Medical Policy

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Title: Low-Level Laser Therapy

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DESCRIPTION

Low-level laser therapy (LLLT), also called photobiomodulation, is being evaluated to treat a variety of conditions including soft tissue injuries, myofascial pain, tendinopathies, nerve injuries, joint pain, lymphedema, and oral mucositis.

Background

Low-level laser therapy (LLLT) refers to the use of red-beam or near-infrared lasers with a wavelength between 600 and 1,000 nm and power from 5–500 MW. (In contrast, lasers used in surgery typically use 300 W.) When applied to the skin, these 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 on tissue healing is unknown; hypotheses have included improved cellular repair and stimulation of the

immune, lymphatic, and vascular systems. LLLT is being evaluated to treat a wide variety of conditions, including soft tissue injuries, myofascial pain, tendinopathies, nerve injuries, and joint pain. LLLT has also been evaluated for lymphedema.

One of the disorders that LLLT has been evaluated for is the treatment of carpal tunnel syndrome. Carpal tunnel syndrome is the most common entrapment neuropathy and the most commonly performed surgery of the hand. The syndrome is related to the bony anatomy of the wrist. The carpal tunnel is bound dorsally and laterally by the carpal bones and ventrally by the transverse carpal ligament. Through this contained space run the 9 flexor tendons and the median nerve. Therefore any space-occupying lesion can compress the median nerve and produce the typical symptoms of carpal tunnel syndrome—pain, numbness, and tingling in the distribution of the median nerve. Symptoms of more severe cases include hypesthesia, clumsiness, loss of dexterity, and weakness of pinch. In the most severe cases, patients experience marked sensory loss and significant functional impairment with thenar atrophy. Mild to moderate cases of carpal tunnel syndrome are usually first treated conservatively with splinting and cessation of aggravating activities. Other conservative therapies include oral steroids, diuretics, nonsteroidal anti-inflammatory drugs (NSAIDs), and steroid injections into the carpal tunnel itself. Patients who do not respond to conservative therapy or who present with severe carpal tunnel syndrome with thenar atrophy may be considered candidates for surgical release of the carpal ligament, using either an open or endoscopic approach.

LLLT is also being evaluated for cancer therapy-induced oral mucositis in patients treated by radiotherapy and/or chemotherapy and hematopoietic stem-cell transplantation (HCST). Oral mucositis describes inflammation of the oral mucosa and typically manifests as erythema or ulcerations that appear 7 to 10 days after initiation of high-dose cancer therapy. Oral mucositis can cause significant pain and increase risk of systemic infection, dependency on total parenteral nutrition, and use of narcotic analgesics. Treatment planning may also need to be modified due to dose-limiting toxicity. There are a number of interventions for oral mucositis that may partially control symptoms, but none are considered a gold standard treatment. When uncomplicated by infection, oral mucositis is self-limited and usually heals within 2 to 4 weeks after cessation of cytotoxic chemotherapy.

Regulatory Status

A number of low-level lasers have received clearance for marketing from the U.S. Food and Drug Administration (FDA) for the treatment of pain. Data submitted to the FDA as part of the FDA 510(k) approval process for the MicroLight 830 Laser consisted of application of the laser over the carpal tunnel 3 times a week for 5 weeks. The labeling states that the "MicroLight 830 Laser is indicated for adjunctive used in the temporary relief of hand and wrist pain associated with Carpal Tunnel Syndrome." In 2006, the FDA provided marketing clearance for the GRT LITE™, which listed the Tuco Erchonia PL3000, the Excalibur System, the Microlight 830 Laser, and the Acculaser Pro as predicate devices. Indications of the GRT LITE for carpal tunnel syndrome are similar to the

predicate devices: “adjunctive use in providing temporary relief of minor chronic pain.” The LightStream™ Low Level Laser device received 510(k) marketing clearance in 2009 for adjunctive use in the temporary relief of pain associated with knee disorders with standard chiropractic practice. A number of clinical trials of LLLT are underway in the United States, including studies of wound healing.

POLICY

Low-level laser therapy is considered **experimental / investigational** for all indications, including but not limited to carpal tunnel syndrome.

Policy Guidelines

Other protocols have used low-level laser energy applied to acupuncture points on the fingers and hand. This technique may be referred to as "laser acupuncture." Laser acupuncture is not reviewed in this policy.

RATIONALE

The principal outcomes associated with treatment of musculoskeletal conditions, including carpal tunnel syndrome, are relief of pain and/or return to work and/or functional status. Relief of pain is a subjective outcome that is 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. In patients with mild to moderate symptoms, low-level laser therapy (LLLT) may be compared to other forms of conservative therapy such as splinting, rest, nonsteroidal anti-inflammatory drugs (NSAIDs), or steroid injection. Second, in a group of patients who have exhausted conservative therapy, LLLT must be compared to surgical intervention. Another relevant outcome measure for treatment is return to work. It is difficult to analyze this outcome because the criteria for returning to work are often variable and job-specific, and it is not known whether this decision is driven by the patient, physician, or employer. Finally, the extraclinical issue of workmen's compensation frequently influences the decision to return to work. Outcomes associated with wound healing include incidence of complete wound closure and time to various stages of wound closure.

Multiple Etiologies of Pain

For the most part, studies of LLLT for treatment of pain compare laser treatment with a sham treatment only, rather than comparison with treatments known to be effective. With very few exceptions, the studies are from centers outside the United States. A 2009 systematic review included controlled trials of LLLT as primary intervention for any tendinopathy. (1) Twenty-five trials were included, with conflicting findings for each indication studied. Twelve studies showed positive effects, and 13 were inconclusive or showed no effect. Thirteen studies investigated LLLT for epicondylitis, 6 of them showing positive results. The largest of these trials had only 58 subjects. Two of the positive studies were of poor quality. Four studies examined LLLT for tendinopathy in the shoulder, 4 of them were of high quality. The largest of these trials had just 30 subjects. Three of these trials found a positive effect of LLLT. Two of the positive studies had placebo controls, and the third compared LLLT with ultrasound (US) or placebo. Of the 5 trials of LLLT for Achilles tendinitis included in the review, 2 demonstrated a benefit of LLLT. One of the

positive and 1 of the negative studies of LLLT for Achilles tendinitis received the highest quality rating. One of the negative studies was the largest study (n=89) included in the review but scored only 5 of 10 possible points for study quality. Three studies included subjects with a variety of indications; all reported inconclusive or no effect of LLLT. The authors reported that dosages used in the positive trials suggested that there is an effective dosage window; however the only parameter reported for all studies was wavelength. Power density and dose were not provided, or there was too little information provided in the studies to calculate the dose.

Jang and Lee conducted a meta-analysis of 22 randomized sham-controlled trials of LLLT for the treatment of joint pain including temporomandibular joints, glenohumeral joints, knee joints, and cervical and lumbar spinal regions. (2) Only trials that had a (Physiotherapy Evidence Database (PEDro) quality rating of 5 or more were included; the average PEDro score of the included trials was 7.96. There were a total of 668 subjects who received laser therapy and 565 subjects who were treated with sham laser. Although half of the trials had negative results, the mean weighted improvement in VAS for pain was 13.96 mm (out of 100 mm). When only trials that were within the range of recommended energy doses for each joint region were included, the mean improvement in VAS for pain increased to 19.88 or 21.05 mm, depending on the specific recommendations. Typically, a 20-30% improvement in pain is considered clinically significant. This meta-analysis did not assess the percentage of subjects in each condition who had a clinically significant improvement in pain.

In 2010, Fulop et al. published a meta-analysis of 22 studies of LLLT for treatment of pain of a variety of etiologies. (3) Inclusion criteria did not specify the timing of measuring outcomes. Some included studies measured outcomes only at the end of treatment and, for some others, the timing of measurement was not reported in the analysis. Given these questions, this analysis was not reviewed further. Key studies of LLLT for specific joints are summarized below.

Carpal Tunnel Syndrome

Sham Controlled Trials*.* The largest body of evidence for LLLT describes its use in treatment of carpal tunnel syndrome. As part of the U.S. Food and Drug Administration (FDA) approval process, the manufacturer of the MicroLight device conducted a double-blind, placebo-controlled study of 135 patients with moderate to severe symptoms of carpal tunnel syndrome who had failed conservative therapy for at least 1 month. However, the results of this study have not been published in the peer-reviewed literature, and only a short summary is available in the FDA Summary of Safety and Effectiveness, (4) which does not permit scientific conclusions.

In November 2010, the Blue Cross and Blue Shield Association Technology Evaluation Center (TEC) published a technology assessment of LLLT for carpal tunnel syndrome and chronic neck pain. (5) For inclusion in the assessment, studies had to: be published in a peer-reviewed journal; be randomized, sham-controlled trials, and, if adjunctive therapies were used, they were applied to both groups; measure outcomes at least 2 weeks beyond the end of the treatment period; and, for neck pain studies, be studies of patients with chronic pain. Four of the studies of carpal tunnel syndrome discussed below (6-9) met the inclusion criteria for the TEC Assessment. TEC concluded that the studies have serious limitations including small sample size and limited follow-up, and no one study is so methodologically sound as to provide definitive results.

Tascioglu et al. reported a randomized double-blind sham-controlled trial of LLLT in 2011. (10) Sixty patients with carpal tunnel syndrome were assigned to 1 of 2 active laser dosages (1.2 J or

0.6 J per painful point) or placebo treatment 5 times per week for 3 weeks. VAS scores, grip strength, and functional status scores improved significantly in all groups. The only nerve conduction measure to improve was sensorial nerve velocity in the active laser groups. There was no significant difference between groups for any of the outcome measures. In this study, LLLT was no more effective than placebo.

A 2007 double-blinded randomized sham-controlled trial with 81 patients (141 hands) found slight pre- to post-treatment improvements in sensory (0.2 msn) and distal (0.3 msn) latencies for the laser group, while sensory nerve velocity improved (by 2.7 and 2.1 msn, respectively) in both groups (a wrist splint was used at night in both groups). (8) Other measures of nerve conduction were not affected by treatment. There were no differences between the groups in visual analogue scales (VAS) for pain or in symptom severity scores. Irvine and colleagues reported on the results of a small double-blinded study of 15 patients with carpal tunnel syndrome who were randomized to receive either LLLT or sham laser therapy. (9) There was a significant improvement in both groups, but there was no significant difference between the groups.

Another small, double-blinded RCT (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). (7) Chang and colleagues report on an RCT with short follow-up comparing LLLT with sham treatment in 36 patients. (6) After 2 weeks of treatment and 2 weeks after the end of treatment, VASs for pain were lower in the treatment group than in the sham group ($p<0.05$). After 2 weeks of treatment, differences in grip strength, symptoms, and functional assessment were not significant but were significant at the 2-week follow-up ($p<0.05$). There were no significant between-group differences on nerve conduction studies at either time point. Another RCT with sham control, a study with 80 patients, was reported by Shooshtari et al. (11) Outcomes were measured at the end of 15 treatment sessions (5 times a week for 3 weeks). In this study, the treatment group showed significant improvement in clinical symptoms, hand grip, and nerve conduction studies.

Active Control Trials. Bakhtiary and Rashidy-Pour reported on the outcomes of 50 consecutive patients with carpal tunnel syndrome who were randomized to receive either US therapy or LLLT. (12) Improvement was significantly better in those randomized to US. Dincer et al. compared splinting with US, splinting with LLLT, and splinting alone in an RCT. (13) Sixty women were randomized; 10 did not complete the study. One hundred hands (50 women), 30 in the splint with US group, 36 in the splint with LLLT group, and 34 with splint only, were followed for 3 months after treatment and included in the analysis. Outcome measures were the Boston Questionnaire Symptom Severity Scale (BQ-SSS) score, the Boston Questionnaire Functional Status Scale (BQ-FSS) score, visual analog scale (VAS), second digit-wrist median nerve sensory velocity (SV), and median nerve motor distal latency (MDL). Splinting with US or LLLT was more effective than splinting alone on all measures 3 months after treatment. LLLT was significantly more effective than US on measures of pain on VAS, BQ-SSS ($p=0.03$), and SV. Patient satisfaction was higher in the US and LLLT groups than the splint-only group ($p=0.05$).

Conclusions. The literature on LLLT for carpal tunnel syndrome consists of a number of randomized controlled trials. However, results of these trials are inconsistent, with many studies showing no benefit with LLLT.

Neck Pain

The 2010 TEC Assessment included 6 trials of LLLT for chronic neck pain and found inconsistent results. (5) In the largest study by Chow et al., 90 patients were randomized to active LLLT or sham treatment. (14) At 5 weeks after the 7-week treatment period, patients in the active treatment group reported a 2.7 point improvement in VAS pain versus a 0.3 point worsening for the sham group. A calculated mean improvement of 43.8% was reported by the active LLLT group while the sham-treated group improved by 2.1%. TEC noted that baseline VAS pain scores were significantly higher in the active treatment group possibly biasing results in favor of LLLT. In a 2004 RCT, possibly a pilot study for the larger trial reported by Chow, 20 patients were randomized to LLLT or sham laser. (15) The VAS pain scores improved 2.1 points in the laser-treated group and 0.7 in the sham-treated group, which was not significant; however the percent change was statistically significant, and the change in the neck pain questionnaire scores, McGill pain questionnaire, and a global measure of self-reported improvement were significantly greater in the laser-treated group.

Gur et al. randomized 30 patients to active or sham laser treatment and reported significant improvement in the active- but not in the sham-treated groups on numerous measures; however, analysis of the presented results was problematic. (16) In a study by Ceccherelli et al., 27 women were randomized to active (n=13) or sham (n=14) laser treatment and, at 3 months after treatment, the VAS pain score was significantly more improved in the active treatment group. (17) An imbalance in patient characteristics may have impacted results. In a study by Altan and colleagues, 48 patients with myofascial pain syndrome were randomized to active or sham treatment, and all were instructed to perform daily isometric and stretching exercises. (18) At 12 weeks, both groups had improved pain VAS, and there were no significant between-group differences. Ilbuldu et al. randomized 40 women with myofascial pain syndrome to active or sham laser. (19) All patients were instructed to do stretching exercises. There were no significant differences between groups for any outcomes measure. (A third group received dry needling; those results were not included in the TEC Assessment.) The TEC Assessment did comment on a systematic review and meta-analysis of randomized placebo or active-treatment controlled trials by Chow et al.(20) and noted “some studies evaluated acute neck pain, some had insufficient follow-up beyond the period of treatment, one had no sham control, ...” Overall, TEC concluded that “the studies are characterized by small sample sizes, limited statistical power, and limited long-term follow-up.”

An RCT of LLLT for acute neck pain with radiculopathy by Konstantinovic and colleagues published in 2010 did not report outcomes at least 2 weeks beyond the end of the treatment period. (21)

Subacromial Impingement

In a 2009 study designed to assess the effectiveness of LLLT in patients with subacromial impingement syndrome, 44 patients were randomized in equal numbers to receive a 12-week home exercise program with or without LLLT. (22) Outcome measures of night pain, shoulder pain, and disability index (SPADI), and University of California-Los Angeles (UCLA) end-result scores were assessed at the second and twelfth weeks of intervention. Both groups showed

significant reductions in night pain and SPADI at 2- and 12-week assessments. UCLA scores improved significantly in both groups at 12 weeks. No distinct advantage was demonstrated by LLLT over exercise alone.

Another RCT compared outcomes of a 3-week program of exercise with either LLLT or sham therapy for treatment of subacromial impingement. (23) Both groups improved significantly, and there were no significant between-group differences on measures of pain, function, disability, and muscle strength.

In a 2010 report, Dogan et al. randomized 52 patients with subacromial impingement syndrome to active or sham LLLT 5 times per week for 14 sessions. (24) All patients were also given an exercise program. Both groups showed improvements in pain, some measures of range of motion, and on the SPADI. There were no significant differences between the 2 groups.

Calis et al. randomized 52 patients with subacromial impingement syndrome to LLLT, US, or exercise in 2011. (25) Patients were treated 5 days a week for 3 weeks with hotpack+ultrasound+exercise, hotpack+laser+exercise, or hotpack+exercise. All 3 groups showed improvement from baseline to post-treatment in pain at rest, range of motion, and function. There were no significant differences between the groups.

In a 2011 publication, Abrisham et al. randomized 80 patients with subacromial syndrome (rotator cuff and biceps tendinitis) to exercise plus pulsed LLLT or sham laser 5 times per week for 2 weeks. (26) At the conclusion of the treatment period, both groups showed improvement in VAS for pain and shoulder range of motion. The improvement was significantly better for the active LLLT group than the sham laser group for VAS (4.4 vs. 2.9), and all measures of range of motion (active and passive flexion, abduction, and external rotation). The durability of this effect was not assessed.

Conclusions. The literature on LLLT for subacromial syndrome consists of a number of medium-sized randomized controlled trials. The majority of these trials do not show a benefit of LLLT compared to sham controls.

Frozen Shoulder

Sixty-three patients with frozen shoulder were included in an RCT comparing an 8-week program of LLLT (n=31) or placebo (n=32). (27) Compared to the sham group, the active laser group had a significant decrease in overall, night, and activity pain scores after 4 weeks and 8 weeks of treatment, and at the end of 8 more weeks of follow-up. At the same time intervals, a significant decrease in shoulder pain, disability index (SPADI) scores, and Croft shoulder disability questionnaire scores was observed, while a significant decrease in disability of arm, shoulder, and hand questionnaire (DASH) scores was observed at 8 weeks of treatment and at 16 weeks' post-randomization; and a significant decrease in health assessment questionnaire scores was observed at 4 weeks and 8 weeks of treatment.

Temporomandibular Pain

A meta-analysis of RCTs on low-level laser therapy for treating TMJ disorders was published in 2011. (28) The investigators identified 6 randomized placebo-controlled trials that met the inclusion criteria. A pooled analysis of data from the 6 trials did not find a statistically significant difference in the primary outcome of interest, change in pain from baseline to endpoint. The

pooled difference in pain, measured on a visual analogue scale (VAS), was a mean difference of 7.77 mm (95% CI: -2.49 to 18.02), p=0.14. All studies had small sample sizes (ranging from a total of 14 to 52 participants), and the confidence interval in the pooled analysis was wide.

Outcomes of individual trials of LLLT for temporomandibular joint (TMJ) pain are inconsistent. In a study from Brazil, 40 patients with TMJ were treated with LLLT or placebo. (29) After 4 weeks of weekly treatment, patients were evaluated for pain on VAS and the Craniomandibular Index (CMI). Both groups improved on both measures ($p<0.05$), and there were no significant differences between groups. Emshoff et al. evaluated LLLT in the management of TMJ in a double-blinded RCT with 52 patients randomized equally to LLLT or sham treatment. (30) After 8 weeks of 2–3 treatments/week, both groups showed improvements in pain during function. Between-group differences were not significant.

Fikackova and colleagues treated 61 patients with TMJ or myofascial pain with LLLT at 1 of 2 densities (10 J/cm2 or 15 J/cm2) and 19 patients with sham LLLT (0.1 J/cm2). (31) Outcomes were measured by self-administered questionnaire. The authors report significantly better outcomes in patients treated with 10 J/cm2 or 15 J/cm2 than in patients given sham treatment. There were no differences in outcomes between patients with TMJ and myofascial pain.

Carrasco et al. randomly assigned 60 patients with myofascial pain and one active trigger point in the anterior masseter and anterior temporal muscles to 6 groups. (32) Three groups received laser treatment twice a week for 4 weeks using different energy levels for each group (25 J/cm2, 60 J/cm2, or 105 J/cm2). The other 3 groups received placebo treatment simulating the same parameters as the treated groups. Pain scores were assessed just before, immediately after the 4th and 8th applications, and at 15 days and 1 month after treatment. An analgesic effect was seen starting from the third evaluation in both the treated and placebo groups, and placebo was as effective as laser ($p<0.05$). Differences in pain VAS between groups treated at different energy levels were not significant.

Venezian et al. randomized 48 patients with myofascial pain to one of 2 doses of laser (25 J/cm2 or 60 J/cm2) or placebo twice a week for 4 weeks. (33) Surface electromyography (EMG) at the conclusion of testing showed no difference between the groups. Pain with palpation was measured by VAS before, at the conclusion of, and 30 days after laser therapy. VAS scores declined in all groups and were more consistently decreased (more regions of the palpated muscles) after active laser therapy. However, there were no significant differences in VAS between the active and sham-controlled groups.

Marini and colleagues compared superpulsed LLLT with NSAIDs for pain caused by temporomandibular joint disorders secondary to disc displacement without reduction or osteoarthritis. (34) Ninety-nine patients were randomized to 1 of 3 groups: 39 received LLLT in 10 sessions over 2 weeks, 30 received sham LLLT on the same schedule, and 30 patients received ibuprofen 800 mg twice/day. Pain intensity was measured at baseline and after 2, 5, 10, and 15 days of treatment. Mandibular function (active and passive mouth openings and right and left lateral motions) was evaluated at baseline, 15 days, and 1 month of treatment. Durability of pain relief beyond the end of treatment is not reported. Mandibular function was significantly better at 1 month after treatment in the active laser-treated group.

Conclusions. There are a number of medium to large randomized sham-controlled trials of LLLT for temporomandibular syndrome. The majority of these trials, along with a recent meta-analysis, do not show a benefit of LLLT.

Low Back Pain

A 2007 update of the Cochrane Database System Review of LLLT for nonspecific low back pain concluded 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 for low-back pain." (35) Chou and Huffman assessed benefits and harms of nonpharmacologic therapies including LLLT for acute and chronic low back pain in a 2007 review of evidence and did not find good evidence of efficacy for LLLT for either indication. (36)

In a large double-blind placebo-controlled study published in 2010, Konstantinovic et al. randomized 546 patients with acute low back pain to 3 groups of 182 patients. (37) All patients received nimesulide 200 mg; patients in group A received active LLLT, patients in group B received only nimesulide, and patients in group C received placebo LLLT. Treatments were given these 5 times per week for 15 weeks. Statistically significant differences after treatment were found on all outcomes ($p<0.001$) but were larger in group A than in B ($p<0.005$) and C ($p<0.0005$). Results in group C were better than in group B ($p<0.0005$). The authors conclude that improvement is better in acute low back pain with LLLT as additional therapy. Durability of these outcomes was not measured.

In 2010, Ay and colleagues randomized 80 patients with acute and chronic low back pain attributed to lumbar disc herniation (LDH) into 4 groups of 20. (38) All patients received hot-packs and group 1 (acute LDH) received laser therapy; group 2 (chronic LDH) received laser therapy, group 3 (acute LDH) received placebo laser therapy; and group 4 (chronic LDH) received placebo laser therapy for 15 sessions over 3 weeks. Outcome measures were pain on VAS, patients' global assessment, physicians' global assessment, and functional capacity and were measured after 3 weeks of treatment. After treatment, all groups had statistically significant improvements in pain severity, patients' and physicians' global assessment, range of motion, Roland Disability Questionnaire, and Modified Oswestry Disability Questionnaire ($p<0.05$). There were no significant differences between treatment groups on any outcomes ($p<0.05$). Durability of the treatment effect was not reported.

In a 2007 study by Djavid et al., 61 patients were randomized to LLLT alone (n=20), LLLT with exercise (n=21), or sham laser treatment with exercise (n=20). (39) Outcomes of pain on VAS, lumbar range of motion (ROM), and disability were measured by blinded assessors after 6 weeks of treatment, after another 6 weeks and 12 weeks without treatment. By intention-to-treat (ITT) analysis, there were no between-group differences for any outcome measure immediately after the 6-week intervention. After 6 weeks without intervention, there was no difference between the LLLT alone group and the placebo laser therapy plus exercise group; however, in the LLLT plus exercise group, pain had reduced by 1.8 cm (95% confidence interval [CI]: 0.1 to 3.3, $p=0.03$), lumbar ROM increased by 0.9 cm (95% CI: 0.2 to 1.8, $p=<0.01$) on the Schober Test and by 15 degrees (95% CI: 5-25, $p<0.01$) of active flexion, and disability reduced by 9.4 points ($p=0.03$) on the Oswestry Disability Index more than in the placebo laser therapy plus exercise group. The authors advised that larger trials are needed to detect differences between groups for some outcomes.

Conclusions. The literature on LLLT for low back pain consists of several medium- to large-sized randomized sham-controlled trials. Results of these trials are inconsistent.

Osteoarthritic (OA) Knee Pain

In 2007, Bjordal et al. published a systematic review of placebo-controlled RCTs to determine the short-term efficacy of physical interventions for OA knee pain. (40) They concluded that transcutaneous electrical nerve stimulation (TENS) (including interferential currents) and LLLT offered clinically relevant pain-relieving effects on VAS scores compared to placebo control. Follow-up data up to 121 weeks were sparse, but positive effects seemed to persist for at least 4 weeks after the course of treatment.

In 2011, Alfredo et al. reported a randomized double-blind sham-controlled trial of LLLT in 40 patients with knee OA. (41) Laser or sham treatments were delivered 3 times per week for 3 weeks, and both groups received exercise sessions 3 times per week for 8 weeks. The active laser group showed significant improvements from baseline in pain scores, activity, range of motion, and functionality, but there were no significant differences between the active and sham laser groups.

Hegedus et al. reported a randomized double-blind sham-controlled trial of LLLT in 35 patients with knee OA in 2009. (42) Eight patients from the sham group left the experiment, leaving 18 patients in the active LLLT group and 9 in the sham group. Treatments were delivered twice a week over a period of 4 weeks at a dose of 6 J/point (48 J/cm2). Follow-up was performed immediately, 2 weeks, and 2 months after completing the therapy. In the group treated with LLLT, a significant improvement was found in pain (5.75 to 1.18), pressure sensitivity (2.33 to 0.77), and flexion (105.83° to 122.94°) at 2 months. In the placebo group, baseline to post-treatment changes in joint flexion and pain were not significant. It was not reported if these changes were significantly improved in comparison with the sham group. Circumference of the joint was not significantly changed for either group. Thermographic measurements at 2 months showed an increase in temperature of equal to or greater than 0.5 degrees in patients in the active laser group who experienced pain relief, suggesting an improvement in circulation.

Conclusions. The literature on LLLT for OA includes a systematic review and some small randomized sham-controlled trials. Results of these studies are inconsistent.

Rheumatoid Arthritis (RA)

A 2005 Cochrane Review included 5 placebo-controlled RCTs and found that relative to a separate control group, LLLT reduced pain by 1.10 points on VAS compared to placebo, reduced morning stiffness duration by 27.5 minutes, and increased tip-to-palm flexibility by 1.3 cm. (43) Other outcomes, such as functional assessment, range of motion, and local swelling, did not differ between groups. For RA, relative to a control group using the opposite hand (1 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.”

A 2010 randomized double-blind placebo-controlled trial comparing outcomes of pain reduction and improvement in hand function in 82 patients with RA treated with LLLT or placebo laser was

reported by Meireles et al. (44) There were no statistically significant differences between groups in most of the outcome measurements including the primary variables, though a few measures significantly favoring either the active or placebo treatment were found. The authors concluded that LLLT at the dosage used in the study was not effective for the treatment of hands among patients with RA.

Elbow Pain

Authors of a systematic review published in 2008 grouped trials by application technique and wave lengths and reported that 7 of the 13 included trials had a 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. (45) Positive results in these trials were consistent on outcomes of pain and function, and significance persisted for at least 3–8 weeks after the end of treatment. The authors noted that the conclusions of their review differed from conclusions of prior reviews of this topic.

Achilles Tendinopathy

Stergioulas and colleagues randomized 52 recreational athletes with chronic Achilles tendinopathy symptoms to an 8-week (12 sessions) program of eccentric exercises (EE) with LLLT or with sham LLLT. (46) By ITT analysis, results for the primary outcome of pain during physical activity on VAS were significantly lower in the EE with LLLT group at 4 weeks ($p=0.0003$), 8 weeks ($p=0.0002$), and 12 weeks ($p=0.007$) after randomization. Results of EE with LLLT at 4 weeks were similar to results for the EE plus sham LLLT group after 12 weeks.

Tumilty et al. reported a randomized double-blinded sham-controlled trial of LLLT as an adjunct to 3 months of EE in 40 patients with Achilles tendinopathy. (47) Active or sham LLLT was administered 3 times per week for 4 weeks, and exercises were performed twice a day for 12 weeks. The primary outcome was the Victorian Institute of Sport Assessment-Achilles questionnaire (VISA-A) at 12 weeks. There was a trend for the active laser group to score lower on the VISA-A at baseline ($p=0.051$). Following treatment, the only significant difference between the groups on an ITT basis was at 4 weeks on the VISA-A and favored the sham-control group. The VISA-A and numerical rating scale for pain were not significantly different between the active and sham groups at 12 weeks or 1-year follow-up.

Myofascial Neck/Shoulder Pain

Rayegani et al. evaluated LLLT in a randomized trial of 49 patients with myofascial pain of the upper trapezius muscle. (48) Following baseline assessments, the patients were randomized to active or sham laser or to ultrasound (5 times a week for 2 weeks). All of the patients received stretching exercises, transcutaneous electrical nerve stimulation (TENS), and hot packs. The patients, assessors, and statisticians were blinded to treatment condition. Compared to sham controls, the LLLT group showed significantly greater improvements in VAS during activity, VAS at rest, VAS at night, the neck disability index (NDI), and pain-provoking threshold. Laser was also found to be more effective than ultrasound for the NDI and pain provoking threshold, but not in the VAS for pain.

Plantar Fasciitis

Kiritsi and colleagues reported a randomized double-blind sham-controlled trial of LLLT in 30 subjects with plantar fasciitis in 2010. (49) Twenty-five patients (83%) completed the study, with treatment 3 times per week over 6 weeks. At baseline, plantar fascia thickness measured by US

was significantly greater in the symptomatic compared with asymptomatic feet (5.3 mm vs. 3.0 mm). Plantar fascia thickness decreased in both LLLT and sham groups over the course of the study. Although plantar fascia thickness after 6 weeks of treatment was not significantly different between the 2 groups (3.6 mm LLLT and 4.4 mm sham), there was a significant difference between the groups in the change in thickness (1.7 mm LLLT vs. 0.9 mm sham). VAS after night rest or daily activities was significantly improved in the LLLT group compared with the sham, with a 59% improvement in the active laser group and a 26% improvement for the sham-treated subjects. At baseline, pain after daily activities was rated as 67/100 by both groups. At the end of treatment, VAS after daily activities was rated as 28/100 for LLLT and 50/100 for sham.

Oral Mucositis

The Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO) published a systematic review of laser and other light therapy for the management of oral mucositis in 2012. (50) A total of 24 trials were included for the review. Based on their review of the evidence, the MASCC/ISOO made a new recommendation for LLLT for the prevention of oral mucositis in adult patients receiving hematopoietic stem-cell transplantation (HSCT) conditioned with high-dose chemotherapy. This recommendation was based on what was considered to be one well-designed placebo-controlled randomized trial (described in more detail below), (51) together with a series of studies classified at a lower level of evidence. Evidence was insufficient to provide a guideline for laser as a treatment of oral mucositis in HSCT patients.

The MASCC/ISOO made a new “suggestion” for low-level laser for the prevention of oral mucositis in patients undergoing radiotherapy, without concomitant chemotherapy, for head and neck cancer. This guideline was based on 3 studies that showed positive results but were considered to have major flaws. Evidence was considered encouraging but insufficient to recommend LLLT in other populations. The authors emphasized that due to the variety of laser devices and the variation in individual protocols, results of each study apply exclusively to the cancer population studied and the specific wavelength and settings used.

The pivotal study for the MASCC/ISOO recommendation was a randomized double-blind sham-controlled trial with 70 patients who were undergoing HSCT. (51) Patients were randomized to 650 nm laser, 780 nm laser, or placebo (randomization method not described). Patients in the 650 nm laser group were more likely to have received a TBI-containing regimen compared to the other 2 groups, otherwise, the groups were comparable. LLLT began on the first day of conditioning and continued for 3 days post-transplant. Of the 70 patients, 47 (67%) had complete or nearly complete mucositis measurements over time; the average number of visits per patient was similar for the 3 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), and this difference between the 650 nm group and placebo approached statistical significance ($p=0.06$). Thus, there was no significant difference in mean oral mucositis scores between the 650 nm and placebo group at the other time points. Patient-specific oral mucositis scores were significantly different between the 2 groups only when adjusted for total body irradiation (TBI) exposure. Of the 70 patients in the study, 17 (24%) were assessed for oral pain. With group sizes of 5 and 6, the 650-nm group had significantly lower patient-specific average pain scores (15.6) compared to placebo (47.2). No adverse events from LLLT were noted. This study, which formed the basis for the MASCC/ISOO recommendation, suffers from limitations that include not achieving statistical significance for the primary outcome measure and a very small percentage of patients with pain assessments.

Gautam et al. reported 2 double-blinded randomized sham-controlled trials in 2012. (52, 53) One of the studies reported LLLT for the prevention of chemoradiotherapy-induced oral mucositis in 121 oral cancer patients. (52) The second publication reported LLLT for the prevention of chemoradiotherapy-induced oral mucositis in 221 head and neck cancer patients. (53) There is an apparent overlap in patients in these 2 reports, with the head and neck cancer report including the 121 patients with a primary tumor site in the oral cavity. In the report on oral cancer, LLLT prior to radiation treatment led to significant reductions in the incidence of severe oral mucositis (29% vs. 89%) and its associated pain (18% vs. 71% with a VAS >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 vs. 13.96 days), severe pain (5.31 vs. 9.89 days), and total parenteral nutrition (14.05 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 vs. 12.86 days) and its associated pain (VAS of approximately 4 vs. 7), total parenteral nutrition (45.0% vs. 65.5%), and opioid analgesic use (9% vs. 26% for step III, all respectively).

Another randomized sham-controlled trial from 2012 evaluated the effect of LLLT on quality of life in 60 patients undergoing radiotherapy in the region of the major salivary glands. (54) Quality of life (QOL) was measured by the University of Washington QOL questionnaire at baseline and after 15 and 30 treatment sessions. QOL decreased significantly in both groups over the 30 treatment sessions, but there was a smaller decrease in QOL in the LLT group compared to the placebo group. The domains of appearance, activity, recreation, speech, taste, pain, chewing, and saliva were less affected in the LLLT group compared to the placebo group at either the mid-treatment or final assessment. More patients in the sham control group had an interruption of radiotherapy (25 vs. 12), which was due primarily to mucositis.

Conclusions. The literature on LLLT for the prevention of oral mucositis includes a systematic review by MASCC/ISOO with a resulting recommendation for LLLT for the prevention of oral mucositis in adult patients receiving HSCT conditioned with high-dose chemotherapy. Review of the pivotal study for this recommendation reveals serious limitations that include a lack of statistical significance for the primary outcome measure. The systematic review by MASCC/ISOO considered the evidence insufficient to recommend LLLT for the prevention or treatment of oral mucositis in any other situation. Since the publication of this systematic review, 2 randomized sham-controlled trials from South America and Asia have reported some efficacy of LLLT for the prevention of oral mucositis in patients with head and neck cancer undergoing radiotherapy or chemoradiotherapy. Additional study in these patient populations is needed to determine the efficacy of LLLT with greater certainty.

Fibromyalgia

Matsutani and colleagues randomized 20 patients with fibromyalgia to receive laser treatment and stretching exercises or stretching alone. (55) Outcome measures were VAS and dolorimetry at tender points, quality of life on the Fibromyalgia Impact Questionnaire (FIQ), and the 36-item Short-Form Health Survey (SF-36). 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.

Wound Healing

A 2004 evidence report on vacuum-assisted and low-level laser wound therapies for treatment of chronic non-healing wounds prepared for the Agency for Healthcare Research and Quality (AHRQ) was based on 11 studies of LLLT. (56) It stated that "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." No newer studies were identified in updated literature searches.

Lymphedema

Omar and colleagues published a qualitative systematic review of LLLT for the management of breast cancer-related lymphedema in 2012. (57) They included 8 studies with a total of 230 patients in the review. Five studies were graded as Sackett evidence level II (small randomized trial with high false-positive or false-negative errors), 2 were graded as level III (non-randomized comparative study), and 1 study was graded as level V evidence (case series). The authors noted major methodologic flaws and little uniformity in the design of the studies.

One of the studies included in the review was a 2011 publication by Omar et al. reporting a randomized double-blind sham controlled trial of LLLT in 50 patients with post-mastectomy lymphedema. (58) The average length of time that patients had swelling was 14 months (range 12-36 month). Patients were treated with active or sham laser 3 times per 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 limb circumference in the active laser group at 8 (20.0 vs. 16.4 cm), 12 (29 vs. 21.8 cm), and 16 weeks (31 vs. 23). 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 of laser therapy (26.2 vs. 22.4 Kg). The durability of these effects was not assessed.

Conclusions. The evidence on LLLT for post-mastectomy lymphedema includes 5 small randomized trials with high potential for false-positive or false-negative errors. Larger sham-controlled studies are needed to determine the efficacy of LLLT for post-mastectomy lymphedema with greater certainty.

Summary

The available literature on low-level laser therapy as a treatment for lymphedema, prevention of oral mucositis, wound healing, or pain of various etiologies and in a variety of anatomical sites presents inconsistent results and methodologic weaknesses, including lack of follow-up evaluation, that prevent drawing firm conclusions regarding efficacy. Therefore, LLLT remains investigational for all indications.

Practice Guidelines and Position Statements

In 2010, the American Physical Therapy Association (APTA) published a guideline on the diagnosis and treatment of Achilles tendinitis. (59) APTA gave a level B recommendation (based on moderate evidence) to consider the use of LLLT to decrease pain and stiffness in patients with

Achilles tendinopathy. APTA states in their review of the evidence, that “given the limited number of studies employing LLLT in this population, additional study is warranted”.

The United Kingdom’s National Institute for Health and Clinical Excellence (NICE) 2009 Guideline on early management of persistent non-specific low back pain does not recommend laser treatment, citing limited evidence. (60)

The 2007 American Pain Society/ guideline states that there is insufficient evidence to recommend LLLT for treatment of low back pain, (61) and LLLT is not mentioned in the 2009 guideline. (62)

The American Academy of Orthopaedic Surgeons (AAOS) 2008 clinical practice guideline on the treatment of carpal tunnel syndrome included laser treatment among treatments that carry no recommendation for or against their use because there is insufficient evidence to recommend their use. (63)

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT/HCPCS

S8948 Application of a modality (requiring constant provider attendance) to one or more areas; low-level laser; each 15 minutes

- In January 2004, a HCPCS code S8948 was added that is specific to this therapy.
- There is no specific CPT code for low-level laser therapy.

DIAGNOSES

Experimental / Investigational for all diagnoses related to this medical policy.

REVISIONS

2005	Policy added to the bcbsks.com web site.
03-12-2013	Title Revised from "Low-Level Laser Infrared Therapy (also known as soft laser therapy, Microlight 830, and cold laser therapy)" to "Low-Level Laser Therapy"
	Description section updated
	In Policy section: ▪ Revised policy language from, "Low-level laser treatment is considered experimental/investigational for all indications, including but not limited to carpal tunnel syndrome and other pain disorders, edema, and to enhance wound healing due to the lack of sufficient studies and published scientific literature." to," Low-level laser therapy is considered experimental/investigational for all indications, including but not limited to carpal tunnel syndrome." This policy language change does not change the intent of the policy position.

	▪ Added the Policy Guidelines of: "Other protocols have used low-level laser energy applied to acupuncture points on the fingers and hand. This technique may be referred to as "laser acupuncture." Laser acupuncture is not reviewed in this policy."
	Added Rationale section
	In Coding section: ▪ Added coding notations.
	Added Revision section
	Added References

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