(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
14 May 2010 (14.05.2010)

PCT

(10) International Publication Number
WO 2010/053811 A2

(51) International Patent Classification:
A61B 5/145 (2006.01) *A61B 5/1455* (2006.01)

(21) International Application Number:
PCT/US2009/062446

(22) International Filing Date:
28 October 2009 (28.10.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/109,161 28 October 2008 (28.10.2008) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

(54) **Title**: IMPLANTABLE SMALL ANIMAL PULSE OXIMETRY SENSOR

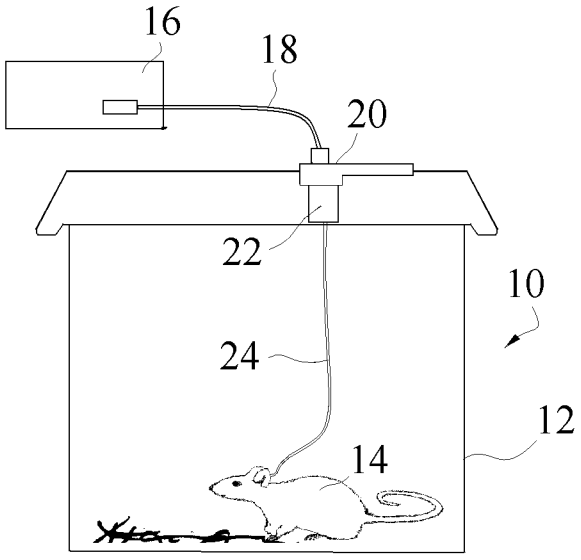

FIG. 4

(57) **Abstract**: An implantable photoplethysmographic sensor for animals such as small rodents, namely rats and mice is provided. This involves making photoplethysmographic measurements on, or more precisely through, the head of the subject specifically, but also subcutaneously by applying sensors directly to the skull of the animal. Not only does the skull provide a location where blood flow will always be available, it also provides a platform for adhering sensor pads such that noise that results from motion of the animal is minimized. The reason is that when sensors are glued to the skull, they cannot move relative to the bone, but more importantly to the brain tissue underneath, assuming that the brain does not "slosh around" while the animal is moving.

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IMPLANTABLE SMALL ANIMAL PULSE OXIMETRY SENSOR

[0001] The present invention claims priority of U.S. Provisional Patent Application Serial No. 61/109,161 entitled "Implantable Small Animal Pulse Oximetry Sensor" filed October 28, 2008.

BACKGROUND OF THE INVENTION

[0002] 1. FIELD OF THE INVENTION

[0003] The present invention relates to photoplethysmographic readings for animal research and more particularly, the present invention is directed to an implantable photoplethysmographic sensor for small animals.

[0004] 2. BACKGROUND INFORMATION

[0005] A photoplethysmograph is an optically obtained plethysmograph, which, generically, is a measurement of changes in volume within an organ whole body, usually resulting from fluctuations in the amount of blood or air that the organ contains. A photoplethysmograph is often obtained by using a pulse oximeter.

[0006] A conventional pulse oximeter monitors the perfusion of blood to the dermis and subcutaneous tissue of the subject. Pulse oximetry is generally a non invasive method that allows for the monitoring of the oxygenation of a subject's arterial blood, generally a human (or possibly animal) patient or an animal (or possibly human) research subject.

[0007] As a brief history of pulse oximetry, it has been reported that in 1935 an inventor Matthes developed the first 2-wavelength earlobe O_2 saturation meter with red and green filters, later switched to red and infrared filters. This was the first device to measure O_2 saturation. Further, in 1949, an inventor Wood added a pressure capsule to squeeze blood out of the earlobe to obtain zero setting in an effort to obtain absolute O_2 saturation value when blood was readmitted. The concept is similar to today's conventional pulse oximetry but suffered due to unstable photocells and light sources and the method was not used clinically. In 1964 an inventor Shaw assembled the first absolute reading ear oximeter by using eight wavelengths of light which was commercialized by Hewlett Packard. This use was limited to pulmonary functions due to cost and size.

[0008] Effectively, modern pulse oximetry was developed in 1972, by Aoyagi at Nihon Kohden using the ratio of red to infrared light absorption of pulsating components at the measuring site, and this design was commercialized by BIOX/Ohmeda in 1981 and Nellcor, Inc. in 1983. Prior to the introduction of these commercial pulse oximeters, a patient's oxygenation was determined by a painful arterial blood gas, a single point measure which typically took a minimum of 20-30 minutes processing by a laboratory. It is worthy to note that in the absence of oxygenation, damage to the human brain starts in 5 minutes with brain death in a human beginning in another 10-15 minutes. Prior to its introduction, studies in anesthesia journals estimated US patient mortality as a consequence of undetected hypoxemia at 2,000 to 10,000 deaths per year, with no known estimate of patient morbidity. Due to the near instantaneous oxygenation measurements, pulse oximetry has become a standard of care for human patients since about 1987.

[0009] Pulse oximetry has been a critical research tool for obtaining associated physiologic parameters in humans and animals beginning soon after rapid pulse oximetry became practical. The patient/research distinction is particularly important in animal subjects wherein in research the data gathering is the primary focus, as opposed to care-giving in which patient care is of utmost importance. In research applications the physiologic data being obtained may, necessarily, be at extreme boundaries for the animal subject. Research animals often have physiologic parameters well outside those of humans, and this fact is exacerbated by the values being at extreme boundaries for the animals in research. For this reason, pulse oximeters that are designed for human use may not lend themselves well to research applications on animals.

[0010] In conventional pulse oximetry a sensor is placed on a thin part of the subject's anatomy, such as a human fingertip or earlobe, or in the case of a neonate, across a foot, and two wavelengths of light, generally red and infrared wavelengths, are passed from one side to the other. Changing absorbance of each of the two wavelengths is measured, allowing determination of the absorbances due to the pulsing artery alone, excluding venous blood, skin, bone, muscle, fat, etc. Based upon the ratio of changing absorbance of the red and infrared light caused by the difference in color between oxygen-bound (bright red) and oxygen unbound (dark red or blue, in severe cases) blood hemoglobin, a measure of oxygenation (the per

cent of hemoglobin molecules bound with oxygen molecules) can be made. The measured signals are also utilized to determine other physical parameters of the subjects, such as heart rate (pulse rate). Starr Life Sciences, Inc. has utilized pulse oximetry measurements to calculate other physiologic parameters such as breath rate, pulse distension, and breath distention, which can be particularly useful in various research applications.

[0011] In addressing animal pulse oximetry, particularly for small rodents, one approach has been to modify existing human or neonate oximeters for use with rodents. This approach has proven impractical as the human based systems can only stretch so far and this approach has limited the use of such adapted oximeters. For example, these adapted human oximeters for animals have an upper limit of heart range of around 400 or 450 beats per minute which is insufficient to address mice that have a conventional heart rate of 400-800 beats per minute, and the intended research can extend the rates needed to be measured. Starr Life Sciences has developed a small mammal oximeter, rather than an adapted human model, that has effective heart rate measurements up to 900-1000 beats per minute, and this is commercially available under the Mouse Ox® oximeter brand.

[0012] There are many difficulties associated with making oximetry measurements in small animals, but one of the paramount issues is the propensity for small animals to divert blood from the tail and appendages, which results in the inability to make oximetry measurements. Moreover, this is exacerbated when certain types of challenges are imparted to the animal that can cause stress, or a form of shock, whereby blood flow is diverted completely from the extremities. Even under these conditions however, blood will always flow to the brain, the organ that is last to suffer losses in perfusion. Thus, oximetry measurements can always be made on the head or neck.

[0013] Further, in pulse oximetry associated with animals there can be an error associated with the sensors moving on the subject relative to the animal. There is a further concern of the skin of the animal moving relative to the tissue.

[0014] A further issue associated with pulse oximetry in research applications is the objectiveness of repeatability of the results of a given experiment. In short it can be helpful for repeatability of testing on a given subject that the sensors are positioned in the exact same location for each trial.

[0015] It is an object of the present invention to address the deficiencies of the prior art discussed above and to do so in an efficient, cost effective manner.

SUMMARY OF THE INVENTION

[0016] The various embodiments and examples of the present invention as presented herein are understood to be illustrative of the present invention and not restrictive thereof and are non-limiting with respect to the scope of the invention.

[0017] According to one non-limiting embodiment of the present invention, an efficient, effective, implantable photoplethysmographic sensor for animals such as small rodents, namely rats and mice is provided. The concept disclosed here involves making photoplethysmographic measurements on, or more precisely through, the head of the subject specifically, but also subcutaneously by applying sensors directly to the skull of the animal. Not only does the skull provide a location where blood flow will always be available, it also provides a platform for adhering sensor pads such that noise that results from motion of the animal is minimized. The reason is that when sensors are glued to the skull, they cannot move relative to the bone, but more importantly to the brain tissue underneath, assuming that the brain does not significantly "slosh around" while the animal is moving.

[0018] Although the primary concept is to make measurements across the skull using sensors adhered directly to the skull, however, there are other locations where it may be useful to locate sensors internally, such as the neck muscles, hind quarters or across internal organs.

[0019] The benefits to this application include reduction of motion relative to the skull and repeatability of measurements from day-to-day since the sensors are not removed.

[0020] One aspect of the present invention provides a method of obtaining photoplethysmographic measurements from a small mammal comprising the subcutaneous application of a photoplethysmographic emitter and receiver on the animal, such as a rat or mouse. The method of obtaining photoplethysmographic measurements from a small mammal according to the invention may provide that the signal from the emitter is transmitted through selected tissue, such as the skull, of the animal to the receiver. The method of obtaining photoplethysmographic measurements from a small mammal according to invention may provide that emitter

and the receiver are glued to the skull of the animal. The emitter and receiver may be attached to a flexible strip adapted for subcutaneous application in the animal, wherein flexible strip includes a gauze mesh substrate and resinous binder. The method of obtaining photoplethysmographic measurements from a small mammal according to invention wherein the sensor is configured to obtain heart rates above 450 beats per minute and up to 900 beats per minute. The method of obtaining photoplethysmographic measurements from a small mammal according to claim 9 further including a wireless transmitter coupled to the subcutaneous emitter and receiver.

[0021] These and other advantages of the present invention will be clarified in the description of the preferred embodiments taken together with the attached figures.

BRIEF DESCRIPTION OF THE DRAWINGS

[0022] The invention is described in connection with the following figures in which common reference numerals represent common elements throughout.

[0023] Figure 1 is a schematic view of an implantable photoplethysmographic sensor according to one embodiment of the present invention;

[0024] Figure 2 is a schematic view of an implanted photoplethysmographic sensor of figure 1;

[0025] Figure 3 is a schematic perspective view of the implantable photoplethysmographic sensor of figure 1;

[0026] Figure 4 is a schematic view of an implanted photoplethysmographic sensor system according to one embodiment of the present invention;

[0027] Figure 5 is a schematic perspective view of an implantable photoplethysmographic sensor according to another embodiment of the present invention;

[0028] Figure 6 is a schematic view of an implantable photoplethysmographic sensor according to one embodiment of the present invention;

[0029] Figure 7 is a schematic exploded view of an implantable photoplethysmographic sensor according to the present invention;

[0030] Figure 8 is a schematic perspective view of an implantable photoplethysmographic sensor according to another embodiment of the present invention.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0031] In summary, the present invention relates to an implantable photoplethysmographic sensor system 30 for animals, such as rats and mice 14 that are utilized in a laboratory environment. In the design proposed here, the sensor pads 32, namely an emitter and receiver, are glued or otherwise attached to a thin plastic form or strip 34 that allows alignment across the skull of the animal 14. The plastic form or strip 34, as well as the sensors 32, would all be glued to the skull, generally as shown in figure 7. The probable location will be behind the ears of the mouse 14 as generally shown, and the sensors 32 allow for transmission of the signal across the skull of the animal 14 as shown.

[0032] In one alternative the strip 34 can be formed of gauze mesh material in which the emitter and receiver sensor pads 32 are placed and the structure dipped into a resinous binder to form a flexible thin assembly adapted for subcutaneous application. The gauze and/or the binder may overlap the emitter or receiver to form a diffuser for the respective pad 32. Alternatively openings in the binder can be used depending on what presents the best signal to noise ratio for the device in the intended operation.

[0033] The plastic strip 34 shown in figure 8 is formed as two halves with a sliding mechanism 50 to allow the two sensor pads 32 to move laterally relative to each other to accommodate different sized skulls. In other words the form or strip 34 is formed of two half portions that can slide toward and away from each other

[0034] Wires 24 soldered or otherwise coupled to the sensor pads 32, or elements, would protrude through the skin of the animal 14. In the embodiment presented, the wires 24 are then connected to small connector 24.

[0035] Fig. 4 is a schematic representation of an implantable photoplethysmographic sensor system 10 for mobile animals 14 such as small rodents, namely rats and mice, in accordance with one embodiment of the present invention. The system 10 is particularly well suited for use in a laboratory environment in which a subject animal, such as a mouse 14, is often maintained within a confinement unit 12 (e.g. a cage, cell, housing, etc). The confinement unit 12 is used herein as a generic term for anything holding the subject animals. The unit 12 could be an integral element of the research, such as a maze or other structured test environment. The unit 12 will

often be a housing area for the animal. The details of the unit 12 will be well known to those of ordinary skill in animal research fields.

[0036] The subject animal may be any subject animal for which photoplethysmographic measurements are desired. A large amount of laboratory research is conducted on rats and mice, however prior art photoplethysmographic measurements have been of limited availability to the researchers when using such subjects. Consequently, the present invention has particular application to research associated with rats and mice. More accurately the present invention provides particular advantages and expands potential research possibilities when utilized with subjects of the order rodentia, and even more precisely, when utilized with the sub-order muroidia. A particularly advantageous aspect of the present invention is that the system 10 allows for photoplethysmographic measurements from a mobile animal. The mobile animals may still be retrained by the confinement unit 12, but the animals may still have a certain range of motion therein. Although useful for mobile animals, there is nothing that prevents the system 10 from being effectively utilized for restrained and/or anesthetized animals.

[0037] The system 10 will include a processor or controller 16 coupled thereto. The controller 16 is shown schematically in figure 4 and can be formed as a component of a laptop or desktop computer. The controller 16 may be the combination of stand alone hardware and software that is coupled with computer for the user interface, display memory and some computation. One particularly advantageous use of the photoplethysmographic measurements of the system 10 is for pulse oximetry, particularly in animals such as rats and mice 14. In this application the controller 16 is the commercially available MouseOx™ product from Starr Life Sciences with the unique sensor 30 and animal coupling as described herein. The details of the controller 16, including the user interface, the user display, memory or the like is not discussed herein in detail.

[0038] A conventional controller cable 18 extends from the controller 16 for transmitting control and power signals from the controller and data back to the controller 16. The controller cable is coupled to a rotation coupling 20, also called a swivel link, slip ring or commutator. A mercury swivel commutator, such as available from Mercotac Inc, is a commutator that has been used in electrophysiological experiments involving moving animals. Another acceptable coupling 20 is a

commutator available from the company Plastics One. Any acceptable rotation coupling 20 can be used that transmits the signals with minimal commutator noise and which avoids twisting of the wires 24.

[0039] A collar cable 24 is attached to and extends from the rotation coupling 20 through attachment plug 22. The rotation coupling 20 allows relative rotation between the controller cable 18 and the cable 24. The rotation coupling 20 provides a convenient location for mounting to the confinement unit 12. The use of the swivel link or rotation coupling 20 allows the animal, e.g. mouse 14, to be effectively freely roaming within the area of the unit 12, wherein twisting of the cables is avoided. The swivel link or rotation coupling 20 also serves to effectively divide the system 10 into an animal specific portion (sensor 30) and the controller 16, whereby the controller 16 can be easily used with a large number of animal specific portions or sensors 30, in a serial fashion. Further, it allows for easy replacement of the specific sensors 30 which is anticipated to have a shorter life span than the controller 16.

[0040] The present invention does anticipate that the controller 16 may be simultaneously (e.g. a parallel attachment) connected to a number of animal specific sensors 30 through separate cables 18 to allow for obtaining numerous study results at the same time, but this configuration does not eliminate the advantages of the coupling 20.

[0041] The present invention preferably has the subcutaneous application of the sensors 32 to the skull of the animal, however, the neck of small mammals such as rats and mice allows for a other advantages for photoplethysmographic pulse oximetry measurements. The necks of animals of the sub-order muroidia tend to allow for both transmissive and reflective pulse oximetry measurements. Transmissive pulse oximetry is where the received light is light that has been transmitted through the perfuse tissue, whereas in reflective pulse oximetry the representative signal is obtained from light reflected back from the perfuse tissue. Each technique has its unique advantages. Transmissive techniques often result in a larger signal of interest, which is very helpful in small animals that have very small quantities of blood being measured to begin with.

[0042] Further, the head and neck region of the animal offers an area with a relatively large blood flow for the animal, which will improve the accuracy of the measurements. In addition to increased blood flow, the blood flow is present under

substantially all conditions. In other areas of the animal, such as the legs, paws and tail, the animal will often cut off blood flow under a variety of conditions. For example if the animal is cold or sufficiently agitated the blood flow to the tail can be shunted. The neck, in contrast represents an area of the animal that will always maintain a constant blood flow for measurements.

[0043] The subcutaneous application and the head or neck location also provides a bite proof location for the sensor pads 32 and external wire 24 mounting.

[0044] The sensor pads 32 include an emitter on the strip 34 configured to be mounted subcutaneously such as glued to the animal's skull, with the emitter having two light sources of distinct wavelengths; and a receiver 32 on the strip 34 subcutaneously such as glued to the animal's skull for detecting light from the emitter that has been transmitted through the intervening tissue of the subject mammal. The emitter and receiver may be configured for transmissive operation as shown, or even reflective operation as noted above.

[0045] The advantages of the sensor system 10 include the location of the sensors 32 as discussed above. Further, this system 10 allows the measurements to be obtained from a mobile animal, which will be free to roam about the confinement unit 12. Neither the sensor pads 32, strip 32 nor the cable 24 will limit motion in this area, and the swivel link 20 prevents cable twisting from interfering with animal motion. This opens the door for researchers to collect photoplethysmographic measurements, in particular pulse oximetry measurements, under a greater number of conditions.

[0046] Additional techniques for improving photoplethysmographic pulse oximetry measurements in mobile subjects could be helpful. For example, adding an accelerometer sensor (see for example 42 of figure 6) on the strip 34 will allow more information to the researcher and this information can be combined with the pulse oximeter measurements so the controller will be able to match periods of rapid acceleration with the pulse oximeter measurements as a method of identifying potentially anomalous readings.

[0047] Figure 5 illustrates a different design for sensor 30 that replaces the cable 24, link 20 and cable 18 with a wireless transmitter/reciever 40 for wireless operation. Controller 16 would similarly have a wireless transmitter/receiver 40 to complete the link. Wireless technology in general, and radio-telemetry on collars for wildlife

studies is very well established and the details need not be discussed further. Wireless operation will generally allow for more freedom of mobility to the animals. It is apparent that the wireless operation allows for wildlife applications in research, or free roaming animals. In this arrangements the transmitter 40 would typically be outside the animal, unless small transmitter become available that allow for subcutaneous applications.

[0048] Figure 6 illustrates the use of multiple sets of sensor pads 32 and 42as the system 10 is not limited to sensors 32 for photoplethysmographic measurements. Additional sensors 42 can be added, such as temperature sensors, accelerometers, and other physiologic and environmental sensors as shown in figure 6. EKG or EEG type sensors would be applicable for the skull application of the system 10. These sensors 42 can have their data utilized by the controller 16 to validate the obtained data of sensors 32, and vice versa. The particular validation methodologies will depend on the particular sensors.

[0049] Further another aspect of the present invention includes boosting the light signal on the collar platform. One method of boosting the signal strength is by increasing the number of emitters and/or increasing the number of detectors or receivers forming the sensor pads 32 to increase the signal strength. Specifically adding several emitters at each wavelength can be used to increase the amount of light directed at the subject and hence increase the detected signal. In a similar fashion, increasing the number of detectors utilized can increase the amount of detected signal and thus also improve the signal. The system strip 34 provides an advantageous base for this modification. Utilizing a more powerful emitter is a further possibility and continued improvements in LED technology will make this a reasonable approach.

[0050] In an alternative embodiment of the invention the lighting or emitter pad 32 and receiver pad 32 could also reside on only one side of the plastic form 34 or on the skull directly without a strip, and operate in a reflectance mode. However the through the skull approach is shown believed to provide preferential results.

[0051] *Adherence to Skull*

[0052] The sensor pads 32 and strip 34 (or frame or form) is designed to be glued to the skull, but it is also possible to use tiny bone screws to adhere the sensor pads 32

and the strip 34 to hold the entire assembly in place and to assure no relative motion between the skull and the sensor placement.

[0053] As described, the implanted sensor 30 is designed to make long-term measurements on conscious animals that are free-roaming within the boundaries of the attached wire 24.

[0054] Additionally, some capacity on the commutator is provided to accommodate more wires passing out of the animal than just those from the oximeter, such as for EEG measurements. In such a case, the commentator could provide open channels for passage of other wires.

[0055] *Embedded Strip*

[0056] An alternate approach to using a strip 34 with wired sensor pads 32 is to use a mylar (or other material) strip 34 in which the components are embedded, with electrical connections made using conductive traces to a connector on the end. This strip 34 could then be adhered in some manner to the skull such that only the conductive trace connector protrudes through the skin for attachment of the wire 24. This configuration could greatly reduce the cost of the disposable sensor.

[0057] The above summarized imbedded pulse oximetry system greatly reduces some of the problems faced in the prior art. The sensor provides the researcher with a simple to install sensor that once installed in a relatively simple subcutaneous operation will provide repeatable accurate readings.

[0058] PRE-INSTALLED SENSORS ON RODENTS

[0059] One further possibility under one version of the present invention is to supply rodents with pre-installed physiologic sensors, such as through the head, subcutaneous pulse oximeters in mice, to medical researchers. This non-limiting aspect of the present invention pre-installs the embedded physiologic pulse oximetry sensor into or within the rodents prior to selling the rodents with attached or embedded sensors to the researcher. In this manner the specialty skills, such as small animal surgical and anesthesia skills, sensor selection, implantation procedure, engineering, sterilization techniques, validation techniques, and all the hardware and software are centralized at a single source or single organization rather than being spread about a collection of researchers. It is further contemplated that the embedded sensors could be of the wireless physiologic hardware. Further, it is anticipated that the embedded sensors may be entirely subcutaneous, as

opposed to having an antenna stick through the subject's skin. The subjects, such as mice, with preinstalled, pre-tested hardware, are sold to the researcher as needed and when needed and in the quantity desired. In addition to the hardware embedded inside the animal, communication hardware and software will be supplied for the user to convert their desktop computer into a wireless monitoring station. The key aspect of this version of the invention is removing the design and implementation of the specific modified rodents from the individual researchers. The design step including selecting the appropriate sensors, locating and/or adapting them for use on the subject small rodents, developing the manufacturing techniques, the sterilization techniques, the validation techniques and all of the associated hardware and software needed. A single organization can design a wide variety of modified rodents using the imbedded through the head (neck or other portion) pulse oximeter.

[0060] NON-INSTALLED SENSORS

[0061] Even when supplying the sensor to the user for installation the invention removes the design and implementation aspects from the individual researchers. The design step including selecting the appropriate sensors, locating and/or adapting them for use on the subject small rodents, developing the manufacturing techniques, the sterilization techniques, the validation techniques and all of the associated hardware and software needed is supplied, although the researchers would need to implement the identified installation techniques.

[0062] In the pulse oximetry field there has been a lack of adequate photoplethysmographic sensors for small mice (and even small rats), until the advent of the Mouse Ox® brand pulse oximeters by Starr Life Sciences. Prior to this development, commercially available pulse oximeters could provide heart rate data up to about 350 or 450 beats per minute (and even this range required special software modifications for some sensors), which were basically suitable for rats but not small mice given that the small mouse will have heart rates in the range of 400 to 800 beats per minute. The Mouse Ox™ brand of pulse oximeters for small rodents has an effective range up to (currently) about 900-1000 beats per minute which has opened up a wider selection of subjects for this type of research. The system 10 of the present invention uses the Mouse Ox® system (controller 16) such as available in October 2008 from Starr Life Sciences. The system may use a conventional

power source as through plug or could use a battery power source. The system couples to a computer such as a lap top through a coupling. The details of the controller, signal processing, display system including the user interface, and data storage on computer is not discussed herein in detail.

[0063] The subject animal may be any subject animal for which photoplethysmographic measurements are desired. A large amount of laboratory research is conducted on rats and mice, however photoplethysmographic measurements have been of limited availability to the researchers when using such subjects. Consequently, the present invention has particular application to research associated with rats and mice. More accurately the present invention provides particular advantages and expands potential research possibilities when utilized with subjects of the order rodentia, and even more precisely, when utilized with the sub-order muroidia.

[0064] Whereas particular embodiments of the invention have been described above for purposes of illustration, it will be evident to those skilled in the art that numerous variations of the details of the present invention may be made without departing from the spirit and scope of the present invention.

What is claimed is:

1. A photoplethysmographic sensor for small animals comprising a through the head transmissive emitter and receiver placed on opposite sides of the small animals skull.

2. The photoplethysmographic sensor for small animals according to claim 1 wherein the sensor is subcutaneous.

3. The photoplethysmographic sensor for small animals according to claim 1 wherein the emitter and receiver are attached to a flexible strip adapted for subcutaneous application in the animal.

4. The photoplethysmographic sensor for small animals according to claim 3 wherein flexible strip includes a gauze mesh substrate and resinous binder.

5. The photoplethysmographic sensor for small animals according to claim 1 wherein the sensor is configured to obtain heart rates above 450 beats per minute.

6. The photoplethysmographic sensor for small animals according to claim 1 further including a wireless transmitter coupled to the subcutaneous emitter and receiver.

7. A method of obtaining photoplethysmographic measurements from a small mammal comprising the subcutaneous application of a photoplethysmographic emitter and receiver on the animal.

8. The method of obtaining photoplethysmographic measurements from a small mammal according to claim 7 wherein the signal from the emitter is transmitted through selected tissue of the animal to the receiver.

9. The method of obtaining photoplethysmographic measurements from a small mammal according to claim 7 wherein the signal from the emitter is transmitted through the skull of the animal to the receiver.

10. The method of obtaining photoplethysmographic measurements from a small mammal according to claim 9 wherein the emitter and the receiver are glued to the skull of the animal.

11. The method of obtaining photoplethysmographic measurements from a small mammal according to claim 9 wherein the emitter and receiver are attached to a flexible strip adapted for subcutaneous application in the animal.

12. The method of obtaining photoplethysmographic measurements from a small mammal according to claim 11 wherein flexible strip includes a gauze mesh substrate and resinous binder.

13. The method of obtaining photoplethysmographic measurements from a small mammal according to claim 9 wherein the sensor is configured to obtain heart rates above 450 beats per minute.

14. The method of obtaining photoplethysmographic measurements from a small mammal according to claim 9 further including a wireless transmitter coupled to the subcutaneous emitter and receiver.

15. The method of obtaining photoplethysmographic measurements from a small mammal according to claim 9 wherein the animal is a mouse.

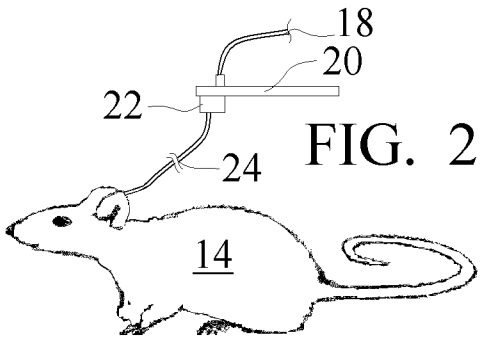

FIG. 2

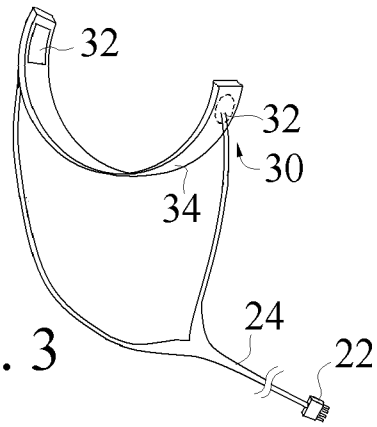

FIG. 3

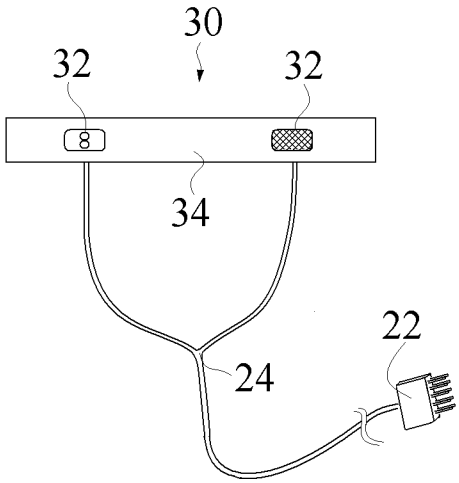

FIG. 1

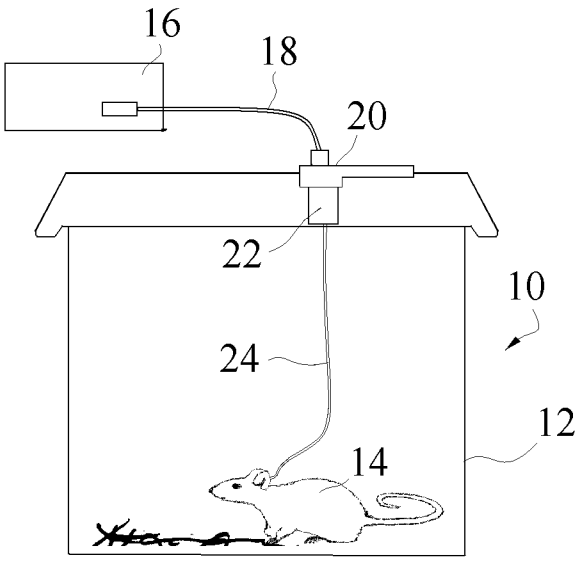

FIG. 4

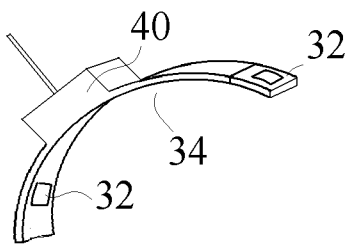

FIG. 5

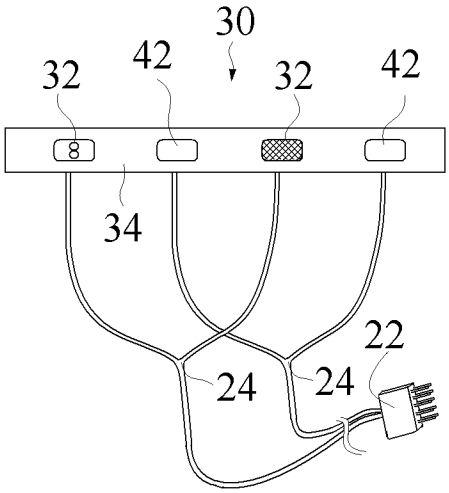

FIG. 6

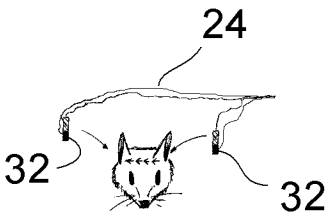

Figure 7

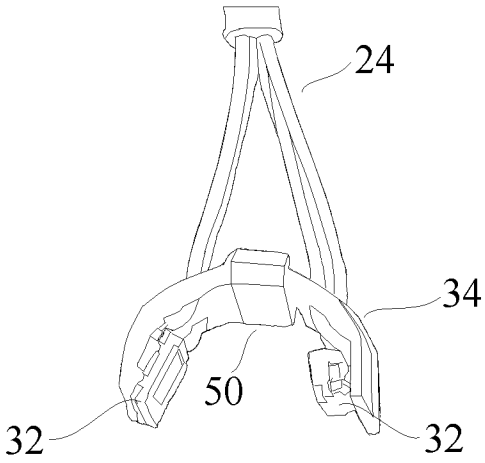

FIG. 8