The Report Committee for James Edwin Casselman
Certifies that this is the approved version of the following report:

A study into the non-invasive manipulation of skin blood flow utilizing electrotherapy techniques integrating Eastern and Western research to create engaging, open-ended classroom experiences

APPROVED BY
SUPERVISING COMMITTEE:

Supervisor: ______________________________
Kenneth Diller

____
David Allen

A study into the non-invasive manipulation of skin blood flow utilizing electrotherapy techniques integrating Eastern and Western research to create engaging, open-ended classroom experiences.

by

James Edwin Casselman, B.A.

Report

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Dedication

This Master's report is dedicated to all who have mentored and encouraged me to further pursue my passion for teaching science. I am indebted to my mother and father, all the professors in the program, and my supervising professor Dr. Kenneth Diller.

Most importantly, I would like to dedicate this work to my inspirational, knowledgeable and understanding wife, Susan. Without Susan's enthusiasm and encouragement, this journey would never begun.

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To Therese Dobbs, thank you is insufficient.   Always the cheer leader, champion, cheer captain, inspirational coach, motivator, and superb administrator keeping all in alignment.

Abstract

A study into the non-invasive manipulation of skin blood flow utilizing electrotherapy techniques integrating Eastern and Western research to create engaging, open-ended classroom experiences.

James Edwin Casselman, M.A.

The University of Texas at Austin, 2013

Supervisor: Kenneth Diller

The research to date, of transcutaneous electric nerve stimulation on cutaneous blood flow, is equivocal. The purpose of this report is to review the TENS body of knowledge, in particular synthesizing the literature on acupuncture stimulation of cutaneous blood flow with the two fold goal of creating a protocol to increase skin blood flow through the exogenous application of electrical stimulation, as well as creating an engaging engineering challenge for high school anatomy and physiology students. The hypothesis developed was TENS stimulation with electrode placement on specific acupuncture points would influence cutaneous blood flow as measured using laser Doppler flowmetry.

The findings of this project did not support the hypothesis of TENS or Interferential electrical stimulation, in combination with acupuncture points or not, influencing skin blood flow. Perhaps this is due to the physiological differences between glabrous and non-glabrous skin and the different electrical resistances of each dermal

layer, nerve stimulation, age and gender of subject or some combination thereof. These equivocal findings may also be the result of inconsistencies in testing protocols, such as subject preconditioning or not, subject's position during administration of stimulation, electrode size and placement to name a few.

Ultimately, this report provides a summary of the research to date, as well as outlining how this research could be adapted to supply engaging bio engineering challenges in the classroom including challenges to develop a model for delivering current to muscle; develop a model for skin blood flow management to name a few.

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Chapter 1: Introduction

Within the curriculum of fourth year science classes lay ample opportunities to utilize Engineering concepts as a means of creating scientific and engineering literacy: to develop an awareness of the engineering process. Altering cutaneous blood flow continues to be an area of ongoing research as biomedical engineers seek non-invasive methods to minimize tissue damage while improving tissue-healing outcomes; if blood flow can be increased patient outcomes and recovery time from such surgeries as knee replacement would be improved.

Ask any student "How does the dermis function in the maintenance of normothermia? Their response typically would be "Humans sweat when the body becomes heated and shiver when the body becomes cooled." Ask a biomedical engineer, and the response frames the view of the integumentary system as a heat exchanger operating with a negative control loop, heating or cooling being utilized when the body core is in need. With an understanding of vasculature and nervous enervation and some electrical means to confuse the sympathetic nervous system one could develop a non-invasive means to manipulate skin blood flow.

1.1 CUTANEOUS ANATOMY

The vasculature of the dermis is a knotted physiological puzzle with two distinct skin types present: glabrous and on-glabrous skin. Glabrous, with its intricate network of AVAs (arteriovascular anastomoses working under the control of the hypothalamus, primary means of control of skin blood flow is based upon a concept called "set point" where maintenance of the body core dictates the flow of blood, for the most part, at the cutaneous level. (Hensel, 1973) Of note is the impact of perspiration upon (sudoriferous glands) upon vascular dilation, or the sensation of cold upon vascular contraction.

Sympathetic nerves control vascular flow, fight or flight to divert blood to internal organs, however other moderators of cutaneous blood flow exist such as sudiferous secretions, neurosensory transmitter or other bio compounds are known or are being researched.

For instance, the fibers innervating most eccrine sweat glands are cholinergic, with perhaps some evidence of noradrenergic control at the glabrous (hairless) surfaces of the hands and feet. Skin blood flow to these glabrous surfaces is determined solely by noradrenergically mediated vasoconstrictor nerves (Kellogg, 2006), while blood flow to the non-glabrous (hairy) skin regions is mediated by separate noradrenergic vasoconstrictor and active vasodilator branches of the sympathetic nervous system; the neurotransmitter for the latter pathway awaits identification (Kellogg, 2006). Perhaps Hales' description of cutaneous vascular anatomy provides insight into the complex and knotted physiology encountered: "Cutaneous capillaries are located just below the epidermis, with hand veins draining into either superficial or deep vessels, the largest of which run along the dorsal hand and foot surfaces. Palmar surfaces of ands and feet also contain arteriovenous anastomoses, and when these shunts are open, dramatic elevations in skin blood flow can occur. Indeed, these vessels are responsible for the extremities behaving as very efficient heat exchangers (radiators), with thermal homeostasis sometimes being achieved entirely through subtle changes in skin blood flow through the anastomoses of the hands, face and feet (Hales, 1985).

1.2 Electro Stimulation

Electro stimulation's ability to influence cutaneous blood flow is an area of some debate in scientific literature, as shall be seen. Perhaps the first use of electro stimulation was in Egypt, 2500 BC with the use of a *Malapterurus electricus* catfish for treatment of an unknown ailment. Research in the 1940's proposed the possible value of using electrical stimulation with paralysis patients. TENS devices were developed to replace invasive percutaneous electrical nerve stimulation therapy, creating a safer, infection free method of electrical stimulation for the sufferer, instead of an needle like electrode, TENS uses superficially applied adhesive electrodes.

Electro stimulation has its most typical uses in pain management, with a growing body of literature and researchers seeking alternative uses for electro stimulation: wound and bone healing, easing labor pain during childbirth, and pain relief from adjunctive symptoms of chronic diseases such as Sjogren's, Reynaud's syndrome.

What success in the manipulation of skin blood flow from the synthesis of acupuncture meridian/energy flows, TENS and subsequent electrode placement? Acupuncture loci are precisely located with palpable anatomical landmarks. These landmarks enable consistency, in experimental trials, of electrode placement, and typically possess some degree of decreased resistance to electrical currents, ideal sites for electrical stimulation (Walsh, 1996)

This project is intellectually grabbing and challenging one, an exciting area of study, developing an understanding of the anatomy and physiology of the dermis, innervation, various modes of electro stimulation all combine to provide a wealth of investigative opportunities: the ultimate real world application.

One result of my exposure to engineering mindset through the MASEE program has been to look for areas where Anatomy and Physiology studies can be linked to additional disciplines, in this case those of engineering. Homeostasis, as most students learn it, is pretty much a static definition in their mind, however as a result of this project, homeostasis will take on the additional dimensions of control theory as well as developing an understanding of the electrical nature of the human body, specifically the resistances of the tissues. Students of anatomy tend to have a perception the electrical nature of the human body is limited to the brain and the nervous system, a perception which is not totally correct. Could this electrical system be overridden, such as reflective foil can jam or fool radar? An engineering challenge what students could not resist the: develop a technique to "jam" the nervous system?

During the course of the challenge, students could seek expert opinions, black box electrical flow through tissues, beginning with the stratum corneum and concluding at the periosteum, including electrical properties of tissues influencing electrical current delivery at depth to the loci of electro stimulation as a beginning.

The non-invasive manipulation of cutaneous blood flow, in both glabrous and non-glabrous skin has been an area of ongoing research within Dr. Diller's labs at UT. Maintenance of normothermia is under the control of the autonomic nervous system, and some form of disruption of these autonomic processes could result from: anesthesia induced hypothermia, hyperthermia as a result of chronic disease such as Multiple Sclerosis or as a result of misadventure such as being caught in a blizzard. Examples where patient recovery prognosis could benefit from an ability to noninvasively locally disrupt these processes is knee replacement: providing a non-invasive means to speed healing due to increased skin blood flow during use of a circulating cold water bath to minimize swelling.

Currently, anesthesia induced hypothermia is controlled by the administration of certain drugs, such as Isoflurane, during the surgery. Exogenous heat is applied to patients by wrapping warm blankets or administration of warm air circulation or some other means. Administration of additional drugs is something to be avoided in any procedure, warm blankets either in combination with warm air treatment or without, are not optimal at best: in hypothermic situations, the autonomic nervous system restricts blood flow to the extremities, conserving blood flow and warmth in the body core minimizing transport and acquisition of exogenously applied heat to the core.

An understanding of anatomical structures and physiological processes of the human body lend insight into why these approaches are not optimal: not all human dermal surfaces have the same density of vasculature or innervation. Using anatomical knowledge plus the differential knowledge gleaned from research with applicable acupuncture loci theory, the non-invasive manipulation of skin blood flow using TENS is a reality.

Chapter 2: Review of the Literature

Manipulation of vascular circulation is an area of abundant research in the literature: through a synthesis of the existing literature regarding electrical simulation, (TENS or other) and utilizing a knowledge of dermal vascular control mechanisms, we were confident of reaching our goal: influencing vascular circulation.

Cutaneous vasculature is an integral component of the human thermoregulatory system, whose primary purpose is the maintenance of the thermal core of the body and controlled by the hypothalamus and central nervous system, receiving inputs from thermal sensors in the dermis. Components of the thermal core control system include two tissue types: glabrous and non-glabrous. Glabrous tissues are found in the hairless regions of the face, ears, hands and feet and possess tremendous heat transfer structures called arteriovenous anastomoses: vascular communications directly between the arteries and the venous plexuses (Grahn 1998) Non-glabrous tissues, making up the bulk of human dermis, while not possessing the dense vascularization, do perform a thermic role, which could be manipulated non-invasively.

The literature reviewed initially concerns the restoration of normothermia in hypothermic patients, hypothermia being a typical response to anesthetic. Exogenously applied heat, to a hypothermic patient, does not influence thermal core temperature. Hypothalamic control of the arteriovenous anastomoses results in a shunting of blood flow away from the extremities back to the body core. Arteriovenous anastomoses are susceptible to manipulation by air pressure: insertion of a hand or foot into a barometric chamber equipped with a warm bath, reduce the atmospheric pressure: the arteriovenous anastomoses vasodilate and body core temperature is influenced (Grahn 1998).

Looking through this lens, at the body of research by Grahn we see a focus on manipulation of the glabrous tissues: using low-pressure environments (portable heated barometric chamber) with or without a water bath, to create an artificial distension of the AVAs, allowing the conduction of the exogenously applied heat to overcome anesthesia-induced hypothermia. While this is a functional approach, adopted by the medical community and used in hospitals, the equipment is clumsy, design specific for hands and feet and requires a sizeable footprint in an already crowded operating room. Another issue is seen this equipment and protocol cannot be used on other body areas such as the patellar region.

Two branches of the sympathetic nervous system affect the neural mechanisms controlling cutaneous vasculature: an active vasodilator system and an active vasoconstrictor system (Wissler 2008). Skin blood flow is a tangled physiology, sympathetic nervous responses are a component of vascular control, however vascular reflex actions exist: in response to warming or cooling of one portion the body reflex vasodilation or vasoconstriction is seen in other portions of the body (Rowell 1977). This cutaneous vascular resistance is regulated by the frequency of impulses over the sympathetic vasoconstrictor nerve fibers (Rowell 1977).

2.1 TENS

Would use of some form of electro-stimulation enable a researcher to over-riding or electrically jam the sympathetic nervous system? Knowledge of the frequency and duration of stimulation should allow constriction or dilation cutaneous vessels, placing a modicum of control of cutaneous vasculature in the control of others.

Medical use of electricity dates to 2500B.C. in Egypt, the application of the African electric catfish, capable of generating 300-400 volts, to the patient's afflicted area. While the neither the patient diagnosis nor outcome is known, this may be the first use of TENS in medicine.

Trans cutaneous electrical nerve stimulation (TENS) has been in therapeutic use for approximately 42 years (Walsh 1996). Typically, TENS is used for pain and aches: a safe, non-invasive treatment enabling patient management of chronic pain. From all appearances TENS use would be ideal for safe, non-invasive manipulation of blood flow.

Research on the impact of transcutaneous electrical nerve stimulation on blood flow has produced equivocal results: some researchers see the effect, others don't. Perhaps this equivocal nature of TENS is due to experimental set up, loci of stimulation electrodes, pre trial conditioning of subjects or lack of conditioning? TENS is a surface effect: the current penetration is confined to the surface and areas adjacent to the electrode. Considering electrode surface areas used in research vary from 1cm^2 to 16cm^2, the TENS influences seen, and the data collected for skin blood flow cannot be correlated.

Utilization of TENS to influence blood flow is seen as early as 1952 in research by K Wakim (Wakim 1952) on anesthetized dogs. In this research, one group of dogs had stimulation to the electrodes affixed on the exposed sciatic and femoral nerves, the second group of dogs received stimulation through electrodes affixed to shaved areas of the thigh and ankle. In both instances, blood flow was increased over control values, regardless of frequency used.

Shifting TENS study to humans, Owens (Owens et al 1979) sought thermo graphic evidence of reduced sympathetic tone. Placement of an electrode over ulnar aspect of the wrist at the point of greatest arterial pulsation, and using medium frequency TENS (75Hz) observed increases in palmar radiation distal to stimulation. This effect continued for 5 to 7 minutes after the conclusion of stimulation, presenting indirect evidence of cutaneous vasodilation (Owens et al 1979). In researching electrode placement other than that of Owens, Tracy et al (1988) researched stimulation of 2 electrodes positioned over the proximal vastus lateralis muscle and 2 electrodes over the distal vastus lateralis produced mean increases in blood flow, attributed to the pulse frequency used as supported by statistical analysis (Tracy et al 1988).

In a response to the variance of frequency of TENS seen in research, Cramp et al (2000) chose to investigate the effect of high frequency (110 Hz) and low frequency (4 Hz) TENS on cutaneous blood flow with the electrodes placed 4-5 cm distal and proximal to the midpoint of the wrist and elbow crease over the median nerve. This study concluded low frequency TENS causes cutaneous vasodilation, perhaps due to some inhibition of the sympathetic nervous system.

Using the protocol of Cramp (2000) McDowell (1999) reported a significant increase in skin blood flows using low frequency TENS stimulation (2 Hz). Unlike previous studies, where skin blood flows were transient post stimulation, McDowell reported, "lasting effects on blood flow post stimulation". During a study of wound healing in chronic leg ulcers, Cosmo et al (2000) using low frequency (2 Hz) TENS saw a "regional increase" in blood flow, with large variation between subjects.

In a follow on study, Cramp et al (2002) again chose the median nerve, with low frequency TENS (4 Hz) varying the intensity of stimulation above and below the motor threshold. Using an intensity of stimulation above motor threshold produced significant cutaneous blood flow increases; interestingly no differences were seen skin temperature or distal blood flow. Perhaps the increased blood flow is a localized effect, limited to those muscles stimulated.

Wong and Jette (1983) using acupuncture loci, typical for treatment of pain in the forearm, for electrode location, while seeing no increase in skin temperature and consequently skin blood flow, did see a decrease in skin temperature and speculated this observation was the result of increased sympathetic activity a localized TENS effect.

Indergand & Morgan (1994) saw no effect on cutaneous skin blood flow when using high frequency (110 Hz) TENS applied through 2 pair of $16cm^2$ electrodes, one placed over the peroneal nerve proximal, the other distal to the fibular head; a second pair of electrodes with one electrodes placed over the tibial nerve above the popliteal fossa and the other immediately distal to the fibular head. No change in blood flow was seen, possibly due to inconsistencies in electrode placements, and ambient room temperatures utilized by Owens.

In partial agreement with Owens findings, but only observing a transient vasodilatory effect on calf blood flow, Sherry (Sherry et al 2001) concluded burst mode of TENS was increased above motor level was responsible. No change in skin temperature was noted, nor were any change in skin blood flow noted in the unstimulated leg of subjects.

Petrofsky (Petrofsky et al 2005) in research on wound healing, using moderate frequency TENS stimulation (30 Hz) observed increased blood flow to non hairy skin, however hairy skin blood flows only increased if a wound were present, due to the immediate wound environment. Of note, blood flow remained elevated in glabrous fingertips after stimulation was over.

Petrofsky (Petrofsky et al 2007), researching the effect of a warm room, 32 °C, on wound healing in diabetics found moderate frequency TENS stimulation (30 Hz) produced a large increase in skin blood flow especially in those subjects with diabetes. Petrofsky (Petrofsky et al 2007) in further research on the effect of moderate frequency TENS (30 Hz) and a room temperature 32 °C on wound healing confirmed earlier findings of warmed room with the additional observation room heating substantially influences the skin blood flow both during and post stimulation.

In another study, Petrofsky et al (2007) using moderate frequency TENS (30 Hz) and placement of 2 pairs of electrodes on the quadriceps saw an increase in skin blood flow, which continued for 4 minutes post stimulation.

Factors, which may have contributed to these seemingly contradictory findings, may include frequency of stimulation (Tracy et al., 1988; Cramp et al 1999) and the intensity of stimulation (Wong & Jette, 1984). Further inconsistencies may be found in ambient temperatures, dissimilar probe sites, patient conditioning, length of stimulation and others. Many of the studies reviewed fail to specify or specify in ambiguous terms electrode placement on the subject, as well as a failure to specify exact stimulation parameters: frequency, pulse duration and wave form. Variability in the experimental set up appeared to be a driving factor in those researchers who did not see an effect. Additional areas of ambiguity include subject compliance: if Laser Flowmetry were utilized to measure blood flow, accuracy of perfusion rate is impacted if the skin under the probe moves, either by a muscle twitch created by the ES or subject repositioning of limb. Petrofsky's protocol (Petrofsky 2007) required the subjects to pre-condition by refraining from smoking, exercise and caffeine intake for 2 hours prior to testing. Cramp (Cramp, F.L.et al 2002) demonstrated significant changes in blood flow seen using low frequency TENS (4Hz, 200μs) without the strict subject protocol used by Petrofsky.

Temperature of laboratory or room where the trials are run on the subject affects blood flow; a warm room would create a situation where vasodilation would be seen, and an increase in blood perfusion rates. A cool room, would create vasoconstriction, with the accompanying vasoconstriction creating lower blood perfusion rates, as seen by (Petrofsky et al, 2007)

2.2 Acupuncture loci and TENS

Location of electrodes in the research may be a larger determinant of success in realizing or not realizing blood flow increases. Armed with the knowledge electrode placement is important to research success, a not insubstantial body of research exists on the efficacy of acupuncture loci for placement of TENS electrodes, which has been utilized by skin blood flow researchers. Walsh (1996) advocates the use of acupuncture loci because of these characteristics: well-defined loci exhibiting decreased resistance to electrical currents frequently innervated superficially and deeply; ideal sites for situating electrodes. To illustrate this point, stomach 36 is located 3 units below the hollow found on the lateral side of the patellar tendon when the knee is flexed, approximately 1 finger width lateral to the tibia through this loci pass lateral cutaneous nerve of the calf, a cutaneous branch of the saphenous nerve with the peroneal nerve passing deeply. Thus acupuncture loci might prove ideal for stimulation by TENS due to the access to cutaneous branches of nerves innervating the limb.

A foundation paper is the work of Lee (1974) on the vasodilatory effects of low frequency stimulation (2 Hz) electro stimulation of acupuncture loci Tsusanli (St36), determined electro stimulation of St 36 inhibited sympathetic vasoconstriction: Lee observed “remarkable vasodilator effect in response to needle-electrical stimulation”. Lin’s (1979) conclusions were opposite to those of Lee; with stimulation of St 36 saw vasoconstriction with manual stimulation of acupuncture needles. Vasodilation, as measured by oral temperature, was observed with stimulation of acupuncture loci Li 11 and Li 4. Perhaps the variation with Lee’s work resulted from manual stimulation of acupuncture needles versus TENS stimulation: a TENS device can be programmed to deliver consistent impulses, whereas human manipulation is prone to inconsistencies both with the same subject and between subjects during trials. Nevertheless, acupuncture loci were found to have an impact on circulation. Lin's further research (1981) using acupuncture loci Li 11 and Li 4 provided data supporting cutaneous vasodilation. This study utilized manual stimulation of acupuncture needles, with attendant variability of reproducibility and actions.

Kaada (1982) successfully used low frequency TENS to achieve cutaneous vasodilation in patients suffering from peripheral ischemia. TENS stimulation of 30- 45 minutes resulted in vasodilation in cold limbs and an attendant temperature rise of 7-10°C for periods of 4-8 hours or more. These responses were more easily elicited with both sympathectomized patients and patients with diabetic neuropathy.

Wong et al (1983) utilizing 4 acupuncture loci commonly used for pain and TENS saw a fall in skin temperature of the subjects, more pronounced on the ipsilateral extremity in contradiction to the expectation of skin temperature rising.

Ernst and Lee (1986) using St 36 as the loci, with both manual and low frequency (1 Hz) TENS, observed a significant skin temperature warming which they believed was due to sympathetic inhibition.

In a study utilizing acupuncture needles, loci were not acupuncture loci, with low frequency (2 Hz) TENS placed into musculocutaneous flaps in rats, Jansen (1989) observed "electro acupuncture increased the blood flow suggesting either sympathetic inhibition and/or the release of a vasodilatory neurotransmitter, release of vasodilatory neurotransmitter was also hypothecated by Kaada (1982).

Blom (1993) utilizing both manual and electro stimulation of acupuncture needles with low frequency (2Hz) TENS on acupuncture loci with patients suffering from Sjogren's syndrome found significant blood flow increases, speculating this effect is due to release of vasodilatory neuropeptides. Sandberg (2003), using manual stimulation of acupuncture needles, inserted superficially or deeply into muscle, concluded skin and muscle blood flow increased with acupuncture, with the greatest increase being observed in needles which were deeply inserted and stimulated manually. In a seeming contradiction, Sandberg's study (2004) saw significant increases in both skin and muscle blood flow in subjects using superficial insertion in those patients with fibromyalgia. These disparate findings perhaps due to the lessened pain thresholds found in fibromyalgia.

Yeh, et al (2012) sought to influence body core temperature through low frequency (2 Hz) electro stimulation of acupuncture loci St 36 and St 37 bilaterally to counter anesthetically induced hypothermia. Those patients receiving electroacupuncture registered a lower drop in body core temperature compared with those not receiving electroacupuncture.

A common thread that developed in the review of acupuncture literature was use of acupuncture needle(s) to deliver electrical stimulation (intensity) at particular loci versus using electrodes with varying surfaces areas to deliver electrical stimulation. Needles, having less surface area, would have be able to conduct the stimulus, with no variance in intensity, to the deeper layers of muscle, Silverio-Lopes (2009). Examination of the effect of skin blood flow TENS in literature, through the lens of acupuncture loci and delivery mode: needle versus electrode patch may account for much of the variance seen within the literature.

Insertion of acupuncture needles is invasive, and the stated goal of this project was to manipulate cutaneous blood flow in a non-invasive manner. During the course of this project, the need for a non-invasive means to deliver current intensity at depth became apparent. New research was initiated to determine the existence of some form of electrical stimulation device addressing this need. Interferential Current appeared through a search of the literature as a possible solution.

2.3 INTERFERENTIAL CURRENT

As research on IFC was pursued it, methodology to influence skin blood flow is almost anecdotal, with a paucity of literature. Interferential current (IFC) is a medium frequency (3000–5100 Hz) alternating current with a beat frequency ranging from 0 to 250 Hz, the beat frequency obtained by subtracting the lower frequency from the higher frequency with the sensory nerves of the skin not be stimulated due to this higher frequency and the deeper layers of the muscle receiving the stimulation.

Johnson and Tabasam (2002) explain the ability of IFC to deliver currents to deep-seated tissue is by using kilohertz frequency pulsed or sinusoidal currents to overcome the impedance offered by the skin. As kilohertz currents are inefficient at exciting nervous tissue, two individual currents are delivered out of phase, interfering with each other within tissue at the point where the currents cross. The resultant amplitude-modulated interference wave has frequencies between 1 and 250Hz and is believed to excite nervous tissues and initiate endogenous mechanisms. Illustration1 is from Johnson and Tabasam (2002)

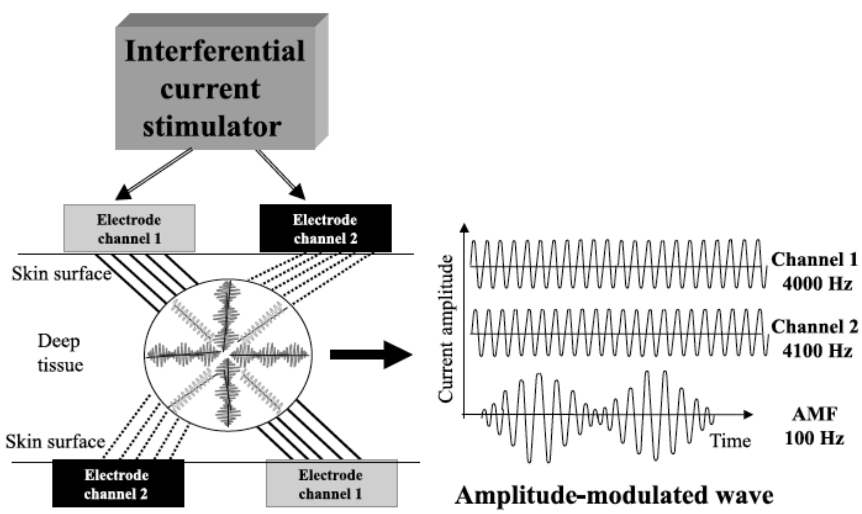

Illustration1: The principle of IFC. An interference current, which is modulated in its amplitude, is produced by the delivery of two out-of-phase currents (Johnson and Tabasam 2002)

To find research for IFC's depth efficiency claim proved to be elusive, as research conducted by Petrofsky et al (2009) does not support the claim nor do the findings of Beatti et al (2011) while stating the observed voltages of IFC were highest on the skin and lowest in the muscle tissue confirmed the penetration of IFC to muscle depth, with a disclaimer of a larger sample size being needed.

Ward (2009) is another author dismissing the depth efficiency claims as unsubstantiated citing a paper by Lambert (Lambert, H.L 1993), who disproved the concept of current intensity at depth with quadripolar stimulation.

Among those researchers finding support for IFC, Goats promotes interferential therapy capable of influencing peripheral blood flow, stimulate bone growth and more (Goats1990), however this appears to be more anecdotal than factual. Nussbaum et al (1990) sought to find an increase of peripheral blood flow with the conclusion IFC does not cause vasodilation.

An investigation with results obtained for skin blood flow was conducted by Noble et al (2000), contradicting Nussbaum's findings. Examining the physiological effect of interferential therapy upon cutaneous blood flow using laser Doppler ¯flowmetry, with concomitant measurement of skin temperature Noble observed results demonstrating a beat frequency of 10±20 Hz produced a significant increase in cutaneous blood flow. This finding supported results of Lamb and Mani (1994) who utilized 3 frequencies of IFC with increases in both arterial and microcirculatory blood flow observed.

Consistence in inconsistent results and lab approaches appeared to be the order of the day: few if any of the TENS, acupuncture, or IFC researchers utilized similar methodologies No clear cut path to success was to be illuminated by the review of the literature, paving the way for a series of interesting laboratory trials discussed in chapter 3.

Chapter 3: Methods

Confident of successfully increasing skin blood flow, as seen in Petrofsky's studies (2005, 2007, 2009), Cosmo, P (2000) and Cramp, (2000) and synthesizing the literature supporting the use of acupuncture loci with TENS stimulation to increase blood flow (Yeh, 2012), the TENS trials were envisioned to have one phase with a successful outcome: utilizing acupuncture loci stimulated by TENS electrodes to influence skin blood flow. This would not prove to be the outcome as derived from the trial data, which will be discussed in the data and analysis section.

Lab investigations into manipulation of skin blood flow ultimately had three iterations. As we attempted to duplicate protocols of published literature by authors observing a vascular effect, both TENS trials utilized acupuncture loci, the second TENS trial used shaped electrodes in an attempt to create a greater current density and achieve deeper penetration. The final iteration of lab trials resulted after conversations between Ken, Sepideh and myself considering the need to achieve a charge depth density at a deeper dermal layer than the achieved by TENS.

The third trials utilized Interferential current technology. After researching alternatives to TENS, and examining other forms of electrical stimulation, research revealed a body of literature, possibly serendipitous, from TENS skin blood flow researchers including Cramp, Noble and Petrofsky whose work supported the hypothesis of vascular effects using TENS.

Ultimately, neither TENS nor IFC trials produced data which supported our hypothesis, which will be discussed in chapter 4, results and data analysis.

3.1 TENS TRIALS

In the first TENS trial subject was seated on a massage table at approximately 75° angle for the duration of each experiment. Temperature was maintained at 23C, however was prone to fluctuation when lab was populated. A light blanket was placed over the subject to eliminate any vascular event, such as constriction in response to the air-conditioning turning on and cooling of the overall skin surface. Temperatures were monitored with ribbon type thermocouples taped to the skin surface peripheral to the sensing element.

All electrical sensor outputs (fiber optic blood perfusion and temperature, thermocouples, heat flux gauge) were read into a data acquisition interface (DAQ) (NI 9172, 9174, 9201, 9205, 921 1, and 9213; National Instruments, Austin, TX) and recorded using NI Lab VIEW Signal Express software running on an ACER laptop computer. Data files subsequently were transferred for analysis and plotting using MATLAB (Math Works, Natick, MA).

5 Laser Doppler perfusion and temperature probes were used to monitor skin blood flow using two laser Moor Doppler flow systems: two Moor InstrumentsVMS-LDF2 two channel perfusion and temperature systems and one Moor Instruments VMS-LDF1-HP single channel high power perfusion probe (Moor Instruments, Oxford, UK). The LDF2 device supports two fiber optic probes that incorporate both laser Doppler and optical temperature measurement. The flow field sampling depth is superficial, centered at about 0.5mm into the skin, extending from near the surface to about 2mm. The LDF1-HP device incorporates is a higher power laser with a wider sensor separation resulting in a deeper sampling depth centered at about 2mm, extending from near the surface to about 4mm. The probe heads, incorporating the fiber optic and sensor surfaces are affixed to the skin via a flexible probe holder and a double-sided adhesive disc.

In the first trial, following a modified protocol of Yeh (2012), 4cm x 4cm electrodes attached to acupuncture loci stomach 36 and stomach 37 respectively, and these electrodes were connected to the LG-TEC TENS unit. LDF probes (P1, O2, P2) were positioned as shown in figure 5. LDF P3 and a heat flux unit were attached to the right palmar surface as seen in figure 6.

The subject was given 20 minutes of preconditioning prior to TENS trials beginning to develop a baseline as well as allowing the probe ware to settle. It was imperative the subject remain motionless for the duration of the lab trial as motion of skin will cause spiking in data Fredriksson, I (2007). Trials were conducted as follows: twenty minutes of preconditioning with no stimulation, thereafter, TENS stimulation was applied for three minutes, with intensity set at 3.5, frequency at 4 and a pulse width of 150µs, and a total of 8 trials were run. No muscle contractions were visible, however the subject reported sensations of movement beneath the electrodes.

Figure 1: LG-TEC TENS unit used in TENS trials.

Figure 2: 2 Moor VMS-LDF2 two-channel LDF analyzers and 1 Moor VMS-LDF1-HP LDF analyzer with fiber optic cables attached.

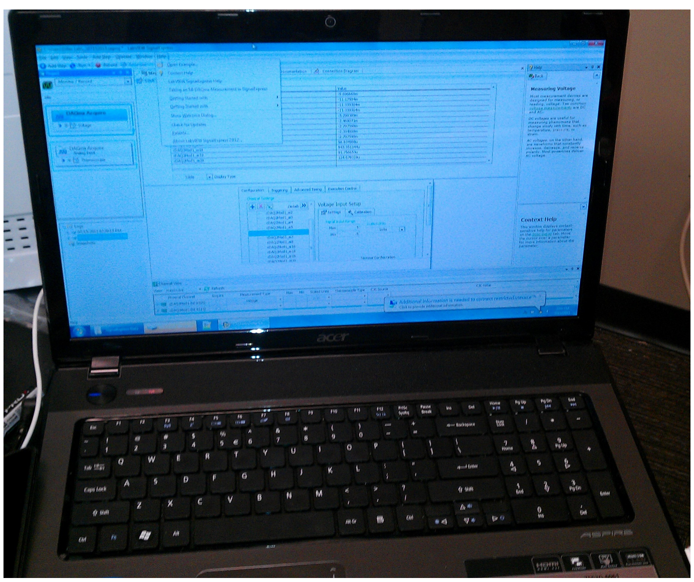

Figure 3 Acer PC collecting data from Moor Laser Doppler Flowmetry probes using Labview Data Express

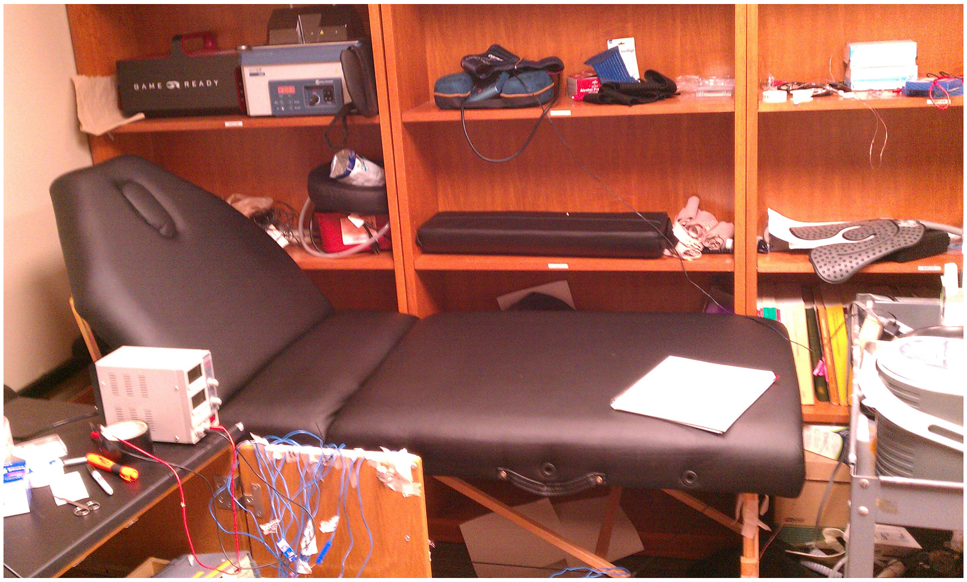

Figure 4: Subject table approximately 75 degree incline.

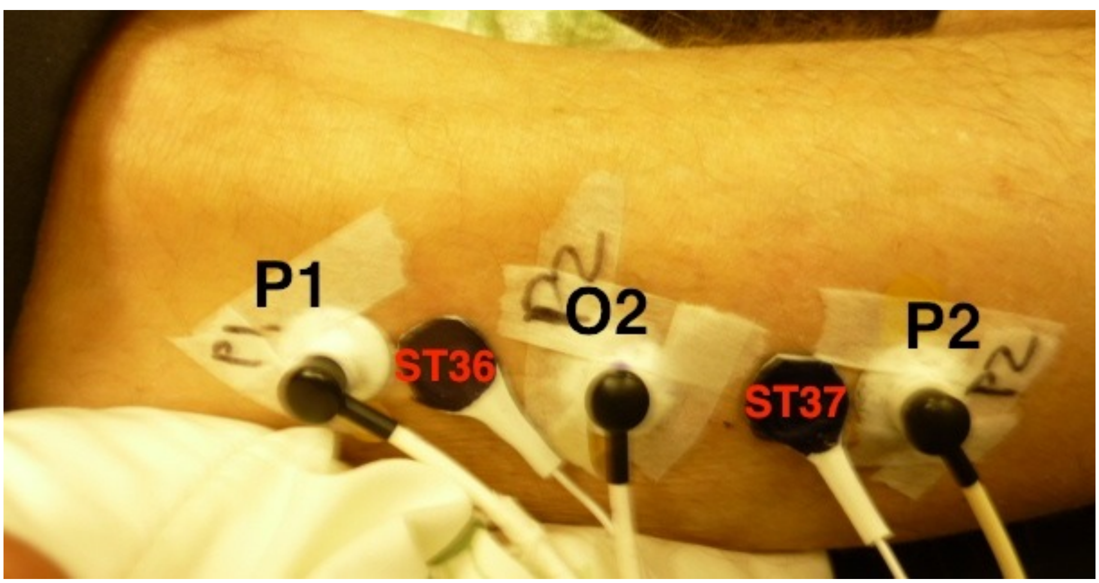

Figure 5: TENS Trial 1 positioning of the 3 LDFs (P1, O2, P3) and 2 TENS (ST36, ST37) electrodes (following Yeh's protocol)

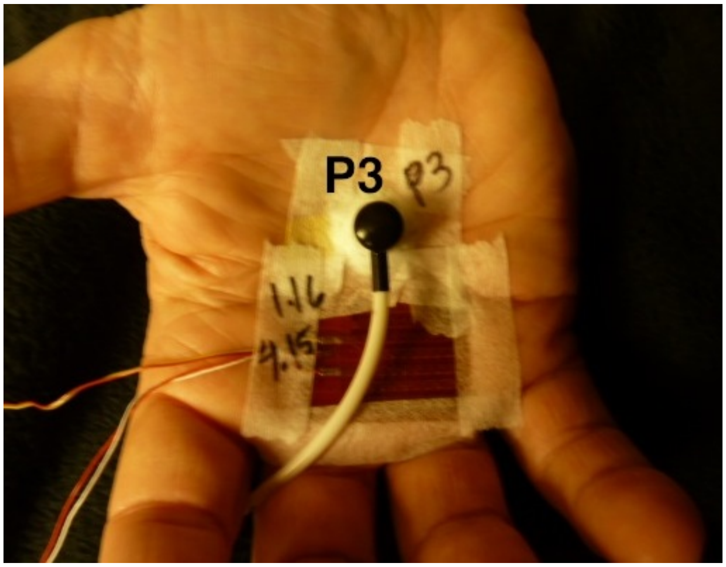

Figure 6: TENS Trial 1 positioning of LDF probe (P3) and heat flux unit on glabrous tissue

TENS trial two utilized the same experimental conditions as the first TENS trial, positioning the electrodes on acupuncture loci, however two channels of TENS stimulation were used with TENS electrodes positioned using acupuncture loci St34, 36 and Sp9, 10. As well, the electrodes attached to St34 and Sp10 were shaped to direct the TENS stimulation towards the center of the acupuncture point. The placements of TENS electrodes and LDF probes are shown in Figure 7.

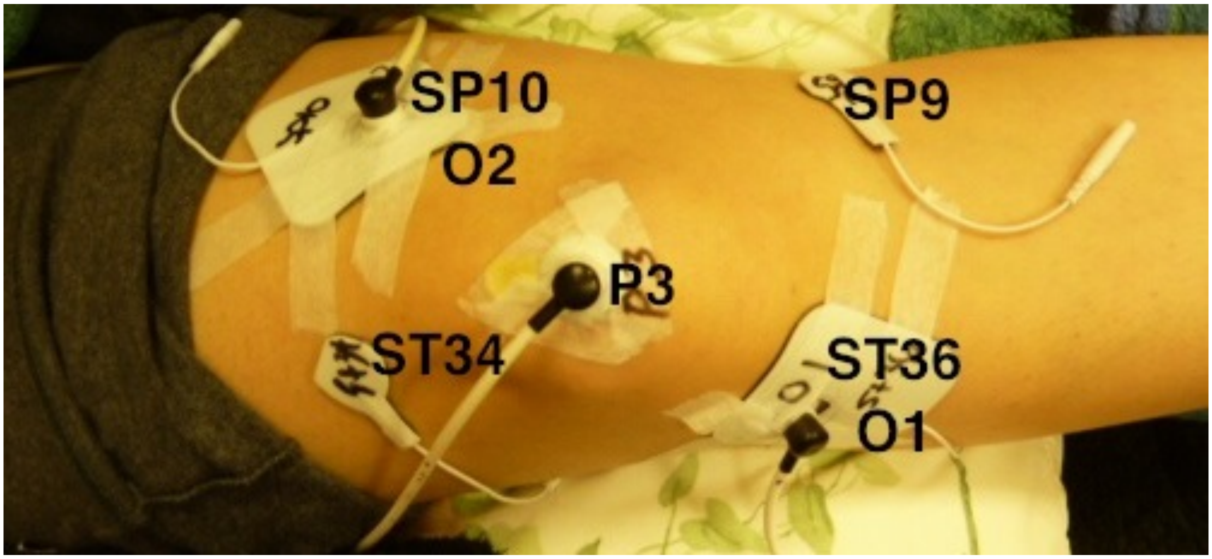

Figure 7: Trial 2 showing TENS Stimulation set up utilizing acupuncture loci SP10, SP9 on medial side, ST34 and ST36 on lateral side. LDF probes O2 is located on SP10 loci, LDF probe P3 patellar perfusion and LDF probe 01 lateral to ST36 loci.

A total of nine stimulation events were conducted: a twenty minute period of conditioning with no stimulation followed by three minutes of TENS stimulation of St34 and St 36 only, three minutes of TENS stimulation Sp 9, 10 only and seven minutes of TENS stimulation all acupuncture loci, followed by a rest period of three minutes with this series of stimulation and no stimulation repeated nine times. Data derived from this TENS trial failed to support the hypothesis as well, with discussion in chapter 4.

3.2 Interferential current trials

This set of three trials were developed subsequent to discovery of a body of research using Interferential Current Therapy to deliver current at depth with the goal of some measurable vascular manipulation. Researchers including Petrofsky and Noble previously reporting success with TENS manipulation of skin blood flow also reported successes in skin blood flow manipulation using Interferential Current. Certainly, equipped with this new knowledge and tool, success would be seen through data supporting our original hypothesis.

IFC Trial 1 was conducted following the TENS protocol previously used with modifications as noted. We chose to follow the methodology of Noble (1999), placing two 4cm x 4cm electrodes on the medial side of the right quadriceps femoris 6 cm and 20 cm from the base of the patella, and placing electrodes on the lateral side of the right quadriceps femoris as seen in figure 8.

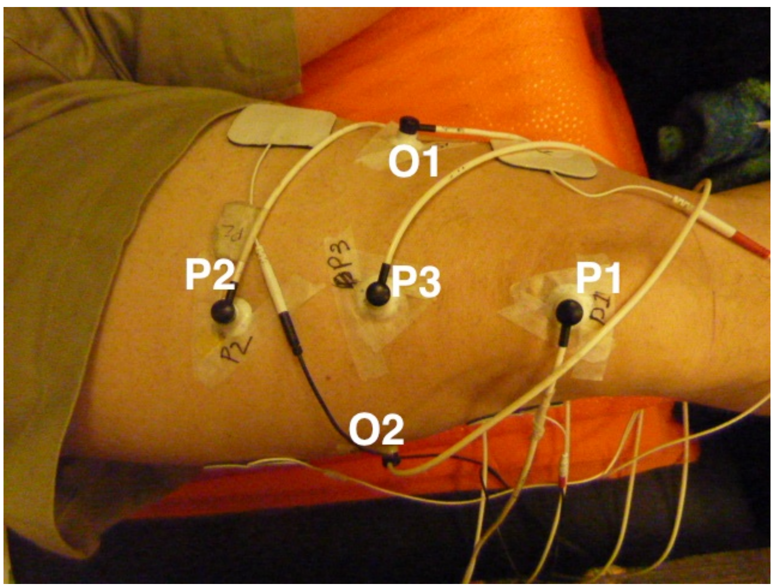

Figure 8: IFC trial 1 loci of Stimulation set up employing J.G. Noble's set up (Noble, JG et al 1999).

To achieve the greatest depth of penetration using IFC, the electrodes are connected contra laterally, with the electrode located medially 20 cm superior to the patella paired with the electrode located laterally 6 cm superior to the patella. Where Noble used one LDF, on the patella, we located five LDF, P1 being located consistent with Noble and probes P2, P3, O1, O2 placed to observe any skin blood flow changes along the dorsal surface of the femoris. Figure 9, from Noble, can be compared against figure 8.

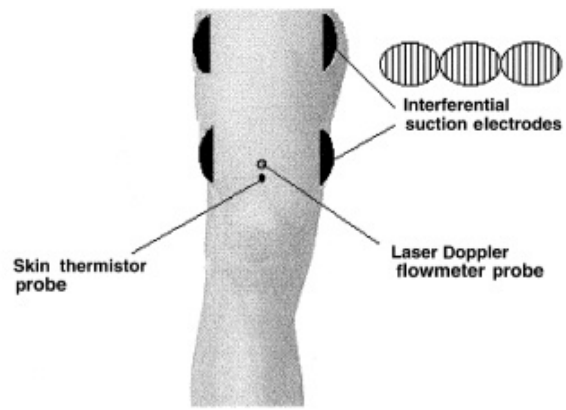

Figure 1 Summary of experimental procedure showing electrode placements (Interactive ADAM version 3·0, ADAM Software, Atlanta, Georgia, USA).

Figure 9: from Noble (1999), showing the placement of electrodes and patellar LDF probe.

Interferential Current stimulation using the LG-TEC IFC device was conducted on the subject with nineteen minutes of conditioning, no IFC stimulation followed by nine minutes of stimulation with a sweep of 10-20Hz and an intensity set to 7. Following a rest period of 6 minutes, another IFC stimulation of nine minutes with a sweep of 10-20 Hz and intensity increased to 15 was administered. Following 6 minutes of rest, IFC stimulation with a sweep of 80-160Hz and intensity of 15 was administered for nine minutes. After a rest period of 6 minutes, IFC administration with a sweep of 40-80Hz and intensity of 15 was administered for nine minutes. Figure 10 shows the IFC unit display set for a sweep of 10-20Hz (the display shows 12Hz), with an intensity of 15, four electrodes were utilized as shown in the lower left of the IFC device.

Figure 10: Interferential Current device exemplar stimulation setting.

A second series of IFC trials were conducted, following the protocol detailed in the first IFC trial using the LG-TEC IFC device on the subject with fifteen minutes of conditioning, no IFC stimulation followed by nine minutes of stimulation with a sweep of 10-20Hz and an intensity set to 8. Following a rest period of 6 minutes, another IFC stimulation of nine minutes with a sweep of 10-20 Hz and intensity increased to 13 was administered. Following 6 minutes of rest, IFC stimulation with a sweep of 80-160Hz and intensity of 12 was administered for nine minutes. After a rest period of 6 minutes, IFC administration with a sweep of 40-80Hz and intensity of 12 was administered for nine minutes. A final IFC administration after 9 minutes of rest with a sweep of 10-20Hz and an intensity of 11was conducted. Initial analysis of data seemed to indicate a reduction in skin blood flow, and led to IFC trial 3.

The third series of IFC trials were conducted incorporating the protocol previously used in IFC trials 1 and 2 with the addition of a patellar cold-water recirculation jacket placed over right knee This trial prototypically models a non-invasive medical device of the future: a patellar cold pack, which improves patient outcomes due to the increase in patellar perfusion rates. Figure 11 shows the experimental set up without patellar cooling, and figure 12 shows experimental set up with patellar cooling.

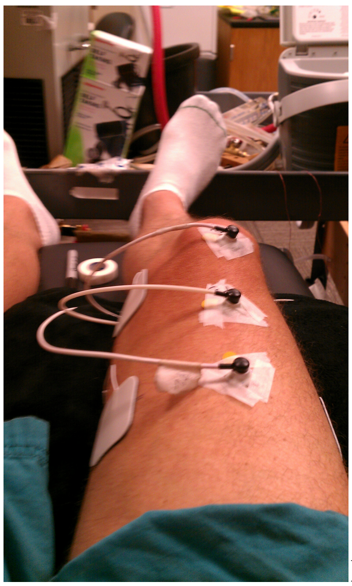

Figure 11: IFC trial 3 experimental setup

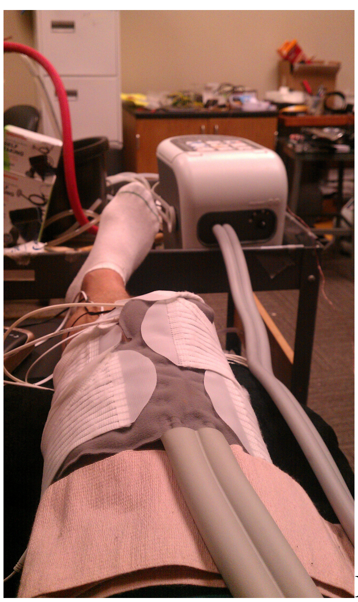

Figure 12: IFC trial 3 experimental setup with patellar cooling

Using the LG-TEC IFC unit, the first trial was run for 9 minutes, with a 10-20Hz sweep and intensity of 11, followed by a 30-minute period of patellar cooling with ice water. After this cooling, 9 minutes of IFC with a 10-20Hz sweep and intensity of 11was administered followed by 6 minutes of cooling only and another IFC administration of 80-160Hz and intensity of 11. After 6 minutes of cooling only, the circulation of the ice water ended. IFC with a sweep of 10-20Hz and an intensity of 11 was administered followed by a 6-minute rest period. After the rest period, IFC was administered with a sweep of 80-160Hz and intensity of 11. Followed by 6 minutes of rest and a final IFC administration of a sweep of 40-80 Hz at intensity of 11. Discussion of data derived from these IFC trials follows in chapter 4.

Chapter 4: Results and Data Analysis

With the data from the two TENS experiments not supporting our hypothesis; initial ebullience seen in the IFC data was proven to be unfounded. Data and results obtained during the IFC trials did not support the hypothesis, either. TENS and IFC data graphs are presented individually with discussion of plausible reasons for the results combined.

4.1 TENS TRIALS:

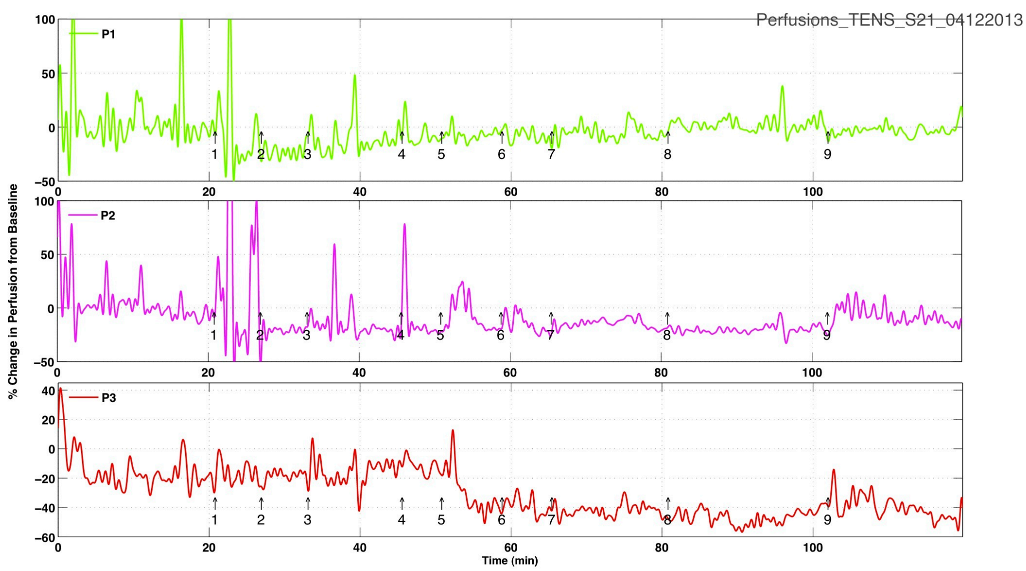

Illustration 2: First TENS trial LDF probes P1, P2, P3 acupuncture loci for TENS electrodes after Yeh protocol (Yeh, et al 2007)

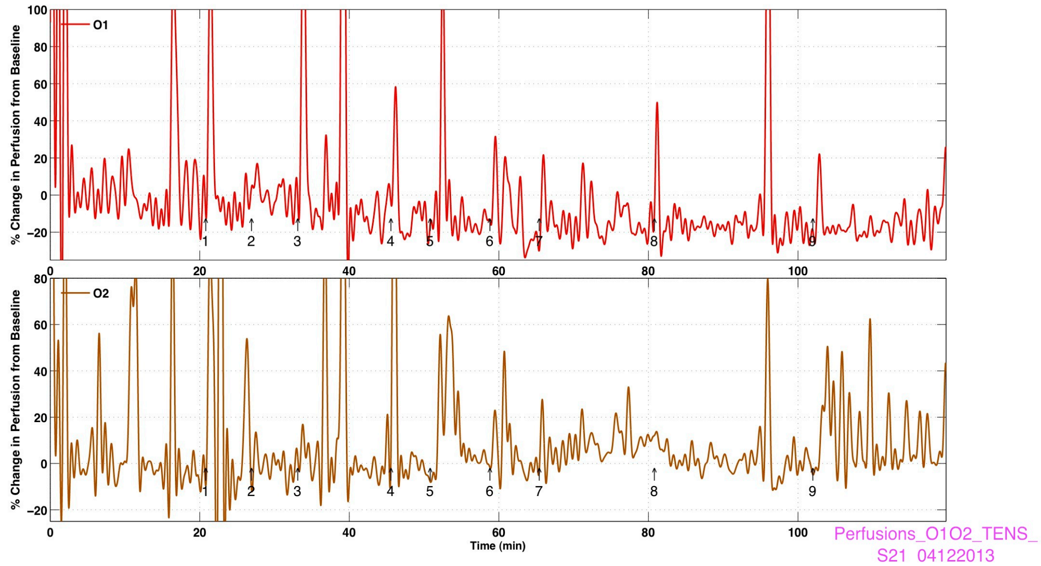

Illustration 3: First TENS trial LDF probes 01, 02, acupuncture loci for TENS electrodes after Yeh protocol (Yeh, et al 2007)

Examining illustrations 2 and 3 large spikes are seen, with perfusion fluxes in all probes striking the upper limit of the graph: at the initiation of TENS with subsequent smaller spiking seen at the termination of TENS. Protocol of the trial called for 3 minutes of TENS stimulation followed by 3 minutes without TENS stimulation. These intervals were changed in duration starting with 7 on the graph to 15 minutes each. Perhaps these spikes are the result of subject movement, placement over a larger vessel or variances in room temperature. While these spikes are "striking", nothing significant was seen when using Friedman analysis.

A second TENS trial utilizing acupuncture loci to manipulate skin blood flow was conducted following the same parameters as used in the first TENS trial with an extension of additional TENS cycles. Data graphs of the perfusion flux from LDFs O1, O2, P3 seen in illustration 4 while those perfusion fluxes from LDF probes P1, P2 are seen in illustration 5.

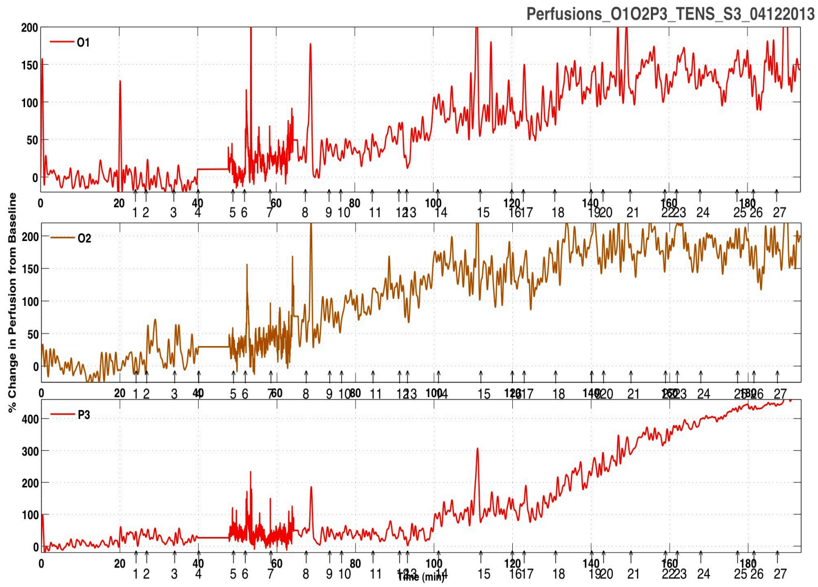

Illustration 4: Second TENS trial, patellar skin blood flow, LDF probes 01, 02, P3

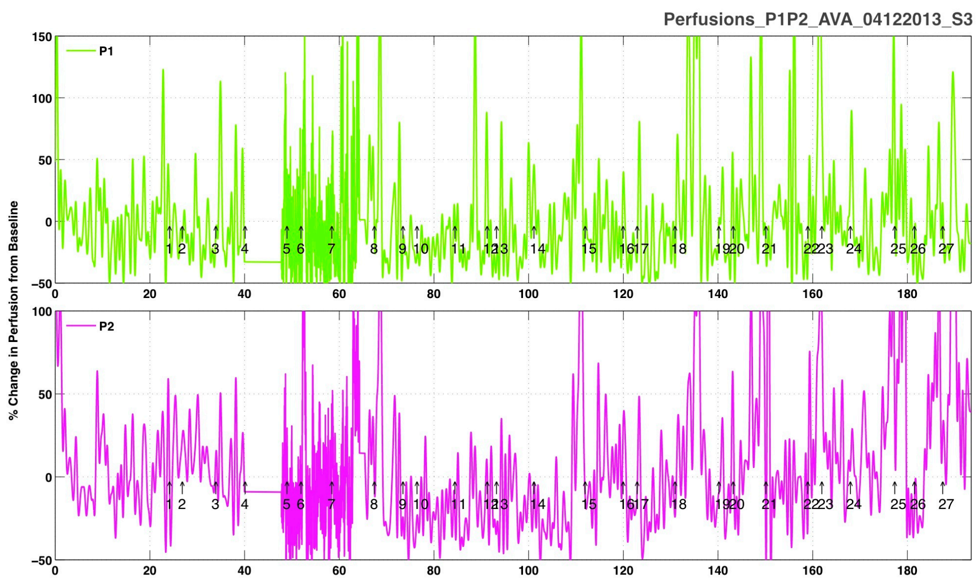

Illustration 5: Second TENS trial patellar skin blood flow, LDF probes P1, P2

Examination of illustrations 5 and 5 reveals extreme spiking of the perfusion fluxes, with the perfusion fluxes striking the upper limit frequently. As seen in the illustrations for the first TENS trial, this spiking might be the result of subject motion causing LDF probe movement, LDF probe positioning over larger vessel or variance in room temperature. Analysis of data obtained from TENS trial 2 did not show any significant data.

4.2 Interferential Current trials

After research a body of literature demonstrating the ability of Interferential Current stimulation to manipulate skin blood flow, excitement flowed through the lab, more so when data from the second IFC trial appeared to support a change in skin blood flow. Ultimately the data from the IFC trials would not support the hypothesis.

Interferential Current trial 1 perfusion flux graphs for probes P1, P2 and P3 is shown in illustration 6.

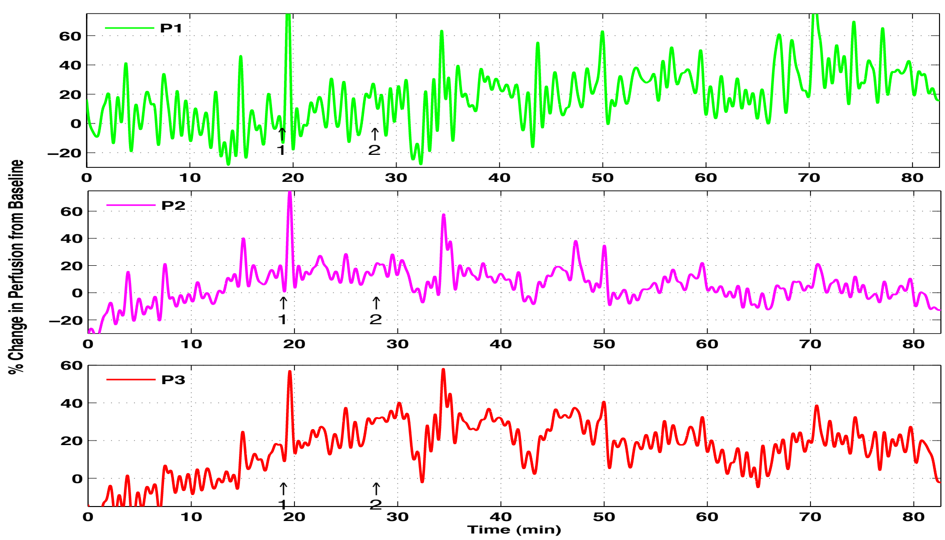

Illustration 6: IFC trial 1 following Noble, JG (2000) LDF probes P1, P2, P3

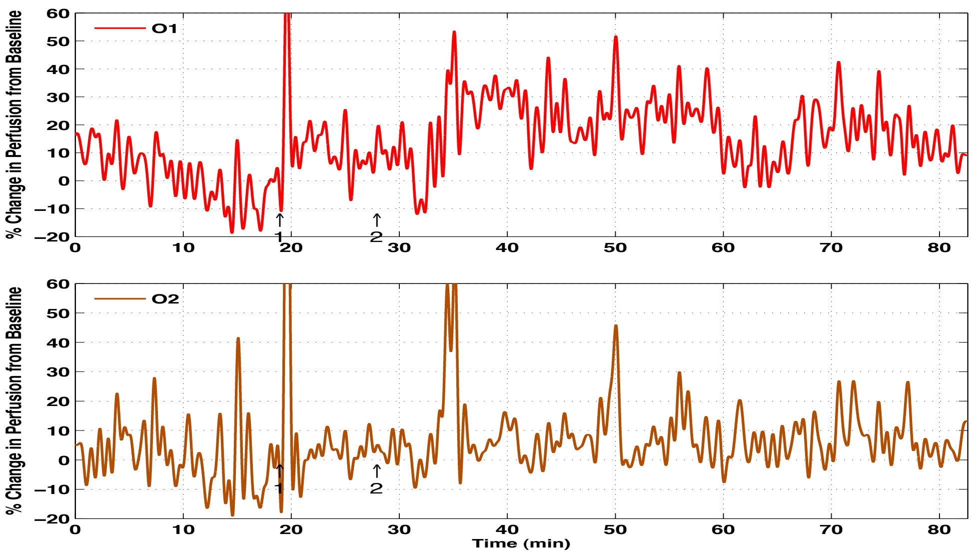

Illustration 7: IFC trial 1 following Noble, JG (2000) LDF probes O1, O2

Interferential Current trial two perfusion fluxes are graphed in illustrations 8 and 9 with illustration 10 the Friedman analysis results of this trial.

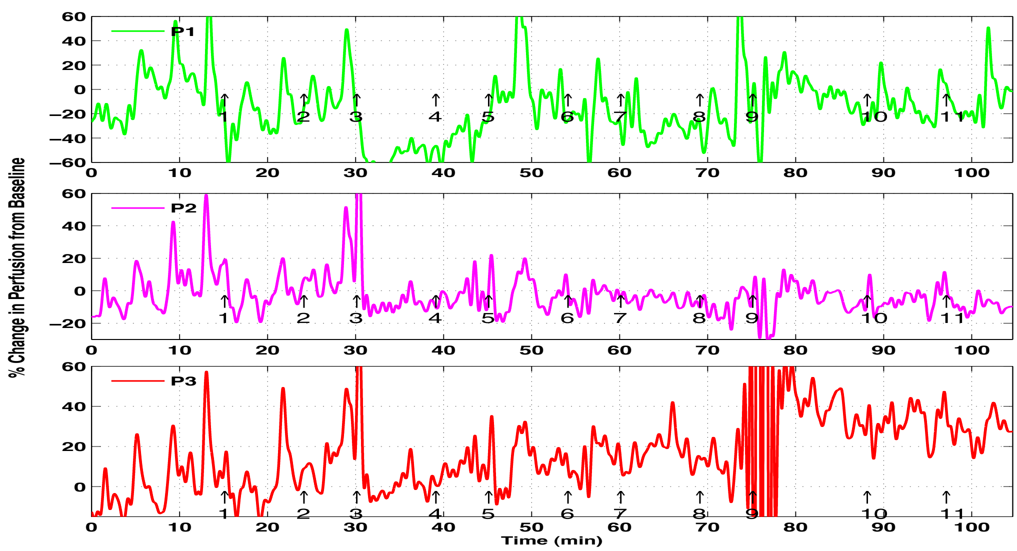

Illustration 8: IFC trial 2 following Noble, JG (2000) LDF probes P1, P2, P3

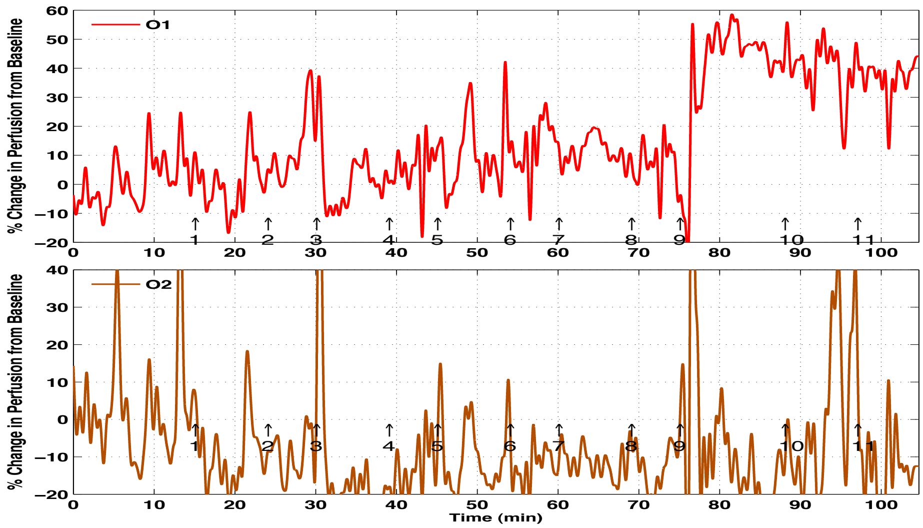

Illustration 9: 2nd IFC trial following Noble, JG (2000) LDF probes O1, O2

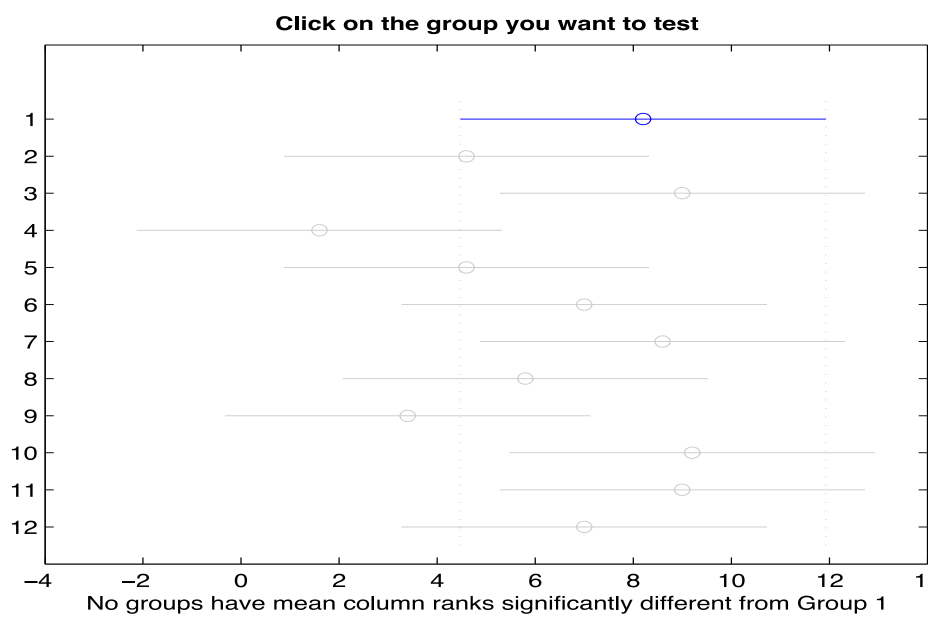

Illustration 10: 2nd IFC trial Friedman test on data, nothing significant

As seen in illustrations 8 and 9 although the spiking is not as extreme, these perfusion fluxes did not support our hypothesis, however some change in blood flow was seen, it was not a statistically significant change. Based on this blood flow change, the third IFC trial was anticipated as supporting the hypothesis.

The third IFC trial perfusion fluxes for P1, P2, P3 are shown in figures 11 and 12.

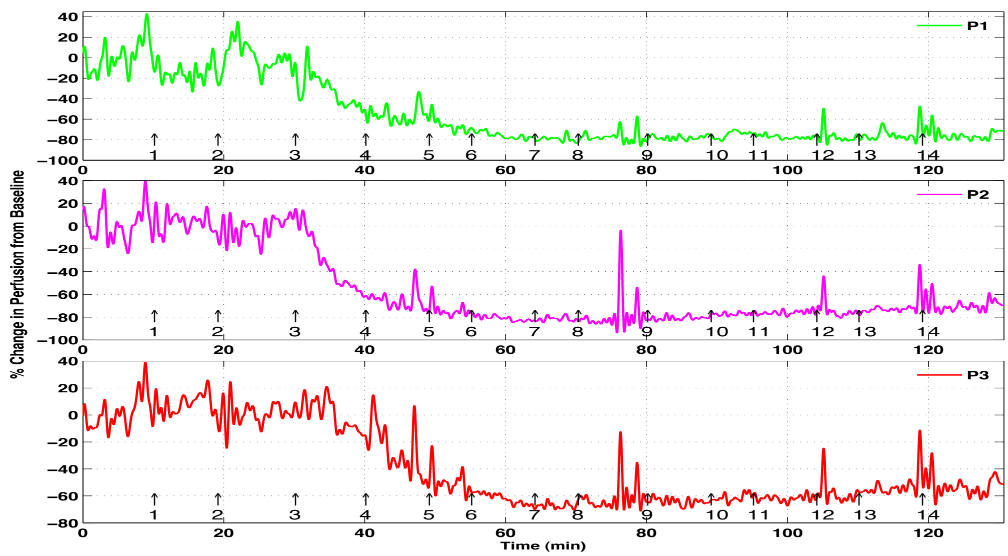

Illustration 11: 3rd IFC trial following Noble, JG (2000) LDF probes P1, P2, P3

Examining illustrations 11 and 12, numbers 1 to 14 on the time axis are to delineate events occurring during the IFC trial. For example, the area between 1 and 2 is the first IFC administration, between 2 and 3 the rest period, 3 and 4 is cooling only. Between 8 and 9 the cooling is ended. The impact of cooling on perfusion flux can be seen as a steady downward trend across all probes, as well as cessation of cooling with a rebound in perfusion flux seen beginning at 9. Again, the spiking seen is of no statistical consequence.

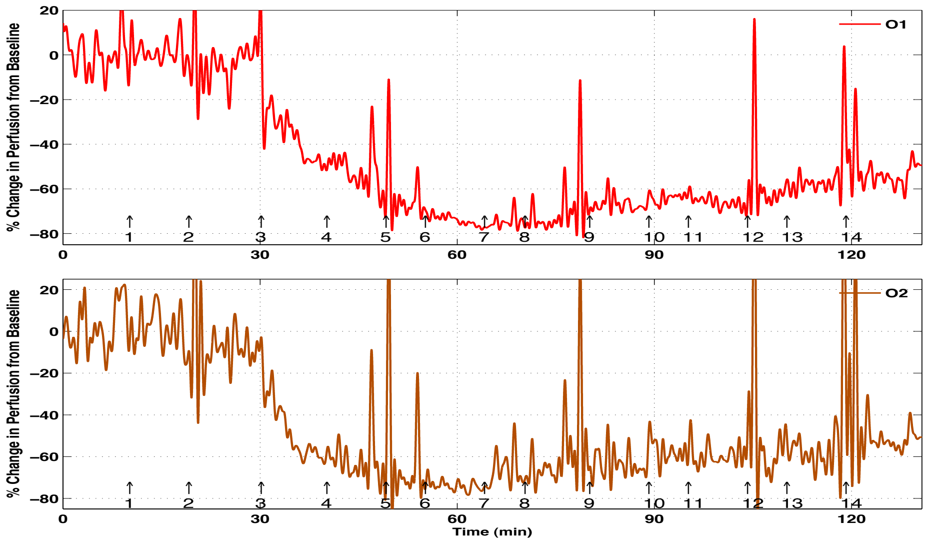

Illustration 12: 3rd IFC trial following Noble, JG (2000) LDF probes O1, O2

4.3 TENS TRIALS DATA ANALYSIS

Our data, and subsequent analysis using Mathlab software determined nothing statistically significant occurred with skin blood flow, neither increase nor decrease. Researchers also experienced this lack of support for the hypothesis in TENS.

Perhaps the data experiences of the two TENS trials is a result of a number of conflicting variables which could include:

1. Subject conditioning prior to TENS trial, as some researchers created strict subject pre-conditioning protocol prohibiting the use of caffeine, tobacco and any exercise for a period of two hours immediately prior to trials.

2. Strict adherence to the protocol reported by those researchers our lab set up was duplicating. TENS trial 1, the Yeh protocol is a bilateral stimulation of 4 acupuncture loci (ST36, 37) using two channels of TENS for a period of 30 minutes. As reported TENS

trial 1 used one channel of TENS stimulating 2 acupuncture loci (St 36, 37) stimulated unilaterally for a duration of 6 minutes.

Room temperature, subject movement, LDF probe placement could also impact negatively on the data gathered, length of stimulation, preconditioning of patient to name a few.

4.4 Interferential current trials data analysis

As with the TENS trial, we were unable to see any significant data from IFC trials. Initially some excitement was generated by the graphs seen in illustration 7 and 8 appearing to show increase in perfusion. Illustration 9, the Friedman test dispelled the thought of significant data trend.

Possible reasons for these results include: Room temperature, subject movement, LDF probe placement, length of stimulation session, preconditioning of patient, to name a few.

4.4 Conclusions

From the data collected in our trials, our hypothesis was not supported. A disappointment and yet a terrific learning experience into laboratory work and the scientific method and the need to keep seeking further knowledge.

The seeming inability to see any form of vascular response, while initially disheartening, is a solid experience in laboratory research: every hypothesis is not supported by data collected, if it were, what a different world of research one would see. After reflecting upon the processes and comparing lab notes with studies we duplicated in the lab, some areas appear which could explain the results observed: consistency of electrode loci, perhaps using acupuncture loci or through the use of physical anatomy landmarks on the body. What Electrode type was used, particularly with the IFC where several investigators used suction electrodes, or did not specify. Subject pre-conditioning protocol, control of ambient room temperature, subject interference of LDF probes through movement during any portion of the trial.

Reflecting upon this project and the research performed, the ability to manipulate skin blood flow using TENS or IFC type device is with grasp. Analyzing the researched literature through the particular lens of what parameters worked, consistently, for researchers and applying these parameters to additional trials. Acupuncture loci continue to present as viable choices for electrode loci. Non-invasive cutaneous blood flow manipulation is an achievable challenge that will be overcome; this author would welcome the opportunity to share more thoughts with the principle investigator at any time.

CHAPTER 5: Applications to Practice

The UTeach Engineering Master of Arts in Science and Engineering Education (MASEE) program has positively impacted my teaching, style approach and extensions from first class days, starting with the ESIT program. Having attended both the ESIT and MASEE programs, my students have benefited from: the open-endedness of challenges created, departures in dichotomous answer/multiple choice assessment to a more student based, risk free and friendlier assessment system whereby students can demonstrate their learning through system diagrams, such as Causal loop diagrams to model various cycles such as carbon, water, phosphate, input/output diagrams, Black box and more.

Always being interested in how things work, MASEE has helped bolster my neophyte skills with the breadth and depth of engineering, pedagogy and classroom skills acquired from the program. Without exception, the professors "walked the talk and talked the walk" exposure and practice with different student engagement techniques was a standard of all MASEE classes. Those skills learned theoretically and in practice benefit my students with higher levels of engagement, developing a thrill of learning and students learning multiple iterations are the norm for this world. Ultimately, my students benefit from these MASEE acquired skills and skillsets: pulling students into engagement through meaningful, real world problems such as are facing the world now.

5.1 Developing engineering awareness

The Greatest Engineering Achievements of the Twentieth Century, tool used in MASEE classes, is my engager for all of my classes. Being fortunate to teach fourth year science electives, my students are not under the performance stress of standardized testing, the real stress is their desire to slide into senior doldrums. Engagement begins with discussion of Greatest Engineering Achievements and flows onto reveal student interests and sometimes goals. A regular activity in my classrooms is tasking students to draw an engineer doing engineering (Fralick et al 2009). Students enjoy this exercise, misconceptions are uncovered this starts a conversation with students which lasts through out the year – graduating seniors have written letters regarding their desire to pursue engineering. A strong testimony to the skills demonstrated, practiced and honed with MASEE program

Perhaps because my background is from sales and marketing to a broad spectrum of industries, the shortcoming seen in my classroom is the need to bring in outside speakers, especially women and minority engineers. The school year 2013-2014 will see a number of speakers for my students, from recently graduated to in the industry, high school students hearing stories from those closer in age is important, as it is easy to dismiss the words of any teacher as coming from another era.

5.2 Developing Engineering habits of mind

Development of the discipline to maintain constant and accurate documentation of thoughts, activities and outcomes, is an engineering habit of mind I have instituted and will institute with greater vigor 2013-2014. Engineering notebooks are started at the beginning of the school year, however after laptops are issued, students are less willing to use pen and paper. In the upcoming school year 2013-2014 will start off with showing my engineering notebook, with all the accompanying markings, table of contents, scratch outs, tears, scotch taped entries. The look of penciled notes in the margins with tidbits of thoughts, or questions, which arose during the course of activity or another. If it was good for Leonardo DaVinci to keep a notebook, it is good for the student. How better to convince then to have an exemplar, such as DaVinci? The engineering notebooks supplied throughout the MASEE course are optimal: these notebooks are what engineers use. Drawing attention to the rationale for the notebook: including legal and practical purposes – as well as ease of having all thoughts, data, pictures, diagrams and reflections in one place. Perhaps framing it, as a "sketchbook" for science would help as many students carry bound sketchbooks. Best would be for Taylor High School to purchase and distribute the professional engineering notebooks as have been supplied to MASEE students, something to discuss with my department head.

Teachers are constantly reminded of the need to teach 21st century skills, logging/diarizing activities within a hand written engineering notebook with an eye for correctness and precision is a transferable skill for entry into any of the sciences, and would definitely spill over into other fields of study as well as life skills in general.

Helping students to develop collaborative skills and non-judgmental acceptance of the ideas and concepts of others, developing the listening and analytical skills start with the creation of a "risk free" classroom. As a direct result of the MASEE program students willingly and without prompting speak of glowingly of knowing our classes are risk free, where all questions or thoughts are entertained and addressed, providing some validation to students of their concept of worth.

Working in small groups, which are randomized has proven to be beneficial in developing these student skills. While I have not utilized the personality test administered at MASEE summer 2011, students do complete an anonymous left brain/right brain survey providing a springboard into conversations and student enlightenment helping each to understand their idiosyncrasies.

5.3 Developing an Understanding of the Design Process

Putting things together and taking them apart, can this be made to run better? These are a few of the basic skills I brought to MASEE. Comprehension of the necessity of the frustration factor, coupled with a belief all life's projects are in "Beta" design stage is a core belief I have developed and continually discuss with students. In my own experiences within my project, the hypothesis was not supported, anticipated results were not seen and personal frustration set in. When students speak of frustration, my response is: enjoy it, you are learning. When the first discussion of frustration is hatched – Thomas Edison's quote regarding finding the correct material for filaments is dusted "I have not failed. I've just found 10,000 ways that won't work".

Preparing students for failure, results expected and not realized all of these are real world. Certainly students will see this as we discuss the happenings during my MASEE summer. Teaching students engineering skills, which are readily transferable to any subject or undertaking: make a survey to determine needs and interests, create a prototype, re-survey using the prototype, then create another iteration, and continue this process in an endless loop until the desired outcome is at hand, or the closest approximation to that desired outcome. Helping students to see the connection between the sciences and humanities, the understandings which arise when one sees the connection between engineering design and making a wall or dog house or?

5.4 DEVELOPING KNOWLEDGE FOR AND OF ENGINEERING TEACHING

Continual creeping change, while the darling moniker of the electronics industry, is my choice for describing those incremental changes made in my teaching and classroom activities which occur year to year and frequently from one class section to the other. In a continuing quest for curriculum, it was the influence of MASEE program which gave me the desire and confidence to have students black box real world problems, such as the lack of a blow out prevention valve in the 2010 BP Gulf oil spill to tasking students to design a protection system for their brain, perhaps these sorts of activities would have been pushed off by myself were it not for the insights gained thru MASEE.

It has been a privilege and an honor to be a part of this MASEE cohort 3, one for which I will ever be grateful.

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