International Journal of Surgery 24 (2015) 147–153

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.journal-surgery.net

Review

Shock wave as biological therapeutic tool: From mechanical stimulation to recovery and healing, through mechanotransduction

M.C. d'Agostino [a, *], K. Craig [b], E. Tibalt [a], S. Respizzi [a]

[a] ESWT Center, Rehabilitation Department, Humanitas Research Hospital, Rozzano, Milan, Italy
[b] Kompass Health Associates, Auckland, New Zealand

HIGHLIGHTS

- SW represents a revolutionary form of mechanotherapy (acustic stimulation).
- Unlike urological lithotripsy (mechanical model), on living tissues, SW exert an anti-inflammatory action and pro-angiogenic and regenerative effects as well (biological model).
- Mechanotrasduction pathways sustain their clinical and experimental results.
- We present a summary of current knowledge of SW mechanisms of action, according to main recent data (mechanobiology).
- Better comprehension of SW mechanobiology could led to new therapeutical perspectives.

ARTICLE INFO

Article history:
Received 21 July 2015
Received in revised form
28 September 2015
Accepted 9 November 2015
Available online 28 November 2015

Keywords:
Shock waves
Mechanotransduction
Tissue regeneration
Tissue
Remodeling
Inflammation
Macrophages

ABSTRACT

Extracorporeal Shock Wave Therapy (ESWT) is a form of "mechanotherapy", that, from its original applications as urological lithotripsy, gained the field of musculo-skeletal diseases as Orthotripsy (mainly tendinopaties and bone regenerative disorders) and Regenerative Medicine as well.

The mechanisms of action of Shock Waves (SW), when applied in non-urological indications, are not related to the direct mechanical effect, but to the different pathways of biological reactions, that derive from that acoustic stimulations, through "mechano-transduction". So, the "mechanical model" of urological lithotripsy has been substituted by a "biological model", also supported by current knowledge in "mechanobiology", the emerging multidisciplinary field of science that investigates how physical forces and changes in cell/tissue mechanics can influence the tissue development, physiology and diseases.

Although some details are still under study, it is known that SW are able to relief pain, as well to positively regulate inflammation (probably as immunomodulator), to induce neoangiogenesis and stem cells activities, thus improving tissue regeneration and healing.

ESWT can be nowadays considered an effective, safe, versatile, repeatable, noninvasive therapy for the treatment of many musculo-skeletal diseases, and for some pathological conditions where regenerative effects are desirable, especially when some other noninvasive/conservative therapies have failed.

Moreover, based on the current knowledge in SW mechanobiology, it seems possible to foresee new interesting and promising applications in the fields of Regenerative Medicine, tissue engineering and cell therapies.

© 2015 IJS Publishing Group Limited. Published by Elsevier Ltd. All rights reserved.

1. Introduction

Shock Waves (SW) were originally introduced in medicine as Extracorporeal Shock Waves Lithotripsy (ESWL) in the early 1980s for kidney stones treatment and these clinical applications widespreaded all over the world until today. After its original introduction in medicine as *urological lithotripsy*, this technology indeed has been increasingly applied also to a broad range of musculoskeletal diseases, up to present day, when it represents an interesting therapeutic tool in the field of Regenerative Medicine [1–4].

Nowadays in fact, Extracorporeal Shock Wave Therapy (ESWT) is currently applied to a wide range of pathologies of different origins

* Corresponding author.
E-mail address: info@cristinadagostino.it (M.C. d'Agostino).

http://dx.doi.org/10.1016/j.ijsu.2015.11.030
1743-9191/© 2015 IJS Publishing Group Limited. Published by Elsevier Ltd. All rights reserved.

and localization, both in orthopedics and rehabilitative medicine (tendon pathologies, bone healing disturbances, vascular bone diseases) [1–3,5–8], dermatology/vulnology (wound healing disturbances, ulcers, painful scars) [9–12] and neurology (spastic hypertonia and related syndromes) [13–15]. More recently, the positive effects of ESWT on soft tissues and the local vasculature allowed its application, in clinical practice, also for some andrologic disturbances (*induratio penis plastic* and erectyle disfunctions) [16–18]. Regenerative and trophic effects have also been demonstrated for ischemic heart diseases, although, at present, SW application in this field has still to be considered as an experimental one [19].

In general, ESWT, in virtue of its noninvasive approach, absence of main side effects, repeatability, good tolerability and compliance by the patients (if properly applied, on the basis of a correct diagnosis), seems to offer new therapeutical perspectives in *Orthopadic and Regenerative Medicine* [1–3]. In particular, it may represent a very useful tool, especially when all other noninvasive treatments were ineffective or surgery failed, especially in the field of orthopedics and rehabilitation [20], better if in synergistic action with some other therapeutical options (as, for example, rehabilitation programs) [21].

2. Shock waves as mechanotherapy: from fisics to mechanobiology and mechanotransduction

SW are "mechanical" waves, whose shape is characterized by an initial positive very rapid phase, of high amplitude, followed, after very few microseconds, by a sudden phase of mild negative pressure, afterwards returning to the ambient (basic) values. Medical SW are generated, through a fluid medium (water), by a *source* (electrohydraulic, piezoelectric or electromagnetic type generator). They are sonic pulses characterized by: high peak pressure, up to 100 mpa (500 bar) or even more, rapid rise in pressure (<10 ns), short duration (<10 μs) and a broad range of frequency [22,23] (Fig. 1).

Independently of the type of generator (source) mounted in the lithotripter, SW are produced as consequence of a rapid increase in pressure (like a "micro-explosion") into the water, and sooner they are "focused" on the *target* (that is the anatomical area to be treated). Focusing is possible for a parabolic lens, which concentrates the front of SW, as soon as they are produced from the source. These *focused* Extracorporeal SW (fesw) are well defined in their characteristics, that differentiate them from the *radial waves* [23,24]. Radial Waves are mechanical stimulations (acoustic waves) as well, but differ from fsw according to their shape, and act

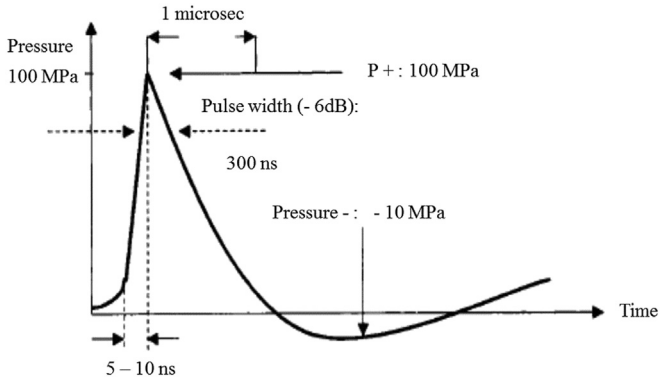

Fig. 1. Typical "biphasic" form of the therapeutical extracorporeal shock waves. (from: Odgen JA, Toth-Kischkat A, Schulteiss R. Principles of Shock Wave Therapy. Clinical Orthopedic and Related Research, 2001; 387: 8 – 17).

through a *ballistic* mechanism. Technically, in the applicator (a barrel handpiece), a metallic bullet is accelerated at very high speed by compressed air (pneumatic source) or by an electromagnetic mechanism. Due to the high kinetic energy produced, it impacts against the tip of the applicator itself, which is directly applied on the body surface: as a consequence, the kinetic energy, forfeited during running, is directly transferred to the skin on the area of treatment. Differently than SW, this *pressure waves* propagate into the body as a spherical or ball-shaped waves, that is in a radial fashion, that gives them the descriptive term of "*radial waves*". They are not focused in the deeper layers, and, at some extent, join the more superficial layers in the area of treatment. From the physical point of view, both fsw and radial waves are mechanical waves, but differ relatively to the shape of the wave itself; nevertheless, they share, as *mechanotherapies*, some useful clinical applications in some soft tissue disorders [23–25].

The importance of mechanical stimuli on living beings, as well as the influence that biomechanical deformations can exert on cellular biology and physiology, in health and diseases, have been recently seen a reneviewed interest in scientific literature, especially with the purpose of possible therapeutical applications [4,26,27].

Mechanical stimulation usually brings to mind the obsolete concept of "physical therapies", especially in the fields of orthopedics and rehabilitation: for a long time, studies and researches for exploring the applications of "physical" stimulations have been generally limited to describe and quantify the final general outcomes of these therapies, without analyzing in details the pathways of actions, at biological level, that these "physical means" may produce on the treated tissues and cells [4].

Only in more recent years, due to the developing of the new branch of science named *Mechanobiology*, researchers began to analyze in details the effects of the physical stimulus and, most of all, to correlate the interactions of physical energies with the various tissues and cell elements [28,29].

It can be considered a field of science at the "cross-road" between biology and engineering of mechanics, whose main goal is to describe *mechanotransduction*, that is all the molecular mechanisms, by which cells can sense mechanical stimulations and adapt their behavior to mechanical signals [30,31].

"Mechanotransduction" is a *biological pathway* to which many cell types are sensible: after sensing and processing the mechanical informations from the extracellular environment, these biomechanical forces are converted in biochemical responses, thus influencing some fundamental cell functions as migration, proliferation, differentiation, and apoptosis [31].

Originally studied in "adhesion biology", where *integrins* have been described to convey force transmission between the extracellular matrix and the intracellular actin cytoskeleton, it has been described that the phenomenon of *mechanosensing* is correlated with the laterally rearrangement of proteins within the membrane, thus inducing some changes in their tridimensional structure and modifying their activity, according to the different and changing biomechanical conditions [32].

Many cells structures have been described to contribute to mechanotransduction: stretch-activated ion channels, caveolae, integrins, cadherins, growth factor receptors, myosin motors, cytoskeletal filaments, nuclei, extracellular matrix, intercellular "gap junctions", "hemi channels" among membrane proteins, "primary cilia" among cell organelles (capable of perceiving possible mechanical, physical or other "perturbations"), "transient receptor potential channels" intracellular mechanical-signalling"pathways" and numerous other molecular structures and signaling molecules. Moreover, endogenous cell-generated traction forces significantly contribute to these responses by modulating

tensional prestress within cells, tissues, and organs that govern their mechanical stability, as well as mechanical signal transmission from the macroscale to the nanoscale [30,31].

If originally the mechanotransduction phenomenon was extensively investigated in endothelial cell biology upon shear stress stimulation, more recent evidences indicate its important role also in function and physiology of many other cell types, including fibroblasts, bone cells, and mesenchymal stem cells [32–34]; even macrophages and some other cells of the immune system, seem to be endowed with some mechanosensing properties [35].

Nowadays, although it is still not completely possible to apply Mechanobiology for diagnosis, treatment, health maintenance and upgrading of various biological systems, and is well known that Human Mechanobiology is still a field of theoretical speculation and research, nevertheless, we can already apply some mechanical stimulations, better known as *Mechanotherapies,* that can be successfully used in clinical practice for many disorders of bone and soft tissues as well. According to a revisited definition of the term, on the basis of the current knowledge in mechanobiology, *Mechanotherapies* have been defined as "all therapeutic interventions that reduce and reverse injury to damaged tissues, or promote the homeostasis of healthy tissues by mechanical means at the molecular, cellular, or tissue level"; in other words, they include all "active mechano – interventions, that aim to convert potentially destructive mechanical effects into constructive influences and target normal mechano – adaptation to promote recovery" [4].

In the field of Mechanotherapies, a specific place is reserved to Extracorporeal Shock Waves Therapy (ESWT): its manifold biological mechanisms of action (based on mechanotransduction) have been partially understood and described over recent years, although still remaining partly under scientific investigation [4].

3. Which biological effects from shock waves as mechanotherapy ?

As already introduced, nowadays it is scientifically recognized that SW, on living structures, although acting as pure physical energy, do not evoke a mechanical disruptive result, but really induce some biological effects on tissues and cells, whose functions and metabolism can be positively regulated and stimulated; in other words, the mechanical stimulus could be only a "trigger", but not properly the direct responsible of the ultimate effects of stimulation itself. This phenomena is supported by some "*mechanotransduction pathways*", which imply the activation of a series of cellular events (largely unknown until now), responsible for the positive effects of ESWT on cell metabolism and cell cycle, which ultimately account for the ductility of the therapy [1–3,36].

Regarding the field of *SW mechanobiology*, it is important to underline that *in vitro* cell experiments may show some different results, according to the type and energy level stimulation applied, from a positive, regenerative and trophic effect, to a dangerous and disruptive one as well. Cell experiments can be considered very useful for understanding basic pathways of reaction, as well as for postulating the mechanisms of interaction at the tissue level, but cannot be used to define clinical protocols and general indications. At the cellular level, in any case, it was demonstrated that SW can induce – as shear stresses - a deformation of some cytoskeletal proteins (actin and tubulin, but not vimentin), but this is only a transient effect, as cells were able to reorganize their original cytoskeletal network within 3 h, with a pattern similar to the control [37].

In the field of mechanotrasduction and possible therapeutical mechano - interventions, definitely, SW, as *mechanotherapy*, can play an important role in positively influencing some cells functions and local homeostasis, thus conditioning the tissue *self-healing* capabilities. Evidences from basic science and clinical trials, in fact, seem to indicate that ultimately this effect involves the SW action of inducing proliferation, migration and differentiation of stem cells, which significantly contribute to tissue healing and regeneration. Besides stem cells and bone marrow – stromal cells, many other cells revealed themselves as targets for mechanotransduction after SW exposure, including tenocytes, bone cells and their precursors, endothelial cells, fibroblasts and some other ones [1–3,38–45].

SW represent a fundamental therapeutic tool for tendinopathies, irrespective of the presence or not of calcifications, with success rates reported in the literature up to 91% (for rotator cuff "tendinitis", trocanteritis, Achilles tendinitis, plantar fasciitis and jumper's knee) [1–3,24]. Many clinical data indicate that SW can be effective in resolving tendon pathologies, especially as an effective intervention to be considered when other nonoperative treatments have failed, although the specific mechanisms of action remain partly unknown [1–3,20,46].

Indeed, between the different cell types, tenocytes, well known since a long time to be very sensible to mechanical stimulations, have been extensively studied regarding SW Mechanobiology.

In animal experiments, it has been observed, for example, that an optimal SW treatment promoted healing of "collagenase - Achilles tendinitis", by inducing TGF-beta1 and IGF-I. Histological observations demonstrated that ESWT resolved edema, swelling, and inflammatory cell infiltration in injured tendons. Lesion site underwent intensive tenocyte proliferation and progressive tendon tissue regeneration. Tenocytes, at the hypertrophied cellular tissue and newly developed tendon tissue, expressed strong proliferating cell nuclear antigen (PCNA) after ESW treatment, coinciding with intensive TGF-beta1 and IGF-I expression, right as in the early stage of tendon healing. So, it has been hypothesized that physical SW stimulation could increase the mitogenic responses of tendons [47].

Moreover, it was described that SW can exert a direct action on tendon cells, as below summarized, thus implying also a possible future involvement in tendon healing and regenerative therapies:

1. Reduced expression of several metalloproteinases and interleukins (MMPs and ILs) [48];
2. Positive regulation of cell vitality and proliferation, besides expression of typical tendon markers and anti-inflammatory citokines [49–51];
3. Stimulus to proliferation and collagen synthesis, firstly mediated by early up-regulation of PCNA and TGF-beta1 gene expression, endogenous NO release and synthesis and TGF-beta1 protein and then collagen synthesis [47];
4. Enhancing of *in vitro* functional activities of ruptured tendon-derived tenocytes (proliferation and migration), which could probably contribute to tendon healing *in vivo* [52];
5. Increased expression of lubrycin [53].

Regarding this topic, very recently some Authors studied with microdialysis, in humans, the biochemical responses of tendons after SW stimulation, and hypothesized that this mechanical stimulus might aid tendon remodeling in tendinopathies, by promoting the inflammatory and catabolic processes, that are associated with removal of "pathological" matrix constituents, thus suggesting a potential argument for future studies [54].

Another important clinical field, where SW play a primary role as *mechanotherapy* is represented by bone healing disorders and bone vascular diseases. Nowadays, many clinical and experimental data seem to confirm SW as an important therapeutic tool for enhancing osteoregenerative processes in pseudoarthrosis and bone healing delays, as a valid alternative to surgery in many cases [1,3,5,55], besides the possibility to positively interphere with

altered local bone turnover (as for example in bone marrow edema syndromes) [8] or to improve local osseous trophism (as in osteonecrosis and related disorders) [6,7].

Bone is perhaps the tissue where mechanobiological pathways are well expressed in their different forms: both due to its particular mechanosensitivity, and its complex structure and physiology as well. Cell experiments seem to demonstrate in fact, that the effects of SW in this tissue can act at different levels: not only directly on bony and periosteal cells and their precursors, but also in the complex *cross – talk* between osteoblasts and osteoclasts, involving osseous vasculature as well [43,56].

More in details, at the bone level, there have been described after SW exposure:

- direct stimulation of osteoblasts and periosteal cells [57–61];
- osteogenic differentiation of mesenchymal stem cells through superoxide–mediated signal transduction, followed by activation of tyrosine kinase–mediated extracellular signal-regulated kinase (ERK) and core binding factor A1 [62];
- accelerated migration of osteoblasts [63];
- early expression of angiogenesis-related growth factors, including endothelial nitric oxide synthase (eNOS), vascular endothelial growth factor (VEGF) and proliferating cell nuclear antigen, thus producing new vessel in-growth with improved blood supply, increasing cell proliferation, accelerating tissue regeneration and healing [55,56,64–66];
- stimulation of periosteum toward orthotopic bone regeneration [42];
- reduction of osteoclasts activity, through inhibition of pro-osteoclastogenic factors [43].

Moreover, as some other mechanotherapies applied in clinical practice, main action of ESWT seems to focus on inducing tissue regeneration and, accordingly, experimental and clinical results indicate that its clinical efficacy is tightly related to its ability to induce neovascularization and matrix remodeling "*in vivo*" [1,3,10,19,38,39,67–72].

From the mechanobiologic point of view, it has been described, for example, that this neoangiogenic capacity, could be related, as first step, to the inhibition of endothelial cells apoptosis and adhesion, occurring in the very early phase after SW stimulation (first 3 h), as initial response to the mechanical stimulus. More in details, it has been hypothesized that some aspects of the early gene response of endothelial cells to SW, as mechanotherapy, are similar to those induced by the laminar shear stress flow, mainly characterized by an anti-apoptotic effect. In other words, at 3 h after SW exposure, still lacking neoangiogenic activity (usually appearing no earlier than 12 h), nevertheless it seems possible to detect some "preparatory" signals, such as downregulation of the genes involved in cell cycle and adhesion, probably correlated to an upcoming detachment of endothelial junction [40]. Although *in vitro* data, they seem to confirm in any case that, from a general point of view, for applying mechanical interventions in view of a therapeutical purpose it is useful to understand many details at the molecular, cellular and tissue level [4,28,73].

As already mentioned, increasing evidences in the literature describe that mechanotransduction events, after SW stimulation, are not only dose-dependent but also can vary in different cell types and stem cells at different stages of differentiation. Moreover, each cell type seems to be responsive to SW, but probably with different optimal patterns and ranges of mechanical stimulation, thus developing different biological answers, including, for example, upregulation of TGF-alfa-1 expression and NO production, as well as suppression of NF-kappa-B activity and pro-inflammatory cytokines production [4,38,39,74,75].

Furthermore, according to the more recent knowledge in SW mechanobiology, there is increasing evidence of SW as mechanotherapy acting as "immunomodulator" in wound healing and tissue regeneration, mainly through an anti-inflammatory strategy [75–78]; very interestingly, some Authors described that SW may modulate inflammation via the Toll-Like Receptor 3 (TLR3) pathway, through the release of cytosolic RNA [79].

These basic science data may be some revolutionary findings, as only in recent years it has been demonstrated the important role and involvement of the innate immunity system in the complex series of interplayed cellular and biochemical events, that lead to tissue regeneration, healing and remodeling. A very critical point in tissue healing and regeneration is represented by the delicate phase, where acute inflammation (as for example in a wound soon after trauma) can shift toward its physiological resolution or chronicization (pathological conditions). It is well known, nowadays, that macrophages play an important role in controlling many phases of the "healing" process, both in the initial inflammatory phase (as M1 or "classically" activated macrophages), and in the resolving stage (as M2 or "alternative activated" one), by regulating this delicate transition. They can perceive in fact some endogenous as well as exogenous "danger signals" (as after local trauma or in the presence of pathogens) and respond with a proinflammatory activity as first response – as M1-, to generate anti-inflammatory and pro-resolving mediators, while recruiting and stimulating stem cells as well in their M2 mode. In other words, macrophages can be considered highly plastic cells, that, in their different stages of activation, during the course of the inflammatory process, can integrate signals from the microenvironment and coordinate the evolution of the local inflammatory response (chronicization *versus* resolution), according to the mediators that dominates [80–82]. Surprisingly, not only macrophages had already been demonstrated to be responsive to mechanical stimuli, but also, a very recent *in vitro* study shows that, after exposure to low energy SW, it is possible to dampen the induction of the pro-inflammatory profile characterizing M1 macrophages, while promoting the acquisition of an anti-inflammatory profile (M2), in synergy with the macrophage alternative activation. These preliminary data seem to suggest this could be a possible another key – point of regulation in SW mechanobiology, both related to tissue regeneration and remodeling as well [83].

On the other hand, some experimental model already described that ESWT application, based on intramuscular silicone injection, reduced formation of the dense fibrous capsule and, when applied as multiple SW sessions, could degrade the fibrous envelope, related to a synergistic alterations in pro- and anti-fibrotic proteins (TGF-beta1 and matrix metalloproteinase 2, respectively), thus suggesting that SW could reduce capsule formation and may induce fibrotic tissue remodeling/resorption [84].

From this one and similar experimental and clinical data, it seems possible to conclude that ESWT would enhance not simply "healing" processes, but properly "regenerative" events, where fibrous tissue can be reduced at the origin, or even remodeled in a second phase (as in scars, for example). These important mechanobiological findings may have multiple, interesting and promising applications in clinical practice, first of all in cardiology, where restoration of tissue integrity, instead of fibrous tissue, is vital for heart performance [79,85].

Another important issue in SW mechanobiology is the possibility of positively interfering with the *nervous system* and some neurophysiological processes at different levels. It is well known since many years, the possible analgesic effect, induced by SW application. If, on one hand, it could be partially explained with the resolution of "inflammation" and all related diseases, nevertheless

some clinical and increasing evidences in the literature seem to suggest an important role of ESWT also in modulating some "neurological" activities, although the mechanisms of action have to be clarified in details [86]. It is well known for example, that SW exposure can modify the presence and/or function of small unmyelinated nerve fibers and some neurotransmitters (as for example Substance P and Calcitonin Gene Related Peptide) [87,88].

On the other hand, if it is well recognized its potential in reducing hypertonia in spastic syndromes, although, in any case, it is less clear how SW can modify these pathologic muscle activities, although some hypothesis have been postulated [89,90].

Moreover, if some studies recently began to demonstrate the possibility of a regenerative effect also on nerves and spinal structures [91,92], already in 2008, Wess O. had published an article, hypothesizing how SW (as mechanical stimulation) could reorganize pathologic memory traces, thus giving cause to a real and permanent pain relief (through a central effect), thus opening the doors for new treatment approaches to chronic pain and several other disorders of the nervous system [93]. Only more recently, Lohse-Busch H. et all. published the first study of focused transcranial ESWT (TESWT), showing the possibility to stimulate vigilance in patients with unresponsive wakefulness syndrome, although the exact neurophysiological mechanism remain to be verified by further studies [94].

Definitely, although more recently introduced and with the necessity of further studies confirming preliminary results, SW, as mechanotherapy, seem to foreshadow new interesting therapeutical implications also in the field of some neurological diseases.

4. Conclusions

In clinical practice, as SW stimulation can positively influence the interplayed chain of biological reactions that, through controlled inflammation lead tissue regeneration and "reset" local metabolism, new horizons and insights seem to be opening, in view of counteracting many acquired pathological conditions (especially post – traumatic sequelae with muscle and skin lesions and heart failure as well), for which fibrosis is the main issue. Further investigations exploring SW application in a very early phases of healing, in order to reduce the amount of fibrous tissue during recovering, could further underline the importance and dignity of this irreplaceable mechanotherapy in the field of Regenerative Medicine.

Already in 1997, Haupt wrote: " .. in patients in whom conservative treatment has failed, surgery used to be the only choice, but its success rate barely exceeds that of shock wave therapy and surgery can still be done if shock wave therapy fails. Extracorporeal shock waves will have an impact on orthopedics comparable to its effect in urology. Scientific evaluations, professional certifications, quality assurance and reimbursement issues present great challenges .." [20]. On the basis of all scientific data about SW and according to its mechanobiology, it seems likehood that those prophetic words of Haupt in that "pioneering era" became realistic, going beyond expectations, even implying for SW new promising perspectives in different fields of Regenerative Medicine, Tissue Engineering and Cells Therapy in the near future [83,95].

Ethical approval

Ethical approval not requested.

Funding

There was no funding of this research.

Author contribution

M. Cristina d'Agostino and Kenneth Craig conceived the idea of the article, studied the scientific articles and wrote the paper.

Elisabetta Tibalt participated in writing the paper and in reviewing scientific literatures.

M. Cristina d'Agostino, Kenneth Craig and Stefano Respizzi revised the final version and gave the final approval of the version to be submitted.

Conflicts of interest

All authors declare, that they have no conflict of interest.

Guarantor

Dr. M. C. d'Agostino.

References

[1] C.J. Wang, Extracorporeal shockwave therapy in musculoskeletal disorders, J. Orthop. Surg. Res. 7 (2012 Mar 20) 11.
[2] A. Notarnicola, B. Moretti, The biological effects of ESWT on tendon tissue, Muscles Ligaments Tendons J. 2 (1) (2012) 33–37.
[3] P. Romeo, V. Lavanga, D. Pagani, V. Sansone, Extracorporeal shock wave therapy in musculoskeletal disorders: a review, Med. Princ. Pract. 23 (1) (2014) 7–13.
[4] C. Huang, J. Holfeld, W. Schaden, D. Orgill, R. Ogawa, Mechanotherapy: revisiting physical therapy and recruiting mechanobiology for a new era in medicine, Trends Mol. Med. 19 (9) (2013 Sep) 555–564.
[5] A. Cacchio, L. Giordano, O. Colafarina, J.D. Rompe, E. Tavernese, F. Ioppolo, S. Flamini, G. Spacca, V. Santilli, Extracorporeal shock-wave therapy compared with surgery for hypertrophic long-bone nonunions, J. Bone Jt. Surg. Am. 91 (11) (2009 Nov) 2589–2597.
[6] C.J. Wang, F.S. Wang, C.C. Huang, K.D. Yang, L.H. Weng, H.Y. Huang, Treatment for osteonecrosis of the femoral head: comparison of extracorporeal shock waves with core decompression and bone-grafting, J. Bone Jt. Surg. Am. 87 (11) (2005 Nov) 2380–2387.
[7] C. D'Agostino, P. Romeo, E. Amelio, V. Sansone, Effectiveness of ESWT in the treatment of Kienböck's disease, Ultrasound Med. Biol. 37 (9) (2011 Sep) 1452–1456.
[8] C. d'Agostino, P. Romeo, V. Lavanga, S. Pisani, V. Sansone, Effectiveness of extracorporeal shock wave therapy in bone marrow edema syndrome of the hip, Rheumatol. Int. 34 (11) (2014 Nov) 1513–1518.
[9] R. Saggini, A. Figus, A. Troccola, V. Cocco, A. Saggini, N. Scuderi, Extracorporeal shock wave therapy for management of chronic ulcers in the lower extremities, Ultrasound Med. Biol. 34 (8) (2008 Aug) 1261–1271.
[10] A. Arnó, O. García, I. Hernán, J. Sancho, A. Acosta, J.P. Barret, Extracorporeal shock waves, a new non-surgical method to treat severe burns, Burns 36 (6) (2010 Sep) 844–849.
[11] P. Romeo, M.C. d'Agostino, A. Lazzerini, V.C. Sansone, Extracorporeal shock wave therapy in pillar pain after carpal tunnel release: a preliminary study, Ultrasound Med. Biol. 37 (10) (2011 Oct) 1603–1608.
[12] R. Mittermayr, V. Antonic, J. Hartinger, H. Kaufmann, H. Redl, L. Téot, A. Stojadinovic, W. Schaden, Extracorporeal shock wave therapy (ESWT) for wound healing: technology, mechanisms, and clinical efficacy, Wound Repair Regen. 20 (4) (2012 Jul-Aug) 456–465.
[13] J.Y. Lee, S.N. Kim, I.S. Lee, H. Jung, K.S. Lee, S.E. Koh, Effects of extracorporeal shock wave therapy on spasticity in patients after brain injury: a meta-analysis, J. Phys. Ther. Sci. 26 (10) (2014 Oct) 1641–1647.
[14] P. Manganotti, E. Amelio, Long-term effect of shock wave therapy on upper limb hypertonia in patients affected by stroke, Stroke 36 (9) (2005 Sep) 1967–1971.
[15] E. Amelio, P. Manganotti, Effect of shock wave stimulation on hypertonic plantar flexor muscles in patients with cerebral palsy: a placebo-controlled study, J. Rehabil. Med. 42 (4) (2010 Apr) 339–343.
[16] E. Chung, R. Cartmill, Evaluation of clinical efficacy, safety and patient satisfaction rate after low-intensity extracorporeal shockwave therapy for the treatment of male erectile dysfunction: an Australian first open-label single-arm prospective clinical trial, BJU Int. 115 (Suppl. 5) (2015 Apr) 46–49.
[17] Y. Abu-Ghanem, N.D. Kitrey, I. Gruenwald, B. Appel, Y. Vardi, Penile low-intensity shock wave therapy: a promising novel modality for erectile dysfunction, Korean J. Urol. 55 (5) (2014 May) 295–299.
[18] G. Paulis, T. Brancato, Inflammatory mechanisms and oxidative stress in Peyronie's disease: therapeutic "rationale" and related emerging treatment strategies, Inflamm. Allergy Drug Targets 11 (1) (2012 Feb) 48–57.
[19] K. Ito, Y. Fukumoto, H. Shimokawa, Extracorporeal shock wave therapy for ischemic cardiovascular disorders, Am. J. Cardiovasc. Drugs 11 (5) (2011 Oct 1) 295–302.

[20] G. Haupt, Shock waves in orthopedics [Article in German], Urologe A 36 (3) (1997 May) 233–238.
[21] J.D. Rompe, J. Furia, N. Maffulli, Eccentric loading versus eccentric loading plus shock-wave treatment for midportion achilles tendinopathy: a randomized controlled trial, Am. J. Sports Med. 37 (3) (2009 Mar) 463–470.
[22] J.A. Odgen, A. Toth-Kischkat, R. Schulteiss, Principles of shock wave therapy, Clin. Orthop. Relat. Res. 387 (2001) 8–17.
[23] L. Gerdesmeyer, M. Henne, M. Gobel, P. Diehl, Physical principles and generation of Shock Waes, in: Extracorporeal Shock Wave Therapy Clinical Results, Technologies, Basics, Data Trace Publishing Company, Towson USA, 2006, pp. 11–20.
[24] C. Speed, A systematic review of shockwave therapies in soft tissue conditions: focusing on the evidence, Br. J. Sports Med. 48 (21) (2014 Nov) 1538–1542.
[25] L. Gerdesmeyer, M. Maier, M. Haake, C. Schmitz, Physical-technical principles of Extracorporeal Shockwave Therapy (ESWT), Orthopade 31 (2002) 610–617.
[26] I. Tadeo, A.P. Berbegall, L.M. Escudero, T. Alvaro, R. Noguera, Biotensegrity of the extracellular matrix: physiology, dynamic mechanical balance, and implications in oncology and mechanotherapy, Front. Oncol. 4 (2014 Mar 4) 39.
[27] K.M. Khan, A. Scott, Mechanotherapy: how physical therapists' prescription of exercise promotes tissue repair, Br. J. Sports Med. 43 (4) (2009 Apr) 247–252.
[28] W.H. Goldmann, Mechanosensation: a basic cellular process, Prog. Mol. Biol. Transl. Sci. 126 (2014) 75–102.
[29] K.A. Jansen, D.M. Donato, H.E. Balcioglu, T. Schmidt, E.H. Danen, G.H. Koenderick, A guide to mechanobiology: where biology and physics meet, Biochim. Biophys. Acta (2015 May 18) S0167–4889.
[30] D.E. Ingber, Tensegrity: the architectural basis of cellular mechanotransduction, Annu. Rev. Physiol. 59 (1997) 575–599.
[31] D.E. Ingber, Cellular mechanotransduction: putting all the pieces together again, FASEB J. 20 (2006) 811–827.
[32] K.L. Marshall, E.A. Lumpkin, The molecular basis of mechanosensory transduction, Adv. Exp. Med. Biol. 739 (2012) 142–155.
[33] S. Alam, D.B. Lovett, R.B. Dickinson, K.J. Roux, T.P. Lele, Nuclear forces and cell mechanosensing, Prog. Mol. Biol. Transl. Sci. 126 (2014) 205–215.
[34] ChA. Lambert, B.V. Nusgens, ChM. Lapiere, Mechano-sensing and mechanoreaction of soft connective tissue cells, Adv. Space Res. 21 (8–9) (1998) 1081–1091.
[35] F.Y. McWhorter, C.T. Davis, W.F. Liu, Physical and mechanical regulation of macrophage phenotype and function, Cell Mol. Life Sci. 72 (7) (2015 Apr) 1303–1316.
[36] J.C. Wang, An overview of shock wave therapy in musculoskeletal disorders, Chang. Gung Med. J. 26 (4) (2003).
[37] S.F. Moosavi-Nejad, S.H. Hosseini, M. Satoh, K. Takayama, Shock wave induced cytoskeletal and morphological deformations in a human renal carcinoma cell line, Cancer Sci. 97 (4) (2006 Apr) 296–304.
[38] S. Tara, M. Miyamoto, G. Takagi, S. Kirinoki-Ichikawa, A. Tezuka, T. Hada, I. Takagi, Low-energy extracorporeal shock wave therapy improves microcirculation blood flow of ischemic limbs in patients with peripheral arterial disease: pilot study, J. Nippon Med. Sch. 81 (1) (2014) 19–27.
[39] C. Tepeköylü, F.S. Wang, R. Kozaryn, K. Albrecht-Schgoer, M. Theurl, W. Schaden, H.J. Ke, Y. Yang, R. Kirchmair, M. Grimm, C.J. Wang, J. Holfeld, Shock wave treatment induces angiogenesis and mobilizes endogenous CD31/CD34-positive endothelial cells in a hindlimb ischemia model: implications for angiogenesis and vasculogenesis, J. Thorac. Cardiovasc. Surg. 146 (4) (2013 Oct) 971–978.
[40] V. Sansone, M.C. D'Agostino, C. Bonora, F. Sizzano, L. De Girolamo, P. Romeo, Early angiogenic response to shock waves in a three-dimensional model of human microvascular endothelial cell culture (HMEC-1), J. Biol. Regul. Homeost. Agents 26 (1) (2012 Jan-Mar) 29–37.
[41] F. Suhr, Y. Delhasse, G. Bungartz, A. Schmidt, K. Pfannkuche, W. Bloch, Cell biological effects of mechanical stimulations generated by focused extracorporeal shock wave applications on cultured human bone marrow stromal cells, Stem Cell Res. 11 (2) (2013 Sep) 951–964.
[42] C.J. Kearney, H.P. Hsu, M. Spector, The use of extracorporeal shock wave-stimulated periosteal cells for orthotopic bone generation, Tissue Eng. Part A 18 (13–14) (2012 Jul) 1500–1508.
[43] R. Tamma, S. dell'Endice, A. Notarnicola, L. Moretti, S. Patella, V. Patella, A. Zallone, B. Moretti, Extracorporeal shock waves stimulate osteoblast activities, Ultrasound Med. Biol. 35 (12) (2009 Dec) 2093–2100.
[44] J. Hausdorf, B. Sievers, M. Schmitt-Sody, V. Jansson, M. Maier, S. Mayer-Wagner, Stimulation of bone growth factor synthesis in human osteoblasts and fibroblasts after extracorporeal shock wave application, Arch. Orthop. Trauma Surg. 131 (3) (2011 Mar) 303–309.
[45] 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 Apr) 457–461.
[46] S. Mani-Babu, D. Morrissey, C. Waugh, H. Screen, C. Barton, The effectiveness of extracorporeal shock wave therapy in lower limb tendinopathy: a systematic review, Am. J. Sports Med. 43 (3) (2015 Mar) 752–761.
[47] Y.J. Chen, C.J. Wang, K.D. Yang, Y.R. Kuo, H.C. Huang, Y.T. Huang, Y.C. Sun, F.S. Wang, Extracorporeal shock waves promote healing of collagenase-induced Achilles tendinitis and increase TGF-beta1 and IGF-I expression, J. Orthop. Res. 22 (4) (2004 Jul) 854–861.
[48] S.H. Han, J.W. Lee, G.P. Guyton, B.G. Parks, J.P. Courneya, L.C. Schon, Effect of extracorporeal shock wave therapy on cultured tenocytes. "J. Leonard Goldner Award 2008", Foot Ankle Int. 30 (2) (2009 Feb) 93–98.
[49] L. de Girolamo, D. Stanco, E. Galliera, M. Viganò, A.B. Lovati, M.G. Marazzi, P. Romeo, V. Sansone, Soft-focused extracorporeal shock waves increase the expression of tendon-specific markers and the release of anti-inflammatory cytokines in an adherent culture model of primary human tendon cells, Ultrasound Med. Biol. 40 (6) (2014 Jun) 1204–1215.
[50] M. Vetrano, F. d'Alessandro, M.R. Torrisi, A. Ferretti, M.C. Vulpiani, V. Visco, Extracorporeal shock wave therapy promotes cell proliferation and collagen synthesis of primary cultured human tenocytes, Knee Surg. Sports Traumatol. Arthrosc. 19 (12) (2011 Dec) 2159–2168.
[51] Y.H. Chao, Y.H. Tsuang, J.S. Sun, L.T. Chen, Y.F. Chiang, C.C. Wang, M.H. Chen, Effects of shock waves on tenocyte proliferation and extracellular matrix metabolism, Ultrasound Med. Biol. 34 (5) (2008 May) 841–852.
[52] L. Leone, M. Vetrano, D. Ranieri, S. Raffa, M.C. Vulpiani, A. Ferretti, M.R. Torrisi, V. Visco, Extracorporeal Shock Wave Treatment (ESWT) improves in vitro functional activities of ruptured human tendon-derived tenocytes, PLoS One 7 (11) (2012) e49759.
[53] D. Zhang, C.J. Kearney, T. Cheriyan, T.M. Schmid, M. Spector, Extracorporeal shockwave-induced expression of lubricin in tendons and septa, Cell Tissue Res. 346 (2) (2011 Nov) 255–262, http://dx.doi.org/10.1007/s00441-011-1258-7.
[54] C.M. Waugh, D. Morrissey, E. Jones, G.P. Riley, H. Langberg, H.R. Screen, In vivo biological response to extracorporeal shockwave therapy in human tendinopathy, Eur. Cell Mater. 29 (2015 May 15) 268–280 discussion 280.
[55] W. Schaden, A. Fischer, A. Sailler, Extracorporeal shock wave therapy of nonunion or delayed osseous union, Clin. Orthop. Relat. Res. (387) (2001 Jun) 90–94.
[56] H.Z. Ma, B.F. Zeng, X.L. Li, Upregulation of VEGF in subchondral bone of necrotic femoral heads in rabbits with use of extracorporeal shock waves, Calcif. Tissue Int. 81 (2) (2007 Aug) 124–131.
[57] L. Martini, G. Giavaresi, M. Fini, P. Torricelli, M. de Pretto, W. Schaden, R. Giardino, Effect of extracorporeal shock wave therapy on osteoblastlike cells, Clin. Orthop. Relat. Res. (413) (2003 Aug) 269–280.
[58] L. Martini, G. Giavaresi, M. Fini, P. Torricelli, V. Borsari, R. Giardino, M. De Pretto, D. Remondini, G.C. Castellani, Shock wave therapy as an innovative technology in skeletal disorders: study on transmembrane current in stimulated osteoblast-like cells, Int. J. Artif. Organs 28 (8) (2005 Aug) 841–847.
[59] L. Martini, G. Giavaresi, M. Fini, V. Borsari, P. Torricelli, R. Giardino, Early effects of extracorporeal shock wave treatment on osteoblast-like cells: a comparative study between electromagnetic and electrohydraulic devices, J. Trauma 61 (5) (2006 Nov) 1198–1206.
[60] K.F. Tam, W.H. Cheung, K.M. Lee, L. Qin, K.S. Leung, Osteogenic effects of low-intensity pulsed ultrasound, extracorporeal shockwaves and their combination - an in vitro comparative study on human periosteal cells, Ultrasound Med. Biol. 34 (12) (2008 Dec) 1957–1965.
[61] F.S. Wang, C.J. Wang, H.J. Huang, H. Chung, R.F. Chen, K.D. Yang, Physical shock wave mediates membrane hyperpolarization and Ras activation for osteogenesis in human bone marrow stromal cells, Biochem. Biophys. Res. Commun. 287 (3) (2001 Sep 28) 648–655.
[62] 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 Apr) 457–461.
[63] J.K. Xu, H.J. Chen, X.D. Li, Z.L. Huang, H. Xu, H.L. Yang, J. Hu, Optimal intensity shock wave promotes the adhesion and migration of rat osteoblasts via integrin β1- mediated expression of phosphorylated focal adhesion kinase, J. Biol. Chem. 287 (31) (2012 Jul 27) 26200–26212.
[64] 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. 41 (1) (2002 Jan-Feb) 16–22.
[65] F.S. Wang, K.D. Yang, Y.R. Kuo, C.J. Wang, S.M. Sheen-Chen, H.C. Huang, Y.J. Chen, Temporal and spatial expression of bone morphogenetic proteins in extracorporeal shock wave-promoted healing of segmental defect, Bone 32 (4) (2003 Apr) 387–396.
[66] Wang FS, Wang CJ, Chen YJ, Chang PR, Huang YT, Sun YC, Huang HC, Yang YJ, Yang KD. Ras induction of superoxide activates ERK-dependent angiogenic transcription factor HIF-1alpha and VEGF-A expression in shock wave-stimulated osteoblasts.
[67] J. Holfeld, C. Tepeköylü, S. Blunder, D. Lobenwein, E. Kirchmair, M. Dietl, R. Kozaryn, D. Lener, M. Theurl, P. Paulus, R. Kirchmair, M. Grimm, Low energy shock wave therapy induces angiogenesis in acute hind-limb ischemia via VEGF receptor 2 phosphorylation, PLoS One 9 (8) (2014 Aug 5) e103982.
[68] G. Haupt, M. Chvapil, Effect of shock waves on the healing of partial-thickness wounds in piglets, J. Surg. Res. 49 (1) (1990 Jul) 45–48.
[69] O. Goertz, H. Lauer, h Hirsc, A. TRing, M. Lehnhardt, S. Langer, H.U. Steinau, J. Hauser, Extracorporeal shock waves improve angiogenesis after full thickness burn, Burns 38 (7) (2012 Nov) 1010–1018.
[70] C.H. Ha, S. Kim, J. Chung, S.H. An, K. Kwon, Extracorporeal shock wave stimulates expression of the angiogenic genes via mechanosensory complex in endothelial cells: mimetic effect of fluid shear stress in endothelial cells, Int. J. Cardiol. 168 (4) (2013 Oct 9) 4168–4177.
[71] A.M. Weihs, C. Fuchs, A.H. Teuschl, J. Hartinger, P. Slezak, R. Mittermayr, H. Redl, W.G. Junger, H.H. Sitte, D. Rünzler, Shock wave treatment enhances cell proliferation and improves wound healing by ATP release-coupled

extracellular signal-regulated kinase (ERK) activation, J. Biol. Chem. 289 (39) (2014 Sep 26) 27090–27104.
[72] A. Stojadinovic, E.A. Elster, K. Anam, D. Tadaki, M. Amare, S. Zins, T.A. Davis, Angiogenic response to extracorporeal shock wave treatment in murine skin isografts, Angiogenesis 11 (4) (2008) 369–380.
[73] S. Obi, K. Yamamoto, J. Ando, Effects of shear stress on endothelial progenitor cells, J. Biomed. Nanotechnol. 10 (10) (2014 Oct) 2586–2597.
[74] A.R. Ciampa, A.C. de Prati, E. Amelio, E. Cavalieri, T. Persichini, M. Colasanti, G. Musci, E. Marlinghaus, H. Suzuki, S. Mariotto, Nitric oxide mediates anti-inflammatory action of extracorporeal shock waves, FEBS Lett. 579 (30) (2005 Dec 19) 6839–6845.
[75] T.A. Davis, A. Stojadinovic, K. Anam, M. Amare, S. Naik, G.E. Peoples, D. Tadaki, E.A. Elster, Extracorporeal shock wave therapy suppresses the early proinflammatory immune response to a severe cutaneous burn injury, Int. Wound J. 6 (1) (2009 Feb) 11–21.
[76] C. Tepeköylü, D. Lobenwein, S. Blunder, R. Kozaryn, M. Dietl, P. Ritschl, E.J. Pechriggl, M.J. Blumer, M. Bitsche, R. Schistek, K. Kotsch, H. Fritsch, M. Grimm, J. Holfeld, Alteration of inflammatory response by shock wave therapy leads to reduced calcification of decellularized aortic xenografts in mice, Eur. J. Cardiothorac. Surg. 47 (3) (2015 Mar) e80–90.
[77] S. Mariotto, A.C. de Prati, E. Cavalieri, E. Amelio, E. Marlinghaus, H. Suzuki, Extracorporeal shock wave therapy in inflammatory diseases: molecular mechanism that triggers anti-inflammatory action, Curr. Med. Chem. 16 (19) (2009) 2366–2372.
[78] Y.R. Kuo, C.T. Wang, F.S. Wang, K.D. Yang, Y.C. Chiang, C.J. Wang, Extracorporeal shock wave treatment modulates skin fibroblast recruitment and leukocyte infiltration for enhancing extended skin-flap survival, Wound Repair Regen. 17 (1) (2009 Jan-Feb) 80–87.
[79] J. Holfeld, C. Tepeköylü, R. Kozaryn, A. Urbschat, K. Zacharowski, M. Grimm, P. Paulus, Shockwave therapy differentially stimulates endothelial cells: implications on the control of inflammation via toll-Like receptor 3, Inflammation 37 (1) (2014 Feb) 65–70.
[80] P.L. Shao, C.C. Chiu, C.M. Yuen, S. Chua, L.T. Chang, J.J. Sheu, C.K. Sun, C.J. Wu, C.J. Wang, H.K. Yip, Shock wave therapy effectively attenuates inflammation in rat carotid artery following endothelial denudation by balloon catheter, Cardiology 115 (2) (2010) 130–144.
[81] F.O. Martinez, A. Sica, A. Mantovani, M. Locati, Macrophage activation and polarization, Front. Biosci. 13 (2008 Jan 1) 453–461.
[82] A. Mantovani, S.K. Biswas, M.R. Galdiero, A. Sica, M. Locati, Macrophage plasticity and polarization in tissue repair and remodelling, J. Pathol. 229 (2) (2013) 176–185.
[83] N.G. Sukubo, E. Tibalt, S. Respizzi, M. Locati, M.C. d'Agostino, Effect of shock waves on macrophages: a possible role in tissue regeneration and remodeling, Int. J. Surg. 24 (2015 Aug 18) 122–128.
[84] S. Fischer, W. Mueller, M. Schulte, J. Kiefer, C. Hirche, S. Heimer, E. Köllensperger, G. Germann, M.A. Reichenberger, Multiple extracorporeal shock wave therapy degrades capsular fibrosis after insertion of silicone implants, Ultrasound Med. Biol. 41 (3) (2015 Mar) 781–789.
[85] G. Alunni, S. Marra, I. Meynet, M. D'amico, P. Elisa, A. Fanelli, S. Molinaro, P. Garrone, A. Deberardinis, M. Campana, A. Lerman, The beneficial effect of extracorporeal shockwave myocardial revascularization in patients with refractory angina, Cardiovasc. Revasc. Med. 16 (1) (2015 Jan-Feb) 6–11.
[86] J. Hausdorf, C. Schmitz, B. Averbeck, M. Maier, Molecular basis for pain mediating properties of extracorporeal shock waves [Article in German], Schmerz 18 (6) (2004 Dec) 492–497.
[87] S. Ohtori, G. Inoue, C. Mannoji, T. Saisu, K. Takahashi, S. Mitsuhashi, Y. Wada, K. Takahashi, M. Yamagata, H. Moriya, Shock wave application to rat skin induces degeneration and reinnervation of sensory nerve fibres, Neurosci. Lett. 315 (1–2) (2001 Nov 23) 57–60.
[88] N. Takahashi, Y. Wada, S. Ohtori, T. Saisu, H. Moriya, Application of shock waves to rat skin decreases calcitonin gene-related peptide immunoreactivity in dorsal root ganglion neurons, Auton. Neurosci. 107 (2) (2003 Sep 30) 81–84.
[89] J.Y. Lee, S.N. Kim, I.S. Lee, H. Jung, K.S. Lee, S.E. Koh, Effects of extracorporeal shock wave therapy on spasticity in patients after brain injury: a meta-analysis, J. Phys. Ther. Sci. 26 (10) (2014 Oct) 1641–1647.
[90] T. Kenmoku, N. Ochiai, S. Ohtori, T. Saisu, T. Sasho, K. Nakagawa, N. Iwakura, M. Miyagi, T. Ishikawa, H. Tatsuoka, G. Inoue, J. Nakamura, S. Kishida, A. Saito, K. Takahashi, Degeneration and recovery of the neuromuscular junction after application of extracorporeal shock wave therapy, J. Orthop. Res. 30 (10) (2012 Oct) 1660–1665.
[91] S. Yamaya, H. Ozawa, H. Kanno, K.N. Kishimoto, A. Sekiguchi, S. Tateda, K. Yahata, K. Ito, H. Shimokawa, E. Itoi, Low-energy extracorporeal shock wave therapy promotes vascular endothelial growth factor expression and improves locomotor recovery after spinal cord injury, J. Neurosurg. 121 (6) (2014 Dec) 1514–1525.
[92] T. Hausner, A. Nógrádi, The use of shock waves in peripheral nerve regeneration: new perspectives? Int. Rev. Neurobiol. 109 (2013) 85–98.
[93] O.J. Wess, A neural model for chronic pain and pain relief by extracorporeal shock wave treatment, Urol. Res. 36 (6) (2008 Dec) 327–334.
[94] H. Lohse-Busch, U. Reime, R. Falland, Symptomatic treatment of unresponsive wakefulness syndrome with transcranially focused extracorporeal shock waves, NeuroRehabilitation 35 (2) (2014 Jan 1) 235–244.
[95] G. Muzio, G. Martinasso, F. Baino, R. Frairia, C. Vitale-Brovarone, R.A. Canuto, Key role of the expression of bone morphogenetic proteins in increasing the osteogenic activity of osteoblast-like cells exposed to shock waves and seeded on bioactive glass-ceramic scaffolds for bone tissue engineering, J. Biomater. Appl. 29 (5) (2014 Nov) 728–736.