First Congress

International Society of Diamagnetic Therapy

13th – 14th September 2024
Magna Graecia University - Catanzaro

"Shock Waves in Tissue Regeneration"

***M. Cristina d'Agostino**, MD – SITOD Past President*

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ISMST Senator & Membership Secretary - International ISMST Instructor - SETOC Honorary Member

HUMANITAS RESEARCH HOSPITAL

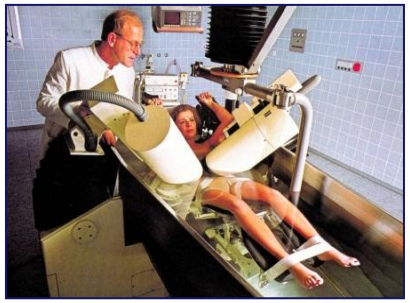
ISMST

S.I.T.O.D

ISDT International Society of Diamagnetic Therapy

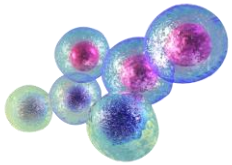
1991 = Urological Lithotripsy

ESWT



BEYOND RENAL STONES FRAGMENTATION

*2024 = **R**egenerative **M**edicine*



TRMOME-878; No. of Pages 10 ARTICLE IN PRESS

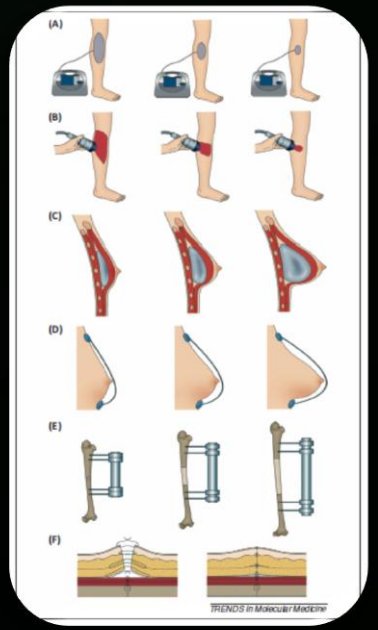
Review

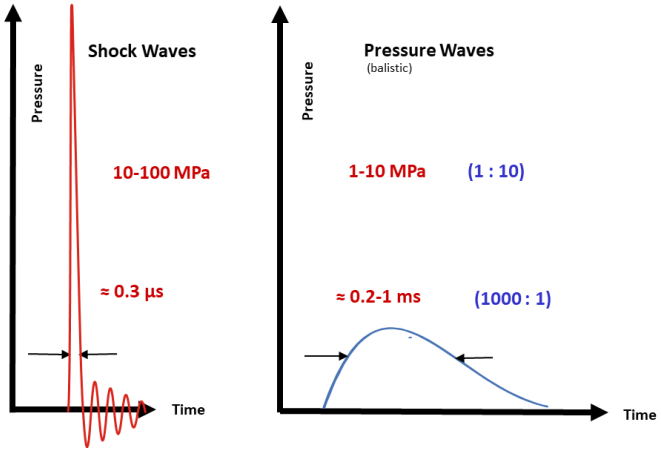
Mechanotherapy: revisiting physical therapy and recruiting mechanobiology for a new era in medicine

Chenyu Huang[1,2,3], Johannes Holfeld[4], Wolfgang Schaden[5], Dennis Orgill[3], and Rei Ogawa[1]

MECHANOTHERAPIES ..

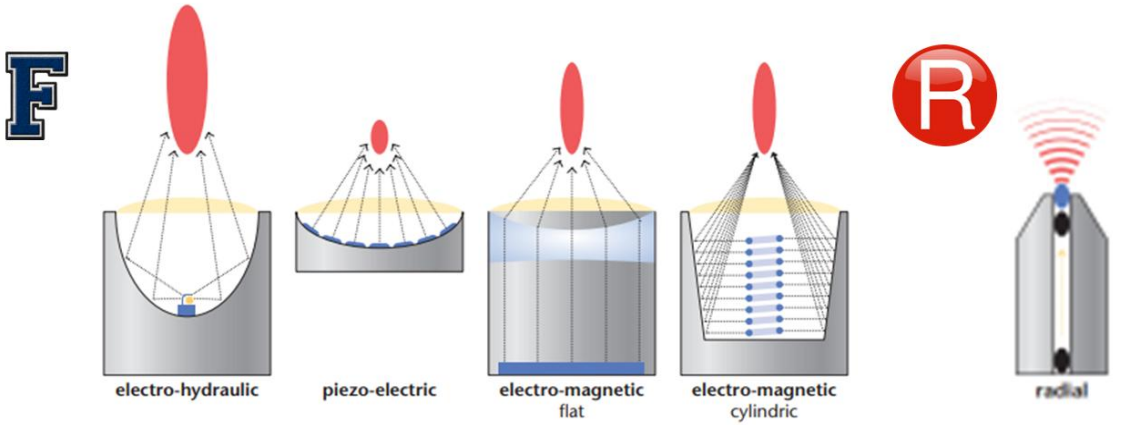
« .. are active mechano – interventions that aim to convert potentially destructive mechanical effects into costructive influences and target normal mechano – adaptation to promote recovery .. «





" .. Focal Shock Waves and Radial Pressure Waves may have similar and/or synergistic THERAPEUTIC EFFECTS .. "

SW



RPW

Fig. 1 Different types of generating pressure waves and shock waves are produced by the diverse devices for ESWT. All these devices produce more or less focused pressure waves and shock waves except the radial devices, which produce pressure waves, which are not focused and have the highest energy in the area where the applicator delivers the mechanical energy into the body, superficially on the skin. Auersperg V et al, *EFORT Open Rev 2020;5:584-592*

Naples, Italy, October 12th, 2016

Consensus Statement on
ESWT Indications and Contraindications

A. Introduction and prerequisites and minimal standards of performing ESWT

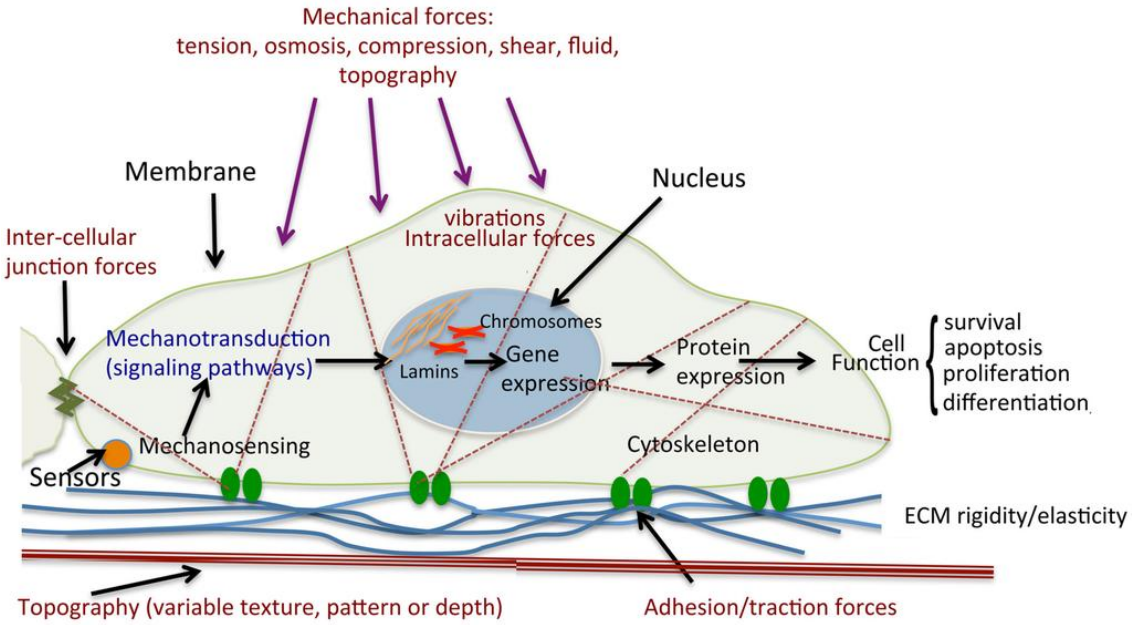
For the treatment on bones, a high-energy, focused shockwave with positioning technology has to be used.

In accordance with most scientific evidence ISMST recommends to use focused generators and high energy levels to treat calcifications.

To treat superficial soft tissue conditions, devices with or without focusing technology may be utilized; close attention must be paid to the depth of penetration of the shockwave source when treating deep tissue structures.

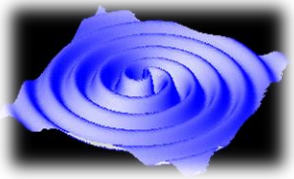
MECHANOTRANSDUCTION

Describes the Cellular and Molecular Processes Through Which Mechanical Stimuli Are Converted into Biochemical Signals



Spyropoulou A. et alL, ***Biochim Biophys Acta. 2015 Sep;1852(9):1700-8***

STATE OF THE ART



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]

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.

Mechanical Model → BIOLOGICAL MODEL

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.

STATE OF THE ART

SW could modulate inflammation via stimulation of TL-R3

F

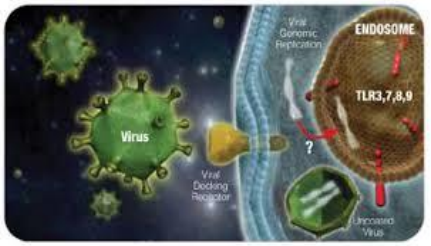
→Early pro-inflammatory
→Late anti-inflammatory response

Inflammation (© 2013)
DOI: 10.1007/s10753-013-9712-1

Shockwave Therapy Differentially Stimulates Endothelial Cells: Implications on the Control of Inflammation *via* Toll-Like Receptor 3

Johannes Holfeld,[1] Can Tepeköylü,[1] Radoslaw Kozaryn,[1] Anja Urbschat,[2] Kai Zacharowski,[3] Michael Grimm,[1] and Patrick Paulus[3,4]

However, the mechanism of how the mechanical stimulus of shock waves is translated into a biological response remains unknown [12]. It was suggested that SWT leads to an increase of cell membrane permeability [13]. Thereby, it could cause the release of cytosolic RNA. In the present experiments, we therefore hypothesized that SWT may modulate inflammation *via* stimulation of toll-like receptor 3 (TLR3). TLR3 is part of the innate immune system and involved in the recognition of double-stranded RNA (dsRNA) and fragmented deoxyribonucleic acid (DNA) from viruses [14, 15]. It therefore could be able to detect released cytosolic RNA from neighbouring cells. TLR3 activation is characterized by an early pro-inflammatory phase and a late anti-inflammatory response. This balancing may create the environment for angiogenesis and repair in ischemic tissue [16].



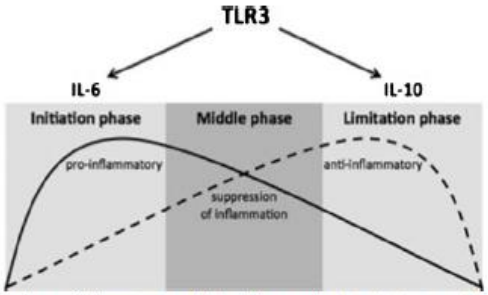
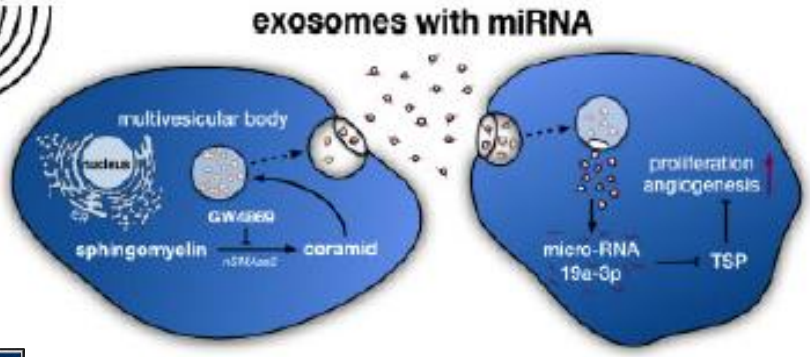


Fig. 6. TLR3 stimulation leads to three phases of inflammatory modulation. The complex interaction between the two main cytokines IL-6 and IL-10 in TLR3 stimulation can be schematically seen as a three-phase regulation over time. After an early pro-inflammatory initiation phase mediated by IL-6, a middle phase showing suppression of inflammation can be seen before the late anti-inflammatory limitation phase of IL-10 results. This modulation of the inflammatory response is prerequisite for angiogenesis and repair in ischemic tissue.

Inflammation. **2014** Feb;37(1):65-70.



ESC European Society of Cardiology
Cardiovascular Research
doi:10.1093/cvr/cvz209

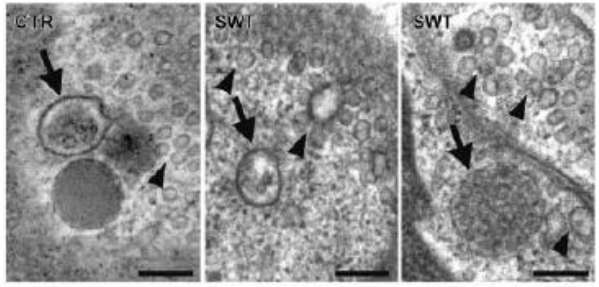
miR-19a-3p containing exosomes improve function of ischaemic myocardium upon shock wave therapy

Can Gollmann-Tepeköylü[1,2†], Leo Pölzl[1,2†], Michael Graber[1,3], Jakob Hirsch[1,2], Felix Nägele[1,2], Daniela Lobenwein[1,3], Michael W. Hess[4], Michael J. Blumer[3], Elke Kirchmair[1,2], Johannes Zipperle[2,5], Carina Hromada[2,5], Severin Mühleder[2,5], Hubert Hackl[6], Martin Hermann[7], Hemse Al Khamisi[8], Martin Förster[9], Michael Lichtenauer[10], Rainer Mittermayr[2,11], Patrick Paulus[12], Helga Fritsch[4], Nikolaos Bonaros[1], Rudolf Kirchmair[13], Joost P.G. Sluijter[8], Sean Davidson[14], Michael Grimm[1], and Johannes Holfeld[1,2*]

Methods and results Mechanical stimulation of ischaemic muscle via SWT caused extracellular vesicle (EV) release from endothelial cells both *in vitro* and *in vivo*. Characterization of EVs via electron microscopy, nanoparticle tracking analysis and flow cytometry revealed specific exosome morphology and size with the presence of exosome markers CD9, CD81, CD63. Exosomes exhibited angiogenic properties activating protein kinase B (Akt) and extracellular signal-regulated kinase (ERK) resulting in enhanced endothelial [illegible] analysis via [illegible] miR-19a-3p was identified as [illegible] angiogenic exosome effects. Exosomes and target miRNA were [illegible] myocardially in mice after left anterior descending artery ligation. Exosomes resulted in improved vascularization, decreased myocardial fibrosis, and increased left ventricular ejection fraction as shown by transthoracic echocardiography.

Conclusion The mechanical stimulus of SWT causes release of angiogenic exosomes. miR-19a-3p is the vesicular cargo responsible for the observed effects. Released exosomes induce angiogenesis, decrease myocardial fibrosis, and improve

the mechanical stimulus of SWT causes release of angiogenic exosomes containing miR-19a-3p.



arrows: multivesicular bodies, arrowheads: caveolae

C. Gollmann-Tepeköylü *et al.*

*M*echanisms of *A*ction

- Changes in cellular membrane permeability

- Production of NO (Nitric Oxide) F
- Stimulation of mitochondria, ATP release F
- Diluition of Substance P (neurotransmitter)
- Riduction of unmyelinated small nerve fibers F R
- Antinociceptive effect (neuropeptides ?!)

(*Othori S et all, 2001, Abed JM, et all, 2007, Klonschinski T et all, 2011*)

F

- Synthesis of Growth Factors (VEGF, BMPs, etc)
- Angiogenesis & Vasculogenesis
- Lymphangiogenesis
- Proliferation, Migration, «*Homing*» and differentiation of Stem cells

- MODULATION of INFLAMMATORY PATHWAYS

Defining M1 and M2 Macrophages

This classification is based upon **macrophage polarization**

polarization process is dynamic, and cells often display characteristics of both states at the same time

M1 macrophages

Produce proinflammatory cytokines, phagocytize microbes,
and initiate an immune response

M2 macrophages

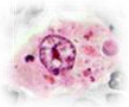
are alternatively activated by IL-4, IL-10, or IL-13.
.. wound healing, tissue repair and collagen production ..

Interaction with cells with stem or progenitor cell properties
is likely an important component of the role of macrophages
in repair and remodeling

*Source: Tamás Rőszer, "Understanding the Mysterious M2 Macrophage through Activation Markers and Effector Mechanisms,
" Mediators of Inflammation, vol. 2015, Article ID 816460, 16 pages, 2015.*

HUMANITAS
FONDAZIONE PER LA RICERCA

Sukubo G. et all., *International Journal of Surgery* 2015 24, 124-130DOI: (10.1016/j.ijsu.2015.07.719)

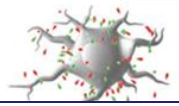


Contents lists available at ScienceDirect
International Journal of Surgery
journal homepage: www.journal-surgery.net

Original research

Effect of shock waves on macrophages: A possible role in tissue regeneration and remodeling

Naths Grazia Sukubo [a,b], Elisabetta Tibalt [c], Stefano Respizzi [c], Massimo Locati [a,b], M.Cristina d'Agostino [c,*]



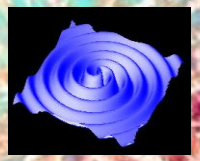
SW ON «IN VITRO» MACROPHAGES INDUCE:

- NO effects on «resting» Macrophages (M0)
- Inhibition of «pro-inflammatory» Macrophages (M1)
- Enhancement of «pro-resolving» Macrophages (M2)

Modulation of the «cross – road» between M1 & M2

for regenerative purposes

«Self – Healing» enhancement through Immuno – Modulation ..



.. without ..

.. BIOLOGICAL MANIPULATION..

Possible Role in Analgesic Effects

- Relief of pain after SW application to the skin, results from rapid degeneration of the intracutaneous (sensory) nerve fibers.
  Reinnervation of the epidermis occured after 2 weeks (*Othori S et all, 2001)*
- SW induce an improved rate of axonal regeneration (*Hausner T et. all. 2012)*
- Local anaesthesia substantially alters the biological response to SW
  SW dose-dependently activates and sensitizes primary afferent C- fibers
  (Klonschinski T et all, 2011)
- Substance-P and CGRP-containing nerve fibers are not disrupted by radial or focused SW (*Abed JM, et all, 2007)*

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SW & Lymphangiogenesis

PLoS One. 2014 Dec 11;9(12):e114806. doi: 10.1371/journal.pone.0114806. eCollection 2014.

Molecular and cellular effects of in vitro shockwave treatment on lymphatic endothelial cells.

Rohringer S[1], Holnthoner W[1], Hackl M[2], Weihs AM[3], Rünzler D[3], Skalicky S[2], Karbiener M[4], Scheideler M[4], Pröll J[5], Gabriel C[5], Schweighofer B[6], Gröger M[7], Spittler A[8], Grillari J[9], Redl H[1].

The results indicate **that IVSWT-mediated proliferation changes of LECs** are highly energy flux density-dependent and LEC 2D as well as 3D migration was enhanced through IVSWT

J Vasc Res. 2013;50(2):124-33. doi: 10.1159/000343699. Epub 2012 Nov 27.

Extracorporeal shock wave therapy combined with vascular endothelial growth factor-C hydrogel for lymphangiogenesis.

Kim IG[1], Lee JY, Lee DS, Kwon JY, Hwang JH.

The VEGF-C hydrogel was applied to the injury site in **a mouse model of lymphedema** and then regularly underwent ESWT .. Four weeks after the treatment, mice treated with VEGF-C hydrogel and ESWT showed signs of the greatest decrease in edema/collagenous deposits when compared with the other experimental group.
These results suggested that VEGF-C and ESWT had a synergistic effect and were very effective in alleviating the symptoms of lymphedema and promoting lymphangiogenesis

J Vasc Surg. 2010 Aug;52(2):429-34. doi: 10.1016/j.jvs.2010.03.017.

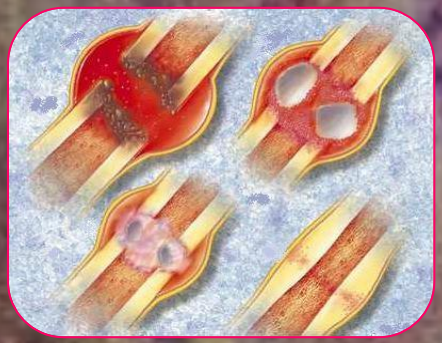
Extracorporeal shock wave therapy ameliorates secondary lymphedema by promoting lymphangiogenesis.

Kubo M[1], Li TS, Kamota T, Ohshima M, Shirasawa B, Hamano K.

A rabbit ear model of lymphedema was created by disruption of lymphatic vessels. Two weeks after surgery, the lymphedematous ear was treated with or without low-energy shock waves ..
Compared with the control group, shock wave treatment led to a significant decrease in the thickness of lymphedematous ears.
Immunohistochemistry for VEGFR3 showed the density of lymphatic vessels was significantly increased by shock wave treatment

EFFECTS of SW on the MUSCULAR - SKELETAL SYSTEM

Bone – Tendon - Muscle



" .. SW in orthopaedics are not used to disintegrate tissues, rather to induce neovascularization, improve blood supply, and tissue regeneration ... "

Wang CJ, 2003

STATE OF THE ART

International Journal of Surgery 24 (2015) 179–183

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Review

Extracorporeal shockwave therapy (ESWT) — First choice treatment of fracture non-unions?

Wolfgang Schaden [a, b], Rainer Mittermayr [a, b, *], Nicolas Haffner [b], Daniel Smolen [b], Ludger Gerdesmeyer [c], Ching-Jen Wang [d]

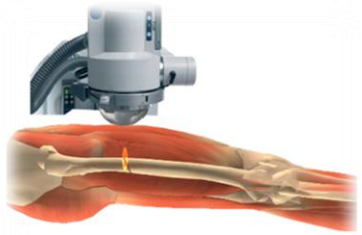


Fig. 2. The image shows the principle of shockwave treatment of a femur non-union. The therapy head is positioned above the femur in a way that the focal area of the shockwave is placed in the non-union gap.

HIGHLIGHTS

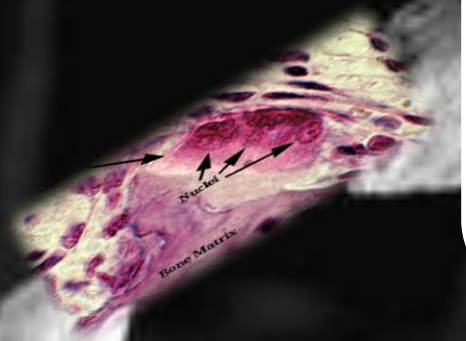
- Non-healing fractures (pseudarthroses, non-unions) still are a challenging problem in orthopedics.
- ESWT is a non-invasive procedure that achieves comparable results to surgical approaches.
- Complications associated with ESWT are on rare occasions and minimal if present.
- Peer-reviewed literature shows excellent results with medium/high energy focused ESWT, with faster return to competition and athletic activity.

As ESWT has been proven to be as effective as surgical procedures but being more economic and practically free of side effects it should be considered progressively as "therapy of first choice" for the treatment of suitable non-union fractures.

O. U. hanno effetti POSITIVI «MULTILEVEL»

sul Tessuto Osseo

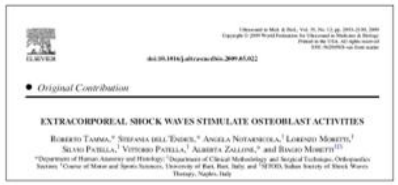
1. CELLULE OSSEE



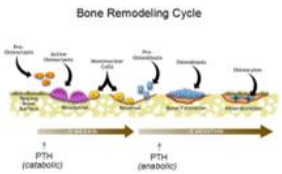
2. RIMODELLAMENTO OSSEO
accoppiamento clasti - blasti

O.U. & Osteogenesi Riparativa

Meccanismi Cellulari



EXTRACORPOREAL SHOCK WAVES STIMULATE OSTEOBLAST ACTIVITIES



" .. OU possono stimolare la rigenerazione ossea anche attraverso una ridotta secrezione di fattori pro – osteoclastogenici .. "

Riduzione del rapporto RANKL/OPG → inibizione osteoclastogenesi

3. VASCOLARIZZAZIONE OSSEA

Häußer et al. Journal of Orthopaedic Surgery and Research (2021) 16:369
https://doi.org/10.1186/s13018-021-02484-5

2021

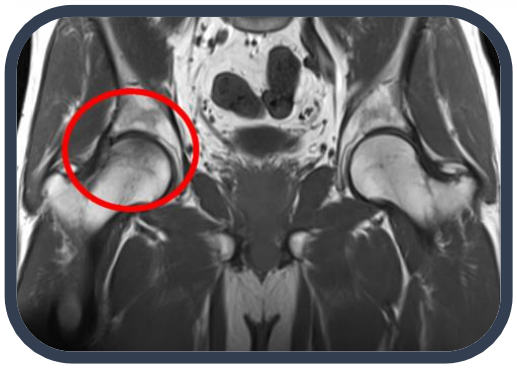
Journal of Orthopaedic Surgery and Research

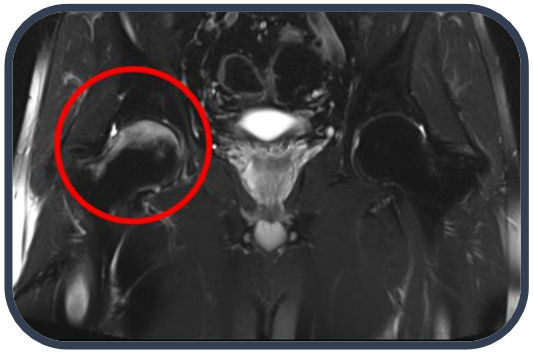
SYSTEMATIC REVIEW Open Access

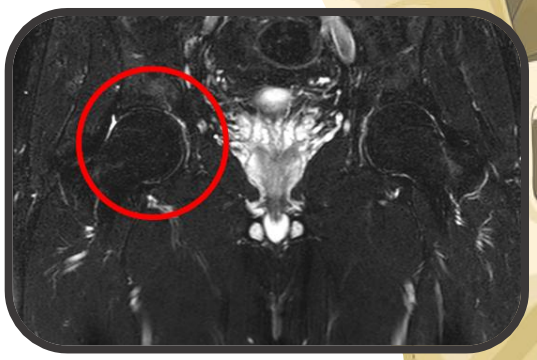
The use of extracorporeal shock wave therapy for the treatment of bone marrow oedema — a systematic review and meta-analysis

Jonathan Häußer[1*], Juliane Wieber[1,2*] and Philip Catalá-Lehnen[1]

Conclusions: Based on the available evidence, ESWT may be an adequate option for conservative therapy in pathologies involving BME.

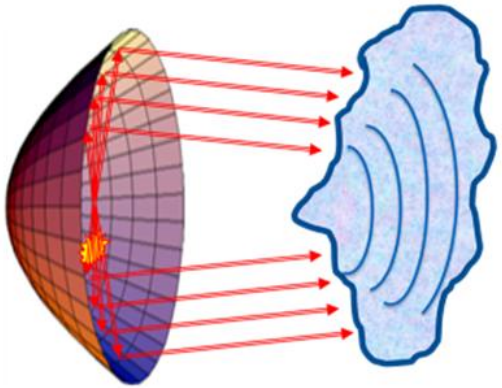






SW & Regenerative Medicine

planar F



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JOURNAL OF BIOLOGICAL REGULATORS & HOMEOSTATIC AGENTS Vol. 30, no. 2, 323-332 (2016)

EDITORIAL

EXTRACORPOREAL SHOCKWAVES AS REGENERATIVE THERAPY IN ORTHOPEDIC TRAUMATOLOGY: A NARRATIVE REVIEW FROM BASIC RESEARCH TO CLINICAL PRACTICE

M.C. D'AGOSTINO[1], R. FRAIRIA[2], P. ROMEO[3], E. AMELIO[4], L. BERTA[5], V. BOSCO[6], S. GIGLIOTTI[7], C. GUERRA[4], S. MESSINA[8], L. MESSURI[9], B. MORETTI[10], A. NOTARNICOLA[10], G. MACCAGNANO[10], S. RUSSO[11], R. SAGGINI[12], M.C. VULPIANI[13] and P. BUSELLI[14]

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.

Nowadays, on the basis of our narrative review, we can declare the "SW pioneering phase" as closed, while opening the very new and revolutionary phase of tissue regeneration, with important therapeutic implications in muscle–skeletal traumatology sequelae and with further promising perspectives in regenerative medicine, cell therapy and tissue engineering in the near future.

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 ..." (45).

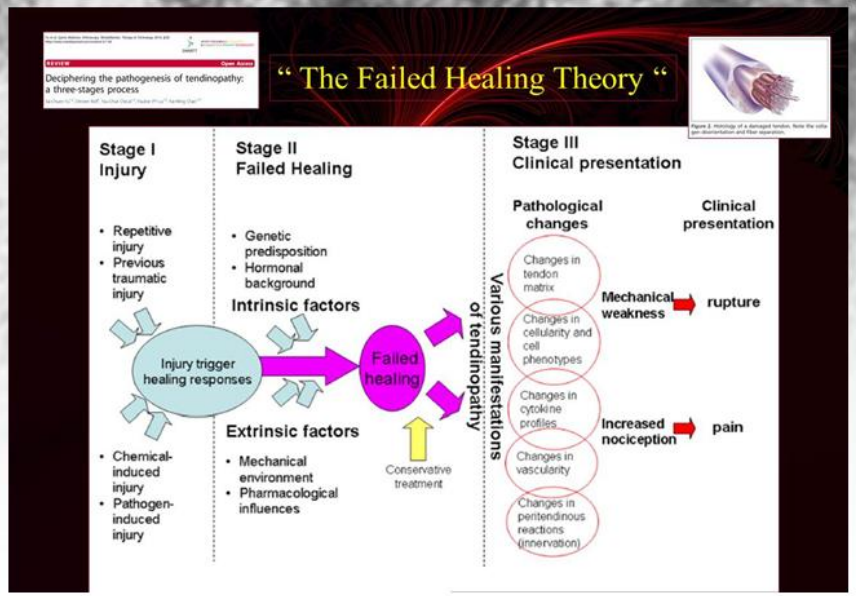
Repair

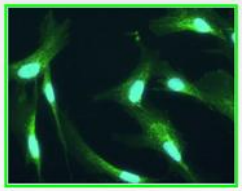
Replace

Restore

Regenerate

Which rationale for applying SWs in tendinopathies ?





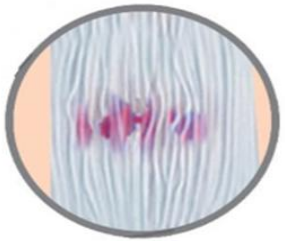
Tendon Stem Cells (TSCs)

Zhang J et all, 2010

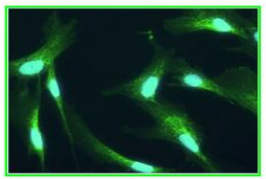
NEWS

Tendons

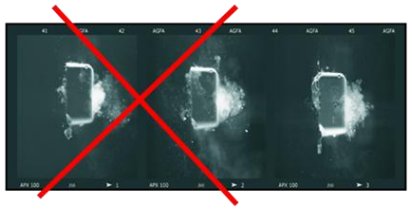
- Possibile role in tendon healing
  (*de Girolamo L. et all, 2014; Visco V et all, 2014*)
- Reduced expression of Metalloproteinasis (MMP) and Interleukine (ILs)
  (*Chao YH et all, 2008*)
- Increased tenocytes metabolism, expression of tendon markers and release of antiinflammtory cytokines (*Bosch G et all 2007*)
- Possible clonogenic potential on hTSPCs
  (*Leone L et all, 2016*)



Not simply «palliative» but really curative effects



Tendon Stem Cells (TSCs)
Zhang J et all, 2010



STATE OF THE ART

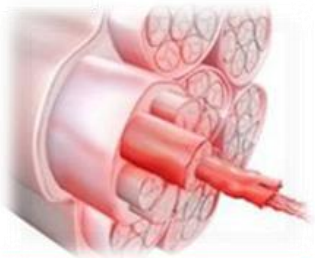
European Cells and Materials Vol. 29 2015 (pages 268-280) ISSN 1473-2262

IN VIVO BIOLOGICAL RESPONSE TO EXTRACORPOREAL SHOCKWAVE THERAPY IN HUMAN TENDINOPATHY

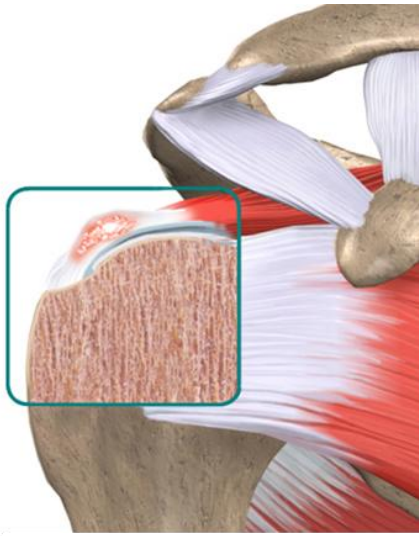
C.M. Waugh[1,2], D. Morrissey[1], E. Jones[3], G.P. Riley[3], H. Langberg[4] and H.R.C. Screen[2,*]

This study provide a novel insight into the biological mechanisms underpinning the observed clinical effects of ESWT in humans in vivo

the mechanical stimulus provided by ESWT might aid the initiation of tendon regeneration in tendinopathy by promoting pro-inflammatory and catabolic processes that are associated with removing damaged matrix constituents.



HUMANITAS
RESEARCH HOSPITAL



O.U. & Calcificazioni – Sistematic Reviews & Meta-Analysis

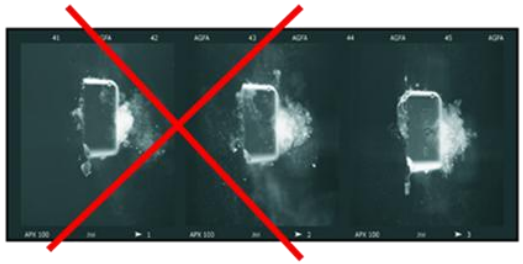
Arch Phys Med Rehabil 2013 Sep;94(9):1699-706

Clinical improvement and resorption of calcifications in calcific tendinitis of the shoulder after shock wave therapy at 6 months' follow-up: a systematic review and meta-analysis.

Ioppolo F. et all.

" .. We found a clinical improvement with a **pooled total resorption ratio of 27.19** (95% confidence interval [CI], 7.20-102.67) and **a pooled partial resorption ratio of 16.22** (95% CI, 3.33-79.01).

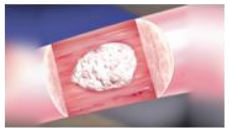
" .. SWT increases shoulder function, reduces pain, and is effective in dissolving calcifications .. "



Ann Intern Med 2014 Apr 15;160(8):542-9.

High-energy extracorporeal shock-wave therapy for treating chronic calcific tendinitis of the shoulder: a systematic review.

Bannuru RR et all.



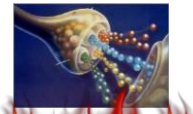
High-energy ESWT is effective for improving pain and shoulder function in chronic calcific shoulder tendinitis and can result in complete resolution of calcifications. This therapy may be underutilized for a condition that can be difficult to manage.

Hackett L, Millar NL, Lam P, Murrell GA
Are the Symptoms of Calcific Tendinitis Due to Neoinnervation and/or Neovascularization ?
J Bone Joint Surg Am. 2016 Feb 3;98(3):186-92.

METHODS:
At arthroscopy, ultrasound was used to identify calcium within the tendon. Samples were taken from the supraspinatus tendon adjacent to the calcific lesion (in the calcific tendinitis group, with ten patients), the torn supraspinatus tendon of patients undergoing rotator cuff repair (the rotator cuff tear group, with ten patients), and the subscapularis tendon of patients undergoing a stabilization surgical procedure (the control group, with ten patients).

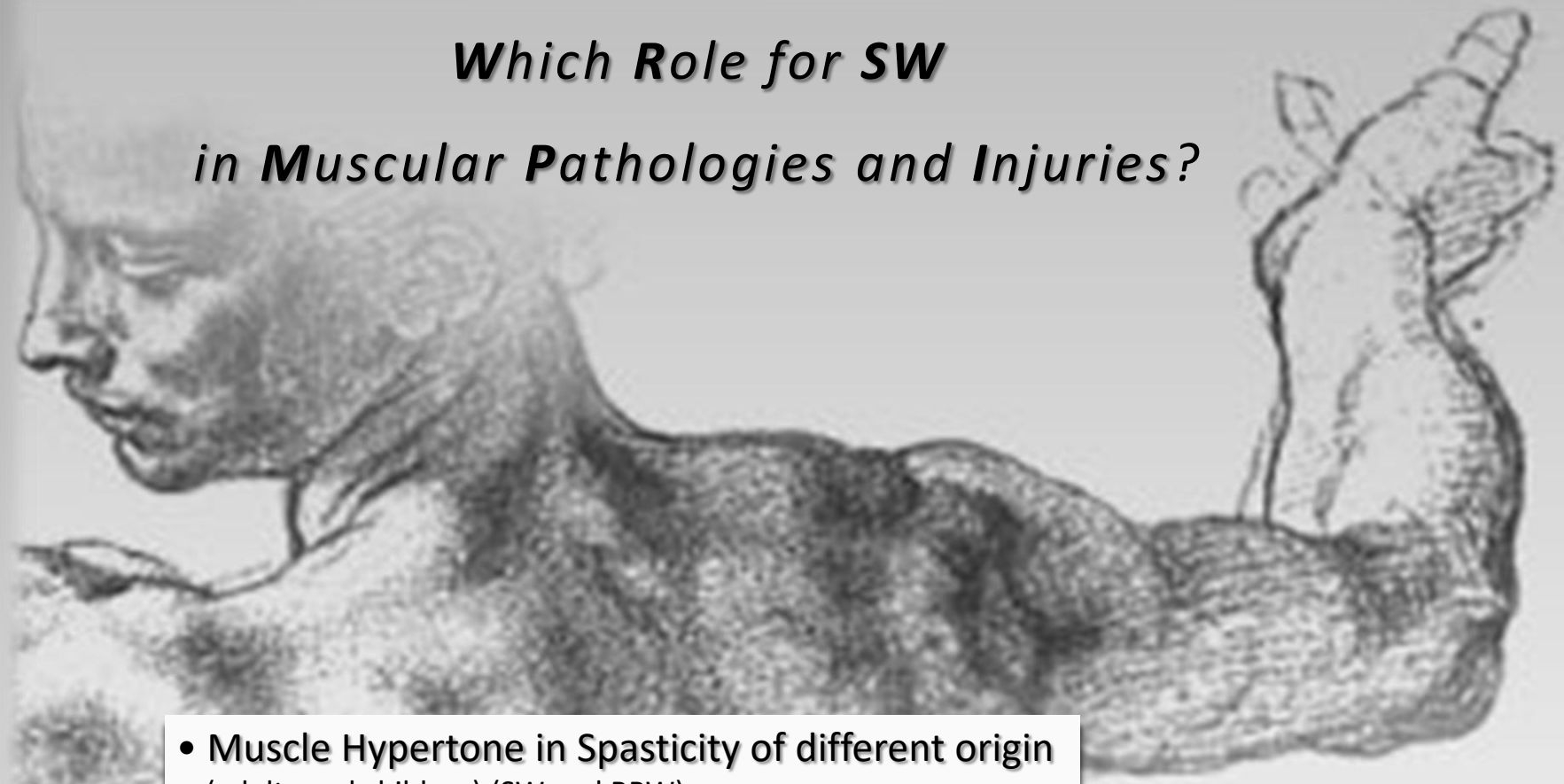
CONCLUSIONS:

This is the first study to show a significant increase in **neovascularization** and **neoinnervation** in calcific tendinitis lesions of the shoulder along with an eightfold increase in **mast cells and macrophages**. The findings are consistent with the hypothesis that, in calcific tendinitis, the calcific material is inducing a **vigorous inflammatory response within the tendon with formation of new blood vessels and nerves**.



Which Role for SW

in Muscular Pathologies and Injuries?



- Muscle Hypertone in Spasticity of different origin
  (adults and children) (SW and RPW)
- Myofascial Pain Syndromes
  (contractures and trigger points) (SW and RPW)
- Localized Ossificans Myositis
  (post-traumatic ossifications) (SW)
- Injury/Muscle Fibrosis of post-trumatic origin

J Surg Res. 2016 Apr;201(2):440-5. doi: 10.1016/j.jss.2015.11.049. Epub 2015 Nov 30.

Repetitive shock wave therapy improves muscular microcirculation.

Kisch T[1], Wuerfel W[2], Forstmeier V[3], Liodaki E[4], Stang FH[4], Knobloch K[5], Mailaender P[4], Kraemer R[4].

F

Am J Sports Med. 2017 Mar;45(3):676-684. doi: 10.1177/0363546516668622. Epub 2016 Oct 13.

Extracorporeal Shock Wave Therapy Accelerates Regeneration After Acute Skeletal Muscle Injury.

Zissler A[1], Steinbacher P[1], Zimmermann R[2], Pittner S[1], Stoiber W[1], Bathke AC[3], Sänger AM[1].

F

Oxid Med Cell Longev. 2018 Apr 2;2018:6012636. doi: 10.1155/2018/6012636. eCollection 2018.

Combined Therapy with Extracorporeal Shock Wave and Adipose-Derived Mesenchymal Stem Cells Remarkably Improved Acute Ischemia-Reperfusion Injury of Quadriceps Muscle.

Yin TC[1], Wu RW[1], Sheu JJ[2], Sung PH[3], Chen KH[4], Chiang JY[5], Hsueh SK[3], Chung WJ[3], Lin PY[6], Hsu SL[1], Chen CC[6], Chen CY[7], Shao PL[8], Yip HK[3,8,9,10,11].

F

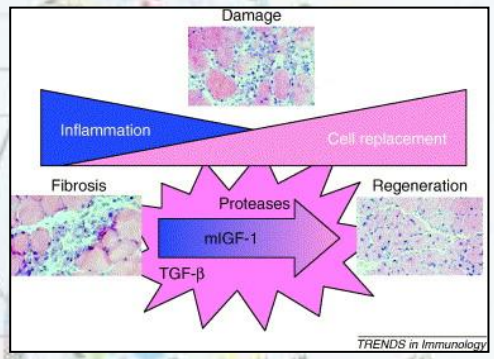
J Orthop Surg Res. 2018 Apr 6;13(1):75. doi: 10.1186/s13018-018-0779-0.

Exposure to radial extracorporeal shock waves modulates viability and gene expression of human skeletal muscle cells: a controlled in vitro study.

Mattyasovszky SG[1], Langendorf EK[2], Ritz U[2], Schmitz C[3], Schmidtmann I[4], Nowak TE[2], Wagner D[2], Hofmann A[2], Rommens PM[2], Drees P[2].

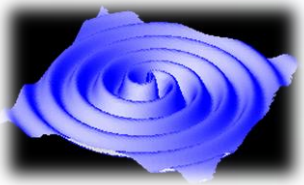
R

.. In tema di *Lesioni Muscolari* ..



.. Effective repair of skeletal muscle after severe injury is unlikely to be achieved with a single intervention ..

myogenic factors



stem cells

.. For full functional recovery of muscle there is a need to:

control inflammation,

stimulate regeneration,

limit fibrosis ..

β-agonists

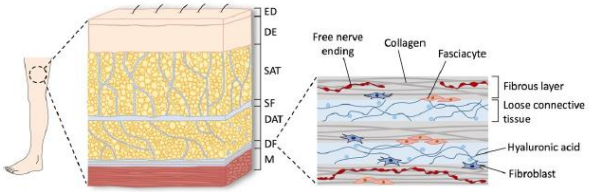
Sports Health. 2014 Jul;6(4):348-55.
Therapeutic approaches to skeletal muscle repair and healing.
Danna NR, Beutel BG, Campbell KA, Bosco JA 3rd.

life *Life* **2022**, *12*, 743. https://doi.org/10.3390/life12050743 MDPI

Review

Molecular Mechanisms Underlying the Pain-Relieving Effects of Extracorporeal Shock Wave Therapy: A Focus on Fascia Nociceptors

Larisa Ryskalin [1,2,*], Gabriele Morucci [1,2], Gianfranco Natale [1,2,3], Paola Soldani [1,2] and Marco Gesi [1,2]



Among numerous biological effects of ESWT, the pain-relieving effect remains the most intriguing one. Experimental results show that ESWT may influence the musculoskeletal system by specifically affecting nerve fibers. ESWT was shown to induce a selective destruction of sensory unmyelinated fibers, reduction and dispersion of pain mediators and nociceptive metabolites, and prevention of local tissue re-innervation, while altering pain neurotransmission. Moreover, ESWT application reduces the number of CGRP- and SP-positive neurons in the dorsal root ganglia.

Though the mechanisms underlying the etiology of MPS are far from being fully elucidated, a key role of intrinsic sensory innervation and pain receptors of the deep fascia is gradually gaining acceptance. Thus, it seems likely that all of these mechanisms might contribute to the analgetic working mechanism of ESW in MPS by reducing pain sensitivity and dorsal horn sensitization.

However, to date, there is no clear evidence on ESWT effects on the fascial nociceptive system.

Reduction of Pain Sensitivity and Dorsal Horn Sensitizazion

biomedicines Biomedicines 2022, 10, 1732. MDPI

Article

Immediate Effects of Extracorporeal Shock Wave Therapy in Fascial Fibroblasts: An In Vitro Study

Carmelo Pirri [1,*], Caterina Fede [1], Lucia Petrelli [1], Enrico De Rose [1], Carlo Biz [2], Diego Guidolin [1], Raffaele De Caro [1] and Carla Stecco [1,*]

The aim of this study was to investigate changes in cell biology of fibroblasts derived from deep/muscular fascia following treatment with ESWs (*100 impulses of 0.05 mJ/mm2 at 2.5 Hz*)

This study demonstrated for the first time that ESWs can lead to in vitro production of hyaluronan-rich vesicles immediately after the treatment. At 1, 4, and 24 h after treatment, Alcian blue and Toluidine blue staining; immunocytochemistry to detect ... acid binding protein (HABP), collagen I, and collagen III; and ... demonstrated that these vesicles are rich in ... vesicles was assessed ... at 4 and 24 h, ... release of hyaluronan-rich vesicles, ... with an increase at 4 h and maintenance by 24 h. These ... that fascial cells respond to ESW treatment by regulating and remodeling the formation of extracellular matrix.

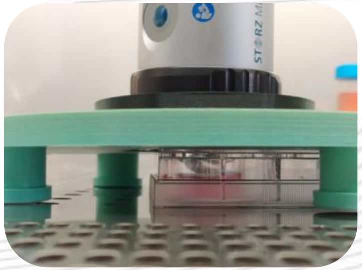
" .. fascial cells respond to ESW treatment by regulating and remodeling the formation of extracellular matrix .. «

→ Hyaluronan

→ Collagen I

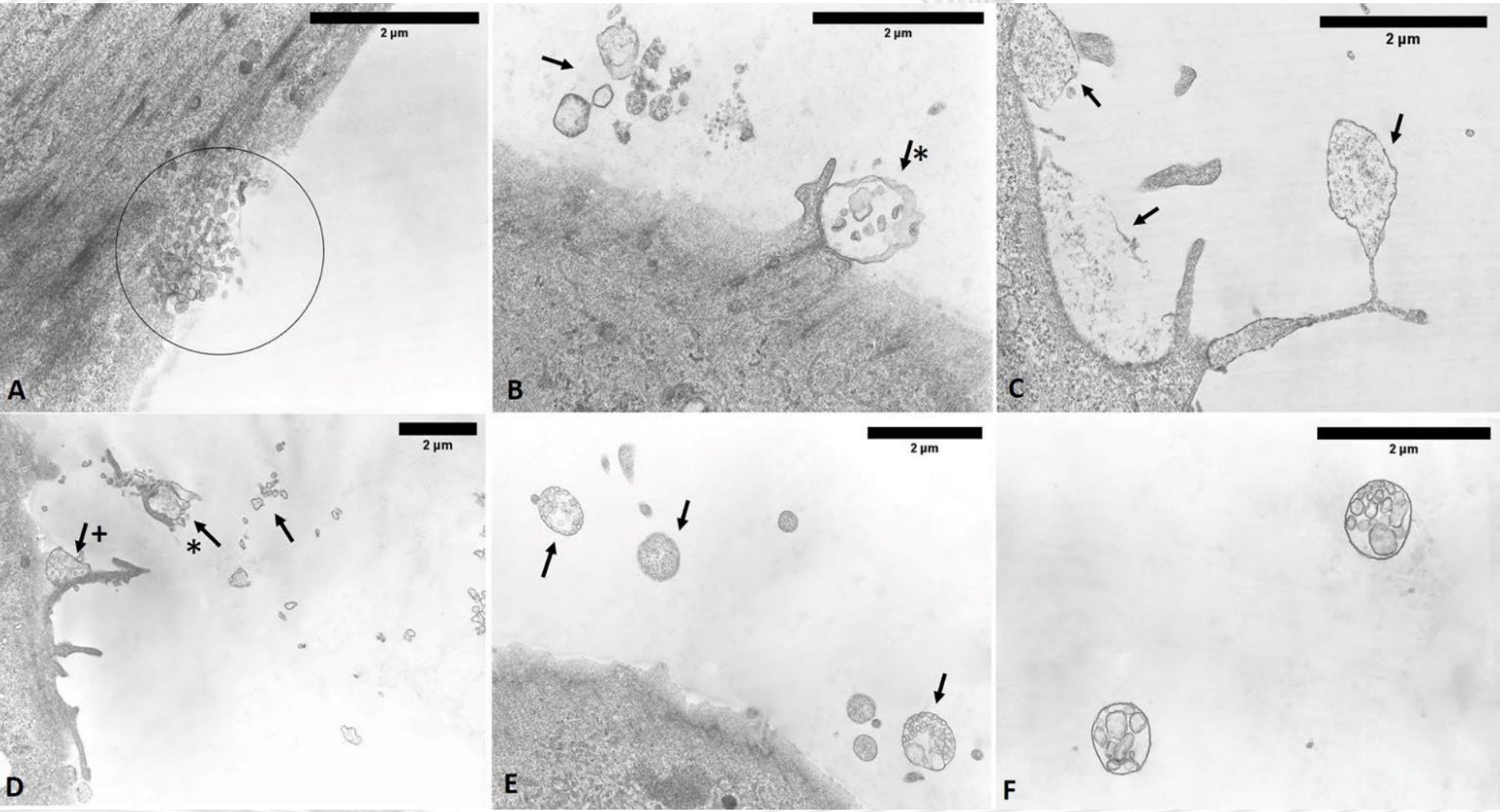
→ Collagen III

1 h → 4h → 24 h



Duolith SD-1 T-Top

This study indicates that fascial fibroblasts are metabolically “activated” by ESWT



*Pirri C et all, Biomedicines **2022**, 10, 1732*

Rehabilitation Programs

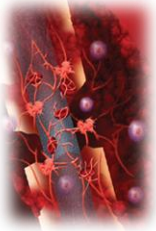
BIOPHYSICAL STIMULATION

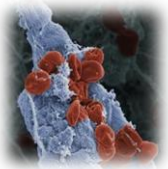
Interesting Therapeutic Strategies …

Mechanical Model

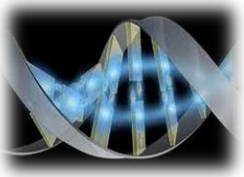
.. Work in Progress ..

Biological Model





SW as " BIOSURGERY "
in Regenerative Medicine ?!



1. Cardiology
2. Implantology
3. *Tissue Engineering*

If correctly applied, according to the

General SITOD - ISMST Reccomandations & "Good Clinical Practice" rules

Shockwaves ***do not*** damage tissues ..

.. via *Mechanotransduction, they*:

- stimulate normal cell functions
- induce biological "regeneration"
- restore physiological tissue *homeostasis*

.. As Biological Processes ..

.. They takes time to heal ..

.. Work in progress..

Take Home Messages

- Ormai passata la fase «pionieristica» → la ESWT trova indicazione versatile, di per sé stessa o anche come «adiuvante», in combinazione con altre terapie, sia conservative che chirurgiche
- In taluni casi puo' rappresentare valida alternativa all'intervento chirurgico, o strategia terapeutica per gli esiti invalidanti
- Offre l'interessante vantaggio di poter trattare contemporaneamente non solo i tendini, ma anche altre strutture sede di patologia ed origine di dolore (osso, muscoli e fasce)
- La ESWT rappresenta un valido strumento terapeutico ai fini della rigenerazione e rimodellamento tissutali → ***R****iabilitazione* ***R****igenerativa*
- E' necessario attendere anche diverse settimane, per apprezzare l'effetto terapeutico di «rigenerazione»

YOU'RE invited

www.sitod.it

Grazie per la

Vostra Cortese

Attenzione !