# International Journal of Complementary and Internal Medicine

# RESEARCH ARTICLE

# Can Photobiomodulation Laser Therapy 'Lighten' Pain in Chronic Osteoarthritis? Facts and Opportunities

# Ray Marks

Research, Osteoarthritis Research Center, Box 5B, Thornhill, ONT L3T 5H3, Canada

**Corresponding Author:** Ray Marks. OARC Clinical Research and Education Director, Ontario L3T 5H3, Canada. E-mail: Dr.RayMarks@osteoarthritisresearchcenter.com; doctorraymarks75@gmail.com

**Received:** November 09, 2025 **Published:** November 19, 2025

**Citation**: Marks R. Can photobiomodulation laser therapy 'lighten' pain in chronic osteoarthritis? Facts and opportunities. Int J Complement Intern Med. 2025;6(4):452–462. DOI: 10.58349/IJCIM.4.6.2025.00164

**Copyright:** ©2025 Marks R. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and build upon your work non-commercially.

## **Abstract**

Among the various non-pharmacological interventions shown to partially relieve joint pain, we elected to review the present 2025 photo or laser therapy data as applied to establishing its potential for alleviating pain in the aging musculoskeletal system. More specifically, we aimed to:

- a) examine current 2025 related research on this topic, from the general standpoint of photo biomodulation or low-level laser applications as applied to preclinical or clinical osteoarthritis, the most common painful disease affecting older adults,
- b) more specifically from laser application influences observed as regards various joint tissues and sites underpinning osteoarthritis pain,
- c) how low-level laser affects pain. Results show consistent post-treatment pain associated improvements even in the face of verifiable osteoarthritis damage and destruction, but that the underlying mechanisms and optimal dosages for maximizing this effect are generally unclear. However, most researchers agree the topic warrants future study and will likely prove of high clinical significance.

**Keywords:** arthritis, cartilage, inflammation, low level laser therapy, osteoarthritis, pain, photobiomodulation, rehabilitation, therapy

# **Background**

Among the health conditions causing immense pain in older life, osteoarthritis, ranked as the most prevalent cause induces immense physical, social, emotional, functional, and psychological challenges among many aging citizens in all parts of the globe. Predominantly impacting the thin shock absorber termed articular cartilage tissue that lines both surfaces of the bones that make up freely moving or synovial joints such as the knee, the disease tends to progress in magnitude and severity especially if poorly treated or ignored. This degrading process

that stems from a breakdown in the balance between cartilage anabolic and catabolic processes has a profound and debilitating array of daily impacts and is hard to restore, attenuate or reverse in an age group with limited or declining reparative capacities as well as an entrenched belief in the inability of cartilage to undergo repair. In addition, pain, the key feature of osteoarthritis often reduces mobility and motivation plus the physical energy needed for moving the joint but is hard to mitigate as well as non-uniform in its causes and pain amplification pathways **Box 1**.

#### PHYSICAL FACTORS

Abnormal joint biomechanics

Bone hypertrophy, bone cysts, osteophytes

Capsulae fibrosis

Joint inflammation/swelling

Increased risk for falling/micro + macro injury

Joint instability

Joint swelling, stiffness

Ligament and tendon damage

Muscle inflammation

Muscle/ligament damage/fatigue, pathology

Muscle weakness/increased fat mass/wasting

Nerve damage, impingement, sensitization, neural inflammation

Limited joint range of motion

Limited mobility/function

Obesity

Poor posture

Reduced proprioception, /balance capacity

Reflex muscle inhibition

# PSYCHOLOGICAL/COGNITIVE ATTRIBUTES OF

Altered cognitive integration

Depression and/or anxiety

Feelings of fear and helplessness

Fatigue, and lack of energy

Limited confidence in ability to function/control pain

Poor coping skills

Sleep disturbances

Stress

## OTHER-

Chronic health conditions

Innate joint damage linked immune responses

Oxidative stresses

Poor nutrition

Sedentary lifestyle

Socioeconomic challenges

Social isolation\

Systemic factors such as diabetes and sarcopenia

**Box 1.** Selected Potentially Treatable Problems Commonly Faced by Older Adults with Symptomatic Osteoarthritis that Could Cause Pain both Local or Referred as well as Neuropathic Pain.

Some evidence has accrued over the years however, implying electromagnetic light waves or photons and others termed 'Laser' a non-invasive form of amplified monochromatic light collimated coherently emitted radiation delivered by a device in various ways may potentially offer a non painful safe means of positively reversing or ameliorating some of the pathology of osteoarthritis, including articular cartilage degradation.<sup>1-4</sup> In particular, photo biomodulation or low-level laser light emitting devices applied statically on the skin via a laser diode[s] or a cluster probe used to cover large tissue areas may well improve local joint status as well as addressing problems that require cell stimulation and intrinsic energy pathway activation, such those need to regenerate ligament, muscle, and tendon tissues. Other data show adverse obesity outcomes in their own right can be ameliorated post laser irradiation, an outcome that would tentatively help many overweight osteoarthritis cases who have mobility as well as possible high degrees of joint loading and inflammatory pain challenges.5 Moreover, its application may foster some form of cartilage repair even if only indirectly<sup>6</sup> and when used alone or in conjunction with other approaches or by those who cannot exercise may yet yield meaningful benefits such as those that implicate adverse bone, ligament, tendon, and muscle alterations.8-11

Since osteoarthritis pain is not readily mitigated by standard interventions the search for alternative ways to treat this osteoarthritis attribute in older adults is an important one. Alternately, relying on potentially harmful narcotic medications and others that have minimally important favorable restorative and anti-inflammatory long-term impacts and safety records may heighten rather than lower future pain. 12-14 Additionally, photo biomodulation therapy may stimulate inherent body healing processes, while reversing structural pathology, as well as fostering function, and the ability to manage the disease. This impact alone is likely to obviate or reduce any need for addictive medications and others to counter osteoarthritis pain and that can induce a negative effect on systemic health, as well as dependence and disruptions of inherent cartilage cell repair mechanisms as well exposure of intact cartilage to excess impact loading.15-16

On the other hand, a fair body of well designed and implemented preclinical studies conducted over the years and currently and that employ low level laser energy in the context of examining its impact on healthy as well as damaged cartilage cells and joints show the cartilage cell is not inert and can be stimulated to render favorable reparative products. Laser light may also foster pain relieving muscle regeneration, alleviate pain nerve transmission or reduce its impact from other health

conditions such as obesity. Its anti-inflammatory impacts alone may help avert excessive use of pain medications and their possible adverse influences on multiple body systems. <sup>17,18</sup>

## Goal

Building on what is known in the realm of low-level light applications in the osteoarthritis context, we currently chose to specifically update what has been shown largely over time, especially within the past year [January 1-mid November 2025] regarding the application of low-level laser therapy in any form to actual osteoarthritis lesions or simulated models of cartilage damage and its apparent influence on pain. The analysis was undertaken to examine if advancements have been made recently that can help solidify if this form of electromagnetic energy offered at a low intensity level is indeed a sufficiently valuable one and whether its promise as a salient line of future inquiry appears desirable. This does not discount the value of high intensity laser approaches, but is one that has more years of testing and a large preclinical set of compelling results.

#### Rationale

Amidst rising numbers of older adults suffering from disabling osteoarthritis, the disease is considered a chronic one deemed incurable and largely progressive and has been largely addressed by pharmacologic and surgical means that may yet prove limited, unsafe, or contra indicated.

As one of many non-pharmacologic toolbox options, laser therapy, a form of light energy, may however have some merit as far as mitigating osteoarthritis due to its observed influence on the key tissue site of influence disrupted by osteoarthritis, namely the cartilage lining of the diseased joint. Apparently able to foster cartilage repair, regeneration, or adequate healing, low level laser therapy or photobiomodulation appears promising in this respect because of its ability to be rapidly absorbed, so as to induce alterations of cell membrane potential, enzyme and energy needs, plus favorable degrees oof intercellular cartilage matrix production of the irradiated cartilage cells.

Laser light similarly impacts other osteoarthritis affected joint tissues such as ligaments, muscles, bone, and tendons impactfully when studied, and can thereby duly relieve pain-the complaint experienced by most active osteoarthritis cases. 19-26 Although it is time consuming and needs to be safely applied it is safer than most medications and offers considerable benefit in attenuating osteoarthritis tissue damage, as well as

perpetuating the disease by warding off excess inflammation and cartilage destruction, <sup>24,27,28</sup> and sedentary ramifications due to immobilizing pain.

## **Ouestions Posed**

As opposed to an umbrella overview of low-level laser therapy or photobiomodualtion as applied to osteoarthritis, this current report specifically assesses the question of whether these approaches are efficacious regardless of independent or complementary osteoarthritis pain treatment approach. Second, it asks if its observed beneficial pain outcomes can be readily explained. Third, it asks if laser light can substitute for exercise or supplement this due to its unique multimodal biochemical, molecular, neural, and structural effects and documented favorable influences.

# **Application**

Based on recent superior pain related results in the clinic and favorable pre-clinical cartilage repair findings,<sup>8</sup> we felt it important to try to discern the degree to which current data can be generalized in the face of a growing osteoarthritis epidemic and global aging.

#### **Methods**

To explore the topic mentioned above, we elected to consult the PUBMED, PubMed Central, Science Direct, and Google Scholar data bases using the search terms - low level lasers and osteoarthritis, laser/light therapy and osteoarthritis, osteoarthritis, pain, and photobiomodulation.

To grasp the content and scope of these data, as many were not of direct current relevance, a fair number of the most currently posted articles [2025] were scanned and those selected were examined individually to uncover if the research report met the present inclusion criteria-of being a full length publication that has recently discussed some applications of low level laser intervention in experimental models of osteoarthritis and/or isolated cartilage tissues or clinical realms. All forms of low-level laser application and research modes were deemed acceptable. Clinical studies examined elsewhere were not systematically reviewed and only a narrative overview is provided. Readers can refer here to references<sup>4,10,19,22,23,28</sup> for more insights. The current search excluded examining experiments of healthy cartilage cells or chondrocytes, lasers as a diagnostic tool, those studies related to rheumatoid arthritis, or laser irradiation in acute conditions. The validity of the osteoarthritis model used in the various preclinical studies was accepted as being

reasonably representative of clinical osteoarthritis and able to thus offer insights into laser irradiation effects on destructive cartilage processes. The laser stimulation parameters employed and outcomes assessed and reported had to be those that could foster some degree of structural favorable change in the cartilage tissue such as cyclic hydrostatic pressure and inflammation control that might yet be applied to the human condition.

Pain, the most important factor that causes osteoarthritis disability and one that can have multiple key clinical influences was studied in isolation. Laser was studied due to its possible impact on pain as well as pain determinants emanating from osteoarthritis muscles, bone, nerves, ligaments and tendons as well as central factors.<sup>27,29</sup>

As opposed to most medications and surgery or invasive therapies, it was believed laser therapy is underutilized, but appears to have immense measurable repair influences that may help restore damaged cartilage and cartilage defects to a more mechanically functional joint tissue status, rather than just ameliorating osteoarthritis symptoms such as pain, but that may or may not restore joint integrity or provide long-term relief and cost savings. The terminology used was that applied in the research and included the terms laser therapy, phototherapy, photobiology, photobiostimulation and photobiomodulation that were deemed comparable modes.

# **Key Findings**

In terms of interest as regards osteoarthritis and pain more than 3400 articles have been posted on PUBMED in 2025, showing the immense interest in and desire to address this burgeoning issue. Among the remedies listed here, a role for ant-inflammatory drugs [1671 cites], surgery [1734 cites], and injections [481 cites] predominate. Laser therapy in osteoarthritis pain relief in 2025 is largely overlooked [with 14 cites], even though its apparent ability to reduce inflammation as well as pain when used at a low level is quite well established, regardless of osteoarthritis mode or site; or type of low intensity laser application mode.<sup>29</sup> In addition, its lack of inclusion in remedial realms is surprising given that photo therapy applications may reduce the extent of osteoarthritis related articular cartilage attrition and degeneration that stems from muscle dysfunction, ligament damage, bone sources, and widespread presende of neuropathic pain states.<sup>28-31</sup>

Indeed, even if only 'positive' studies are being published in 2025, most clearly report low level laser light as having favorable impacts on tissue homeostasis imbalances, the

modulation of oxidative stresses that fosters cartilage degradation, and possible important chondroprotection effects, as well as reductions in chronic inflammation.<sup>32,33</sup>

In this regard, Wang<sup>28</sup> earlier found the application of low-level laser of at least six weeks duration applied to a rabbit osteoarthritis model to positively influence pain and inflammation. In another earlier study, Milares<sup>29</sup> who conducted a multi-group comparison of different experimental model rat groups subjected to an aquatic and low-level laser therapy, data showed laser therapy efficacious in fostering joint degenerative modifications as well as fostering anti-inflammatory mediation processes. Overall results of a four-group comparison showed both the exercise and laser treated groups had better tissue organization, and less structural damage post irradiation than the controls. The exercise and the laser-exercise combinations showed reduced expression of inflammatory markers, as well as a statistically significant lower matrix metalloprotease-13 inflammatory marker level, implying a strong inflammation mediating effect.

Other results show joint morphology may well improve post laser stimulation,<sup>34</sup> as may its biomechanical properties that could indeed be predicted to have an immense bearing on osteoarthritis pain generation<sup>35</sup> and when combined with exercise, laser therapy may afford an immense degree of pain relief.<sup>36-40</sup>

In terms of mechanisms of action, laser light applications may relieve pain because the waves can accelerate tissue repair and a return to tissue homeostasis and with this the probable ability to withstand joint forces more optimally as well as to function more ably. They can also foster passive chondroprotection, reshape and stimulate regenerative cellular and molecular, reactions in multiple joint tissues. Photobiomodation also appears to have the potential to impact pain by repairing or minimizing bone lesion sources as well as reducing synovial membrane inflammation, inflammatory gene expression, pain related behavior, synovitis, cartilage damage, and capsular fibrosis. 9,45

Martins<sup>46</sup> likewise found the application of laser therapy effective in helping arthritis-induced joint tissues to recover from the presence of excess oxidative stressors-a strong pain determinant. Other data reveal structurally, biochemically, neurologically, and mechanically induced effects that may foster pain relieving articular cartilage tissue repair. As well, by reducing swelling, and fostering ligament repair as well as muscle regeneration, joint stability and shock absorption and thus less impact loading pain sources may be realized.

Due to its apparent beneficial and crucial ability to foster stress relaxation cycles as well as cell proliferation states at the affected joint, <sup>54</sup> as well its impact on multiple neural pathways, laser light may reduce pain sensitivity, <sup>55</sup> as well as pain sources such as oxidative and musculoskeletal tissue damage, joint inflammation, and muscle degeneration, and cross talk between sensory and sympathetic nerves. <sup>26,50,54,56-60</sup>

Tim<sup>61</sup> who undertook a controlled photobiomodulation application study using rat chondrocytes found the light waves increased cell proliferation rapidly and sustainably for a short period thereafter. The researchers also found that the laser impacted tissue degradation extent favorable and suggested phototherapy can foster a possible return to cartilage cell tissue homeostasis, thus promoting being able to promote a chondroprotective effect. This may be helpful not only in reducing cartilage degradation rates and magnitudes, but susceptibility to pain provoking impact stresses in those suffering chronic pain and varying degrees of muscle damage, poor proprioception, and possible joint instability. Indeed, although somewhat untested at present in humans, these findings seem well founded, robust, and to hold promise and support based on investigative studies by Sen<sup>62</sup> and Auger. 63 Moreover, their application can speed up wound healing that could otherwise be very painful.66 Their combined usage with other therapies could produce even stronger effects than those applied alone, and despite a belief in the limited intrinsic degree of cartilage self repair or renewal in the face of osteoarthritis damage, laser waves may clearly be harnessed to render bone and cartilage interface repair processes, favorable cognitive responses, as well as fostering joint protection and the ability to exercise safely that can offset pain. 54,40,64,65,70 In addition, it appears there may be favorable impacts post laser stimulation even in the high age adult population such as those involving:

- Favorable cellular metabolic, energetic, and microenvironment status benefits
- Nerve regeneration and/or pain transmission slowing
- Systemic as well as local joint antiinflammatory effects
- Venous and lymphatic microcirculation
- Healing processes in muscle, ligaments, bone, and articular cartilage
- Muscle performance and fatigue recovery post exercise
- Reductions in joint effusion and sensory input deficits
- Reductions in anxiety/distress

However, to achieve success, it appears this is likely to only be truly possible if an insightful step by step action plan is forged and implemented with fidelity and is one that involves and embraces patient education about the crucial role of joint protection. Moreover, the plan should be targeted, tailored, and delivered for an adequate time period using optimal light energy parameters. A belief by the clinician in the therapy as an important complimentary one, as well as the patients like beliefs appear essential as is correcting any underlying remedial problem such as instability by using a brace, or preventing excess weight gain.

Moreover, in accord with well-established management principles, due consideration should be given to:

- 1) the unique attributes of the diseased joint, the stage of the disease, the age and health status of the older adult;
- 2) how, when and for how long therapy should be applied,
- 3) the most appropriate irradiation method and set of parameters,
- 4) the outcomes assessed tools and their reliability, sensitivity, and validity properties,
- 5) the overall the rapeutic dosage and follow up plans.  $^{62,67,68,73,86}$

Dose dependent effects may also wane over time, thus long-term benefits may be lost if no other remedial strategy is forthcoming and follow up sessions are only sporadic rather than regular.<sup>73,74</sup>

# **Discussion**

Osteoarthritis, studied for more than 100 years with limited understandings of its origins and treatment success, remains an increasingly prevalent disabling joint disease causing immense late life suffering and multiple functional limitations no matter where it occurs. Associated with immense direct as well as indirect health care costs that are clearly advancing incrementally and exponentially, the use of low-level laser therapy as one potential disease mediator or moderator was presently revisited as a promising treatment option for remediating osteoarthritis disability due to pain. Although fraught over time with no uniformly definitive outcome or explanatory findings and multiple research gaps and flaws, laser light energy has apparent promising attributes uncovered for well over 50 years, but unfortunately has been one not readily translated clinically to any meaningful disease modifying observable degree. This is despite its effect on metabolic processes both stimulatory as well as inhibitory73 along with its impact on neuropathic pain and overall function demonstrated in an increasing number of preclinical studies.<sup>75,78</sup> However most cannot be confirmed as mirroring the actual 'in

vivo' osteoarthritis disease processes at all successfully.

Additionally, even if laser light may induce a short-lived array of beneficial outcomes that may be helpful to the sufferer, 83 as of November 1 2025, this mode of therapy has not been well substantiated or supported to date. Yet, it does seem a topic of clinical relevance as supported by numbers increasing of low-level laser photobiomodulation therapy studies that show laser light can combat or suppress joint inflammation differentially and successfully. Several have shown interesting effects on pain and inflammation, key problems in the clinical context of osteoarthritis tissue impacts and trends indicating favorable extracellular matrix production, chondrocyte cell metabolism improvements and pain reduction.<sup>79-82</sup> Moreover, unlike medication, surgery, or injections alone, it appears laser therapy in various dosages and wave lengths can not only foster repair of damaged cartilage, but has a favorable impact on nerves, muscles, bones, soft tissues, and sleep that may be affected negatively by chronic osteoarthritis.87 New forms of laser therapy that can penetrate deep tissues may be especially efficacious in this regard and appear promising as well. 50,84

Indeed, regardless of whether recent laser therapy osteoarthritis studies have been observational or comparative, a reader cannot fail to be impressed by the enormous 'healing' potential of laser therapy and its impact on effectively reducing pain, stiffness, and overall joint and mobility dysfunction. <sup>10,75</sup> Moreover, it seems laser light impacts seem to occur regardless of treatment methods and disease durations and in clinical as well as cartilage lesions introduced artificially. <sup>74,77</sup> In addition, the full scope of any long term or structural post laser benefit may be larger than its short term benefits, but is still largely unexplored in joints other than the knee or where its unique effects are potentially contaminated by combination therapies.

It can be hypothesized however, that careful selection and delivery of stand-alone laser light pulses applied to a compromised joint will vary with modes of application, and application durations and thus should be designed to evoke mechanisms that may help in averting injurious degrading enzymatic joint fluid processes, regardless of osteoarthritis damage magnitude and site. New technologies may also enable better characterization of osteoarthritis cartilage pathology that allow it to be treated at an early stage as well as how to prevent or counteract damaging inflammatory receptor pathways from mediating osteoarthritis cartilage damage at the individual level. Moreover, the application of a wider range of objective clinically relevant biomechanical, neurogenic, and biomarker estimates and less reliance on

subjective data that may be memory dependent may help to foster more confidence in the application of low-level laser light to foster or maintain optimal mechanical, radiological, kinematic and kinetic, and regenerative osteoarthritis disease states in the older adult.

In this regard, establishing whether low level laser therapy applied externally can be designed to precisely target, or heighten the activation of older adult osteoarthritis cartilage cells, matrix repair, bone and muscle damaged cells, nerve lesions, or the prevention of progressive downward cartilage destruction, which appears plausible and possible, is strongly encouraged. Supported by most current as well as past research, insightful clinically relevant observations that foster healing and life quality benefits even in chronic longstanding cases can be anticipated. 69,85,88 Moreover, the implied value of data showing the likelihood of endogenous light sensitive opioid or distant neural receptors that appear to have the potential to specifically modify or influence immune functions and central sensitization processes when stimulated selectively appears highly promising. A more intense examination of possible beneficial morphological impacts osteoarthritis soft tissue structures and function, such as ligaments, and inflammatory pathways in the older population, rather than failing to do so, may further help to expand its utility, functional successes, and strengthen its neuro mechanistic underpinnings, and thereby maximize its application so as to avert a need for addictive pain killers, surgery, as well as antiinflammatory drugs [NSAIDS] and others, especially where the older adult is NSAID resistant and can benefit from the ability to exercise with less pain post laser therapy.81

However, to affirm, clarify or discern the unique effects of low-level laser light in osteoarthritis contexts, and until agreement of its efficacy is conclusively established, we believe the role of multi-intervention trial approaches should be discouraged in order to uncover any unique stand-alone effects.

To this end, research based on well-defined and careful sampling, disease staging and age, instituting a washout period of at least two weeks prior to treatment session one, and controlling activity levels between treatments are indicated. In addition, careful parameter and laser delivery modes are strongly indicated. Moreover, long-term rather than short term observational studies using carefully selected devices, laser dosages, and reliable as well as sensitive objective outcome measures applied with methodological rigor are especially encouraged. 76,77

But preceding this in both the laboratory and clinical practice is the key issue of paying persistent attention to addressing and preventing muscle fatigue, muscle hypotonia, sensory-sympathetic nervous system crosstalk, and overloading the joint.

## **Conclusion**

In the absence of any cure, and limitations on what is therapeutically safe for older adults with disabling osteoarthritis, this brief review of low-level laser therapy approaches leads us conclude that a role for laser light applications in fostering function, averting or delaying joint surgery or fostering cartilage repair or both is highly promising, albeit one not aligned with mainstream approaches.

Given its strong pre-clinical support and safety record we conclude the modality is one worthy of consideration, and applicable, and acceptable for pain relief in the older disabled osteoarthritis case who cannot take medication or undergo surgery. To aid this quest however, we conclude further research be conducted.

Until then, we conclude that the use of low-level laser therapy, while not well accepted to date, is worthy of consideration. In addition, its validated use may have a strong bearing on social and public health costs, and an additive long-lasting temporal effect in selected cases of osteoarthritis in the older adult population who can remain in their own homes if harnessed accordingly. As well, enormous suffering may be allayed if laser therapy can activate endogenous opioid receptors or distant neural structures that influence immune function and central sensitization processes favorably.

Allied health workers who take the time to carefully analyze their client's health situation, and carefully and clearly educate the importance of safe versus unsafe treatments and management of the disease and carry out periodic reviews can expect high success rates, probable healing or regenerative or restorative trends in function, as well as desirable outcomes that save societal costs, as well as the high costs of immense personal suffering and independence losses.

Acknowledgements

None.

**Conflicts of interest** 

None.

**Funding** 

None.

# References

- Son Y, Lee H, Yu S, et al. Effects of photobiomodulation on multiple health outcomes: an umbrella review of randomized clinical trials. Sits Rev. 2025;14(1):160.
- Karadayı G, Akbulut N, Deresoy FA, et al. Comparison of the effectiveness of the new generation dual wavelength laser with the conventional laser type in treating rabbit model temporomandibular joint osteoarthritis. BMC Oral Health. 2025;25(1):980.
- Gatta C, Calzaretta G, Musco N, et al. Laser acupuncture effects on chronic pain, inflammatory response, and biochemical and oxidative stress markers in osteoarthritic dogs: a randomized controlled trial. *Animals (Basel)*. 2025;15(17):2568.
- Kunimatsu R, Nakatani A, Sakata S, et al. Effects of photobiomodulation on osteoarthritis from in vivo and in vitro studies: a narrative review. *Int J Mol Sci*. 2025;26(18):8997.
- Sun W, Zhuang Z, Yang L, et al. Effectiveness of photobiomodulation therapy in improving health indicators in obese patients: a systematic review and meta-analysis of RCTs. BMC Complement Med Ther. 2025;25(1):133.
- 6. Giaretta S, Magni A, Migliore A, et al. A review of current approaches to pain management in knee osteoarthritis with a focus on Italian clinical landscape. *J Clin Med*. 2024;13(17):5176.
- 7. Chen X, Fan Y, Tu H, et al. Clinical efficacy of different therapeutic options for knee osteoarthritis: a network meta-analysis based on randomized clinical trials. *PLoS One*. 2025;20(6):e0324864.
- Dos Santos Maciel T, Corrêa Lima Chamy N, Dos Santos Maciel M, et al. Effect of photobiomodulation (low-level laser therapy) in patients with knee osteoarthritis: a randomized controlled trial. Lasers Med Sci. 2025;40(1):293.
- Carvalho VA, Martins AA, Desiderá AC, Nascimento GC, Magri LV, Leite-Panissi CRA. Preclinical evaluation of dose-dependent effects of photobiomodulation therapy on persistent inflammation in the temporomandibular joint. J Oral Facial Pain Headache. 2025;39(2):183-192.
- Hennessy SN, Corcoran GD. Low-level laser therapy in osteoarthritic pain: a narrative review with an approach to integrated clinical use. Osteoarthr Cartil Open. 2025;7(4):100685.
- Malik S, Sharma S, Dutta N, et al. Effect of low-level laser therapy plus exercise therapy on pain, range of motion, muscle strength, and function in knee osteoarthritis - a systematic review and meta-analysis. Somatosens Mot Res. 2023;40(1):8-24.
- Whittaker JL, Kalsoum R, Bilzon J, et al. Toward designing human intervention studies to prevent osteoarthritis after knee injury: a report from an interdisciplinary OARSI 2023 workshop. Osteoarthr Cartil Open. 2024;6(2):100449.
- Aparecido Monteiro Duque da Fonseca G, Carvalho Roxo D, Moreira Figueira M et al. Evaluation of laserphotobiomodulation different irradiation parameters on macrophages (RAW 264.7) inflammatory mediators' production. Lasers Med Sci. 2025;40(1):366.
- 14. Assis L, Domigos H, Tim C, et al. Influence of an aquatic resistance progressive exercise and low-level laser therapy on musculoskeletal atrophy: an experimental model of knee osteoarthritis. *Lasers Med Sci.* 2025;40(1):43.
- Zhang R, Qu J. The mechanisms and efficacy of photobiomodulation therapy for arthritis: a comprehensive review. *Int J Mol Sci.* 2023;24(18):14293.

- Zhang Z, Wang R, Xue H, et al. Phototherapy techniques for the management of musculoskeletal disorders: strategies and recent advances. *Biomater Res.* 2023;27(1):123.
- Martinez-De la Torre A, Weiler S, Bräm DS, et al. National Poison Center calls before vs after availability of high-dose acetaminophen (Paracetamol) Tablets in Switzerland. *JAMA* Netw Open. 2020;3(10):e2022897.
- 18. Parigi M, Tani A, Palmieri F, et al. Shining a light on skeletal muscle regeneration: red photobiomodulation boosts myoblast differentiation in vitro. *FASEB J.* 2025;39(21):e71107.
- Pasin T, Dogruoz Karatekin B. Comparison of short-term effects of extracorporeal shock wave therapy, low-level laser therapy and pulsed electromagnetic field therapy in knee osteoarthritis: a randomized controlled study. *J Clin Med*. 2025;14(2):594.
- 20. Fatu AM, Ciobotaru RO, Balta A, et al. The efficiency of combined capacitive and resistive energy transfer (tecar) therapy and low-level laser therapy (LLLT) in pain reduction on patients with musculoskeletal disorders: a clinical study. *Cureus*. 2025;17(9):e92670.
- 21. Oliveira S, Andrade R, Valente C, et al. Effectiveness of photobiomodulation in reducing pain and disability in patients with knee osteoarthritis: a systematic review with meta-analysis. *Phys Ther*. 2024;104(8):pzae073.
- 22. Karadayı G, Akbulut N, Deresoy FA, et al. Comparison of the effectiveness of the new generation dual wavelength laser with the conventional laser type in treating rabbit model temporomandibular joint osteoarthritis. *BMC Oral Health*. 2025;25(1):980.
- 23. Mi L, Gao J, Liu Y, et al. Photodynamic therapy for arthritis: a promising therapeutic strategy. *Rheumatol & Autoimmunity*. 2023;3(04):205-219.
- 24. Yap BWD, Lim ECW. 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*. 2025;38(6):1232-1256.
- 25. Alexandrovskaya Y, Feldchtein F, Glatz A, et al. Therapeutic window of laser dosimetry for the treatment of knee osteoarthritis. *Lasers Surg Med.* 2025.
- Hang NLT, Aviña AE, Chang CJ, et al. Photobiomodulation in promoting cartilage regeneration. *Int J Mol Sci.* 2025;26(12):5580.
- 27. Guastaldi FPS, Matheus HR, Hadad H, et al. A regenerative approach for temporomandibular joint repair: an in vitro and ex vivo study. *J Oral Rehabil*. 2024;51(8):1521-1529.
- Wang P, Liu C, Yang X, et al. Effects of low-level laser therapy on joint pain, synovitis, anabolic, and catabolic factors in a progressive osteoarthritis rabbit model. *Lasers Med Sci*. 2014;29(6):1875-1885.
- Milares LP, Assis L, Siqueira A, et al. Effectiveness of an aquatic exercise program and low-level laser therapy on articular cartilage in an experimental model of osteoarthritis in rats. Connect Tissue Res. 2016;57(5):398-407.
- 30. El-Qashty R, Elkashty OA, Hany E. Photobiostimulation conjugated with stem cells or their secretome for temporomandibular joint arthritis in a rat model. *BMC Oral Health*. 2023;23(1):720.
- Kaneguchi A, Ozawa J, Minamimoto K, et al. Low-level laser therapy attenuates arthrogenic contracture induced by anterior cruciate ligament reconstruction surgery in rats. *Physiol Res*. 2022;71(3):389-399.
- 32. Martins LPO, Santos FFD, Costa TED, et al. Photobiomodulation Therapy (Light-Emitting Diode 630 nm) favored the oxidative stress and the preservation of articular cartilage in an induced knee osteoarthritis model. *Photobiomodul Photomed Laser Surg.* 2021;39(4):272-279.

- S GN, Kamal W, George J, et al. Radiological and biochemical effects (CTX-II, MMP-3, 8, and 13) of lowlevel laser therapy (LLLT) in chronic osteoarthritis in Al-Khari, Saudi Arabia. *Lasers Med Sci.* 2017;32(2):297-303.
- Travessini GR, Villanova B, de Alcantara BFR, et al. Evaluation of photobiomodulation for modulating peripheral inflammation via the lumbosacral medullary region. J Complement Integr Med. 2025.
- Agostini F, Capuano F, Sebastiani C, et al. The effects of laser therapy on pain, functionality and biomechanical parameters in patients suffering from gonarthrosis: an observational study. Clin Ter. 2025;176(3):330-335.
- Yang X, Liu TC, Liu S, et al. Promoted viability and differentiated phenotype of cultured chondrocytes with low level laser irradiation potentiate efficacious cells for therapeutics. Front Bioeng Biotechnol. 2020;8:468.
- Anbari F, Khalighi H, Baharvand M, et al. Effect of low-level laser irradiation on the proliferation of human chondrocytes: an in vitro study. *J Lasers Med Sci.* 2024;15:e55.
- 38. Lou X, Zhong H, Fan X, et al. Low-intensity laser alleviates cartilage degradation in a rat model of knee osteoarthritis by improving the biomechanics of joint muscles and cartilage. *Acta Mechanica Sinica*. 2025;41(11):623656.
- 39. Retameiro ACB, Neves M, Tavares ALF, et al. Resistance exercise and low-level laser therapy improves grip strength and morphological aspects in the ankle joint of Wistar rats with experimental arthritis. *Anat Rec (Hoboken)*. 2023;306(4):918-932.
- Tanideh N, Ali Behnam M, Mohit Ghiri S, et al. The effects of combined and independent low-level laser and mesenchymal stem cell therapy on induced knee osteoarthritis: An animal study. *Knee*. 2024;47:208-218.
- Fernandes GHC, Labat Marcos R, Almeida Dos Santos S, et al. Photobiomodulation control the expression of MMP, TNF-α and NK-1 receptors, improving allodynia and cartilage resistance in rheumatoid arthritis model. *Lasers Med Sci.* 2025;40(1):306.
- 42. Fan Y, Guastaldi FPS, Runyan G, et al. Laser ablation facilitates implantation of dynamic self-regenerating cartilage for articular cartilage regeneration. *J Funct Biomater*. 2024;15(6):148.
- 43. Kang YT, Tri TT, Jo DS, et al. Impact of Red and Red/NIR OLEDs photobiomodulation effects towards promoting ADMSCs chondrogenic differentiation. *Tissue Cell*. 2025;96:102948.
- Mendelsohn DH, Walter N, Cheung WH, et al. Targeting mitochondria in bone and cartilage diseases: A narrative review. *Redox Biol.* 2025;83:103667.
- 45. Fan T, Xia P, Ahmed S, et al. Wavelength-dependent photobiomodulation attenuates synovial inflammation in fibroblast-like synoviocytes and a collagenase-induced osteoarthritis model. *J Photochem Photobiol B*. 2025;272:113276.
- Wen X, Zhang G, Cui J, et al. Efficacy and safety of laser acupuncture on osteoarthritis: a systematic review and metaanalysis. Front Aging Neurosci. 2025;16:1462411.
- 47. Zhu Y, Zhou X, Peng X, et al. 1064nm Nd:YAG laser promotes chondrocytes regeneration and cartilage reshaping by upregulating local estrogen levels. *J Biophotonics*. 2024;17(2):e202300443.
- Sargolzaei N, Gerayeli M, Ekhlasi A, et al. The effect of low-level laser therapy on the healing of soft tissue graft donor and recipient sites: a randomized clinical trial. J Maxillofac Oral Surg. 2025;24(5):1448-1457.
- Dellalbaşı AB, Cihan M. Evaluate the effects of photobiomodulation of blue led light combined with different graft materials on bone healing in the rat model. *Lasers Med Sci.* 2025;40(1):388.

- Seo SH, Kang SM, You YH, et al. Effects of 650 nm laser acupuncture on cartilage, bone, and skeletal muscle in osteoarthritis. *Bone Rep.* 2025;26:101864.
- Nambi G. Does low level laser therapy has effects on inflammatory biomarkers IL-1β, IL-6, TNF-α, and MMP-13 in osteoarthritis of rat models-a systemic review and metaanalysis. *Lasers Med Sci.* 2021;36(3):475-484.
- Feng Z, Wang P, Song Y, et al. Photobiomodulation for knee osteoarthritis: a model-based dosimetry study. *Biomed Opt Express*. 2023;14(4):1800-1817.
- Chia WT, Wong TH, Jaw FS, et al. The impact of photobiomodulation therapy on swelling reduction and recovery enhancement in total knee arthroplasty: a randomized clinical trial. *Photobiomodul Photomed Laser* Surg. 2025;43(2):65-72.
- Okita S, Sasaki R, Kondo Y, et al. Effects of low-level laser therapy on inflammatory symptoms in an arthritis rat model. *J Phys Ther Sci.* 2023;35(1):55-59.
- Hasanin ME, Aly SM, Taha MM, et al. The Effect of laser biostimulation at sensitized acupoints on chronic pelvic pain and quality of life in women with pelvic inflammatory disease: a randomized controlled trial. *Medicina (Kaunas)*. 2025;61(2):354.
- 56. Bomfim FRCD, Gomes BS, Lanza SZ, et al. Photobiomodulation effects on synovial morphology, iNOS gene, and protein expression in a model of acute inflammation. *Acta Cir Bras.* 2024;39:e392024.
- 57. Ma Z, Wan Q, Qin W, et al. Effect of regional crosstalk between sympathetic nerves and sensory nerves on temporomandibular joint osteoarthritic pain. *Int J Oral Sci.* 2025;17(1):3.
- Barale L, Monticelli P, Adami C. Effects of low-level laser therapy on impaired mobility in dogs with naturally occurring osteoarthritis. *Vet Med Sci.* 2023;9(2):653-659.
- Vassão PG, de Souza ACF, da Silveira Campos RM, et al. Effects of photobiomodulation and a physical exercise program on the expression of inflammatory and cartilage degradation biomarkers and functional capacity in women with knee osteoarthritis: a randomized blinded study. Adv Rheumatol. 2021;61(1):62.
- Liu H, Cheema U, Player DJ. Photobiomodulation therapy (PBMT) in skeletal muscle regeneration: a comprehensive review of mechanisms, clinical applications, and future directions. Photodiagnosis Photodyn Ther. 2025;53:104634.
- Tim CR, Martignago CCS, Assis L, et al. Effects of photobiomodulation therapy in chondrocyte response by in vitro experiments and experimental model of osteoarthritis in the knee of rats. *Lasers Med Sci.* 2022;37(3):1677-1686.
- Şen SB, Koçyiğit BF, Ortaç EA, et al. Comparison of the effects of high-intensity laser therapy and low-level laser therapy in knee osteoarthritis. Clin Rheumatol. 2025.
- Auger K, Shedlock G, Coutinho K, et al. Effects of osteopathic manipulative treatment and bio-electromagnetic energy regulation therapy on lower back pain. *J Osteopath Med*. 2021;121(6):561-569.
- 64. Heng C, Zhou Y, Luo H, et al. Hydroxyapatite injectable hydrogel with nanozyme activity for improved immunoregulation microenvironment and accelerated osteochondral defects repair via mild photothermal therapy. *Biomater Adv.* 2026;178:214462.
- de Guzzi Tremarin RF, Zambetta ML, Park J, et al. Revitalizing minds and muscles: a narrative review of potential impact of transcranial photobiomodulation and exercise on cognitive and motor enhancement in the elderly. Physiother Res Int. 2025;30(3):e70062.
- Bozkurt E, Özdemir EÇ. The efficacy of injectable plateletrich fibrin versus photobiomodulation therapy on palatal wound healing: a randomized, controlled, clinical trial. *Clin Oral Investig.* 2025;29(11):512.

- de Souza V, da Palma Cruz M, Chaves Bittencourt C, et al. Dosimetric parameters and clinical outcomes of photobiomodulation in diabetic neuropathy: a concise review. Lasers Med Sci. 2025;40(1):436.
- 68. Soares JM, Carneiro BD, Pozza DH. The role of biomarkers in temporomandibular disorders: a systematic review. *Int J Mol Sci.* 2025;26(13):5971.
- Chen P, Zou Y, Liu Y, et al. Low-level photodynamic therapy in chronic wounds. *Photodiagnosis Photodyn Ther*. 2024;46:104085.
- Labanca L, Platano D, Tedeschi R, et al. Multi-wave locked system laser therapy in chronic non-specific neck pain: a double-blind placebo randomized-controlled trial. Eur J Phys Rehabil Med. 2025;61(4):645-654.
- 71. Attiyah HS, Moharrum HS, El Dakrory UAERM. Efficacy of photobiomodulation therapy using 980 nm versus 635 nm diode lasers for treatment of myofascial pain: a randomized controlled trial. *BMC Oral Health*. 2025;25(1):1511.
- 72. Canez MS, da Silva LI, Ferreira GD, et al. Effects of photobiomodulation, intermittent pneumatic compression and neuromuscular electrical stimulation on muscle recovery: systematic review with meta-analysis. *J Bodyw Mov Ther*. 2025;44:570-584.
- Spivak JM, Grande DA, Ben-Yishay A, et al. The effect of low-level Nd:YAG laser energy on adult articular cartilage in vitro. *Arthroscopy*. 1992;8(1):36-43.
- 74. Lan X, Li L, Jia Q, et al. Physical modalities for the treatment of knee osteoarthritis: a network meta-analysis. *Aging Clin Exp Res.* 2025;37(1):121.
- Araujo LC, Silva DPFB, Rocha-Braga LC, et al. Therapeutic synergy between swimming and photobiomodulation in a rat model of neuropathic pain. *Lasers Med Sci.* 2025;40(1):444.
- Zhao FY, Fu QQ, Ho YS. Interpreting the evidence for laser acupuncture in knee osteoarthritis management: a call for methodological rigor and nuance [letter]. J Pain Res. 2025;18:4787-4790.
- Zeng DH, Yuan DN, Zhou QQ, et al. Laser acupuncture for the pain of knee osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. *J Pain Res*. 2025;18:3833-3841.
- Yan Y, Lin L, Cheng K, et al. Therapeutic analysis of laser moxibustion for different KL graded knee osteoarthritis. *Medicine (Baltimore)*. 2024;103(25):e38567.
- Yang X, Liu TC, Liu S, et al. Promoted viability and differentiated phenotype of cultured chondrocytes with low level laser irradiation potentiate efficacious cells for therapeutics. Front Bioeng Biotechnol. 2020;8:468.
- 80. Hang NLT, Chuang AE, Chang CJ, et al. Photobiomodulation associated with alginate-based engineered tissue on promoting chondrocytes-derived biological responses for cartilage regeneration. *Int J Biol Macromol.* 2024;280(Pt 4):135982.
- 81. Tay YL, Ahmad MA, Mohamad Yahaya NH, et al Effects of photobiomodulation combined with rehabilitation exercise on pain, physical function, and radiographic changes in mild to moderate knee osteoarthritis: A randomized controlled trial protocol. *PLoS One*. 2025;20(1):e0314869.
- 82. Parizotto NA, Millan C, Kamamoto F, et al. Photobiomodulation with IR and RED light acutely applied to lipedema patients: preliminary study with 3 cases. *Lasers Med Sci.* 2025;40(1):437.
- de Oliveira MFD, Leal-Junior ECP, Machado CDSM, et al. Effects of photobiomodulation therapy combined with static magnetic field on pain and function in patients with lateral epicondylitis: a multicentre, randomised, placebo-controlled trial. *BMJ Open.* 2025;15(10):e104789.

- 84. Leal-Junior ECP, Hess F, Dias LB, et al. Light transmission and thermal impact of different photobiomodulation therapy devices on the Achilles tendon of human volunteers: a comparative study. *Photodiagnosis Photodyn Ther*. 2025;56:105234.
- Kasim AH, Viventius Y. Reduced pain and improved quality of life after laser acupuncture therapy for trigger finger. *Med Acupunct*. 2022;34(4):261-265.
- Fan T, Xia P, Ahmed S, et al. Optimizing LED photobiomodulation parameters to prevent cartilage matrix degradation in knee osteoarthritis: in vitro and in vivo study. *J Orthop Surg Res*. 2025;20(1):933.
- Mehdizadeh M, Farnam A, Nikzad B. Transcranial photobiomodulation improves sleep quality, reduces daytime sleepiness, and modulates delta power in chronic insomnia: a randomized controlled trial. *Lasers Med Sci.* 2025;40(1):451.
- 88. Murriky A, Bloom M, Matei IC, et al. Bone regeneration therapy using low level laser treatment in a rabbit model: pilot study. *Lasers Med Sci.* 2025;40(1):403.