Low-Frequency Ultrasound in Wound Healing: Cavitating its way into Patient Wounds

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Disclosures

• None
Therapeutic Ultrasound

- Modality that delivers energy through mechanical vibration in the form of sound waves
- These frequencies are above the detection by the human ear
Musculoskeletal Ultrasound: Therapeutic

- MHz (1.0 – 3.0 watts/cm²)
- Gel or water bath is needed to transmit energy (coupling medium)
- Transducer needs to be in contact with the substrate
Low-Frequency Ultrasound: Therapeutic

- kHz (22.5 - 40 kHz)
- Contact or non-contact system
- Saline solution is atomized at the transducer tip (55 - 60 micron particle)
- Acoustic streaming carries the small particles to the wound surface
- Cavitation at the surface occurs
  - The effect to a cell wall or cell membrane has different outcomes
Delivery of Low-Frequency Ultrasound

- Contact
- Non-contact
- Both
Science and Applications of Low-Frequency US

**Stages of Wound Healing**
- Inflammatory
- Proliferative
- Remodeling

**Low Frequency US applications:**
- Acute Wounds
  - High velocity, blunt trauma, degloving, lacerations, crush injuries
- Chronic Wounds
  - DFU, Arterial, Venous, Neuropathic, Pressure, Metabolic, Infectious, Factitious, Radiation
- Burns
  - 2\textsuperscript{nd} and 3\textsuperscript{rd} degree
Wound Healing Science: What is Important

Wound Bed Preparation
• Debridement
• Infection
• Arterial
• Venous
• Moisture Balance
• Nutrition
• Offloading
• Compression

Triad predisposing to LE amputation
(72% of non-traumatic amputations were preceded)
• Minor trauma
• Cutaneous ulceration
• Wound healing failure

Evidence Base Medicine Validating the Efficacy of Low-Frequency Ultrasound in Wound Healing

**Basic Science**
- Antimicrobial
- Disrupts Biofilm
- Increases Microcirculation
- Increases Angiogenesis
- Increased Fibroblast Activity
- Increased Collagen Deposition
- Release of Growth Factors
- Cytokine and MMP 9 Reduction

**Clinical Science**
- Diabetic Foot Ulcers
- Ischemic Ulcers
- Venous Leg Ulcers
- Neuropathic Ulcers
- Metabolic Disease with Ulcers
- Autoimmune Disease with Ulcers
- Radiation Ulcers
- Burns
Current literature supporting LFU use in wound healing

1 Meta-analysis
8 Prospective Randomized Controlled Trials
3 Prospective Studies
7 Retrospective Studies
30 Articles – Case Series
> 100 Abstract/Poster Presentations
Antimicrobial Effect

SEM / TEM 40k Mag
Staph. aureus Experimental

Antimicrobial Effect

SEM / TEM 40k Mag

P. aeruginosa Experimental

Antimicrobial and Biofilm Disruption

• **P. aeruginosa, S. epidermidis, S. aureus** - planktonic cells
  • Decreased by a mean of 5.10, 4.99 and 5.22 log$_{10}$ cfu/ml with 4 min of treatment

• **P. aeruginosa, S. epidermidis, S. aureus** – biofilm
  • Deceased by a mean of 1.34, 1.46, and 1.02 log$_{10}$ cfu/cm$^2$ with 10 min of treatment

• Increased activity of fibroblast DNA synthesis
  • Increased Extracellular signal-related kinases (ERK), 2 hrs - 2 days
  • Increased c-Jun N terminal kinase (JNK), 2 hrs - 2 days
• Increased KGF - promotes the proliferation and migration of keratinocytes
• Increased TGF-β – stimulates the regeneration of soft tissue and production and deposition of collagen by fibroblasts
Decreased Pro-Inflammatory Cytokines, MMP 9

- Pilot study of DFU patients
- Biochemical and histological analysis indicated a trend towards reduction of pro-inflammatory cytokines (IL-6, IL-8, IL-1B, TNF-a)
- Decrease in MMP-9

**Clinical Evidence Based Medicine**


- 40.7% vs. 14.3% DFU healing
- LFU 9.12 weeks vs. 11.74 weeks


- 63% vs. 29% > 50% healing in 12 weeks
- TcPO$_2$: 0-20mmHg
  - 21-40mmHg
Clinical Evidence Based Medicine


  - 62% vs. 45% wound reduction after 4 weeks of treatment
  - Pain score reduction: 3.0 to 0.6 vs. 3.0 to 2.4


  - 163 LFU vs. 47 SOC
  - 53% vs. 32% healing of all wound etiology
  - Ischemic, Venous, Neuropathic, Multifactorial
    - All represented at least 50% or greater healing with LFU vs. SOC
Low-Frequency Ultrasound Medical Devices

- CUSA Tissue Ablation - Integra LifeSciences
- MIST Therapy System - Alliqua Biomedical
- Qoustic Wound Therapy System - Arobella Medical
- SonicOne - Misonix, Inc.
- Sonoca 180 - Söring, Inc.
Thank you