ASURIS NORTHWEST HEALTH

Medical Policy Manual Medicine, Policy No. 105

Low-Level Laser Therapy

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Next Review: June 2025
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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Low-level laser therapy (LLLT) uses red-beam or near-infrared lasers at much lower intensity than surgical lasers. It is proposed as a treatment for a variety of conditions.

MEDICAL POLICY CRITERIA

I. Low-level laser therapy may be considered **medically necessary** for prevention of oral mucositis in patients undergoing cancer treatment associated with increased risk of oral mucositis, including chemotherapy and/or radiotherapy, and/or hematopoietic cell transplantation.

II. Low-level laser treatment and laser acupuncture are considered **investigational** for all other indications.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

LIST OF INFORMATION NEEDED FOR REVIEW

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

- History and Physical/Chart Notes
- Current Symptomology and indication
- Documentation of need for prevention of oral mucositis in cancer patients with high risk of developing oral mucositis including cancer treatment causing this risk

CROSS REFERENCES

None

BACKGROUND

Low-level laser therapy (LLLT), also called photobiomodulation (PBM), refers to the use of red-beam or near-infrared lasers with a wavelength between 600 and 1000 nm and power from 5 to 500 milliwatts. This contrasts with surgical lasers that typically use 300 watts. Low-level laser energy that is applied to acupuncture points on the body may be referred to as “laser acupuncture.”

When applied to the skin, low level lasers produce no sensation and do not burn the skin. Because of the low absorption by human skin, it is hypothesized that the laser light can penetrate deeply into the tissues where it has a photobiostimulative effect. The exact mechanism of its effect is unknown; hypotheses have included improved cellular repair and stimulation of the immune, lymphatic, and vascular systems.

LLLT has been proposed as a treatment of carpal tunnel syndrome, painful musculoskeletal disorders such as temporomandibular joint disfunction and low back pain, soft tissue injuries, tendinopathies, and osteoarthritis. LLLT has been used outside the U.S. to treat oral mucositis associated with radiation and chemotherapy, stimulate healing of chronic wounds, treat nerve injuries, and as an adjunct to antituberculosis drug treatment.

REGULATORY STATUS

A number of low-level lasers have received US Food and Drug Administration (FDA) 510(k) clearance, including:

- Super Pulsed Laser (Multi Radiance Medical)
- MicroLight ML830® (MicroLight Corporation of America)
- GRT LITE™ PRO-8A (GRT Solutions, Inc.)
- LightStream™ Low Level Laser (RJ Laser Canada Corp.)
- TouchOne™ (OTC)
- FX-635 (Erchonia Corporation)

EVIDENCE SUMMARY

The principal outcomes associated with treatment of musculoskeletal conditions, including carpal tunnel syndrome, are relief of pain and/or functional status. Relief of pain is a subjective outcome typically associated with a placebo effect. Therefore, blinded and randomized controlled trials (RCTs) are required to control for the placebo effect and determine its magnitude and whether any treatment effect provides a significant advantage over the placebo. The technology must also be evaluated in general groups of patients: (1) in patients with mild-to-moderate symptoms, low-level laser therapy (LLLT) may be compared with other

forms of conservative therapy such as splinting, rest, nonsteroidal anti-inflammatory drugs (NSAIDs), or steroid injection; and (2) in patients who have exhausted conservative therapy.

The focus of this policy is on peer-reviewed publications of RCTs, which follow patients (with the exception of those undergoing preventive treatment for oral mucositis) for at least two weeks beyond the end of the treatment period.[1]

LOW-LEVEL LASER TREATMENT

ACHILLES TENDINOPATHY

Systematic Review

A systematic review with meta-analysis on LLLT for Achilles tendinopathy was published by Martimbianco (2020).[2] Four trials (N=119) were included in the analysis, two of the studies were conducted in Norway, the other two in New Zealand. One of the trials compared LLLT to sham, the other three evaluated the addition of LLLT to eccentric exercises, and treatment duration ranged from one session to eight weeks of treatment. High risk of attrition bias was found in three trials and three trials did not report prospectively published protocols. LLLT associated with eccentric exercises when compared to eccentric exercises and sham had very low to low certainty of evidence in pain and function assessment. While one trial reported favorable outcomes with LLLT laser therapy at two months (mean difference (MD) -2.55, 95% confidence interval (95% CI) -3.87 to -1.23), the CIs did not include important differences between groups at three and 13 months. Functional outcomes were not significantly improved in the LLLT groups for any timepoint evaluated. Adverse event reporting was poor across trials. Sub-group and sensitivity analyses were not possible due to insufficient data. The authors conclude “there were insufficient data to support clinical effects of low-level laser therapy for Achilles tendinopathy.”

Section Summary

There is not enough research to show that LLLT improves health outcomes for people with Achilles tendinopathy.

BELL’S PALSY

Systematic Review

Javaherian (2020) published a SR of randomized controlled trials (RCTs) that compared the efficacy of the LLLT with placebo laser, exercise, massage, or no intervention in patients with Bell's palsy (BP).[3] Four studies (N=171) were included in the review, and the patients of all trials were in the sub-acute (less than one week) stage. Studies by Ordahan (2017) and Alayat (2013) summarized below were included in the review, the other two were published in Spanish. The only common outcome measure was the facial disability index (FDI), which was reported in only two studies. Significant differences between the groups after six weeks of laser application (830 nm, 100 mW) was found in two studies, and the other two studies did not identify any effectiveness following LLLT treatment with 670 and 830 nm wavelengths. Meta-analysis was not possible due to data limitations. No data on adverse effects during treatment and/or follow-up sessions were reported.

Randomized Controlled Trials

LLLT as an addition to facial exercise was evaluated in a study by Ordahan (2017).[4] There were 46 patients (40 women) randomized to a facial exercise intervention alone or the exercise intervention plus LLLT. LLLT was performed three times a week for six weeks. Facial exercises were performed five times a week for the six weeks. The main outcome measured was the facial disability index (FDI) questionnaire. FDI scores showed significant improvement in the exercise only group at week six, and in the exercise plus LLLT group at weeks three and six. The improvements in the FDI were greater with the LLLT plus exercise group than in the exercise only group. However, the lack of blinding and of long-term follow-up, and use of combination therapy make it difficult to draw conclusions from this study.

Alayat (2013) reported on a randomized double-blind placebo-controlled trial of laser therapy for the treatment of 48 patients with Bell's palsy.[5] Facial exercises and massage were given to all patients. Patients were randomized to one of three groups: high intensity laser therapy, low level laser therapy or exercise only. Each group included 17 patients that were blinded to treatment. Laser treatment was given three times per week to eight points of the affected side for six weeks. At three and six weeks after treatment, outcomes were assessed using the facial disability scale (FDI) and the House-Brackmann scale (HBS). The authors reported that significant improvements in recovery were seen in both laser therapy groups over exercise alone with the most improvement seen with high intensity laser.

Section Summary

The current evidence is limited to two small RCTs published in English that do not report long-term health outcomes and do not establish the clinical utility of LLLT for the treatment of Bell’s palsy.

CARPAL TUNNEL SYNDROME

Systematic Reviews and Technology Assessments

Evidence for the use of LLLT in carpel tunnel syndrome (CTS) was evaluated in a 2010 BlueCross BlueShield Association (BCBSA) Technology Evaluation Center (TEC) Assessment, which concluded that the existing randomized clinical trials were insufficient to determine the effect of low-level laser therapy on CTS.[1]

For inclusion in the assessment, studies had to meet the following: published in a peer-reviewed journal; randomized and sham-controlled; if adjunctive therapies were used, they had to be applied to both groups of patients; and outcomes had to be measured at least two weeks beyond the end of the treatment period. Only four studies met the above inclusion criteria, and findings from these studies were inconsistent. No one study was so methodologically sound that its results were considered definitive. Overall, the available studies were small and most did not follow patients for sufficient periods of time beyond the treatment period to determine the durability of the treatment effects.

A systematic review by Bekhet (2017) included eight RCTs that compared functional and electromyographic outcomes of LLLT with those of placebo.[6] A random effects model meta-analysis found that there were no significant differences between groups for all primary outcomes: visual analogue scale (VAS), symptom severity scale (SSS), and functional status scale (FSS) scores. Grip strength was the only measure that was improved with LLLT compared to placebo. Another 2017 systematic review included nine RCTs, but did not perform a meta-analysis due to study heterogeneity.[7] The authors similarly concluded that

there was no strong evidence of LLLT efficacy on pain and function outcomes in carpal tunnel syndrome.

A 2017 Cochrane report assessed the benefits and harms of LLLT compared with placebo and compared with other non-surgical interventions in the management of CTS.[8] Twenty-two RCTs (N=1153) were evaluated. Risk of bias varied across the studies but was high or unclear in most assessed domains in most studies. At short-term follow-up (less than three months), there was very low-quality evidence for any effect over placebo of LLLT on CTS for the primary outcome of Symptom Severity Score (scale 1 to 5, higher score represents worsening; MD -0.36, 95% CI -0.78 to 0.06) or Functional Status Scale (scale 1 to 5, higher score represents worsened disability; MD -0.56, 95% CI -1.03 to -0.09). The authors concluded the quality of evidence was very low and found no data to support a clinical effect of LLLT in treating CTS.

Li (2016) published a systematic review (SR) that included seven RCTs of this topic, with similar results to those of the Bekhet (2017) review.[9] Meta-analyses were conducted for the outcomes hand grip strength, pain measured by a VAS, SSS, and FSS. Short-term follow-up was defined as less than six weeks after treatment and long-term follow-up as at least 12 weeks after treatment. For six of the eight meta-analyses, there were not statistically significant between-group differences in outcomes. These include short-term assessment of hand grip, short-term assessment of pain by VAS, and short- and long-term assessment of SSS and FSS. Meta-analyses found stronger hand grip (three studies) and greater improvement in VAS score (two studies) at the long-term follow-up in the LLLT group compared with the control. Most data for these two positive analyses were provided by a single RCT. Reviewers concluded that additional high-quality trials with similar LLLT protocols are needed to confirm that the intervention significantly improves health outcomes.

Randomized Controlled Trials

RCTs not addressed in the 2016 Cochrane SR are discussed below.

Badıl Güloğlu (2022) published the results of a RCT comparing LLLT and corticosteroid injection in 87 patients (143 wrists) with moderate carpal tunnel syndrome (CTS).[10] Outcomes were assessed at baseline and one- and six-months post-treatment. Outcome measures were numbness and pain, QuickDASH questionnaire, grasping tests, Tinel and Phalen tests, electrophysiological tests and MRI evaluations. Six-month outcome data were available for 80 patients (133 wrists). Corticosteroid injection and LLLT groups showed statistically significant difference at one-month post-treatment in favor of the corticosteroid group and no significant group difference at the six-month timepoint was found.

Barbosa (2015) evaluated the efficacy of orthoses and patient education with or without the addition of LLLT in patients with mild and moderate carpal tunnel syndrome.[11] Laser treatment was provided twice a week for six weeks. Forty-eight patients were randomized and 30 (63%) completed the study protocol. Compared with baseline, outcomes, including scores on the Boston Carpal Tunnel Questionnaire and its domains, did not differ significantly between groups after treatment.

Section Summary

The evidence for LLLT for the treatment of CTS includes several SRs, a technology assessment, and RCTs, and generally does not demonstrate that LLLT is an effective treatment for CTS.

CHRONIC NECK PAIN

Systematic Reviews

In a 2013 SR and meta-regression, Gross (2013) evaluated 17 trials on LLLT for neck pain.[12] Ten of these trials were found to demonstrate high risk of bias. Two trials consisting of 109 subjects were considered to be of moderate quality and found LLLT produced better outcomes than placebo for chronic neck pain treatment. Evidence showed improved outcomes with LLLT compared to placebo for acute neck pain, acute radiculopathy and cervical osteoarthritis but was considered to be low quality. There was conflicting evidence on chronic myofascial neck pain.

A SR by Kadhim-Saleh (2013) analyzed eight RCTs (n=443 patients) to determine the efficacy of LLLT in reducing acute and chronic neck pain as measured by VAS.[13] Authors concluded the evidence was inconclusive and the benefit seen in the use of LLLT did not constitute the threshold of minimally important clinical difference.

The 2010 BCBSA TEC Assessment also determined that the evidence was insufficient to allow conclusions regarding the effect of LLLT on chronic neck pain.[1] The six trials that met the assessment inclusion criteria reported variable results, and no single study was methodologically sound. It was not possible to explain the differences in results due to the numerous differences in patient selection, treatment regimens, and trial co-interventions.

Randomized Controlled Trials

Subsequent to the publication of the 2010 technology assessment, an additional RCT was published.[14] However, interpretation of results from this trial is limited by lack of study of treatment durability (follow-up for at least two weeks beyond end of the treatment period).

Section Summary

The current evidence on the use of LLLT for the treatment of chronic neck pain has methodological limitations and the conclusions of the reports are conflicting. Therefore, it cannot be determined if LLLT improves health outcomes.

ELBOW PAIN

Systematic Reviews

A single SR has been identified on the use of LLLT in elbow pain.[15] Published in 2008, the review grouped placebo-controlled randomized clinical trials by application technique and laser wave length and reported on the 7 of 13 included trials with a common, narrowly defined regimen where lasers of 904 nm wavelength with low output (5-50 MW) were used to irradiate the tendon insertion at 2–6 points on the lateral elbow. Positive results in these trials were consistent with outcomes of pain and function, and significance persisted for at least 3–8 weeks after the end of treatment. However, among the articles included in this review, there were considerable differences in treatment protocol and type of patient treated, indicating that

these results may not be generalizable to all patients with elbow pain. The authors noted that the conclusions of their review differed from conclusions of prior reviews of this topic.

Section Summary

The current evidence on LLLT for the treatment of elbow pain is insufficient due to the variability across studies in the patient population and treatment protocols used. Based on this evidence, it cannot be determined if health outcomes are improved on the use of LLLT for the treatment of elbow pain.

FIBROMYALGIA

Systematic Reviews

A SR with meta-analysis by Yeh (2019) included nine RCTs with 325 patients with fibromyalgia undergoing LLLT or placebo laser treatment with or without an exercise program.[16] Primary outcomes evaluated were the total scores on the Fibromyalgia Impact Questionnaire (FIQ), pain severity, and number of tender points. Secondary outcomes were changes in fatigue, stiffness, anxiety, and depression. Significantly greater improvement in FIQ scores (SMD: 1.16; 95% CI, 0.64-1.69), pain severity (SMD: 1.18; 95% CI, 0.82-1.54), number of tender points (SMD: 1.01; 95% CI, 0.49-1.52), fatigue (SMD: 1.4; 95% CI, 0.96-1.84), stiffness (SMD: 0.92; 95% CI, 0.36-1.48), depression (SMD: 1.46; 95% CI, 0.93-2.00), and anxiety (SMD: 1.46; 95% CI, 0.45-2.47) were found in patients receiving LLLT compared to those receiving placebo laser. The methodological quality of the included RCTs was considered to be low-to-middle, as there was no clear allocation process and only patients were blinded in most studies. Considerable heterogeneity in study protocols such as differences in laser types, energy sources, exposure times, and associated medication status were noted.

Honda (2018) published a SR with meta-analysis of RCTs evaluating pain relief modalities for fibromyalgia. Eleven studies with a total of 498 patients (range, 20-80) were included.[17] Compared with control, LLLT was not associated with a reduction of VAS-measured pain (MD -4.0; 95% CI -23.4 to 15.4; p=0.69). A significant reduction in tender points (MD -2.21; 95% CI -3.51 to -0.92; I2=42%; p=0.0008) and in Fibromyalgia Impact Questionnaire score (MD -4.35; 95% CI -6.69 to -2.01; I2= 62%; p=0.03) were found for LLLT compared with control groups. The analysis was limited by including only English language studies and studies with a pure control group or placebo group (ie, no other intervention) as well as by the high heterogeneity score for included studies.

Section Summary

LLLT for treatment of fibromyalgia has been evaluated in several small RCTs and in two SRs. Although significant improvements in outcomes including disease severity and pain were found in one SR, another SR found no significant reduction in pain between LLLT and control groups. Studies are limited by small sample sizes and heterogeneity of study protocols. Additional RCTs with sufficient numbers of patients are needed.

LOW BACK PAIN

Systematic Reviews

Chen (2022) published a systematic review with meta-analysis of RCTs on LLLT for treating nonspecific chronic low back pain compared to placebo.[18] Eleven trials were included that

compared LLLT to placebo (N=836 patients); seven of these trials assessed LLLT alone compared to placebo and four trials assessed LLLT plus acupuncture compared to placebo. For the overall risk of bias in LLLT trials, eight were identified as low risk, two as having some concerns, and one as high risk. The primary outcomes of interest were changes from baseline in pain scores, measured by visual analogue scale (VAS), and disability measured by the ODI score. In pooled analyses, reviewers found a significant reduction in pain scores with all LLLT interventions compared to placebo posttreatment (SMD, -0.22; 95% CI, -0.38 to -0.05) and in disability scores for trials comparing LLLT therapy alone to placebo (SMD, -0.50; 95% CI, -0.79 to -0.21). In trials comparing LLLT plus acupuncture to placebo, there was no significant difference in disability scores posttreatment (SMD, 0.10; 95% CI, -0.15 to 0.35).

Glazov (2016) published a SR with meta-analysis of blinded sham-controlled trials evaluating LLLT for treatment of chronic low-back pain.[19] Fifteen RCTs (total n=1039 patients) met reviewers' eligibility criteria. Reviewers found that 3 of the 15 trials were at higher risk of bias (using a modified Cochrane tool), mainly due to lack of blinding. The primary outcomes of interest to reviewers were pain measured by a VAS or a numeric rating scale, and a global assessment measure evaluating overall improvement and/or satisfaction with the intervention. Outcomes were reported immediately posttreatment (<1 week) and at short-term (1 to 12 weeks) follow-up. Longer term outcomes at 6 and 12 months were considered secondary measures. For the pain outcome, meta-analysis of 10 trials found significantly greater reduction in pain scores in the LLLT group at immediate follow-up (weighted mean difference [WMD] = -0.79 cm, 95% confidence interval [CI] -1.22 to 0.36 cm). In a meta-analysis of six trials, there was no significant difference in pain reduction at short-term follow-up. However, in subgroup analyses, there was significantly greater pain reduction with LLLT in trials that used a higher dose (>3 J/point), but not a lower dose, and in trials that included patients with a short duration of back pain (5 to 27 months) but not long duration (49 months to 13 years). The decisions regarding the cutoff to use for laser dose and duration of back pain was made post hoc and considered review findings. Findings were similar for the global assessment outcome. Meta-analyses found significantly higher global assessment scores at immediate follow-up (five trials) but not short-term follow-up (three trials). Only two trials reported pain or global assessment at six months and 12 months, and neither found statistically significant differences between the LLLT and sham groups.

Huang (2015) published a SR of RCTs on LLLT for treatment of nonspecific chronic low back pain.[20] The review included trials comparing LLLT and placebo that reported pain and/or functional outcomes and reported a PEDro quality score. Seven trials (total n = 394 patients: 202 assigned to LLLT, 192 assigned to placebo) were included. Six of the seven trials were considered high quality (i.e., a PEDro score ≥7; maximum score, 11 points). Primary outcomes of interest were posttreatment pain measured by VAS score and disability measured by the Oswestry Disability Index (ODI) score. Range of motion and change in pain scores were secondary outcomes. In pooled analyses of study data, the authors found a statistically significant benefit of LLLT on pain outcomes, but not disability or ROM. For the primary outcome (posttreatment pain scores) in a meta-analysis of all seven trials, mean VAS scores were significantly lower in the LLLT group than in the placebo group (WMD = -13.57, 95% CI -17.42 to -9.72). In a meta-analysis of four studies reporting the other primary outcome (ODI score), there was no statistically significant differences between the LLLT and the placebo groups (WMD = -2.89, 95% CI -7.88 to 2.29).

An update of the Cochrane Database SR of LLLT for nonspecific low back pain was conducted in 2008.[21] The authors stated that “based on the heterogeneity of the populations, interventions, and comparison groups, we conclude that there are insufficient data to draw firm conclusions on the clinical effect of LLLT groups for low-back pain.”

A SR by Chou (2007) assessed benefits and harms of nonpharmacological therapies including LLLT for acute and chronic low back pain.[22] The reviewers did not find good evidence of efficacy for LLLT for either indication.

Randomized Controlled Trials

Since publication of the Glazov (2016) SR described above, additional RCTs have been published.

Taradaj (2019) published a RCT evaluating LLLT for the treatment of nonspecific lumbar pain (NSLP).[23] Sixty-eight patients were were randomly assigned to four groups: high-intensity laser therapy for 10 minutes (HILT), sham (HILT placebo), low-level laser therapy for eight minutes (LLLT), and sham (LLLT placebo). Postural stability measurements were taken pre- and post-laser sessions (three weeks) and at follow-up time points (one and three months). The authors concluded that neither LLLT nor HILT lead to a significant improvement in postural sway in patients with NSLP compared with standard stabilization training based on short- and long-term observations.

Koldaş Doğan (2017) reported a RCT that compared two different LLLT regimens for chronic low back pain.[24] Forty-nine patients were randomized to receive either hot-pack plus LLLT 1 (1850 nm Gallium-Aluminum-Arsenide [Ga-Al-As] laser) or hot-pack plus LLLT 2 (650 nm Helium-Neon [He-Ne], 785 ve 980 nm Gal-Al-As combined plaque laser), with a total of 15 sessions per treatment. Both groups reported improvements in pain and function, and neither regimen was superior for pain treatment. However, there was no non-LLLT control group for comparison in the study.

Section Summary

The literature on LLLT for low back pain consists of RCTs and several SRs of RCTs. Meta-analyses found that LLLT resulted in significantly greater reductions in pain scores and global assessment scores than a placebo control in the immediate posttreatment setting. Meta-analyses also found that other outcomes (eg, disability index, ROM) were significantly better immediately after treatment with active versus placebo LLLT, though not at longer-term follow-up.

LYMPHEDEMA

Systematic Reviews

Chiu (2023) published a systematic review and meta-analysis on LLLT on the treatment of breast cancer-related lymphedema.[25] The systematic review included 11 RCTs published between 2003 and 2021. There were positive effects in the LLLT group compared to the control group in post-treatment QOL (3 studies; n=73; SMD, 0.47; 95% CI, 0.00 to 0.94; I^2=0%; p=.05), reduction in swell at post-treatment (6 studies; n=204; SMD, -0.41; 95% CI, -1.01 to 0.18; I^2=76%; p=.18), and reduction in swelling at one to three months post-treatment (5 studies; n=193; SMD, -1.06; 95% CI, -2.11 to -0.02; I^2=90%; p=.05). Overall, limitations

included a high heterogeneity among studies and varying follow-up periods among studies. The authors note larger studies with long-term follow-up are needed.

A 2019 SR with meta-analysis was published by Chen evaluating effectiveness of LLLT for the treatment of breast cancer–related lymphedema.[26] The SR included nine RCTs. Six studies (N=316) were included in the meta-analysis. The primary outcome was the arm circumference or volume, and secondary outcomes were grip strength and pain scores. No significant difference in the reduction of the arm circumference or arm volume was found between LLLT and control groups after treatment, or at one-month, or at three-month follow-up. In addition, no significant differences in the change in grip strength or pain scores at any timepoint were identified between groups.

Smoot (2015) published a SR of studies on the effect of LLLT on symptoms in women with breast cancer–related lymphedema.[27] The authors identified nine studies, seven RCTs and two single-group studies. Three studies had a sham control group, one used a waitlist control, and three compared LLLT to an alternative intervention (e.g., intermittent compression). Only three studies had blinded outcome assessment and, in three studies, participants were blinded. A pooled analysis of four studies found significantly greater reduction in upper-extremity volume with LLLT than with the control condition (effect size [ES], -0.62, 95% CI -0.97 to -0.28). Only two studies were suitable for a pooled analysis of the effect of LLLT on pain. This analysis did not find a significant difference in pain between LLLT and control (ES = -1.21, 95% CI -4.51 to 2.10).

Randomized Controlled Trials

Kozanoglu (2022) published a RCT evaluating the long-term effectiveness of combined intermittent pneumatic compression (IPC) therapy plus LLLT compared to IPC therapy alone in patients with postmastectomy upper limb lymphedema (PML).[28] Group 1 received combined treatment with IPC plus LLLT (n = 21) and group 2 received only IPC (n = 21) for five sessions per week for four weeks. Clinical outcomes were assessed pre- and post-treatment at 3, 6, and 12-months. Statistically significant improvements in the circumference difference and grip strength were observed in both groups (for circumference, p=0.018 and p=0.032, respectively; for grip strength, p=0.001 and p=0.046, respectively). Visual analog scale values for arm pain and shoulder pain during motion decreased only in the combined treatment group (group 1).

A randomized double-blind sham-controlled trial of LLLT in 50 patients with post-mastectomy lymphedema was published by Omar (2010).[29] The average length of time that patients had swelling was 14 months (range, 12 to 36 months). Patients were treated with active or sham laser three times a week for 12 weeks over the axillary and arm areas. In addition, all participants were instructed to perform daily arm exercises and to wear a pressure garment. Limb circumference, shoulder mobility, and grip strength were measured before treatment and at 4, 8, and 12 weeks. Limb circumference declined over time in both groups, with significantly greater reduction in the active laser group. Shoulder flexion and abduction were significantly better in the active laser group at 8 and 12 weeks. Grip strength was significantly better in the active laser group after 12 weeks (26.2 kg vs 22.4 kg). The durability of these effects was not assessed.

Section Summary

There is insufficient evidence in the available literature to determine if the use of LLLT for the treatment of lymphedema improves health outcomes.

MEDIAL TIBIAL STRESS SYNDROME

Systematic Reviews

In a SR by Winters (2013) of treatments for medial tibial stress syndrome, LLLT was not found to be effective.[30] All studies included in the SR were considered to have methodological bias.

Section Summary

The evidence is insufficient due to the methodological limitations identified in the available literature; therefore, it cannot be determined if the use of LLLT for the treatment of medial tibial stress syndrome improves health outcomes.

MENISCAL KNEE PAIN

Systematic Reviews

There are no reports of SRs of LLLT for meniscal knee pain.

Randomized Controlled Trials

Malliaropoulos (2013) reported on a randomized, double-blind, placebo-controlled study of LLLT in 64 patients with unilateral medial knee pain for more than six weeks that was related to meniscal pathology (i.e., grade 3 tiny attenuation or intrasubstance tears on MRI). Pain improved significantly more with LLLT than placebo ($p<0.0001$). However, four patients (12.5 %) did not have improvement with LLLT. Pain returned in three patients at six months and in five patients after one year. Repeat MRIs were not performed.

Section Summary

The current evidence consists of one RCT that is limited by a small study population, does not report long-term health outcomes, and does not establish the clinical utility of LLLT for the treatment of meniscal knee pain.

ORAL MUCOSITIS

Systematic Reviews

A SR with meta-analysis evaluating the relative effects of LLLT and/or cryotherapy in cancer patients with oral mucositis (OM) was published by Lai (2021).[31] Twenty-six RCTs (N=1830) comparing groups receiving interventions of combined cryotherapy and LLLT, LLLT, cryotherapy and usual care (the control group) in patients with cancer were included. Treatment effects of combined cryotherapy and LLLT were better than those of usual care for none/mild and severe OM (ORs=106.23 [95% CI=12.15 to 929.17] and 0.01 [95% CI=0 to 0.57], respectively). Treatment effects with cryotherapy alone and LLLT alone were better than those with usual care for none/mild and severe OM (ORs = 3.13 [95% CI=1.56 to 6.27]; ORs=7.56 [95%CI = 3.84 to 14.88] and 0.25 [95% CI = 0.11 to 0.54]; ORs = 0.13 [95%CI0.07 to 0.24], respectively). For patients with none/mild OM, treatment effects with combined cryotherapy and LLLT were better than those with only LLT or cryotherapy (ORs=14.06 [95% CI=1.79 to 110.30] and 33.95 [95% CI=3.50 to 329.65], respectively). No difference in

treatment effects among cryotherapy and/or LLLT intervention in cancer patients with moderate OM was found. Heterogeneity in treatment protocols and outcome measures were noted limitations across studies.

Peng (2020) conducted a SR with meta-analysis comparing LLLT to placebo, usual care, or no therapy in patients receiving chemotherapy or radiotherapy for hematologic malignancies with or without hematopoietic stem cell transplant (HCT) or head and neck squamous cell cancer (HNSCC).[32] The SR included 30 studies including one with a stratified analysis. For the purposes of the meta-analysis, this was treated as an additional trial. Fourteen studies were conducted in Brazil and 10 were published between 2014 and 2018. Patients underwent HCT or chemotherapy in 19 studies: radiotherapy in five studies, and chemoradiotherapy in six studies. The application of LLLT was prophylactic in 26 studies and six studies reported on therapeutic LLLT use. Nineteen were considered high-quality (Jadad score of ≥3 out of 5) and 10 trials were low risk for bias. For use of prophylactic LLLT, a total of 22 studies (N=1190) evaluated the incidence of the primary outcome of severe oral mucositis during the treatment of hematologic disorders or head and neck cancer. Severe oral mucositis occurred significantly less in patients receiving LLLT compared to control (relative risk, 0.40; 95% CI, 0.25 to 0.57; p <0.01). This significant reduction in severe oral mucositis incidence with LLLT therapy was sustained in multiple subgroup analyses including assessment by underlying condition/ treatment regimen: HCT (relative risk, 0.46; 95% CI, 0.23 to 0.94; p =0.03), chemotherapy (relative risk, 0.2; 95% CI 0.05 to 0.92; p =0.04), and radiotherapy (relative risk, 0.36; 95% CI, 0.27 to 0.50; p <0.01). An analysis of 15 trials (N=900) found that prophylactic LLLT numerically, but not significantly, reduced the incidence of oral mucositis of any grade (relative risk, 0.90; 95% CI, 0.98 to 1.00; p =0.06). A subgroup analysis of patients receiving chemotherapy showed a significant reduction in any grade of mucositis with LLLT (relative risk, 0.73; 95% CI, 0.55 to 0.96; p =0.03); this difference was not significant in patients receiving radiotherapy and chemoradiotherapy (relative risk, 1.00; 95% CI, 0.92 to 1.09; and relative risk, 1.00; 95% CI, 0.98 to 1.01, respectively).

Anschau (2019) published a SR with meta-analysis of RCTs on oral mucositis (OM) in patients during and/or after cancer therapy and in which the therapeutic approach was LLLT.[33] Grade of OM was analyzed as a dichotomous variable, as improvement or no improvement in severe OM on the seventh day of therapy. Across the five RCTs (N= 315) a 62% risk reduction of severe mucositis on the seventh day of evaluation (RR = 0.38 [95% CI, 0.19-0.75]) was identified. A mean reduction of 4.21 days in the time of complete resolution of OM (CI - 5.65 to - 2.76) was found with LLLT.

In 2014, the Multinational Association of Supportive Care in Cancer (MASCC) and the International Society of Oral Oncology (ISOO) issued guidelines that reiterated findings from their 2012 SR recommending LLLT for the prevention of oral mucositis in patients receiving hematopoietic stem cell transplantation (HSCT) conditioned with high-dose chemotherapy and for patients undergoing head and neck radiotherapy, without concomitant chemotherapy.[34] The 2012 SR included 24 trials on a variety of prophylactic treatments. The recommendation on which LLLT for prevention of oral mucositis in patients receiving HSCT was based on what the authors considered to be one well-designed, placebo-controlled, randomized trial (described in more detail next),[35] together with observational studies. The trial was double-blind and sham-controlled with 70 patients. Patients were randomized to 650 nm laser, 780 nm laser, or placebo.[35] Patients in the 650-nm laser group were more likely to have received a total body irradiation (TBI)–containing regimen compared with the other two groups; otherwise, the groups were comparable. LLLT began on the first day of conditioning and continued for

three days posttransplant. Of the 70 patients, 47 (67%) had complete or nearly complete mucositis measurements over time; the average number of visits per patient was similar among the three groups. The difference between groups in mean oral mucositis scores was greatest at day 11 (placebo, 24.3; 650 nm, 16.7; 780 nm, 20.6), but this difference between the 650-nm group and placebo group was not statistically significant (p=0.06). Patient-specific oral mucositis scores differed significantly between the two groups only when adjusted for TBI exposure. Of the 70 patients in the study, 17 (24%) were assessed for oral pain. With group sizes of five and six, the 650-nm group had significantly lower patient-specific average pain scores (15.6) than the placebo group (47.2). No adverse events from LLLT were noted. This study was flawed because it did not achieve statistical significance for the primary outcome measure and had a very small percentage of patients with pain assessments.

The MASCC/ISOO recommendation for LLLT for the prevention of oral mucositis in patients undergoing radiotherapy, without concomitant chemotherapy, for head and neck cancer was based on “weaker evidence” from three studies that showed positive results but had major flaws. Evidence was considered encouraging but insufficient to recommend LLLT in other populations. The authors emphasized that due to the range of laser devices and variations in individual protocols, results of each study applied exclusively to the cancer population studied and the specific wavelength and settings used.

Additional SRs have been published since the 2012 MASCC/ISOO SR.[36, 37] Oberoi (2014) reported on a SR and meta-analysis of 18 RCTs on LLLT versus no treatment or placebo for oral mucositis.[37] Eight RCTs assessed patients undergoing HSCT, eight evaluated head and neck cancer patients receiving radiotherapy or chemoradiation, and the rest studied patients with other conditions receiving chemotherapy. The investigators used the Cochrane risk of bias tool to evaluate the RCTs. Most studies were considered at low risk of bias on most domains. For example, 68% were at low risk of bias for blinding of patients and personnel, and 89% were at low risk of bias on incomplete outcome data. The primary outcome measure for the review was the incidence of severe mucositis. Ten studies (total N=689 patients) were included in a pooled analysis of this outcome. The overall incidence of severe mucositis (grades 3-4) decreased with prophylactic LLLT, with a risk ratio (RR) of 0.37 (95% CI 0.20 to 0.67, p=0.001). Moreover, the absolute risk reduction in the incidence of severe mucositis (-0.35) significantly favored LLLT (95% CI -0.48 to -0.21, p<0.001). Among secondary outcomes, LLLT also significantly reduced the overall mean grade of mucositis (standardized mean difference [SMD], -1.49; 95% CI, -2.02 to -0.95), duration of severe mucositis (WMD -5.32, 95% CI -9.45 to -1.19), and incidence of severe pain (VAS; RR=0.26, 95% CI 0.18 to 0.37). In a subgroup analysis of the primary outcome (incidence of severe mucositis), the investigators did not find a statistically significant interaction between the type of condition treated and the efficacy of LLLT.

Randomized Controlled Trials

de Carvalho e Silva (2023) published an RCT evaluating the effectiveness of LLLT in the management of both xerostomia and oral mucositis in 53 patients with squamous cell carcinoma of the head and neck.[38] The participants were being treated with radiation therapy or chemoradiotherapy with curative intent. Twenty-six patients were randomized to LLLT and 27 were randomized to a sham treatment on the first day of treatment. There was no significant different in baseline dental health between the two groups (p>0.05). Outcome measures were arithmetic means of a xerostomia-related quality of life (QOL) questionnaire and the presence or absence of oral mucositis lesions. Differences in mean scores on the

QOL questionnaire were considered clinically relevant if they were ≥20%. In the sham treatment group, there was an increase in mean score for several items that indicated symptoms of xerostomia ($p<0.0001$). In the treatment group, mean scores decreased, indicating absent or very mild xerostomia ($p=0.0074$). Differences in mean scores were ≥20% for eight of the 15 questions on the QOL questionnaire. Higher grades of oral mucositis were found in the sham group compared to those treated with LLLT ($p=0.0001$). The study findings indicate that LLLT reduces both xerostomia and oral mucositis in patients being treated for head and neck cancer.

Legouté published the results of a phase III trial of LLLT to treat OM lesions grade ≥ 2 in patients with oral cavity or oro/hypopharyngeal cancers (stage III or IV) from seven French oncology centers.[39] Severity of OM (incidence and duration of grades ≥3) was the primary endpoint. Among the 97 randomized patients, 83 (85.6%) were assessed; 32 patients had no laser therapy because of unreachable OM lesions. An acute OM (grade ≥ 3) was observed in 41 patients (49.4%): 23 patients (54.8%) of the active laser group versus 18 (43.9%) in the control group (modified intend to treat, $p = 0.32$). Tolerance was noted as excellent for every session for 91% of patients and 4.5% in most sessions. The five-year follow-up is targeted for March of 2021.

Two large RCTs evaluating LLLT for prevention of oral mucositis were published by Gautam in 2012.[40, 41] One of these studies reported LLLT for the prevention of chemoradiotherapy-induced oral mucositis in 121 oral cancer patients.[41] The second publication reported LLLT for the prevention of chemoradiotherapy-induced oral mucositis in 221 head and neck cancer patients.[40] There is an apparent overlap in patients in these two reports, with the head and neck cancer study including the 121 patients with a primary tumor site in the oral cavity. Patients in these studies received LLLT before radiotherapy at 66 Gy delivered daily in 33 fractions, five days per week and concurrent with cisplatin. LLLT was delivered at a wavelength of 632.8 nm, power density of 24 mW/cm^2, and a dosage of 3 to 3.5 J. In the report on oral cancer, LLLT before radiotherapy led to significant reductions in the incidence of severe oral mucositis (29% vs 89%) and its associated pain (18% vs 71%, with a VAS score >7), opioid analgesic use (7% vs 21%), and total parenteral nutrition (30% vs 39%), all respectively, during the last weeks of chemoradiotherapy. LLLT also reduced the duration of severe oral mucositis (4.07 days vs 13.96 days), severe pain (5.31 days vs 9.89 days), and total parenteral nutrition (14.05 days vs 17.93 days), all respectively. In the 221 patients treated for head and neck cancer, LLLT was reported to lead to significant reductions in the incidence and duration of severe oral mucositis (8.19 days vs 12.86 days) and its associated pain (VAS score of approximately 4 vs 7), total parenteral nutrition (45.0% vs 65.5%), and opioid analgesic use (9% vs 26% for step III), respectively.

The next year, Gautam (2013) published an assessment of patient-reported outcomes from the same study of 221 head and neck cancer patients using the Oral Mucositis Weekly Questionnaire-Head and Neck (OMWQ-HN) and the Functional Assessment of Cancer Treatment- Head and Neck (FACT-HN) questionnaire.[42] Patients received LLLT as described earlier in this paragraph. Patients in the LLLT group reported significantly better outcomes than the placebo group with lower scores on both the OMWQ-HN ($p<0.001$) and FACT-HN ($p<0.05$).

A number of small, double-blind, sham-controlled RCTs on prevention of oral mucositis in patients undergoing cancer treatment were published in the last several years. Gautam (2015) reported on 46 patients with head and neck cancer scheduled for radiotherapy and found

significant reductions in the incidence and duration of severe oral mucositis (p=0.002) and severe pain (p=0.023) after LLLT versus sham.[43] Oton-Leite (2015) reported on 30 head and neck cancer patients undergoing chemoradiation and found that oral mucositis grades were significantly lower in the LLLT group than in the control group at the week 1, 3, and 5 evaluations.[44] For example, at the last clinical evaluation (week 5), the rates of grade 3 oral mucositis were 25% in the LLLT group and 54% in the control group. The third RCT, by Ferreira (2015), included 36 patients with hematologic cancer undergoing HSCT.[45] The overall incidence of oral mucositis did not differ significantly between groups (p=0.146). However, the rate of severe oral mucositis (grade 3 or 4) was significantly lower in the laser group (18%) than in the control group (61%; p=0.015).

Section Summary

The literature on LLLT for the prevention of oral mucositis includes several SRs. A 2014 SR of LLLTs for prevention of oral mucositis included 18 RCTs, generally considered at low risk of bias, and found statistically significantly better outcomes with LLLT than with control conditions on primary and secondary outcomes. These findings were recapitulated in a 2019 SR which focused on only RCTs. A 2020 SR not limited to patients undergoing HCT showed benefit with using prophylactic LLLT compared to control in reducing the incidence of severe oral mucositis in patients undergoing chemotherapy or radiotherapy. A large SR including 26 RCTs and 1830 patients found LLLT to be beneficial for the reduction of mild and severe OM in patients with cancer.

OROFACIAL PAIN

Systematic Reviews

A SR on studies using LLLT for the treatment of trigeminal neuralgia was published by Ibarra in 2021.[46] The review included five RCTs and one nonrandomized clinical trial. Sample sizes ranged from 12 to 53 across studies, for a total sample of 193. Study designs included one sham-controlled study, one study evaluating the same population at two timepoints, one comparing LLLT to electromagentic therapy, one evaluating LLLT as an adjuvant therapy to ganglion block, and two studies evaluating photobiomodulation as an adjuvant therapy to pharmacotherapy. Risk of bias ranged from high (two studies) to low (three studies). Low sample size precluded pooled analysis. While the authors found that, qualitatively, LLLT appears to be as effective as conventional therapies for trigeminal neuralgia, they conclude that additional data with consistent outcome parameters and longer follow-up are needed.

DePedro (2020) published a SR of LLLT for the management of neuropathic orofacial pain which included 13 studies (eight RCTs, two prospective studies, and three case series).[47] Ten of the studies were on burning mouth syndrome, three were on trigeminal neuralgia, and one on occippital neuralgia. Although all studies showed a reduction in pain intensity, not all were statistically significant. No meta-analysis was reported. The authors concluded that studies assessing medium and long-term outcome measures of chronic pain are needed, as is standardization of the technique.

Tengrungsun (2012) assessed the effectiveness of LLLT as a treatment for orofacial pain in 33 studies[48] represented by 1,522 chronic pain patients meeting inclusion criteria in a SR. Trials were included if they were randomized, had a comparison group, had a study population with an orofacial pain condition including dentin hypersensitivity and musculoskeletal pain, and

included a measurement of pain relief. In addition, a high-quality scoring system was used the literature was analyzed by two independent researchers. Of the 23 RCTs reviewed, all but two were rated as low quality. The review concluded there was limited evidence to conclude that LLLT was more effective than placebo, sham laser, and other active treatments.

Randomized Control Trials

Manca (2014) investigated the effects of ultrasound and LLLT on myofascial trigger points (MTP) of the upper trapezius muscle (uTM).[49] In the double-blind, randomized, placebo-controlled study, 60 participants with at least one active MTP in uTM (28 women and 32 men; mean age 24.5 ± 1.44 years) were recruited and randomly assigned to one out of five groups: active ultrasound (n = 12), placebo US (n = 12), active LLLT (n = 11), placebo LLLT (n = 11) and no therapy (control, n = 14). After the 2-week intervention, all groups showed pressure pain threshold, numerical rating scale and cervical lateral flexion significant improvements ($p < 0.05$), which were confirmed at the follow-up. The authors concluded that ultrasound and LLLT provided significant improvements in pain and muscle extensibility.

A double-blind, randomized trial by Magri (2017) compared LLLT with placebo in a group of women with temporomandibular disorders.[50] LLLT was performed twice a week for a total of eight sessions. Both LLLT (n=31) and placebo (n=30) groups showed decreases in pain from baseline, though only the LLLT group maintained a reduction in pain after 30 days. There were no changes in pain sensitivity noted with either treatment.

In a small RCT not included in the above SR, the effects of LLLT on masticatory performance, pressure pain threshold (PPT), and pain intensity in 21 patients with myofascial pain were evaluated.[51] Patients were either assigned to the laser group (n=12) or the placebo group (n=9). A reduction in the geometric mean diameter of crushed particles and an increase in PPT were seen only in the laser group when comparing the baseline and end-of-treatment values. Both groups showed a decrease in pain intensity at the end of treatment. Authors concluded that LLLT promoted an improvement in MP and PPT of the masticatory muscles. This is a study of limited sample size and the randomization of the patient population is not clear.

Section Summary

Findings from published RCTs on the use of LLLT in orofacial pain are insufficient to determine the added benefit of the technology on net health outcomes due to the methodological limitations in the study designs.

ORTHODONTIC PAIN

Systematic Reviews

He (2013) investigated the efficacy of LLLT in the management of orthodontic pain.[52] Four RCTs, two quasi-RCTs, and two controlled clinical trials (CCTs) were selected from 152 relevant studies, including 641 patients. The meta-analysis demonstrated that 24% risk of incidence of pain was reduced by LLLT (RR = 0.76, 95% CI range 0.63-0.92, P = 0.006). In addition, compared to the control group, LLLT brought forward "the most painful day" (MD = -0.42, 95% CI range -0.74- -0.10, P = 0.009). Furthermore, the LLLT group also implied a trend of earlier end of pain compared with the control group (MD = -1.37, 95% CI range -3.37-0.64, P = 0.18) and the pseudo-laser group (MD = -1.04, 95% CI range -4.22-2.15, P = 0.52). Authors concluded due to the methodological shortcomings and risk of bias of included trials, the evidence for LLLT in delaying pain onset and reducing pain intensity was insufficient.

Randomized Controlled Trials

Owayda published the results of a RCT on analgesic effects of LLLT and paracetamol-caffeine in controlling orthodontic pain induced by elastomeric separators in a total of 54 patients.[53] Group 1 (n = 18) received a single dose of laser treatment with a placebo medication, group 2 (n = 18) received paracetamol-caffeine tablets with a placebo light-emitting diode (LED) light, and patients in group 3 (n = 18) were exposed to the two placebo procedures. An 11-point numeric rating scale was used to assess spontaneous and chewing pain perception immediately and at one hour, 24 hour, 48 hours, and one week after separator placement. The authors report similar pain levels in the laser and drug groups and decreased pain in the LLLT group compared with the placebo group. No impact of paracetamol-caffeine or LLLT were found for overall health related quality of life measures.

Celebi (2019) found no significant reduction in pain with LLLT compared to control or mechanical vibration following placement of an orthodontic archwire in 60 subjects [54] However, reduction in pain levels were found in LLLT treated patients compared to control in 84 subjects following placement of an orthodontic archwire in a study published by Lo Giudice (2019).[55] Martins (2019) published the results of a randomized, double-blinded, placebo-controlled study in 62 patients, which found reduced pain immediately following separation of an orthodontic device, but no difference at 24 hours in patients treated with LLLT compared to control.[56] AlSayed Hasan (2017) evaluated two levels of LLLT (4 Joule or 16 Joule) in 26 patients treated with a fixed orthodontic appliance.[57] The study used a blinded, split-mouth design, in which one molar from each patient received the laser treatment, while one molar had sham treatment. The outcome measures of pain by VAS scale during mastication at various timepoints after LLLT were not significantly different between treatment groups.

Section Summary

The evidence from published studies on the use of LLLT to reduce orthodontic pain has not demonstrated consistent findings of improved outcomes. These inconsistent findings may be due to methodological limitations of the published studies.

OSTEOARTHRITIC (OA) KNEE PAIN

Systematic Reviews

Malik (2023) published a systematic review and meta-analysis assessing the effect of LLLT plus exercise on pain, range of motion (ROM), muscle strength, and function.[58] Fourteen RCTs involving 820 patients were included. There was a significant difference in pain both immediately after therapy (SMD: -058, p=0.001) and during follow-up (SMD: -1.35, p=0.05) but no significant differences in ROM, strength, or knee function either right after therapy or during follow-up.

Huang (2015) published a SR of RCTs comparing at least eight treatment sessions of LLLT and sham laser treatment in knee osteoarthritis patients.[59] To be eligible for inclusion in the review, trials had to report pain and/or functional outcomes and a PEDro quality score. A total of nine trials (total n=518 patients) met eligibility criteria. In these studies, interventions included between eight and 20 laser or sham sessions over two to six weeks. All nine trials were considered high quality, as assessed using the PEDro scale (score of 7; maximum score, 11 points). Primary outcomes of interest were posttreatment pain measured by VAS scores and the Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores (Pain

and Function). Meta-analyses did not find that LLLT led to significantly better pain scores than the sham control, either immediately after treatment or at the three-month follow-up. For example, a meta-analysis of five studies that reported 12-week pain scores did not find a statistically significant between-group difference (SMD = -0.06; 95% CI, -0.30 to 0.18). Moreover, there were no statistically significant differences between active and sham laser interventions on WOMAC Stiffness scores or WOMAC Function scores. The secondary outcome (range of motion after therapy) also did not significantly favor LLLT over a sham intervention.

Bjordal (2007) published a SR of placebo-controlled RCTs to determine the short-term efficacy of physical interventions for osteoarthritic knee pain.[60] They included a total of 36 RCTs. The largest proportion of trials evaluated transcutaneous electrical nerve stimulation (n=11), followed by eight trials on LLLT and seven on pulsed electromagnetic fields. Also included were trials on electroacupuncture, manual acupuncture, static magnets, and ultrasound. The authors did not report findings of pooled analyses on LLLT for knee osteoarthritis. In a qualitative analysis, they stated that all the physical interventions but two (manual acupuncture, ultrasound) showed better results with active treatment over placebo.

Randomized Controlled Trials

Elboim-Gabyzon (2023) published a single-blinded RCT comparing LLLT to pulsed electromagnetic field therapy (PEFT) in 40 people with low-grade knee osteoarthritis.[61] Twenty patients were treated with LLLT and 20 were treated with PEFT. Primary outcomes were pain intensity and functional level. All patients completed therapy and no adverse events were documented. Both groups had significant improvement in pain intensity ($p<0.0001$), but the PEFT group had a greater effect size in three of four activities (resting, standing, and climbing stairs). Similarly, both groups had significant improvement in function after therapy ($p\leq0.0003$), but the PEFT group had a larger effect size. Limitations of the study include the results may not be generalizable to people with higher grades of knee osteoarthritis, and the researchers did not take participants medication usage into account.

De Matos Brunelli Braghin (2018) published the results of a RCT of LLLT on pain, stiffness, function, and spatiotemporal gait in patients with bilateral knee osteoarthritis.[62] Patients with knee OA (Grades 1-3) were and randomized into four groups: Control Group (CG), untreated; Laser Group (LG), treated with LLLT; Exercise Group (EG), treated with exercise; and Laser + Exercise Group (LEG), treated with laser and exercises. Treatment was twice a week for two months. Significant improvement in pain ($p = 0.006$) and function ($p = 0.01$) was found only in the EG. At eight weeks, all groups receiving intervention showed a significant increase in gait speed: LG versus CG ($p = 0.03$); EG versus CG ($p = 0.04$) and LEG versus CG ($p = 0.005$). Only the LEG group showed a significant increase in the cadence and duration of single right limb support ($p=0.009$ and 0.04, respectively), and only the EG and LEG groups showed significant decreases in the duration of right limb support ($p = 0.035$ and $p = 0.003$, respectively) compared to the CG. No long-term outcomes were reported.

Gopal Nambi (2016) evaluated LLLT in 34 patients with knee osteoarthritis in a double-blind, randomized trial.[63] The placebo treatment consisted of laser therapy with the minimum emission of energy. The 17 subjects each in the LLLT group and placebo group had treatment sessions three times a week for four weeks, with additional exercise therapy and Kinesio taping. Pain was assessed by VAS. After eight weeks, VAS scores were significantly lower in the LLLT group than in the placebo group.

Section Summary

Though RCTs are available on the use of LLLT for the treatment of osteoarthritic knee pain, the interpretation of the results is limited due to small patient sizes and limited long-term follow-up of patients. Study results have been inconsistent. Systematic reviews have not shown that LLLT consistently improves pain and function for people with osteoarthritic knee pain.

PLANTAR FASCIITIS

Systematic Reviews

Ferlito (2023) published a systematic review and meta-analysis of 19 RCTs involving 1089 participants to assess the effects of LLLT related to pain and disability due to plantar fasciitis when compared to control conditions, other interventions, and adjunct treatments.[64] The analysis found that LLLT may reduce short-term pain compared to placebo/control intervention with moderate certainty evidence (mean difference (MD) = -22.02, 95% CI -35.21 to -8.83, I^2=46%, p<0.001) based on three trials, but a fourth study found LLLT did not improve short-term pain compared to placebo with low certainty evidence (MD-3.08, 95% CI –15.90 to 22.06). LLLT with exercise compared to exercise alone was associated with improved pain intensity based on moderate certainty evidence (MD= -21.84, 95% CI -26.14 to -17.54, p<0,00001). When compared to extracorporeal shockwave therapy (ESWT) an analysis of six studies found LLLT with exercise was better than ESWT with exercise with low certainty evidence (MD= -19.59, 95% CI -29.03 to -10.15, I^2 = 67%, p=0.0005). LLLT with exercise compared to ultrasound therapeutic (UST) plus exercise in four studies found LLLT was not superior to UST for short-term pain based on low certainty evidence (MD= -5.05, 95% CI -8.19 to -1.91, p=0.02). One study found LLLT to be superior to UST for medium term pain with low certainty evidence (MD=-10.79, 95% CI -14.51 to -7.07). LLLT with or without exercise did not improve disability when compared to placebo/control, exercise alone, or ESWT. There is some evidence LLLT with exercise is superior to UST with exercise for disability but the effect size is small so its clinical relevance is questionable (SMD = -.039, 95% CI -0.77 to 0.01, p=0.04). The authors point out that the LLLT dosage was not addressed. Further research is needed to understand if there is a dose-response relationship that is important in the delivery of LLLT to achieve therapeutic goals.

Guimaraes (2023) published a systematic review and meta-analysis of multiple therapeutic interventions for plantar fasciitis that have been evaluated with RCTs.[65] Nineteen treatments from 236 studies were evaluated. Outcomes were short, medium, and long-term pain. For short-term pain, LLLT was compared to a control group in five studies involving 231 participants. The meta-analysis found improvement in pain with moderate quality evidence (p<0.01). Two studies involving 172 subjects compared high-intensity laser therapy to LLLT and found no significant difference in short-term pain (p=0.28). No studies evaluated LLLT for medium or long-term pain.

Naterstad (2022) published a systematic review and meta-analysis of 18 RCTs evaluating LLLT in patients with lower extremity tendinopathy (seven trials of patellar or Achilles tendinopathy) or plantar fasciitis (11 trials).[66] In an analysis of LLLT versus any control, both pain and disability were improved with LLLT. VAS scores were reduced immediately after therapy (n=260; SMD, 0.39; 95% CI, 0.09 to 0.7; I2=30%) and at 4 to 9 weeks follow-up (n=222; SMD, 0.32; 95% CI, 0.05 to 0.59; I2=4%) compared with control. LLLT did not significantly improve disability compared with other interventions immediately after therapy

(n=76; SMD, 0.25; 95% CI, -0.21 to 0.7; I2=0%) or at 4 to 8 weeks follow-up (n=76; SMD, 0.24; 95% CI, -0.21 to 0.7; I2=0%).

Guimaraes (2022) published a systematic review (SR) with meta-analysis of 14 studies (N=817) comparing LLLT (alone or combined with other interventions) and control (placebo and other interventions) in patients with plantar fasciitis.[67] Compared to the placebo group, LLLT improved pain in the short term of 0 to 6 weeks (four studies, N=234; moderate-quality evidence; MD, -2.28; 95% CI, -2.58 to -1.97; p<0.00001; I^2=0%). No significant difference in short-term disability was found for individuals in the LLLT group compared to the placebo group. Compared to the conventional rehabilitation alone group, LLLT combined with conventional rehabilitation improved pain in the short term of 0 to 6 weeks (two studies, N=90; moderate-quality evidence; MD, -2.01; 95% CI, -2.89 to -1.13; p<0.00001; I^2=0%). However, compared to extracorporeal shock wave therapy (ESWT), LLLT did not significantly reduce pain intensity in the short term (four studies, N=175; low-quality evidence; MD, 0.45; 95% CI, -2.0 to 2.9; p=.72; I^2=94%). The meta-analysis was limited by insufficient data for longer-term outcomes, the lack of multicenter studies, and lack of a large sample. Additionally, the quality of evidence for the outcome disability were low.

Wang (2019) published a SR with meta-analysis of six RCTs (N=315) comparing LLLT (alone or combined with other interventions) and controls (placebo or other interventions) in the treatment of plantar heel pain or plantar fasciitis.[68] Compared with controls, VAS for pain was significantly reduced after treatment (SMD=-0.95; 95% CI -1.20 to -0.70; p<0.001), as well as remaining significantly better at 3 months (SMD= -1.13; 95% CI -1.53 to -0.72; p<0.001). The meta-analysis was limited by the small number of studies included, its small sample size, and insufficient data for longer-term outcomes.

Randomized Controlled Trials

Cinar (2018) conducted a prospective, single-blinded RCT investigating combination therapy consisting of LLLT plus exercise and orthotic care compared with orthotic care alone in persons with plantar fasciitis.[69] Forty-nine individuals were randomized to LLLT (n=27) or a control therapy (n=22). Each person performed a home exercise routine and received orthotic care; persons in the LLLT group received treatment three times a week for a total of ten sessions. The function subscale of the American Orthopedic Foot and Ankle Society Score, a VAS, and the 12-minute walk test were used to measure progress. Scores were recorded at baseline, three weeks, and three months after treatment. At week three, both groups saw a significant improvement in American Orthopedic Foot and Ankle Society total score (LLLT, p<0.001; control, p=0.002). However, at the three-month follow-up, only the LLLT group progressed as assessed on the American Orthopedic Foot and Ankle Society total score (p=0.04). At all check-ins, the group scores for the 12-minute walk test were comparable. Both groups showed significant pain reductions at the three-month follow-up (LLLT, p<0.001; control, p=0.01); however, the LLLT group had a more significant reduction in pain at month three (p=0.03). Thus, reviewers concluded that combination therapy plus LLLT was more effective in reducing pain and improving function for patients with plantar fasciitis than orthotic care alone. Limitations included a lack of a control group, which would have accounted for the natural progression of recovery in patients with plantar fasciitis; another limitation is that the LLLT dose may or may not have been precise enough for the conditions of this study. The same group also published a randomized trial comparing LLLT (n=24) to extracorporeal shock wave therapy (ESWT) (n=25) or usual care (n=17).[70] Significant improvements in pain were seen over three months for all groups, with the LLLT group demonstrating lower pain than the

ESWT group (p=0.003) and control group (p=0.043). It was not clear whether different patients were used for these trials.

A double-blinded RCT by Macias (2015) assessed 69 patients with unilateral chronic plantar fasciitis and chronic heel pain of three months or longer that was unresponsive to conservative treatments (e.g., rest, stretching, physical therapy).[71] Patients were randomized to twice weekly treatment for three weeks of LLLT or sham treatment. The primary efficacy outcome, reduction of heel pain pre- to posttreatment, differed significantly between groups (p<0.001). Mean VAS scores decreased from 69.1 to 39.5 in the LLLT group and from 67.6 to 62.3 in the sham group. The difference in Foot Function Index scores did not differ significantly between groups.

An RCT on LLLT was reported by Kiritsi (2010) on LLLT in 30 subjects with plantar fasciitis.[72] The trial was double-blinded and sham-controlled trial and included 30 patients. Twenty-five (83%) patients completed the study, with treatment three times a week over six weeks. At baseline, plantar fascia thickness, measured by ultrasound was significantly greater in symptomatic compared with asymptomatic feet (5.3 mm vs 3.0 mm). Plantar fascia thickness decreased in both the LLLT and the sham groups during the study. Although plantar fascia thickness after 6 weeks of treatment did not differ significantly between the two groups (3.6 mm in LLLT, 4.4 mm in sham), there was a significant difference between groups in the change in thickness (1.7 mm LLLT vs 0.9 mm sham). VAS scores after night rest or daily activities improved significantly more in the LLLT group (59% improvement) than in the sham group (26% improvement). At baseline, pain after daily activities was rated as 67 out of 100 by both groups. At the end of treatment, VAS scores after daily activities were rated as 28 out of 100 for LLLT and 50 out of 100 for sham.

Section Summary

Sham-controlled RCTs have evaluated LLLT for plantar fasciitis, but findings were inconsistent. One RCT compared LLLT plus therapy with orthotic care alone, and while a significant advantage was observed in the LLLT treatment group, this treatment was a part of combination therapy. None of the studies presented long-term follow-up data. Three systematic reviews found that studies of LLLT for the treatment of plantar fascitis are limited by a lack of high quality evidence, small sample sizes, absence of long-term outcomes.

RHEUMATOID ARTHRITIS (RA)

Systematic Reviews

Lourinho (2023) conducted a systematic review and meta-analysis on the effects of LLLT in adults with rheumatoid arthritis.[73] Their literature search included 18 RCTs (n=793). There were varying intervention durations of four weeks to six months among the studies. Also, treatment regimens and comparisons varied among the studies. Some studies investigated laser acupuncture. The meta-analyses for the outcomes of interest, including pain, morning stiffness, handgrip strength, functional capacity, inflammation, and disease activity, were reported in subgroups of two to four studies, with no statistically significant differences in effects. The authors noted that 17 of the 18 studies had an overall high risk of bias and the results show a low quality of evidence for LLLT in rheumatoid arthritis.

A 2005 Cochrane Review included five placebo-controlled randomized trials and found that relative to a separate control group, LLLT reduced pain and morning stiffness, and increased

tip-to-palm flexibility.[74] Other outcomes did not differ between groups, including functional assessment, range of motion, and local swelling. For RA, relative to a control group using the opposite hand (one study), there was no difference observed between the control and treatment hand for morning stiffness duration and no significant improvement in pain relief. The authors noted that "despite some positive findings, this meta-analysis lacked data on how LLLT effectiveness is affected by four important factors: wavelength, treatment duration of LLLT, dosage and site application over nerves instead of joints."

Randomized Controlled Trials

A randomized double-blind placebo-controlled trial comparing outcomes of pain reduction and improvement in hand function in 82 patients with RA treated with low-level laser or placebo laser was reported by Meireles (2010).[75] However, co-treatment (such as pain medication) was not controlled during the trial and durability of treatment effects was not measured, limiting interpretation of these findings.

Section Summary

Studies on the use of LLLT for the treatment of rheumatoid arthritis have methodological limitations that preclude the interpretation of the results; therefore, valid conclusions cannot be made to determine if the use of LLLT leads to improved health outcomes.

SHOULDER PAIN

Systematic Reviews

A 2015 SR and meta-analysis evaluated 17 RCTs (13 high quality; four moderate quality) LLLT studies that included outcome measures of pain relief by VAS and relative risk for global improvement.[76] Results showed that patients treated with LLLT experienced significant and clinically relevant pain relief compared with placebo, for LLLT as monotherapy and as adjunct to exercise therapy. In addition, when LLLT was used in combination with physiotherapy, patients achieved significant pain reduction on VAS compared with placebo. Relative risks for global improvement were also statistically significant at 1.96 (95% CI 1.25 to 3.08) and 1.51 (95% CI 1.12 to 2.03), for laser as monotherapy or adjunctive in a physiotherapy regime, respectively. Study authors concluded that LLLT can offer clinically relevant pain relief and hasten improvement, both alone and in combination with physiotherapy.

A 2014 Cochrane review evaluated LLLT and other electrotherapy modalities for frozen shoulder.[77] The review found limited evidence to draw conclusions on the effectiveness of electrotherapy modalities for frozen shoulder. Only one RCT of 40 patients compared LLLT with placebo. This trial administered LLLT for six days. On the 6th day, LLLT was considered to have some improvement in a global assessment of treatment success when compared to placebo. However, this study was considered to be of low quality and the small size and short follow-up limited interpretation of results. Another RCT on LLLT discussed in the Cochrane review, by Stergioulas (2008), was considered to be of moderate quality.[78] In this study, 63 patients with frozen shoulder were included in an RCT comparing an 8-week program of LLLT (n=31) or placebo (n=32). Both groups also participated in exercise therapy. Compared with the sham group, the active laser group had a significant decrease in overall, night, and activity pain scores after four weeks and eight weeks of treatment, and at the end of eight more weeks of follow-up. At the same time intervals, a significant decrease in SPADI scores, and Croft shoulder disability questionnaire scores was observed, while a significant decrease in

Disability of Arm, Shoulder, and Hand Questionnaire scores was observed at eight weeks of treatment and at 16 weeks postrandomization; and a significant decrease in health assessment questionnaire scores was observed at four weeks and eight weeks of treatment. However, 11 patients included in the original randomization were excluded from analysis after leaving the study to seek other treatments. It is not known how this loss might have biased the final outcomes of the study.

Favejee (2011) published results from a SR of RCTs on the use of non-surgical treatment (including LLLT) for frozen shoulder (adhesive capsulitis).[79] Five Cochrane reviews and 18 RCTs were evaluated. The researchers reported finding a strong association between LLLT and reduced pain and disability. However, commentary on these findings points to the lack of distinction between primary (or idiopathic) capsulitis versus secondary adhesive capsulitis (due to trauma, diabetes, or thyroid dysfunction).[80] Because secondary capsulitis is less responsive to treatment, lack of sub-group analysis of treatment outcomes by patient type may limit the generalizability of these results to a specific patient population.

Randomized Controlled Trials

Badil Güloğlu (2021) randomized 64 patients with a recent diagnosis of subacromial impingement syndrome without treatment in the preceding four weeks to 15 sessions of LLLT (n=34) every weekday for three weeks or to weekly sessions of extracorporeal shock wave treatment (ESWT; n=30) for three weeks.[81] In both groups, all range of motion measurements, visual analogue scale pain scores, and SPADI scores showed significant improvements both at the end of treatment and at the third month after treatment ($p<0.05$). There was no significant difference in abduction between the groups except the change at the end of treatment. The ESWT group showed greater improvements in terms of SPADI disability and total scores at the end of treatment compared to LLLT. The improvements in VAS pain scores and SPADI scores at the third month after treatment was significantly more evident in the ESWT group ($p<0.05$).

Alfredo (2021) randomized 122 patients to LLLT plus exercise (group 1, n=44; 42 included in analysis), exercise alone (group 2, n=42), or LLLT alone (group 3, n=42) for the treatment of subacromial impingement syndrome:[82] Therapy was given three times a week for eight weeks. The primary outcome was the change in shoulder pain and disability index (SPADI) and numeric pain rating scale and medication intake were secondary outcomes. SPADI scores at baseline, two month, and three month follow-up ($p=0.001$) were 60.8 (37.7 to 70.8), 3.8 (0.0 to 10.8) and 2.3 (0.8 to 10.8) for group 1; 61.5 (41.5 to 71.5), 9.2 (3.8 to 29.2) and 14.2 (1.5 to 38.0) for the group I2; and 73.3 (59.2-80.8), 34.2 (16.9 to 54.6) and 33.1 (22.3 to 49.2) for the group 3, respectively, all $p<0.05$. Pain scores at baseline ($p=0.829$), two- month ($p=0.057$) and three- month follow-up ($p=0.004$) were 6.8 (4.7 to 7.7), 0.2 (0.0 to 0.5) and 0.3 (0.0 to 1.0) for group 1; 6.6 (5.7 to 8.0), 0.5 (0.2 to 2.0) and 0.2 (0.0 to 3.3) for group 2; and 6.5 (5.1 to 7.4), 2.4 (0.1 to 6.7) and 4.0 (2.0 to 5.0) for group 3, respectively. While patients in the LLLT plus exercise group had a significantly greater improvement in SPADI compared to other groups, no between-group comparison was performed for patients receiving LLLT alone and exercise alone. This study was also limited by lack of blinding.

Eslamian and others evaluated the effects of LLLT in combination with conventional physiotherapy endeavors in 50 patients with rotator cuff tendinitis.[83] A total of 25 patients were randomly assigned to the control group and received only routine physiotherapy. The additional 25 patients were assigned into the experimental group and received conventional

therapy plus LLLT. Authors concluded that LLLT combined with conventional physiotherapy had superiority over routine physiotherapy in decreasing pain and improving the patient's function, but no additional advantages were detected in increasing shoulder joint range of motion in comparison to other physical agents. This study had a limited study population and did not include a sham group for comparison.

Results from additional RCTs remain limited by lack of sham control [83-86] and/or lack of treatment durability assessment.[87-89]

Section Summary

In sumary, conflicting results from available RCTs limit the conclusions that can be drawn about the effectiveness of LLLT in shoulder disorders.

TEMPOROMANDIBULAR JOINT PAIN

Systematic Reviews

Zhang (2023) published a systematic review and meta-analysis of laser therapy on temporomandibular disorders, including 28 RCTs.[90] Overall, laser therapy had a statistically significant effect on VAS (21 studies; n=934; SMD: -1.88; 95% CI, -2.46 to -1.30; p<.00001; I^2, 93%), maximum active vertical opening (17 studies; n=732; MD, 4.90; 95% CI, 3.29 to 6.50; p<.00001; I^2, 72%), maximum passive vertical opening (5 studies; n=300; MD, 5.82; 95% CI, 4.62 to 7.01; p<.00001; I^2, 40%), and right lateral movement (6 studies; n=261; MD, 0.73; 95% CI, 0.23 to 1.22; p=.004; I^2, 0%). The authors note that while the results demonstrated effective pain relief, but limited effect on improvement of mandibular movement. There was variation among the included studies, including various laser parameter settings. RCTs with larger sample sizes are needed for higher quality evidence.

Arribas-Pascual (2023) published systematic review and meta-analysis on the effects of various physiotherapy interventions on pain and mouth opening in temporomandibular disorders.[91] They conducted a sub-analysis on four studies of LLLT. The found a statistically significant effect of LLLT on pain intensity (SMD, 0.8; 95% CI, 1.44 to 0.17; p<.001; I^2, 27%) and maximum mouth opening (SMD, 0.95; 95% CI, 1.5 to 0.39; p<.001; I^2, 21%). The overall confidence of studies included in the systematic review were low or critically low. The systematic review did not adequately report sample sizes among the studies used in the LLLT sub-analyses. Overall, the results are of a low quality of evidence.

Tournavitis (2023) published a systematic review and meta-analysis that assessed conservative treatments for temporomandibular joint (TMJ) related pain.[92] Twenty-eight studies were included and of those five included LLLT. Two studies used PMB, which the authors state is an umbrella term that includes LLLT. LLLT and PBM offered short-term improvement in TMJ pain when compared to a control group (LLLT vs. control; p = 0.001; LLLT vs. PBM vs control; p=0.033), but were less effective than occlusal splint (p = 0.35).

Hanna (2021) published a large systematic review of 44 RCTs of LLLT for temporomandibular joint (TMJ) pain.[93] All included trials were at low risk for reporting missing outcome data. Seventy percent of the included trials were at low risk, 28% were at high risk, and 2% had some concerns in terms of reporting outcome measurement. Of the RCTs included, 98% were at low risk of bias for selective reporting of the results. Overall, 38% of studies had a low risk of bias, 46% were at high risk, and 16% had some concerns. Comparators across RCTs included sham placebo, drug therapy and physiotherapy. The primary outcome of interest was was

change in pain intensity reduction from baseline, measured by a visual analogue scale (VAS). Thirty-three studies (N=1163) were eligible for inclusion in the meta-analysis. In a meta-analysis, pooled change in VAS score from baseline to final follow-up evaluation demonstrated a significantly greater reduction with LLLT compared to comparator groups (pooled SMD, -0.55; 95% CI, -0.82 to -0.27; p<0.0001), however, heterogeneity was high (I^2=78%).

Jing (2021) published the results of a SR with meta-analysis of 16 RCTs to evaluate the effects of different energy density LLLT in patients with TMJ pain.[94] D1 laser therapy (energy density ranging from 0 to 10 J/cm2) was associated with more pain reduction than placebo (MD = 2.49, 95% CI ranging from 1.28 to 3.71) immediately following treatment based on "moderate" quality evidence. One month following treatment, d1 laser therapy also performed better than placebo (MD = 1.69, 95% CI = -0.78, 4.16) based on "low" quality evidence.

Chang (2014) published a meta-analysis of seven RCTs on LLLT for TMJ pain.[95] Included RCTs compared LLLT to no treatment or placebo. Only six studies were sufficient to be included in the meta-analysis for a total of 223 patients. The number of treatment sessions ranged from 4 to 20. The pooled effect size of pain relief using the VAS was a mean decrease of 0.6 [95% confidence interval (CI) −0.47 to −0.73].

A SR by Maia (2012) investigated the effect of LLLT on TMJ disorders (TMD).[96] Of the 14 studies reviewed, authors concluded the lack of standardization across the studies limited the interpretation of the review's results. Authors suggested further research is necessary to obtain a consensus regarding the best application protocol for pain relief in patients with TMD.

Melis (2012) reviewed 14 studies evaluating the efficacy of LLLT for the treatment of TMD.[97] The outcomes of the trials were controversial and not related to any features of the laser beam, to the number of laser applications, or their duration. Authors concluded that based on the results of the review no definitive conclusions could be drawn on the efficacy of LLLT for the treatment of TMD.

A SR by Petrucci (2011) included six sham-controlled randomized clinical trials of LLLT for TMD.[98] Using change in pain by VAS as the primary treatment outcome, the researchers concluded that LLLT was not more effective than placebo alone.

Randomized Controlled Trials

Chamani (2024) randomized 42 patients with temporomandibular disorders into three groups: LLLT (n=14), placebo (n=15), or standard treatment (n=13).[99] The LLLT group received treatment twice per week for 10 sessions. All groups showed a statistically significant improvement in VAS (p=.0001), lateral jaw movements (p=.0001) forward jaw movement (p=.007), but not in maximum mouth opening. There was no significant difference between groups. The authors conclude that LLLT may be effective in treating temporomandibular disorders, but there was no difference to standard therapy. This study is limited by its small sample size and single-center design, so further evidence is needed.

Tanhan (2023) compared physical therapy (manual pressure release) with exercise to LLLT with exercise and to exercise alone in 75 participants with myofascial jaw pain and cervical myofascial pain.[100] Compared to baseline all groups had improvement in pain (p<0.01). The combination of LLLT with exercise and manual release pressure with exercise relieved pain better than exercise alone. The authors conclude that multimodal approaches to TMJ pain should include exercise.

Desai (2022) randomized 60 patients with TMJ disorders to LLLT or placebo given for 20 sessions over 8 weeks.[101]74, By week 8 both the placebo group and LLT group had improvements from baseline with a final mean VAS of 5.2 in the placebo group and 3.2 in the LLLT group. There was no statistical comparison reported between groups. Mouth opening and lateral movement were also improved in both groups compared to baseline; however, improvements were numerically greater in the LLLT group. The small sample size, single-center design, and lack of comparison between active and placebo treatment limit generalizability of these finding.

Del Vecchio (2021) randomized 90 patients between the ages of 18 and 73 years old with TMJ disorders to home LLLT (808 nm, 5 J/min, 250 mW, 15 KHz for eight minutes twice daily), sham control, or standard conventional drugs (nimesulide 100 mg daily with five days of cyclobenzaprine 10 mg daily) for one week.[102] Pain was measured using a 100-mm VAS, and the examiner was blinded. At the end of treatment, the reduction in VAS was greater in the LLLT group (MD, 13.030; p=0.036) and the drug group (MD, 14.409; p=0.17) compared to the sham group. However, no significant difference in pain reduction was observed between the LLLT group and the drug group (MD, 1.379; p=1). This study evaluated a specific at-home LLLT protocol limiting the generalizability of the findings to other LLLT regimens.

Aisaiti (2021) randomized 78 patients with TMJ pain to receive LLLT (810 nm, 6 J/cm2, applied at five points for 30 seconds) or placebo once daily for seven consecutive days.[103] Pain was measured on a 0 to 10 numerical rating scale and pressure pain thresholds. Only 50 patients, 25 per group, remained in the study to contribute data to analysis. Greater reduction in numerical rating scale pain scores were seen with LLLT than with placebo (p=0.014), but no significant interaction between time and intervention was found (p=0.35). For pressure pain thresholds, there was no significant difference found between interventions or interaction between time and intervention.

Madani (2020) published a randomized, double-blind clinical trial in 45 patients with TMD.[104] Patients were randomized to group 1 (LLLT applied to the painful masticatory muscles two times a week for 5 weeks), group 2 (laser acupuncture therapy [LAT] emitted bilaterally on acupuncture points with the same settings as the LLLT group) or group 3 (placebo underwent treatment with sham laser). Patients were evaluated before treatment, after five and ten laser applications, and at month. No significant difference in mouth opening between the groups was identified ($p > 0.05$), but the amount of lateral excursive and protrusive movements was significantly greater in LLLT and LAT groups than the placebo group at some intervals ($p< 0.05$). No mid- or long-term follow-up data were reported.

A double-blind, placebo-controlled randomized trial by Shobha (2017) investigated the effectiveness of LLLT in patients with TMJ pain.[105] Forty TMJ patients were evenly randomized to an active or a placebo group. Treatment included two to three weekly sessions of LLLT for a total of eight sessions. Patients were evaluated at baseline, after treatment, and at a 30-day follow-up. Both groups experienced pain reduction at all evaluation points. The most significant pain reduction was reported at the 30-day follow-up (p=0.001). There were no significant differences between groups at baseline (p=0.214), final session (p=0.000), or the 30-day follow-up (p=0.230). For a secondary outcome (the ability to open one’s mouth), while both groups showed improvement, the difference between groups was not significant (p=0.330). Therefore, LLLT was determined to have no greater impact on healing or pain reduction over placebo.

Another clinical trial, by Ahrari (2013), assessed LLLT in 20 patients with myogenic TMD.[106] Patients were randomly divided into laser and placebo groups. There was a significant increase in mouth opening and a significant reduction of pain symptoms in the laser group that was not observed in the placebo group. Between-group comparisons revealed no significant differences in pain intensity and mouth opening measurements at any of the evaluation time points. Using a very limited sample size, authors concluded that LLLT can produce a significant improvement in pain level and mouth opening in patients affected with myogenic TMD.

Additional RCTs lacking study of durability of treatment effects have also been published.[107-114]

Nonrandomized studies

Nonrandomized studies have been published evaluating the effectiveness of LLLT in TMD, but have not identified significant impacts on health outcomes.

Section Summary

There are several SRs of LLLT for TMJ syndrome. Findings from these reviews, as well as from RCTs of this treatment, are mixed, and most trials do not show a benefit of LLLT. RCTs have not compared the impact of LLLT with physical therapy on health outcomes.

WOUND HEALING

Systematic Reviews

Li (2018) published a SR and meta-analysis of 7 RCTs (N=194) evaluating LLLT as a treatment for a diabetic foot ulcer.[115] Ulcer area was significantly reduced with LLLT compared with control (WMD 34.18; 95% CI 19.38–48.99; p<0.001), and the complete healing rate significantly improved with LLLT (OR 6.72; 95% CI 1.99–22.64; p=0.002). The analysis was limited by the number of studies included and small sample size, and by each study having different parameters, demographic information, ulcer characteristics, follow-up time, and treatment period.

Machado (2017) published a SR evaluating the treatment of pressure ulcers with LLLT.[116] Reviewers identified four studies meeting eligibility requirements (total n=210 patients). Outcomes were the ulcer area, healing rate, and overall healing rate. Two of the four studies used LLLT with a single wavelength;[117, 118] and the other two used LLLT with probe cluster, which employs the simultaneous assimilation of different types of diodes and wavelengths.[119, 120] In the study that employed the 658 nm wavelength, reviewers found that particular frequency reduced pressure ulcers by 71%. The other wavelengths did not produce any significant findings related to the study outcome; moreover, the studies using the probe cluster technique were also not successful in producing significant findings. While studies should be conducted to investigate further the success found in single wavelength at 658 nm, at this time there is insufficient evidence to suggest LLLT can significantly benefit patients with pressure ulcers.

Suter (2017) published a SR on the use of LLLT in patients with aphthous stomatitis, also known as canker sores.[121] There were 11 studies included in the review, 10 of which were RCTs, and outcomes included pain relief, duration of wound healing, and reduction in frequency of episodes. Controls in the studies received either placebo, no therapy, or topical

corticosteroids. LLLT was associated with reductions in immediate pain in five out of six studies, reductions in late pain in seven out of 10 studies, and with faster wound healing in five out of nine studies. The authors noted, however, that only two of the studies were double-blinded and studies were of a generally low quality, with a mean Jadad score of 1.0 out of 5.

Santinoni (2017) evaluated LLLT and maxillofacial wound healing in a SR focused on six studies that evaluated bone repair.[122] Four of the studies showed improved bone formation with LLLT, two showed improvements at only one follow up point, and one showed no benefit. Because the LLLT treatments were not standardized, no specific conclusions could be drawn.

Additional evidence on LLLT for wound healing includes a SR from the Agency for Healthcare Research and Quality (AHRQ) in 2004 and a 2014 Cochrane review.

The evidence report on vacuum-assisted and low-level laser wound therapies for treatment of chronic non-healing wounds prepared for the AHRQ was based on 11 studies of LLLT.[123] The review concluded:

> "The best available trial [of low level laser wound therapy] did not show a higher probability of complete healing at 6 weeks with the addition of low-level laser compared to sham laser treatment added to standard care. Study weaknesses were unlikely to have concealed existing effects. Future studies may determine whether different dosing parameters or other laser types may lead to different results."

In 2014 a Cochrane review of RCTs on light therapy, including phototherapy, ultraviolet and laser, for pressure ulcers was published.[124] The few trials available for analysis were of small size and very low quality. The reviewers found the available evidence overall was insufficient to draw conclusion on the effects light therapy on pressure ulcers.

Randomized Controlled Trials

Since the publication of the Cochrane review described above, there have been a number of RCTs evaluating LLLT for the healing of various wounds, including diabetic ulcers,[125] sternotomy incisions,[126] hip arthroplasty incisions,[127] skin graft donor wounds,[128] soft tissue injuries due to trauma,[129] and periodontal wounds.[130-134] For the most part, these have been small studies of varied quality, and they have yielded mixed results.

Section Summary

Evidence is limited on the use of LLLT for the treatment of wound healing and therefore valid conclusions cannot be made to determine if the use of LLLT leads to improved health outcomes.

OTHER INDICATIONS

LLLT has been studied in RCTs for use in indications such as treatment of venous leg ulcers,[117] perineal pain after episiotomy,[135] chronic periodontitis,[136] sternotomy healing,[137] and improvement of visual acuity in amblyopia.[138] A SR of active-control clinical trials (some lacking randomization to treatment) has also been published on the use of LLLT for treatment of hypertrophic scars.[139] A SR of LLLT in the management of tinnitus evaluated ten RCTs and concluded the effectiveness of the technology was not established and adequately powered RCTs with longer-term outcomes were needed.[140] A SR evaluating studies of LLLT for acceleration of orthodontic tooth movement concluded that further studies are needed to

overcome limitations resulting from heterogeneity among study designs.[141] Before this evidence can be used to make determinations about treatment benefit in this indications, all individual studies require replication with one or more subsequent RCTs to validate any findings of treatment benefit.[117, 135, 136, 138] Where present evidence lacks placebo control,[117, 136, 139] any such replication should include comparison with sham.

Section Summary

Available evidence is therefore considered insufficient to make conclusions about the effectiveness of LLLT in venous leg ulcers, perineal pain after episiotomy, chronic periodontitis, and improvement of visual acuity in amblyopia.

LASER ACUPUNCTURE (LA)

HEADACHE

Ebneshahidi (2005) performed a single-blind, randomized, placebo-controlled trial of 50 patients with chronic tension headache and reported that laser acupuncture using a LLLT device may provide benefit over placebo.[142] The study was small and the acupuncturists administering the true or sham treatments as well as the assessors were aware of the allocation and thus could have positively influenced the laser acupuncture group. In addition, the baseline measures were different from the subsequent measurements performed in follow-up. The results from this small study need to be validated in a larger, randomized, double-blind clinical trial.

A trial of laser acupuncture on 43 children with both migraine and tension headaches provided highly individualized treatment and additional therapies which do not permit conclusions regarding the independent effects of laser treatment.[143]

LOW BACK PAIN

Yang (2023) published a RCT of laser acupuncture for low back pain in nurses in China.[144] Seventy-six nurses were randomized to have low-level laser acupuncture combined with auricular acupressure or sham acupuncture without laser energy output. Outcome measures were pain using the Brief Pain Inventory and quality of life measured with the Roland-Morris Disability Questionnaire. Pain was measured at 2.4, and 8 weeks after intervention, and significant differences were seen in favor of laser acupuncture at each time-point. Quality of life was also better in the treatment group at weeks 4 and 8. Participants were similar in their usage of pain medication and muscle relaxants but the study results do not account for medication usage.

Cheng (2022) performed an RCT comparing laser acupuncture to usual care in post-partum women with low back pain.[145] The study included 106 women and the treatment group had 10 sessions of laser acupuncture. Laser acupuncture was associated with significantly lower pain ($p<0.001$), fewer limitations of daily activities ($p<0.001$) and physical activities ($p<0.001$) and less perceived stress ($p=0.001$). Salivary cortisol levels were also lower in the treatment group ($p=0.02$). It is not known if the participants also used medication for low back pain.

Glazov (2014) assessed the effect of infrared LA for reducing pain and disability in treatment of chronic low back pain (LBP).[146] The double-blind sham laser controlled trial included 144 adults with chronic non-specific LBP. Participants were followed-up at one and six weeks, and six and 12 months post-treatment. The analysis showed no difference between sham and the

laser groups at six weeks for pain or disability. There was a significant reduction in mean pain and disability in all groups at six weeks ($p<0.005$); Numerical Pain Rating Scale (NPRS): sham (-1.5, 95% CI -2.1 to -0.8), low dose (-1.3, 95% CI -2.0 to -0.8), high dose (-1.1, 95% CI -1.7 to -0.5). ODI: sham (-4.0, 95% CI -7.1 to -1.0), low dose (-4.1, 95% CI -6.7 to -1.5), high dose (-2.6, 95% CI -5.7 to 0.5). All secondary outcomes also showed clinical improvement over time but with no differences between groups. The authors concluded that laser acupuncture using energy density range (0-4 J/cm^2) for the treatment of chronic non-specific LBP resulted in clinical improvement unrelated to laser stimulation.

A randomized, placebo-controlled, double-blind trial by Shin (2015) evaluated laser acupuncture for low back pain.[147] Study participants were randomly assigned to either the laser acupuncture group (n = 28) or the sham laser acupuncture group (n = 28). The study only lasted for one week and included three sessions. There were no significant differences in any of the measured outcomes.

OTHER MUSCULOSKELETAL PAIN

Da Silva Mira (2024) published a systematic review and meta-analysis of the use of LLLT to acupuncture points to treat TMJ.[148] Seven studies were included that involved 275 participants. Three studies were placebo-controlled RCTs. The included studies had low to moderate heterogeneity. Compared to a control group, LLLT at acupoints reduced spontaneous pain ($p<0.0001$). The increase in mouth opening was statistically significantly improved after LLLT application ($p=0.002$). However, the studies were inconsistent in the density and dose of laser irradiation, as well as irradiation time. The authors note the importance of determining the irradiation parameters for safe and effective delivery of LLLT at acupuncture points.

Han (2024) published a systematic review and meta-analysis of laser acupuncture (LA) use for knee osteoarthritis.[149] Twenty-five RCTs involving 2075 participants were included. Comparators to LA included for the meta-analysis were sham treatment, LLLT without acupuncture, LA plus acupuncture compared to LA alone, acupuncture without LLLT. The authors concluded that LA is “more or less effective” for osteoarthritis, and its overall efficacy is similar to LLLT. However, some studies found LA superior to acupuncture alone. The authors noted barriers to outcome comparisons included variability in disease staging and laser parameters, as well as selection of acupoints; and called for standardization of participant selection and LA interventions in future research.

Huang (2022) published a single-blind, placebo-controlled RCT that randomized 82 patients who had total knee arthroplasty (TKA) to receive post-operative laser acupuncture or placebo acupuncture.[150] The laser acupuncture group had less pain at hours 10-72 post surgery ($p<0.05$) and less morphine consumption at hours 48 and 72 ($p<0.05$).

A sham-controlled study by Kibar (2017) randomized 73 patients with subacromial impingement syndrome.[151] At baseline and after 15 sessions of laser or sham treatment, pain (VAS), range of motion, and functional status were assessed. All outcomes showed significantly more improvement in laser acupuncture group compared with the sham group.

Fleckenstein (2016) reported results of a five-arm RCT comparing needle acupuncture, laser acupuncture, sham needle acupuncture, sham laser acupuncture, and no intervention for delayed-onset muscle soreness.[152] There were 60 participants that had delayed-onset muscle

soreness induced in the study. None of the interventions were found to improve the outcomes assessed: pain intensity, pain threshold, or maximum isometric voluntary force.

Two studies reported no significant difference between patients treated with active vs. sham laser acupuncture for the treatment of whiplash injury[153] and knee osteoarthritis[154]. A third RCT[155] assessed the effectiveness of acupuncture plus stretching to reduce pain and improve range of motion in patients afflicted by cervical myofascial pain syndrome (n=19). Health outcomes were measured immediately after treatment and up to 30 minutes following treatment. Patients had significantly increased range of motion after the application of acupuncture and stretching compared with sham placebo ($p<0.05$). However, the study was limited by lack of generalizability to wider patient populations.

Results of laser acupuncture are conflicting for knee osteoarthritis. An RCT evaluated laser acupuncture for the treatment of knee osteoarthritis among older adults.[156] Results showed that neither laser nor needle acupuncture resulted in treatment benefits compared with sham therapy in this patient population, and study authors do not recommend its use. Another small RCT[157] showed that short-term application of LLLT to specific acupuncture points in association with exercise and advice is effective at significantly reducing pain and improving quality of life (QOL) in patients with knee osteoarthritis. Both studies evaluated small patient populations and lacked statistical power. Results were generally not generalizable to wider patient populations.

WEIGHT LOSS

In a study by Tseng (2016), 52 obese subjects were randomly assigned to either the laser acupuncture group or the sham group.[158] Treatment lasted for eight weeks and then after a two-week washout period, the opposite treatment. The authors concluded that laser acupuncture improved anthropometric measurements and appetite sensations in obese subjects. This was a small study with methodological limitations. A similar, single-blind study by Hung (2016) randomized 66 postpartum patients to laser acupuncture or sham for weight loss.[159] Treatment was performed five times per week for 12 sessions. There were no significant differences between groups for any of the outcomes measured, including body mass index and body fat percentage.

A study by El-Mekawy (2015) evaluated laser acupuncture combined with a diet and exercise intervention for metabolic syndrome.[160] Twenty-eight obese, post-menopausal women were randomly assigned and followed for 12 weeks. Both groups showed a significant decrease in the anthropometric and metabolic parameters. The laser acupuncture group showed a significantly greater decrease in the waist and hip circumferences, cholesterol, and insulin levels compared to the control group.

OTHER INDICATIONS

Abd El Azeem (2023) conducted an RCT comparing laser acupuncture along with behavioral therapy and dietary modification to a laxative combined with behavioral therapy and dietary modification in 40 children with chronic constipation.[161] The therapy was over four weeks with four-month follow-up. Both groups had higher median frequency of bowel movements from baseline, but the laser acupuncture group was higher than the control group both after treatment ($p=0.01$) and at three months ($p=0.03$). Laser acupuncture was also associated with improved stool consistency after treatment compared to the laxative group ($p=0.03$). The authors noted that prior research has shown conflicting results and more study is needed to

know whether laser acupuncture is superior to other treatments for chronic constipation in children.

Laser acupuncture with usual vitamin supplementation was studied in post-menopausal women by Hassan (2023) to determine if laser acupuncture is an effective therapy for pain and osteoporosis.[162] Sixty-eight women were randomized to receive laser acupuncture with usual vitamin therapy (calcium and vitamin D3) or vitamin therapy alone. Both groups showed increased bone density after treatment. The laser acupuncture group had a significantly higher increase in bone density and improved pain scores than the vitamin group alone ($p<0.0001$). The study is limited by short follow-up and small sample size.

Kannon (2022) published a systematic review and meta-analysis on the use of acupuncture in children for the treatment of nocturnal enuresis.[163] Thirteen studies involving 890 participants were included and six studies used laser acupuncture. Only one study was deemed to have low risk of bias. Meta-analysis did not find significant differences in studies that compared laser acupuncture to sham acupuncture or in studies comparing laser acupuncture to pharmacologic intervention.

Juan (2019) published the results of a RCT on efficacy of laser acupuncture in patients with idiopathic mild-to-moderate carpal tunnel syndrome (CTS).[164] Eighty-four consecutive patients were randomly divided into the treatment arm, treated once a day, five times a week for four weeks ($n = 43$) or the sham arm using the same device and protocol with the laser acupuncture device switched off ($n = 41$). Patients completed the Global Symptom Score (GSS) at baseline and two and four weeks later. Nerve conduction studies (NCSs) were performed at baseline and repeated at the end of the study. There was a significantly greater reduction in GSS in the treatment group than in the placebo group at week two (-9.30 ± 4.94 vs. -2.29 ± 4.27, respectively, $p < 0.01$) and at week four (-10.67 ± 5.98 vs. -2.90 ± 5.61, respectively, $p < 0.01$). However, no significant difference in NCS between the two groups was found. No long-term outcomes were reported.

Laser acupuncture was evaluated as a treatment for pain from kidney biopsy in mainly pediatric patients in a double-blind trial by Oates (2017).[165] A total of 69 treatments were given to patients aged 7 to 26 years: 33 low-level laser applications to 10 acupuncture points and 36 low-level laser applications to sham points. There were significant differences in favor to the acupuncture group for changes pain scores (0.044), heart rate ($p=0.043$), and respiratory rate ($p=0.045$), but the clinical significance of these differences is uncertain.

Alsharnoubi (2017) reported the results of a trial comparing laser acupuncture to treatment with desmopressin for nocturnal enuresis in children.[166] The 45 children in the study were randomized to receive either laser acupuncture, desmopressin acetate, or a combination of both treatments. Laser treatments were given twice a week for three months, and desmopressin (60µg) was given daily for three months. All patients were provided with behavioral therapy in addition to other treatments. There was a significantly higher rate of complete recovery in the acupuncture group (73.3%) compared with the desmopressin alone group (20.0%), or the combination therapy group (13.3%). The authors explained the surprisingly low cure rate in the combination group by stating that only seven of the 15 children in this group actually received the complete treatment course, but there was no mention of the compliance rate in the other groups.

Dabbous (2016) evaluated low-level laser on acupuncture points compared to conventional physiotherapy in hemiplegic spastic cerebral palsy children.[167] Forty spastic hemiplegic

cerebral palsy children aged one to four years were randomly divided into control (n=20) and study groups (n=20). The low-level laser group had significantly better muscle tone (wrist flexors and plantar flexors) but there was no different for range of motion. The authors concluded that laser acupuncture has a beneficial effect on reducing spasticity in spastic cerebral palsy, however there was no blinding in the study, which indicates significant potential for bias.

A study by Lee (2016) compared the effects of laser acupuncture, manual acupuncture, and electromagnetic field stimulation on heart rate variability in 56 patients.[168] Patients were randomized to four groups: the three treatment groups and a control group that received no stimulation. Heart rate variability was calculated from electrocardiogram (ECG) and assigned to high frequency (HF: 0.15 to 0.4 Hz), low frequency (LF: 0.04 to 0.15 Hz) domains. The LF and LF/HF ratio were found to be higher in the laser acupuncture group and lower in the manual acupuncture and electromagnetic stimulation groups, compared to controls, while this pattern was reversed for variation in the HF domain. The authors attribute these findings to differential stimulation of the parasympathetic and sympathetic nervous systems, but did not offer a potential mechanism for these differences.

Section Summary

The current evidence base does not permit conclusions concerning the impact of laser acupuncture on health outcomes for any of these conditions. The evidence is limited by small sample size and short-term follow-up and is significantly heterogenous.

PRACTICE GUIDELINE SUMMARY

NORTH AMERICAN SPINE SOCIETY

In 2020, the North American Spine Society published a guideline on the diagnosis and treatment of low back pain. The guideline was based on a systematic review of the literature to address key clinical questions regarding the diagnosis and treatment of adults with nonspecific low back pain and included the following regarding laser therapy:

Guideline Recommendation (Grade of Recommendation)

- It is suggested that the combination of laser therapy (low-level or high-level) with exercise provides better short-term relief of pain than either exercise or laser therapy alone. (B=Fair evidence [Level II or III studies with consistent findings] for or against recommending intervention)
- There is conflicting evidence that the combination of laser therapy with exercise provides better short-term improvement in function compared to exercise or laser therapy alone. (I=Insufficient or conflicting evidence not allowing a recommendation for or against intervention.)
- It is suggested that there is no short-term benefit of laser therapy (low-level or high-level) when compared with exercise alone. (B=Fair evidence [Level II or III studies with consistent findings] for or against recommending intervention)

AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS (AAOS)

The AAOS published an updated guideline on the management of carpal tunnel syndrome in 2024 that includes laser therapy as a non-operative treatment that does not improve long-term outcomes for carpal tunnel syndrome.[169] The quality of evidence was rated “high.”

The AAOS 2016 clinical practice guideline on the treatment of carpal tunnel syndrome rated laser therapy as having “limited evidence.”[170] The guidelines state: “limited evidence supports that laser therapy might be effective compared to placebo.”

AMERICAN COLLEGE OF PHYSICIANS (ACP)

In 2020, the ACP and American Academy of Family Physicians published joint guidelines on the nonpharmacologic and pharmacologic management of acute pain from non-low back, musculoskeletal injuries in adults.[171] The guideline recommends interventions that improved at least two outcomes related to pain and function. The guideline notes that laser therapy improved only one outcome (symptom relief) and with low-certainty evidence.

The 2017 ACP clinical practice guideline on noninvasive treatments for acute, subacute, and chronic low back pain list LLLT among a number of potentially recommended treatments for patients with chronic low back pain based on low-quality evidence.[172]

AMERICAN PHYSICAL THERAPY ASSOCIATION (APTA)

In 2023, the APTA published clinical practice guidelines for plantar fasciitis that state, “Clinicians should use low-level laser therapy as a part of a rehabilitation program in those with acute or chronic plantar fasciitis to decrease pain in the short term;” Grade B (moderate evidence).[173]

In 2018, the American Physical Therapy Association published an updated guideline on the diagnosis and treatment of Achilles tendinitis.[174] The use of LLLT was given a level D recommendation, meaning that no recommendation could be made due to contradictory evidence.

AMERICAN COLLEGE OF OCCUPATIONAL AND ENVIRONMENTAL MEDICINE (ACOEM)

- In recommendations regarding treatment of carpal tunnel syndrome (CTS) published in 2011, the ACOEM recommended against the use of LLLT for CTS.[175] This recommendation was based upon Level C evidence (at least intermediate evidence that harms and costs exceed benefits based on limited evidence”).

- In a 2009 update to existing guidelines on disorders other than CTS of the hand, wrist, and forearm, the ACOEM recommended against the use of LLLT for treatment of hand or finger osteoarthrosis based upon a Level B recommendation (“moderately not recommended,” based upon “intermediate evidence that the intervention is ineffective, or that harms or costs outweigh benefits”).[176]

MUCOSITIS PREVENTION GUIDELINE DEVELOPMENT GROUP

In 2021, the Clinical Practice Guideline for the Prevention of Oral and Oropharyngeal Mucositis in Pediatric Cancer and Hematopoietic Stem Cell Transplant Patients was updated from the 2017 Mucositis Prevention Guideline Development Group.[177] Regarding PBM, the guideline states:

- Use intraoral photobiomodulation therapy in the red light spectrum (620–750 nm) for pediatric patients undergoing autologous or allogeneic HSCT and for pediatric patients who will receive radiotherapy for head and neck carcinoma (Strong recommendation, high-quality evidence).
- Consider using intraoral photobiomodulation therapy in the red light spectrum (620–750 nm) for pediatric patients who will receive radiotherapy for head and neck cancers other than carcinoma (Conditional recommendation, moderate quality evidence).

MULTINATIONAL ASSOCIATION OF SUPPORTIVE CARE IN CANCER AND INTERNATIONAL SOCIETY OF ORAL ONCOLOGY

In 2020, the Multinational Association of Supportive Care in Cancer (MASCC) and the International Society of Oral Oncology (ISOO) updated the guidelines on the management of mucositis secondary to cancer therapy.[178] The guidelines state:

- The panel recommends the use of intraoral PBM therapy using low-level laser therapy for the prevention of OM in adult patients receiving HSCT conditioned with high-dose CT, with or without TBI, using one of the selected protocols listed in Table 2 (Level of evidence: I).
- The panel recommends the use of intraoral PBM therapy using low-level laser therapy for prevention of OM in adults receiving RT to the H&N (without CT) (Table 2); safety considerations unique to patients with oral cancer should be considered (Level of evidence: II).
- The panel recommends the use of intraoral PBM therapy using low-level laser therapy for the prevention of OM in adults receiving RT-CT for H&N cancer (Table 2); safety considerations unique to patients with oral cancer should be considered (Level of evidence: I).
- For all PBM guidelines, it is recommended that the specific photobiomodulaton therapy parameteres of the selected protocol will be followed for optimal therapy.

Table 2: Recommended Intraoral Photobiomodulation Therapy Protocols for the Prevention of Oral Mucositis

Cancer Treatment Modality	Wavelength, nm	Power Density (Irradiance), mW/cm^2	Time per Spot, s	Energy Density (Fluence), J/cm^2	Spot Size, cm^2	No. of Sites	Duration
HSCT	632.8	31.25	40	1.0	0.8	18	From the d after cessation of conditioning for 5 d
	650	1000	2	2.0	0.04	54-70	From the first d of conditioning to d +2 post-HSCT (for 7-13 d)
RT	632.8	24	125	3.0	1.00	12	Entire RT course

RT-CT	660	417	10	4.2	0.24	72	Entire RT course
	660	625	10	6.2	0.04	69	Entire RT course

Abbreviations: CT, chemotherapy; HSCT, hematopoietic stem-cell transplantation; RT, radiotherapy.

SUMMARY

There is enough research to show that low-level laser therapy (LLLT) can improve health outcomes for people with an increased risk of oral mucositis due to some cancer treatments and/or hematopoietic cell transplantation. Therefore, LLLT may be considered medically necessary for prevention of oral mucositis in patients undergoing cancer treatment associated with increased risk of oral mucositis, including chemotherapy and/or radiotherapy, and/or hematopoietic cell transplantation.

There is not enough research to show that low-level laser therapy (LLLT), including laser acupuncture, can improve health outcomes for patients that have conditions other than oral mucositis, including but not limited to carpal tunnel syndrome, various musculoskeletal conditions, and wound healing. Therefore, low-level laser therapy (LLLT) remains investigational for all indications except prevention of oral mucositis.

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CODES

Codes	Number	Description
CPT	0552T	Low-level laser therapy, dynamic photonic and dynamic thermokinetic energies, provided by a physician or other qualified health care professional
	97037	Application of a modality to 1 or more areas; low-level laser therapy (ie, nonthermal and non-ablative) for post-operative pain reduction
	97039	Unlisted modality (specify type and time if constant attendance)
HCPCS	S8948	Application of a modality (requiring constant provider attendance) to one or more areas; low level laser, each 15 minutes

Date of Origin: *January 2003*