Effects of exposure of musculoskeletal tissue to extracorporeal shock waves

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Supplementary Material

Table S1: effects of the exposure of bone and cartilage tissue to extracorporeal shock waves

Reference No.	Author	Year	Study type	Utilized device	Cell type investigated	Morphological, functional, radiological findings	Findings of molecularbiological examinations	Findings of histological examinations
[18]	Li et al.	2021	Primary cell culture + animal experiment	Epos Ultra, Dornier MedTech, Wessling, Germany	Rabbit femur BMSC	Increased mineral apposition rates, trabecular bone volume, number, thickness; decreased trabecular separation	Increased expression of ALP, OCN, RUNX2, OPG /// SMAD2	
[19]	Inoue et al.	2021	Animal experiment	Physio ShockMaster, SAKAI Medical Co., Ltd., Tokyo, Japan	Rat osteoporotic model	Increased trabecular bone microarchitecture and bone strength	Decreased RANKL	
[20]	Inoue et al.	2021	Animal experiment	Physio ShockMaster, SAKAI Medical Co., Ltd., Tokyo, Japan	Rat osteoporotic fracture models	Increased bone volume/tissue volume		Increased osteoblast surface, decreased number of sclerostin positive osteocytes
[21]	Zhao et al.	2021	Primary cell culture + animal experiment	Swiss DolorClast Master (Electro Medical Systems SA, Switzerland).	Human SBC-SPCs // rabbit osteochondral injury model		Unaltered expression of OCN, RUNX2, COL2, SOX9; decreased expression of CEBPα and PPARγ; increased expression of YAP	Increased proliferation
[22]	Kobayashi et al.	2020	Animal experiment + secondary cell culture	Duolith® SD1-Storz Medical AG, Tagerwilen, Switzerland	Rat femur delayed union // ATDC5 cells	Increased bone union rate, radiographic score		Increased enchondral ossification, chondrogenic differentation without inhibing proliferation
[23]	Alshihri et al.	2020	Primary cell culture	PiezoClast EMS, RICHARD WOLF GmbH, Knittingen, Germany	Goat iliac crest BMSC			Unaltered cell migration; increased proliferation and osteogenic differentation
[24]	Hsu et al.	2020	Animal experiment	Duolith® SD1-Storz Medical AG, Tagerwilen, Switzerland	Rat osteoporotic model	Increased bone strenght, bone mineral density, trabecular thickness, bone volume/tissue volume, porosity		Increased expression of BMP2, BMP4, and Wnt3a signaling; unaltered expression of IGF1
[25]	Ramesh et al.	2020	Animal experiment	Radial Spec., Medi Spec., Gaithersburg, MD, USA	Cultured fetal rat metatarsal bones	Increased bone length		Increased number of proliferative chondrocytes of growth plate's cartilage and diameter of hypertrophic chondrocytes; activation of IGF1 and NFkb; increased levels of Bcl2 and Bcl-xL
[26]	Colbath et al.	2020	Primary cell culture	Pulse Veterinary Technologies, LLC	Equine BMSC		Increased expression of ALP, decreased expression of TGFb, VEGF	
[27]	Hashimoto et al.	2019	Animal experiment	Dornier MedTech; Dornier ARIES Vet	Rat meniscus model		Increased expression of COL2a1, ACAN, CCN2, SOX9	Increased meniscal healing score and BrdU/CCN2-ratio
[28]	Senel et al.	2019	Animal experiment	Orthogold 100, MTS Medical, Konstanz, Germany	Rabbit osteotomy model	Bone mineral density, bone mineral content		
[29]	Kim et al.	2019	Primary cell culture + animal experiment	Dornier AR2 electromagnetic head applicator	Rat chondrocytes // rat temporomandibular joint osteoarthritis model	Increased structure and bone quality	Decreased expression of TNFa, IL1b, IL6, MMP3, MMP13, BMP7	Increased cell viability; decreased number of apoptotic cells and pro-inflammatory, cartilage degradation markers
[30]	Buarque de Gusmao et al.	2019	Animal experiment	Evotron, SwiTech Medical AG, Kreuzlingen, Switzerland (fok.) // MP 100, Storz Medical, Tägerwilen, Switzerland (rad.)	Rat tibial defects		fESWT: increased Akt and FAK activity and TGFb1 expression rESWT: increased FAK activity, decreased FAK activity	
[31]	Cheng et al.	2019	Animal experiment	Duolith® SD1-Storz Medical AG, Tagerwilen, Switzerland	Rat knee osteoarthritis model: subchondral bone / articular cartilage	Enhanced bone volume and trabecular thickness		Reduced synovitis and cartilage damage, decreased expression of MMP-13, enhanced expression of RUNX-2, SOX-9 and Collagen Xα1, enhanced expression of IGF-1, TGF-β1, type II collagen and decreased TUNEL activity
[32]	Ginini et al.	2019	Animal experiment	Dermagold 100, Tissue Regeneration Technologies, Woodstock, GA, manufactured by MTS, Konstanz, Germany	Distraction osteogenesis in rats mandible: ESWT during distraction period	Increased mineral density, enhanced bone formation		Higher collagen orientation index, expression of type I collagen and osteocalcin proteins
[33]	Ginini et al.	2018	Animal experiment	Dermagold 100, Tissue Regeneration Technologies, Woodstock, GA, manufactured by MTS, Konstanz, Germany	Distraction osteogenesis in rats mandible: ESWT during consolidation period	Higher degree of bone formation and mature bone, increased bone mineral density, bone volume fraction, and trabecular thickness		Enhanced expression of bone morphogenetic protein-2, vascular endothelial growth factor, and proliferating cell nuclear antigen
[34]	Qi et al.	2018	Animal experiment	STORZ device (STORZ Medical, Tägerwilen, Switzerland) (radial)	Treatment of osteochondral defects of rabbit knees with scaffolds	Improved International Cartilage Repair Society (ICRS) score and macroscopic osteochondral appearance		
[35]	Koolen et al.	2018	Animal experiment	Orthogold 180 c; MTS Medical, Konstanz, Germany	Screw fixation of rat cortical and cancellous bones	Cortical screws: increased bone formation and screw fixation; cancellous screws: no alterations		
[36]	Mackert et al.	2017	Animal experiment	Duolith® SD1-Storz Medical AG, Tagerwilen, Switzerland	Osteoporotic fracture of rats tibia	Improved average stiffness and yield load	Increased expression of Collagen 1-alpha-1, Estrogen Receptor-α, Insulin-like Growth Factor 1, Osteocalcin, Tartrate-resistant Acid Phosphatase	Improved average ventral, dorsal and endosteal callus formation
[37]	Tan et al.	2017	Primary cell culture	KDE-2001 Extracorporeal Shockwave Lithotripter	HMSCs under 3D culture conditions		ESWT alone: increased levels of A2B receptors; ESWT in combination with adenosine and A2BR-agonists downregulated ACAN, COL1A2, COL2A1, SOX9 and SOX6	ESWT + adenosine and A2BR-agonists: inhibited chondrogenic differentation
[38]	Hsu et al.	2017	Animal experiment	not specified	Rat knee osteoarthritis model		Increased expression of ERK1, OPG, ALP, MMP13; potential activation of the 1α,25-Dihydroxyvitamin D3 Rapid Membrane Signaling Pathway	Increased expression of Pdia-3
[39]	Yilmaz et al.	2017	Animal experiment	Duolith® SD1-Storz Medical AG, Tagerwilen, Switzerland	Rat knee osteoarthritis model	Increased osteoblastic activity, improved pain score		Lower modified Mankin score
[40]	Wang et al.	2017	Animal experiment	OssaTron (SANUWAVE Health, Inc., Alpharetta, GA)	Rat knee osteoarthritis model	Improved OARSI score and gross pathological changes, less cartilage defect, higher bone mineral density and bone volume, improved bone porosity and yield stress		Increased expression PCNA and osteocalcin, decreased expression of TUNEL
[41]	Chen et al.	2017	Primary cell culture	Huikang type IV (Huikang, Shengzhen, China)	BMSC in osteogenic medium and implantation in mid-femur bone defects in rats	In vivo: improved bone volume, trabecular volume, BV/TV, bone thickness and bone mineral density	In vitro: increased expression of Col1, Runx2, osterix, and ALP	In vitro: enhanced proliferation and osteogenic differentation; in vivo: increased bone formation and expression of Runx2 and Osterix
[42]	Onger et al.	2017	Animal experiment	OE050 focused applicator, Orthogold 100, MTS, Konstanz, Germany	Distraction osteogenesis in rats mandible: ESWT during consolidation period	500 impulses per treatment: unaltered bone volume/bone density 1000 impulses per treatment: enhanced bone volume, bone density		500 impulses per treatment: enhanced capillary volume, decreased connective tissue volume 1000 impulses per treatment: enhanced capillary volume more positive areas of staining with VEGF, collagen antibody, BMP7 compared to control, but decreased capillary volume compared to 500 impulses; unaltered connective tissue volume;
[43]	Wang et al.	2017	Animal experiment	OssaTron (SANUWAVE Health, Inc., Alpharetta, GA)	Rat knee osteoarthritis model	Improved OARSI score and gross pathological changes, less cartilage defect, improved BV/TV ratio, improved bone porosity and trabecular thickness		Decreased expression of TUNEL, higher amount PCNA-positive cells and increased vascular density; increased cartilage thickness and sectional cartilage area, decreased modified Mankin score
[44]	Lama et al.	2017	Animal experiment	Duolith® SD1-Storz Medical AG, Tagerwilen, Switzerland	Rat osteoporotic model	Prevention of bone weight reduction and trabecular microarchitecture deterioration; restored serum parameters of alkaline phosphatase, receptor activator of nuclear factor kappa-B ligand, osteoprotegerin, and PTH due to illness	Reduced cathepsin k, TNF-α levels, PPARγ and adiponectin transcription; increased runt-related transcripiton factor 2 and bone morphogenetic-2 expression	
[45]	Catalano et al.	2017	Primary cell culture	Piezoson 100, Richard Wolf, Knittlingen, Germany	Human adipose-derived mesenchymal stem cells		Increased ERK phosphorylation, ROS formation, RUNX2, ALP, BMP2	Increased Smad phosphorylation

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Reference No.	Author	Year	Study type	Utilized device	Cell type investigated	Morphological, functional, radiological findings	Findings of molecularbiological examinations	Findings of histological examinations
[46]	Ma et al.	2017	Animal experiment	Orthospec (Medispec, Gaithersburg, MD, USA)	Rabbit necrotic femoral head model	Higher bone volume per tissue volume, trabecular thickness, trabecular number, osteoblast surface/bone surface, osteoid surface/bone surface, osteoid thickness, mineralizing surface/bone surface, mineralizing apposition rate, and bone formation rate as well as a reduced trabecular separation		
[47]	Huang et al.	2016	Animal experiment	Orthospec™ (Medispec, Israel)	Osteoporotic fracture of rats tibia		Increased expression of osteoprotegerin and bone morphogenetic protein-2	
[48]	Notarnicola et al.	2016	Primary cell culture	Minilith SL1 (STORZ, Germany)	Human bone marrow stem cells		Increased expression of BMP, alkalaine phosphatase, osteocalcin, COL1A1 and RUNX2	Enhanced cell adhesion and proliferation
[49]	Zhai et al.	2016	Primary cell culture	MFL 5000 Lithotriptor, Dornier Medizintechnik, Wessling, Germany	Human bone mesenchymal stem cells from patients with avascular femoral head necrosis		Increased expression of osteocalcin (OCN), core binding factor α1 (Cbfα1) and decreased peroxisome proliferator-activated receptor γ	Increased alkaline phosphatase content
[50]	Dias dos Santos et al.	2015	Animal experiment	EVOTRON-Vet® (SwiTech, Switzerland)	Bone drilled femurs of rats		Increased contents of sulfated glycosaminoglycans and hyaluronic acid	
[51]	Wang et al.	2014	Animal experiment	OssaTron (SANUWAVE Health, Inc., Alpharetta, GA)	Rat osteoporosis and/or osteoarthritis model	Reduced arthritic area of injury joint, enhanced BMD and bone strength, improved subchondral plate thickness and bone porosity, reduced cartilage damage		Increased Mankin and safranin O score, improved alterations of the molecular levels due to the illness of Dickkopf-1 (DKK-1), PCNA, VEGF, and BMP-2
[52]	Muzio et al.	2014	Secondary cell culture	Piezoson 100, Richard Wolf, Knittlingen, Germany	Blocking of BMP of ESW-treated human osteoblast-like cells		Decreased alkalaine phosphatase and osteocalcin	Increased cell growth
[53]	Oktas et al.	2014	Animal experiment	Stonelith PCK® lithotripter (Turkey, Ankara)	Fractures with both intact periosteum and excised periosteum in rats	No radiologic differences		Excised periosteum group: positive effect on bone healing
[54]	Sun et al.	2013	Primary cell culture	KDE-2001 Extracorporeal Shockwave Lithotripter	Osteogenic differentation of human bone marrow mesenchymal stem cells		Shockwave-dependent ATP release, that activated P2X7 receptors and downstream signaling events, which induced the differentation	
[55]	Suhr et al.	2013	Primary cell culture	Duolith®SD1 (Storz Medical AG, Trägerwilen, Switzerland)	Human bone marrow stromal cells			Extended growth rate, proliferation, migration, cell tracking and wound healing; ameliorated cell migration meditated by active remodeling of the actin cytoskeleton as indicated by increased directed stress fiber formations
[56]	Lyon et al.	2013	Animal experiment	not specified	Osteochondrosis dissecans of rabbit knees	Increased bony density		More mature bone formation, better healing, higher density of the cartilage
[57]	Wang et al.	2013	Animal experiment	OssaTron (SANUWAVE Health, Inc., Alpharetta, GA)	Rat knee osteoarthritis model	Increased bone mineral density		Improved Makin and Safranin O score, increased collagen II, decreased MMP13
[58]	Wang et al.	2013	Animal experiment	OssaTron (SANUWAVE Health, Inc., Alpharetta, GA)	Rat knee osteoarthritis model			Treamtent 1-2 times per week: improved Makin and Safranin O score, increased collagen II, decreased MMP13, increased vWF, VEGF, BMP-2 and osteocalcin; deteriorated effects after 3 treatments per week
[59]	van der Jagt et al.	2013	Animal experiment	Dermagold, Tissue Regeneration Technologies, Woodstock, GA, manufactured by MTS, Konstanz, Germany	Rat osteoporotic model	Increased cortical volume (CtV), higher trabecular connectivity and, more plate like and thicker trabeculae, increased trabecular bone volume fraction		
[60]	Oztemur et al.	2013	Animal experiment	Storz Masterpuls MP200 (STORZ, Germany)	Immature epiphysis of rats	No changes in bone length		Increased blood vessel density, highly basophilic matrix and abundance of the differentiating chondrocytes
[61]	Gollwitzer et al.	2013	Animal experiment	Swiss Dolorclast® (Electro Medical Systems SA, Switzerland)	Rabbit femurs	New bone formation		
[62]	Altuntas et al.	2012	Animal experiment	Storz Masterpuls MP200 (STORZ, Germany)	Rat subcondylar mandibular fracture model			Higher specimens' mean score in bone fracture healing
[63]	Notarnicola et al.	2012	Primary cell culture	enPuls, Zimmer MedizinSysteme GmbH, Germany	Murine calvaria osteoblasts		Reduction in type 1 collagen, osterix, bone sialoprotein and receptor activator NF kappa ligand expression, osteocalcin, and osteopontin; in summary: inhibing effect on osteoclastogenesis	
[64]	Zhao et al.	2012	Animal experiment	Swiss Dolorclast® (Electro Medical Systems SA, Switzerland)	Rabbit knee osteoarthritis model	Decreased NO level, and severity of cartilage lesions		Decreased chondrocyte apoptosis, enhanced Mankin score
[65]	Kearney et al.	2012	Animal experiment	OssaTron (SANUWAVE Health, Inc., Alpharetta, GA)	Rabbit tibia			Increased cambium cell number, cambium cell thickness, osteous tissue and callus area, larger amount of osteoprogenitor tissue; improved results in combination with a bioactive scaffold
[66]	Xu et al.	2012	Primary cell culture	Huikang type IV (Huikang, Shengzhen, China)	Rat osteoblasts		Promotion of Integrin alpha-5 and beta-1-expression; induction of phosphorylation of the focal adhesion kinase, which led to an increased adhesion and migration of osteoblasts	
[67]	Wang et al.	2012	Animal experiment	OssaTron (SANUWAVE Health, Inc., Alpharetta, GA)	Osteoarthritis of rat knees			Improved Makin and Safranin O score, increased collagen II, VEGF, BMP-2 and osteocalcin expression
[68]	Ertürk et al.	2012	Animal experiment	Multimed Ortho (ElmedElectronics & Medical Industry & Trade Inc., Ankara, Turkey)	Intervertebral cartilage endplate in rabbits	No alterations in MRI		Edema, increased fibroblastic activity, neovascularisation
[69]	Wang et al.	2011	Animal experiment	OssaTron (SANUWAVE Health, Inc., Alpharetta, GA)	Osteoarthritis of rat knees	Increased BMD, bone strength, modulus of elasticity		Decreased Mankin score, improved Safranin O staining results, increased expression of VWF, VEGF, BMP2, OCN, ALP, decreased expression of CTXII, COMP
[70]	van der Jagt et al.	2011	Animal experiment	Dermagold; TissueRegeneration Technologies, Woodstock, Georgia, manufactured by MTS, Konstanz, Germany	Rat tibia	Increased 99mTc-MDP uptake, increased trabecular and cortical bone volume, higher bone stifness; no alterations in microcrack analysis		Soft tissue damage, no periostal damage, de novo bone with active osteoblasts and osteoids
[71]	Notarnicola et al.	2011	Primary cell culture	Minilith SL1 (STORZ, Germany)	Murine calvaria osteoblast culture		Increased expression of RUNX2, COL1, OCN, IGF-1, IGFBP-3; decreased expression of IGFBP-4 and -5	
[72]	Hausdorf et al.	2011	Secondary cell culture	XL 1 (Dornier MedTech, Wessling, Germany)	Human osteoblasts and fibroblasts		Increased FGF-2; no significant alterations in TGF-b	
[73]	Wang et al.	2011	Animal experiment	OssaTron (SANUWAVE Health, Inc., Alpharetta, GA)	Rabbit tibia acute fracture healing model	Increased BMC		Increased bone tissue, decreased fibrous tissue; increased expression of VEGF, VWF, PCNA, OCN, BMP2, decreased expression of TUNEL

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[74]	Mayer-Wagner et al.	2010	Animal experiment	XL 1 (Dornier MedTech, Wessling, Germany)	Rat knee		Increased COL2A1 expression	Ultrastructural expansion of the rough-surfaced endoplasmatic reticulum, detachment of the cell membrane and necrotic chondrocytes; increased tenascin-C and Chi3L1; no alterations in Mankin Score
[75]	Muzio et al.	2010	Secondary cell culture	Piezoson 100, Richard Wolf, Knittlingen, Germany	Human osteoblast-like cells		Increased expression of ALP, COL1, BMP-4, OCN	Increased osteoblast activity as well as number and size of calcium deposits
[76]	Lai et al.	2010	Animal experiment	OssaTron (High Medical Technology, Kreuzlingen, Switzerland)	Distraction osteogenesis of rat mandible	Treatment with 14kV: increased mineral densitiy, biomechanical bone strength, intense osteoblastic cell recruitment, new bone formation		Treatment with 14kV: intense osteoblastic cell recruitment, new bone formation, neovascularisation, increased PCNA, VEGF, BMP-2; opposite effects after treatment with 21kV
[77]	Qin et al.	2010	Animal experiment	Dornier MedTech Epos, Wessling, Germany	Rabbit osteotendinous junction	Higher fraction of new bone		Increased VEGF expression in hypertrophic chondrocytes, promotion of regeneration of the fibrocartilage zone
[78]	van der Jagt et al.	2009	Animal experiment	Dermagold/Orthowave 180, Tissue Regeneration Technologies, Woodstock, GA	Rat tibiae osteoporotic model	Diminished bone loss, higher trabecular bone volume fraction		No differences in mineralization or osteoid appearance
[79]	Iannone et al.	2009	Primary cell culture	MINILITH SL1; Storz Medical, Kreuzlinger, Switzerland	Human osteoarthritic and healthy osteoblasts		Increased expression of IL10, no alterations in TGFa, CD29, CD105 expression	
[80]	Tamma et al.	2009	Primary cell culture	MINILITH SL1; Storz Medical, Kreuzlinger, Switzerland	Murine calvaria osteoblasts		Increased expression of Bax, RUNX2, OPN, BSP, OCN, COL1, decreased RANKL/OPG-ratio suggesting inhibition of osteoclasogenesis	
[81]	Lee et al.	2009	Animal experiment	OssaTron (High Medical Technology, Kreuzlingen, Switzerland)	Rabbit spinal fusion model	Increased callus formation and both extension and flexion stiffness		
[82]	Tam et al.	2009	Animal experiment	Epos Ultra with EMSE O-140-AL source, Dornier MedTech, Wessling, Germany	Calcaneus of ovariectomized goats	Enhanced trabecular bone mineral density, trabecular bone volume fraction (BV/TV), trabecular thickness		Increased mineral apposition rate
[83]	Hofmann et al.	2008	Primary cell culture	Sonocur Plus device (Siemens AG)	Primary human cancellous bone osteoblasts		Altered expression of several genes involved in bone formation, osteoblast differentation and skeletal development; no alterations in Runx2, osterix, osteopontin, osteonectin, OC, TGFb1 expression	Enhanced mineralization and number of AP-positive osteoblasts
[84]	Tam et al.	2008	Primary cell culture	Dornier MedTech, Wessling, Germany	Human periosteal osteoblasts		Decreased cell viability 6 days after treatment, increased viability 18 days after treatment; increased cell proliferation 18 days after treatment	Enhanced mineralization 35 days after treatment and AP activity 18 days after treatment
[85]	Lee et al.	2008	Animal experiment	OssaTron (High Medical Technology, Kreuzlingen, Switzerland)	Rabbits with dissociated transverse processes	New bone formation		Superior fusion mass
[86]	Wang et al.	2008	Animal experiment	OssaTron (Sanuwave, Alpharetta, GA, USA)	Rabbit femur closed fracture model	Increased bone strength		Increased cortical bone formation, higher number of neovessels, increased expression of VEGF, eNOS, PCNA, and BMP-2
[87]	Moretti et al.	2008	Primary cell culture	MINILITH SL1; Storz Medical, Kreuzlinger, Switzerland	Human osteocytes: healthy and osteoarthritic		Decreased expression x of IL-10, TNFa in both groups; no alteration in b1-integrin expression	
[88]	Tischer et al.	2008	Animal experiment	Epos + XL 1 (Dornier MedTech, Wessling, Germany)	Rabbit intact femur model	Dose-depending new bone formation		Dose-depending new bone formation
[89]	Ozturk et al.	2008	Animal experiment	PCK, Stonalith Smart Lithotripter	Rabbit tibia epiphysis			Increased epiphyseal plaque thickness and number of chondrocytes
[90]	Ma et al.	2007	Animal experiment	Orthospec (Medispec, MD, USA)	Necrotic femoral head in rabbits		Increased VEGF expression	Increased bone and osteoblast number; increased VEGF expression and microvessel density
[91]	Murata et al.	2007	Primary cell culture	Swiss Dolorclast® (Electro Medical Systems SA, Switzerland)	Rabbit chondrocytes		Augmented uniform gene transfection and increased activity of vector-expressed genes	
[92]	Benson et al.	2007	Primary cell culture	pneumatically driven radial shock wave generator (Electro Medical Systems, Dallas, TX, USA)	Equine chondrocytes		Decreased synthesis of GAG, no alterations in NO or PGE2 synthesis	
[93]	Martini et al.	2006	Secondary cell culture	Modulith SLX (Storz Medical AG, Kreuzlingen, Switzerland) + Ossatron (High Medical Technologies AG, Lengwil, Switzerland)	Human osteoblast-like cells (MG63)		Dose- and device-dependent cell viability and expression of ALP, CICP, OCN, TGFb	
[94]	Bulut et al.	2006	Animal experiment	PCK, Stonalith Smart Lithotripter	Rabbits bony nonunion model	Increased callus volume		Advanced bone healing
[95]	Martini et al.	2005	Secondary cell culture	Modulith SLX (Storz Medical AG, Kreuzlingen, Switzerland)	Human osteoblast-like cells (MG63)	Enhanced transmembrane current and voltage dependence of Ca-activated-/K- channels		
[96]	Saisu et al.	2005	Animal experiment	Piezolith 2300 (Richard Wolf Inc., Knittlingen, Germany)	Acetabulum of immature rabbits	Increased breadth of the acetabular roof and transient woven bone formation on the lateral margin		
[97]	Chen et al.	2004	Animal experiment	Ossatron (HMT High Medical Technologies GmbH, Kreuzlingen. Switzerland)	Rat segmental defect model		Increased TGFb1 and VEGF-A expression	Increased cell density and cell number of RP59-pos. mesenchymal stem cells, subsequently enhanced differentation into chondrocytes and osteocytes
[98]	Saisu et al.	2004	Animal experiment	Piezolith 2300 (Richard Wolf Inc., Knittlingen, Germany)	Immature rabbit femurs	Enhanced bone mineral content, long-bone length and width		
[99]	Chen et al.	2004	Animal experiment	Ossatron (HMT High Medical Technologies GmbH, Kreuzlingen. Switzerland)	Rat segmental defect model		Increased ALPase, COL1, COL2, OCN expression and [3H]-thymidine uptake, increased expression and phosphorylation of ERK and p38	Activated ERK and p38 expression
[100]	Pauwels et al.	2004	Ex vivo	Equitron (HMT High Medical Technologies, Kreuzlingen, Switzerland) // Swiss Dolorclast Vet (Electro Medical Systems, Dallas, TX, USA)	Equine cortical bone	No alterations in bone elasticity		No histological alterations
[101]	Wang et al.	2004	Primary cell culture	not specified	Mesenchymal progenitor cells of human umbilical cord blood		Induced superoxide production, enhanced TGFb1, RUNX2, OCN and COL1 expression, increased bone alkaline phosphatase activity	Increase in bone nodule formations, promotion of the CFU-Stroma formation but not CFU-Mix formation
[102]	da Costa Gomez et al.	2004	Ex vivo	Swiss DolorClast Vet Radial ESWT machine (Electro Medical Systems, Dallas, TX) + Equitron focused ESWT machine (High Medical Technologies Health Tronics Inc, Kennesaw, GA)	Ex-vivo metatarsal bones of horses			rESWT: increased microcrack length; fESWT: increased microcrack density
[103]	Takahashi et al.	2004	Animal experiment	Lithotripter A (Dornier MedTech, Munich, Germany)	Rat femur shafts	Increased cortical thickening, bone mineral density, bone mineral content		Enhanced expression of COL1A1, COL2A1, OC, OPN; no alterations in expression of COL10A1
[104]	Chen et al.	2003	Animal experiment	Ossatron (HMT High Medical Technologies GmbH, Kreuzlingen. Switzerland)	Rats segmental femoral defect model	Increased callus size and calcium content, bone mineral density	Increased AP activity, OCN production, PCNA, TGFb1 and BMP-2 expression	Increased bone tissue formation, progressive mesenchymal aggregation, enchondral ossification and hard callus formation

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[105]	Martini et al.	2003	Primary cell culture	Ossatron (HMT High Medical Technologies GmbH, Kreuzlingen. Switzerland)	Primary sheep osteoblasts cultures		High intensity treatment (28kV): decreased viability, detrimented cell respiration, depressed ALP and NO synthesis, decresed expression of OCN, TGFb and PICP; low intensity treatment (14kV) showed contrary effects with increased viability and cell respiration, increased ALP and NO synthesis as well as OCN and PICP expression; generally negative affection of PICP production	
[106]	Martini et al.	2003	Secondary cell culture	Ossatron (HMT High Medical Technologies GmbH, Kreuzlingen. Switzerland)	Human osteoblastlike cells		Increased NO, OCN, TGFb1 production after low energy application (14kV); decreased cell viability and expression of all examined proteins at high application intensities (28kV)	
[107]	Dorotka et al.	2003	Primary cell culture	Modulith SLK (Storz Medical AG, Kreuzlingen, Switzerland)	Human articular chondrocytes and ovine bone marrow stromal cells		Increased cytotoxity in both chondrocytes and BMSCs at high application intensities (0.17mJ/mm2) compared to lower energy levels and control; unaltered cell proliferation at all energy levels	
[108]	Wang et al.	2003	Animal experiment	Ossatron (HMT High Medical Technologies GmbH, Kreuzlingen. Switzerland)	Rat segmental femoral defect model		Increased expression of BMP-2, BMP-3, BMP-4, and BMP-7	Intensive mesenchymal cell aggregation, hypertrophic chondrogenesis, and endochondral/intramembrane ossification; increased levels of PCNA, BMP-2, BMP-3, BMP-4
[109]	Maier et al.	2002	Animal experiment	Epos Ultra (Dornier MedTech, Wessling, Germany)	Intact distal rabbit femur	Scintigraphic decreased bone metabolism after 10 days, but increased metabolism after 28 days; signs of soft-tissue oedema, epiperiosteal fluid and bone-marrow oedema on MRI		Epiperiostal deposits of hemosiderin
[110]	Wang et al.	2002	Animal experiment	Ossatron (HMT High Medical Technologies GmbH, Kreuzlingen. Switzerland)	Rat femur bone-marrow stromal cells		Increased AP activity and TGFb1 expression	Promotion of bone marrow stromal, but not hematopoetic cell growth; dose-dependent effect on formation of CFU-osteoprogenitors
[111]	Wang et al.	2001	Secondary cell culture	Ossatron (HMT High Medical Technologies GmbH, Kreuzlingen. Switzerland)	Human bone marrow stromal cells		Induction of cell membran hyperpolarization and consecutive Ras-activation, induction of osteogenic transcription factor CBFA1, increased activity of bone alkalaine poshphatase, increased expression of OCN, COL1	Increased bone nodule formations
[112]	Wang et al.	2001	Animal experiment	Ossatron (HMT High Medical Technologies GmbH, Kreuzlingen. Switzerland)	Dog tibia facture model	More callus formations		More cortical bone and thicker, denser, and heavier bone tissues
[113]	Väterlein et al.	2000	Animal experiment	Osteostar (Siemens,Erlangen, Germany)	Rabbit femur joint cartilage	Neither macroscopic nor radiological alterations after high intensity treatments		No histological alterations after high intensity treatments
[114]	Peters et al.	1998	Primary cell culture	Siemens Lithostar Plus (Siemens, Erlangen, Germany)	Embryos of Oryzias latipes			Several damages of tissues after low intensity treatment
[115]	Augat et al.	1995	Animal experiment	XL2, Dornier Medical Systems, Munich, Germany	Ovine tibia fracture model	Neither alterations in biomechanical outcomes nor altered radiological results; tendency to deterioration of facture healing with increasing application intensities		
[116]	Forriol et al.	1994	Animal experiment	Osteostar (Siemens,Erlangen, Germany)	Osteotomized lambs tibia	No effect on the periosteal surface of mature cortical bone, but on the endosteal surface induction of some new trabecular bone, delayed bone healing		
[6]	Graff et al.	1988	Animal experiment	Dornier HM3 (Dornier Medical Systems, Munich, Germany)	Rabbit femur	Soft tissue bleeding		Bone marrow hemorrhage and osteocyte damage 48h after ESWT; increased callus and bone formation, focal regeneration, apposition of new bone, bone remodeling

Table S2: effects of the exposure of connective tissue to extracorporeal shock waves

Reference No.	Author	Year	Study type	Utilized device	Cell type investigated	Morphological, functional, radiological findings	Findings of molecularbiological examinations	Findings of histological examinations
[117]	Haberal et al.	2021	Animal experiment	Storz Masterpuls MP100 (STORZ, Germany)	Rat post-laminectomy			Decreased epidural fibrosis; unaltered acute/chronic inflammation and vascular proliferation
[118]	Heimes et al.	2020	Fertilized Chicken Eggs	Swiss Dolorclast® (Electro Medical Systems SA, Switzerland)	Fertilized chicken eggs.CAM-Assay		Increased expression of MMP-9; decreased expression of MMP-13; unaltered expression of iNOS2, HIF-1α, VEGF	Increased coverage of the transplant by vasculature, percentage of the vascularized area, increase of the vascularized area and number of vessel junctions
[119]	Lu et al.	2020	Primary cell culture	Duolith®SD1 (Storz Medical AG, Trägerwilen, Switzerland)	Human ACL remnant cells + BMSC		Increased ACL remnant cell viability; BMSC: increased expression of Ki67, COL1, COL3, unaltered expression of TGFb, VEGF	ACL-cells: increased expression of COL-I A1, TGF-β, and VEGF BMSC: increased migration and expression of EdU, COL1, COL3; unaltered expression of VEGF, TGFb
[120]	Basoli et al.	2020	Secondary cell culture	Orthogold 100, MTS Medical, Konstanz, Germany	Human foreskin fibroblasts		Increased proliferation, ATP release, ROS production, expression of IL8, MCP1, HSP90, HSP27; unaltered expression of IL-6	
[121]	Schnurrer-Luke-Vrbanić et al.	2018	Animal experiment	Swiss Dolorclast® / Piezoclast® (Electro Medical Systems SA, Switzerland)	Soft tissue regeneration in a rat fibula fracture model			Higher multiplication of collagen fibers; faster organisation of muscle fibers and vascularization by treatment with radial shockwaves
[122]	Cui et al.	2018	Primary cell culture	Duolith®SD1 (Storz Medical AG, Trägerwilen, Switzerland)	Human hypertrophic scar tissue fibroblasts		Decreased expression of TGFb, a-SMA, vimentin, COL1a1, N-Cad, twist; increased expression of ID1, ID2, E-cad, FN after 24h, but decreased expression of FN after 72h	Decreased cell migration
[123]	Cai et al.	2016	Primary cell culture	Dermagold 100, Tissue Regeneration Technologies, Woodstock, GA, manufactured by MTS, Konstanz, Germany	Human periodontal ligament fibroblasts		Initial decreased of IL-6, IL-8, MCP-1, TNF-α; after 4 and more hours: increase of IL6 and IL8, unaltered expression of MCP-1, TNF-α	
[124]	Hochstrasser et al.	2016	Secondary cell culture	Swiss Dolorclast® (Electro Medical Systems SA, Switzerland)	Human foreskin fibroblasts // human placental choriocarcinoma cells (JEG-3)		Induced mechanical cell distruction, dose-dependent decreased cell viability, increased growth potential of fibroblasts (not of JEG-3 cells), shift in proportion from G0/G1 to G2/M phase in fibroblasts (not in JEG-3 cells)	Cellular detachments, holes in monolayers, disruption of actin filaments
[125]	Leone et al.	2016	Primary cell culture	Modulith SLK (Storz Medical AG, Kreuzlingen, Switzerland)	Human Tendon-derived Stem/Progenitor cells (hTSPCs)		Increased expression of COL2A, SOX9, ALP, PPARγ; unaltered expression of BGLAP, RUNX2	Increased expression of differentiation markers in cells grown in specific differentiation media
[126]	Kisch et al.	2015	Animal experiment	Duolith®SD1 (Storz Medical AG, Trägerwilen, Switzerland)	Skin of the contralateral leg to the treated side in rats	Increased capillary blood velocity; unaltered postcapillary venous filling pressure		
[127]	Waugh et al.	2015	Human experiment	Swiss Dolorclast® (Electro Medical Systems SA, Switzerland)	Microdialysate from peri-tendinous tissue		Increased expression of IL-6, IL-8, MMP2 complex and ProMMP9; unaltered expression of (IL)-1β, IL-2, IL-4, IL-10, IL-12p70, IL-17A, VEGF, interferon-γ, Active MMP9, ProMMP2 and Active MMP2	
[128]	de Girolamo et al.	2014	Primary cell culture	Orthogold 100, MTS Medical, Konstanz, Germany	Human tendon cells		Increased expression of SCX, IL-1β, IL-6, IL-10 , TGFβ , VEGF; unaltered expression of MMP-3, MMP-13, COL1 A1, COL3 A1, and TNFα; reduced NO synthesis	
[129]	Chow et al.	2014	Animal experiment	Epos (Dornier MedTech, Wessling, Germany)	Rabbit delayed tendon bone insertion healing			Increased fibrocartilage area and thickness, proteoglycan deposition, expression of SOX9, COLII, Vickers hardness; unaltered expression of COL1
[130]	Cinar et al.	2013	Animal experiment	Swiss Dolorclast® (Electro Medical Systems SA, Switzerland)	Rat Achilles tendinitis	Decreased Load to failure		Decreased collagen fiber density
[131]	Contaldo et al.	2012	Animal experiment	Swiss Dolorclast® (Electro Medical Systems SA, Switzerland)	Mice wound healing model			Enhanced expression of caspase-3, PCNA, eNOS; increase of functional angiogenetic density and total wound score
[132]	Chow et al.	2012	Animal experiment	Epos (Dornier MedTech, Wessling, Germany)	Rabbit delayed tendon bone insertion healing	Increased Load to failure, new bone area and new bone volume		Increased fibrocartilage zone and ratio of bone forming
[133]	Yoo et al.	2012	Animal experiment	Dornier AR2 (Dornier MedTech, Wessling, Germany)	Rat collagenase-induced achilles tendinitis			Increased fibrillary diameter, vascularity, fibroblast activity, lymphocyte and plasma cell infiltration, dense histocytes; transient disorganization of collagen fibers
[134]	Leone et al.	2012	Primary cell culture	Modulith SLK (Storz Medical AG, Kreuzlingen, Switzerland)	Human ruptured / healthy tenocytes		Ruptured tenocytes: decreased expression of COL1, SCX; unaltered COL3, TNM, TN-C	Healthy tenocytes: increased cell proliferation and migration
[135]	Zhang et al.	2011	Animal experiment	OssaTron + EvoTron (SANUWAVE, Alpharetta, GA, USA)	Rat various tendons and septa			Increased lubricine expression
[136]	Penteado et al.	2011	Animal experiment	OssaTron® (Barueri, SP, Brazil)	Rabbit Patellar tendon			Unaltered blood vessel number
[137]	Kubo et al.	2010	Animal experiment	Medispec Ltd, Germantown, Md	Rabbit ear lymphedema	Reduced ear thickness	Increased expression of VEGF-C, VEGF-R3	Increased density of lymphatic vessels
[138]	Sugioka et al.	2010	Primary cell culture	Swiss Dolorclast® (Electro Medical Systems SA, Switzerland)	Rat Achilles tendon cells			Increased introduction of NF-κB decoy-FITC, activation of NF-κB; decreased activation of NF-κB after pretreatment with ESW+NF-κB decoy-FITC
[139]	Berta et al.	2009	Secondary cell culture	Piezoson 100, Richard Wolf, Knittlingen, Germany	Human fibroblasts		Decreased viability; increased expression of TGF−β1; increase of COL1 and COL3 expression after 6 days after a primary decreased expression	
[140]	Bosch et al.	2009	Animal experiment	Equitron, High Medical Technologies, Lengwil, Switzerland	Various pony tendons		Increased expression of COL1 and MMP14; decreased expression of MMP3	Unaltered total collagen content, disorganisation of normal collagen structure; decreased percentage of degraded collagen 6 weeks after treatment after an increase 3h after treatment
[141]	Han et al.	2009	Primary cell culture	Sonocur (Siemens Medical Solutions, Iselin, NJ)	Healthy and diseased tenocytes		Healthy: increased expression of IL1; unaltered expression of MMP1, MMP2, MMP9, MMP13, IL6 and IL13 diseased: decreased expression of MMP1, MMP13 and IL6; unaltered expression of MMP2, MMP9, IL1 and IL13	Decreased cell viability
[142]	Byron et al.	2009	Animal experiment	Swiss DolorClast Vet, EMS Electro Medical Systems, Nyon, Switzerland	Palmar heel pain in horses	Radiographic scores, scintigraphic navicular pool phase, delayed phase ROI density ratios		
[143]	Chao et al.	2008	Primary cell culture	Dornier Electromagnetic Shock Wave Emitter (EMSE 220F; Dornier MedTech GmbH, Wessling, Germany)	Rat tenocytes		Increased total collagene concentration, NO production, expression of PCNA, COL1, COL3, TGFb	Decreased cell viability; increased cell proliferation
[144]	Wang et al.	2008	Animal experiment	Epos (Dornier MedTech, Wessling, Germany)	Rabbit Patella-patellar tendon healing junction	Increased new bone formation, bone mineral status, tensile load and strength		Increased remodeling / alignment of collagen fibers, thicker and mature regenerated fibrocartilage zone
[145]	Bosch et al.	2007	Animal experiment	Equitron, High Medical Technologies, Lengwil, Switzerland	Various pony tendons		Unaltered DNA content, 3h after treatment: increased GAG, total protein synthesis; 6weeks after treatment: decreased GAG, collagen synthesis, noncollagenous protein synthesis, total protein synthesis	Unaltered total collagen content, disorganisation of normal collagen structure; decreased percentage of degraded collagen 6 weeks after treatment after an increase 3h after treatment
[146]	Kersh et al.	2006	Animal experiment	Equitron, High Medical Technologies, Lengwil, Switzerland	Horse superficial digital flexor tendinitis model			Unaltered percentage lesion, percentage disruption and grey scale, external width, fibroblast and tenocyte number, increased capillary density

Table S2: effects of the exposure of connective tissue to extracorporeal shock waves

Reference No.	Author	Year	Study type	Utilized device	Cell type investigated	Morphological, functional, radiological findings	Findings of molecularbiological examinations	Findings of histological examinations
[147]	Wang et al.	2005	Animal experiment	Ossatron (HMT High Medical Technologies GmbH, Kreuzlingen. Switzerland)	Rabbit tendon-bone interface healing	Increased trabecular bone around the tendons and tensile strength of tendon/bone-interface, better bone/tendon contacting		
[148]	Chen et al.	2004	Animal experiment	HMT High Medical Technologies GmbH, Kreuzlingen, Switzerland	Rat Achilles tendinitis	Increased load to failure		Decreased edema, swelling, inflammatory cell infiltration; increased expression of TGF-b, IGF-I, tenocyte proliferation, neovascularization and progressive tendon tissue regeneration
[149]	Orhan et al.	2004	Animal experiment	Breakstone 200 Lithotripter System (Breakthrough Medical Corp, Gaittersburg, Maryland)	Rat Achilles tendon injury	Higher force to rupture		Less adhesion formation, increased number of capillaries
[150]	Hsu et al.	2004	Animal experiment	Orthospec, Medispec, Israel	Rabbit patellar tendinopathy	Increased ultimate tensile load		Increased hydroxyproline concentration; decreased pyridinoline concentration; unaltered number of blast-like tenocytes (4 weeks); increased number of mature tenocytes (16 weeks)
[151]	Orhan et al.	2004	Animal experiment	mobile ELMED lithotriptor, 2001, Ankara, Turkey	Rat healthy Achilles tendon			Disorganisation of collagen fibers
[152]	Wang et al.	2003	Animal experiment	not specified	Rabbit Achilles tendon-bone junction			Increased number of neo-vessels and expression of eNOS,VEGF and PCNA
[153]	Maier et al.	2002	Animal experiment	EPOS Ultra, Dornier MedTech, Wessling,Germany	Rabbit Quadriceps tendon			High intensities: tendon: increased staining affinity, nuclear and fibrillar appearance paratendon: increased thickness, edema, capillary density
[154]	Wang et al.	2002	Animal experiment	Ossatron (HMT High Medical Technologies GmbH, Kreuzlingen. Switzerland)	Dog Achilles tendon bone junction			New capillary and muscularized vessels, newly appeared myofibroblasts; no alterations in bone matrix, bone vascularization and osteocyte activity
[155]	Johannes et al.	1994	Cell culture	Osteostar (Siemens,Erlangen, Germany)	Human fibroblasts			Decreased cell viability, no alterations in cell growth

Table S3: effects of the exposure of muscle and nerve tissue to extracorporeal shock waves

Reference No.	Author	Year	Study type	Utilized device	Cell type investigated	Morphological, functional, electrophysiological findings	Findings of molecularbiological examinations	Findings of histological examinations
[156]	Huang et al.	2021	Animal experiment	Swiss Dolorclast® (Electro Medical Systems SA, Switzerland)	Rabbit immobilization-induced fibrosis and contracture of muscle	Decreased total contracture angle, muscle contracture angle	Decreased expression of TGFb, HIF1a	Decreased proportion of collagen fiber area
[157]	Kenmoku et al.	2021	Animal experiment	Swiss Dolorclast® (Electro Medical Systems SA, Switzerland)	Neuromuscular junction in rats	Energy flux density- and total energy-dependent decrease of CMAP, unaltered CMAP latency		
[158]	Park et al.	2020	Animal experiment	Dornier MedTech, Wessling, Germany	Rat sciatic nerve crush model	Increased print width, print area	Tendential increased expression of myelin basic protein	
[159]	Matsuda et al.	2020	Animal experiment	Duolith®SD1 (Storz Medical AG, Trägerwilen, Switzerland)	Spinal cord contusion injury model in rats	Improved BBB locomotor function, increased withdrawal threshold, abbreviated latency of MEPs, no alterations in MEP amplitude	Increased expression of BDNF and TrkB	Increased expression of BDNF, reduced myelin damage and oligodendrocyte loss, decreased axonal damage
[160]	Langendorf et al.	2020	Animal experiment	Swiss Dolorclast® (Electro Medical Systems SA, Switzerland)	Rat musculus rectus femoris grade III muscle tear		Increased expression of MyoD and myosin	First higher amount of mononucleated cells, at day 7 newly formed muscle fibers with less MNCs; unaltered number of CD31-pos. cells.
[161]	Sagir et al.	2019	Animal experiment	OE050 focused applicator, Orthogold 100, MTS, Konstanz, Germany	Rat peripheral nerve injury	Decreased EMG amplitude, increased EMG latency, improved sciatic functional index		Decreased Myelin thickness, axon area and number
[162]	Feichtinger et al.	2019	Animal experiment	Dermagold; TissueRegeneration Technologies, Woodstock, Georgia, manufactured by MTS, Konstanz, Germany	Rat rotator cuff reconstruction	Improved load-to-failure testing results, intensity measurements in functional gait analysis	Unaltered expression of CXCL12, TGF-β1, TGF-β3, VEGFR2	
[163]	Yang et al.	2019	Animal experiment	not specified	Neuropathic pain // rat L4/5 dorsal root ganglions and sciatic nerve	Improved mechanical paw withdrawal treshold and thermal paw withdrawal latency	Decreased TNF-α, NF-κB, MMP-9, IL-1ß, NOX-1, NOX-2, NOX-4, oxidized protein, cleaved caspase 3, cleaved PARP, γ-H2AX, (p)-p38, p-JNK, p-ERK1/2, Nav.1.3, Nav.1.8 and Nav.1.9	
[164]	Mattyaszovszky et al.	2018	Primary cell culture	Swiss Dolorclast® (Electro Medical Systems SA, Switzerland)	Human sceletal muscle cells		Dose-dependent increase of Myf5, MyoD, Pax7, NCAM; down-regulation of these proteins at double exposure of the highest energy flux density	Increased cell viability at low energy flux densities, no alterations at higher energy flux densities
[165]	Yin et al.	2018	Animal experiment	Cardiospec, Medispec, Israel	Rat limb ischemia-reperfusion injury of quatriceps muscle	Increased angiogenesis, decreased serum myoglobin/creatine phosphokinase	Decreased NOX-1, NOX-2, cleaved caspase 3, cleaved PARP, TGF-β, (p-)Smad3, ICAM-1, MMP-9, TNF-α, NF-κB, RANTES, TLR-2, TLR-4, IL-1β, cytosolic cytochrome C, γ-H2AX; increased Bcl-2, p-Smad1/5, BMP-2, mitochondrial cytochrome C	Decreased muscle-damaged/fibrosis/collagen-deposition areas
[166]	Shin et al.	2018	Animal experiment	Swiss Dolorclast® (Electro Medical Systems SA, Switzerland)	Rat chronic contusive SCI model		Increased expression of DCX, SOX-2, GAP-43, MAP-2	Increased expression of DCX, SOX-2, GAP-43, MAP-2
[167]	Luh et al.	2018	Animal experiment	Piezoson 100, Richard Wolf, Knittlingen, Germany	Rat caudal nerves anaesthetic drug delivery			
[168]	Kenmoku et al.	2018	Animal experiment	Swiss Dolorclast® (Electro Medical Systems SA, Switzerland)	Rat neuromuscular junction	Decreased CMAP amplitude, unaltered CMAP latency		Irregular end plates, unchanged axon terminals and muscle fibers, increased mean interjunctional fold interval
[169]	Chen et al.	2017	Animal experiment	not specified	Neuropathic pain // rat L4/5 dorsal root ganglions and sciatic nerve	Improved mechanical paw withdrawal treshold and thermal paw withdrawal latency	Decreased expression of TNF-α, NF-κB, MMP-9, IL-1ß, GFAP, ox42, NOX-1, NOX-2, NOX-4, oxidized protein, γ-H2AX, cytosolic mitochondria, cleaved capase-3, PARP, p-P38, p-JNK, p-ERK1/2, Nav.1.3, Nav.1.8, Nav.1.9	Decreased expression of p-P38+, peripherin+ cells, P38+, NF200+ cells
[170]	Yahata et al.	2016	Animal experiment	Duolith®SD1 (Storz Medical AG, Trägerwilen, Switzerland)	Rat SCI model	Improved BBB locomotor score, withdrawal latency, 50% withdrawal threshold		Increased expression of VEGF, CD31, a-SMA, 5-HT, increased area of spared white matter, decreased number of TUNEL-pos. cells
[171]	Schuh et al.	2016	Primary cell culture	Dermagold 100, Tissue Regeneration Technologies, Woodstock, GA, manufactured by MTS, Konstanz, Germany	Schwann cells of rats peripheral nerves(sciatic nerves)		Increased cell yield, BrdU assays, population doublings, S100b, c-Jun, GFAP, and P75 expression, decreased P0 and P16 expression, increased extracellular ATP levels immidiately after application	
[172]	Lee	2016	Animal experiment	HAEMIL, Soltar, Korea	Locomotion in a rats CNS injury model	Decreased knee joint angle		
[173]	Kisch et al.	2016	Animal experiment	Duolith®SD1 (Storz Medical AG, Trägerwilen, Switzerland)	Rat hind limb muscle	Increased muscular blood flow		
[174]	Lee & Kim	2015	Animal experiment	HAEMIL, Soltar, Seoul, Korea	Rat sciatic nerve injury	Increased ankle angles (toe off + foot contact), improved Sciatic functional index	Increased expression of NT-3	
[175]	Yamaya et al.	2014	Animal experiment	Duolith®SD1 (Storz Medical AG, Trägerwilen, Switzerland)	Rat SCI model	Improved BBB locomotor score	Increased expression of VEGF and Flt-1	Increased NeuN-positive cells, VEGF staining
[176]	Fu et al.	2014	Animal experiment	Storz Masterpuls MP100 (STORZ, Germany)	Neuropathic pain / rat chronic constriction injury	Improved mechanical withdrawal threshold, thermal withdrawal latency		
[177]	Ishikawa et al.	2013	Animal experiment	Swiss Dolorclast® (Electro Medical Systems SA, Switzerland)	Rat CCI hind limb muscle	Transfection of POMC gene		
[178]	Mense & Hoheisel	2013	Animal experiment	Duolith®SD1 (Storz Medical AG, Trägerwilen, Switzerland)	Rat distal sciatic nerve injury (Gastrocnemius–Soleus or Sural Nerve)	Decreased pressure pain threshold, improved locomotor activity		Increased number of PGP 9.5 IR nerve fibers
[179]	Hausner et al.	2012	Animal experiment	Orthowave 180 shockwave machine (MTS Europe,Switzerland)	Rat sciatic nerve autograft	Increased amplitude, CNAP area		Increased number of myelinated axons, unaltered number of endoneural vessels
[180]	Kenmoku et al.	2012	Animal experiment	Swiss Dolorclast® (Electro Medical Systems SA, Switzerland)	Rat gastrocnemius muscle neuromuscular junction	Decreased amplitude, unaltered CMAP latency		Decreased number of acetylcholine receptors
[181]	Yamashita et al.	2009	Primary cell culture + animal experiment	not specified	POMC transfection in rat muscle cells	Decreased mechanical allodynia		Increased ratio of β-endorphin-IR muscle cells and number of β-endorphin-IR muscle fibers; decreased number of CGRP-IR DRG neurons
[182]	Wu et al.	2008	Animal experiment	Piezoson 100, Richard Wolf, Knittlingen, Germany	Rat sciatic nerve	Decreased motor nerve conduction velocity; unaltered Sciatic functional index and withdrawal reflex latency		Damage to the myelin sheath of large-diameter myelinated fibers
[183]	Hausdorf et al.	2008	Animal experiment	XL 1 (Dornier MedTech, Wessling, Germany)	Rabbit distal femoral region			Decreased number of unmyelinated nerve fibers of femoral nerve; unaltered number of unmyelinated nerve fibers of sciatic nerve; unaltered size, number and myelin sheet of myelinated nerve fibers
[184]	Hausdorf et al.	2008	Animal experiment	XL 1 (Dornier MedTech, Wessling, Germany)	Rabbit distal femoral region // dorsal root ganglion			Decreased number of neurons immunoreactive for substance P
[185]	Lee et al.	2007	Animal experiment	Ossatron (HMT High Medical Technologies GmbH, Kreuzlingen. Switzerland)	Rabbit spinal cord	No changes in motor and vegetative functions		Decreased number of neurons at high intensity treatment (0.68mJ/mm2), dose-dependent myelin damage
[186]	Ochiai et al.	2007	Animal experiment	Epos (Dornier MedTech, Wessling, Germany)	Rat knee osteoarthritis // dorsal root ganglion	Increased walking duration		Decreased ratio of CGRP-positive dorsal root ganglion neurons
[187]	Wu et al.	2007	Animal experiment	Piezoson 100, Richard Wolf, Knittlingen, Germany	Rat sciatic nerve	Decreased motor nerve conduction velocity, unaltered sciatic functional index		
[188]	Murata et al.	2006	Animal experiment	Epos (Dornier MedTech, Wessling, Germany)	Rat foot pad // dorsal root ganglion			Increased number of ATF3 and ATF-3/GAP-43 dual-IR neurons

Table S3: effects of the exposure of muscle and nerve tissue to extracorporeal shock waves

Reference No.	Author	Year	Study type	Utilized device	Cell type investigated	Morphological, functional, electrophysiological findings	Findings of molecularbiological examinations	Findings of histological examinations
[189]	Takahashi et al.	2006	Animal experiment	Epos (Dornier MedTech, Wessling, Germany)	Rat foot pad			Decreased number of epidermal nerve fibers
[190]	Bolt et al.	2004	Animal experiment	Swiss DolorClast Vet, EMS Electro Medical Systems, Nyon, Switzerland	Horse digital palmar nerves	Decreased sensory nerve conduction velocity		Disruption of myelin sheet
[191]	Hausdorf et al.	2004	Animal experiment	XL 1 (Dornier MedTech, Wessling, Germany)	Rabbit periosteoum of distal femur		Increased Substance P release 6 and 24 hours after treatment, decreased Substance P release 6 weeks after treatment; unaltered Prostaglandine E release	
[192]	Takahashi et al.	2003	Animal experiment	Epos (Dornier MedTech, Wessling, Germany)	Rat foot pad // dorsal root ganglion			Decreased percentage of CGRP-immunoreactive dorsal root ganglion neurons
[193]	Maier et al.	2003	Animal experiment	XL 1 (Dornier MedTech, Wessling, Germany)	Rabbit distal femur			Increased Substance P release after 6 and 24 hours; decreased SP release after 6 weeks; no alterations in PGE2 release
[194]	Haake et al.	2002	Animal experiment	MINILITH SL1; Storz Medical, Kreuzlinger, Switzerland	Rat hind paw // spinal chord		Unaltered c Fos expression	Unaltered c Fos expression
[195]	Ohtori et al.	2002	Animal experiment	Epos (Dornier MedTech, Wessling, Germany)	Rat hind paw epidermis			Decreased number of nerve fibres immunoreactive for PGP 9.5 and CGRP
[196]	Haake et al.	2001	Animal experiment	MINILITH SL1; Storz Medical, Kreuzlinger, Switzerland	Rat hind paw // spinal chord			Unaltered expression of met-enkephalin (MRGL) and dynorphin (Dyn)
[197]	Rompe et al.	1998	Animal experiment	Osteostar (Siemens,Erlangen, Germany)	Rabbit sciatic nerve			Vacuolic swelling of the axons, no disruption of nerve's continuity