International Journal of Surgery 24 (2015) 115–119

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.journal-surgery.net

Original research

Osteogenetic effect of extracorporeal shock waves in human

L. Gerdesmeyer [a, c, *], W. Schaden [b], L. Besch [a], M. Stukenberg [a], L. Doerner [a], H. Muehlhofer [c], A. Toepfer [c]

[a] Dept Orthopaedic Surgery and Traumatology, University Schleswig Holstein, Campus Kiel, Arnold Heller Strasse, 24105 Kiel, Germany
[b] Ludwig Boltzmann Institute for Experimental and Clinical Traumatology, Donaueschingenstrasse 13, 1200 Vienna, Austria
[c] Dept for Orthopedics, Klinikum rechts der Isar, Technical University Munich, Ismaningerstr. 22, 81675 Munich, Germany

HIGHLIGHTS

- This study shows efficacy of extracorporeal shock wave therapy in osteogenesis.
- Focused shock wave therapy increases bone mass density in human.
- Focused shock wave therapy increases bone mass concentration in human.
- Focused shock wave therapy applied in heel pain is free of adverse effects.

ARTICLE INFO

Article history:
Received 30 June 2015
Received in revised form
18 August 2015
Accepted 13 September 2015
Available online 9 October 2015

Keywords:
ESWT
Shock wave therapy
Bone
Mass
Density
Osteogenesis
Osteoporosis

1. Introduction

The plantar heel pain is known as an insertional tendinopathy of the plantar fascia at the medial aspect of the calcaneus. Many predisposing factors are discussed, such as muscle contractures, obesity, overuse or anatomical malalignment.

Most patients complain about a stabbing-like pain in the plantar, medial heel region radiating to the foot and occurring mainly load-dependent after prolonged standing, walking or running. Pain during first steps in the morning or after rest are significant clinical findings with characteristic tenderness at the medial tuberculum calcanei. In chronic cases rest pain and pain during the night can occur. Numerous therapeutic procedures have been reported.

Conservative therapeutically options like different manual therapeutic concepts (especially stretching), orthotic fittings with special inserts and night splinting as well as cortisone injections are well described but efficacy according evidence based medicine is still lacking. Promising alternatives include local application of autologous growth factors (PRP) [1], local radiofrequency ablation [2], ultrasound therapy [3] or radiation therapy [4]. Extracorporeal shock wave therapy (ESWT) is recently the best proven therapy and indicated as a first line option with regards to evidence based medicine [5,6].

ESWT was found to improve blood perfusion and thus metabolism of the surrounding soft-tissue which is altered by chronic inflammation. In addition to a proven analgesic effect, research by Wang et al. showed that perfusion in the tendon area is significantly improved by low energy ESWT [7,8]. Furthermore it was recognized in the late 80s that shock waves have effects on bone metabolism. Haupt et al. observed in his kidney stone patients that the iliac crests thickened when they were located in the treatment area of the shock wave [9]. Later on shock wave were firstly used for bone pathologies [10–12]. Depending on the amount of acoustic energy shock wave can damage the bony structures. Even complete fractures were observed if energy level far beyond proven clinical treatment level is applied [13]. If shock wave therapy is used in a proper way consolidation of non-unions can be found even in patients with multiple revision surgeries. For this indication, hypertrophic non-unions have a much better prognosis than atrophic nonunions [14]. Several studies have confirmed this positive osteogenic effect [15,8] which is based on induction of

* Corresponding author. Dept Orthopaedic Surgery and Traumatology, University Schleswig Holstein, Campus Kiel, Arnold Heller Strasse, D-24105 Kiel, Germany.
E-mail address: Gerdesmeyer@aol.com (L. Gerdesmeyer).

http://dx.doi.org/10.1016/j.ijsu.2015.09.068
1743-9191/© 2015 IJS Publishing Group Limited. Published by Elsevier Ltd. All rights reserved.

neovascularization by increased angiogenetic factors and bone marrow cells as well as bone progenitor cells [16,8].

Until now the osteogenetic effect on unaffected human bone is still unknown. This study analysis the effect of focused extracorporeal shock waves on human calcaneus.

2. Materials and methods

The aim of this study was to investigate the effect of extracorporeal shock waves on not pathologically altered bone in human. It should be investigated whether medium-energy shock waves have an osteoinductive effect. To determine this effect, bone mineral density (BMD) and bone mineral content (BMC) of the treated calcaneus are measured as the primary target. Furthermore, it was examined whether treatment of the calcaneus can lead to a change in the target bone mineral density in remote areas.

45 patients (34 female, 11 male) with a clinically relevant and radiologically documented plantar heel spur were treated as part of a standardized focused extracorporeal shock wave therapy. Patients were treated according to the inclusion and exclusion criteria (Table 1). Patients who had already received ESWT or had local cortisone injections before were excluded from the study to avoid any therapeutically effect on bone density.

36 out of 45 patients were available for follow-up after six and twelve weeks. Nine patients (eight women and one man) were excluded for follow up: Five patients have withdrawn study consent subsequently, two patients discontinued the therapy protocol due to ongoing pain and two patients could not be contacted.

All shock wave treatments were performed with the EPOS FLUORO© by Dornier (Wessling, Germany). This device generates the shock waves electromagnetically. Measurements of bone mass density and bone mass concentration were performed with a Lunar Prodigy© (Madison, Wisconsin, USA). The technology is based on the DEXA principle. The Lunar Prodigy Osteodensitometer is equipped with a combination of two conventional measuring beam devices – spot-beam and fan-beam. With the combined measurement methods, the unit can recalibrate automatically which gives a high precision and constancy despite short measurement time for each measured level.

The evaluation and data analysis were carried out by a blinded observer. The effected site was treated by extracorporeal shock waves and analyzed to calculate the effect size as the unaffected heel of the patient which did not get any shock wave treatment served as a control group. The study design was a prospective single blinded intra-individual controlled study.

Patients who met inclusion and exclusion criteria and consented to the study were treated twice with an interval of two weeks with focused extracorporeal shock wave therapy. The mean energy flux density was 0.32 mJ/mm^2, 2000 shock waves at a frequency of 2 Hz were applied per session. The localization of the most painful area was achieved with the so-called biofeedback mechanism. By this method, shock waves were applied from plantar to assure intraosseous penetration to the center of the calcaneus by treating the chronic inflammation originating from the insertion of the plantar fascia. The large and oval shaped focal zone was placed at the origin of the fascia and reached the central calcaneus as well. This precise focus positioning was done radiologically controlled. No local anesthesia was used [17,18]. Patients were allowed for full weight bearing after the treatment. Bone density measurement was performed directly before the first ESWT as well as six and twelve weeks after ESWT in a standardized manner. After each measurement an automatic calibration (of the unit) was carried out. Patient data were matched with a reference group, which is comparable in terms of age, height, weight, gender and ethnicity.

The square-shaped analysis field (Region of Interest, ROI) was

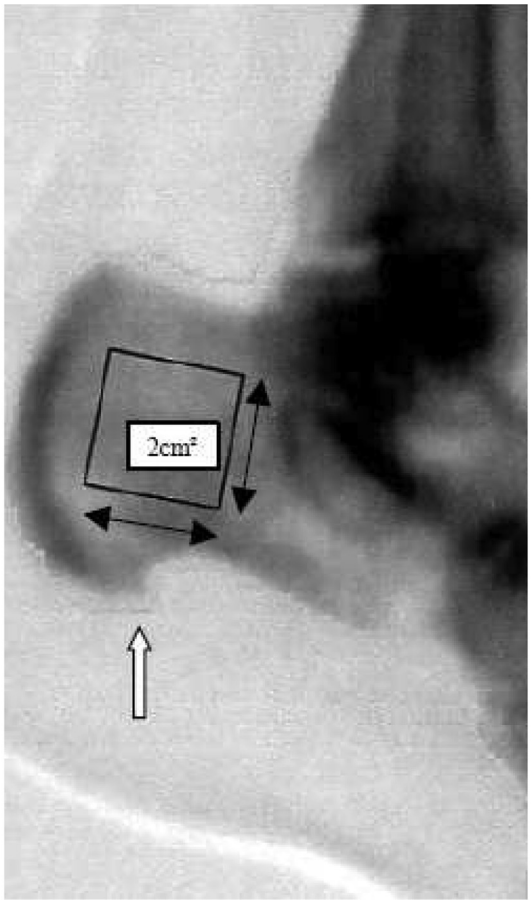

Fig. 1. Measuring surface of the calcaneus, Region of Interest (ROI) = 2 cm^2, standardized.

Table 1
In- and exclusion criteria.

Inclusion criteria	Exclusion criteria
Pain history > 6months	Age < 18years
Unsuccessful conservative treatment	Mechanical dysfunction of ankle- and/or foot joints
Clinically relevant pain of plantar heel spur	Degenerative or rheumatoid arthritis
	Neuro-vascular pathologies
	Tarsal tunnel syndrome
	Pregnancy
	Coagulation disorders
	Infections
	Tumors
	Preceding injection therapy for plantar heel spur

placed in the cancellous part of the calcanei and BMD and BMC were measured. ROI was placed in the middle of the calcaneal cancellous bone area to increase preciseness of BMD and BMC measurement (Fig. 1). With a standardized measurement area of 2 cm^2, we obtained the results of the bone mineral content (BMC) in grams and the bone mineral density (BMD) in g/cm^2 as the quotient of the two measured variables (i.e. the mineral mass per measuring surface).

As primary defined criteria BMD and BMC were measured in the calcaneus 12 weeks after last ESWT. Secondary criteria included the change of BMD and BMC in the skull, humerus, greater trochanter, trunk, ribs, pelvis and L5. Statistical analysis was performed with a "Q–Q plot" which is a graphical method for comparing two probability distributions by plotting their quantiles against each other to show normal distribution of values. After proven normal distribution paired T-Test analysis were calculated to calculated significance.

3. Results

At baseline the mean age of participants was 53 years (28.6–80.1y). The average height was 170.4 cm (150–193 cm), mean body weight was 80.7 kg (50.5–117 kg). This was calculated for a mean BMI of 27.74 (women: 23.0; men 28.2). For women, the values reached from 20.7 to 34.0, for men from 22.8 to 31.8. During the 12-week follow-up period, there were no significant changes in size and weight of the participants.

The plantar heel spur was located on the right side in 22 out of 36 cases (61%). In all patients the calcaneal spur was radiologically evident.

The primary targets of this study were bone mineral density (BMD) and bone mineral content (BMC). Additionally, BMD of the secondary target areas were analyzed during the course of treatment. The mean values of BMD in the secondary target areas are listed in Table 2 for all three measurements. None of the regions but at the calceneus showed a significant change in BMD over the course of time.

4. BMD

In Fig. 2, the mean values of bone mineral density for the control group and ESWT group are displayed over the course of time (Fig. 2). The mean BMD values at baseline were 0.50 g/cm^2 (±0.10) in the ESWT group, the median was 0.48 g/cm^2, the minimum 0.30 g/cm^2 and the maximum 0.69 g/cm^2. For the control group the mean value was 0.54 g/cm^2 (±0.10), median was 0.52 g/cm^2, with a minimum of 0.36 g/cm^2 and a maximum of 0.75 g/cm^2.

Six weeks after the second therapy, BMD in the ESWT group showed an average of ø0.529 g/cm^2 (±0.10), median was 0.51 g/cm^2, minimum 0.34 g/cm^2 and maximum 0.75 g/cm^2. In the control group the average value was 0.529 g/cm^2 (±0.09), median was 0.51 g/cm^2, minimum 0.35 g/cm^2, maximum 0.71 g/cm^2.

Table 2
BMD mean values (±standard deviation) for all secondary target areas for all three measurements.

Secondary target area	Baseline	6 Weeks	12 Weeks
Skull [g/cm^2]	2.12 (±0.23)	2.09 (±0.24)	2.09 (±0.24)
Arms [g/cm^2]	0.88 (±0.16)	0.88 (±0.10)	0.88 (±0.10)
Trochanter [g/cm^2]	1.29 (±0.17)	1.28 (±0.17)	1.29 (±0.17)
Trunk [g/cm^2]	0.92 (±0.08)	0.95 (±0.09)	0.94 (±0.10)
Ribs [g/cm^2]	0.67 (±0.67)	0.70 (±0.20)	0.66 (±0.07)
Pelvis [g/cm^2]	1.11 (±0.13)	1.15 (±0.13)	1.15 (±0.13)
L5 [g/cm^2]	1.07 (±0.12)	1.11 (±0.13)	1.09 (±0.13)
Overall [g/cm^2]	1.17 (±0.11)	1.17 (±0.10)	1.17 (±0.11)

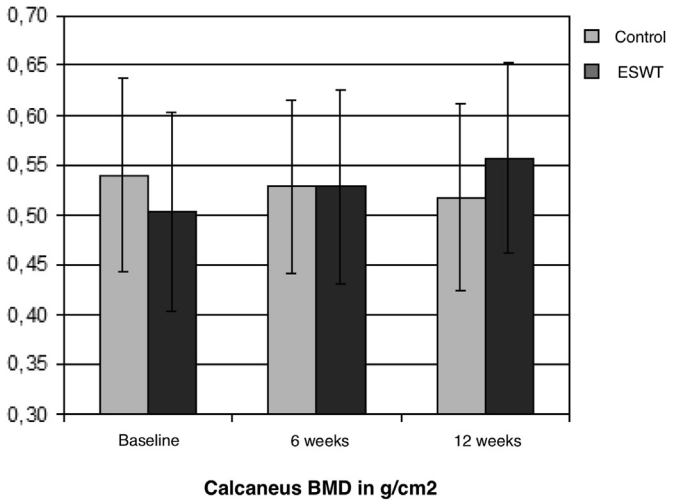

Fig. 2. Calcaneus BMD, control and ESWT-group.

12 weeks after last ESWT the following results were determined for the treatment side: Mean value 0.557 g/cm^2 (±0.10), median 0.55 g/cm^2, minimum 0.35 g/cm^2 and maximum 0.75 g/cm^2. The control group shows a mean value of 0.52 g/cm^2 (±0.09), median of 0.51 g/cm^2, minimum of 0.34 g/cm^2 and a maximum of 0.71 g/cm^2. This demonstrates that the BMD increase on the treated side is highly significant in all intervals with $p < 0.0001$.

4.1. BMD-difference compared to baseline

Fig. 3 illustrates the differences in bone mineral density after 6 and 12 weeks compared to the values at baseline (Fig. 3). The difference of change compared to baseline (6 weeks FU) at the ESWT-group showed an increase of 0.03 g/cm^2 (±0.03), median was 0.02 g/cm^2, minimum −0.04 g/cm^2und maximum 0.10 g/cm^2. After another six weeks the averaged increase in BMD-difference was 0.05 g/cm^2 (±0.04), the median 0.06 g/cm^2. Values ranged from −0.06 g/cm^2 (min.) to 0.13 g/cm^2 (max.).

In the control group an average reduction of −0.01 g/cm^2

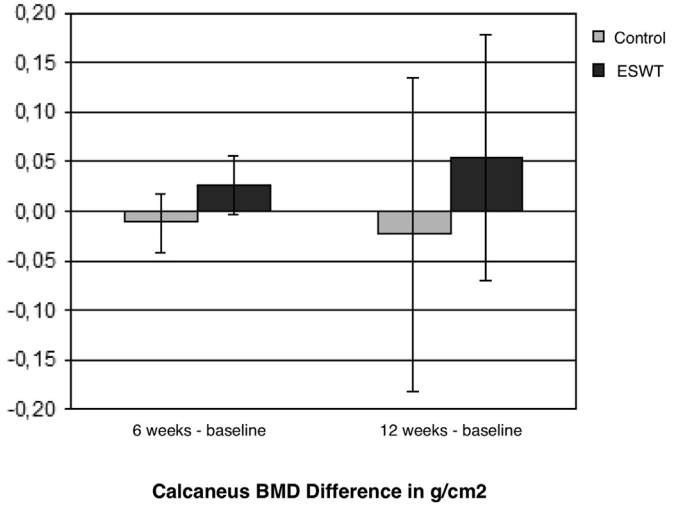

Fig. 3. Differences of change of BMD calcaneus 6 weeks and 12 weeks after last ESWT.

(±0.03) with a median of −0.01 g/cm^2, a minimum of −0.09 min g/cm^2 and a maximum of 0.03 g/cm^2 was noticed after 6 weeks and an average of −0.02 g/cm^2 (±0.04), median −0.02 g/cm^2, minimum −0.12 g/cm^2, maximum 0.06 g/cm^2 after 12 weeks. The differences are significant for the treatment group at 12 weeks with $p = 0.001$.

5. BMC

The average BMC of the ESWT group to the baseline was 2.03 g (±0.38), median was 2.00 g, with a range of 1.30 g (min.) and 2.70 g (max.). BMC of the control group was 2.16 g (±0.40), median was 2.10 g, minimum 1.40 g and maximum 3.00 g. 6 weeks after the last ESWT an average value of 2.12 g (±0.39), a median of 2.00 g, a minimum of 1.40 g and a maximum of 3.00 g was recorded on the treated heel. On the contralateral control side, an average value of 2.14 g (±0.37), with a median of 2.10 g, a minimum of 1.40 g and a maximum of 2.90 g was recorded.

Another six weeks later (12 weeks after last ESWT) the average BMC of the ESWT group was 2.22 g (±0.38), median 2.15 g, minimum 1.40 g and maximum 3.00 g whereas the control group showed ø 2.08 g (±0.36) with a median of 2.00 g, ranging between 1.30 g (min.) and 2.80 g (max.). Fig. 4 illustrates the average values of BMC of both groups for all measurements (baseline, 6 weeks and 12 weeks). The values of the treatment group were significantly higher compared to the control group at each measurement with $p < 0.0001$ (Fig. 4).

5.1. Change of BMC-differences

The mean difference of the BMC after 6 weeks was on the ESWT side at 0.09 g (±0.12), median was 0.10 g, minimum −0.50 g and maximum at 0.30 g (Fig. 5). After 12 weeks the mean difference was 0.19 g (±0.17), median 0.20 g with values ranging between −0.20 g (min.) and 0.60 g (max.). After 12 weeks the average BMC was 0.19 g (±0.17), the median was 0.20 g with a minimum of −0.20 g and a maximum of 0.60 g.

For the control group a mean difference of −0.02 g (±0.16) could be observed. The values ranged between −0.40 g (min) and −0.30 g (max.) with a median of 0.01 g after 6 weeks. After 12 weeks the following data was recorded: mean difference −0.18 g (±0.18), median 0.02 g, minimum −0.40 g and maximum 0.30 g. Again, the values of the treatment group increased significantly with $p < 0.0001$, whereas the increase in the control group was

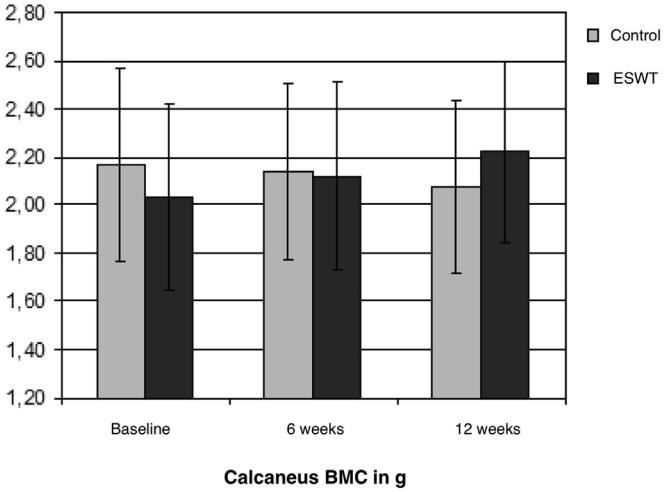

Fig. 4. Bone mineral concentration of calcaneus, control and ESWT group.

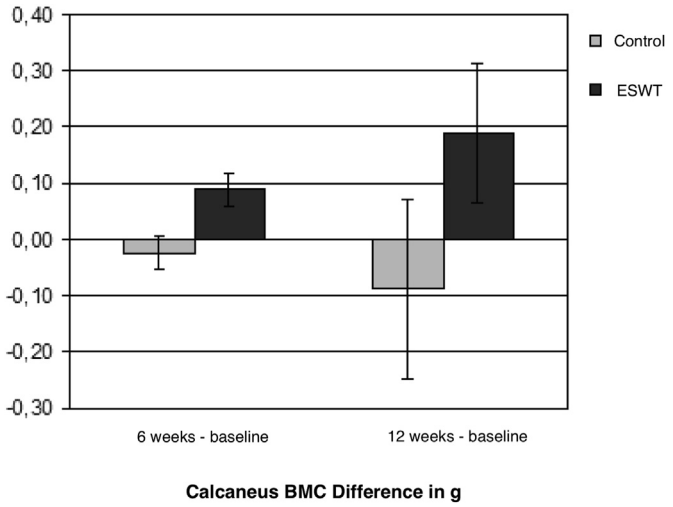

Fig. 5. Differential values for BMC calcaneus 6 weeks vs. baseline (left) und 12 weeks vs. baseline (right).

significant only after 12 weeks compared to baseline with $p = 0.005$.

5.2. Side-effects

There were no clinically relevant side-effects. Some patients reported increased pain for a few days after ESWT as well as minor hematoma at the coupling area which disappeared after some days.

6. Discussion

A plantar heel spur is a widespread medical condition that may affect both professional and recreational daily life predominantly through load-dependent pain. For this indication extracorporeal shock wave therapy is an established method of non-surgical treatment with the best evidence. So far no studies on the relationship between shock wave therapy and bone density in humans have been reported in human. Van der Jagt et al. published the outcome after unfocused shock wave ware applied in an animal model especially when this treatment is combined with an anti-resorptive treatment [21].

Our study was firstly able to demonstrate that six weeks after ESWT with 0.31 mJ/mm^2 an increase in bone mineral density could be observed in human. This effect turned out to be statistically significant twelve weeks after therapy. Similar to the findings of Maier et al. and Wang et al. [19,7] a temporal latency of the osteogenesis could be observed in our patients.

So it can be assumed that an increase of calcified tissue (BMD and BMC) needs a time period after treatment to reach significant level. Wang et al. were able to demonstrate that osteoblasts can be stimulated by shock waves [8]. Furthermore ESWT can improve blood perfusion which leads to vasculogenesis with improved osseous perfusion [16]. In the long term, this osteogenetic effect may help to reduce fracture risk. Even low-energy shock wave therapy leads to a significant increase in neovascularization and angiogenetic markers only one week after therapy [20,16]. Due to the fact that mechanical stress is the strongest stimulus on bone proliferation, extracorporeal shock wave therapy can be interpreted as mechanical load with a local piezoelectric effect.

The present study does not demonstrates that partial weight bearing due to pain can led to a significant reduction in bone density on the affected side because patients will do full weight bearing despite severe pain and hardly use walking aids. At baseline

no statistically significant difference in BMD and BMC was found. Furthermore a small local osteoporotic effect can be discussed in chronic local inflammation processes such as chronic heel pain. But again the difference in BMC and BMC does not differ significantly at baseline. This has to be addressed in larger sample size studies.

As an increase in BMD ad BMC was detected at low levels other stimuli besides micro fractures with subsequent callus induction such as a hormonal influence and vessel proliferation have to be taken into consideration. This is nowadays described as mechanotransduction. Assuming a general hormonal effect, a systemic influence on bone density resulting from ESWT has to be examined but could not found in our study.

Since bone density after ESWT increased only at the calcaneal bone in our study, the probability of systemic humoral influence can be excluded.

Our own results clearly demonstrate that bone density remains unchanged in areas remote from the actual ESWT site and ESWT did not have any influence to our secondary measured and analyzed localizations.

These results are limited by the small sample size which goes along with a lower statistic power. Furthermore the limited number of subjects enrolled within a larger age range (28.6–80.1y) does not allow more detailed analysis regarding the effect of age regarding the outcome after ESWT. More studies with larger study population are needed to verify the results. Further studies have to determine the best level of energy flux density to optimize the osteogenetic effect. Current studies about ESWT do not address bone density. The observation period of twelve weeks is clearly enough to detect that bone density increases after ESWT. Long term effects have to be addressed in the future whether this shock wave effect can be increase by further treatment options such as magnetic field or not. Until now it remains unclear if this effect lasts permanently or regresses a few months after treatment to the prior level. If the effect of shock wave therapy is in fact time-limited an adequate regime of repeated ESWT has to be established to maintain the positive therapeutic success.

Our results lead to the reasoned statement that osteogenesis can also be stimulated in the non-pathologically altered bone using ESWT. Shock wave therapy could be an option in patients suffering from impaired bone quality such as osteoporosis. This has to be addressed in the future.

Ethical approval

None.

Funding

None.

Author contribution

None.

Conflicts of interest

None.

Guarantor

Prof. Dr. med. Ludger Gerdesmeyer MD, PhD, Dept Orthopaedic Surgery and Traumatology, University Schleswig Holstein, Campus Kiel, Arnold Heller Strasse, D-24105 Kiel, Germany. Tel.: +49 431 597 5505, e-mail: Gerdesmeyer@aol.com.

References

[1] N. Martinelli, A. Marinozzi, S. Carni, U. Trovato, A. Bianchi, V. Denaro, Platelet-rich plasma injections for chronic plantar fasciitis, Int. Orthop. 37 (5) (2013) 839–842, http://dx.doi.org/10.1007/s00264-012-1741-0.

[2] H.Y. Erken, S. Ayanoglu, I. Akmaz, K. Erler, A. Kiral, Prospective study of percutaneous radiofrequency nerve ablation for chronic plantar fasciitis, Foot Ankle Int. 35 (2) (2014) 95–103, http://dx.doi.org/10.1177/1071100713509803.

[3] N. Konjen, T. Napnark, S. Janchai, A comparison of the effectiveness of radial extracorporeal shock wave therapy and ultrasound therapy in the treatment of chronic plantar fasciitis: a randomized controlled trial, J. Med. Assoc. Thai. Chotmaihet thangphaet 98 (Suppl. l) (2015) S49–S56.

[4] H. Badakhshi, V. Buadch, Low dose radiotherapy for plantar fasciitis. Treatment outcome of 171 patients, Foot 24 (4) (2014) 172–175, http://dx.doi.org/10.1016/j.foot.2014.07.005.

[5] L. Gerdesmeyer, C. Frey, J. Vester, M. Maier, L. Weil Jr., L. Weil Sr., M. Russlies, J. Stienstra, B. Scurran, K. Fedder, P. Diehl, H. Lohrer, M. Henne, H. Gollwitzer, Radial extracorporeal shock wave therapy is safe and effective in the treatment of chronic recalcitrant plantar fasciitis: results of a confirmatory randomized placebo-controlled multicenter study, Am. J. Sports Med. 36 (11) (2008) 2100–2109, http://dx.doi.org/10.1177/0363546508324176.

[6] H. Gollwitzer, P. Diehl, A. von Korff, V.W. Rahlfs, L. Gerdesmeyer, Extracorporeal shock wave therapy for chronic painful heel syndrome: a prospective, double blind, randomized trial assessing the efficacy of a new electromagnetic shock wave device, J. Foot Ankle Surg. – Off. Publ. Am. Coll. Foot Ankle Surg. 46 (5) (2007) 348–357, http://dx.doi.org/10.1053/j.jfas.2007.05.011.

[7] C.J. Wang, H.Y. Huang, C.H. Pai, Shock wave-enhanced neovascularization at the tendon-bone junction: an experiment in dogs, J. Foot Ankle Surg. – Off. Publ. Am. Coll. Foot Ankle Surg. 41 (1) (2002) 16–22.

[8] F.S. Wang, K.D. Yang, R.F. Chen, C.J. Wang, S.M. Sheen-Chen, Extracorporeal shock wave promotes growth and differentiation of bone-marrow stromal cells towards osteoprogenitors associated with induction of TGF-beta1, J. Bone Jt. Surg. Br. 84 (3) (2002) 457–461.

[9] G. Haupt, A. Haupt, A. Ekkernkamp, B. Gerety, M. Chvapil, Influence of shock waves on fracture healing, Urology 39 (6) (1992) 529–532.

[10] W. Heinrichs, U. Witzsch, R.A. Burger, Extracorporeal shock-wave therapy (ESWT) for pseudoarthrosis. A new indication for regional anesthesia, Der Anaesth. 42 (6) (1993) 361–364.

[11] J.D. Rompe, C. Schoellner, B. Nafe, Evaluation of low-energy extracorporeal shock-wave application for treatment of chronic plantar fasciitis, J. Bone Jt. Surg. Am. 84-A (3) (2002) 335–341.

[12] V.D. Valchanou, P. Michailov, High energy shock waves in the treatment of delayed and nonunion of fractures, Int. Orthop. 15 (3) (1991) 181–184.

[13] D.M. Kaulesar Sukul, E.J. Johannes, E.G. Pierik, G.J. van Eijck, M.J. Kristelijn, The effect of high energy shock waves focused on cortical bone: an in vitro study, J. Surg. Res. 54 (1) (1993) 46–51.

[14] S. Beutler, G. Regel, H.C. Pape, S. Machtens, A.M. Weinberg, I. Kremeike, U. Jonas, H. Tscherne, Extracorporeal shock wave therapy for delayed union of long bone fractures – preliminary results of a prospective cohort study, Der Unfallchirurg 102 (11) (1999) 839–847.

[15] H. Gollwitzer, T. Gloeck, M. Roessner, R. Langer, C. Horn, L. Gerdesmeyer, P. Diehl, Radial extracorporeal shock wave therapy (rESWT) induces new bone formation in vivo: results of an animal study in rabbits, Ultrasound Med. Biol. 39 (1) (2013) 126–133, http://dx.doi.org/10.1016/j.ultrasmedbio.2012.08.026.

[16] C.J. Wang, F.S. Wang, K.D. Yang, L.H. Weng, C.C. Hsu, C.S. Huang, L.C. Yang, Shock wave therapy induces neovascularization at the tendon-bone junction. A study in rabbits, J. Orthop. Res. – Off. Publ. Orthop. Res. Soc. 21 (6) (2003) 984–989, http://dx.doi.org/10.1016/S0736-0266(03)00104-9.

[17] T. Klonschinski, S.J. Ament, T. Schlereth, J.D. Rompe, F. Birklein, Application of local anesthesia inhibits effects of low-energy extracorporeal shock wave treatment (ESWT) on nociceptors, Pain Med. 12 (10) (2011) 1532–1537, http://dx.doi.org/10.1111/j.1526-4637.2011.01229.x.

[18] J.D. Rompe, A. Meurer, B. Nafe, A. Hofmann, L. Gerdesmeyer, Repetitive low-energy shock wave application without local anesthesia is more efficient than repetitive low-energy shock wave application with local anesthesia in the treatment of chronic plantar fasciitis, J. Orthop. Res. – Off. Publ. Orthop. Res. Soc. 23 (4) (2005) 931–941, http://dx.doi.org/10.1016/j.orthres.2004.09.003.

[19] M. Maier, H.R. Durr, S. Kohler, D. Staupendahl, M. Pfahler, H.J. Refior, Analgesic effect of low energy extracorporeal shock waves in tendinosis calcarea, epicondylitis humeri radialis and plantar fasciitis, Z. Orthop. Ihre Grenzgeb. 138 (1) (2000) 34–38.

[20] D. Kusnierczak, D.R. Brocai, U. Vettel, M. Loew, Effect of extracorporeal shockwave administration on biological behavior of bone cells in vitro, Z. Orthop. Ihre Grenzgeb. 138 (1) (2000) 29–33, http://dx.doi.org/10.1055/s-2000-10109.

[21] O.P. van der Jagt, J.H. Waarsing, N. Kops, W. Schaden, H. Jahr, J.A. Verhaar, H. Weinans, Unfocused extracorporeal shock waves induce anabolic effects in osteoporotic rats, Orthop Res. 31 (5) (2013 May) 768–775, http://dx.doi.org/10.1002/jor.22258.