

The Effectiveness of Therapeutic Class IV (10 W) Laser Treatment for Epicondylitis

Delia B. Roberts, PhD, FACS¹,*¹ Roger J. Kruse, MD, FACS²,² and Stephen F. Stoll, MD³³

¹Selkirk College, Castlegar, British Columbia, Canada, V1N 4L3

²Sports Care, ProMedica Health System, Toledo, Ohio, 43615

³Diagnostic Radiologist, Toledo Radiological Associates, Toledo, Ohio, 43606

Background and Objective: Photobiomodulation has been shown to modulate cellular protein production and stimulate tendon healing in a dose-dependent manner. Previous studies have used class IIIb lasers with power outputs of less than 0.5 W. Here we evaluate a dual wavelength (980/810 nm) class IV laser with a power output of 10 W for the purpose of determining the efficacy of class IV laser therapy in alleviating the pain and dysfunction associated with chronic epicondylitis.

Methods: Sixteen subjects volunteered for laser therapy, or an identically appearing sham instrument in a randomized, placebo-controlled, double-blinded clinical trial. Subjects underwent clinical examination (pain, function, strength, and ultrasonic imaging) to confirm chronic tendinopathy of the extensor carpi radialis brevis tendon, followed by eight treatments of $6.6 \pm 1.3 \text{ J/cm}^2$ (laser), or sham over 18 days. Safety precautions to protect against retinal exposure to the laser were followed. The exam protocol was repeated at 0, 3, 6 and 12 months post-treatment.

Results: No initial differences were seen between the two groups. In the laser treated group handgrip strength improved by $17 \pm 3\%$, $52 \pm 7\%$, and $66 \pm 6\%$ at 3, 6, and 12 months respectively; function improved by $44 \pm 1\%$, $71 \pm 3\%$, and $82 \pm 2\%$, and pain with resistance to extension of the middle finger was reduced by $50 \pm 6\%$, $93 \pm 4\%$, and $100 \pm 1\%$ at 3, 6 and 12 months, respectively. In contrast, no changes were seen until 12 months following sham treatment (12 months: strength improved by $13 \pm 2\%$, function improved by $52 \pm 3\%$, pain with resistance to extension of the middle finger reduced by $76 \pm 2\%$). No adverse effects were reported at any time.

Conclusions: These findings suggest that laser therapy using the 10 W class IV instrument is efficacious for the long-term relief of the symptoms associated with chronic epicondylitis. The potential for a rapidly administered, safe and effective treatment warrants further investigation. *Lasers Surg. Med.* 2013 Wiley Periodicals, Inc.

Key words: epicondylalgia; photobiomodulation; tendinopathy; tendinosis; tenosynovitis

INTRODUCTION

Tendinopathy is a common and painful condition that occurs following damage to a tendon [1–3]. The onset of

symptoms is associated with overuse, increased load, vibration and/or repetitive movements and while tendon injuries are sometimes acute, they are most often chronic in nature resulting in significant restriction of activity and lost work-time [3,4]. Characteristic findings include necrosis [3], abnormal neovascularization [5], edema, crepitus, and impaired function [4,6]; however, the etiology remains incompletely understood. Furthermore, while most cases resolve themselves within 12 months of rest, approximately 15–20% are persistent, with reoccurrence of symptoms when activity is resumed [6,7].

There is little consensus regarding effective treatments for tendinopathy [4,8]. Rest, ice, and analgesics are general guidelines used to provide pain relief. Orthotic devices [9], ultrasonography [10] and deep transverse friction massage [11] are often recommended, although there is no conclusive evidence as to the effectiveness of these treatments. Similarly, while eccentric exercises have been shown to be more effective than no treatment in relieving symptoms for some tendinopathies, compliance can be problematic and there is a great deal of heterogeneity in protocols [12]. Randomized controlled studies of epicondylitis have determined that oral non-steroidal anti-inflammatory treatment was not significantly better than placebo [13] and although early corticosteroid injection did provide symptom relief in some patients, studies that were extended to 3 [14] and 12 [13] months post-injection indicated that corticosteroid injection could even produce a detrimental outcome. Extracorporeal shock therapy for treatment of tendinopathy is also not supported by systematic reviews of the literature [15], except perhaps for cases resistant to conventional treatments [16].

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

RCT Registration: BioMed Central Current Controlled Trials ISRCTN04330904.

Contract grant sponsor: LiteCure LLT

*Correspondence to: Delia Roberts, PhD, FACS¹, School of University Arts and Sciences, Selkirk College, 301 Frank Beinder Way, Castlegar, BC V1N 4L3.

E-mail: droberts@selkirk.ca

Accepted 26 March 2013

Published online in Wiley Online Library

(wileyonlinelibrary.com).

DOI 10.1002/lsm.22140

Another drawback is that there is a significant amount of pain associated with this therapy [17].

In contrast, low level laser therapy (LLLT), also known as photobiomodulation (PBM) has been shown to be effective at the cellular level increasing cytochrome C oxidase production and reversing the effects of cellular inhibitors of respiration [18]. Accelerated tissue healing has been reported, including an increase in collagen fibril size [19] and a decrease in prostaglandin E₂ levels [20,21] in a dose dependent manner [22]. Samoilova et al. [23] reported activation of nitric oxide synthase, and recently increased blood flow in the treated limb has been demonstrated [24]. Given that tendinopathies have been shown to be associated with matrix degeneration, these combined effects would be likely to have an influence in improved healing of damaged tendon. While one meta-analysis of LLLT for lateral epicondylitis suggested that LLLT was not more effective than placebo [25], two more recent examinations of the literature based upon treatment protocol concluded a positive effect. In studies where the tendon was directly irradiated using wavelengths between 630 and 1,064 nm, doses of 0.5–8 J were effective in achieving improvements in decreased pain and increased strength both acutely and up to 8 weeks following treatment [26,27].

Previous clinical studies on LLLT have used lasers with a typical output of less than 0.5 W. However, a dual wavelength (980 and 810 nm) laser with an output power of up to 10 W has recently been developed for use in laser therapy. At full power (10 J/seconds) these instruments can deliver 8–9 J/cm² at the skin surface, achieving a distributed photochemical biomodulatory dose in only minutes. The body of evidence indicating that LLLT is efficacious suggests that the using a higher power laser would allow for an effective treatment to be delivered in a shorter time over a larger area, and with a more uniform dose than the point administration of low power lasers. However, to date, no randomized placebo controlled trials have been undertaken utilizing this instrumentation. Hence, the purpose of this investigation was to investigate the efficacy of a laser with a higher power output for the treatment of tendinopathy of the extensor carpi radialis brevis tendon in a clinical setting.

METHODS

The study design was a single center randomized (1:1), placebo-controlled, double-blinded, parallel group clinical trial, conducted in the United States. Level of Evidence: Therapy, 2 [28]. Independent ethical review was conducted by the IRB Promedica Health Systems, Toledo, OH. Volunteers were recruited by advertisement for 4 months. Of the 28 subjects who volunteered for this randomized controlled trial, 16 subjects were accepted into the study. Exclusion criteria included factors which may have affected treatment administration such as photosensitivity or pigment around the cubital area which could have resulted in different levels of absorption of the administered light. The use of corticosteroids or, injection of the cubital area within the past 3 months also precluded

participation. Informed consent was obtained and the rights and privileges of the patients were observed at all times. Clinical evaluation of lateral epicondylitis was made by blinded Sport Medicine Fellows on the basis of standard clinical tests including: Handgrip strength from three maximal trials using the using the Smedley III Digital Grip Strength Tester (Creative Health Products, Plymouth, MI) according to standard protocol of Ashford et al. [29]; Ratings of pain using the Visual Analog Scale (VAS) of 1–10 (where 10 is intolerable pain) with maximal handgrip using the Ashford et al. protocol [29], with moderate palpation of the common extensor tendon, and with resistance to extension of the middle finger (affected elbow stabilized at 90°, forearm pronated, wrist in neutral); And functional impairment (scale of 1–5 with 5 being no impairment and 1 being unable to use hand during daily tasks). Participants also underwent ultrasonic imaging of the extensor carpi radialis brevis tendon to confirm the diagnosis based upon the presence of tendon thickening relative to the adjacent osseous structures, discriminate focal areas of hypoechogenicity or anechromicity, focal tears, and the presence of calcifications. Ultrasonographs were evaluated by an experienced radiologist with specialization in musculoskeletal radiology who was also blinded to the treatment groups.

Subjects were then randomly assigned to placebo (sham) or laser treatment (LT) groups by drawing sealed envelopes from a box. Two identically appearing 10 W lasers were used for treatments (LiteCure LLT, Newark, DE), however the sham laser light was disabled and only the aiming beam (identical to that utilized on the true device) remained, subjects and clinicians were unable to discriminate between which instrument was which. The true laser was a solid-state diode dual wavelength (980/810 nm fixed ratio 80:20) laser. The aiming beam was a single wavelength class 3a laser (650 nm), with a power output 4 mW. All treatments were administered in a sport medicine clinic (Toledo, OH) by a trained technician according to the following schedule: three treatments on consecutive days, four additional treatments over the next 10 days and one final treatment during the third week. The testing protocol was repeated following the final treatment, and again at 3, 6, and 12 months to generate the primary outcome measures. The study flow diagram is shown in Figure 1.

Subjects abstained from all other forms of treatment including non-steroidal anti-inflammatory or topical medications, braces, physical therapy, ultrasound, acupuncture and shock wave therapy until completion of the study. If a patient chose to institute an alternative treatment they were withdrawn from the study at that point, their data was only included in analyses performed when the original laser or sham was the only treatment. Activities causing pain or irritation of the tendon were restricted until the laser treatment was complete (the first 3 weeks), after which subjects were encouraged to resume normal activity.

Due to ethical considerations subjects randomized into the sham group were offered the true treatment after the 3-month follow up (Fig. 1), since any sham subjects

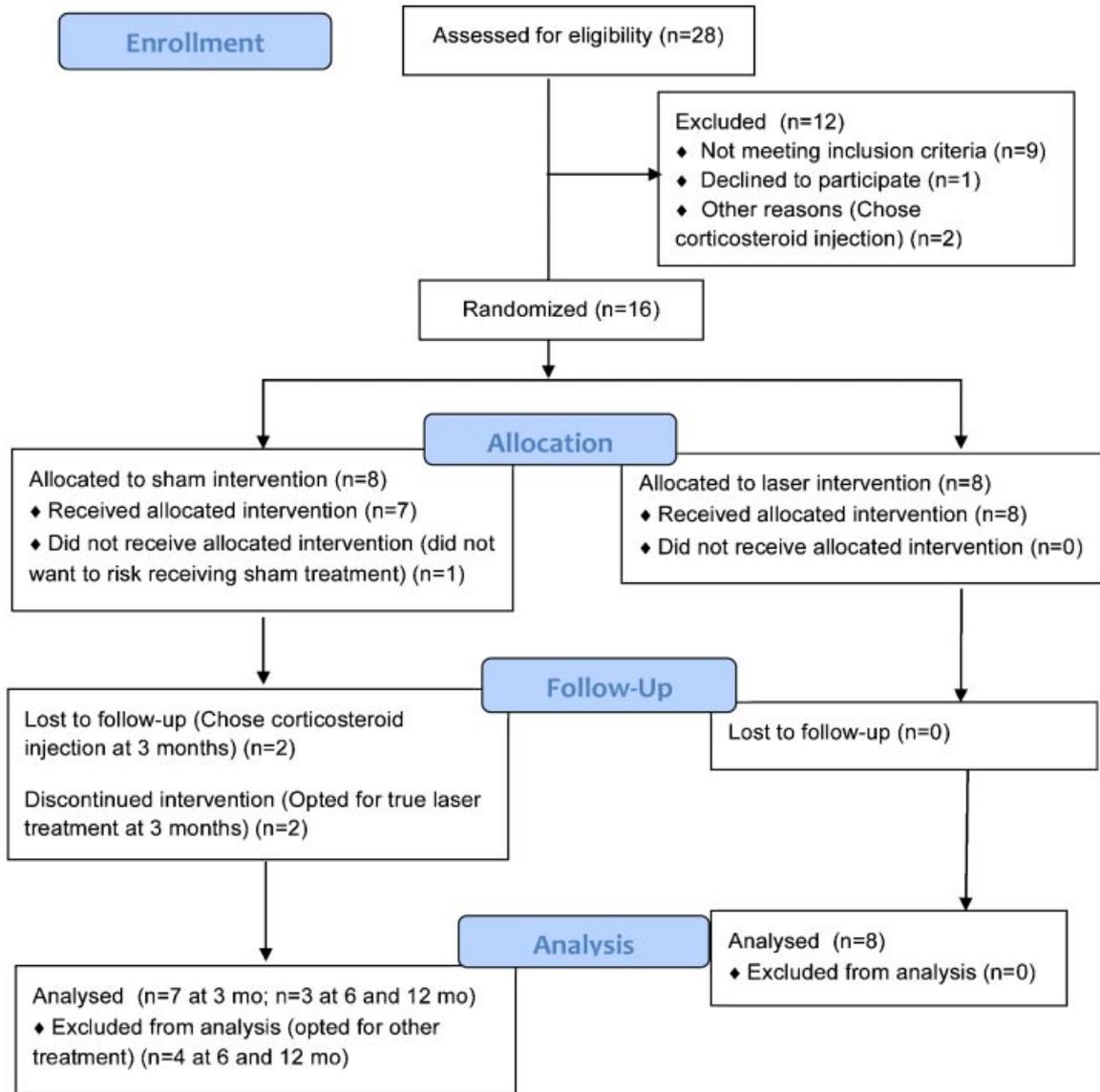


Fig. 1. CONSORT flow diagram for the laser study.

choosing the true treatment were no longer blinded to the treatment their data was not crossed over and was not included in the treatment data analysis after the 3-month assessment.

Procedure For Administration of the Laser Treatment

The area to be treated was demarcated at 1/2 the distance from the lateral epicondyle to the ulnar styloid and 1/3 of the distance from the lateral epicondyle to the acromion process. The non-contact laser probe was kept perpendicular to, and approximately 2.5 cm above the surface of the dermis, creating a spot size 5.7–9.6 cm². The laser was set at full power output of 10 W with a continuous wave form generating a total dose per treatment of 3000 J in 5 minutes or 6.6 ± 1.3 J/cm²,

within the recommended therapeutic guidelines [26,30]. The first 2.5 minutes of the laser treatment were administered with the arm in full extension, and the second 2.5 minutes were administered while passively moving the joint through its range of motion in order to better allow full illumination of the tissue. The laser probe was moved in a “painting” fashion with half of the treatment delivered along the long axis to the tendon, with the other half delivered transverse to the tendon while covering the anterior, lateral and posterior aspects of the lateral epicondyle.

Safety precautions were placed in effect to minimize the risk of exposure of the retina of the eye to laser light. Both clinician and subject wore specifically designed safety goggles provided by the manufacturer to shield against reflected laser light. Jewelry and other reflective surfaces were removed from the treatment area which was

TABLE 1. Demographic Information for Sham and Laser Treatment Groups

	Sex		Age (years)	Duration of pain (months)
	% female	% male		
Sham ($n = 7$)	40	60	48 ± 7	15 ± 12
Treatment ($n = 8$)	36	64	53 ± 9	16 ± 15

Data presented as mean \pm SD.

designated by MSDS signage, and was restricted access. At no time was the laser probe directed upwards towards the head of the clinician or subject.

Statistical Analysis

The data analysis was generated using the MIXED procedure for repeated measures with unbalanced design [31] (SAS/STAT software, Version 9.2 of the SAS System for Windows, Cary, NC) with the level of significance taken at $P < 0.05$. Power analyses were performed for each parameter using G*Power3 [32].

RESULTS

Demographic information is presented in Table 1. No differences were observed between the two groups prior to treatment. Clinical exams and ultrasonography confirmed a diagnosis of chronic tendinopathy of the extensor carpi radialis brevis tendon in all subjects. The ultrasonography revealed tendons to be thickened, with heterogeneous areas. Regions of hypoechogenicity and anechogenicity were noted, and in some cases, proximal calcifications were also visible.

All subjects tolerated the treatments well; there were no reports of discomfort during the laser therapy or adverse reports made at any time, and all LT subjects completed the full treatment course as well as returning for the full 12 months of follow-up testing. One SG subject withdrew prior to the beginning of the treatment course because they did not want to risk being randomized into the sham treatment group, two SG subjects chose to obtain the true

treatment when it was offered following the 3-month exam (their data were included prior to and including the 3-month assessment, but not afterwards as they were no longer blinded to the treatment), two SG subjects opted for corticosteroid injections following the 3-month assessment (their data were included prior to and including the 3-month assessment, but not following the injection), and the remaining three control subjects continued with no alternate treatment until completion of the 12-month follow up (Fig. 1). No significant differences were observed in any of the primary outcome measures of strength or pain in the sham group until 12 months (Figs. 2–6). In contrast, all pain measures as well as perceived functional impairment were significantly improved by the end of the treatment protocol in the laser group (Figs. 3–6). Handgrip strength was slower to recover and was not significantly improved over pre-treatment levels until 6 months post-treatment (Fig. 2).

DISCUSSION

This study is the first report of a clinical trial of a10 W laser for treatment of tendinopathy. Our findings confirm the positive effects of PBM in enhancing tendon healing that have previously been reported with LLLT trials [19,21,27]. In the current study, reductions in pain and return of strength and function were observed in the treatment group with greater speed and magnitude than in the sham group (Figs. 3–6), with improvement continuing up to and including the final time point at 12 months post-treatment. While it is possible that these effects were due

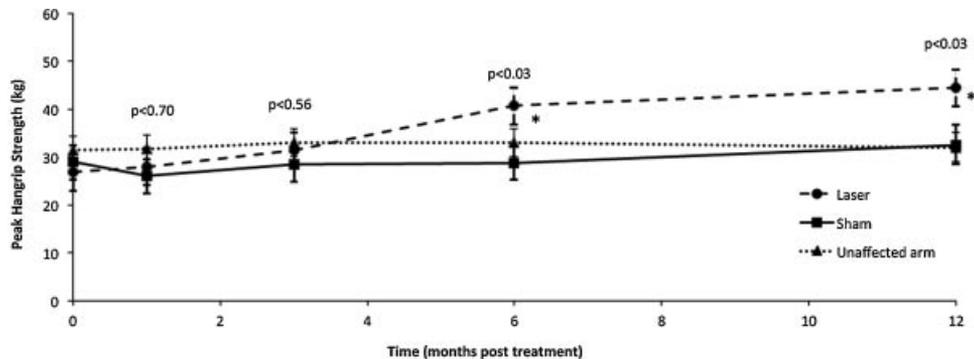


Fig. 2. Handgrip strength (kg) in the affected arm, pre and post laser and sham treatment. Shown P values are for the difference in strength between laser and sham treatment ($df = 48$). Results for the unaffected arm are also shown for comparison. *Significantly different from pre-treatment. $P < 0.0001$. Power = 0.74.

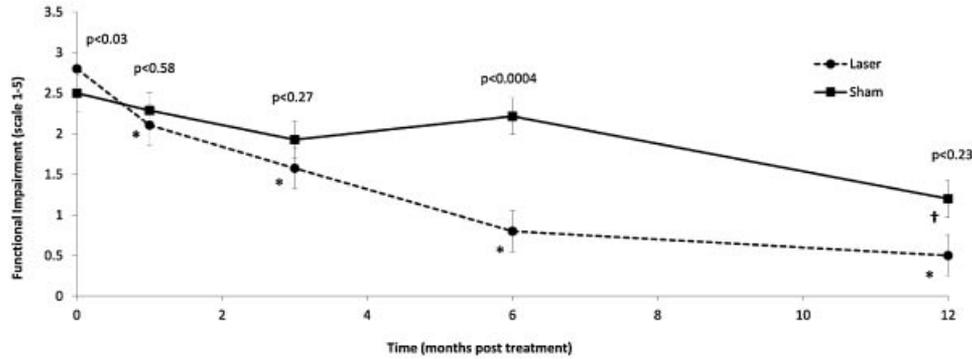


Fig. 3. Functional Impairment (1–5, 1 = Useless). Shown P values are for the difference in perceived functional impairment between laser and sham treatments ($df = 48$). Significantly different from pre-treatment. * $P < 0.0001$ for the laser group, † $P < 0.002$ for the sham group at 12 months. Power = 0.77.

at least in part to neurological changes [33], we propose that the improvements in the primary outcome measures may have occurred due to tendon repair over time as patients reported continued reduction of pain and increased strength even though they increased their use of the affected tendon over the same time period. In contrast, pain, strength, and functional impairment in the sham group remained undiminished until 12 months (Figs. 2–6). This outcome is as expected, as tendinopathy has been shown to resolve itself in approximately 12 months without treatment other than reduced use [6]. That the laser group showed continued decline of tendinopathy symptoms in spite of increased function immediately post-treatment through to 12 months (Fig. 3) indicates that PBM treatment provides a superior outcome to no treatment.

One weakness in the current study is the small sample size, particularly in the sham group. With continued pain and dysfunction at 3 and 6 months, the majority of patients in the sham group switched to the true treatment or sought other modalities (Fig. 1). However, our statistical power analysis of 0.62–0.89 supports the validity of our observations in spite of the small sample size [32].

The higher power output of the 10 W laser allowed for the delivery of an effective PBM dose in minutes. Here, a total of 3000 J were delivered over the entire area of the extensor carpi radialis brevis tendon from 1/2 the distance from the lateral epicondyle to the lateral styloid of the carpus and 1/3 of the distance from the lateral epicondyle to the acromion process in 5 minutes. This fluence ($6.6 \pm 1.3 \text{ J/cm}^2$) is within the published guidelines for LLLT [30] which are designed for much lower power lasers using point treatment as opposed to the current beam diameter of 5.7–9.6 cm^2 . The wider beam diameter and higher power allow for a much more even distribution of energy over a larger areas such as a whole muscle or large tendon which is likely to be advantageous due to the dose response effect of PBM. Furthermore, because the point delivery of lower power lasers is so narrow, some of the inconsistency in outcomes following laser treatment has been attributed to the heterogeneity of delivery of the laser to the affected tissue [34].

Studies of LLLT treatment with 0.5 W lasers and point treatment have been shown to have beneficial outcomes in the treatment of tendinopathy [26,27], thus we cannot exclude that the 4 mW laser light in the aiming beam

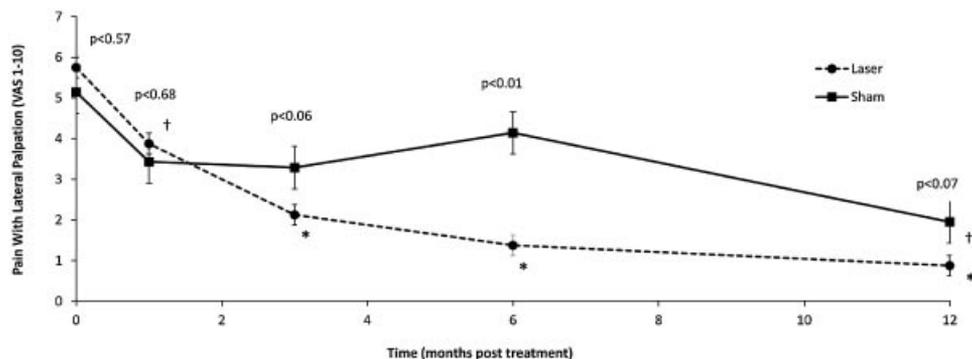


Fig. 4. Lateral Pain With Palpation (VAS 1-10). Shown P values are for the difference in perceived pain between laser and sham treatments ($df = 48$). *Significantly different from pre-treatment $P < 0.001$. †Significantly different from pre-treatment. $P < 0.05$. Power = 0.74.

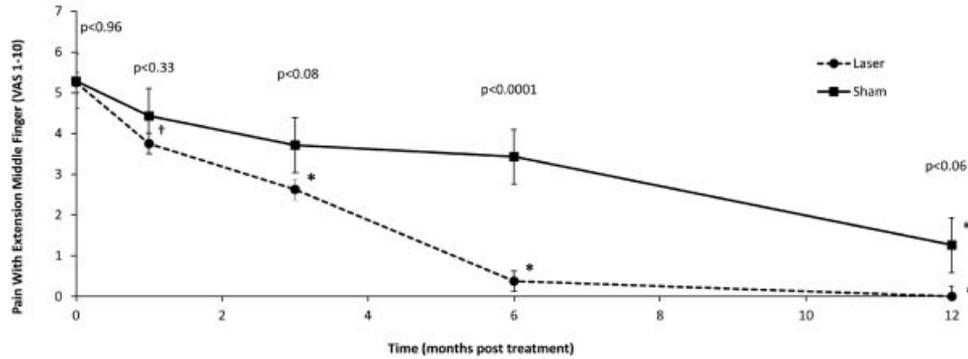


Fig. 5. Pain with resistance extension middle finger (VAS 1-10). Shown P values are for the difference in perceived pain between laser and sham treatments ($df = 48$). *Significantly different from pre-treatment, $P < 0.001$; † $P < 0.02$. Power = 0.89.

(650 nm) used in both the 10 W laser and the sham device contributed to the PBM dose applied in the current investigation. However, due to the short time period of exposure the total energy delivered by the aiming beam would have only amounted to 1.2 J, well under the level that has been identified as being an effective dose [30], making it unlikely that the aiming beam had any therapeutic effect. Furthermore, in the current study there was a clear difference in the effectiveness of the two devices in ameliorating the pain, weakness and dysfunction associated with lateral epicondylitis. There is also a possibility that the higher power output of the 10 W laser resulted in some heating of the tissue exposed to the laser and that the kinetic energy rather than PBM may have had an effect on the tendon repair. While this cannot be entirely discounted it is highly unlikely as the increase in skin temperature after a 5 minutes exposure to the laser was only 8°C (unpublished results) and there are no conclusive reports of heat being an effective treatment for epicondylitis in the literature.

Numerous cellular findings support the suggestion that the mechanism of the positive effect of laser treatment on tendinopathy is increased function, strength, and reduced

pain may be due to enhanced repair of tendonous tissues. Reports of reduced levels of pro-inflammatory mediators TNF- α , IL-6, TGF- β cytokines, and COX-2 enzyme [35], PGE₂ [21], and increased activation of NO [23] in damaged tendon have been made following LLLT treatment. Fibroblast metabolism appears to be enhanced with increased fibroblast proliferation [35] reduced fibroblast apoptosis [36] and an increase in collagen fibril size [19] and biomechanical strength [37] in response to PBM. Given that tendinopathy tends to be characterized by tendon degeneration that is persistent to existing treatment modalities, these findings are very promising to the many individuals who suffer from chronic tendon dysfunction.

CONCLUSION

Laser therapy using a 10 W class IV solid state diode dual wave-length (980/810 nm) laser with eight treatments of 3,000 J each over 18 days was found to be a safe and efficacious treatment for the reduction of pain and loss of strength seen with chronic tendinopathy of the extensor carpi radialis brevis tendon. The potential for a quickly

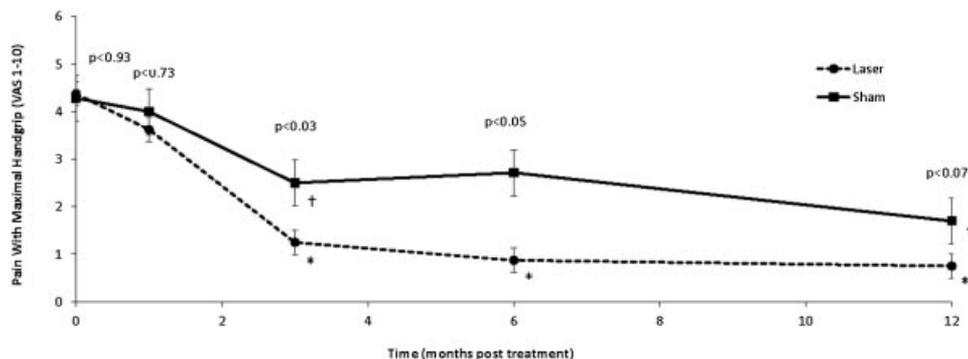


Fig. 6. Pain With Maximum handgrip contraction (VAS 1-10). Shown P values are for the difference in perceived pain between laser and sham treatments ($df = 48$). Significantly different from pre-treatment; * $P < 0.001$, † $P < 0.02$. Power = 0.62.

administered, safe and effective treatment of tendinopathy warrants further investigation.

ACKNOWLEDGEMENTS

The authors wish to recognize Dr. M. Petznick, Dr. J. Kiefer, Dr. P. Alasky, F. Hurley, and K. Zicarelli for their assistance with the data collection as well as Dr. D. Sachs for his assistance with the statistical analysis and A. Roberts and H. Gerelle for their assistance with data handling and manuscript preparation.

REFERENCES

1. Fredberg U, Stengaard-Pedersen K. Chronic tendinopathy tissue pathology, pain mechanisms, and etiology with a special focus on inflammation. *Scand J Med Sci Sports* 2008;18:3–15.
2. Khan KM, Cook JL, Kannus P, Maffulli N, Bonar SF. Time to abandon the “tendinitis” myth. *BMJ* 2002;324:626–627.
3. Potter HG, Hannafin JA, Morwessel RM, et al. Lateral epicondylitis: Correlation of MR imaging, surgical, and histopathologic findings. *Radiology* 1995;196:43–46.
4. Khan KM, Cook JL, Bonar F, Harcourt P, Astrom M. Histopathology of common overuse tendon conditions: Update and implications for clinical management. *Sports Med* 1999;27:393–408.
5. Knobloch K. The role of tendon microcirculation in Achilles and patellar tendinopathy. *J Ortho Surg Res* 2008;3:18–31.
6. Jozsa LG, Kannus P. *Human tendons: Anatomy, physiology, and pathology*. Champaign, IL: Human Kinetics; 1997.
7. Johnson GW, Cadwallader K, Scheffel SB, Epperly TD. Treatment of lateral epicondylitis (disease/disorder overview). *Am Fam Physician* 2007;76:843–848.
8. Wilson JJ, Best TM. Common overuse tendon problems: A review and recommendations for treatment. *Am Fam Physician* 2005;72:811–818.
9. Struijs PA, Smidt N, Arola H, Dijk CN, Buchbinder R, Assendelft WJ. Orthotic devices for the treatment of tennis elbow. *Cochrane Database of Syst Rev* 2002;1:CD001821. DOI: 10.1002/14651858.CD001821
10. Green S, Buchbinder R, Hetrick SE. Physiotherapy interventions for shoulder pain. *Cochrane Database of Syst Rev* 2003;2:CD004258. DOI: 10.1002/14651858.CD004258
11. Brosseau L, Casimiro L, Milne S, Robinson VA, Shea BJ, Tugwell P, Wells G. Deep transverse friction massage for treating tendinitis. *Cochrane Database of Syst Rev* 2002;4:CD003528. DOI: 10.1002/14651858.CD003528
12. Woodley BL, Newsham-West RJ, Baxter GD. Chronic tendinopathy: Effectiveness of eccentric exercise. *Br J Sports Med* 2007;41:188–198. DOI: 10.1136/bjsm.2006.029769
13. Coombes BK, Bisset L, Brooks P, Khan A, Vicenzino B. Effect of corticosteroid injection, physiotherapy, or both on clinical outcomes in patients with unilateral lateral epicondylalgia. A randomized controlled trial. *JAMA* 2013;309(5):461–469.
14. Stahl S, Kaufman T. The efficacy of an injection of steroids for medial epicondylitis: A prospective study of sixty elbows. *J Bone Joint Surg Am* 1997;79:1648–1652.
15. Buchbinder R, Green SE, Youd JM, Assendelft WJ, Barnsley L, Smidt N. Shock wave therapy for lateral elbow pain. *Cochrane Database of Syst Rev* 2005;4:CD003524. DOI: 10.1002/14651858.CD003524.pub2
16. Rompe JD, Furia J, Maffulli N. Eccentric loading compared with shock wave treatment for chronic insertional achilles tendinopathy: A randomized, controlled trial. *J Bone Joint Surg Am* 2008;90:52–61.
17. Hearnden A, Desai A, Karmegam A, Flannery M. Extracorporeal shock wave therapy in chronic calcific tendinitis of the shoulder—Is it effective? *Acta Orthop Belg* 2009;75(1):25–31.
18. Eells JT, Wong-Riley MTT, VerHoevec J, et al. Mitochondrial signal transduction in accelerated wound and retinal healing by near-infrared light therapy. *Mitochondrion* 2004;4:559–567.
19. Fung DT, Ng GY, Leung MC, Tay DK. Effects of a therapeutic laser on the ultrastructural morphology of repairing medial collateral ligament in a rat model. *Lasers Surg Med* 2003;32(4):286–293.
20. Bjordal JM, Lopes-Martins AM, Iverson VV. A randomized, placebo controlled trial of low level laser therapy for activated Achilles tendinitis with microdialysis measurement of peritendinous prostaglandin E₂ concentrations. *Br J Sports Med* 2006;40:76–80.
21. Marcos RL, Leal Junior EC, Messias Fde M, de Carvalho MH, Pallotta RC, Frigo L, dos Santos RA, Ramos L, Teixeira S, Bjordal JM, Lopes-Martins RA. Infrared (810 nm) low-level laser therapy in rat achilles tendinitis: A consistent alternative to drugs. *Photochem Photobiol* 2011;87(6):1447–1452. Epub 2011 Oct 7 DOI: 10.1111/j.1751-1097.2011.00999.x
22. Houeld NN, Abrahamse H. Laser light influences cellular viability and proliferation in diabetic-wounded fibroblast cells in a dose- and wavelength-dependent manner. *Lasers Med Sci* 2008;23:11–18.
23. Samoilova KA, Zhevago NA, Petrishchev NN, Zimin AA. Role of nitric oxide in the visible light-induced rapid increase of human skin microcirculation at the local and systemic levels II: Healthy volunteers. *Photomed Laser Surg* 2008;26(5):443–449.
24. Larkin KA, Martin JS, Zeanah EH, True JM, Braith RW, Borsari PA. Limb blood flow after class 4 laser therapy. *J Athl Train* 2012;47(2):178–183.
25. Bisset L, Paungmali A, Vicenzino B, Beller E. A systematic review and meta-analysis of clinical trials on physical interventions for lateral epicondylalgia. *Br J Sports Med* 2005;39:411–422.
26. Bjordal JM, Rodrigo JM, Lopes-Martins AM, et al. A systematic review with procedural assessments and meta-analysis of low level laser therapy in lateral elbow tendinopathy (tennis elbow). *BMC Musculoskeletal Disorders* 2008; 9:75–90.
27. Tumilty S, Munn J, McDonough S, Hurley DA, Basford JR, Baxter GD. Low level laser treatment of tendinopathy: a systematic review with meta-analysis. *Photomed Laser Surg* 2010;28(1):3–16.
28. OCEBM Levels of Evidence Working Group. The Oxford 2011 Levels of Evidence. Oxford Centre for Evidence-Based Medicine. Available at: <http://www.cebm.net/index.aspx?o=5653> Accessed Jan 16, 2013.
29. Ashford RF, Nagelburg S, Adkins R. Sensitivity of the Jamar dynamometer in detecting submaximal grip effort. *J Hand Surg (Am)* 1996;21:402–405.
30. World Association of Laser Therapy [Internet]. Dosage Recommendations and Scientific Guidelines. Revised 2010. <http://www.walt.nu/dosage-recommendations.html>
31. SAS Institute Inc. 2008. *SAS/STAT 9.2. User's Guide*. Cary, NC: SAS Institute Inc.
32. Faul F, Erdfelder E, Lang AG, Buchener A. G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods* 2007;39(2):175–191.
33. Moges H, Wu X, McCoy J, Vasconcelos OM, Bryant H, Grunberg NE, Anders JJ. Effect of 810 nm light on nerve regeneration after autograft repair of severely injured rat median nerve. *Lasers Surg Med* 2011;43(9):901–906.
34. Chow RT, Johnson MI, Lopes-Martins RA, Bjordal JM. Efficacy of low-level laser therapy in the management of neck pain: A systematic review and meta-analysis of randomised placebo or active-treatment controlled trials. *Lancet* 2009;374:1897–1908.
35. Pires D, Xavier M, Araújo T, Silva JA, Aimbire F, Albertini R. Low-level laser therapy (LLLT; 780 nm) acts differently on mRNA expression of anti- and pro-inflammatory mediators in an experimental model of collagenase-induced tendinitis in rat. *Lasers Med Sci* 2011;26:85–94.
36. Frigo L, Fávero GM, Lima HJ, et al. Low-level laser irradiation (InGaAlP-660 nm) increases fibroblast cell proliferation and reduces cell death in a dose-dependent manner. *Photomed Laser Surg* 2010;28(Suppl 1):S151–S156.
37. Fung DT, Ng GY, Leung MC, Tay DK. Therapeutic low energy laser improves the mechanical strength of repairing medial collateral ligament. *Lasers Surg Med* 2002;31(2):91–96.