatively or in addition, a component may be implemented by several components.

[00116] The above description illustrates the aspects of the invention by way of example and not by way of limitation. This description enables one skilled in the art to make and use the aspects of the invention, and describes several embodiments, adaptations, variations, alternatives and uses of the aspects of the invention, including what is presently believed to be the best mode of carrying out the aspects of the invention. Additionally, it is to be understood that the aspects of the invention is not limited in its application to the details of construction and the arrangement of components set forth in the following description or illustrated in the drawings. The aspects of the invention are capable of other embodiments and of being practiced or carried out in various ways. Also, it will be understood that the phraseology and terminology used herein is for the purpose of description and should not be regarded as limiting.

[00117] Having described aspects of the invention in detail, it will be apparent that modifications and variations are possible without departing from the scope of aspects of the invention as defined in the appended claims. It is contemplated that various changes could be made in the above constructions, products, and methods without departing from the scope of aspects of the invention. In the preceding specification, various preferred embodiments have been described with reference to the accompanying drawings. It will, however, be evident that various modifications and changes may be made thereto, and additional embodiments may be implemented, without departing from the broader scope of the aspects of the invention as set forth in the claims that follow. The specification and drawings are accordingly to be regarded in an illustrative rather than restrictive sense.

CLAIMS:

What is claimed is:

1. A system for providing an indication of pain of a person such as measuring pain or a surrogate of pain symptoms of a person, said system for use with the tissue of the person, said system comprising:

A light source adapted for illuminating the tissue of the person;

An optical sensor adapted for sensing light emitted or reflected by the tissue of the person, said optical sensor generating a light signal indicative of a light parameter of the sensed light;

A surface electrode adapted for sensing an electrical parameter of the tissue of the person, said surface electrode generating an electrode signal indicative of an electrical parameter of the sensed electrical parameter;

A temperature sensor adapted for sensing a temperature of the tissue of the person, said temperature sensor generating a temperature signal indicative of the sensed temperature;

One or more circuits adapted for receiving the light signal, the electrode signal, and the temperature signal and providing corresponding signals;

A controller adapted for receiving and processing the corresponding signals and adapted for providing a pain indication signal which is a function of the corresponding signals;

An indicator adapted to be responsive to the controller for providing an indication which is indicative of the pain indication signal; and

A power supply for supplying power to the system.

2. The system of claim 1 further comprising a motion sensor adapted for sensing a motion of the person, said motion sensor generating a motion signal indicative of the sensed motion; and wherein the controller is adapted for receiving and processing the motion signal and is adapted providing the pain indication signal as a function of the motion signal and as a function of the corresponding signals.

3. The system of claim 2 wherein the motion sensor comprises at least one of:

an accelerometer;

a GPS sensor; and

a gyroscope.

4. The system of claim 1 wherein the light source comprises at least one of:

A light source emitting light having a frequency in the range of near infrared wavelengths (e.g., about 10^{14} Hz; about 1000nm in wavelength);

An LED;

An LED emitting visible light; and

An LED emitting light having a frequency in the range of infrared wavelengths (e.g., between 10^{11} to 10^{15} Hz; between 1000nm to 1 cm in wavelength).

5. The system of claim 1 wherein the optical sensor comprises at least one of:

A photodetector; and

A light sensitive element.

6. The system of claim 1 wherein the light parameters comprises at least one of:

Light intensity;

Light frequency;

Light wavelength; and

A light emitting pattern (chirp pattern).

7. The system of claim 1 wherein the surface electrode comprises at least one of:

an electrode; and

Conductive elements adapted to contact the tissue.

8. The system of claim 1 wherein the electrical parameters comprises at least one of:

Voltage;

Current;

Resistance;

Capacitance;

Inductance;

Impedance; and

Charge.

9. The system of claim 1 wherein the temperature sensor comprises at least one of:

A resistive temperature sensitive element;

A bi-metallic element; and

A MEMS temperature sensor.

10. The system of claim 1 wherein the one or more circuits comprise:

An analog to digital circuit;

A signal conditioning circuit;

A filtering circuit; and

Hardware and drivers for optical transceivers in both normal and chirp modulation modes.

11. The system of claim 1 wherein the light source, the optical sensor, the surface electrode, the temperature sensor and the one or more circuits comprise one unitary, integrated component and the controller is a separate, unitary, integrated component and further comprising a wireless link between the controller and the one or more circuits.

12. The system of claim 1 wherein the light source, the optical sensor, the surface electrode, the temperature sensor, the one or more circuits, the power supply, and the controller comprise one unitary, integrated component.

13. The system of claim 1 wherein the indicator comprises at least one of:

One or more LEDs;

An LCD device;

A screen; and

A set of LEDs operating in visible wavelength as indicators of hemodynamic change rate and/or pain level.

14. The system of claim 1 wherein the controller comprises a processor having a memory device storing computer executable instructions which estimate hemodynamic parameters and wherein the processor is adapted to execute the instructions.

15. The system of claim 14 wherein the hemodynamic parameters comprise at least one of the following:
hemoglobin oxygenation;
hemoglobin deoxygenation;
heart rate;
respiration rate;
forehead and/or body temperature; and
forehead and/or body impedance.

16. The system of claim 1 wherein the controller comprises a processor having a memory device storing computer executable instructions wherein the processor processes the received, corresponding signals according to at least one of the following: instructions for an algorithm to compute the pain indication signal based on hemodynamic parameters and hemodynamic response to external and/or internal stimulus in real-time or near real-time; instructions for comparing the signals to a reference (history of hemodynamic parameters and hemodynamic response; and instructions for scaling the hemodynamic response to the range of [0, 10].

17. The system of claim 16 wherein at least one of the following:

the instructions for the algorithm executed by the processor comprises instructions for fusing over a preset time interval a plurality of samples of a magnitude of the light signal LS, the electrode signal ES, and the temperature signal TS, adjusted by preset weights a, b, and c, to compute a pain indicative signal PS corresponding to a fused signal according to the following: Fused Signal = Σ (a*LS + b*ES + c*TS); and

the instructions for the algorithm executed by the processor comprises instructions for using over a preset time interval a plurality of samples of a magnitude of a light pain signal LPS indicative of a pain level, an electrode pain signal EPS indicative of a pain level, and a temperature pain signal TPS indicative of a pain level, adjusted by preset weights a, b, and c, to compute an estimated pain indicative signal PS corresponding to a fused signal according to the following: Fused Signal = Σ (a*LPS + b*EPS + c*TPS).

18. The system of claim 16 wherein the instructions for the algorithm executed by the processor comprises instructions for summing over a preset time interval of a plurality of samples of a magnitude of the light signal LS, the electrode signal ES and the temperature signal TS, wherein

each sample is compared to a preset range and the magnitude of the signals is adjusted according to a relationship between each signal and the preset range.

19. The system of claim 1 further comprising instructions for inputting personal input into the controller by an input device such as a keypad or keyboard, said personal input including conditions and/or environments of the person and wherein the pain indication signal is coordinated with the personal input whereby improved person pain management is provided.

20. The system of claim 16 wherein the personal input includes a level of consciousness indicator, such as:
0 Awake;
2 Light/Moderate Sedation;
4 General Anesthesia;
6 Deep Hypnotic State;
8 Burst Suppression; and
10 Fully unconscious.

21. The system of claim 1 the controller processes at least one of the corresponding signals according to chirp based optical modulation.

22. The system of claim 1 wherein the optical sensor comprises a blood oxygenation sensor for sensing a blood oxygenation of the person and wherein the chirp based optical modulation by the processor comprises measuring the light signal in different wavelengths as indicative of blood oxygenation.

23. The system of claim 1 wherein the chirp based optical modulation comprises varying a carrier frequency in optical modulation over time to mimic hemodynamic response in different wavelengths over time to detect hemodynamic response recursively over time in a serial (recursive) approach.

24. The system of claim 1 wherein the controller calculates respirations and heart rate by evaluating different frequency components in raw sensor data from the optical sensor.

25. The system of claim 1 wherein a respiratory signal is a frequency component of the raw data [2-5Hz] which can be extracted using a band pass frequency with cut off [2-5Hz], and wherein the processor evaluates frequency components of 5-100Hz to get heart rate.

26. The system of claim 1 wherein the controller comprises a processor having a memory device storing computer executable instructions comprising machine learning techniques and wherein the processor is adapted to execute the instructions, wherein said machine learning techniques includes at least one of:
Adaptive and non-adaptive noise cancelation of noise in the signals;
Signal Envelope Detection;
Low pass, band-pass, band-stop and high pass digital filters to extract different hemodynamic parameters from sensor data spectrum; and
supervised or unsupervised clustering including at least one of k-means, fuzzy c-means artificial neural networks, support vector machine, fuzzy systems to characterize hemodynamic response across different persons (persons) and across days (inter and intra subject variability characterization).

27. The system of claim 1 wherein the controller calibrates the system using a baseline wander correction algorithm based on at least one of adaptive or non-adaptive filtering.

28. The system of claim 1 further comprising providing data to the controller indicative of feedback from a person to train the controller or set a range.

29. The system of claim 28 wherein the data comprises subjective pain measurements from the person synchronized with pain indicator measurements by the system, wherein the subjective pain measurement comprise:
0-1 No pain;
2-3 Mild pain;
4-5 Discomforting - moderate pain;
6-7 Distressing - severe pain;
8-9 Intense - very severe pain;
10 Unbearable pain.

30. The system of claim 1 wherein the controller synchronizes objective hemodynamic parameters of the sensor signals with subjective measurements provided by the person so that the sensor and person or a physician establish communication and coordination between the sensors and the person or physician.

31. The system of claim 1 at least one of the following:
wherein the controller generates commands to which the person responds to at a particular point to define a baseline;
wherein the controller is responsive to a person or physician to trigger the hemodynamic monitor to make measurements and define a baseline;
wherein a person indicates his/her pain status among environmental parameters to train the device for threshold definition; and
wherein the device communicates with the person regarding its pain status in order to define a baseline and threshold for device training and personalization.

32. The system of claim 1 wherein said system is configured to be implantable within a person.

33. The system of claim 1 said system is configured to measure at least one of the following:
pain associated with an addiction;
predict rising pain levels;
track uterus-related pain or uterus contractions;
epidural pain management;
post-childbirth pain management;
teething or other child-related pain;
post-surgery pain;
pain medication drug discovery; and
neurological disorders.

34. The system of claim 1 for use in combination with a PCA (patent controlled analgesia) infusion pump for controlling the delivery of medication to treat pain.

35. The system of claim 1 wherein the controller includes telemetry circuitry to communicate information indicative of the pain indicative signal to another device.

36. A method for providing an indication of pain of a person such as measuring pain or a surrogate of pain symptoms of a person, said method comprising:

illuminating the tissue of the person;

sensing light emitted or reflected by the tissue of the person;

generating a light signal indicative of a light parameter of the sensed light;

sensing an electrical parameter of the tissue of the person;

generating an electrode signal indicative of an electrical parameter of the sensed electrical parameter;

sensing a temperature of the tissue of the person;

generating a temperature signal indicative of the sensed temperature;

processing the light signal, the electrode signal and the temperature signal and providing a pain indication signal which is a function of the processed signals; and

providing an indication which is indicative of the pain indication signal.

37. A system for cerebral monitoring of a person, said system for use with the tissue of the person, said system comprising:

A light source adapted for illuminating the tissue of the person;

A optical sensor adapted for sensing light emitted or reflected by the tissue of the person, said optical sensor generating a light signal indicative of a light parameter of the sensed light;

A surface electrode adapted for sensing an electrical parameter of the tissue of the person, said surface electrode generating an electrode signal indicative of an electrical parameter of the sensed electrical parameter;

A temperature sensor adapted for sensing a temperature of the tissue of the person, said temperature sensor generating a temperature signal indicative of the sensed temperature;

One or more circuits adapted for receiving the light signal, the electrode signal, and the temperature signal and providing corresponding signals;

A controller adapted for receiving and processing the corresponding signals and adapted for providing a cerebral monitoring signal which is a function of the corresponding signals;

An indicator adapted to be responsive to the controller for providing an indication which is indicative of the cerebral monitoring; and

A power supply for supplying power to the system.

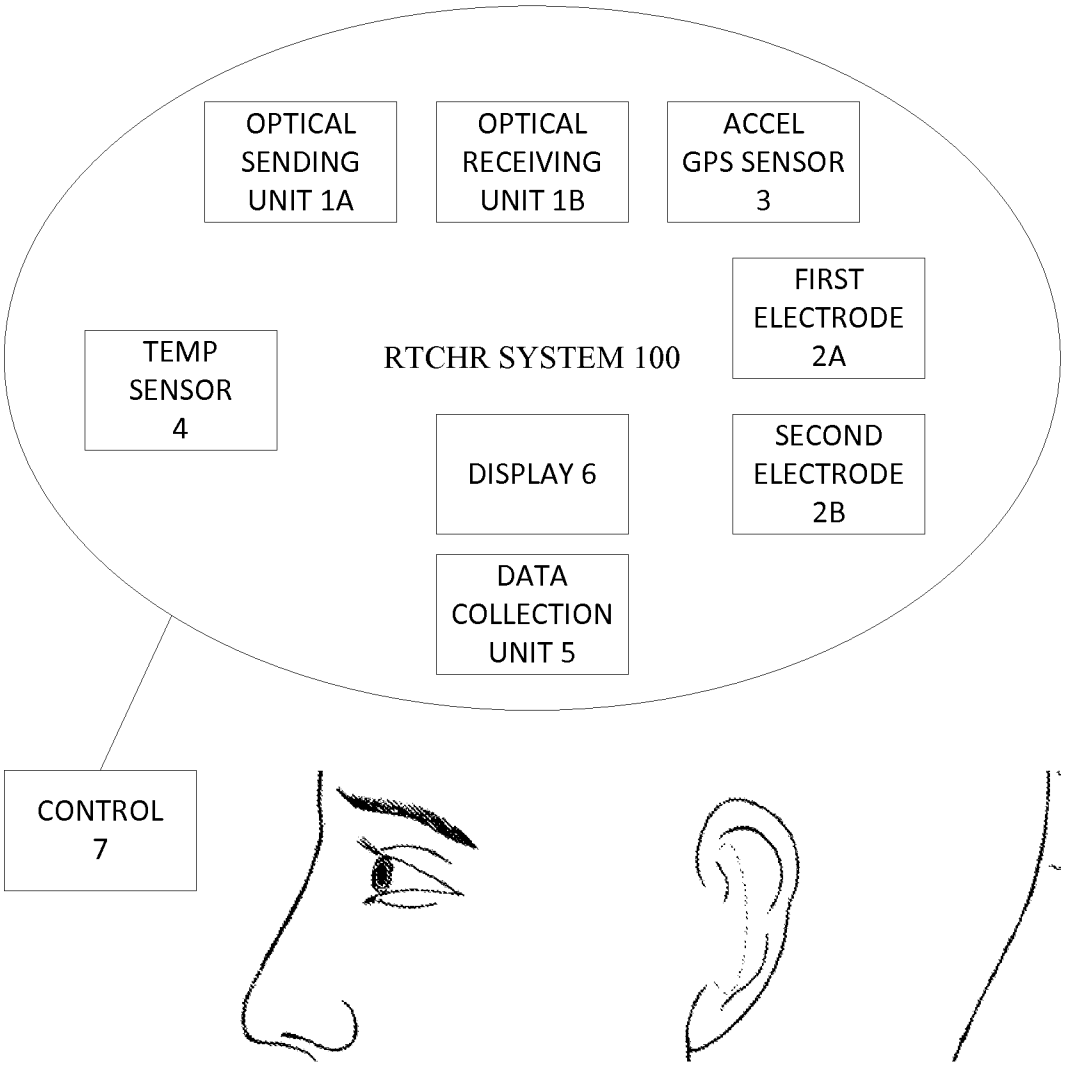

OPTICAL SENDING UNIT 1A
OPTICAL RECEIVING UNIT 1B
ACCEL GPS SENSOR 3
FIRST ELECTRODE 2A
TEMP SENSOR 4
RTCHR SYSTEM 100
DISPLAY 6
SECOND ELECTRODE 2B
DATA COLLECTION UNIT 5
CONTROL 7

FIG. 1

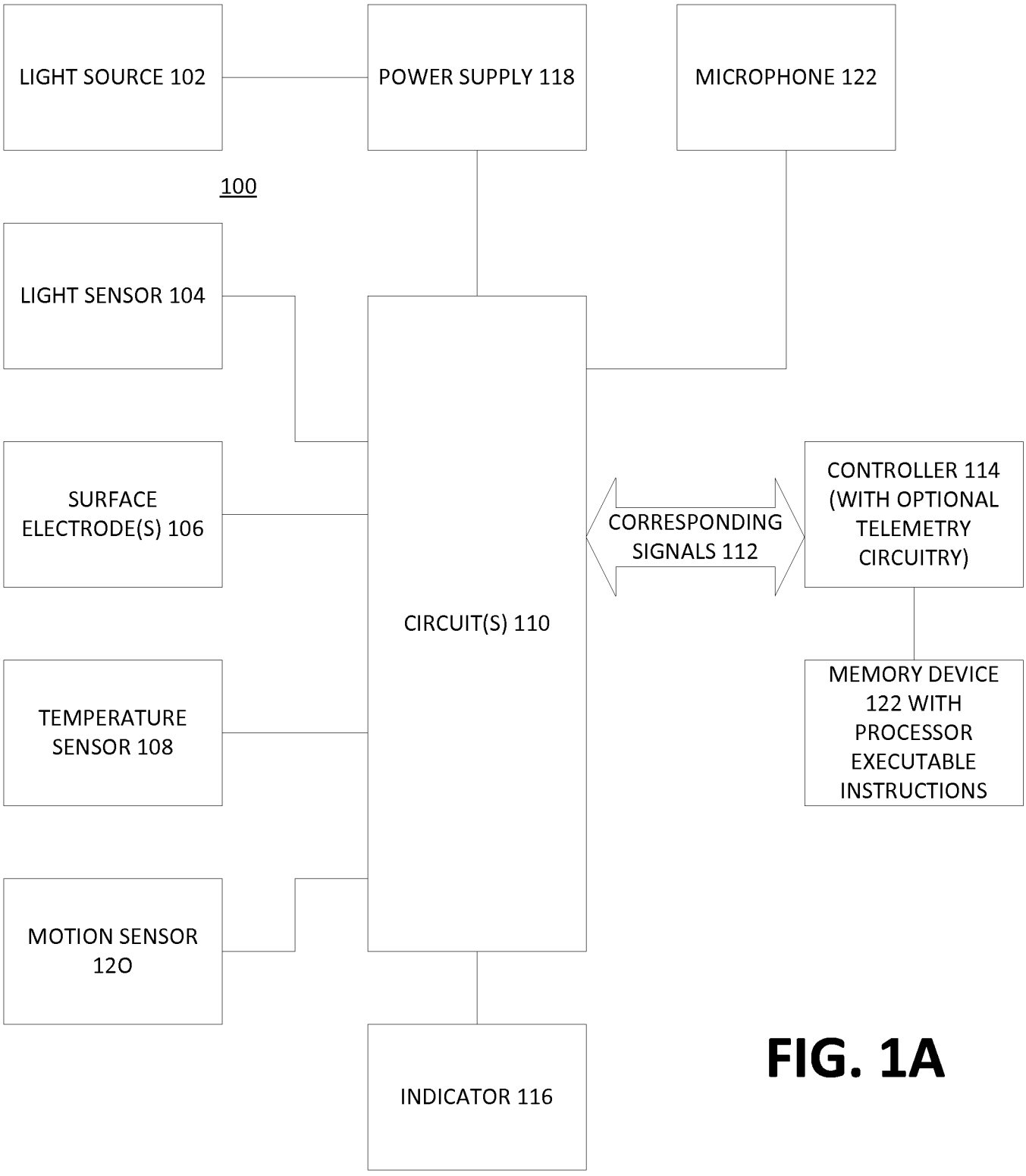

LIGHT SOURCE 102
POWER SUPPLY 118
MICROPHONE 122
100
LIGHT SENSOR 104
SURFACE ELECTRODE(S) 106
CIRCUIT(S) 110
CORRESPONDING SIGNALS 112
CONTROLLER 114 (WITH OPTIONAL TELEMETRY CIRCUITRY)
MEMORY DEVICE 122 WITH PROCESSOR EXECUTABLE INSTRUCTIONS
TEMPERATURE SENSOR 108
MOTION SENSOR 12O
INDICATOR 116

FIG. 1A

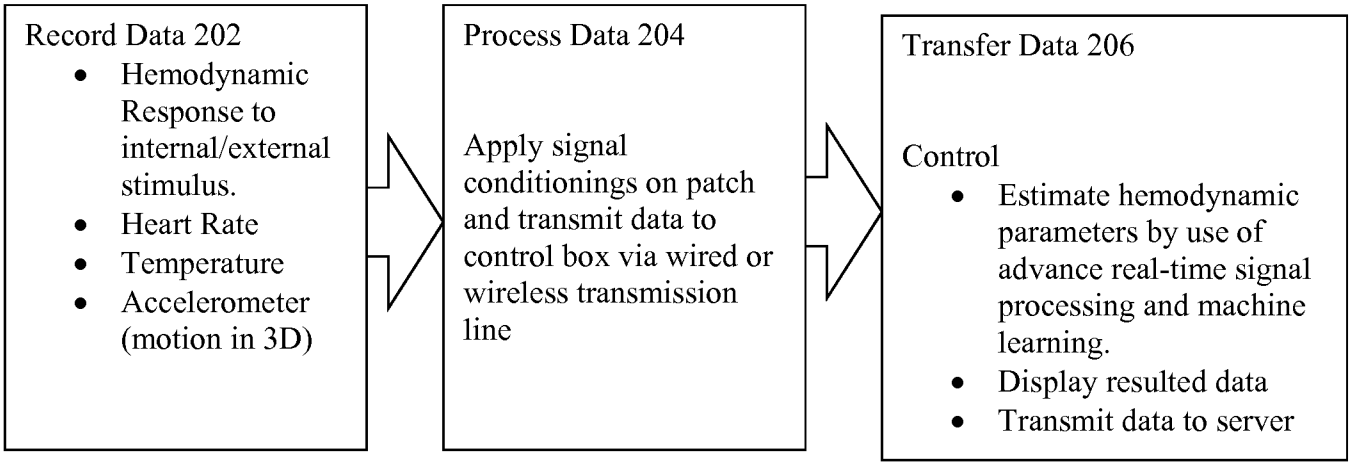
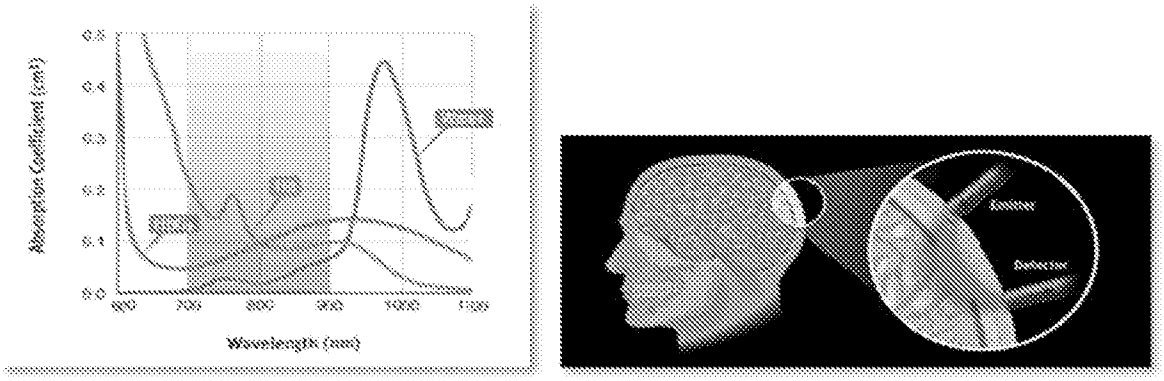

Record Data 202
Hemodynamic Response to internal/external stimulus.
Heart Rate
Temperature
Accelerometer (motion in 3D)
Process Data 204
Apply signal conditionings on patch and transmit data to control box via wired or wireless transmission line
Transfer Data 206
Control
Estimate hemodynamic parameters by use of advance real-time signal processing and machine learning.
Display resulted data
Transmit data to server

FIG. 2



Absorption spectra of oxy-Hb and deoxy-Hb in the near infrared range and path of light on human head.

FIG. 3A

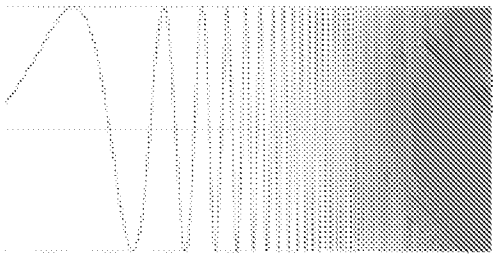


FIG. 3B

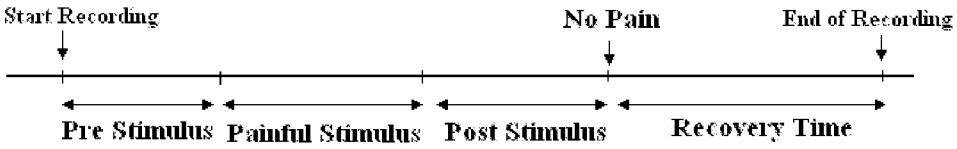

Start Recording
No Pain
End of Recording
Pre Stimulus
Painful Stimulus
Post Stimulus
Recovery Time

FIG. 4

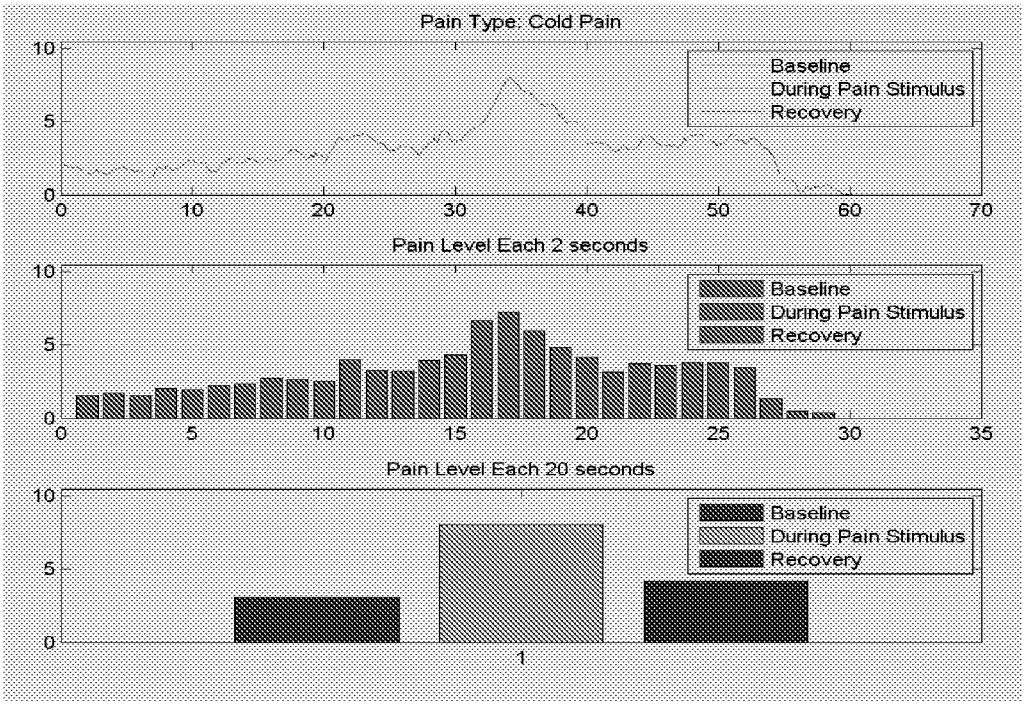

Pain Type: Cold Pain
Baseline
During Pain Stimulus
Recovery
Pain Level Each 2 seconds
Baseline
During Pain Stimulus
Recovery
Pain Level Each 20 seconds
Baseline
During Pain Stimulus
Recovery

FIG. 5

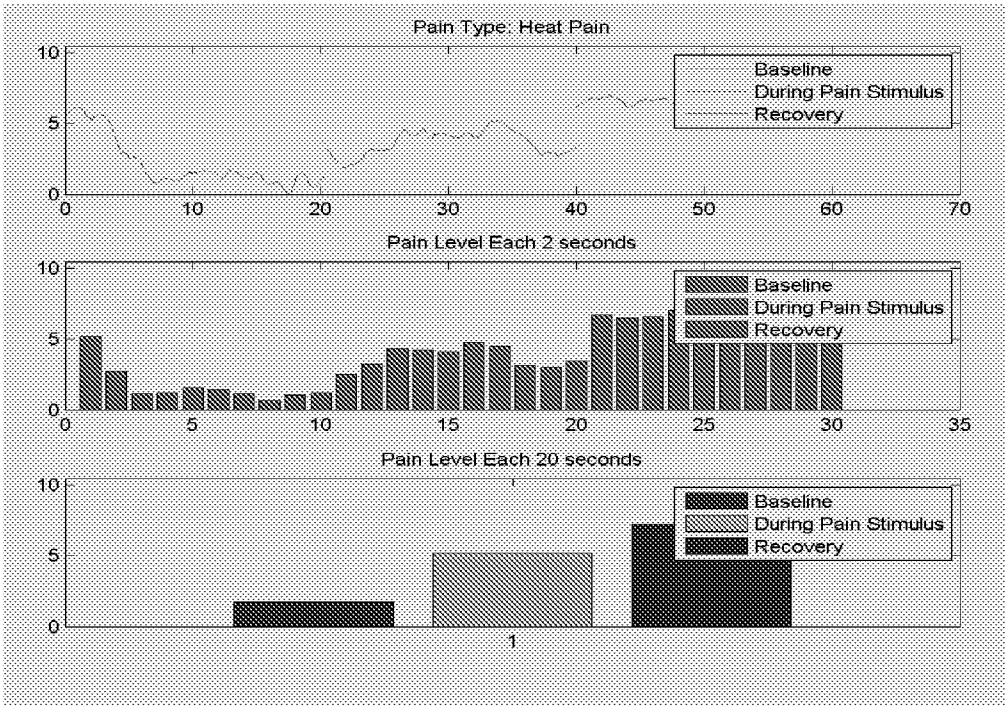

Pain Type: Heat Pain
Baseline
During Pain Stimulus
Recovery
Pain Level Each 2 seconds
Baseline
During Pain Stimulus
Recovery
Pain Level Each 20 seconds
Baseline
During Pain Stimulus
Recovery

FIG. 6

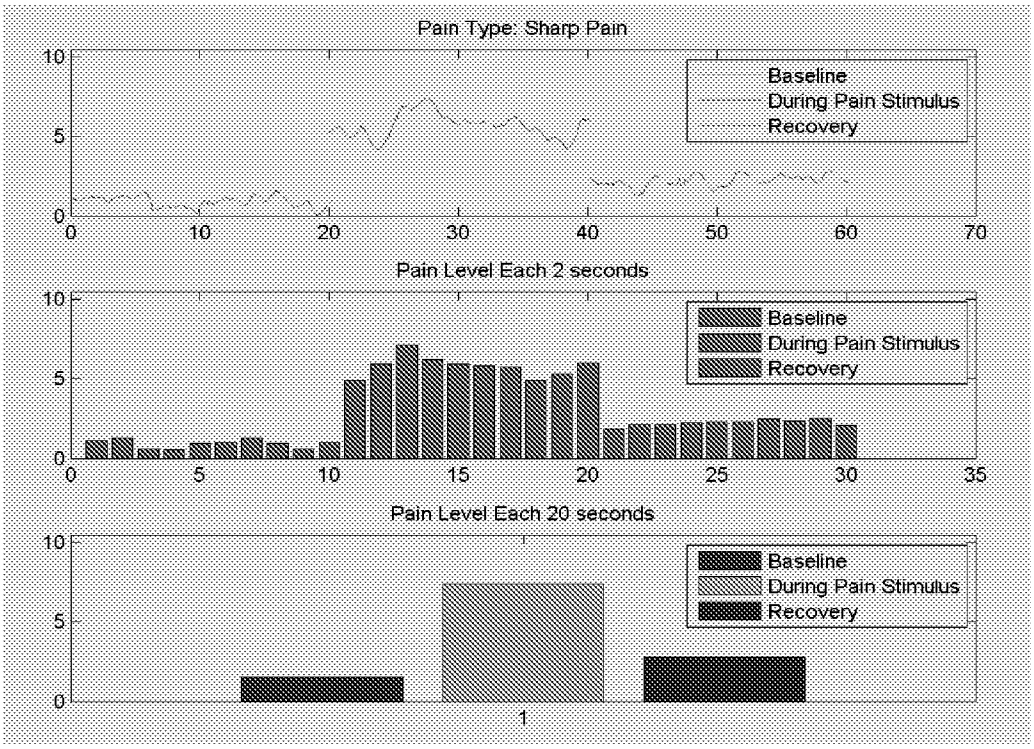

Pain Type: Sharp Pain
Baseline
During Pain Stimulus
Recovery
Pain Level Each 2 seconds
Baseline
During Pain Stimulus
Recovery
Pain Level Each 20 seconds
Baseline
During Pain Stimulus
Recovery

FIG. 7

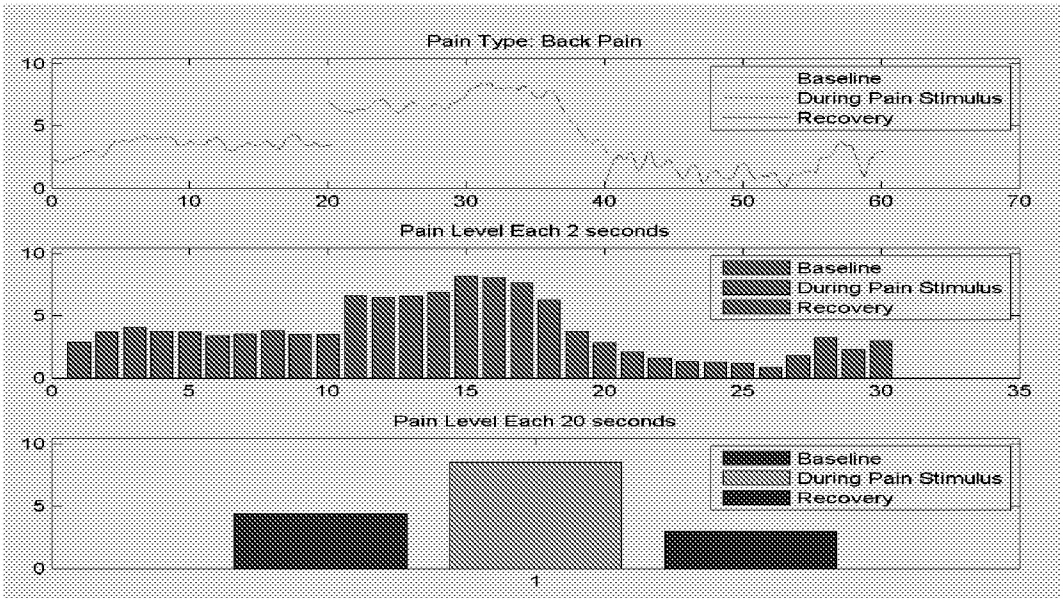

Pain Type: Back Pain
Baseline
During Pain Stimulus
Recovery
Pain Level Each 2 seconds
Baseline
During Pain Stimulus
Recovery
Pain Level Each 20 seconds
Baseline
During Pain Stimulus
Recovery

FIG. 8

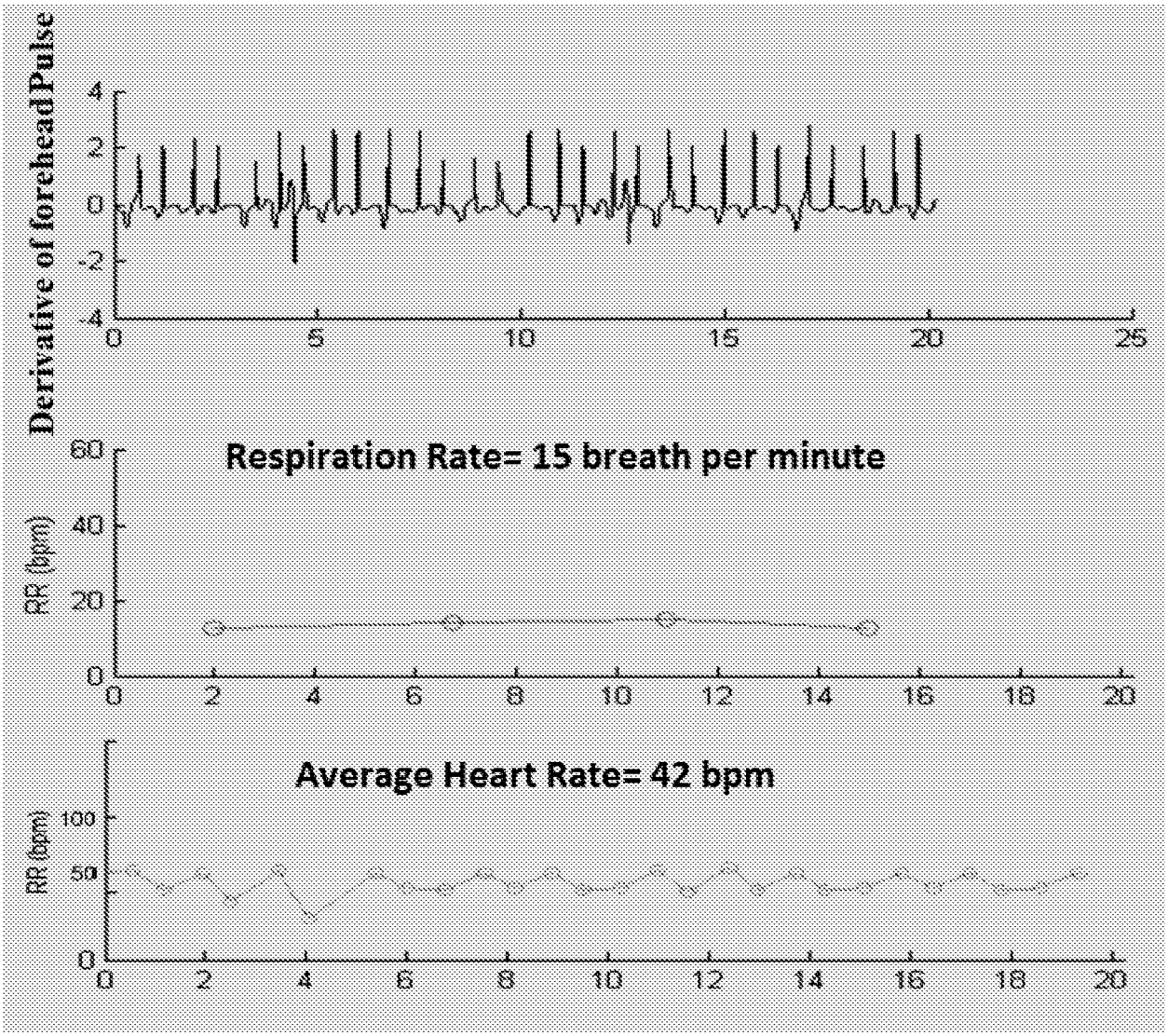

Derivative of forehead Pulse
4
2
0
-2
-4
0
5
10
15
20
25
Respiration Rate= 15 breath per minute
RR (bpm)
60
40
20
0
0
2
4
6
8
10
12
14
16
18
20
Average Heart Rate= 42 bpm
RR (bpm)
100
50
0
0
2
4
6
8
10
12
14
16
18
20

FIG. 9

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 14/23296

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61B 5/00 (2014.01)
USPC - 600/301
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
USPC: 600/301

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 600/300, 306, 547, 549, 557, 561
IPC: A61B 5/05, 19/00 (keyword limited; terms below)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Patbase; Google Patents; Google
Search Terms Used: monitor*, anesthesia, consciousness, pain, sensor%, integrated, battery, power supply, circuit*, photoplethysmograph*, pulse oximet*, electrode%, temperature, cpu, microprocessor, controller, accelerometer, gyro*

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2010/134068 A1 (ZUCKERMAN-STARK et al) 25 November 2010 (25.11.2010) pg 4, ln 16-20, pg 5, ln 3-5, pg 6, ln 2-6, pg 16, ln 30-33, pg 20, ln 8-14, pg 27, ln 31 to pg 28, ln 4, pg 29, ln 8-18, pg 31, ln 6-11	1-3, 10, 13, 33-34, 37
Y		9, 11-12, 25, 32
Y	US 2012/0130203 A1 (STERGIOU et al) 24 May 2012 (24.05.2012) fig 6, para [0032], [0056]-[0060]	9, 11, 32
Y	US 2008/0091089 A1 (GUILLORY et al) 17 April 2008 (17.04.2008) para [0039]-[0040], [0043]-[0046], [0056]	12
Y	US 2012/0132211 A1 (HALPERIN et al) 31 May 2012 (31.05.2012) para [0216], [0720]	25

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
18 August 2014 (18.08.2014)	11 SEP 2014

Name and mailing address of the ISA/US	Authorized officer:
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 14/23296

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

This application contains the following species of the generic invention which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid

Group I: Claims 1-3, 9-13, 25, 32-34, 37 directed to specifics of the motion sensors.

Group II: Claims 1, 4-6, 9-13, 22-23, 25, 32-34, 37 directed to specifics of the optical sensors/emitters.

Group III: Claims 1, 7-13, 25, 32-34, 37 directed to specifics of the electrodes.

Group IV: Claims 1, 9-21, 24-35, 37 directed to specifics of the controllers.

----Continued on Supplemental Page----

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-3, 9-13, 25, 32-34, 37

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 14/23296

Continuation of Box III: Observations where unity of invention is lacking

Group V: Claim 36 directed to a method for providing an indication of pain of a person such as measuring pain or a surrogate of pain symptoms of a person.

Claims 1, 9-13, 25, 32-34, 37 are generic to groups I-IV.

The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

SPECIAL TECHNICAL FEATURES

The special technical feature of each species (Groups I-IV) is provided in the group descriptions above. None of these special technical features are common to the other species, nor do they correspond to a special technical feature in the other species.

Group V includes the special technical feature of a method for providing an indication of pain of a person such as measuring pain or a surrogate of pain symptoms of a person, said method comprising: illuminating the tissue of the person; sensing light emitted or reflected by the tissue of the person; generating a light signal indicative of a light parameter of the sensed light; sensing an electrical parameter of the tissue of the person; generating an electrode signal indicative of an electrical parameter of the sensed electrical parameter; sensing a temperature of the tissue of the person; generating a temperature signal indicative of the sensed temperature; processing the light signal, the electrode signal and the temperature signal and providing a pain indication signal which is a function of the processed signals; and providing an indication which is indicative of the pain indication signal, not required by Groups I-IV.

COMMON TECHNICAL FEATURES

Groups I-V share the technical features of claims 1 and 37. Groups I-IV are species of generic independent claim 1. Groups I-V are related as an apparatus (Groups I-IV) and methods for using the apparatus (Group V). The apparatus is known in prior art as shown in WO 10/134068 A1 to Zuckerman-Stark, et al. (hereinafter Zuckerman-Stark).

Regarding claim 1, Zuckerman-Stark discloses a system for providing an indication of pain of a person such as measuring pain or a surrogate of pain symptoms of a person, said system for use with the tissue of the person, said system comprising:
a light source adapted for illuminating the tissue of the person (light source inherent in PPG system - pg 5, ln 3-5);
an optical sensor adapted for sensing light emitted or reflected by the tissue of the person, said optical sensor generating a light signal indicative of a light parameter of the sensed light (optical sensor inherent in PPG system - pg 5, ln 3-5);
a surface electrode adapted for sensing an electrical parameter of the tissue of the person, said surface electrode generating an electrode signal indicative of an electrical parameter of the sensed electrical parameter (col 4, ln 16-20);
a temperature sensor adapted for sensing a temperature of the tissue of the person, said temperature sensor generating a temperature signal indicative of the sensed temperature (pg 16, ln 30-33);
one or more circuits (102) adapted for receiving the light signal, the electrode signal, and the temperature signal and providing corresponding signals (pg 29, ln 8-12);
a controller (104) adapted for receiving and processing the corresponding signals and adapted for providing a pain indication signal which is a function of the corresponding signals (pg 29, ln 12-18);
an indicator adapted to be responsive to the controller for providing an indication which is indicative of the pain indication signal (display, pg 31, ln 1-5); and
a power supply for supplying power to the system (power supply inherent in computer - pg 27, ln 31 to pg 28, ln 4).

Regarding claim 37, Zuckerman-Stark discloses a system for cerebral monitoring of a person, said system for use with the tissue of the person, said system comprising:
a light source adapted for illuminating the tissue of the person (light source inherent in PPG system - pg 5, ln 3-5);
a optical sensor adapted for sensing light emitted or reflected by the tissue of the person, said optical sensor generating a light signal indicative of a light parameter of the sensed light (optical sensor inherent in PPG system - pg 5, ln 3-5);
a surface electrode adapted for sensing an electrical parameter of the tissue of the person, said surface electrode generating an electrode signal indicative of an electrical parameter of the sensed electrical parameter (col 4, ln 16-20);
a temperature sensor adapted for sensing a temperature of the tissue of the person, said temperature sensor generating a temperature signal indicative of the sensed temperature (pg 16, ln 30-33);
one or more circuits (102) adapted for receiving the light signal, the electrode signal, and the temperature signal and providing corresponding signals (pg 29, ln 8-12);
a controller (104) adapted for receiving and processing the corresponding signals (pg 29, ln 12-18) and adapted for providing a cerebral monitoring signal which is a function of the corresponding signals (intended use);
an indicator adapted to be responsive to the controller (display - pg 31, ln 1-5) for providing an indication which is indicative of the cerebral monitoring (intended use); and
a power supply for supplying power to the system (power supply inherent in computer - pg 27, ln 31 o pg 28, ln 4). The device as taught in Zuckerman-Stark is capable of performing the intended function as the signals are capable of being interpreted in various manners, including a cerebral monitoring/level of consciousness manner.

As the common features were known in the art at the time of the invention, they cannot be considered special technical features that would otherwise unify the groups.

Therefore, Groups I-V lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.

专利名称(译)	基于血液动力学参数实时跟踪受试者的脑血流动力学反应（RTCHR）		
公开(公告)号	EP2967357A1	公开(公告)日	2016-01-20
申请号	EP2014779148	申请日	2014-03-11
[标]申请(专利权)人(译)	ROPAMEDICS		
申请(专利权)人(译)	ROPAMEDICS LLC		
当前申请(专利权)人(译)	ROPAMEDICS LLC		
[标]发明人	AKHBARDEH ALIREZA TEHRANI AMIR		
发明人	AKHBARDEH, ALIREZA TEHRANI, AMIR		
IPC分类号	A61B5/00 A61B5/01 A61B5/02 A61B5/024 A61B5/0476 A61B5/08 A61B5/11 A61B5/1455		
CPC分类号	A61B5/01 A61B5/02028 A61B5/024 A61B5/0476 A61B5/0816 A61B5/1112 A61B5/14553 A61B5/4064 A61B5/4824 A61B5/7278		
优先权	61/776482 2013-03-11 US		
其他公开文献	EP2967357A4		
外部链接	Espacenet		

摘要(译)

一种用于测量人的疼痛的系统，该系统用于人的组织。组织上的各种传感器和检测器向控制器提供信号，以确定和指示人的疼痛程度。所有组件可以集成到一个单元中或分成与处理单元无线通信的传感单元。