

6º Congresso Brasileiro de Tratamento por Ondas de Choque

Fundamentos • Indicações • Protocolo • Hands-on



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EFFECTS OF F-ESWT



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Shock Wave technique:

- stimulates tissue regeneration (metabolism and vascularity);
- reduces inflammation;
- relieves chronic localized pain.



Shock Waves can increase cell proliferation and collagen synthesis.

Integrated into a physiotherapy and rehabilitation program, they can be used as a complementary treatment to support tissue regeneration and the management of chronic muscle pain improving the quality of muscle tissue.



ESWT

Best statistically results in **ESWT VS PLACEBO**

Wang (2003) Gerdesmeyer (2003)

Reduction of pain and improvement of functional outcomes in more 90%

Malliaropoulos (2017) Pan (2003)

Reduction in number and size of calcification in 40-60%

Rebuzzi (2008) Cosentino (2003) Wang (2003)

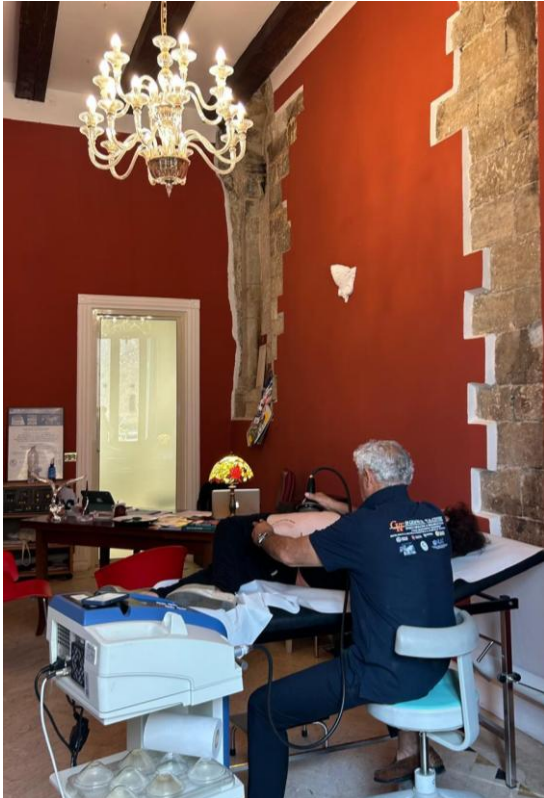
Overlapping clinical outcomes between surgery and ESWT (in early stage)

Rompe (2011) Rebuzzi (2008)

Protocol – ESWT

Treatment protocol:

- **N° of sessions:** variable (minimum of 6 sessions, once a week) and repeatable in the following months
- **N° of pulses:** 3.000 pulses per session
- **Frequency:** 5 Hz
- **Duration of each session:** 10 minutes
- **Energy Flux Density:** variable (according to patient's tolerance) between 0,10 and 0,20 mJ/ mm²



PROTOCOL TREATMENT

- **Pressure Exerted**: depending on operator
- **Manipulus angolation** : depending on operator
- **Manipulus movement**: depending on operator
- **Pre-Treatment with Local anesthesia**: no

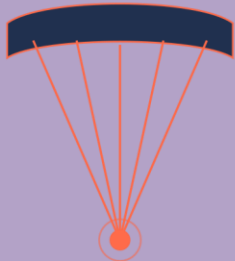
From Mechanical Impulse to Biological Signal: The Physics of Focal Shock Waves

- Focal shock waves: high-amplitude, sub-microsecond acoustic pulses
- Generated by electrohydraulic, electromagnetic, or piezoelectric sources and converged onto a defined focal volume → distinct from radial/ballistic pressure waves
- Energy flux density (EFD, mJ/mm^2) is the key clinical parameter: "same tool, different dose," from lithotripsy ($>100 \text{ MPa}$) down to ultra-low regenerative protocols ($<0.1\text{--}0.2 \text{ mJ}/\text{mm}^2$)
- Tissue-level effects: direct compressive/tensile stress, transient cavitation (microbubble formation and collapse generating microjets), and acoustic microstreaming
- These physical events open mechanosensitive channels, transiently permeabilize the membrane, and engage integrin-focal adhesion complexes → the starting point of mechanotransduction

From Mechanical Impulse to Biological Signal: The Physics of Focal Shock Waves

Focused vs. Radial Wave Geometry

Focused (Focal)



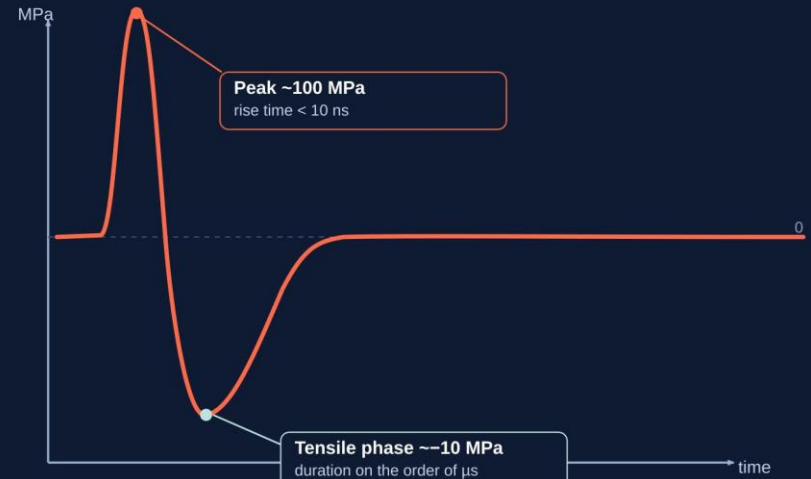
Converges at a focal point
reaches deep tissue targets
high, tightly-defined peak pressure

Radial (Ballistic)



Diverges from the applicator
superficial, lower amplitude
peak pressure ≈ 1 MPa

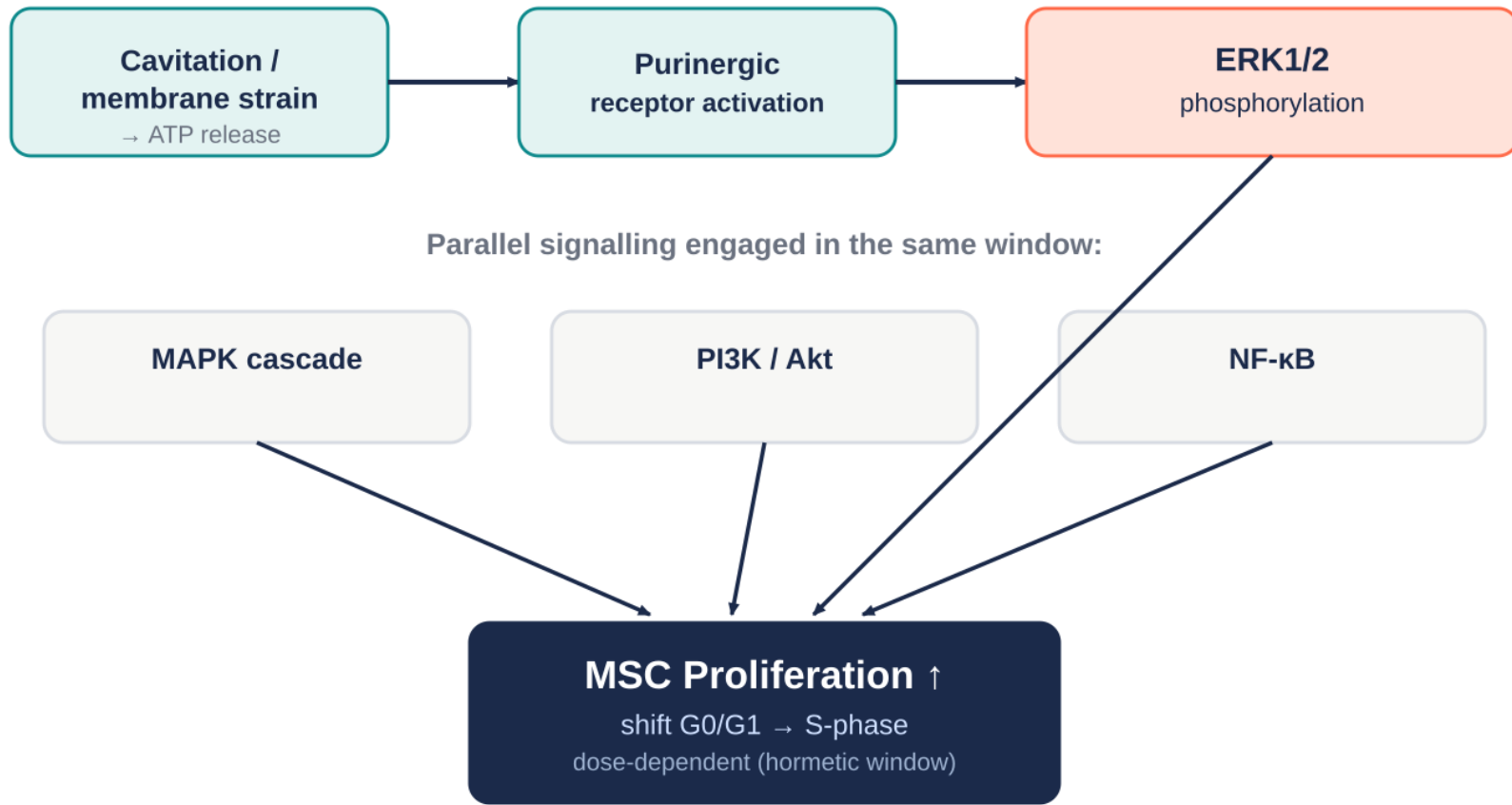
Shock-Wave Pressure–Time Profile



Biphasic pulse $\rightarrow$ direct compressive/tensile strain + cavitation at the cell membrane

Cell-Cycle Kinetics

- F-ESWT increase MSC proliferation across sources: bone-marrow-derived, adipose-derived, and umbilical-cord-blood MSCs
- F-ESWT on human BMSCs: increased proliferation and migration, reduced apoptotic rate, differentiation potential preserved
- Cell-cycle shift from G0/G1 into S-phase: a genuine mitogenic, not purely metabolic, effect
- Extracellular ATP release → purinergic receptor activation → ERK1/2;
MAPK, PI3K/Akt, and NF-κB pathways also implicated
- Dose-response ceiling: cytotoxicity and necrosis reported near 0.27 mJ/mm²



MSC Migration / Homing

- Enhanced MSC/progenitor migratory capacity in vitro and increased recruitment to the treated microenvironment in vivo

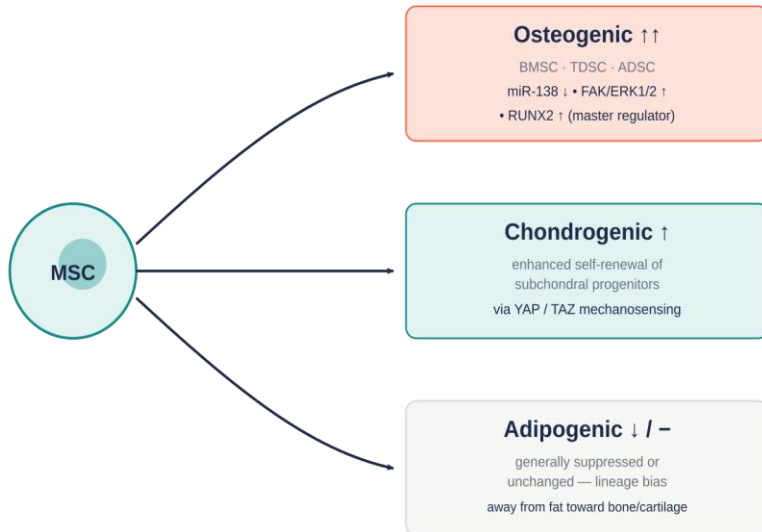
Central axis: SDF-1 (CXCL12) / CXCR4, with integrin-mediated arrest (VLA-4–VCAM-1) and FAK activation

- F-ESWT locally upregulate SDF-1 in target tissue (skeletal muscle, corpus cavernosum, myocardium, pancreas) creating a chemotactic gradient
- Downstream requirement: ERK1/2 and PI3K/Akt activation for the migratory response

Translational rationale: shock-wave "preconditioning" of the tissue bed to improve homing efficiency of co-administered or endogenous MSCs

MSC Lineage Differentiation

Sequential recruitment → proliferation → chondrogenic/osteogenic differentiation

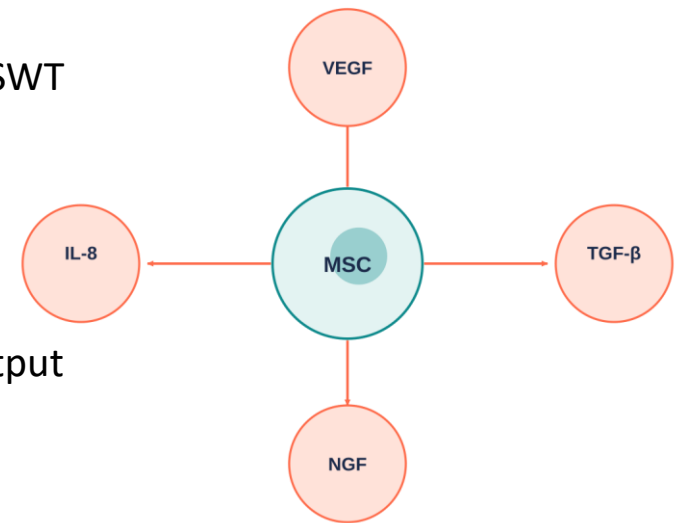


- Osteogenic differentiation is the best-characterized effect: F-ESWT ($\sim 0.16 \text{ mJ/mm}^2$) promotes osteogenesis in BMSCs, tendon-derived, and adipose-derived stem cells via a shared axis
- Chondrogenic potential: shock-wave-preconditioned MSCs show enhanced self-renewal and improved cartilage-defect healing, partly via YAP/TAZ mechanosensitive coactivators
- Adipogenic differentiation: generally suppressed or unchanged

Effects are dose, source, and protocol dependent: not a universal, one-size-fits-all response

MSC Secretome

- MSC-mediated regeneration is largely paracrine/trophic: F-ESWT amplifies this secretory phenotype
- Increased secretion of VEGF, TGF- β , NGF, and IL-8 following stimulation
- Mechanistic axis in adipose-derived MSCs:
FAK/p38-MAPK $\rightarrow$ GATA4 upregulation $\rightarrow$ increase VEGF/NGF output



Improved graft maturation after ACL reconstruction; enhanced revascularization/reinnervation in diabetic bladder and erectile tissue; improved re-endothelialization in chronic limb ischemia

FAK $\rightarrow$ p38 MAPK $\rightarrow$ GATA4 $\rightarrow$ $\uparrow$ VEGF / NGF secretion
(shown in adipose-derived MSCs)

F-ESWT acts as a "volume knob" on the MSC's native trophic program, not a scalpel

MSC-Derived Extracellular Vesicles

- Newest mechanistic layer (2024–2026 literature): F-ESWT trigger release and cargo remodeling of MSC-derived extracellular vesicles (EVs) (exosomes and microvesicles), not just soluble factor secretion

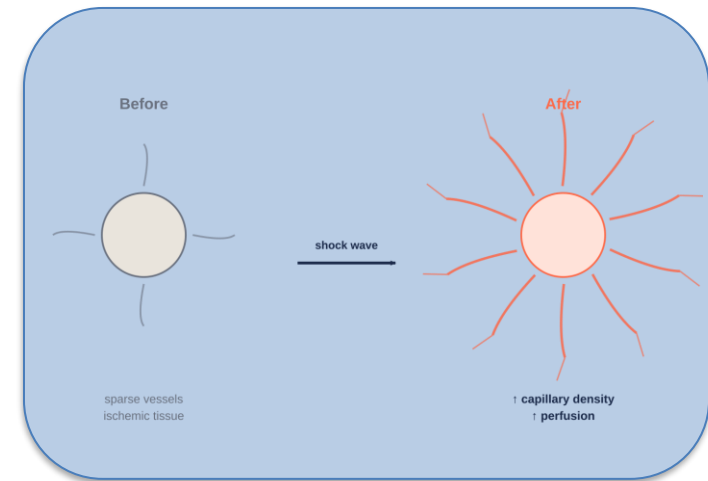
ATP release → P2X7 receptor → p38 MAPK, alongside nSMase2/ceramide-driven multivesicular body formation

- F-ESW-conditioned EVs enriched in pro-angiogenic, anti-apoptotic, antioxidative, and immunomodulatory microRNAs, proteins, and transcription factors
- Conceptual meaning: reframes the MSC as a cell-free "signal factory" SW-primed EVs are being explored as off-the-shelf regenerative products

Regenerative Effects on Tissue: Angiogenesis and Neovascularization

- Angiogenesis is the best-validated in vivo regenerative endpoint of focal shock wave therapy
- Dose-response data: angiogenic gene expression, AKT/ERK phosphorylation, and endothelial proliferation increase progressively up to $\sim 0.15 \text{ mJ/mm}^2$ EFD; necrosis only appears above $\sim 0.27 \text{ mJ/mm}^2$
- Molecular mediators: VEGF-A upregulation (Ras $\rightarrow$ superoxide $\rightarrow$ ERK $\rightarrow$ HIF-1 axis), eNOS, PCNA, chemoattractant factor expression

In vivo outcome: increased capillary density, improved tissue perfusion, functional recovery of ischemic tissue



Regenerative Effects on Tissue: Inflammation Modulation and Clinical Translation

M1 (pro-inflammatory)



M2 (reparative)



- F-ESWT shift macrophage polarization from pro-inflammatory M1 toward reparative M2 (decreased TNF- α /IL-23, increased IL-10/TGF- β)

Combined effect across all mechanisms discussed: clinical benefit in delayed/non-union fracture, tendon-to-bone healing, chronic/diabetic wound healing, diabetic erectile dysfunction, adjunctive treatment of chronic myocardial ischemia

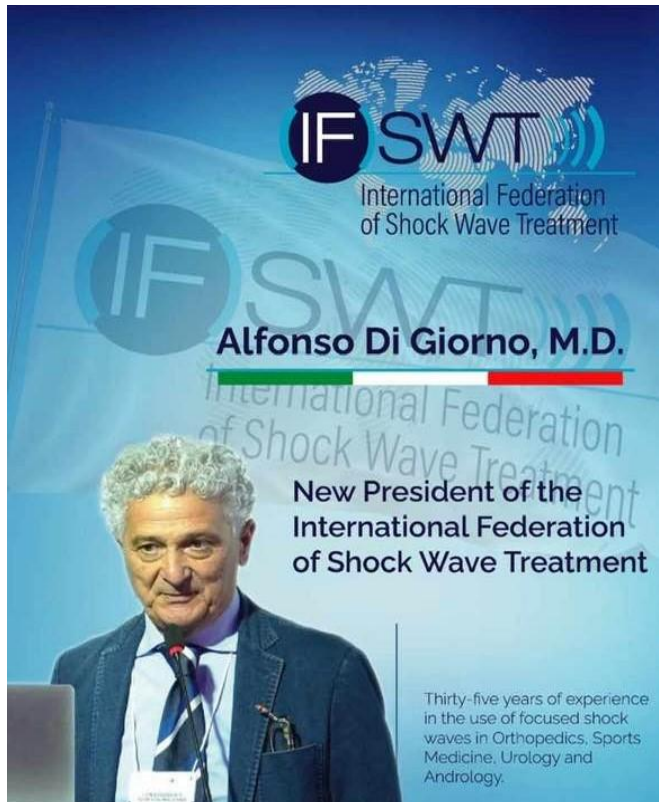
F-ESWT is a physical stimulus that recalibrates the local regenerative niche

→ Barrier to consensus: heterogeneity in reported EFD, pulse number/frequency, and focal geometry across devices and trials

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