RESEARCH RESULTS – ANNOTATED BIBLIOGRAPHY

TENNIS ELBOW:

Roberts, Delia, et al. "The effectiveness of therapeutic class IV (10W) laser treatment for epicondylitis." *Lasers in Surgery and Medicine* (2013) doi: 10.1002/lsm.22140. (LiteCure® Laser used in study) 15 patients with documented chronic tendinosis of the elbow were randomized into sham or laser therapy treatment. The laser group received eight 5.5 minute treatments of 10 J/cm2 every-other day for 18 days. Follow-up evaluations were made at 3, 6 and 12 months. Multiple pain measures, handgrip strength and functional impairment all improved with respect to sham treatment. Statistical significance was maintained to 1 year follow-up.

PLANTAR FASCIITIS

A recent study demonstrates the effectiveness of low level laser on the reduction of pain with plantar fasciitis as well as changes in the thickness of the fascia after laser treatment.

FROZEN SHOULDER:

Favejee M. M., B M A Huisstede,and B W Koes. "Frozen shoulder: the effectiveness of conservative and surgical interventions— systematic review." *British Journal of Sports Medicine* 45.1 (January 2011): 49-56.70 patients with clinically verified subacromial impingement were randomized to receive 10 treatments (5 days a week for 2 weeks) of either ultrasound or laser therapy. Ultrasound was administered at 1 MHz for 10 minutes. 2050 J of laser therapy was administered to the same treatment area over 10 minutes. After the treatment period the laser therapy group had reduced pain, improved articular movement, functionality and muscle strength in the affected shoulder compared to the ultrasound group ($P<0.005$).

A significant improvement in laser therapy compared to the control group. The treatment group experienced significantly less pain and significantly improved disability scores. Range of motion in the treatment group was better than placebo. *Photomed Laser Surg. 2008 Mar 16.*

ACHILLES TENDONITIS:

Carcia, Christopher R., et al. "Achilles Pain, Stiffness, and Muscle Power Deficits: Achilles Tendinitis–Clinical Practice Guidelines Linked to the International Classification of Functioning, Disability, and Health from the Orthopaedic Section of the American Physical Therapy Association." *Journal of Orthopaedic & Sports Physical Therapy* 40.9 (September 2010): A1-A26. The Orthopaedic Section of the APTA recommends that clinicians should consider the use of laser therapy to decrease pain and stiffness in patients with Achilles tendinopathy.

Tumilty, Steve, et al. "Low Level Laser Treatment of Tendinopathy: A Systematic Review with Meta-analysis." *Photomedicine and Laser Surgery* 28.1 (February 2010): 3-16.A review of 25 clinical trials of laser therapy for the treatment of tendinopathy. 12 trials had positive results and 13 were inconclusive or showed no significant effect. Dosing in the 12 positive trials supports the existence of an effective dosing window from 1-9 J/cm2 depending on the depth of the tendon.

FIBROMYALGIA:

Panton, Lynn, et al. "Effects of class IV laser therapy on fibromyalgia impact and function in women with fibromyalgia." *Journal of Alternative and Complementary Medicine* (2013) 19.5: 445-452. (LiteCure® Laser used in study) 39 women with

fibromyalgia syndrome were randomized to receive laser therapy treatment or sham heat gun treatment. Treatments were administered twice a week for 4 weeks at eight tender points across the neck, shoulders and back. Laser therapy treatment significantly improved upper body flexibility, fibromyalgia impact score and a composite measure of pain compared to the sham treatment.

MYOFASCIAL PAIN:

International Association for the Study of Pain. "Myofascial Pain." Global Year Against Musculoskeletal Pain. IASP. October 2009-October 2010. Web. August 4, 2012. < http://www.iasp-pain.org/Content/NavigationMenu/GlobalYearAgainstPain/20092010MusculoskeletalPain/FactSheets/default.htm>.Position paper from the International Association for the Study of Pain that recommends the use of laser therapy in the treatment of Myofascial Pain: "Laser Therapy shows strong evidence of effectiveness for pain relief."

NERVE HEALING:

Knapp, Daniel J. "Postherpetic neuralgia: Case study of class 4 laser therapy intervention." *The Clinical Journal of Pain* (April 17, 2013) Published online ahead of print. (LiteCure® Laser used in study) Case study of laser treatment on a woman diagnosed with PHN (postherpetic neuralgia). The 73-year-old woman had pain in her upper back, shoulder and arm that had lasted for 15 years after a case of shingles. Pain decreased after 8 weekly class 4 laser treatments (2 to 4 W, 3.5 to 7.1 J/cm2).

Contolled trial showed regeneraton of sciatic nerve and myelination in rat. *Rochkind. Photomed & Laser Surg. 2007, 25(3): 137-143.*

*Saidu, Edward, et al. "980 nm wavelength light decreases mechanical allodynia in a rat neuropathic pain model." ASLMS 2013 annual meeting. Presentation abstract. (LiteCure® Research Collaboration)Study examined the effects of laser treatment on rats with nerve injury. Rats were injured and either treated with a 980 nm wavelength laser (LT) or in a control group (CTRL). Laser treatment significantly decreased mechanical allodynia. In the LT group there was also regeneration of the intra-epidermal nerve fibers, re-innervation of the LC and a decrease in expression of PGP9.5.

*Anders, Juanita J., Stefano Geuna and Shimon Rochkind. "Phototherapy promotes regeneration and functional recovery of injured peripheral nerve." *Neurological Research* 26 (March 2004): 233-239.This review presents several studies that evaluate the efficacy of laser therapy to promote regeneration and recovery of injured peripheral nerve. Studies include a crush injury model of the rat facial nerve, injured rat sciatic nerve and regeneration after surgical repair. All studies demonstrated the efficacy of laser therapy for treating nerves and the technique was identified as "one of the most promising therapies to date" for these difficult pathologies.

Chow, Roberta, et al. "Inhibitory Effects of Laser Irradiation on Peripheral Mammalian Nerves and Relevance to Analgesic Effects: A Systematic Review." *Photomedicine and Laser Surgery* 29.6 (2011): 365-381. 44 studies of laser therapy were reviewed for inhibitory effects on peripheral nerve pain. In 13 of 18 human studies laser therapy was shown to slow conduction velocity and/or reduce the amplitude of compound action potentials. Several mechanisms for the analgesic effects of laser therapy are also discussed.

PERIPHERAL NEUROPATHY:

After treatment, there was an improvement of 71%. Only 43% continued to have loss of protective sensation. Light treatment associated with a reduced incidence of diabetic foot wounds and amputations
J Am Podiatr Med Assoc. 2005 Mar-Apr; 95 (2)
*Anders, Juanita, et al. “Light interaction with the peripheral nervous system: in vivo and in vitro models of neuropathy.” WALT. Queensland, Australia. September 2012. Presentation abstract. (LiteCure® Research Collaboration). Dr. Anders presented a series of studies on the effect of laser therapy on nerves. Cell culture experiments on rat cortical and dorsal root ganglion neurite extension were used to determine optimal laser dosing at 980 nm and 810 nm. After measuring real penetration to the target tissue, these dosing criteria were then tested successfully in functional models of rabbit peroneal nerve injury and a rat spared nerve injury. Preliminary histology results were presented to support the functional result.

BONE HEALING:

LOW-LEVEL LASER THERAPY VS LOW-INTENSITY PULSED ULTRASOUND (LIPUS): LIPUS enhanced bone repair by promoting bone resorption; LLLT accelerated this process through bone formation. *Photomed Laser Surg. 2006 Dec; 24 (6):735-40*
Laser creates an increase in Osteoblasts & Calcium in fracture sites.
Pinheiro L, Photomed Laser Surg. 2006 Jun;24 (2):169-171
Laser improves osteoblastic formation, bone strength in fractures, implant stability, and can improve osteonecrosis of the jaw.
Lasers Med Sci. 2010 Jul; 25(4): 559-69), Photomed Laser Surg. 2010 Jun; 28(3): 365-9 Lasers Surg Med 2009 Apr;41(4):298-304, J Orthop Surg Res. 2010 Jan 4;5(1):1

NECK PAIN:

Lee, Eric, et al. “A pilot study to determine the efficacy of therapeutic class IV laser treatment on local muscle spasm associated with myofascial pain syndrome in patients with neck pain.” AAPM 2013 annual meeting. Poster abstract. (LiteCure® Laser used in study)Pilot study consisting of ten patients with at least one month of myofascial pain. Patients underwent two weeks of class IV laser treatment. A majority of the patients who underwent laser therapy showed improvement in pain assessment at 25 and 30 days post treatment. This study warrants a larger, controlled clinical study.
Chow, Roberta T., et al. “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.” *The Lancet* 374 (5 December 2009): 1897–1908.Seminal review of Laser Therapy for Neck Pain published in a top-tier medical journal. 16 RCTs including 820 individual patients were included in the review. Laser therapy was found to immediately reduce neck pain and maintained results up to 22 weeks after completion of treatment. Also, most statistical heterogeneity disappeared when Chow excluded studies with small doses or flaws in
95% EFFECTIVENESS AT RELIEF OF NECK PAIN; RECURRENCE OF PAIN 58% IN PLACEBO GROUP, BUT ONLY 14% IN LASER TREATED GROUP
Soriano et al, Laser Therapy, 1996 (8) pp 149-154

LOW BACK PAIN:

Fiore, P., et al. “Short-term effects of high-intensity laser therapy versus ultrasound therapy in the treatment of low back pain: a randomized controlled trial.” *European*

Journal of Physical and Rehabilitation Medicine 47.3 (September 2011): 367-373.30 consecutive patients with clinically verified sub-acute or chronic low back pain. Patients were randomized to receive 15 treatments (5 days a week for 3 weeks) of either ultrasound or laser therapy. Ultrasound was administered at 1 MHz for 10 minutes. 2600 J of laser therapy was administered to the same treatment area over 10 minutes. The laser therapy group "showed a statistically significant reduction of Visual Analog Scale pain and Oswestry Low Back Pain Disability Questionnaire scores with respect to Ultrasound at the end of treatment ($P<0.005$)."
Morries, L.D. "Class IV Laser Therapy; Effective For Back And Neck/Shoulder Pain." 2010 ACBSP Annual Conference. University of Colorado Denver. Los Angeles. June 2010. Poster Presentation. (LiteCure® Laser used in study) 55 patients with low back pain were randomized to receive either manual adjustment or adjustment followed by laser therapy. After 4 weeks the laser therapy group had a 71% reduction in pain score (VAS) and was significantly better than manipulation alone.

INFLAMMATION:

Pires, Débora, et al. "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 in Medical Science* 26 (January 2011): 85–94. A rat model of induced tendonitis was used to evaluate the effect of laser therapy on inflammatory signaling. 42 rats were randomized evenly into laser and control populations. Rats in the laser group were treated at 780 nm with a fluence of 7. 7 J/cm2 every-other day starting at 12 h or day 7 through the end of the study. The laser group had significantly lower IL-6, COX-2 and TGF-β than control animals in both acute and chronic phases. Laser therapy significantly reduced TNF-α only at the chronic phase. Laser therapy is effective for the reduction of mRNA expression for pro-inflammatory mediators.

ULTRASOUND vs. LASER

Animal study; laser treatment provided a much greater increase in the wound strength than ultrasound.
J Rehab Res & Dev, Volume 41 Number 5, September/October 2004
LOW-LEVEL LASER THERAPY VS LOW-INTENSITY PULSED ULTRASOUND (LIPUS): LIPUS enhanced bone repair by promoting bone resorption; LLLT accelerated this process through bone formation. *Photomed Laser Surg. 2006 Dec; 24 (6):735-40*

CORTISONE vs LASER:

Animal study; 810-nm laser was almost as good as cortisone at reducing swelling. Higher doses showed most benefit. Laser therapy reduced joint swelling and correlated with decreased serum prostaglandins
Castano AP, Lasers Surg Med 2007 Jul;39(6):543-50

NON-STEROIDALS vs LASER:

Laser as effective as NSAIDs
Bjordahl J, Photomed Laser Surg. 2006 Jun; 24 (2):158-168

TEMPORMANDIBULAR JOINT (TMJ):

Dostalová, Tatjana, et al. "Effectiveness of Physiotherapy and GaAlAs Laser in the Management of Temporomandibular Joint Disorders." *Photomedicine and Laser Surgery* 30.5 (2012): 275–280.27 patient prospective case series on patients with clinically verified TMJ disorder. Subjects received 5 weekly treatments using a 830 nm

laser on 3 points in contact mode at an energy density of 15.4 J/cm2. After treatment population VAS was reduced by 85% and jaw range of motion increased by 24%. “The laser therapy was effective in the improvement of the range of temporomandibular disorders (TMD) and promoted a significant reduction of pain symptoms.”
Kulekcioglu, Sevinc, et al. “Effectiveness of low-level laser therapy in temporomandibular disorder.” *Scandinavian Journal of Rheumatology* 32 (January 2003): 114-118. 35 patients with TMJ verified by MRI were randomized to laser therapy treatment or control. Patients in the treatment group received 15 treatments of 3 J/cm2 at 904 nm. Both groups improved in all measures over the study period. The laser group had significantly better improvement in the number of tender points and all range of motion measures.
Decreased of pain and anti-inflammatory effects; Confirmed by thermographic examination.
Photomed Laser Surg. 2006 Aug;24 (4):522-7

OTHER:

Borsa, Paul A., et al. “Does phototherapy enhance skeletal muscle contractile function and **postexercise recovery**? A systematic review. *Journal of Athletic Training* 48.1 (2013): 57-67. Review of published laser therapy studies. Phototherapy before resistance exercise may enhance contractile function, reduce exercise-induced muscle damage, and facilitate post-exercise recovery.
Larkin, Kelly, et al. “Phototherapy prolongs time to task failure in older adults.” Neuroscience 2012. New Orleans, LA. October 2012. Presentation abstract. (LiteCure® Research Collaboration) 42 right-hand dominant subjects, equally divided in age groups 18-35 yrs or 65-90 yrs, were randomized to treatment and control groups. The treatment group received 10 J/cm2 pre-treatment to the first dorsal interosseus before **exercise to failure.** Results indicate that laser therapy shows promise to enhance time to task failure, prevent loss of muscular strength and delay the onset of **musculoskeletal fatigue** in older adults.
Naeser, Margaret A., et al. “Improved Cognitive Function After Transcranial, Light-Emitting Diode Treatments in Chronic, **Traumatic Brain Injury**: Two Case Reports.” *Photomedicine and Laser Surgery* 29.5 (May 2011): 351-358. 2 case studies are presented that demonstrate the potential effectiveness of laser therapy applied transcranially to the forehead and scalp for the treatment of traumatic brain injury (TBI).
Moges, Helina, et al. “980 nm laser irradiation improved functional recovery after **peroneal nerve injury** in rabbits.” ASLMS. Dallas, TX. April 2011. Presentation Abstract. (LiteCure® Research Collaboration) 12 rabbits were subjected to peroneal nerve injury followed by primary repair and randomized into laser therapy and control groups. The laser group received 10 daily treatments at 980 nm light for 40 seconds totaling 7.5 J/ cm2. Functional recovery was assessed weekly for 9 weeks using the toe-spread reflex. At week 6 the laser therapy group showed statistically significant functional recovery over the sham group and continued to improve to week 9. Functional recovery in the laser therapy group was 86.9% at week 9. “980 laser irradiation successfully promoted earlier and faster functional recovery after peroneal nerve transection and surgical repair.”

Frigo, Lucio, **F**et al. “Low-Level Laser Irradiation (InGaAlP-660 nm) Increases Fibroblast Cell Proliferation and **Reduces Cell Death** in a Dose-Dependent Manner.” *Photomedicine and Laser Surgery* 28.1 (August 2010): S151–S156. In cell culture, primary fibroblasts treated with laser at 660 nm were shown to increase proliferation and decrease cell death at an irradiance of 2.5 W/cm2 and a fluence of 150 J/cm2.

Hashmi, J.T., et al. “Effect of Pulsing in Low Level Light Therapy.” *Lasers in Surgery and Medicine* 42.6 (August 2010): 450–466. 33 studies comparing continuous wave (CW) and pulsed laser treatments were reviewed. A common criticism of these studies is the lack of direct, like-for-like comparison of pulsed treatment to CW. The article concludes “**CW is the gold standard** and has been used for all LLLT applications” and “there is no consensus on the effects of different frequencies and pulse parameters on the physiology and therapeutic response of various disease states that are often treated with laser therapy. This has allowed manufacturers to claim advantages of pulsing without hard evidence to back up their claims.”

Wu, Xingjia, et al. “Differential response of neurons to light irradiation in an in vitro **diabetic** model.” ASLMS. Phoenix, AZ. April 2010. Presentation abstract. (LiteCure® Research Collaboration) Primary cortical and dorsal root ganglion neurons were pre-treated in high glucose media to induce die-back in a cell culture model of diabetic cell damage. In cortical neurons 980 nm irradiation at 0.01, 0.05 and 0.2 J/cm2 significantly increased neurite extension. For DRG’s subjected to high glucose media, 810 nm light at 0.01 J/cm2 significantly increased neurite extension.

Erbele, Isaac, et al. “Optimization of dose and power density of 980 nm and 810 nm light based on **mitochondrial activity**.” SPIE. The Moscone Center, San Francisco. 23 January 2010. Presentation Abstract. (LiteCure® Research Collaboration) Human fibroblasts were exposed to 980 nm and 810 nm irradiation at a range of irradiance and fluence parameters in cell culture. Response was measured by MTS assay for mitochondrial activity. A 980 nm dose of 5 J/cm2 at 10 mW/cm2 caused an 11% increase in mitochondrial activity. 810 nm doses of 1 and 5 J/cm2 at 50 mW/cm2 caused a 40% increase. Results indicate that different wavelengths require different dosing to increase mitochondrial activity.

Bashkatov, A N, et al. “Optical properties of **human skin**, subcutaneous and mucous tissues in the wavelength range from 400 to 2000 nm.” *Journal Of Physics D: Applied Physics* 38 (2005): 2543–2555. Bashkatov investigates the optical properties of human tissue in the visible and near infrared. Tissue penetration depth, defined as the depth of 37% of surface exposure, is found to be between 2.25 mm and 2.50 mm into skin and between 4.5 mm and 6.0 mm in mucous tissue for the wavelengths used in laser therapy devices.

Al-Watban, Farouk A.H., and X. Y. Zhang. “The Comparison of Effects between Pulsed and CW Lasers on **Wound Healing**.” *Journal of Clinical Laser Medicine & Surgery* 22.1 (2004) 15-18.\This study evaluated both continuous wave (CW) and pulsed laser therapy in an elliptic wound model in rats. This study is one of the few published reports that evaluates both pulsed and CW therapy compared to a sham control. All laser parameters improved wound healing. Maximal benefit was achieved using CW laser therapy. Optimal dosing for wound healing was 5 J/cm2.

Whelan, Harry T., et al. “NASA Light-Emitting Diodes for the Prevention of Oral Mucositis in Pediatric **Bone Marrow Transplant** Patients.” *Journal of Clinical Laser Medicine & Surgery* 20.6 (December 2002): 319-324. 23 consecutive pediatric patients that received chemotherapy in preparation for bone marrow transplant were given 4 J/cm2 phototherapy daily for 14 days at 670 nm. Ulcerative oral mucositis rates in this case series were reduced by 20-40% compared to historical controls.