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The effects of therapeutic ultrasound on open wounds

Martha Henao Bloyer
Florida International University

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FLORIDA INTERNATIONAL UNIVERSITY

Miami, Florida

THE EFFECTS OF THERAPEUTIC ULTRASOUND ON OPEN WOUNDS

A thesis submitted in partial fulfillment of the

requirements for the degree of

MASTER OF SCIENCE

in

PHYSICAL THERAPY

by

Martha Henao Bloyer

1999

To: Dean DeLois P. Weekes
College of Health Sciences

This thesis, written by Martha Henao Bloyer, and entitled The Effects of Therapeutic Ultrasound on Open Wounds, having been approved in respect to style and intellectual content, is referred to you for judgment.

We have read this thesis and recommend that it be approved.

Ann Marie Knecht

Helen Z. Cornely

Leonard Elbaum, Major Professor

Date of Defense: April 2, 1999

The thesis of Martha Henao Bloyer is approved.

Dean DeLois P. Weekes
College of Health Sciences

Dean Richard L. Campbell
Division of Graduate Studies

Florida International University, 1999

DEDICATION

I dedicate this thesis to my husband Brent. Without his love, understanding and support during this past year, the completion of my Master's degree would not have been possible.

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I have found my coursework throughout the Curriculum and my Graduate Assistantship to be rewarding and fulfilling.

ABSTRACT OF THE THESIS

THE EFFECTS OF THERAPEUTIC ULTRASOUND ON OPEN WOUNDS

by

Martha Henao Bloyer

Florida International University, 1999

Miami, Florida

Professor Leonard Elbaum, Major Professor

The purpose of this study was to evaluate the evidence for the effectiveness of therapeutic ultrasound (US) therapy in the treatment of open wounds as an adjunct to the usual and customary treatment provided by physical therapists. An exhaustive search of all published studies on the effects of therapeutic ultrasound on open wounds was performed. Every article, which met certain criteria, was reviewed in detail. Criteria included the use of human subjects, animal subjects, or human cells in vitro, publication in referred journals indexed by MEDLINE, CINAHL and availability of full text in the English language. Fourteen studies met the selection criteria. A total of 31 possible outcomes were available from these studies. Outcomes were categorized as positive, negative or non-significant. The results indicated a total of seventeen positives, eight negatives and six non-significant outcomes. The results of the analysis indicate that there is evidence in the literature to suggest that therapeutic US is beneficial in the treatment of open wounds.

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Introduction

The problem of wound healing has long presented challenges to those in the medical profession. The goals of facilitating wound healing, repairing injured tissues, preventing infection, maximizing wound strength and preventing disability have been sought by many throughout history. Wound management is best attained by using a multidisciplinary team approach,(McCulloch, Kloth, & Feedar, 1995; Sparks, 1994) and physical therapists play a logical role in this team. Physical therapists can add unique treatments to the plan of care in wound management. These treatments include electrotherapy, ultrasound (US), and hydrotherapy, as well as mobility and positioning techniques and devices.

Byl, McKenzie, West, Whitney, Hunt, and Sceuenstuhl (1992) wrote that the most frequently used technique to accelerate wound healing is the application of heat. However, they hypothesized that deep heat such as US might be more effective than superficial heat. Their study concluded that low-dose ultrasound would facilitate wound healing. Riet, Kessels, and Knipschild (1996) found in their research that the data did not support the idea that US speeds up the healing of pressure ulcers. The literature on the effectiveness of US in accelerating healing is incomplete, conflicting and inconclusive.

Wound healing is a complex process involving the synthesis of intracellular and extracellular materials. Vascular responses and release of chemical mediators within wounded tissues combine to form inherent interrelated components of the healing process (McCulloch et al., 1995). The biological effects of US, if applied correctly, should produce physiological changes that could accelerate wound healing and other tissue repair (McCulloch et al., 1995).

Research Purpose

The purpose of this study is to evaluate the evidence for the effectiveness of therapeutic ultrasound (US) therapy in the treatment of open wounds as an adjunct to the usual and customary treatment provided by physical therapists. Usual and customary treatments provided by therapists include but are not limited to: cleansing or irrigating wounds with agents, application of hydrotherapy, US, electrical stimulation, or vasopneumatic compression treatments, debridement of wounds, selecting appropriate dressings for the wound and determining the frequency and duration of treatments (Ennis & Meneses, 1995; McCulloch, 1995; Sparks, 1994).

Review of Literature

Physics of Ultrasound

Ultrasound (US) has been used in medicine for over 50 years, and its biological effects on tissue were first reported by Wood and Loomis in 1927. Lysis of red blood cells and decreased mobility in mice following exposure to high-frequency (300kHz), high intensity sound waves were demonstrated. Ultrasound for medical treatment was introduced in Germany in the late 1930's according to Michlovitz (1996) and in the United States in the late 1940's (Michlovitz, 1996). Ultrasound has a variety of uses in contemporary medicine including diagnostic imaging of internal structures, functional restoration and healing of soft tissue conditions, tissue destruction, and hyperthermia for tumor irradiation according to Michlovitz (1996). The intensity of US in each varies, with the lowest intensity used for diagnostic purposes and the highest for tissue destruction.

Ultrasound is defined as a non-ionizing radiation; an inaudible, acoustic, mechanical vibration transmitted at a frequency above the upper limit of human hearing (McCulloch et al. 1995). Solids and liquids consist of molecules held together by elastic forces that behave like rubber bands connecting each molecule to its neighbor. If the molecule is vibrated, it will cause the neighboring molecule to vibrate. This will continue until the vibration has propagated throughout the entire material (Michlovitz, 1996). The propagation of this vibratory motion creates sonic waves.

Haar (1987) described a wave as "nature's way of transferring energy from one point to another" (p. 2). Ultrasound waves are transmitted in the form of mechanical compressional waves. These waves consist of regions where the molecules are alternately pushed together, or compressed, and pulled apart, or rarefied. When

traveling through liquids and soft tissues, the waves are longitudinal. Longitudinal waves cause the particles of a medium to oscillate in the direction of the wave, giving rise to alternate conditions of compression and rarefaction (McCulloch et al., 1995). In solids, transverse or shear waves, in which molecular displacement is perpendicular to the direction of wave propagation, are also transmitted. These transverse waves cannot travel through fluids (Haar, 1987). With the exception of compact bone, all the tissues of the body support only longitudinal waves (McCulloch et al., 1995).

The number of oscillations a molecule undergoes in 1 second defines the frequency (f) of a sound wave and is expressed in units of hertz (Hz). One Hz = 1 cycle/second, 1 kHz = 1000 cycles/second, and 1 MHz = 1 million cycles/second. Humans hear frequencies between 16 Hz and 20,000 Hz. Any waves above 20,000 Hz are considered ultrasound (Michlovitz, 1996). The time taken to complete one cycle is termed a period (T). The wavelength (λ) of a longitudinal wave is the distance from the middle of one compression to the middle of the next or the distance between two adjacent peaks. The wavelength is related to the frequency and the velocity (c) of the wave by the equation $\lambda = c/f$. Velocity is the speed at which the vibratory motion is propagated through the material. The velocity of US in water, blood, interstitial fluid, and soft tissue is approximately 1500 meters per second. Therefore, at a frequency of 1 MHz, the wavelength is 1.5 mm. At a frequency of 3 MHz, the wavelength is 0.5 mm (McCulloch et al., 1995). For therapeutic purposes, US frequencies range from 0.7 to 3.0 MHz. For diagnostic purposes, frequencies range up to 10 MHz (Gann, 1991).

Amplitude as defined by Haar (1987) is the term used to describe the magnitude of the disturbance in a wave. Amplitude increases as the intensity is increased. It can be

expressed either as the displacement amplitude, or as the variation in pressure found along the path of the wave, either negative or positive, measured from zero. Amplitude is expressed in units of distance (centimeters or meters) (Haar, 1987).

Energy contained within a sound beam is decreased (attenuated) as it travels through tissue. This results from two processes: scattering and absorption. Scattering is the deflection of sound out of the beam that results when it strikes a reflection surface. Absorption is the transfer of energy from the sound beam to the surrounding tissues. Absorption of sound increases as the frequency increases. At frequencies greater than 20 MHz, superficial absorption becomes so great that less than 1% of the sound penetrates beyond the first centimeter (Michlovitz, 1996). The amount of attenuation also depends on the type of tissues through which the US passes. Tissue with a high protein content, such as muscle, attenuates US more readily than do tissues with a high fat or water content. US at 3 MHz is more suitable for treating superficial injuries of the epidermis and collagenous dermis, as seen in skin wounds. Ultrasound of 1MHz is suitable if the injury extends more deeply (McCulloch et al., 1995).

Sound waves can be produced as continuous or pulsed wave. A continuous wave is one in which the sound intensity remains constant without interruption. If US is being used primarily to heat tissues, continuous application is appropriate (McCulloch et al., 1995). A pulsed US is intermittently interrupted. Pulsed waves are further characterized by specifying what fraction of the time the sound is present over one pulse period. This fraction is called duty cycle and is calculated by the equation $\text{duty cycle} = \frac{\text{duration of pulse (time on)}}{\text{pulse period (time on + time off)}}$ (Michlovitz, 1996).

Haar (1987) defined power as “the total energy in the beam, measured in watts” (p. 3). The strength of an US beam is determined by its intensity. Intensity is the rate at which energy is delivered per unit area, expressed in units of watts per square centimeter (W/cm^2) (Michlovitz, 1996). Measurement of intensity is derived by measuring the total power output (in watts) of an US applicator and dividing by the area (cm^2) of the applicator face. This intensity is called the spatial peak intensity. When pulsed US is being used, the intensity is highest during the pulse and zero when the sound is off. The maximum intensity is called the temporal peak intensity. The temporal average intensity is obtained by averaging the intensity over both the “on” and “off” periods. For example, a pulsed sound beam with a duty cycle of 50% and a temporal peak intensity of $2.0 \text{ W}/\text{cm}^2$ would have a temporal average intensity of $1.0 \text{ W}/\text{cm}^2$. The amount of heating depends on the temporal average intensity. Therefore, by interrupting a continuous wave, the temporal average is decreased and less heating will occur (Michlovitz, 1996). For therapeutic uses, intensities range from 0.2 to $3.0 \text{ W}/\text{cm}^2$. The World Health Organization (WHO) limits the spatial average intensity to a maximum of $3.0 \text{ W}/\text{cm}^2$. Intensities above $10.0 \text{ W}/\text{cm}^2$ are used to destroy tissue surgically, while intensities below $1.0 \text{ W}/\text{cm}^2$ are used for diagnostic purposes (Michlovitz, 1996).

According to Haar (1987) the total time of irradiation must be adequately quoted if the exposure is to be repeatable. This time is expressed in minutes. Duration is usually based empirically on the surface area to be treated. The area to be treated should be divided into zones each 1.5 times the area of the active surface of the applicator. One to two minutes should be allowed for treating each zone (McCulloch et al., 1995).

Therefore, if the effective radiating area (ERA) of the applicator is 5 cm^2 and the area to

be treated is 30 cm² , then there would be four zones. Total treatment time in this area would be between 4 and 8 minutes.

The equipment used in the generation of therapeutic levels of ultrasound typically consists of a microcomputer-controlled high frequency generator linked by coaxial cable to an applicator or treatment head containing a disc of piezoelectric material (McCulloch et al. 1995). There are two forms of the piezoelectric effect – direct and reverse (indirect). The direct effect is the generation of an electric voltage across a crystal when the crystal is compressed due to tension or pressure. If the crystal is expanded instead of compressed, a voltage of opposite polarity is induced. The direct effect is utilized for converting US into an electrical signal that replicates the sound pattern and can be conveniently and accurately processed and analyzed (Michlovitz, 1996).

Therapeutic US generators use the reverse piezoelectric effect. This reverse effect is the contraction or expansion of a crystal in response to a voltage applied across its face. Each change in the polarity of the applied voltage causes a contacted crystal to expand and contract. An alternating voltage incites the crystal to vibrate at the frequency of the alternating current, resulting in generated US. Therefore, the piezoelectric crystal is a transducer that converts electrical energy into sound energy (Michlovitz, 1996).

The transducer is any device that converts one form of energy into another. Commonly, naturally occurring crystals, such as quartz, possess the property of piezoelectricity. However, synthetic ceramic crystals, such as barium titanate or lead zirconate titanate (PZT), are almost always used in US because of their superior mechanical and electrical properties (Michlovitz, 1996).

When US in a therapeutic frequency range encounters a boundary or interface between two media with different acoustic properties, reflection occurs. The amount of reflected energy depends on the difference in the amount of impedance the media offers the US. There is little difference between the acoustic impedance of soft tissue and water, but much more between soft tissue and bone, and even more between soft tissue and air. Therefore, if US is to enter the body to treat tissue injuries successfully, air must be excluded from its path. This is achieved by placing a coupling or contact medium with acoustic properties similar to those of soft tissue between the applicator and the skin or wound surface (McCulloch et al. 1995).

Williams (1987) reported the functions of a coupling medium are simply to exclude air from the region between the transducer and the patient so that US can get to the site to be treated. McCulloch et al. (1995) described the ideal coupling medium. They felt that it should have the same acoustic impedance as skin, excellent ultrasonic propagation properties, and the ability to double as a wound dressing. In addition, the ideal coupling medium should be sterile, nonstaining, nonirritating, chemically inert, not too rapidly absorbed, slow to evaporate, free from gas bubbles and other inclusions, transparent, and inexpensive. However, this ideal medium does not exist.

William (1987) described how degassed water had the acoustic properties to make an excellent contact medium transmitting US for considerable distances with little loss in power. Due to the low viscosity of water, it has to be held in a container within or through which it can be linked to the skin. The container also has to be lined with ultrasound absorbing material, to reduce the problem of unwanted reflection. Often body

part and the applicator are submerged in the container, and US is delivered in the container.

Another choice includes aqueous gels. These gels are more convenient to use than water because their higher viscosity allows them to be applied to the skin without being held in a container. Unless sterile and inert, however, they should not be placed over broken skin, but only over adjacent intact skin or re-epithelialized scar tissue (McCulloch et al. 1995).

Open wounds can most conveniently be treated with US via sterile wound dressings. However, these dressings must have acoustic properties similar to soft tissue. In addition, these dressings must have the ability to be coupled to, and exclude air from, the wound area. Examples of such dressings are transparent polyarylamide agar gel, which is impermeable to bacteria and contains 96% water. Commonly available hydrogel (HDG) dressings come in sheets and are used to rehydrate wounds and to transmit ultrasonic energy in wound treatment protocols (McCulloch et al. 1995). Ultrasound is transmitted into the tissue by placing the applicator on the dressing. An aqueous gel contact medium can be applied to the applicator and moved gently over the treatment area (McCulloch et al. 1996).

Physiological Effects of Ultrasound

Ultrasound has been shown to have thermal and biophysical effects when applied to tissues. Dyson (1987) states that ultrasonic therapy can produce physiological heating at high intensities. In order to achieve a therapeutic effect through heating, the tissue temperature has to be maintained between 40°C and 45° C for at least five minutes.

Michlovitz (1996), Dyson (1987), Kitchen & Partridge (1990) list the physiological effects of heating. Including a temporary increase in the extensibility of collagenous structures, a decrease in joint stiffness, a reduction of pain, an increase in nerve conduction velocities, a reduction of muscle spasms, and the production of a mild inflammatory reaction, including a temporary increase in blood flow. Dyson (1987), Kitchen & Partridge (1990) warn that the possible problems of heating at higher doses can be damaging to tissue.

McCulloch et al. (1995) report that some of the physiological changes induced by therapeutic US that can affect the healing process are primarily of nonthermal origin. These physical effects include cavitation, defined by Dyson (1987) as “the formation and pulsation of gas or vapour-filled bubbles in fluid as a result of ultrasonically induced pressure changes” (p. 118). McCulloch et al (1995) described how these bubbles vibrate when exposed to ultrasonic waves. As a result, changes in cell membrane structure and permeability and the diffusion of metabolites can occur, giving rise to considerable therapeutic value. Cavitation occurs more readily at lower frequencies such as 1 MHz as reported by McCulloch et al. (1995).

Another physical effect of nonthermal US is acoustic streaming. This is defined by Dyson (1987) as “a steady circulation of fluid induced by radiation forces” (p. 118). When induced by US, a small object, such as a cell or a bubble will vibrate. Microscopic movements near the vibrating object have been termed “microstreaming” as reported by Dyson (1987) from Nyborg (1965). This microstreaming results in high velocity gradients that give rise to high viscous forces. These viscous forces can alter cell membrane structure and, in consequence, affect cell activity (McCulloch et al. 1995).

According to Dyson (1987), as long as the cell membrane has not been damaged, microstreaming could be of therapeutic use in acting as a signal leading to an influx of the cellular messenger calcium. Microstreaming can also facilitate diffusion of other ions and metabolites across the membrane. Depending on the cell type, the response to the intra-cellular calcium ions can be synthesis of collagen, secretion of chemotactic agents and wound factors, or motility changes of fibroblasts and endothelial cells. All of these could possibly accelerate repair process (Dyson, 1987).

Last of the non-thermal physical effects of US is standing wave formation. This can form if part of a wave of US traveling through tissue is reflected from an interface between two materials with different acoustic properties as previously described. This incident wave becomes superimposed in such a manner that peaks (antinode) of maximum intensity or pressure form at fixed positions half a wavelength apart (Dyson 1987). Midway between adjacent antinodes are areas of zero pressure called nodes (McCulloch et al. 1995). Gas bubbles floating in fluid collect at pressure antinodes, while cells, if they are free to move around, collect at nodes. Microstreaming in the fluid surrounding the bubbles can cause shear stresses, damaging the membranes of immobile cells, such as endothelial cells lining a blood vessel (McCulloch et al. 1995). Another problem reported by Dyson (1987) is that standing waves can impede or even arrest the movement of blood cells locally. In order to avoid the formation of damaging standing waves, the applicator should be moved throughout the treatment when administering US (Dyson, 1987).

Maxwell (1992) performed a review of literature on the effects of therapeutic US on cellular and molecular mechanisms of inflammation and repair. She summarized that,

despite the extensive research on diagnostic US, very little is known about the pathophysiological effects of therapeutic US. She found that research had been extensive with respect to the thermal effects of US due to the absorption of ultrasonic energy and its conversion to heat. Non-thermal effects such as cavitation and resultant shear forces have been less thoroughly investigated. In conclusion, Maxwell (1992), found it apparent that US might potentiate or inhibit inflammation due to its capacity to generate free radicals. Ultrasound also increased blood flow, the mediation of inflammation, leukocyte migration and function, angiogenesis, collagen synthesis and maturation, and scar formation. She felt further research was required to determine the precise cellular and molecular effects of US in order to provide a more rational basis for its use. She also thought research necessary to determine the most appropriate dosage at the most effective stage of the wound healing process.

Falconer, Hayes and Chang (1990) performed a quantitative synthesis of the literature addressing the effectiveness of US in selected musculoskeletal conditions. They reviewed published studies of therapeutic US on human subjects who had periarticular inflammatory conditions such as bursitis, capsulitis, epicondylitis, tendonitis, low back pain, spondylitis, frozen shoulders, osteoarthritis, and other chronic inflammatory conditions such as rheumatoid arthritis. It was concluded that patients with acute periarticular inflammatory conditions or osteoarthritis may experience relief of pain and immobility following US treatment. However, they were not confident that the US was causing these responses. They felt the literature concerning the therapeutic efficacy of US for pain and immobility in musculoskeletal conditions was inconclusive. Well-designed clinical trials were needed to resolve this.

Precautions and/or Contra-indications for Ultrasound

Ultrasound parameters and exposure conditions used for therapeutic purposes induce physiological effects that can be potentially damaging to tissues according to Dyson (1987). According to Dyson (1987) and McCulloch et al. (1995), a conservative approach should be taken when administering therapeutic US. Ultrasound should not be applied over the eyes, heart, pregnant uterus, gonads, malignancies and pre-cancerous lesions, tissue already treated by radiation therapy, vascular abnormalities including deep vein thrombosis and arteriosclerosis, the cranium, or on hemophiliacs without factor replacement. Caution should be used when administering US to subjects with decreased ability to perceive changes in temperature and pain. Epiphyseal areas in children should be exposed only minimally to US according to McCulloch et al. (1995).

Biology of Wound Healing

The fashion in which wounds heal is a complex process that involves cellular and biochemical events that must take place. There are three overlapping phases of the wound healing process; inflammatory, proliferative and matrix formation/remodeling phase (McCulloch et al. 1995). Harding (1990) described that an initial normal clotting mechanism was required to trigger succeeding events. This initial stage ensures that homeostasis takes place, releasing vasoactive substances resulting in an inflammatory response. This results in polymorphs and macrophages appearing in large numbers in the wound area. Collagen formation occurs over a period of time to help restore the tensile strength of the wound.

The first phase is the inflammatory phase. According to Ennis and Meneses (1995), this phase begins immediately after injury and lasts for approximately two days.

There is a brief period of vasoconstriction mediated by chemicals such as norepinephrine and serotonin to prevent excessive bleeding. Vasodilation follows as a result of stimulation by local sensory nerve endings and an accumulation of vasodilatory substances, such as histamine, in the tissue (McCulloch, 1996). A process of phagocytosis begins and, within three days after injury, macrophages are the predominant cells in the wound environment. Macrophages engulf bacteria and debris and also secrete growth factors which regulate and mediate many processes in skin repair (Ennis & Meneses, 1995). Clinical signs of inflammation as described by Ennis and Meneses (1995) are redness, warmth, edema, and pain. It is important to realize that all wounds need to pass through this phase in order for healing to occur.

The second phase of wound healing is the proliferative phase. This phase overlaps with the inflammatory phase and is distinguished by the formation of granulation tissue and the process of re-epithelialization (Ennis & Meneses, 1995). In this phase fibroblasts change shape and function to become myofibroblasts. The myofibroblast proliferate and migrate into the wound space. As fibroplasia occurs, there is a concurrent re-establishment of circulatory network within the wound. The clinical result of this angiogenic event is the development of granulation tissue (McCulloch, 1996).

Granulation tissue is red due to capillary formation. Wound contraction is also noted during this phase of wound healing. Contraction as defined by McCulloch (1996) is “the process by which a full thickness wound closes by centripetal movement of surrounding tissues” (p. 67). Myofibroblasts are predominantly responsible for this phenomenon. If however, there are forces resisting closure greater than myofibroblast’s closure, this process will stop. The wound will then heal via epithelialization and scarring (McCulloch

1996). Epithelial cells have a silvery appearance surrounding the red granulation tissue. The epithelialization process occurs via inward migration of cells from the wound edges (Ennis & Meneses, 1995).

The final phase of wound healing is the maturation phase. It usually begins three weeks after the injury and continues for months and even years (Ennis & Meneses, 1995). During this phase collagen re-organizes and strengthens. In order to achieve maximal healing, a balance of collagen production and breakdown is necessary. The maturation phase presents as pale scar tissue which results from capillary regression (McCulloch, 1996).

Weingarten (1993) reviewed the obstacles associated with wound healing. A number of physiological conditions, as well as pathological and iatrogenic problems, can interrupt or alter the wound healing process. These factors include age, obesity, inadequate perfusion, anemia, edema, repeated trauma, foreign body, infection, nutritional deficiencies, smoking, radiation, medications and topical agents. Harding (1990) listed local factors adversely affecting wound healing as blood supply, denervation, hematoma, lack of protection, mechanical stress, surgical technique, and type of tissue.

There are a number of diseases that predispose patients to the development of chronic wounds. Diabetes might predispose an individual to injury and delayed healing. According to Weingarten (1993), atherosclerosis (usually involving the tibial vessels) and neuropathies found in diabetics leave the patients more prone to injury. Diabetics also suffer from multiple disorders of the immune defense mechanism and are, therefore,

susceptible to bacterial invasion. Wound healing is also impaired as a direct result of the metabolic abnormalities associated with diabetes (Weingarten, 1993).

Other predisposing factors, according to Weingarten (1993), are inherited disorders of wound healing. For example, patients with epidermolysis bullosa have an inherited failure of adhesion of the epidermis, dermis, and basement membrane of the skin, leading to skin breakdown. In addition carcinoma may arise in chronic wounds, even without predisposing factors like radiation. Connective tissue disorders such as osteoarthritis and rheumatoid arthritis can lead to non-healing ulcers due to scleroderma (Weingarten, 1993). Hematological disorders and lymphedema are also considered predisposing factors that can lead to chronic wounds according to Weingarten (1993).

Wound Facts

According to the American Physical Therapy Association (APTA) Wound Management Fact Sheet (1998) pressure ulcers affect up to 30 % of all patients in hospitals and 23 % of patients in nursing homes. These ulcers are caused by unrelieved pressure resulting in the damage of underlying tissue, usually at bony prominences.

McCulloch et al. (1995) report leg ulcers account for the greatest number of wounds secondary to vascular insufficiency. These can be a result of arterial or venous origin. Arterial (ischemic) ulcers typically present as well demarcated lesions lacking epithelium. They are usually located over the toes, interdigital spaces, dorsum of the foot or lateral malleolus (McCulloch et al., 1995). These ulcers can vary in depth. Their base is pale due to lack of granulation tissue. They may be surrounded by gangrenous skin which is dry and scaly and they are usually painful. Symptoms of arterial insufficiency

ulcers include can be decreased pulses, intermittent claudication, pallor on elevation, slow nail growth, and loss of hair on the skin (McCulloch et al., 1995).

Venous insufficiency ulcers, according to Ennis and Meneses (1995), are the most common of the lower extremity ulcers resulting from vascular impairments. These ulcers are usually located above the medial malleoli. Pain may be present and is usually alleviated by elevating the leg. Venous ulcers are usually shallow, irregular in shape and classically have a red granulating wound base. The peri-wound skin is often hyperpigmented with hemosiderin stain and thickened. Venous ulcers represent the end stage of venous insufficiency according to Weingarten (1993).

Scurr and Coleridge-Smith (1992) report that microcirculation is recognized as playing an important role in the etiology of venous ulcers. Therefore there is an inability to reduce venous pressure on exercise. Damage to the valves in veins and failure of the muscle pump leads to a prolonged rise in venous pressure. Another current hypothesis for the cause of venous ulceration has also been attributed to skin hypoxia (Scurr & Coleridge-Smith, 1992).

Physical Therapists Role in Wound Care

Weingarten (1993) addressed the economic impact of patients with venous ulcers on society beyond the cost of medical care. One third of these patients are unable to work. Physical therapists play a role in management of wounds based on assessment of these wounds and choosing the appropriate treatment modalities. As a result physical therapists may be able to reduce healing costs by decreasing healing time. Sparks (1994) believed physical therapists were ideal to assist in the wound healing process due to their knowledge of soft tissue injury and treatment. Although wounds differ widely in etiology

and individual characteristics, they can be considered a type of soft tissue injury (Sparks, 1994).

Physical therapy modalities used to provide an environment conducive to wound healing include hydrotherapy, compression therapy (pumps, garments, or dressings), electrical stimulation, and ultrasound. Sussman (1992) reported that these modalities have the most supporting research for their effects on the phases of wound healing. McCulloch (1995) discussed the goals of vasopneumatic devices including reducing venous hypertension and edema by assisting venous return. The treatment goals of hydrotherapy include debriding loosely attached devitalized tissue and promoting circulation in ischemic limbs (McCulloch, 1995). Sparks (1994) wrote of the positive results of high volt pulsed current on the reduction of edema as well as increasing blood flow for wound management.

Methodology

The literature on the efficacy of therapeutic ultrasound on facilitating wound healing has been contradictory and inconclusive in assisting therapists to determine its use as part of their treatment plan. Dyson (1987) & Michlovitz (1996) discuss the physiological mechanisms involved in the response of injured tissue to ultrasound. McDiarmid & Burns (1987) address the clinical applications of therapeutic ultrasound, and facilitating wound healing is one of the intended clinical uses. Some studies have shown a positive effect of therapeutic ultrasound on wound healing, others, such as the one performed by Riet et al (1996) found that US did not speed up the healing of wounds. The purpose of this Meta-analysis was to evaluate the literature on the efficacy of therapeutic ultrasound in the treatment of open wounds.

Selection of Papers

An exhaustive search of all published studies on the effects of therapeutic ultrasound on open wounds was performed. Articles were indexed using MEDLINE and CINAHL. Search keyword terms used were; therapeutic ultrasound, ultrasound, wounds, open wounds, wound healing, wound care, burn care, and physical therapy. More than one thousand article results were found with these search topics. Article abstracts were reviewed and selected if they met a certain criteria. Every article, which met the criteria, was reviewed in detail. Criteria included the use of therapeutic ultrasound on human subjects, animal subjects, or human cells in vitro, publication in referred journals indexed by MEDLINE, CINAHL and availability of full text in the English language and published in 1985 to the present. Fourteen articles met the study selection criteria. Exclusion criteria included articles not published in English, studies involving non-traditional therapeutic US use such as 30 kHz continuous US at 100mW/cm^2 .

All references contained within obtained papers were also reviewed for selection. The goal was to select every paper that contained research on the efficacy of therapeutic ultrasound on open wounds. The articles selected for this analysis were all published studies on the efficacy of therapeutic ultrasound on open wounds performed in vitro, on animal subjects or human subjects. The following 14 articles were the selected ones for the meta-analysis.

De Deyne and Kirsch-Volders (1995) felt that the biological and cytological effects of therapeutic US in response to sonication at a frequency of 1 MHz with intensities in the range of 0.5 to 3 W/cm^2 were poorly documented. Previous research suggested a supporting role for US in the treatment of wound healing. The purpose of

their investigation was to determine whether (1) an in vitro approach could be used to study the effect of therapeutic US at the cellular level, (2) therapeutic US induced a change in the number of cells, and (3) therapeutic US had any effect on the morphology of chromosomes or the presence of mitotic spindles. They concluded the dose-dependent lytic effect of non-thermal US could result in fractionation of cells, which might facilitate phagocytosis during chronic inflammation. It was also observed that an increase in chromosomal aberrations and a loss of mitotic spindles resulted from extremely short US treatment (30 seconds). They stated that it was possible that, in their in vitro experiments, the US received was greater than would occur in a clinical situation (Deyne & Kirsch-Volders, 1995).

Ramirez, Schwane, McFarland, and Starcher (1997) performed an investigation to determine the effects of ultrasound on the rate of collagen synthesis and cell proliferation using cultured fibroblasts derived from Achilles tendons of neonatal rats. Ultrasound was administered at 0.4 W/cm^2 and 1MHz frequency to the experimental cells growing as monolayers in cultured flasks. Their results concluded that continuous US had no effect on the rate of collagen synthesis by tendon fibroblasts after 9 days of treatment. They also concluded, in collagenase-treated fibroblast cultures, that ultrasound treatment resulted in significant increase in rate of collagen synthesis during a 5 day period. Their results indicated that the greatest stimulation of collagen synthesis by ultrasound occurred soon after matrix disruption and most beneficial early in the repair process.

Byl, McKenzie, Wong, West, and Hunt (1993) performed a controlled, single blind, posttest experimental study to compare differences in wound breaking strength and collagen deposition. They performed forty-eight incisions on three mini Yucatan pigs.

Each incision was assigned to a control group or an US group and the sonicated incisions were further randomly assigned to 5 or 10 days of US treatment with either high dose US ($1.5\text{W}/\text{cm}^2$, continuous mode, 1 MHz, 5 minutes) or low dose US ($0.5\text{W}/\text{cm}^2$, pulsed mode, 20% duty cycle, 1 MHz, 5 minutes). They concluded that wound breaking strength was significantly higher in the sonicated incisions compared to the control group without significant difference in collagen deposition levels. They did find a significant interaction between the number of days of treatment and the dose of US. Collagen deposition was significantly higher in the low-dose US compared to the high-dose US after 5 days of US. Also, both the wound breaking strength and the collagen depositions were significantly higher in the low-dose US group compared with the high-dose US group after 10 days. Researchers suggest that physical therapists can use either low-dose US or high-dose US for approximately one week to enhance wound breaking strength in an acute incisional wound. If treatment is continued for 2 weeks or more, they suggest low-dose US should be used.

Young & Dyson (1990) investigated the effects of US on angiogenesis in full-thickness excised lesions in the flank skin of adult rats. Angiogenesis was defined by them as “the development of new blood vessels”(p. 261), a vital part of wound healing. They studied the wounds of one group during the late inflammatory phase of repair and the other group during the proliferative phase of repair. They used two methods to quantify angiogenesis: scanning microdensitometry, which gave information about vessel numbers, and image analysis, which gave information about vascularization in terms of total vessel area occupying the wound bed. Their results revealed US at frequency of 0.75

MHz caused a greater effect on angiogenesis than 3.0 MHz. This suggested that there may be a non-thermal component of the US involved in the stimulatory process. Their results also suggested that US could be effective in the early phase of the repair process. In the later phase of repair, the US treatment did not appear to have further significant effects on angiogenesis.

Byl, McKenzie, West, Whitney, Hunt and Scheuenstuhl (1992) studied the effects of low dose US on wound healing of surgically induced incisions and full-thickness and partial-thickness lesions in Yucatan pigs. Their research questioned if low dose US facilitated healing in the early stage of repair. Tensile strength, collagen deposition, quality of collagen, wound size and depth, visual quality and mast-cell degranulation were measured 7 days post-healing and after 5 days of sonation. The results of their study showed tensile strength was almost twice as high in sonated lesions. There were no measurable differences of size of the lesions, and the greatest difference in collagen deposition and tensile strength was associated with 1.5 W/cm^2 pulsating at 20% at 1 MHz. Visually, differences were nil. Byl et al. (1992) concluded one week of US treatment did not affect the apparent visual quality of healing, but it significantly increased the strength of incisional wounds and the rate of closure of full-thickness lesions. They also found there was a significantly higher degranulation of mast cells in lesions sonicated. They felt more studies were needed to clarify the specific physiological mechanisms of US wound enhancement and how it varies by dose, treatment time, and duration of treatment.

Enwemeka (1989) studied the effects of 1 MHz therapeutic US on healing strength of tendons in the tenotomized, repaired, and immobilized right Achilles tendon of 26 rabbits. Twelve of the tendons were sonicated with continuous wave of 1 W/cm^2

for 5 minutes for a duration of nine days. They concluded that, on the basis of their biomechanical study, the daily application of therapeutic US augmented the tensile strength and energy absorption capacity of rabbit Achilles tendons during the first 10 days of healing. It was stated that healing in rabbits may not translate directly to healing in humans, but the findings suggested that surgically repaired human Achilles tendons may heal faster if therapeutic US is applied during the early stages of healing.

Huys, Siang Gan, Sherebrin, and Scilley (1993) studied the efficacy of ultrasound treatment on flexor tendon healing in chickens, as this animal model was reported to closely resemble humans in regard to flexor tendon anatomy and collagen composition. They compared the effects of US given at six weeks postoperatively and US started seven days postoperatively. Their goal was to decrease morbidity secondary to tendon injury by improving tendon strength and to decrease adhesion formation. They concluded that early use of US was significant for tendon healing.

Young & Dyson (1990) studied the effect of therapeutic ultrasound on the healing of the dermis of full-thickness excised lesions made in the flank skin of adult rats. Wounds were either sham-treated or exposed to pulsed US at an intensity of $0.1\text{W}/\text{cm}^2$ and frequency either 0.75MHz or 3.0 MHz. The results indicated that by five days after injury, ultrasound-treated wounds contained more extensive granulation tissue, fewer polymorphs and macrophages, and more fibroblasts than the sham-irradiated control group. By seven days after injury there was no significant difference in cellularity. The results indicated that ultrasound can be useful in accelerating the inflammatory and early proliferative stages of repair.

Cambier & Vanderstraeten (1997) studied the effects of therapeutic ultrasound in healing burn injuries that were inflicted on 20 female rats. Two groups of 10 animals each were studied. In group 1 the experimental burn was treated with pulsed US at 0.25 W/cm^2 and in group 2 the burn was treated with continuous US at 0.3 W/cm^2 . Their results indicated that there was no statistically significant difference in favor of pulsed or continuous US. Histologically no differences in general aspect or in the amounts of fibroblasts, endothelial cells could be observed. These results discourage the clinical administration of therapeutic US to enhance healing of burns.

Callam, Harper, Dale, Ruckley and Prescott (1987) conducted a controlled study of US therapy in chronic leg ulceration. One hundred and eight (108) patients were entered into the study. Fifty-six patients were randomized to standard treatment, and 52 received standard treatment plus pulsed US given weekly. They concluded that the proportion of healed ulcers was 20% greater in the US group than the control group after 12 weeks.

Riet, Kessels and Knipschild (1996) performed a randomized clinical trial of US in the treatment of pressure ulcers. The purpose of their study was to assess the effects of US in conjunction with standardized treatment. Eighty-eight patients were randomly assigned to either an US group or a sham US group. Wound survival, healing rates of wound surfaces, and changes on a clinical rating scale were measured over a 12-week period. Their results concluded that the data did not support the idea that US speeds up the healing of pressure ulcers.

Nussbaum, Biemann and Mustard (1994) performed a study to compare the effect of wound healing with nursing care alone to wound healing with nursing care combined

with either laser treatment or a regimen of US and ultraviolet-C (US/UVC) in a group of patients with spinal cord injury. Twenty patients were randomly assigned to one of the three groups: a control group, a US/UVC group and laser group. The results of their study concluded that US/UVC treatment combined with standard wound care had an advantage over standard wound care combined with laser treatment and standard treatment alone when treating wounds in patients with spinal cord injury. These results were obtained from a total of 18 wounds.

Eriksson, Lundeberg and Malm (1991) performed a placebo-controlled trial of US therapy in 38 patients with chronic leg ulcerations. Patients were randomly assigned into two groups: placebo US or US group with the dose of 1.0 W/cm^2 at 1MHz for 10 minutes two times per week. Percentage of healed ulcer area and number of healed ulcers were compared after 2, 4, 6 and 8 weeks. Their study concluded there was no significant difference between US and placebo US in the treatment effect of venous ulcers. It was stated, however, that the number of patients completing the study was insufficient to detect a less than 40% difference in healing.

McDiarmid, Burns, Lewith and Machin (1985) performed a double-blind randomized trial to test the efficacy of ultrasound therapy on pressure sores. Forty patients were randomly assigned to either the ultrasound group or a group receiving mock-US. Only 18 patients could be followed until their sores were completely healed. It was found that ultrasound appears to be of value in the treatment of pressure sores. However, the complexity of other factors involved in wound healing means that a large trial involving more than 1,000 patients would be required for the study to be statistically valid.

Analysis

Meta-Analysis

Meta-Analysis is a technique which requires access to at least one of three types of data from research reports: a) information that can be used to calculate effect size estimates, such as means, standard deviations, or test statistic values, b) information about whether the hypothesis tests found statistically significant relations, and c) information about the direction of the outcome. Vote counting procedure is useful in the second and third type of data. For the purpose of this review, information about the direction of the outcome was looked at using the conventional vote-counting procedure (Cooper & Hedges, 1994).

This traditional voting method consists of a tabulation of significant and nonsignificant findings. Hunter, Schmidt and Johnson (1982) and Cooper and Hedges (1994) used the description by Light and Smith (1971) for this method:

All studies which have data on a dependant variable and a specific independent variable of interest are examined. Three possible outcomes are defined. The relationship between the independent variable and the dependent variable is either significantly positive, significantly negative, or there is no specific relationship in either direction. The number of studies falling into each of these three categories is then simply tallied. If a plurality of studies falls into any of one of these three categories, with fewer falling into the other two, the modal category is declared the winner. This modal categorization is then assumed to give the best estimate of the direction of the true relationship between the independent variable and dependent variable (p.130).

To analyze the articles, each article was numbered and arranged by starting with the In Vitro studies then the animal studies and finally the human subjects research articles. Table I provides the title of each article selected, its' author(s), year of

publication, number of subjects used and if other treatments were rendered in conjunction with therapeutic ultrasound along with the usual and customary wound care treatments.

Other information abstracted from the articles included a) type of study: in vitro, on animals, or on human subjects b) number of subjects in the study c) subject groupings d) any additional treatments given in conjunction with US other than the usual and customary wound care dressings e) Frequency, intensity, mode and ultrasound treatment times f) number of treatments rendered to each group g) purpose of the study h) study results: effectiveness of therapeutic US on the treatment of wounds. The level of significance used to determine which category the studies would be classified was the level of significance used by each author in his/her study. Studies were classified as indicated by using the traditional voting method as “Positive” if the author(s) concluded that US was beneficial in the treatment of wounds or “Negative” if the authors did not consider US to be beneficial in the process of wound healing, or “Non significant” if the evidence was not conclusive to support the role of US in wound healing. Table II shows a summary of this abstracted information.

To evaluate the effectiveness of US therapy across all the studies, the probability of getting k out of n outcomes, where k equals the total number of positive outcomes and n equals the total number of outcomes was computed. The traditional voting method was used and a qualitative critique of the studies as a group was performed.

Table I. Summary of selected articles. Article title, author/s, type of study, number of subjects, other treatments given.

#	Title	Author/s	Year	Type of study	Subjects	Additional Treatments
1	In Vitro Effects of Therapeutic Ultrasound on the Nucleus of Human Fibroblasts	De Deyne & Kirsch-Volders	1995	In vitro: Human male fibroblasts	5 to 6 dishes of cells per treated group	N/A
2	The Effect of Ultrasound on Collagen Synthesis and Fibroblast proliferation in Vitro	Ramirez et al.	1997	In vitro: Achilles tendon fibroblasts from neonatal rats	3 to 5 flasks of cells for each time point	Vitamin C and Collagenase separately
3	Incisional Wound Healing: A Controlled Study of Low and High Dose Ultrasound	Byl et al.	1993	Animal: Mini Yucatan Pigs	48 incisions on three mini Yucatan pigs	N/A
4	The Effect of Therapeutic Ultrasound on Angiogenesis	Young & Dyson	1990	Animal: Flank skin of adult rats	36 Female rats	N/A
5	Low-dose Ultrasound Effects on Wound Healing: A Controlled Study with Yucatan Pigs	Byl et al.	1992	Animal: Mini Yucatan Pigs	88 lesions on 11 Yucatan pigs	N/A
6	The Effects of Therapeutic Ultrasound on Tendon Healing	Enwemeka	1989	Animal: Achilles tendons of Rabbits	26 rabbits	N/A
7	Comparison of Effects of Early and Late Ultrasound Treatment on Tendon Healing in the Chicken Limb	Huys et al.	1993	Animal: Chicken	76 chicken tendons	N/A
8	Effect of Therapeutic Ultrasound on the Healing of Full-thickness excised skin lesions	Young & Dyson	1990	Animal: Flank skin of adult rats	36 Female rats	N/A
9	Failure of Therapeutic Ultrasound in Healing Burn Injuries	Cambier & Vanderstraeten	1997	Animal: Female rats	20 Female rats	N/A
10	A Controlled Trial of Weekly Ultrasound Therapy in Chronic Leg Ulceration	Callam et al.	1987	Human: leg ulcers	108 patients	N/A
11	A Randomized Clinical Trial of Ultrasound in the Treatment of Pressure Ulcers	Riet et al.	1996	Human: Pressure ulcers	88 patients	N/A
12	Comparison of Ultrasound/Ultraviolet-C and Laser for Treatment of Pressure Ulcers with Spinal Cord Injury	Nussbaum et al.	1994	Human: Pressure ulcers	22 wounds from 20 patients	US combined with UVC
13	A Placebo Controlled Trial of Ultrasound Therapy in Chronic Leg Ulceration	Eriksson et al.	1991	Human: Venous leg ulcers	25 total patients	N/A
14	Ultrasound and the Treatment of Pressure Sores	McDiarmid et al.	1985	Human: Pressure sores	40 patients	N/A

Table III. Shows them frequency, intensity, mode of ultrasound used. Also the subject groupings, number of ultrasound treatments given, purpose of the study and the results.

Study #	US Frequency	Intensity	Mode	Type of subject	Groups	Number of US treatments	Purpose of the study	Results
1	1 MHz	1.0 W/cm ²	20% pulsed	In vitro human fibroblasts 5 to 6 dishes of cells per group	0 sec= control 30 seconds 60 seconds 90 seconds	One time	To test if: 1. US induces a change in the number of cells 2. US has any effect on the morphology of chromosomes or presence of mitotic spindles	1. Positive for Time dependent decrease in # of cells 2. Positive for a fourfold increase in mitotic index. *Result US used to facilitate the resolution of chronic inflammation
2	1 MHz	0.4W/cm ²	Continuous Or 20 % pulsed	Fibroblasts from rats 3 to 5 flasks of cells for each	3minutes each group with continuous ----- control Vit C & no US Vit C & US US & no Vit C ----- 3 minutes for	9 days 5 days 1, 3 or 5 days	To compare the: 1. Effect of continuous US on collagen synthesis 2. Effect of vitamin C on collagen synthesis with or without US 3. Effect of US on collagen synthesis in Collagenase treated cultures	1. No Effect 2. No effect with or without US 3. Positive increase in rate of collagen synthesis
3	1MHz	1.5 W/cm ² 0.5 W/cm ²	Continuous 20% pulsed	48 incisions on three Yucatan pigs	12 for control 8 low dose US 18 high dose 24 wounds for 5 days 12 wounds for 10 days	5 min/day for 5 days 10 days	To compare: 1. Control Vs Sonated at 2 weeks a. Breaking strength b. Collagen deposition 2. One week of healing Vs 2 weeks 3. Low Vs High dose US in: a. Breaking strength b. Collagen deposition 4. Sonation for 5 days and 10 days a. Breaking strength b. Collagen deposition 5. Sonation for 5 & 10 days: Low Vs High dose US a. At 1 week and 5 days of US b. At 2 weeks and 5 days	1a. Positive for sonated wounds stronger than control 1b. Negative for collagen deposition 2. Positive for more collagen deposition during the 2 nd week compared with the 1 st . 3a. Negative 3b. Negative Breaking strength and collagen deposition are similar with low or high dose US 4a. Negative 4b. Negative No differences btwn treatment for 5 or 10 days 5a. Positive After 1 week and 5 days of US breaking strength greater with Low dose US 5b1. Negative No difference btwn Low and High dose at 2 weeks 5b2. Positive Greater collagen with low dose US

								of US in terms of 1.breaking strength 2.collagen deposition c. At 2 weeks of healing & 10 days in terms of 1. breaking strength 2. collagen deposition	5c1. Positive 5c2. Positive Wound breaking strength and collagen were higher after 10 days of US and low dose compared to high
4	0.75 MHz 3.0 MHz	0.1 W/cm ²	20% pulsed	Flank skin of adult rats	Group 1 5 days post op control group 0.75MHz and 3.0MHz Group 2 7 days post op control group 0.75 MHz 3.0 MHz	One treatment for 5 minutes each	To test if: US could promote angiogenesis in full thickness excised lesions	Positive for greater vascularization in US groups at 5 days post op. No significant difference at 7 days pots op	
5	1 MHz	0.5 W/cm ² 1.5 W/cm ²	20% pulsed	Yucatan pigs	Experimental side Full thickness and partial thickness incisions Control group	10 min at 0.5 W/cm ² for 3 days and 1.5 W/cm ² for 2 days 5 minutes at the same intensities similar times	To test if: Low dose US facilitate healing in the early stage of repair?	Positive for tensile strength, collagen deposition, reduction in wound size and mast cell degranulation on the sonated lesions compared to the control. Low dose US facilitates wound healing in the first week of healing	
6	1 MHz	1 W/cm	Continuous	26 Achilles tendons of rats	Treatment group and control group	5 minutes for 9 treatments	To determine the biomechanical effects of US on healing Achilles tendons.	Positive for tensile strength and energy absorption capacity with US treatments in early stage of healing	
7	3 MHz	0.8W/cm ²	Pulsed	76 chicken flexor digitorum profundus	Group 1= control Group 2=Us at 6 weeks Group 3= US at 7 days	3 minutes for 10 days	To compare the effects of flexor tendon healing with US initiated at 6 and at 7 days	Positive for early use of US was significant for tendon healing. No significant difference in tensile strength Positive for better alignment of collagen in the early US group	
8	0.75 MHz 3.0 MHz	0.1W/cm ²	20% pulsed	2 groups of 18 flank skin of adult rats	Group 1= (6)Control, (6)0.75 MHz	5 minutes for 5 days post op	To study the effects of US with sham US on the rate of dermal healing	Positive for accelerating the inflammatory and early proliferative stages of wound healing	

						and (6) 3.0 MHz Group 2 = same	5 minutes for 7 days post op 5 minutes/week for 6 weeks for both groups	To study the effects of US on burns		
9	3.0 MHz	0.25 W/cm ² 0.3 W/cm ²	20% pulsed continuous	Burns on 20 rats		Group 1 = control and 20% US Group 2 = control and continuous US		Negative for enhancing healing of burns		
10	1 MHz	0.5 W/cm ²	pulsed	56 patient with chronic leg ulcers		Group 1 = Standard treatment group Group 2 = standard treatment plus US	1 minutes/probe head area per wound weekly until healing or 12 weeks	To ascertain whether US given weekly in conjunction with standard treatment improves healing rate	Positive. After 12 weeks the proportion of healed ulcers was 20% greater in the US group	
11	3.38 MHz	0.1 W/cm ²	20% pulsed	88 patients		US group Control group	Treatment time varied per wound size. Daily treatments for 5 days/week over 12 week period	To assess the effects of US in the treatment of pressure ulcers as an adjunct to standard treatment	Negative. Data does not support the idea that US speeds up the healing process.	
12	3 MHz	0.2 W/cm ²	1:4 pulsed	22 pressure ulcers		Control group Laser group US/UVC group	US given usually 3 times/week	To compare in patient with SCI the effect of wound healing of nursing care alone or combined with either laser or US/UVC	Positive wound healing in the US/UVC group	
13	1 MHz	1.0 W/cm ²	Not reported in study	38 patients with venous leg ulcers (13 withdrawals)		Control group Treatment group	10 minutes of US twice a week for 8 weeks	To study the effects of US on healing chronic leg ulcers	No significant difference in the proportion of healed ulcers or ulcer area in the US group compared to placebo.	
14	3 MHz	0.8 W/cm ²	20% pulsed	40 patients (18 followed until wound healed)		Control group Treatment group	Minimum of 5 minutes for pressure sores up to 3cm ² . For three times/week	To test the efficacy of US on pressure sores	No significant result US appears to be of value in the treatment of pressure sores, but the authors recommend studies with larger populations involving more than 1000 patients to be statistically significant	

Results

Fourteen papers published met the study selection criteria. Two papers were studies performed In Vitro, seven on animal subjects and five on human subjects. Each paper had a total number of outcomes based on the number of hypotheses being tested. There were a total of 31 possible outcomes from the 14 published papers. Therefore the total number of outcomes exceeds the number of published papers. Table III shows the total number of Positive, Negative or Non significant outcomes. There were a total of 3 positive, 0 negative and 2 non-significant In Vitro studies outcomes. Twelve animal studies were positive, 7 negative and 2 had non-significant outcomes. In the human studies, there were 2 positive, 1 negative and 2 non-significant outcomes. The overall totals were 17 positive, 8 negative and 6 non-significant outcomes. The results of this analysis (17 positive outcomes out of 31) therefore indicate that there is evidence in the literature to suggest that therapeutic US is beneficial in the treatment of open wounds.

Table III. Summary of total number of Positive, Negative, and Non significant outcomes from the published papers.

	Positive Outcome	Negative Outcome	Non significant Outcome	Totals
In Vitro Studies	3	0	2	5
Animal Studies	12	7	2	21
Human studies	2	1	2	5
Totals	17	8	6	31

Discussion

Literature on the efficacy of US in the treatment of open wounds has demonstrated to be somewhat inconclusive. Due to the biophysical effects of US, if applied correctly, according to Dyson (1987), Haar (1987), & Michlovitz (1996), ultrasound therapy should accelerate the wound healing process. Four of the studies used in this analysis, concluded that US would be most beneficial during the early phases of wound healing (Byl et al, 1993, Enwemeka, 1989, Huys et al, 1993 & Young & Dyson, 1990). In the later phase of repair ultrasound treatment does not appear to have any further significant effect. Byl et al. (1993) cautions the clinician not to assume that the effects of ultrasound are consistent throughout all phases of healing or for all types of wounds.

The study by McDiarmid et al (1985) reports that in order for a clinical trial to be statistically significant, 1000 or more patients (wounds) should be included due to all the possible variables involved in wound healing. The number of patients (wounds) used in the human studies in this analysis ranged from 22 to 88, far less than what is recommended in order to obtain a significant outcome due to the many variables involved in the wound healing process.

Clinicians should be cautious when deciding if US treatment should be a part of their wound care treatment. The clinician should be aware of the conflicting data available in the use of US on wound healing. Entry level books on the use of US in open wounds, such as Michlovitz (1996) and McCulloch et al. (1995) suggest the use of 3.0 MHz for the treatment of superficial wounds, however in the studies mentioned in this analysis, there were seven studies using 1.0 MHz and six using 3.0 MHz and two studies

examined the use of US at 0.75 MHz as the frequency. These textbooks also recommend low dose pulsed ultrasound for the treatment of acute wounds, which does appear to be consistent with the literature addressed in this analysis.

Weaknesses of this study were performing the simple voting method of meta-analysis and not performing a more advanced method. This method of analysis has had some criticism. First, it does not incorporate sample size into the vote. As sample size increases, the probability of obtaining a statistically significant result increases. Second, this method does not allow the meta-analysis to determine whether a treatment won by a little or a lot, and the margin of victory is not known. Third, this method has very low power for the range of sample sizes and effect sizes most common in the social sciences. That is, when effect sizes are medium to small, the conventional vote-counting procedure frequently fails to detect the effects. For medium to small effect sizes, the power of this procedure tends to zero as the number of studies to be integrated increases.

Limitations of the study include: limiting articles to the efficacy of US on wounds and not any other conditions, and limiting the analysis to articles published in English only and within the years of 1985 to the present. Another limitation was not being able to perform a specific clinical trial on the efficacy of therapeutic ultrasound on open wounds due to limited sample sizes available.

Conclusion

Specific clinical guidelines cannot be provided for the use of ultrasound on open wounds from this analysis due to the limited human subject studies available that provide a positive outcome. Suggestions for treatment guidelines can be given based on the physiological effects of ultrasound and the physiology of wound healing. In treating

superficial injuries, 3 MHz is recommended and for deeper wounds, 1 MHz is indicated. Low dose pulsed ultrasound has been shown to have positive effects on wound healing during the early stages with regard to increased vascularization and accelerating the inflammatory and early proliferative stages of wound healing.

Clinicians choosing to incorporate therapeutic ultrasound as part of their treatment should be knowledgeable on the effects of US on wound healing. They should also be aware of the limited number of clinical trials available on the efficacy of US on wound healing, the different parameters used for those studies that are available, and the relatively small sample sizes used in most studies that may result in outcomes that are not statistically significant. Well-designed clinical trials are still needed to statistically prove the efficacy of ultrasound in wound healing.

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