CuraMedix

Innovative Technologies for Advanced Healing

What is Shock Wave?

The Technology, The Treatment & How it Fits Into Your Medical Practice

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Introduction

Shock waves in medicine, also known and referred to as Extracorporeal Pulse Activation Technology (EPAT) and/or Extracorporeal Shock Wave Treatment (ESWT), is an evidence-based, non-invasive technology platform that uses unique sets of acoustic pressure waves to elicit healing responses from diverse tissues. A growing body of clinical literature supports the safety and efficacy of EPAT/ESWT in multi-discipline medicine and a broad range of musculoskeletal disorders that are often challenging to treat with traditional methods. [1]

The discovery of shock waves began during World War II with engineers and physicists attempts at determining the cause of cracks in aircraft associated with flying at supersonic speed in the rain.

The theory of using shock waves in medicine dates back to the 1940s, but the first demonstration of its clinical use in humans occurred in 1980, when Professor Christian Chaussy, MD used shock waves to disintegrate renal pelvic stones in humans [2]. He found that 20 of the 21 patients were able to successfully pass the disintegrated stones without surgical intervention.

Since Dr. Chaussy's demonstration in the area of urology, the term "shock wave" was established and later referred to as Extracorporeal Shock Wave Lithotripsy (ESWL).

Shock wave technologies have continued to evolve and expand in multi-discipline medicine and have been clinically proven to be a powerful therapeutic modality. The term Extracorporeal Shock Wave Therapy/ Treatment/ Technology (ESWT) was later established to differentiate other clinical applications.

The first orthopedic indication(s) approved by the FDA occurred in 2000 for the treatment of plantar fasciitis, followed by lateral epicondylitis in 2002 [3].

Today, physicians are turning to shock wave to successfully treat patients who suffer from a broad range of musculoskeletal disorders, with consistently high efficacy levels and patient satisfaction scores.

In addition, new indications/applications for shock wave are being identified and researched regularly to improve the fields of urology, orthopedics, sports medicine, pain management and rehabilitation, wound healing, plastics and aesthetic dermatology, neurology, cardiology, and veterinary medicine. Shock wave technologies are making a significant impact on treatment strategies, clinical and economic outcomes, and patient satisfaction.

Despite the evolution and technological advancements, there continues to be confusion with different technology platforms, products, performance variables, protocols and dosages. As with many products, devices and technologies, not all shock wave systems are created equal.

Shock Wave Terminology

There are three types of shock wave technology platforms that are used in medicine: Focused Shock Waves (F-SW), Planar Shock Waves (P-SW) and Radial Pressure Waves (R-PW).

Physically speaking, radial pressure waves are not shock waves, and the technology is more correctly referred to as radial pressure waves (R-PW). However, R-PW is colloquially known as radial shock wave therapy (R-SW, RSWT, or rESWT).

Focused Shock Waves (F-SW)

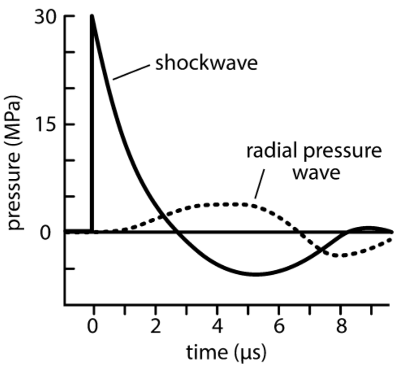


Fig. 2
Illustration showing the difference in pressure waveform between a shockwave and a radial pressure wave as used in medical applications.

Moya, D., et al., The Role of Extracorporeal Shockwave Treatment in Musculoskeletal Disorders. J Bone Joint Surg Am, 2018. 100(3): p. 251-263

Focused shock waves are unique sets of acoustic pressure waves that propagate faster than sound in the propagating medium. They have a characteristic biphasic pressure profile that includes an initial, abrupt high positive pressure amplitude followed by a small negative pressure amplitude.

The focused shock wave front is a region of sudden, dramatic changes in the stress, density, and temperature of the medium. The pressure profile of a focused shock wave includes an initial high positive pressure amplitude that rises rapidly, followed by a small negative pressure amplitude. The positive component of the wave directly transfers energy to the medium, while the negative pressure component is associated with the development of vapor-filled cavitation bubbles, which collapse explosively (an indirect effect), creating a secondary focused shock wave that is characterized by powerful fluid microjets that radiate out from the point of collapse.

Focused shock waves are subject to the physical laws of reflection, refraction, and deflection. F-SW takes advantage of this by reflecting acoustic pressure waves and/or acoustic energy to a single focal point underneath the skin.

F-SW applications are beneficial for deeper sited pathologies to include soft tissue, bone and vascular structures. They have a smaller focal zone than radial pressure waves, allowing for precise targeting of deeper tissue structures.

Planar Shock Waves (P-SW)

Planar shock waves (P-SW) are a unique type of focused wave that combines features of focused shock waves and radial pressure waves. Planar shock waves propagate radially, similar to radial pressure waves.

Focused Shock Wave Generation

There are three basic types of focused shock wave generators that can produce a focused shock wave:

1. Electrohydraulic sources also referred to as “spark gap” pass use a high-voltage electrical current across a submerged spark-gap electrode (spark plug). The resulting discharge creates a high-energy shock wave front that is focused into the target tissue with a semi-ellipsoid reflector. Electrohydraulic sources typically have the largest focus size of the shock wave technologies.

2. Electromagnetic sources are based on the principles of electromagnetic induction, in which the rate of change of magnetic flux inside a coil determines the current. Here, a metallic membrane is placed opposite a coil, and electromagnetic forces cause the membrane to accelerate away from the coil, which generates the acoustic pulse.

There are two types of electromagnetic systems, flat coils and cylindrical coils, which affect how the wave is focused. Currently, cylindrical-coil systems are the preferred system because of the large aperture of the shock wave source compared to the focal zone which allows for a less painful transfer of energy into the body as well as a more consistent delivery of energy per pulse.

3. Piezoelectric sources form acoustic waves based on the piezoelectric effect, which describes the ability of certain materials to create an electric charge when mechanical stress is exerted on them. With this approach, a high voltage pulse is applied to submerged piezoelectric crystals, which expand and generate a low-pressure pulse in the surrounding water. This is the only self-focusing method, and it produces the smallest focus size.

Each of these platforms generate the spark in water, which has an acoustic impedance that is similar to biological tissue. This minimizes energy loss at the interface, and wave propagation into the body is facilitated. However, electrohydraulic sources create the shock wave immediately after the spark-gap, while electromagnetic and piezoelectric generators produce the focused shock wave in the focal region.

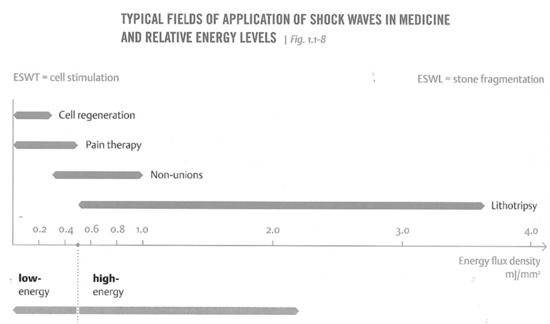
Focused Shock Wave Propagation

In F-SW applications, focused shock waves are generated in water and transmitted to the tissue via a dry-coupling system. Because water and tissue have similar impedances, focused shock waves propagate with little loss of energy. However, ultrasonic gel is used as a coupling agent to eliminate air between the skin and the treatment head, otherwise energy transfer will be inhibited.

An understanding of shock wave propagation becomes important when considering how a shock wave will interact with a targeted surface. In the case of Dr. Chaussy's lithotripsy, a dramatic difference existed between the acoustic impedance of water and the kidney stone, which blocks wave propagation. It is this difference in impedance that gives acoustic waves the power to pulverize kidney stones.

When a shock wave propagating in water hits a surface with a very different impedance, e.g. a kidney stone, the wave is slowed substantially. Subsequent shock waves arrive too quickly for the first wave to dissipate, and pressure on the stone increases, causing internal stress and microcrack development. In addition, the dramatic pressure drop that is associated with each wave generates vapor-filled cavitation bubbles that implode violently, directing intense secondary shockwaves towards the stone. Over time, these acoustic shock waves are sufficient to break up kidney stones.

So, if focused shock waves can break stones, why are they safe for use on tissues? A key reason is because the propagating media (water and tissue) have similar acoustic impedances, so a shock wave can move from one into the other with relative ease and continue to propagate unhindered. Focused shock wave (F-SW) can safely propagate acoustic energy to a focus as deep as 200 mm under the skin [4]. In addition, energy levels used in ESWT are much less than for lithotripsy.

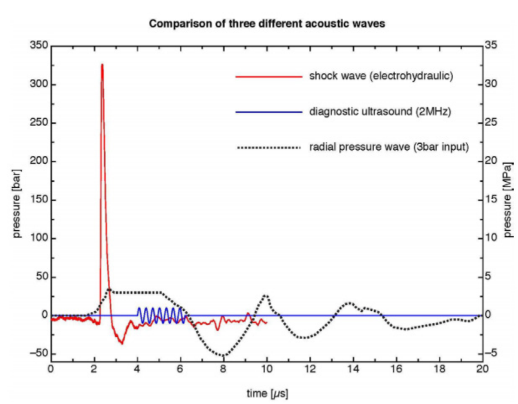


Radial Pressure Waves

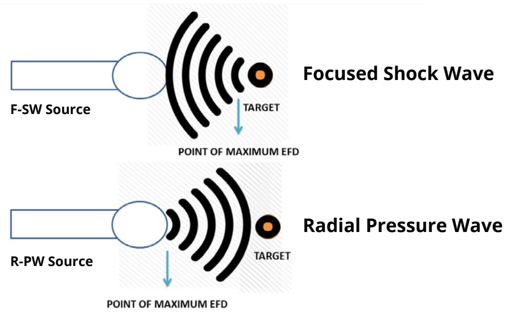
Like focused shock waves, radial pressure waves are sound waves. However, rather than abrupt biphasic pressure disturbances, pressure waves are characterized by an oscillating pressure gradient with a much smaller amplitude and a much longer duration. Although normal pressure waves don't have the same intensity level as shock waves, they are still able to produce cavitation bubbles at an interface [5].

Radial Pressure Waves

Oscillating sound waves that propagate outwards from a focus are called radial pressure waves. While focused shock waves target deeper tissues, radial pressure waves are most effective on superficial tissues (up to 50 mm).



DIGEST Guidelines for ESWT (page 4)
https://www.shockwavetherapy.org/fileadmin/user_upload/ISMST_Guidelines.pdf



Simplicio et al. Extracorporeal Shock Wave Therapy Mechanisms in Musculoskeletal Regenerative Medicine. Journal of Clinical Orthopaedics and Trauma, 2020. https://doi.org/10.1016/j.jcot.2020.02.004

Radial Pressure Wave Generation

Radial pressure waves are generated by way of pneumatic acceleration of a projectile that is accelerated towards an applicator/transmitter. Upon impact at the refractory point (the surface of the skin), ballistic energy in the form of a spherical acoustic pressure wave is propagated radially through the target tissue.

Radial Pressure Wave Propagation

Radial pressure waves lack the explosive, non-linear qualities of focused shock waves, so they follow the inverse square law (1/r2), which says that when a linear wave is twice as far from its source, it will have half the amplitude. Consequently, the highest energy levels delivered by radial pressure waves are at the surface of the skin.

Shock Waves		Pressure Waves
10-100 MPa	**Pressure**	0.1-1 MPa
≈0.2 μs	**Pulse Duration**	≈0.2-5 ms
0.5-2mNs	**Impact**	100-200 mNs
20-35 mJ	**Energy**	150-200 mJ
100-150 MPa/mm	**Pressure Gradient**	0.1-0.5 kPa/mm
Focused	**Pressure Field**	Radial, divergent
Large, up to 200 mm	**Penetration Depth**	Small, superficial, up to 50 mm
Cells	**Effects**	Tissue

Fig 16: Main differences between shock waves and pressure waves

STORZ: The Art of Shock Wave

Approaches to Shock Wave

Focused shock waves and radial pressure waves use varying forms of acoustic energy respectively to promote healing. Focused shock waves target deeper sited pathologies (soft tissue or bone), while radial pressure waves target larger, more superficial areas.

Use of either focused shock wave or radial pressure wave treatments have consistently demonstrated remarkable results, and anecdotal data on the use of combined shock and pressure wave treatments demonstrate that they deliver complementary results and improved clinical outcomes.

F-SW and R-PW are also readily combined with other treatment modalities, including laser therapy, ultrasound, platelet-rich plasma (PRP) and other regenerative therapies, and physical therapy. Ideally, F-SW/R-PW will be introduced early in the continuum of care and not left as a last resort to surgery, but people often report significant improvements in pain and function even when F-SW/R-PW is introduced later in treatment. Since F-SW/R-PW is a non-invasive procedure with little to no downtime and no adverse side effects, it is an ideal way to augment current clinical practices and enhance outcomes.

Mechanisms of Action

The mechanisms of action of focused shock waves are becoming clear, and a great deal of molecular and biochemical evidence supports the impressive effects of F-SW on diverse healing processes. Both focused shock waves and radial pressure waves exert their effects via propagation of sound waves through biological tissues. While there are differences in their mechanisms and effects, they share key characteristics.

A framework for understanding the mechanisms of action of focused shock wave has been proposed to include four phases [6]:

1. The Physical Phase

The physical phase is characterized by energy transfer from propagating acoustic waves to biological tissues [7]. Two forces are particularly important: tensile forces and shear stress. Tensile forces affect cellular morphology, activating mechanotransduction pathways and increasing cell permeability. Shear stress induces shedding of cargo-rich membrane-bound extracellular vesicles, which act in both autocrine and paracrine fashion to affect downstream signaling.

2. The Physicochemical Phase

Vesicles released during the physical phase are endocytosed, stimulating release of adenosine triphosphate (ATP) and diffusible radicals and upregulating multiple signaling pathways.

3. The Chemical Phase

Activation of signaling pathways alters ion channel function and increases calcium mobilization.

4. The Biological Phase

Biochemical signaling cascades drive myriad biological responses, including angiogenesis, tissue and nerve regeneration, osteogenesis, analgesia, reduced inflammation, chondroprotection, and neuroprotection.

Angiogenesis

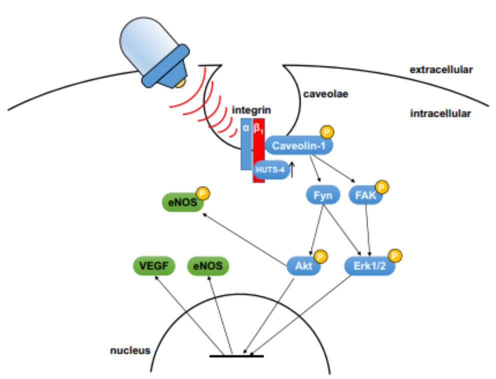


Fig. 6. Possible molecular mechanisms for the angiogenic effects of SW. Mechanoreceptors in caveolae and its downstream pathways may play pivotal roles in the SW-induced angiogenesis.

Hatanaka et al. Molecular mechanisms of the angiogenic effects of low-energy shock wave therapy: roles of mechanotransduction. Am J Physiol Cell Physiol 2016 https://journals.physiology.org/doi/pdf/10.1152/ajpcell.00152.2016

One of the most well understood shock wave mechanisms underlies angiogenesis (sprouting off of existing vessels) and vasculogenesis (de novo vessel formation). Using the 4-stage approach outlined above, focused shock wave and radial pressure waves promote angiogenesis in the following manner:

Physical phase: Focused shock waves or radial pressure waves induce capillary shear stress and tensile forces, which activate mechanotransduction signaling pathways in endothelial cells via caveolin-1 and α2β1-integrin [8].

Physicochemical phase: Caveolin-1 and α2β1-integrin-induced ATP release activates biochemical signaling pathways via Piezo1 channel-dependent mechanoregulation and activation of purinergic P2X7 receptors [9].

Chemical phase: Endothelial nitric oxide synthase (eNOS) leads to nitric oxide (NO) generation.

Biological phase: NO activates the PI3K/Akt pathway, which upregulates vascular endothelial growth factor (VEGF) and its receptors VEGFR1 and VEGFR2, leading to angiogenesis and vasculogenesis [10, 11].

Notably, focused shock wave or radial pressure wave-induced VEGF signaling depends on eNOS activation of VEGF, which further upregulates eNOS signaling, illustrating the complexity of signaling pathways.

Osteogenesis

Evidence has shown that focused shock wave stimulates bone lacunae-canalicular networks, which promotes osteogenesis, increases bone strength, and enhances cortical bone formation [7]. Osteogenesis and angiogenesis share several common pathways, most notably VEGF, and studies of F-SW-induced osteogenesis reliably find increased neovascularization in bone structures [12]. The biological phase of F-SW-induced osteogenesis is driven by ATP-induced activation of the p38 MAPK pathway, which upregulates key osteogenic factors including BMP-2 and RUNX2 [13-15].

Immunomodulation

Macrophage phenotype is an important regulator of immune function, with the pro-inflammatory M1 phenotype acting to restrict cell proliferation, and the anti-inflammatory M2 phenotype procytokines and growth factors. One study found that ESWT shifts macrophages from the M1 to the M2 phenotype [16]. In addition, ESWT upregulates activity of the immunomodulatory toll-like receptor 3 (TLR3), which promotes wound healing and protects against atherosclerosis [17-19].

Analgesia

F-SW and R-PW induced analgesia involves reductions in the pro-analgesic and pro-inflammatory molecules substance P (SP) and calcitonin gene-related peptide (CGRP), however, research remains ongoing to clarify the mechanism [20]. Two hypotheses have been proposed to describe F-SW-induced analgesia [7]: Degeneration of nerve fibers from small immunoreactive neurons, and hyperstimulation of the descending inhibitory system (conditioned pain modulation).

Applications of Focused Shock Wave (F-SW) and Radial Pressure Wave (R-PW)

The diverse biological effects of both focused shock wave and radial pressure wave are largely related to upregulating activity in regenerative pathways. Taken together, data support a model where tissues respond to F-SW/R-PW as if an acute injury had occurred. Consequently, healing processes can be initiated without an acute injury. New applications for both F-SW and R-PW are being evaluated all the time, and there are several clinical indications with strong supporting evidence for safety and efficacy [1].

Important Information for U.S. Customers:

Certain devices and references made herein to specific indications of use may have not received clearance or approval by the United States Food & Drug Administration. Practitioners in the United States should first consult with their local CuraMedix representative in order to ascertain product availability and specific labeling claims. Federal (USA) law restricts certain devices referenced herein to sale, distribution, and use by, or on the order of a physician, dentist, veterinarian, or other practitioner licensed by the law of the state in which she/he practices to use or order the use of the device.

Calcifying Tendinopathy of the Shoulder

The rotator cuff tendon or subacromial bursa are prone to developing painful calcific tendinitis after overuse or degeneration. In the past, people who did not respond to conservative treatment had few alternatives to surgery. However, numerous Level-I studies have demonstrated that focused ESWT is an effective non-surgical treatment, with calcium resorption approaching 90% in some studies [21].

Lateral epicondylopathy of the shoulder

Focused Shock Wave was approved by the FDA in 2002 as a treatment for lateral epicondylopathy. While there are some conflicting data, Level-I studies have found significant improvements in pain and function at 6 and 12 months [22]. Notably, no other treatment methods have proven to be consistently reliable for lateral epicondylopathy.

Greater trochanter pain syndrome

Initial data supporting the use of shock wave for greater trochanter pain syndrome suggests that it is a more effective treatment option than other common interventions [23]. Although the available data are limited, some evidence suggests that radial pressure wave delivers greater improvements in pain and function than focused shock wave.

Patellar tendinopathy

Patellar tendinopathy is a challenging disorder to manage, and common treatments have inconsistent results. Recent research into the efficacy of shock wave for patellar tendinopathy has delivered promising results, both proving to be safe and effective treatment modalities [24].

Plantar fasciitis

Both focused shock wave and radial pressure wave have Level-I evidence to support their use in treating plantar fasciitis, and the American College of Foot and Ankle Surgeons recommended in 2010 that F-SW be a non-surgical treatment of choice for plantar fasciitis with or without a plantar spur when conservative treatments fail [25].

Case Study:

48 yo woman; Primary school teacher

- Chronic, debilitating unilateral heel pain (3 years)
- 3 podiatrists, but VAS was still 8/10 at its worst, every day

High-energy ESWT under sedation:

- First follow-up (2 weeks): 50% reduction in perceived pain
- At 3 months: 90% resolution of symptoms

5 year follow up:

"...she felt that ESWT had "given her life back.""

- Lost 50 pounds
- Ran 2 marathons

https://www.podiatrytoday.com/eswt-plantar-fasciitis-what-do-long-term-results-reveal

Achilles tendinopathy

Both insertional and non-insertional (midportion) Achilles tendinopathies respond well to focused shock wave and radial pressure wave, as has been shown by multiple Level-I trials. One randomized control trial (RCT) found that radial pressure wave is more effective than eccentric loading exercises for insertional Achilles tendinopathy 15-months after treatment, suggesting the long-term value of R-PW treatments [26].

Bone non-union

In 1991, Valchanou & Michailov demonstrated that focused shock wave had an 84% success rate in treating non-unions in 82 patients [27]. Since then, focused shock wave has been shown to promote osteogenesis and angiogenesis in bone, and Level-I and II evidence has demonstrated that focused shock wave is as effective as surgery for treatment of non-unions. Early results also suggest that F-SW may improve adult osteochondritis dissecans [28].

Lower back pain

Lower back pain is one of the most common pain conditions, and it is notoriously difficult to treat. Walewicz et al. recently published the results from an RCT showing that radial pressure wave significantly reduced lower back pain and improved function and range of motion [29].

Acute and chronic soft tissue injuries

A 2018 systematic review and meta-analysis of 10 randomized controlled trials found that focused shock wave/ ESWT significantly improved the healing rate of acute and chronic soft tissue wounds 2.73-fold. They found that acute wounds healed 3 days faster with shock wave treatment, and chronic wounds healed 19 days faster than with conventional wound therapy alone [30].

How to Incorporate Shock Wave into Your Practice

Both focused shock wave (F-SW) and radial pressure wave (R-PW) have demonstrated impressive efficacy in treatment of various musculoskeletal disorders with the added advantage of having little to no downtime, meaning patients can get back to doing the activities they love. Clinicians appreciate the convenience and ease of use associated with shock wave, and patients appreciate the immediate, long-lasting improvements in pain, mobility, and functionality.

Unlike conventional treatment options, shock wave provides immediate results without requiring long periods of downtime and/or immobility. In addition, shock wave may attenuate pathogenesis of musculoskeletal abnormalities, making it a promising preventative approach.

Athletes are a unique demographic that has wholeheartedly embraced shock wave treatments and sports medicine and interventional pain physicians are key proponents. Physiotherapists and physical therapists are also finding success treating myofascial trigger points.

F-SW/R-PW can also augment treatments that patients are currently familiar with, including laser therapy. Although clinical trials on the effectiveness of combined F-SW/ R-PW and biologics (platelet-rich plasma (PRP), Stem Cells & Amniotic injections) remain ongoing, preliminary studies suggest that they are highly complementary [31].

Economic benefits

In the US, shock wave is typically not reimbursed by insurance companies. However, there are substantial clinical and economic benefits of shock wave for both clinicians and patients. Traditional interventions including surgery, even if they are covered by insurance, often require patients to provide thousands of dollars out-of-pocket with copay and deductible obligations.

Elective-pay modalities can be intimidating to patients. However, studies have shown that shock wave is as (or more) effective than surgery for plantar fasciitis, and patients often spend less money. In fact, one study determined that the patient's costs associated with surgery are 5-7 times higher than for shock wave, when including lost function, productivity and wages during recovery [32].

The Future of Shock Wave

Mounting evidence supports the incredible value offered by shock waves in overuse injuries and pain treatment, and ongoing research is finding new ways to use this technology. For example, current research is investigating everything from neurological pathologies like post-herpetic neuralgia [33] and post-stroke muscle spasticity [34] to the use of shock waves in nanomaterial-based drug delivery [35].

A systematic review and meta-analysis published in March 2020 found that focused shock wave (F-SW) is a valuable treatment option for people with diabetic foot ulcers, including intractable and recurrent ulcers [36].

In addition, plastic surgeons and aesthetic dermatologists are incorporating shock wave into their practices, as mounting evidence shows that this treatment tightens, regenerates and rejuvenates skin and underlying connective tissues [37].

The applications of shock wave are vast and continue to grow. Combined use of focused shock waves and radial pressure waves with other treatment modalities like physical therapy, ultrasound, biologics, laser and other pain treatments is a very exciting area of ongoing investigation.

New technological innovations, product developments, indications, protocols, and implementation strategies are a constant priority, allowing medical professionals to focus on optimal patient centered outcomes.

Conclusion

Extracorporeal Pulse Activation Treatment (EPAT) also referred to as Extracorporeal Shock Wave Treatment (ESWT) is evidence-based, evidence-guided and has consistently demonstrated that it is a highly safe and effective treatment across multi-discipline medicine for a broad range of musculoskeletal disorders conditions that affect muscles, tendons, ligaments, fascia, bones, joints and other vascular structures.

CuraMedix is a long-standing and proud partner of STORZ Medical with more than 20 years of shock wave experience and offers a complete suite of focused shock wave and radial pressure wave devices. Made in Switzerland, STORZ Medical is the industry leader in shock wave technology development and manufacturing.

CuraMedix is committed to providing evidence-based and evidence-guided, non-surgical regenerative and restorative technologies that improve clinical and economic patient outcomes.

References

1. Moya, D., et al., The Role of Extracorporeal Shockwave Treatment in Musculoskeletal Disorders. J Bone Joint Surg Am, 2018. 100(3): p. 251-263.

2. Chaussy, C., W. Brendel, and E. Schmiedt, Extracorporeally induced destruction of kidney stones by shock waves. Lancet, 1980. 2(8207): p. 1265-8.

3. Wang, C.J., Extracorporeal shockwave therapy in musculoskeletal disorders. J Orthop Surg Res, 2012. 7: p. 11.

4. STORZ Medical, The Art of Shock Wave.
5. Császár, N.B.M., et al., Radial Shock Wave Devices Generate Cavitation. PloS one, 2015. 10(10): p. e0140541-e0140541.

6. Haupt, G., Use of extracorporeal shock waves in the treatment of pseudarthrosis, tendinopathy and other orthopedic diseases. J Urol, 1997. 158(1): p. 4-11.

7. Simplicio, C., et alExtracorporeal Shock Wave Therapy Mechanisms in Musculoskeletal Regenerative Medicine, Journal of Clinical Orthopaedics and Trauma, 2020.

8. Hatanaka, K., et al., Molecular mechanisms of the angiogenic effects of low-energy shock wave therapy: roles of mechanotransduction. Am J Physiol Cell Physiol, 2016. 311(3): p. C378-85.

9. Wei, L., et al., Adenosine Triphosphate Release and P2 Receptor Signaling in Piezo1 Channel-Dependent Mechanoregulation. Front Pharmacol, 2019. 10: p. 1304.

10. Milkiewicz, M., et al., Nitric oxide, VEGF, and VEGFR-2: interactions in activity-induced angiogenesis in rat skeletal muscle. Am J Physiol Heart Circ Physiol, 2005. 289(1): p. H336-43.

11. Gollmann-Tepeköylü, C., et al., Shock Wave Therapy Improves Cardiac Function in a Model of Chronic Ischemic Heart Failure: Evidence for a Mechanism Involving VEGF Signaling and the Extracellular Matrix. J Am Heart Assoc, 2018. 7(20): p. e010025.

12. Hu, K. and B.R. Olsen, Osteoblast-derived VEGF regulates osteoblast differentiation and bone formation during bone repair. The Journal of clinical investigation, 2016. 126(2): p. 509-526.

13. Sun, D., et al., Shockwaves induce osteogenic differentiation of human mesenchymal stem cells through ATP release and activation of P2X7 receptors. Stem cells (Dayton, Ohio), 2013. 31(6): p. 1170-1180.

14. Mukherjee, A. and P. Rotwein, Akt promotes BMP2-mediated osteoblast differentiation and bone development. J Cell Sci, 2009. 122(Pt 5): p. 716-26.

15. Wang, T., S. Guo, and H. Zhang, Synergistic Effects of Controlled-Released BMP-2 and VEGF from nHAC/PLGAs Scaffold on Osteogenesis. Biomed Res Int, 2018. 2018: p. 3516463.

16. Abe, Y., et al., Extracorporeal low-energy shock-wave therapy exerts anti-inflammatory effects in a rat model of acute myocardial infarction. Circ J, 2014. 78(12): p. 2915-25.

17. Holfeld, J., et al., Shockwave therapy differentially stimulates endothelial cells: implications on the control of inflammation via toll-Like receptor 3. Inflammation, 2014. 37(1): p. 65-70.

18. Nelson, A.M., et al., dsRNA Released by Tissue Damage Activates TLR3 to Drive Skin Regeneration. Cell stem cell, 2015. 17(2): p. 139-151.

19. Cole, J.E., et al., Unexpected protective role for Toll-like receptor 3 in the arterial wall. Proceedings of the National Academy of Sciences of the United States of America, 2011. 108(6): p. 2372-2377.

20. Hausdorf, J., et al., Selective loss of unmyelinated nerve fibers after extracorporeal shockwave application to the musculoskeletal system. Neuroscience, 2008. 155(1): p. 138-44

21. Gerdesmeyer, L., et al., Extracorporeal shock wave therapy for the treatment of chronic calcifying tendonitis of the rotator cuff: a randomized controlled trial. Jama, 2003. 290(19): p. 2573-80.

22. Pettrone, F.A. and B.R. McCall, Extracorporeal shock wave therapy without local anesthesia for chronic lateral epicondylitis. J Bone Joint Surg Am, 2005. 87(6): p. 1297-304.

23. Rompe, J.D., et al., Home training, local corticosteroid injection, or radial shock wave therapy for greater trochanter pain syndrome. Am J Sports Med, 2009. 37(10): p. 1981-90.

24. Everhart, J.S., et al., Treatment Options for Patellar Tendinopathy: A Systematic Review. Arthroscopy, 2017. 33(4): p. 861-872.

25. Thomas, J.L., et al., The diagnosis and treatment of heel pain: a clinical practice guideline-revision 2010. J Foot Ankle Surg, 2010. 49(3 Suppl): p. S1-19.

26. Rompe, J.D., J. Furia, and N. Maffulli, Eccentric loading compared with shock wave treatment for chronic insertional achilles tendinopathy. A randomized, controlled trial. J Bone Joint Surg Am, 2008. 90(1): p. 52-61.

27. Valchanou, V.D. and P. Michailov, High energy shock waves in the treatment of delayed and nonunion of fractures. Int Orthop, 1991. 15(3): p. 181-4.

28. Thiele, S., R. Thiele, and L. Gerdesmeyer, Adult osteochondritis dissecans and focussed ESWT: A successful treatment option. Int J Surg, 2015. 24(Pt B): p. 191-4.

29. Walewicz, K., et al., Effect of Radial Extracorporeal Shock Wave Therapy on Pain Intensity, Functional Efficiency, and Postural Control Parameters in Patients with Chronic Low Back Pain: A Randomized Clinical Trial. J Clin Med, 2020. 9(2).

30. Zhang, L., et al., Efficacy and safety of extracorporeal shock wave therapy for acute and chronic soft tissue wounds: A systematic review and meta-analysis. Int Wound J, 2018. 15(4): p. 590-599.

31. Seabaugh, K.A., M. Thoresen, and S. Giguère, Extracorporeal Shockwave Therapy Increases Growth Factor Release from Equine Platelet-Rich Plasma In Vitro. Frontiers in veterinary science, 2017. 4: p. 205-205.

32. Haake, M., M. Rautmann, and T. Wirth, Assessment of the treatment costs of extracorporeal shock wave therapy versus surgical treatment for shoulder diseases. Int J Technol Assess Health Care, 2001. 17(4): p. 612-7.

33. Lee, S.H., et al., Efficacy of extracorporeal shockwave therapy in the treatment of postherpetic neuralgia: A pilot study. Medicine (Baltimore), 2020. 99(12): p. e19516.

34. Dymarek, R., et al., Shock Waves as a Treatment Modality for Spasticity Reduction and Recovery Improvement in Post-Stroke Adults - Current Evidence and Qualitative Systematic Review. Clin Interv Aging, 2020. 15: p. 9-28.

35. Wang, S., et al., Improved Healing of Diabetic Foot Ulcer upon Oxygenation Therapeutics through Oxygen-Loading Nanoperfluorocarbon Triggered by Radial Extracorporeal Shock Wave. Oxid Med Cell Longev, 2019. 2019: p. 5738368.

36. Huang, Q., et al., Extracorporeal Shock Wave Therapy for Treating Foot Ulcers in Adults With Type 1 and Type 2 Diabetes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Can J Diabetes, 2020. 44(2): p. 196-204.e3.

37. Adatto, M.A. and R.M. Adatto-Neilson, Facial treatment with acoustic wave therapy for improvement of facial skin texture, pores and wrinkles. J Cosmet Dermatol, 2020.

38. International and Society for Medical Shockwave Treatment. Consensus statement on ESWT indications and contraindications. 2016 [cited 2020 March 26]; Available from: https://www.shockwavetherapy.org/fileadmin/user_upload/dokumente/PDFs/Formulare/ISMST_consensus_statement_on_indications_and_contraindications_20161012_final.pdf.

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