evocell® II – Mechanical Transductoin in Science

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1. What is mechanical transduction?

Mechanical transduction describes the transmission of mechanical stimuli or a process in which an extracorporeal mechanical stimulation results in an intracorporeal biological response (Cheng & Wang, 2015). Thus, our body's ability to convert acting forces into an electrical signal (Marshall & Lumpkin, 2012). Over 80% of our cell components are sensitive to mechanical stress (Ingber, 2006). It could be shown that physical input can activate cells through their mechanosensitive parts (e.g., focal adhesions), transmitting signals into the cell interior (Ingber, 1997).

High and low energy shock waves have been used for decades to treat numerous diseases. The mechanism responsible for stimulating diverse physiological processes (e.g., gene expression TGF-beta 1, neovascularization, an anti-inflammatory reaction, regulation of PCNA, Notarnicola & Moretti, 2012, Frairia & Berta, 2012) is known as mechanical transduction. It can consequently initiate migration, proliferation, differentiation, growth, and apoptosis of cells and result in a cellular restructuring of the extracellular matrix (binding forces of integrins or focal adhesions, d'Agostino et al., 2015).

Wang (2006) already discussed the importance of each cell component for mechanical transduction and provided considerable evidence of his hypotheses: „Note that there are many excellent reviews in the literature that focus on different types of cells, including cardiac fibroblasts (MacKenna et al., 2000), cardiac myocytes (Sadoshima and Izumo, 1997), smooth muscle cells (O-sol, 1995), endothelial cells (Davies, 1995; Resnick and Gimbrone, 1995), bone cells (Duncan and Turner, 1995), lung cells (Liu and Post, 2000), and dermal fibroblasts (Silver et al., 2003a). Interested readers should consult these references for an in-depth understanding of the topic of cellular mechanotransduction mechanisms" (p.1573).

Further Information:

- Berta, L., Fazzari, A., Ficco, A. M., Enrica, P. M., Catalano, M. G., Frairia, R. (2009). Extracorporeal shock waves enhance normal fibroblast proliferation in vitro and activate mRNA expression for TGF-beta1 and for collagen types I and III. Acta Orthopedica, 80(5):612-617.
- Cheng, J.H. & Wang, C.J. (2015). Biological mechanism of shockwave in bone. Int J Surg. 2015;24(Pt B):143-146. doi:10.1016/j.ijsu.2015.06.059
- Ingber, D. E. (2006). Cellular mechanotransduction: putting all the pieces together again. The FASEB Journal,20,811-27.
- Marshall, K.L., Lumpkin, E.A. (2012). The molecular basis of mechanosensory transduction. Adv Exp Med Biol;739:142-155. doi:10.1007/9781-4614-1704-0_9
- Wang, J. (2006). An introductory review of cell mechanobiology. Biomech. Model. Mechnobiol. 5:1-16.

2. What is the difference between extracorporeal shockwaves (eswt) and mechanical transduction?

ESWT describes a method and mechanical transduction its' effect, e.g., this very one. With ESWT, the result is caused by frequency or intensitydependent transmission of forces utilizing a transducer. The application of a mechanical force stimulates the transduction of the body/cells. As a result, cells are activated by setting various processes in motion, as described below.

3. Which effects are evidence-based?

The effects attributed to stimulation of mechanical transduction by ESWT include:

- Increase in immune defense (reduction of leukocyte migration, fewer cytokines, interleukin and chemokines ➤ reduction of the body's inflammatory response)
- Pain reduction (via hyper-stimulation of analgesics and use of the gate control mechanism
- Edema, swelling, and inflammation reduction
- Gene expression (TGF-beta 1 / IGF1)
- Support of bone formation (stimulation of osteoblast activity, promotion of spread and multiplication)
- Neovascularization (wound healing)
- Formation of neurotransmitters (nitric oxide)
- Tenocyte stimulation and, as a result, the regeneration of collagen structures

Mechanical transduction plays a vital role in the immune system: cell-cell adhesions are crucial for leukocytes' migration through vessels (Kobayashi, 1995). Their strength and quality are mainly influenced by integrins and selectins (Ingber, 2006; Takada et al., 2007). Because the interaction of integrin clusters and the actomyosin complex enables the reception of chemotactic signals, chemokines guide the leukocytes to their migration site (Nourshargh & Alon, 2014). To migrate through the endothelium, the cadherins responsible for the mechanotransmission decrease, as they are responsible for the adhesion between the individual cells (Ingber, 2006; Sun et al., 2016). After this migration, interactions with other immunologically relevant blood components such as macrophages, T & B lymphocytes, and platelets occur (Scapini & Cassatella, 2014). According to Jansen et al. (2017), shock waves can influence (increase stiffness) the extracellular matrix and cell adhesions. However, the opposite is necessary for the migration of leukocytes (Nourshargh & Alon, 2014).

Shock wave-induced reduction in proinflammatory cytokines or chemokines (Notarnicola & Moretti, 2012; Davis et al. 2009, Weihs et al., 2014) could lead to reduced migration of leukocytes as well. One reason may be the cytokinecontrolled reduction of cell apoptosis. Another that the lack of activation of integrin complexes due to a reduced number of cytokines and chemokines makes migration or the building of essential adhesions more difficult (Jansen et al., 2017, Sun et al., 2016). Integrins can, however, also be activated by mechanical stress (Ingber, 2006). Thus, an increase in hematopoietic stem cells (Lim et al., 2013, Suhr et al., 2013), potentially stimulated by mechanotransduction, leads to a higher amount of Blood leukocytes, thus enables a higher number of migrating cells. These processes have not yet been scientifically clarified. Such findings, however, focus on the importance of functioning mechanical transduction and underline realistic scenarios for the importance of the stimulation of the mechano-sensitive cell components.

Two different mechanisms can explain pain-reducing effects: On the one hand, shock waves have a hyperstimulating effect on analgesics (Rompe et al., 1996). The stimulation of peripheral endogenous nerve endings and the release of endogenous morphine are already considered one of the causes of pain reduction within acupuncture (Sjölund et al., 1977, Flowerdew et al., 1997). The role of an excessive release of substance P (Maier et al., 2003; Hausdorf et al., 2004), a neuropeptide, is still unclear. Presumably, the irritation of sensory afferents leads to its' release and activity as a neurotransmitter. What influence this ultimately has on pain perception is still unclear.

On the other hand, the welldocumented gate control theory (Melsack & Wall, 1965) seems to impair the transmission of painful perceptions. A mechanical stimulus transmitted via A-beta fibers suppresses

a painful stimulus by activating an inhibiting neuron (the gate to pain is closed). This directly reduces the projection neurons' activity and reduces/prevents the transmission of pain signals to the sensory cortex. Therefore, whole-body stimulation forms a sensory flood, which is followed by a preferred activation of the A-beta fibers.

Further Information:

- Jansen, K. A., Atherton, P. & Ballestrem, C. (2017). Mechanotransduction at the cell-matrix interface. Seminars in cell / developmental biology, 71, 75-83. Doi: 10.1016/j.semcdb.2017.07.027.
- Matthews, B. D., Overby, D. R., Mannix, R., & Ingber, D. E. (2006). Cellular adaptation to mechanical stress: role of integrins, Rho, cytoskeletal tension, and mechano-sensitive ion channels. J. Cell Sci., 119(3), 508.
- Melzack R, Wall PD.: Pain mechanisms: a new theory. Science. 1965 Nov 19;150 (699): 971–9.
- Notarnicola, A. & Moretti, B. (2012). The biological effects of extracorporal shock wave therapy (eswt) on tendon tissue. Muscles, ligaments and Tendons Journal,2(1):33-7.
- Noursargh, S. & Alon, R. (2014). Leukocyte migration into inflamed tissues. Immunity, 41(5), 694-707. Doi; 10.1016/j.immuni.2014.10.008.

4. What do we know about evocell?

evocells stimulation of mechanical transduction is regarded as a low-energy process due to its energy transfer. So far, there have been several theses (B.Sc.), one clinical study, and various articles on this treatment method, as well as countless reports from everyday clinical practice and professional sports. In terms of clinical experience, the medical team around Prof. Dr. Crevenna, Dr. Schaden, and Dr. Gallei from the (University-) Clinic for Physical Medicine, Rehabilitation and Occupational Medicine Vienna has already successfully used the device on several thousand patients. Since 2016, Dr. Schneider from the Orthopedic Center Theresie in Munich works with evocell as well. His focus lies on the treatment of elite athletes or evocell as an object of scientific research. Two studies concerning the treatment of chronic lower back pain have been conducted, which ascribe evocell a significantly pain-reducing character (measured using VAS, also compared to traditional methods such as heat therapy or without intervention) (Haag et al., 2016, Crevenna et al., 2016). Scientific theses (B. Sc.) at the Technical University of Munich were only able to identify trends in tiny samples (< 20) about the promotion of short-term regenerative ability after exercise (lactate, cortisol, leukocytes). A study further investigating these results using larger samples will be finished by the end of 2021.

Physicians report (based on patients' feedback and experience) a relaxing impact on musculature and a painreducing effect. The range of side effects is limited to mild nausea, dizziness, or minor headaches (1 in 100). Indications are predominantly patients with chronic (back) pain or other complaints of the musculoskeletal system.

In elite sports, evocell is used to support recovery and or in combination with physio-therapeutic procedures (manual therapy, heat, e.g.). Athletes at the Olympic Training Center in Garmisch-Partenkirchen (Germany) reported these effects over the past seven years of use: loosening, relaxation, increased blood circulation, tingling, better elasticity, and pain reduction. Slight dizziness and headache (1 out of 100) were documented as side effects. These subjective reports from users' experiences partly coincide with the previously published experiences and potential impact of shock waves in the low-energy range.

According to this, regeneration of injured tendons of the lower extremity (tibia, heel & Achilles) as well as damaged skin areas could be successfully supported by the use of low-energy shock waves (Chen et al., 2004, Haupt & Chvapil, 1990, Rompe et al., 1996 and Rompe et al., 2010). Amongst other effects, a proliferation of PCNAs is described as a potential consequence of higher gene expression TGF-ß1 and IGF-1 in the context of cell regeneration. Low energy shock waves seem to miss the destructive effects of previously documented treatments (Delius, 1994). The shock waves evocell emit are not sufficient to form cavitation bubbles. As a result, shattering effects, which can also lead to other potential side effects, are not expected (positive and negative, Delius, 1994). On

the other hand, low-energetic shock waves do seem to improve myocardial ischemia, neovascularization, and expression of vascular endothelial growth factors (Ito et al., 2009).

Besides, positive effects on erectile function (Vardi et al., 2012) and postprostatectomy-related incontinence (Crevenna et al., 2016) have also been documented. Remarkably, low-energy shock waves (1-20Hz) even seem to have a supporting effect on cementless implants' biological fixation (Rubin, 1984). The applied mechanical stress at low amplitudes also appears to positively impact osteoblast activity, as it is known for intense shock waves (Haupt et al., 1992).

Further Information:

- Chen, Y.-J., Wang, C.-J., Yang, K. D., Kuo, Y.R., Huang, H.-C., Huang, Y.-T. et al. (2004). Extracorporeal shock waves promote healing of collagenase-induced Achilles tendinitis and increase TGF-beta1 and IGF-I expression. Journal of Orthopaedic Research: official publication of the Orthopaedic Research Society, 22 (4), 854-861.
- Cho, W.; Kim, S.; Jeong, M.; Park, Y.M. Shockwaves Suppress Adipocyte Differentiation via Decrease in PPARγ. Cells 2020, 9, 166.
- Haupt, G., & Chvapil, M. (1990). Effect of shock waves on the healing of partial thickness wounds in piglets. Journal of Surgical Research, 49(1), 45-8.
- Rompe, J.D., Hopf, C., Nafe, B., & Bürger, R. (1996). Low-energy extracorporeal shock wave therapy for painful heel: a prospective controlled single-blind study. Archives of Orthopaedic and Trauma Surgery; 115(2),75-9.
- Rubin, C. T. & McLeod, K. J. (1984). Promotion of bony ingrowth by frequency-specific, low-amplitude mechanical strain. ClinOrthopRelat Res, 298,165-74.

FACTS ABOUT MECHANICAL TRANSDUCTION

- Over 80% of our cell parts are sensitive to mechanical stress
- Cells can be activated mechanically
- The ECM is continuously restructuring
- Mechanical transduction increases the ability to communicate with cells
- Mechanical transduction increases the sensibility of cells (mechanical prestension, d'Agostino et al., 2015)
- Molecules can change in energetic potential depending on their spatial arrangement (Conformation)
- Disturbance in mechanical transduction can be a cause or consequence of diseases (z.B. Aneurysma, Atherosklerosis, Osteoporosis, Cardiomyopathies, Heydemann & McNally, 2007; Tietse et al., 2020; Gimbrone et al., 2000)
- Low-energy shock waves do have a stimulating effect, and high-energy shock waves (although used for different indications).

5. Scientific evidence

"As an example, neurotransmitter release from motor nerve terminals can be detected within 10–20 msec after cell surface integrins are mechanically stressed."

Chen, B.M. & Grinnell, A.D. (1995). Integrins and modulation of transmitter release from motor nerve terminals by stretch. Science 269:1578–1580, pmid:7667637. Source: https://science.sciencemag.org/content/269/5230/1578

„Mechanotransduktion erhöht die Sensibilität von Zellen (mechanische Vorspannung) und kann wichtige Zellfunktionen wie Migration, Proliferation, Differenzierung sowie den programmierten Zelltod, die Apoptose beeinflussen."

d'Agostino, M. C., Craig, K., Tibalt, E. & Respizzi, S. (2015): Shock wave as biological therapeutic tool: From mechanical stimulation to recovery and healing, through mechanotransduction. In: International journal of surgery (London, England) 24 (Pt B), S. 147–153. DOI: 10.1016/j.ijsu.2015.11.030. Source: https://pubmed.ncbi.nlm.nih.gov/26612525/

„Vinculin liegt in einer inaktiven Konformation vor und wird z.B. durch Phosphorylierung konformationell aktiviert."

Flad, V. (2015). Phosphorylierung von Vinkulin und Kraftübertragung in zellulären fokalen Adhäsionen (Dissertation). Universität Erlangen-Nürnberg. Source: https://opus4.kobv.de/opus4-fau/files/6491/Dissertation_Vera+Flad.pdf

„Zellen reagieren auf Zugkräfte an der ECM. Zugkräfte können Genexpression oder weitere intrazelluläre Prozesse wie das Zellüberleben oder die Bewegungsgeschwindigkeit der Zellen beeinflussen."

Humphrey, J.D., Dufresne, E.R. & Schwartz, M.A. (2014). Mechanotransduction and extracellular matrix homeostasis. Nat Rev Mol Cell Biol;15(12):802-812. doi:10.1038/nrm3896. Source: https://pubmed.ncbi.nlm.nih.gov/25355505/

„Mechanical signals, therefore, may be integrated with other environmental signals and transduced into a biochemical response through force-dependent changes in scaffold geometry or molecular mechanics."

Ingber, D. E. (1997). Tensegrity: the architectural basis of cellular mechanotransduction. Annu. Rev. Physiol., 59(1), 575–599. https://doi.org/10.1146/annurev.physiol.59.1.575. Source: https://www.annualreviews.org/doi/abs/10.1146/annurev.physiol.59.1.575

„Über 80% aller Zellbausteine sind sensitiv für mechanische Reize."

Ingber, D. E. (2006). Cellular mechanotransduction: putting all the pieces together again. The FASEB Journal,20,811-27. Source: https://pubmed.ncbi.nlm.nih.gov/16675838/

„Consequently, defects in mechanotransduction–often caused by mutations or misregulation of proteins that disturb cellular or extracellular mechanics–are implicated in the development of a wide array of diseases, ranging from muscular dystrophies and cardiomyopathies to cancer progression and metastasis. Jaalouk & Lammerding provide detailed information about the biological components of mechanotransduction (box 1)."

Jaalouk, D. E., &Lammerding, J. (2009). Mechanotransduction gone awry. Nature Reviews Molecular Cell Biology10,63-73 (Januar 2009). Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2668954/pdf/nihms98005.pdf

„Talin und Vinculin, die auf der Cytoplasmaseite der Zellmembran zu finden sind essenziell für die Mechanotransduktion."

Jansen, K.A., Atherton, P. & Ballestrem, C. (2017). Mechanotransduction at the cell-matrix interface. Semin Cell Dev Biol;71:75-83. doi:10.1016/j.semcdb.2017.07.027. Source: https://pubmed.ncbi.nlm.nih.gov/28754442/

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"In principle, the articles presented in this book prove that the issue of mechanoelectric feedback considering transformation of mechanical signals into electrical one has grown into a global field of investigating with special respect to the pathways activated by stretch."

Kamkin A. &Kiseleva I., (2005). Mechanosensitivity of Cells from Various Tissues.Moscow: Academia. Source: https://www.ncbi.nlm.nih.gov/books/NBK7493/

"In conclusion, on the basis of our data and the proposed model, we suggest that connective tissue cells can coordinate their responses to mechanical forces through adherens junctions. These junctions mediate the activation of stretch-activated ion channels and subsequently facilitate the reorganization of actin filaments."

Ko, K. S., Arora, P. D., & McCulloch, C. A. (2001). Cadherins-mediate intercellular mechanical signaling in fibroblasts by activation of stretch-sensitive calcium-permeable channels. The Journal of Biological Chemistry, 276, 35967–35977. Source: https://www.jbc.org/content/276/38/35967.full.pdf

"Results indicate that cells and nuclei are literally built to respond directly to mechanical stresses applied to cell surface receptors, such as integrins. Other types of adhesion receptors that couple to the CSK (e.g., cadherins) may exhibit similar behavior. The demonstration of direct mechanical linkages throughout living cells raises the possibility that regulatory information, in the form of mechanical stresses or vibrations, may be rapidly transferred from these cell surface receptors to distinct structures in the cell and nucleus"

Maniotis, A. J., Chen, C. S., & Ingber, D. E. (1996). Demonstration of mechanical connections between integrins, cytoskeletal filaments, and nucleoplasm that stabilize nuclear structure. Proceedings of the National Academy of Sciences of the United States of America, 94(3), 849–854. Source: https://www.pnas.org/content/94/3/849.

"Zellen lassen sich rein mechanisch aktivieren. Ionenkanäle können durch Krafteinwirkung geöffnet werden. Dadurch ist der Ionenaustausch durch die Zellmembran und damit die Umwandlung eines mechanischen Signals möglich."

Marshall, K.L., Lumpkin, E.A. (2012). The molecular basis of mechanosensory transduction. Adv Exp Med Biol; 739:142-155. doi:10.1007/978-1-4614-1704-0_9. Source: https://pubmed.ncbi.nlm.nih.gov/22399400/

"Cells use multiple mechanisms to sense and respond to static and dynamic changes in the level of mechanical stress applied to integrins. (immediate viscoelastic response, early adaptive pulse-to-pulse attenuation, later adaptive cell stiffening/static stress, large-scale repositioning."

Matthews, B. D., Overby, D. R., Mannix, R., & Ingber, D. E. (2006). Cellular adaptation to mechanical stress: role of integrins, Rho, cytoskeletal tension and mechanosensitive ion channels. J. Cell Sci., 119(3), 508. Source: https://jcs.biologists.org/content/joces/119/3/508.full.pdf

"Knochen können mechanische Signale detektieren und ebenfalls in biologische Signale umsetzen wodurch der Knochen Auf- und Umbau beeinflusst wird: „Finally, we summarize the published data on bone cell accommodation, whereby bone cells stop responding to mechanical signaling events. Collectively, these data highlight the complex yet finely orchestrated process of mechanically regulated bone homeostasis."

Robling, A. G., & Turner, C. H. (2009). Mechanical Signaling for Bone Modeling and Remodeling. Critical reviews in eukaryotic gene expression, 19(4), 319–338. Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3743123/pdf/nihms-281049.pdf

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„Extrakorporale Stoßwellentherapie können durch eine Hyperstimulation von Analgetika für eine signifikante Schmerzlinderung bei einer Epicondylitis lateralis (Rompe, Hope, Küllmer, Heine & Bürger, 1996; Thiel, 2001; Yu, Junger, Yuan, Jin, Zhao, Zheng, Zeng & Liu, 2010) sowie auch bei einer Tendinitis in der Achillessehne (Chen, Y.-J., Wang, Yang, Kuo, Huang, Huang, Sun & Wang, 2004) oder einer kalzifizierten Schulter verantwortlich gemacht werden."

Rompe, J. D., Hope, C., Küllmer, K., Heine, J. & Bürger, R. (1996). Analgesic effect of extracorporeal shock-wave therapy on chronic tennis elbow. The Journal of bone and joint surgery. British volume, 78 (2), 233-237. Source: https://pubmed.ncbi.nlm.nih.gov/8666632/

„Mechanical transduction „is essential to the survival of both cells and higher organisms"."

Sachs, F (1988). Mechanical transduction in biological systems. Crit Rev Biomed Eng;16(2):141-169. Source: https://pubmed.ncbi.nlm.nih.gov/2460290/

"During mechanotransduction, force allosterically alters the functions of mechanosensitive proteins within adhesions to elicit biochemical signals that regulate both rapid responses in cellular mechanics and long-term changes in gene expression. Integrin-mediated mechanotransduction plays important roles in development and tissue homeostasis, and its dysregulation is often associated with diseases."

Sun, Z., Guo, S.S. & Fässler, R. (2016). Integrin-mediated mechanotransduction. J Cell Biol;215(4):445-456. doi: 10.1083/jcb.201609037. Source: https://pubmed.ncbi.nlm.nih.gov/27872252/

„Eine gestörte Mechanotransduktion wird als Ursache oder Folge von Krankheiten gesehen (z.B. Aneurysmen, Atherosklerose)."

Tietze, S., Hofmann, A., Wolk, S. & Reeps, C. (2020). Grundlagen der zellulären Mechanotransduktion. Gefässchirurgie;25,244-8. Source: https://link.springer.com/journal/772/volumes-and-issues/25-4.

„While the major focus in the search for mechanosensory units has been on membrane proteins such as ion channels, integrins, and associated cytoplasmic complexes, a multimodular design of tandem repeats of various structural motifs is ubiquitously found among extracellular matrix proteins, as well as cell adhesion molecules, and among many intracellular players that physically link transmembrane proteins to the contractile cytoskeleton."

Vogel, V. (2006). Mechanotransduction involving multimodular proteins: Converting Force into Biochemical Signals. Annu. Rev. Biophys. Biomol. Struct., 35(1), 459–488. https://doi.org/10.1146/annurev.biophys. 35.040405.102013. Source: https://www.annualreviews.org/doi/pdf/10.1146/annurev.biophys.35.040405.102013

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"These results suggest that integrins act as mechanoreceptors and transmit mechanical signals to the cytoskeleton. Mechanotransduction, in turn, may be mediated simultaneously at multiple locations inside the cell through force-induced rearrangements within a tensionally integrated cytoskeleton."

Wang, N., Butler, J. P., & Ingber, D. E. (1993). Mechanotransduction across the cell surface and through the cytoskeleton. Science, 260(5111), 1124. https://doi.org/10.1126/science.7684161. Source: https://science.sciencemag.org/content/260/5111/1124

"We found cortical bone adaptation to mechanical loading to increase with increasing loading frequency up to 5-10 Hz and to plateau with frequencies beyond 10 Hz."

Warden, S. J. & Turner, C. H., (2004). Mechanotransduction in cortical bone is most efficient at loading frequencies of 5-10 Hz. Bone,34,261-70. Source: https://pubmed.ncbi.nlm.nih.gov/14962804/

"Quantitative measurements of both static and dynamic mechanical behaviors in cells also were consistent with specific a priori predictions of the tensegrity model. These findings suggest that tensegrity represents a unified model of cell mechanics that may help to explain how mechanical behaviors emerge through collective interactions."

Wang, N., Naruse, K., Stamenović, D., Fredberg, J. J., Mijailovich, S. M., Tolić-Nørrelykke, I. M.,. . . Ingber, D. E. (2001). Mechanical behavior in living cells consistent with the tensegrity model. Proceedings of the National Academy of Sciences of the United States of America, 98(14), 7765–7770. https://doi.org/10.1073/pnas.141199598. Source: https: //europepmc.org/article/med/11438729

"The results demonstrate that shear stress and vascular smooth muscle cells promote endothelial differentiation of EPCs via activation of Akt, which provide a new insight to clinical application on the regeneration of the vascular endothelium."

Ye, C., Bai, L., Yan, Z.-Q., Wang, Y.-H., & Jiang, Z.-L. (2008). Shear stress and vascular smooth muscle cells promote endothelial differentiation of endothelial progenitor cells via activation of Akt. Clinical Biomechanics, 23, S118-S124. https://doi.org/10.1016/j.clinbiomech.2007.08.018. Source: https://www.clinbiomech.com/article/S02680033(07)00173-8/abstract.

„Over a period of 6 weeks after starting treatment, the patient regained continence (usage of 1 safety pad)."

Crevenna R, Cenik F, Margreiter M, Marhold M, Komanadj TS, Keilani M (2016). Whole body vibration therapy on a treatment bed as additional means to treat postprostatectomy urinary incontinence. Wie Med Wochenschr, 167:139-141, DOI 10.1007/s10354-016-0469-7

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- Luginbuehl H, Lehmann C, Gerber R, et al. Continuous versus intermittent stochastic resonance whole body vibration and its effect on pelvic floor muscle activity. Neurourol Urodyn. 2012;31(5):6837.
- Maehr B, Keilani M, Wiltschke C, et al. Cancer rehabilitation in Austria-aspects of Physical Medicine and Rehabilitation. Wien Med Wochenschr. 2016;166(1–2):39–43.
- Pfefferkorn, M. (2020). Evaluation des Einflusses mechnotransduktiver Stoßwellenbehandlung auf die Immunabwehr nach Belastung. Abschlussarbeit (B.Sc.) an der Technischen Universität München. Lehrstuhl für Trainingswissenschaft und Sportinformatik: Prof. M. Lames.
- Pilotstudie (EK-Nr. 1593/2015) der Meduni Wien: Wissenschaftliche Untersuchung der Akzeptanz, Effektivität und Effizienz einer Schmerzbehandlung mit der medizinischen Ganzkörperliege mit biomechanischer Wellentechnologie an 200 Probanden (Rückenschmerz)
- Schuster, C. (2019). Der Einfluss von Stoßwellen auf die Cortisolproduktion. Abschlussarbeit (B.Sc.) an der Technischen Universität München. Lehrstuhl für Trainingswissenschaft und Sportinformatik: Prof. M. Lames.
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- Vom Brocke, J. (2015).Der Regenerationsprozess und dessen Optimierung bei männlichen Athleten des Landeskaders Ski Alpin: Fahrradergometer vs. Ganzkörperstoßwelle – Ein Vergleich. Abschlussarbeit (B.Sc.) an der Hochschule Fresenius. Fachbereich Gesundheit Physiotherapie: M. Zwiorek.
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