MEASURING BRACHIAL ARTERY BLOOD FLOW FOLLOWING A 3MHZ, 1.0 W/CM^2 THERMAL THERAPEUTIC ULTRASOUND TREATMENT

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Measuring Brachial Artery Blood Flow Following A 3 MHz, 1.0 W/cm^2 Thermal Therapeutic Ultrasound Treatment

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The Supervisory Committee certifies that this ***disquisition*** complies with North Dakota State University's regulations and meets the accepted standards for the degree of

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ABSTRACT

Ultrasound has been suggested to be one of the most commonly used therapeutic modalities in clinical practice. One of the purported benefits of thermal ultrasound, is the ability to increase blood flow to local tissue. This benefit however, has not been sufficiently supported by current literature and research. The purpose of this study was to determine if there is a significant increase in blood flow to the brachial artery following a 3MHz thermal ultrasound at 1.0 W/cm^2 treatment over the brachial artery. Blood flow was measured in time-averaged mean velocity using a diagnostic ultrasound machine prior to, and following an ultrasound treatment given at these parameters. Results indicated that thermal ultrasound delivered for 5 minutes at 3MHz and 1.0 W/cm^2 has the capability of producing a statistically significant increase in blood flow (α=0.015).

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CHAPTER I. INTRODUCTION

After numerous studies demonstrated the ability of ultrasound to safely deliver heat to bodily tissues several centimeters below the skin's surface, it was introduced as a therapeutic modality in the 1950's.[1] Since the introduction into clinical practice, the use of ultrasound has become widespread and frequent. Some sources report that it is the most widely used modality in practice.[2,3] Prior to the 2007 study by Wong et al.[1], it had been nearly twenty years since a study was conducted regarding the use of ultrasound by clinicians in the United States. At the time of the initial study, 79% of respondents used ultrasound at least once per week and 45% reported that they used it more than ten times each week. In the most recent study, results indicated that these trends remained fairly consistent over 20 years.[1]

Despite the popularity and utilization of ultrasound, the effects and benefits of the treatment are the subject of great scrutiny. This modality lacks research that clearly confirms or denies that it effectively delivers the proposed results and benefits. One study on the use of ultrasound in physical therapy examined fifteen systematic reviews of the modality. Of the fifteen reviews, eleven of them could not draw any significant or definitive conclusions about the effectiveness of this treatment due to insufficient evidence.[1] In spite of the lack of evidence supporting clinical efficacy, ultrasound is used to induce an assortment of physiological responses and as a tool to aid in the treatment of a wide variety of pathologies.

Ultrasound can be performed in order to gain thermal or nonthermal benefits based on the settings employed.[5] Among the proposed therapeutic benefits of thermal ultrasonic treatment is the ability to heat tissues at both superficial and deep levels.[4] Heat causes local blood vessels to dilate at the area of application and in surrounding tissues.[6] Thus, it is generally accepted that the application of thermal ultrasound causes an increase in local blood flow.[2,5,7,8] An increase in blood flow to tissue damaged as the result of an acute or chronic injury has been postulated to enhance the influx of nutrients and cellular components, as well as aid in removing metabolic waste products and tissue debris.[7]

Statement of the Problem

Research has indicated that there is no consensus on the efficacy of this modality and its physiological benefits.[4,7] Traditionally, ultrasound has been most commonly utilized for the perceived thermal benefits, including the aforementioned increase in local blood flow.[2] Without any definitive evidence, there seems to be a disparity in knowledge between the actual and proposed benefits of thermal ultrasound treatment on blood flow.

Purpose of the Study

The purpose of this study was to determine if there is a significant increase in blood flow to the brachial artery following a 3MHz thermal ultrasound at 1.0 W/cm^2 treatment over the brachial artery.

Research Question

The primary research question is “does thermal ultrasound cause a significant increase in blood flow to the brachial artery in the healthy individual set at the parameters of continuous, 3 MHz, 1.0 W/cm^2 for 5 min?”

Definitions

Diagnostic Ultrasound: A method of imaging that produces images of internal body structures by sending high frequency sound waves into the body. Also referred to as sonography or medical sonography.[9]

Doppler Ultrasound: A form of diagnostic ultrasound that utilizes high-frequency sound waves that are reflected by red blood cells in the body to produce information about blood flow.[10]

Therapeutic Ultrasound: A therapeutic modality that uses acoustical energy to penetrate deep into the body and create changes in the tissue from thermal and non-thermal effects.[6]

Blood Flow: The amount of blood flowing through an organ, tissue or blood vessel in a given time.[11]

Thermal: The transfer of energy that causes an increase in tissue temperature. A continuous output of ultrasonic energy or 100% duty cycle produces thermal effects during an ultrasound treatment.[6]

Vasodilation: "The widening of a blood vessel due to relaxation of the muscle of its tunica media and the outward pressure of blood exerted against the wall.[11]

Significance

Based on the empirical and anecdotal evidence currently available, researchers of this study believe that thermal ultrasound performed proximal to the medial epicondyle of the elbow will cause an increase of blood flow to the brachial artery, but not at a significant level. In order to substantiate the use of thermal ultrasound to increase local blood flow and stimulate healing, it is imperative that clinicians have evidence to indicate that there truly is a measurable increase in blood flow following such a treatment.

Limitations

1. The researchers had no control over extraneous variables such as hydration status, amount of adipose tissue, etc. that may alter the results of the study.
2. All sonography was performed by a certified athletic trainer that is trained and practiced in the procedure. Although the researcher is proficient in scanning and interpreting the Doppler output, significant training is needed to master the skill.
3. The study used a population of healthy individuals and therapeutic ultrasound is used on injured individuals.
4. Researchers were unable to monitor blood flow changes during the ultrasound treatment.

Delimitations

1. Only subjects who were healthy and had no history of injury to the treatment area were included.
2. Subjects who were between ages 18 and 35 were included in the population of interest.
3. The subject pool drew from only North Dakota State University students and staff.
4. The parameters of 3MHz, 1.0 W/cm^2, 100%, for 5 min were used.
5. Dynatron Solaris® Series 700 therapeutic ultrasound machine was used to provide treatment
6.

CHAPTER II. REVIEW OF LITERATURE

The purpose of this study was to determine if there is a significant increase in blood flow to the brachial artery following a 3MHz thermal ultrasound at 1.0 W/cm^2 treatment over the brachial artery. The research question that guided this study was: Does thermal ultrasound cause a significant increase in blood flow to the brachial artery in the healthy individual set at the parameters of continuous, 3 MHz, 1.0 W/cm^2 for 5 min? The review of literature is organized into the following areas: therapeutic ultrasound, therapeutic effects, nonthermal effects, parameters, biophysical effects, intermanufacturer variance, efficacy of treatment, and the role of blood flow.

Therapeutic Ultrasound

Humans have the ability to hear up to a frequency of approximately 20,000 Hz. When acoustic vibrations exceed that level, they are considered ultrasonic.[6,12] This type of mechanical energy is often utilized as a form of therapeutic intervention in the medical field and to serve as a catalyst to healing of a variety of pathologies. Unlike many other electrophysical agents, the use of the acoustic nature of ultrasound provides for the ability for tissue change through both thermal and nonthermal mechanisms. Although the frequency used for therapeutic benefits does lie on the same spectrum as what is audible to humans, it is significantly higher ranging from 750,000 to 3,300,000 Hz.[6] The production of ultrasound is a complex process that occurs when alternating current flows through a synthetically produced piezoelectric crystal. When the current passes through the crystal, it contracts and expands causing a vibration and a subsequent transfer of kinetic energy between molecules. This causes the production of the ultrasonic sound waves.[6] There are currently three types of ultrasound used in regular clinical practice; conventional therapy, low-intensity pulsed ultrasound (LIPUS), and MIST therapy.[12]

Conventional ultrasound is the original and still most widely used form of ultrasonic therapy. It is characterized by a high frequency and high intensity delivery. The typical frequency used in conventional ultrasound ranges from 1-3 MHz and the intensity generally lies between 0.1 and 3 W/cm^2.[12] This type of ultrasound is thought to be capable of producing both the mechanical and thermal benefits that ultrasound therapy has proposed to offer and is employed for a variety of pathological conditions excluding fracture. Conventional ultrasonic treatments deliver acoustic energy with a dynamic transducer by making contact with the skin over the treatment area and using a coupling medium to prevent loss or blocking of acoustic energy via the air.[12] Conversely, low-intensity pulsed ultrasound (LIPUS) produces only the mechanical effects of ultrasound with a lower frequency ranging from 1-1.5 MHz and lower intensity that is typically set at 0.03 W/cm^2. LIPUS is almost exclusively reserved for the treatment of fresh and slow-to-heal fractures and is delivered with a stationary device by applying the transducer to the area of skin directly over the fracture site. When casting has been employed, this form of ultrasound can be non-directly applied on top of the cast.[12]

The third and newest form of ultrasonic therapy was introduced in the early 2000s and has since been branded and sold exclusively under the name MIST therapy system®.[12] MIST therapy is delivered at a frequency lower than both of the previously identified forms of ultrasound (40 KHz) and at a moderate intensity. This form of insonation is used for debridement and stimulation of the healing process of wounds that are problematic. MIST therapy uses a non-contact method of pushing a mist of sterile saline into the wound bed by ultrasonic waves, thus transferring the ultrasonic energy into the wound without any direct contact that may put the patient at risk for infection or cause pain.[12]

Although LIPUS and MIST therapies have an important place in the clinical setting and the use is reserved mostly for very specific purposes, therapeutic ultrasound in the conventional form is frequently utilized in the medical field for a wide variety of pathologies and conditions. It has been postulated that ultrasound is capable of increasing the rate of tissue repair and wound healing, aiding in the breakdown of calcium deposits, increasing tissue extensibility, reducing pain and muscle spasm, creating changes in nerve conduction velocity and cell membrane permeability, and increasing local blood flow.[6,13] While the potential benefits and uses have been well established, much exists to be learned about this modality.

Usage Trends

As new technology continues to be introduced into the medical field to aid in the healing of musculoskeletal impairments, the frequent use of one of the oldest modalities remains consistent. It has been reported that despite these advancements, therapeutic ultrasound appears to be one of the most widely used adjunct modality in clinical practice.[2,3] Researchers across the world have examined the clinical use of ultrasound repeatedly. In the last several decades, surveys of its use have been conducted in Australia, Canada, and the Netherlands. Both Canadian and Australian clinicians reported very high utilization of this modality at 93.7% and 84.7% respectively. Dutch health care providers also reported regular use of ultrasound in their everyday practice [1].

Prior to a study by Wong et al.[1] in 2007, the usage rate of ultrasound by healthcare providers in the United States had not been examined for over twenty years.[1] This study surveyed the responses of 213 Orthopedic Certified Specialists about their regularity of use of ultrasound for specific musculoskeletal conditions and their perception of its clinical importance in accomplishing the therapeutic goals involved in treating those conditions. Results indicated that clinicians who reported using therapeutic ultrasound for at least one in four of their patients frequently used this modality with their patients that had soft tissue inflammatory conditions (83.6%) such as tendinitis or bursitis, tissue extensibility issues (70.9%), and for scar tissue remodeling (68.8%) [1]. Clear anecdotal evidence has been established by the historical and frequent use of therapeutic ultrasound by clinicians around the world. While empirical evidence has also been presented on the subject, the conflicting results and controversial nature of the proposed benefits call into question its efficacy. It is imperative that irrefutable evidence is established to support the use of this modality and to ensure that best practice guidelines are being followed.

Therapeutic Effects

Therapeutic ultrasound is capable of producing physiological changes in the tissue through both thermal and non-thermal/mechanical mechanisms. Although heat is not necessary for some of these changes to occur, as will be discussed in the section regarding the non-thermal effects of therapeutic ultrasound, many of these changes are accomplished when heat is absorbed into the tissues from the ultrasonic waves.[14] The amount of absorption, and thus heat production, determines the therapeutic benefits of treatment. The tissue temperature increase and the therapeutic effects to which they correlate are generally accepted and suggest that a 1ºC increase in tissue temperature causes mild inflammation and accelerates metabolic rate, a 2-3ºC change causes decreased muscle spasm and pain, increased blood flow, and a reduction in chronic inflammation, and a change of 3-4ºC results in tissue elongation, scar tissue reduction, and sympathetic inhibition.[6,15] The thermal benefits, as previously discussed, are seen most frequently in the 3-4ºC change from baseline range.[16] There are many factors that play an imperative role in the rate of absorption. Tissues that are high in protein and rich in vascularization absorb heat produced by ultrasound at a greater rate.[2,13] Additionally, ultrasound applied at a higher frequency has the tendency to absorb at a greater rate as well.[2]

While related by the same general principles, thermal and non-thermal ultrasound vary greatly in many aspects including indications for use, biophysical changes produced, and efficacy. What does remain consistent between the two types of therapeutic ultrasound is the fact that evidence exists both in favor and against its clinical utilization based on clinical efficacy.[2,14,17]

Nonthermal Effects

Nonthermal effects of therapeutic ultrasound are achieved through changes in parameters. Most commonly, this change occurs in the pulse ratio, which alters the percentage of time that ultrasound is being disbursed and effectively decreases the temporal average intensity.[6] Nonthermal ultrasound treatments are most commonly utilized when the heating effects of thermal ultrasound are contraindicated or unwanted. Although attributed to the nonthermal effects of ultrasound, the cavitation and acoustical streaming found following a pulsed treatment, are also seen in thermal ultrasound. Cavitation and acoustical streaming are the mechanical changes that are thought to be responsible for the biophysical alterations that occur as a result of application of this modality. Acoustical streaming occurs when fluid in the body moves in one direction and ultimately cause small bubbles to flow through the acoustical stream and alter membrane permeability. Additionally, cavitation occurs when small gas bubbles form and oscillate while traveling in a circular pattern due to pressure changes that arise as the ultrasound waves pass through the tissue.[6] In addition to the major mechanisms by which nonthermal ultrasound is capable of altering the healing process, there are a cascade of physiological changes that occur as a result of insonation. Phagocytosis is initiated, there is an increase in the quantity of free radicals, the cell membrane permeability and cellular proliferation is altered, and fibrinolysis is stimulated.[6] Each of the aforementioned elements of the cascade of biophysical changes that occur with the application of nonthermal ultrasound serve to accelerate the healing process of soft tissue injuries and other pathological conditions. Phagocytosis allows for the extraction of inflammatory debris while the increase in free radicals causes the ionic conductance to go up allowing nutrients to easily flow in and out of the cell membrane. Specifically, this change in permeability and proliferation permits calcium to penetrate the cell and subsequently release protein which aids in the remodeling of collagen.[6]

Parameters

Historically and in recent clinical practice, therapeutic ultrasound has most frequently been utilized for its thermal effects.[2,6] Thermal ultrasound effects can be accomplished through employing continuous output parameters and thus, thermal ultrasound is also commonly termed ‘continuous ultrasound’. Continuous output means that ultrasound is being delivered for 100% of the duration of the treatment. This allows for the tissues being treated to absorb the ultrasonic rays, effectively heating the target area.[6] Pulsed output means that the ultrasound unit is not delivering ultrasonic waves for the entire duration of the treatment but instead, in a pre-determined on-to-off ratio of time. This setting produces the mechanical effects previously described in the section of the literature review regarding the nonthermal effects of ultrasound.[6]

As previously discussed, the thermal qualities and physiological benefits received from therapeutic ultrasound are dependent on the parameters by which treatment is delivered. It has been suggested that of these parameters, alterations in intensity and time are most responsible for the resulting outcomes.[18] In order to understand the current literature that exists surrounding the most appropriate parameters for achieving the proposed benefits of thermal ultrasound, it is vital that the components of parameter selection be understood. Most important of the components are the frequency, power, and intensity settings as they play a key role in the outcome and efficacy of accomplishing treatment goals.

Frequency

The frequency of ultrasound controls the depth of penetration of a treatment and is measured in megahertz (MHz). As frequency is adjusted when parameters are selected, it describes the number of waves generated and emitted in one second. While most ultrasound units emit only 1MHz or 3MHz ultrasound, some have a mid-range frequency setting that produces a 2MHz frequency.[6] Frequency and depth of penetration share an inverse relationship in which higher frequencies penetrate to a much more superficial level than seen in lower frequency settings. In terms of absorption of ultrasonic energy, more energy is attenuated, or lost, during high frequency ultrasound which inhibits the ability of the ultrasound waves to penetrate into deeper tissues.[6] Although some literature offers evidence that ultrasound delivered at 3MHz has a penetration range from below the skin's surface up to 2.5cm, it is believed that 3 MHz ultrasound is also capable of penetrating to tissues up to 3 cm deep.[19]

Often, the efficacy of a treatment parameter includes discussion of the half-layer value. The half-layer value describes the depth of the tissue at which 50% of the original amount of energy emitted has been absorbed.[6] This value helps clinicians understand exactly how much energy the target tissue is receiving and at what depth. The half-layer value is key for making sure that tissue temperature increases for specific therapeutic goals are achieved in the tissue being treated. For example, if ultrasound is applied using an intensity setting of 1 W/cm^2, it loses 50% of its energy when it reaches 2.3cm below the skin's surface and thus, the intensity of beam becomes just 0.5 W/cm^2.[15]

Power and Intensity Outputs

Two additional key elements to understanding ultrasound treatment parameters are the power and intensity outputs. While both are products of the strength of the ultrasound wave, they represent this measure at different locations. The power is the amount of energy being produced by the transducer and is the pure amount of energy being emitted. As the energy from the ultrasonic waves penetrate through tissue, attenuation occurs, or energy is lost and by the time it reaches the target tissue, the resulting strength of the sound wave is represented by the intensity.

In order to be able to describe the intensity of a treatment or output of a machine, it is also vital that one knows the ERA or effective radiating area. Ultrasound transducers do not emit waves from their entire surface. The portion of the transducer head that actually produces waves and registers as producing at least 5% of the maximum power output is described as the ERA.[6] When these measurements are collected, they are taken at least 5mm from the face of the sound head, as the outermost edge of the sound head does not produce any energy. For example, a 5cm sound head would have an ERA that is less than $5cm^2$ and is generally centered around the location of the crystal. The smaller the unit's ERA, the more divergent the beam.[6] It has become apparent that the ability of a transducer to heat tissues may vary up to 61%, which may help to explain the equivocal outcomes of therapeutic ultrasound.[20] One of the major causes of these intramanufacturer and intermanufacturer variances is a difference in ERA which leads to variable amount of energy passing through a given area, or spatial average intensity (SAI).[6,21] The US Food and Drug Administration (FDA) lack strict standard regulatory guidelines for this important measure to prevent unsafe or inappropriate use of therapeutic ultrasound treatment. Although it is required that the error band for ERA be reported and most manufacturers report a ±20-25% error band, the FDA has not yet established any guidelines for an acceptable and safe percentage.[21] Because of these discrepancies, it is even more difficult for parameter guidelines for treatment to be established. However, the FDA has established a regulatory standard for power output on all therapeutic ultrasound machines that must report a ±20% variability.[18]

Biophysical Effects

The biophysical effects of an ultrasound treatment can be defined as the resultant changes that occur within the treated tissue as a direct result of the increase in tissue temperature.[6] The amount of temperature change that occurs in the area of treatment is highly dependent on several factors including application parameters (frequency, intensity, etc.), vascularity of the target area, type of tissue, size of the treatment area, type of ultrasound generator, and rate of movement of the machine transducer.[6] In general, the physiological changes attributable to a temperature increase following ultrasonic treatment follow the same principles of all other forms of thermal therapy. Although these effects are generally the same, deep-heating agents penetrate depths up to 2 cm below the skin's surface and deeper while superficial forms of heat are only capable of heating the tissues up to 2cm deep.[6] However, specific research on therapeutic ultrasound has shown that ultrasound applied at a frequency of 1MHz reaches target tissues 2.5 to 5 cm deep and 3MHZ ultrasound penetrates tissues up to 2.5 cm.[19,22]

In order for ultrasonic waves to enter the tissues in the area to which it is applied, treatments must utilize a coupling medium to prevent dispersion of ultrasound waves and allow transmission of the therapeutic agent into the desired tissue.[2,13] After the ultrasound waves are emitted from the transducer and pass through the coupling medium and the skin, conduction causes the heat that is generated to penetrate into deeper tissues.[6]

Increased Cell Metabolism

Physiologically, several changes occur in the body as the tissue is warmed. Primarily, cell metabolism is increased by the application of heat. These results can be amplified through microstreaming which is defined by the pulsation of tissue particles that occurs as a direct result of the flow of interstitial fluids initiated by therapeutic ultrasound.[6,23] Although microstreaming is traditionally thought of as a nonthermal result of ultrasound, it can also be seen during a thermal treatment because of the mechanical effects that are seen in both non-thermal and thermal applications. During thermal ultrasound, cell membrane permeability changes as a direct result of the microstreaming. This causes a change in the diffusion rate which eventually aids in accelerating the inflammation process. The increased metabolic rate creates a demand for the oxygen and nutrients necessary for resolution at the site of injury. In addition to heat inducing an increase in metabolic rate, the increase in metabolic rate is also responsible for generating additional heat within the treated tissue. This resultant reciprocal relationship stemming from increased cell metabolism also plays a key role in the increase in blood flow seen following ultrasound treatment.[2,6,24]

Increased Inflammation

An additional product of thermal ultrasound is its ability to increase inflammation. A mild increase in inflammation is thought to be seen when tissue temperature is increased by 1ºC.[6,25] Although many may initially view the increase in inflammation to an injury site as detrimental to healing, when timed correctly, an increase in inflammation is purported to serve as a facilitator to healing. An increase in blood flow to an active site of bleeding may cause further damage to the area and thus, is contraindicated during the acute inflammatory phase.[2] However, following that period, inflammation at the site of injury allows for metabolic rate and blood flow increases as well as enhanced delivery of oxygen and leukocytes. Growth factors and platelets are also released in conjunction with fibroblast proliferation, increased macrophage activity, and increased cell division.[6]

Alterations of Edema Levels

Ultrasound and other thermal modalities are also capable of altering edema levels through physiological mechanisms that lead to a more rapid recovery from soft tissue injury. As edema increases, the body responds in attempts to restore homeostatic balance and is much more efficient at removing the edema than allowing it to increasing in volume. Capillary pressure raises in order to remove the edema and facilitate the removal of harmful metabolites. Lymphatic permeability also increases which allows more edema to be absorbed and aids in the reduction of hematomas.[6] While Starkey[6] reported edema reduction as product of thermal application, these types of outcomes are typically thought to be the result of a pulsed or mechanical output.[15]

Decreasing Pain

Although the data is contradictory, it has been proposed that biophysical changes occur following a thermal ultrasound treatment that alter the perception of pain [1]. Typically, the deep heating of tissues results in increased rates of chemical reaction and cell metabolism, as previously discussed. This change facilitates an increased nerve conduction velocity and improved function of sensory and motor nerves. The most common mechanisms by which a thermal treatment, such as ultrasound, are able to be altered include decreases in mechanical pressure at nerve endings, decreasing muscle spasm, reducing ischemia, and by serving as an alternate stimuli to increase the pain threshold.[6]

Pain is a result of one of two mechanisms; chemical or mechanical. Both of these mechanisms are physiologically relevant at different times throughout the healing process. Mechanical deformation is seen during the acute phases of injury when actual physical damage exists in the tissue at the injury site. This causes pain by creating pressure at the nerve endings, usually by means of muscle spasm. As the injury begins to heal and the physical insult to the tissue subsides in the sub-acute and chronic phases of injury, pain perception is attributed to the result of chemical changes within the body. Those changes include ischemia and irritation caused by chemical mediators.[6] The increased circulation proposed to be a direct effect of a thermal ultrasound treatment helps to deliver oxygen to ischemic areas and increase the removal of pain-causing chemicals. It has also been suggested that the heat increase seen in tissues treated with thermal ultrasound breaks the pain-spasm-pain cycle by desensitizing muscles to the secondary gamma afferents that are often responsible for the mechanical sources of pain. Typically these benefits are seen when the tissue temperature has been raised 2-3º C.[6,25] This temperature increase is also capable of producing a sense of analgesia to decrease the perception of pain.[6]

Increasing Tissue Extensibility

Tissue extensibility is also a physiological property that has been studied in great detail with regards to its changes following application of deep heat. Given that the tissue reaches a temperature great enough to warrant physical effects, the tissue is more easily manipulated to elongate for injury prevention or contracture resolution.[6] Research indicates that the tissue must reach an increase of at least 3-4º C greater than the resting or baseline temperature.[6,25] Among the most valuable and beneficial physiological changes that occurs with the application of thermal modalities including continuous wave ultrasound is the increase in blood flow and change in blood dynamics. Increased blood flow after a rise in tissue temperature is responsible for aiding in many of the aforementioned biophysical changes that expedite the healing process. This topic will be investigated in more depth at a later time.

Intermanufacturer Variance

Although the components of the settings necessary to initiate an ultrasound treatment are well understood and established, the most appropriate parameters for accomplishing these therapeutic benefits are the subject of great debate as there is a lack of consensus of best practices for this modality. Several studies have sought to reduce the disparity in knowledge that exists between the physiological benefits and the parameters necessary to accomplish them. Of the existing studies, one has been repeatedly cited as having come the closest to bridging this disparity by examining the rate of temperature increases with a variety of settings. Draper, Castel, and Castel[15] performed four different ultrasound treatments of varying intensities on each of their 24 subjects, 12 of whom received 1MHz ultrasound while the other 12 received 3MHz ultrasound. These treatments were performed using an Omnisound 3000™ ultrasound machine and lasted 10 minutes or until the patients could no longer withstand the discomfort.[15] The results of this study are depicted in Appendix A and have frequently been used to guide parameter selection as it is included in many modality textbooks used to guide the education of athletic trainers and health care professionals across the country.[6,22,26] Although the study is sound in procedure, it lacks applicability to different ultrasound brands and needs to be validated and reproduced using other machines and ultrasound devices.[16]

As it has become clearer that the parameters outlined in Draper et al.[15] may only be applicable when the Omnisound 3000™ is used for treatment, other studies have been conducted in attempts to corroborate their findings. Many of the later studies also sought to determine whether or not these findings could be seen in other brands of ultrasound units. Leonard et al.[16] evaluated the changes in intramuscular temperatures after at 10-minute, 1.0 MHz ultrasound treatment using a Rich-Mar Theratouch 7.7 ultrasound unit. This study also evaluated a variety of intensity parameters including, 0.5, 1.0, 1.5, and 2.0 W/cm^2. Researchers reported that the intramuscular temperatures observed were different than those reported by other studies, thus, confirming the lack of consensus to the most appropriate parameters.[16]

Variability in machine output and ability to produce consistent results is often blamed for the lack of clear cut data about how ultrasound settings should be used. These differences have been noted when brands of machines are different.[27,28] Both studies noted that the Omnisound 3000™ heated tissues at a better rate than those to which they were compared. Rubley et al.[25] suggest that the variability seen in these studies may be due to a variety of mechanical components of ultrasonic parameters including the effective radiating area (ERA), the special average intensity (SAI), and the beam nonuniformity ratio (BNR). While the ERA is the area of the ultrasound that is actually emitting ultrasonic energy, the SAI describes the amount of energy passing through this area measured as the power per unit area of the sound head. The BNR is a representative measurement of how the intensity of the ultrasound beam varies as it is measured in different areas and is expressed by a ratio.[6] Although the FDA regulates that the standard for power output on all therapeutic ultrasound machines, the variability in this modality feature has the ability to greatly affect the actual amount of energy being delivered to the target tissue. That means that given the ultrasound machine meets FDA standards, a treatment intensity after attenuation occurs can be 20% lower or 20% greater than the intended dosage.[18] A dosage lower than expected may void any hopes for achieving therapeutic outcomes and thus, rendering treatment irrelevant. A treatment that reaches higher than expected intensity has the potential to increase tissue temperature to uncomfortable or damaging levels.

Efficacy of Treatments

Significant amount of disparities exist regarding the ability of thermal ultrasound to produce the proposed benefits at a clinically significant level. Research exists supporting its ability to effectively heat the tissue to a temperature that is conducive to accomplishing therapeutic goals such as increasing tissue extensibility and increasing blood flow. Conversely, there is also evidence that suggests that while measureable thermal tissue changes have been identified, they are not significant enough to warrant its use as a valuable clinical tool.

A 2006 study compared the change in tissue extensibility, one of the proposed benefits of thermal ultrasound, between thermal ultrasound and a hot water bottle applied to the treatment location. Results of the study revealed that the ultrasound treatment did sufficiently heat the tissues to cause an increase in tissue extensibility measured by a functional weight-bearing lunge test, but appeared to have no clinical benefit over the other thermal modality in question. The results actually demonstrated a slight tendency towards the other thermal modality having a greater effect on tissue extensibility than thermal ultrasound.[29] Similarly, Garrett et al.[30] demonstrated that a 20-minute pulsed shortwave diathermy treatment (800 bursts per second, 400- microsecond burst duration, 850-microsecond interburst interval, peak root mean square amplitude of 150 W per burst, and an average root mean square output of 48 W per burst) produced a level of tissue heating greater than that of the 20-minute thermal (continuous) 1MHz ultrasound with 1.5 W/cm^2 intensity to which it was compared. Although study participants who received the ultrasound treatment reported feeling a sensation of warmth, the level of tissue heating did not penetrate deep enough to produce therapeutic benefit.[30] Although Draper's previous work[15] with similar equipment to that that was used in the study suggests that with a 1MHz, 1.5 W/cm^2 treatment, the depth of penetration of 2.5cm should be achieved, this change was not identified and thus, the selected parameters may not have been appropriate, in particular the intensity may have been too low signifying that Draper's work may, in fact, not apply to all clinical situations. In contrast, Draper and Ricard[31] demonstrated that ultrasound employed for the purpose of increasing tissue temperature caused a significant and useful increase in tissue temperature. The study did, however, indicate that the tissue temperature returned to baseline quickly after application, decreasing its clinical benefit.

A systematic review of research concerning the effectiveness of ultrasound was conducted in 2001 by Robertson and Baker[17]. The reviewers ultimately drew conclusions from a group of ten articles that were chosen after an initial 5-filter screening process that excluded 25 other articles concerning the topic. Of the 10 articles reviewed, only two were found to demonstrate improvements in a variety of their respective outcome measures.[17] Despite repeated reports of inadequate results of research regarding thermal ultrasound, it remains one of the most frequently used modalities in clinical practice.[2,3]

Although it seems that, based on the current reports, ultrasound should be dismissed from clinical practice, more research is needed to investigate its proposed benefits more thoroughly. Many of the existing research articles are fundamentally and methodically flawed. A review of clinical trials involving ultrasound treatment revealed methodological flaws such as lack of control groups, standardized treatments, and assessment criteria for most of the 18 studies reviewed. Another article reports that only about 8% of the 293 articles that they reviewed surrounding ultrasound treatments were of adequate standards to be considered scientifically sound.[32]

Role of Blood Flow

Although the supporting evidence is contradictory, it has been reported by numerous sources that continuous, thermal ultrasound causes an increase in blood flow to the treated area.[2,5,6,7,14,33] While many articles support that there is in fact an increase in blood flow, the consensus on clinical significance of these rate changes is inconsistent.

If ultrasound really does have the capability to increase blood flow to the tissue surrounding the treatment area, the physiological benefits to healing are numerous. Heat causes the blood vessels to dilate thus, increasing the volume and velocity of the blood flowing to the injury site. Other mechanisms have been found to contribute to the dilation of blood vessels including the release of histamines and changes in cell membrane permeability. Once perfused to the site of injury, the blood flowing through the damaged tissue delivers nutrients and oxygen necessary for healing.[6] Additionally, blood flow helps flush the metabolic waste products and debris from damaged tissue away from the site of injury.[7]

Measuring Blood Flow

As the technology available in the medical field has grown, the ability to measure blood flow effectively has also dramatically improved. There seems to be no consensus about the gold standard for measuring the rate of blood flow, despite the fact that several methods have been introduced. Early studies utilized a method called occlusion plethysmography. This process was utilized by one of the pioneer studies on the effect of ultrasound treatment on blood flow in 1953.[34] Plethysmography can be defined as the use of an instrument that is designed to identify modifications to the size of an organ, limb, or other body part such as arteries or veins as a result of a change in the volume of blood.[35] Although this practice dates back to some of the original studies involving blood flow, it is still frequently utilized with new and updated technology that has made obtaining these readings easier and more accurate. Another study employed the use of more recent technology called tissue viability imager. A 2014 study examining the sensory and cutaneous vascular changes in the human forearm following a therapeutic ultrasound treatment utilized this technology that is able to identify changes in blood flow by imaging the target tissue and quantifying the concentration of red blood cells present.[4]

Among the other common noninvasive forms of viewing changes in blood flow is Doppler Ultrasound. This method of measurement utilizes the same methods of sending and receiving ultrasonic waves into the tissue specifically targeting blood vessels via the machines transducer. The high frequency ultrasound waves bounce off of the red blood cells in the area of interest to provide information about the rate and volume of blood flow. It is capable of measuring this rate of flow by identifying changes in the frequency being received by the transducer from the red blood cells flowing through the area of interest.[10] The ability to measure the change in these frequencies is traditionally used for diagnostic purposes. It is frequently utilized for diagnosing conditions such as blood clots, aneurisms, heart valve defects, congenital heart disease, and a variety of other cardiovascular and vascular diseases. However, for the purposes of this study, it was used solely for visualizing the change in blood flow following an ultrasound treatment to the brachial artery.

Existing Evidence for the Effects of Ultrasound on Blood Flow

Currently, research with definitive findings regarding the true effects of thermal ultrasound on the physiological changes that occur following insonation is lacking. While other studies have been conducted that examine other physiological effects such as tissue extensibility, spasm reduction, and effectiveness in treating specific conditions, few studies exist exploring the effect of ultrasound on blood flow, which allegedly plays a significant role in the healing process.

Early research by Bickford and Duff[34] in 1953 studied the influence of ultrasound on temperature and blood flow in the forearm using the occlusion plethysmography method. Results of this study suggested that although readings of blood flow (ml/100ml/min) did increase following a 2.0 W/cm^2 treatment, the changes were of insignificant clinical and statistical value.

A group of subjects were also treated at an intensity ranging from 3.0-3.5 W/cm^2 for 10-15 minutes. While treatment at this intensity did raise the rate of blood flow to a significant level (3.0-4.3 ml/100ml/min), patients reported a fair amount of discomfort with treatment at this level.[34] Similarly, Robinson and Buono[5] also utilized strain-gauge plethysmography to measure the change in blood flow in their study. The authors concluded that after application of continuous ultrasound (1.5W/cm^2, 1.0 MHz, 5min) to the forearm, there was no significant difference between the blood flow in the control arm and the one treated with thermal ultrasound.[5]

Another study investigated the ability of therapeutic ultrasound to cause a perfusion of blood flow to the area treated. Researchers used laser Doppler to measure the effects of a 6-minute, 1.0 W/cm^2, 3 MHz ultrasound treatment over the forearm in 3 treatment groups; control, placebo, pulsed, and continuous ultrasound. Results of this study supported the use of therapeutic ultrasound suggesting that a therapeutic ultrasound treatment can significantly increase the rate of blood flow in both thermal and nonthermal ultrasound.[7] Researchers conducting this study also measured skin temperature to determine the extent to which a warming effect from the transducer movement contributed to the increase in blood flow. Since they found significant differences between the treatment groups with increased blood flow following therapeutic ultrasound treatment and skin temperatures throughout the groups remained relatively similar, results could more confidently be attributed to the ultrasound.[7]

Conclusion

Existing research regarding therapeutic ultrasound is most frequently concerned with parameters and outcomes, but a wide variety of other topics about how best to utilize this modality have also been examined. It is well established that a 1ºC increase in tissue temperature causes mild inflammation and accelerates metabolic rate, a 2-3ºC change causes decreased muscle spasm and pain, increased blood flow, and a reduction in chronic inflammation, and a change of 3-4ºC results in tissue elongation, scar tissue reduction, and sympathetic inhibition.[6,15] Based on this information, clinicians have sought to identify parameters that can reliably produce these desired healing effects. Although many studies have been conducted since Draper et al.'s 1995 study[15], the parameter suggestions developed (Appendix A) based on these results are often thought of as the go-to reference standard for parameter selection. Though the benefits to thermal ultrasound have been supported through anecdotal and empirical evidence, research to back the claims to the physiological changes that occur following a thermal ultrasound treatment are lacking. Specifically, it is generally accepted that thermal ultrasound increases blood flow to the treatment area, however there is very little research available to substantiate this claim.[5] The research that is available provides conflicting data about the ability of this modality to improve blood flow. Therefore, it is vital that more research be conducted to determine the actual vascular benefit of thermal ultrasound.

CHAPTER III. METHODOLOGY AND PROCEDURE

The purpose of this study was to determine if there is a significant increase in blood flow to the brachial artery following a 3MHz thermal ultrasound at 1.0 W/cm^2 treatment over the brachial artery. Therefore, researchers sought to answer the following research question developed to bridge the disparity of knowledge about the true effects of thermal ultrasound on the proposed benefit of increased blood flow: does thermal ultrasound cause a significant increase in blood flow to the brachial artery in the healthy individual set at the parameters of continuous, 3 MHz, 1.0 W/cm^2 for 5 min? The purpose of this chapter is to address the type of experimental design, population of study, instrumentation, procedures, and statistical analysis methods.

Experimental Design

This study followed a pre-test post-test experimental design. The researchers collected measurements of blood flow using time-averaged mean velocity readings gathered with the diagnostic ultrasound machine and then performed a thermal ultrasound treatment. Immediately following the thermal ultrasound treatment, researchers again collected a blood flow measurement. The dependent variable was the time-averaged mean velocity reading that was collected to measure the change in blood flow. The independent variable was the thermal ultrasound treatment.

Population of Study

A convenience sample of 30 healthy individuals were recruited for participation in this study through Listserv emails distributed to North Dakota State University students and staff and by word of mouth on the North Dakota State University campus. In order to be considered for participation in the study, an individual must have been between 18-35 years old and reported being healthy. Those with an upper extremity injury that had occurred within the three weeks prior to participation in the study, history of surgery in the area, any type of vascular disorder or disease including peripheral vascular disease, open wounds, ecchymosis, or skin infections, those with sensation deficits, pacemakers, or heart monitoring devices, and individuals who reported being pregnant were excluded from participating in the study. All participants read the consent form presented to them, and the researcher answered all questions they had. Those who wished to go forth with participation in the study then signed the consent form. There was no subject attrition throughout the study, however one subject's data was thrown out due to the inability to obtain an accurate blood flow measurement.

Instrumentation

A Dynatron Solaris® 700 Series ultrasound machine (Dynatronics Corp., Salt Lake City, UT) was used to deliver treatment to the target area. The Dynatron Solaris® 700 Series machine has the capability of producing 1, 2, and 3 MHz frequencies which determines the depth of penetration. Deeper tissues require a lower frequency and more superficial tissues typically utilize a higher frequency setting.[4] The manufacturers report an effective radiating area of $5cm^2$

and a beam non-conformity ratio of 6:1. In order to maintain the recommended treatment area of 2-3 times the effective radiating area, a foam template was made within which the therapeutic ultrasound was performed. Aquasonic® 100 (Parker Laboratories, Inc., Fairfield, NJ) brand ultrasound gel was used as a coupling medium to aid in the transmission of ultrasonic energy into the tissues without excessive loss. Researchers utilized the Color Doppler setting on a Phillips HD11 XE Ultrasound System (Phillips Healthcare, Andover, MA) to measure the blood flow before and after a thermal therapeutic ultrasound treatment.

Procedure

Study subjects reported to room 14 in the Bentson Bunker Fieldhouse on the campus of North Dakota State University for participation. Upon arrival, researchers explained the study procedure along with any known risks and the benefits of participation and informed consent was obtained. This document also released the information as well as any images gathered during the study to the researchers. Demographics included gender, upper extremity dominance, and age were collected in addition to a survey of health questions for the purpose of exclusionary criteria (Appendix B). Each participant's data collection session lasted approximately fifteen minutes

All subjects that meet the inclusion criteria completed the study design as follows: initially, the subject was asked to lie supine on a treatment table with their dominant arm in 90 degrees of abduction, 90 degrees of elbow flexion, and in full shoulder external rotation so their hand was resting palm-up above their head on the treatment table. After the subject was situated in the correct position the diagnostic ultrasound machine was readied for data collection. Though this method for visualizing internal structures including vascular anatomy has been used in several research studies, the technology lacks research that ascertains its validity and reliability as a diagnostic instrument.[36,37] Much of the difficulty in identifying these measures lies in the experience level of the sonographer which plays a significant role in appropriately and effectively utilizing this technology. The diagnostic ultrasound transducer was used to locate the brachial artery after a coupling medium is applied to the head of the transducer by positioning it in short axis proximal to the medial epicondyle over the medial bicep. Once the brachial artery was identified, the transducer was rotated counter-clockwise into long axis to display the artery longitudinally across the screen. After the general placement of the transducer was located, the transducer was removed and a template was placed at this location and then the transducer was replaced in the center of the template. The brachial artery was again located in long axis. Once the researcher located and maintained a clear and well optimized picture, the research assistant wrapped cohesive bandage around the bicep and ultrasound treatment template. The treatment area template aligned with the superior border of the transducer and the research assistant also made a mark on the bandage at the center of the transducer head in order to optimize the transition from the therapeutic ultrasound to the post-ultrasound blood flow measurement. Following location of the artery and application of the treatment area template, appropriate steps were initiated to analyze the time-averaged mean velocity (TAVM), which was used to determine the blood flow.

After the TAVM was acquired using the ‘Trace’ feature, the subject received a therapeutic ultrasound treatment at the parameters of 3MHz, 1.0 W/cm^2, 100%, for 5 min. Since the existing literature lacks a clear consensus on the most efficacious parameters for achieving the desired therapeutic outcomes, which was increased blood flow in this case, parameters were selected based on knowledge of anatomy, various relevant research, and articles published by other researchers at this university using the same equipment. It has been well established that in order to induce a physiological increase in blood flow, the target tissue temperature must be raised by a minimum 2-3ºC.[6,15] Based on a sample collected by researchers, the average brachial artery lies between 1.0 and 1.4cm below the skin surface. Taking into account the target tissue depth of the brachial artery and the desired temperature change, researchers selected parameters of 3MHz at 1.0 W/cm^2 for 5 minutes at a 100% pulse-ratio based on current research being conducted by a faculty member at North Dakota State University using the Dynatron Solaris® 700 Series ultrasound machine. The transducer was moved at a rate of 4cm/sec as measured by a metronome to result in even heating throughout the treatment area within the previously placed template that was taped to the skin to maintain a 2-3 times ERA treatment area. None of the participants reported any sensations of heat or warmth. Upon completion of the therapeutic ultrasound treatment, the researcher replaced the diagnostic ultrasound transducer at the previously marked site to ensure a quick reading to not allow the effects of the thermal ultrasound treatment to wear off. Once the picture was optimized, the research assistant again obtained the TAVM measurement. Once the subject completed a pre- and post- treatment TAVM reading as well as their therapeutic ultrasound treatment, the session was completed.

Data Analysis

Descriptive statistics were performed for age, gender, upper extremity dominance and brachial artery depth. Data collected was analyzed using SPSS version 21 (SPSS Software. 21st edition; IBM, Upper Saddle River, NJ) and a paired samples dependent T-Test was performed with the level of significance set at $p \leq .05$

CHAPTER IV. MANUSCRIPT

Abstract

Background: Ultrasound has been suggested to be one of the most commonly used therapeutic modalities in clinical practice. One of the purported benefits of thermal ultrasound, is its ability to increase blood flow to tissue. This benefit however, has not been sufficiently supported by current literature and research. The purpose of this study was to determine if there is a significant increase in blood flow to the brachial artery following a 3MHz thermal ultrasound at 1.0 W/cm^2 treatment over the brachial artery. **Methods:** 30 healthy individuals (mean age 22.3 ± 3.1 years) were recruited to participate in the study. Blood flow was measured using a Phillips HD11 XE Diagnostic Ultrasound System in time-averaged mean velocity (cm/sec) prior to, and following a thermal ultrasound treatment. The therapeutic thermal ultrasound was performed using a Dynatron Solaris® 700 Series ultrasound machine at continuous, 3MHz, 1.0W/cm^2, for 5 min. A paired samples dependent T-Test was performed with the level of significance set at $p \leq .05$ to identify any significant changes in blood flow. **Results:** Results indicated that ultrasound performed at 3MHz, 1.0W/cm^2, for 5 min caused a statistically significant increase in blood flow (α=.015). **Conclusion:** This study demonstrated that ultrasound performed at 3MHz, 1.0W/cm^2, for 5 min can be effectively used to promote healing through increases in blood flow.

Keywords: blood flow, brachial artery, therapeutic ultrasound, thermal ultrasound

Background

Since the introduction in the 1950's, therapeutic ultrasound has been widely used to deliver heat to bodily tissues several centimeters below the skin's surface.[1] Some sources report that it is the most widely used modality in clinical practice.[2,3] Despite the popularity and utilization of ultrasound, the effects and benefits of the treatment have been unconfirmed. The proposed effects and physiological benefits have been neither confirmed nor denied in the existing literature. One of the many physiological benefits that is proposed to occur following a therapeutic ultrasound treatment is its ability to induce an increase in blood flow. [2,5,7,8] An increase in blood flow is accomplished by the modality's ability to heat tissues deep and superficial.[4] Heating is accomplished as the acoustic sound waves emitted from the machine's transducer to penetrate the skin and into the depths of the body's soft tissue structures. As tissues absorb the ultrasonic waves, tissue temperatures rises and the targeted treatment area is effectively heated. Heat causes local blood vessels to dilate at the area of application and in surrounding tissues thus, increasing blood flow.[6] When the tissue targeted for treatment is the site of an acute or chronic injury, an increase in blood flow aids in the healing and recovery process by enhancing the influx of nutrients and cellular components, as well as aiding in removing metabolic waste products and tissue debris.[7]

While an increase in blood flow following a rise in local tissue temperature seems both anatomically and physiologically feasible, literature is contradicting in the actual efficacy of treatments. Research exists supporting the ability to effectively heat the tissue to a temperature that is conducive to accomplishing therapeutic goals such as increasing tissue extensibility and increasing blood flow. Conversely, there is also evidence that suggests that while measureable thermal tissue changes have been identified, they are not significant enough to warrant its use as a valuable clinical tool.[29,30,31]

A systematic review of research concerning the effectiveness of therapeutic ultrasound was conducted in 2001 by Robertson and Baker.[17] Of the 10 articles reviewed, only two were found to demonstrate improvements in a variety of their respective outcome measures.[17] Despite repeated reports of inadequate results of research regarding thermal ultrasound, it remains one of the most frequently used modalities in clinical practice.[2,3] Among those reports, research specifically regarding the true effects of thermal ultrasound on the physiological changes that occur following insonation is lacking. Although several studies have been conducted about other physiological effects such as tissue extensibility[29], and effectiveness in treating specific conditions[17], few studies exist exploring the effect of ultrasound on blood flow, which has the potential to play a significant role in the healing process.

In 1953, Bickford and Duff [34] studied the influence of ultrasound on temperature and blood flow in the forearm using the occlusion plethysmography method. The results indicated that although readings of blood flow (ml/100ml/min) did increase following a 2.0 W/cm^2 treatment, the changes were of insignificant clinical or statistical value. A group of subjects were also treated at an intensity ranging from 3.0-3.5 W/cm^2 for 10-15 minutes. While treatment at this intensity did raise the rate of blood flow to a significant level (3.0-4.3 ml/100ml/min), patients reported a fair amount of discomfort with the treatment.[34] Similarly, Robinson and Buono[5] concluded that after application of continuous ultrasound (1.5W/cm^2, 1.0 MHz, 5min) to the forearm, there was no significant difference between the blood flow in the control arm and the one treated with thermal ultrasound.[5] However, Noble, Lee, Griffith-Noble[5] reported the use of a therapeutic ultrasound treatment (1.0 W/cm^2, 3 MHz, for 6 minutes) did significantly increase the rate of blood flow in both thermal and nonthermal ultrasound.[7]

In order to provide the most effective and evidence-based care, clinicians must ensure that the treatments they use have substantial and irrefutable research to support their use. Though many of the benefits of thermal ultrasound are well supported in the existing literature, several of the specific physiological changes that are anticipated following such a treatment lack clear consensus on their existence. Specifically, research provides conflicting data about the ability of thermal therapeutic ultrasound to increase local blood flow to the targeted tissue.[5] Therefore, this study was designed to bridge the gap in knowledge between the proposed and actual benefits of therapeutic ultrasound on blood flow by determining if there is a significant increase in blood flow to the brachial artery following a 3MHz thermal ultrasound at 1.0 W/cm^2 treatment over the brachial artery.

Methods

A convenience sample of 30 healthy individuals (age 22.3 ± 3.1 years; 15 males, 15 females) were recruited for participation in this study through Listserv emails distributed to university students and staff and by word of mouth on the researching campus. In order to be considered for participation in the study, an individual must have reported being generally healthy and were required to be between the ages of 18 and 35. Those with an upper extremity injury that had occurred within the three weeks prior to participation in the study, history of surgery in the area, any type of vascular disorder or disease including peripheral vascular disease, open wounds, ecchymosis, or skin infections, those with sensation deficits, pacemakers, or heart monitoring devices, and individuals who reported being pregnant were excluded from participating in the study. All participants read the consent form presented to them, and the researcher answered all questions they had. Those who wished to go forth with participation in the study then signed the consent form. There were no subject withdrawals throughout the duration of the study.

Table 1. Demographic characteristics of participants

Brachial Artery Depth, cm (M±SD)	**0.96 ± 0.3292**
Age, years (M±SD)	**22.3 ± 3.1**
Gender	
Male, *n* (%)	15 (50%)
Female, *n* (%)	15 (50%)
Dominance	
Right *n*, (%)	27 (90%)
Left *n*, (%)	3 (10%)

M mean, SD standard deviation, *n* number of participants

Instrumentation

A Dynatron Solaris® 700 Series therapeutic ultrasound machine (Dynatronics Corp., Salt Lake City, UT) was used to deliver treatment to the target area. The Dynatron Solaris® 700 Series machine has the capability of producing 1, 2, and 3 MHz frequencies which determines the depth of penetration. The manufacturers report an effective radiating area of 5cm^2 and a beam non-conformity ratio of 6:1. Aquasonic® 100 (Parker Laboratories, Inc., Fairfield, NJ) brand ultrasound gel was used as a coupling medium to aid in the transmission of ultrasonic energy into the tissues without excessive loss. In order to maintain the recommended treatment area of 2-3 times the effective radiating area, a foam template was attached to the treatment area within which the therapeutic ultrasound was performed. Researchers utilized the Color Doppler setting on a Phillips HD11 XE Ultrasound System (Phillips Healthcare, Andover, MA) to measure the blood flow before and after a thermal therapeutic ultrasound treatment.

Procedure

Study subjects reported to the research room. Upon arrival, researchers explained the study procedure along with any known risks and the benefits of participation and informed consent was obtained. This document also released the information as well as any images gathered during the study to the researchers. Demographics including gender, upper extremity dominance, and age were collected in addition to a survey of health questions for the purpose of exclusionary criteria. Each data collection session lasted approximately fifteen minutes.

All subjects that met the inclusion criteria completed the study design as follows: initially, the subject was asked to lie supine on a treatment table with their dominant arm in 90 degrees of abduction, 90 degrees of elbow flexion, and in full shoulder external rotation so their hand was resting palm-up above their head on the treatment table. After the subject was situated in the correct position, the diagnostic ultrasound machine was readied for data collection. Though this method for visualizing internal structures including vascular anatomy has been used in several research studies, the technology lacks research that ascertains its validity and reliability as a diagnostic instrument. [15,16] Much of the difficulty in identifying these measures lies in the experience level of the sonographer which plays a significant role in appropriately and effectively utilizing this technology. The primary investigator of the current study was well trained and practiced in the protocol used to obtain blood flow readings. In addition to a 17-week long course familiarizing the researcher with the use of diagnostic ultrasound, professional sonographers from a local health institution were brought in to further train the researcher on collecting blood flow measurements. The diagnostic ultrasound transducer was used to locate the brachial artery after a coupling medium was applied to the head of the transducer by positioning it in short axis proximal to the medial epicondyle over the medial bicep. Once the brachial artery was identified, the transducer was rotated counter-clockwise into long axis to display the artery longitudinally across the screen. After the general placement of the transducer was located, the transducer was removed and a template was placed at this location and then replaced in the center of the template. The brachial artery was again located in long axis. Once the researcher located and maintained a clear and well optimized picture, the research assistant wrapped cohesive bandage around the bicep and ultrasound treatment template. The treatment size template aligned with the superior border of the transducer and the research assistant also makes a line on the bandage at the center of the transducer head in order to optimize the transition from the therapeutic ultrasound to the post-ultrasound blood flow measurement. Following location of the artery and application of the treatment size template, appropriate steps were initiated to analyze the time-averaged mean velocity (TAVM), which was used to determine the blood flow.

After the TAVM was acquired using the 'Trace' feature on the diagnostic ultrasound, the subject received continuous therapeutic ultrasound treatment at the parameters of 3MHz, 1.0 W/cm^2, for 5 min. Since the existing literature lacks a clear consensus on the most efficacious parameters for achieving the desired therapeutic outcomes, which was increased blood flow in this case, parameters were selected based on knowledge of anatomy, various relevant research, and articles published by other researchers at this university using the same equipment. It has been well established that in order to induce a physiological increase in blood flow, the targeted tissue temperature must increase by a minimum 2-3ºC. [8,16] While the researcher practiced the technique of measuring blood flow in the brachial artery, the depth of the arteries were scanned to obtain an average depth of approximately 1cm below the skin. Taking into account the target tissue depth of the brachial artery and the desired temperature change, researchers selected parameters of 3MHz at 1.0 W/cm^2 for 5 minutes at a 100% pulse-ratio. The parameters were based on unpublished research that has been performed on the Dynatron Solaris® 700 Series therapeutic ultrasound machine at the institution. The unpublished research results indicated an increase of 3.77°C the 1.0 cm depth. The transducer was moved at a rate of 4cm/sec as measured by a metronome to result in even heating throughout the treatment area within the previously placed template that was taped to the skin to maintain a 2-3 times ERA treatment area.[6] No participants reported any sensations of heat or warmth. Upon completion of the therapeutic ultrasound treatment, the researcher replaced the diagnostic ultrasound transducer at the previously marked site to ensure a quick reading and to not allow the effects of the thermal ultrasound treatment to wear off. Once the picture was optimized the research assistant again, obtained the TAVM measurement. Once the subject completed a pre- and post- treatment TAVM reading as well as their therapeutic ultrasound treatment, their session was completed.

Data Analysis

Descriptive statistics were performed for age, gender, upper extremity dominance and brachial artery depth. Data collected was analyzed using SPSS version 21 (SPSS Software. 21st edition; IBM, Upper Saddle River, NJ) and a paired samples dependent T-Test was performed with the level of significance set at $p \leq .05$.

Results

A paired-samples t-test was conducted to compare blood flow through the brachial artery prior to and following insonation. There was a significant difference in the scores for before thermal therapeutic ultrasound (M=11.1860, SD= 11.5555) and after thermal therapeutic ultrasound (M=16.4837, SD= 9.40805) conditions; $t(29)= -2.596$, $p = 0.015$. These results support that a 5 minute thermal therapeutic ultrasound treatment delivered with a frequency of 3MHz and an intensity of 1.0 W/cm^2 has the capability to cause a statistically significant increase in blood flow at the treatment site.

Discussion

Previous research has outlined the physiological changes that occur as tissues are heated. Among these physiological changes that are now generally accepted, a change in tissue temperature of 2-3^{o}C causes decreased muscle spasm and pain, reduction in chronic inflammation, and increased blood flow.[6,15] In order to ensure an increase in blood flow, researchers sought to increase tissue temperature in the treatment area to at least 2-3ºC above baseline or resting temperature. Researchers in the current study calculated an average brachial artery depth of the participating subjects to ensure that the chosen parameters caused a tissue temperature increase of this magnitude. Therapeutic ultrasound parameters were based on an average brachial artery depth of approximately 1.0 cm. A study currently being conducting at the researching institution was designed to identify tissue temperature changes that were associated with a 3MHz, 1.0 W/cm^2 therapeutic ultrasound treatment. As the mean depth of the targeted treatment in participants was slightly less than 1.0 cm (0.96 ± 0.3292cm), one can reasonably assume that the tissue temperature increase was marginally larger than the 3.77°C change that was measured at five minutes of ultrasonic treatment in the unpublished research study. This temperature is well above 2-3°C tissue temperature change that is postulated to increase blood flow. Therefore, the results of the unpublished research at the 1.0cm depth support the findings of this study that indicate an increase in blood flow occurs following a 5-minute, continuous, 3 MHz, 1.0 W/cm^2 ultrasound treatment.

Other studies conducted on this topic have varying results. While most acknowledge that an increase in blood flow does occur, several deny that this change is of a statistically significant difference. Two studies that used plethysmography to measure blood flow changes reported similar findings. Plethysmography identifies changes in limb size in order to measure an increase in blood flow. This method operates under the assumption that any change in limb circumference can be associated with an increase in blood flow. However, there are several other variables to which these fluctuations can be attributed such as hydration status or muscle activity. Researchers in the current study chose to utilize Doppler ultrasound to measure blood flow for its seemingly more scientific and accurate methodology. Doppler ultrasound isolates changes in velocity of the blood flowing through the targeted area by using high frequency ultrasound waves that bounce off of the red blood cells in the area of interest to provide information about the rate and volume of blood flow. The advantages of using Doppler ultrasound as opposed to other methods such as plethysmography include the ability to measure the blood flow to an individual vessel or artery, the option to continuously monitor blood flow during the application of other treatments, and the ability to monitor blood flow in anatomical locations that are not cylindrical or have large tissue volumes.[39] Bickford and Duff[34] found that although readings of blood flow (ml/100ml/min) did increase following a 2.0 W/cm^2 treatment, the changes were of insignificant clinical value or statistical significance. A small group of five subjects were also treated at an intensity ranging from 3.0-3.5 W/cm^2 for 10-15 minutes. While treatment at this intensity did raise the rate of blood flow to a significant level (3.0-4.3 ml/100ml/min), patients reported a fair amount of discomfort with treatment at this level.[34] Similarly, Robinson and Buono[5] concluded that although an increase in blood flow was seen after application of continuous ultrasound (1.5W/cm^2, 1.0 MHz, 5min) to the forearm, there was no significant difference.[5]

Although both of the aforementioned studies do not support the use of thermal therapeutic ultrasound for the purpose of increasing blood flow, both studies have aspects of their methodology that make their applicability to currently clinical practice questionable. Bickford and Duff[34] used an ultrasound machine that is no longer in production or use. When the Sonostat was still in production, frequency was measured in kilocycles which also makes comparison to the current study and other more recent literature difficult. Variability exists between brands of machines[27,28] and thus, the physiological effects seen in one machine may be drastically different in another brand. Therefore, comparing results of a study in which a machine that is no longer used to current clinical practice can be misleading.

Certain aspects of the study performed by Robinson and Buono also make their results difficult to compare to the current study. Their choice of the parameter settings are contradictory for the forearm where they performed their data collection. The soft tissue in the forearm is fairly superficial in nature. One MHz ultrasound is designed to penetrate tissues 2.5-5.0 cm in depth which is much deeper than most of the forearm tissue.[19] Although this depth is sufficient enough to reach both the forearm tissue and tissues much deeper, the lack of increase in blood flow may be attributable to the ultrasound not being absorbed by the more superficial, target tissues. Therefore, the 1 MHz parameter selection was inappropriate for the treatment goals. The current study uses a frequency of 3 MHz since the target tissue (brachial artery) lies approximately 1cm below the skin surface and 3MHz ultrasound is believed to be capable of penetrating up to 3 cm.[19]

Both of the aforementioned studies used plethysmography to measure changes in blood flow associated with thermal therapeutic ultrasound. A third study, almost identical to this study in methodology with the exception of the treatment time being one minute longer, supports the results of the current study indicating that ultrasound performed at 3MHz and 1.0 W/cm^2 can cause a statistically significant increase in blood flow. Noble, Lee, and Griffith-Noble[7] administered one of four treatments each week for four weeks at the same time of day to each of their participants. The treatment groups included a control group in which no ultrasound was administered, a placebo group in which the application technique was performed but no output was emitted from the ultrasound machine, a pulsed ultrasound treatment delivered at a 1:2 ratio, and finally the continuous thermal ultrasound treatment in question. Furthermore, the research being conducted at the current study's institution indicated that when a Dynatron Solaris® 700 series was used for six minutes of insonation, the tissue temperature heated to 4.18ºC. The increases in the Noble et al.[7] study provides additional physiological evidence that blood flow should increase just as the results of the present study indicate.

While the statistical significance of the results are irrefutable, research successes and failures must be measured by their clinical utility and applicability. Because research on this topic lacks a gold-standard for measuring blood flow, it is difficult to discern what can be considered clinically significant. However, it can be reasonably assumed based on anatomical and physiological knowledge that any increase in blood flow is clinically beneficial. Time-averaged mean velocity is measured in centimeters per second. Assuming that ultrasound produces an increase in the velocity of the blood as it travels throughout the body, as the current study indicates, the rate and overall amount of blood that passes through an injury site would be increased following such a treatment. The benefits of increased blood flow include the transport of nutrients, hormones, metabolic wastes, oxygen, and carbon dioxide in order to maintain cell metabolism, osmotic pressure, and body temperature, regulation of pH levels throughout the body, and protection from microbial and mechanical threats.[10] Although it is currently unknown how ultrasound affects injured tissue, it can be assumed that based on the physiological benefits, it could immensely contribute to the healing and repair of such tissue.

This research has provided a basis for future research that may be conducted concerning ultrasound and blood flow. Because of the wide clinical use of therapeutic ultrasound as a modality, it is imperative that there be knowledge of how effective insonation is when different parameters and machines are used. Additionally, since the current study examined the effect of ultrasound on blood flow in healthy tissue, the effects should also be studied in damaged or diseased tissue as this is the most common use for therapeutic ultrasound.

Conclusions

The results of this study indicate that blood flow can be effectively increased following a continuous, 5-minute, 3 MHz, 1.0 W/cm² ultrasound treatment with the Dynatron Solaris® 700 Series Ultrasound machine. With the use of this machine and said parameters, healthy tissue at about 1cm in depth will heat up about 3.77ºC and blood flow has the potential to increase approximately 150% (5.3 cm/sec). Increasing blood flow to the site of an injury serves to create an optimal environment for healing by facilitating the delivery of nutrients and eliminating metabolic wastes present as a result of tissue damage. Clinically, this information provides evidence to support the use of ultrasound for a catalyst to accomplishing this important therapeutic goal.

CHAPTER V. DISCUSSION AND CONCLUSIONS

The purpose of this study was to determine if there is a significant increase in blood flow to the brachial artery following a 3MHz thermal ultrasound at 1.0 W/cm^2 treatment over the brachial artery. Existing literature regarding this topic is inconsistent in its findings, so it was imperative that a research question that aided in substantiating this claim of physiological benefit be formulated. Therefore, researchers used the following question to guide the study: does thermal ultrasound cause a significant increase in blood flow to the brachial artery in the healthy individual set at the parameters of continuous, 3 MHz, 1.0 W/cm^2 for 5 min?

As one of the many proposed physiological benefits of one of the most widely used modalities in clinical practice, [2,3] blood flow induced by thermal therapeutic ultrasound has not been sufficiently studied, nor has the existing literature been able to identify consistent or reliable findings. Should ultrasound have the capability to increase blood flow as postulated, it stands to provide a wealth of benefits to injured and healing tissue. The most significant of these benefits include flushing the metabolic waste products produced by the injury and the deliverance of nutrients and oxygen that are critical to the healing process.

In order to determine if an increase in blood flow occurs following an ultrasound treatment set at the parameters of continuous, 3 MHz, 1.0 W/cm^2 for 5 min, researchers employed a pretest-posttest research design. Thirty healthy participants were scanned using the Doppler setting on a diagnostic ultrasound machine to determine their blood flow rate. Following the initial measurement, the subjects received a therapeutic ultrasound treatment. Immediately after completion of their treatment, they were scanned again to identify any changes in blood flow rate which would indicate an increase in blood flow. Results of the study indicated that following a 5-minute, continuous, 3 MHz, 1.0 W/cm^2 ultrasound treatment, blood flow as measured by time-averaged mean velocity increased at a statistically significant level. On average, blood flow showed an increase of nearly 150% with an average of approximately 5.3 cm/sec increase in time-averaged mean velocity.

Previous research has outlined the physiological changes that occur as tissues are heated. It is generally accepted that a 1ºC increase in tissue temperature causes mild inflammation and accelerates metabolic rate. Additionally, a 2-3ºC change causes decreased muscle spasm and pain, increased blood flow, and a reduction in chronic inflammation, and a change of 3-4ºC results in tissue elongation, scar tissue reduction, and sympathetic inhibition.[6,15] For the purposes of this study, researchers sought to reach the window in which the tissue temperature rose to 2-3°C above the subject's resting, baseline temperature. This would ensure that, based on current research available, blood flow would increase.

The results of unpublished research currently being conducted at North Dakota State University provided support for the parameters used in the current study. Participants in the unpublished study had three thermocouples inserted into the belly of their gastrocnemius muscle at the depths of 1.0cm, 1.75cm, and 2.5cm and were subsequently treated with thermal therapeutic ultrasound (3MHz, 1.0 W/cm^2). At the 1.0cm depth, the tissue temperature increased an average of 3.77°C in five minutes of treatment. For the current study, brachial artery depths were measured using the caliper feature on the diagnostic ultrasound machine. Based on those measurements, the average depth of the brachial arteries of participating subjects was 0.96±0.3292 cm below the skins surface. As the mean depth of the targeted treatment was slightly less than 1.0 cm, one can reasonably assume that the tissue temperature increase would be marginally larger than 3.77°C. This temperature is well above 2-3°C tissue temperature change that is postulated to increase blood flow. Therefore, the results of the unpublished research at the 1.0cm depth support the findings of this study that indicate an increase in blood flow following a 5-minute, continuous, 3 MHz, 1.0 W/cm² ultrasound treatment.

The results of this study are consistent with much of the existing literature that suggests that blood flow does increase following an ultrasound treatment. However, the data collected in this study demonstrated that the increase in blood flow is of a statistically significant value. This suggestion is contradictory to several studies that also identified an increase in blood flow, but not to a significant level. Bickford and Duff (1953) found that although readings of blood flow (ml/100ml/min) did increase following a 2.0 W/cm^2 treatment, the changes were of insignificant clinical value or statistical significance. A small group of five subjects were also treated at an intensity ranging from 3.0-3.5 W/cm^2 for 10-15 minutes. While treatment at this intensity did raise the rate of blood flow to a significant level (3.0-4.3 ml/100ml/min), patients reported a fair amount of discomfort with treatment at this level.[34] Bickford and Duff's study was conducted using Siemens "Sonostat" Universal Ultrasonic Generator on a total of 26 subjects (20 males; 6 females).

The legitimacy and relevance of the 1953 study to current practice is questionable. While the method used to assess blood flow during this study (plethysmography) is still credited to be used in varying forms in more recent studies[39], technology has drastically improved to make this a more reliable source of measurement. Bickford and Duff[34] indicated that following the therapeutic ultrasound treatment, the plethysmographic readings were used to "estimate" blood flow and it can take anywhere from three to five minutes to obtain a post-treatment blood flow reading which may have altered the results and significance of the study. In addition, the ultrasound machine they used is no longer used or sold in clinical practice. When the Sonostat was still in production, frequency was measured in kilocycles which makes comparison to the current study and other more recent literature difficult. Similarly, Robinson and Buono[5] conducted a study in 1995 that concluded that though an increase in blood flow was seen after application of continuous ultrasound (1.5W/cm^2, 1.0 MHz, 5min) using a Chattanooga Corporation Intellect 205 portable ultrasonicator to the forearm, there was no significant difference. This study reported a total of twenty subjects (10 males; 10 females).[5] While the methods and instrumentation used in Robinson and Buono's study have more current clinical applicability than those used in the Bickford and Duff study[34], the parameters used do not parallel the most frequently used parameters.

As technology has improved since the conduction of the 1995 study, Chattanooga Corporation continues to improve their products and remains a competitor in the modality industry. Moreover, the instrumentation of Robinson and Buono's study[5] may be considered more reliable than previous studies. However, the parameter choices are contradicting for the treatment area selected. Insonation was performed on the forearm at 1MHz. Based on anatomical knowledge of the forearm, the soft tissue in the forearm is fairly superficial in nature. One MHz ultrasound is designed to penetrate tissues 2.5-5.0 cm in depth which is much deeper than most of the forearm tissue.[19] Therefore, the 1 MHz parameter selection was inappropriate for the treatment goals. The current study uses a frequency of 3 MHz as the target tissue (brachial artery) lies approximately 1cm below the skins surface and 3MHz ultrasound is believed to be capable of penetrating up to 3cm.[19]

Both of the aforementioned studies used plethysmography to measure changes in blood flow associated with thermal therapeutic ultrasound. A 2006 study by Noble, Lee, and Griffith-Noble used a methodology much more similar to the methods used in the current study. Nobel et al.[7] used Doppler ultrasound and similar therapeutic ultrasound parameters. Ten healthy subjects received a treatment delivered by a Medilink ultrasound machine at 3MHz, 1.0 W/cm^2 for 6 min on the forearm in conjunction with the constant monitoring of blood flow via a laser Doppler probe. While the methodology does not clearly state from which artery blood flow rates were measured, the arteries supplying blood to the forearm are branches of the brachial artery and it can be estimated that they lie approximately as deep or slightly more superficial than the brachial artery which was measured in the present study. Participants completed one of four treatments each week for four weeks at the same time of day. The treatment groups included a control group in which no ultrasound was administered, a placebo group in which the application technique was performed but no output was emitted from the ultrasound machine, a pulsed ultrasound treatment delivered at a 1:2 ratio, and finally the continuous thermal ultrasound treatment in question. The results of the 2006 study, consistent with the findings of this study, supported the use of therapeutic ultrasound suggesting that a therapeutic ultrasound treatment can significantly increase the rate of blood flow in both thermal and nonthermal ultrasound.[7] The striking similarities seen in both methodology and results of the 2006 study when compared to the present study help to support the conclusion that thermal therapeutic ultrasound administered with at 3MHz, 1.0 W/cm^2 for five minutes has the capability of producing a statistically and clinically significant increase in blood flow. Furthermore, the research conducted at North Dakota State University indicated that when a Dynatron Solaris® 700 series, which was used in the current study, was used for six minutes of insonation, the tissue temperature heated to 4.18ºC. The increases seen in the Noble et al.'s study provides additional physiological evidence that blood flow should increase just as the results of the present study indicate.

The primary findings of the present study are difficult to compare to existing literature due to the nature of their methodologies. There are many approaches available to measure blood flow however, a gold-standard does not exist. Many of the pioneer studies used a plethysmography that identifies changes in the size of a limb. This method operates under the assumption that any change in limb circumference can be associated with an increase in blood flow. However, there are many other variables to which these fluctuations can be attributed such as hydration status or muscle activity. This method also lacks the ability to measure the blood flow to one specific vascular structure as it is measuring the change in volume of the limb in its entirety. Additionally, it is not possible to continuously monitor blood flow or follow rapid or transient changes. Measurements can be made at a frequency of approximately two to four minutes.[38] Plethysmography could be perceived as an inferior method for obtaining blood flow measurements when compared to Doppler ultrasound based on the aforementioned drawbacks however, both were found to have a high correlation (r^2= 0.87-0.98) when measuring brachial artery blood flow. [39]

Other studies have utilized newer technologies such as tissue viability imaging which lacks research. The current study used Doppler ultrasound which identifies changes in velocity of the blood flowing through the targeted area by using high frequency ultrasound waves that bounce off of the red blood cells in the area of interest to provide information about the rate and volume of blood flow. While the science behind both tissue viability imaging and Doppler ultrasound are similar, Doppler ultrasound has been used much more frequently in recent scientific studies.[7,39] The advantages of using Doppler ultrasound as opposed to other methods include the ability to measure the blood flow to an individual vessel or artery, the option to continuously monitor blood flow during the application of other treatments, and the ability to monitor blood flow in anatomical locations that are not cylindrical or have large tissue volumes.[39] Doppler ultrasound is a skill that takes mastery however, the researchers were well trained and practiced in the protocol used for the current study.

In addition to the variability in methods used to measure blood flow, there is also an inconsistency in the machines used. The 1995 Draper et al.[15] study is often regarded as the standard for the parameter selection and used in therapeutic modality textbooks. [6,22,26] However, other studies have been performed that refute the applicability of these parameters to all machines. Leonard et al.[16] evaluated the changes in intramuscular temperatures after a 10 minute, 1.0 MHz ultrasound treatment using a Rich-Mar Theratouch 7.7 ultrasound unit. This study evaluated a variety of intensity parameters and reported that the intramuscular temperatures observed were different than those reported by other studies, thus, confirming the lack of consensus to the most appropriate parameters.[16] Contributing to the variability seen in treatment outcomes are the inconsistencies in effective radiating area, power, and spatial average intensity (SAI). Straub and Howard[20] evaluated the inter- and intramanufacturer variability when a frequency of 3 MHz was used in five different insonation machines. Results confirmed the wide variance that exists in ultrasound machine stating that all manufacturers, with the exception of the Omnisound brand machine, showed a difference between the reported and measured effective radiating area values, all transducers were within FDA guidelines for power, and that the Chattanooga brand machine had a lower SAI than all other manufacturers when ultrasound was delivered at 3 MHz. Intramanufacturer variability in SAI ranged from 16% to 35%, and intermanufacturer variability ranged from 22% to 61%.[21] A variance in the ability of an ultrasound machine to effectively heat tissue to the expected temperatures may affect the amount or lack of blood flow increases seen in some of the existing studies.

While research successes and failures are most frequently measured by the amount of statistical significance, in healthcare professions it is imperative that we allow clinical utility and significance to be the measure. It is difficult to discern what can be considered clinically significant as there is a lack of standard for measuring blood flow. However, it can be reasonably assumed based on anatomical and physiological knowledge that any increase in blood flow is clinically beneficial. Time- averaged mean velocity is measured in centimeters per second. Assuming that ultrasound produces an increase in the velocity of the blood as it travels throughout the body, as the current study indicates, the rate and overall amount of blood that passes through an injury site would be increased following such a treatment.

It has been well established that blood flow increases linearly with exercise. In order to better compare the results of the present study and draw more clear clinical implications, the increases in blood flow can be paralleled to the increases seen following physical exertion. A study by Saltin et al.[41] demonstrated this physiological regulation mechanism by evaluating changes in the hemodynamics of the femoral artery. Researchers used Doppler ultrasound to obtain blood flow readings at rest and in conjunction with dynamic knee-extensor exercise. At rest, subjects had an average reading of approximately 0.3 L $min^{-1}$and during knee-extensor exercise the rate of blood flow increased to an average of 6-10 L min^{-1}.[40] While the units of blood flow were quantified differently than the current study, a valuable comparison can be made about the magnitude of change. The change in blood flow seen after exercise are extremely significant with a change in velocity being over twenty times as large. Although the increases seen following thermal therapeutic ultrasound delivered at a frequency of 3MHz and an intensity of 1.0 W/cm^2 for 5 minutes are not nearly as large (M=5.29767 cm/s), the ability to mechanically produce an increase in blood of just a marginal amount in comparison to exercise is tremendously beneficial to the healing of injured tissue.

As blood flows through the body, it facilitates the transport of nutrients, hormones, metabolic wastes, oxygen, and carbon dioxide in order to maintain cell metabolism, osmotic pressure, and body temperature, regulate pH levels throughout the body, and protect the body from microbial and mechanical threats.[11] It is clear that blood flow is beneficial even to the healthy, uninjured body. When there is an increase in blood flow at the site of an injury, these physiological changes that occur can be even more beneficial, aiding in healing and recovery. Based on the findings of this research, ultrasound delivered at the protocol parameters is capable of increasing blood flow at the site to which it is delivered. When the treatment area is the site of an injury, the physiological benefit of an ultrasound treatment can immensely contribute to healing and repair. Clinicians must rely on research to determine the best and most efficacious treatment protocols for their patients. This research substantiates the use of thermal therapeutic ultrasound for increasing blood flow in the healthy individual.

The findings of this research open the door to a variety of future studies that may be conducted in conjunction with the results that were obtained. Of the most clinically relevant, may be the potential to determine the effect of ultrasound on blood flow using other parameters and other machines. As previously discussed, research indicates that variability exists among different ultrasound machines and the ability to effectively heat the tissues at similar rates. Many clinicians follow guidelines for parameter selections that was established using the Omnisound 3000 ultrasound unit.[15] However, when treatment goals include increasing blood flow, it would be advantageous to have substantiated evidence to back the use of ultrasound for increasing blood flow on other brands of machines. Additionally, current research being conducted at North

Dakota State regarding tissue temperature changes using different parameters indicate that there are a variety of other parameter selections that produce a change in tissue temperature in the 2-3° C target window. Determining the most efficacious parameters to select in order to increase blood flow is highly valuable to clinical practice. As this study was conducted on healthy individuals, it may also be beneficial to a health care professional's clinical practice to conduct a study on the effect of ultrasound treatments on damaged or diseased tissue. When an injury occurs and blood vessels are damaged, normal blood flow is compromised. Currently there is no research to determine how blood flow is affected after an ultrasound on injured tissue. Therefore, a study to clarify this effect would provide valuable information to the treatment of injuries.

The results of this study indicate that blood flow can be effectively increased following a 5-minute, 3 MHz, 1.0 W/cm² ultrasound treatment with the Dynatron Solaris® 700 Series Ultrasound machine. With the use of this machine and said parameters, healthy tissue at about 1cm in depth will heat up about 3.77ºC and blood flow has the potential to increase approximately 150% (5.3 cm/sec). Increasing blood flow to the site of an injury serves to create an optimal environment for healing by facilitating the delivery of nutrients and eliminating metabolic wastes present as a result of tissue damage. Clinically, this information provides evidence to support the use of ultrasound for a catalyst to accomplishing this important therapeutic goal.

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MHz	W/cm^2	Depth (cm)	$\bar{X}$	SD
1	.5	2.5	.04	.054
3	.5	.8	.30	.135
1	.5	5.0	.06	.035
3	.5	1.6	.31	.132
1	1.0	2.5	.16	.072
3	1.0	.8	.58	.242
1	1.0	5.0	.16	.059
3	1.0	1.6	.58	.229
1	1.5	2.5	.34	.007
3	1.5	.8	.82	.276
1	1.5	5.0	.31	.115
3	1.5	1.6	.96	.242
1	2.0	2.5	.40	.084
3	2.0	.8	1.5	.354
1	2.0	5.0	.34	.018
3	2.0	1.6	1.3	.602

TABLE. *Means and standard deviations for the rate of heating (°C) per minute at doses of .5, 1.0, 1.5, and 2.0 W/cm^2. At 1 MHz, the tissue depths are 2.5 and 5.0 cm. At 3 MHz, the tissue depths are .8 and 1.6 cm.*

APPENDIX B. HEALTH QUESTIONNAIRE

Subject #	

Age: _______________

Gender (circle one): Male Female

Dominant Arm: Right Left

Health History:

1. Have you had an injury to any part of your dominant arm in the last 3 weeks?
   YES NO
2. Have you ever had surgery on any part of your dominant arm?
   YES NO
3. Do you have any diagnosed skin infections?
   YES NO
4. Have you ever been diagnosed with a vascular disease or disorder (ie: peripheral vascular disease)?
   YES NO
   If yes, please explain:
   ____
5. Has anyone ever told you that you have high cholesterol or blood pressure?
   YES NO
6. Do you have diabetes?
   YES NO
7. Do you have normal sensation in your arms?
   YES NO
   If yes, please explain:
   ____
8. Do you have a pacemaker or any other heart monitoring device?
   YES NO
9. Are you or is there any chance that you are pregnant?
   YES NO

OFFICE USE ONLY:

Open Wounds?	YES	NO
Sign of Infection?	YES	NO
Ecchymosis?	YES	NO
Check Sensation:	WNL	NWNL

If NWNL explain: ____