Marquette University e-Publications@Marquette

Physical Therapy Faculty Research and Publications

Health Sciences, College of

9-1-2016

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

Luther C. Kloth Marquette University, luther.kloth@marquette.edu

Accepted version. *Plastic and Reproductive Surgery,* Vol. 138, No. 3S (September 2016): 105S-106S. DOI. © 2016 American Society of Plastic Surgeons. Used with permission.

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

Luther C. Kloth

College of Health Sciences, Department of Physical Therapy, Marquette University, Milwaukee, WI

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.

Plastic and Reconstructive Surgery, Vol 138, No. 3 supplement (September 2016): pg. 1055-1065. <u>DOI</u>. This article is © American Society of Plastic Surgeons and permission has been granted for this version to appear in <u>e-</u><u>Publications@Marquette</u>. American Society of Plastic Surgeons does not grant permission for this article to be further copied/distributed or hosted elsewhere without the express permission from American Society of Plastic Surgeons.

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.^{1–3} In addition, numerous in vitro research publications are cited that have reported enhanced angiogenesis,⁴ protein and DNA synthesis,⁵,⁶ and augmented migration of fibroblasts⁷ and endothelial cells³ 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.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.^{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 μ C/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.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

Plastic and Reconstructive Surgery, Vol 138, No. 3 supplement (September 2016): pg. 1055-1065. DOI. This article is © American Society of Plastic Surgeons and permission has been granted for this version to appear in <u>e-</u> <u>Publications@Marquette</u>. American Society of Plastic Surgeons does not grant permission for this article to be further copied/distributed or hosted elsewhere without the express permission from American Society of Plastic Surgeons.

frequency with 2 animal studies¹³,¹⁴ and 2 human subject studies.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.

Plastic and Reconstructive Surgery, Vol 138, No. 3 supplement (September 2016): pg. 1055-1065. <u>DOI</u>. This article is © American Society of Plastic Surgeons and permission has been granted for this version to appear in <u>e-</u> <u>Publications@Marquette</u>. American Society of Plastic Surgeons does not grant permission for this article to be further copied/distributed or hosted elsewhere without the express permission from American Society of Plastic Surgeons. I applaud the authors for their time, effort, and expertise spent in finding the research evidence that best supports their coverage of 3 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).

REFERENCES

- ¹McCaig CD, Rajnicek AM, Song B, et al. Controlling cell behavior electrically: current views and future potential. *Physiol Rev* 2005 85 943–978
- ²Pullar CE. The biological basis for electric stimulation as a therapy to heal chronic wounds. *J Wound Technol* 2009 620–24
- ³Zhao M. Electrical fields in wound healing-an overriding signal that directs cell migration. *Semin Cell Dev Biol* 2009 20 674–682
- ⁴Ud-Din S, Sebastian A, Giddings P, et al. Angiogenesis is induced and wound size is reduced by electrical stimulation in an acute wound healing model in human skin. *PLoS One* 2015 10 e0124502
- ⁵Bourguignon GJ, Bourguignon LY. Electric stimulation of protein and DNA synthesis in human fibroblasts. *FASEB J* 1987 1398–402
- ⁶Cheng N, Van Hoof H, Bockx E, et al. The effects of electric currents on ATP generation, protein synthesis, and membrane transport of rat skin. *Clin Orthop Relat Res* 1982 264–272
- ⁷Uemura M, Maeshige N, Koga Y, et al. Monophasic pulsed 200-muA current promotes galvanotaxis with polarization of actin filament and integrin alpha2beta1 in human dermal fibroblasts. *Eplasty* 2016 16 e6
- ⁸Spadaro JA, Chase SE, Webster DA. Bacterial inhibition by electrical activation of percutaneous silver implants. *J Biomed Mater Res* 1986 20 565–577
- ⁹Kloth LC. Electrical stimulation technologies for wound healing. *Adv Wound Care (New Rochelle)* 2014 381–90
- ¹⁰Houghton PE. Clinical trials involving biphasic pulsed current, microcurrent, and/or low-intensity direct current. Adv Wound Care (New Rochelle) 2014 3 166–183

Plastic and Reconstructive Surgery, Vol 138, No. 3 supplement (September 2016): pg. 1055-1065. <u>DOI</u>. This article is © American Society of Plastic Surgeons and permission has been granted for this version to appear in <u>e-</u><u>Publications@Marquette</u>. American Society of Plastic Surgeons does not grant permission for this article to be further copied/distributed or hosted elsewhere without the express permission from American Society of Plastic Surgeons.

- ¹¹Polak A, Franek A, Taradaj J. High-voltage pulsed current electrical stimulation in wound treatment. Adv Wound Care (New Rochelle) 2014 3 104–117
- ¹²Kloth LC. Wound healing with conductive electrical stimulation- it's the dosage that counts. J Wound Technol 2009 630–37
- ¹³Weinheimer-Haus EM, Judex S, Ennis WJ, et al. Low-intensity vibration improves angiogenesis and wound healing in diabetic mice. *PLoS One* 2014 9 e91355
- ¹⁴Sari Y, Sanada H, Minematsu T, et al. Vibration inhibits deterioration in rat deep-tissue injury through HIF1-MMP axis. *Wound Repair Regen* 2015 23 386–393
- ¹⁵Arashi M, Sugama J, Sanada H, et al. Vibration therapy accelerates healing of stage I pressure ulcers in older adult patients. *Adv Skin Wound Care* 2010 23 321–327
- ¹⁶Wilson JM, Arseculeratne YM, Yang Y, et al. Healing venous ulcers with cycloidal multidirectional vibration therapy. *J Wound Care* 2002 11 395–398