

FLEX CEUs



Low-Level Laser Therapy



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Introduction

Low-Level Laser Therapy is a treatment that is utilized in many fields of therapy and medicine on patients who suffer from a variety of acute and chronic conditions in order to help eliminate pain, swelling, reduce spasms and increase functionality, amongst other concerns. Low-Level Laser Therapy is also known as Cold Therapy, Biostimulation, low-intensity light therapy, and soft laser therapy. Low-Level Laser Therapy is a type of Photobiomodulation Therapy, which is therapy that uses light to treat a patient. This treatment applies low-level laser or light-emitting diodes (LEDs) to the surface of the body, in comparison to high-level laser treatments that are used to cut or burn tissues.

Theodore Maiman developed the first working laser at Hughes Research Lab in 1960. His work was based on theoretical work by Charles Hard Townes and Arthur Leonard Schawlow. In 1967, Professor Endre Mester began using low power lasers in medicine. Dr. Mester is recognized by many as the founder of low laser therapy. He began treatment of laser therapy on skin cancer. Endre Mester accidentally discovered that low-level red laser light could regrow hair during an attempt to replicate an experiment that such lasers could reduce tumors in mice. The laser he was using was faulty and was not as powerful as he had thought. It failed to affect the tumors, but he noticed that in places where he has shaved the mice in order to perform his experiments that the hair grew back more quickly on the treated mice than on the mice in the control group. He went on to show that low-level laser light could accelerate wound healing in mice. By the 1970s he was treating patients with skin ulcers using Low-Level Laser Therapy. In 1974 he founded the Laser Research Center at the Semmelweis Medical University in Budapest. He is credited as the discoverer of the positive biological effects of low power lasers. The first experimental FDA clearance lasers for medical reasons occurred in February of 2002, after a successful study for carpal tunnel syndrome on workers at General Motors. Since the discovery of Low-Level Laser Therapy, advancements have been made for the types of ailments treated by lasers.

This course will describe the role of Low-Level Laser Therapy in Physical Therapy applications, highlight the risks and benefits, and the many occasions which can call for this treatment.

Section 1: Defining Low-Level Laser Therapy

LASER is an acronym for Light Amplification by Stimulated Emission of Radiation. All lasers must have the following parts: an energy source (power supply), lasing or amplifying medium (solid, gas, or liquid), and a resonating cavity (mirrors). A laser light is monochromatic with parallel rays (**collimated**), and **coherent** (meaning all light beams have the same frequency).

Low-Level Lasers on the other hand are divergent, as in not focused or collimated, which also means that the risk to the eyes diminishes with distance. Low-Level Laser Therapy is a type of Photobiomodulation Therapy, which is the use of light in medical treatments. There are four classes of lasers, as defined by the International Engineering Consortium. Level 1 is akin to a CD player. Level 2 includes laser pointers, such as for presentation pointers or pet toys. LLLT is a Level 3 laser, which means that it is non-heat emitting. Level 3 includes LLLT, and CD and DVD writers. Level 4 lasers are heat-emitting and are those used to cut or cauterize tissues in medical procedures and surgery. The Federal Drug Administration (FDA) classifies medical lasers into three categories, as Class 4 Surgical Lasers, Class 3B Non-surgical Lasers, and Class 3A Low-Level Lasers. Class 3A lasers help heal superficial wounds and conditions and will typically not penetrate below the skin's surface. However, Class 3B low-level lasers are most commonly the type used in Low-Level Laser Therapy and have the ability to penetrate and assist in the healing process of deep tissue and joint problems.

Low-Level Laser Therapy is primarily used to help damaged tissue recover, and is often used as an alternative to medications or invasive methods such as surgery. The lasers used in Low-Level Laser Therapy are small, and instead of heating the targeted tissue, they emit low levels of light that are absorbed by the body's **mitochondria** (the energy-producing organelles in many of the body's cells) which in turn increases cellular energy production and helps to encourage healing of the surrounding tissues.

When the body is subjected to ultraviolet light it encourages the production of **Vitamin D**. The body naturally produces Vitamin D in response to sunlight, and Low-Level Laser Therapy is intended to focus and improve the production, although the entirety of the benefits regarding improved Vitamin D production via laser light is not fully known. Vitamin D is essential for the following;

- Promoting the health of teeth and bones
- Support of the immune, brain and nervous system
- Influencing the expression of genes involved in cancer development
- Regulation of insulin levels and supporting diabetes management

- Supporting lung function and cardiovascular health

Vitamin D deficiency can be dangerous. Without Vitamin D the body cannot function as it was intended. Some things that inhibit Vitamin D production and can cause a Vitamin D deficiency include darker skin pigments, sunscreen with a sun protection factor (SPF) of 30 or more, and low exposure to sunlight. The symptoms of Vitamin D deficiency include;

- Regular sickness or infections
- Bone pain
- Back pain
- Impaired wound healing
- Low or depressed mood
- Hair loss
- Muscle pain

Besides promoting Vitamin D production, Low-Level Laser Therapy has been shown to help many illnesses and injuries. It can help in tissue regeneration, reduction of inflammation, pain reduction, and immune response enhancement. It has shown to be effective in treating many conditions, such as stroke, plantar fasciitis, rheumatoid arthritis, temporomandibular joint disorder (TMJ), exercise-induced muscle fatigue and injury prevention, traumatic brain injury, and certain skin conditions.

Low-Level Laser Therapy is beneficial on a cellular level as well. Phototherapy has been shown to affect cellular activity in the following ways:

- stimulates cell growth
- increases cell metabolism
- improves cell regeneration
- promotes an anti-inflammatory response
- promotes edema reduction
- reduces **fibrous tissue formation**, which reduces the scar tissue that forms from injury
- stimulates nerve function
- reduces the production of **substance P**, which acts as a mediator of pain transmission
- stimulates long term production of nitric oxide. In mammals including humans, nitric oxide is a signaling molecule involved in many physiological and pathological processes. It is a powerful vasodilator with a half-life of a few seconds in the blood.

- decreases the formation of **bradykinin**, **histamine**, and **acetylcholine**
- stimulates the production of **endorphins**, the “happy chemical”

There are three types of effects on the cellular bodies. Primary effects of Low-Level Laser Therapy are a result of the interaction of photons and cell mitochondria which capture, direct, and transduce photon energy to chemical energy used to regulate cellular activity.

Secondary effects occur **intracellular**, in which photons produce the primary effects and are induced by these primary effects. Secondary effects include **myofibroblast contraction**, cell **proliferation**, **protein synthesis**, **degranulation**, growth factor secretion, and neurotransmitter modification.

Tertiary effects are the indirect responses of distant cells, or the surrounding cells, to changes in the initial cells that have interacted directly with photons. They are the least predictable due to the fact they are dependent on both variable environmental factors and intercellular interactions. Tertiary effects include all the systemic effects of Low-Level Laser Therapy. Primary, secondary, and tertiary events combine to produce phototherapeutic activity.

The wavelengths of visible light are minuscule, ranging from 400 to 700 billionths of a meter. A billionth of a meter is called a nanometer, or nm. Lasers with different wavelengths, varying from 600 to 1070 nm, are used in Low-Level Laser Therapy. Wavelengths in this range have the ability to penetrate the skin and soft tissues and are considered the optimal range. Low-Level Laser Therapy has a power of less than 500 mW (milliwatts), as more than 500 mW is considered High-Level Laser Therapy. High-Level Laser Therapy creates heat on the surface of the targeted skin area due to the higher irradiance (power density), hence why Low-Level Laser Therapy is commonly referred to as Cold Therapy.

Properties of Low-Level Lasers are as follows;

- The power output of lasers being 0.001- 0.1 Watts (W)
- Wavelengths in the range of 300-10,600 nanometers (nm)
- Pulse rate from 0, meaning continuous, to 5000 Hertz (cycles per second, known as H)
- Intensity of 0.01-10 W/cm² and dose of 0.01 to 100 Joules/cm²

These are the properties for a laser to be considered low level for therapy, otherwise, they are known as High-Level Laser Therapy (HLLT).

Low-Level Laser Therapy devices are normally handheld apparatuses, approximately the size of a flashlight. The laser is placed over the desired treatment area for anywhere from thirty seconds to several minutes, depending on the size of the area being treated and the dose being provided by the laser unit. The photons of the light that are emitted during the treatment pass through the skin and underlying tissues, or the dermis, epidermis, and subcutaneous tissues. The light triggers biochemical changes within cells and can be compared to the process of photosynthesis in plants, where the photons are absorbed by cellular photoreceptors and trigger chemical changes. Specifically, the photons affect the mitochondria, or the powerhouse of the cell. This causes increased adenosine triphosphate (**ATP**) production, modulation of reactive oxygen species, and induction of **transcription factors**. These effects in turn lead to increased cell proliferation and migration (particularly by **fibroblasts**).

Increased ATP production increases blood flow, which contributes to numerous bodily processes including cell growth and oxygen supply. Increased blood flow plays a key role in the clearing of metabolic waste products, lactic acid, tissue healing, and muscle growth. Modulation of reactive oxygen species is important because a build-up of reactive oxygen species in cells may cause damage to DNA, RNA, and proteins, and may cause cell death. Transcription factors are necessary to regulate the amount of messenger RNA in cells, which is a nucleic acid present in all living cells whose principal role is to act as a messenger carrying instructions from DNA for controlling the synthesis of proteins. Increased cell proliferation, or increased cell production, is vital to healing. Fibroblasts, which are affected by laser therapy, are a type of biological cell that synthesizes the extracellular matrix and collagen, produces the structural framework (stroma) for animal tissues, and plays a critical role in wound healing. Fibroblasts are the most common cells of connective tissue in animals.

Once the light energy passes through the layers of skin and reaches the target area, it is absorbed and interacts with the light-sensitive elements in the cell. This process produces a **photochemical effect** and can be compared to photosynthesis in plants. Low-Level Laser Therapy makes use of the first law in photochemistry, the **Grotthuss-Draper Law**, which states that light must be absorbed by a chemical substance in order for a photochemical reaction to take place. In photosynthesis, sunlight is absorbed by plants, and is then converted to usable energy so that the plant can grow. In LLLT that chemical substance is represented by the **respiratory enzyme** known as **cytochrome c oxidase** which is involved in the **electron transport** chain in mitochondria. When cells absorb the light energy, it initiates a series of events in the cell that are theorized to result in normalizing damaged or injured tissue, a reduction in pain, inflammation, edema and an overall decrease in healing time by increasing

intracellular metabolism, increasing ATP production, and promoting increased cell proliferation.

For LLLT to be effective, the irradiation parameters (wavelength, power, power density, pulse parameters, energy density, total energy, and time) need to be within specified ranges. There are four clinical targets for LLLT:

- The site of injury to promote healing, remodeling, and reduce inflammation
- Lymph nodes to reduce edema and inflammation
- Nerves to induce analgesia
- Trigger points to reduce tenderness and relax contracted muscle fibers

Treatment times vary, upwards of 30 seconds to each target area. There could be only one target per treatment session, or multiple target areas in excess of 10 for complex dysfunctions such as cervical radiculopathy.

LLLT continues to require much study, but has shown itself to be a valuable asset for healing and pain relief amongst other health issues. The changes intracellularly are promising for future applications that have yet to be discovered and researched.

Section 1 Summary

Low-Level Laser Therapy is a non-heat emitting laser treatment used in the treatment of many diseases and ailments. The properties include a power output of lasers being 0.001- 0.1 Watts (W), wavelengths in the range of 300-10,600 nanometers with an ideal range of 600-1070 nm, pulse rate from 0, meaning continuous to 5000 Hertz (cycles per second, known as H), Intensity of 0.01-10 W/cm², and a dose of 0.01 to 100 Joules/ cm². Lasers work intracellularly, increasing adenosine triphosphate (ATP) production, cell proliferation, and cell migration. When laser light is absorbed through the skin and reaches the target area, it is absorbed by the light-sensitive elements in the cells. This process is comparable to photosynthesis in plants. In photosynthesis, sunlight is absorbed by plants, and is then converted to usable energy so that the plant can grow. When cells absorb the light energy, it initiates a series of events in the cell that are theorized to result in normalizing damaged or injured tissue, a reduction in pain, inflammation, edema and an overall decrease in healing time by increasing intracellular metabolism, increasing ATP production, and promoting increased cell proliferation.

Section 1 Key Concepts

- **Acetylcholine** - Acetylcholine is a neurotransmitter, which is a chemical released by a nerve cell or neuron. Acetylcholine causes muscles to contract, activates pain responses, and regulates endocrine and REM sleep functions. Deficiencies in acetylcholine can lead to myasthenia gravis, which is characterized by muscle weakness. Too much acetylcholine causes muscle spasms.
- **ATP** - adenosine triphosphate, a compound consisting of an adenosine molecule bonded to three phosphate groups, present in all living tissue. ATP provides energy for physiological processes such as muscular contraction.
- **Bradykinin** - potent endothelium-dependent vasodilator and a mild diuretic, which may cause a lowering of the blood pressure. It also causes contraction of non-vascular smooth muscle in the bronchus and gut, increases vascular permeability, and is also involved in the mechanism of pain. Reducing this reduces nerve sensitivity
- **Coherent** - meaning all light beams have the same frequency
- **Collimated** - a light whose rays are parallel
- **Cytochrome c oxidase** - This is a large transmembrane protein complex found in bacteria, archaea, and in eukaryotes in their mitochondria. It is the last enzyme in the respiratory electron transport chain of cells located in the membrane.
- **Degranulation** - cellular process that releases antimicrobial cytotoxic or other molecules from secretory vesicles called granules found inside some cells. It is used by several different cells involved in the immune system, including granulocytes (neutrophils, basophils, and eosinophils) and mast cells.
- **Electron transport chain** - The electron transport chain consists of a series of redox reactions in which electrons are transferred from a donor molecule to an acceptor molecule. The underlying force driving these reactions is the free energy (energy available to do work) of the reactants and products.
- **Fibroblasts** - Biological cells that synthesize the extracellular matrix and collagen, produces the structural framework for animal tissues. Most common cells of connective tissue in animals, which play a critical role in wound healing.
- **Fibrous tissue formation** - Fibrosis, also known as fibrotic scarring, is a pathological wound healing in which connective tissue replaces normal parenchymal tissue to the extent that it goes unchecked, leading to considerable tissue remodeling and the formation of permanent scar tissue
- **Grotthuss-Draper Law** - The Grotthuss-Draper law (also called the Principle of Photochemical Activation) states that only that light which is absorbed by a system can bring about a photochemical change.
- **Growth factor** - growth factor is a naturally occurring substance capable of stimulating cellular growth, proliferation, healing, and cellular differentiation.

- **Histamine** - a compound which is released by cells in response to injury and in allergic and inflammatory reactions, causing contraction of smooth muscle and dilation of capillaries.
- **Intracellular** - located or occurring within a cell or cells
- **LASER** - an acronym for Light Amplification by Stimulated Emission of Radiation
- **Mitochondria** - the powerhouse of the cell, the energy-producing organelles in many of the body's cells.
- **Myofibroblast contraction** - Myofibroblasts can contract by using smooth muscle type actin-myosin complex, rich in a form of actin called alpha-smooth muscle actin. These cells are then capable of speeding wound repair by contracting the edges of the wound.
- **Photochemical effect** - a chemical reaction initiated by the absorption of energy in the form of light. The consequence of molecules' absorbing light is the creation of transient excited states whose chemical and physical properties differ greatly from the original molecules.
- **Proliferation** - rapid reproduction of a cell, or organism
- **Protein Synthesis** - the process by which cells make proteins
- **Respiratory enzyme** - An enzyme, such as oxidase, that catalyzes the transfer of electrons from its substrate to molecular oxygen during cellular respiration.
- **Substance P** - Substance P is a neuropeptide that acts as a mediator of pain transmission in the central nervous system and during neurogenic inflammation in the periphery.
- **Transcription Factor** - a transcription factor (TF) (or sequence-specific DNA-binding factor) is a protein that controls the rate of transcription of genetic information from DNA to messenger RNA, by binding to a specific DNA sequence.
- **Vitamin D** - a a nutrient found in some foods or by absorption of sunshine that is needed for health and to maintain strong bones. It does so by helping the body absorb calcium (one of bone's main building blocks) from food and supplements. It is vital to support the immune, brain, and nervous system, to regulate insulin levels, and to support lung function and cardiovascular health.

Section 2: Applications for Laser Therapy

Low-Level Laser Therapy can be used to treat many illnesses or disorders, including to treat hair loss, chemoradiotherapy-induced mucositis, lymphedema, promote healing in injuries, wounds, or lesions, for use as an antimicrobial, and even to treat tuberculosis. Some indications for Low-Level Laser Therapy include;

Hair loss, while not seen as a devastating disorder, does have an effect on quality of life due to a decline in self-esteem and is a high-stress producer. Low-Level Laser Therapy is a nonsurgical treatment that stimulates cell growth and supercharge hair follicles. It can combat hair loss and improve the volume and appearance of hair.

LLLT has been shown effective to help treat **traumatic brain injury (TBI)**, **spinal cord injuries (SCI)**, and stroke patients. TBI affects millions worldwide, being the leading cause of neurological disorder in people under 50, and is without effective treatment. The current treatment for TBI includes treating brain edema, reducing intracranial pressure, fighting against shock and hypoxia, and physical, occupational, and speech therapies to assist the patient in regaining quality of life and functional ability in activities of daily living (ADLs). In the United States alone, 2 million brain injuries occur each year, resulting in over 56,000 deaths. A traumatic brain injury can be caused by car accidents, falling from heights, or any other type of forceful impact to the cranial area. The **pathophysiology** of TBI is complicated and still poorly understood. It is known that immediately following the primary impact, activation of several pathways begins resulting in secondary brain injury. This includes inflammation, oxidative stress, ionic imbalance, increased vascular permeability, mitochondrial dysfunction, and excitotoxic damage. These things result in brain edema, increased intracranial pressure (ICP), and impaired cerebral perfusion. This combination of cellular and physiologic disturbances causes enlargement of infarct size, increased neuronal cell death, and neurological, motor, and cognitive impairment.

LLLT has been purported to treat TBI by increasing respiration in the mitochondria, causing activation of transcription factors, reducing inflammatory mediators and oxidative stress, and inhibiting **apoptosis** (cell death). These positive factors promote healing. Transcription factors are the protein that controls the rate of transcription of genetic information from DNA to messenger RNA, by binding to a specific DNA sequence. The flow of information from DNA to RNA to proteins is one of the fundamental principles of molecular biology.

There was a study performed on adult mice who were placed under anesthesia to induce a closed head injury (CHI) via a weight-drop device. A 69-gram weight was dropped through a 15 cm tube, and dropped onto a Teflon tipped cone placed on a lateral incision on the cranial aspect to induce a trauma that could be considered moderate to severe. After the suture of incision, the neurological condition was assessed using the Neurological Severity Score (NSS). The Neurological Severity Score has ten tasks and was designed to test mice after a traumatic injury. These tasks

include the inability to walk on beams of differing width, loss of startle behavior, and loss of seeking behavior. One point is awarded for each task failed, with the higher number indicating a higher degree of brain injury. For this study, only mice with an NSS score of 6-8 were utilized. Half of the mice were treated with sham laser therapy, while the other half were subjected to laser therapy. Four laser-treated groups of mice received a single treatment with 665, 730, 810, or 980 nm laser (36 J/cm² over 4-min) 4-hour post-injury at 150 mW/cm². NSS measurements in the control sham group of mice displayed a gradual improvement from a mean score of 7.3 at 1-hour post-TBI to 4.5 at 5 days, to 3.4 at 15 days, and to 2 at 28 days. Mice treated with 665 nm laser at 4-hour post-TBI started to show a significantly greater improvement than sham-treated mice on day 5. Scores on day 5 for mice treated with lasers were 2.78 versus 4.5 for the sham mice. On day 9, scores were 2.78 for treated mice and 4.5 for the sham mice. Improvement continued for day 9 at 1.55 versus 3.75. Day 14 resulted in treated mice measuring 1.22 versus sham mice at 3.37. On day 21, the improvement began to taper off a bit at 0.89 for treated mice versus 2.62 for sham mice, and at day 28 treated mice measured 0.78 versus 2.0 for sham mice.

Mice treated at 665 and 810 nm showed a higher recovery rate, with mice treated at 730 and 980 nm showing little significant difference between those mice and sham control mice. This study proved that Low-Level Laser Therapy including red laser (665 nm) and near-infrared (810 nm) can significantly improve neurobehavioral activity of mice following a closed head injury traumatic brain injury. This leads experts to believe that this shows promise for the application of low-level laser therapy on human subjects for brain damage from stroke or TBI.

Low-Level Laser Therapy is used to promote wound healing in superficial lesions as well as deeper injuries. Lasers or Light Emitting Diodes (LEDs) are useful in healing wounds in that they promote cell proliferation and migration (particularly by fibroblasts). They increase blood flow and collagen production which promotes healing and muscle growth. In a double-blind study performed with twenty-two healthy subjects aged 20-22 years old with height and weight in small variable ranges, two standardized 1.27 cm² abrasions were induced on the anterior forearm. After wound cleaning, standardized digital photos were recorded. Each subject received Low-Level Laser Therapy to one of the two randomly chosen wounds at 8 J/cm² for a treatment time of two minutes, five seconds, with a pulse rate of 700 Hz. Laser therapy was applied from either a laser or a sham 46-diode cluster head. Subjects reported back to the laboratory on days two through ten to be photographed and receive more Low-Level Laser Therapy, then again on day twenty to be photographed. Collected data was analyzed for wound contraction (reduction of area), color changes

to wound (chromatic red), and luminance (the homogeneity of the wound as the tissue heals).

It was found that at days six, eight, and ten, follow up testing and observance revealed that the laser groups had smaller wounds than the sham group for both the treated and untreated wounds. The conclusion stated that the Low-Level Laser Therapy resulted in enhanced healing as measured by wound contraction. The untreated wounds in subjects treated with lasers contracted more than the wounds in the sham group, so it is theorized that Low-Level Laser Therapy may produce an indirect healing effect on the surrounding tissues. The results indicate that lasers are an effective modality to facilitate wound contraction of partial-thickness wounds.

It should also be noted that lasers can have a cauterizing, or sealing, effect and may be used to;

- Seal nerve endings to reduce pain after surgery
- Blood vessels to help stem blood loss
- Lymph vessels to reduce swelling and limit the spread of tumor cells

It has been proven that low-level laser therapy, particularly UVC (ultraviolet light) with wavelengths between 200-280 nanometers, can be used for disinfecting water, sterilizing surfaces, and destroying harmful microorganisms in the air or on surfaces. UVC is often used to disinfect equipment such as safety goggles, instruments, medical scissors, pipettes, scalpels, and other devices. Lab personnel also disinfect glassware and plasticware using low-level laser therapy. Microbiology laboratories use UVC to disinfect surfaces inside biological safety cabinets (also known as "hoods") between uses. Some sources claim that wounds actually heal faster due to the laser light killing microbes and bacteria in the wound. This is useful due to drug-resistant bacterial strains, which are evolving and placing a strain on healthcare providers and encouraging them to use broad-spectrum antibiotics. It has been shown in studies that a laser using 658 nm wavelength evidenced a significant difference in bacterial growth when infrared (IR) or blue laser lights were utilized.

Lymphedema is swelling that generally occurs in one arm or leg. Lymphedema is a chronic and progressive condition that is characterized by the accumulation of protein-rich lymph fluid in the interstitial spaces. It can lead to chronic inflammation, fibrosis, and repeated infection. Cancer survivors with lymphedema may suffer from multiple symptoms, including inflammation, heaviness, firmness, tenderness, pain, numbness, aching, decreased range of motion (ROM), and stiffness. Consequently, physical deficits such as limb weakness and decreased range of motion may develop,

which limits a patient's ability to perform their activities of daily living (ADLs) or work duties. These issues cause psychological issues such as depression and anxiety and decreased quality of life.

This disorder is usually caused by the removal of or damage to the lymph nodes, such as damage caused by cancer treatments. Low-level laser therapy has been used in order to stimulate **lymphangiogenesis** (the formation of lymphatic vessels from pre-existing lymphatic vessels in a method believed to be similar to **angiogenesis**, which is blood vessel development), encourage lymphatic motility, and reduce **lymphatic fibrosis** (a progressive hardening of the skin that occurs in all patients with lymphedema).

Many case studies have been performed on breast cancer sufferers who were stricken with lymphedema. They are many varied, however most agree that a significant reduction in limb volume is evident. Skin improvement can be noted in each group that receives Low-Level Laser Therapy. Symptom distress of sadness and self-perception improved in most groups, with one case study improving from 76% to 33% symptom sadness, and self-perception improving from 36% to 0%. There was high evidence that symptoms such as stiffness, tenderness, and range of motion were reported to improve over long term application. It seems that while most agree that some volume reduction is evident, the real key to this therapy is that LLLT decreases the number of lymphedema symptoms, relieves symptoms of impaired mobility, and improves emotional distress. Low-Level Laser Therapy in conjunction with conventional treatments plays an important role in treating lymphedema, with a focus on symptom management.

Tuberculosis (TB, M. Tuberculosis) continues to be a worldwide health issue. According to the CDC (Centers for Disease Control), tuberculosis is the leading cause of death from a single infectious disease agent, and also the leading cause of death among persons living with human immunodeficiency virus (HIV) infection. In 2017, worldwide, 10 million people fell ill with tuberculosis. Of those, 1.6 million died including 300,000 deaths among people with HIV. An estimated one million children became ill with TB, with 230,000 of those stricken dying. Approximately 95% of TB cases and deaths occur in low- and middle-income countries, due to limited access to treatment. India has a reported majority, with one-third of total worldwide TB cases. The United Nations (UN) Sustainable Development Goals and the World Health Organization (WHO) have implemented a TB Strategy which defines ambitious targets for 2020-2035, including a 35% reduction in the absolute number of TB deaths and a 20% reduction in TB incidence by 2020, as compared with the 2015 reports. Since

2000, WHO has produced annual TB estimates for all countries to track the progression of their attempts to limit this disease.

The main treatment for tuberculosis is antituberculosis medications. The emergence of multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant TB (XDR-TB) is a major threat to global TB control and treatment since the therapeutic cure rate is low in such cases. As such, it is vital to explore other treatment options. The first goal in the control of tuberculosis is to promote rapid conversion to acid-fast bacillus (AFB) smear negativity of TB patients, since every open case of TB is likely to generate eight more cases of tuberculosis in one year. A negative AFB smear test may mean that no infection is present, or that bacteria is present in numbers not sufficient to be seen under a microscope. Low-Level Laser Therapy laser has been shown to have direct antibacterial effects, and also accelerates intracellular killing of phagocytosed bacteria within the **macrophages**. Macrophage activation is necessary for the killing of intracellular organisms such as bacteria. The activated macrophages produce cytokines like **TNF-alpha** (Tumour Necrosis Factor-alpha) and **GM-CSF** (Granulocyte-macrophage colony-stimulating factor) which inhibit the growth of *M. tuberculosis* within macrophages. The efficient intracellular killing of **phagocytosed** *M. tuberculosis* is key in the control of tuberculosis.

Low-level laser therapy at 337 nm and 2 W has shown to be very effective in inhibiting the growth of and killing *M. Tuberculosis*. There have been multiple case studies performed to explore the efficiency of this treatment. In one such study, a 19-year-old male presented with ABF positive sputum and drug resistance for two and a half months. An X-ray of his chest area showed a cavity in his right mid-zone. In this instance, an intracavity laser was applied for ten minutes. The patient subsequently became asymptomatic with negative ABF sputum. The cavity in his right mid-zone had disappeared within six weeks, and there had been no recurrence of a cavity or positive sputum in the following three years of follow up.

A 46-year-old female had been undergoing various types of treatment for over 20 years with no success. An x-ray of the chest revealed multiple large cavities on both sides of the lungs combined with heavy infiltration. She was supplied with two treatments of intracavity laser therapy of ten minutes duration. She experienced good improvement, with no fever, no hemoptysis, a mild cough, with ABF negative sputum. A follow-up x-ray showed that some of the cavities had disappeared.

It is apparent that Low-Level Laser Therapy is effective in a majority of tuberculosis case treatments. Symptoms such as cough and pain were relieved. Sputum negativity

is shown in 75% of treatments performed and studied, which is important in slowing the spread of this deadly disease.

The use of Low-Level Laser Therapy in treating chemoradiotherapy-induced mucositis is a novel treatment. Chemoradiotherapy-induced mucositis is evidenced by tissue swelling and lesions in the mouth as a result of receiving chemotherapy for cancer. It is considered the most common and debilitating side effect of chemotherapy and radiation. Mucositis occurs when cancer treatments break down the rapidly dividing epithelial cells lining the gastrointestinal tract (which goes from the mouth to the anus), leaving the mucosal tissue open to ulceration and infection. The part of this lining that covers the mouth, called the oral mucosa, is one of the most sensitive parts of the body and is particularly vulnerable to chemotherapy and radiation. The oral cavity is the most common location for mucositis. This disorder can cause pain, and lead to nutritional problems as a result of restricted oral intake, and increased risk of infection due to open wounds. It has a significant effect on quality of life, and can lead to limiting doses of chemotherapy resulting in less effective treatment.

Laser therapy can be applied directly to the mucosal membranes, usually at a wavelength of 10.6 nm and continuous wave at 1.0-1.5 W. Application of a gel with a high water content should be applied prior to use to protect from possible dehydrating effects. Near immediate pain relief has been reported from patients after treatment, with fast healing noted (often within 5-7 days). The laser therapy reduces the inflammation of the lesions, accelerates tissue regeneration, and lessens the pain associated with mucositis. As a result, patients report better quality of life due to the ability to ingest more food, thereby receiving better nutrition, and improved mood and outlook due to the decrease in pain.

Low-Level Laser Therapy has been mentioned in treating mood disorders. Laser therapy is proven to have success in treating wounds and providing pain relief, which in itself would naturally boost the quality of life and thereby mood. Specifically, Major Depressive Disorder is a leading form of psychiatric disorder. Also known as clinical depression, major depression, unipolar disorder, and recurrent depression, this disorder is characterized by aversion to mobility, neurotransmitters deficiency, low mood, low self-esteem, loss of interest in normally enjoyable activities, pain without a clear cause, and energy metabolic decline. Major Depressive Disorder affects approximately 16% of the world's population with high risk of suicide, increased probability to develop disorders such as;

- Coronary Artery Disease
- Parkinson's Disease

- Autoimmune Diseases
- Stroke
- Cancer
- Type 2 Diabetes
- Insomnia
- Eating disorders
- Chronic pain
- Chronic fatigue
- Decreased sex drive
- Increased risk for substance abuse

Besides the massive drain on the patient, depression leads to a detrimental effect on family and interpersonal relationships, and substantially contributes to a global burden of public health. Low-Level Laser Therapy has been studied in a variety of neurodegenerative disorders associated with mitochondrial dysfunction and functional impairments. Low-Level Laser Therapy has been shown to modulate many biological processes, such as anti-oxidation, anti-inflammation, cell proliferation, and angiogenesis. Low-Level Laser Therapy has also shown evidence to increase ATP biosynthesis and the level of mitochondrial complex IV expression activity. Elevated ATP supply enhances cell growth, biosynthesis, export of target products, and increases the acid tolerance of cell factories. Adenosine triphosphate (ATP) is the organic compound that provides energy to drive many processes in living cells such as muscle contraction, nerve impulse propagation, and chemical synthesis. ATP is found in all forms of life and is often referred to as the unit of currency of intracellular energy transfer.

Mitochondria produces the energy, ATP, in the cell and regulates cellular metabolism. If someone has a Mitochondrial Complex IV deficiency, they can suffer from many symptoms including muscle weakness, exercise intolerance, developmental delay, delayed motor development, hypertrophic cardiomyopathy, **hepatomegaly**, liver dysfunction, and mental retardation. In addition to stemming the negative effects of a deficiency, increased mitochondria improves the body's ability to produce energy. In other words, the more mitochondria a person has, the more energy that can be generated during activity, and the faster and longer a body can function. Studies on mitochondrial associated chronic depression models have found that the levels of several mitochondrial complexes were reduced in the brain cortex area. There exists compelling evidence that Low-Level Laser Therapy can preserve mitochondrial function by increasing cytochrome c oxidase activity.

Research has suggested that the **pathogenesis** of depression is linked to an imbalance of monoamine transmitters in the brain with regards to serotonin and dopamine. Serotonin is a chemical nerve cell produce that sends signals between your nerve cells. Often called the happy chemical, it contributes to wellbeing and happiness. Serotonin is involved in the regulation of quite a few important physiological functions, including sleep, aggression, eating, and mood. Dopamine is also a happy chemical, and plays roles in regulating mood and emotion. Dopamine plays a heavy role in the regulation of the drive to seek out rewards, as well as the ability to obtain a sense of pleasure. Research suggest that a decrease in serotonin and dopamine production will lead to depression, and difficulty in handling the effects of stress efficiently

Distinct depression symptoms correspond to specific neurotransmitter deficiencies, suggesting that the pathology of depression is neurotransmitter dependent. This has been targeted by anti-depressant drug treatments such as Selective Serotonin Reuptake Inhibitors (SSRIs). These drugs treat depression by increasing levels of serotonin in the brain. SSRIs include such drugs as Celexa, Prozac, Zoloft, and Paxil. The problem with SSRI drugs are the numerous side effects. Patients may suffer from nausea, vomiting, diarrhea, headache, drowsiness, dry mouth, insomnia, nervousness, agitation, restlessness, and dizziness amongst others. To counteract this, LLLT can be used as an alternative or complementary treatment.

A study was performed and published to the US National Library of Medicine National Institutes of Health using male adult mice as subjects in 2018. Tests were performed to introduce stress into the mice. These tests were necessary to create stress in the mice, and all mice were returned to their warm, dry cages after testing with free access to food and water. For example, mice were individually placed into a modified, well ventilated 50 ml centrifuge tube for 2 hours every day for 2 weeks to develop a depression **phenotype**. In this centrifuge, the mice movements were restricted and they were unable to move forward or backward. This is referred to as Spatial Restraint Stress. Control mice remained undisturbed in their cages to serve as comparison models. The Forced Swimming Test is a procedure by which mice were individually placed in a 2-liter glass beaker filled with 1.5 liters of water at 77 degrees Fahrenheit and allowed to swim freely for 6 minutes. The Tail Suspension Test was performed by attaching a wood rod to the tail by adhesive tape that kept the mouse to be suspended at 35 centimeters above the surface for six minutes. During the Tail Suspension Test and Forced Swimming Test, immobility of the mice was measured and recorded. Mitochondrial Complex and ATP levels were measured in each mouse to determine depression rates. It was noted that the stressed mice exhibited significantly greater immobility and less motor activity than the control mice,

indicating a representative depressive phenotype after repeated Spatial Restraint Stress tests. Results of testing showed dramatically decreased dopamine levels in the hippocampus of the stress mice compared with the control mice. Taking into account the demonstrated neurotransmitter decline and motor activity decrease, data suggested that the depressive phenotype had been successfully developed in mice subjected to the Spatial Restraint Test.

Laser therapy treatment was administered using a diode laser with a continuous wave of 808 nm and a maximum power output of 30 mW. During the treatment, mice were positioned on a plastic plate with the head covered by an aluminum sheet with a 1 cm diameter hole centered over the cerebral cortex. After positioning of the mice, laser therapy was initiated with a power output density of 23 mW/cm² by focussing the distal tip of the fiber optics on the top of the head over a shaved scalp. The duration of laser irradiation was 30 minutes per day for a total of 28 days immediately after Spatial Restraint Testing. It was discovered that immobility time as measured by the Tail Suspension Test and Forced Swimming Test was significantly reduced in comparison with mice who were in the depression group who did not receive Low-Level Laser Therapy. These differences were maintained at a noticeably stable level from the 21st day of testing on. This study found that LLLT of 808 nm exerts efficient depressive relief of depression-like behaviors by decreasing the immobility and promoting motor activity.

Section 2 Summary

LLLT can treat many diseases, including tuberculosis, depression, hair loss, chemoradiotherapy induced mucositis, lymphedema, treat traumatic brain injuries, stroke, and promote wound and injury healing, amongst other things. Mice are commonly used as test subjects due to the physiological symmetry to humans. Low-Level Laser Therapy is a wonderful tool to promote healing, reduce inflammation, and improve cell regeneration. The indications for Low-Level Laser Therapy are varied and are still being discovered and researched.

Section 2 Key Concepts

- ***Angiogenesis*** - blood vessel development
- ***Apoptosis*** - the death of cells that occurs as a normal and controlled part of an organism's growth or development.
- ***Biosynthesis*** - the production of complex molecules within living organisms or cells.
- ***Cardiomyopathy*** - is a disease of the heart muscle that makes it harder for your heart to pump blood to the rest of your body. This disease can lead to heart failure.

- **Chemoradiotherapy-induced mucositis** - Mucositis is the painful inflammation and ulceration of the mucous membranes lining the digestive tract, usually as an adverse effect of chemotherapy and radiotherapy treatment for cancer. Hence the term chemoradiotherapy induced, meaning caused by.
- **Cytokines** - a large group of proteins secreted by specific cells of the immune system, responsible for mediating and regulating immunity, inflammation, and hematopoiesis.
- **GM-CSF** - also known as colony-stimulating factor 2 (CSF2). This is a monomeric glycoprotein secreted by macrophages, T cells, mast cells, natural killer cells, endothelial cells, and fibroblasts that functions as a cytokine.
- **Hepatomegaly** - abnormal enlargement of the liver
- **Macrophage** - a large phagocytic (white blood) cell found in stationary form in the tissues or as a mobile white blood cell, especially at sites of infection
- **Pathogenesis** - the manner of development of a disease, the source
- **Pathophysiology** - the disordered physiological processes associated with disease or injury.
- **Phagocytosed** - from phagocytosis, with phagein meaning 'to eat', and kytos meaning 'cell'. This is the process by which a cell uses its plasma membrane to engulf a large particle.
- **Phenotype** - the set of observable characteristics of an individual resulting from the interaction of its genotype with the environment.
- **TNF-Alpha** - an inflammatory cytokine produced by macrophages/monocytes during acute inflammation and is responsible for a diverse range of signaling events within cells, leading to necrosis (premature death of cells) or apoptosis (natural death of cells). The protein is also important for resistance to infection and cancers.
- **Traumatic Brain Injury (TBI)** - Brain dysfunction caused by an outside force, usually a violent blow to the head.

Section 3: Low-Level Laser Therapy and Pain Relief

Low-Level Laser Therapy is often used in situations requiring pain relief. It has been shown to reduce inflammation, accelerate tissue regeneration, and promote the production of endorphins (peptides that provide an analgesic, or pain-relieving, effect). Low-Level Laser Therapy can be used for acute and chronic pain. Acute pain is considered to last less than thirty days, while chronic pain is of more than six months duration or as “pain that extends beyond the expected period of healing”.

Nociceptive pain and neuropathic pain are the most common types of pain. Clinically, Low-Level Laser Therapy can treat both types of pain. It has not been proven to treat *central pain*, which is pain that is caused by damage or disease to the central nervous system. Nociceptive pain is pain that has been caused by an injury or physical damage, while neuropathic pain is caused by illness or injury to the central nervous system. Nociceptive pain is caused by the activation of specific pain receptors in response to noxious stimuli, while neuropathic pain reflects nervous system damage, dysfunction, or illness. Pain is typically treated with the use of NSAIDs (Non-steroidal anti-inflammatory drugs), opioids (narcotic pain relievers), hot and cold therapy, massage, hydrotherapy, exercise, acupuncture, and various other methods.

Opioids and NSAIDs are often prescribed as long term treatment, yet they each have their dangers. NSAIDs work by reducing the sensitivity of nociceptors, which are the body's pain receptors, in the peripheral nervous system, but they can have significant or even life-threatening side effects. Aspirin, Advil, Motrin, and Aleve are examples of NSAIDs. Side effects of NSAIDs include;

- Stomach pain
- Heartburn
- Stomach ulcers
- Headaches
- Dizziness
- “Thinning” of the blood, or tendency to bleed more
- High blood pressure
- Ringing of the ears
- Liver or kidney problems, up to and including kidney failure
- Fluid retention
- Gas
- Bloating
- Nausea
- Increased risk for stroke and heart attack

Opioids include drugs such as Fentanyl, Vicodin, Codeine, Morphine, and many others. These drugs work by attaching to proteins called opioid receptors on nerve cells in the brain, spinal cord, gut, and other parts of the body. When this happens, the opioids block pain messages sent from the body through the spinal cord to the brain, effectively reducing the sensation of pain.

Side effects of opioids include;

- Nausea and vomiting
- Dizziness
- Sedation
- Confusion
- Respiratory depression
- Constipation
- Dependency and addiction
- Muscle rigidity
- Overdose and death

Opioids are dangerous due to the high potential for abuse. When taken, they produce a feeling of pleasure due to the strong release of endorphins. This makes people more likely to abuse medication, causing addiction and dependency. Taken at high levels, these pleasurable feelings increase, but respiratory and heart rates are also slowed which increases the risk of death.

Instead of using medications to treat pain, Low-Level Laser Therapy is a viable alternative. Low-Level Laser Therapy can treat both **nociceptive** and **neuropathic** pain by interfering with action potential propagation in axons of the **A-delta** and **C-nerve** fibers. This means that it interferes with the information sent down the axon away from the cell body of the A-delta and C-nerve fibers. The A-delta nerve fibers carry information related to touch, and the C-nerve fibers carry information related to pain, temperature, and touch. It is a superior alternative to NSAIDs, without the known side effects.

Pain conditions that may benefit from Low-Level Laser Therapy treatment for pain include, but are not limited to;

- Rheumatoid Arthritis is a disease in which the body's immune system attacks its own healthy tissues. The attack happens mostly in the joints of the hands and feet and causes redness, pain, swelling, and heat around the joints. Laser therapy is used to decrease pain, increase range of motion (ROM), decrease stiffness, and decrease edema (swelling).
- Osteoarthritis of the joints is the degeneration of joint cartilage and the underlying bone, most common from middle age onward. It causes pain and stiffness, especially in the hip, knee, and thumb joints. Laser therapy is used to relieve this stiffness and pain, improve range of motion, and reduce edema.
- TMD (Temporomandibular Joint Disorders) are disorders of the jaw joint, which is the sliding joint joining the lower jaw to the skull. Jaw pain, difficulty chewing, and clicking and locking of the jaw joint are some of the symptoms.

Laser therapy is used to reduce the pain intensity, number of tender points in the jaw, decrease joint sounds, and improve range of motion.

- Shoulder Impingement Syndrome occurs when there is impingement of the bursa or tendons in the shoulder. This can be caused by repetitive motions and is typically characterized by persistent pain from reaching overhead or behind the back. Laser therapy is effective to relieve pain, edema, and improve functional ability.
- Bursitis is the inflammation of the fluid-filled sacs around the joints, commonly of the shoulder, hip, or knee. Laser therapy is used to reduce inflammation, thereby reducing pain felt from said inflammation.
- Disc Herniation is when a fragment of the disc nucleus is pushed out of the annulus (the tough circular exterior of the intervertebral disc that surrounds the soft inner core, the nucleus pulposus), into the spinal canal through a tear or rupture in the annulus. Discs that become herniated usually are in an early stage of degeneration. Low-Level Laser Therapy is used to assist in pain reduction and inflammation management.
- Disc Degeneration occurs when the discs in the spine begin to show signs of wear and tear, usually from age. This causes pain and loss of mobility. Laser therapy can benefit the patient by reducing inflammation, improving range of motion, and lessening pain symptoms.
- Neuropathic pain is caused by damage or injury to the nerves that transfer information between the brain and spinal cord from the skin, muscles, and other parts of the body. This can be caused by nerve damage, spinal cord injury, or diseases such as diabetes. Laser therapy can be beneficial in repairing the myelin sheath, which is the insulating layer that forms around the nerves. It is made up of protein and fatty substances and allows electrical impulses to transmit quickly and efficiently along the nerve cells.
- Tendonitis is inflammation of a tendon, caused by overuse or injury. Laser therapy increases blood flow to the damaged tendon, promoting healing. It also reduces pain and inflammation.
- Sciatica is back pain caused by the impingement of the sciatic nerve. This pain can spread to the hips, buttocks, and legs. Besides pain and edema relief, Low-Level Laser Therapy has been proven to promote the regeneration of peripheral nervous tissue, which can relieve the pressure on the sciatic nerve.
- Tennis Elbow is an inflammation of the tissue connecting the forearm muscle to the elbow. This is usually caused by repetitive motion injury, such as playing a lot of tennis. Laser therapy can relieve pain and improve functional mobility without resorting to surgery.
- Plantar Fasciitis is the inflammation of the thick band of tissue connecting the heel bone to the toes. It is caused by repetitive stress to the area, by way of

excessive running or walking, improper footwear, and jumping injuries. Laser therapy can be used to help with inflammation, pain relief, and to help the area heal.

- Sprains, which are stretching or tearing of the connective ligaments. Laser therapy can help promote blood flow and healing and assist with inflammation and pain relief.

Musculoskeletal pain is reported to be the number one pain-related reason for missing work or school days. Musculoskeletal disorders comprise over 150 diagnoses that affect the locomotor system. It was estimated in a Global Burden of Disease (GBD) study in 2017 that 20-33% of people around the globe suffer from some form of musculoskeletal condition. Low back pain is a musculoskeletal condition, and remains the number one cause for disability since it was first measured in 1990. In America alone, musculoskeletal pain affects over 110 million individuals a year with a monetary loss of more than \$600 billion a year in loss of productivity, medical bills, and missed work or school.

It is reported that the majority of neuro-musculoskeletal conditions respond better to a higher power and a higher dosage, which is a function of power output and time. The best results are purported to be obtained with a laser that has 30 W of power or more. A 10-minute treatment with a 30 W laser will produce 18,000 joules, which gives a significant anti-inflammatory, healing, and pain-relieving effect.

A case study was performed in 2015 regarding the effects of Low-Level Laser Therapy on musculoskeletal pain. This study analyzed over 4000 case studies and concluded that the majority of laboratory and clinical studies have demonstrated that LLLT has a positive effect on acute and chronic musculoskeletal pain. It is recognized that due to the diversity of populations, interventions, and comparison groups, not every single study has been positive. LLLT regimens are complicated by different lengths of treatment, in addition to no standardization of wavelengths and dosages. There have been no long term case studies of LLLT as of this time (none longer than two years). Case studies have however been overall positive, although LLLT is currently classified as experimental by most insurance companies.

Many sufferers of neck pain are seeking relief from symptoms using Low-Level Laser Therapy. Neck pain is a common musculoskeletal condition that affects nearly 10% of the American population. Common conditions associated with neck pain include degenerative disc disease, degenerative joint disease, and disc herniations. Low-Level Laser Therapy has been shown to have a significant effect on pain reduction for patients suffering from neck pain. It is advised that the pain site should be targeted

for 3-4 minutes at 1000 Hz (30-50 J) in a static position to keep the delivered dose constant. With FDA approval for temporary relief of muscle and joint pain, this emphasizes the need for further well-designed clinical studies.

In one case study concerning pain and wound care, a 29-year-old female was treated who had second-degree scalding burns to right and left thighs, abdomen, and flank. The patient was injured during a hot water bottle leak that had been placed on the pelvic and abdominal region for the reduction of pain for menstrual cramps. The patient was a nonambulatory and nonverbal with cerebral palsy. When the hot water bottle leaked she was unable to alert the caregiver of the scalding water in a timely manner to avoid injury. In addition to Tylenol with Codeine for pain, Augmentin as an antibiotic, and Bacitracin and Silver Sulfadiazine for wound healing, the patient was prescribed Low-Level Laser Therapy for additional relief. A second-degree burn was noted on the right thigh measuring 11 cm x 7 cm with a large, waxy white center. On the left thigh, a second-degree burn measuring 12 cm by 7 cm was noted. A second-degree burn on the left abdominal flank and back was noted measuring 31 cm x 12 cm with a waxy, white centering surrounded by erythema.

Low-Level Laser Therapy was applied to lesion sites to facilitate the cellular responses to inflammation, pain, circulation, and lymph drainage. The goal was to accelerate wound healing by affecting fibroblasts with the laser light to improve cellular ATP production, collagen synthesis, and scar tissue remodeling. The Low-Level Laser that was used in this treatment combined the following characteristics;

- IR laser radiation 0.4-1.6 mW 900 +/- 50 nm
- IR LED radiation 30-90 mW 860-960 nm
- Red LED radiation 2-10 mW 600-740 nm
- Static magnetic field 25-45 mt
- Total radiation of 60-90 mW, with pulsed laser power at 8-24 W

The Low-Level Laser Therapy treatment protocols called for treatment in two-day intervals for the first week using programmed frequencies for wounds, burns, and inflammation by focusing on the cells well below the skin surface and treating cells in the different skin layers on three treatment dates. The emitter was held at 90 degrees to the tissues and scanned 1 cm over the waxy, white centralized lesions.

For the first week, dosimetry with a total of two applications of 1000 Hz frequency at 4 minutes intervals (for skin layers), and with applications of 50 Hz at five-minute intervals (for the below skin layer) was delivered to the total area of the injured sites. Due to the size of the wounds, the total body size of the patient (42 cm tall and

39 lbs), the quantity of injured tissue, and patients' neurological integrity, scanning techniques using both non-contact and contact methods were practiced.

During the second and third weeks, the dosimetry applied was with programmed frequencies of 2x of 1000-3000 Hz for edema reduction, lymphatic drainage, cellular proliferation, and cellular turnover. Programmed frequencies 2x of 1000 Hz for skin cell regeneration, increase of circulation and reduction of scar tissue formation were also applied. It was noted that the patient experienced hypertrophic scarring and raised margins around each wound, reddened centers of increased circulation, and decreasing waxy, white plaques. The patient comfort level was considerably improved, resulting in discontinued use of Tylenol with Codeine. There was no evidence of bacterial intrusion of the wounds. Wound dressing was changed from Bacitracin and Silver Sulfadiazine was changed to Silver Shield Cosmetic Gel with Aqua Sol Technology. The course of Augmentin oral antibiotics was completed.

The dosage applied during the fourth to eighth-week protocols was a programmed frequency of 1x 1000-3000 Hz, 1 x 1000 Hz, 1 x 50 Hz. Dose was applied at 90-degree scanning from central to peripheral margins with non-contact. Treatment intervals varied between five to seven days, and up to 14 days. During this time, the wounds exhibited less **suppuration** with lessening areas of hypertrophic scarring, wound area narrowing, and continues to be absent of signs of bacterial activity. Patient comfort levels continued to improve, with no signs of distress noted. Silver Shield Cosmetic Gel with Aqua Sol Technology was discontinued. Vitamin E ointment over wounds and scars was begun.

During the ninth to fourteenth week, dosimetry was applied with program frequencies of 1 x 1000-3000 Hz or 1 x 1000 Hz with 1 x 50 Hz per treatment. A scanning method was utilized from the center to the periphery of each wound with non-contact at centers and contact at outer margins to avoid contact of most compromised areas. The treatment schedule varied from seven to fourteen-day intervals. Wounds began to exhibit diminished total length and width of necrotic and damaged tissues. New epidermal layers flattened without hypertrophic scarring, and outer peripheral margins were noted to exhibit melanin layering. It was decided to continue LLLT at seven to ten-day intervals until all burn lesions were completely healed and all scar margins were cosmetically acceptable.

Over fourteen weeks, the size of each burn lesion decreased as healed tissue replaced necrotic areas. There was no visible evidence of bacterial infection or invasion. The new skin showed evidence of increased **tensile elasticity**. Scar formation improved from raised margins to flattened, smooth blending patterns. Inflammatory markers

such as edema, redness, heat, and pain improved along with the levels of tissue healing per treatment with the laser. The initial white, waxy burned centers were replaced with healthier pink cutaneous tissue as granulation ensued. Increases in lymphatic drainage allowed for cellular waste removal and reduction of inflammatory mitigators. Overall comfort level of the patient improved each week as determined by the patient's improved demeanor and sleeping patterns.

This clinical case demonstrated the speed and efficiency of the use of Low-Level Laser Therapy in cases of skin conditions and wounds. Because of the direct skin contact, in this case, the visible outcomes of the effects on the second-degree burns were seen rapidly at the cellular level, largely due to the turnover rate at the epidermis. Vascularity was improved, which played a large role in the healing process. The decreased edema and increased lymphatic drainage as well as the improved phagocyte activity brought the reduction of central wound margins as the tissues were healing from the center out. Between treatments, increased fibroblast activity was seen in the cellular proliferation rates. Increased epithelial production and increased collagen production caused new skin margins to develop without overproduction of scarred, inelastic tissues on the outer margins of the wounds.

It was determined that the wavelengths needed to stimulate cellular ATP production appear to be the 635 nm and 820 nm ranges. The use of light therapy sources with these two wavelengths induce more protein synthesis and result in increased cell proliferation benefiting wound healing. Low-Level Laser Therapy does not raise the temperature of the tissue being irradiated by more than one degree, which means that change arrives via bioelectrical, biomagnetic, and biochemical effects. The repetition of the doses of pulsed laser light amplified cellular and systemic effects. Utilizing proper technique when scanning the burned tissues, frequency of treatment, repair time intervals, and medications supplied to the wound areas were all beneficial and contributed to the efficient healing of the wounds and limiting of the keloid and hypertrophic scarring. These results regarding wound healing are encouraging and should promote clinicians to use this modality as a tool to accelerate healing, relieve pain, reduce scarrings, and improve all symptoms and outcomes for patients with burns or other wounds.

Osteoarthritis (OA) also appears to be positively affected by Low-Level Laser Therapy. Osteoarthritis, also known as degenerative arthritis, is the degeneration of joint cartilage and the underlying bone, most common from middle age onward. It causes pain and stiffness, especially in the hip, knee, and thumb joints. Osteoarthritis is the most common type of arthritis, and according to the United States Arthritis Foundation affects more than 27 million people in the United States. When a patient

has osteoarthritis, the cartilage in the joints breaks down, which will eventually cause the bones to rub together and joints to become inflamed with subsequent pain, bone injury, and even bone spur formation. The periarticular tissues are also affected by the disease, resulting in muscle atrophy and ligament dysfunction. Some factors for the development of Osteoarthritis include advancing age, obesity, injuries, family history, and overuse of the joint. Common symptoms include;

- joint soreness
- morning stiffness
- Loss of balance and lack of coordination
- Increasing disability due to loss of function
- Pain upon rest or weight-bearing upon affected extremity

Many studies have been performed on osteoarthritis patients. One such case study involves patients with osteoarthritis of the knee in conjunction with static stretching exercises. This study aimed to examine the effects of Low-Level Laser Therapy and stretching as monotherapy and in combination with pain relief, quality of life, function, mobility, and range of motion (ROM) in patients with knee osteoarthritis. The study involved 145 people aged 50-75 years with osteoarthritis. The patients were allocated into five groups;

- True LLLT and stretch
- Sham LLLT and stretch
- Stretch alone
- LLLT alone
- Control group

Treatment frequency was three sessions per week for all active groups. Treatment involved the use of a **Gallium-Arsenide laser** at 904 nm, 40 mW, 3 J per point, 27 J per knee for 24 sessions for the monotherapy group, and nine sessions for the LLLT and stretch groups. Stretching consisted of seven exercises completed over 24 sessions. Participants were treated for 2 months (stretch, Low-Level Laser Therapy, and Control groups) or 3 months (Low-Level Laser Therapy and stretch groups). Participants and outcome assessors were blind to treatment allocation throughout the study. The **Visual Analog Scale (VAS)** was used to measure the pain throughout the treatment and at the outcome. Secondary outcomes included quality of life as assessed by **Western Ontario and McMaster Universities Arthritis Index**, function was measured by **Lequesne Algofunctional Index**, mobility by the **Timed Up and Go Test**, and knee range of motion was measured by goniometry of knee flexion.

Low-Level Laser Therapy has been used as a resource to increase the therapeutic effects of Physical Therapy. The specific dose and treatment frequency have not been well defined. Physical Therapy treatment aims to relieve pain, improve function, quality of life, mobility, joint function, knee stabilization, reduce the load on the joint, promote the adaptation of certain activities, prevent deformities, and slow the progression of the disease. Exercise and weight reduction have had high-quality effects on the improvement in pain and function. Acupuncture, **transcutaneous electrical nerve stimulation (TENS)** have had moderate quality of evidence for the same variables. Prior conflicting reports have been published over the efficacy of Low-Level Laser therapy in regards to osteoarthritis treatment, more than likely due to the great variability in relation to the wavelength, dosage, localization of application points, frequency and duration of treatment, and the absence of calibration of the lasers. It has already been shown that laser therapy has been utilized successfully to control the pain of various musculoskeletal disorders. It is believed that in regards to the inflammatory nature of osteoarthritis, that laser therapy can have a beneficial effect by modulating the inflammatory process.

In the combination of Low-Level Laser Therapy and stretching, the aim was to relieve pain with the initial use of the laser to enhance the effect and implementation of stretching exercises. The five intervention groups part of the study were treated as follows;

- Low-Level Laser Therapy and Stretch- 3 weeks of Low-Level Laser Therapy followed by 8 weeks of stretching exercises
- LLLT Sham and stretch- 3 weeks of placebo LLLT followed by 8 weeks of stretching exercises
- Stretch- 8 weeks of stretching exercises alone
- LLLT- 8 weeks of active LLLT
- Control group- minimal intervention provided through educational booklet

Patients were assessed prior to starting treatment and reassessed after each intervention. Patients who continuously use NSAIDs and/or medications such as glucosamine sulfate and chondroitin to control Osteoarthritis were instructed to discontinue said drugs until the end of the study to avoid possible research bias. For pain control during the intervention study period only analgesics such as Tylenol and heat therapy were allowed, but none 48 hours prior to reassessment in order to avoid possible confusion.

The control group received an educational booklet at the baseline visit consisting of explanations about the disease, postures during activities of daily living, and

information for the management of pain. The Physical Therapist educated the patient in detail of each point, and performed weekly telephone follow-ups to answer and ask questions regarding the educational content and the patients' state of health. Reassessment occurred after 8 weeks.

Stretching was performed by patients after a 10 minute warm-up period on a stationary bike with a light load and comfortable machine or on a treadmill at a speed of 2.0 km per hour and no slope. This treatment was conducted at a frequency of 3 times per week and lasted approximately 45 minutes. The treatment consisted of seven segmental stretching exercises, repeated 4 times, and sustained for 30 seconds each. The intensity of the stretches followed the recommendation of the American College of Sports Medicine positioning with middle discomfort. Patients were correctly positioned and guided by a Physical Therapist to be aware of body positioning and movement, breathing, and alignment throughout the therapy. The muscles stretched were the major muscles of the posterior and anterior-internal hip muscle chains, such as the paraspinal muscle, gluteus, iliopsoas, hamstrings, quadriceps, hip adductors, and gastrocnemius.

The Low-Level Laser Therapy was performed using a pulsed laser with a wavelength of 904 nm. The Gallium Arsenide diode laser has the technical specs of peak power 70 W, pulse duration 60 ns, pulse repetition rate 9500 Hz, and beam area of 0.1 cm². Exposure duration was 11 minutes and 25 seconds with 3 J per point energy. Nine points per knee were irradiated with contact pressure, meaning a total of 27 total J per knee. The dose of the 3 J was 75 seconds per treatment point.

The nine points irradiated with Low-Level Laser Therapy include three on the medial joint line, two on the lateral joint line, and four points over the borders of the knee cap. Participants, sham and active, were positioned in a seated position. The laser probe was placed on the knee points sequentially and perpendicularly, in full contact with the skin.

Results indicated that while minimal to moderate improvement was noted with the Control (min), sham LLLT and stretch (min-mod), and stretch alone (min-mod), LLLT and stretch patients reported an overall decline in pain, reduction in inflammation, improvement in functional ability, and better quality of life. The study seems to be a positive indicator that LLLT is a novel accessory to the treatment of osteoarthritis. Of course, more study is needed before conclusively identifying treatment parameters and all of the benefits that could be available.

Section 3 Summary

Specifically for Physical Therapists, Low-Level Laser Therapy is most commonly used to assist in pain relief and to simultaneously promote healing. Musculoskeletal pain is the most common reason for loss of school or work hours and costs millions of dollars worldwide in loss of productivity, medical bills, and lost income. Of musculoskeletal pain disorders, low back pain is the leading cause of disability claims worldwide. The most common treatments for pain include NSAIDs and opioids, which have mild to severe and even life-threatening side effects. Opioids also have a high tendency for abuse, resulting in addiction and even death. Low-Level Laser Therapy has the potential to mitigate some of these issues, and lessen the dependency on drugs which may cause more harm than good. Physical Therapy, chiropractic treatments, and surgical intervention are also used to assist in different types of pain relief. Surgeries are invasive procedures with risk of infection, complications, and stemming medical issues. Surgeries are often the last result. Low-Level Laser Therapy has multiple applications in wound healing by promoting ATP production, improved cell proliferation, decreased scar tissue, improved new skin elastic, improved mitochondrial function, increased fibroblast activity, and increased epithelial and collagen production are all benefits of Low-Level Laser Therapy treatments. It has been shown that Low-Level Laser Therapy can hold a large supporting role in conjunction with medication and other treatments for wounds and pain relief.

Section 3 Key Concepts

- **A-Delta nerve fiber** - nerve fibers that carry information to the brain concerning touch
- **Analgesic** - pain relieving
- **C-Nerve Fibers** - nerve fibers that carry information to the brain concerning pain, temperature, and itch
- **Central pain** - a neurological condition caused by damage to or dysfunction of the central nervous system (CNS), which includes the brain, brainstem, and spinal cord. Central pain syndrome can be caused by stroke, multiple sclerosis, tumors, epilepsy, brain or spinal cord trauma, or Parkinson's disease, amongst others.
- **Endorphins** - a group of hormones secreted within the brain and nervous system that have a number of physiological functions. Endorphins are peptides which activate the body's opiate receptors, causing an analgesic effect.
- **Gallium-Arsenide laser** - The aluminum gallium arsenide laser is a diode laser, having similar characteristics as that of the aluminum gallium indium phosphide laser.
- **Lequesne Algofunctional Index** - A questionnaire composed of 11 questions about pain, discomfort, and function. Each answer has an equivalent score, with total

score ranges from 0 to 24 and is divided into five categories of functional impairment. Response options are no, bit, moderate, severe, very severe, and extremely severe with scores of 0, 1-4, 5-7, 8-10, 11-13, and more than or equal to 14. The higher the score, the greater the functional impairment.

- **Lymphangiogenesis** - the formation of lymphatic vessels from pre-existing lymphatic vessels in a method believed to be similar to angiogenesis (blood vessel development). Lymphangiogenesis plays an important physiological role in homeostasis, metabolism, and immunity.
- **Lymphostatic Fibrosis** - a progressive hardening of the skin that occurs in all patients with lymphedema
- **Neuropathic pain** - pain caused by damage or injury to the somatosensory nervous system, which is a complex system of sensory neurons and neural pathways that responds to changes at the surface or inside the body
- **Nociceptive pain** - a term used to describe the pain from physical damage or potential damage to the body, such as a physical sports injury, or surgical site
- **Osteoarthritis** - degeneration of joint cartilage and the underlying bone, most common from middle age onward. It causes pain and stiffness, especially in the hip, knee, and thumb joints.
- **Suppuration** - this is the term for the formation of pus, which is the result of the body's natural immune system automatically responding to an infection, usually caused by bacteria or fungi
- **Tensile elasticity** - the elasticity of the skin, return of normal elasticity
- **Timed Up and Go (TUG) test** - participants are asked to rise from a standard armchair, walk at a safe and comfortable pace to a mark 3 m away, then returned to a sitting position in the chair. Gait aids and chair armrests are utilized to assist with sit to stand and stand to sit transfers as needed. The longer the time spent to complete the test, the worse the patient's mobility. This test has been shown to be reliable, reproducible, and responsive to change.
- **Transcutaneous electrical nerve stimulation** - Transcutaneous electrical nerve stimulation (TENS) is a therapy that uses low voltage electrical current to provide pain relief. A TENS unit consists of a battery-powered device that delivers electrical impulses through electrodes placed on the surface of your skin
- **Visual Analog Scale** - The VAS is used in many healthcare settings as a general pain indicator, and has been shown to be reliable and a valid measure of pain. It consists of a 10 cm line anchored at each end. The left-hand side reads "no pain" and the right-hand side reads "worst possible pain". The participant marks a line to represent their pain level. The higher values of course represent more severe pain.
- **Western Ontario and McMaster Universities Arthritis Index** - A questionnaire that contains 24 questions of which 5 evaluate pain, 2 evaluate joint stiffness, and 17 evaluate function. Each question is graded qualitatively, with response options of

none, low, moderate, severe, and very severe and corresponding scores of 0, 1, 2, 3, and 4 respectively. Higher scores indicate a greater impact on quality of life.

Section 4: Low-Level Laser Therapy Equipment and the Use Thereof

Firstly, keep in mind that during treatments patients should be positioned in a comfortable manner. Since in Physical Therapy pain relief is a major reason for treatment involving Low-Level Laser Therapy, it is important to take the proper precautions to avoid causing patients any additional discomfort. For the treatment of extremities, it is acceptable to perform the therapy in any position the patient is comfortable. This includes prone, supine, seated, or long sitting. Pillows, mats, or bolsters are encouraged to position the extremity in a neutral position. For treatment of the core, supine, prone, and seated leaning forward onto support are all also acceptable. Positioning is important in any Physical Therapy treatment.

The vast majority of therapeutic lasers are semiconductor lasers. A semiconductor laser is a solid-state laser, constructed like a semiconductor diode, in which electrons and holes come together at the junction of cathode and anode, emitting bandgap radiation as in a light-emitting diode. There are three diode types;

- Indium, Gallium-Aluminum-Phosphide (InGaAlP) laser. This is a visible red light laser diode that operates in the 630-700 nm range. These lasers output light in a continuous manner. They may also be pulsed by an electro-mechanical method (duty cycle). A duty cycle output means that the power is switched off for part of a second then switched back on. If it were off for one second and on for one second it would be referred to as a 50% duty cycle. This reduces the average power output by 50%. Red light lasers have the least amount of penetration of the three lasers with a range of 6-10 mm. They affect the skin and superficial tissues.
- Gallium-Aluminum Arsenide (GaAlAs) semiconductor laser. This is a near-infrared (NIR) laser, which means that the light emitted is invisible to the naked eye. This laser operates in the 780-890 nm range. This type of laser has a continuous output of power and is often pulsed on a duty cycle as described previously. This laser can penetrate 2-3 cm in depth. These lasers are often utilized for medium to deep tissue structures such as muscles, tendons, and joints.

- Gallium-Arsenide (GaAs) semiconductor laser. This laser is different in that it is always operated in superpulsed mode, which means that the laser produces very short pulses of high peak power. The peak power spikes are usually in the 10-100 W range but only last for 100-200 nanoseconds while maintaining a mean power output that is relatively low. This is similar to what happens in a camera flash. Superpulsing allows for deep penetration into body tissues without causing the unwelcome tissue effects of continuous high power output such as a heating effect. Super pulsing also allows for deeper penetration than a laser of the same wavelength that is not super pulsed but has the same average output power. Penetration is achieved of 3-5 cm or more. Superpulsing also allows for treatment times to be as short as possible. This laser is extremely well suited for medium and deep tissues such as tendons, ligaments, and joints.

Several studies have been performed utilizing light-emitting diodes (LEDs) and infrared emitting diodes (IREDs). LED/IRED diodes have approximately 80% of the effect on tissues as lasers. The most commonly used diodes for laser therapy are visible red at 630 nm, 640 nm, 650 nm, and 660 nm, and IRED at 830 nm, 880 nm, and 950 nm. These diodes are driven by power outputs of up to 100 mW or more and are most often used in clusters of several diodes. Some diodes use clusters of diodes of a single frequency and others use a mix of LEDs and IREDs of various wavelengths.

Red light at 640 nm has been shown to affect skin so it may be most effective in treating scars, cuts, and wounds. The usual depth of laser penetration is less than 10 mm. Infrared lasers at 880 nm have been shown to affect deeper structures such as bone, tendons, tissues, or deep muscle structures up to 30-40 mm. Advantages include broad coverage due to the noncoherent light used and no tissue devices, while disadvantages include the possible thermal effects in devices that cover large surface areas and have several watts of power output.

There are many types of instruments available for the application of Low-Level Laser Therapy. The most common type utilized in Physical Therapy are handheld, small devices. Being small allows the unit to be applied in hard to reach areas and increases the ease of use by the therapist, while the handheld feature provides improved maneuverability. There are static devices available, which could be useful in a situation requiring constant application instead of moving the device around. They are usually able to be strapped to the body and worn. There are also laser therapy instruments that double as a TENS (transcutaneous electrical nerve stimulation) unit, which adds a benefit for increased pain relief.

Laser therapy can be applied on pulsed mode, super pulsed mode, or continuous mode. Pulse-modulated diodes create a 'pulse' by cutting the beam, or turning the laser on and off at regular intervals. Super pulsed diodes emit a series (**frequency**) of radiation impulses with high amplitude in an extremely short duration (typically 100 to 200 nanoseconds, or nm). Continuous Wave diodes emit continuous laser energy with a fixed power output for the entire duration of the treatment. Compared to continuous-wave lasers (with similar power parameters), super pulsed lasers seem to achieve more effective penetration into the tissue by virtue of the controlled light energy being delivered at very high peak power (25-100 Watts) but very short duration (100-200 nanosecond) pulses and low average intensity. These methods deliver the same laser light, it is just delivered to the tissues differently.

Continuous mode delivers a stable and constant light and is ideal for most situations. Pulsed modes can deliver higher doses to the treatment area, and in deeper areas up to six inches, but at a decreased risk of burning the surrounding tissue due to the on/off cycle. By turning the laser on for a brief period at very high power, you achieve the benefit of deep penetration without the risk of heating or burning that arises when using higher power, continuous wave diodes for long periods.

Laser therapy can be applied via laser or light-emitting diode (**LED**). When lasers come into contact with cells, they act on the mitochondria to increase adenosine triphosphate (ATP) production. In turn, that increased ATP production can lead to faster production of collagen, vascular structures, **DNA**, **RNA**, and other materials essential to the healing process. In contrast, LEDs emit incoherent light in a broader range of wavelengths. Their power output is significantly lower than that of lasers, which tends to make them less invasive and less potentially harmful to targeted tissues. Still, they exert the same end effect on ATP production and healing as lasers, albeit to a different degree. There are also devices that can switch between laser and LED, so the therapist can make their own determination as to the effectiveness. The difference in treatments is viewed by most to be minimal, so it is really to be determined on a case by case basis.

Dosimetry, or the determination of the dose to be administered, is a debatable topic. There are many factors to take into consideration such as wavelength, irradiance, and pulse structure. Irradiation parameters are as follows;

- Wavelength-measured in nm, or **nanometers**. Wavelength is visible in the 400-700 nm range. Wavelength determines which **chromophores** will absorb the light. Low-Level Laser Therapy devices are typically in the ranges of

600-1000 nm. Some clinicians believe that wavelengths above 900 nm are probably more absorbed by water than the cellular structures.

- **Irradiance** - often called power density, and is calculated as Power (W)/Area (cm²) = Irradiance
- **Pulse structure** - Measured in **peak power** (W), Pulse Frequency (Hz), duty cycle (%) and pulse width (s). If the beam is pulsed then the power reported should be calculated as Peak Power- (W) x Pulse Width (s) x Pulse Frequency (Hz) = Average Power (W). Optimal frequencies and pulse duration (or intervals) are yet to be determined.

Time/Energy/Dose can be defined as;

- **Energy** - measured in Joules (J), this is calculated as Power (W) x time (s) = Energy (Joules)
- **Energy Density** - Measured in Joules/cm². Most common expression of LLLT dose.

Due to the interrelated parameters, this means that there has not yet been a comprehensive study reported that examined the effect of varying all the individual parameters one by one. It is unlikely that there will ever be a study carried out due to the complexity of all parameters involved. The parameters often depend on the practitioner's personal preference or experience rather than on a consensus statement by an authoritarian body. Equipment ordered for a Physical Therapy practice will contain a manual to assist with selecting recommended parameters. Please see the chart below to compare studies on animals with Low-Level Light Therapy for different conditions.

Disease	Parameters	Subject	Effect
Myocardial Infarction (Heart Attack)	804 nm; 38 mW; 4.5 ± 0.1 mW/cm ² ; 0.27 J/cm ² ; CW, 1.5 ! 3.5 mm	Rats	Reduced the loss of myocardial tissue
Myocardial Infarction (Heart Attack)	635 nm, 5 mW, 6 mW/cm ² ; 0.8 J–1 J/cm ² ; CW; 0.8 cm ² ; 150 s	Rats	The expression of multiple cytokines was regulated in the acute phase after LLLT

Myocardial Infarction (Heart Attack)	804 nm; 400 mW 8 mW/cm ² ; 0.96 J/cm ² ; CW; 2 cm ² ; 120	Rats and dogs	VEGF and iNOS expression markedly upregulated; angiogenesis and cardioprotection enhanced
Stroke	808-nm; .5 mW/cm ² ; 0.9 J/cm ² at cortical surface; CW; 300 μ s pulse at 1 kHz; 2.2 ms at 100 Hz	Rabbits	The results showed that laser administered 6 h following embolic strokes in rabbits in P mode can result in significant clinical improvement and should be considered for clinical development
Stroke	808-nm; 7.5 mW/cm ² ; 0.9 J/cm ² ; 3.6 J/cm ² at cortical surface; CW and 70 Hz, 4-mm diameter	Rats	LLLT issued 24 h after acute stroke may provide a significant functional benefit with an underlying mechanism possibly being induction of neurogenesis
Traumatic Brain Injury (TBI)	808 \pm 10 nm; 70 mW; 2230 mW/cm ² ; 268 J/cm ² at the scalp; 10 mW/cm ² ; 1.2 J/cm ² at cortical surface; CW; 2 mm ²	Mice	LLLT given 4 h following TBI provides a significant long-term functional neurological benefit

Traumatic Brain Injury (TBI)	660 nm or 780 nm, 40 mW; 3 J/cm ² or 5 J/cm ² ; CW; 0.042 cm ² (3 s and 5 s) irradiated twice (3 h interval)	Rats	LLLT affected TNF-alpha, IL-1beta, and IL-6 levels in the brain and in circulation in the first 24 h following cryogenic brain injury
Spinal Cord Injury (SCI)	830 nm; 100 mW; 30 mW/cm ² ; 250 J/cm ² ; CW, 0.028 cm ²	Rats	LLLT initiated a positive bone-tissue response, maybe through stimulation of osteoblasts. However, the evoked tissue response did not affect biomechanical or densitometric modifications
Spinal Cord Injury (SCI)	810 nm; 1589 J/cm ² ; 0.3 cm ² , 2997 s; daily for 14 days	Rats	Promotes axonal regeneration and functional recovery in acute SCI
Arthritis	632.8 nm; 5 mW; 8 J/cm ² , CW; 2-mm diameter; 50 s; daily for 5 days	Rats	Laser reduced the intensity of the inflammatory process in the arthritis model induced by hydroxyapatite and calcium pyrophosphate crystals
Arthritis	632.8-nm; 3.1 mW/cm ² CW, 1 cm diameter; 15 min; 3 times a week for 8 weeks	Rats	laser treatment enhanced the biosynthesis of arthritic cartilage

Arthritis	810-nm; 5 or 50 mW/cm ² ; 3 or 30 J/cm ² ; CW; 4.5-cm diameter; 1, 10 or 100 min; daily for 5 days	Rats	Highly effective in treating inflammatory arthritis. Illumination time may be an important parameters
Wound Healing	632.8-nm laser; 635, 670, 720 or 810-nm (± 15 -nm filtered lamp); 0.59, 0.79, and 0.86 mW/cm ² ; 1, 2, 10 and 50 J/cm ² ; CW; 3-cm diameter	Mice	635-nm light had a maximum positive effect at 2 J/cm ² . 820 nm was found to be the best wavelength. No difference between non-coherent 635 \pm 15-nm light from a lamp and coherent 633-nm light from a He/Ne laser. LLLT increased the number of α -smooth muscle actin (SMA)-positive cells at the wound edge
Familial amyotrophic lateral sclerosis (FALS)	810 nm; 140-mW; 12 J/cm ² ; CW; 1.4 cm ²	Mice	Rotarod test showed significant improvement in the light group in the early stage of the disease. Immunohistochemical expression of the astrocyte marker , glial fibrillary acidic protein, was significantly reduced in the cervical and lumbar enlargements of the spinal cord as a result of LLLT

The World Association for Laser Therapy provided dosage recommendations in 2010 that have been reviewed yearly. Provided are tables for 780-860 nm and 904 nm. These tables are subject to change, and are just recommendations for reference. As always, dosages are adjustable on a case by case basis.

The dosage recommendations for 780-860 nm, continuous or pulsed, with a mean output of 5-500 mW are defined in the table below. Irradiation times are recommended to range between 20 and 300 seconds.

Tendinopathies	Min area/points cm ²	Joules 780-820 nm	notes
Carpal Tunnel	2-3	8	Min 4 J per point
Lateral Epicondylitis	1-2	4	Max 100 mW/ cm ²
Biceps Humeri c.l.	1-2	6	
supraspinatus	2-3	8	Min 4 J per point
Infraspinatus	2-3	8	Min 4 J per point
Trochanter major	2-4	8	
Patellartendon	2-3	8	
Tract Iliobialis	1-2	4	Max 100 mW/ cm ²
Achilles Tendon	2-3	8	Max 100 mW/ cm ²
Plantar fasciitis	2-3	8	Min 4 joules per point
Arthritis			
Finger PIP or MCP	1-2	4	

Wrist	2-4	8	
Humoradial Joint	1-2	4	
Elbow	2-4	8	
GLenohumeral Joint	2-4	8	Min 4 J per point
Acromioclavicular	1-2	4	
Temporomandibular	1-2	4	
Cervical Spine	4-12	16	Min 4 J per point
Lumbar Spine	4-8	16	Min 4 J per point
Hip	2-4	12	Min 6 J per point
Knee medial	3-6	12	Min 5 J per point
Ankle	2-4	8	

The dosage recommendations for 904 nm lasers are included in the table below. (Peak pulse output >1 Watt, mean output >5 mW and power density > 5mW/cm²) Irradiation times are recommended to range between 30 and 600 seconds. Daily treatment for 2 weeks or treatment every other day for 3-4 weeks is recommended. Irradiation should cover most of the pathological tissue in the tendon/synovia. Start with an energy dose in the table, then reduce by 30% when inflammation is under control. Therapeutic dose windows typically range from +/- 50% of given values, and doses outside these windows are inappropriate and should not be considered as Low-Level Laser Therapy.

Tendinopathies	Min area/points cm ²	Joules 904 nm	notes
Carpal Tunnel	2-3	4	Min 2 J per point

Lateral Epicondylitis	2-3	2	Max 100 mW/cm ²
Biceps Humeri c.l.	2-3	2	
supraspinatus	2-3	4	Min 2 J per point
Infraspinatus	2-3	4	Min 2 J per point
Trochanter major	2-3	2	
Patellartendon	2-3	2	
Tract Iliobialis	2-3	2	Max 100 mW/cm ²
Achilles Tendon	2-3	2	Max 100 mW/cm ²
Plantar fasciitis	2-3	2	Min 2 J per point
Arthritis			
Finger PIP or MCP	1-2	1	
Wrist	2-3	2	
Humoradial Joint	2-3	2	
Elbow	2-3	2	
Glenohumeral Joint	2-3	2	Min 1 J per point
Acromioclavicular	2-3	2	
Temporomandibular	2-3	2	

Cervical Spine	4	4	Min 1 J per point
Lumbar Spine	4	4	Min 1 J per point
Hip	2	4	Min 2 J per point
Knee medial	4-6	4	Min 1 J per point
Ankle	2-4	2	

Daily treatment for 2 weeks or treatment every other day for 3-4 weeks is recommended, Irradiation should cover most of the pathological tissue in the tendon/ synovia. Start with an energy dose in the table, then reduce by 30% when inflammation is under control. Therapeutic dose windows typically range from +/- 50% of given values, and doses outside these windows are inappropriate and should not be considered as Low-Level Laser Therapy.

During treatment, laser therapy can be applied in a contact setting or non-contact setting depending on the sensitivity of the patient, presence of wounds, and other considerations. Non-contact methods do result in a scattering effect of the laser lights and less efficient absorption into the skin and the underlying layers thereof, however sometimes non-contact methods are sometimes necessary due to the ability to treat open wounds, sterile sites, sensitive areas, and exudative lesions. Even when operating within non-contact perimeters, the laser must still be applied directly to the skin. Laser therapy cannot be applied to skin covered by casts, bandages, clothing, splints, or tape.

Another important fact to take into consideration is the possibility of a topical ointment, lotion, or cream being part of the treatment plan. For example, a topical ointment may have been prescribed by an attending physician for wound care. In such a case, Low-Level Laser Therapy should be applied without the presence of said topical agent. Due to the local vasodilation that occurs with the application of laser therapy, as well as angiogenesis, there could be a change in the absorption rate of a topical product, causing more medication to be absorbed than is advised. Another concern is whether or not a laser beam may inactivate or otherwise alter the normal chemical functioning of a topical product. With these considerations in mind, the practitioner should ensure that laser treatments are applied prior to applications of

topical creams or that any topical be removed prior to laser therapy. Skin should be clean and wiped with wipes prior to beginning.

Regardless of performing contact or non-contact treatment, the practitioner must keep the handpiece perpendicular to the tissues being irradiated. This ensures an even application of the laser beam to the tissues of the skin and ensures even irradiation of the tissues which will produce an effective, thorough treatment.

There are small and large heads available for treatment machines. It is important to fit the applicator head to the patient and circumstances. Using a small head would enable the therapist without contaminating surrounding tissues or widening the beam spot to the point where a decreased dose is delivered to the target tissues. With the use of a large applicator head, this allows the therapist or medical practitioner to treat larger areas. Some would say it is best to be in contact with the patient skin for the following two reasons;

- The laser light can scatter and the dosage can be drastically reduced even with a half of centimeter of space between the surface of the area being treated and the lens of the probe. Therefore, to ensure that you are delivering enough joules to have an effective treatment, contact mode is crucial.
- When applying your dose in contact mode, the pressure of the probe on the skin pushes a bit of the fluid in the tissue out of the way to allow for deeper penetration of the laser light.

Low-Level Laser Therapy was proven in a clinical trial published in March of 2020 to be more effective in a non-contact mode in relieving pain and reducing the healing time during the treatment of oral ulcers compared to laser treatment in contact mode. It was also seen that there was less recurrence in patients seen after one year of follow up.

Section 4 Summary

There are multiple considerations to take into account when using Low-Level Laser Therapy. This includes the use of machines using light-emitting beams or LEDs (laser emitting diodes). There are determinations concerning whether to use contact therapy or non-contact. Dosimetry is a confusing subject due to the multiple factors to be considered such as wavelength, irradiance, pulse structure, and energy output.

Section 4 Key Concepts

- **Axonal Regeneration** - recovery of damaged nerves
- **Astrocyte marker** - star-shaped glial cells found in the central nervous system. They serve a variety of functions, including maintenance of extracellular ion balance, provision of nutrients (such as lactate) to neurons, supporting repair & regeneration after CNS damage, and modulation of synaptic transmission
- **Cardioprotection** - represents a way to guard the heart from the damage inflicted by different insults, including ischemia, ischemia/reperfusion injury (I/R) and chemical, metabolic, and physical stressors, and to reduce the incidence of heart failure (HF) and mortality.
- **Chromophores** - the functional group of a molecule which contains the electrons responsible for the absorption of light and resulting UV-visible spectrum.
- **DNA** - Deoxyribonucleic acid, a self-replicating material that is present in nearly all living organisms as the main constituent of chromosomes. It is the carrier of genetic information.
- **Embolic Stroke** - occurs when a blood clot that forms elsewhere in the body breaks loose and travels to the brain via the bloodstream. When the clot lodges in an artery and blocks the flow of blood, this causes a stroke. This is a type of ischemic stroke.
- **Energy** - measured in Joules (J), this is calculated as Power (W) x time (s) = Energy (Joules)
- **Energy Density** - Measured in Joules/cm². Most common expression of LLLT dose.
- **Frequency** - the number of waves that pass a point in space during any time interval, usually one second. We measure it in units of cycles (waves) per second, or hertz. The frequency of visible light is referred to as color, and ranges from 430 trillion hertz, seen as red, to 750 trillion hertz, seen as violet.
- **Irradiance** - often called power density, and is calculated as Power (W)/Area (cm²) = Irradiance
- **Light Emitting Diode (LED)** - a semiconductor light source that emits light when current flows through it
- **Nanometers** - one billionth of a meter, serve to measure extremely small distances or objects
- **Neurogenesis** - the process by which nervous system cells, the neurons, are produced by neural stem cells (NSC)s. It occurs in all species of animals except the porifera (sponges) and placozoans.
- **Peak Power** - (W) x Pulse Width (s) x Pulse Frequency (Hz) = Average Power (W). Optimal frequencies and pulse duration (or intervals) are yet to be determined.
- **Pulse Structure** - measured in peak power
- **RNA** - ribonucleic acid, a nucleic acid present in all living cells. Its principal role is to act as a messenger carrying instructions from DNA for controlling the synthesis of

proteins, although in some viruses RNA rather than DNA carries the genetic information.

- **Rotarod Test** - the rotarod performance test is a performance test based on a rotating rod with forced motor activity being applied, usually by a rodent. The test measures parameters such as riding time (seconds) or endurance.
- **SCI** - spinal cord injury is damage to the spinal cord that causes temporary or permanent changes in its function.
- **TBI** - traumatic brain injury, a nondegenerative, noncongenital insult to the brain from an external mechanical force, possibly leading to permanent or temporary impairment of cognitive, physical, and psychosocial functions, with an associated diminished or altered state of consciousness.

Section 5: Side effects, Contraindications, Precautions, and Safety regarding Low-Level Laser Therapy

The North American Association for Laser Therapy conference in 2010 held a consensus meeting on safety and contraindications. Their main recommendations were:

- **Eye Precautions** - Do not aim laser beams into the eyes and everyone present should wear appropriate safety spectacles.
- **Cancer** - Do not treat over the site of any known primary carcinoma or secondary metastasis unless the patient is undergoing chemotherapy when LLLT can be used to reduce side effects such as mucositis. LLLT however can be considered in terminally- ill cancer patients for **palliative** relief.
- **Pregnancy** - Do not treat directly over the developing fetus.
- **Epilepsy** - Be aware that low frequency pulsed visible light (<30Hz) might trigger a seizure in photosensitive epileptic patients.

That being said, there are other contraindications and alleged contraindications, or precautions, that therapists should be aware of. These contraindications should be considered professional in regard to each individual patient. This is not a comprehensive list, and is constantly evolving due to continued studies. Knowledge from over five decades of research and clinical application has rewritten the recommendations against using laser therapy on many conditions and anatomical sites once thought to be contraindicated. Most historical contraindications require special permission, consideration, or observance, but are now not quite true

contraindications and can be seen more as precautions. Please consider each of these advised precautions and contraindications;

- Eye precautions - The only absolute contraindication for laser therapy is direct or reflected exposure through the pupil onto the retina. When performing laser therapy practitioners and patients should wear appropriate eye protection. Laser beams should never be shone into someone's eyes, nor should laser therapy be performed over the eye itself. Direct irradiation of the eyes can cause permanent damage to the eyes. Other guidelines should be considered precautionary.
- Immunosuppressive therapy - Do not treat patients that are on **immune suppression therapy** without prior approval from the physician. The light may boost the immune system.
- Cancer - Laser therapy should not be applied over the site of any known carcinoma or secondary metastasis. LLLT can be used for palliative relief, to heal wounds, or assist in the relief and healing of mucositis. Practitioners should never treat a known or suspected cancerous site or tumor without approval from an oncologist or primary physician. There is the potential that the laser could stimulate the cells and promote cancerous growth.
- Pregnancy - As previously mentioned, laser therapy should not be applied over the abdomen in pregnant women. A study on chicken embryos showed that they suffered cell damage after laser light had been applied through an opening in the egg. There is no documentation of damaging effects on human embryos, nor is there any documentation indicating that treatment in areas not related to the uterus or abdomen would have any damaging effects.
- Epilepsy - Pulsed visible light in the 5-10 Hz range can cause epileptic seizures. Low-Level Laser Therapy lights rarely have visible pulsing light. A study was performed showing that an epileptic patient was only able to tolerate laser light with a frequency below 800 Hz. As a precaution if laser therapy is required in an epileptic patient, the patient should be provided with goggles for the duration of the treatment.
- Treatment of the thyroid - Some studies have shown positive results in the treatment of thyroid disorders such as **hypothyroidism**, including an improvement in thyroid function. The thyroid is light sensitive, so unless specifically advised by a physician, it is not advisable to treat the thyroid directly without more study.
- **Coagulation** disorders - Patients with coagulation disorders such as **thrombocytopenia** should be treated with caution. It is known that laser therapy has effects upon the coagulation process, and it could increase blood flow with unexpected consequences. On the other hand, a study from

Massachusetts General hospital reports that Low-Level Laser Therapy increased the generation of platelets from precursor cells called megakaryocytes.

- Children - laser light dosage should be adjusted to the weight of a child. There are no indications prohibiting the treatment of a child.
- Tattoos - Tattoos are not a contraindication per se, but they should be treated with caution due to the fact that the pigments of a tattoo will absorb the laser light and the area could begin to warm and turn painful. It is therefore advised to begin the treatment at a distance from the skin and to move the laser closer to the skin based on feedback from the patient.
- Bacterial infections - Do not treat directly over a bacterial infection unless directed by a physician. Although there has been evidence suggesting that some wavelengths of light may inhibit or kill bacteria in a wound, there has not been enough comprehensive study to prove the parameters involved or the possible side effects. It is possible that bacterial growth could increase.
- Implants - A therapist should not treat a patient with laser therapy directly over a pacemaker, cochlear implant, or any internal electronics. The light could interfere with the function of the devices.
- Ports - It is not advisable to treat a patient over their port site. A laser may stimulate the cells to block the port, resulting in decreased usefulness and possible necessity of port relocation.
- Fever - Patients with a fever should not be treated due to the chance that a laser may increase the fever.
- Sensitive skin - Patients with sensitive skin should be treated with caution to avoid burns or adverse reactions. A patient with **photosensitivity** could have a strong reaction to light. Keep in mind this includes patients taking light sensitive drugs such as thyroid medication, Retin-A, tetracycline, and St. John's Wort.
- Sunburns - A patient with a sunburn or recent high sun exposure including tanning booths should be avoided. The laser may increase the reaction of these areas and increase the level of sunburn.
- Irradiation of the brain - The brain should not be directly treated. There is a lot of ongoing research regarding the successful use of therapy and brain damage, or TBI. However, this is more suited for a specialist physician, not for a physical therapist.
- Diabetes - There are many physicians who specialize in treating diabetic neuropathy using a laser to treat the numb and painful areas, and the studies show good results. The purported cell regeneration is beneficial, as well as treatment of the wounds associated with diabetes. However, again, this is an area best suited for a specialist to administer and monitor due to the

decreased sensation and decreased wound healing properties present in a diabetic.

- Patients with very dark skin pigmentation - These patients should be observed closely due to some may experience an unpleasant heating sensation. If treatment is painful, remove the treatment probe from contact and treat approximately 15 mm from the surface of the skin.
- Cranial treatment - When treating the head and neck, a patient may experience pain as the melanin in the fine superficial hair follicle absorbs a lot of the laser energy. Once again, if treatment is painful remove the treatment probe from contact and treat approximately 15 mm from the surface of the skin.
- Gonads - Irradiation in the gonad area is not recommended due to the unknown effect of light therapy on the sperm and reproductive organs in general.

Pins, metal plates, and plastics including joint replacements or other nonelectrical implants are not contraindicated. Any concerns should be discussed with a physician, and issues should be acknowledged and explored.

As with any medical treatment, there are some risks involved. There are no known long term side effects of Low-Level Laser Therapy. Some minor short term side effects include redness, swelling, itching, acne, skin rash, and minor numbness in the surrounding areas. All side effects need to be reported and monitored, and Low-Level Laser Therapy should be halted until the physician can be consulted.

Section 5 Summary

The only true contraindication for Low-Level Laser Therapy is to avoid shining light into someone's eyes due to the possible permanent damage that may occur. Patients and providers are suggested to wear appropriate eye protection during treatment. There are however several precautions to consider including immunosuppression therapy, cancer, gonad regions, dark-skinned patients, sunburns, brain irradiation, diabetes, cranial treatment over hair, sensitive skin, ports, electrical implants, pregnancy, epilepsy, thyroids, coagulation disorders, tattoos, bacterial infections, fever, and patients with sensitive skin. All patients skin integrity should be viewed pre and post-treatment and monitored for redness, swelling, rashes, or other adverse reactions. There are no known long term effects of Low-Level Laser Therapy. There are known minor short term side effects such as redness, edema, itching, acne, rash, and minor numbness to surrounding treatment areas. Low-Level Laser Therapy is an evolving treatment that continues to require much study and consideration.

Section 5 Key Concepts

- **Coagulation** - the action or process of a liquid, especially blood, changing to a solid or semi-solid state, ie clotting
- **Hypothyroidism** - is a condition in which the thyroid gland is not able to produce enough thyroid hormone. Since the main purpose of the thyroid hormone is to "run the body's metabolism," it is understandable that people with this condition will have symptoms associated with a slow metabolism.
- **Immune suppression therapy** - Immunosuppressive therapy is a medical procedure that uses drugs to suppress or reduce immune activity to (1) transplant patients so the new organ will not be rejected by the recipient's body and (2) patients with autoimmune disease and myelodysplastic syndrome. The immune system is the body's natural defense.
- **Megakaryocytes** - (mega- + karyo- + -cyte, "large-nucleus cell") is a large bone marrow cell with a lobulated nucleus responsible for the production of blood thrombocytes (platelets), which are necessary for normal blood clotting.
- **Palliative** - (of a medicine or medical care) relieving pain without dealing with the cause of the condition.
- **Photosensitivity** - sometimes referred to as a sun allergy, is an immune system reaction that is triggered by sunlight. Sunlight can trigger immune system reactions. People develop itchy eruptions or areas of redness and inflammation on patches of sun-exposed skin.
- **Precursor cells** - In cell biology, a precursor cell, also called a blast cell or simply blast, is a partially differentiated cell, usually referred to as a unipotent cell that has lost most of its stem cell properties. A precursor cell is also known as a progenitor cell but progenitor cells are multipotent.
- **Thrombocytopenia** - deficiency of platelets in the blood. This causes bleeding into the tissues, bruising, and slow blood clotting after injury.

Conclusion

Low-Level Laser Therapy is a form of treatment that applies low-level lasers or light-emitting diodes (LEDs) to the surface of the body. It is believed that applications of low-level laser therapy relieve pain and stimulate and enhance cell function. The effects of Low-Level Laser Therapy seem to be most effective within a specified set of wavelengths, as those too high are considered cutting lasers that destroy tissue, and those too low have no effect. Photochemical reactions are well known in biological research and Low-Level Laser Therapy makes use of the first law in photochemistry

known as the Grotthuss-Draper Law. Laser lights affect the body on an intracellular level, improving mitochondrial function, cell proliferation and migration, and ATP function. It also helps produce endorphins and serotonin, the happy chemicals that improve mood, and helps to block the pain receptors of the body. These effects help improve mood and decrease pain.

Low-Level Laser Therapy is a complex treatment method that can be utilized in many varied health applications. These can be cosmetic such as tattoo removal and hair growth, or in the treatment of wound healing, musculoskeletal treatment, pain relief, neurological ailments, and many other health issues. Due to the multiple treatment variables, it is difficult to pinpoint the correct dosage, however, there are many references available to assist in the determination, including references available specific to each device that is included with the device used by clinicians. Low-Level Laser Therapy has shown much promise in Physical Therapy and other medical areas. Practitioners should only perform Low-Level Laser Therapy under the direction of a physician due to the precautions associated. Therapists should follow all safety guidelines and monitor patient progress.

Although more study is needed, laser therapy has been proven effective to be a valuable resource to treat patients. In Physical Therapy applications, it is especially relevant in treating pain, healing wounds, and treatment of musculoskeletal disorders, and should be studied at length and utilized when necessary to further the validation required to bring this therapy into mainstream usage.

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