Woundshield Background

Selection of ultrasound application parameters is based on the desired effect and the location and density of the tissue to be treated. These decisions are best made by the physician and the therapist experienced in performing therapeutic ultrasound.

Common indications for high frequency ultrasound therapy include treatment of tendon injuries and short-term pain relief. (**1 -3**) Ultrasound has also been shown to promote healing of some acute bone fractures, venous and pressure ulcers, and surgical incisions (**1 ,4 -6**). However, conventional therapeutic ultrasound can cause burns or endothelial damage if applied incorrectly (**1 ,7 ,8**)

Recently, low frequency ultrasound was tested and introduced to the market. The motivation of looking for alternative ultrasound parameters was due to the fact that application of high-frequency US in clinical medicine is limited due to tissue heating. Thus, using low-frequency US with less tissue heating, thereby acting as a "slow release" mechanism, may become the standard care in treating slow-to-heal lesions, skin ulcers and nonunion fractures. In addition it may be able to facilitate protein secretion and enzymatic reactions.

Prescription for a modality

The elements in the prescription for a modality should include indication or diagnosis, choice of modality, location, intensity, and duration and frequency specifications. Before selecting a modality, one must understand the physiologic effects each exerts on tissues. The target tissue, the depth and intensity of heat or cooling desired and patient characteristics are all factors to consider when deciding what modality to use. The patient’s body habitus (amount of adipose tissue), co-morbid conditions (e.g., cancer, neuropathy, peripheral vascular disease), implants (e.g., pacemaker, metallic implants), age, and sex

(during pregnancy) should all be considered in the equation

Low frequency Ultrasound

High power, high frequency ultrasound is defined as ultrasound of 0.5-10 MHz and up to 1500W/cm^2 while low power, low frequency ultrasound is defined as an ultrasound of 20120 kHz and 0.05-1.0 W/cm^2). Low frequency/low intensity US is mainly reflected in the skin or wound surface. Only a small portion of the energy transmitted by the probe reaches deeper tissue layers and the major effect is mechanical effect, which is the opposite for high frequency US that combine mostly thermal with mechanical effects.

There is growing evidence-based information that shows the various clinical effects resulting from low frequency US therapy. A range of biological effects can be induced by ultrasound, depending on the exposure levels used. At low levels, beneficial, reversible cellular effects may be produced, whereas at high intensities instantaneous cell death is sought. The ‘‘low power’’ group includes physiotherapy, fracture repair, sonophoresis, sonoporation and gene therapy. Therapeutic effect through the intensity spectrum is obtained by both thermal and non-thermal interaction mechanisms. At low intensities, acoustic streaming is likely to be significant, but at higher levels, heating and acoustic cavitation will predominate. While useful therapeutic effects are now being demonstrated clinically, the mechanisms by which they occur are often not well understood.

In the physiotherapy setting ultrasound is used mainly in the treatment of soft tissue injuries, for the acceleration of wound healing, the resolution of edema and softening of scar tissue. It is also used, amongst other things, for bone injuries and circulatory disorders. Ultrasound was originally thought of as an alternative diathermy treatment, competing with hot packs, microwave, and radiofrequency methods to produce gentle heating. As the basic understanding of all the therapeutic mechanisms of ultrasound improves, treatment regimes are being altered in an attempt to make use of any beneficial non-thermal mechanisms that may exist (by use of lower intensities and of pulsed beams). There is a dearth of scientifically designed controlled clinical trials, and so the ultrasonic treatment regime used is usually empirically determined, and often to each department’s particular ‘‘recipe’’. Until more rigorous scientific studies are available, the mechanism by which therapeutic benefit, if any, is obtained will be the subject of speculation and it will not be possible to optimize treatments using an understanding of interaction mechanisms. A survey of randomized clinical trials of physiotherapy ultrasound was unable to find a relationship between ‘‘dose’’ and therapeutic outcome, although the majority of effective treatments were pulsed, with spatial average temporal average intensities lying between 0.16 and 0.5W/cm^2 (9)

There is some evidence in the literature that while high intensities of ultrasound can damage bone or delay healing (**1 0,1 1**) low intensities can enhance repair rates and reduce healing times (**1 2,1 3**). It has been shown experimentally in rat fibulae that when ultrasound exposures are carried out during the inflammatory and early proliferative phases of bone repair following fracture, healing can be accelerated, with direct ossification being observed. If treatment is delayed until the late proliferative phase, it is cartilage growth that is stimulated. 1.5MHz ultrasound has been found to be more effective than 3MHz (I_{SATP} ¼ 0.5 W/cm^2, pulsed 2 ms: 8ms for 5 min) (**1 2**). This suggests a non-thermal mechanism of action.

Low intensity ultrasound has also been used for clinical treatment of fracture non-unions (**1 4,1 5**). An additional paper has demonstrated the results of treating 67 patients with nonunions using a commercial device (Exogen GmbH) (**1 6**). This high frequency device operates at 1.5MHz (0.03 W/cm^2 I_{SATA}, 0.065 W/cm^2 I_{SPTA}, 200ms, with a p.r.f. 1kHz). Daily exposures lasting 20min are administered by the patient themselves. Again, no placebo group was presented. Non-union for these patients was defined as a failure to heal for 8 months following fracture. When analyzed on an ‘‘intention to treat’’ basis, repair was found in 82% of patients with a mean healing time of 168 days. Healing rates following surgery have been reported as 68–90% with a mean healing time of 200 days

(**1 7-1 9**).

There are clinical evidences of the beneficial effects of very low ultrasound intensities on bone repair. However, the mechanisms by which this is produced are unclear, and warrant further study. At these low exposure levels, thermal effects are unlikely to be involved.

Ultrasound may be used to increase the penetration of pharmacologically active drugs through the skin. This technique is known as sono- or phonophoresis (**2 0,2 1**). Mechanisms by which sonophoresis is achieved are unclear. It is thought that the stratum corneum is rendered temporally permeable by acoustic cavitation or streaming, thus allowing the enhanced perfusion (**2 0,2 2,2 3**). Low frequencies (less than 100 kHz) appear generally to be more effective than high,

Sonoporation is the term used for the phenomenon by which ultrasound may transiently alter the structure of the cellular membrane, and thus allow enhanced uptake of low and high molecular weight molecules into the cell. There have been a large number of studies in which a synergistic effect between ultrasound and different drugs has been sought (**2 0,2 4**). Many of the studies reported have been carried out in vitro. It should be noted that while effects may be identified in these studies, the mechanisms of action in the aqueous in vitro environment, where acoustic cavitation and streaming may predominate and significant amounts of heating are not to be expected, may not be relevant when exposures are carried out in vivo. Results should therefore be interpreted with caution.

The mechanisms for the enhancement of the thrombolytic effect are poorly understood, but a number have been suggested. It has been proposed that streaming may facilitate the permeation of the drug into the clot, or that the mechanical action of the ultrasound affects the fibrin mesh, allowing better access for the drug

Low frequencies provide the advantage of increased penetration through the skull that may be advantageous in stroke applications. Frequencies in the range 26 kHz–5MHz have been studied (2 5). However, at high intensities, there is the suggestion that these low frequencies can lead to enhanced platelet and fibrin deposition. Investigation of various intensities in the range 1.1–3.2 W/cm^2 Showed that whereas at 0.5–1 W/cm^2 clot lysis was produced, at 4 W/cm2 there was less clot lysis than in the presence of fibrinolytic agents alone (2 6).

Leg ulcers are a big problem for both patients and health service resources.1–3 Most ulcers are associated with venous disease, but other causes or contributing factors include immobility, obesity, trauma, arterial disease, vasculitis, diabetes, and neoplasia. Care for patients with leg ulcers has improved in the past two decades as research based approaches have been adopted.

It appears that exposure to ultrasound during the initial 'inflammatory' phase of tissue repair can lead to an acceleration of this phase, although ultrasound is not in itself an antiinflammatory agent. The second phase of healing is the 'proliferative' stage. This is the stage at which cells migrate to the site of injury and start to divide, granulation tissue is formed, and fibroblasts begin to produce collagen. Ultrasound has been shown to enhance collagen synthesis by fibroblasts and repairing of epithelium (**2 7-2 9**).

The final phase of tissue repair is one of 'remodelling'. There is also evidence that scar tissue treated with ultrasound may be stronger and more elastic that 'normal' scar tissue. During the recent years there is an accumulative data from clinical trials, case reports and observational results demonstrated that ultrasound can accelerate the healing of various ulcers through different mediators (**3 0-3 4**). Moreover, using low frequency ultrasound in burs care was also tested in few cases (**3 5,3 6**). In addition, since ultrasound known as a generator for nitric oxide release, it serves as an auxiliary tool for vasodilatation and pain relief in the treated wound (**3 7-3 8**)

1. Kibler WB, Duerler K. Electrical stimulation and application of heat. In: DeLee J, Drez D, Miller MD. DeLee & Drez's Orthopaedic Sports Medicine: Principles and Practice. 2nd ed. Philadelphia, Pa.: Saunders, 2003:349-51,356-9.
2. Casimiro L, Brosseau L, Robinson V, Milne S, Judd M, Well G, et al. Therapeutic ultrasound for the treatment of rheumatoid arthritis. Cochrane Database Syst Rev 2002;(3):CD003787.
3. Robertson VJ, Baker KG. A review of therapeutic ultrasound: effectiveness studies. Phys Ther 2001;81:1339-50.

4. Cameron MH. Thermal agents: cold and heat, ultrasound, and electrical currents. In: Cameron MH. Physical Agents in Rehabilitation: From Research to Practice. 2nd ed. St. Louis, Mo.: Saunders, 2003:133-259.
5. Van der Windt DA, van der Heijden GJ, van den Berg SG, ter Riet G, de Winter AF, Bouter LM. Ultrasound therapy for musculoskeletal disorders: a systematic review. Pain 1999;81:257-71.
6. Busse JW, Bhandari M, Kulkarni AV, Tunks E. The effect of low-intensity pulsed ultrasound therapy on time to fracture healing: a meta-analysis. CMAJ 2002;166:437-41.
7. Guide to Physical Therapist Practice. Part 1: A description of patient/client management. Part 2: Preferred practice patterns. American Physical Therapy Association. Phys Ther 1997;77:1160–656.Brosseau L, Welch V, Wells G, DeBie R, Gam A, Harman K, et al. Low level laser therapy (classes I, II and III) for treating osteoarthritis. Cochrane Database Syst Rev 2004;(3):CD002046.
8. Flemming K, Cullum N. Therapeutic ultrasound for venous leg ulcers. Cochrane Database Syst Rev 2000;(4):CD001180.
9. Robertson, V. 2002. Dosage and treatment response in randomised clinical trials of therapeutic ultrasound. Physical Ther. Sport 3, 124–133.
10. Reher, P., Elbeshir, E.-N.I., Harvey, W., Meghji, S., Harris, M., 1997. The stimulation of bone formation in vitro by therapeutic ultrasound. Ultrasound Med. Biol. 23, 1251–1258.
11. Tsai, C.-L., Chang, W.H., Liu, T.-K., 1992. Preliminary studies of duration and intensity of ultrasonic treatments on fracture repair. Chin. J. Physiol. 35, 21–26.
12. Dyson, M., Brookes, M., 1983. Stimulation of bone repair by ultrasound. In: Lerski, R.A., Morley, P. (Eds.), Ultrasound ‘82. Pergamon Press, Oxford, pp. 61–66.
13. Pilla, A.A., Mont, M.A., Nasser, P.R., Khan, S.A., Figueiredo, M., Kaufman, J.J., Siffert, R.S., 1990. Non-invasive low intensity pulsed ultrasound accelerates bone healing in the rabbit. J. Orthopaed. Trauma 4, 246–253.
14. Frankel, V.H., 1998. Results of prescription use of pulsed ultrasound therapy in fracture management. In: Szabo, Z., Lewis, J.E., Fantini, G.A., Salvagi, R.S. (Eds.), Surgical Technology International VII. Universal Medical Press, San Francisco, pp. 389–393.
15. Rutten S, Nolte PA, Korstjens CM, van Duin MA, Klein-Nulend J. Low-intensity pulsed ultrasound increases bone volume, osteoid thickness and mineral apposition rate in the area of fracture healing in patients with a delayed union of the osteotomized fibula Bone: 2008 Aug;43(2):348-54.
16. Gebauer, D., Mayr, E., Orthner, E., Ryaby, J.P., 2005. Low-intensity pulsed ultrasound: effects on non-unions. Ultrasound Med. Biol. 31, 1391–1402.
17. Healy, W.L., Jupiter, J.B., Kristiansen, T.K., White, R.R., 1990. Nonunion of the proximal humerus. J. Orthop. Trauma 4, 424–431.
18. Barquet, A., Fernandez, A., Luvizio, J., Masliah, R., 1989. A combined therapeutic protocol for aseptic nonunions of the humeral shaft. J.Trauma 29, 95–98.

19. Webb, L.X., Winquist, R.A., Hansen, S.T., 1986. Intramedullary nailing and reaming for delayed union or non-union of the femoral shaft. Clin. Orthop. 212, 133–141.
20. Mitragotri, S., 2005. Healing sound: the use of ultrasound in drug delivery and other therapeutic applications. Nat. Rev.: Drug Discovery 4, 255–260.
21. Mitragotri, S., Kost, J., 2004. Low frequency sonophoresis: a review. Adv. Drug. Deliv. Rev.
56, 589–601.

1. Mitragotri, S., Blankschtein, D., 1995. Ultrasound mediated transdermal protein delivery. Science 269, 850–853.
2. Tezel, A., Mitragotri, S., 2003. Interactions of inertial cavitation bubbles with stratum corneum lipid bilayers during low frequency sonophoresis. Biophys. J. 85, 3502–3512.
3. Rosenthal, I., Sostaric, J.Z., Riesz, P., 2004. Sonodynamic therapy—a review of the synergistic effects of drugs and ultrasound. Ultrason. Sonochem. 11, 349–363.
4. Daffertshofer, M., Hennerici, M., 2003. Ultrasound in the treatment of ischemic stroke.
Lancet—Neurol. 2, 283–290.

1. Nilsson, A.M., Odselius, R., Roijer, A., et al., 1995. Pro-and antifibrinolytic effects of ultrasound on streptokinase induced thrombolysis. Ultrasound Med. Biol. 21, 833–840.
2. Zhang, ZJ. Huckle, J. Francomano, CA. Spencer, RG. The effects of pulsed low-intensity ultrasound on chondrocyte viability, proliferation, gene expression and matrix production Ultrasound Med Biol. 2003 Nov;29(11):1645-51
3. Hill, GE. Fenwick, S. Matthews, BJ. Chivers, RA. Southgate, J. The effect of low-intensity pulsed ultrasound on repair of epithelial cell monolayers in vitro. Ultrasound Med Biol. 2005 Dec;31(12):1701-6
4. Zhou, S. Schmelz, A. Seufferlein, T. Li, Y. Zhao, J. Bachem, MG. Molecular mechanisms of low intensity pulsed ultrasound in human skin fibroblasts J Biol Chem. 2004 Dec 24;279(52):54463-9
5. Kavros, SJ. Miller, JL. Hanna, SW. Treatment of ischemic wounds with noncontact, lowfrequency ultrasound: the Mayo clinic experience, 2004-2006 Adv Skin Wound Care. 2007 Apr;20(4):221-6
6. Tan, J. Abisi, S. Smith, A. Burnard, KG. A painless method of ultrasonically assisted debridement of chronic leg ulcers: a pilot study Eur J Vasc Endovasc Surg. 2007 Feb;33(2):234-8
7. Breuing, KH. Bayer, L. Neuwalder, J. Orgill, DP. Early experience using low-frequency ultrasound in chronic wounds Ann Plast Surg. 2005 Aug;55(2):183-7
8. Uhlemann, C. Heinig, B. Wollina, U. Therapeutic ultrasound in lower extremity wound Management. Int J Low Extrem Wounds. 2003 Sep;2(3):152-7
9. Johnson S. Low-frequency ultrasound to manage chronic venous leg ulcers J. Nurs. 2003 Oct;12(19 Suppl):S14-24
10. Waldrop, K. Serfass, A. Clinical effectiveness of noncontact, low-frequency, nonthermal ultrasound in burn care. Ostomy Wound Manage. 2008 Jun;54(6):66-9

11. Samies, J. Gehling, M. Acoustic pressure wound therapy for management of mixed partial- and full-thickness burns in a rural wound center. Ostomy Wound Manage. 2008 Mar;54(3):56-9
12. Sugita, Y. Mizuno, S. Nakayama, N. Iwaki, T. Murakami, E. Wang, Z. Nitric oxide generation directly responds to ultrasound exposure Ultrasound Med Biol. 2008 Mar;34(3):487-93

1. Altland, OD. Dalecki, D. Suchkova, VN. Francis, CW. Low-intensity ultrasound increases endothelial cell nitric oxide synthase activity and nitric oxide synthesis. Thromb. Haemost. 2004 Apr;2(4):637-43