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(54) Title: MONITORING SOMATOSENSORY EVOKED POTENTIALS (SSEPs) FOR COMPARTMENT SYNDROME

Fig. 1

Electrodes Applied Distal and Proximal to Examined Compartment

Examined Compartment

Unaffected Limb

SSEPs Reflect Nerve Function and Compartment Status

Altered SSEPs

Normal SSEPs

(57) Abstract: Described herein is the use of longitudinal/continuous somatosensory evoked potentials (SSEPs) for monitoring e.g., lower and upper limb nerves as a surrogate measure of compartment status in patients at high risk for developing compartment syndrome or manifesting for diagnosis of chronic compartment syndrome. Therein, a novel, non-invasive or minimally invasive telem medicine approach to monitoring compartment status is achieved where compression of the nerve within the affected compartment is detected using both individualized threshold values and rate of change increments.
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MONITORING SOMATOSENSORY EVOKED POTENTIALS (SSEPs) FOR COMPARTMENT SYNDROME

RELATED APPLICATIONS


FIELD

This invention relates to assessment and monitoring for a medical condition known as compartment syndrome (acute and chronic).

BACKGROUND

Compartment syndrome is a serious complication of upper and lower limb injury that can lead to irreversible loss of limb function; soft tissue swelling reduces perfusion to muscle, resulting in necrosis (muscle cell death). Patients at high risk of compartment syndrome are observed closely with clinical observation and fasciotomies (surgical open release of muscle pressure) are performed in patients that have symptoms and signs of compartment syndrome. Clinical cues include disproportionate pain in the affect limb and loss of function; direct, invasive compartment pressure measurements aid to confirm the diagnosis. Although curative, fasciotomies are morbid procedures and are associated with increased infection risk and decreased mobility/function, and should only be performed only when necessary.

Currently, observation of compartment pressures and diagnosis of compartment syndrome remains difficult, particularly in the obtunded or unconscious patient. Despite being a medical emergency, the clinical options available for monitoring (intermittent invasive direct pressure measurement) are difficult to deliver, unreliable and result in delayed diagnosis or unnecessary fasciotomy. Thus, development of a non-invasive or minimally invasive method for monitoring compartment pressures using Somatosensory Evoked Potentials (a nerve response to a stimulus) presents a novel clinical approach to this problem by detecting longitudinal alterations in nerve function as the result of compression and ischemia on a nerve running through an examined myofascial compartment.

Summary

In some embodiments, the invention disclosed herein comprises a method for monitoring a subject for compartment syndrome comprising the steps of applying a n
electrical stimulus to a nerve within a compartment at risk of compartment syndrome and
detecting a measurable waveform resulting from the electrical stimulus, wherein the
measurable waveform represents a somatosensory evoked potential (SSEP). In some
embodiments, the method further includes determining if there is a difference in the
somatosensory evoked potentials for the compartment at risk as compared to somatosensory
evoked potentials in a similarly situated compartment that does not have compartment
syndrome. The similarly situated compartment may be in the opposite (unaffected) limb of
the subject. In some aspects of the invention, an alteration in somatosensory evoked
potentials in the compartment at risk indicates an increase compartment pressure and/or a
decrease in nerve function.

Some methods according to the invention include a stimulating electrode. The
stimulating electrode may be a skin electrode or a needle electrode. In some methods, the
stimulating electrode is positioned distal to the examined compartment and may be used to
apply the electrical stimulus. A detecting electrode may be used to detect somatosensory
evoked potentials. Detecting electrodes may be positioned proximal to the examined
compartment. In some embodiments, a detecting electrode is positioned on the scalp.

Some methods of the invention further comprise notifying a healthcare professional if
the somatosensory evoked potential is outside of an individualized threshold range or is
changing faster than a pre-determined threshold rate of change. Methods of the invention
may be used to diagnose compartment syndrome. Methods for monitoring SSEPs may be
performed in a surgical or non-surgical setting. The patient or subject being monitored may
be conscious, obtunded or unconscious. In some embodiments, a healthcare professional
monitors the subject remotely.

Some aspects of the invention include a device for monitoring a patient for
compartment syndrome comprising a component for applying an electrical stimulus to a
nerve in a compartment at risk for developing compartment syndrome and a component for
detecting a measurable waveform resulting from the electrical stimulus, wherein the
measurable waveform represents a somatosensory evoked potential.

Some embodiments of the invention include a system for monitoring a patient for
compartment syndrome, comprising a component for applying an electric stimulus to a nerve
in a compartment at risk for developing compartment syndrome, a component for detecting a
measurable waveform resulting from the electrical stimulus, wherein the measurable waveform represents a somatosensory evoked potential, and a component for quantifying or analyzing the somatosensory evoked potential. A system may further include a component for transmitting the measured somatosensory evoked potentials, or results from analysis of the measured somatosensory evoked potentials, to a remote user.

Some aspects of the invention include non-transitory computer readable media comprising computer code for applying an electrical stimulus to a nerve in a compartment at risk of compartment syndrome and detecting a measurable waveform resulting from the electrical stimulus, wherein the measurable waveform represents somatosensory evoked potentials.

**BRIEF DESCRIPTION OF THE FIGURES**

The present invention may be better understood by referring to the following non-limiting figures.

**Figure 1** is a schematic for monitoring SSEPs according to one embodiment of the invention. The schematic shows parallel monitoring on the limb with the compartment of concern and the unaffected limb for comparison of SSEPs.

**Figure 2** illustrates an example of an SEP monitoring configuration according to an embodiment of the invention. Stimulating electrodes on the ankles apply an electrical stimulus which is conducted through the compartment of concern to the central nervous system. Detecting electrodes on the scalp receive the SEP signal.

**Figure 3** is a schematic showing possible configurations for SEP data management, according to some embodiments of the invention.

**DETAILED DESCRIPTION**

The following description recites various aspects and embodiments of the present invention. No particular embodiment is intended to define the scope of the invention. Rather, the embodiments merely provide non-limiting examples of various methods and systems that are at least included within the scope of the invention. The description is to be read from the perspective of one of ordinary skill in the art; therefore, information well-known to the skilled artisan is not necessarily included.
Definition and Abbreviations

The following terms, unless otherwise indicated, shall be understood to have the following meanings:

As used herein, the terms "a," "an," and "the" can refer to one or more unless specifically noted otherwise.

The term "or" is not to be construed as identifying mutually exclusive options. For example, the phrase "X contains A or B" can mean that X contains A and not B, X contains B and not A, or X contains both A and B. That is, the term "or" is used to mean "and/or" unless explicitly indicated to refer to alternatives only or the alternatives are mutually exclusive, although the disclosure may support a definition that refers to only alternatives and "and/or."

As used herein "another" can mean at least a second or more.

The term "SSEPs" as used herein, refers to Somatosensory Evoked Potentials, which are electrical signals generated by the nervous system in response to sensory stimuli, specifically consisting of a series of waves that reflect sequential activation of neural structures (including peripheral nerves) along examined somatosensory pathways.

The term "compartment syndrome" as used herein refers to a condition characterized by increased pressure in a confined myofascial compartment that interrupts perfusion of tissues and results in irreversible muscle loss.

The term "individualized thresholds" as used herein refers to the use of initial baseline SSEP measurements of the examined compartment as well as SSEP measurements from the unaffected limb to determine the nature and/or extent of change in SSEPs needed to trigger the system to send an alert to a healthcare professional. Rate of change is considered, in addition to the actual amplitude and latency of each waveform recorded, in arriving at individualized thresholds.

The terms "compartment at risk" or "examined compartment" are used interchangeably herein. Both refer to a compartment that is believed to be susceptible to (at risk of) developing compartment syndrome.

The terms "distal" and "proximal" as used herein, refer to locations of limb anatomy with respect to the point of attachment to the torso. Distal means farther from the point of attachment to the torso, whereas proximal means closer to that point. In embodiments where
the examined compartment is not in a limb, the point of reference is the midline, central nervous system and/or brain.

The term "obtunded" as used herein refers to a state of less than full alertness. That is, it refers to patients having altered level of consciousness, often as a result of a medical condition.

The terms "subject" and "patient" are used interchangeably herein and may refer to a person being monitored, diagnosed, or treated for compartment syndrome.

**Description**

There is a current clinical need for a precise, reliable, longitudinal non-invasive or minimally invasive method to diagnose compartment syndrome. Compartment syndrome is monitored in hundreds of thousands of trauma patients that are "at risk" annually, due to the devastating consequences of a missed diagnosis. Invasive compartment pressure measurement is generally reserved for confirming a diagnosis of compartment syndrome. Specific monitoring of patients for compartment syndrome is lacking, often resulting in a delayed treatment.

Compartment syndrome is defined as increased pressure in a confined myofascial compartment that interrupts perfusion of tissues and results in irreversible muscle loss. It is usually monitored clinically by asking the patient how much pain they have in the affected limb (disproportionate pain is pathognomonic) and with compartment checks using an invasive pressure needle/catheter to make the definitive diagnosis. However, compartment syndrome can evolve in patients that remain asymptomatic or who are obtunded, with resultant muscle damage. Delayed treatment has clearly been demonstrated to lead to poor outcome and is a leading cause of litigation in medicine. Currently used continuous direct measures of compartment pressure are invasive and consist of serial measurement of compartment pressure using a needle catheter. From a patient perspective this method of measurement is uncomfortable, and from the perspective of the healthcare professional, it can be unreliable (demonstrated in clinical studies) and not without associated risk to the patient.

Moreover, this invasive procedure often leads to incorrect diagnosis of compartment syndrome, which may then lead to unnecessary fasciotomy. Fasciotomy is a surgical procedure that involves cutting the fascia (cutting into the compartment) to relieve tension or
pressure in order to treat the resulting loss of circulation to an area of tissue or muscle. Fasciotomy is a limb-saving procedure when used to treat acute compartment syndrome, but it is never desirable to have fasciotomy performed unnecessarily.

Specifically, the rate of unnecessary fasciotomy is not decreased by direct invasive measures of compartment pressures and is associated with significant cost to the healthcare provider. Development of a novel application of non-invasive Somatosensory Evoked Potentials (SSEPs) as a continuous surrogate measure of compartment status in patients "at risk" of compartment syndrome can provide an alternative to direct pressure monitoring. In addition, non-invasive monitoring of SSEPs may be undertaken in the sedated, obtunded, or alert patient in the operating room, ward and intensive care unit, with the ultimate goal of accurately detecting evolving compartment syndrome for a rapid and appropriate response. The continuous monitoring of SSEPs to detect nerve compression and ischemia as a result of increasing compartment pressure in evolving compartment syndrome may improve detection and treatment of compartment syndrome. Longitudinal assessment of the affected limb may be non-invasive or minimally invasive and therefore more comfortable for the patient as well as having a decreased associated risk (of infection, e.g.) and decreased incidence of unnecessary fasciotomy.

Somatosensory Evoked Potentials (SSEPs) are utilized routinely in spinal surgery to monitor soft tissue handling of the nervous system during surgical dissection in close proximity to vulnerable nervous structures. One case report in the literature describes a patient undergoing cervical spinal surgery who had altered SSEPs in the upper limb, which were coincident with evolving compartment syndrome caused by iatrogenic intravenous fluid extravasation in the upper limb during the neck surgery. Bronson, et al. Evolving compartment syndrome detected by loss of somatosensory- and motor-evoked potential signals during cervical spine surgery. *Orthopedics.* 35(9):e1453-1456 (2012). In this patient, removal of the infiltrating intravenous line and reduction in swelling and compartment pressures caused normalization of the SSEPs. In addition, alterations in SSEP were previously described in a primate model during evolving compartment syndrome. Present, et al. The evaluation of compartmental syndromes using somatosensory evoked potentials in monkeys. *Clinical orthopaedics and related research.* 1993(287):276-285. The publications cited are incorporated by reference herein.
SSEPs have been recorded and characterized in conscious patients (adults and children) and unconscious surgical patients undergoing spinal surgery, including those with diabetic peripheral neuropathy, with accuracy and reproducibility. Strahm, et al. Reliability of perioperative SSEP recordings in spine surgery. *Spinal cord.* 2003;41(9):483-489.  

However, SSEPs have not been used in the clinical setting to monitor patients continuously for the spontaneous development of compartment syndrome. The invention disclosed herein comprises methods, devices, and systems for continuous SSEP monitoring of, e.g., the upper and lower limbs, within a novel telemedicine paradigm as a minimally invasive tool to monitor compartment pressures in patients at high risk of compartment syndrome. Applications include monitoring for both acute and/or chronic compartment syndrome.

Generally, a device (e.g., an electrode) may be applied to a portion of a patient's body (e.g., a limb) distal to a compartment of concern, in order to generate an electrical stimulus at that location. A detection device may be applied to a different portion of the patient's body (e.g., scalp) for receiving signals being conducted through the nerve in the compartment. Nerve function can be impaired by increased pressure in the compartment, so increased pressure may be observed indirectly via changes in conduction seen as altered detection of waveforms (including the loss of detection or alterations in amplitude and latency in detected waveforms). Specifically the conduction of a signal may be slower if nerve function is impaired by compression. Some drugs also affect the use of SSEPs. For example, anaesthetic drugs including inhaled agents (isoflurane) and intravenous agents (propofol) are known to alter the amplitude and latency of SSEPs. A baseline SSEP measurement of the affected limb and a direct comparison with the unaffected limb may be used to differentiate the systemic (bodily) effects of drug administration from the more localized effects of compartment compression. Integration of drug administration and nursing notes in a SSEP compartment monitoring interface, as well as the comparison of multiple waveforms in the
affected and unaffected limbs may deliver enhanced capability of differentiating artifact phenomena.

The continuous monitoring of SSEPs to detect nerve compression as a result of increasing compartment pressure in evolving compartment syndrome represents a new approach for detection and diagnosis of this condition. Longitudinal assessment of the affected limb may be achieved using non-invasive or minimally invasive devices and therefore more comfortable for the patient as well as having a decreased associated risk. These non-invasive devices will be easily administered by healthcare professionals and may be monitored remotely on the ward or with a hand-held device such as a smartphone. The application of this technology to this particular problem allows the development of an early warning system utilizing a telemedicine approach.

Methods for Monitoring SSEPs to Detect Compartment Syndrome

Some embodiments of the invention disclosed herein include methods for monitoring a patient for increased compartment pressure, which may be indicative of compartment syndrome, comprising the steps of applying an electrical stimulus to a nerve in a compartment at risk of compartment syndrome, and detecting a measurable waveform resulting from the electrical stimulus, wherein the measurable waveform represents a somatosensory evoked potential.

Some methods further include comparing SSEPs from a compartment being examined to SSEPs from a similarly situated compartment that does not have compartment syndrome. For example, the unaffected limb of the same patient or subject may be monitored for comparison.

Some methods for monitoring SSEPs include at least one stimulating electrode. A stimulating electrode may be placed on a patient’s limb, distal to the compartment of interest (i.e., the compartment to be monitored). Some embodiments include at least one detecting electrode, which may be placed proximal to the examined compartment, e.g., on the patient’s scalp. A detecting electrode may receive sensory signals conducted through a nerve in the compartment into the central nervous system. Thus the proximal electrodes will detect a signal evoked distally by the stimulating electrode.

As an example, SSEPs from the lower limb may be obtained from stimulation of the common peroneal nerve (deep peroneal nerve at the ankle) and the posterior tibial nerve, with
special emphasis on monitoring the anterior compartment of the lower leg, where compartment syndrome is most commonly encountered. A plate or band electrode over the lower limb or foot may be used as a ground electrode.

Electrodes may be secured distal to the compartments, for example at the level of the ankle when monitoring the lower leg. Thereby, the nerve segment in the investigated compartment is examined. Standard disk EEG electrodes or sterile subdermal needle electrodes, for example, may be attached at the anatomic sites corresponding with the respective nerves. This may be achieved, for example, using a customized sticker/stockinet for accurate placement, or velcro bands may be used to attach electrodes. Disk EEG electrodes are less invasive and thus preferred to subdermal needle electrodes and may be applied to the scalp with collodion, as per SSEP monitoring in spinal surgery with impedance < 5 Kohms, for example.

A montage of recording electrodes for lower limb monitoring may typically be placed at CPz, CP3 and CP4 scalp locations, with additional scalp electrodes about the mid-sagittal plane. An initial montage of mid-sagittal electrodes may aid in the selection of the electrode derivation that produces the highest amplitude cortical response, as well as to provide redundancy allowing acquisition of reliable responses with fewer repetitions. Emerson and Adams, Intraoperative monitoring. Current practice of clinical electroencephalography, 3rd ed. J. S. Ebersole and T. A. Pedley. Philadelphia, Lippincott Williams & Wilkins: 936-954 (2003); MacDonald, Al Zayed, et al., Tibial somatosensory evoked potential intraoperative monitoring: recommendations based on signal to noise ratio analysis of popliteal fossa, optimized P37, standard P37, and P31 potentials. Clin Neurophysiol 116(8): 1858-69 (2005). For example, electrodes may be placed in the popliteal fossa to record the nerve action potential following posterior tibial nerve stimulation. A multichannel montage that includes cortical near-field as well as subcortical far-field including non-cephalic Erb's point signals may be optimal, if possible.

The lower limbs may be stimulated unilaterally, with SSEPs obtained independently from the affected (injured) and unaffected sides. This also provides a control for the systemic effects that may alter SSEPs including certain medications. Multiple-channel recording allows recording a combination of subcortical and cortical SSEPs. For patients in the
operating room or the Intensive Care Unit (ICU) under intravenous anesthesia, obtaining subcortical responses may not be necessary in some cases.

Since stimulation of the posterior tibial nerve can produce plantar flexion of the great toe (hallux), it may be associated with discomfort in patients that are at higher risk of developing compartment syndrome. Caution should be exercised in increasing stimulus intensity in a pharmacologically paralyzed patient. Although a stimulus intensity of 20 mA is often sufficient to activate the tibial nerve, this may vary in patients with certain disease states and a higher stimulus may be required. Stimulation rates between 2 and 10/s are commonly utilized in the monitoring setting with initial adjustments of stimulus rate helping to minimize line noise artifact from recordings. Longitudinal, regular stimulation of patients on the wards will provide a longitudinal assessment of nerve and compartment status. Analysis time depends on the usual latency of the nerve of interest (usually at least two intervals). For example, the lower limb may initially require 60 ms and the upper limb may require 40 ms. The number of repetitions to be averaged may be determined during initial setup on the patient and is sensitive to montage.

As initial measurements are taken, the waveforms which are most pronounced and rapidly acquired may be identified, highlighted and analyzed more closely. It is important to note that the analysis of SSEP waveforms may be based on initial readings and comparison with readings from the contralateral (unaffected side), with each patient serving as their own control/reference. Thus the analysis can be individualized for the specific patient.

SSEP data may be further evaluated, for example, by assessing two parameters - 1) the individualized amplitudes and latencies for the monitored nerves (and compartments), and 2) the rate of change in such parameters, based on the current measurement and recent measurements. Both of these parameters may have thresholds assigned to trigger an alert or other feedback and assigned/individualized to each patient during initial setup based on baseline affected and unaffected limb measurements. If an alert is triggered, a remote server may alert the medical personnel directly, or a server may first send feedback to the patient site which is then relayed to the medical personnel remotely monitoring the patient. In addition, integration of nursing notes and drug administration using device or system interfaces will allow a fuller understanding of patient status by healthcare professionals monitoring the patient remotely.
Figure 1 is a schematic for monitoring SSEPs according to one embodiment of the invention. Stimulating electrodes are first attached to a part of the patient's body distal to the compartment of concern (i.e., the examined compartment). Detecting electrodes are attached proximal to the examined compartment (e.g., on the scalp). The same electrode configuration is applied to the unaffected (opposite) limb for comparison. The stimulating electrodes apply a current to the body 110 which is conducted through the nerve or nerves in the compartment of interest. If the examined compartment experiences increased pressure 120, the blood flow also decreases and the nerve does not conduct the signal as efficiently, resulting in altered SSEPs from that limb 130. By contrast, the nerve function in the unaffected limb is fully intact 140 such that the SSEPs detected from the unaffected limb are normal 150.

Figure 2 illustrates an example configuration for monitoring SSEPs according to an embodiment of the invention. Initially, stimulating electrodes 210 are attached to a patient at the ankles, and thus distal to the examined compartment. Detecting electrodes 220 are attached to the patient's scalp. Both the stimulating electrodes 210 and the detecting electrodes 220 may be coupled to a device that registers SSEP waveform data 230. The data registering device 230 may be in wireless communication with a CPU, the internet, or other devices. When a stimulating electrode delivers an electrical current to the patient's body 240, the signal travels through the nerve or nerves in the compartment 250 and is detected by the detecting electrodes 220 as SSEPs. If the examined compartment 260 experiences increased compartment pressure, the nerve function 250 will be affected, resulting in altered SSEP detection by the detecting electrodes 220. Multiple compartments and their constituent nerves are illustrated in cross-section of the leg 270.

Alterations of SSEPs may be monitored at the bedside and remotely by the healthcare team in the context of regular clinical (nursing) monitoring. An early warning system (i.e., alert) may be initiated if there is, for example, a contiguous 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, or 95 % drop in amplitude and a 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 40, 50, 60, 70, 80, or or 90% prolongation in latency. Sudden absence of SSEPs may also initiate such an alert. Nuwer and Packwood, Somatosensory evoked potential monitoring with scalp and cervical recording. Intraoperative monitoring of neural function. M. R. Nuwer. Amsterdam, Elsevier: 180-189 (2008). However, incremental distinct longitudinal changes may also initiate a clinical response.
Communication between any of the various devices (e.g., feedback) may be achieved using systems of the invention.

Devices

In some embodiments, the invention comprises a device for eliciting SSEPs. In some embodiments, the invention comprises a device for measuring SSEPs. In some embodiments, the invention comprises electrodes for eliciting and/or measuring SSEPs in combination with the devices. In some embodiments, the invention comprises hardware and/or software for measuring and/or monitoring SSEPs. In some embodiments the invention comprises educational systems for training in administering the devices and measuring/monitoring SSEPs.

In some embodiments, existing devices may be adapted for use in a system for monitoring SSEPs to detect increased compartment pressure. In other embodiments, specialized devices may be developed for the particular application of monitoring SSEPs in order to detect increased compartment pressure. For example, there are a wide variety of disk electrodes and needle electrodes that may be adapted for use to monitor SSEPs. Some electrodes and/or other devices may be disposable. The electrodes may be attached to a patient by velcro bands, for example, or by any conventional means.

Stimulating and detecting electrodes may be coupled to a device for registering SSEP waveforms. Such a device may include at least one processor for processing and/or evaluating data. Alternatively or additionally, the registering device may send the data to another device having a processor, which is able to evaluate the data. In some embodiments, a single device for registering SSEP waveforms may be designed to accommodate monitoring of multiple patients being monitored by any number of medical personnel (e.g., in a hospital-based monitoring system). Alternatively a web-based application may receive data from the registering device for processing, or an application on a personal device may process data (e.g., a smart phone), or various other configurations are possible.

A variety of devices may be used to evaluate SSEP data, to determine whether any intervention is needed. Regardless of whether data processing occurs at the site where the patient is located, on a device located (proximally or remotely) with one or more healthcare professionals who monitor the patient, or at a third location (e.g., a remote server), a remote device may be used by a healthcare professional to monitor the results of SSEP data.
processing. In some embodiments, the personal smart phone of the healthcare professional may include an application that allows monitoring. In other embodiments the healthcare professional may carry a device dedicated for monitoring SSEPs. Or other configurations are possible.

**Systems**

In some embodiments, systems for monitoring SSEPs may include some or all of the devices described above in communication with hardware and/or software for remotely monitoring a patient and, as needed, for initiating an early warning clinical response to healthcare professionals who are monitoring the patient.

Some embodiments of the invention include a system for monitoring a patient for compartment syndrome, comprising a component for applying an electric stimulus to a nerve in a compartment at risk for developing compartment syndrome, a component for detecting a measurable waveform resulting from the electrical stimulus, wherein the measurable waveform represents a somatosensory evoked potential, and a component for quantifying or analyzing the somatosensory evoked potential. A system may further include a component for transmitting the measured somatosensory evoked potentials, or results from analysis of the measured somatosensory evoked potentials, to a remote user.

Some systems of the invention further include a component for comparing the measured somatosensory evoked potentials to somatosensory evoked potentials in a similarly situated compartment that does not have compartment syndrome. The similarly situated compartment may be in the opposite (unaffected) limb of the subject. Some systems further include a component for transmitting the comparison of the measured somatosensory evoked potentials and the somatosensory evoked potentials from the similarly situated compartment that does not have compartment syndrome to a remote user.

Some embodiments include a stimulating electrode, a detecting electrode, a device for receiving SSEP data, a component for processing SSEP data, and a component for evaluating the results of data processing. The stimulating electrode may be programmed to provide a stimulus at regular intervals continuously and longitudinally (i.e., repeatedly examining or observing measurements over time). The duration may be set, for example, to allow continuous monitoring for 24 hours. Or the duration may be indefinite.
In some embodiments, systems include at least one processor. The processor may be located at the same site as the patient, in a device carried by a healthcare professional monitoring the patient, or at a third location such as a remote server. For example, the SSEP waveform data may be sent by a device that collects the data from the patient to a remote server or device for processing, where an application or program evaluates the data and determines whether an alert should be sent to the monitoring healthcare professional.

Some aspects of the invention include non-transitory computer readable media comprising computer code for applying an electrical stimulus to a nerve in a compartment at risk of compartment syndrome and detecting a measurable waveform resulting from the electrical stimulus, wherein the measurable waveform represents somatosensory evoked potentials. The computer readable media may include code for transmitting the measured somatosensory evoked potentials, or results from analysis of the measured somatosensory evoked potentials, to a remote user. It may also include code for comparing the measured somatosensory evoked potentials to somatosensory evoked potentials in a similarly situated compartment that does not have compartment syndrome. Again, the similarly situated compartment may be in the opposite (unaffected) limb of the subject. Computer readable media may further include code for determining the rate of change in detected somatosensory evoked potentials.

Computer readable media (e.g., software) may be included in systems for monitoring SSEPs. SSEP monitoring software may be incorporated into any of numerous devices. Such software may assign and individualize warning parameters, including the assessment of longitudinal incremental changes and initiate an early warning response by interacting with automatic hospital paging systems and cellular messaging/calling. Software may be designed to allow user input regarding, e.g., drugs administered to the patient, or other details that could be factored into the evaluation of SSEP data. Thus some embodiments include computer readable code for analyzing SSEP data by comparison with SSEP data obtained initially from the limb of concern and also obtained simultaneously from the unaffected limb. In some embodiments, systems may include for-fee monitoring services offered by a third party via telemedicine.

The components of systems for monitoring SSEPs may further include hardware (disposable electrodes, electrode gel, device to register waveforms or SSEP measurements),
software (applications for phones, computer systems and tablets), crossover or cooperation with existing systems for monitoring patients, and educational programs (multidisciplinary healthcare education; systems management courses).

Figure 3 is a schematic of configurations according to some embodiments of the invention. The stimulating and detecting electrodes 310 may be in communication with a device near the site of the patient 320. This device 320 may register SSEP measurements, and it may contain a processor for evaluating the measurements as well. Alternatively, the registering device may send the SSEP measurements to a remote server or web-based application 330, or directly to a device in the possession of a healthcare professional who is remotely monitoring a patient. The SSEP data processing could be performed at the remote server or web-based application 330, by the healthcare professional's device 340. Alternatively, the results from data processing could be sent by the registering device 320 or the remote server or web-based application 330 directly to the healthcare professional's device 340 for monitoring the patient.

**Monitoring, Feedback, and Evaluation**

A goal for remote monitoring of SSEPs as provided by the methods, devices, and systems of the present invention is to develop an early warning system and rapid surgical response with increased lead time to a surgical intervention, while increasing the accuracy of the diagnosis. In some methods for monitoring SSEPs, the patient may be used as their own reference/control with baseline measurement and stimulation of the unaffected limb for comparison (and to investigate any systemic phenomena that may alter SSEPs including medications). This configuration for obtaining a baseline measurement is relatively non-invasive. Finally, rapidity of change in longitudinal SSEPs monitoring may further enhance the opportunity for early close examination and intervention.

In some embodiments of the methods and systems of the present invention, an application or program evaluates the data by assessing both the individualized baseline compartment pressure and the rate of change in compartment pressure, based on the current measurement and recent measurements. For example, the actual compartment pressure may be only slightly increased at a given time, but the rate of change may cause concern and generate an automatic alert to medical personnel. Or conversely, the rate of change may be slow, but if it reaches an actual compartment pressure that is likely to cause damage to the
compartment tissues, an alert will trigger intervening measures. Both of these parameters may have thresholds assigned to trigger an alert or other feedback.

The thresholds may be assigned on an individualized basis (i.e., by comparison with initial baseline measurements and the unaffected limb of the same patient) and/or may also be designated to account for tendencies observed in clinical trials. Rate of change thresholds, in particular, may be more widely applicable and may be developed based on data from clinical trials. That is, the rate of change in SSEPs designated as a threshold to trigger an alert to a healthcare professional may be very similar from one patient to another. The devices, systems, and/or software of the present invention may facilitate signal conversion from amplitude and latency to a warning binary signal as the parameters reach a threshold. Devices, systems and/or software may be designed to account for interpolation of the SSEP output signals on an individualized and/or generalized basis.

In certain embodiments of methods, devices, and systems of the invention, the resulting alerts and/or feedback may be customizable based on user inputs. At minimum the application may at least send an alert to the healthcare professional monitoring the patient if the increase in compartment pressure from the patient's baseline (and compared to unaffected limb) is too high, or if the rate of change is rapid enough to cause concern.

In certain embodiments, specific telemedicine strategies may be implemented to integrate this new technology with a user-friendly interface. Telemedical strategies may include applications for smartphones, programs for desktop or laptop computers, processing at a remote server which hosts the program or application for evaluating collected data, or other arrangements. Further provisions to allow the monitoring system to integrate with existing healthcare monitoring systems may be developed.

Currently, compartment syndrome is monitored clinically by assessing a patient's pain and disproportionate or worsening pain is clinically indicative of compartment syndrome, warranting invasive compartment checking and/or fasciotomy. However, patient pain is subjective and very often obscured by significant amounts of analgesics and sedatives in the trauma patient. In addition the unconscious patient cannot currently be clinically monitored without invasive large bore needle compartment checks that are prone to inaccuracy; continuous slit catheter monitoring has demonstrated some efficacy in this patient population but poses concerns relating to infection and migration of the sensing elements and

An alert that notifies a healthcare professional early in the development of compartment syndrome may allow more time for further evaluation before the situation escalates to the point of emergency. Thus, fasciotomy may not be performed so hastily in some cases (or at all in other cases) in the context of examining longitudinal trends in compartment status as a result of SSEP monitoring.

A healthcare professional monitoring a patient may react to such an alert by intervening or causing other medical personnel to intervene. This may initiate intense monitoring with a higher degree of clinical suspicion towards compartment syndrome directing a timely invasive compartment pressure check using the established needle technique. In some cases fasciotomy may be necessary, but it is also possible that a patient may have simply shifted position or need cast removal or loosening of an external dressing that may have contributed to nerve irritation and potentially increased compartment pressure.

The present invention establishes continuous SSEP monitoring of conscious and unconscious patients at high risk of developing compartment syndrome in the operating room, intensive care unit, and on surgical wards as a new standard of care for "at risk" patients. This includes the establishment of telemedical algorithms to alert the multidisciplinary team of concerning data. Compared to the present intra-compartmental pressure measurement, this method offers two major advantages: i) it is minimally invasive and therefore has minimal infectious risk and discomfort; and ii) it may be used continuously to constantly evaluate for evolving status changes. This SSEP monitoring approach may also facilitate diagnosis of chronic exertional compartment syndrome and may be applied in the context of other similar diagnoses such as abdominal compartment syndrome.

While the present invention has been disclosed with references to certain embodiments, numerous modifications, alterations and changes to the described embodiments are possible without departing from the scope and spirit of the present invention, as defined in the appended claims. Accordingly, it is intended that the present invention not be limited to the described embodiments, but that it have the full scope defined by the language of the following claims, and equivalents thereof.
EXAMPLES

Example 1 - Early medical response after trauma using objective detection

A patient undergoes surgical procedure to address a high-risk fracture. During the post-operative recovery, the patient may be monitored for SSEPs in the fracture compartment. Individualized SSEP values and rate of change of SSEP values that correspond to evolving compartment syndrome in patients may be in the ranges of 50% drop in amplitude and a 10% prolongation in latency during the post-operative period following fixation of a high risk fracture pattern (Nuwer and Packwood, Somatosensory evoked potential monitoring with scalp and cervical recording. Intraoperative monitoring of neural function. M. R. Nuwer. Amsterdam, Elsevier: 180-189 (2008)).

Since changes in SSEPs are objective, quantifiable and less likely to be diminished by analgesics than subjective pain assessment (clinical monitoring is the gold standard with large bore needle pressure as the diagnosis), the medical team are alerted of the apparent nerve compression/ischaemia of the affected nerve within the compartment, which may represent an earlier presentation of impending compartment syndrome.

The patient is seen timely and the limb is examined, with cast removal, repositioning and loosening of external dressings. Analgesia is reviewed to rule out masking of painful symptoms and longitudinal readings and trends are reviewed. If there is no improvement as observed by SSEPs, a diagnostic needle pressure is undertaken with escalation to fasciotomy as necessary. In this case, the medical team are alerted to compartment compromise in the absence/before of clinical symptoms, representing a clear advantage over the current practice.

Example 2 - Chronic, exertional compartment syndrome diagnosis

Chronic compartment syndrome is caused by exercise and exertion. It is associated with athletes who participate in activities with repetitive motions, such as biking, running, or swimming. The pain associated with chronic compartment syndrome is usually relieved by discontinuing the exercise. Although it is not usually dangerous, clinical diagnosis is challenging and currently requires large bore, invasive compartment pressure monitoring that is extremely uncomfortable to patients. SSEP assessment pre-exercise, during exercise and post exercise provides a non-invasive diagnostic strategy when correlated with the development of painful symptoms.
Example 3 - ICU, unconscious or obtunded patient

Monitoring of compartment syndrome in the sedated or obtunded patient, e.g., in the ICU is currently a substantial clinical challenge. Where pain assessment of the patient is not possible, invasive compartment pressure monitoring is incrementally undertaken. In some cases, prophylactic fasciotomy is also undertaken. Situation of an indwelling pressure catheter represents an infection risk with migration of the sensing elements in physical pressure detection posing a continuous concern, while intermittent measurement of compartment pressures is prone to error since pressure measurements are sensitive to the proximity of the fracture. There is a current clinical need for a non-invasive, continuous, longitudinal assessment of compartment status in unconscious patients and it is a clinical reality that patients undergo prophylactic and potentially unnecessary fasciotomy in this setting, given the lack of monitoring strategies, contributing to significant patient morbidity.

SSEP monitoring can thus allow the unconscious ICU patient to avoid being subject to fasciotomy and all the accompanying negative effects of fasciotomy. SSEP monitoring of the contralateral (unaffected) limb accounts for the systemic (entire body) effects of drug administration on SSEPs and can be used to discern these from the localized effects of nerve compression and ischemia within the compartment.

Example 4 - Intra-operative and peri-operative monitoring

Non-invasive monitoring for compartment syndrome away from the operative field during elective surgical procedures that present a high risk (e.g., multi-ligament reconstruction in the knee) is not currently available. In addition, the post-operative period is characterized by high analgesic prescription and a prolonged period of sedation, making clinical monitoring for compartment syndrome only possible with invasive compartment checks. In high-risk cases, SSEP compartment monitoring provides a monitoring strategy to bridge periods of sedation and analgesia. In some cases prophylactic fasciotomy is unnecessarily performed due to these concerns. The opportunity to diagnose compartment syndrome and perform fasciotomy in an adjacent myofascial compartment manifesting during the surgery obviates a return to the operating room, while an early diagnosis in the post-operative period also improves patient care.
Example 5 - EMT and Emergency Department

SSEP monitoring may be applied to the acutely injured patient in the field and in the Emergency Department. Compartment Syndrome is a commonly consulted diagnosis of exclusion for orthopaedic surgeons. Equipping emergency physicians with a strategy to assess compartment status non-invasively and even remotely in the out-patient setting will enable enhanced efficiency of the Emergency Department on orthopaedic hospital services while enhancing patient care standards. Specifically, remote telemonitoring for SSEPs can involve i) the development of computer, telemedicine tablet and phone applications; ii) course-directed education of the staff; and iii) incorporation of continuous SSEP monitoring into existing protocols within the healthcare system, including the establishment of best practice guidelines with continued peer review and research.
Claims

1. A method for monitoring a subject for compartment syndrome comprising the steps of:

   applying an electrical stimulus to a nerve in a compartment at risk of compartment syndrome; and

   detecting a measurable waveform resulting from the electrical stimulus, wherein the measurable waveform represents a somatosensory evoked potential.

2. The method of claim 1, further comprising determining if there is a difference in the somatosensory evoked potential for the compartment at risk as compared to a somatosensory evoked potential in a similarly situated compartment that does not have compartment syndrome.

3. The method of claim 2, wherein an alteration in somatosensory evoked potentials in the compartment at risk indicates an increase compartment pressure and/or a decrease in nerve function.

4. The method of claim 2 wherein the similarly situated compartment is in the opposite limb of the subject.

5. The method of claim 1 wherein a stimulating electrode is used for applying the electrical stimulus.

6. The method of claim 5 wherein the stimulating electrode is a skin electrode positioned distal to the examined compartment.

7. The method of claim 5 wherein the stimulating electrode is a needle electrode positioned distal to the examined compartment.

8. The method of claim 1 wherein a detecting electrode is used to detect somatosensory evoked potentials.
9. The method of claim 8, wherein the detecting electrode is positioned proximal to the compartment at risk.

10. The method of claim 9, wherein the detecting electrode is positioned on the scalp.

11. The method of claim 1, further comprising the step of notifying a healthcare professional if the somatosensory evoked potentials are outside of an individualized threshold range or are changing faster than a pre-determined threshold rate of change.

12. The method of claim 1, wherein the monitoring is performed in a non-surgical setting.

13. The method of claim 1, wherein the subject is unconscious or obtunded during at least a portion of the monitoring.

14. A device for monitoring a patient for compartment syndrome comprising a component for applying an electric stimulus to a nerve in a compartment at risk for developing compartment syndrome; and a component for detecting a measurable waveform resulting from the electrical stimulus, wherein the measurable waveform represents a somatosensory evoked potential.

15. A system for monitoring a patient for compartment syndrome comprising:

   a component for applying an electric stimulus to a nerve in a compartment at risk for developing compartment syndrome;

   a component for detecting a measurable waveform resulting from the electrical stimulus, wherein the measurable waveform represents a somatosensory evoked potential; and

   a component for quantifying or analyzing the somatosensory evoked potential.

16. The system of claim 15, further comprising a component for transmitting the measured somatosensory evoked potentials, or results from analysis of the measured somatosensory evoked potentials, to a remote user.
17. The system of claim 15, further comprising a component for comparing the measured somatosensory evoked potentials to somatosensory evoked potentials in a similarly situated compartment that does not have compartment syndrome.

18. The system of claim 17, further comprising a component for transmitting the comparison of the measured somatosensory evoked potentials and the somatosensory evoked potentials from the similarly situated compartment that does not have compartment syndrome to a remote user.

19. The system of claim 17 or 18, wherein the similarly situated compartment is in the opposite limb of the subject.

20. Nontransitory computer readable media comprising computer code for applying an electrical stimulus to a nerve in a compartment at risk of compartment syndrome; and detecting a measurable waveform resulting from the electrical stimulus, wherein the measurable waveform represents somatosensory evoked potentials.

21. The computer readable media of claim 20, further comprising code for transmitting the measured somatosensory evoked potentials, or results from analysis of the measured somatosensory evoked potentials, to a remote user.

22. The computer readable media of claim 20, further comprising code for comparing the measured somatosensory evoked potentials to somatosensory evoked potentials in a similarly situated compartment that does not have compartment syndrome.

23. The computer readable media of claim 20, further comprising code for determining the rate of change in detected somatosensory evoked potentials.

24. The method of claim 1, wherein a healthcare professional monitors the subject remotely.

25. The method of claim 1, wherein the monitoring comprises providing a diagnosis of compartment syndrome.
Fig. 1

Electrodes Applied Distal and Proximal to Examined Compartment

Examined Compartment

Unaffected Limb

SSEPs Reflect Nerve Function and Compartment Status

Altered SSEPs

Normal SSEPs

110

120

140

130

150
Fig. 3
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61A5/05
ADD.

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)
A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
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Further documents are listed in the continuation of Box C.

See patent family annex.

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Van Dop, Eric
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