Stem Cell Research and Therapeutics
SCRT, 9(1): 241-252
www.scitcentral.com

ISSN: 2474-4646

Review Article: Open Access

Energy, Signal and Load: A Comparative Functional Taxonomy of Physical Therapies as Adjuncts to Stem Cell and Orthobiologic Regenerative Medicine

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Received October 19, 2026; Revised October 22, 2026; Accepted October 23, 2026

ABSTRACT

Background: Physical modalities, including photobiomodulation (PBM), extracorporeal shockwave therapy (ESWT), pulsed electromagnetic fields (PEMF), electrotherapy, thermal therapies and manual interventions, are increasingly combined with platelet-rich plasma (PRP), bone marrow aspirate concentrates and mesenchymal stromal/stem cell (MSC) treatments, yet are usually compared one device at a time.

Methods: Structured comparative critical review of the modalities in the clinical guide Physical Therapies in Regenerative Medicine (Kume, 2026). Each modality was coded across eleven prespecified dimensions, and key efficacy statements were checked against primary trials and recent meta-analyses.

Results: We propose a five-class functional taxonomy: structural/mechanotransductive stimulators (ESWT, PEMF for bone, NMES), a bioenergetic modulator (PBM), thermal tissue preparers, neural/contextual enablers, and symptomatic modulators with an adaptive cost (cryotherapy). Independent evidence supported high-energy ESWT for calcific rotator cuff tendinopathy, ESWT for greater trochanteric pain and nonunion, adequately dosed PBM for knee osteoarthritis and NMES after knee surgery. It did not support adding ESWT to eccentric loading in patellar tendinopathy, or whole-body cryotherapy. Most modalities converge on calcium and nitric oxide signaling and show biphasic dose responses; factorial data with orthobiologics are scarce.

Conclusions: Physical therapies are best framed as adjuncts that prepare, amplify or permit the signals delivered by progressive loading and orthobiologics. An essentiality test, peri-injection timing rules and factorial add-on trials are proposed to reduce redundancy and overclaiming.

Keywords: photobiomodulation; extracorporeal shockwave therapy; pulsed electromagnetic field; mesenchymal stem cells; platelet-rich plasma; regenerative rehabilitation.

INTRODUCTION

Regenerative medicine for musculoskeletal disorders has moved from single biological products toward combined strategies in which an injected biologic, such as PRP, BMAC or a culture-expanded MSC preparation, is followed by structured rehabilitation [1]. The concept of regenerative rehabilitation recognizes that cells respond to their mechanical and physiological environment, and that the rehabilitation program is therefore part of the biology rather than an afterthought [1,2]. Mesenchymal cells are known to read substrate stiffness and cytoskeletal tension through myosin-dependent and YAP/TAZ-dependent pathways that bias lineage commitment [3,4]. Physical energy delivered to tissue is therefore a plausible means of shaping the environment in which endogenous or transplanted progenitor cells act.

In parallel, the market offers a growing range of devices that deliver light, acoustic pressure waves, electric currents,

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Citation: Kume MH, Furlan B, Boaventura CG, Probst MA, Peracchi E, et al. (2026) Energy, Signal and Load: A Comparative Functional Taxonomy of Physical Therapies as Adjuncts to Stem Cell and Orthobiologic Regenerative Medicine. Stem Cell Res Ther, 9(1): 241-252.

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DOI: https://doi.org/10.5281/zenodo.23762654

magnetic fields, heat or cold. Each modality has its own literature, dose vocabulary and commercial narrative. The clinician who must decide whether to add PBM, ESWT, PEMF or TECAR to an injection-plus-exercise plan rarely finds a framework that compares them on common terms. Single-modality reviews answer the question "does X work for condition Y?" but not the more practical questions: what does X add that loading and the biologic do not already provide, when in the repair timeline should it be used, and which combinations are redundant?

The clinical guide Physical Therapies in Regenerative Medicine (Kume, 2026) organizes these modalities within one framework, covering mechanism, parameters, indications, contraindications, evidence and integration with orthobiologics across 31 chapters [5]. The present article is not a summary of that book. It uses the book's content as a structured source corpus and performs an explicit cross-modality comparison that the book does not present as a single analysis. The aims were (i) to build a functional taxonomy of physical therapies according to the biological axis they primarily target; (ii) to compare modalities across common dimensions in a single matrix; (iii) to check the main efficacy statements against independent primary trials and meta-analyses; (iv) to identify convergence and redundancy among modalities; and (v) to derive timing rules, decision rules and a research agenda relevant to stem cell and orthobiologic practice.

METHODS

Design

This is a structured comparative critical review with a narrative synthesis. It is not a systematic review: no exhaustive database search, risk-of-bias assessment or quantitative pooling was performed, and no GRADE certainty ratings were generated. Where certainty ratings are mentioned, they are those reported by the cited meta-analyses.

Source corpus

The primary corpus was the full text of Physical Therapies in Regenerative Medicine, first edition (2026; 159 pages, 7 parts, 31 chapters, 94 references) [5]. The book covers the foundations of regenerative rehabilitation (Part I; chapters 1 to 4), PBM (chapters 5 to 9), ESWT (chapters 10 to 15), bioelectric and electromagnetic modalities (chapters 16 to 19), thermal and cold modalities (chapters 20 to 23), manual, needle and neuromodulatory interventions (chapters 24 to 28), and clinical integration (chapters 29 to 31).

Comparative coding

Each modality described in the corpus was coded across eleven dimensions defined before extraction: (1) physical energy form; (2) primary biological target, using the five healing-microenvironment axes defined in the corpus (vascular/oxygen supply, mechanical load signaling, metabolic/mitochondrial state, resolution of inflammation and neural regulation); (3) effective tissue depth; (4) onset and time course of effect; (5) repair-phase window; (6) parameter dependence; (7) strength of clinical evidence; (8) principal risks and contraindications; (9) cost and logistic burden; (10) interface with MSC and orthobiologic therapies; and (11) explicit limits of claims. Evidence was described qualitatively as consistent, moderate, modest or heterogeneous, limited, or insufficient. These labels are the author's interpretation and are not a validated grading instrument.

External verification

Because the corpus is a clinical guide written by the author of this review, its key quantitative and efficacy statements were checked against independent sources. These were landmark randomized controlled trials (RCTs) and recent systematic reviews or meta-analyses identified by targeted searches of PubMed, PubMed Central and publisher websites (search completed October 2026). During this step, several mismatches between in-text citation numbers and the reference list of the source book were identified. Only references verified directly against their original records are cited here.

RESULTS

Five energy forms, one convergent biology

The corpus groups physical therapies by the form of energy delivered: photons (PBM), mechanical waves (focused and radial ESWT, therapeutic ultrasound), electric currents and fields (TENS, interferential current, NMES, peripheral nerve stimulation), magnetic or electromagnetic fields (PEMF, TECAR as radiofrequency diathermy), and thermal energy in either direction (superficial heat, cryotherapy, contrast) [5]. Manual and needle-based interventions add mechanical input with a large neurophysiological and contextual component [6]. **Table 1** summarizes the physical characteristics of each energy form and its first transduction step.

Despite these physical differences, the downstream signaling converges. Photon absorption by cytochrome c oxidase leads to nitric oxide dissociation, increased ATP, a brief burst of reactive oxygen species and modulation of calcium [7]. Shockwaves and pressure waves act through cavitation and membrane strain, opening mechanosensitive channels and inducing nitric oxide synthase, vascular endothelial growth factor and growth factor release [8,10]. PEMF is thought to act on calcium/calmodulin and adenosine receptor signaling [9]. Heat raises enzymatic rate and perfusion. The corpus therefore treats calcium and nitric oxide as a shared node through which several modalities act [5]. This convergence has a practical corollary. When two modalities act mainly through the same node at the same time, the second may add cost without adding biology.

Table 1. Physical energy forms used in regenerative rehabilitation and their first transduction step (synthesized from the source corpus [5] and mechanistic reviews [6–9]).

Energy form	Modalities	Effective depth	First transduction step
Photons (red/near-infrared)	PBM (laser, LED)	Red 630–685 nm: superficial; 780–860 nm: intermediate; 904–1064 nm: deeper	Cytochrome c oxidase absorption; NO dissociation; ATP and transient ROS; Ca^{2+} modulation
Mechanical pressure waves	Focused ESWT; radial pressure-wave therapy; therapeutic ultrasound	Focused: adjustable focal depth; radial: maximal at skin, decays with depth	Cavitation, membrane strain, mechanosensitive channels (e.g., Piezo), integrin–cytoskeleton signaling
Electric currents/fields	TENS, IFC, NMES, PNS, electroacupuncture	Peripheral nerve and muscle under electrodes or leads	Axonal depolarization; segmental and descending pain modulation; motor-unit recruitment
Magnetic/electromagnetic fields	PEMF; capacitive coupling	Penetrates soft tissue and bone without contact	Induced electric fields; Ca^{2+}/calmodulin, adenosine A2A/A3 and NO signaling
Radiofrequency diathermy	TECAR (capacitive/resistive, 300 kHz–1 MHz)	Capacitive: superficial, water-rich tissue; resistive: denser deep tissue	Endogenous heating and possible athermal current effects
Thermal (heat)	Hot packs, infrared, warm water	Superficial heat: about 1–2 cm	Temperature-dependent enzymatic rate (Q10 ≈ 2–3), vasodilation, collagen extensibility
Thermal (cold)	Ice, cold-water immersion, whole-body cryotherapy	Skin and superficial tissue; systemic autonomic effects	Reduced metabolic rate and nerve conduction; vasoconstriction
Manual/needle mechanical input	Mobilization, manipulation, massage, OMT, acupuncture, dry needling	Local tissue plus central nervous system	Mechanoreceptor afferents; descending inhibition; contextual and expectation effects

A functional taxonomy

Grouping modalities by device type (laser, shockwave, electrical) does not predict clinical role. We therefore propose a functional taxonomy based on the primary biological axis targeted and on the relationship of each modality to the main regenerative stimulus, which is progressive mechanical loading with or without an orthobiologic (**Table 2; Figure 1**).

Table 2. Proposed functional taxonomy of physical therapies in regenerative medicine (original classification by the author).

Functional class	Modalities	Defining role	Relationship to loading/biologic
A. Structural / mechanotransductive stimulators	Focused ESWT (calcific, bone); PEMF for bone; NMES for muscle	Deliver a mechanical or electrical stimulus capable of driving a tissue-level structural response	Can supply a signal that loading cannot deliver (e.g., non-weight-bearing nonunion; inhibited quadriceps)
B. Bioenergetic modulator	PBM	Modulates mitochondrial function, oxidative balance and inflammatory phenotype	Prepares tissue and cells; may improve exercise tolerance and recovery
C. Thermal tissue preparers	Superficial heat, TECAR, contrast therapy	Change temperature, perfusion and tissue extensibility	Best used immediately before loading; limited stand-alone effect
D. Neural / contextual enablers	TENS/IFC, PNS, manual therapy, massage, OMT, acupuncture/dry needling, taVNS (research)	Reduce pain, inhibition and threat; improve movement confidence	Make loading possible; should not be described as regenerative
E. Symptomatic modulators with adaptive cost	Cryotherapy (local, cold-water immersion, whole-body)	Short-term analgesia and perceived recovery	May blunt inflammatory and anabolic signals; timing must be periodized

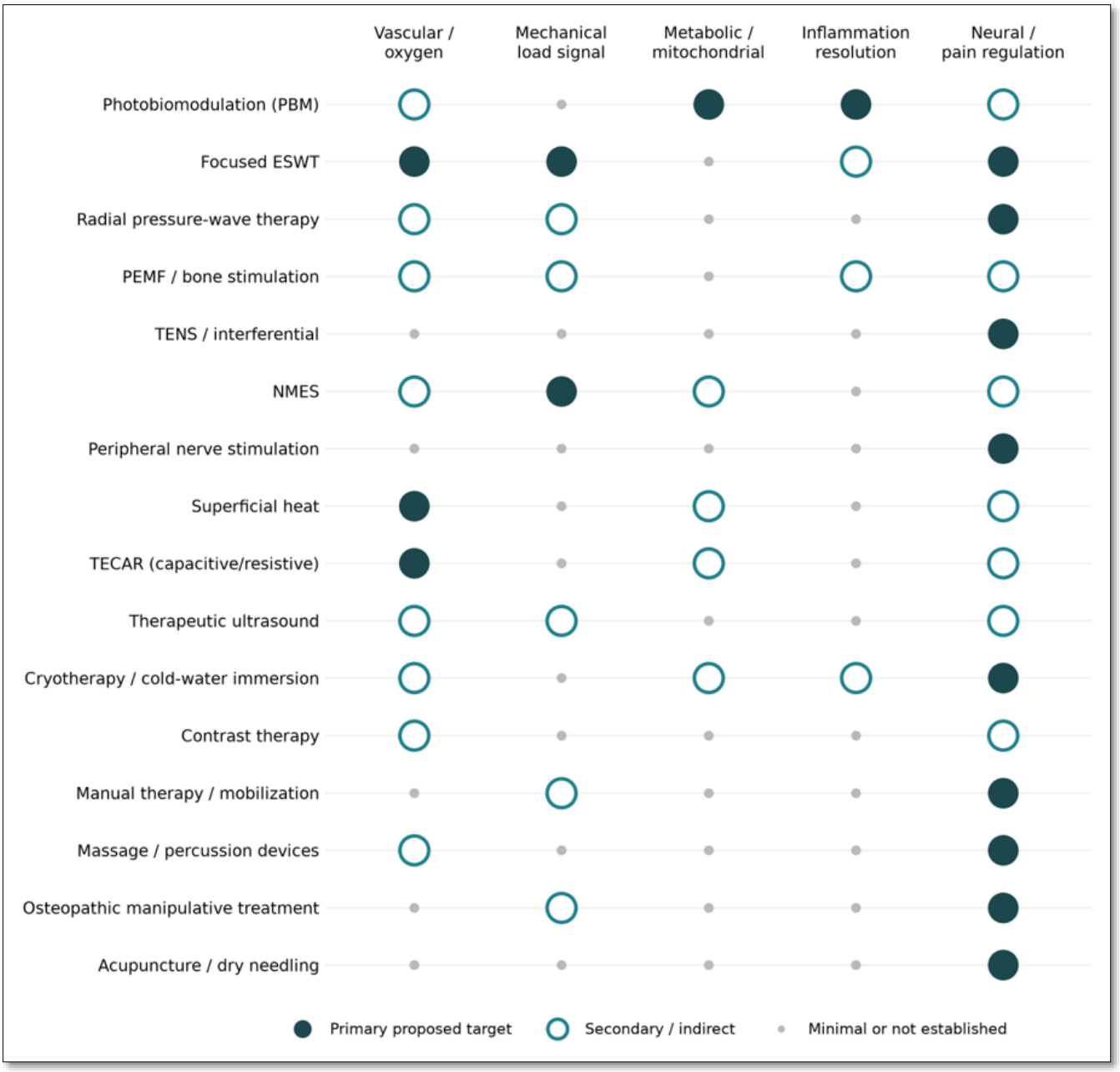


Figure 1. Modality-by-target map. Primary and secondary targets of each physical therapy across the five healing-microenvironment axes defined in the source corpus [5]. Filled circles indicate primary proposed targets, open circles secondary or indirect effects, and small grey dots minimal or unestablished effects. Classification is the author's interpretation and has not been validated.

Two features of the taxonomy deserve emphasis. First, only the structural/mechanotransductive class delivers a stimulus that, by itself, can plausibly initiate a tissue-level repair response, as with ESWT in calcific tendinopathy or nonunion and PEMF in bone. Even in this class, the corpus positions the modality as an adjunct to loading rather than a replacement [5]. Second, the largest class, neural/contextual enablers, acts mainly on pain, motor inhibition and patient experience. These are clinically valuable because they make loading possible, but they should not be described as regenerative.

Comparative matrix

Table 3 presents the comparative matrix across the main coded dimensions. Parameter ranges are those proposed in the corpus [5] and, where indicated, in the cited trials.

Table 3. Comparative matrix of physical therapies. Parameters are those proposed in the source corpus [5] unless otherwise stated; evidence labels are the author's qualitative interpretation and are not formal certainty ratings.

Modality (class)	Key parameters	Onset / repair window	Clinical evidence (interpretation)	Main risks / contraindications	Orthobiologic and MSC interface
PBM (B)	5–500 mW/cm²; 2–10 J/point; 4–12 points; 30–150 J/session; 2–3×/week for 3–6 weeks	Hours to days; inflammatory and proliferative phases	Moderate in knee OA and exercise recovery at adequate dose; modest in tendinopathy; heterogeneous in nerve	Eye exposure; photosensitizing drugs; active malignancy over field	Start ≥72 h after PRP; MSC/EV priming is a research frontier; factorial RCTs lacking
Focused ESWT (A)	EFD low <0.10, medium 0.10–0.28, high >0.28 mJ/mm²; 2000–4000 pulses; usually 3 weekly sessions	Weeks (angiogenic response peaks at weeks); remodeling phase	Supported in calcific cuff (high energy; very low certainty in 2024 meta-analysis) and hypertrophic nonunion; modest in plantar fascia and lateral elbow; no added benefit over eccentrics in patellar tendinopathy	Pregnancy; malignancy; coagulopathy; open physes; lung in acoustic path; infection	Combine with PRP 7–14 days after last session (corpus); one RCT shows earlier pain relief only
Radial pressure waves (A/D)	Ballistic; energy maximal at skin; 2000–3000 pulses	Days to weeks	Moderate in greater trochanteric pain (medium term); variable elsewhere	As above; superficial bruising	As for focused ESWT, with less depth
PEMF (A)	Device-specific; bone: 3–10 h/day for 3–6 months	Months; proliferative and remodeling phases	Most robust in nonunion; low to very low certainty in OA	Pacemakers and implanted electronics; pregnancy	Pro-osteogenic and chondrogenic MSC effects in vitro; adherence-dependent
TENS / IFC (D)	80–100 Hz (segmental) or 2–4 Hz (opioid-mediated); IFC ≈ TENS	Minutes; any phase	Moderate certainty of pain reduction vs placebo	Pacemakers; anterior neck; impaired sensation	Analgesic enabler; no regenerative effect expected
NMES (A)	250–450 µs; 35–75 Hz; ≥50% MVIC	Weeks; early post-operative and remodeling	Moderate for quadriceps strength after ACL surgery and TKA	Pacemakers; DVT risk zones; skin	Counteracts arthrogenic inhibition so that loading can progress
Superficial heat (C)	40–45 °C; 15–20 min; 1–2 cm depth	Minutes; before loading in subacute and chronic phases	Modest; mainly symptomatic and preparatory	Acute inflammation; impaired sensation; bleeding	Avoid over fresh injection site; useful before loading
TECAR (C)	300 kHz–1 MHz; capacitive vs resistive	Minutes; late rehabilitation (weeks 4–12)	Limited; small, heterogeneous trials	Metal implants in field; pregnancy; pacemakers	Can be applied during movement; add-on value unproven
Cryotherapy (E)	Local ice; CWI 10–15 °C for 10–15 min; WBC −100 to −140 °C	Minutes; acute symptomatic	Short-term analgesia; WBC evidence very low certainty; CWI blunts hypertrophy	Cold urticaria; Raynaud's; cardiovascular risk (WBC)	Avoid prolonged cold after biologic injection
Contrast therapy (C)	38–40 °C for 3–4 min / 10–15 °C for 30–60 s	Minutes; subacute distal edema	Limited	Vascular disease; sensory loss	Defer 48–72 h after injection
Manual therapy / massage / OMT (D)	Mobilization preferred to manipulation; percussion devices 20–50 Hz	Minutes to days; movement and tolerance stage	Small to moderate effects on pain (e.g., OMT in low back pain)	Cervical HVLA risk; anticoagulation; fragile tissue	No direct pressure on injection site ≥1 week; no HVLA over injected structure for 1–2 weeks
Acupuncture / dry needling (D)	Electroacupuncture 2/100 Hz; STRICTA reporting	Minutes to weeks	Modest specific effect over sham; larger effect vs no acupuncture	Pneumothorax; infection; bleeding	Analgesic enabler; avoid needling through injected tissue

Table 4. Main efficacy positions of the source corpus compared with independent trials and syntheses.

Indication / modality	Position in corpus [5]	Independent evidence	Agreement
PBM, knee osteoarthritis	Benefit at adequate dose	22 placebo-controlled RCTs (n = 1063): clinically relevant pain reduction with recommended doses (4–8 J at 785–860 nm; 1–3 J at 904 nm) [11]	Agrees
PBM, tendinopathy	Modest benefit, dose-dependent	25 trials: positive results associated with WALT-consistent doses [12]	Agrees
PBM, muscle performance/recovery	Among the more consistent uses	Meta-analysis: best effect when applied before exercise, about 5–6 J per point [13]	Agrees
Focused ESWT, calcific rotator cuff	High energy preferred	RCT n = 144: high energy > low energy > sham [14]; 2024 meta-analysis: high > low energy, but ultrasound-guided needling > ESWT for pain; very low certainty [15]	Agrees, with a caveat
Radial ESWT, greater trochanteric pain	Superior to corticosteroid in medium term	RCT n = 229: success at 4 months 68% (rESWT) vs 51% (injection) vs 41% (home training); at 15 months home training 80%, rESWT 74%, injection 48% [16]	Agrees; loading catches up
ESWT, hypertrophic nonunion	Union about 70–80% at ≥0.35 mJ/mm²	RCT: ESWT union rates comparable to surgery [17]	Agrees
ESWT, patellar tendinopathy	Adjunct for refractory cases after loading	Living NMA: no added benefit to eccentric exercise (moderate strength) [18]; 2026 NMA: no effect over placebo [19]	Tempers the corpus
ESWT, plantar fasciitis	Among best-supported indications	2024 meta-analysis (14 RCTs): reduced fascia thickness, no significant pain advantage over other non-surgical care [20]	Partly tempers
PEMF, nonunion and OA	Nonunion most robust; OA moderate	Original nonunion series [21]; OA meta-analysis: pain benefit, low to very low quality evidence [22]	Agrees; OA certainty low
TENS, pain	Analgesic enabler	381 RCTs: pain reduction vs placebo, moderate certainty [23]	Agrees
NMES, post-surgical quadriceps	Supports early strength recovery	Meta-analysis after ACL surgery: improved quadriceps strength in the short and long term [24]	Agrees
Whole-body cryotherapy	Safety concerns; limited role	Cochrane review: very low-certainty evidence; optimal protocol and safety unknown [25]	Agrees
Acupuncture, chronic pain	Modest effect over sham	IPD meta-analysis: effect over sham and over no acupuncture, the latter larger [26]	Agrees
OMT, low back pain	Modest effect	Meta-analysis: effect size about −0.30 for pain [27]	Agrees

Independent evidence: where it agrees and where it tempers

Table 4 contrasts the main efficacy positions of the corpus with independent trials and syntheses. Agreement was found for most core indications. For PBM in knee osteoarthritis, a meta-analysis of 22 placebo-controlled RCTs (n = 1063) reported clinically relevant pain reduction when recommended doses were used (4 to 8 J per point at 785 to 860 nm; 1 to 3 J at 904 nm) [11]. For tendinopathy, positive PBM trials clustered around doses consistent with World Association for Laser Therapy (WALT) recommendations [12], and pre-exercise application improved performance and recovery markers [13]. For calcific rotator cuff tendinopathy, high-energy focused ESWT outperformed low-energy and sham treatment in a randomized trial of 144 patients [14]. A 2024 meta-analysis confirmed the high- versus low-energy gradient but found that ultrasound-guided needling was superior to ESWT for pain, with very low certainty overall

[15]. In greater trochanteric pain syndrome, radial ESWT outperformed corticosteroid injection and home training at 4 months, while home training caught up by 15 months [16]. In hypertrophic long-bone nonunion, ESWT achieved union rates comparable to surgery [17]. These results agree with the corpus's position that modality benefit is dose-specific and time-limited.

Independent evidence was less favorable in three places. First, in patellar tendinopathy, a living network meta-analysis found moderate-strength evidence that ESWT adds no short-term pain or function benefit when combined with eccentric exercise [18]. A 2026 network meta-analysis likewise found no significant effect of ESWT over placebo in this condition [19]. Second, for plantar fasciitis, a 2024 meta-analysis found reduced fascia thickness but no significant pain advantage over other non-surgical treatments [20]. Third, for whole-body cryotherapy, a Cochrane review found very low-certainty evidence and no established safe or effective protocol [25]. Evidence for TECAR also remains preliminary, with small samples, few sham-controlled trials and variable protocols [28]. These findings support the corpus's general rule that loading comes first. They also argue for applying that rule more strictly in patellar tendinopathy than a device-led protocol might suggest.

Convergence, redundancy and the inverted-U dose curve

Two cross-cutting properties emerged from the comparison. The first is convergence: PBM, ESWT, PEMF, heat and, to a lesser extent, electrical stimulation all modulate calcium handling, nitric oxide availability and perfusion [7–9]. When the target is the same node, adding a second modality is more likely to be redundant than synergistic. The corpus notes that adding TECAR, PEMF or neuromodulation to an already adequate program of ESWT or PBM plus loading rarely adds measurable benefit [5]. The second is biphasic dosing. PBM has a well-described Arndt–Schulz-type biphasic response, in which low fluence stimulates and high fluence inhibits [29]. Similar inverted-U behavior is visible in MSC studies of PBM [30] and in the energy dependence of ESWT effects on progenitor cells [10]. Mechanical loading itself has a therapeutic window bounded by under-stimulation and overload [2]. A practical inference is that stacking modalities increases total delivered dose and may move tissue beyond the stimulatory window, especially early after injection.

The stem cell and orthobiologic interface

Preclinical data show that several modalities can modify MSC behavior. PBM increases MSC proliferation, migration and, depending on parameters and cell source, differentiation [30]. ESWT enhances proliferation, migration and homing of bone marrow and adipose-derived progenitors and has been used as a preconditioning strategy [8]. PEMF promotes osteogenic and chondrogenic differentiation of MSCs through BMP/TGF-β, adenosine and mTOR pathways [9,10]. These data justify research into using physical energy to prime cells ex vivo or condition the recipient site in vivo. However, they do not establish clinical benefit when a modality is added to an injected cell or platelet product.

Direct clinical evidence for combinations remains sparse. In an RCT of 33 athletes with chronic patellar tendinopathy, adding a focused ESWT session to PRP accelerated pain relief at 1 month, with no between-group differences at 1 year [31]. For PBM plus PRP or BMAC, the corpus identifies no adequately powered factorial trial and treats the combination as a research question [5]. Timing therefore relies on biological reasoning rather than outcome data. **Table 5** summarizes the peri-injection timing rules proposed in the corpus. Their common logic is to protect the early platelet- and cell-driven inflammatory cascade, avoid mechanical dispersion of the injectate, and introduce loading progressively.

Table 5. Peri-orthobiologic timing rules proposed in the source corpus [5]. These rules are based on biological reasoning and expert opinion and have not been tested in dedicated trials.

Intervention	Timing relative to PRP/BMAC/cell injection	Rationale
Direct manual pressure over injection site	Avoid for ≥1 week	Avoid dispersion of injectate and disruption of early clot/matrix
HVLA manipulation of injected structure	Avoid for 1–2 weeks	Protect early repair and injectate retention
Massage around (not over) the site	From 48–72 h	Manage edema and guarding without loading the site
PBM	From ≥72 h (typically days 3–7)	Avoid interfering with the platelet-driven inflammatory phase
ESWT then PRP	PRP 7–14 days after last ESWT session	Allow the angiogenic and mechanotransductive response to develop first
Contrast therapy	Defer 48–72 h	Avoid vasomotor disturbance during early phase
Prolonged cryotherapy and NSAIDs	Avoid in the early post-injection window	May blunt the inflammation the biologic is meant to start
Loading progression	Isometrics within days; isotonics at 1–2 weeks; heavy slow resistance at 3–4 weeks	Load is the main regenerative stimulus and is introduced progressively

The cold rule deserves specific mention. Post-exercise cold-water immersion attenuated anabolic signaling and long-term hypertrophy in a controlled training study [32], and the PEACE and LOVE framework advises against reflexive anti-inflammatory strategies in the acute phase of soft-tissue injury [33]. By analogy, prolonged cold after a biologic injection may blunt the inflammatory phase that the biologic is designed to start. The corpus applies the same reasoning to non-steroidal anti-inflammatory drugs [5]. This analogy is plausible but has not been tested in trials of orthobiologic outcomes.

Stage-by-modality map

The corpus organizes rehabilitation into five stages: protection, movement and tolerance, remodeling, performance, and resilience [5]. Figure 2 maps each modality to these stages. Progressive loading is the only intervention present in every stage after protection. Neural/contextual enablers are concentrated in stages 1 and 2, where pain and inhibition limit loading. Structural stimulators are concentrated in stage 3, after a loading program has been established. Thermal preparers are most useful in stages 2 and 4, where they prepare tissue before loading.

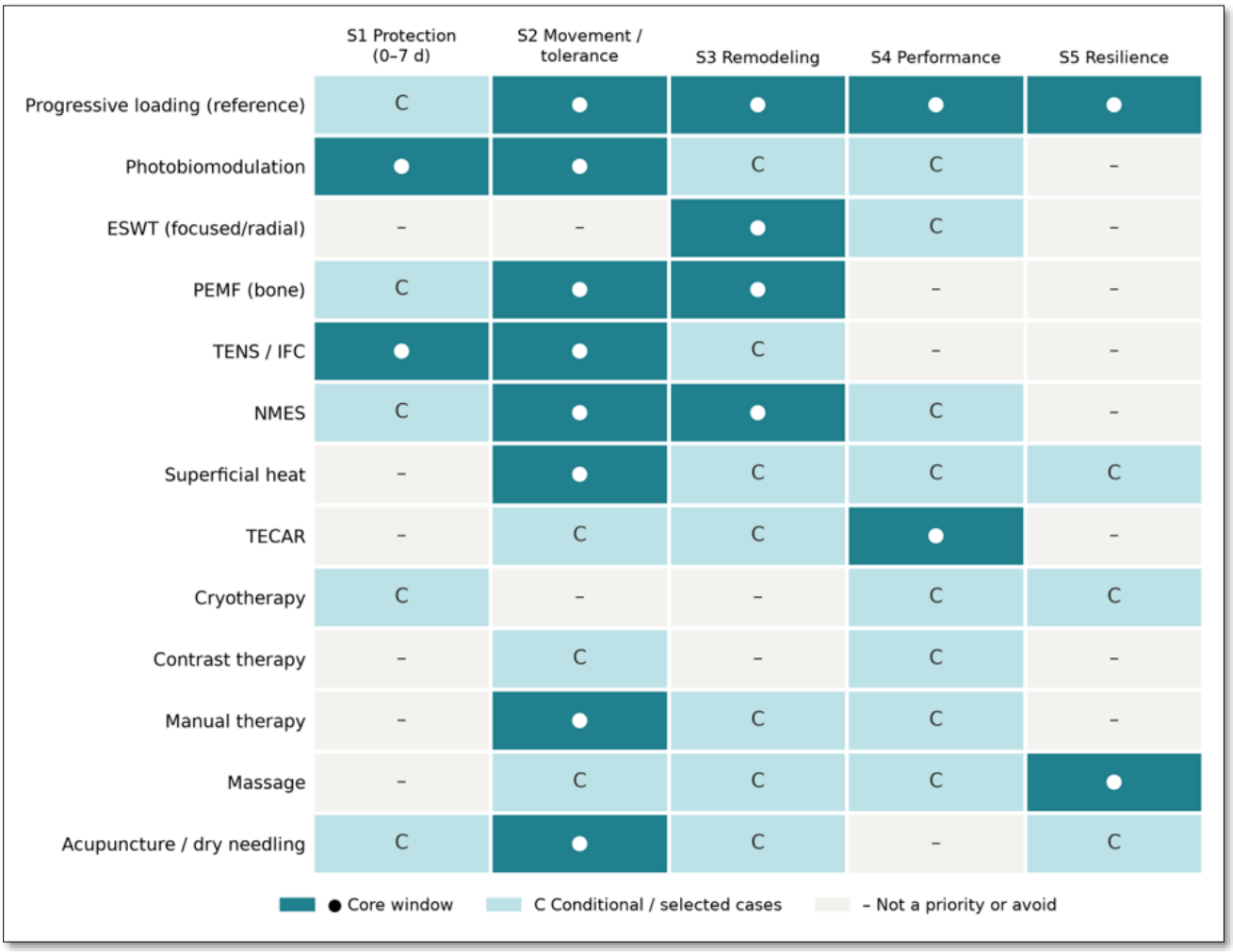


Figure 2. Stage-by-modality map. Suggested use of each physical therapy across the five rehabilitation stages described in the source corpus [5] (S1 protection; S2 movement/tolerance; S3 remodeling; S4 performance; S5 resilience). ● core window; C conditional or selected cases; – not a priority or to be avoided. Progressive loading is shown as the reference intervention. Classification is the author's interpretation and has not been validated.

Decision rules and the essentiality test

Across modalities, the corpus applies a consistent set of decision rules (**Table 6**). We summarize them here as an essentiality test: if the modality were removed, would the intended biological signal still be delivered? If the answer is yes, because loading and the biologic already provide it, the modality is optional and should be justified by symptom control or adherence rather than by regenerative claims. If the answer is no, as with high-energy ESWT for calcific deposits or PEMF in a nonunion where weight-bearing is restricted, the modality has a defensible structural role.

Table 6. Decision rules for adding a physical modality to a regenerative plan (synthesized from the source corpus [5]).

Rule	Practical application
No clear diagnosis, no modality	A structural diagnosis, confirmed by imaging when needed, must precede device selection
Loading first	A 6–12-week progressive loading program precedes ESWT in tendinopathy; if the patient will not load, defer the modality
Predefined outcome	No modality is started without a predefined outcome measure and review point
Reassess early	Reassess after 3 sessions; if there is no benefit after 6, reconsider diagnosis, dose and plan
One mechanism, one modality	If two modalities act on the same node in the same phase, one is redundant
Essentiality test	If the modality were removed, would the intended biological signal still be delivered? If yes, it is optional
Claim discipline	Mechanistic plausibility is not efficacy; request device-specific parameters and independent trial data from manufacturers

DISCUSSION

This comparison suggests that the most useful question about a physical therapy in regenerative medicine is not whether it "works", but which signal it adds that the main regenerative stimulus does not already provide. Organized this way, the field becomes simpler. A small number of modalities deliver a structural signal with independent clinical support for specific indications: ESWT for calcific tendinopathy, greater trochanteric pain and nonunion; PEMF for nonunion; and NMES for quadriceps strength after knee surgery [14,16,17,21,24]. One modality, PBM, acts mainly on cellular bioenergetics and inflammation, with dose-dependent support in knee osteoarthritis, tendinopathy and exercise recovery [11–13]. Most remaining modalities are enablers. Their value lies in reducing pain, inhibition or fear enough to make loading tolerable, as shown by the moderate-certainty effect of TENS on pain [23], the modest specific effect of acupuncture over sham [26] and the small-to-moderate effect of osteopathic treatment in low back pain [27].

This framing has three implications for stem cell and orthobiologic practice. First, it discourages a common pattern in which several devices are added to an injection protocol without a defined mechanism or outcome. Second, it prioritizes timing. Modalities that act on inflammation, such as cold or high-dose anti-inflammatory strategies, can conflict with the early phase that platelet and cell products are designed to start, whereas loading and structural stimulators belong to the remodeling window. Third, it identifies where research is most needed. Preclinical data on PBM, ESWT and PEMF effects on MSCs are extensive [8–10,30], but clinical data on whether these effects add to an orthobiologic in patients are almost absent. The single RCT located for ESWT added to PRP showed only a short-lived advantage [31].

The comparison also highlights a reporting problem shared by all modalities. Light-based trials often omit wavelength, irradiance, energy per point or total energy. Shockwave trials often omit energy flux density, device type or focal depth. PEMF studies frequently omit waveform, flux density or daily exposure. Without these parameters, negative and positive trials cannot be compared, and dose-response curves cannot be built. We therefore propose that trials combining a physical modality with an orthobiologic report, at minimum: (i) full physical dose parameters; (ii) timing relative to injection; (iii) the concurrent loading program; (iv) a predefined primary outcome and minimal clinically important difference; and (v) a sham or attention control for the modality.

Claim limits and device governance

The comparison also has implications for how physical therapies are described to patients and in commercial material. Loading remains the reference intervention: heavy-load eccentric training established it as first-line care in chronic Achilles tendinopathy [34], and the independent syntheses reviewed here repeatedly found that devices add little once an adequate loading program is in place [18]. The corpus recommends that clinicians ask manufacturers for device-specific physical parameters, independent controlled trials in the target indication and disclosure of conflicts of interest, and that mechanistic plausibility not be presented as clinical efficacy [5]. In the context of stem cell and orthobiologic practice, this means that terms such as regenerative, stem cell-activating or exosome-boosting should be reserved for effects shown in humans at the doses used, not inferred from in vitro data.

Research agenda

Three study designs would resolve most of the uncertainty identified here. First, a 2 × 2 factorial RCT (biologic versus saline, modality versus sham, all with standardized progressive loading) would separate the main effects and the interaction of the modality and the biologic. Second, an add-on design for refractory cases, in which patients who have not responded to 6 to 12 weeks of standardized loading are

randomized to modality or sham, would test the incremental value claimed in practice. Third, mechanistic sub-studies using imaging, biomarkers or tissue sampling would test whether modality-induced changes in MSC behavior seen in vitro occur in vivo at clinically used doses. Where cells are primed ex vivo, the priming dose should be specified as rigorously as the cell dose.

LIMITATIONS

This review has important limitations. Its primary corpus is a clinical guide written by the author of this review, which creates a risk of confirmation bias. We mitigated this by checking key statements against independent trials and meta-analyses and by reporting where they disagreed. The comparison is narrative and not systematic. Evidence labels and the classifications shown in Table 3 and in Figures 1 and 2 are the author's qualitative interpretation and have not been validated. The external verification was targeted rather than exhaustive and may have missed relevant trials. Finally, the timing rules in Table 5 derive from biological reasoning and expert opinion rather than from trials designed to test them.

CONCLUSION

Physical therapies used with stem cell and orthobiologic treatments fall into five functional classes. Only a minority deliver a structural signal with independent clinical support. Most act as bioenergetic modulators, tissue preparers or neural and contextual enablers whose main value is to make progressive loading possible. Shared signaling nodes and biphasic dose responses mean that combining modalities is often redundant and sometimes counterproductive, especially in the early post-injection window. An essentiality test, explicit timing rules, standardized reporting of physical parameters and factorial add-on trials offer a practical way to reduce overclaiming and to identify where physical energy adds to regenerative biology.

DECLARATIONS

Acknowledgements: None.

Author contributions: M.K. conceived the review, developed the source corpus, designed the comparative framework, interpreted the evidence, and drafted and all authors approved the final manuscript.

Funding: No specific funding was received for this work.

Conflict of interest: The author wrote the clinical guide used as the primary source corpus for this review [5]. There is no financial relationships with manufacturers or distributors of photobiomodulation, shockwave, electromagnetic, radiofrequency or other devices, or with orthobiologic products

Ethics approval and consent: Not applicable. This review involves no human participants, animals or patient data.

Data availability: No new data were generated. The coding matrix underlying Tables 2 to 6 and Figures 1 and 2 is available from the author on reasonable request.

Use of AI-assisted tools: An AI-based writing assistant was used to help structure the comparison, check references against public bibliographic records and edit the language. The author reviewed and verified all content and takes full responsibility for the manuscript.

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