ESWT in skin & aesthetic indications

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Disclosures Prof. Knobloch, FACS

Lecturer & travel expenses

Publishers honoraries for books & chapters

- Springer
- Thieme
- UNI-MED Verlag AG
- Level 10
- De Gruyter

ISMST Beijing 2019 Conference
ESWT in skin graft epithelization
3 days faster healing

Prospective Randomized Trial of Accelerated Re-epithelization of Skin Graft Donor Sites Using Extracorporeal Shock Wave Therapy

Christian Ottmann, MD, Bernd Hartmann, MD, Josh Tyler, MD, Heike Maier, MD, Richard Thiele, MD, Wolfgang Schaden, MD, Alexander Stojadinovic, MD, FACS

Figure 2. Time to complete split thickness skin graft donor site re-epithelialization in patients with and without single postharvest defocused shock wave treatment to the donor site. ESWT, extracorporeal shock wave therapy.

3 days faster healing by ESWT
ESWT in 2a° burn injuries
3 days faster healing

Randomized Clinical Trial

Prospective Randomized Phase II Trial of Accelerated Reepithelialization of Superficial Second-Degree Burn Wounds Using Extracorporeal Shock Wave Therapy

Christian Ottmann, MD,* Alexander Stojadinovic, MD, FACS,†† Philip T. Lavin, PhD,§ Francis H. Gannon, MD,¶
Michael H. Heggeness, MD,¶¶ Richard Thiele, MD,|| Wolfgang Schaden, MD,** and Bernd Hartmann, MD*
Reduced burn scar pruritus/itchiness after 3x focused electromagnetic ESWT

The clinical utility of extracorporeal shock wave therapy for burn pruritus: A prospective, randomized, single-blind study

So Young Joo, Yoon Soo Cho, Cheong Hoon Seo

Fig. 2 - The extracorporeal shock wave therapy was administered to burn patients. The administered shock wave dose was 100 impulses/cm² at 0.05 to 0.20mj/mm² with a total of 1000-2000 impulses.
Reduced burn scar pruritus/itchiness after 3x focused electromagnetic ESWT

Table 3 – The changes in numerical rating scale (NRS), 5-D pruritus scale, Leuven Itch Scale.

<table>
<thead>
<tr>
<th></th>
<th>ESWT Before therapy</th>
<th>ESWT After 3rd therapy</th>
<th>p</th>
<th>Control Before therapy</th>
<th>Control After 3rd therapy</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRS</td>
<td>6.30 ± 1.29</td>
<td>3.57 ± 2.09</td>
<td>&lt;0.001</td>
<td>6.87 ± 1.32</td>
<td>5.35 ± 2.31</td>
<td>0.002</td>
</tr>
<tr>
<td>5-D pruritus scale</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration</td>
<td>1.96 ± 1.87</td>
<td>1.39 ± 0.66</td>
<td>0.046</td>
<td>2.00 ± 1.17</td>
<td>1.65 ± 1.07</td>
<td>0.118</td>
</tr>
<tr>
<td>Degree</td>
<td>3.52 ± 0.79</td>
<td>2.52 ± 0.59</td>
<td>&lt;0.001</td>
<td>3.48 ± 0.73</td>
<td>2.96 ± 0.93</td>
<td>0.017</td>
</tr>
<tr>
<td>Direction</td>
<td>4.17 ± 0.83</td>
<td>2.78 ± 0.90</td>
<td>&lt;0.001</td>
<td>4.21 ± 0.90</td>
<td>3.48 ± 1.08</td>
<td>0.028</td>
</tr>
<tr>
<td>Disability</td>
<td>3.30 ± 1.15</td>
<td>2.35 ± 1.23</td>
<td>0.004</td>
<td>3.21 ± 1.04</td>
<td>2.87 ± 1.18</td>
<td>0.057</td>
</tr>
<tr>
<td>Leuven Itch Scale</td>
<td>78.26 ± 18.93</td>
<td>67.39 ± 23.15</td>
<td>0.075</td>
<td>79.35 ± 12.28</td>
<td>72.83 ± 19.81</td>
<td>0.107</td>
</tr>
<tr>
<td>Frequency</td>
<td>33.00 ± 34.47</td>
<td>20.09 ± 25.83</td>
<td>0.12</td>
<td>45.91 ± 34.09</td>
<td>43.04 ± 37.80</td>
<td>0.79</td>
</tr>
<tr>
<td>Duration</td>
<td>63.04 ± 12.95</td>
<td>35.22 ± 20.20</td>
<td>&lt;0.001</td>
<td>68.70 ± 13.25</td>
<td>53.48 ± 23.08</td>
<td>0.002</td>
</tr>
<tr>
<td>Severity</td>
<td>32.51 ± 21.50</td>
<td>17.19 ± 16.24</td>
<td>&lt;0.001</td>
<td>37.85 ± 23.39</td>
<td>32.60 ± 21.84</td>
<td>0.20</td>
</tr>
</tbody>
</table>

Values are mean ± standard deviation.

a Wilcoxon signed rank test.
b Paired t-test.
* p < 0.05 between groups.
Literature
ESWT in soft tissue wounds

- 208 pts with non-healing wounds with 75% complete wound epithelization
  - ESWT: 100-1000 shots/cm² 0.1mJ/mm², 3x
- Potential mechanisms for ESWT in wounds:
  - Initial neovascularisation with functional angiogenesis
  - Recruitment of mesenchymal stem cells
  - Anti-inflammatory effects
  - Antimicrobial effects
Modulation of vascular endothelial growth factor and mitogen-activated protein kinase-related pathway involved in extracorporeal shockwave therapy accelerate diabetic wound healing.

Chen RF, Cheng CH, Weng CT, Xiong MX, Weng CP, Kuo TT, Lin YC, Tsai YJ.

Abstract

Extracorporeal shockwave therapy (ESWT) has a significant positive effect to accelerate chronic wound healing. This study investigated whether the vascular endothelial growth factor (VEGF)-related pathway has involved in ESWT enhancement of diabetic wound healing. A dorsal skin defect (area, 6 × 5 cm) in a streptozotocin-induced diabetes rodent model was used. Thirty-two male Wistar rats were divided into four groups. Group I consisted of nondiabetic control; group II, diabetic control without treatment; group III, diabetic rats received ESWT; and group IV, rats received Avastin (a VEGF monoclonal antibody) on day 0 (post-wounding immediately) to day 7 and ESWT on day 3 and day 7. The wound healing was assessed clinically. The VEGF, endothelial nitric oxide synthase (eNOS), and Ki-67 were analyzed with immunohistochemical staining. The mRNA expression of mitogen-activated protein kinase-related genes was measured by real-time quantitative real-time polymerase chain reaction. The results revealed wound size was significantly reduced in the ESWT-treated rats as compared to the diabetic control (p < 0.01). The positive effect of ESWT-increasing wound healing was significantly suppressed in pretreatment of the Avastin group. Histological findings revealed significant increase in neo-vessels in the ESWT group as compared to the control. In immunohistochemical stain, significant increases in VEGF, eNOS, and Ki-67 expressions were noted in the ESWT group as compared to that in controls. However, Avastin suppressed the shockwave effect and down-regulation of VEGF, eNOS, and Ki-67 expressions in the Avastin-ESWT group as compared to that in the ESWT alone group. We found that highly mRNA expression of Kras, Raf1, Mek1, Jnk, Jnk, and Jun at early stage in the ESWT group, as compared to the diabetic control. These evidences indicated treatment with multiple sessions of ESWT significantly enhanced diabetic wound healing associated with increased neovascularization and tissue regeneration. The bio-mechanism of ESWT-enhanced wound healing is correlated with VEGF and mitogen-activated protein kinase-mediated pathway.
ESWT for diabetic foot ulcers

• Meta-Analysis of 5 trials with 255 patients

• ESWT was superior to standard wound care
  • At complete wound healing (Odds ratio 2.66)
  • Time to healing (65±8days vs. 81±4days)
  • ESWT was better than hyperbaric oxygenation (HBO) for diabetic foot ulcers
ESWT for diabetic foot ulcers

- Randomized-controlled trial (N=23)
  - Six ESWT treatments in 3 weeks and standard care vs. standard care alone
    - 250 shots/cm² plus 500 shots on arterial beds supplying ulcer location
  - Transcutaneous oxygen saturation was significantly increased in ESWT vs. standard therapy alone (p=0.044)
  - Ulcer area reduction was 35% in the intervention and 6% in the standard care group at week 7
Proposed region for ESWT application on ulcers (darker point) with the recommended treatment area (orange) 

Jeppesen S/Lund L. ESWT in diabetic foot

IN: Knobloch: ESWT in Aesthetics, Burns and Dermatology, 2018

Figure 3
Illustration of the area that was treated with 500 shocks deep focus ESWT using the DUOLITH SD1 (STORZ MEDICAL AG). ESWT was aimed at the medial plantar artery if the ulcer was located on the plantar surface medially (1), the small calcaneal branches if the ulcer was located on the heel (2), the lateral plantar artery if the ulcer was located on the plantar surface laterally (3), the interdigital arteries on each side of the metatarsal bone if the ulcer was located on a toe (4), and the proximal perimeter of the ulcer if the ulcer was located on the dorsum of the foot (5)
FDA approval for Sanuwave for diabetic foot ulcer

Diabetic foot ulcer treatment with focused shockwave therapy: two multicentre, prospective, controlled, double-blinded, randomised phase III clinical trials.

Snyder R1, Galindo P2, Meyer P3, Rogers LC4, Alvarez C5, Sanuwave Trial Investigators.

Abstract

OBJECTIVE: To investigate the efficacy of focused extracorporeal shockwave therapy (ESWT) as an adjunctive treatment for neuropathic diabetic foot ulcers (DFU) (1A or 2A on the University of Texas grading scheme), compared with sham treatment.

METHOD: We performed two multicentre, randomised, sham-controlled, double-blinded, phase III clinical trials using focused ESWT compared with sham examining DFUs that did not reduce in volume by ≥50% over 2 weeks' standard treatment immediately prior to randomisation. Patients were enrolled into the trials and randomised for either standard care and focused ESWT (pulsed acoustic cellular expression, dermaPACE System, SANUWAVE Health Inc.) active therapy, or standard care and sham therapy. Both active and sham therapy were administered four times in 2 weeks in study 1 and a maximum of eight times over 12 weeks in study 2. Standard care continued in both studies throughout the 12-week treatment phase. The proportion of DFUs that closed completely by 12, 20 and 24 weeks was measured.

RESULTS: The two studies evaluated 336 patients; 172 patients treated with active therapy and 164 managed with a sham device. The demographic characteristics of patients in the two arms of both studies were balanced and statistical comparison of the two studies justified pooling datasets for analysis. Statistically significantly more DFU healed at 20 (35.5% versus 24.4%; p=0.027) and 24 weeks (37.8% versus 26.2%; p=0.022) in the active treatment arm compared with the sham-controlled arm. At 12 weeks the active therapy arm trended to significance (22.7% versus 19.3%).

CONCLUSION: The outcome of these two trials suggests that ESWT is an effective therapeutic modality in combination with standard care for neuropathic DFU that do not respond to standard care alone.

KEYWORDS: PACE technology; chronic wound; diabetic foot ulcers; extracorporeal shockwave therapy; randomised controlled trial

PMID: 30557108 DOI: 10.12968/wound.2019.27.12.822
Recommended ESWT wound protocol

- De/-Focused ESWT
  - 0.1-0.2mJ/mm²
  - 2-5 Hz
  - 3-6 sessions
  - Wound size:
    - 350+100 impulses/cm²

<table>
<thead>
<tr>
<th>wound size</th>
<th>wound area</th>
<th>number of pulses</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 x 1 cm</td>
<td>1 cm²</td>
<td>350 + 100 = 450</td>
</tr>
<tr>
<td>2 x 2 cm</td>
<td>4 cm²</td>
<td>350 + 400 = 750</td>
</tr>
<tr>
<td>2 x 4 cm</td>
<td>8 cm²</td>
<td>350 + 800 = 1.150</td>
</tr>
<tr>
<td>4 x 4 cm</td>
<td>16 cm²</td>
<td>350 + 1.600 = 1.950</td>
</tr>
</tbody>
</table>
Timeline of ESWT in cellulite
26 females with cellulite with lymphdrainage with or without ESWT

ESWT reduces oxidative stress and improves cellulite
Fig. 3. Improvement of biomechanic skin properties during a 2 weeks-period with 6 sessions of shock wave application each for 8 minutes (1,000 impulses) in 5 patients with cellulite. In this part of the study the patients were treated only with SWT, but without parallel CPDT. Therefore, the increases of smoothening and elasticity (Young modul or stiffness index) which are given as difference between Young modul/stiffness index of the treated and untreated extremity are completely due to SWT. Values as Young modul/stiffness index without dimension; trend was calculated as linear trend.
CelluShock RCT Knobloch K

Intervention group
- 6 sessions of focused extracorporeal shockwave therapy 0.35 mJ/mm² 2000 shocks and daily gluteal strength training (Storz Duolith SD1)

Control group
- 6 sessions of SHAM focused extracorporeal shockwave therapy 0.01 mJ/mm² 2000 shocks and daily gluteal strength training
RCT Cellushock Knobloch et al.
Before and after 6x focused ESWT

Intervention group A
baseline
CSS 15

Intervention group A
3 months post intervention
CSS 7
RCT Cellushock Knobloch et al.
Before and after 6x focused ESWT

Intervention control

Baseline

10,9
p<0,01
8,3

12 weeks

10
10,1
Review

Extracorporeal shock wave therapy (ESWT) for the treatment of cellulite – A current metaanalysis

Karsten Knobloch a, *, Robert Kraemer b

a SportPraxis Prof. Dr. Karsten Knobloch, Hannover, Germany
b Plastic, Hand and Burn Surgery, University of Schlewig Holstein, Lubeck, Germany

HIGHLIGHTS

- Both, focused & radial ESWT devices are effective in treating cellulite.
- Typically, one or two weekly sessions and 6–8 sessions overall were studied.
- Outcome parameters mainly focused on photographs, circumference measurements and ultrasound.
- Reporting quality showed substantial heterogeneity from 22 to 82 points with a mean of 57 points.
<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Study design</th>
<th>Level of evidence</th>
<th>Number of patients</th>
<th>Type of ESWT</th>
<th>Device type</th>
<th>Energy flux densities</th>
<th>Pressure</th>
<th>Number of sessions</th>
<th>Follow-up</th>
<th>Outcome measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Siems et al.</td>
<td>2005</td>
<td>Cohort study</td>
<td>3</td>
<td>26 (intra-individual control, one treated leg)</td>
<td>Focused ESWT</td>
<td>DermaSelect, Storz Medical Activator-Derma</td>
<td>0.16 mJ/mm², 1000 impulses</td>
<td></td>
<td>3–6 sessions</td>
<td>2 weeks</td>
<td>Mitigation of oxidative stress, Improvement of high resolution ultrasound with collagen remodelling, Epidermal improvement, neocollagenogenesis</td>
</tr>
<tr>
<td>Angehrn</td>
<td>2007</td>
<td>Cohort study</td>
<td>3</td>
<td>21 (intra-individual control, one treated leg)</td>
<td>Low-energy defocused ESWT</td>
<td>0.018 mJ/mm², 40,000 shots</td>
<td></td>
<td>12 (twice a week)</td>
<td>8 weeks</td>
<td></td>
<td></td>
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<tr>
<td>Kuhn</td>
<td>2008</td>
<td>Case study</td>
<td>4</td>
<td>1 (intra-individual control, one treated leg)</td>
<td>Focused ESWT</td>
<td>Activator-Derma electrohydraulic device, SwiTechMedical</td>
<td>0.115 mJ/mm², 4 Hz, 800 impulses on 2 x 2 cm² sample</td>
<td></td>
<td>4</td>
<td>unclear</td>
<td></td>
</tr>
<tr>
<td>Christ</td>
<td>2008</td>
<td>Cohort study</td>
<td>3</td>
<td>59</td>
<td>Planar ESWT</td>
<td>Storz CellActor SC1</td>
<td>0.25 mJ/mm², 1200 impulses per session</td>
<td></td>
<td>6 (n = 15) or 8 (n = 44) (twice a week)</td>
<td>3 &amp; 6 months</td>
<td>Skin elasticity improvement 105% at 6 months (µ); Improvement on skin roughness, number of depressions and elevations</td>
</tr>
<tr>
<td>Adatte</td>
<td>2010</td>
<td>RCT, 1:1 allocation</td>
<td>1b</td>
<td>25 (intra-individual control, one treated leg)</td>
<td>Radial ESWT</td>
<td>Storz D-Actor 200</td>
<td>2.6–3.5 bar, 15 Hz, 3000 impulses on 10 x 15 cm rectangle</td>
<td></td>
<td>6 twice a week</td>
<td>12 weeks</td>
<td>Reduction of subcutaneous fat layer, Mean fat thickness reduction by 3 cm, Circumference reduction by 4.5 cm</td>
</tr>
<tr>
<td>Adatte</td>
<td>2011</td>
<td>Cohort study</td>
<td>3</td>
<td>14</td>
<td>Radial and focused ESWT</td>
<td>Storz CellActor SC1</td>
<td>0.45–1.24 mJ/mm², 1500 impulses</td>
<td></td>
<td>3–4 bar, 3000 impulses</td>
<td>12 weeks</td>
<td></td>
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<tr>
<td>Ferraro</td>
<td>2012</td>
<td>Cohort study</td>
<td>3</td>
<td>50</td>
<td>Radial ESWT + cryo-lipolysis</td>
<td>Proshockico (Prinosoftballa)</td>
<td>50–500 bar, 1–6 Hz combined with a freezing probe for cryolipolysis</td>
<td></td>
<td>4 sessions every 15 days</td>
<td>12 months</td>
<td></td>
</tr>
<tr>
<td>Knobloch</td>
<td>2013</td>
<td>RCT, 1:1 allocation</td>
<td>1b</td>
<td>53</td>
<td>Focused ESWT</td>
<td>Storz Duolith</td>
<td>0.35 mJ/mm², 2000 impulses</td>
<td></td>
<td>6 (once a week)</td>
<td>12 weeks</td>
<td>Improvement of Cellulite Severity scale CSS from 10.9 to 8.1 by 24% (double-blind standardized photographic evaluation)</td>
</tr>
<tr>
<td>Russe-Willingseder</td>
<td>2013</td>
<td>RCT, 2:1 allocation</td>
<td>1b</td>
<td>16 (11 verum, 5 placebo)</td>
<td>Radial ESWT</td>
<td>Storz D-Actor 200</td>
<td>2–3 bar, 3500 impulses</td>
<td></td>
<td>8 (once a week)</td>
<td>12 weeks</td>
<td>Subjective patient improvement, Photoscore improvement, Improvement of cellulite grade by 0.93 grades, Crossline study, Reduction of subcutaneous fat layer from 1.4 ± 0.4 cm to 1.0 ± 0.3 cm at 3 months follow-up, 1.7 cm circumference reduction</td>
</tr>
<tr>
<td>Schlaußaff</td>
<td>2014</td>
<td>RCT, 1:1 allocation</td>
<td>1b</td>
<td>14 (intra-individual control, one treated leg)</td>
<td>Radial ESWT</td>
<td>EMS Swiss DolorClast</td>
<td>3.5–4 bar, 15,000 impulses, 15 Hz</td>
<td></td>
<td>8 (twice a week)</td>
<td>4 weeks</td>
<td></td>
</tr>
<tr>
<td>Nassar</td>
<td>2015</td>
<td>RCT, 1:1 allocation</td>
<td>1b</td>
<td>15 (crossleg study, 1 leg being treated, one served as intra-individual control)</td>
<td>Focused and radial ESWT</td>
<td>Storz SC1</td>
<td>0.56–1.24 mJ/mm², 1500 impulses, per leg</td>
<td>2.6–5 bar, 16 Hz, 3,000 impulses</td>
<td></td>
<td>8 (twice a week)</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>
Metaanalysis ESWT in Cellulite
Knobloch & Krämer 2015

- Both, focused as well as radial ESWT devices have been found effective in treating cellulite so far
- Typically, one or two sessions per week and 6–8 sessions overall were studied in the published clinical trials
- Follow-up typically ranged between three and six months
- Overall, outcome parameters mainly focused on digital standardized photographs, circumference measurements and specific ultrasound examinations
- Only one RCT to date used a non-validated patients' questionnaire to assess the patients' evaluation of the treatment
Timing of ESWT

Therapeutic ESWT

Improved function

Less pain

Preventive ESWT

Less scaring

Faster healing

Preconditioning
ESWT - Improved scaring after body lift

Thanks to Dr. Wolfgang Schaden, AUVA Vienna
Improved scaring after a single preventive F-SW

Russe E et al. in press

45yrs female 6 weeks postoperatively

(BMI: 24.4 kg/m2)
THE DIFFERENCES BETWEEN NORMAL WOUND HEALING

I. Inflammation
- Platelets
- Macrophages
- Neutrophiles
- Monocytes
- Lymphocytes

II. Cell Proliferation
- Fibroblasts
- Keratinocytes
- Endothelial Cells

III. Matrix Remodeling
- Myofibroblasts

A. Normal Wound Healing
- TGF-β1
- TGF-β2
- PDGF
- IGF-1
- IL-4
- IL-10
- Collagen
- Fibronectin
- Glycosaminoglycan
- TIMP 1, II

B. Excessing Scarring
- MMO-9
- INF-γ
- TGF-β3
- Collagenase
- Proteoglycans
- MMP 2

Time

Figure 1: The differences between normal wound healing and excessive scarring (Gauglitz et al., 2015, Hypertrophic Scarring and Keloids: Pathomechanisms and Current and Emerging Treatment Strategies).
CASCADE OF WOUND HEALING PROCESSES AFTER SWT

Wound Healing

- NO + VEGF expression ↗
- Vasodilatation ↗
- Angiogenesis ↗
- Vascular and capillary density ↗
- Local blood flow ↗
- Apoptosis ↘
- ECM ↗

SUGGESTED SWT SETTINGS FOR FOCUSED ELECTROMAGNETIC DEVICES WHEN TREATING WOUNDS OR SCARS

<table>
<thead>
<tr>
<th></th>
<th>Energy Flux Density</th>
<th>Number of pulses</th>
<th>Pulse Frequency</th>
<th>Treatment interval</th>
<th>Number of treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWT for Wound Healing</td>
<td>0.03–0.20 mJ/mm²</td>
<td>500–1,000</td>
<td>4–6 Hz</td>
<td>1 x per week</td>
<td>1–3</td>
</tr>
<tr>
<td>SWT for scar treatment</td>
<td>0.15–0.33 mJ/mm²</td>
<td>800–1,500</td>
<td>4–6 Hz</td>
<td>1 x per week</td>
<td>8–12</td>
</tr>
</tbody>
</table>

ISMST Certification Course
ESWT can
- Accelerate skin epithelization
  - in burns
  - in diabetic ulcers
- Improve scaring
- Improve cellulite