June 25, 2014: Instructional Certification Course

Abstract Book
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Award for the Best Presentation of the ISMST-BRM Meeting in Frankfurt:
Shock Wave Induced Bone Regeneration and Neovascularisation: the Involvement of Wnt-signaling
Influence of Different In-Vitro Setups on Shockwave Treatment Parameters – a Guide for More Comparable Results
Kristin Dietz-Laursonn, Matias de la Fuente

Institution: Chair of Medical Engineering, RWTH Aachen University, Germany

Device and producing company

Introduction: Since the end of the 1980’s shockwave induced therapeutical effects have been demonstrated in-vitro for different cell types using different setups. However, the mechanisms of shockwave therapy are still not understood. One reason is that depending on the chosen setup the pressure field interacting with the cells varies extensively and is not comparable to the data published by the manufacturers. Therefore, there is a need for a standardized setup.

Methods: An extensive literature review of different published in-vitro setups has been conducted to get an overview of the variety of experimental setups used. Problematic parts of different setups are described and compared. Several key parameters are identified and their influence is quantified using FEM simulations.

Results: Most in-vitro setups are not described sufficiently in journal articles. Therefore a comparison of different studies is mostly impossible. Due to errors regarding the setup, like too little distance from the cells in the focal area to air or to other materials the pressure distribution is changed substantially. Thereby the mechanical forces interacting with the cells are altered which is likely to change also the biological reaction.

Discussion: The comparability of experimental results of different researchers is the main requirement to be able to confirm the results and find correlations between physics and biology. In order to gain comparable results the reproducibility of studies is most important.

Conclusion: The experimental setup used for in-vitro shock wave treatment has to be described more detailed. If a few major tips and tricks are applied to those setups, it is possible to avoid major changes of the sound field compared to the manufacturers’ data.
Combination of ESW and Doxorubicin-loaded Nanobubbles: Anti-Tumor Effects in Anaplastic Thyroid Cancer
Francesca Marano (1), Maria Graziella Catalano (1), Aloe Adamini (1), Roberta Cavalli (2), Ornella Bosco (1), Nicoletta Fortunati (3), Roberto Frairia (1)

Institution: (1) Dept. of Medical Sciences, (2) Dept. of Drug Science and Technology, University of Turin, (3) Oncological Endocrinology, AO Città della Salute e della Scienza, Turin, Italy

Device and producing company: Piezoson 100, Richard Wolf

Introduction: Anaplastic thyroid cancer (ATC) is a lethal neoplasia resistant to traditional chemotherapy. Nanobubbles (NBs) can target anticancer agents to tumor cells; moreover, combining drug-loaded NBs with an external “trigger” (e.g. ultrasounds) may control drug action at the target region. The features of Extracorporeal Shock Waves (ESW) make ESW-triggered drug delivery a new strategy for cancer therapy. The aim of the present work was to evaluate the cytotoxic effects of combining doxorubicin-loaded NBs and ESW.

Methods: CAL-62 cells were treated with: doxorubicin, coumarin-loaded NBs, and doxorubicin-loaded NBs in the presence or absence of ESW (0.59 mJ/mm2, 500 shots), generated by a piezoelectric device (Piezoson 100). Cell viability was evaluated by Trypan Blue exclusion and WST-1 proliferation assay. The uptake of drug and NBs was evaluated by fluorescence microscopy and FACS analysis.

Results: ESW and empty NBs did not affect CAL-62 cell growth. NBs entered the cells and doxorubicin-loaded NBs had a greater cytotoxic effect with respect to free doxorubicin, being GI50=1.57 microM for doxorubicin and 1.13 microM for doxorubicin-loaded NBs. ESW treatment further enhanced the cytotoxic effect of drug-loaded NBs (GI50=0.95 microM).

Discussion: The combined treatment with doxorubicin-loaded NBs and ESW allowed to obtain the same cytotoxic effect with a dose of doxorubicin 60% lower compared to treatment with free doxorubicin alone.

Conclusion: The combination of ESW with drug-loaded NBs defines the possibility of using this multimodal approach in the treatment of ATC, with the ultimate goal of improving the prognosis and limiting the systemic side-effects of chemotherapy.
In Vitro Shockwave Treatment Influences Lymphatic Endothelial Cell Marker Expression and Proliferation
Sabrina Riedl (1), Anna Weihs (2), Marion Gröger (3), Matthias Hackl (4), Johannes Grillari (5), Heinz Redl (1), Wolfgang Holnthoner (1)

Institution: (1) Ludwig Boltzmann Institute; (2) City of Vienna Competence Team Tissue Engineering Bioreaktoren; (3) Medical University; (4) TAmiRNA GmbH; (5) University of Natural Resources and Life Sciences; Vienna, Austria

Device and producing company: MTS Dermagold 100

Introduction: Extracorporeal shockwave treatment (ESWT) is a promising therapy for treating orthopaedic diseases and chronic wounds and further induces blood and lymphatic vessel growth. In this study we analyzed the effects of shockwaves on lymphatic endothelial cells (LEC) in vitro.

Methods: LEC were stimulated in a waterbath with a MTS Dermagold 100 device. Twenty four hours later, flow cytometry analyses for endothelial marker expression were performed. The LEC proliferation and viability changes after ESWT were determined by manual counting and MTT assays. 2D and 3D migration changes were investigated by scratch and bead assays. Furthermore, miRNA expression changes were evaluated.

Results: The proliferation rates of LEC varied when stimulation with different energy flux densities was applied and 2D and 3D migration was significantly enhanced by ESWT. The endothelial markers CD31, VE-Cadherin, VEGFR2 as well as the LEC marker VEGFR3 expression did not change after ESWT. However, we found an energy density- and population-dependent increase in the expression of the LEC-specific podoplanin. Different miRNA level alterations after ESWT including podoplanin-regulating miR-29b were identified.

Discussion: Since lymphatic vessels play a key role in tissue hemostasis, regeneration of lymphatic vessels is of crucial interest for tissue engineering purposes or for lymphedema patients. Our results add new insights into ESWT-induced changes of LEC behaviour and reveal podoplanin as one of the target molecules of ESWT.

Conclusion: ESWT influences the proliferation and migration of isolated lymphatic endothelial cells and mediates podoplanin upregulation in these cells.
A Development of Biological Reparative Model in Human Tendon Derived from Fibroblasts Healing Process with Unfocused ESWT

Raoul Saggini (1), Giuseppe Soda (2), Nicolò Scuderi (2), Rosa Grazia Bellomo (1)

Institution: (1) "G. d'Annunzio" University, Chieti; (2) "Sapienza" University, Rome; Italy

Device and producing company: Orthogold, MTS, Europe GmbH, Germany

Introduction: Alterations of tendon collagen due to overload are represented by degeneration, disorganization and thickening of collagen fibers, increase in collagen degradation and interfibrillar glycosaminoglicans, alteration in the normal ratio between type I and type III collagen. A similar process happens in pathological skin scarring, so recently we investigated biological and histopathological modifications of human skin in pathological scars after ESWT.

Methods: We compared 2 groups of subjects with retracting scars; the first group was treated with ESWT, the second did not receive the treatment (control group). 4 mm punch-biopsy of human skin samples were taken from all patients. We made histopathological and immunoistochemical analysis to get a quantitative evaluation of fibroblasts, angiogenesis and collagen concentrations in human skin samples.

Results: Results in the ESWT group showed: a significant increase of fibroblasts infiltration and increase in angiogenesis at the immunohistochemical analysis with Factor XIII marker; a significant increase in type I collagen concentration and an increase in angiogenesis in CD34 stained samples; an improvement in angiogenesis in CD31 stained samples. The collagen fibers were placed parallel to the skin surface and type III collagen was replaced by type I collagen. Dermal collagen appeared finer and more fibrillar if compared to pretreatment. No increase in fibroblasts infiltration and angiogenesis and no change in collagen composition was found in the control group.

Discussion: We can assume that the biological response to ESWT is the same in the different tissues and shock waves are able to get deep up to tendon thanks to the possibility of modulating the depth of treatment through parameters of focal pressure and intensity.

Conclusion: Compatibly with what observed in the human skin, where the tissue regeneration process is characterized by fibroblasts infiltration and collagen remodeling, with the replacement of type III with type I collagen, and considering the scientific evidence of the clinical effectiveness of ESWT on tendon diseases, we can assume a similar model of tissue repair in vivo also in human tendon.
Shockwave Treatment Promotes the Expression of Alox15 in Pro-Resolving Macrophages
Naths Grazia Sukubo (1), Stefano Respizzi (2), Alberto Mantovani (1), Maria Cristina D'Agostino (2), Massimo Locati (1)

Institution: Dept. of Medical Biotechnologies and Translational Medicine, University of Milan; (2) Humanitas Research Hospital, Milan, Italy

Device and producing company: OrthoGold 100, MTS Germany

Introduction: Extracorporeal Shock Wave (SW) treatment is broadly used as a non-surgical therapy in various diseases, demonstrating its pro-angiogenic and anti-inflammatory effects. However, the molecular mechanisms translating shock waves in a biological response with potential therapeutic activity are largely unknown. As macrophages take part in both the onset and amplification of the inflammatory response, and well in its resolution, we investigated the effect of SWT on their biology.

Methods: Human monocyte-derived macrophages were polarized to pro-inflammatory classic macrophages (M1) by overnight exposure to LPS+IFN-γ or anti-inflammatory alternative macrophages (M2) by overnight exposure to IL-4. Using an Orthogold100 device as electrodraulyc SW source, macrophages were then exposed in a thermostated water bath to SW (400 impulses, 3.5Hz, 0.1-0.03 mJ/mm²) at different time points. RNA was then extracted and expression levels of M1 (CD80, CCL5, CXCL9, CXCL10, COX2) and M2 (CD206, ALOX15, IL-10, TGFβ) genes were analyzed by qRT-PCR.

Results: SW had no direct effect on any transcript investigated, when applied to resting macrophages. Though the effect did not reach statistical significance for the elevated variability among different experiments, when applied to inflammatory macrophages SW showed a faint downmodulatory effect on some M1 markers (CCL5, CD80), while others (including COX2) were not affected. Conversely, at low energy level (0.03 mJ/mm²) SW had a significant reproducible and time-dependent synergistic effect with IL-4 for the induction of ALOX15 in M2 macrophages. Interestingly, other M2 genes (including IL-10) were not affected by SW exposure.

Discussion: Synergism with IL-4 in the induction of some M2 genes, suggesting that SW therapeutic potential may be at least in part mediated by their effect on macrophage biology.

Conclusion: Our results demonstrate that SW at low energy level act in an conclusion, we did not detect any synergistic effect of SW on the anti-inflammatory cytokine IL-10, but we identified ALOX15 as a SW-responsive gene in M2 macrophages. ALOX15 has a key role in the resolution of the inflammatory response via production of the pro-resolving eicosanoid lipoxin A4 and of endogenous agonists of the PPARγ pathway and could therefore be involved in the therapeutic effects observed after exposure to SW.
Shockwave Therapy as a Component of Multimodal Regenerative Medicine in Horses
Scott McClure

Institution: Iowa State University, USA
Device and producing company: Equitron

Introduction: Shockwave therapy (SWT) has been demonstrated to have multiple regenerative effects in the horse. In tendons a transient stimulatory effect on glycosaminoglycan production, neovascularization, increased collagen fiber production and expression of growth factors has been seen. In bone, osteoblastic activity has been increased and subchondral bone remodeling stimulated by SWT. Developing parallel to shock wave therapy has been a group of other modalities that fit into the regenerative therapy grouping. Platelet rich plasma (PRP), collagen matrices, and stem cells are all routinely being used. Clinically we frequently combine therapies with them being used sequentially or simultaneously.
At this time we lack controlled studies of the effects of multiple treatments being administered. We justify our treatment protocols based on knowledge of each treatment separately. In vivo healing always involves multiple cytokines and growth factors and processes occurring simultaneously. Therefore, utilizing therapies that may stimulate neovascularization and cell recruitment into a collagen scaffold or any other combination may improve the overall rate and quality of tissue.
There is some flexibility from regulatory issues in veterinary medicine that allow us to utilize combination therapies and therapies that may not be currently approved for use in humans. The objective of this paper will be to share some of the reasoning for and cases in which we have utilized SWT in combination with other regenerative methods.

Methods: not applicable
Results: not applicable
Discussion: not applicable
Conclusion: not applicable
Prognostic Factors for the Failure of the Shockwaves in the Treatment of Tendinopathy

Angela Notarnicola, Alessandra Fiore, Cristina Margiotta, Angela Dantone, Maria Grazia Ricchiuti, Biagio Moretti

Institution: Faculty of Medicine and Surgery of University of Bari, General Hospital; Italy

Device and producing company: Minilith, STORZ MEDICAL

Introduction: The purpose of this clinical study is to verify whether the response to shock waves therapy is related to the presence of the risk factors for tendinopathy.

Methods: We set up an observational study monitoring the epidemiological characteristics of patients treated with shock waves and reassessed at follow-up at 2 months. We have compiled a questionnaire that includes the demographic variables (gender, age, blood group, etc), anthropometric data (weight, height, BMI), the side of treatment, the number of cycles, the energy, the sport activity, diet, co-morbidities such as hypertension, dyslipidemia, hypothyroidism, rheumatologic diseases, neurological disorders, taking medication that could adversely affect the outcome of therapy, previous treatments, and the Roles and Maudsley score. For the purposes of this analysis were considered failures cases with the Roles and Maudsley > 2. The study of the association between exposure factors and failure has been made before by univariate analysis and by multivariate analysis.

Results: From the preliminary results, relating to a case series of 218 patients, there was a statistically significant correlation with the male gender, the bilateral location, repeated cycles of therapy, weight, blood group 0 Rh + and the presence of co-morbidities.

Discussion: These preliminary data may be useful to the clinician to select patients that may not have benefit from shockwaves therapy.

Conclusion: In these patients at greater risk of failure it could be necessary to change the shockwaves protocol or to integrate the treatment with other physical therapies.
The Significance of Inflammatory Tendon Hypervascularization for the Treatment Results with ESWT: Are the Actual Recommendations Still Valid?
Markus Gleitz

Institution: Orthopaedic Practice, Luxembourg, Luxembourg

Device and producing company: Orthogold 100 (MTS) with a planar applicator, Storz Duolith with a focused applicator

Introduction:
Although ESWT of chronic tendinopathies is judged as efficient and is partly considered as a standard indication according to the ISMST/DIGEST guidelines, results vary according to the indications. Former personal results with Power Doppler examinations in radial epicondylopathy (ISMST 2013) have shown that chronic tendinopathies develop variable amounts of a secondary tendon hypervascularization that is decisive for the pain sensation and for the reliability of good treatment results.

Methods:
In a retrospective study of 160 patients with chronic tendinopathies (> 3 months: radial epicondylopathy of the elbow, Achilles tendinopathy, patella tendinopathy, plantar fasciitis), ultrasound examinations including grey-scale changes and Power Doppler were performed (1 examiner, not blinded) before and every 3 months after 3 ESWT sessions, up to 24 months. Power Doppler changes were quantified according to the percentage of surface of neovessels within the tendon insertion area. Treatment results were evaluated using the Visual Analogue Scale (VAS in mm, 0-100) during function. The correlation between pre-treatment ultrasonographic changes and the treatment pain as well as the VAS during function 3 months after ESWT was calculated.

Results:
The amount of neovessels in the different tendons and fasciae varied significantly at the beginning of the treatment and it correlated with the treatment pain during ESWT (r=0.72, p<0.05) and the length of the symptoms after ESWT (r=0.68, p<0.05). The VAS during function 3 months after ESWT was significantly higher (r=0.77, p<0.05) in patients with an increased amount of neovessels before ESWT. No correlation was found between the amount of neovascularity and the duration of symptoms before ESWT and the amount of neovascularity and the mean pain VAS before ESWT.
The highest neovascularity was found in radial epicondylopathy, Achilles and patella tendinopathy, followed by the plantar fasciitis, which has the best clinical results.
The amount of neovascularity determined the length of the healing period. The typical 3 months interval showed to be an inappropriate time span, as highly vascularized tissues need 6-12 months to heal, even without surgery.

Discussion:
Hypervascularity is considered to be associated with an active inflammatory response and is highly correlated with pain intensity. Neovascularity in Power Doppler seems to be a valid parameter for the estimation of pain during ESWT and for the prediction of treatment results. The classical time span of 3 months after ESWT is not a valid parameter to clinically decide about the final treatment results.
The unknown presence of neovessels might be the reason for the heterogeneous study results in the literature, as this parameter has never been considered in the highly ranked studies that are usually taken as a reference.

Conclusion:
Pre-treatment tissue conditions of the different tendinopathies vary and determine the time span for treatment results: The classical 3 months are no longer valid. For this reason ultrasound examinations using grey-scale pictures and Power Doppler should be performed as a routine before and after ESWT.
Local Blockage Decrease the Effect of Radial Extracorporeal Shockwaves Therapy for Achilles Tendinitis

Yayun Liu, Longhao Zhang

Institution: Orthopaedic ESWT center, Beijing Jishuitan Hospital

Device and producing company: STORZ MASTERPULS® MP100

Introduction: To explore the influence of local blockage on the effect of radial extracorporeal shockwaves therapy for Achilles tendinitis.

Methods: Fifty-six patients were divided into two groups based on whether they had the history of local blockage therapy. Among them, 35 cases not have local blockage before (A group) and 21 cases had local blockage before (B group). All patients accepted the RESW therapy according to the standard procedure and were followed up for at least 12 weeks. Visual analogue scale (VAS) was taken to evaluate the therapy effect.

Results: Before the therapy, the VAS scores of the two groups are no statistic difference (A group: 7.57±1.77; B group: 7.14±2.08). Four and 12 weeks after the therapy, the VAS scores decreased in both groups (at four-weeks FU: A group 3.17±1.42 and B group 4.42±2.24; at 12 weeks FU: A group 1.66±1.51 and B group 2.95±2.13). The VAS before and after therapy had significant differences in both groups (P<0.05). Group A had better cure rate (at four-weeks FU 28.6% and 12 weeks 74.3%) and effective rate (at four-weeks FU 97.1% and 12 weeks 100%) than Group B (cure rate at four-weeks FU 14.3% and 12 weeks 33.3%; effective rate at four-weeks FU 35.7% and 12 weeks 61.9%), and the difference had statistic significance (P<0.05).

Discussion: Therapy of Achilles tendinitis with RESW is safe and effective, and for the patients with history of local blockage, the therapy efficacy decreased.

Conclusion: Local blockage decrease the effect of radial extracorporeal shockwaves therapy for Achilles tendinitis.
Extracorporeal Shock Waves Trigger Tenogenic Differentiation of Human Adipose Derived Stem Cells

Maria Graziella Catalano (1), Letizia Rinella (1), Laura Annaratone (1), Isabella Castellano (1), Marco Fraccalvieri (2), Laura Berta (3), Roberto Frairia (1)

Institution: (1) Department of Medical Sciences, University of Turin, (2) Plastic Surgery Unit, University of Turin, (3) Med&Sport 2000 S.r.l., Italy

**Device and producing company:** Piezoson 100, Richard Wolf

**Introduction:** Repair of tendon ruptures is difficult, due to the low cellularity and poor vascularization. Moreover, current strategies to treat damaged tendons are often associated with limitations like injury relapse, donor site morbidity and risk of disease transmission, respectively. Human Adipose derived Stem Cells (hASCs), because of their capacity of self-renewal and multipotent differentiation, are a promising candidate cell type for tissue engineering applications. Extracorporeal Shock Waves (ESW) may induce some signals for growth and maturation of mesenchymal progenitors. The aim of the present study was to evaluate the effects of ESW on the differentiation of hASCs towards tenoblast-like cells.

**Methods:** hASCs were obtained from lipoaspirates of healthy donors. After combined treatment with tenogenic medium (DMEM-F12, 10% FBS, 50 ng/ml IGF-1, 10 ng/ml TGF-β) and ESW (0.32mJ/mm², 1000 shots), generated by a piezoelectric device (Piezoson 100), we determined: cell morphology, using an inverted phase contrast microscope; cell viability by Trypan Blue exclusion; cell proliferation by WST-1 proliferation assay; expression of tenogenic differentiation markers, scleraxis (Scx), tenascin C (TNC), and biglycan (BGN) by RT-real time PCR; collagen deposition by Masson’s trichrome staining.

**Results:** Combined treatment with ESW and tenogenic medium determined the expression of the differentiation markers Scx, TNC and BGN and the deposition of collagen fibers. Moreover, cells exhibited elongated, spindle-shaped, fibroblast-like appearance.

**Discussion:** These data indicates that ESW in combination with tenogenic medium may trigger differentiation of hASCs towards tenoblast like cells.

**Conclusion:** This preliminary study provides the basis for using hASCs and ESW in tendon tissue engineering.
High-Energetic Focused Extracorporeal Shockwave (ESWT) Reduces Pain Levels in the Nodular State of Dupuytren’s Disease (DupuyShock) – an Update with 1-year Follow-up data
Marie Kühn (1), Heiko Sorg (1), Peter M. Vogt (1), Karsten Knobloch (2)

Institution: (1) Hannover Medical School; (2) SportPraxis; Hannover, Germany

Device and producing company: none

Introduction: To study the effect of focused ESWT on Dupuytren’s disease in the nodular stage (Tubiana N) in a randomized-controlled trial.

Methods: In this prospective, randomized, blinded, placebo-controlled single center trial we included 52 patients (mean age: 58.2±9.2, 35 males,) with nodular Dupuytren’s disease Tubiana N. Randomization was done to either:
• 3 treatments with high-energetic focused ESWT (2000 shots, 3Hz, mean: 49mJ/mm2/hand, Storz Duolith SD1, n=27, 15 males, mean age 57.6±8.1)
• or placebo ESWT (2000 shots, 3 Hz, 0.01mJ/mm2/hand, n=25, 17 male, mean age 58.9±10.9) in a weekly interval

Outcome was assessed by three validated quality of life instruments
• DASH score (0=perfect, 100= maximal impairment)
• MHQ score (0=maximal impairment, 100=perfect)
• URAM scale (0=perfect, 45=maximal impairment)

In addition, pain on a visual analogue scale and grip strength (JAMAR) were assessed before and after three, six and twelve months.

Results: Treatment with three sessions of focused ESWT reduced pain from 3.6±1.8 to 1.9±1.2 at six and to 1.7±1.6 after twelve months in the intervention group (54% reduction, p<0.05). In the placebo group, pain on VAS increased from 2.2±1.4 to 3.4±1.7 at six and 3.5±1.4 at twelve months (55% increase, p<0.05). Quality of life score tented to improve in the intervention group (MHQ: 77±19 to 85±10, DASH: 12±18 to 10±8, URAM: 3±4 to 3±3) while it deteriorated in the placebo group as Dupuytren’s disease was progressing (MHQ: 80±15 to 73±17, DASH: 6±10 to 12±15, URAM: 1±2 to 3±3) twelve months after treatment. The strength of the affected hand and fingers did not change significantly in either of the groups (JAMAR Intervention: 37±12kg to 37±13kg, Placebo: 39±14kg to 40±14kg). No adverse events were reported beside a moderate pain during treatment.

Discussion: This RCT demonstrates a significant reduction of pain at six and twelve months after treatment with focused ESWT. Improvement of life quality is beneficially influenced within the first six months after focused ESWT.

Conclusion:
Soft Focused Extracorporeal Shockwaves Increase the Expression of Tendon-Specific Markers and the Release of Anti-Inflammatory Cytokines in an Adherent Culture Model of Primary Human Tendon Cells

Marco Viganò (1), Pietro Romeo (1), Laura De Girolamo (1), Deborah Stanco (1), Arianna Barbara Lovati (1), (Emanuela Galliera (2), Valerio Sansone (1)

Institution: IRCCS Istituto Ortopedico Galeazzi, Dipartimento di Scienze Biomediche, Chirurgiche ed Odontoiatriche, Università degli Studi di Milano, Milan, Italy
Device and producing company: OP155-Orthogold 100, MTS

Introduction: Few in vitro reports investigate the response of tendon cells (TCs) to shockwaves. In particular no one study has already reported data about TCs treated while adhering on culture plate rather than in suspension as usually applied. In this study we first investigated the effect of soft-focused shockwaves on adherent TCs culture, which represents a more physiological-like condition, where cell-to-cell contact could influence the cell response.

Methods: TCs, deriving from 7 healthy donors, were treated while adherent on culture plate, with 1000 shots of soft-focused extracorporeal shockwaves (SF-ESW) at energy of 0.17 mJ/mm². Cells were plated accordingly to the size of the SF-ESW SW focus, in order to treat the whole cell culture. The culture flask was treated after the immersion in a devoted water bath. Viability, proliferation, gene expression of specific markers and release of cytokines and growth factors were assessed.

Results: Shockwaves were able to induce positive modulation of cell viability, proliferation and tendon-specific marker expression, as well as release of anti-inflammatory cytokines and growth factors.

Discussion: We devised an original model to investigate the in vitro effects of soft-focused shock waves on TCs in adherent culture, and demonstrate that this kind of treatment could enhance TCs activation, in terms of tissue regeneration, thanks to its anti-inflammatory, proliferative, pro-tenogenic and pro-angiogenic effect.

Conclusion: Our findings could prefigure a new modality of in vitro cell treatment with SF-ESW, where a more physiological-like condition is preserved, allowing more reliable results.
Shockwaves Exposure Improves Tendon Regeneration
Vincenzo Visco, Maria Chiara Vulpiani, Mario Vetrano, Maria Rosaria Torrisi, Andrea Ferretti

Institution: Sant'Andrea Hospital, Sapienza University, Rome; Italy
Device and producing company: MODULITH® SLK - STORZ MEDICAL AG

Introduction: Several authors stated that EWST effectiveness on tendon pathologies could be ascribed to the transduction of the acoustic shock wave signal into biological signals, which results in cell proliferation and/or differentiation.

Methods: In two recent studies, we reported -for the first time- the specific effects of shock-wave treatment on human cultured tenocytes derived either from healthy semitendinosus (ST) or ruptured Achilles tendons (AT). ESWT mediated-effects were compared in tenocytes established from ST collected for arthroscopic anterior cruciate ligament (ACL) reconstruction or from ruptured AT.

Results: We showed that ESWT significantly interferes with by impairing the typical cell de-differentiation previously documented by several authors. Moreover, our results indicated that ESWT significantly enhances the proliferation of tendon-derived cells, when compared to untreated controls (p<0.05), although those effects were mainly observed in tenocytes explanted from ruptured versus healthy tendons (p<0.05).

Discussion: A further significant increase in collagen (mainly type I) synthesis by stimulated tenocytes compared to control cells (p<0.005) was found. Lastly, in order to validate the reliable repairing capacity of the exposed cultured tenocytes, we performed a classical scratch test of cell migration. The shock wave exposure induced a typical migratory phenotype in the majority of the cultured tenocytes and this effect was significantly more evident for cells derived from ruptured tendons (p<0.05).

Conclusion: Our findings suggest that human cultured tenocytes are metabolically “activated” by ESWT and significantly induced to proliferate, migrate and synthesize collagen, compared to untreated controls. Nevertheless, the shock wave efficacy was more evident in tenocytes explanted from ruptured than from healthy tendons.
Shockwave Treatment for Deep Orthopaedic Infections
Richad Coombs, Moustafa Hafez, Milad Hanna, Nikki Horwood

Institution: Imperial College London; UK

**Device and producing company:** Modulith, Storz

**Introduction:** Some Patients with deep orthopaedic infection are resistant to traditional treatments.

**Methods:** Seven patients have been treated with three to twelve sessions of Shockwave treatment.

**Results:** All our patients have noted symptomatic improvement.

**Discussion:** Our experience is anecdotal but reflects our previously reported experimental studies.

**Conclusion:** Shockwave treatment appears helpful for deep orthopaedic infections.
Intractable Bone Marrow Edema Syndrome of the Hip: 
High Energy Extracorporeal shockwave is an Amazing Technology

Wie Sun, Fuqiang Gao, Zirong Li,

Institution: China-Japan Friendship Hospital, Beijing, China

**Device and producing company:** Dornier compact Delta II

**Introduction:** Bone Marrow Edema Syndrome (BMES) of the Hip is a rare condition of unclear etiology characterized by hip pain, limited osteopenia on plain radiography and characteristic magnetic resonance image (MRI) findings. There is a need for an effective and non-invasive method of treatment for BMES. The aim of this study was to compare the short-term clinical effect of high-energy extracorporeal shock wave therapy (ESWT) for intractable bone marrow edema syndrome of the hip (BMESH), with the one treated by femoral head core decompression (FHCD).

**Methods:** Twenty one patients who had gotten intractable bone marrow edema syndrome of the hip from March 2010 to January 2013 were retrospectively studied. In ESWT group, there were 9 patients (12 hips) included, and in FHCD group, 12 patients (17 hips). We located edema lesions of each femoral head relying on the use of intraoperative X-ray fluoroscopy and preoperative MRI findings. 4-6 shockwave treatment points were applied on each femoral head. ESWT Orthopaedic Settings: Number of levels 3-4, with 2,000-3,000 impulses each administered at 0.50 MJ/mm², The affected limb should be protected under the crutch during the weight-bearing walking in 4-6 weeks post-treatment. Clinical assessments included assessment of preoperative and postoperative pain VAS score, Harris hip score (HHS), intraoperative fluoroscopy radiation dose, operation time, operation costs, and the symptoms disappeared time and MRI findings. Follow-up examinations were scheduled at 1, 3, 6 and then 10 months.

**Results:** For Unilateral lesion, pre-operative VAS, pre-operative HHS were calculated to be 7.9±0.9, 47.6±6.4 for U-ESWT and 8.0±0.8, 46.4±10.6 for U-PHCD (no significant difference, p>0.05). For Bilateral lesion, pre-operative VAS, pre-operative HHS were calculated to be 7.8±1.2, 43.2±9.3 for B-ESWT and 7.1±1.3, 52.4±5.7 for B-PHCD (no significant difference, p>0.05). There was much significant difference between ESWT and PHCD groups regarding post-operative instant VAS (Unilateral: p=0.008, Bilateral: p=0.014), regarding post-operative HHS, also much significant difference between two groups for Unilateral lesion (p=0.002), but no significant difference for Unilateral lesion (p=0.460). Daily activities were begun significantly earlier in ESWT. Average overall operation time for each treated group was similar, with no statistical difference (p>0.05). All retrospectively collected data assessing pain relief were dichotomised using 6 months of impairment as the cut-off point. The time when their symptoms disappeared in ESWT was significantly shorter (p<0.01) in Unilateral lesion group, and in Bilateral lesion group approximately similar (p=0.089). Hospital costs were shown significantly lower in ESWT than in FHCD, in Unilateral or Bilateral lesion group. In Unilateral group, intraoperative fluoroscopy radiation dose in ESWT was lower than in PHCD (p=0.010), the same as Bilateral group (p=0.000). MRI imaging follow-up period two hip bone marrow edema were improved.

**Discussion:** All patients remained free of pain with normal radiographs and MRI scans through high energy ESWT.
**Conclusion:** ESWT showed to be a valid, sure, noninvasive tool, has a low complication rate, and a relatively low cost compared to other types of conservative and surgical approaches, to solve intractable rapidly BMESH.
Results of Piezoelectric Shockwave Therapy for the Treatment of Bone Non-unions: Four Years Experience
Galina Konstantinovna Sermyazhko

Institution: Tula State University, Medical Institute, Russia

Device and producing company: Piezo Wave, Richard Wolf

Introduction: For over four years we have applied Piezoelectric Shockwave Therapy (ESWT) for the treatment in bone non-unions. The goal of research was study of stimulative effect of ESWT on the reparative regeneration of bone tissue in case of delayed union of fractures and pseudarthrosis of patients in the setting of city rehabilitation center and the search for optimal of treatment protocols.

Methods: ESWT was applied to 89 patients with delayed union diaphyseal fractures of extremities and pseudarthrosis. Selection criteria were fractures with delayed consolidation for 4 months or more. The time elapsed from the date of the injury varied from 4 months to 7 years. Patients were aged from 20 to 65 (mean age: 48.5 years, 39 males, 50 females). They received ESWT treatment. 5 sessions with high-energetic focused ESWT (2000-4000 shots, a frequency of 4 - 5 Hz, mean energy density: 0.45 MJ/mm²).

ESWT procedures were performed on outpatient basis in a weekly interval of sessions.

Results: According to our data, consolidation of fracture occurred in 96.6 % (86 patients). ESWT accelerates the union of fractures on 2-4 weeks compared to the control group, after the fourth procedure the pain reduced from 7.8 ±1.5 to 1.4 ±1.1 (78% reduction, p<0.05).

Discussion: The leading factors in pathogenesis of delayed union are deterioration of blood supply in damaged segment of the limb. The impact by high-energetic focused ESWT on fracture zone or nonunion induces neovascularization and osteogenesis. Thus it can be assumed that neovascularization plays a fundamental role in improving the blood supply of bone fragments, which in turn contributes to bone remodeling and regeneration.

Conclusion: ESWT should be more widely applied in cases with a need of fast rehabilitation (athletes, socio active patients). A combination of surgical treatment with high-intensity focused ESWT should be the gold standard in the treatment of long bone fracture nonunions.
Extracorporal Shockwaves in the Treatment of High Energy Lower Limbs Long bone Non Union
Carlos Eduardo Sandoval (1), Alvaro Fernando Valenzuela (1), Carlos Rojas (1), Sebastian Monge (1), Manuel Brañes (2)

Institution: (1) Hospital de Trabajador; (2) Clinica Araucosalud; Santiago de Chile, Chile

Device and producing company: DUOLITH SD1 STORZ MEDICAL AG

Introduction: Delayed union and non-union of femur and tibia are common in trauma hospitals. The purpose of this study was to examine the effect of focused extracorporeal shock wave therapy (ESWT) on the treatment of non-unions in high energy lower limb long bone diaphyseal fractures.

Methods: Prospective nonrandomized study patients were investigated at a single referral trauma center of worker compensation insurance. Inclusion criteria was a minimum duration of non-union for 6 months after first surgery (ORIF). We applied two sessions of ESWT (10000 pulses /0,35mJ/mm² - 0,55mJ/mm², Storz DuolithSD1) spaced by 4 to 6 weeks period. Re-evaluation was performed once a month after treatment, with clinical examination and radiologic control. We considered "success" with 70% of bone consolidation (that include 3 corticals) within follow-up period (4 to 10 months). Cases considered "failures" comprised, a) absence of any biological reactivity in the treated area for three months after first treatment (patients underwent new surgical procedures); b) less of 70% of bone healing at the end of 10 months (f-u).

Results: We included 35 patients (average age, 38.5 years) with a diagnosis of nonunion. The average onset of therapy time since the accident was 10,6 months (range 6-20,3 months). At the time of last follow up, 24 of 35 (68.6%) patients have demonstrated complete fracture healing. Mean time from first shock wave therapy to complete healing of the nonunion was 4.1 months (range 2 – 9.6 months). In 22 patients (62.9%) one or more re-intervention had been performed prior to ESWT, in this subgroup following ESWT we found a success rate of 54.5% (n=12).

Discussion: Our series of patient studied have a rate of consolidation similar to the current literature reports.

Conclusion: ESWT appears to represent an additional treatment option in patients with non-union after high energy fractures.
“Fractures at Risk” – Which Patient Will Benefit of Shockwave Therapy (ESWT)?
Frank Bätje

Institution: Private General Medicine Office, Hannover, Germany
Device and producing company: Duolith Ultra®, Modulith SLK®, Storz Medical

Introduction: It does not appear very good skilled to wait for defined periods in osseous healing before a timely shock wave therapy would be capable to prevent the development of bone healing disorder in a given indication. It is at an early stage to identify those cases that have such critical conditions that treatment in early stages should prevent delayed fracture healings, treatment in delayed unions should prevent non-unions and treatment in non-unions should prevent surgery.

Methods: Between 2006 and 2013 1064 consecutive fracture-, osteotomy- or arthrodesis-patients with existing or expected bone healing disorders have been treated with highenergetic focused shockwaves. We have used two different devices, depending on the given case. Most patients have been subsequently interviewed and only meaningful results were introduced in this evaluation. Retrospectively, it was decided by means of questionnaires, radiological controls and doctor's opinion, if treated bones or joint were completely healed or not healed.

Results: Preliminary) Overall 745/1064 (75%) showed sufficient bony consolidation ("healing") after ESWT. Cases of "fresh" fractures or arthrodeses were healed in 76%, cases of delayed unions in 73% and cases of non-unions in 70% - the respective next degree of impaired bone healing was avoided therefore. Depending on localization and indication and also based on the above three therapy-groups, certain cases proved more successful treatable than others.

Discussion: It is still the gold standard in most industrial nations to treat bone healing disorders surgically with or without osteoconductive and / or osteoinductive materials. The highenergetic focused shock wave therapy should be an alternative to surgical procedures justified because their retrospective controls in an exceptionally large clientele show that "fractures at risk" and "arthrodoses at risk" benefit from it. Certain subpopulations, such as arthrodeses of the subtalar joint, show poor results, others, such as scaphoid fractures and non-unions, show good results, similar or better compared with surgery.

Conclusion: Surgeons should assess individual prognoses of patients after fractures or arthrodesis. As ESWT is a serious alternative to surgery in cases of “fractures at risk” or delayed bone healing all physicians who treat their patients with shockwaves should have knowledge about probable outcomes and have to use comparable shockwave devices in the interest of improvement of successful therapy protocols for different impaired bone healings.
Serum Proteomic Analysis of Extracorporeal Shockwave Therapy Enhanced Diabetic Wound Healing in a STZ-Induced Diabetes Model

Yur-Ren Kuo (1), Yu-Ting Huang (1), Ching-Jen Wang (2)

Institution: (1) Dept. of Plastic and Reconstructive Surgery, (2) Dept. of Orthopedics, Kaohsiung Chang Gung Memorial Hospital, Taiwan

Device and producing company: Derma PACE, Sauwave, USA

Introduction: Previous studies demonstrated extracorporeal shockwave therapy (ESWT) has a significant positive effect on accelerating diabetic (DM) wound healing. However, the systemic effect after ESWT is still unclear.

Methods: This study investigated the plasma protein expressions between the ESWT group and DM controls using proteomic study. A dorsal skin defect (6×5 cm) in a streptozotocin-induced DM Wistar rat model was used. DM rats receiving no ESWT and received ESWT post-wounding were analyzed. The spots of interest were subjected to in-gel trypsin digestion and MALDI-TOF mass spectrometry to elucidate the peptide mass fingerprints. The mass spectrometric characteristics of the identified proteins including their theoretical pIs, molecular weights, sequence coverage, and MASCOT score were analyzed. Protein expression was validated using immunohistochemical analysis of topical peri-wounding tissues.

Results: The proteomic study revealed the rats at both day 3 and day 10 post-ESWT had significantly higher abundance of haptoglobin (Hp) and significantly lower levels of the vitamin D-binding protein (DBP) precursor as compared to the DM controls. Immunohistochemical stain of topical peri-wounding tissue also revealed significant up-regulation of Hp and down-regulation of DBP expressions in the ESWT group which was consistent with the systemic proteome study.

Discussion: This proteomic study uncovered the differential plasma protein expressions that enhance wound healing in ESWT DM rats are involved in angiogenesis and anti-inflammatory effects. Our results provide the basis for further elucidation of the bio-mechanism of these proteins and the related signaling pathway of wound healing enhancement by ESWT.

Conclusion: This proteomic study uncovered the differential plasma protein expressions that enhance wound healing in ESWT DM rats are involved in angiogenesis and anti-inflammatory effects. Our results provide the basis for further elucidation of the bio-mechanism of these proteins and the related signaling pathway of wound healing enhancement by ESWT.
Comparison the Effects of Extracorporeal Shockwave Therapy and Hyperbaric Oxygen Enhanced Diabetic Wound Healing in a Rat Model of STZ-induced Diabetes
Yur-Ren Kuo (1), Chun-Tin Wang (1), Ching-Jen Wang (2)

Institution: (1) Dept. of Plastic and Reconstructive Surgery, (2) Dept. of Orthopedics, Kaohsiung Chang Gung Memorial Hospital, Taiwan

Device and producing company: Derma PACE, Sauwave, USA

Introduction: Extracorporeal shockwave therapy (ESWT) and hyperbaric oxygen (HBO) therapy both have a significant positive effect to accelerate chronic wound healing. However, the effectiveness between ESWT and HBO enhanced diabetic wound healing are still debate and bio-mechanisms remain unclear. This study investigated the effectiveness of ESWT and HBO in the enhancement of diabetic wound healing.

Methods: In this study, we used a dorsal skin defect (area, 6×5 cm) in a streptozotocin (STZ)-induced diabetes rodent model. Fifty male Wistar rats were divided into 5 groups. Group I consisted of non-diabetic control; group II, diabetic control receiving no treatment; group III, rats received 2 sessions of ESWT (800 impulses at 0.09mJ/mm²) on days 3 and 7; and group IV, rats received HBO (1hr /2.5atm/day from day 1 to day 14. The wound healing was assessed clinically. The VEGF, eNOS, and PCNA were analyzed with immunohistochemical stain.

Results: The wound size was significantly reduced in the ESWT-treated and HBO-treated rats as compared to the control (P< 0.01). However, the wound healing speed in ESWT-treatment group is faster than HBO terhaps (5.7 ± 1.7 weeks versus 7.5 ± 1.05 weeks). Histological findings revealed significant reduction in pro-inflammatory reaction in leukocytes and increase in neo-vessels in ESWT and HBO groups as compared to the control. In immunohistochemical stain, significant increases in VEGF, eNOS, and PCNA expressions were noted in the treatment group as compared to the control. However, the ESWT have higher percentage expressions in HBO group.

Discussion: Treatment with ESWT and HBO both significantly enhanced diabetic wound healing associated with increased neo-vascularization and tissue regeneration, and anti-inflammatory response. However, ESWT indicated more effective than HBO and compatible our previous clinical outcome.

Conclusion: This study inidcated ESWT has more effective than HBO for wound healing. Further studies are needed to elucidate bio-mechanisms.
Functional and Molecular Characteristic of Underactive Bladder Induced by Lumbar Canal Stenosis in Rats and Effects of Low Energy Shockwave Therapy

Hung-Jen Wang (1), Yao-Chi Chuang (1), Chao-Cheng Huang (1), Michael B. Chancellor (2), Ching-Jen Wang (1)

Institution: (1) Kaohsiung Chang Gung Memorial Hospital, Taiwan; (2) Oakland University, Michigan, USA

Device and producing company: EvoTron, Sanuwave

Introduction: Lumbar canal stenosis (LCS) compromised neurological function is a common problem in elderly patients and may cause underactive bladder (UAB). Low energy shock wave (LESW) therapy has been used clinically to improve tissue regeneration. We investigate the mechanism and molecular change underlying the LCS induced UAB in rats and the effects of LESW therapy.

Methods: One small hole was drilled at the fifth lumbar vertebral arch (sham), and a rectangular piece of silicone rubber was inserted into the L5–L6 epidural space (LCS) of female Sprague-Dawley rats. LCS rats underwent bladder expression twice a day. Some LCS rats at week two were treated with LESW at bladder for 3 times. Continuous cystometry (CMG) was performed at day 14, or 28 under urethane anesthesia. The bladder was then harvested for histology, expression of M2 and M3 receptors, NGF, and agrin by western blotting.

Results: LCS induced urinary retention, overflow incontinence, and progressive increase of bladder weight. LCS bladder showed edematous change of the lamina propria, thinning of muscle layer, and decreased of agrin expression, which conditions were improved after LESW therapy.

Discussion: LESW therapy did not get the recovery of voiding function. LCS rats showed no obvious difference in M2, M3 receptor, and NGF compared with the sham rats.

Conclusion: LCS induced UAB, and altered bladder morphology and agrin expression. LESW improved bladder morphology change and agrin expression, but not the functional recovery. Further study is needed to get the best use of LESW for neurogenic UAB.
Umbilical Cord Mesenchymal Stem Cell Therapy Enhanced Islet Cells Repair

Chang-Chun Hsiao (1), Fang-Cheng Huang (2), Kuang-Hung Cheng (3), Te-Yao Hsu (1, 4), Cheng-Chan Lin (1), Shin-Yi Chen (1)

Institution: (1) Chang Gung University; (2) Cheng Shiu University; (3) National Sun Yat-Sen University; (4) Chang Gung Memorial Hospital-Kaohsiung Medical Center, Kaohsiung, Taiwan

Device and producing company: HMT Evotron, Sanuwave, Inc

Introduction: The type 1 diabetes (T1D) is caused by autoimmune destruction of pancreatic β-cells and lead to inefficient secretion of insulin. Mesenchymal stem cells (MSCs) with immunosuppressive and anti-inflammatory functions, the use of MSCs to treat T1D are a very viable methods.

Methods: We use hyaluronic acid (HA) coated 6 × 10^6 human umbilical cord MSCs (hUCMSCs) transplanted into liver capsule of T1D mice.

Results: After 4 days of treatment, the T1D mice with HA coating hUCMSCs therapy can effectively lowering blood glucose to normal 142.5 ± 13.8 mg / dL, and after 28 days of treatment, the HA coating hUCMSCs in treated mice has maintain the same level of blood glucose with normal mice.

After four days of treatment, the liver of T1D mice with HA coating hUCMSCs treatment exists on human nuclear protein, CD44 and ki67 performance. Confirmed that the HA coating hUCMSCs transplanted into liver capsule of T1D mice are present in the mouse liver with proliferation function. The islet cells in T1D mice have been damaged and smaller, and have a high degree of apoptosis generated, so the insulin expression is very weak. The islet cells in T1D mice with HA coating hUCMSCs therapy are relatively large and apoptosis is less, and has a very strong insulin expression.

Discussion: Transplant HA coated PKH-26 labeled hUCMSCs into liver capsule of T1D mice, four days after we discovery of traces of hUCMSCs in the mouse liver, but also in the pancreas of mice found a large number of hUCMSCs. This proves that the HA-coated hUCMSCs transplanted into liver capsule of T1D mice indeed migrate to the damaged pancreas doing repair islet cell function.

Conclusion: Transplantation HA-coated hUCMSCs can indeed effective in treating diabetic mice, their blood glucose drop back to normal level and to promote the restoration of islet cells or regeneration and has the function of insulin-secreting.
Benefit of Combined Extracorporeal ShockWave and Bone Marrow-Derived Endothelial Progenitor Cells in Protection Against Critical Limb Ischemia in Rats

Jiunn-Jye Sheu (1), Hon-Kan Yip (2)

Institution: (1) Dept. of Surgery, (2) Dept. of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, Taiwan

Device and producing company: none

Introduction: We hypothesized that combined treatment with extracorporeal shock wave (ECSW) and bone marrow-derived endothelial progenitor cell (BMDEPC) might exert enhanced protection against critical limb ischemia (CLI) in rats.

Methods: Male Sprague-Dawley rats (n=9 for Laser Doppler study and n=6 for laboratory examinations in each group) were divided into group 1 (sham control), group 2 (CLI treated with culture medium), group 3 [CLI treated with intramuscular BMDEPCs (2.0 x10^6 cells)], group 4 [CLI treated with ECSW (280 impulses at 0.1 mJ/mm2), and group 5 (combined BMDEPC-ECSW) after CLI induction.

Results: By day 21, Laser Doppler showed substantially lower ratio of ischemic/normal blood flow in group 2 compared with other groups (p<0.001). The protein expressions of mitochondrial cytochrome c, SDF-1, CXCR4, VEGF and eNOS were remarkably higher in group 5 than in groups 2 to 4 and notably higher in groups 3 and 4 than in group 2 (all p<0.01). The mRNA expressions of pro-inflammatory and apoptotic biomarkers, and oxidative stress were reduced in group 5 compared with groups 2 to 4, and notably lower in groups 3 and 4 than in group 2 (all p<0.01). The mRNA expression of anti-inflammatory and anti-apoptotic biomarkers were lower in group 2 than in other groups (all p<0.01).

Discussion: Immunofluorescent staining showed higher number of CD31+ SDF-1+, CXCR4+ and vWF+ cells, and vessels in ischemic area in group 5 than in groups 2 to 4, and in groups 3 and 4 than in group 2 (all p<0.04).

Conclusion: Combined treatment with BMDEPC and ECSW is superior to either BMDEPC or ECSW treatment alone in improving ischemia in rodent CLI.
Shockwave Triggers Cultured Mesenchymal Stem Cell Proliferation via Activating mTOR-FAK Signaling Axis

Fan-Yen Lee (1), Yen-Yi Zhen (2), Hon-Kan Yip (2)

Institution: (1) Dept. of Surgery, (2) Dept. of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, Taiwan

Device and producing company: Evotron, Switzerland

Introduction: Previous studies demonstrated extracorporeal shockwave therapy (ESWT) has a significant positive effect on accelerating diabetic (DM) wound healing. However, the systemic effect after ESWT is still unclear.

Methods: To elucidate the role of cytoskeletons in SW-induced FAK phosphorylation, we administered cytochalasin D to depolymerize actin filament before applying the optimal energy of 0.12 mJ/mm² to MSCs.

Results: The results showed a failure in stimulating FAK phosphorylation, highlighting the essential role of microfilament in SW-induced FAK phosphorylation. To further identify the upstream regulator, three kinases, namely GSK-3β, Akt, and mTORC1, which are activated in pressure-stimulated mechanotransduction, are assayed for SW-stimulated FAK phosphorylation. Of the three specific inhibitors, only rapamycin, an inhibitor of mTORC1, was found to inhibit FAK phosphorylation, suggesting that mTORC1 is the upstream regulator in SW-elicited FAK phosphorylation. Microscopic examination revealed not only SW-induced increase in the number of actin stress fibers, but also alternative subcellular localization of mTORC1 as vesicle-like inclusions on microfilaments. Besides, rapamycin was found to destruct the vesicle-like pattern of mTORC1, while dissociation between actin and mTORC1 was noted after cytochalasin D administration.

Discussion: Since mTORC1 is essential for cell proliferation, we performed proliferation assay for MSCs with and without SW/rapamycin treatment. The results demonstrated significant enhancement of cell proliferation after SW treatment.

Conclusion: Our findings suggest that mTORC1 and microfilament synergistically regulate FAK phosphorylation and mTORC1-FAK signalling participates in MSC proliferation.
Extracorporeal Shockwave Therapy Reverses Ischemia-Related Left Ventricular Dysfunction and Remodeling: Molecular-Cellular and Functional Assessment

Jiunn-Jye Sheu (1), Chin-Jen Wang (2)

Institution: (1) Dept. of Surgery, (2) Dept. of Orthopedic Surgery, Kaohsiung Chang Gung Memorial Hospital, Taiwan

Device and producing company: none

Introduction: An optimal treatment for patients with diffuse obstructive arterial disease unsuitable for catheter-based or surgical intervention is still pending. This study tested the hypothesis that extracorporeal shock wave (ECSW) therapy may be a therapeutic alternative under such clinical situation.

Methods: Myocardial ischemia was induced in male mini-pigs through applying an ameroid constrictor over mid-left anterior descending artery (LAD). Twelve mini-pigs were equally randomized into group 1 (Constrictor over LAD only) and group 2 [Constrictor over LAD plus ECSW (800 impulses at 0.09 mJ/mm²) once 3 months after the procedure].

Results: Results showed that the parameters measured by echocardiography did not differ between two groups on days 0 and 90. However, echocardiography and left ventricular (LV) angiography showed higher LV ejection fraction and lower LV end-systolic dimension and volume in group 2 on day 180 (p<0.035). Besides, mRNA and protein expressions of CXCR4 and SDF-1α were increased in group 2 (p<0.04). Immunofluorescence staining also showed higher number of vWF-, CD31-, SDF-1α, and CXCR4-positive cells in group 2 (all p<0.04). Moreover, immunohistochemical staining showed notably higher vessel density but lower mean fibrosis area, number of CD40-positive cells and apoptotic nuclei in group 2 (all p<0.045). Mitochondrial protein expression of oxidative stress was lower, whereas cytochrome-C was higher in group 2 (all p<0.03). Furthermore, mRNA expressions of MMP-9, Bax and caspase-3 were lower, whereas Bcl-2, eNOS, VEGF and PGC-1α were higher in group 2 (all p<0.01).

Discussion: none

Conclusion: In conclusion, ECSW therapy effectively reversed ischemia-elicited LV dysfunction and remodeling through enhancing angiogenesis and attenuating inflammation and oxidative stress.
Extracorporeal Shockwave Effectively Attenuate Brain Infarct Size Improve Neurological Function in Rat Mode
Chun-Man Yuen, Han-Kan Yip

Institution: Kaohsiung Chang Gung Memorial Hospital; Taiwan
Device and producing company: none
Introduction: We tested hypothesis that extracorporeal shock wave (ECSW) therapy effectively attenuated rat brain ischemic area (BIA) and improved neurological function in acute ischemic stroke (AIS) that was induced by occlusion of distal left internal carotid artery.

Methods: Adult-male SD rats (n=20) were divided into AIS, and AIS-ECSW (energy dosage of 0.15mJ/mm2/300 impulses) and sacrificed by day 21 after the procedure.

Results: In normal animals, the intra-cranial pressure was found to be increased from 5 mmHg (baseline) to 15 mmHg during applying the ECSW to the rat skull. Additionally, the brain protein levels of apoptotic (cleaved caspase 3 and PRAP) and DNA-damaged (γ-H2A) markers did not differ between with and without ECSW therapy. Furthermore, p-S6K and focal adhesion molecule (FAK) were the earliest proteins to be activated (2 hr post-ECSW), followed by heat shock protein 70 and the brain glial cells (≥ 16 hr after ECSW application).

By day 21, brain MRI demonstrated that that BIA was larger in AIS than in AIS-ECSW (p<0.001). Sensorimotor functional test (Corner test) identified a higher frequency of turning movement to left in AIS than in AIS-ECSW (p<0.05). The cellular and protein expressions of angiogenesis biomarkers in BIA (CD31, VEGF, CXCR4, SDF-1α) were higher in AIS-ECSW than in AIS animals (all p<0.001). Number of apoptotic nuclei on TUNEL assay and protein expressions of cleaved caspase 3 and PRAP, and γ-H2A, MMP-9, and TNF-α were significantly higher in AIS-ECSW than in AIS animals (all p<0.001).

Discussion: none

Conclusion: Application of ESCW with energy dosage of 0.15mJ/mm2/300 to the rat brain was safe and effectively reduced BIA and improved neurological function through inhibiting inflammation and cellular apoptosis and enhancing angiogenesis.
Combined Therapy with Extracorporeal Shockwave and Bone Marrow Derived Mesenchymal Stem Cell Alleviates Left Ventricular Dysfunction and Remodeling through Inhibiting Inflammatory Stimuli & Enhancing Angiogenesis in a Swine Acute Myocardial Infarction Model
Jiunn-Jye Sheu (1), Hon-Kan Yip (2)

Institution: (1) Dept. of Surgery, (2) Dept. of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, Taiwan

Device and producing company: none

Introduction: We hypothesized that combined therapy with extracorporeal shock wave (ECSW) and bone marrow-derived mesenchymal stem cells (BMDMSCs) offered an additional benefit as compared with each treatment modality alone in alleviating left ventricular (LV) dysfunction through enhancing angiogenesis, exerting cytokine/paracrine effects, and suppressing inflammatory response/oxidative stress.

Methods: Male mini-pigs, weighting 18-20 kg, were equally divided into group 1 (normal control), group 2 [AMI (by ligation of left anterior descending artery), group 3 (AMI-ECSW), group 4 (AMI-BMDMSC) and group 5 (AMI-ECSW- BMDMSC). The animals were sacrificed at day 60 after.

Results: The baseline LV injection fraction (LVEF) did not differ among five groups (p>0.5). However, by day 60, the LVEF was highest in group 1 and lowest in group 2, higher in group 5 than in groups 3 and 4, and higher in group 3 than in group 4 (p<0.001), whereas the LV chamber size showed an opposite pattern of VLEF among the five groups (p<0.001). The cellular and protein levels of VEGF, CXCR4 and SDF-α in infarct area (IA) were progressively increased from groups 1 to 5 (all p<0.005). The small-vessel number and CD31 protein expression in IA were highest in groups 1 and 5, lowest in group 2, higher in group 4 than in group 3 (p<0.001). The protein (MMP-9, TNF-1α and NF-kB, oxidized protein) and cellular (CD14+, CD40+) biomarkers in IA were highest in group 2 and lowest group 1, lower in group 5 than in groups 3 and 4, and lower in group 4 than in group 3 (all p<0.001).

Discussion: none

Conclusion: Combined therapy is superior to either one alone for improving LVEF and inhibiting LV remodeling mainly through regulating angiogenesis and inflammation/oxidative stress.
Extracorporeal Shockwave Therapy Enhanced Diabetic Wound Healing is Associated with Modulation of wnt/β-Catenin Expression

Kuender Yang (1), Yur-Ren Kuo (2), Chun-Ting Wang (2), Ching-Jen Wang (2)

Institution: (1) Show Chwan Memorial Hospital, Changhua; (2) Kaohsiung Chang Gung Memorial Hospital, Taiwan

Device and producing company: none

Introduction: Our previous studies demonstrated extracorporeal shockwave therapy (ESWT) has a significant positive effect to accelerate chronic wound healing. However, the bio-mechanisms operating during ESWT of wounds remain unclear. Studies have been proved that Wnt/β-catenin signaling induces epithelial differentiation during cutaneous wound healing. This study investigated the effectiveness of ESWT in the enhancement of diabetic wound healing is related of wnt/β-catenin pathway.

Methods: In this study, we used a dorsal skin defect (area, 6×5 cm) in a streptozotocin (STZ)-induced diabetes rodent model. Wistar rats were divided into different groups. Group I consisted of non-diabetic control; group II, diabetic control receiving no ESWT; group III, rats received 1 session of ESWT (800 impulses at 0.099mJ/mm2) on day 3; group IV, rats received 2 sessions of ESWT on days 3 and 7; group V, rats received BIO as a GSK-3β inhibitor to mimic the β-catenin effect. The wound healing was assessed clinically. The tissue samples were analyzed with immunohistochemical (IHC) stain and RT-PCR after different time -periods.

Results: The wound size was significantly reduced in the ESWT-treated rats as compared to the control (P< 0.01). In IHC stain, Wnt3a and Wnt5a expressions were significant increase in 3 days and 10 days post-ESWT in 2 sessions, as compared to that in controls without treatment. The β-catenin expression was significant increase in 3 days and 10 days post two-sessions of ESWT as compared to that in controls.

Discussion: In this study, the results demonstrated that Wnt/β-catenin pathway is involved in ESWT enhanced wound healing.

Conclusion: Treatment with multiple sessions of ESWT significantly enhanced diabetic wound healing associated with increased wnt / β-catenin and tissue regeneration.
Introduction: Patients that have received a total knee arthroplasty (TKA) are more active day by day, not only because of the current lifestyle of the senior citizens, but because of the modern surgical and rehabilitation techniques in knee surgery. It is a common fact to have sport rehabilitation programs in our total knee patients that would have been almost a sin a decade ago, including low impact sports like golf or cycling. The major concern is the risk of loosening in the short term and wear in the long term. Anterior knee pain during exercise is common, and usually directs the knee surgeon to rule out infection or loosening. However, many patients have an extensor mechanism overload in a somehow un-natural biomechanical environment. We have found a number of TKA patients that clearly have a patellar tendinopathy and not a joint or prosthetic problem. We have treated patients with patellar tendinopathy with Shockwave Medicine for the past 15 years with excellent results. We hypothesize that the use of low energy radial shockwaves could safely provide pain control and tendon regeneration in our TKA patients with patellar tendinopathy. In this short case series we followed four patients with patellar tendinopathy and a TKA treated with radial shockwave therapy.

Methods: We treated four volunteer patients with previous TKA that signed an informed consent to receive shockwave therapy for their patellar tendinopathy. All cases had a total knee arthroplasty operated by the senior author. All cases had the same implant and technique: a Genesis II total knee implant, with no patellar implant (Smith & Nephew – London England). The average age was 64 years o, and had the surgery done between 18 and 26 months before (avg. 22 months). They all were male active executive patients that play golf twice a week regularly for more than 20 years. They were symptomatic for anterior knee pain for 7 -12 months (avg. 9.5 months). All had normal X-rays, bone scans and lab tests that ruled our infection or implant loosening. They all had at least three physical therapy protocols in the past six months without results. They all have been prescribed with NSAIDS and pain medication with temporary relief. The main complaint was pain during and after walking or golfing. They all received a standard 6000 radial LPSP shockwave protocol in two weekly sessions, with 2000 initial analgesic shockwaves, 2000 therapeutic shockwaves over 2 BAR and 2000 final analgesic shockwaves on each session. In all cases, the treatment was performed by the authors, using a BTL5000-Power Radial Shockwave device (BTL Industries Checz Rep). Patients were followed for three months and assessed for pain-VAS and function Roles and Maudsley scores, and any adverse effect was recorded. At the end of the study we performed a new X Ray and bone Scan in order to determine possible changes or signs of loosening. The study was done independently with no financial or material support from the manufacturers of the mentioned devices or implants.

Results: All patients improved pain and function. Three patients improved the VAS score over 50% after one session, and one improved only 26% with an average of 46%. After the first month follow up the average VAS improvement was of 65%, and did not change much, to a 63% and 69% after two and three months. The functional score
showed an improvement in all patients. All four had a poor rating at the beginning of the study, and ended with two excellent, one good and one fair rating. All patients revealed satisfaction with the treatment, and a good return to golf with little or no pain during or after sports. No complications or side effects were found or reported by the patients. No X ray or Bone Scan Changes were found at the three-month follow up.

**Discussion:** This is the first report of Extracorporeal Shockwave Therapy for this medical condition. Even though the series is a short one, the results are very encouraging in active patients that had no results with previous conventional treatments. The low energy and the low depth of the radial pressure waves did not cause any damage, symptoms or changes on the implants or the bone-cement-prosthesis interfaces. Our previous experimental studies using high-energy focused shockwaves on an experimental hip prosthesis cemented model did not show any changes in the interfaces. More studies must be performed in order to provide the solid evidence we require as knee surgeons to use this promising procedure as a standard in our patients.

**Conclusion:** The use of shockwave therapy in this series of patellar tendinopathy patients with previous total knee arthroplasty is favorable, has similar results as those found in other patients with the same condition and without a knee implant.
Shockwave Therapy in Pes Anserinus Tendinopathies: Report of 239 Cases

Authors: Rosanna Audain,Alejandra Guevara, Roberto Audain, Yarila Avarez, Nahin Perez
Institution: Unitrond CA, Venezuela
Device and producing company: Orthospec, Medispec

Introduction: The pes anserinus tendinitis is the inflammation of the insertion of the conjoined tendons of three muscles: sartorius, gracilis and semitendinosus.

Methods: A retrospective study on 309 cases of anterior knee pain was performed between January 2009 and March 2012. Patients with Anterior Knee Pain Syndrome were included in the study: AKPS 239/309 (77.34%), Female 121/239 (50.67%), Male 118/239 (49.37%), mean age: 45 years. Patients were defined as false negative when MRI were not conclusive for tendinopathy, but the patients complained of anterior knee pain in the pes anserinus region. Patients were treated with one session of 3000 focused shockwaves, with an intensity of 0,12-0,16 mJ/mm2. No sedation was used. We analyzed the variations in the Lysholm score and the pain Visual Analogue Scale at 21 days, 45 days, 3 and six months. Patients were surveyed via telephone to determine the level of satisfaction. Data was studied by analytical and inferential statistical analysis.

Results: The incidence of AKPS tendinopathies was 70/239 (29.28%). Pes anserinus tendinitis associated with another MRI diagnosis were 49/70 (70%). Patients treated with focused shockwaves were 49/49 (100%). Level of satisfaction in false negatives: very satisfied 19/49 (38.78%) satisfied 23/49 (46.94%) dissatisfied 7/49 (14.28%) Lysholm Score: Initial 59 - Final

Discussion: We found a low correlation between clinical diagnosis and Pes Anserinus tendinopathy with MRI findings. These patients treated with ESWT improved the level of satisfaction without complications.

Conclusion: The best diagnosis of tendinopathy’s pes anserinus is through clinical evaluation and not MRI images. Due the high incidence of false negatives ESWT should be considered as a treatment of choice.
Effect of Extracorporeal Shockwave Therapy on Variable Foot & Ankle Musculoskeletal Diseases

Kiwon Young, Hunki Cho

Institution: Eulji Hospital Foot & Ankle Clinic, Seoul, Korea
Device and producing company: PiezoWave, WOLF

Introduction: ESWT is widely used in Orthopaedic Foot and Ankle Musculoskeletal disease. Most commonly applied disease is plantar fasciitis. However, many other disease can be applied for treatment between conservative and surgical treatment. We applied ESWT on variable foot and ankle disease, that failed to treat conservative method and before surgical treatment. Here we analyze variable disease and their effect of ESWT in foot and ankle musculoskeletal fields.

Methods: Variable foot and ankle disease that is not effective in conservative treatment were treated ESWT.

The diseases are plantar fasciitis, post op persistent pain(Excision of accessory navicular, Ankle instability with modified Brostrom procedure), acute and chronic ankle sprain, pain at previous fracture site, bursitis, osteoarthritis and chondral lesion, Morton's neuroma, contusion, and achilles tendinitis.

Retrospective analysis of prospectively collected clinical data of patients treated with ESWT. 201 patients' data (Male: 69, Female: 134) were collected satisfaction that graded by 4 (Excellent-Good-Fair-Poor) at before and 2 weeks after the last treatment. We defined the term 'Excellent' as pain relieved much better than before and the term "Good" as pain relieved better than before, but not as much as "Excellent". "Fair" for on change in pain, "Poor" defined as pain get worse than before. All the patient were failed to other conservative treatment and before treatment of ESWT, satisfaction were F or P state.

Results: The percentage of patients for
(1)Plantar fasciitis group was 58.7% of all patients and the results is 28% for Excellent, 50% for Good, 20% for Fair, 2% for Poor. (2)Post operative persistent pain was 8.9% of all patients and the results is 28% for Excellent, 50% for Good, 20% for Fair, 2% for Poor. (3)Acute and chronic ankle sprain / Inflammatory disease such as tenosynovitis was 8.9% of all patients and its clinical outcome was 22% for Excellent, 67% for Good, 11% for Fair, 0% for Poor. (4)Pain at previous fracture site that was treated by conservative method was 2.9% of all patients and its clinical outcome was 33% for Excellent, 67% for Good, 0% for Fair, 0% for Poor. (5)Bursitis was 2.9% of all patients and its clinical outcome was 0% for Excellent, 83% for Good, 17% for Fair, 0% for Poor. (6)Osteoarthritis and chondral lesion was 3.4% of all patients and 0%, 29%, 57%, 14%. (7)Morton's neuroma was 5.9% of all patients and 16%, 16%, 68%, 0%. (8)Contusion was 0.9% of all patients and 50%, 50%, 0%, 0%. (9)Achilles tendinitis was 6.9% of all patients and 0%, 71%, 29%, 0% for Excellent, Good, Fair, Poor each.

We defined "Effectiveness of ESWT" when more than half of patient get better (that feel Excellent or good). The disease being effective is Bursitis, both acute and chronic ankle sprain, tenosynovitis, plantar fascia, Achilles tendinitis, fracture that didn't need to operate, and contusion.

ESWT did not bring a satisfactory effect on Morton's neuroma. No serious complications were observed.
Discussion: no
Conclusion: The ESWT can be applied variable foot and ankle disease as well as plantar fasciitis. The effect of ESWT on variable foot and ankle disease is around 70% and good result especially painful post op or after fracture status.
The Effectiveness of Extracorporeal Shockwave Therapy in Patients with Plantar Faciitis
Tuğçe Köse (1), Ummuhan Baş Aslan (2)

Institution: (1) Denizli State Hospital, (2) Pamukkale University School of Physical Therapy and Rehabilitation, Denizli, Turkey

Device and producing company: EMS Swiss Dolor Clast Master

Introduction: Focused extracorporeal shock waves (ESWT) has been used in the treatment of plantar fasciitis. The purpose of this study was to determine whether ESWT application combined with exercise treatment is more effective than ESWT treatment alone in chronic plantar fasciitis patients or not.

Methods: Forty chronic plantar fasciitis patients were participated in this retrospective study. Patients were into two groups for treatment by ESWT: group 1(n=20), patients received ESWT application, and group 2(n=20), patients received ESWT application combined with combined exercise. Each group had three session of ESWT at 1-week intervals. Patients in group 2 also received plantar stretching and foot muscle strengthening exercise. Morning pain, activity pain and resting pain were assessed at pre-treatment, post-treatment and 6 week follow up period.

Results: In both groups, pain reduction was found at post-treatment and 6 weeks follow up period (p>0.05). On the other hand, no significant differences were noted between the groups.

Discussion: We hypothesized that additional exercise treatment to ESWT is increase the effectiveness of ESWT treatment in patients with plantar fasciitis.

Conclusion: Our results suggests that ESWT is effective in the treatment of chronic plantar fasciitis. Additional exercise treatment to ESWT is not increase the effectiveness of therapy.
Combined Focused and Radial Shockwave Therapy in the Treatment of Plantar Fasciitis

Authors: Gabriele Verratti, Myriam Capasso, Miguel Guedez, Carlos Lamanna, Ciro Quintero, Ambiorix Utrera, Marta Betancourt

Institution: Servicios Medicos Orthoshock, Caracas, Venezuela

Device and producing company: Epos Ultra, Dornier // Swiss Dolorclast, Ems // Duoliht Sd1, Storz Medical

Introduction: The combination of two different types of shock waves in soft tissue injuries seeks to improve the effectiveness of the resolution of the inflammatory process. This is a prospective comparative analysis on the application of shock waves with a Focused and Radial combination method under two different protocols in the treatment of chronic plantar fasciitis.

Methods: 4 sessions of the combined method using focused and radial devices were applied to 254 patients. They were divided in a control group and an experimental group, evaluating pain level. Patients were followed for 3 weeks and 6 months after completing the treatment. The control group received two focused sessions of 2000 shockwaves every week at 0,34mJ/mm, and then two weekly radial sessions of 3000 shockwaves at 1.8 Bar. The experimental group received the same protocol, but divided into two sessions with interval of seven days and then two more sessions every fifteen days.

Results: After the second session, 75 patients showed a 70% decrease of pain in the control group. At four weeks, 121 patients of the control group had 90% of pain reduction, and at six months 122 patients showed 90% of pain reduction. In the experimental group, 114 patients had 80% of pain reduction after the second session. After 4 weeks 122 patients showed 90% of pain reduction, and 124 patients reported 96% of pain reduction after six months.

Discussion: Both groups showed the same pain relief by the time of the last evaluation. The experimental group had a lower VAS at the beginning of the treatment, while the control group showed improvement only after the third session.

Conclusion: Combined focused and radial seems to be a better approach in the treatment of plantar fasciitis with ESWT.
Juan Maria Alarcon Garcia, Adolfo Santos Lian

Institution: Ibermutuamur, Spain
Device and producing company: Epos Ultra Dornier

Introduction: To describe structural characteristics and sonographic alterations of the common extensor tendon (CET) pre and post ESW treatment. Lateral epicondylopathy, is a tendinopathy caused by overuse. Affecting the common extensor tendon (CET). It is widely accepted that the deeper and more anterior fibers belong to the extensor carpi radialis brevis, and those closest to the surface belong to the extensor digitorum. Moreover, it is thought that the extensor digiti minimi and extensor carpi ulnaris contribute to tendon formation to a much lesser extent.

Methods: In patients, we determined; sonographic CET thickness, morphologic characteristics, and alterations; and color Doppler measurements of the epicondylar artery width and peak systolic velocity. Age, sex, epicondylalgia history, activities (work), and dominant and non dominant elbows were noted.

We performed U.S pre and post treatment with esw. Focal system.

Results: We have a homogeneus group of work accident pathology. All the group had history of tennis elbow. All the group, 100 % was studied by ultrasound, B and PW doppler. 50 % with peak sistolic study. all cases, were dominant elbow.

100% we find images compatibles with epicondilophaty in grade I %; II %; III % and none in IV degree.

Alteration in vertex %. Calcium %. Deep fibrilar pattern alteration % located in the posterior área in % and % in lateral área. We check this images in longitudinal and transversal.

Morphologic abnormalities were found in 79.5% of patients with a history of epicondylalgia; 7.7% with no history had abnormalities; and 55.9% with abnormalities but no history were older than 55 years. Bone spurs (49.2% versus 16.4% [P < .001]), tendon calcifications (21.5% versus 3.9% [P < .001]), and bone cortex abnormalities (12.3% versus 1.7% [P < .001]) were found more often in non-normal elbows; 79.4% of bone spurs in normal elbows occurred in patients older than 55 years.

We get good/ excelent results in 90.02 % of cases in pain.

Discussion: Lateral epicondylopathy is a progressive clinical process resulting in progressive and secuential sonographic changes. We also believe that some of the sonographic alterations thought to be associated with the disease could appear in those who have never had it.

We believe, ultrasound is a real good way for diagnosis, location and following the patients.

We try to detect as prognosis pre treatment depending of the peak sistolic study by pulse doppler.

Conclusion: b US is an excelent in the treatment of esw. Power doppler helps to determine the prognosis of evolution. Peak sistolic/ pulse doppler helps us in the pronosis and the evolution of flow an resistance index.

We can predict the result before using esw.
**Effectiveness of Shockwave Treatment Compared With Eccentric Exercises and Mobilization for Chronic Lateral Epicondylitis of the Elbow.**

**A Prospective, Randomized, Blinded, Multicentric Study**

Jose Ramon Aranzabal (1), Mireia Gonzalez Osinalde (2), Javier Garcia-Ariño (1), Ricardo Trujillo (2), Jorge Martinez Ezquerra (2), Pilare Aranzamendi (1), Maria Isabel Hernandez (1), Maria Jose Fernandez (2), Jose Ignacio Emparanza (2), Jaime Usabiaga (2)

Institution: (1) Hospital Bidasoa, (2) Hospital Universitario Donostia, Spain,

**Device and producing company:** Epos Ultra Dornier

**Introduction:** The purpose of this investigation is to evaluate the efficacy of High Energy ESWT without anesthesia compared to an Eccentric Exercises and Mobilization (EEM) protocol.

**Methods:** A prospective, randomized, multicentric, single blinded study performed at the University of the Basque Country (UPV-EHU). CEIC of Hospital Donostia supervision.

78 patients who fulfilled the Inclusion and Exclusion Criteria included into ESWT and EEM groups.

ESWT: 4 treatments of High Energy focused ESWT without anesthetics. Four weeks interval.

The protocol of EEM: 16 weeks electrotherapy, Kinesitherapy and Elongating and Eccentric Exercises.

After 16 weeks, patients were evaluated by a blind Orthopaedic Surgeon. The tests included Subjective Pain VAS, Dynamometric Strength, Satisfaction and other provocation clinical tests.

**Results:** During two years a total of 60 of the 78 randomized patients completed all treatments (30 ESWT and 30 in the EEM group).

All the tests demonstrated an improvement in both groups.

A significant difference (p=0.02) in pain reduction was observed in the ESWT (VAS initial mean 4.54 to final 7.94) group compared with the EEM group (5.32 to 6.98).

No significant differences were observed in the other parameters evaluated.

**Discussion:** Satisfaction, Strength and other Parameters improved in both groups but differences were not significant.

Subjective pain score improved in both groups. The improvement was better in the ESWT group and a statistically significant difference (p=0.02) was observed between the groups.

**Conclusion:** These results demonstrate that High Energy ESWT is useful in the treatment of the CLE.

ESWT has been more efficient in Pain reduction than EEM.
Piezoelectric Shockwave Therapy in Management Lateral Epicondylitis of the Elbow
Ayman Elwey Balabel, Eman Mohammed Alkhalfan, Amani Ahmed Yaccob

Institution: Ahmadi Hospital, Kuwait
Device and producing company: Piezoson 300

Introduction: Tennis elbow is the common term used to describe the pain of undefined pathology over the common extensor origin at the lateral aspect of the elbow and that interferes with the activities of daily living, computer use, sport and at workplace. Treatment for each case remains controversial and is based on the professional judgment of the health care provider. Tennis elbow is usually easily diagnosed by a physical examination. Up to 90% of cases can be remedied by nonsurgical treatments, non-steroidal anti-inflammatory medications, physiotherapy modalities in form of cold packs, and ultrasound additionally eccentric exercises program and elbow support brace, lastly is steroid, symptoms usually diminish within four to six weeks with appropriate treatment. Surgical treatment is necessary in 5% of patients in case of failure to conservative line and still persist. The outcome of surgical treatment is not satisfactory.

Methods: Retrospective study including 20 patients with tennis elbow, ages 30-55 years old, with a pain VAS rating of 8-9, with pain in daily living activities and sometime at rest, they were clinically diagnosed as lateral epiconylitis elbow. Painful elbow present for a minimum of 3-5 months, pregnancy, infectious or tumorous diseases were excluded. We performed the treatment as an outpatient procedure without anesthesia our protocol at least 3and maximum 5 Focused ESWT sessions every two weeks, with a 3000 pulses, energy level of 0.15 – 0.20 mJ/mm². All patients had been advised to start stretching exercise and eccentric loading exercises after 4 weeks after last treatment. Patients were advised to continue exercises for 12 weeks.

Results: We followed patients after 5-6 month, and found that 16 patients showed 80% patients were free from pain, significantly better 10%, 2 patients, Pain had been reduced to VAS 2-3 and range of motion had significantly improved. 5% of our patients were slightly better and 5% no changes. Mean pain score before treatment was 8.78 ± 0.65 and after we recorded 4.35 ± 1.40. ROM changed from 27.50 ± 7.26 to 78.25 ± 10.11 with a highly significant P-value > 0.001.

Discussion: Focused piezoelectric Shock wave therapy produces significant relief of pain, improves ROM in tennis elbow and decrease physical incapacity produced by tennis elbow.

Conclusion: FESWT treatments should be considered as line of treatment in elbow epicondylities, it is very effective, noninvasive, and safe procedure with no complications or any side effects, exercise program is also recommended.
Radial Shockwave Therapy and High Frequency Laser Combined Treatment in Elbow Tendinopathies
Carlos Leal, Diana Lemus, Jenny Juschten

Institution: Fenway Medical; Bosque University; Bogota, Colombia
Device and producing company: BTL5000 POWER; BTL HILT UNIT; ORTHOGOLD 100 / MTS

Introduction: The treatment of elbow tendinopathies with radial pressure waves (RSWT) has showed good and excellent results in over 75% of the cases in most of the series in the literature. In the past ten years we have used a two-session RSWT protocol with 2000 therapeutic radial shockwaves above 2 BAR, preceded by 2000 analgesic shockwaves with high number of repetitions per second, followed by another analgesic 2000 shockwaves. This protocol has allowed us to have 81% success rate in the treatment of chronic elbow tendinopathies. Our protocol includes a follow up visit two weeks after the final SWT session. If the patient reports a VAS pain scale improvement lower than 50%, we proceed to a third and final session, usually with a higher power focused device. Our group has been working in the past year with High Intensity Laser Therapy (HILT) for acute musculoskeletal painful conditions with excellent results. We hypothesize that the use of HILT may have a significant control of pain if combined with RSWT. In this study we compare the outcome of a combined therapy of RSWT and HILT on the third session of Focused Shockwaves in patients that did not improve pain over 50% in their follow up evaluation.

Methods: We performed a case control study on 21 patients diagnosed for chronic lateral epicondyle elbow tendinopathy, that did not improve pain control over 50% in the VAS scale on the follow up visit two weeks after the second RSWT session. We had 14 female and 7 male subjects with and average age of 35.5 y/o (19-52 y/o). They were divided in two groups of 10 and 11 patients. The two groups were statistically similar. They all signed an informed consent. In all cases we used for the first two sessions a Radial SWT generator (BTL 5000 Power – BTL Industries Checz Rep). All subjects were tested and evaluated by ISMST & ONLAT certified specialists. In the Cases Group (RSWT+HILT ) we applied a progressive protocol using 200 shocks on 15 Hz, 200 shocks on 10 Hz and 200 shocks on 5 Hz, plus the application of 2500 laser shots over the elbow epicondyle painful region. We used a HILT unit (BTL Industries Checz Rep). The laser treatment was then repeated every 4 days in four more sessions. In the Control Group (RSWT+FSWT) we used a our regular protocol of 1000 focused shockwaves using an electrohydraulic device ( MTS Orthogold – OE155 – soft focused applicator - MTS Medical – Konstanz, Germany). We followed up the patients for four months, with a monthly record of VAS pain score, the Roles and Maudsley scale, and a record for any adverse effects. All data was recorded and analyzed using a One-Way ANOVA, and the P value was based in <0.01. The study was done independently with no financial or material support from the manufacturers of the mentioned devices.

Results: Both the cases group and the control group patients improved pain and function in the four-month follow up. The RSWT+HILT treated patients had a 71% VAS pain reduction after 5 months, as compared with a 70% in the RSWT+FSWT control group. The Roles and Maudsley scores showed good and excellent results in 70% of the cases group patients, as compared with 73% in the control group. 9/11 patients
improved 25%-50% their pain in the four-month follow up, and 2/11 improved over 50% in the cases group. The control group had similar results, with 7/10 patients that improved 25%-50% and 3/10 over 50%. All reported data in pain control, functional score and improvement rates were not statistically significant. No patients showed increase in pain or any complications.

**Discussion:** The use of HILT has proven efficacy and safety in pain control of musculoskeletal lesions, and it’s regenerative power is still under research. Shockwave medicine has proven to be a great tool in tissue regeneration, neovasculogenesis and healing, but pain control is still a short and long-term issue. This study shows a possible use of the best of both technologies in benefit of our tendinopathy patients. We do have better results in our cases with RSWT that did not require a third session, with a 81% pain control, as compared with the 71% and 70% of the patients included in this study, who were the poor-results individuals who required a third treatment session. In future studies we will compare primary patients using RSWT, FSWT and combined RSWT+HILT.

**Conclusion:** The use of a combined therapy of radial shockwaves and high intensity laser therapy showed similar results as the use of focused shockwaves in the recurrent pain after a primary shockwave treatment for tennis elbow.
Extracorporeal Shockwave Therapy in Calcific Tendinosis of the Rotator Cuff: Comparision of Radial and Focal Treatment
Edson Serrano, Karim Flores, Jean Carlos Criado

Institution: Neomedica Shockwave Unit; Lima, Peru
Device and producing company: ORTHOGOLD 100, MTS; BTL 5000, BTL 6000
Introduction: Calcific tendinosis of the shoulder is often associated with chronic pain and impairment of function. Extracorporeal shockwave therapy (ESWT) is considered to be a treatment option. We compared the effects of two different ESWT technologies: focal and radial.

Methods: Forty eight shoulders were followed in 2 groups of twenty-four each. The treatment was weekly consisted of 3 x 2000 focal electrohidraulic shockwave with an energy flux density of 0.14-0.2 mJ/mm2 without anesthesia (group A) and 5 x 6000 impulses of radial impulses with progressive protocol (group B). The patients were examined at a 4 weeks, 3 and 6 months after treatment. X-rays were performed at each visit.

Results: In six months of following after treatment the Constant Score improved from 52.5 to 78.4 in group A and from 54.2 to 72.6 in group B (p < 0.05). The values on the visual analog scale which ranges from 0 (no pain) to 10 (maximal pain) improved from 7.7 to 3.1 (group A) and from 7.4 to 3.3 (group B) before and 6 months after treatment respectively. X-rays showed a complete or subtotal calcific resorption in 56% in group A, and 38% in group B of patients.

Discussion: This is a preliminary study indicates that three sessions of extracorporeal electrohidraulic focal shockwave therapy with energy flux density of 0.14-0.2 mJ/mm2 may be as effective as five applications of a radial extracorporeal shockwave therapy with progressive protocol for calcific tendinosis of rotator cuff. Focal technology shortens the treatment time, but the radial treatment is more accessible to people.

Conclusion: Both technologies of ESWT (focal and radial) had successful and comparable result in the treated patients with calcific tendinosis of rotator cuff of the shoulder. No complications seen in six months of following. Subjectively, 84% of group A and 76% of group B judged the treatment to be successful.
Combination of Shockwave Therapy with Exercise in Shoulder Tendinopathy: Preliminary Results on Perceived Functional Outcome

Gianluca Ruggiero, Elisabetta Tibalt, Maria Cristina D'Agostino, Stefano Respizzi

Institution: Humanitas Research Hospital, Milan, Italy
Device and producing company: SLK STORZ MEDICAL

Introduction: Purpose of the study was to investigate whether association of exercise therapy with ESWT, resulted in better and early functional outcome in patients with rotator cuff tendinopathy.

Methods: Eighteen patients (average age 57.4, 12 female, 8 male) with rotator cuff tendinopathy, were randomly assigned into two groups. Both groups (A and B) were treated with ESWT. Patients in Group B were even instructed, by a Physiotherapist, with a self-assisted exercise program and provided with a therapy kit for home exercise. A weekly session of supervised physiotherapy was scheduled in order to verify and update the exercise program. Patients were evaluated at baseline and 1 and 2 months after beginning of treatment. Clinical assessment included pain and R.O.M. Subjective functional assessment included SST and D.A.S.H.

Results: At 2 months follow-up the average Pain score (assessed with V.A.S.) improved 16.5% with non significant difference between two groups (16.7% in Group A and 16.4% in Group B), confirming an overall benefit in pain relief even in short term results. Subjective functional assessment increased 3.3 (SST) and 13.6 (DASH) average points in Group A (52.3% for SST and 19.8% for DASH); Group B increased 1.8 (SST) and 12.3 (DASH) average points (28.9% for SST and 18.4% for DASH). All patients completed exercise program but one patient in Group B didn't participate at final assessment at follow-up.

Discussion: There is no significative evidence that association of exercise with ESWT for patients with rotator cuff tendinopathy seems to result in better functional improvement. However results in Group B (patients instructed with a home based, self-assisted rehabilitation program with PT supervising) seem to achieve better functional results in a shorter period.

Conclusion: Further investigations are needed to assess long term-results and different ESWT-exercise combination modalities. Updated data will be presented.
The Effects of Radial Extracorporeal Shockwave Therapy on Function, Range of Motion, Strength and Pain in Patients with Chronic Rotator Cuff Tendinosis: A Prospective Pre-Test Post-Test Design

Paolo Sanzo

Institution: Lakehead University, Thunder Bay, Canada

Device and producing company: D Actor 100 Radial Shockwave Unit; Storz Medical

Introduction: Shoulder pain is the third most common cause of musculoskeletal pain. 16-34% of the population suffers from shoulder pain with rotator cuff tendinosis (RCT) comprising a good portion of this subpopulation. Many treatments exist for RCT but few are supported by strong scientific evidence. Much needs to be learned about the etiology, pathophysiology, and management of RCT. As a result, the purpose of this investigation was to assess the effects of ECSWT on shoulder pain, function, ROM and strength in patients with RCT.

Methods: ROM, strength, functional status via the Upper Extremity Functional Scale (UEFS), and pain was measured with the P4 Scale pre- and 3 months post-treatment. 24 subjects received 3 treatments (2000 shockwaves, 2.5 bars, 10-15 Hz, 11.5 Mp) completed over the painful site (clinical focusing) and insertion of the painful tendon (anatomical focusing). A Wilcoxon Test and dependent t-Test was used to analyze the data.

Results: A significant improvement was found in UEFS scores (p=.0001); P4 scores (p=.0001); ROM for shoulder flexion (p=.013); abduction (p=.002); internal rotation (p=.02); and external rotation (p=.001); and strength for shoulder abduction (p=.01); and external rotation (p=.002).

Discussion: not applicable Radial ECSWT has been reported to be an effective treatment in some trials and ineffective in others, but the evidence and efficacy remains controversial. The results add to the merit and body of literature supporting its use.

Conclusion: Radial ECSWT is an effective treatment for patients diagnosed with RCT and is able to decrease shoulder pain, and improve shoulder function, ROM, and strength.
Dynamic Myofascial Treatment and ESWT
Jiri Nedelka (1), Tomas Nedelka (2)

Institution: (1) Rehabilitation Center and Pain Clinic, (2) Charles University, 2nd Faculty of Medicine, Dept. of Neurology Praha, CZ

Device and producing company: BTL 5000, 6000, Storz Duolith Radial Applicator

Introduction: The authors are presenting the original method of treatment of locomotive system. This technique proceeds from experience of Prague rehabilitation school, rehabilitation techniques in combination with the effect of shockwave therapy based on the principle of mechanotransduction. Long time experience with shockwave therapy used at the functional and structural disorders of locomotive system are presented here.

Methods: Manual medicine techniques allow to relieve painful muscle spasm for follow up dynamic application of radial ESWT. This affects not only painful muscle spasm but also referred pain and peripheral pain perception itself.

Results: Combination of manual therapy and dynamic application ESWT is very effective in the acute and chronic disorders of locomotive system with prompt pain relieve. Best effect was observed in non-specific cervical and low back pain and radial epicondylitis.

Discussion: Manual therapy and dynamic application of ESWT has been much more effective than static one. This technique is enabling to affect multisegmental disorders of spine, fascias, joints.

Conclusion: Authors are presenting own technique of treatment concerned in musculoskeletal system. Optimal combination seems to be manual therapy according Prague’s school and dynamic application of ESWT.
Radial Extracorporeal Shockwave Therapy in Fibromyalgia
Silvia Ramon (1), Leonor Hernandez-Sierra (1), Antonio Gomez-Centeno (2), Elena Morales-Espeleta (1), Oscar Ares (3), Maria Garcia-Manrique de Lara (2), Fernando Vidiella (1), Ramon Cugat (3)

Institution: (1) Dept. of Rehabilitation, (2) Dept. of Rheumatology, (3) Dept. of Orthopedic Surgery, Hospital Quiron, Barcelona, Spain

Device and producing company: Physiogold 50, MTS

Introduction: The purpose of this study is to evaluate the evidence of rESWT in fibromyalgia (FM).

Methods: We performed a randomized, prospective study with 24 FM patients. All patients were female, mean age 52, 13 years (45-67). Patients were divided into two groups and asked to select the 3 most painful myofascial and asymmetrical regions. Both groups received 5 weekly sessions of radial ESWT (rESWT), using 2000 shocks of rESWT at each of the 3 points. Group 1 (treatment) N= 13 treated with 500 shocks, 1,5 bar, 5 Hz; then 1000 shocks, 2 bar, 8 Hz; and 500 shocks, 1,5 bar, 15 Hz; Group 2 (placebo) N= 11 (using a soft rubber cap leaving air between transmitter and the cap) received 500 shocks, 15 Hz; then 1000 shocks, 8 Hz; and 500 shocks, 15 Hz, with the pressure constant 1,5 bar.

Outcome variables were: 1) Pain: VAS, algometer (Wagner instruments®) at 3 points and contralateral; McGill Questionnaire; 2) Emotional status (BDI; Hamilton test) and 3) QOL measures: Fibromyalgia-Impact-Questionnaire; Fibromyalgia-R808-NP2; SF-36. Both groups received a home FM exercise program, according to Fibromyalgia Information Foundation. All patients were assessed for pain before each rESWT and at 6 weeks post treatment.

Results: We found clinical improvement on pain at 6 weeks after treatment and excellent-good results according to Roles and Maudsley in FM patients treated compared to placebo, without side effects.

Discussion: Patient follow-up 6 to 12 months post-treatment will determine shockwave efficacy over time.

Conclusion: In a multi-disciplinary approach, rESWT appears to be safe and effective as an early adjunctive therapy in fibromyalgia.
How to Increase Good Clinical Practice in Shockwave Therapy: The Importance of a Correct Communication Between ESWT Specialist and General Practitioner

Maria Cristina Ottone (1), Silvio Roldi (1), Emanuela Maria Roldi (2), Francesca Maria Roldi (3)

Institution: (1) ASL AL; Tortona; (2) no inst.; Tortona; (3) List S.p.A.; Milan, Italy

Device and producing company: Piezoson 300 - Wolf

Introduction: The General Practitioner is the first contact between the Specialist and the patient, so it is necessary to explain a new method of treatment or diagnostic system correctly, but also to have a direct contact with the General Practitioner.

Methods: At first we sent a paper with general informations about the musculoskeletal pathology that is possible to treat with ESWT and the controindications; then we organized the educational course and the general practitioners could learn the physical mechanisms of ESWT, the applications in orthopaedic pathology with the controindications, the importance of radiology for correct diagnosis avoiding mistakes in indication.

Results: The course that was carried out gave an immediate result in the reduction of number of patients with contraindications: we had an adherence to SITOD guidelines of 95% compared to 74% before the course.

Discussion: Over the last fifteen years we have had an increasingly large application of ESWT in the treatment of orthopaedic pathology and consequently a greater importance of the General Practitioner in the management of these pathologies. We made a study with SIMG (Italian Society of General Practitioners). We wanted to verify the importance and the utility of these instructional courses. We realized that if the GP has a good knowledge of SITOD guidelines about indications, contraindications and the results of the treatment with SW, it is possible to have a faster and better management of these patients.

Conclusion: We presented the results of this study to the National Meeting of SIMG in Florence, in Novembre 2011. The data analysis shows that correct information for GPs about ESWT through instructional courses allows a correct approach for diagnosis and treatment of patients with orthopaedic pathologies sensitive to ESWT. This study confirms the importance of direct contact between both Society - SITOD and SIMG - also for other projects.
The Smartphone App- a Tool For Enhancing Patient Education
John Furia

Institution: SUN Orthopedics-Evangelical Community Hospital, Lewisburg, USA
Device and producing company: DolorClast, EMS Inc

Introduction: Although educational smartphone apps are widely utilized in many medical sub-specialties, their efficacy as teaching tools has not been proven. The purpose of this study was to assess patient acceptance and efficacy of an orthopedic smartphone app designed to enhance education.

Methods: Following an initial evaluation, patients with newly diagnosed Achilles tendinopathy were requested to download an educational smartphone app designed to explain the condition and treatment options. At final follow-up, the number of downloads, frequency of app usage, overall satisfaction with the app as a teaching tool, and patient understanding of their medical condition and treatment options was determined.

Results: Fifty-two of the 59 qualified patients (88%) downloaded the app, and of these, 40 patients (77%) used the app on 2 or more occasions. Fifty-one of the 52 patients (98%) were either “very satisfied” or “satisfied” with the app as a means of education. The mean comprehension score for patients in the download group was 74 compared to 23 for patients in the non-download group (p <0.05).

Discussion: The data from this pilot study indicates that orthopedic smartphone apps are another effective means of providing accurate, physician derived content regarding a medical condition. Novel treatment options such as ESWT can be demonstrated in a patient-friendly manner. In contrast to other studies, both download rate and short-term app retention are high. Larger studies utilizing more sophisticated apps and validated forms of patient assessment are required to verify these preliminary findings.

Conclusion: Patient acceptance, utilization, and overall satisfaction with the app were high. Smartphone apps may be effective tools for enhancing patient education.
Extracorporeal Shock Wave Therapy Inhibits Cyclophosphamide-Induced Rat Acute Interstitial Cystitis
Yen-Ta Chen (1), Yen-Yi Zhen (2), Hon-Kan Yip (2)

Institution:(1) Division of Urology, Dept. of Surgery, (2) Division of Cardiology, Dept. of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, Taiwan

Device and producing company: none

Introduction: We investigated whether extracorporeal shock wave (ECSW) therapy can attenuate cyclophosphamide (CYP)-induced acute interstitial cystitis (AIC) in rats.

Methods: Eighteen male-adult Sprague-Dawley rats were equally divided into group 1 (sham control), group 2 (AIC induced by 150 mg/kg CYP by intra-peritoneal injection) and group 3 (AIC + ECSW 200 impulses at 0.11 mJ/mm2). ECSW was applied to the urinary bladder using skin surface approach at 3 and 24 h after CYP treatment.

Results: The results demonstrated that 24-hour urine amount and microscopic findings of red blood cell count (i.e., hematuria) were significantly higher in group 2 than in groups 1 and 3, and significantly higher in group 3 than in group 1 (all p<0.001). The urine levels of albumin and interleukin-6 showed an identical pattern of hematuria among all three groups (all p<0.001). The cellular and mRNA expressions of macrophage migration inhibitory factor (MIF)+, CD74+, CD68+, substance p+, and Cox-2+ cells in the bladder tissue exhibited an identical pattern of hematuria among all three groups (all p<0.0001). The integrity of epithelial layer and collagen-deposition area as stained by Sirius red displayed an opposite pattern of hematuria among the three groups (p<0.0001). The protein expression of IL-12, iNOS, TNF-α, NF-κB, MMP-9, NOX-1, NOX-2, RANTES, and Oxyblot in the bladder displayed an identical pattern of hematuria among all three groups (all p<0.01).

Discussion: none

Conclusion: ECSW therapy markedly attenuated CYP-induced AIC through inhibition of the inflammatory reaction and the generation of reactive oxygen species and oxidative stress.
Functional and Molecular Characteristic of Cyclophosphamide Induced Cystitis in Rats and Effects of Low Energy Shock Wave Therapy

Yao-Chi Chuang (2), Hung-Jen Wang (2), Chao-Cheng Huang (3), Michael B. Chancellor (4), Ching-Jen Wang (1)

Institution:(1) Kaohsiung Chang Gung Memorial Hospital, Taiwan; (2) Dept of Urology, (3) Dept. of Pathology, Kaohsiung Chang Gung Memorial Hospital, Taiwan; (4) Dept. of Urology, Oakland University, USA

Device and producing company: Sanuwave, EvoTron

Introduction: Cyclooxygenase 2 (COX-2) elevation and subsequent prostaglandin E2 (PGE2) production play a major role in bladder inflammation and hyperactivity. Low energy shock wave (LESW) therapy has been used clinically to improve tissue regeneration as well as anti-inflammatory effects. We investigate the mechanism and molecular change underlying the cyclophosphamide (CYP) induced cystitis in rats and the effects of LESW therapy.

Methods: Experimental and control animals were injected with CYP (75mg/kg intraperitoneally) or saline on day 1, and 4. The bladders were explored on lower midline incision and treated with LESW (0.12 mJ/mm2, 300 pulse) or sham operation on day 2. Continuous cystometry (CMG) was performed on day 8 under urethane anesthesia. The bladder was then harvested for histology, and inflammatory biomarkers.

Results: CYP induced increased bladder inflammatory reaction, bladder hyperactivity, and COX-2 expression in the bladder. The CYP effects were suppressed by LESW. LESW treatment decreased inflammatory reaction, and suppressed bladder hyperactivity (contraction amplitude decrease).

Discussion: CYP injection activated COX2 expression in the bladder and induced bladder inflammation and hyperactivity, which effects were suppressed by LESW treatment.

Conclusion: These findings suggest a potential benefit of LESW treatment for bladder inflammatory conditions.
Does Extracorporeal Shockwave Therapy (ESWT) have an Effect on Erectile Dysfunction – Preliminary Results
Peter Lyngdorf, Jesper Lyngdorf,

Institution: Clinic for Sexual Dysfunction, Gentofte, Denmark
Device and producing company: Aries ESWT, Dornier

Introduction: Treatment with ESWT has shown to be a new modality in the area of erectile dysfunction. The aim was to demonstrate the effects of ESWT applied to men with erectile dysfunction of vascular origin. To demonstrate the effect, IIEF and Duplex-ultrasonography was used.

Methods: A prospective study of 10 men with erectile dysfunction of vascular etiology unable to perform sexual intercourse with or without medication. The participants had ED for more than 6 months. After history was taken the men completed IIEF score and all men had penile ultrasonic scans performed before and after intracavernous injection of prostaglandine. Patients received 12 treatments over a 9 week period. 1-2 months after the final treatment the IIEF and Duplex scans were repeated.

Results: Ten men participated, mean age 63 years, range 45-82. Nine patients showed a significant increase in IIEF score and 6 of these 9 men had no needs for medication. Six patients had signs of better penile flow.

Discussion: ESWT is a new treatment for erectile dysfunction with a high rate of success. It can be applied to men with reduced vascular capacity.

Conclusion: Treatment with ESWT showed a significant effects in erectile function. The treatment is without side effects.
Extracorporeal Shockwave Therapy for Osteoporotic Osteoarthritis of the Knee in Rats: An Experiment in Animals

Chin-Jen Wang

Institution: Kaohsiung Chang Gung Memorial Hospital, Taiwan
Device and producing company: OssaTron, Sanuwave

Introduction: No study showed the effective method in the most severe osteoporotic osteoarthritis of the knee. The purpose of this study was to investigate the effectiveness of ESWT in osteoporotic osteoarthritis of the knee in rats.

Methods: Sixty-four female Sprague Dawley rats were divided into four groups. The control group received sham ovariectomy (OVX) and sham anterior cruciate transection (ACLT) and medial meniscectomy (MM). The osteoarthritis (OA) group received ACLT and MM, but no OVX. The osteoporosis (OP) group underwent bilateral OVX, but no ACLT and MM. The OA + OP group received bilateral OVX, ACLT and MM. One half of animals also received ESWT. The evaluations included the areas of gross arthritic changes, bone mineral density (BMD), micro-CT scan, bone strength test, histopathological examination and immunohistochemical analysis.

Results: Group OA + OP showed larger areas of arthritic changes than groups OA and OP as compared to sham group. BMD and bone strength significantly decreased in groups OA, OP and OA+OP versus sham group, and ESWT significantly improved the changes. In micro-CT scan, subchondral plate thickness significantly decreased and bone porosity increased in groups OA, OP and OA+OP, and ESWT significantly improved the changes. Mankin and Safranin O scores significantly increased in groups OA and OA+OP, relative to sham group, and ESWT significantly improved the changes. DKK-1 significantly increased, and VEGF, PCNA and BMP-2 decreased in groups OA, OP and OA+OP relative to sham group, and ESWT significantly reversed the changes.

Discussion: The main findings of this study showed that osteoporosis increased the severity of osteoarthritis of the knee. ESWT for the first time was shown effective to ameliorate osteoporotic osteoarthritis of the knee.

Conclusion: ESWT is effective in osteoporotic osteoarthritis of the knee in rats.
Efficacy of Extracorporeal Shockwave Therapy for Knee Osteoarthritis: A Randomized Controlled Trial

Gengyan Xing, Zhe Zhao

Institution: Dept. of Orthopaedic Surgery, The General Hospital of Chinese People’s Armed Police Force, Beijing, China

Device and producing company: Swiss DolorClast, Electro Medical Systems

Introduction: Extracorporeal shockwave therapy (ESWT) has been widely used for pain relief and treatment of musculoskeletal disorders. We aimed to assess ESWT for knee osteoarthritis (OA) over 12 wk by comparison with placebo treatment.

Methods: We randomized 70 patients to receive placebo (n = 36) or ESWT (n = 34). For ESWT, patients received 4000 pulses of shockwave at 0.25 mJ/mm² weekly for 4 wk. In the placebo group, patients received shockwave at 0 mJ/mm² in the same area. The effect on OA was assessed by pain on a visual analog scale and disability on the Lequesne index, Western Ontario and McMaster University Osteoarthritis Index, and patient perception of the clinical severity of OA. Evaluation was performed at baseline and after 1, 4, and 12 wk.

Results: We found no adverse events during and after ESWT. ESWT was more effective than placebo in reducing pain on movement at each period (P < 0.01). The mean visual analog scale score with ESWT was 3.83 at 12 wk versus 7.56 at baseline (P < 0.01). The Lequesne index and the Western Ontario and McMaster University Osteoarthritis Index score were reduced with ESWT. Moreover, patient perception of clinical severity of OA was significantly greater with ESWT than that with placebo (P < 0.01).

Discussion: Basic science studies have shown that ESWT application for OA is safe with proper dosing. Shockwaves applied at >0.50 mJ/mm² caused degenerative changes in hyaline cartilage in OA of rats. We selected an energy flux density of 0.25 mJ/mm² and found no adverse damage to knees of patients; only the skin of the knee showed transient reddening after treatment and swelling for several days. To our knowledge, no clinical trials have tested the effect of ESWT on human knee OA. ESWT could have a beneficial effect for pain and physical function in patients with knee OA.

Conclusion: ESWT is effective in reducing pain and improving knee function, with better results than placebo during the 12-wk treatment. However, further pilot studies are needed to determine whether ESWT should be recommended at an early or later stage of OA or combined with conventional therapies.
Extracorporeal Shockwave Therapy and Alendronate Demonstrate Equal Protective Effects in Osteoarthritis Knee

Chin-Jen Wang, Shan-Ling Hsu, Wen-Yi Chou, Jai-Hong Cheng

Institution: Kaohsiung Chang Gung Memorial Hospital, Taiwan
Device and producing company: OssaTron, Sanuwave

Introduction: This study compared the effects of extracorporeal shockwave therapy (ESWT) and alendronate (Alen) in osteoarthritis (OA) of rat knee.

Methods: The control group received sham anterior cruciate ligament transaction (ACLT) and medial meniscectomy (MM) of the knee, but received no ESWT or Alen. The OA group underwent ACLT and MM but received no ESWT or Alen. The ESWT group underwent ACLT and MM and received ESWT. The Alen group received Alen after ACLT and MM. The evaluations included radiograph, bone mineral density (BMD), serum C-telopeptide collagen II (CTX II), cartilage oligometric protein (COMP), alkaline phosphatase and osteocalcin, histopathological examination and immunohistochemical analysis.

Results: Radiographs of knee at 12 weeks showed more pronounced OA changes in OA group, and mild OA in control, ESWT and Alen groups. BMD values significantly decreased in OA group, and increased in ESWT and Alen groups, but no difference noted between ESWT and Alen group. Serum CTX-II and COMP significantly increased and alkaline-phosphatase and osteocalcin decreased in OA group, but no significant difference was observed between ESWT and Alen groups. In histopathology, Mankin and Safranin O scores significantly increased in OA, ESWT and Alen groups, but no significant difference noted between ESWT and Alen group. In immunohistochemical analysis, the vWF, VEGF, sVCAM, PCNA, BMP-2, and osteocalcin expressions in articular cartilage and subchondral bone significantly decreased in OA, ESWT and Alen groups, but no difference noted between ESWT and Alen groups.

Discussion: The principal findings of the current study revealed that application of ESWT to subchondral bone and injection of alendronate sodium showed equal protective effective in rats from developing osteoarthritis of the knee. These innovative findings may unveil a new concept in the management of early osteoarthritis of the knee by changing the initial focus of intervention from the articular cartilage to the subchondral bone. Furthermore, ESWT and alendronate sodium may be used as the alternatives in the treatment of early osteoarthritis of the knee.

Conclusion: ESWT and Alen demonstrate equal protective effects in rats from developing osteoarthritis of the knee.
Extracorporeal Shockwave Therapy Treatment of Chronic Osteochondral Lesions of the Talus: Long-term Results
Gengyan Xing

Institution: Dept. of Orthopaedic Surgery, The General Hospital of Chinese People’s Armed Police Force, Beijing, China

Device and producing company: Swiss DolorClast, Electro Medical Systems

Introduction: Osteochondral lesions of the talus are relatively uncommon but may be a cause of significant pain and disability in symptomatic patients. However, arthroscopic treatment of osteochondral lesions of the talus will not result in good long-term clinical outcomes in the majority of patients. To investigate the efficacy, safety and the duration of treatment effectiveness of extracorporeal shockwave therapy (ESWT) in patients with chronic osteochondral lesions of the talus (OLT).

Methods: Fifty patients with chronic OLT underwent ESWT treatment. Average age was 32 years (range, 12-72 years). Average follow-up was 71 months (range, 24-152 months). Treatment consisted of either drilling of the osteochondral lesions of the talus in situ (n = 4), excision of the osteochondral lesions of the talus and abrasion arthroplasty (n = 6), or excision of the osteochondral lesions of the talus and drilling (n = 40). Preoperative and intraoperative staging of the osteochondral lesions of the talus was performed. Follow-up evaluation included 3 clinical rating systems: Alexander, modified Weber, and American Orthopaedic Foot and Ankle Society Ankle/Hindfoot scores. In addition to plain radiographic studies, preoperative computed axial tomography (CAT) scans, magnetic resonance imaging (MRI) studies were used to evaluate their efficacy of ESWT in patients with OLT.

Results: There were 72% excellent/good, 20% fair, and 8% poor results on the Alexander scale. According to the modified Weber scale, there were 64% excellent/good, 30% fair, and 6% poor results. The average American Orthopaedic Foot and Ankle Society Ankle/Hindfoot score was 84 (range, 34-100). We found no correlation between plain radiographs, computed tomography, or magnetic resonance imaging staging and clinical results. However, there was significant correlation between arthroscopic stage and clinical outcome.

Discussion: To our knowledge, this was the first study to examine the effect of ESWT on patients with chronic osteochondral lesions of the talus (OLT). The six-month trial period in our study was relatively short, and it is unclear how much longer the clinical benefits would have been maintained.

Conclusion: ESWT treatment of chronic symptomatic osteochondral lesions of the talus results in good clinical outcomes in the majority of patients. However, pain and functional limitation may persist in some patients, especially those noted to have unstable osteochondral defects.
Medical Shockwaves a Treatment Option for Complex and Neuropathic Pain Syndromes? A Compilation of Case Reports

Kenneth Craig (1), Bradley Takai (1), Daniel Poratt (2)

Institution: (1) Kompass Health Associates, (2) Auckland University of Technology, Auckland, New Zealand

Device and producing company: OrthoSpec, MediSpec

Introduction: The impervious nature of complex and neuropahtic pain syndromes that are often inodcile to conventional treatments warrants the exploration of treatment methods that limit intrinsic risk while modifying disease patterns. This compilation of 12 case-reports discusses the use of medical shock waves for the treatment of complex and neuropathic pain syndromes of the lower extremity, and its outcomes after a 24 month follow-up period.

Methods: Four treatments of extracorporeal-shockwaves propagated by an electro – hydraulic generator (MediSpec, Germantown) were administered at one week intervals. Energy density flux levels ranged from 0.08mj/mm² - 0.18mj/mm². Pain, physical function and emotional measures were performed utilizing visual analogue scale (VAS), Neuropathic Pain Diagnostic Questionnaire (DN4), and Pain Outcomes Profile questionnaire (POP3), at baseline and post-treatment. Use of anti-inflammatory and pain medications were ceased prior to treatment, and in the positive response cases remained discontinued throughout the entire 24 week follow-up period.

Results: Ten out of the twelve patients responded to treatment and their scores are reflected as: subjective neuropathic pain experience (VAS / DN4), physical capacity (POP3), and emotional disposition (affective Index POP3). An overall improvement in (n=10) over each domain: mean average subjective pain scores (VAS) improved (baseline 8.87/10; post-treatment 2/10). Average DN4 (baseline 6.4/10: 0/10 post-treatment). POP3 questionnaire recorded improvements in both the Physical Index (baseline 53.47; post-treatment 2.77), and the Affective Index (baseline 85.49; post-treatment 10.22) respectively.

Discussion: The exact mechanism of ESWT is yet to be fully elucidated; however a dose and stimulus dependant shockwave triggers a neuro-bio-chemical regulatory cascade resulting in the resolution of the associated neuro-physical pathology and cognitive response in the subjects of this case series. In the cases that showed a positive response (n=10), their benefits were clinically noted from week two upon receiving treatments. In the two cases which did not respond to treatment, there was no response at all from the initiation of treatment right throughout.

Conclusion: The findings of these case-report corroborates with the findings of earlier investigations utilizing shockwaves for complex regional pain syndrome of the knee conducted by Nortarnicola and colleagues (2010). ESWT may provide a non-invasive, non-pharmacogenic disease modifying treatment option for peripheral neuropathic and complex pain conditions. This encourages further investigations of ESWT to be conducted on neuropathic and complex pain syndromes of the upper and lower extremity.
Focused Extracorporeal Shockwaves Improve Pareses in 8 Cases of Spinal Cord Injury and 3 Cases of Myelomeningocele
Henning Lohse-Busch, Ulrike Reime, Ruth Falland

Institution: Rheintalklinik, Bad Krozingen, Germany
Device and producing company: Duolith, Storz Medical

Introduction: Focused extracorporeal shockwave therapy (ESWT) promotes endothelial nitric oxide production, is stimulating angiogenesis and neurogenesis. Former investigations with rats show that ESWT of the damaged spinal cord improves the motor activity and the sensibility.

Methods: With 8 patients*, 43 years of age, suffering from different degrees of severity of posttraumatic paraparesis and 3 children** from 9-12 years of age suffering from a myelomeningocele, a longitudinal observation case study was carried out. They received ESWT (“Duolith” shockwave generator, Storz Medical) to the region of the spinal cord lesion several times a week. Treatment was part of a complex therapy regime. The courses of treatment were documented using surface EMG, manual muscle test (MMT), and functional reach test (FR).

Results: Previously non-innervated muscles that were rated subsequently showed increasing EMG activity and an average improvement in strength to about 2.45* 2.6 ** in MMT. The patients improved their FR when seated to 8.9*/ 8 cm** on average. Superficial and deep sensibility increased below the lesion level. There were no undesirable side effects.

Discussion: Suitable doses of ESWT stimulate the spinal cord directly and may lead furthermore to the release of neurotrophic substances. Questions of intensity and frequency of the ESWT are not yet answered sufficiently.

Conclusion: ESWT enhances muscular function and superficial sensibility in the lower adjacent region of the spinal cord lesion. The neurophysiological effects need to be verified on larger number of patients.
The Activating Effect of ESWT on Schwann Cells
In Vitro and In Vivo
David Hercher, Christina Schuh

Institution: Ludwig Boltzmann Institut, Vienna; Austria
Device and producing company: DermaGold 100, MTS

Introduction: Peripheral nerve injuries are common and a frequent cause of hospitalization displaying a major burden to patients and social health-care systems. Extracorporeal shockwave therapy (ESWT) has been shown to accelerate peripheral nerve regeneration but the underlying mechanisms are still unclear. Schwann cells (SCs) are activated after injury, switch from a myelinating to a proliferating, axonal growth promoting state. In this study we investigated the effect of ESWT on SCs and peripheral nerve regeneration on a molecular level.

Methods: Schwann cells have been isolated from motor, sensory and mixed nerves, respectively, using an established protocol. Dissected nerves have been treated with ESWT prior to isolation. Their activation status has been evaluated using FACS analysis. Additionally, an in vivo femoral nerve defect model in the rat has been established. RNA has been extracted from whole nerves at different timepoints after injury to evaluate the influence of ESWT on the expression profiles of injured and regenerating nerves by qPCR.

Results: Myelination markers like P0 are down-regulated in ESWT treated SCs whereas p75 is upregulated, representing an activated state of SCs. This effect is confirmed by in vivo data, where an upregulation of p75 and other pro-regenerative markers is observed up to 10 weeks after injury in the ESWT treated animals.

Discussion: In vitro and in vivo data indicate a strong influence of ESWT on the activation status of Schwann cells.

Conclusion: We hypothesize that ESWT has a beneficial effect on the pro-regenerative status of SCs in vitro and in vivo.
Symptomatic Treatment of Unresponsive Wakefulness Syndrome with Transcranially Focused Extracorporeal Shockwaves (TESWT).

Henning Lohse-Busch, Ulrike Reime, Ruth Falland

Institution: Rheintalklinik, Bad Krozingen, Germany

Device and producing company: Duolith, Storz Medical

Introduction: The results of extracorporeal shockwave therapy (ESWT) treating spastic disorders nurture the idea that this treatment stimulates neural structures. The question was, whether transcranial ESWT (TESWT) may restore originally existing, but malfunctioning synaptic connections in the brain of patients with apallic syndrome.

Methods: Between 8 and 18 years after the brain lesion 5 patients with unresponsive wakefulness syndrome of differing severity received TESWT with the device Duolith (Storz Medical) during 4-week physicomical complex therapies. The patient were assessed with the 24 points German Coma Remission Scale (KRS, which is quite similar to the JFK Coma Recovery Scale revised) and with the Glasgow Coma Scale (GCS).

Results: After 2-4 years and an average of 5.2 treatment series the patients improved their abilities by 135.9%, from 7.8 to 18.4 points on the KRS and by 43.6% on the GCS. In the motor area of the KRS, the patients improved by 64.3%. Three PEG feeding tubes could be removed, nonverbal communication initiated 4 times.

Discussion: In the animal model, some neurotransmitters as the endothelial nerve growth factor and the endothelial vascular growth factor, promote functional regeneration after experimental injuries of periphereal nerves and the spinal cord. According to the literature ESWT upregulates these neurotransmitters for more than 4 weeks. Our casuistic study shows an enduring improvement of the vigilance in patients with unresponsive wakefulness syndrome treated with TESWT.

Conclusion: The TESWT improves the life quality of patient with apallic syndrome. Looking on the clinical results the precise neurophysiological effects, questions of treatment frequency etc. must be verified.
Shockwaves Induce Postnatal Vasculogenesis in Infarcted Myocardium by Recruitment of Bone Marrow Derived Endothelial Progenitors

Johannes Holfeld (1), Can Tepeköylü (1), Markus Theurl (1), Wolfgang Mathes (1), Daniela Lobenwein (1), Radoslaw Kozaryn (1), Patrick Paulus (2), Rudolf Kirchmair (1), Michael Grimm (1)

Institution: (1) Medical University; Innsbruck; Austria; (2) Goethe-University Hospital; Frankfurt; Germany

Device and producing company: TRT DermaGold

Introduction: Recently shock waves at low energy levels were described to induce angiogenesis and regeneration in ischemic tissue. Improvement of myocardial perfusion and relief of angina symptoms in human patients with severe coronary artery disease have been shown. We hypothesized that the recruitment of progenitor cells from bone marrow to infarcted myocardium may be involved as well.

Methods: Sub-lethally irradiated C57Bl/6 wild-type mice received bone marrow transplantation (BmTx) from transgenic GFP mice (C57BL/6Tg(CAG-EGFP)1Osb/J) (n=6 per group). 4 weeks after BmTx, myocardial infarction was induced by LAD ligation. Treatment group (SWT) received shock wave therapy (0.38mJ/mm², 200 impulses, 3Hz) 3 weeks after infarction, whereas control animals (CTR) underwent sham treatment. Hearts were harvested 3 weeks after therapy. GFP positive bone marrow derived cells in the heart were detected by immunofluorescence microscopy. Lectin counterstaining revealed endothelial progenitor cells (EPCs). Gene expression of pivotal factors SDF-1, CXCR4, VEGF receptors and others was performed. Functional outcome was measured with a pressure catheter inserted into the left ventricle. For further mechanistic findings an in-vitro migration assay using human umbilical vein endothelial cells (HUVECs) was performed.

Results: Higher numbers of bone marrow derived endothelial progenitor cells per high power field have been found in the treatment group (CTR 3.98 ± 0.6 vs. SWT 17.89 ± 1.6, p<0.0001). The main chemoattractant for EPC recruitment SDF-1 mRNA, was increased (CTR 1.86 ± 0.68 vs. SWT 5.19 ± 1.18, p=0.02). Migration assay revealed higher migration rates (CTR 171.9 ± 15.89 vs. SWT 234.5 ± 25.9, p=0.04). Functional outcome as assessed by pressure catheter showed an increase in dPdtmax (CTR 1957 ± 343 vs. SWT 3007 ± 617.4, p>0.059), a decrease in dPdtmin (CTR -1532 ± 251.3 vs. SWT -2603 ± 346.7, p=0.03) and an increase in Tau (CTR 33.68 ± 5.99 vs SWT 124.7 ± 42.15, p=0.09) indicating functional improvement after SWT.

Discussion: Low energy shock waves induce postnatal vasculogenesis in infarcted myocardium by the recruitment of bone marrow derived endothelial progenitor cells.

Conclusion: Shock wave treatment may develop a regenerative adjunct or alternative treatment option to state of the art revascularization in myocardial infarction. Notably, it has already been applied in angina patients without causing any severe side effects.
Focused Low-Energy Extracorporeal Shockwaves with Distally Symmetric Polyneuropathy (DSPNP). A Pilot Study
Henning Lohse-Busch (1), Ernst Marlinghaus (2), Ulrike Reime (1), Uwe Möwis (1)

Institution: (1) Rheintalklinik, Bad Krozingen, Germany; (2) Storz Medical, Switzerland

Device and producing company: Duolith, Storz Medical

Introduction: The results of extracorporeal shockwave treatment (ESWT) on nerve regeneration in the rat and incidental observations led to the question whether ESWT could alleviate the still difficult-to-improve symptoms of DSPNP.

Methods: In a pilot study out of an original 24 patients with DSPNP, 10 patients with diabetes mellitus were excluded because of their inhomogeneous performances. Of the 14 patients remaining, 6 received one sham treatment at the beginning. All 14 patients were then treated with ESWT to the soles of the feet using the Duolith® shock wave generator (Storz Medical) 3 times weekly for 2 weeks. The assessments were carried out before and after the sham treatment, the first ESWT and after 2, 4 and 8 weeks.

Results: The placebo treatment did not influence pain or paraesthesia. After the 2 weeks of ESWT, the intensity decreased from 100% to 23.6%, rising again after 8 weeks to 45.7% of the original state (p<0.01). But the placebo treatment had a great effect on walking abilities. The results of ESWT did not become significant until the 8th week. Step length improved by 14.6% (p<0.001), walking speed by 24.8% (p<0.001) and time of dual support during the stance phase of the gait declined by 12.2% (p<0.009).

Discussion: In the beginning there was a high placebo effect on the motor parameters, which later became an enduring treatment related improvement. The treatment of diabetes patients with ESWT has to be undertaken with a greater number of patients.

Conclusion: Despite the small number of cases it appears that ESWT can alleviate some symptoms of DSPNP.
Shockwave Treatment Enhances Proliferation and Wound Healing via Purinergic Signaling Linked Erk1/2 Pathways

Anna M. Weihs (1), Christiane Fuchs (1), Andreas Teuschl (1), Joachim Hartinger (2), Paul Slezak (2), Rainer Mittermayr (2), Heinz Redl (2), Wolfgang G. Junger (3), Harald H. Sitte (4), Dominik Rünzler (1)

Institution: (1) University of Applied Sciences Technikum Wien; (2) Ludwig Boltzmann Institute for Experimental and Clinical Traumatology, Vienna, Austria; (3) Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, USA; (4) Institute of Pharmacology, Center for Physiology and Pharmacology, Medical University of Vienna; austria

Device and producing company: dermagold100, MTS

Introduction: Shockwave treatment (SWT) accelerates poor wound healing, though the principle underlying the beneficial effect has not been fully revealed yet. As proliferation is a major phase in the wound healing cascade our hypothesis is that shockwave induced ATP release induces proliferation via purinergic signaling coupled to Erk1/2 signaling.

Methods: In our in vitro model C3H10T1/2 mouse mesenchymal stem cells were subjected to SWT and ATP release was assessed. Cell cycle phase distribution after application of shockwaves was evaluated and proliferating cells were quantified using a BrdU incorporation assay. Western blot analysis was performed to identify the role of the Erk1/2 pathway. Inhibitors for purinergic receptors were used to evaluate if ATP is essential for the effect of shockwave treatment on proliferation.

Results: SWT released ATP in C3H10T1/2 cells in an energy- and pulse-number dependent manner. SWT significantly increased proliferation and purinergic signaling was found to be essential for this proliferative effect. Shockwaves enhanced Erk1/2 signaling via ATP release. Furthermore, the crucial importance of Erk1/2 signaling in the proliferative effect of SWT was verified in a rodent ischemic wound healing model.

Discussion: We demonstrate for the first time that SWT releases cellular ATP which consequently activates Erk1/2 signaling via purinergic receptors, ultimately causing the proliferative effects of SWT. Moreover, Erk1/2 signaling is essential for shockwave induced wound healing in an in vivo model.

Conclusion: Our in vitro as well as in vivo data identify the Erk1/2 signaling cascade as one of the major mechanisms underlying the beneficial effects of shockwave treatment in wound healing.
Defocused ESWT as Strategical Tool in Vulnology: Our Experience

Elena Maria Abati (1), Maria Cristina D’Agostino (2), Elisabetta Tibalt (2)

Institution: (1) Humanitas Gavazzeni, Bergamo; (2) Humanitas Research Hospital, Milan; Italy

Device and producing company: Duolith®SD1-T-Top (STORZMEDICAL)

Introduction: Defocused Extracorporeal Shock Wave Therapy (dESWT), reached the field of Regenerative Medicine. We report our successful experience with dESWT in complex “wounds”, thus confirming its validity in Vulnology.

Methods: In Humanitas Gavazzeni, a Vulnologic Service-Reference Center opened many years ago. Eighteen months ago, we introduced dESWT for non-healing refractory wounds and ulcers. Beginning to the present, we treated 76 patients, selected between the most complicated cases (lower and upper limb lesions). We use the Duolith® SD1-T-Top (STORZMEDICAL), defocused electromagnetic applicator, EL 0.25-0.33 mJ/mm², 350 shots + 100 shots/cm², weekly, until healing.

Results: 6 patients (7.9%) interrupted for concomitant general diseases; 8 patients (10.52%) still under treatment; 46 patients (60.53%) healed; 16 patients (21.05%) suspended the treatment (inefficacy or worsening).

Among these patients:
- 3 osteomyelitis (late diagnosis)
- 1 bilateral elephantiasis
- 2 thrombophilic attitudes
- 1 paraplegic
- 1 suspected pyoderma gangrenosum
- 8 arteriovenous ulcers.

Only 2 of them (12.5%) healed after other types of treatments; the other ones are monthly controlled at the Vulnologic Service.

Discussion: dESWT can improve skin healing in complex, non-healing wounds and sores. Failed treatments (12.5%) seem to suggest us some interesting considerations about concomitant diseases and indications, that will be discussed extensively.

Conclusion: dESWT can be considered a strategical tool in Vulnologic Service for improving wound healing, in all its aspects, named “TIME” (T = tissue; I = infection or inflammation; M = moisture imbalance; E = epidermal margin). Failures can teach and explain us new insights as well.
The Role of ESWT and Manual Lymphatic Drainage in the Treatment of Grade II Chronic Ulcers

Raoul Saggini (1), Ira Dodaj (1), Alexandra di Stefano (1), Giovanni Barassi (1), Maria Giuseppina Onesti (2), Rosa Grazia Bellomo (1), Nicolò Scuderi (2)

Institution: (1) "G. d'Annunzio" University, Chieti; (2) "Sapienza" University, Rome; Italy

Device and producing company: Dermagold, MTS, Europe GmbH, Germany

Introduction: The purpose of this study was to verify the effectiveness of two temporal modalities of ESWT administration in chronic ulcers and compare them to each other and to the combined therapy with manual lymphatic drainage in presence of Lymphedema.

Methods: 28 patients with stage II chronic ulcers were evaluated and treated. They were divided into 2 groups (A and B) of 14 subjects according to the absence or presence of associated lymphedema. Each group was then randomly divided into two subgroups (A-I, A-II, B-I, B-II) who made ESWT at different weekly frequency; subjects with lymphedema also underwent manual lymphatic drainage.

Results: At the end of the 5 weeks treatment (T1) we found:
In group A-I reduction of wound dimensions from 1.87 (T0) to 0.77; reduction of the subjective pain from 5.7 (T0) to 1.8. In group A-II reduction of wound dimensions from 1.69 (T0) to 0.45; reduction of the subjective pain from 5.1 (T0) to 0.5. In group B-I reduction of wound dimensions from 2.83 (T0) to 1.88; reduction of the subjective pain from 5.5 (T0) to 2.9. In group B-II reduction of wound dimensions from 2.71 (T0) to 1.54; reduction of the subjective pain from 5.3 (T0) to 2.3.

Discussion: We found a significative reduction of wound dimension and subjective pain in all groups (p<0.05).

In terms of absolute value, the best results were found in group A-II and B-II, who performed the treatment with ESWT twice a week and 500 pulses per session also even using the lymphatic drainage.

Conclusion: Our results show that it is preferable to administer ESWT in chronic ulcers with fractionated energy in 2 weekly steps; probably in this way there is greater regenerative activation. The results obtained in subjects with lymphedema, where the presence of edema represents a delay element for healing, can encourage us in confirming that the healing process is based on angiogenesis, that is very important to promote drainage, but above all to confirm that shock waves are crucial in reactivating and accelerating the healing process of chronic wounds.
Extracorporaenal Shockwave Therapy in Chronic Ulcers
Treatment: Experience in a Vulnologic Center
Stefania Chiarenza, Sabina Terragni, Roberta Brambilla

Institution: Istituti Clinici Zucchi, Centro di Vulnologia, Monza, Italy

Device and producing company: none

Introduction: Extracorporaenal Shockwave Therapy (ESWT) is a very well known practice in treatment of musculoskeletal disease since 2000. ESWT has been formerly involved in the treatment of stress shielding tendinopathy, sports injuries and non-healing bone fractures. Over the years ESWT has shown good results in the treatment of chronic ulcers, expecially in diabetic patients.

Methods: 33 patients, (13 M; 20 F) with unresponsive chronic leg ulcers (from various etiology) have been treated with ESWT. The duration of the treatment ranged from 2 to 28 sessions, once or twice a week. After ESWT session each patient has been medicated with antimicrobial silver wound dressing and multi-layer compression bandage. In 7 cases ESWT has been associated with surgical treatment and coverage of the wound with cellular or acellular dermal substitute.

Results: Only one case of complete wound healing has been observed after ESWT; in 2 cases a worsening of the ulcer has been evident. In 30 cases we observed dimensional reduction of the wounds. No patients showed clinical signs of infection during and immediately after ESWT sessions.

Discussion: Several Authors demonstrated an increase in osteogenic growth factors, of TGF – beta1 and an increase in neoangiogenesis after ESWT. Neoangiogenesis, in particular, is due to a rise in proliferative factors such as eNOS, VEGF e PCNA, directly involved in tissue regeneration. ESWT has also shown the ability of reducing cellular apoptosis through a decrease of TUNEL expression in traumatic injuries, burns, diabetic ulcers and after reconstruction flap surgery, with better results than Hyperbaric Oxygen Therapy.

Conclusion: ESWT can be considered a very good ally within chronic ulcers treatment, through a continuous neoangiogenetic and regenerative stimulation of the tissues and it can be successfully associated with surgical treatment with bioengineered tissues.
Influence of treatment frequency on healing outcome in subacute and chronic wounds.

Rainer Mittermayr, Sebastian Weber, Daniel Smolen, Wolfgang Schaden

1) AUVA Trauma Center Meidling, Vienna, Austria
2) Ludwig Boltzmann Institute for Experimental and Clinical Traumatology – AUVA Research Center, Vienna, Austria
   Austrian Cluster for Tissue Regeneration, Vienna, Austria

Device and producing company: Dermagold, Activitor, MTS/TRT

Introduction: We could show in our open prospective study in the retrospective data analysis that extracorporeal shock wave therapy has great potential in the treatment of delayed or non healing wounds. Detection of differences in outcome based on the treatment frequency has major impact in adequately planning therapy sessions.

Methods: In our open study patient study enrollment is done during routine clinical work. Between August 2004 and April 2014 patients of both sexes with sub-acute and chronic soft tissue wounds of different etiology were included. The primary outcome measure was complete wound healing based on treatment frequency.

Results: Until April 2014 we already included 850 patients. 661 patients were analyzed with respect to ESWT frequency. Similar as previously found we could not detect differences in healing outcome when wounds were treated with extracorporeal shockwaves weekly (n=176), every 2 (n=183) or every 3 (n=37) weeks. (complete healing in 74, 73, and 76%, respectively). However, applying shockwaves only every 4 weeks complete healing was only observed in 69% of the patients (n=30). Interestingly, these lower number encounters not to more frequently not healed wounds but rather to patients missing follow up (20% in comparison to 9% (weekly) 14% (every 2 weeks), and 11% (every 3 weeks).

Conclusion: In the open clinical trial performed in the trauma Center Meidling since 2004 we could show consistently excellent results in treating sub-acute and chronic wounds with ESWT without observing any clinical relevant adverse effects. Due to comparable high percentage of missing patients in the follow up period then shock waves were applied only every 4 weeks, ESWT repetition within 3 weeks is recommended.
Regenerative Model with ESWT in atrophic and Retracting Scars

Raoul Saggini (1), Andrea Saggini (2), Ira Dodaj (1), Alexandra di Stefano (1), Giuseppe Soda (3), Rosa Grazia Bellomo (1), Nicolò Scuderi (3)

Institution: (1) "G. d'Annunzio" University, Chieti; (2) University of Rome Tor Vergata, Rome; (3) "Sapienza" University, Rome; Italy

Device and producing company: Dermagold, MTS, Europe GmbH, Germany

Introduction: The aim of our study was to evaluate the efficacy of the treatment of hand scars with unfocused shock waves alone and in combination with manual therapy.

Methods: 40 patients with an history of surgical painful scars after hand surgery were treated between November 2012 and May 2013. Treatment consisted of 10 ESWT sessions (twice a week for 5 weeks). Subjects were randomly divided in 3 groups. Group A received unfocused ESWT; Group B received unfocused ESWT and Manual Miofascial Therapy; group C did not receive any treatment (control group).

Results: Group A: the mean scar vascularity before treatment (T0) was 2.3 and after (T1) 0.2 (P<0.05); scar pigmentation was 2.4 at T0 and 0.5 at T1 (P<0.05); scar height was 2.3 at T0 and 0.5 at T1 (P<0.05); scar thickness was 3.5 at T0 and 1.6 at T1 (P<0.05). Pain assessment by VAS was 4.3 before treatment and 2.1 after (P<0.05).

In group B: the mean scar vascularity before treatment (T0) was 2.2 and after (T1) 0.5 (P<0.05); scar pigmentation was 2.4 at T0 and 0.3 at T1 (P<0.05); scar height was 2.4 at T0 and 1.3 at T1 (P<0.05); scar thickness was 3.1 at T0 and 1.2 at T1 (P<0.05). Pain assessment by VAS was 5.2 before treatment and 2 after (P<0.05).

In group C: the mean scar vascularity before treatment (T0) was 2.4 and after (T1) 1.9; scar pigmentation was 1.4 at T0 and 0.9 at T1; scar height was 2.5 at T0 and 2.2 at T1; scar thickness was 3.4 at T0 and 2.7 at T1. Pain assessment by VAS was 5.3 before treatment and 4.3 after.

In summary we found a significant improvement of vascularity, color, height, thickness, pigmentation, a significant reduction of ipersensibility and a remission of pain in groups A and B which received ESWT. The reduction of hand disability and the return to daily activity was very significant for groups A and B. The control group, C group, didn’t have any significative benefit at the second evaluation.

Discussion: Multiple sources of dermal damage may induce deposition of new collagen through activation of dermal fibroblasts. Fibroblasts are mesenchymal cells playing a critical role in wound healing. Fibroblasts are capable of secreting the precursors of Extracellular Matrix (ECM) components, including basal substance, collagens, glycosaminoglycans, reticular and elastic fibers, glycoproteins. Shock-wave treatment has been shown to induce an increase in the number of activated fibroblasts, CD34+ fibrocytes, and fXIII+ dendritic cells; this process leads to the deposition of new collagen, characterized by thinner collagen fascicles and parallel orientation to the dermo-epidermal junction. Indeed, a strong correlation may be observed between such histologic features and scar macroscopic appearance in treated patients. Additionally, shock-wave therapy may be regarded as playing a significant role in the increase in CD31+ vessel density in the dermis of treated patients, allowing an improved tissue metabolism.
Conclusion: In this way and considering the significative clinical results we can confirm that ESWT can be an elective treatment in skin healing disorders, even without other contribution like Manual Miofascial Therapy.
Shockwave Therapy as a Part of the Reconstructive Clockwork – a Conceptual Work
Karsten Knobloch (1), Peter M. Vogt (2)

Institution: (1) SportPraxis; (2) Hannover Medical School; Hannover, Germany

Device and producing company: none

Introduction: The plastic surgeons Mathes and Nahai introduced the conventional reconstructive ladder in 1982 to address tissue defects starting with primary and secondary closure of wounds followed by autologous skin grafting. Regional and local pedicled flaps, tissue expansion and free tissue transfer were further steps. Despite enormous achievements and refinements in these techniques, clinical situations and problems occur beyond the scope of these conventional reconstructive measures.

Methods: Regeneration and tissue engineering are of distinct interest in reconstructive surgery. Adipose-derived stem cell transfer is able not only to improve contour defects by volume effects, but also to improve the quality of the overlying skin.

Results: ESWT has shown to accelerate skin healing such as following burn injuries as well as in complicated chronic wound conditions. There is an increasing number of evidence that stem-cell activation is one mode of action of ESWT in this regard. Furthermore, skin rejuvenation has been postulated following ESWT, such as in the case of cellulite, where a number of clinical studies, some even in randomized-controlled design, have shown a significant improvement of the degree of clinical cellulite. Further aesthetic indications are pending currently using ESWT.

Discussion: To overcome the concept of the reconstructive ladder, and to underpin the more combinatory multimodal way to address reconstructive issues currently, we would propose that these novel reconstructive techniques should be considered as potential future integral parts in the reconstructive mechanism for the 21st century with the patient being at the centre of the reconstructive efforts.

Conclusion: A reconstructive clockwork is thus in our view an appropriate concept for up-to-date current reconstructive understanding in this regard.
Introduction

In previous research we have shown that unfocused extracorporeal shock waves (UESW) induce de novo intramembranous bone formation. Wnt signaling molecules are evolutionarily conserved and play key roles in many developmental processes, like bone formation. Stimulation of this pathway is known to differentiate between endochondral and intramembranous ossification. Since UESW induce pronounced and quick bone regeneration after application it is likely that Wnt signaling is involved. With the ability to target Wnt signaling pathway to enhance bone regeneration, shock wave therapy could further optimize and redirect future clinical applications. In the current study we specifically analyzed the effect of UESW on Wnt signaling in bone.

Methods

In a pilot study four wild type mice and four Axin2LacZ mice were treated with 1000 shock waves on the right tibia. These Axin2LacZ mice are known as Wnt reporter mice; because Axin2 is part of the Wnt signaling pathway and the staining of LacZ with X-gal enables the visualization of Wnt signaling. X-gal staining of the bones of the Axin2LacZ mice was performed at day 1 and day 7. The wild type mice underwent in vivo micro-CT scans at day 0 and day 14. Immunohistochemistry of the bones of the wild type mice was performed at day 14 (wnt-3a, Col-2, Col-10, CD-34 and vWf).

Results

The Axin2LacZ mice increased X-gal expression especially at day 7 after UESW (fig 1). Fourteen days after UESW on wild type mice micro-CT analysis shows an increase of trabecular and cortical bone (fig 2), and show a high expression of Wnt-3a in the cortex and bone marrow (fig 3), which is a known characteristic of bone regeneration. Next to this, we showed a higher expression of CD-34 after shock wave therapy, indicating neovascularization.

Conclusion

This study exposed how the mechano-physical stimuli of UESW are transferred to cellular signals that direct bone formation. The Wnt reporter mice showed clear activation of Wnt after UESW and Wnt 3a was detected in UESW treated wild type mice, both indicating the involvement of Wnt-signaling after shock wave therapy. This study elucidates the pathway of bone formation after UESW and might guide new directions or optimal protocols for clinical applications of shock wave therapy in the treatment of bone regeneration disorders.
Figure 1. X-gal expression was high in the $Axin^{2LacZ}$ mice seven days after shock wave therapy. The blue staining (X-gal) in both the marrow (BM) and in the de novo bone region (B) indicates Axin2 expression, which is part of the Wnt signaling pathway. The cortex (C) did not stain blue.

Figure 2. Micro-CT scan analysis show that UESW (shockwave) of the tibia increases trabecular (A) and cortical (B) bone volume compared to the contralateral side (control), and to the start of the experiment in wild type mice.
Figure 3. Micro-CT scans of the shock waved tibia (B) show an obvious raise in bone volume after fourteen days compared to the control tibia (A) in wild type mice. UESW showed a higher expression of Wnt-3a (pink staining) in the cortex and bone marrow (D) compared to the contralateral side (C) in wild type mice. B = de novo bone formation, BM = bone marrow, C = cortex