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Injury and inflammation detection by the application of microcurrent through the skin

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Objective: To determine the efficacy and reliability of measuring direct current microcurrent applied through the skin to determine injury in the underlying tissues.
Design: Case control study.
Methods: First, microcurrent was measured as decreased blood flow induced hypoxia in healthy subjects. Next, reliability was assessed by measuring over ten days with set variations in pressure and distance between the electrodes. Finally, measurements over sprained ankle were compared to measurements over comparable uninjured areas on the same injured subject.
Results: For the blood flow test phase, microcurrent significantly decreased an average of 17% after 5 minutes ($p<0.05$), remained decreased for 30 seconds, and returned to non-occlusive levels after 2 minutes of normal circulation. The results indicate that the microcurrent decrease was not due to blood flow, and most likely from hypoxic cellular damage. For the reliability phase, the coefficients of variation averaged 10.3% for the shoulder, 14.8% for the low back, and 29.1% for the knee. Changing distance 2.5 cm between the electrodes resulted in insignificant changes. Changes in pressure had some significant effect after an increase in force of 2.6 N, affirming the need for consistent pressure for measurement. For the injury test phase, a significant 69% decrease occurred comparing injured areas to the same area on the uninjured side, and a significant 74% occurred comparing injured and non-injured areas on the same limb.
Conclusions: Microcurrent through the skin shows promise as an objective method of assessing a soft tissue injury by detecting damage likely due to hypoxia.

Key Words: Diagnosis, Electric impedance, Inflammation, Sprains and strains

Introduction

Musculoskeletal injuries are prevalent in society, with conditions such as tendonitis in the extremities and back pain common amongst people of all activity levels [1,2]. The severity of these conditions can range from minor to disabling, interfering with the activities of daily life [3]. These injuries can be sub-classified as bone or soft tissue injuries. While radiographs are excellent for bone injuries, quantifying soft tissue injuries requires special studies which are much more expensive [4,5]. Other measurements and tests, such as blood tests, MRI, and diagnostic ultrasound, have been attempted, with varying success [6,7]. However, there may be promise using electrical measurements.

Soft tissue injuries lie in the muscles, ligaments, fascia, and other structures outside of the bones and joints of the body. These structures can be visualized by MRI and diagnostic ultrasound, expanding knowledge on injuries and giving more objective information than a physical examination [4,5]. For example, sprains, strains, and arthritis can be

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sometimes be objectively visualized using these special studies and their severity can be assessed [4-6].

However, in common practice, soft tissue injuries are generally evaluated by clinical presentation, including observation, orthopedic tests, muscle strength and flexibility tests, and range of motion [7]. Functional tests specific to tasks and disability indexes have also been created and test both upper and lower extremities and spinal regions, and may be specific for certain professions and tasks [8,9]. Although these tests give a numerical score, they rely on subjective information supplied by the patient.

For a purely objective measure, blood markers have been attempted to quantify soft tissue injury. Associated with the inflammatory processes of muscular damage, markers may provide a composite picture of the muscle [10]. Some serum markers include creatine kinase, lactate dehydrogenase, aldolase, myoglobin, troponin, aspartate aminotransferase, and carbonic anhydrase [10]. It has been shown that with delayed onset muscle soreness, creatine kinase and myoglobin concentrations increased significantly [11]. Interleukin-6 is a major cytokine mediator with acute inflammation and injury, but tests for its concentration may overestimate or underestimate its concentrations and its complexes with other molecules [12,13]. Also, there were only minor changes in cytokine concentration and other inflammatory mediators [11]. Cytokine gene expression has also been tested after severe trauma, but unexpected cytokine genes involving fibrosis and osteogenesis were up-regulated, and more investigation was determined to be needed [14]. Also, blood markers are very unreliable with small injuries due to dilution from systemic blood circulation and clearance from circulation through the kidneys [11].

Other research has attempted to quantify soft tissue injuries by tracking cartilage gene markers in repetitive stress tendonitis. After creating supraspinatus tendonitis in rats, the tendon showed expression of the cartilage genes, while the undamaged patellar tendon did not show the same [15]. Although the results were promising, this was an extremely invasive procedure, requiring removal of the tendon.

One objective, non-invasive evaluative method that shows some promise is the detection of inflammation by the opposition to electrical current by a circuit, called electrical impedance or resistance. Electrical impedance is a vector quantity and uses alternating current (AC). It is measured with electrode pads placed on the subject's body, and does not break or puncture the skin [16-18]. Impedance changes have been shown in extracellular inflammation, with high Cohen's kappa agreement between impedance and the inflammation in rhinitis and asthma [16]. Significant differences in impedance and specific resistivity have also been shown in myocardium damaged by ischemia, with increased impedance and resistivity (resistance per unit volume) in ischemic myocardium [17]. Urinary bladders with carcinoma also resulted in increased impedance compared to normal, with a possible model being an increased lymphocyte density from an inflammatory response [18]. More complicated cancer detection methods, such as 3D electrical impedance tomography of the breast have also been attempted, but results are not conclusive and improvements need to be made [19].

Aside from inflammation, total body water and fat free mass have been investigated using impedance, specifically bioimpedance analysis, and through many studies [20]. The more common method is to use a four electrode system for testing impedance with AC, but electrical impedance has also been previously tested with a two electrode system on a specific body part [21]. Overall, skin acts as the greatest resistor to electric current, with electricity better able to flow through the fluid and electrolyte-rich tissue underneath, especially muscles and nerves [22]. Also, current flows through the body more easily with a changing voltage, such as with AC current, than with a constant voltage direct current (DC) current [22]. However, at least two points of contact are required for electricity to flow [22].

For DC circuits, opposition to current flow is referred to as resistance, a scalar quantity, and is calculated with Ohm's law, I=V/R, with I=current, V=voltage, and R=resistance. This calculation is simpler compared to impedance on AC circuits. Pain in infants has been studied with skin conductance measurements, with conductance being the inverse of resistance [23]. (conductance=1/resistance) Here, skin conductance increased with pain, though it was thought to have been from increased sweating. Ischemia created a decrease in whole heart conductance tested with DC current, hence an increase in resistance like was seen with AC current [17,24].

With constant voltage, changes in resistance are inversely proportional to current. So, it is possible that testing DC microcurrent, using constant voltage, probes closely spaced, and with a reliable stretch and pressure on the skin could detect changes directly over an injured area. There is some evidence that skin resistance will change with an injection of

1% lignocaine and adrenaline [24]. Inflammation brings more fluid into an injured areas and should reduce resistance, and there is evidence of edema reducing resistance [25]. However, ischemia creates hypoxia in tissues, and hypoxia also occurs in inflamed tissue, with wounds showing hypoxia from increased metabolic activity and decreased blood supply from damaged vascular structures [26]. So, an increase in current could be possible if current travels through edema, while a decrease in current could be a result of current travelling through ischemic tissues. Therefore, the purpose of this study was to determine the reliability and efficacy of applying a DC microcurrent through the skin to determine soft tissue injury.

Methods

Subjects

The subjects for this study were split into blood flow test, reliability, and injury test portions. For the blood flow test portion fourteen healthy young subjects, free of any orthopedic or neurological conditions were recruited. The general characteristics are given in Table 1.

For the reliability portion, ten healthy young subjects, free of any orthopedic or neurological conditions were recruited. The general characteristics are given in Table 2.

For the injury test portion, ten subjects with sprained ankles were recruited. All had visible swelling around one ankle only. The general characteristics are in Table 3. Subjects were recruited from the students and faculty of Loma Linda University, or from the community. The experimental protocol, IRB #5110308 approved by the Institutional Review Board of Loma Linda University, was explained to each subject and the subjects gave their written informed consent for the study.

Methods

The electrical measurement used was resistance from a prototype device from Mettler Electronics (Anaheim, CA) that was called a zone finder. It supplied a constant 9 volts between two probes and measured the resulting microcurrent in microamps (uA), generally measuring around 100 uA. The two probes were tipped with cotton pads and mounted in a housing where the distance between probes could be changed, and the force of each probe on the skin could be measured on two separate force gauges. Due to the angle of the probes, pressure caused the skin between the probes to stretch. During each test, the cotton pads on the probes were first soaked with 0.9% saline. Then they were placed onto

Table 1. Demographic information for blood flow testing portion (N=14)

Sex	Mean age	Standard deviation of age	Mean height (m)	Standard deviation of height (m)	Mean weight (kg)	Standard deviation of weight (kg)	Side tested
Male (n=6)	30.5	9.3	1.8	0.070	77.7	11.5	Right: 3, left: 3
Female (n=8)	29.3	5.3	1.6	0.078	56.1	8.0	Right: 3, left: 5

Table 2. Demographic information on subjects for reliability portion (N=10)

Sex	Mean age	Standard deviation of age	Mean height (m)	Standard deviation of height (m)	Mean weight (kg)	Standard deviation of weight (kg)	Side tested
Male (n=6)	26.7	3.7	1.8	0.074	77.1	13.8	Right: 5, left: 5
Female (n=4)	24.8	2.5	1.6	0.062	56.4	6.9	

Table 3. Demographic information for injury testing portion (N=10)

Sex	Mean age	Standard deviation of age	Mean height (m)	Standard deviation of height (m)	Mean weight (kg)	Standard deviation of weight (kg)	Ankle injured
Male (n=5)	31.0	10.4	1.8	0.042	70.4	2.1	Right: 8, left: 2
Female (n=5)	39.8	20.0	1.7	0.075	67.2	21.9	

the subject so that equal pressure was applied on each probe, as measured by each force gauge. Only then would the current be recorded. Also, the skin was first cleaned to minimize the effects of dirt, sweat, or anything else on the surface of the subject. This was repeated for all areas, distances, and forces. Less than 1 mA of current was applied and could not be felt by the patient [22].

Procedures

There were three parts to this study. First, the effects of blood flow on microcurrent measurements were determined. Second, the reliability of microcurrent measurements was evaluated over multiple days and differing forces and separation distances. Finally, microcurrent measurements were measured with injury in the underlying tissues.

The effect of blood flow on tissue resistance

The blood flow response to four minutes of occlusion is used to assess endothelial function. After occlusion, tissue blood flow increases by at least fifty fold. It returns to normal in two minutes.

Subjects were tested a single time. First, a blood pressure cuff was placed around the subject's arm. Their forearm was cleaned with alcohol and a testing spot was selected. Then the zone finder was calibrated to 100 uA. All tests were performed at 2.54 cm separation and 226.8 g pressure. A measurement was taken with the cuff deflated. Then the cuff was inflated to 200 mmHg to create ischemia in the forearm. Measurements were taken at one minute intervals. Then the cuff was deflated at 5 minutes. Measurements were taken 30 seconds, 1 minutes, 2 minutes, and 5 minutes after release.

Reliability testing

Subjects were tested for 10 days at different times of the day. There were 5 areas tested; middle deltoid, infraspinatus, erector spinae near L3, quadriceps tendon, and the fibularis muscle bellies. The spots to be tested were marked with a marking pen, and the side was preselected as seen in Table 1. Areas were tested with a 2.54 cm separation, measured between the metal probes, at 2.2 newtons (N), 3.6 N, and 4.9 N of pressure on each probe. The area was then tested at 3.81 cm and 5.08 cm of separation with the same pressures. This was repeated for each of the 5 areas tested.

Subjects lay or sat on a plinth, allowing the specific area to be tested to face upwards. Areas to be tested where cleaned with alcohol. The zone finder was first calibrated by recording a reading while touching a copper sheet. Then all areas listed previously were tested at the separation distances and pressures listed. The instrument was recalibrated at each change of distance.

Injury testing

Sprained ankles were chosen because they were a common condition with easily visible signs of inflammation that also carried little risk of complications. Subjects were tested bilaterally on their ankles, calves, feet, and quadriceps tendons. In this portion, only a 2.54 cm separation was used, with only 2.2 N. Areas tested included the bilateral calf and ankle anteriorly, posteriorly, laterally, and medial, as well as the dorsum of the foot and the quadriceps tendon.

Subjects sat with their knees extended, allowing easy access to the feet. Both feet were examined for signs of inflammation. Both feet and legs were then cleaned with alcohol. The zone finder was calibrated by touching a copper sheet, same as before. Then bilateral calves and ankles were tested, as listed. The instrument was recalibrated when switching sides.

Data analysis

Measurements were normalized by dividing the calibration reading by the reading recoded by the instrument. For the reliability portion, mean, 95% confidence intervals, coefficient of variation, and standard deviation were calculated. Differences in separation and force were measured with a one-way ANOVA. For the injury test portion, readings over the injured areas were compared with uninjured areas using a two sample t-test assuming unequal variances, two-tail. Cohen's d was used to assess effect size. Pearson's correlation was used to compare various areas on both feet. Values of 0 were recorded as 0.4. For the hypoxia test phase, readings were compared using a two sample t-test assuming unequal variances, two-tail.

Results

For the blood flow testing portion, microcurrent significantly decreased 17% after five minutes of occlusion, and did not change significantly for 30 seconds after the cuff was deflated as seen in Figure 1. Little change was observed after three minutes of occlusion. Neither was there much change from the second to the fifth minutes after blood flow was restored.

For the reliability portion, current measurements ranged from 0.76 to 0.86 for the upper body and low back areas, and 0.45 for the lower extremities as shown in Figure 2, with standard deviations from 0.08 to 0.14. Altering probe separation created insignificant changes with no more than a 5% change in values for a 1.27 cm or 2.54 cm change. As shown in Figure 3, a pressure change of 2.7 N resulted in significant changes for certain areas and a mean percent change of 20%. Also, current was virtually undetectable on the electrical gauge unless the skin was stretched from pressure on the probes.

For the injury testing portion, measurements over injured areas decreased by 69.5% versus the same spot on the opposite limb, and 73.8% versus an adjacent non-injured spot on the same limb. Percent changes for non-injured areas ranged from 15% for the adjacent areas tested in the reliability portion, to 35% for comparisons on the non-injured ankle for subjects in the test portion as shown in Figures 4 and 5. All comparisons for the injured area against all other areas were significant ($p < 0.05$). Cohen's d calculated all large effect sizes for all comparisons ($d > 0.8$). Pearson's correlation comparing non-injured spots on each particular subject ranged from 0.53-0.81, which indicated a strong correlation ($r > 0.5$). Strong correlation was also found comparing the percent change in injured versus adjacent spots, with injured versus the same spot on the opposite limb (r=0.96).

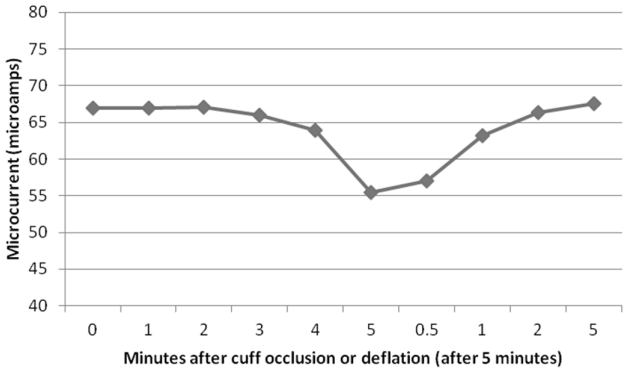

Figure 1. Microcurrent tested during and after hypoxia was created. Hypoxic condition ended after 5 minutes. 0.5, 2, and 5 indicate time after cuff deflation. p=0.04 comparing values at time 0 and 5 minutes. p=0.84 comparing times at 5 minutes and 30 seconds after deflation.

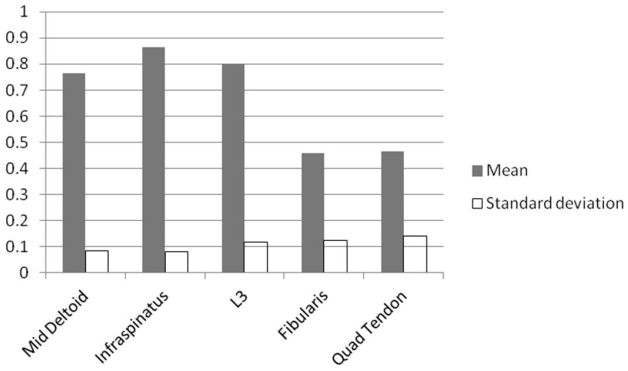

Figure 2. Mean and standard deviation at 2.54 cm separation and 2.2 N pressure as tested in reliability portion. Values are measured values divided by calibration value.

Discussion

Currently, the only objective measurements for soft tissue injury are special studies like MRI or diagnostic ultrasound [4-6]. Functional tests still require subjective information [8,9], blood tests are limited by dilution and excretion while not necessarily specific [12,13], and tissue tests are extremely invasive [15]. We were interested in testing the reliability of using microcurrent, to detect soft tissue injury by changes in tissue resistance, specifically the inflammation associated with injury, and to investigate the mechanism for microcurrent changes.

The blood flow test phase demonstrated significant decreases that were unrelated to blood flow. Occlusion stopped the blood flow, but there was no change in microcurrent measurements once occlusion began. Significant decreases did not occur until after 5 minutes of occlusion. Also, the decrease remained for over 30 seconds after the release of

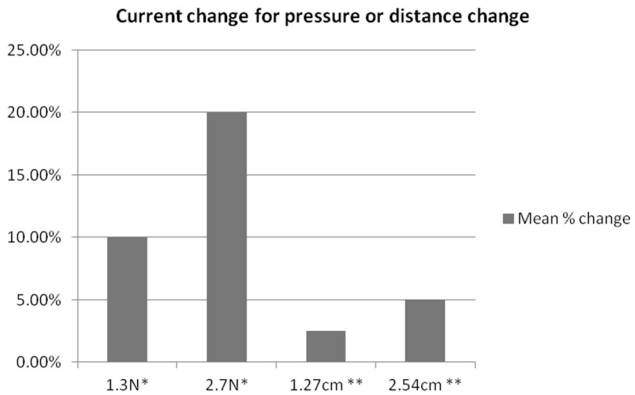

Figure 3. Percentage current change for either a change in pressure or distance between probes. *All separation distances included, 2.54 cm to 3.81 cm and from 3.81 cm to 5.04 cm. p-value < 0.05 for 2.7 N change in mid deltoid, infraspinatus, and L3. **Separation distance changed from 2.54 cm to 3.81 cm and from 3.81 cm to 5.04 cm. p-values 0.74-0.99.

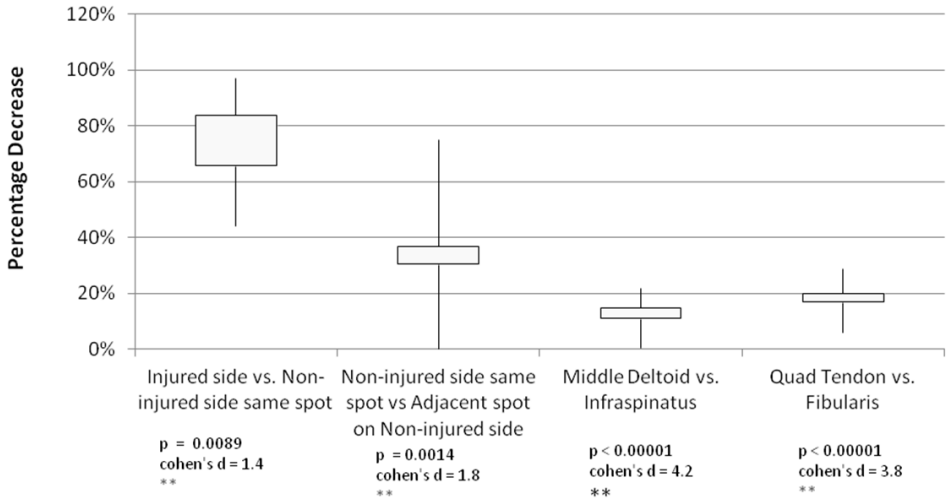

Figure 4. Whisker plot showing various comparisons. Injured side indicates the particular spot on the injured side. Spots were designated as either the anterior ankle, Achilles tendon, just under the lateral malleolus, and just under the medial malleolus. Middle deltoid, infraspinatus, fibularis, and quadriceps tendon information taken from same subject comparisons in the reliability portion.
*Comparing the values for injured side versus the same spot on the uninjured side. **Comparing the percentage change from injured side versus the same spot on the uninjured side with the indicated comparison.

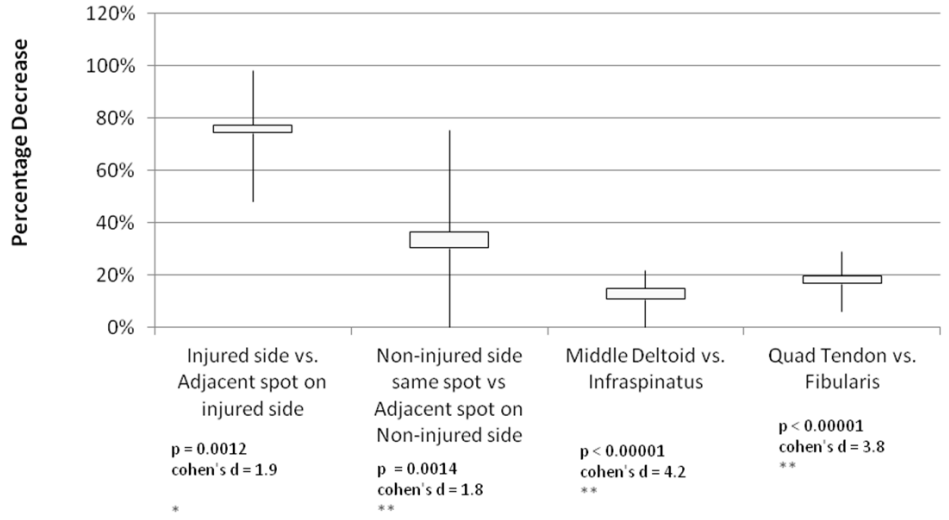

Figure 5. Whisker plot showing various comparisons. Injured side indicates the particular spot on the injured side. Middle deltoid, infraspinatus, fibularis, and quadriceps tendon information taken from same subject comparisons in the reliability portion.
*Comparing the values for injured side versus an adjacent spot on the injured side. **Comparing the percentage change from injured side to an adjacent spot on the injured side with the indicated comparison.

occlusion. Prior research has shown that after occlusion is released, blood flow increases over the first 30 seconds, reactive hyperemia peaks at 20 seconds [27] and blood flow increases over 600% [28]. The lack of microcurrent change in these first 30 seconds further indicates that microcurrent measurements are independent from blood flow. These findings suggest that the microcurrent changes are due to a cellular reaction to the decreased blood flow, and not the blood flow itself. Cellular reactions could include hypoxic damage, a buildup of noxious metabolites, or a change to the cell membranes. Since there is evidence of increased resistance in ischemic tissue [25], and ischemia creates hypoxia in tissues, it is likely that changes are due to hypoxic damage. Also, since five minutes passed before significant microcurrent changes, it appears that some damage must occur before a current decrease. It is likely that further ischemia

would create a greater decrease in microcurrent, but longer testing times could cause injury to subjects.

For reliability, changing the distance between the probes appeared to have insignificant effects on resistance measures. Since the greatest change was only 2.54 cm, no conclusions can be made about changes greater than that. Changing the pressure could create significant effects, however. A 2.7 N increase was able to create significant change in 3 of 5 tests, so investigations must maintain a reasonably consistent pressure for accuracy. This pressure creates a conformational change in the tissues, so it may be important to test in the same body position to minimize conformational change in tissues from body movement. This was not tested in the study since the same body positions were used for repeated measurements. It is also important to note that changing the distance from 2.54 cm 5.08 cm means that the spot tested is more like a small surface area instead of the same exact spot. Since these changes were insignificant, it appears that minor placement changes have little effect on readings.

For the injury test phase, sprained ankles were selected because they are a common soft tissue injury. Significant differences were seen comparing the changes in injured areas to non-injured areas. Cohen's d also indicated a large effect size. From this, it appears that microcurrent measured by the zone finder detected changes related to soft tissue injury. Comparing the interquartile range for percentage change, it appears that there is a range from 65-100% change for injury, and 0-35% for uninjured tissue as shown in Figures 3 and 4. Also, the Pearson's correlation indicated a very strong correlation, suggesting that comparisons can be made against an uninjured area on either limb. Since each measurement was non-invasive and made in a few seconds, and because this instrument would be much less expensive than those needed for a diagnostic ultrasound or an MRI, this may be an excellent instrument for use in a typical healthcare examination. From Ohm's law, current=voltage/resistance. Since the voltage was constant, all decreases in current were due to increases in resistance. Hypoxia occurs in inflamed tissue, with wounds showing hypoxia from increased metabolic activity and decreased blood supply from damaged vascular structures [26]. Ischemic tissues show increased resistance [17,25], and are damaged by hypoxia. Since the microcurrent decreased over injured tissue, it appears that the microcurrent flowed through hypoxia-damaged inflamed tissues and not the edema, which would have reduced resistance [25]. Some factors that may have influenced this current flow were the DC current, which does not penetrate into deep tissues as well as AC, microcurrent which may not overcome the resistance of the skin [22], and the change in the alignment of tissues from the stretch of the skin.

Still, a 35% change for uninjured tissue is high. Looking at the reliability measurements, the standard deviation for three of the five areas is over 10% of the measurement, as shown in Figure 1. However, changes due to injury were still easily identified due to the large effect size. A 25% decrease is easily distinguishable from a 50% or 75% decrease. Also, despite varied baseline measurements for non-injured areas on the injured subjects, the Pearson's correlation is high when making comparisons on the same subject, either with an uninjured area on either limb, or two uninjured areas on either limb. This suggests the presence of a confounding variable. For electric current, the obvious confounding variable is dirt and oil on the skin, which acts as an insulator and blocks electrical current. This was addressed by attempting to clean the skin, and visible dirt and oil were often seen on the cleaning cloth. However, this may not have been sufficient to fully clean the area. Also, from Figure 1, areas on the lower extremity, which gather more dirt and may sweat more, have a much higher variance of values. Another possible confounding variable is altered gait as a result of the injury. This could explain the outliers on the non-injured side. However, this will require more study. Finally it is important to note that dirt acting as an insulator and further injury from altered gait would both result in a decrease in the current flowing from probe to probe. Therefore, a high current likely indicates an uninjured area. This suggests that microcurrent resistance could work as a sensitive measurement, with few false negatives though with some false positives.

Compared to other measures for soft tissue injury, microcurrent appears to have advantages. Microcurrent measurements show significant changes and a large effect size to injuries, while blood tests show minor changes and may be unreliable [11-13]. The fact that the measurement is focused in a small area is similar to the gene testing, but the non-invasiveness of this instrument is a major advantage. Also, microcurrent decreases are related to cellular damage, likely hypoxic damage. Finally, microcurrent measurement requires no subjective information from the subject being tested, making this a completely objective measurement.

In conclusion, microcurrent, applied with consistent pres-

sure through the skin, appears to have good promise as a measurement of soft tissue injury by detecting the ischemic damage caused by the inflammation. Consistent pressure is necessary for accurate measurements, though distance between probes is not as crucial. Even though baseline error exists, the large effect size creates an easily visible change. Therefore, also taking time and cost factors into consideration, microcurrent shows excellent clinical potential for use an objective measure of soft tissue injury.

Limitations to this study were: Each portion of this study had only 10 or 14 subjects. More subjects would give a more accurate picture. Although all ankles were swollen, the injuries were of different severities. Cleaning of oil and dirt was attempted, but does not appear to have been sufficient. Changes resulting from healing were not sufficiently measured. Ischemia times greater than five minutes may show greater microcurrent decreases, but were not tested due to a risk of injury to subjects.

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