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Low-Level Laser Treatment of Neuromuscular Pain Disorders and Other Miscellaneous Conditions

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Next Review: June 2019
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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.

POLICY GUIDELINES

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, 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:

- MicroLight ML830® (MicroLight Corporation of America)
- GRT LITE™ PRO-8A (GRT Solutions, Inc.)
- LightStream™ Low Level Laser (RJ Laser Canada Corp.)
- TouchOne™ (OTC)

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

Randomized Controlled Trials

The available literature on LLLT for Achilles tendinopathy consists of a single randomized controlled trial.[2] However, because durability of treatment effects was not studied for any length of time past treatment, interpretation of these results is limited. Additional trials are needed to identify and establish an estimate of treatment effect and durability.

Section Summary

Current evidence is not available to determine if LLLT improves health outcome for the treatment of Achilles tendinopathy.

BELL’S PALSY

Randomized Controlled Trials

LLLT as an addition to facial exercise was evaluated in a study by Ordahan (2017).[3] 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.[4] 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 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 (CTS)
The literature on the use of LLLT for CTS consists of several systematic reviews, a technology assessment, and RCTs (both sham and active control).

**Systematic Reviews and Technology Assessments**

The largest body of evidence for LLLT describes its use in the treatment of CTS. This evidence 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 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.\(^2\) 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.\(^6\) The authors similarly concluded that there was no strong evidence of LLLT efficacy on pain and function outcomes in carpal tunnel syndrome.

Li (2016) published a systematic review that included seven RCTs of this topic, with similar results to those of the Bekhet (2017) review.\(^7\) 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**

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.\(^8\) 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.
A small, double-blind RCT that included 19 patients with rheumatoid arthritis and carpal tunnel syndrome found slight improvement in subjective scales of pain and function (e.g., 27-point improvement vs. 13-point improvement on VAS) compared with sham laser therapy, but no differences between groups in objective functional measures (e.g., grip strength, 0.3 vs. 0.3, respectively), or in measures of nerve conduction (e.g., motor nerve conduction velocity, 55 vs. 55, respectively) 10 weeks following the end of treatment.[9]

Chang and colleagues reported on an RCT with short follow-up comparing LLLT with sham treatment in 36 patients.[10] After two weeks of treatment and two weeks after the end of treatment, VASs for pain were lower in the treatment group than in the sham group (p<0.05). After two weeks of treatment, differences in grip strength, symptoms, and functional assessment were not significant but were significant (p<0.05) at the two-week follow-up. There were no significant between-group differences on nerve conduction studies at either time point.

Although additional randomized controlled trials have since been published, the lack of a placebo treatment group[11,12] or the lack of study of durability of treatment effects (at least two weeks following the treatment period)[13-15] limit the interpretation of these findings.

Section Summary

CTS is the indication for which LLLT has been studied the most. The evidence includes several systematic reviews, 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 systematic review and meta-regression, Gross (2013) evaluated 17 trials on LLLT for neck pain.[16] 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 systematic review by Kadhim-Saleh (2013) analyzed eight randomized controlled trials (n=443 patients) to determine the efficacy of LLLT in reducing acute and chronic neck pain as measured by VAS.[17] 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 this technology assessment, an additional randomized controlled trial was published.[18] 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 systematic review has been identified on the use of LLLT in elbow pain.[19] 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**

**Randomized Controlled Trials**

Several small RCTs evaluating LLLT for treating fibromyalgia have been published. A double-blind study by Germano Maciel (2018) compared a functional exercise program plus LLLT to the exercise program plus sham LLLT.[20] There were 22 women in the study, 11 in each treatment group, and treatments were performed three times per week for a total of eight weeks. Study outcomes included evaluations of pain, muscle performance, functional tests, depression and quality of life. Improvements were seen in these outcomes in both groups, with no significant differences.

Ruaro (2014) reported on 20 patients randomized to receive LLLT or sham treatment three times a week for four weeks (12 total treatments).[21] Outcomes included scores in the Fibromyalgia Impact Questionnaire (FIQ), which measures physical function, ability to work, pain, fatigue, and depression; the McGill Pain Questionnaire (MPQ); and a pain VAS. All three outcomes were significantly better in the active than in sham after treatment. Mean overall FIQ scores were 18.6 in the LLLT group and 5.2 in the sham group (p=0.003). Mean change scores also differed significantly between groups for MPQ score (p=0.008) and VAS score (p=0.002).
Matsutani (2007) randomized 20 patients with fibromyalgia to receive laser treatment and stretching exercises or stretching alone.\textsuperscript{[22]} Outcome measures were VAS scores and dolorimetry at tender points, QOL on the FIQ, and the 36-Item Short-Form Health Survey (SF-36) scores. At the end of treatment, both groups demonstrated pain reduction, higher pain threshold at tender points (all p<0.01), lower mean FIQ scores, and higher SF-36 mean scores (all p<0.05). No significant differences were found between groups.

**Section Summary**

Few RCTs evaluating LLLT for treatment of fibromyalgia are available and existing trials are small (i.e., < 25 patients each). One RCT with 20 patients found significantly better outcomes with LLLT than with sham, and two other small RCTs did not find statistically significant between-group differences for similar outcomes. Additional RCTs with sufficient numbers of patients are needed.

**LOW BACK PAIN**

**Systematic Reviews**

Glazov (2016) published a systematic review and meta-analysis of blinded sham-controlled trials evaluating LLLT for treatment of chronic low-back pain.\textsuperscript{[23]} 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 (5-27 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 systematic review of RCTs on LLLT for treatment of nonspecific chronic low back pain.\textsuperscript{[24]} 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 systematic review of LLLT for nonspecific low back pain was conducted in 2008.[25] 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 systematic review by Chou (2007) assessed benefits and harms of nonpharmacological therapies including LLLT for acute and chronic low back pain.[26] The reviewers did not find good evidence of efficacy for LLLT for either indication.

Randomized Controlled Trials

Since publication of the Glazov (2016) systematic review described above, Koldaş Doğan (2017) reported an RCT that compared two different LLLT regimens for chronic low back pain.[27] 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 a number of RCTs and several systematic reviews of RCTs. The systematic reviews did not consistently find that LLLT improved outcomes for patients with nonspecific low back pain.

LYMPHEDEMA

Systematic Reviews

Smoot (2015) published a systematic review of studies on the effect of LLLT on symptoms in women with breast cancer‒related lymphedema.[28] 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

A randomized double-blind sham-controlled trial of LLLT in 50 patients with post-mastectomy lymphedema has been identified in the literature.[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 systematic review by Winters (2013) of treatments for medial tibial stress syndrome, LLLT was not found to be effective.[30] All studies included in the systematic review 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 systematic reviews 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**
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 systematic review 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. The 2012 systematic review 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), 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. 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 systematic reviews have been published since the 2012 MASCC/ISOO systematic review. Oberoi (2014) reported on a systematic review and meta-analysis of 18 RCTs on LLLT versus no treatment or placebo for oral mucositis. 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

Two of the larger RCTs evaluating LLLT for prevention of oral mucositis were published by Gautam in 2012.[35,36] One of these studies reported LLLT for the prevention of chemoradiotherapy-induced oral mucositis in 121 oral cancer patients.[36] The second publication reported LLLT for the prevention of chemoradiotherapy-induced oral mucositis in 221 head and neck cancer patients.[35] 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/cm², 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.[37] 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.[38] 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.[39] 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.[40] 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

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The literature on LLLT for the prevention of oral mucositis includes several systematic reviews. A 2014 systematic review 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. In addition, three double-blind RCTs published in 2015 found significantly better outcomes in patients undergoing LLLT compared with sham treatment prior to or during cancer treatment.

OROFACIAL PAIN

Systematic Reviews

Tengrungsun (2012) assessed the effectiveness of LLLT as a treatment for orofacial pain in 33 studies represented by 1,522 chronic pain patients meeting inclusion criteria in a systematic review. 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). 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. 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 systematic review, the effects of LLLT on masticatory performance, pressure pain threshold (PPT), and pain intensity in 21 patients with myofascial pain were evaluated. 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 due to the methodological limitations in the study designs; therefore, it is uncertain that use of LLLT leads to improved health outcomes.

ORTHODONTIC PAIN

Systematic Reviews

He (2013) investigated the efficacy of LLLT in the management of orthodontic pain.[45] 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

Since the systematic review by He (2013), AlSayed Hasan (2017) evaluated two levels of LLLT (4 Joule or 16 Joule) in 26 patients treated with a fixed orthodontic appliance.[46] 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 in orthodontic pain is insufficient to demonstrate that use of LLLT leads to improved health outcomes due to methodological limitations.

OSTEOARTHRITIC (OA) KNEE PAIN

Systematic Reviews

Huang (2015) published a systematic review of RCTs comparing at least eight treatment sessions of LLLT and sham laser treatment in knee osteoarthritis patients.[47] 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 systematic review of placebo-controlled RCTs to determine the short-term efficacy of physical interventions for osteoarthritic knee pain.\textsuperscript{[48]} 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**

Since the publication of the systematic review by Huang (2015), Gopal Nambi (2016) evaluated LLLT in 34 patients with knee osteoarthritis in a double-blind, randomized trial.\textsuperscript{[49]} The control 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 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. The more recent systematic review, which pooled study findings, did not find that LLLT significantly improved pain and functional outcomes compared with a sham intervention.

**PLANTAR FASCIITIS**

**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.\textsuperscript{[50]} 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). 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). 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. 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

At least two 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. Given all factors, further studies are needed to validate the technology.

RHEUMATOID ARTHRITIS (RA)

Systematic Reviews

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. 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).[55] 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 systematic review and meta-analysis[56] 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. 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.[57] 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.[58] 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 systematic review of randomized controlled trials on the use of non-surgical treatment (including LLLT) for frozen shoulder (adhesive capsulitis).[59] Five Cochrane reviews and 18 randomized controlled trials 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).[60] 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

Eslamian and others evaluated the effects of LLLT in combination with conventional physiotherapy endeavors in 50 patients with rotator cuff tendinitis.[61] 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[61-64] and/or lack of treatment durability assessment.[65-67]

Section Summary

In summary, 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

Chang (2014) published a meta-analysis of seven RCTs on LLLT for temporomandibular joint (TMJ) pain.[68] 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 systematic review by Maia (2012) investigated the effect of LLLT on TMJ disorders (TMD).[69] 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.[70] 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 systematic review by Petrucci (2011) included six sham-controlled randomized clinical trials
of LLLT for TMD.\textsuperscript{[71]} 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**

RCTs since the systematic reviews above include a double-blind, placebo-controlled
randomized trial by Shobha (2017) that investigated the effectiveness of LLLT in patients with
TMJ pain.\textsuperscript{[72]} 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. A study limitation is that
MRI was not used, which is the traditional method for diagnosing TMJ disorders.

Another clinical trial, by Ahrari (2013), assessed LLLT in 20 patients with myogenic TMD.\textsuperscript{[73]}
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.\textsuperscript{[74-81]}

**Section Summary**

There are several systematic reviews 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.

**WOUND HEALING**

**Systematic Reviews**

Machado (2017) published a systematic review evaluating the treatment of pressure ulcers
with LLLT.\textsuperscript{[82]} 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;\textsuperscript{[83,84]} and the other two used LLLT with probe
cluster, which employs the simultaneous assimilation of different types of diodes and
wavelengths.\textsuperscript{[85,86]} 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.

Additional evidence on LLLT for wound healing includes a systematic review 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.[87] 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.[88] 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.

Suter (2017) published a systematic review on the use of LLLT in patients with aphthous stomatitis, also known as canker sores.[89] 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.

Another systematic review evaluated LLLT and maxillofacial wound healing, and focused on six studies that evaluated bone repair.[90] 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.

**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,[91] sternotomy incisions,[92] hip arthroplasty incisions,[93] skin graft donor wounds,[94] and periodontal wounds.[95-99] 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 randomized controlled trials for use in indications such as treatment of venous leg ulcers,[83] perineal pain after episiotomy,[100] chronic periodontitis,[101] and improvement of visual acuity in amblyopia.[102] A systematic review of active-control clinical trials (some lacking randomization to treatment) has also been published on the use of LLLT for treatment of hypertrophic scars.[103] However, 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 randomized controlled trials to validate any findings of treatment benefit.[83,100-102] Where present evidence lacks placebo control,[83,101,103] 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.[104] 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.[105]

LOW BACK PAIN
Glazov (2014) assessed the effect of infrared LA for reducing pain and disability in treatment of chronic low back pain (LBP).[106] 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/cm²) 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.[107] 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

A sham-controlled study by Kibar (2017) randomized 73 patients with subacromial impingement syndrome.[108] 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.[109] 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[110] and knee osteoarthritis.[111] A third RCT[112] 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.[113] 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[114] 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.[115] 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.[116] 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.[117] 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**

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

Laser acupuncture was evaluated as a treatment for pain from kidney biopsy in mainly pediatric patients in a double-blind trial by Oates (2017). 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. 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.

A study by Lee (2016) compared the effects of laser acupuncture, manual acupuncture, and electromagnetic field stimulation on heart rate variability in 56 patients. 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.
AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS (AAOS)

The AAOS 2016 clinical practice guideline on the treatment of carpal tunnel syndrome rated laser therapy as having "limited evidence."[122] The guidelines state: "limited evidence supports that laser therapy might be effective compared to placebo."

AMERICAN COLLEGE OF PHYSICIANS (ACP)

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.[123]

AMERICAN PAIN SOCIETY (APS) AND AMERICAN COLLEGE OF PHYSICIANS

The 2007 joining APC/APS guideline states that there is insufficient evidence to recommend LLLT for treatment of low back pain and LLLT is not mentioned in the updated 2009 guideline.[124]

AMERICAN PHYSICAL THERAPY ASSOCIATION

The 2010 guidelines released by the Orthopaedic Section of the American Physical Therapy Association recommend the use of LLLT for Achilles tendinitis, stating: “Clinicians should consider the use of low-level laser therapy to decrease pain and stiffness in patients with Achilles tendinopathy.”[125] This is a grade B recommendation, based upon a “single high-quality randomized controlled trial or a preponderance of level II studies.” Although these guidelines state that they are evidence-based, it is unclear how the evidence was appraised in making this recommendation. In 2014, the Association stated in a press release, based on a Cochrane review,22 that “It could be that low-level laser therapy (LLLT) is a useful electrotherapy modality for treatment of adhesive capsulitis, but the effects are marginal, and evidence is a long way from conclusive….”[126]

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.[127] 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”).[128]

MUCOSITIS PREVENTION GUIDELINE DEVELOPMENT GROUP

In 2017, the Mucositis Prevention Guideline Development Group published guidelines on preventing oral and oropharyngeal mucositis in children undergoing hematopoietic cell transplantation.[129] The guidelines were based on an evidence review consisting of randomized controlled trials that evaluated interventions such as cryotherapy and LLLT. The guidelines suggested that LLLT could be offered to children but classified this recommendation as weak.
MULTINATIONAL ASSOCIATION OF SUPPORTIVE CARE IN CANCER AND INTERNATIONAL SOCIETY OF ORAL ONCOLOGY

In 2014, the Multinational Association of Supportive Care in Cancer (MASCC) and the International Society of Oral Oncology (ISOO) published a guideline on the management of mucositis secondary to cancer therapy.[31] For the prevention of oral mucositis, the MASCC/ISOO recommended the following treatments, based on strong evidence: LLLT (650 nm, power of 40 mW) in patients receiving hematopoietic stem cell transplantation (HSCT) conditioned with high-dose chemotherapy with or without total body irradiation; oral cryotherapy in patients receiving bolus 5-fluorouracil chemotherapy; recombinant human keratinocyte growth factor-1 in patients receiving high-dose chemotherapy and total body irradiation, followed by autologous stem cell transplantation for a hematological malignancy; benzydamine mouthwash in patients with head and neck cancer receiving moderate-dose radiotherapy without concomitant chemotherapy.

Additionally, the following treatments were recommended for the prevention of oral mucositis based on weaker evidence: LLLT (approx. 632.8 nm) in patients undergoing radiotherapy, without concomitant chemotherapy, for head and neck cancer; oral care protocols for patients undergoing any cancer treatment; oral cryotherapy in patients receiving high-dose melphalan as conditioning for HSCT; oral zinc supplements in oral cancer patients receiving radiotherapy or chemoradiation.

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 stem 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, chemotherapy-induced mucositis, and wound healing. Therefore, low-level laser therapy (LLLT) remains investigational for all indications except prevention of oral mucositis.

REFERENCES


47. Huang, Z, Chen, J, Ma, J, Shen, B, Pei, F, Kraus, VB. Effectiveness of low-level laser therapy in patients with knee osteoarthritis: a systematic review and meta-analysis. Osteoarthritis and cartilage / OARS, Osteoarthritis Research Society. 2015 Sep;23(9):1437-44. PMID: 25914044


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<thead>
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<th>Codes</th>
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<th>Description</th>
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<td>CPT</td>
<td>None</td>
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<tr>
<td>HCPCS</td>
<td>S8948</td>
<td>Application of a modality (requiring constant provider attendance) to one or more areas; low level laser, each 15 minutes</td>
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*Date of Origin: January 2003*