Prevention of pressure-induced deep tissue injury using intermittent electrical stimulation

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Prevention of pressure-induced deep tissue injury using intermittent electrical stimulation. J Appl Physiol 102: 1992–2001, 2007. First published February 1, 2007; doi:10.1152/japplphysiol.01092.2006.—Pressure ulcers develop due to morphological and biochemical changes triggered by the combined effects of mechanical deformation, ischemia, and reperfusion that occur during extended periods of immobility. The goal of this study was to test the effectiveness of a novel electrical stimulation technique in the prevention of deep tissue injury (DTI). We propose that contractions elicited by intermittent electrical stimulation (IES) in muscles subjected to constant pressure would induce periodic relief in internal pressure; additionally, each contraction would also restore blood flow to the tissue. The application of constant pressure to the quadriceps muscles of rats generated a DTI that affected 60 ± 15% of the compressed muscle as assessed by magnetic resonance imaging. In contrast, in the groups of rats that received IES at 10- and 5-min intervals, DTI of the muscle was limited to 16 ± 16 and 25 ± 13%, respectively. Injury to the muscle was corroborated by histology. In an experiment with a human volunteer, compression of the buttocks reduced the oxygenation level of the muscles by ~4%; after IES, oxygenation levels increased by ~6% beyond baseline. Concurrently, the surface pressure profiles of the loaded muscles were redistributed and the high-pressure points were reduced during each IES-induced contraction. The results of this study indicate that IES significantly reduces the amount of DTI by increasing the oxygen available to the tissue and by modifying the pressure profiles of the loaded muscles. This presents a promising technique for the prevention of pressure ulcers in immobilized and/or insensate individuals.

PRESERVED ULCERS ARE TYPICALLY associated with individuals of compromised mobility, namely the infirm, the elderly, and people with spinal cord injury (10, 12, 31, 49, 60, 61). A pressure ulcer is any lesion caused by unrelieved pressure resulting in damage of underlying tissue (1), involving the skin, fat, fascia, muscle, and bone. Pressure ulcers develop following a prolonged period of compression of the tissue between a bony prominence and a surface (13, 24, 48, 53, 60), which causes the occlusion of capillaries and leads to ischemia. Ischemia, therefore, has historically been considered a major factor leading to pressure ulcer formation (27–29). Paradoxically, the restoration of blood flow, vital to preserving tissue viability, has also been identified to cause extended damage of the tissue (20, 23, 41, 55). In instances where the ischemic state has been maintained for extended periods, the influx of oxygen-rich blood causes the activation of free radicals, further damaging the cells in the tissue (20, 23, 41, 55). In addition to the injury caused by biochemical changes occurring during tissue ischemia and ensuing reperfusion, high stress levels at the bone-muscle interface and the duration of their application have also been reported as direct causes of tissue injury (7, 8, 11, 35–37). Furthermore, injury to the muscle results in the formation of scar tissue, thus creating more foci for increased stress and leading to injury of adjacent previously healthy tissue (18, 36). It is the combined effects of these processes that cause the edema, inflammation, and necrosis that ultimately lead to formation of a pressure ulcer (14, 19, 20, 47, 56, 57).

Pressure ulcers can be initiated at the dermis, usually in the presence of excessive friction and/or compromised dermal integrity and progress toward the deeper layers of tissue. Muscle is considered to be more susceptible to tissue degradation from mechanical loading and oxygen deprivation (7, 31) than dermis; consequently injury can also be induced in the deep tissue and progress outward (11), evolving into a severe full-thickness pressure ulcer. This type of pressure-related injury to the deep tissue under intact skin has been defined by the National Pressure Ulcer Advisory Panel as deep tissue injury (DTI) (2, 3). DTI can be extremely perilous, as it can evolve undetected until a significant destruction of the tissue has occurred. Presently, pressure ulcers are detected by visual inspection of the skin (45), which often belies existing extensive damage to deeper tissue (11).

At the present time, techniques employed to prevent ulcer formation include frequent repositioning (12) as well as the use of specialized cushions and mattresses that provide either static or dynamic pressure relief of the tissues at risk (22, 46).

Recognizing the absence of a significant reduction in the incidence of pressure ulcers (10, 15, 16, 30, 42, 49, 50, 54), new preventative interventions are needed, especially for DTI. This study investigated the effectiveness of applying intermittent electrical stimulation (IES) to reduce muscle injury due to the presence of persistent external pressure. We hypothesized that the IES-induced muscle contractions would prevent the formation of DTI. These periodically induced contractions may parallel the effects of voluntary or assisted repositioning, which is the standard method for preventing the formation of DTI. We suggested that the mechanism of action of IES is twofold. 1) IES-induced contractions would reshape the underlying muscle, thereby reducing the high stress levels experi-
enced at the muscle-bone interface, minimizing the amount of damage caused by the mechanical deformation and compression of the tissue. 2) Each contraction would also periodically restore blood flow and increase the oxygenation of the compressed tissue, reducing the amount of damage caused by long periods of ischemia and subsequent reperfusion.

IES may be a useful medical intervention that allows immobilized individuals to remain seated or supine for prolonged periods of time, reducing the frequency of assisted repositioning, and, most importantly, reducing the development of DTI.

METHODS

Overview of Experimental Procedures

To investigate the effectiveness of IES in the prevention of DTI, a series of experiments were conducted in four groups of rats. The control group received 2 h of external load applied to the quadriceps muscle of one hindlimb. Experimental groups 1 and 2 received the load application as well as IES at either 10-min or 5-min intervals. Experimental group 3 received the application of IES at 5-min intervals but no load application. DTI was quantified 24 h later by in vivo transverse relaxation time (T2)-weighted magnetic resonance imaging (MRI) and postmortem histological assessment of the extracted quadriceps muscles. In MRI, T2* values reflect irreversible signal loss and are characteristic of the local freedom of water motion in the tissue. The untreated contralateral legs of all animals served as healthy controls (contralateral control group).

To obtain an insight into the mechanisms of action of IES, the effect of IES on tissue oxygenation was measured in two experiments with able-bodied human volunteers. Tissue oxygenation measurements were obtained from an able-bodied volunteer by means of T2*-MRI quantification in muscles in both unloaded and loaded conditions. T2* values reflect, in addition to the T2 effects, the presence of local variations in the static magnetic field in the tissue, for example, paramagnetic agents, such as the iron atoms in deoxyhemoglobin that are exposed to water. T2* images are thus very sensitive to the level of oxygenation in the blood, while T2 images are sensitive to material densities in the local environment that impede Brownian motion. A single experiment in an able-bodied volunteer was also performed to measure changes in the surface (bed-buttocks interface) pressure profiles generated by the IES-elicited contractions. All volunteers provided written consent. All experimental protocols were approved by the Animal Care and Welfare Committee and the Health Research Ethics Board at the University of Alberta.

Effectiveness of IES Preventing DTI

Pressure application and electrical stimulation setup. Eighteen adult female, Sprague-Dawley rats (weight = 320 ± 36 g) were anesthetized with isoflurane (2–3% isoflurane in 500 ml/min oxygen), and a nerve cuff was implanted around the femoral nerve of each hindlimb. Following implantation, the rat was placed on a flat surface and a nerve cuff was implanted around the femoral nerve of each hindlimb. Following implantation, the rat was placed on a flat surface and a nerve cuff was implanted around the femoral nerve of each hindlimb. The knees and upper calf in the experimental leg were tended and a padded strap was placed around each ankle to tether the legs in place. The knee and upper calf in the experimental leg were also restrained using a padded clamp to prevent any off-sagittal movement of the leg.

Pressure was applied to the quadriceps muscle of the experimental leg using a 3-mm-diameter indenter. The contralateral leg served as an internal control. Rats were randomly assigned to three groups of six animals each (control group, experimental group 1, experimental group 2). Rats in experimental group 1 received the application of pressure and simultaneous electrical application of a 10-s stimulus bout (biphasic, charge balanced, constant current, 10–40 mA, 250 μs, 50 pulses/s) to the femoral nerve of the experimental leg every 10 min throughout the duration of pressure application. Rats in experimental group 2 received pressure and simultaneous electrical stimulation to the treated leg (10-s bouts) every 5 min. Rats in the control group received the pressure application but no electrical stimulation. In all animals, pressure was applied for a period of 2 h. The load applied was normalized to 38% of the body weight of each rat, which is the expected unilateral amount of loading in the buttocks and thighs in seated individuals (9). Loads were measured with a miniature beam force transducer (Interface, Scottsdale, AZ). The force was recorded at a sampling rate of 100 samples/s using a CED Power 1401 A/D board (Cambridge Equipment Design, Cambridge, UK) and SIGNAL 2 software (Cambridge Equipment Design) throughout the duration of the experiment (Fig. 1B). The indenter was adjusted as required using a micromanipulator (Narshige, East Meadow, NY) to maintain the desired level of applied force (Fig. 1B). Throughout the experiments, the pressure applied to each group was 164 ± 6.7 kPa for the control group, 167 ± 26.6 kPa for experimental group 1, and 165.2 ± 25.1 kPa for experimental group 2. Following the period of pressure application, the leg was unloaded, the nerve cuffs from both limbs were removed, and the skin was sutured. Postoperatively, buprenorphine (0.05 mg/kg) was administered subcutaneously to alleviate any discomfort.

To test the effect that IES alone may have on the stimulated muscles, experiments were conducted in a fourth group of six rats (285 ± 6 g), designated experimental group 3. The experimental procedures previously described were maintained with the exception of no pressure application. The stimulation paradigm utilized was that of experimental group 2, with IES being applied to one hindlimb of the animal every 5 min for a period of 2 h.

Assessment of deep tissue health using MRI. MRI was used to obtain an in vivo assessment of DTI following pressure application and to quantify the effectiveness of IES in preventing such injury (6, 52). Twenty-four hours after the removal of pressure, each rat was

Fig. 1. Experimental setup. A: constant pressure was applied to the quadriceps muscle of the right hindlimb of each rat. B: 50-min record of the force applied to the quadriceps muscle. The sharp increases in force correspond to the contraction of muscle due to intermittent electrical stimulation (IES).
anesthetized with an intraperitoneal injection of pentobarbital sodium (40 mg/kg). The rat’s hindlimbs were secured inside a 7-cm-diameter birdcage coil and placed inside a 3.0-T magnet (Magnex Scientific PCL). A T2-weighted spin-echo sequence (echo time = 80 ms, relaxation time = 2,000 ms) was employed to detect the presence of edema (as indicated by increased water content) within the quadriceps muscles in both hindlimbs of each rat. Data were collected during a 30-min scanning session, and 20 MRI slices (images) were acquired from each rat, with slice thickness of 2 mm and slice separation of 1 mm (every other slice shown in Fig. 2). The acquisition matrix size was 256 × 256 pixel within a field of view of 120 × 120 mm, resulting in an in-plane resolution of 0.47 × 0.47 mm. Both hind legs were imaged in the same slice. MRI slices were obtained in the sagittal, coronal and transverse planes in relation to the rat’s femur.

All MRI data were imported to MATLAB 7.0.1 (Mathworks, Natick, MA) for analysis using custom-written routines. The left and right quadriceps muscles were manually selected from every slice, and all analyses were restricted to the pixels inside these two regions (Fig. 3A). To quantify the amount of increased water content present within the experimental leg from each slice, the signal intensity of each pixel in that leg was compared with a threshold intensity level obtained from the contralateral leg (Fig. 3B). The mean + 2 SDs in the signal intensity from the quadriceps muscle of the contralateral leg was chosen as the threshold intensity level. If the signal intensity of a pixel in the experimental leg was higher than the threshold, the pixel was considered to have increased water content, or edema (Fig. 3C). A percentage of the affected area relative to the total area of the muscle was obtained from each slice, and the total affected volume was calculated for each rat by summing the results from all slices. The threshold was also applied to each control (contralateral) limb from each rat to quantify the amount of increased water content that could be attributed to factors other than the application of pressure or IES, such as the electrode cuff implantation or normal variation in the signal intensity. Results from the untreated contralateral limbs of all 24 rats were designated as the contralateral control group. For measured comparisons between groups both one-way ANOVA and Tukey post hoc tests were used. All P values <0.05 were considered statistically significant.

Histological assessment. To corroborate the extent of injury in the muscle from the MRI assessment, histological evaluation of the tissue was also performed. Under deep anesthesia (pentobarbital sodium, 40 mg/kg), the animal was transected by perfusing with a formaldehyde (1%)-glutaraldehyde (2.25%) fixative and the quadriceps muscles from both hindlimbs were removed. The muscles were photographed, weighed, and their volume calculated. The muscle tissue was stored in the same fixative, and it was subsequently dehydrated through washing in a graded series of ethanol dilutions and embedded in paraffin.

Muscle sections obtained from the region identified by the magnetic resonance images as containing edema were longitudinally bisected. A 2- to 3-mm-thick longitudinal section was obtained, as well as five 2- to 3-mm-thick transverse sections. A 5-μm slice was obtained from each section and stained with hematoxylin and eosin.

A veterinary pathologist blinded to the experimental groups performed all histological analyses. A 4.9-mm² area from each slice was assessed to identify muscle fiber necrosis, inflammatory cell infiltration, hemorrhage, and tissue mineralization. A necrosis score (0–4) was assigned to each longitudinal slice based on the approximate area exhibiting necrosis out of the slice total area. Subsequently, the transverse slices from each animal were used to confirm the extension of necrosis throughout the muscle. The estimated volume of the muscle affected by necrosis from the histological assessment was compared against the estimated volume of the corresponding muscle affected by edema as calculated from MRI slices. Scoring of histological muscle sections between groups was assessed by a Kruskal-Wallis nonparametric test. All P values <0.05 were considered statistically significant. All results are expressed as means ± SD.

Mechanisms of Action of IES

Muscle oxygenation measurements. In addition to testing the effectiveness of IES in preventing DTI, we sought to understand the mechanisms of action of IES. An initial experiment was conducted in an able-bodied volunteer (male, 22 yr) to assess changes in tissue oxygenation associated with contractions elicited by IES in an unloaded muscle. Surface, nonmagnetic electrodes were placed over the motor point of the medial gastrocnemius (MG) muscle of one leg.
Tissue oxygenation levels were estimated by quantifying changes in the \( T_2^* \) signal in MR scans of the muscle in which an increase in the \( T_2^* \) signal is attributed to an influx of oxygenated hemoglobin to the tissue (26, 39). MR scans were acquired with a 1.5-T whole body Siemens Sonata scanner (Siemens Medical Solution, Malvern, PA) and a 27-cm-diameter transmit-receive knee coil circumscribing the lower leg. A custom-prepared multigradient-echo sequence (repetition time = 51.8 ms, 8 echo times ranging from 3.6 to 47 ms, single slice, 6-mm slice thickness, flip angle = 20°, field of view = 208 × 205 mm, readout matrix = 160 pixel × 158 pixel, in-plane resolution = 1.3 × 1.3 mm) was utilized for all data acquisitions. Baseline levels of oxygenation in MG were obtained as well as simultaneous measurements from the lateral gastrocnemius (LG), medial soleus (MS), and lateral soleus (LS) muscles for comparison. Following the acquisition of baseline scans, successive scans were acquired immediately after 30-s bouts of electrical stimulation delivered through the surface electrodes (biphasic, charge balanced, constant current, 70 mA, 250 ms, 50 pulses/s).

To mimic a simulated sitting position in which muscles are compressed, albeit around the ischial tuberosities, a second experiment was performed on the gluteus maximus muscles of an able-bodied volunteer (male, 26 yr). Because of space limitations within the MRI scanner, which prohibits volunteers from sitting upright, muscle compression during sitting was simulated by adding weight over the pelvis of the person lying supine inside a 1.5-T whole body scanner. Oxygenation measurements were obtained at 1) rest, 2) with a 20-kg (30% of body weight) load applied over the pelvis, and 3) with a 20-kg load and IES applied simultaneously. Surface coils placed below the subject and a multi-gradient-echo sequence (repetition time = 90.3 ms, 20 echo times ranging from 3.8 to 89.6 ms, single slice, 8-mm slice thickness, flip angle = 30°, field of view = 223 × 397 mm, readout matrix = 72 × 128 pixel, in-plane resolution = 3.1 × 3.1 mm) were utilized for imaging the gluteus in the transverse plane. Three successive 31-s scans were acquired at rest to obtain baseline levels of oxygenation in the left and right gluteus maximus muscles. A 20-kg load was placed over the pelvic region to compress the gluteus muscles, and ten 31-s scans were acquired over a 10-min period of loading. Subsequently, six 31-s scans were obtained each immediately following a 10-s stimulus bout (biphasic, charge-balanced, constant current, 70 mA, 250 ms, 50 pulses/s, 3-s ramp up, 3-s ramp down) applied every minute to the gluteus muscles with the load in place. The stimulation parameters utilized did not cause pain or discomfort to the volunteer (data not shown).
Magnetic resonance data were imported into MATLAB 7.0.1 (Mathworks) to measure changes in the T$_{2}^{*}$ signal in each muscle using a monoexponential nonnegative least squares fit routine (59). A region of interest (ROI) was selected around each target muscle (MG, LG, SM, and SL, or right gluteus maximus, and left gluteus maximus) in each MR slice, and the T$_{2}^{*}$ levels in each ROI were determined. The T$_{2}^{*}$ values were normalized to their corresponding baseline levels obtained at rest.

Surface pressure measurements. In addition to injury due to ischemic changes, high stress levels and cell deformation have also been associated with tissue damage (7, 8, 11, 35, 36). Ideally, stress levels should be measured at the bone-muscle interface, the place of origin for DTI. However, due to the lack of noninvasive measuring techniques at this deep level, an alternative and commonly used technique is to measure superficial pressure levels at the support surface-skin interface (5). To obtain insight into the effects of IES in reshaping the gluteus maximus muscles, and modifying the surface pressure profiles with each contraction, a single experiment was performed. The experiment was conducted in the same able-bodied volunteer (male, 26 yr), using the same testing conditions as those utilized to assess oxygenation levels in the gluteus maximus muscles: 1) rest, 2) weight, and 3) weight + IES. To elicit contractions in the left and right gluteus maximus muscles, surface electrodes were placed over the motor point of each muscle. The volunteer was placed in a supine position with the buttocks over an X-3 System pressure-sensitive mattress (XSensor, Calgary, AB, Canada). Measurements of surface pressure in the sacral region of the buttocks were obtained over a 1-min period of rest. A 20-kg load, equivalent to 30% of the body weight of the volunteer, was applied over the pelvis to compress the tissue of the buttocks. Surface pressure measurements were acquired for 1 min under this condition. Electrical stimulation was then applied simultaneously to both gluteus maximus muscles. A series of three 15-s stimulus bouts (biphasic, charge balanced, constant current, 70 mA, 250 μs, 50 pulses/s) were applied with the load in place. Changes in surface pressure associated with IES were measured during each bout of stimulation.

RESULTS

Effectiveness of IES in Preventing the Formation of DTI

The main objective of this investigation was to determine whether IES is an effective technique for preventing DTI. Our results show that edema and tissue injury can develop after a 2-h application of constant pressure. In all test groups and at the completion of the study, the skin under the pressure indenter did not exhibit any indication of inflammation or injury, underscoring the difficulty of identifying DTI by visual inspection of the skin.

In the control group (pressure, No IES), the application of external pressure for 2 h generated edema in 60 ± 15% of the muscle. In contrast (see Fig. 5, left axis, filled circles), experimental groups 1 (pressure + IES every 10 min) and 2 (pressure + IES every 5 min) exhibited a significantly reduced region of edema in the muscle (16 ± 16% for experimental group 1 and 25 ± 13% for experimental group 2). Experimental group 3 (no pressure, IES every 5 min) and contralateral control group (untreated contralateral limbs) exhibited increased water content in 5 ± 4% of the muscle. The extent of increased water content in all three experimental groups was significantly different from that in the control group (one-way ANOVA test, $P = 0.0001$), but was not significantly different from each other (Tukey post hoc test, experimental group 1 1 vs. experimental group 2, $P = 0.59$; experimental group 1 vs. experimental group 3, $P = 0.45$; experimental group 2 vs. experimental group 3, $P = 0.06$).

Histological assessment of the quadriceps muscle tissue (Fig. 4) showed that the severity of muscle injury varied between the control and experimental groups. In general, the lesions within the muscle were characterized by swelling, loss of striations, and fragmentation of muscle fibers. The connective tissue surrounding affected muscle fibers was often infiltrated by numerous neutrophils admixed with smaller numbers of macrophages. Hemorrhage into muscle bundles was most apparent in severely affected tissue. Figure 5 (right axis, open

Fig. 4. Histological assessment of deep tissue injury. Sample hematoxylin and eosin-stained cross sections from different animals in each group. The amount of edema observed with magnetic resonance imaging correlated well with the amount of necrotic fibers assessed from the histological slides. All histological sections were viewed at $\times 100$ magnification. Cnt Grp: control group; Exp Grp 1–3, experimental groups 1–3; Contra Cnt Grp: contralateral control group.
circles) summarizes the extent of tissue necrosis in the control and experimental groups. The control group had the largest extension of necrotic fibers in the tissue with a score of 3.2/0.8. This score represented a necrotic area occupying 25–50% of the area analyzed. The extent of tissue necrosis was significantly larger in the control group than that in experimental group 1, which had a score of 1.0/0.9 (Kruskal-Wallis nonparametric test, \(P < 0.01\)), representing a necrotic area of \(<10\%\).

Experimental group 2 also exhibited a significantly smaller area of muscle necrosis than the control group (Kruskal-Wallis nonparametric test, \(P = 0.03\), with a score of 1.2 ± 1.5, equivalent to a necrotic area between 10 and 20%. The necrosis score was also significantly smaller in experimental group 3 (Kruskal-Wallis nonparametric test, \(P = 0.004\)), with a score of 0.5 ± 0.6. There was no significant difference between all three experimental groups in the amount of necrosis assessed. The infiltration of neutrophils and macrophages, as well as the presence of red blood cells and mineralization of the tissue, were not significantly different between the control and experimental groups.

**Increases in Tissue Oxygenation Due to IES-Elicited Contractions**

Two experiments were performed with the goal of measuring the changes in tissue oxygenation levels associated with the use of IES. The effects of IES-elicited contractions on muscle oxygenation were first tested in a condition where the muscle was at rest and unloaded. Figure 6A summarizes the effect of IES on the level of oxygenation in the muscles of the lower leg. Normalized T2* levels in MG, LG, LS, and MS are shown. Interestingly, IES selectively increased the T2* level of MG, the stimulated muscle. This increase in oxygenation was maintained throughout the experiment. Oxygenation levels in LG, LS, and MS did not show any change compared with baseline measurements.

The second experiment measured the increase in tissue oxygenation following IES-elicited contractions of loaded muscles. These loaded muscles had a corresponding reduction in oxygen supply, a situation that represents the state of tissue around the ischial tuberosities in a seated individual. Figure 6B summarizes the effect of IES on the level of tissue oxygenation in the gluteus maximus muscles in the presence of an external pressure. Normalized T2* levels in the right and left gluteus maximus muscles are shown for each condition tested (rest, weight, weight + IES). The oxygenation levels in both muscles decreased immediately by \(\sim 4\%\) after the load application; oxygenation remained at this lower level throughout the 10 min in which this condition was maintained. Following IES, the oxygenation levels in the muscles increased above the initial baseline levels by \(\sim 6\%\).

**Changes in Surface Pressure Profiles Due to IES-Elicited Contractions**

In a third experiment (Fig. 6C), surface pressure measurements of the buttocks were obtained under the same three conditions previously tested (rest, weight, weight + IES). The average pressure throughout the buttocks at rest was 10.9 kPa, distributed over a 487-mm² area. As expected, the region of highest pressure was that surrounding the bony prominence (the sacrum in this case), and it exhibited an average pressure of 21.7 kPa.

Following the loading of the pelvis, the average pressure throughout the buttocks increased to 13.9 kPa and was distributed over a 511-mm² area. The average pressure in the region...
around the sacrum increased to 25.8 kPa. Simultaneous bilateral application of IES to the loaded (compressed) gluteus maximus muscles induced contractions that reconfigured the shape of the muscles. The average pressure throughout the buttocks became 14.3 kPa distributed over an area of 424 mm², and the average pressure around the sacrum was reduced to 19.5 kPa, a level lower than that seen even during the rest condition.

**DISCUSSION**

*Effectiveness of IES in Preventing the Formation of DTI*

Several studies have reported the beneficial effects of both alternating- and direct-current electrical stimulation for healing chronic wounds, including pressure ulcers (4, 17, 21, 25, 43, 51, 58). The consensus is that when combined with traditional treatments, electrical stimulation improves wound healing.
Very few studies, however, have investigated electrical stimulation alone as a method for preventing the formation of pressure ulcers.

Levine et al. first proposed using electrical stimulation to prevent pressure ulcers and measured the effect of electrical muscle stimulation on (1) pressure at the seating interface (32), (2) muscle shape (33), and (3) blood flow (34). Their results indicated that during each contraction of the gluteus muscles (1) the superficial pressure surrounding the ischial tuberosities was reduced, (2) the shape of the compressed muscle was modified, and (3) blood flow increased in the stimulated muscle. Based on these observations, it was suggested that electrical stimulation might be an effective technique to prevent pressure ulcers.

Following the seminal studies of Levine et al. (32–34), Rischbieth et al. (44) and Bogie et al. (4) reported that an increase in muscle mass was achieved through long-term electrical stimulation. The increase in muscle mass was suggested to provide individuals with improved cushioning, which, in turn, could prolong the time they can remain seated. Recently, Bogie et al. (5) analyzed the long-term effects of electrical stimulation of the gluteus muscles in one individual with spinal cord injury. Measurements of surface interface pressure, transcutaneous oxygen levels, and muscle thickness were similar to observations previously reported by Levine et al. (32–34), Rischbieth et al. (44), and Bogie et al. (4). It was also determined that any benefits gained during the period of electrical stimulation were abolished once the electrical stimulation was discontinued. While the evidence from these studies suggested the potential effectiveness of IES in preventing the formation of pressure ulcers, heretofore no study had investigated the effects of IES on the integrity of deep muscle exposed to constant pressure.

The present study examined the efficacy of IES in preventing DTI in a rat model and its mechanism of action in human volunteers. Our results show, that within defined parameters of electrical stimulation, a considerable reduction in DTI was observed. Traditionally, tissue injury generated by ischemia following long periods of tissue compression, has been considered the principal etiological factor behind pressure ulcers (27–29). Within this precept, more frequent stimulation should restore oxygenation in the tissue to normal or near-normal levels, potentially eliminating tissue injury caused by ischemia. The finding that there was no significant difference between our experimental groups (IES every 10 min vs. 5 min) could indicate that the beneficial effects of an increase in oxygenation to the tissue may have reached their threshold when stimulation occurred every 10 min. It is possible that the amount of damage observed in both experimental groups could be attributed to damage generated directly by the high stress levels at the bone-muscle interface and the resulting excessive cell deformation. This factor that was further exaggerated in our experimental set up due to the fixation of the hindlimb, which led to an increase, rather than a decrease, in focal pressure during the IES-induced contractions (evident in the increases in recorded force in Fig. 1B). Although the application of pressure to the rats’ limbs was done outside the MRI scanner, utmost care was taken in the placement of the indenter, such that it was as centered as possible over the QM and the femur.

Comparison of experimental group 3 and the contralateral control group demonstrated that the use of IES as frequently as every 5 min does not cause an increase in the water content of the muscle. The minimal amount of water content identified in the contralateral control group, as calculated in this study, indicates that ∼5% of the tissue water content quantified in the control group and experimental groups 1 and 2 was not caused by the load application.

It has been suggested that high stress levels at the bone-muscle interface is a primary factor in the development of pressure ulcers (7, 8, 11, 35, 36), but the extent of tissue injury that is associated with these mechanical forces (shear and stress) has yet to be determined. Although complete elimination of DTI has not been achieved, our results suggest that IES delivered every 10 min is sufficient to reduce greatly the extent of damage in deep tissue exposed to constant external pressure.

None of the rats in this study showing indications of DTI displayed injury to the overlying skin. This emphasizes that skin appearance is a poor indicator of deep tissue health, and it supports the need for alternative methods to detect DTI. The results of this study, as well as those reported previously by Bosboom et al. (6) and Stekelenburg et al. (52), show that MRI is an effective tool for the detection of muscle edema associated with the presence of DTI, even when injury occurs in muscles as small as those in the rat hindlimbs (Fig. 3A). Although MRI currently may not be ideal for screening patients with DTI due to cost and availability, in situations where an individual is considered to be at high risk of developing an ulcer or has a long history of ulcer development, it might be necessary to perform periodic screenings. Identifying DTI before it fully evolves into a pressure ulcer would not only have a significant beneficial impact on the health and quality of life of the individual but also could greatly reduce costs associated with further medical and surgical treatments.

Mechanisms of Action of IES

Our results demonstrated that the levels of available oxygen in the tissue of gluteus maximus were reduced immediately after compressing the muscles (Fig. 6). However, instantly following the first IES-induced contraction of the muscles, the levels of tissue oxygen increased. This increase was greater than baseline levels, and it was most likely caused by reactive hyperemia, a process in which there is an increase in blood flow into the capillaries after brief periods of occlusion (38). This increase in oxygenation was maintained after each of the six IES-induced contractions. While oxygenation levels in the unloaded MG muscle also increased with IES, the increase was less than that in the gluteal measurements. This may be due to the fact that blood flow to the MG muscle was not altered, and consequently oxygenation levels were already at normal levels.

While periodical increases in tissue oxygenation should have the beneficial effect of negating tissue injury associated with ischemia-reperfusion, pressure relief is still needed to prevent further damage from persistent high stress levels of muscle cells. Our results demonstrated that IES of the compressed gluteus muscles reconfigured the shape of the muscles and distributed the pressure laterally in the
buttocks. The net result was a periodical relief of the superficial pressure around the bony prominence and reduction in the overall pressure throughout the buttocks. The use of superficial pressure measurements combined with recently developed finite-element models (37, 40) of the gluteal muscles, which can estimate the stress levels at the bone-muscle interface, could provide a more accurate tool for predicting the risk of developing DTI.

In conclusion, IES is a potentially effective means for reducing the incidence and recurrence of DTI in immobi- lized and/or insensate individuals. Use of IES could be applied in wheelchair-dependent individuals who are community dwellers, long-term care and nursing home residents, and acute care patients. Identification of the best stimulation parameters that would provide maximal enhancements in deep tissue oxygenation and decline in stress levels at the bone-muscle interfaces, thus maximal reductions of DTI, is necessary to determine.

GRANTS
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