# Analysis of treatment protocols: application of ESWT for wound healing disorders

Shock waves are high-energy acoustic waves characterized by an initial rise of high pressure within a very short rise time, followed by a low tensile amplitude.
Extracorporeal shock wave therapy has been documented to have various effects on bones and soft tissue. ESWT acts through mechanotransduction and leads to biological responses at cellular level including the release of angiogenic growth factors known to play an important role in wound healing, associated with neovascularization, improved blood supply, cell proliferation and a significant bacterial effect.
Recent researches show that shock waves have highly beneficial effects on skin lesions since they stimulate the healing processes and in acute conditions appears to initiate a more rapid and effective healing phase.

Shockwave energy, frequency, number of pulses and number of re-treatments are important characteristics of treatment description in order to compare different ESWT studies and standardize shock wave treatment for various indications.

For shock waves application on wounds the number of pulses depends on the wound size.
Furthermore, the number of treatments is very case specific and depends on the type of wound healing disorders: some wounds react very well with fewer treatments while others require more treatments.

The following table shows an overview of recently published literature and MTS studies for wound indications, showing positive results and proving the effectiveness of ESWT in wound healing:

## HUMAN STUDIES

## MTS Spark Wave Therapy - Scientific Research: Wounds

| RESEARCH INSTITUTION | INDICATION | PUBLICATION | AUTHOR | JOURNAL | IMPULSES AND ENERGY FLUX DENSITY | RESULTS |
|---|---|---|---|---|---|---|
| Centre for Severe Burns with Plastic Surgery, Unfallkrankenhaus Berlin, Berlin, Germany | **Second degree burn wounds** Clinical application | **Prospective randomized phase II trial of accelerated reepithelialization of superficial second-degree burn wounds using extracorporeal shock wave therapy.** | Ottomann C, Stojadinovic A, Lavin P, et al. | *Ann Surg*. 2012; 255(1):23-9. | **100 impulses per $cm^2$ 0.1 $mJ/mm^2$** | *Pos.* 100% |
| Institute for Neuropalliative Rehabilitation, Royal Hospital for Neuro-disability, London, UK | **Chronic decubitus ulceration** Clinical application | **Randomized control of extracorporeal shock wave therapy versus placebo for chronic decubitus ulceration.** | Larking AM, Duport S, Clinton M, et al. | *Clin Rehabil.* 2010; 24(3):222-9. | **200 + 100 impulses per $cm^2$ 5 pulses per sec 0.1 $mJ/mm^2$** | *Pos.* - Completely healed: 74% - 10% had 50% of epithelialization |
| Centre for Severe Burns with Plastic Surgery, Unfallkrankenhaus Berlin, Berlin, Germany | **Re-epithelization of skin graft donor sites** Clinical application | **Prospective randomized trial of accelerated re-epithelization of skin graft donor sites using extracorporeal shock wave therapy.** | Ottomann C, Hartmann B, Tyler j, et al. | *J Am Coll Surg* 2010; 211(3):361-7. | **100 impulses per $cm^2$ 0.1 $mJ/mm^2$** | *Pos.* |
| Chang Gung Memorial Hospital, Kaohsiung Medical Center, Chang Gung University College of Medicine, Kaohsiung, Taiwan | **Diabetic foot ulcers** Clinical application | **Extracorporeal shockwave treatment for chronic diabetic foot ulcers.** | Wang C, Kuo Y, Wu R, et al. | *J Surg Res*. 2009; 152:96-103. | **300 + 100 impulses per $cm^2$ 0.11 $mJ/mm^2$** | *Pos.* - Completely healed: 31% - Improved: 58% |
| Centre for Severe Burns with Plastic Surgery, Unfallkrankenhaus Berlin, Berlin, | **Termal lesion** Clinical application | **Accelerated reepitheliasation of a IIb° scald through extracorporeal shock wave therapy** | Ottoman C, Thiele R, Hartmann B | *GMS Verbrennungmedizin,2009, 3: Doc01* | **100 impulses per $cm^2$ 0.1-0.14 $mJ/mm^2$** | *Pos.* |

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|---|---|---|---|---|---|---|
| Germany | | | | | | |
| Department of Cardiothoracic Surgery, Medical University of Vienna, Austria | **Wound healing after vein harvesting** Clinical application | **Prophylactic low-energy shock wave therapy improves wound healing after vein harvesting for coronary artery bypass graft surgery: A prospective, randomized trial.** | Dumfarth J, Zimpfer D, Vögele-Kadletz, et al. | *Ann Thorac Surg.* 2008; 86:1909-13. | **25 per cm**<br>**0.1 mJ/mm²** | *Pos.* |
| AUVA-Trauma Center Meidling, Vienna, Austria | **Chronic wounds** Clinical application | **Shock wave therapy for acute and chronic soft tissue wounds: A feasibilty study.** | Schaden W, Thiele R, Kolpl C, et al. | *J Surg Res.* 2007; 143:1-12. | **100 per cm²**<br>**0.1 mJ/mm²** | *Pos.* 75% |

## ANIMAL STUDIES

## MTS Spark Wave Therapy - Scientific Research: Wounds

| RESEARCH INSTITUTION | INDICATION | PUBLICATION | AUTHOR | JOURNAL | IMPULSES AND ENERGY FLUX DENSITY | RESULTS |
|---|---|---|---|---|---|---|
| Ludwig Boltzmann Institute for Experimental and Clinical Traumatology, Vienna, Austria | **Tissue revascularisation** Animal model | **Extracorporeal shockwave therapy (ESWT) minimizes ischemic tissue necrosis irrespective of application time and promotes tissue revascularization by stimulating angiogenesis.** | Mittermayer R, Hartinger J, Antonic V, et al. | *Ann Surg.* 2011; 253(5):1024-32. | **300 impulses per cm²**<br>**5 pulses per sec**<br>**0.1 mJ/mm²** | *Pos.* |
| Chang Gung Memorial Hospital, Kaohsiung Medical Center, Chang Gung University College of Medicine, | **Enhanced wound healing in rat model of STZ-induced diabetes** Animal model | **Extracorporeal shock-wave therapy enhanced wound healing via increasing topical blood perfusion and tissue regeneration in a rat model of** | Kuo, YR, Wang CT, Wang FS et al. | *Wound Rep Reg*. 2009; 17:522-530. | **800 impulses per cm²**<br>**0.9 mJ/mm²** | *Pos.* |

| | | | | | | |
|---|---|---|---|---|---|---|
| Kaohsiung, Taiwan | | **STZ-induced diabetes.** | | | | |
| Naval Medical Research Center, Combat Casualty Care Department of Regenerative Medicine, Silver Spring, USA | **Burn injury** Animal model | **Extracorporeal shock wave therapy surpresses the early proinflammatory immune response to a severe cutaneous burn injury.** | Davis T, Stojadinovic A, Anam K, et al. | *Int Wound J.* 2009; 6:11-21. | **200 impulses per cm$^2$ 5 pulses per sec 0-1 mJ/mm$^2$** | *Pos.* - Significant reduction of neutrophils: 60-68% - Significant reduction of macrophages: 55-66% |
| Walter Reed Army Medical Center, Combat Wound Initiative Program, Department of Surgery, Washington, USA | **Angiogenic response in skin isografts** Animal model | **Angiogenic response to extracorporeal shock wave treatment in murine skin isografts.** | Stojadinovic A, Elster E, Anam EA, et al. | *Angiogenesis*. 2008; 11(4):369-380. | **200 impulses per cm$^2$ 3 pulses per sec 0.1 mJ/mm$^2$** | *Pos.* |
| University of Kentucky Chandler Medical Center, Division of plastic and reconstructive surgery, Department of Internal Medicine and College of Dentistry, Lexington, KY | **Skin flap model** Animal model | **A study of the biological factors and wound healing of a skin flap model treated with unfocused extracorporeal shockwave therapy** | Edelmann S, Fink BF, et al. | *University of Kentucky Chandler Medical Center* | **500 impulses per cm$^2$ 0.15 mJ/mm$^2$** | *Pos.* |
| Ludwig Boltzmann Institute for experimental and clinical Traumatology, Austrian Cluster for Tissue Regeneration –Trauma Center Meidling, AUVA, Vienna,Austria | **Skin flap model** Animal model | **How many shockwaves are enough? Dose-response relationship in ischemic challenged tissue** | Mittermayr R, Hartinger J, Hofmann M, et al. | *Annual Congress ISMST 2008, Abstract No. 64* | **30 impulses per animal** **300 impulses per animal** **1000 impulses per animal** | *Best treatment:* **300 impulses per animal** |

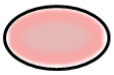
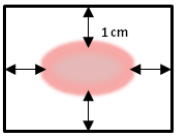
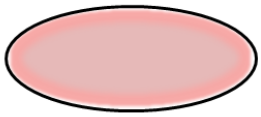
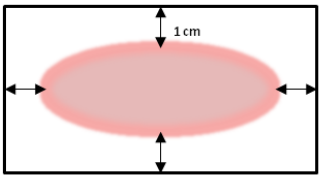
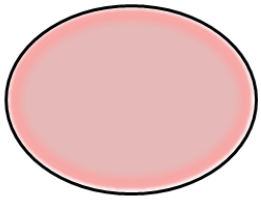
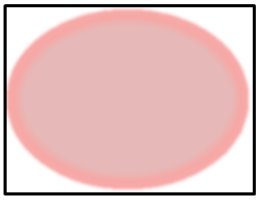
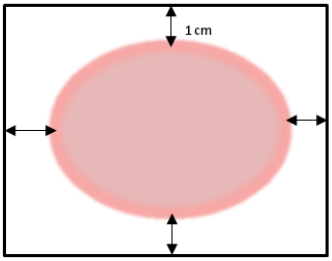
# Comparison treatment protocols Wang et al. (energy-impulses-intervals)

| | Wang et al. (2009) "Extracorporeal shock wave treatment for chronic diabetic foot ulcers" | Wang et al. (2011) "Treatment of diabetic foot ulcers: a comparative study of extracorporeal shockwave therapy and hyperbaric oxygen therapy" |
|---|---|---|
| | MTS Orthowave180<br>New: Orthogold100 | Sanuwave DermaPACE |
| **Indication** | Chronic diabetic foot ulcers | Chronic diabetic foot ulcers |
| **Impulses** | 300 + ($cm^2$ x 10)<br>Total surface | 500 + ($cm^2$ x 8)<br>1 cm plus in all directions |
| **Energy Flux Density** | Unfocused<br>0.11 $mJ/mm^2$ | Focused<br>0.23 $mJ/mm^2$ |
| **Intervals** | Once every 2 weeks<br>(total 3 treatments in 6 weeks) | 2 times per week for 3 weeks<br>(total of 6 treatments) |

# PROTOCOL CALCULATION ANALYSIS

| | | MTS Dermagold100 | Sanuwave DermaPACE | X wound size: (1x2) $cm^2$ | Y wound size: (2x5) $cm^2$ | Z wound size: (4x5) $cm^2$ |
|---|---|---|---|---|---|---|
| OLD | A) MTS IFU | 100 shocks/$cm^2$ | | 157 | 785 | 1587 |
| OLD | B) MTS User guide | 350 + ($cm^2$ x 10) | | 365,7 | 428 | 507 |
| NEW | C) MTS Proposal I | 50 shocks/$cm^2$ Total surface | | 100 | 500 | 1000 |
| NEW | D) MTS Proposal II | 350 + ($cm^2$ x 30) Total surface | | 410 | 650 | 950 |
| NEW | E) MTS Proposal III | 30 shocks/$cm^2$ Total surface | | 60 | 300 | 600 |
| NEW | F) MTS Proposal IV | 350 + ($cm^2$ x 20) Total surface | | 390 | 550 | 750 |
| | G) Sanuwave Measurement | | 500 + ($cm^2$ x 8) 1 cm plus in all directions | 596 | 724 | 836 |

# Examples of calculation impulses

| | MTS old | MTS new | Sanuwave |
|---|---|---|---|
| X |  Wound size (1x2) cm² total surface 1.57 cm² |  Wound size (1x2) cm² total surface 2 cm² |   Wound size (1x2) + 1 cm in all directions: 12 cm² |
| Y |  Wound size (2x5) cm² total surface 7.85 cm² |  Wound size (2x5) cm² total surface 10 cm² |   Wound size (2x5) + 1 cm in all directions: 28 cm² |
| Z |  Wound size (4x5) cm² total surface 15.7 cm² |  Wound size (4x5) cm² total surface 20 cm² |   Wound size (4x5) + 1 cm in all directions: 42 cm² |

| MTS old | | | MTS new | | | Sanuwave | |
|---|---|---|---|---|---|---|---|
| A | 157 | | C | 100 | E 60 | G | 596 |
| B | 365,7 | | D | 410 | F 390 | | |
| A | 785 | | C | 500 | E 300 | G | 724 |
| B | 428 | | D | 650 | F 550 | | |
| A | 1587 | | C | 1000 | E 600 | G | 836 |
| B | 507 | | D | 950 | F 750 | | |

Conclusions:

The different way to calculate the surface of the wound and the number of required impulses can lead to different results!

As reported in the analysed literature studies (both human and animal studies), most of them showed a number of impulses equal to 100 impulses per $cm^2$.
There is only one scientific evidence for a doses-outcome-relation from Mittermayr et al., who investigated skin flap outcome in respond to various total amounts of impulses, in an animal flap model.
In the ischemic area of a rodent epigastric flap, different amounts of total shock wave impulses were applied (30, 300, and 1000) to reduce tissue necrosis. They found out that the best dose is 300 impulses. Thus, they showed that more impulses are not necessary and that a higher amount does not improve the final outcome.

The proposed protocol reflects also the latest Wang et al. study (2011) in which it is shown that the protocol with 8 impulses per cm2 is similar to the one used for Dermapace, but the energy flux density is different: in Wang study they used the double amount of energy.

Based on this scientific paper, a certain minimum dose is required and the maximum doses should be limited. Therefore it is justified to limit the impulses with 20 impulses per $cm^2$, plus a minimum quantity equal to 350 shocks (Proposal IV). This means to have more shocks on small wounds, and less shocks in large wounds compared to a linear formula, used in previous protocols.

Konstanz, 20.06.2013
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