Laser-Accelerated Inflammation/Pain Reduction and Healing

Low Level Laser Therapy (LLLT) precipitates a complex set of physiological interactions at the cellular level that reduces acute inflammation, reduces pain, and accelerates tissue healing.

by Richard Martin, BS, CLT

Compromised cells and tissues respond more readily than healthy cells or tissues to energy transfers that occur between LLLT-emitted photons and the receptive chromophores found in the various cells and sub-cellular organelles. Cells and tissues that are ischemic and poorly perfused as a result of inflammation, edema and injury have been shown to have a significantly higher response to LLLT irradiation than normal healthy structures. Cell membranes, mitochondria and damaged neurological structures exhibit less than optimal metabolism and stasis conditions. Multiple studies have demonstrated that under these compromised conditions, the introduction of energy transfers and the resultant enhancement of metabolic activity is most pronounced in biologically challenged components. While it may appear that LLLT is thus selectively targeting compromised cells, in reality, these cells exhibit a lowered reaction threshold to the effects of laser light and are more easily triggered to energy transfer responses. The result is that LLLT has a significant effect on damaged cells and tissues while normative biological constituents are appreciably less affected.[1]

The cellular cascade effect — precipitated by the actions of enzymes and having a significant in the presence of LLLT — has a significant impact on cellular and tissue function. Since a considerable number of the reactive proteins that respond to laser stimulation are enzymes, laser light effects are amplified in the stimulation of beneficial enzymes and depression of deleterious enzymes.

At the cellular level, cytochromes can be defined as electron or proton-transfer proteins that act as energy producers for human biological functions. Both of the cytochrome enzymes, Cytochrome c Oxydase and Nitric Oxide Synthase (NOS) have been found to be particularly reactive to laser photon stimulation. The particular affinity of these and other photoreactive enzymes to accelerate their functions in the presence of LLLT provides critical increases in the molecule ATP and Nitric Oxide (NO) which enhances cellular metabolism, circulatory improvement and nerve function.

Although the various actions of LLLT in regards to inflammation, pain and healing have been separated categorically here for the purpose of process identification, their interactions are not so easily distinguished. In response to LLLT, the reduction in inflammation, pain and healing time all compliment each other and many of the processes are either simultaneous or overlapping.

Acute Inflammation Reduction

Immediately after an acute injury event, the body, in response to the disruption of the integrity of vascular, soft tissue, connective tissue and neurological processes, initiates a series of biological responses. The inflammatory reaction consists of both vascular and cellular events. Injury responsive components such as Mast cells, Bradykinins and Prostaglandins are activated along with the vascular responses and cellular membrane reactions. All of these combined processes and events are represented by the symptoms of edema, inflammation, pain and functional debility. LLLT can be effective in mediating both the symptoms and the underlying inflammatory process by the following actions:

1. Stabilization of cellular membrane — Ca^{++}, Na^{+} and K^{+} concentrations as well as the proton gradient over the mitochondria membrane are positively influenced. This is accomplished in part by

the production of beneficial Reactive Oxygen Species (ROS) wherein triplet oxygen molecules absorb laser light producing singlet oxygen molecules. These ROS modulate intracellular Ca++ concentrations and laser therapy improves Ca++ uptake in the mitochondria.[2,3,4]

2. ATP production and synthesis are significantly enhanced, contributing to cellular repair, reproduction and functional ability. Laser stimulation of Cytochrome c Oxidase, a chromophore found on the mitochondria of cells, plays a major role in this rapid increase in production and synthesis of ATP.[3]

3. Vasodilation is stimulated via Histamine, Nitric Oxide (NO) and Serotonin increases, resulting in reduction of ischemia and improved perfusion. Laser-mediated vasodilation enhances the transport of nutrients and oxygen to the damaged cells and facilitates repair and removal of cellular debris.[5,6]

4. Beneficial acceleration of leukocytic activity results in enhanced removal of non-viable cellular and tissue components, allowing for a more rapid repair and regeneration process.

5. Increased Prostaglandin synthesis, particularly in conversion of the prostaglandins PGG2 and PGH2 periosides into prostaglandin PGI2. PGI2 (Prostacyclin), has a vasodilating and anti-inflammatory action with some attributes similar to Cox-I and Cox-II inhibitors.[7]

6. Reduction in Interleukin 1(IL-1). Laser irradiation has a reducing effect on this pro-inflammatory cytokine that has been implicated in the pathogenesis of rheumatoid arthritis and other inflammatory conditions.[8]

7. Enhanced lymphocyte response. In addition to increasing the number of lymphocytes, laser irradiation mediates the action of both lymphatic helper T-cells and suppressor T-cells in the inflammatory response. Along with laser modification of beta cell activity, the entire lymphatic response is beneficially affected by LLLT.[9]

8. Increased angiogenesis. Both blood capillaries and lymphatic capillaries have been clinically documented to undergo significant increase and regeneration in the presence of laser irradiation. The resulting improvement in circulation and perfusion enhances all repair and healing processes. Laser induced increases in NO and the growth factors — in particular cytokine INF-g — are contributory to this process.[10,11]

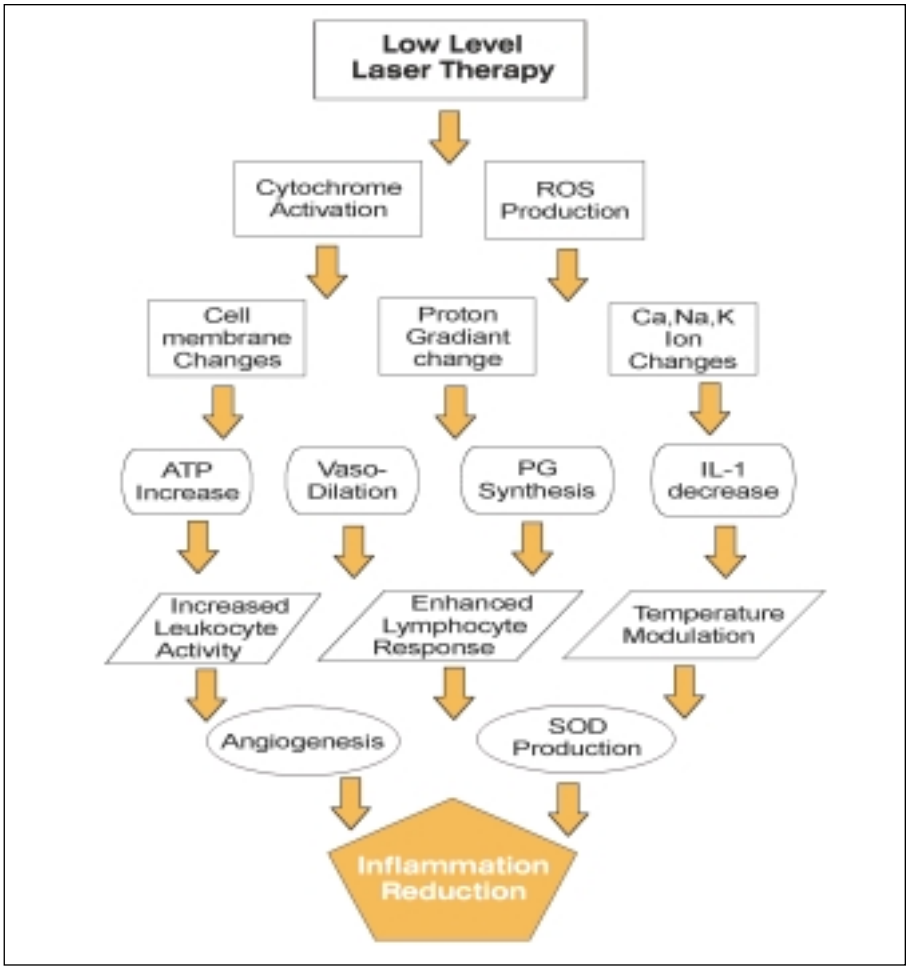

FIGURE 1. *LLLT cellular cascade effects that promote inflammation reduction.*

9. Temperature modulation. Areas of inflammation typically demonstrate temperature variations with the inflamed portion having an elevated temperature. Laser therapy has been shown to accelerate temperature normalization, demonstrating its beneficial influence on the inflammatory process.

10. Enhanced superoxide dismutase (SOD) levels. Laser stimulated increases in cytokine SOD levels interact with other anti-inflammatory processes to accelerate the termination of the inflammatory process. Interactions between SOD and Reactive Oxygen Species (ROS) production subsequent to LLLT balance free radical activity and allows for the beneficial effects of ROS while inhibiting detrimental interactions.[12]

11. Decreased C-reactive protein and neopterin levels. Laser therapy has been shown to lower the serum levels of these inflammation markers, particularly in rheumatoid arthritis patients. Decreased marker levels are indicative that the combined effects of all LLLT-induced anti-inflammatory actions are effectively reducing the inflammatory process.

A summary flowchart of the cellular cascade in reducing tissue inflamation is presented in Figure 1. The cumulative effect of these multiple inter-active processes and events is an accelerated inflammatory cycle with diminished symptoms and earlier normalization.

Since LLLT does not exacerbate the inflammatory process but rather condenses the time frame from onset to resolution through acceleration of processes, it can be used immediately post injury. This rapid initiation of therapy in acute inflammation will assist in limiting the scope and duration of the inflammatory event and minimize the pain and severity associated with it.

Most of the beneficial effects seen from LLLT in the treatment of acute inflammatory events will also have medical efficacy as LLLT is initiated in more chronic

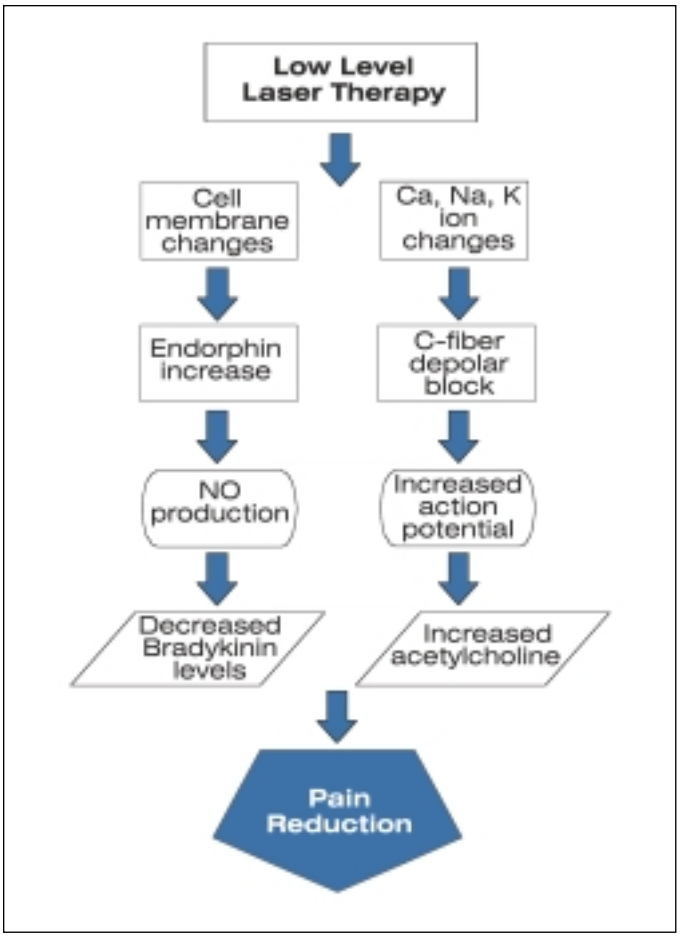

FIGURE 2. *LLLT cellular cascade effects that promote pain reduction.*

inflammatory conditions. While the treatment regimen and course of therapy may be modified in chronic situations, the physiological responses and interactions remain consistent. Chronic conditions may require longer treatment times and results will vary with the patient, condition and length of the chronic condition.

Pain Reduction

The unique pain reduction abilities of LLLT have been extensively researched and documented in numerous clinical studies and medical papers. While there remains much to learn in respect to the various processes through which LLLT achieves its pain reduction characteristics, there is a wealth of knowledge currently available to demonstrate the effectiveness of laser therapy in this regard.

Because the pain amelioration capabilities of LLLT are accomplished via the combination of local and systemic actions — utilizing enzymatic, chemical and physical interventions — the process is very complex. However, there is a preponderance of medical evidence that justifies a conclusion that effective pain reductions can be achieved via LLLT. Following are processes and events that are promoted by LLLT therapy:

1. Increase in b-Endorphins. the localized and systemic increase of this endogenous peptide after LLLT irradiation has been clinically reported in multiple studies with subsequent pain reductions.

2. Blocked depolarization of C-fiber afferent nerves. The pain blocking effect of LLLT can be pronounced, particularly in low velocity neural pathways, such as non-mylenated afferent axons from nociceptors. Laser irradiation suppresses the excitation of these fibers in the afferent sensory pathway.[13,14]

3. Increased nitric oxide production. NO has both a direct and indirect impact on pain sensation. As a neurotransmitter it is essential for normal nerve cell action potential in impulse transmission activity and, indirectly, the vasodilation effect of NO can enhance nerve cell perfusion and oxygenation.

4. Increased nerve cell action potential. Healthy nerve cells tend to operate at about -70 mV and fire at about -20 mV. Compromised cells membrane potential approximates -20 mV thereby resulting in pain stimulus. LLLT can help restore the action potential closer to the normal -70 mV range. Both compound muscle action potential (CMAP) values and nerve latency values have shown improvement with laser therapy.[15]

5. Axonal sprouting and nerve cell regeneration. Several studies have documented the ability of LLLT to induce axonal sprouting and some nerve regeneration in damaged nerve tissues. Where pain sensation is being magnified due to nerve structure damage, cell regeneration and sprouting may assist in pain decrease.[16,17]

6. Decreased Bradykinin levels. Since Bradykinins elicit pain by stimulating nociceptive afferents in the skin and viscera, mitigation of elevated levels through LLLT can result in pain reduction. Laser-induced decrease in plasma kallikrein, increase in Kininase II, and increase in NO are considered the contributors to this Bradykinin decrease.

7. Increased release of acetylcholine. By increasing the available acetylcholine, LLLT helps in normalizing nerve signal transmission in the autonomic, somatic and sensory neural pathways.

8. Ion channel normalization. LLLT promotes normalization in Ca++, NA+ and K+ concentrations resulting in beneficial pain reduction results from these ion concentration shifts.

Figure 2 presents a simplified representation of the effects of LLLT on pain improvement at the cellular level.

Tissue Healing

One of the truly unique characteristics of LLLT is that it has the ability to actually promote and enhance healing, not just treat symptoms. The irradiation by low-level laser light accelerates and enhances healing activities carried out by the body. Several of the unique characteristics of LLLT that work to alleviate pain and inflammation also play an important role in accelerating the healing process; the LLLT-mediated reduction in inflammation and pain frees the body's natural ability to repair and heal itself.

As wound healing progresses through the stages of inflammation, proliferation, remodeling and maturation, laser therapy presents the opportunity to impact each of these phases in positive and beneficial ways. LLLT can provide the following beneficial impacts in both open surface wounds and closed connective or soft tissue injuries as follows:

1. Enhanced leukocyte infiltration. LLLT stimulates activity involving neutrophils, monocytes and lymphocytes.

2. Increased macrophage activity. LLLT accelerates macrophage activity in phagocytosis, growth factor secretion and stimulation of collagen synthesis.

3. Increased neovascularization. The significant angiogene-

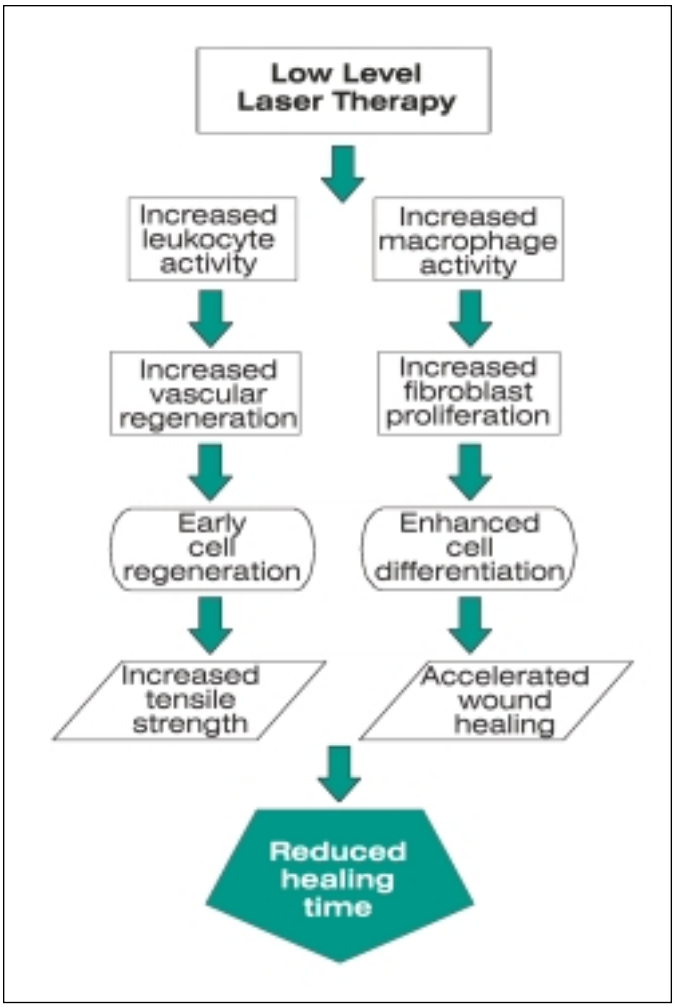

FIGURE 3. *LLLT cellular cascade effects on accelerated tissue healing.*

sis that occurs with laser therapy promotes revascularization with subsequent improvement in perfusion and oxygenation. Endothelial cell regeneration is accelerated.[18]

4. Increased fibroblast proliferation. LLLT stimulation increases fibroblast numbers and fibroblast-mediated collagen production.[19]

5. Keratinocyte proliferation. The beneficial synthesis activities and growth factor ability of keratinocytes are enhanced by proliferation secondary to LLLT.[20]

6. Early epithelialization. Laser-stimulated acceleration of epithelial cell regeneration speeds up wound healing, minimizes scarring, and reduces infection opportunities.

7. Growth factor increases. Two to five fold increases in growth-phase-specific DNA synthesis in normal fibroblasts, muscle cells, osteoblasts and mucosal epithelial cells irradiated with IR light are reported. Increases in vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF-2) secondary to IR light irradiation have also been reported.

8. Enhanced cell proliferation and differentiation. Laser-induced increases in NO, ATP and other compounds that stimulate higher activity in cell proliferation and differentiation into mature cells. Increased numbers of myofibroblasts, myofibrils, myotubes etc., as well as bone cell proliferation, have been clinically documented after LLLT. Satellite cells, the precursor cells in the process of muscle regeneration, show significant increase in proliferation when irradiated with LLLT.[21,22,23]

9. Greater healed wound tensile strength. In both soft tissue and connective tissue injuries, LLLT 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, laser therapy contributes to improved tensile strength.[24,25,26,27]

The preceding effects combine to achieve an accelerated healing rate (see Figure 3). The time from onset of injury to mature healed wound is reduced.[28]

Conclusion

The FDA has recently cleared multiple laser and LED devices for treatment of a variety of medical conditions including carpal tunnel syndrome, cervical neck pain, low back pain, joint pain, generalized muscle pain and acceleration of wound healing. Governmental agencies such as NASA are currently using technical light therapy for medical conditions in space applications. The U.S. Olympic training facilities have just released statements of endorsement for laser therapy for athletes. All of these events validate the growing acceptance in mainstream medicine for the medical efficacy of laser therapy as a viable, often superior therapeutic treatment modality.

With over 200 clinical studies — many of which are double-blind, placebo-controlled — and in excess of 2000 published articles on LLLT, this innovative new technology has a well-documented research and application history. Having grown far beyond its distant Institutional Review Board (IRB) and experimental treatment status, LLLT is now being considered a therapy of choice for many difficult pain management challenges such as fibromyalgia and myofascial pain. New and ongoing clinical investigations offer growing potential for even more widespread applications of this truly unique light therapy. ■

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