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Discussion: Advanced Technologies to Improve Wound Healing: Electrical Stimulation, Vibration Therapy, and Ultrasound—What Is the Evidence?

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This article is a must read literature review of 3 forms of physical energy; electrical stimulation energy (ESE), vibration energy (VE), and ultrasound energy (USE) that when delivered therapeutically into wound tissues elicit biophysical responses that enhance wound healing. The authors acknowledge that enhanced chronic wound healing with ESE is supported with more research evidence from in vitro, animal, and clinical trials.
ESE as stated includes the biological skin battery voltage signals that exist in healthy and wound tissues and that exogenous ESE signals delivered into chronic wounds may amplify the biological signals, leading to enhanced cellular responses and healing. However, as indicated, the evidence supporting the alluded to phenomenon of galvanotaxis or electrotaxis comes primarily from in vitro research.\textsuperscript{1-3} In addition, numerous in vitro research publications are cited that have reported enhanced angiogenesis,\textsuperscript{4} protein and DNA synthesis,\textsuperscript{5,6} and augmented migration of fibroblasts\textsuperscript{7} and endothelial cells\textsuperscript{3} all of which the authors indicate a need of further verification of mechanisms involved from in vivo animal and human studies.

On the use of ESE for additional clinical uses related to wound healing, the authors alert readers to several possible future applications that are presently supported by in vitro and human research. Included are wound bioburden studies showing that positively charged silver ions embedded in dressing materials have enhanced antimicrobial effects when anodal current is applied to the dressings.\textsuperscript{8} This has obvious implications for the treatment of infected wounds. The recent findings of ESE stimulated angiogenesis in ischemic patients and acute human skin wounds is very exciting and is supported by increased skin flap viability in animals, but more research is needed.

The use of ESE to determine its effects on chronic wound healing in humans has resulted in publications that report wounds treated with ESE plus standard wound care heal more than wounds treated with standard wound care alone.\textsuperscript{9-12} Also, readers of ESE wound healing research may not understand that clinical trials that have used different pulse frequencies, durations, and amplitudes produce an electrical current charge delivered to the wound that falls within the range of 250 to 500 μC/s as mentioned by the authors. This range of charge is the dosage of the reproducible electrical energy delivered to the wound tissues that have resulted in positive wound healing outcomes.\textsuperscript{11,12}

VE is relatively new as far as wound treatment is concerned. VE is a form of mechanical energy that is generated by a number of sources, including megahertz and kilohertz ultrasound. However, the vibrations described in the studies cited were low intensity and low
frequency with 2 animal studies\textsuperscript{13,14} and 2 human subject studies.\textsuperscript{15,16} The interesting effects elicited by VE in the animal studies included angiogenesis and granulation tissue formation, as well as increases in wound levels of monocyte chemoattractant protein-1, vascular endothelial growth factor, and insulin-like growth factor-1. The VE treatment of pressure ulcers in humans also produced rather surprising results with 8 of 16 wounds closed with 15-minute treatments 3 times daily. Other studies cited enhanced blood flow in different tissue types. The future of VE for wound healing likely will depend on the outcomes of future human subject research and the instrumentation that becomes available for administering this form of physical energy to intractable wounds.

USE can be high-frequency (MHz) mechanical energy that when produced at 1 and 3 MHz is used to introduce thermal energy into musculoskeletal tissues to enhance blood flow or to phonophoretically deliver analgesic and anti-inflammatory medications to tissues. USE at high frequencies is applied to the patient through transducer gel coupling direct contact or noncontact via water immersion of the body part. USE for wound healing applications is low-frequency (kHz) nonthermal, mechanical energy that is delivered through noncontact and produced at frequencies of 22.5, 25, 35, and 40 kHz. USE delivered to tissues at high and low frequencies has a physical property described by the authors as cavitation, which refers to the formation of microbubbles that develop in biological fluids (blood, lymph, and wound exudates) because of the accumulation of microsized gas bubbles (cavities) that form in the path of the USE beam. Periods of high and low pressures in the USE beam can cause the microbubbles to decrease and increase in size but not to the point of rupture or implosion with stable MHz USE. Low-frequency kHz USE cavitation is unstable because at a sufficiently high intensity, microbubbles significantly increase in size and violently implode during the low-pressure part of the wave cycle releasing energy that can be used to effectively debride necrotic tissue from wound surfaces. It is important to remember that the cavitation effect on efficacy of debridement with the 4 kHz frequencies mentioned is inversely related to frequency. The other research evidence related to the effects of kHz noncontact USE is covered exceptionally well.
I applaud the authors for their time, effort, and expertise spent in finding the research evidence that best supports their coverage of numerous other physical energies that elicit biophysical responses from cells, molecules, microbes, and various tissues related to wound healing. All 3 of the physical energies they addressed are used in physical therapy practice on a daily basis depending on the specialty area of practice. In fact, all of the physical energies fall under the domain of “physical” therapy. Ultimately, the same work needs to be done for electromagnetic energies [infrared (nonthermal), ultraviolet, laser, and pulsed radio frequency] and other mechanical energies that include positive and negative pressure, shockwaves, traction, and thermal energy (infrared, cryotherapy, and conductive heat) and electrical energy (microcurrents, AC, DC, and PC).

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