

Interventional Therapy

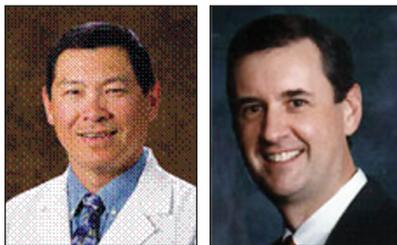
Treating Sports-Related Injury and Pain with Light Therapy

Light therapy is a non-invasive, non-drug modality that stimulates the body's own healing mechanisms via both molecular signaling and circulatory modulation.



This article addresses the likelihood of increasing sports injuries as Baby Boomers age, the limitations and dangers of current pain medications (NSAIDs, opioids), and the need for new, effective, non-invasive technology to speed recovery from sports-related injuries. One such technology is infrared (IR) therapy that demonstrates effective stimulation of the the body's own healing process from sports-related injuries and also appears to have value for pain control. The writers introduce a device (manufactured by BioCare Systems, Inc.) that is meant to provide treatment in a home use setting.

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By Joseph Hsin, MD and Jon Weston, MBA

50's deny the inevitable aging of their bodies in order to keep a youthful intensity to their sports activities. Meanwhile American children are being pushed into high intensity training and new levels of competitiveness at younger ages than ever before. And in the middle, X-treme sports rule. All of these factors are resulting in escalating levels of sports related injuries and pain. New modalities to treat injury and pain are proliferating and now a few "old" modalities are gaining broad audiences in the U.S.

The Evolution of Sports Medicine¹

Galen was a second century AD Greek physician who was one of the first to rigorously depict human anatomy. Working with gladiators in Rome, he gained first hand knowledge of anatomy and physiology through treating their wounds. As such, he might be considered the first "Sports Medicine Specialist." He was also a keen observer who used the gladiatorial athletes to test treatment modalities. Galen was also a creature of his time, prescribing what today would be considered odd treatments and curatives, including purgatives, blistering agents, and that foundation of medical intervention for 2,000 years: bleeding. But the Romans also understood the value of a hot bath and massage to health. Other modalities have made their way through the centuries as well. Acupuncture has been practiced in China for over a thousand years. Societies around the world and throughout time have taken advantage of the medicinal properties of a variety of plants containing natural opiate substances.

Modern Western Medicine: Approach to Injury and Pain

In the middle and late 19th century, western medicine made great strides forward in pain management with the chemical determination and synthesis of opiates for anesthesia and pain

control, and the isolation of salicylates from the bark of the willow tree to treat pain and inflammation. The powerful effectiveness of opiate treatments led western medicine to focus on pharmaceutical treatment of pain, almost to the exclusion of non-pharmaceutical approaches through much of the 20th century.

"New" Modalities for Treating Injury and Pain

However, drug therapy comes at a price. Non-steroidal anti-inflammatory drugs cause significant bleeding stomach ulcers in 2% of patients.² Twenty percent of these die of the bleeding. Newer COX-2 selective inhibitors obviate most of this risk, but bring in additional risks for those with concomitant cardiovascular disease. This has resulted in the withdrawal of several popular COX-2s including Vioxx and Bextra. Opiates have long been recognized for their addictive side effects. According to the Drug Enforcement Administration, 6.2 million people abuse prescription drugs.³ Therefore, new approaches to injury and pain management have emerged in western medicine over the past twenty years. The side effects and potential addiction problems associated with pharmaceutical approaches have contributed to the search for complimentary and alternative medicine for pain.

Acupuncture, electrical stimulation, acupressure, relaxation, and biofeedback are all being explored as alternatives or adjuncts to drug therapy. Electrical stimulation and ultrasound have been used more recently for stimulation of fracture healing. Controlled studies measuring the effectiveness of these therapies have brought them into the mainstream of legitimate approaches to therapy.

Light Therapies

A novel therapy introduced to western medicine over the past 15-20 years is photo-biostimulation, or light therapy. Phototherapy is the application of specific light wavelengths and energies to body tissues that elicits a complex chain of biochemical responses. Most of the focus is on red and near infrared wavelengths. Much of the early work was conducted in the former

Soviet Union and its East European satellite countries. The impetus was to improve performance and injury recovery in both military and athletic patients.

The technology currently being used in the U.S. is largely in the form of lasers. More recently, a number of devices have emerged which use Light Emitting Diodes (LEDs). LEDs provide a safer and more affordable technology for delivering light therapy (also referred to as phototherapy). Physiotherapists and sports medicine specialists are treating a wide variety of acute and chronic musculoskeletal injuries and pain with phototherapy. The benefits of light therapy are that they reduce the discomfort of pain and inflammation while promoting blood flow and the body's own tissue repair mechanisms.

Mechanisms of Action: IR and Tissue Healing

Infrared (IR) therapy stimulates the body's natural healing mechanisms. Evidence suggests that this occurs at both the molecular signaling level and at a more macro level through circulatory modulation. One of the most important mechanisms of action for near infrared light therapy is the release of nitric oxide. A naturally occurring chemical in the body, nitric oxide (NO) is a key signaling molecule which can set off a number of beneficial effects. Most notably, it has a critical role in promoting blood flow to tissues and increasing lymphatic drainage. Through the increase in lymphatic drainage, IR indirectly inhibits inflammation processes and thus reduces swelling.

IR Stimulation of Signaling Pathways

Recent work has shed light on the underlying mechanisms of tissue repair within the body. Conboy et al,⁴ investigated the influence of systemic factors on aged progenitor cells (specifically, satellite cells) of peripheral tissues such as muscle and liver. Muscle satellite cells are quiescent precursors interposed between myofibrils and a sheath of external lamina. Their activation and recruitment enables muscle repair and adaptation. Conboy's team conducted an experiment wherein they established parabiotic pairings (that is, a shared circulatory system) between young and old mice (heterochronic parabioses), exposing old mice to factors present in young serum. Notably, heterochronic parabiosis restored the activation of Notch signaling as well as the proliferation and regenerative capacity of aged satellite cells in muscle tissue. In vitro, the exposure of satellite cells from old mice to young serum enhanced the expression of the Notch ligand (Delta), increased Notch activation, and enhanced proliferation.

More insight into possible signaling mechanisms comes from work on nitric oxide in muscle tissue. Evidence points to nitric oxide as a mediator of satellite cell activation. Cell isolation and histology experiments showed that pharmacological inhibition of nitric oxide synthase (NOS) activity prevented the immediate injury-induced myogenic cell release and delayed the hypertrophy of satellite cells in muscle. NOS inhibition delayed and restricted the extent of repair and resulted in fiber branching (scarring).⁵

Modified muscle use or injury can produce a stereotypic inflammatory response in which neutrophils rapidly invade and are followed by macrophages. This inflammatory response coincides with muscle repair, regeneration, and growth involving activation and proliferation of satellite cells and followed by their terminal differentiation. New evidence also shows that muscle cells can release positive and negative regulators of inflammatory cell invasion, and thereby play an active role in modulat-

ing the inflammatory process. In particular, muscle-derived nitric oxide can inhibit inflammatory cell invasion of healthy muscle and protect muscle from lysis by inflammatory cells both in vivo and in vitro.⁶ This hypothesis is supported by recent work demonstrating that inhibition of nitric oxide synthase (NOS) activity increases muscle cell killing in neutrophil-muscle co-cultures. NO can normally protect muscle from damage by free radicals and thus play an important role in determining the course of muscle injury and repair.⁷

The net result in clinical studies suggests increased strength of tissue repair and minimal scarring. In both soft tissue and connective tissue injuries, infrared light therapy can increase the final tensile strength of the healed tissue. By increasing the amount of collagen production/synthesis and by increasing the intra and inter-molecular hydrogen bonding in the collagen molecules, IR therapy contributes to improved tensile strength.⁸⁻¹¹ The preceding effects combine to achieve an accelerated healing rate. The time from onset of injury to mature healed wound is reduced.¹²

IR Modulation of Local Circulatory Systems

There is evidence that the IR, via NO release, increases lymphatic circulation by increasing the diameter of the lymphatic vessels—not just by increased flow rates within the vessel at an unchanged diameter. This diameter increase helps explain the presence of large diameter protein cells within the normal bone circulation

“Light therapy works instead by stimulating natural biological processes in the area where the light is applied. Light emitting diodes (LEDs) offer a concentrated source of light energy in a narrow portion of the spectrum.”

that cannot be attributed to the vascular circulation. It also explains how debris and larger protein cells are removed from traumatized areas that are additionally stimulated by the use of IR.¹³

One study sought to determine the functional role of nitric oxide (NO) in regulating vascular conductance during high intensity dynamic exercise in skeletal muscles composed of all major fiber types. Administration of a nitric oxide synthase inhibitor reduced vascular conductance in 20 of the 28 individual hind limb muscles or muscle parts of rats examined during high speed treadmill exercise. These results suggest that NO contributes substantially to the regulation of vascular conductance within and among muscles during high intensity exercise.¹⁴

Mechanisms of Action: IR and Pain Reduction

IR has also been shown to have direct effects on pain signaling pathways. Studies of the effectiveness of light therapy on a number of chronic pain conditions suggest that it may have activity on specific nerve fibers involved in “slow conduction” of pain signals.¹⁵⁻¹⁷ Human and animal studies have found elevated levels of endorphins (small proteins which block pain signals in nerves) in response to light therapy. Infrared irradiation of intact rats results in an increase in ATP levels in their brains.¹⁸ In addition to serving as the energy currency of the cell, ATP can serve as a neurotransmitter itself or, metabolized to adenosine, bind to adenosine receptors that oppose excitatory nociceptive

responses that elicit the signaling of pain to the central nervous system. Acetylcholine is another critical neurotransmitter whose release¹⁹ and metabolism²⁰ is modulated by low-level light treatment. Light treatment also suppresses the action potentials elicited by the neuropeptide bradykinin in cultured murine dorsal root ganglion neurons.²¹ Suppression of bradykinin signaling in dorsal root ganglion will inhibit central transmission of pain signals.

Human Studies of IR Therapy

Sports injuries usually involve trauma to muscles, joint ligaments, tendons or bones. Combining the NO-induced enhancement of arterial/venous circulation with lymphatic drainage, a possible application is suggested for soft tissue and bone injury. Enhanced arterial circulation delivers more nutrients to the site of injury while increased venous circulation and lymphatic drainage reduces swelling and increases debridement of damaged tissue.

Clinical Studies of Sports-Related Trauma

The following prospective clinical study is illustrative. Forty-seven soccer players with second degree ankle sprains, were selected at random, and divided into three groups. The first group (n = 16) was treated with the conventional initial treatment (RICE—rest, ice, compression, elevation), the second group (n = 16) was treated with the RICE method plus placebo laser, and the third group (n = 15) was treated with the RICE method plus an 820-nm GaAlAs diode laser. Before the treatment, and 24, 48, and 72 hours later, the volume of the edema was measured. Results from a three by three repeated measures ANOVA with a follow up post hoc test revealed that the group treated with the RICE and an 820-nm infrared light presented a statistically significant reduction in the volume of the edema after 24, 48 and 72 hours compared to RICE alone.²²

Kumar reported a comparative study in 50 patients with inversion injuries of the ankle. He found that IR treated patients showed a more rapid resolution of symptoms and an earlier return to full weight bearing compared to conventional physiotherapy-treated patients.²³

A broad clinical study was performed on 74 patients with injuries to the following anatomic locations: ankle and knee, bilaterally, Achilles tendon; epicondyles; shoulder; wrist; interphalangeal joints of hands, unilaterally. All patients had surgical procedure performed prior to infrared light treatment. Comparison of the healing process between two groups of patients showed that wound healing was significantly accelerated (25%-35%) in the group of patients treated with infrared light.²⁴

Finally, a review of nine separate placebo controlled trials measuring pain and range of motion scores in tendinopathies showed an average 32% improvement in treated over untreated patients.²⁵

Studies of Bone Healing

As far as is known, the first attempt at treating bone fracture with infrared light was reported by Shugaharov and Voronkov. In 1974 they used low level laser radiation (infrared wavelengths) on fracture sites while observing intramedullar osteosynthesis.²⁶ Gatev studied the effect of stimulating repair of fractures with He-Ne laser. The majority of patients had fractures of the distal radius treated with a plaster cast. On the 5th

to 8th day after injury a hole was cut out of the cast over the fracture site and laser radiation applied. Evaluations were made based on radiographic evidence and clinical assessment. Results showed statistically significant differences [$p < 0.001$] from the control group in favor of light treated fractures.²⁷ Numerous other case studies are in the literature, some quite dramatic. But the authors have as yet to see a large controlled clinical trial on fracture outcomes with IR therapy.

Studies of Pain

In a study of pain, sixty patients between 20 and 65 years of age with clinically and radiologically diagnosed cervical osteoarthritis were randomised into two equal groups according to the therapies applied, either with infrared light therapy or placebo treatment. Patients in each group included pain-related physical findings, such as increased paravertebral muscle spasm, loss of lordosis — and range of neck motion restriction — before and after therapy. Functional improvements were also evaluated. Pain, paravertebral muscle spasm, lordosis angle, the range of neck motion and function were observed to improve significantly in the treatment group, but no improvement was found in the placebo group.²⁸

In a double blind study of post-operative pain, 20 patients undergoing elective cholecystectomy were randomly allocated for either IR treatment or as controls. Results showed a significant difference in the number of doses of intra-muscular narcotic analgesic injections required between the two groups. Controls required more than double the pain medication. No patient in the IR group required pain medication after 24 hours. Similarly, the requirement for oral analgesia was reduced in the IR group. Once again, controls required double the doses compared to the treated group. Control patients assessed their overall pain as moderate to severe compared with mild to moderate in the IR group.²⁹

LED Versus Laser Light Sources

Light therapy simply refers to the use of portions of the electromagnetic spectrum—from the far red to near infrared—to elicit beneficial biological responses. Since many of the studies originally involved the use of lasers as a source of well-controlled, narrow-spectrum light, the term 'low level' is used to distinguish it from the high power applications of surgical lasers designed for cutting or ablation of tissue. Light therapy works instead by stimulating natural biological processes in the area where the light is applied. Light emitting diodes (LEDs) offer a concentrated source of light energy in a narrow portion of the spectrum. LEDs are a cheaper, easier alternative to lasers as an output source for controlled, narrow-spectrum light. In this way one can tap the beneficial portion of the spectrum, such as near infrared, without the potentially harmful regions of the spectrum of sunlight such as ultraviolet. Results of light therapy are a direct effect of light itself, generated at specific wavelengths, and are not necessarily a function of the characteristics of coherency and polarization associated with lasers.³⁰

Practical Application of Infrared Modalities

Numerous infrared laser modalities exist. Most of this equipment is for office based use. Recently a number of LED based IR modalities have appeared, again in office based configurations. On the other end of the scale, a myriad of home use de-

vices have been introduced by way of “in-fomercials” with very little science behind the devices, and very little effectiveness. Most of them have been removed from the market due to non-compliance with FDA standards.

Among the most recently FDA-cleared and compliant over-the-counter devices, is the LumiWave Infrared Therapy Device (manufactured by BioCare Systems, Inc.). This small portable unit consists of a flexible bracelet with four, 4cm. X 5cm. pods, each arrayed with 49 LEDs, and a hand held control pod with two settings for high and low temperatures. The LumiWave emits 900 nm wave length near infrared light and maintains a temperature of 42°C (high setting) or 41°C (low setting). Well-suited for home use, it is light, portable, and contains automated features to control the amount of energy deposited. It holds a consistent temperature, and turns itself off once the appropriate dosage has been applied. Treatments are local. The bracelet is simply wrapped over the affected body area (knee, ankle, shoulder) and turned on.

Treatments are typically given twice per day, or as often as every six hours. More frequent treatments mean faster progress toward healing. Due to the benefits of frequent treatment, infrared therapy is best suited for home use. With product cost a fraction of office based modalities, the LumiWave can be purchased in numbers and rented to patients for home use, or patients can be directed to self-purchase a unit.

Conclusion

With the proliferation of sports activities at all ages—predictably resulting in increased presentation of sports injuries—the clinician needs more treatment options at their disposal. Infrared light therapy is likely to grow in popularity as evidence of its efficacy and range of applications becomes more widely known. Non-invasive treatments and non-drug modalities, such as IR therapy, provide inviting and valuable options for the clinician's armamentarium. ■

Joseph Hsin, MD, specializes in sports medicine and general orthopaedics, and has been a part of the Denver Metro community since 1976. Dr. Hsin is involved in numerous community activities including serving as a team physician for several local high schools, Colorado Christian University, and the Denver Barbarians Rugby Club. He periodically

speaks to local community gatherings on orthopedic topics and writes on the subject of sports medicine for local papers. He is a clinical instructor at Denver Health and Hospitals and precepts medical students and internships.

Jon Weston serves as Vice President and Chief Operating Officer to BioCare Systems, Inc. Mr. Weston received a B.A. in molecular, cellular and developmental biology from the University of Colorado and an M.B.A. from the University of Denver. Previously, Mr. Weston was director of global marketing for Navigant Biotechnologies — a wholly owned subsidiary of Gambro, Inc. — a company focused on developing a process for eliminating viruses and other pathogens from donated blood. Before Navigant, he served respectively as senior business unit manager/e-business, business development manager and marketing manager for Gambro BCT. Earlier in his career, Mr. Weston held business and marketing positions with G.D. Searle, Inc. (now Pfizer), and Coors Biotech, Inc.

References

1. Wiley GW. "The Evolution of Athletes," side bar in "Fifty Years of Sports Medicine: The Arthroscope and a Glean in the MRI." *Orthopedic Technology Review*. May/June 2005. p 24.
2. Cooke C. Disease management: Prevention of NSAID-induced gastropathy. *Drug Benefit Trends*. 1996. 8(3):14-15,19-22.
3. Speech by Karen P. Tandy, Administrator, U.S. Drug Enforcement Administration, Operation Cyber Chase Press Conference. Washington, D.C. April 20, 2005. <http://www.usdoj.gov/dea/speeches/s042005.html>
4. Irina M, Conboy MJ, Wagers AJ, Girma ER, Weissman IL, and Rando TA. Rejuvenation of aged progenitor cells by exposure to a young systemic environment. *Nature*. 17 February 2005. 433, 760-764 | doi: 10.1038/nature03260.
5. Anderson JE. A Role for Nitric Oxide in Muscle Repair: Nitric Oxide-mediated Activation of Muscle Satellite Cells. *Molecular Biology of the Cell*. May 2000. 11:1859-1874.
6. Tidball JG. Inflammatory processes in muscle injury and repair. *Am J Physiol Regul Integr Comp Physiol*. Feb 2005. 288(2):R345-53.
7. Ibid.
8. Reddy GK, Stehno-Bittel L, and Enwemeka CS. Laser photo stimulation accelerates wound healing in diabetic rats. *Wound Repair and Regeneration*. 2001. 9:248-255.
9. Stadler I, et al. 830 nm irradiation increases the wound tensile strength in diabetic murine model. *Lasers in Surgery and Medicine*. 2001. 28 (3):220- 226.
10. Parizotto N, et al. *Structural analysis of collagen fibrils after He-Ne laser photostimulation*. 2nd Congress, World Association for Laser Therapy. Kansas City. 1998.
11. Simunovic Z, et al. Low level laser therapy of soft tissue injuries upon sport activities and traffic accidents: a multicenter, double-blind, placebo-controlled clinical study on 132 patients. Pain Center-Laser Center, Locarno, Switzerland. Abstract from II Congress of the Internat. Assn for Laser and Sports Medicine, Rosario, Argentina. March 10-12, 2000.
12. Naeser MA, Hahn, HK, Lieberman, BE, and Branco KF. Carpal tunnel syndrome pain treated with low-level laser and microamperes Transcutaneous Electric Nerve Stimulation: a controlled study. *Archives of Physical Medicine and Rehabilitation*. 2002. 83: 978-988.
13. *Bone Stimulation by Low Level Laser - A Theoretical Model for the Effects*. Philip, Gable B App Sc PT. G Dip Sc Res (LLT) MSc, Australia, Jan Tunér, D.D.S., Sweden.
14. Musch TI, McAllister RM, Symons JD, Stebbins CL, Hirai T, Hageman KS, Poole DC. Effects of nitric oxide synthase inhibition on vascular conductance during high speed treadmill exercise in rats. *Experimental Physiology*. 2001. 86(6):749-757.
15. Tsuchiya K, Kawatani M, Takeshige C, Sato T, and Matsumoto I. Diode laser irradiation selectively diminishes slow component of axonal volleys to dorsal roots from the saphenous nerve in the rat. *Neurosci Lett*. 1993. 161:65-68.
16. Wakabayashi H, Hamba M, Matsumoto K, and Tachibana H. Effect of irradiation by semiconductor laser on responses evoked in trigeminal caudal neurons by tooth pulp stimulation. *Lasers in Surgery and Medicine*. 1993. 13:605-610.
17. Ohno T. Pain suppressive effect of low power laser irradiation. A quantitative analysis of substance P in the rat spinal dorsal root ganglion. *Journal of the Japanese Medical School*. 1997. 64:395-400.
18. Mochizuki-Oda N, Kataoka Y, Cui Y, Yamada H, Heya M, and Awazu K. Effects of near-infrared laser irradiation on adenosine triphosphate and adenosine diphosphate contents of rat brain tissue. *Neuroscience Letters*. 2002. 323:207-210.
19. Vizi E, Mester E, Tisza S, and Mester A. Acetylcholine releasing effect of laser irradiation on Auerbach's plexus in guinea-pig ileum. *Journal of Neural Transmission*. 1977. 40:305-308.
20. Kujawa J, Zavodnik L, Zavodnik I, and Bryszewska M. Low-intensity near-infrared laser radiation-induced changes of acetylcholinesterase activity of human erythrocytes. *Journal of Clinical Laser Medicine and Surgery*. 2003. 21:351-355.
21. Jimbo K, Noda K, Suzuki K, and Yoda K. Suppressive effects of low-power laser irradiation on bradykinin evoked action potential in cultured murine dorsal root ganglion cells. *Neuroscience Letters*. 1998. 240: 93-96.
22. Stergioulas A. Low-level laser treatment can reduce edema in second degree ankle sprains. *J Clin Laser Med Surg*. Apr 2004. 22(2):125-8.
23. Kumar PS, et al. A comparative study of low level laser therapy and conventional physiotherapy for the treatment of inversion injuries of the ankle. *Lasers and Medical Science*. 1988. Abstract issue 298.
24. Simunovic Z, Ivankovich AD, and Depolo A. Wound healing of animal and human body sport and traffic accident injuries using low-level laser therapy treatment: a randomized clinical study of seventy-four patients with control group. *J Clin Laser Med Surg*. Apr 2000. 18(2):67-73.
25. Bjordal JM, Couppe C, and Ljunggren E. Low Level Laser Therapy For Tendinopathy. Evidence of a Dose-Response Pattern. *Physical Therapy Reviews*. 2001. 6:91-99.
26. Shugarov NA and Voronkov DV. Osseous tissues restoration in treatment by intramedullary osteosynthesis combined with the influence of laser radiation. *Proceedings of the 2nd Thematic Symposium of Scientific Practical Papers on the Problem of Physical Self Regulation*. USSR. 1974. pp 336-368.
27. Loc. Cit. 18 (Gatev, S. Helium-Neon laser radiation in the rehabilitation of fracture patients. *Voprosy Kurortologii Fizioterapii i Lechebnoi Fizicheskoi Kultury*. 1989. 2:28-30.)
28. Ozdemir F, Birtane M, and Kokino S. The clinical efficacy of low-power laser therapy (III) on pain and function in cervical osteoarthritis. *Clin Rheumatol* 2001. 20(3):181-184.
29. Moore KC, et al. The effect of infrared laser irradiation on the duration and severity of postoperative pain: a double blind trial. *Laser Therapy*. 1996. 8:247-252.
30. Basford JR. Low-energy laser therapy: Controversies and new research findings. *Lasers Surg. Med*. 1989. 9:1-5.