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(54) **APPARATUS AND METHOD FOR CAUSING VASOCONSTRICTION BY ELECTRICAL STIMULATION**

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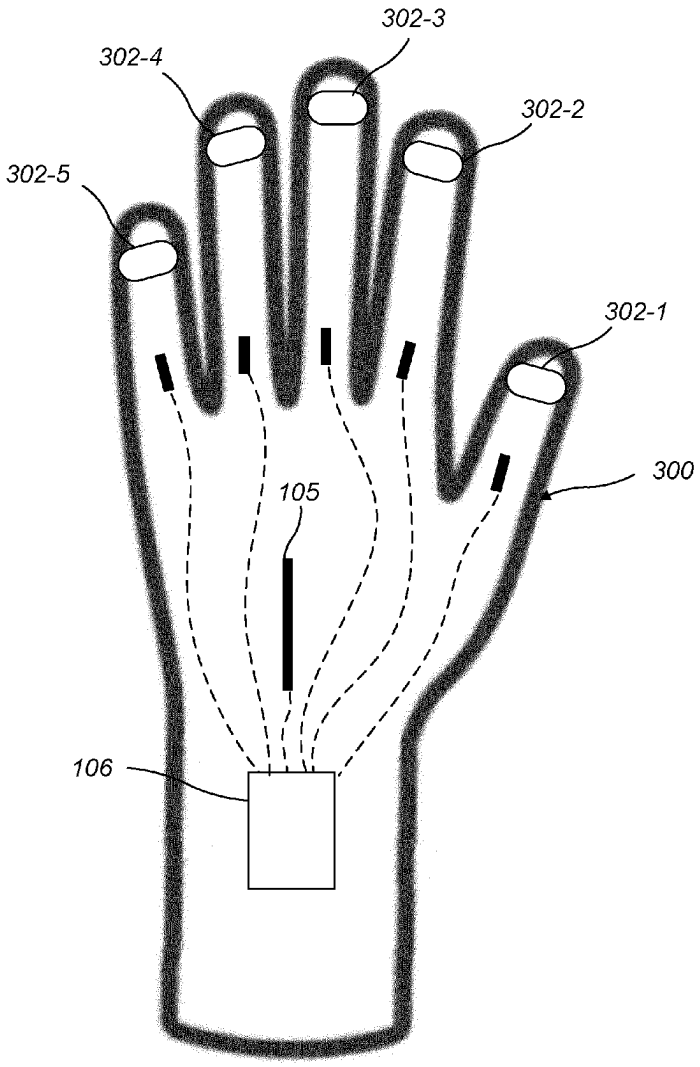
(57) **ABSTRACT**

An apparatus configured to be worn on the hand or foot, comprising: a plurality of electrodes arranged so as to be positioned over one or more respective phalanges when the apparatus is attached to the hand or foot; a supporting structure configured to attach the apparatus to the hand or foot and to retain the plurality of electrodes; and a controller configured to control the application of signals to the plurality of electrodes. Feedback sensors may be provided and positioned on a digits to monitor a property of underlying tissue.



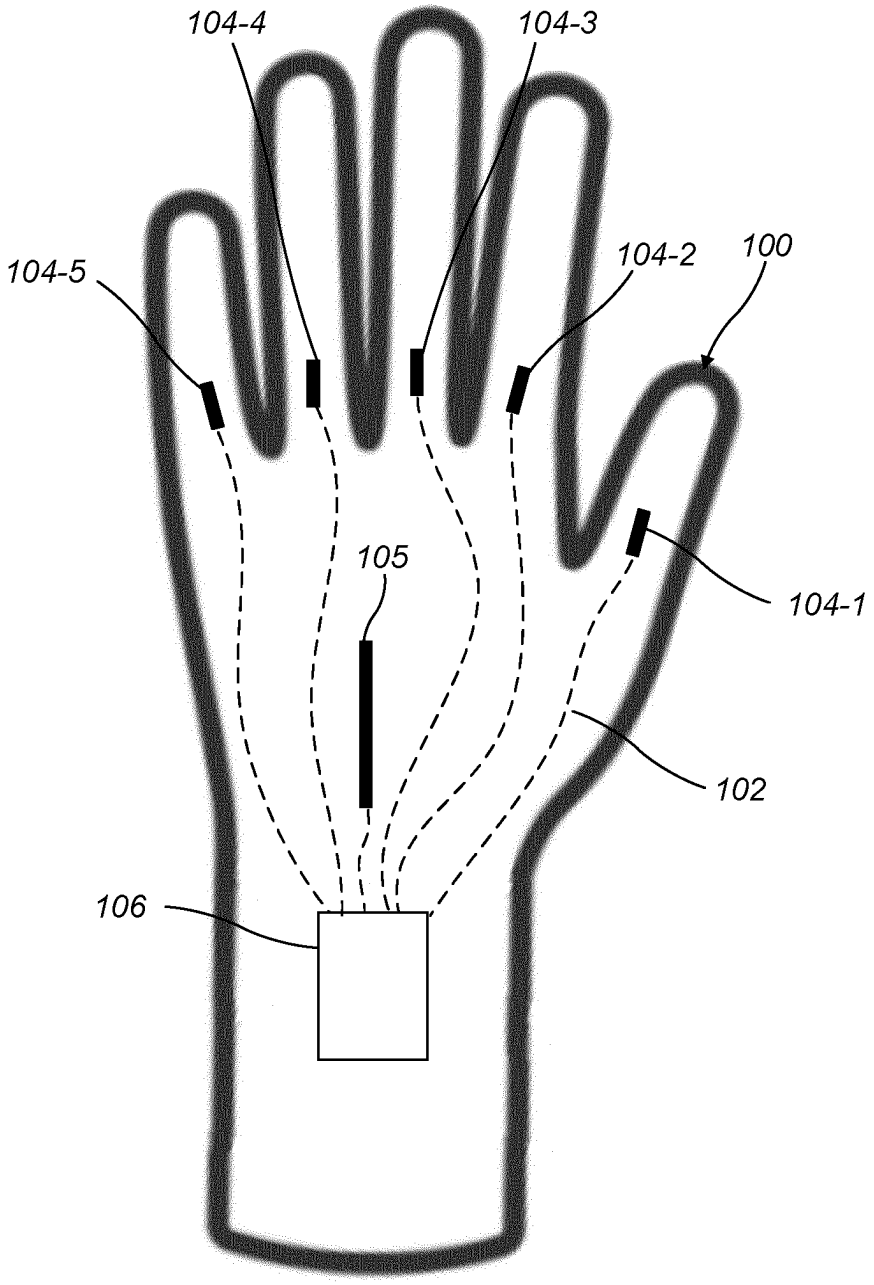


Fig. 1

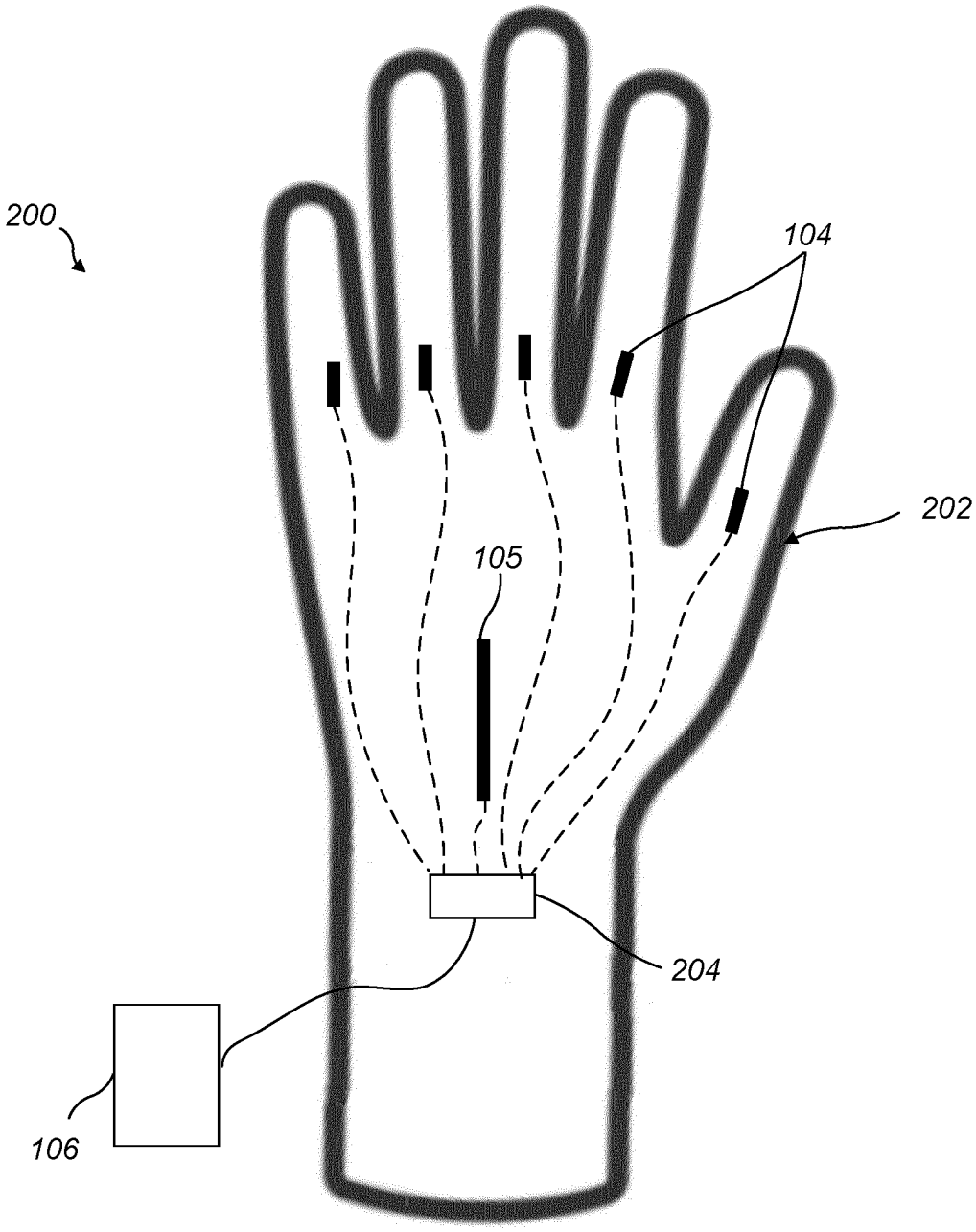


Fig. 2

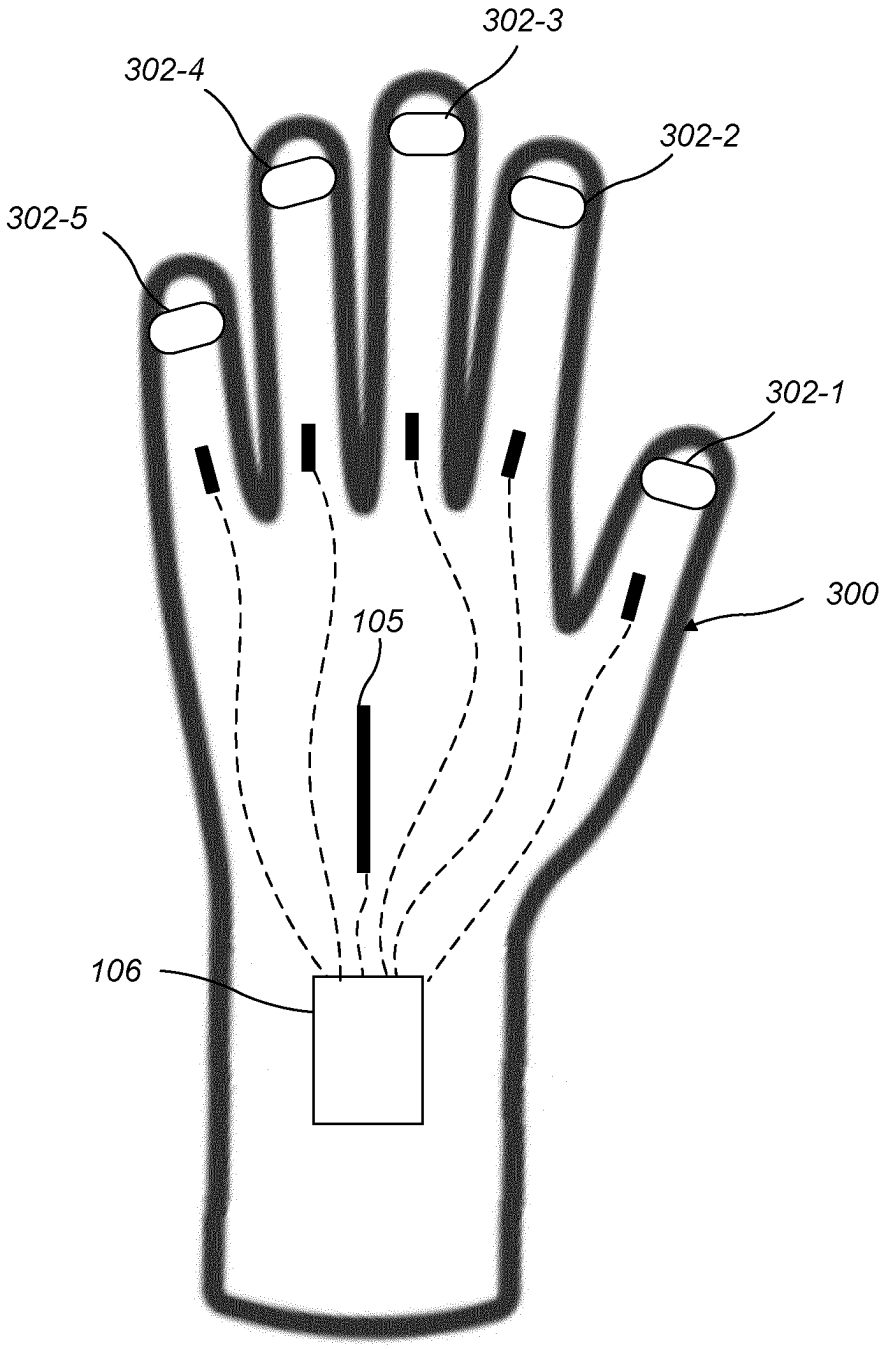


Fig. 3

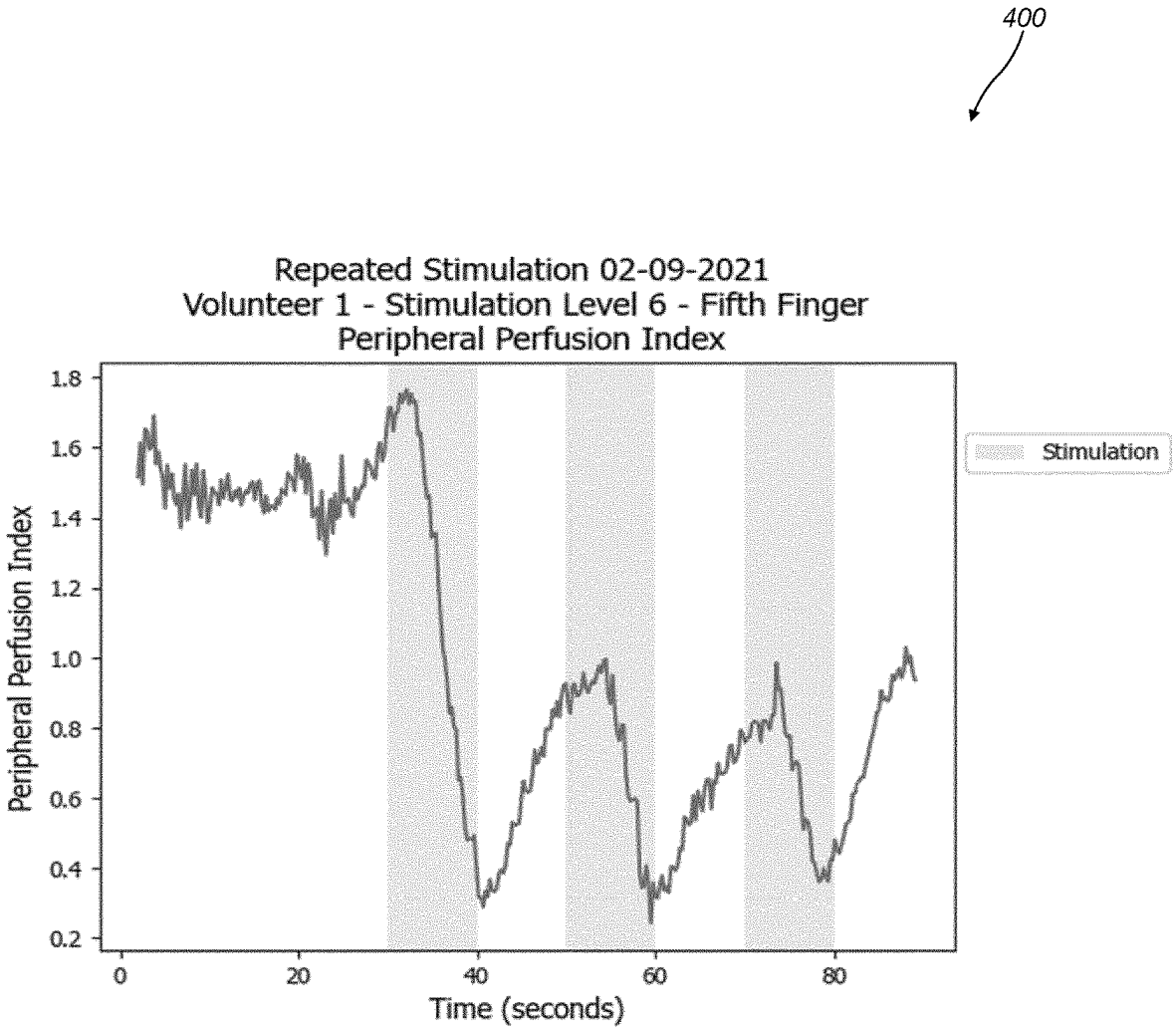

400
Repeated Stimulation 02-09-2021
Volunteer 1 - Stimulation Level 6 - Fifth Finger
Peripheral Perfusion Index
Peripheral Perfusion Index
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
20
40
60
80
Time (seconds)
Stimulation

Fig. 4a

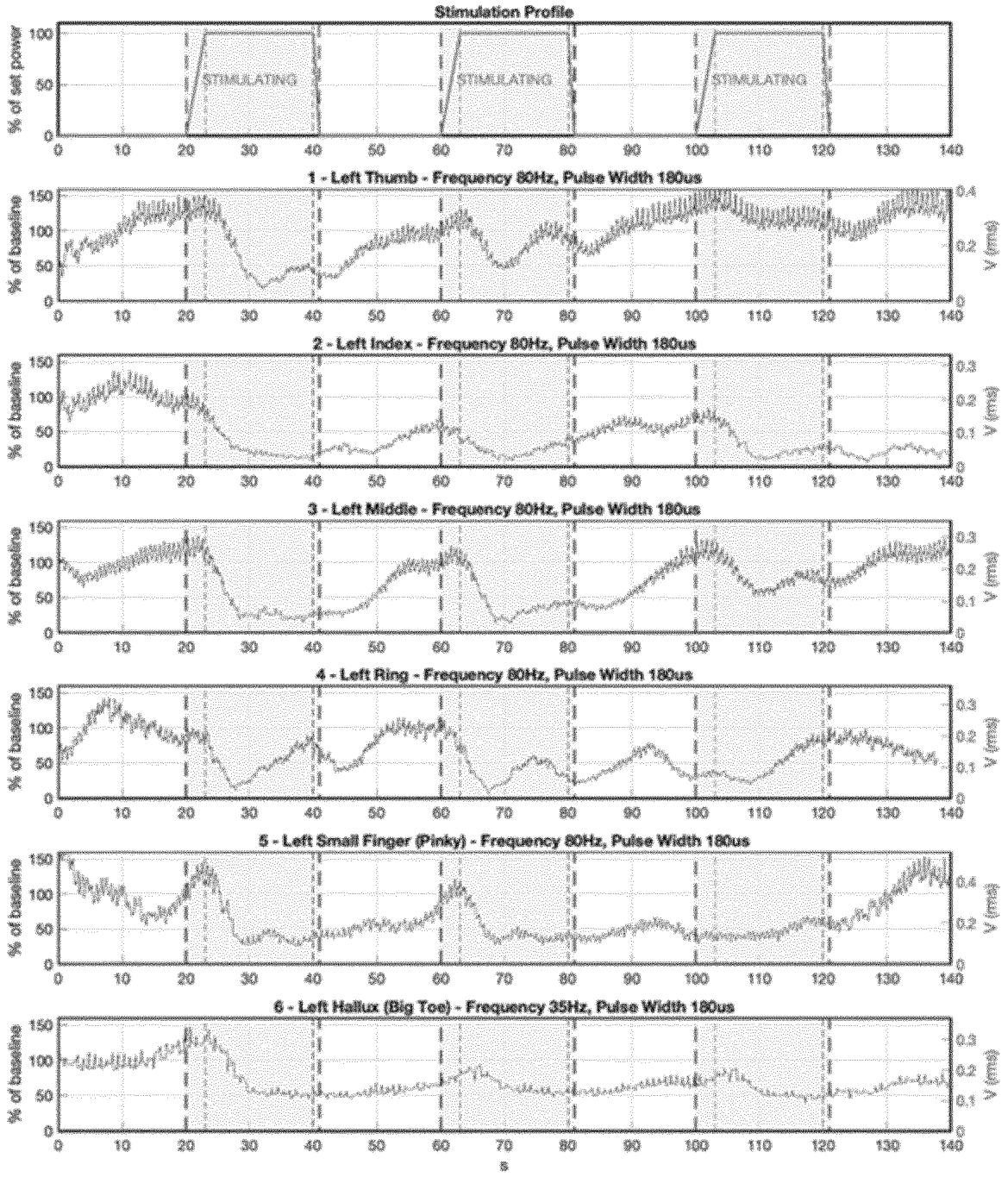

Stimulation Profile
% of set power
STIMULATING
STIMULATING
STIMULATING
1 - Left Thumb - Frequency 80Hz, Pulse Width 180us
2 - Left Index - Frequency 80Hz, Pulse Width 180us
3 - Left Middle - Frequency 80Hz, Pulse Width 180us
4 - Left Ring - Frequency 80Hz, Pulse Width 180us
5 - Left Small Finger (Pinky) - Frequency 80Hz, Pulse Width 180us
6 - Left Hallux (Big Toe) - Frequency 35Hz, Pulse Width 180us
% of baseline
V (rms)
s

Fig. 4b

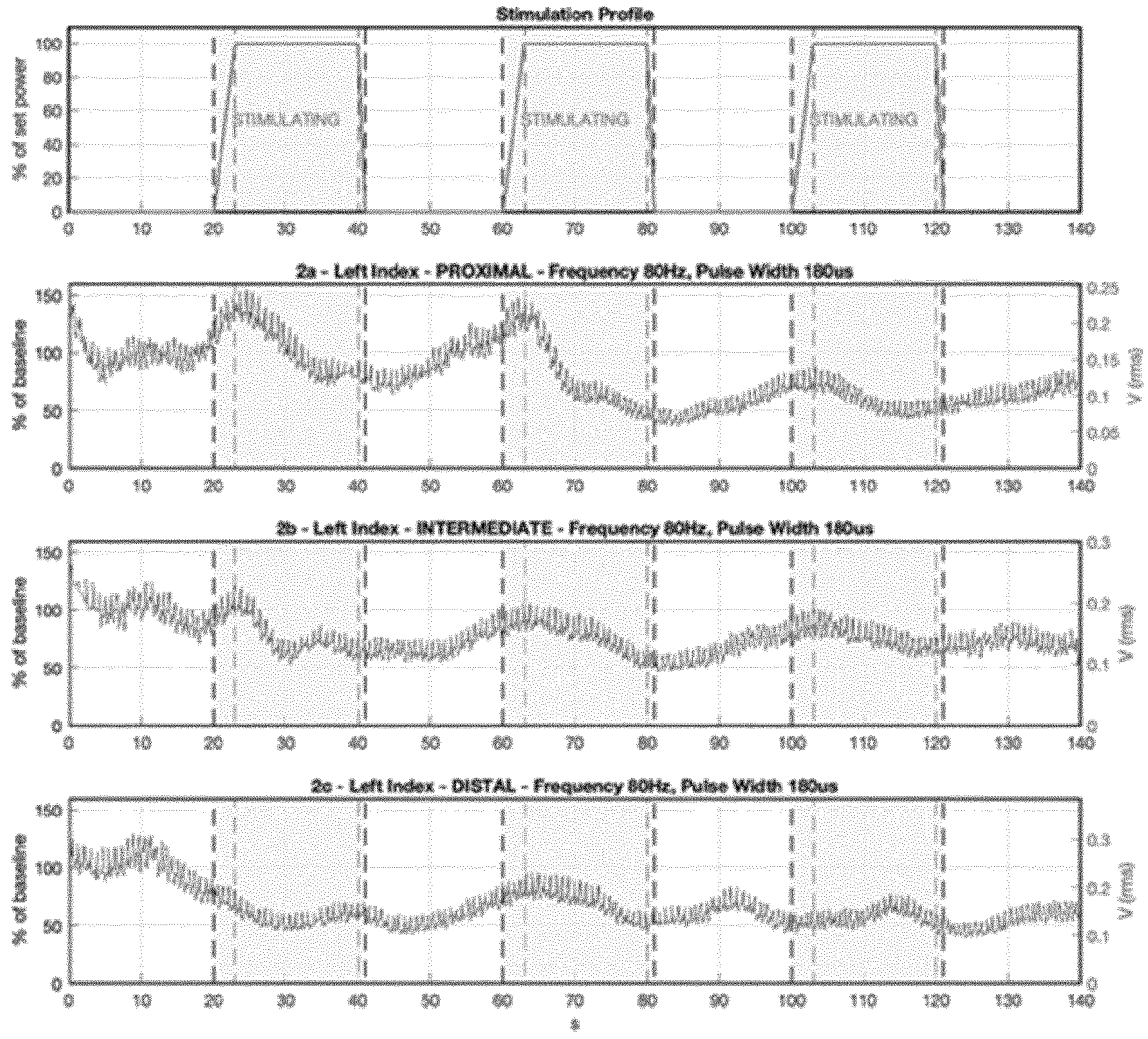

Stimulation Profile
% of set power
STIMULATING
STIMULATING
STIMULATING
2a - Left Index - PROXIMAL - Frequency 80Hz, Pulse Width 180us
% of baseline
V (rms)
2b - Left Index - INTERMEDIATE - Frequency 80Hz, Pulse Width 180us
% of baseline
V (rms)
2c - Left Index - DISTAL - Frequency 80Hz, Pulse Width 180us
% of baseline
V (rms)
s

Fig. 4c

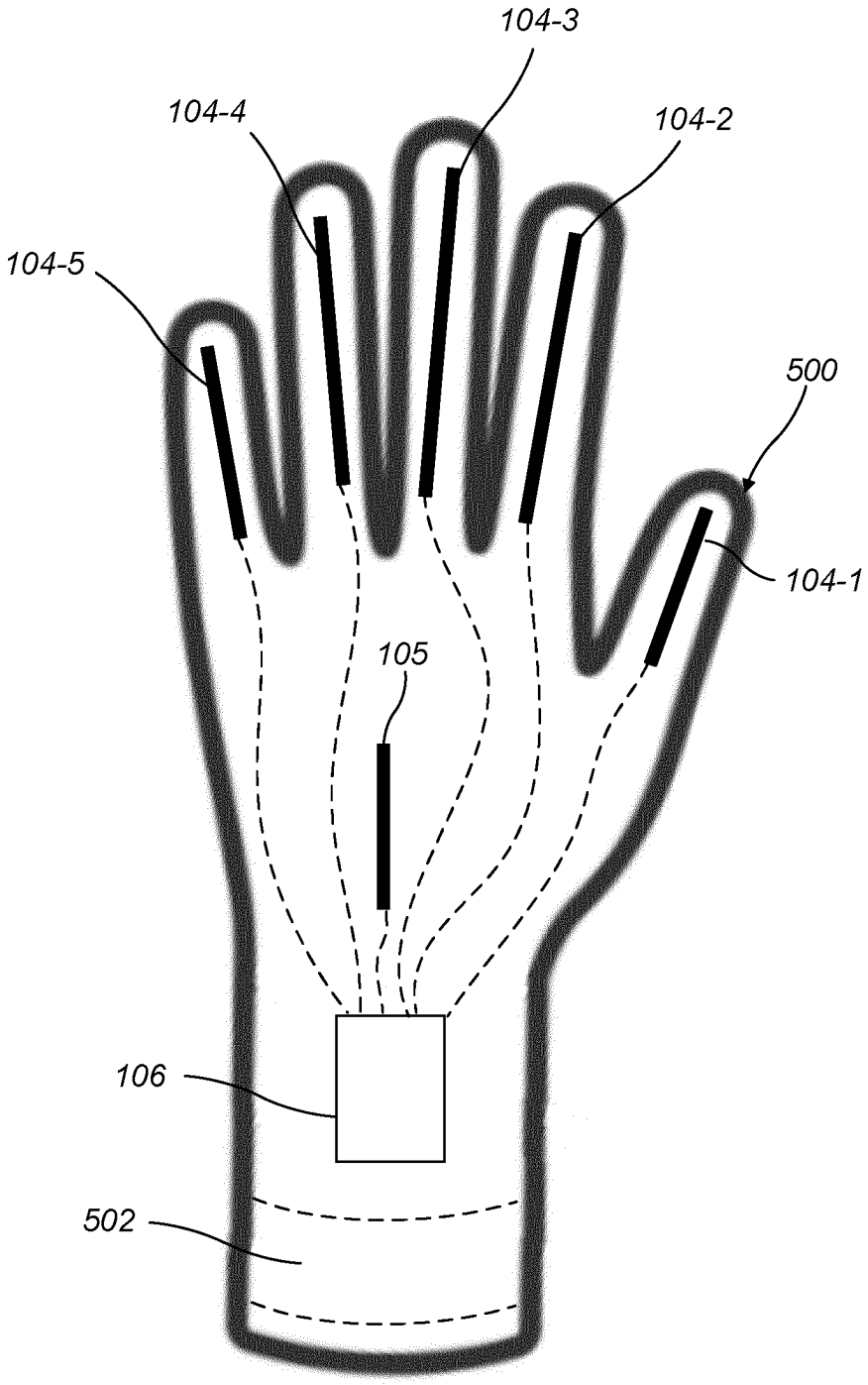


Fig. 5

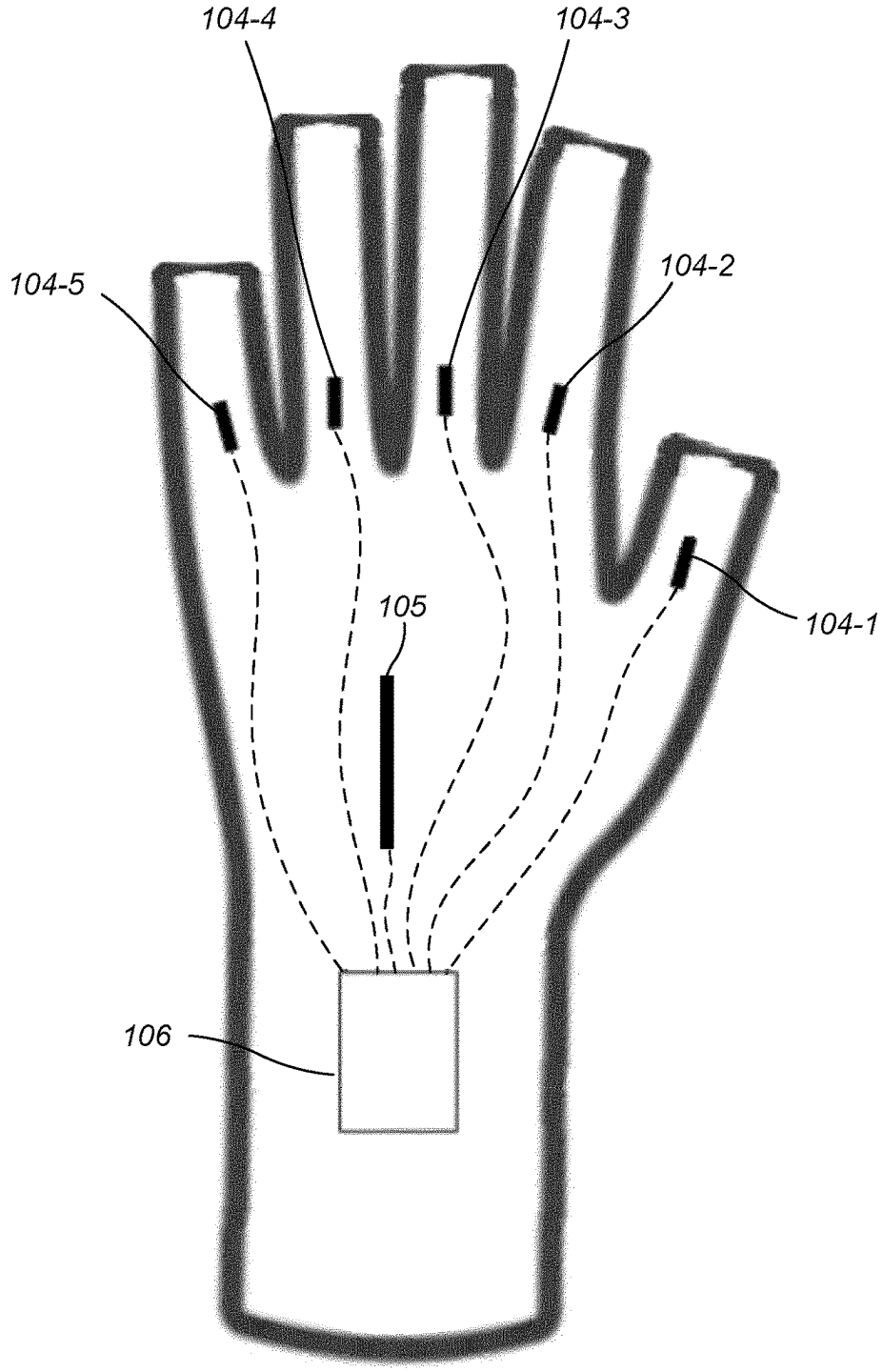


Fig. 6

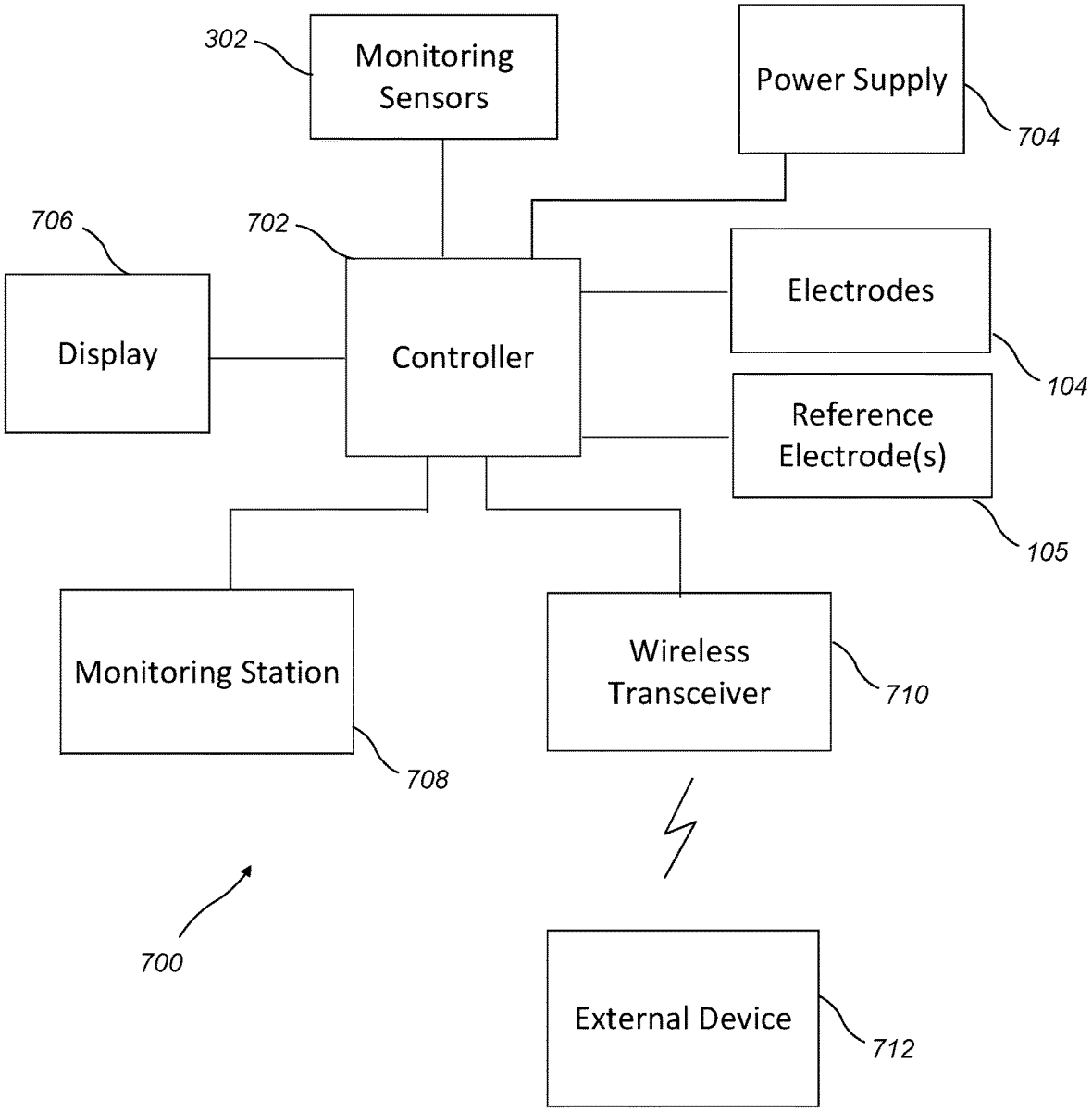

302
Monitoring Sensors
Power Supply
704
706
702
Display
Controller
Electrodes
104
Reference Electrode(s)
105
Monitoring Station
708
Wireless Transceiver
710
700
External Device
712

Fig. 7

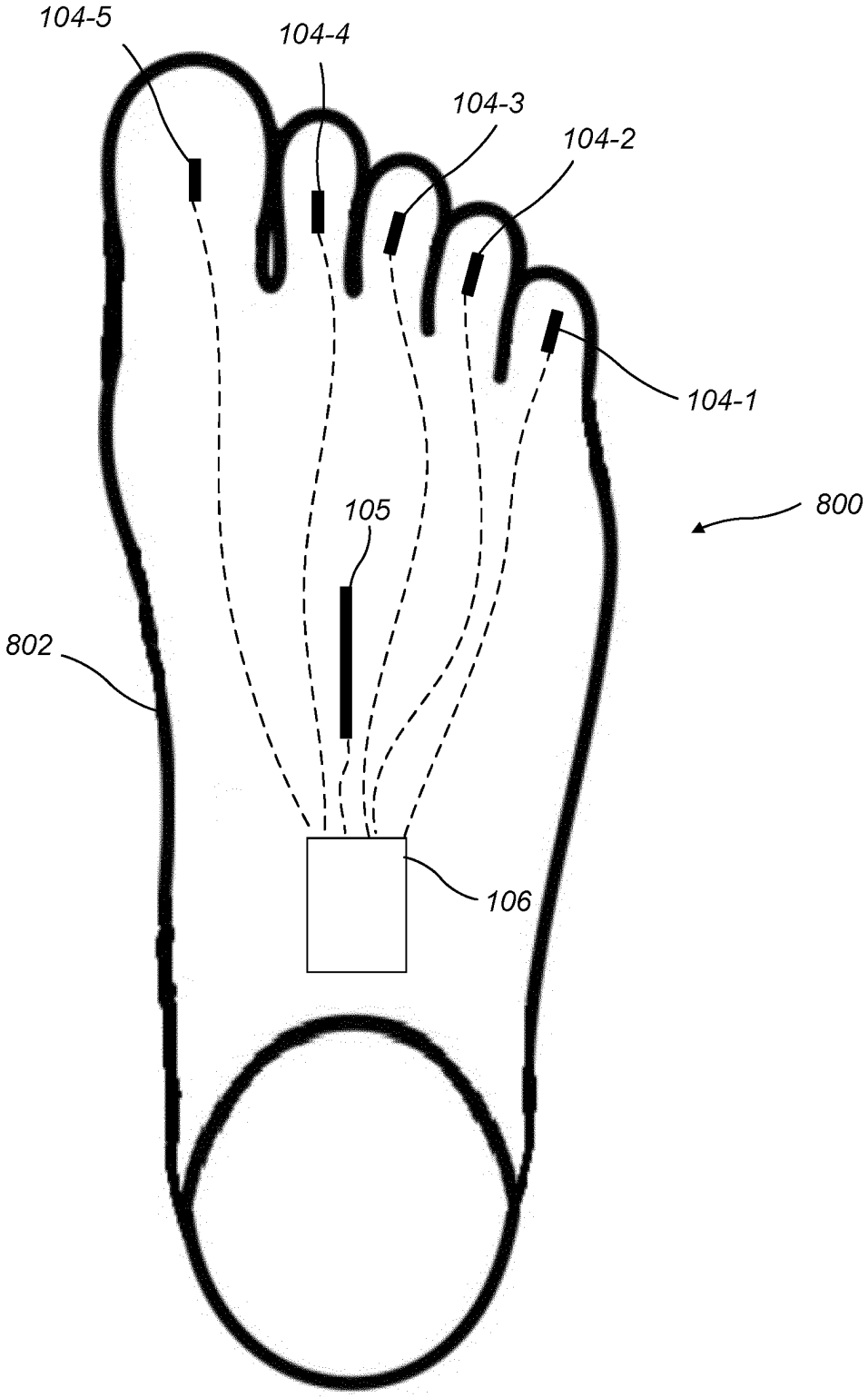


Fig. 8

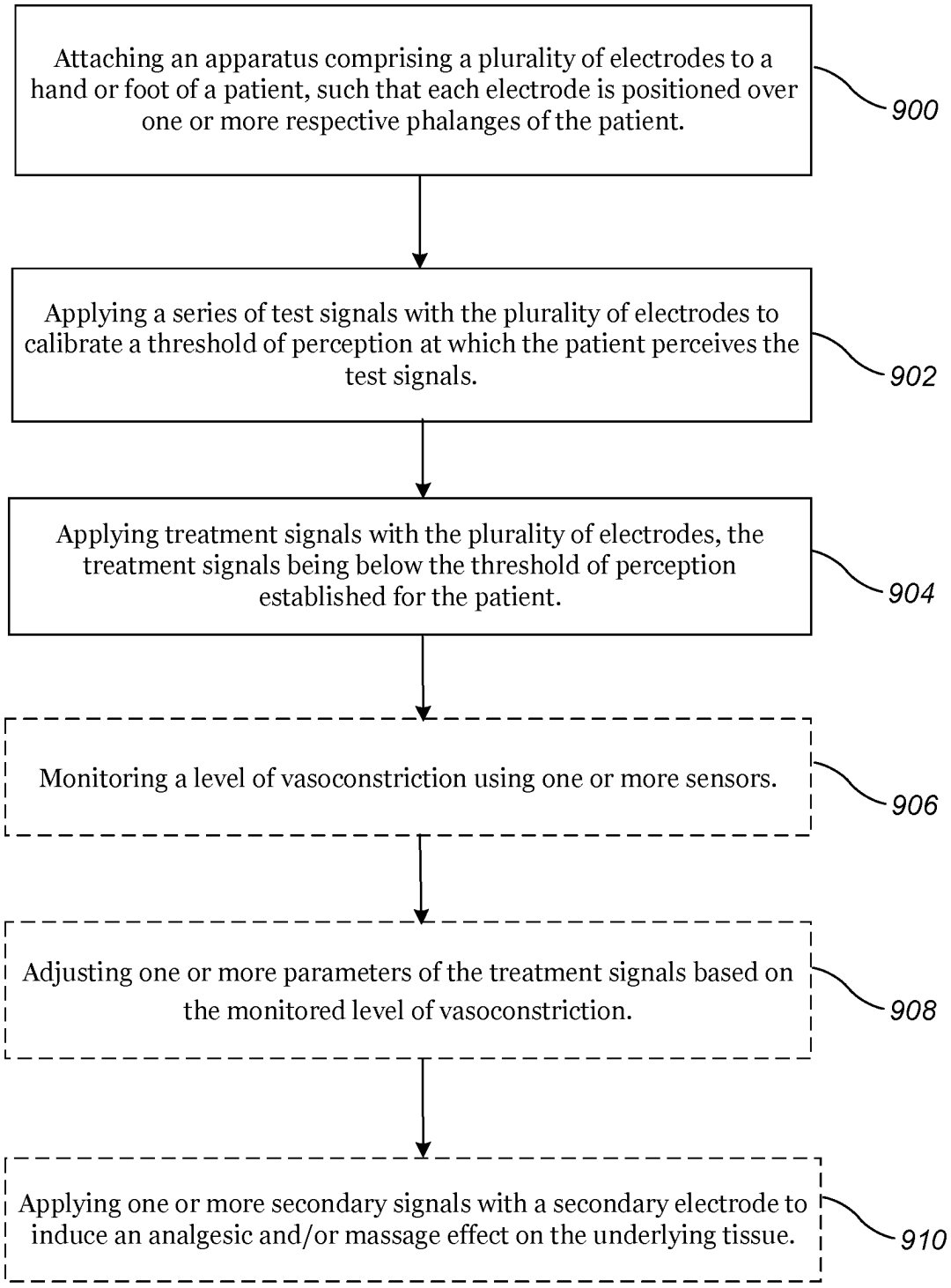

Attaching an apparatus comprising a plurality of electrodes to a hand or foot of a patient, such that each electrode is positioned over one or more respective phalanges of the patient.
900
Applying a series of test signals with the plurality of electrodes to calibrate a threshold of perception at which the patient perceives the test signals.
902
Applying treatment signals with the plurality of electrodes, the treatment signals being below the threshold of perception established for the patient.
904
Monitoring a level of vasoconstriction using one or more sensors.
906
Adjusting one or more parameters of the treatment signals based on the monitored level of vasoconstriction.
908
Applying one or more secondary signals with a secondary electrode to induce an analgesic and/or massage effect on the underlying tissue.
910

Fig. 9

APPARATUS AND METHOD FOR CAUSING VASOCONSTRICTION BY ELECTRICAL STIMULATION

FIELD OF THE INVENTION

[0001] The present invention relates to a wearable apparatus configured to apply electrical stimulation to the autonomous (sympathetic) nervous system, to achieve targeted vasoconstriction.

BACKGROUND

[0002] In the field of chemotherapy treatment, one of the side effects widely observed is Chemotherapy-Induced Peripheral Neuropathy (CIPN). Peripheral neuropathy may manifest as a tingling or numbness in the hands and feet, pain in the hands and feet and loss of function post chemotherapy leading to a deterioration in quality of life.

[0003] Toxicity from the chemotherapy medication is thought to cause nerve damage, leading to CIPN. This is a cumulative effect as the toxicity levels increase with each chemotherapy treatment. This can often lead to the reduction or cessation of chemotherapy, resulting in poorer therapeutic outcomes. CIPN is thought to affect the majority of patients undergoing chemotherapy treatment meaning that addressing the condition is an urgent unmet clinical need.

[0004] Current methods for treating CIPN are not well tolerated by patients and are not easy for healthcare professionals to apply. One existing solution is cold therapy to cause vasoconstriction. However, such devices have poor patient comfort and tolerability due to the very low temperatures involved. Due to the length of some chemotherapy sessions, a cold insert must be changed regularly, or several devices are required, which is time intensive for healthcare professionals. Such devices have also been known to cause thermal injuries such as frostbite.

SUMMARY OF THE INVENTION

[0005] According to a first aspect of the invention, there is described an apparatus configured to be worn on the hand or foot, the apparatus comprising: a plurality of electrodes arranged so as to be positioned over one or more respective phalanges when the apparatus is attached to the hand or foot; a supporting structure configured to attach the apparatus to the hand or foot and to retain the plurality of electrodes; and a controller configured to control the application of signals to the plurality of electrodes.

[0006] Each of the plurality of electrodes may be arranged so as to be positioned over the proximal phalanx of a respective digit. Alternatively, each of the plurality of electrodes may be arranged so as to be positioned over the intermediate phalanx of a respective digit. Alternatively, each of the plurality of electrodes may be arranged so as to be positioned over the distal phalanx of a respective digit. Alternatively, each of the plurality of electrodes may be arranged so as to be positioned over the proximal and intermediate phalanges of a respective digit. Alternatively, each of the plurality of electrodes may be arranged so as to be positioned over all of the phalanges of a respective digit. The apparatus may further comprise one or more reference electrodes positioned on the hand or foot, away from the fingers or toes. The one or more reference electrodes may be positioned on the palm of the hand. The one or more reference electrodes may be positioned on the back of the hand. The one or more reference electrodes may be positioned on the sole of the foot. The one or more reference electrodes may be positioned on the top of the foot.

[0007] The apparatus may further comprise a sensor retained by the supporting structure, wherein the sensor is positioned on a digit and is configured to monitor a property of underlying tissue.

[0008] The sensor may comprise a photoplethysmography sensor configured to output signals to the controller. The controller may be configured to derive a peripheral perfusion index in the underlying tissue based on the signals.

[0009] The sensor may comprise a peripheral autonomic surface potential sensor configured to measure activity of autonomic nervous tissue underlying the sensor.

[0010] The sensor may comprises a surface electromyography sensor configured to measure activity of somatic nervous tissue underlying the sensor.

[0011] The controller may be configured to dynamically adjust a property of the signals applied to the plurality of electrodes based on signals received from the sensor.

[0012] The apparatus may comprise a plurality of sensors, each of the plurality of sensors positioned on a respective digit. Alternatively, some subset of the digits may have corresponding sensors.

[0013] The controller may be configured to apply signals to the plurality of electrodes periodically, with a duty cycle of 50%.

[0014] The apparatus may further comprise a secondary electrode arranged to be positioned on the forearm or foreleg when the apparatus is attached to the hand or foot. The secondary electrode may be positioned so as to provide an analgesic effect when a stimulus is applied.

[0015] The apparatus may comprise a garment configured to be worn on the hand and optionally wherein the garment is a glove or mitt. Configuring the garment as a glove may be advantageous, as the patient retains some degree of dexterity while the electrical stimulus is being applied and can therefore continue to perform some tasks during the treatment.

[0016] The apparatus may comprise a garment configured to be worn on the foot and optionally wherein the garment is a sock or shoe.

[0017] According to a second aspect of the invention, there is described a method of inducing vasoconstriction in peripheral nerves using electrical stimulation, the method comprising: attaching an apparatus comprising a plurality of electrodes to a hand or foot of a patient, such that each electrode is positioned over one or more respective phalanges of the patient; applying a series of test signals with the plurality of electrodes to calibrate a threshold of perception at which the patient perceives the test signals; and applying treatment signals with the plurality of electrodes, the treatment signals being below the threshold of perception established for the patient.

[0018] The method may further comprise: monitoring a level of vasoconstriction using one or more sensors; and adjusting one or more parameters of the treatment signals based on the monitored level of vasoconstriction.

[0019] The apparatus may comprise a secondary electrode arranged to be positioned on the forearm or foreleg when the apparatus is attached to the hand or foot of the patient, and the method may further comprise subsequent to applying the treatment signals, applying one or more secondary signals

with the secondary electrode to induce an analgesic and/or massage effect on the underlying tissue.

BRIEF DESCRIPTION OF THE FIGURES

[0020] So that the general concepts set out in the foregoing sections can be more fully understood, embodiments thereof will be described with reference to the accompanying drawings, in which:

[0021] FIG. **1** shows an apparatus having the form of a glove with an integrated control system;

[0022] FIG. **2** shows a system according to some other embodiments, in which a control system is located externally to the apparatus;

[0023] FIG. **3** shows an apparatus according to further embodiments comprising monitoring sensors;

[0024] FIG. **4***a* is a graph showing results from a prototype apparatus in which a single electrode was attached to the fifth finger;

[0025] FIG. **4***b* shows a series of graphs showing experimental results with electrodes positioned over the proximal phalanges;

[0026] FIG. **4***c* shows a series of graphs showing experimental results in which different positions of the electrodes were tested;

[0027] FIG. **5** shows an apparatus according to further embodiments comprising elongated electrodes and an optional secondary electrode;

[0028] FIG. **6** shows an apparatus according to further embodiments in which the end portions of the fingers sections are omitted;

[0029] FIG. **7** illustrates schematically an electronic system for controlling operation of the apparatus of any of FIGS. **1-3**, **5-6** and **8**;

[0030] FIG. **8** shows an apparatus according to further embodiments having the form of a sock; and

[0031] FIG. **9** is a flow chart illustrating an exemplary method for applying a treatment for inducing vasoconstriction in peripheral nerves using electrical stimulation.

DETAILED DESCRIPTION

[0032] Referring to FIG. **1**, an apparatus **100** is shown having the form of a glove. The apparatus **100** comprises a supporting structure **102** allowing it to be attached to the hand of the user. The apparatus **100** also comprises a plurality of electrodes **104-1** to **104-5** (generally denoted as **104**). Each electrode **104** is located in a respective finger of the glove so as to be positioned on a respective finger of the user when the user is wearing the glove. The electrodes **104** may be positioned on the upper side of each glove finger so as to contact an upper surface of each finger, or on a lower side of each glove finger so as to contact an lower surface of each finger. Alternatively, each electrode **104** may have a ring or partial ring shape so as to wrap partially or completely around the respective finger.

[0033] The electrodes **104** may extend longitudinally along the length of the user's finger, as shown in FIG. **1**. Alternatively, the electrodes **104** may be positioned transverse to the user's fingers. In such an arrangement, each electrode **104** may wrap partially around the respective finger so as to cover both the medial and lateral sides of the finger.

[0034] In the embodiment shown in FIG. **1**, the electrodes **104-1** to **104-5** are each positioned on a proximal phalanx of the respective finger. In some other embodiments, described below, the electrodes **104-1** to **104-5** may be positions on the intermediate or distal phalanges or extend over two or more phalanges.

[0035] In addition to these, a reference electrode **105** is placed on/around the palm or wrist. Each of the electrodes **104-1** to **104-5** may share a common reference electrode **105**. Alternatively, multiple reference electrodes **105** may be provided, such that each electrode **104** has a corresponding reference electrode **105**. The reference electrode **105** may extend longitudinally along the length of the user's palm, as shown in FIG. **1**. Alternatively, the reference electrode **105** may be positioned across the user's palm (transverse to the direction of the fingers). In general, the reference electrode (s) **105** is positioned away from the fingers.

[0036] Placing the reference electrode **105** on the user's palm has been observed to have the greatest vasoconstriction effect. However, the reference electrode **105** may alternatively be positions on the back of the user's hand.

[0037] The electrodes **104-1** to **104-5** may be the anodes of the system while the reference electrode may be the cathode. With this arrangement, the signals applies to the electrodes **104** stimulate along the user's fingers.

[0038] The apparatus **100** also comprises a control system **106**, which in this embodiment is supported on a wrist portion of the glove.

[0039] The supporting structure **102** may be a glove with modified regions for retaining the electrodes **104**, and an elongated wrist portion with a modified region or pocket for retaining the control system **106**. The supporting structure **102** may comprise holes or other access points to allow adjustment or replacement of each electrode **104**. In some other embodiments, the supporting structure **102** may comprise a frame or web structure. This may allow increased airflow to the hand compared with a glove. The electrodes **104**, **105** and control system **106** may be retained by adjustable and/or resilient straps. Alternatively, or in addition, the electrodes may have a sticky portion for securing them to the user's skin.

[0040] The control system **106** may comprise a power supply, pulse generator and a processing unit (optionally incorporating feedback circuitry) for controlling the application of electrical signals to the electrodes **104**. Each of the electrodes **104** may have a separate connection to the control system **106** for this purpose. In some embodiments, the reference electrode may be located directly underneath the control system and/or may be integral with the control system. The control system may also comprise further elements described in more detail with respect to FIG. **6**.

[0041] FIG. **2** shows a system **200** according to some other embodiments, in which the control system **106** is located externally to the apparatus **202**. The apparatus **202** comprises a hub **204** into which all of the electrodes **104** and the reference electrode **105** are connected. The hub **204** can in turn be connected and disconnected from the control system **106** via a port on the hub **204** and/or control system **106**. This arrangement reduces the complexity of the apparatus **202** and allows the control system **106** to be used with different apparatuses **202**, meaning that fewer control systems **106** are required.

[0042] In both of the embodiments of FIGS. **1** and **2**, the electronic parts of the apparatus **100**, **202** may be removable from the supporting structure **102**, which allows the supporting structure to be washed. Alternatively, some or all of

the electronic parts may be sown into or otherwise permanently attached to the supporting structure **102**. The supporting structure **102** may be made of a resilient material to allow it to be used on patients having different sized hands. Alternatively, or in addition, the apparatus **100**, **202** may come in a variety of different sizes.

[0043] Referring to FIG. **3**, an apparatus **300** is shown according to further embodiments. The apparatus **300** comprises the same arrangement of electrodes **104**, reference electrode **105** and control system **106** disclosed in the embodiment of FIG. **1**. In addition, the apparatus **300** comprises at least one sensor **302-1** to **302-5** (generally denoted as **302**) retained by the supporting structure **102**. Each sensor **302** is arranged so as to be positioned on a digit and is configured to monitor a property of underlying tissue.

[0044] Although FIG. **3** illustrates a sensor **302** positioned on each finger, in some embodiments, only a subset of the illustrated sensors may be present. In some embodiments only a single sensor may be used. A number of different sensing technologies may be employed for the sensors **302**. In some embodiments the sensors may comprise photoplethysmography (PPG) sensors configured to output signals to the controller system **106**. The PPG sensors are positioned on the lower side of the glove so as to be in contact with the pad of each finger when the patient is wearing the glove. The control system **106** is configured to receive the signals from the PPG sensors and to derive an indication of peripheral perfusion (such as the peripheral perfusion index—PPI) in the underlying tissue based on the received optical signals. The PPI gives a measure of blood flow in the finger.

[0045] In some other embodiments, the sensors comprise peripheral autonomic surface potential sensors. These are configured to measure an electric potential which is indicative of the activity of autonomic nervous tissue underlying the sensor. The control system **106** receives signals from the peripheral autonomic surface potential sensors and is configured to determine a measure of blood flow in the finger.

[0046] In some other embodiments, the sensors comprise surface electromyography sensors. These are configured to measure activity of somatic nervous tissue underlying the sensor.

[0047] In some embodiments, the electrodes **104** used to apply a stimulus to the fingers may also be used as sensors. In the embodiments described above, the peripheral autonomic surface potential sensors or surface electromyography sensors comprises electrodes. These may be the same electrodes **104** that are used to stimulate the fingers. As described below with reference to FIG. **4**, the stimulus is applied periodically. During the periods where no signal is applied to the electrodes **104**, they may be used as sensors.

[0048] Measuring the current blood flow in the fingers as the electrical stimuli are applied to the electrodes allows the effectiveness of the treatment to be monitored in real time. The information from the sensors can also be used as a feedback mechanism to dynamically alter the strength, frequency and/or periodicity of the signals being applied to the electrodes to achieve the highest ongoing levels of vasoconstriction during a chemotherapy session.

[0049] FIG. **4***a* is a graph **400** showing results from a prototype apparatus in which a single electrode was attached to the fifth finger, with a reference electrode attached to the palm. The electrode extended over both the proximal and intermediate phalanges. A PPG sensor was placed on the finger tip of the fifth finger. Values for peripheral perfusion index were derived from the optical signals received from the PPG sensor during the test. An acclimatization period of 30 seconds was given before the application of any signal. Then an electrical stimulus was applied for 10 seconds, followed by an off period of 10 seconds, repeated periodically. The frequency of the applied signal was ~50 hz, with a current of 15mA and pulse width ~100 μs.

[0050] As can be seen, during the initial period of electrical stimulation the PPI fell sharply down to approximately 20% of the pre stimulus value. When the stimulus was removed for, the PPI rose over the period of no stimulus, but dropped again when the stimulus was re-applied. As can be seen from the graph **400**, applying the electrical stimulus periodically for 10 seconds, with a duty cycle of 50%, resulted in an average PPI over the period of testing of approximately 40% of the pre-stimulus value. This result indicates that substantial vasoconstriction can be achieved by the targeted application of periodic electrical signals on the phalanges. The likely mechanism is by the inhibition of local nitric oxide release, and therefore the activation of a local autonomic (sympathetic) response.

[0051] FIG. **4***b* contains a series of graphs showing firstly a stimulation profile and then a number of experimental results of root-mean-square PPG signals against time. These results were obtained with an apparatus as shown in FIG. **3**, with electrodes **104** positioned on the proximal phalanges of the fingers and a reference electrode positioned on the palm. PPG sensors **302** were positioned in contact with the pad of each finger. After attaching the apparatus **300** to the user, an extended settling period occurred in which no signals were applied.

[0052] The electrical stimulus was then applied periodically for 20 seconds, with a duty cycle of 50%. The frequency of the applied signal was ~80 hz, with a pulse width ~180 μs. The first 20 seconds of the measurement period, in which no signal was applied, was used as a baseline, against which the signal is normalized in plotting, allowing for comparison of the response between fingers. As can be seen in the first plot in FIG. **4***b*, when beginning or resuming stimulation, the apparatus has a linear ramp up over a period of 3 s. On pausing, the apparatus would cease stimulation via a linear ramp down over a period of 1 s.

[0053] Six different configurations are then shown, representing results from the thumb, index, middle, ring and small fingers of the left hand of the user. The last configuration shows results from the hallux (big toe) of a user (see description of FIG. **8** below). As can be seen there is a significant drop in PPG signal strength when the stimulation signal is applied, caused by substantial vasoconstriction in the peripheral nerves of the finger pads. These tests demonstrate a clear ability to induce vasoconstriction and to maintain this reduced blood flow over a prolonged period.

[0054] During these tests, the inventors noted difficulties in retaining the PPG probe against the thumb as it deforms, as is evident in the progressive degradation of the detected vasoconstrictive effect in configuration 1.

[0055] FIG. **4***c* contains a series of graphs showing firstly a stimulation profile and then a number of experimental results of root-mean-square PPG signals against time, in which different positions of the electrodes **104** were tested. The stimulation profile is the same as that described with reference to FIG. **4***b*. After attaching the apparatus to the user, an extended settling period also occurred in which no signals were applied. The first 20 seconds of the measure-

ment period, in which no signal was applied, was again used as a baseline, against which the signal is normalized in plotting.

[0056] Configuration 2a in FIG. **4***c* comprised an electrode positioned on the proximal phalanx of the left index finger, with a reference electrode positioned on the palm and a PPG sensor on the left index finger pad. Configuration 2b in FIG. **4***c* comprised an electrode positioned on the intermediate phalanx of the left index finger, with a reference electrode positioned on the palm and a PPG sensor on the left index finger pad. Configuration 2c in FIG. **4***c* comprised an electrode positioned on the distal phalanx of the left index finger, with a reference electrode positioned on the palm and a PPG sensor on the left index finger pad.

[0057] As can be seen, the largest drop in PPG signal during stimulation was observed when the electrode is positioned over the proximal phalanx, and in general the effect appears more pronounced with stimulation at the proximal and intermediate phalanges. However, in all cases a sustained long term reduction in PPG signal is observed, resulting from a sustained vasoconstriction and reduction in blood flow in the finger tips.

[0058] Referring to FIG. **5**, an apparatus **500** is shown according to further embodiments. The apparatus **500** comprises elongated electrodes **104** which extend along all of the phalanges of the fingers. The electrodes **104** are otherwise the same as those previously described. A reference electrode **105** is position on the palm (or back of the hand) as previously described. The electrodes are connected to and controlled by a control system **106** similar to that already described. In addition, the apparatus **500** may optionally comprise a secondary electrode **502** supported on the elongated wrist portion of the glove, so as to be positioned on the forearm of the patient when the patient is wearing the glove. The position of the secondary electrode **502** is such that applying a stimulus will result in vasodilation of the underlying tissue. The secondary electrode may be a standard TENS electrode. As such, the secondary electrode **502** is not used during a chemotherapy session, but may be activated post therapy for the purpose of increasing peripheral blood-flow, causing an analgaesic effect or massage effect.

[0059] Referring to FIG. **6**, an apparatus **600** is shown according to further embodiments. The apparatus **600** comprises the same arrangement of electrodes **104**, reference electrode **105** and control system **106** disclosed in the embodiment of FIG. **1**. However, the end portions of the fingers of the glove are removed, so that the patient's finger tips will be exposed when they are wearing the apparatus **600**. This allows the apparatus **600** to be used in combination with an existing PPI monitor such as a pulse oximeter. This design may also allow the patient greater dexterity to carry out tasks while undergoing a chemotherapy treatment.

[0060] FIG. **7** illustrates schematically an electronic system **700** for controlling operation of the previously described apparatus. The electronic system **700** comprises a controller **702**, the previously described electrodes **104**, reference electrode(s) **105**, one or more of the previously described monitoring sensors **302** and a power supply **704**. Optionally, the electronic system may also include a display **706**, monitoring station **708** and/or wireless transceiver **710**.

[0061] The controller **702** is configured to control operation of the other components of the electronic system **700**. The controller **702** may for instance be a microprocessor, a Digital Signal Processor (DSP), Application Specific Integrated Circuit (ASIC), Field Programmable Gate Array (FPGA) or the like. Alternatively, the controller **702** may comprise specialized processing hardware, for instance a RISC processor or programmable hardware with embedded firmware. The controller **702** may comprise multiple processors. The controller **702** may also comprise a memory, for example a program memory storing program code (e.g. software or firmware). The program memory may for instance be a non-volatile memory, such as a Read-Only Memory (ROM), a Flash memory or a magnetic drive memory.

[0062] The display **706** may be a standard LCD display or a touch sensitive display based on capacitive or resistive sensing technology. The display **706** may be attached, either removably or permanently, to the supporting structure **102** of the apparatus. Where the apparatus is a glove, the display **706** may be positioned on the elongated wrist portion of the glove, so that it can be easily viewed by the patient, without interfering with either the chemotherapy treatment or the electrical stimulus being provided by the apparatus. The power supply **704** may be a battery of any suitable kind and may provide power for all of the other elements of the electronic system **700**. The power supply **704** may also be retained on or in the supporting structure **102**.

[0063] The electronic system **700** may also optionally comprise a wireless transceiver **710** for communicating with an external device **712**. The wireless transceiver **710** comprises the network interfaces necessary to communicate over 3G, 4G, 5G, Bluetooth, WiFi, Zigbee or any combination of these protocols and may also include an antenna. The wireless transceiver **710** may communicate directly with the external device **712**, or the communication may be routed through an intermediate device, router, server or base station. The external device **712** may be a smartphone, tablet, PDA or other mobile computing device. The external device **712** may be assigned to the patient or the patient's doctor or other health care professional. The external device **712** may run an app or other software to display information relating to the operation of the electronic system **700**. Further information about the patient's chemotherapy may be integrated into the app, such as the duration of the current treatment, time remaining. Information received from the monitoring sensors **302** may be displayed on a display of the external device **712**. The app or other software on the external device **712** may also allow for control of the electronic system **700**, for example to start, stop and/or pause the electrical stimulus or change a parameter of the applied signals, such as the current or periodicity (duty cycle). The external device **712** also comprises a memory (not shown) which may be used to record any information received from the monitoring sensors **302** for subsequent review or onward transmission.

[0064] In some embodiments, the controller **702** and power supply **704** may be incorporated in the control system **106** shown in FIGS. **1**, **2**, **5** and **6**. The display **706** and wireless transceiver **710**, if present, may also be part of the control system **106**. The electrodes **104** and monitoring sensors **302** (if present) are necessarily remote from the control system **106**, so that these components can be located on the user's fingers.

[0065] In some other embodiments, the electronic system **700** comprises a monitoring station **708**, to which the controller **702** can be connected. The monitoring station **708** is external to the apparatus and may comprise a computer

terminal. The monitoring station **708** may receive information from the monitoring sensors **302** while the apparatus is in use. This may allow a doctor, nurse or other healthcare professional to observe the effects of the electrical stimulus in real time. In some embodiments, the monitoring station **708** may be capable of issuing instructions to the controller **702** to alter a parameter of the applied signals, such as the current or periodicity (duty cycle). This may be done automatically as a result of feedback from the monitoring sensors **302**, in order to maximize the reduction in peripheral blood flow, or to keep the peripheral blood flow at or within defined limits.

[0066] In use the controller **702** controls application of electrical signals by the power supply **704** to the electrodes **104**, according to a pre-set program. The pre-set program may be stored in a memory on the controller, a separate memory (not shown) forming part of the electronic system **700** or on the monitoring station **708**.

[0067] The controller **702** receives feedback signals from the monitoring sensors **302** and controls display of this information on the display **706**, if present. The feedback information may be communicated to the monitoring station **708** for display and/or storage. The feedback information may also be communicated via the wireless transceiver **710** to the external device **712**, for display and/or storage. The controller **702** may receive instructions from the monitoring station **708** or the external device **712** to alter one or more parameters of the applied signals.

[0068] Referring to FIG. **8**, an apparatus **800** is shown according to further embodiments. The apparatus **800** comprises a sock or other garment arrangement to be worn on the foot of a patient. The apparatus **800** comprises a supporting structure **802** allowing it to be attached to the foot of the user.

[0069] The apparatus **800** comprises a plurality of electrodes **104**. Each electrode **104** is located in a respective toe of the sock so as to be positioned on a respective toe of the user when the user is wearing the sock. The electrodes **104** may be positioned on the upper side of each toe area so as to contact an upper surface of each toe, or on a lower side of each toe area so as to contact an lower surface of each toe. Alternatively, each electrode **104** may have a ring or partial ring shape so as to wrap partially or completely around the respective toe. In addition to these, a reference electrode **105** is placed on/around the sole of the foot. In some alternative embodiments, the reference electrode **105** is positioned on the top of the foot part of the sock or on the ankle part of the sock. In general, the reference electrode(s) **105** is positioned away from the toes.

[0070] The apparatus **800** also comprises the control system **106** as previously described, which in this embodiment is supported on the top of the foot part of the sock. The control system **106** in FIG. **8** may comprise some of the elements of the electronic system **700** as previously described and may be able to be connected to a monitoring station **708** and/or communicate with an external device **712**, as previously described.

[0071] The supporting structure **802** may be a sock with modified regions for retaining the electrodes **104**. The supporting structure **802** may comprise holes or other access points to allow adjustment or replacement of each electrode **104**.

[0072] As with the glove embodiments described, above, the electrodes **104** in the sock embodiment of FIG. **8** are positioned so as to apply electrical stimulation directly to the phalanges, in this case the phalanges of the toes. Application of an electrical signal in this manner results in vasoconstriction of the blood vessels in the toes, which reduces the build up of toxicity as a result of chemotherapy medication in the toes and a resulting reduction in nerve damage. The electrodes **104** may also act as sensors for determining activity of the underlying nerve tissue in order to monitor the effectiveness of the electrical stimulation and to act as a feedback for altering the electrical stimulus if necessary. In some other embodiment, one or more of the toe sections of the apparatus **800** may additionally be provided with a PPG sensor to independently monitor blood flow and allow a PPI to be derived. Alternatively, the end portions of one or more of the toe section may be omitted to allow a separate PPG sensor to be attached to the toe.

[0073] The apparatus **800** may also comprise a secondary electrode (not shown) supported by an elongated ankle portion (not shown) of the sock, such that the secondary electrode is positioned on the foreleg of the patient. As previously described, the secondary electrode is not used during a chemotherapy session, but may be employed post therapy to provide an analgesic or massage effect.

[0074] Although the apparatus **800** has been shown with separate section for each toe, the apparatus **800** may instead comprise a single internal space, with the electrodes **104** positioned so that they can be accurately placed on the toes of the patient. Additionally, although he apparatus **800** is depicted as a sock with separate sections for each toe, the apparatus may instead take the form of a slipper or shoe.

[0075] Referring again to FIG. **4***b*, experimental results obtained by applying a signal to the hallux (big toe) are shown in chart 6. In this experiment, the electrode was positioned on the proximal phalanx of the big toe and a PPG sensor attached to the toe pad. As can be seen, a significant and sustained vasoconstriction can be obtained in the toe using this apparatus.

[0076] FIG. **9** is a flow chart illustrating an exemplary method for applying a treatment for inducing vasoconstriction in peripheral nerves using electrical stimulation. The treatment may be applied simultaneously with a chemotherapy sessions, i.e. during administration of a chemotherapy medication, for the purpose of reducing the accumulation of toxicity in peripheral nerves during chemotherapy, which can lead to peripheral neuropathy.

[0077] The process begins at step **900**, by attaching an apparatus comprising a plurality of electrodes to a hand or foot of a patient, such that each electrode is positioned over one or more respective phalanges of the patient. The apparatus may be any of those described with reference to FIG. **1-3**, **5**, **6** or **8**.

[0078] At step **902** a series of test signals are applied with the plurality of electrodes to calibrate a threshold of perception at which the patient perceives the test signals. Ideally, the level of electrical signal used during treatment will be mostly imperceptible to the user, both for increased comfort and for improved uptake of the treatment. Each patient will have a different perception threshold and so it is necessary to establish a calibrated perception level for each patient before treatment.

[0079] At step **904**, treatment signals are applied with the plurality of electrodes, the treatment signals being below the threshold of perception established for the patient.

[0080] At optional further step **906**, one or more sensors are used to monitor a level of vasoconstriction. These sensor may be any of the sensors **302** previously described. At optional further step **908**, one or more parameters of the treatment signals are adjusted based on the monitored level of vasoconstriction. The adjustments to the treatment signals are made within predefined limits and also take into account the perception threshold of the individual patient. At optional further step **910**, one or more secondary signals are applied with a secondary electrode to induce an analgesic and/or massage effect on the underlying tissue. This step is performed after the treatment signals are completed.

REFERENCE NUMERALS

[0081] **100** Apparatus
[0082] **102** supporting structure
[0083] **104** electrodes
[0084] **104-1** first electrode etc.
[0085] **105** reference electrode
[0086] **106** control system
[0087] **200** System
[0088] **202** Apparatus
[0089] **204** hub
[0090] **300** apparatus
[0091] **302** sensors
[0092] **302-1** first sensor etc.
[0093] **400** graph
[0094] **500** Apparatus
[0095] **502** Secondary electrode
[0096] **600** apparatus
[0097] **700** Electronic System
[0098] **702** controller
[0099] **704** power supply
[0100] **706** display
[0101] **708** monitoring station
[0102] **710** wireless transceiver
[0103] **712** external device
[0104] **800** apparatus
[0105] **802** supporting structure

1. An apparatus configured to be worn on the hand or foot, the apparatus comprising:

a plurality of electrodes arranged so as to be positioned over one or more respective phalanges when the apparatus is attached to the hand or foot;

a supporting structure configured to attach the apparatus to the hand or foot and to retain the plurality of electrodes; and

a controller configured to control the application of signals to the plurality of electrodes.

2. The apparatus of claim **1**, wherein each of the plurality of electrodes is arranged so as to be positioned over the proximal phalanx of a respective digit.

3. The apparatus of claim **1**, wherein each of the plurality of electrodes is arranged so as to be positioned over the intermediate phalanx of a respective digit.

4. The apparatus of claim **1**, wherein each of the plurality of electrodes is arranged so as to be positioned over the distal phalanx of a respective digit.

5. The apparatus of claim **1**, wherein each of the plurality of electrodes is arranged so as to be positioned over the proximal and intermediate phalanges of a respective digit.

6. The apparatus of claim **1**, wherein each of the plurality of electrodes is arranged so as to be positioned over all of the phalanges of a respective digit.

7. The apparatus of any preceding claim, the apparatus further comprising one or more reference electrodes positioned on the hand or foot, away from the fingers or toes.

8. The apparatus of any preceding claim, the apparatus further comprising a sensor retained by the supporting structure, wherein the sensor is positioned on a digit and is configured to monitor a property of underlying tissue.

9. The apparatus of claim **8**, wherein the sensor comprises a photoplethysmography sensor configured to output signals to the controller.

10. The apparatus of claim **9**, wherein the controller is configured to derive a peripheral perfusion index in the underlying tissue based on the signals.

11. The apparatus of claim **8**, wherein the sensor comprises a peripheral autonomic surface potential sensor configured to measure activity of autonomic nervous tissue underlying the sensor.

12. The apparatus of claim **8**, wherein the sensor comprises a surface electromyography sensor configured to measure activity of somatic nervous tissue underlying the sensor.

13. The apparatus of any of claims **8** to **12**, wherein the controller is configured to dynamically adjust a property of the signals applied to the plurality of electrodes based on signals received from the sensor.

14. The apparatus of any of claims **8** to **12**, wherein the apparatus comprises a plurality of sensors, each of the plurality of sensors positioned on a respective digit.

15. The apparatus of any preceding claim, wherein the controller is configured to apply signals to the plurality of electrodes periodically, with a duty cycle of **50**%.

16. The apparatus of any preceding claim, wherein the apparatus further comprises a secondary electrode arranged to be positioned on the forearm or foreleg when the apparatus is attached to the hand or foot.

17. The apparatus of any preceding claim, wherein the apparatus comprises a garment configured to be worn on the hand and optionally wherein the garment is a glove or mitt.

18. The apparatus of any of claims **1** to **16**, wherein the apparatus comprises a garment configured to be worn on the foot and optionally wherein the garment is a sock or shoe.

19. A method of inducing vasoconstriction in peripheral nerves using electrical stimulation, the method comprising:

attaching an apparatus comprising a plurality of electrodes to a hand or foot of a patient, such that each electrode is positioned over one or more respective phalanges of the patient;

applying a series of test signals with the plurality of electrodes to calibrate a threshold of perception at which the patient perceives the test signals; and

applying treatment signals with the plurality of electrodes, the treatment signals being below the threshold of perception established for the patient.

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

monitoring a level of vasoconstriction using one or more sensors; and

adjusting one or more parameters of the treatment signals based on the monitored level of vasoconstriction.

21. The method of claim **19** or **20**, wherein the apparatus comprises a secondary electrode arranged to be positioned on the forearm or foreleg when the apparatus is attached to the hand or foot of the patient, the method further comprising subsequent to applying the treatment signals, applying

one or more secondary signals with the secondary electrode to induce an analgesic and/or massage effect on the underlying tissue.

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