

WHITE PAPER

Synergistic Applications of Extracorporeal Shockwave Therapy (ESWT) and Photobiomodulation Therapy (PBMT) for Musculoskeletal Regeneration and Pain Management

Prepared by: Dr. David Kunashko, Medical Director BIOFLEX Laser Therapy

Date: December 2025

Executive Summary

Extracorporeal Shockwave Therapy (ESWT) and Photobiomodulation Therapy (PBMT) are two of the leading evidence-based, non-invasive therapeutic modalities used in modern regenerative and musculoskeletal rehabilitation. Individually, both therapies have demonstrated effectiveness in reducing pain, stimulating tissue repair, and improving functionality. When applied together, emerging research suggests synergistic improvements in clinical outcomes—particularly for chronic tendinopathies, plantar fasciitis, and soft tissue injuries. BIOFLEX® is pioneering the synergistic use of these two effective therapies to help you improve patient efficacy and expand your clinical practice.

This White Paper reviews the underlying biological mechanisms, clinical evidence, therapeutic benefits, and combined application potential of ESWT and PBMT, drawing on peer-reviewed literature, meta-analyses, and controlled trials.

1. Introduction

Chronic musculoskeletal pain affects hundreds of millions worldwide and represents one of the leading causes of disability. Traditional interventions—pharmacological agents, corticosteroid injections, immobilization, and, in severe cases, surgical intervention—present limitations including risk, expense, and failure to address underlying tissue pathology.

Non-invasive regenerative modalities have emerged as viable alternatives for conditions involving:

- tendinopathy
- chronic inflammation
- myofascial pain
- soft-tissue injury

- plantar fasciitis
- osteoarthritis and joint degeneration
- slow or impaired tissue healing

ESWT and PBMT, both supported by growing scientific literature, target tissue regeneration and pain modulation via distinct but complementary mechanisms, making their combined use biologically logical and clinically promising.

2. Extracorporeal Shockwave Therapy (ESWT)

2.1 Mechanism of Action

ESWT delivers focused or radial acoustic shockwaves into tissue, triggering mechanotransduction, where mechanical forces are converted into biological signals causing interstitial and extracellular responses leading to tissue regeneration. Demonstrated biological effects include:

2.1.1 Neovascularization

Shockwaves promote angiogenesis (formation of new blood vessels from existing ones) and increased blood flow via upregulation of VEGF (vascular endothelial growth factor) which act as a signal to promote angiogenesis. They also upregulate eNOS (endothelial nitric oxide synthase) which produces NO essential for long-term muscle regeneration after injury. Evidence: Wang et al. demonstrated increased neovascularization in tendons following ESWT in animal and human models.⁴⁷

2.1.2 Collagen Remodeling & ECM Repair

ESWT stimulates fibroblast proliferation and type I collagen synthesis—reversing degenerative tendon changes.

Evidence: Notarnicola & Moretti reviewed ESWT-induced collagen regeneration and improved tendon organization.³⁴

2.1.3 Anti-Inflammatory Effects

Shockwave exposure downregulates inflammatory mediators such as COX-2, IL-6, and Substance P. By regulating these mediators, shockwave therapy helps reduce inflammation in the treated area.

Evidence: Vetrano et al. reported reduced inflammatory cytokines in tendinopathy after ESWT.⁴⁶

2.1.4 Analgesic Effects

Shockwave therapy delivers intense mechanical energy to the tissues, which can overstimulate nerve fibers temporarily. This overstimulation disrupts the pain signals being sent to the brain, resulting in pain relief and decreased sensitivity in the treated region. Pain reduction is attributed to:

- hyperstimulation analgesia
 - decreased nerve fibre sensitivity
 - improved tissue oxygenation
 - diminishing the concentration of the neuropeptide Substance P at the injury site, a primary cause of pain in the affected tissue
-

2.2 Clinical Evidence for ESWT

Plantar Fasciitis

- A 2023 systematic review + meta-analysis concluded ESWT is effective in reducing pain intensity (both for focal-ESWT and radial-ESWT) in PF.⁴²
- A 2024 controlled study combining ESWT with “trigger-points” (in calf musculature / triceps surae) reported improved plantar temperature and plantar pressure in PF patients, suggesting potential biomechanical and vascular effects in addition to symptom relief.⁴⁸
- A 2025 randomized controlled trial (rESWT vs physiotherapy + ultrasound) in 129 PF patients showed significant VAS pain score reductions in both groups at follow-up, supporting clinical benefit of rESWT in a more “real world” rehab setting.²¹
- Another recent trial (2023) showed that ESWT resulted in better pain relief and functional improvement compared with corticosteroid injection + kinesio-taping in PF.³⁶

Clinical interpretation: ESWT — both radial and focused — appears to be a safe and effective non-surgical option for PF, particularly when conventional treatments have failed. It seems to improve both pain and function, and may also effect structural changes (e.g. reduced plantar fascia thickness).

Rotator Cuff Tendinopathy (RCT) / Shoulder Tendinopathy

- A 2024 meta-analysis of RCTs (up to Feb 2024) found that ESWT significantly reduces shoulder pain (VAS) and improves functional scores (e.g., Constant-Murley, UCLA, ASES) compared with controls in rotator cuff tendinopathy (calcific and non-calcific).⁵⁰
- The same meta-analysis noted that improvement in shoulder abduction range of motion (ROM) was *not* statistically significant, suggesting function gains may be more about pain reduction and general use rather than marked ROM gains.⁵⁰

- Another meta-analysis of upper-limb tendonitis (including rotator cuff, lateral epicondylitis, long bicipital tendonitis etc.) concluded ESWT is effective in relieving pain at 3 and 6 months, especially with radial-ESWT (rESWT).⁴⁹

Clinical interpretation: There is growing evidence that ESWT can be a useful non-invasive therapy for shoulder tendinopathy / rotator cuff problems, improving pain and functional measures. It may be considered when conservative therapies have not sufficed, particularly when patients seek non-surgical options.

Achilles Tendinopathy (insertional & non-insertional / midportion)

- A 2013 (older) review already found satisfactory evidence for low-energy ESWT in chronic insertional and non-insertional Achilles tendinopathies, with improvements in pain and function at a minimum 3-month follow-up.³
- A 2022 systematic review focused on midportion Achilles tendinopathy identified 7 RCTs (out of many screened), with 4 RCTs showing consistent benefit — reduced pain and improved function. They recommended ESWT as “safe and effective,” often with augmentation by eccentric exercises and stretching.¹³
- A 2024 clinical trial comparing ESWT vs conventional physiotherapy in chronic Achilles tendinopathy noted both interventions produced significant VAS reductions and functional improvements; but ESWT was superior in improving tendon thickness and heterogeneity (on ultrasound), though not affecting calcifications or neovascularization.¹

Clinical interpretation: ESWT may be considered for Achilles tendinopathy, particularly for patients who fail first-line conservative management. It might offer structural benefits (on ultrasound) with uncertain impact on long-term function and pain. Combining ESWT with exercise (eccentric loading, stretching) may yield better outcomes.

Upper Limb Tendinopathies

- A 2024 meta-analysis of 18 RCTs covering upper-limb tendonitis (rotator cuff, lateral epicondylitis, long bicipital tendonitis, etc.) reported pain relief by ESWT vs placebo at 3 and 6 months — especially for radial ESWT.⁴⁹
- However, a more general meta-analysis (published 2024) of 45 studies across various tendinopathies (upper and lower limb) showed: significant pain reduction, but large heterogeneity; the standardized mean differences (SMD) varied by condition (e.g. plantar fasciitis, lateral epicondylitis, Achilles, rotator cuff).³⁰
- A 2023-2024 review focused on shoulder (rotator cuff) tendinopathy concluded ESWT “may be efficacious” but highlighted limitations — variation in treatment parameters, small number of high-quality trials, and unclear optimal dosing/protocol.⁵⁰

Clinical interpretation: ESWT remains a potential “adjunct / alternative” for upper-limb tendinopathies (shoulder, elbow, biceps). It might be useful when other therapies fail or combined with standard-of-care treatments.

Larger-scale Evidence Syntheses (Meta-Analyses & Reviews)

- A 2023 meta-analysis of 45 clinical studies (up to March 2023) found ESWT significantly reduces pain across a spectrum of tendinopathies (PF, lateral epicondylitis, Achilles tendinopathy, rotator cuff).³⁰
- A 2024 study analyzing upper-limb tendonitis (18 RCTs) found ESWT more effective than placebo in pain relief at 3–6 months — especially radial ESWT.⁴⁹
- A 2024 review focusing on athletes / physically active individuals (56 studies, 32% Level I evidence) suggested ESWT may be effective alone (or with exercise) for plantar fasciitis, lateral epicondylitis, proximal hamstring tendinopathy; and as adjunct to exercise for other conditions (e.g. medial tibial stress syndrome, osteitis pubis).³⁹

3. Photobiomodulation Therapy (PBMT)

3.1 Definition & Mechanism of Action

NAALT and WALT defines Photobiomodulation Therapy (PBMT) as “A form of light therapy that utilizes non-ionizing forms of light sources, including LASERS, LEDs, and broad-band light, in the visible and infrared spectrum. It is a non-thermal process involving endogenous chromophores eliciting photophysical (i.e. linear and non-linear) and photochemical events at various biological scales. This process results in beneficial therapeutic outcomes including but not limited to the alleviation of pain or inflammation, immunomodulation, and promotion of wound healing and tissue regeneration.” <https://www.naalt.org/>

PBMT most commonly uses red to near-infrared wavelengths (630–680 and 800–900 nm) applied in direct contact with skin to stimulate cellular repair without heat or tissue damage.

3.1.1 Mitochondrial Activation

Light absorption by mitochondrial chromophores (especially Cytochrome c oxidase, CCO)¹⁸

- A central hypothesis is that PBMT relies on red or near-infrared (NIR) light (commonly ~630–680 and 800–900 nm) being absorbed by chromophores located in mitochondria — in particular CCO, which is part of complex IV of the electron transport chain.
- When CCO absorbs the photon energy, it can trigger downstream effects: increased electron flux through the respiratory chain, enhanced proton gradient across the inner mitochondrial membrane, and thereby increased production of adenosine triphosphate (ATP).
- One proposed molecular detail: in some cells, nitric oxide (NO) can bind to CCO and inhibit its activity; PBMT may “photodissociate” NO from CCO, freeing the enzyme to resume more efficient respiration and ATP production.

Effects on mitochondrial respiration, biogenesis, and cellular energy metabolism¹⁸

- PBMT has been associated with increased ATP production, presumably via enhanced mitochondrial respiration.
- In some cellular contexts (e.g., adipose tissue), PBMT has been shown to stimulate markers associated with mitochondrial dynamics and biogenesis (e.g., proteins involved in fission/fusion: DRP1, FIS1, MFN2, OPA1) — implying that PBMT might increase not only per-mitochondrion activity but also mitochondrial number / turnover.
- Through these mitochondrial effects (improved energy production, redox signaling, biogenesis), PBMT may influence broader cellular behaviors: proliferation, differentiation, migration, survival — which underlie its therapeutic applications (wound healing, tissue repair, reduction of inflammation, neuroprotection, etc.)

3.1.2 Reduced Oxidative Stress

PBMT modulates reactive oxygen species (ROS), preventing oxidative tissue damage and supporting healing.¹⁷

- PBMT often increases mitochondrial membrane potential (MMP) in healthy or stressed cells. This suggests more efficient function (better proton gradient, ATP generation).
- PBMT causes a transient rise in reactive oxygen species (ROS) production. While excessive ROS is harmful, this mild, transient ROS increase can act as a signaling mechanism, activating redox-sensitive cellular pathways, including transcription factors that govern cell survival, antioxidant defenses, mitochondrial biogenesis, inflammation, etc.
- Particularly in cells under stress (e.g. oxidative stress, hypoxia, or mitochondrial dysfunction), PBMT may reduce excessive ROS over time, helping restore redox balance and mitigate oxidative damage.

3.1.3 Anti-Inflammatory Effects

Effects on inflammatory mediators (cytokines, immune cells, oxidative stress)

- Reduction in pro-inflammatory cytokines / chemokines: In a study of human periodontal ligament fibroblasts (stimulated with inflammatory triggers like IL-1 β and TNF- α), 810 nm PBMT significantly suppressed production of several inflammatory mediators (e.g., IL-6, IL-17A/F, IFN- γ , MCP-1), whereas 660 nm had a less favourable or even pro-inflammatory effect in that context.²
- Modulation of wound healing inflammation: A systematic review of preclinical (animal) studies on diabetic wound healing found that PBMT reduced levels of inflammatory cytokines — including Interleukin-1 β (IL-1 β), Interleukin-6 (IL-6), and Tumour Necrosis Factor-alpha (TNF- α) — which are typically elevated in chronic, non-healing wounds. This downregulation was associated with improved tissue repair (cell proliferation and migration) and accelerated healing.²²
- Effects on immune cell infiltration & vascular/ cellular inflammation: In an acute inflammation model (various inflammatory mediators injected into mouse paw), PBMT at low dose (1 J/cm²) reduced paw edema, inhibited neutrophil migration, and decreased

vascular permeability. Higher dose (5 J/cm²) showed less consistent effects, underscoring the dose dependency.⁹

- In osteoarthritis (OA) inflammation & joint-associated inflammation: In a rat model of acute OA, PBMT (808 nm, specific dosing) lowered levels of TNF- α and a chemokine (CINC-1), attenuated expression of bradykinin receptors (B1/B2) and increased mechanical pain threshold (less hyperalgesia)¹⁰
- Neuroinflammation & central nervous system (CNS) effects: In a recent mouse model of experimental autoimmune encephalomyelitis (EAE, a model for multiple sclerosis), PBMT reduced peripheral immune cell infiltration into the spinal cord, decreased glial activation, and prevented neuronal hyperexcitability — suggesting PBMT can modulate inflammatory and immune processes in the CNS, with neuroprotective consequences.¹¹

PBMT appears capable of lowering pro-inflammatory cytokines and chemokines, reducing immune cell recruitment, limiting oxidative and nitrosative stress, and modulating immune cell phenotype (e.g., macrophage polarization, glial activation), depending on context and dosing.

3.1.4 Enhanced Tissue Repair

Activation of growth factor signaling and extracellular matrix (ECM) remodeling

- PBMT has been shown to activate endogenous growth-factor signaling — notably the transformation of latent Transforming Growth Factor Beta 1 (TGF- β 1), which in turn triggers downstream signaling (Smad2 phosphorylation) leading to gene expression that supports tissue regeneration (fibroblast activation, myofibroblast differentiation, collagen production, wound contraction).²³
- In wound healing models, PBMT modulates the expression of genes involved in ECM remodeling: for example, down-regulating genes for matrix-degrading proteases (e.g., MMP-2, MMP-9) and pro-inflammatory cytokines, while upregulating genes for growth factors (like basic fibroblast growth factor, bFGF) supportive of repair.³⁷
- PBMT also boosts fibroblast proliferation, collagen synthesis, and collagen deposition — all vital to building new tissue and strengthening the repair site.³⁷

Promotion of angiogenesis (new blood vessel formation) and improved microcirculation⁹

- Especially in bone and tissue defect models, PBMT has been shown to enhance vascular proliferation, supporting oxygen and nutrient delivery to regenerating tissues.
- Better vascularisation aids not only in bringing nutrients but also in removing waste products, which helps the tissue maturation and remodeling phases proceed more effectively.

Enhanced cell proliferation, migration, and re-epithelialization (for skin / surface tissues)

- In full-thickness skin wound models, PBMT stimulated keratinocyte migration, increased expression of ECM proteins (e.g., collagen), increased expression of

cytoskeletal/migration-associated markers (like vimentin, α -SMA), and promoted re-epithelialization, supporting faster closure of wounds.²⁵

- In aged-animal skin wounds (where healing is typically slower), PBMT increased fibroblast numbers, collagen I/III production, and modulated inflammatory mediator expression (e.g., lowered IL-6, MMP-3, MMP-9, altered VEGF and TIMP levels), resulting in improved healing despite age-related impairment.¹⁴

3.2 Clinical Evidence for PBMT and Musculoskeletal Conditions

Tendinopathy

Meta-analysis: general tendinopathy (pain & function)

- A 2021 meta-analysis of 17 RCTs (n = 835) found that when PBMT was used in addition to exercise (vs sham+exercise), there were significant reductions in pain and improvements in function.⁴⁴
- Meta-analysis: lower-extremity tendinopathy & plantar fasciitis
 - A more recent meta-analysis focused on lower-extremity tendinopathies / plantar fasciitis (RCTs only) found that PBMT significantly reduced pain (mean ~13 mm on VAS) immediately post-therapy, with effects lasting 4–12 weeks; disability scores also improved (SMD ~0.39 immediately, ~0.32 at 4–9 weeks).³³
 - When applied at recommended doses, PBMT significantly reduced pain versus placebo — and as an add-on to exercise therapy, the benefit was even larger.
 - No serious adverse events were reported in those trials.
- Recent meta-analysis (2025) on chronic tendinopathy pain
 - A 2025 meta-analysis (“Shedding more light...”) including 35 controlled trials (RCTs and other controlled trials) reported that for chronic tendinopathy, PBMT was more effective than minimal intervention in relieving pain (pooled SMD -0.57 , 95% CI -0.93 to -0.20 , $p = 0.002$).⁵²
 - That analysis identified total number of treatment sessions as a significant predictor of effect size — suggesting more sessions lead to greater pain relief.

Early-era systematic review — potential benefit when dosed correctly

- A classic review (25 controlled trials) concluded that when PBMT is applied using “recommended dosages,” positive effects on tendinopathy are possible.⁴⁵
- For instance, in studies of Achilles tendinopathy, mean pain reduction was ~ 13.6 mm on a 100 mm VAS scale; for lateral epicondylitis (common “tennis elbow”), grip strength improved compared to controls.⁴⁵

Knee osteoarthritis (OA) / knee pain & function

- A recent systematic review and meta-analysis (10 RCTs; 542 participants) found that PBMT significantly reduced pain at rest compared to placebo (SMD ≈ -0.7 ; 95% CI -1.1 to -0.2 ; “moderate effect”).³⁵
- That same review noted some within-group improvements (pain, functional scores, gait) after PBMT, though differences vs placebo for functional mobility (e.g. Timed Up & Go) were **not** significant.³⁵
- A more recent meta-analysis focusing on older adults doing regular exercise found that adding PBMT can yield additional benefits: reductions in pain (visual analog scale / numeric rating), improvements in total joint-related scores (WOMAC total, WOMAC-pain and WOMAC-function), and slight increase in knee range of motion.²⁷
- Taken together, this suggests PBMT helps with symptom relief (pain, some function) in knee OA — especially as an adjunct to exercise or rehab.

Evidence for Neck Pain

Early / Foundational Reviews

- A landmark meta-analysis by The Lancet (2009) included 16 randomized controlled trials (RCTs), ~820 patients: for *acute neck pain*, LLLT yielded a relative risk (RR) of 1.69 (95% CI 1.22–2.33) for pain improvement vs placebo; for *chronic neck pain*, RR was 4.05 (2.74–5.98). Based on trials reporting visual analogue scale (VAS) pain scores, pain intensity was reduced by ~ 19.9 mm (on a 100 mm scale) on average. Follow-up up to 1–22 weeks showed sustained pain relief (reduction ~ 22 mm). Side-effects were generally mild and comparable to placebo.⁸
- An updated systematic review + meta-regression (to Feb 2012) of 17 trials concluded: there is moderate-quality evidence (from 2 small trials) that LLLT may improve pain, disability, QoL, and global perceived effect (GPE) in chronic neck pain.¹⁶

More Recent / Specific Analyses

- A 2022 meta-analysis focused on myofascial neck pain (MNP) — 13 RCTs, 556 patients. PBMT significantly reduced pain (mean difference ≈ -1.29 , 95% CI -2.36 to -0.23). Secondary outcomes — pressure pain threshold (PPT) and right-bending range-of-motion (ROM) — improved.⁴³

Take-Home

Overall, for neck pain (especially chronic), PBMT/LLLT shows modest but consistent evidence for pain relief, sometimes with improved QoL or ROM. PBMT should be considered a useful adjunct for neck pain in conjunction with exercise and manual therapy.

Evidence for Low Back Pain (LBP) / Back Pain

- A 2015 meta-analysis on chronic non-specific low back pain (CNLBP) looked at 15 studies with 1039 participants. It found a significant, short-term pain reduction in favour of LLLT (weighted mean difference ~ -1.40 cm on a 10 cm VAS), but this benefit was only observed in trials using at least 3 Joules per point, in participants whose baseline pain was <30 months, and in non-acupuncture LLLT protocols. Global assessment showed improved outcomes immediately after treatment (risk ratio ~ 2.16).¹⁵
- Another meta-analysis of chronic non-specific low-back pain (7 RCTs, ~ 394 patients) found that LLLT significantly reduced pain (WMD ~ -13.6 on 100-point VAS) compared with placebo.¹⁹

Take-Home

For low back pain, PBMT/LLLT has evidence of pain reduction. The effects appear more likely when certain parameters (e.g. adequate dose, shorter pain duration) are met.

Myofascial Pain

- A recent meta-analysis of 17 studies (944 patients) on PBMT for myofascial pain syndrome (MPS) of the upper trapezius found that PBMT alone produced a medium effect size for pain reduction (SMD ≈ -0.54 , 95% CI -1.05 to -0.02), and when PBMT was combined with exercise (PBMT + EX) the effect was larger (SMD ≈ -0.80 , 95% CI -1.35 to -0.26).⁵
- For myofascial pain related to temporomandibular disorders (TMD), a 2018 meta-analysis of 8 RCTs found that LLLT significantly reduced pain (on a 0–10 VAS scale by ~ 2.2 units immediately, and ~ 2.4 units at 3–4 weeks), and increased interincisal opening at 1 month.³²
- A more recent cost-effectiveness and systematic review (2021) on PBMT for myofascial TMD pain (17 SR studies, 4 included in meta-analysis) concluded that laser-treated groups showed superior improvement vs placebo in pain intensity, and PBMT was more cost-effective than placebo in pain control.⁴¹
- A 2025 study combining LLLT with pharmacotherapy for myofascial pain disorder (with/without other TMD) reported that both LLLT alone and LLLT + drugs significantly reduced pain and improved mouth opening, with faster improvement when combined.⁴⁰

PBMT appears to have a modest analgesic effect in various types of myofascial pain (neck pain, trapezius MPS, temporomandibular myofascial pain), often improving pain and sometimes function or range of motion. The added benefit seems stronger when PBMT is combined with exercise or other therapies (manual therapy, conventional care), suggesting PBMT may be best considered as a synergistic treatment.

4. Synergistic Effects of Combined ESWT + PBMT

4.1 Biological Rationale

Although both therapies are effective individually, their mechanisms target different stages of tissue repair:

ESWT	PBMT
Mechanical stimulation	Cellular & biochemical stimulation
Neovascularization	ATP production & mitochondrial enhancement
Collagen remodeling	Anti-inflammatory & antioxidant effects
Breaking pathological tissue patterns	Accelerating tissue regeneration

Combining both therapies may provide a full-spectrum regenerative environment.

4.2 Clinical Evidence of Synergy

4.2.1 Plantar Fasciitis RCT (120 participants)

Study: Alayat et al., 2018⁴

Groups:

1. ESWT + PBMT
2. ESWT alone
3. PBMT alone
4. Sham PBMT

Results:

- All active groups improved significantly.
- The ESWT + PBMT group had the greatest improvement in:
 - VAS pain
 - Pressure pain threshold
 - Functional scores
- Benefits were sustained at 12-week follow-up.
- The combined therapy significantly outperformed each monotherapy.

This remains one of the clearest demonstrations of synergy in musculoskeletal medicine.

4.3 Proposed Mechanistic Synergy

1. ESWT initiates mechanical-driven biological change:
 - microtrauma
 - angiogenesis
 - collagen turnover
 2. PBMT optimizes the cellular environment to accelerate repair:
 - higher ATP levels
 - reduced oxidative stress
 - decreased inflammation
 - boosted fibroblast activity
 3. Sequential application (ESWT → PBMT) likely maximizes results.
 4. Enhanced blood flow from ESWT may improve PBMT photon delivery and cellular response.
-

5. Applications in Clinical Practice

5.1 Indications where combination therapy is most promising:

- chronic plantar fasciitis
- chronic Achilles tendinopathy
- patellar tendinopathy
- rotator cuff tendinopathy
- lateral & medial epicondylitis
- myofascial trigger points
- post-surgical soft tissue recovery
- chronic soft-tissue inflammation
- stubborn overuse injuries unresponsive to exercise and manual therapy

5.2 Situations where PBMT alone may be ideal:

- acute soft tissue injuries
 - early inflammation
 - patients sensitive to mechanical stimulation
 - neuropathic pain
 - post-operative healing phase
 - pain sensitive patients
-

6. Safety Profile

Both ESWT and PBMT demonstrate excellent safety profiles:

ESWT Risks

- transient soreness
- mild swelling
- bruising
- rare nerve irritation

PBMT Risks

- minimal; typically none
- considered to have no side effects based on published clinical trials

No major adverse effects have been reported with combined therapy.

7. Limitations of Current Research

- Heterogeneity in ESWT and PBMT protocols
- Limited large-scale RCTs on combined therapy
- Variation in energy, wavelength, and dosing parameters
- Limited long-term data (>1 year)

Despite this, current data strongly support the rationale and benefits of combination therapy.

8. Conclusion

Both ESWT and PBMT are powerful non-invasive modalities that promote pain reduction, tissue regeneration, and improved function through different, yet complementary biological mechanisms.

Growing evidence—including randomized controlled clinical trials—demonstrates significant synergistic benefits when ESWT and PBMT are combined, particularly for chronic tendinopathy and plantar fasciitis.

Clinicians integrating these therapies may achieve:

- faster recovery
- greater pain reduction
- enhanced tissue repair
- improved patient satisfaction
- reduced reliance on medication or invasive procedures

Combined ESWT + PBMT represents a promising frontier in regenerative musculoskeletal medicine.

References

¹ Abd elazeem, W., et al. (2024). Effectiveness of extracorporeal shockwave therapy versus conventional physiotherapy in treatment of chronic Achilles tendinopathy. *QJM: An International Journal of Medicine*, Volume 117, Issue Supplement_2, October, hcae175.982

² Abidi, A., et al. (2021). Immunomodulatory activity seen as a result of photobiomodulation therapy in stimulated primary human fibroblasts. *Arch Oral Biol*. Jan;121:104968.

³ Al-Abbad, H., et al. (2013). The effectiveness of extracorporeal shock wave therapy on chronic achilles tendinopathy: a systematic review. *Foot Ankle Int*. Jan;34(1):33-41.

⁴ Alayat, M. S. M., et al. (2018). Effect of shockwave therapy and low-level laser therapy combined vs. either therapy alone on plantar fasciitis. *Journal of Lasers in Medical Sciences*, 9(2), 81–87.

⁵ Alayat, M. S. M., et al. (2022). Effectiveness of Photobiomodulation Therapy in the Treatment of Myofascial Pain Syndrome of the Upper Trapezius Muscle: A Systematic Review and Meta-Analysis. *Photobiomodul Photomed Laser Surg*. Oct;40(10):661-674.

⁶ Al Balah, O.F., et al. (2025). Immunomodulatory effects of photobiomodulation: a comprehensive review. *Lasers Med Sci*. Apr 11;40(1):187.

⁷ Bathini, M., et al. (2022). The Molecular Mechanisms of Action of Photobiomodulation Against Neurodegenerative Diseases: A Systematic Review. *Cell Mol Neurobiol*. May;42(4):955-971.

⁸ Chow, R.T., et al. (2009). Efficacy of low-level laser therapy in the management of neck pain: a systematic review and meta-analysis of randomised placebo or active-treatment controlled trials. *Lancet*. Dec 5;374(9705):1897-908.

⁹ Costa, M., et al. (2022). Photobiomodulation exerts anti-inflammatory effects on the vascular and cellular phases of experimental inflammatory models. *Lasers Med Sci*. Feb;37(1):563-571.

- ¹⁰ De Oliveira, V.L.C., et al. (2017). Photobiomodulation therapy in the modulation of inflammatory mediators and bradykinin receptors in an experimental model of acute osteoarthritis. *Lasers Med Sci.* Jan;32(1):87-94.
- ¹¹ Escarrat, V., et al. (2024). Dorsoventral photobiomodulation therapy safely reduces inflammation and sensorimotor deficits in a mouse model of multiple sclerosis. *J Neuroinflammation.* Dec 18;21(1):321.
- ¹² Escudero, J.S., et al. (2019). Photobiomodulation therapy (PBMT) in bone repair: A systematic review. *Injury.* Nov;50(11):1853-1867.
- ¹³ Feeney, K. (2022). Therapy for Midportion Achilles Tendinopathy: A Systematic Review. *Cureus.* Jul 18;14(7):e26960.
- ¹⁴ Fiorio, F.B., et al. (2017). Photobiomodulation therapy action in wound repair skin induced in aged rats old: time course of biomarkers inflammatory and repair. *Lasers Med Sci.* Nov;32(8):1769-1782.
- ¹⁵ Glazov, G. et al. (2016). Low-level laser therapy for chronic non-specific low back pain: a meta-analysis of randomised controlled trials. *Acupunct Med.* Oct;34(5):328-341.
- ¹⁶ Gross, A. R., et al. (2013). Low Level Laser Therapy (LLLT) for Neck Pain: A Systematic Review and Meta-Regression. *Open Orthop J.* 2013 Sep 20;7:396–419.
- ¹⁷ Hamblin, M. R. (2017). Mechanisms and applications of the anti-inflammatory effects of photobiomodulation therapy. *AIMS Biophysics,* 4(3), 337–361.
- ¹⁸ Hamblin, M. (2018). Mechanisms and Mitochondrial Redox Signaling in Photobiomodulation. *Photochem Photobiol.* Mar;94(2):199-212.
- ¹⁹ Huang, Z., et al. (2015). The effectiveness of low-level laser therapy for nonspecific chronic low back pain: a systematic review and meta-analysis. *Arthritis Res Ther.* Dec 15;17:360.
- ²⁰ Huang, Z., et al. (2019). Effectiveness of photobiomodulation therapy for knee osteoarthritis: A systematic review and meta-analysis. *Clinical Rehabilitation,* 33(3), 337–350.
- ²¹ Ines, L., et al. (2025). The effectiveness of radial extracorporeal shock wave therapy (rESWT) in plantar fasciitis: a 12 months randomised controlled trial in a Tunisian rehabilitation department. *BMC Musculoskelet Disord.* Oct 8;26(1):938.
- ²² Karkada, G., et al. (2023). Effect of photobiomodulation therapy on inflammatory cytokines in healing dynamics of diabetic wounds: a systematic review of preclinical studies. *Arch Physiol Biochem.* 2023 Jun;129(3):663-670.

- ²³ Khan, I., et al. (2021). Accelerated burn wound healing with photobiomodulation therapy involves activation of endogenous latent TGF- β 1. *Sci Rep.* Jun 28;11(1):13371.
- ²⁴ Kim, J. et al. (2024). Extracorporeal shockwave therapy for myofascial pain syndrome: Meta-analysis. *American Journal of Physical Medicine.*
- ²⁵ Kim, J.H., et al. (2025). Multispectral Pulsed Photobiomodulation Enhances Re-Epithelialization via Keratinocyte Activation in Full-Thickness Skin Wounds. *Cells.* Sep 10;14(18):1415.
- ²⁶ Leal-Junior, E. C. P., et al. (2015). Photobiomodulation in muscle performance and injury recovery. *Journal of Athletic Training,* 50(10), 1091–1103.
- ²⁷ Li, B-M., et al. (2024). The Effects of Photobiomodulation on Knee Function, Pain, and Exercise Tolerance in Older Adults: A Meta-analysis of Randomized Controlled Trials. *Arch Phys Med Rehabil.* Mar;105(3):593-603.
- ²⁸ Liu, H., et al. (2025). Photobiomodulation therapy (PBMT) in skeletal muscle regeneration: A comprehensive review of mechanisms, clinical applications, and future directions. *Photodiagnosis Photodyn Ther.* Jun:53:104634.
- ²⁹ Lorenzo L., et al. (2024). Efficacy and tolerability of extracorporeal shock wave therapy in patients with plantar fasciopathy: a systematic review with meta-analysis and meta-regression. *Eur J Phys Rehabil Med.* 2024 Oct;60(5):832-846.
- ³⁰ Majidi, L., et al. (2024). The effect of extracorporeal shock-wave therapy on pain in patients with various tendinopathies: a systematic review and meta-analysis of randomized control trials. *BMC Sports Sci Med Rehabil.* 2024 Apr 24;16(1):93.
- ³¹ Modena, D., et al. (2023). Photobiomodulation therapy with light-emitting diode in stimulating adipose tissue mitochondria. *Lasers Med Sci.* 2023 Oct 18;38(1):238.
- ³² Munguia, F.M., et al. (2018). Efficacy of Low-Level Laser Therapy in the Treatment of Temporomandibular Myofascial Pain: A Systematic Review and Meta-Analysis. *J Oral Facial Pain Headache.* Summer;32(3):287–297.
- ³³ Naterstad, I.F., et al. (2022). Efficacy of low-level laser therapy in patients with lower extremity tendinopathy or plantar fasciitis: systematic review and meta-analysis of randomised controlled trials. *BMJ Open.* Sep 28;12(9):e059479.
- ³⁴ Notarnicola, A., & Moretti, B. (2012). Shockwave therapy and tendon regeneration. *Muscles, Ligaments and Tendons Journal,* 2(1), 33–37.
- ³⁵ Oliveira, S., et al. (2024). Effectiveness of Photobiomodulation in Reducing Pain and Disability in Patients With Knee Osteoarthritis: A Systematic Review With Meta-Analysis. *Phys Ther.* Aug 2;104(8):pzae073.

- ³⁶ Orhan, O., et al. (2023). Pain relief and functional improvement provided by extracorporeal shock wave therapy in plantar fasciitis is better than corticosteroid injection and kinesio taping: A randomized trial. *Turk J Phys Med Rehabil.* Aug 23;69(4):469–478.
- ³⁷ Pilar, E.F.S., et al. (2024). Modulation of gene expression in skin wound healing by photobiomodulation therapy: A systematic review in vivo studies. *Photodermatol Photoimmunol Photomed.* Jul;40(4):e12990.
- ³⁸ Pinho, A. C., et al. (2021). Mitochondrial responses to photobiomodulation. *Photochemistry and Photobiology,* 97(3), 517–530.
- ³⁹ Rhim, H.C., et al. (2024). Use of extracorporeal shockwave therapies for athletes and physically active individuals: a systematic review. *Br J Sports Med.* Feb 7;58(3):154-163.
- ⁴⁰ Shah, J. S., et al. (2025). Low-Level Laser Therapy with Pharmacotherapy in the Management of Myofascial Pain Dysfunction Syndrome with or without Other Temporomandibular Disorders. *Indian J Dent Res.* Jan 1;36(1):37-41.
- ⁴¹ Sobral, A-PT., et al. (2021). Photobiomodulation and myofascial temporomandibular disorder: Systematic review and meta-analysis followed by cost-effectiveness analysis. *J Clin Exp Dent.* Jul 1;13(7):e724-e732.
- ⁴² Stania, M., et al. (2023). The Efficacy of Extracorporeal Shock Wave Therapy as a Monotherapy for Achilles Tendinopathy: A Systematic Review and Meta-Analysis. *J Chiropr Med.* Dec;22(4):294-301.
- ⁴³ Tehrani, M.R., et al. (2022). Efficacy of low-level laser therapy on pain, disability, pressure pain threshold, and range of motion in patients with myofascial neck pain syndrome: a systematic review and meta-analysis of randomized controlled trials. *Lasers Med Sci.* Dec;37(9):3333-3341.
- ⁴⁴ Tripodi, N., et al. (2021). The effect of low-level red and near-infrared photobiomodulation on pain and function in tendinopathy: a systematic review and meta-analysis of randomized control trials. *BMC Sports Sci Med Rehabil.* Aug 14;13(1):91.
- ⁴⁵ Tumilty, S., et al. (2010). Low level laser treatment of tendinopathy: a systematic review with meta-analysis. *Photomed Laser Surg.* Feb;28(1):3-16.
- ⁴⁶ Vetrano, M., et al. (2013). Anti-inflammatory response of ESWT. *International Orthopaedics,* 37(12), 2349–2353.
- ⁴⁷ Wang, C. J., et al. (2003). Shockwave therapy and tissue angiogenesis. *Journal of Orthopaedic Research,* 21(6), 984–989.
- ⁴⁸ Wang, B., et al. (2024). Evaluation of the efficacy of trigger points combined with extracorporeal shock waves in the treatment of plantar fasciitis: heel temperature and plantar pressure. *BMC Musculoskelet Disord.* Mar 2;25(1):191.

⁴⁹ Xiong, Y., et al. (2024). Efficacy and safety of extracorporeal shock wave therapy for upper limb tendonitis: a systematic review and meta-analysis of randomized controlled trials. *Front Med (Lausanne)*. 2024 Jul 30;11:1394268.

⁵⁰ Xue, X., et al. (2024). Effect of extracorporeal shockwave therapy for rotator cuff tendinopathy: a systematic review and meta-analysis. *BMC Musculoskelet Disord*. May 4;25(1):357.

⁵¹ Yang, L., et al. (2020). Mitochondria as a target for neuroprotection: role of methylene blue and photobiomodulation. *Transl Neurodegener*. Jun 1;9(1):19.

⁵² Yap, B.W.D., et al. (2025). Shedding more light on the short-term effect of low-level laser therapy on pain in tendinopathy: A systematic review with meta-analysis. *J Back Musculoskelet Rehabil*. Nov;38(6):1232-1256.

⁵³ Yousefi-Nooraie, R., et al. (2008). Low level laser therapy for nonspecific low-back pain. *Cochrane Database Syst Rev*. 2008 Apr 16;(2):CD005107.