Laser is the acronym for **light amplification by stimulated emission of radiation**. The light has unique properties in that it is coherent, monochromatic and collimated, and has many applications in industry, communication, and medicine. Unlike high power laser which has been used as a surgical tool to cut and coagulate tissue, low level laser (LLL) uses a power level that is 500 mW or less, generates almost no thermal energy, and cannot cut or coagulate tissue. The LLL light is generally safe on all human tissue, with exception of the retina, and has potential applications in wound healing, anesthesia, and pain management. With the emergence of low power laser diodes, namely the gallium-aluminum-arsenide (830 nm wavelength) or the gallium-arsenide (904 nm wavelength), the LLL light can be delivered from a small, lightweight, convenient, portable laser unit. The purpose of this paper is to evaluate the current status of LLL in the clinical management of pain.

**Fundamental Actions of Low Level Laser**

Since Mester et. al. first described the potential application of low level laser (LLL) light in wound healing in 1971 (1), the data on the non-surgical medicinal effects of light have been robust. The literature is replete with the LLL affecting cellular processes including fibroblast proliferation, collagen synthesis, and tissue repair (2-6). Some mechanisms have been elucidated to explain the beneficial effects of LLL in accelerating healing include absorbing light by receptors and enzymes within components of the respiratory chain and increasing ATP synthesis within the mitochondria, signaling and expressing various genes that enhance cell proliferation, suppressing the body’s immune responses, promoting anti-inflammatory effect, increasing microvascular circulation and improving lymphatic drainage of edematous fluid (7-15).

**Clinical Effects of Low Level Laser on Pain**

Numerous papers have been published showing the benefits of LLL in relieving pain. Wong and colleagues have shown its efficacy of the 830 nm LLL in patients with migraine and migrainous-type headaches, based on methodically examining and treating the actual sites of soft tissue injury (16). By this similar method, LLL has also been shown to reduce pain in patients with temporomandibular joint dysfunction (17), temporal headaches relating to the styloid process (18), carpal tunnel syndrome, and repetitive stress injury (19, 20). The use of the LLL was safe, and major adverse effects were non-existent. Using a similar 830 nm laser and a treatment modality devised by Wong, Chow and colleagues in a double-blind randomized placebo-controlled trial demonstrated the effectiveness in providing pain relief for patients with chronic neck pain over a three-month period using Visual Analogue Scale and other established questionnaires as outcome measures (21). Adverse effects were described as mild in nature and nearly the same for both groups. Interestingly, nausea was more frequent in the placebo and stiffness more in the LLL group (21). In other randomized studies using different
protocols, Ozdemir et. al. found relief of pain and improvement in function following LLL in cervical osteoarthritis (22).

In patients with musculoskeletal chest pain after other conditions mimicking chest pain such as cardiac ischemia, pulmonary and gastrointestinal problems have been ruled out, an 830 nm LLL appears to be a useful modality for relief of cervicothoracic pain when the culprit soft tissue lesions are determined (23). Saunders in a double-blind, randomized study found patients with supraspinatus tendonitis had less pain, less tenderness and less muscle weakness after LLL than a placebo laser (24).

Other laser wavelengths have also been shown to be effective in mitigating pain. Vasseljen et. al. applied the 904 nm wavelength LLL to patients with lateral epicondylitis and found significant improvement in pain relief and grip strength in a double-blind, randomized, controlled study (25). Gur and colleagues reported salutary effect using LLL therapy in patients with chronic low back pain; they noted significant improvements in reducing pain and functional disabilities based on the visual analogue scale, Schor test, Roland Disability Questionaire and Modified Oswestry Disability Questionaire (26). Soriano and Rios also found effective pain relief in elderly patients with chronic back pain without producing adverse side effects (27). Basford and others also showed reduction in pain and improvement in function in patients with low back pain using a neodymium-yttrium-garnet (Nd:YAG) laser at 1.06 um (28).

In rheumatoid arthritis patients, the LLL treatment reduced joint pain, improved strength and walking time (29, 30). The histological findings in LLL-treated rheumatoid arthritic knees showed suppression of inflammation in the synovial membranes when compared to the non-treated areas (31). Gur et. al. also demonstrated efficacy of 904 nm wavelength LLL to relieve pain and to improve function and quality of life measures using different laser regimens in osteoarthritis of the knee in a double-blind, randomized controlled trial (32).

LLL appears to have salutary effects in the oral mucosa. It is useful in controlling pain in patients with stomatitis and a host of other mucosal diseases (33). Schindl and Neumann found the 690 nm wavelength LLL to be effective in a randomized double-blind placebo-controlled trial in patients with recurrent herpes simplex infections of the perioral region (34). Besides directing the light at injury sites to reduce pain, LLL has been applied as acupuncture anesthesia. Zhou has demonstrated its efficacy in more than 7000 patients for tooth extractions and minor maxillofacial surgery (35, 36). One possible explanation for its anesthesia and analgesic action may be by raising endogenous opioid levels as demonstrated by Laakso et. al. (37).

**Conflicting Reports**

Despite the many propitious studies on the LLL in managing pain, there are several published conflicting papers reporting no effects using LLL, especially in treating shoulder and ankle pains. For example, Bingol and colleagues studied patients with shoulder pain using a 904 gallium-arsenide laser applied for twelve sessions during a
two-week period (38). The LLL or placebo unit was directed for one minute per site; the sites included the tuberculum majus and minus, the bicipital groove, and the anterior and posterior capsules. Their protocol and LLL did not reduce pain when compared to the control group with shoulder pain (38). DeBie and co-workers also showed no beneficial effects using a 904 nm gallium-arsenide laser over placebo; twelve treatment sessions of 200 seconds each using the laser were applied over a 14-week period on the lateral side of the ankle (39).

While such negative studies report no salutary effects of LLL in shoulders and ankles, it is not known whether the application of another laser wavelength, a higher dose, an alternative treatment location, or a longer duration of therapy may have produced a different outcome. It is not known whether a better understanding of the types of the shoulder and ankle injuries that may be treated or whether the more severe traumatic injuries can be ameliorated by brief exposures of LLL. Moreover, it is highly important to thoroughly acknowledge the extent of the injury and the pathology of these complex joints. Many types and different severities of soft tissue lesions and injuries of the shoulder can give rise to shoulder pain, including tears of the rotator cuff, tears of the acromioclavicular joint, adhesive capsulitis, osteoarthritis, rheumatoid arthritis, septic arthritis, tears of the glenohumeral joint, etc. In another trial, Saunders performed a study confined to a group of patients who had supraspinatus tendonitis and found the LLL to be beneficial (24). There are also different types of injuries present in ankle traumas, varying from mild to severe, that may require different LLL dose and treatment parameters, assuming the light is directed at the correct culprit site.

Thus, a good knowledge of pain physiology and functional anatomy while applying LLL is crucial in managing pain. Two of the authors (EW and GL) conducted several seminars and conferences teaching anatomy and pain physiology since the 1990’s in countries such as the United States, Singapore, Japan, Indonesia, Australia, China and Canada. LLL was applied systematically in the management of head, neck, shoulder and back pains after eliciting a thorough history and performing a complete examination. Attendees were taught the principles and underlying basis of musculoskeletal pain, and the uses and limitations of LLL. Practicing physicians and other practitioners were encouraged to bring their own complicated or difficult patients who had refractory pain in the head, neck, shoulder, and back; they had tried numerous medications and modalities without benefit. It is noteworthy that many of these “difficult” patients had immediate improvement with LLL during these demonstration courses. There are numerous accounts in these courses where patients reported little or no relief from LLL when directed at presumed painful sites by novice learners and practitioners. However, these same patients had significant relief of pain when LLL was directed at precise areas of tissue damage as determined by knowledgeable and experienced practitioners and instructors, after careful history taking and examination of the injured sites.

**Meta-analysis of Randomized Controlled Trials**

LLL therapy is not a panacea for all pain syndromes and conditions; the conditions where the modality is most beneficial must still be defined. Published data from multi-center,
randomized double-blind placebo controlled studies in comparable large groups of patients are lacking. Meta-analysis data on LLL combining several smaller published randomized controlled trials to achieve a larger sample size have thus far yield more convincing results for certain pain syndromes. However, limitations in the varying methodologies, laser parameters, and outcome measures among the different studies should be kept in mind when considering these data. Here are a few that have been published. Chow and Barnsley showed the favorable use of infrared LLL in acute and chronic neck pain in four of five randomized controlled trials (40). The same authors also later published a double-blind, randomized, placebo-controlled study demonstrating efficacy and relief of chronic neck pain over a three-month period (21).

Bjordal and others performed a Medline and library literature search on randomized controlled trials applying LLL to treat plantar fascia, Achilles, patellar, lateral epicondyle and rotator cuff tendinopathy (41). They looked at 78 trials, 20 of them involved tendinopathy. They predetermined their inclusion criteria, which consisted of treatments using various ranges of power or energy densities. When optimal treatments for specific tendinopathies were applied, there was a high correlation with successful treatment. They concluded that there was a significant effect using LLL if a valid treatment procedure and location-specific dose was used.

Enwemeka and colleagues searched the literature to determine the effects of LLL on pain control and tissue repair. Of the hundreds of randomized controlled trials, they found 34 tissue repair studies and nine pain control papers that met their inclusion criteria. Their results show that LLL was effective in promoting tissue repair and pain relief. They further statistically determined a “fail safe number” or the number of neutral of negative studies needed to nullify the positive LLL effects, which was 370 and 41 for tissue repair and pain control respectively (42).

Evaluating Pain Has its Limitations

The task of evaluating LLL in the management of pain is quite challenging because the subject of pain is still not yet completely understood. The greatest limitation is that there are no laboratory values and simple imaging studies to measure pain. Pain is what patients say it is, and reporting pain can be very subjective. What one person says is terribly painful; another may relate it as a minor ache. According to the International Association for the Study of Pain (IASP), pain is defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.” Stating it another way, pain is an individual’s perception and expression of existing tissue damage. Perceived pain by the patient is subjectively measured by a visual analogue scale based on a numerical scale from 0 (no pain) to 10 (very severe pain). When evaluating pain, assumptions are made that the patient can accurately and consistently provide a score that measures the actual or potential tissue damage.
Understanding Pain as it Relates to Tissue Damage

When human soft tissue is traumatized, the injured tissues release chemical mediators and breakdown products from phospholipids. A variety of chemical mediators including prostanglandins, kinins, serotonin, histamine, substance P and other inflammatory chemicals are liberated causing a cascade of events including vasomotor changes, edema, increased muscle tension and spasm, and release of substances from platelets and mast cells. Pain receptors (nociceptors) or free nerve endings in the skin, scalp, periosteum, fascia, muscles, cranial sinuses, and arterial wall may be activated by either one or a combination of mechanical, thermal and chemical stimuli. Damage to any of the aforementioned tissue can incite pain. The pain impulse is propagated along one or two types of nerve fibers, the A delta and C fibers, to the central nervous system via the dorsal horn of the spinal cord. The A delta fibers are myelinated, fast-acting fibers producing sharp and stabbing pains, while the C fibers are unmyelinated, thin, slow-acting fibers causing dull, aching, burning pain. Stimulating the A delta fibers allows one to precisely localize the site of injury, while activating C fibers produces the perception of diffuse widespread injury.

Once the pain impulse crosses the dorsal horn of the spinal cord, it continues up the ascending pathway of the spinothalamic tract to the reticular system and the thalamus in the midbrain, and then to the cerebral cortex, where the pain is interpreted. While the ascending pathway is activated, the descending inhibitory pathway is stimulated by releasing morphine-like substances like endorphins and enkephalins to modulate the oncoming train of pain impulses. Some of the incoming impulses from the dorsal horn can innervate the anterior horn cell, which cause increase tension and contraction of extrafusal muscles. Muscle spasm and ischemia result giving rise to additional sites of pain. In some severe situations, some of the incoming impulses can innervate the lateral horn of the cord to activate the autonomic nervous system, and in particular, stimulating sympathetic nerves that not only carry the sensation of pain and paresthesia but other activities which include vasoconstriction, sweating and smooth muscle contraction.

The Challenges and Pitfalls of Pain Studies

Since there are many conflicting reports in the literature regarding the LLL modality in treating pain, it is important to elucidate the challenges and pitfalls of pain studies. Pain may not always be perceived at the site of actual tissue damage, and even when pain is perceived at the site of damage, all injuries are not the same. It is imperative to meticulously perform a detailed history and physical examination of patients to determine the site of the injury, define the type of injury, and specify the amount and extent of tissue damage. Furthermore, pain can be reported at sites distant from the original tissue injury. As tissue is damaged, pain impulses go to the dorsal root ganglia and up ascending pathways to the cortex, some impulses innervate the anterior horn cell, giving rise to increased tension, contraction, spasm and ischemia of muscles; resulting in the perception of additional sites of pain. Classically, anginal pain due to cardiac muscle ischemia may be referred to the jaw, neck and the arms. Thus, the area of perceived pain
may not necessarily be the exact location of the original culprit site of injury. In addition, finding the source and defining the extent of tissue damage can be even more daunting when C fibers are activated and are playing a significant role in this milieu. Furthermore, the reticular system can interact with the limbic system to invoke emotions such as anxiety and fear as well as pain modulation.

Performing chronic pain trials especially require vigilant documentation. Patients perform a variety of different tasks and activities in their daily lives that are central to the success or failure of a pain study. Many of their daily activities could be potentially or actually injurious and can affect the outcome of the study. In chronic trials, it is paramount to carefully interview patients, and to determine and document the types and amounts of all daily physical activities, both new and routine. These activities must relate to whether they exacerbate and cause further tissue injury, and affect the patient’s perception of pain. Many soft tissue injuries are best kept immobilized until they heal. Clinical protocols that involve partially or fully mobilize an injury before it has healed will not likely improve over the placebo controls. There is also the example of a patient apparently improving from a study treatment that casually performed a single brief event, such as lifting a heavy object or grabbing onto something to avoid a fall, and then re-injured the shoulder, neck or back within days before the weekly or monthly study visit. Such brief but significant events are pivotal to the study outcome, and may be remembered or even forgotten by patients.

Complicating the study of pain are patients who are consuming analgesics and various physicians who are prescribing medications during the trial. Aspirin and non-steroidal anti-inflammatory drugs block prostaglandins and decrease activation at the peripheral nociceptors. Opioids affect lateral spinothalamic tracts, and tricyclics and other antidepressant agents reduce pain at the descending tracts and dorsal root ganglia. Merely counting and recording the drugs and frequency a patient takes them may not suffice. Some pain medications are not easily metabolized and have interactions with other drugs. Drugs taken by the elderly may have cumulating effects that clearly affect pain outcome measures. Patients may also be using herbal medications and other home remedies that have not been accounted for.

Conclusion

Evidence is mounting that the low level laser (LLL) is useful in relieving certain clinical pain syndromes. Randomized double-blind studies have demonstrated its effectiveness in relieving acute and chronic neck pain. It appears to be useful in reducing migraine and migrainous headache pain, musculoskeletal chest and back pain, specific types of tendonitis and other pain conditions when the LLL is directed at the culprit soft tissue injury site(s). LLL therapy is generally safe and devoid of major adverse effects, and could be used as an adjunct to pain management. Despite the heterogeneity of published reports, different LLL parameters such as wavelengths, power and energy densities have been shown to be effective. However, LLL therapy is not a panacea for managing all pain conditions. There are conflicting reports; some soft tissue injuries may be more suited for LLL treatment than others; for example, it has not yet been shown to be
efficacious in all shoulder and ankle pain conditions, which include varying types and degrees of tissue damage. Clinical trials evaluating pain, and in particular chronic pain studies, have their limitations. Importantly, merely directing the LLL on a painful site may not be sufficient to treat the tissue injury; it is vital to improve our understanding of the anatomy and physiology of different pain syndromes, to define the types and extent of injuries, and to determine whether the LLL can be used to manage the specific types and extent of traumatic lesions that cause pain. Further, chronic studies must monitor the patient’s activities in order to protect the damaged site and avoid any re-injuries. Despite limitations, several meta-analysis papers have shown the efficacy of LLL therapy. The management of pain using LLL appears exciting and promising, and more controlled trials are underway to verify these early salutary observations and clinical studies.
REFERENCES


