Let There Be Light: Diverse Applications for Low Level Laser Therapy in Oncology Practice

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Heliotherapy, the therapeutic use of sunlight, has long been a core treatment in naturopathic tradition. Current understanding of vitamin D’s importance in oncology supports the value we have placed on heliotherapy. With the advent of laser technology, the benefit of specific wavelengths of light have been investigated and yielded fascinating information.

This article discusses applications for light therapy in the form of low level laser therapy (LLLT) in the oncology patient population. Some applications, such as mucositis and carpal tunnel syndrome, are well-established. Other applications, such as for acute ischemic stroke and ototoxicity, are in the preliminary stages of research. Overall, LLLT is a safe therapy with multiple benefits to this patient population, while offering physicians opportunities for expanding their physical medicine practices.

Oncology studies

Among oncology patients, LLLT has specifically been assessed in clinical trials as a treatment for iatrogenic mucositis and lymphedema.

Mucositis

Patients diagnosed with squamous cell carcinomas of the head and neck, typically receive radiation therapy with concurrent low dose platinum chemotherapy. Dose intensity is critical to the efficacy of this regimen, so treatment delays adversely affect prognosis. Oral mucositis is the dose limiting toxicity for this regimen. At the hospital where the author practices, PEG tube placement is a routine step in the initiation of chemoradiation therapy since these patients are likely to develop grade 2-3 oral mucositis during treatment.

In multiple clinical trials involving both adults and children, low level laser therapy has been shown to both prevent and treat oral mucositis associated with chemotherapy, radiation, or allogenic stem cell transplant. A Belgian trial examined patients who had previously developed chemotherapy-associated mucositis, healed, and then restarted the identical chemotherapy. Among these high-risk patients, LLLT prevented mucositis in 81%. Furthermore, LLLT resolved 83% of existing mucositis lesions, compared to 11% in those treated with sham therapy. A phase II trial at the Seattle Cancer Care Alliance confirmed these findings.

Lymphedema

Post-treatment lymphedema develops in 15-20% of breast cancer patients due to axillary node radiation or resection. Established treatments include therapeutic exercise, lymphatic drainage massage, and compression garments. Botanical lymphagogues have also been discussed in this journal.

LLLT has been studied as a treatment for post-mastectomy lymphedema in clinics in China, Turkey, and Australia. A placebo-controlled clinical trial published in Cancer found that two LLLT treatments
decreased total limb volume and extracellular fluid volume in 33% of patients treated, with results continuing at 3 month follow up.\textsuperscript{14}

\textbf{Co-morbidities:}

LLLT has also been assessed in other patient populations as a treatment for several co-morbid conditions that frequently impact quality of life for oncology patients. These include musculoskeletal pain, neuropathy, fatigue, weakness, decreased exercise tolerance and wound healing.

\textbf{Cardiology}

Oncology patients can be at increased risk for cardiovascular disease due to paraneoplastic hypercoagulability and due to side effects of cardiotoxic chemotherapies and biotherapies. Co-morbid cardiovascular disease also limits patient access to radiation and surgical oncology therapies. LLLT is being studied to improve patient outcomes after acute ischemic cerebrovascular accident and also as a treatment for blood hypercoagulation. The University of California at San Diego is studying the use of infrared transcranial laser therapy within the first 24 hours of acute ischemic stroke. In two double blind randomized studies involving 120 and 600 patients respectively, this therapy improved outcomes on the National Institutes of Health Stroke Score and the Glasgow Outcome Score.\textsuperscript{15} \textsuperscript{16}

Hypercoagulability is a common paraneoplastic syndrome and co-morbid condition in oncology patients. Current therapy involves medications with narrow therapeutic index and significant toxicity. Preliminary LLLT research in other patient populations with hypercoagulability poses intriguing possibilities for enhancing this aspect of oncology care. Chinese scholars are investigating the impact of LLLT on blood hypercoagulability in obstetrics patients, finding decreases in PT, aPTT, TT, and fibrinogen with intranasal laser therapy.\textsuperscript{17}

\textbf{Neurology}

Peripheral neuropathy and peripheral nerve injury are common issues in oncology practice. This includes chemotherapy-induced peripheral neuropathy, diabetic peripheral neuropathy, and post-surgical peripheral nerve injury.

A Serbian randomized study assessed 45 patients with chronic diabetic peripheral neuropathy, comparing the efficacy of 780 nm LLLT with oral multivitamin therapy over the course of 12 weeks. Outcomes included statistically significant improvements in electroneurographic conductivity and spatial perception threshold in the LLLT group.\textsuperscript{18}

The Israelis are studying LLLT as a treatment for chronic peripheral nerve injury. A small pilot study assessed the effects of 780 nm LLLT in a randomized double blind placebo-controlled trial involving 18 patients.\textsuperscript{19} Patients were treated daily for 21 days and then followed for 6 months. Interestingly, treatment durations were 2-3 hours per treatment. Nevertheless, this study with extended treatment times found improvements in motor function and electroneurographic activity at 3 months and 6 months following LLLT.

Ototoxicity is also common in oncology practice, often manifesting as chronic tinnitus. Cisplatin, vincristine, and antibiotics such as gentamycin are common causes. Three preliminary clinical trials have assessed the efficacy of LLLT for chronic tinnitus of diverse causes. A small Italian study assessed the use a 650 nm laser applied daily for 3 months in 26 patients with chronic idiopathic tinnitus of at least 3 years duration. 61% of treated patients improved at least one level on a standardized tinnitus severity
scale, compared with 35% in the placebo group.\textsuperscript{20} Another Italian study of tinnitus in patients with sensorineural hearing loss found no significant benefit as measured by the Tinnitus Handicap Index, though the laser group was noted to have a significant improvement in subjective and objective hyperacusis.\textsuperscript{21} A Turkish study assessed transmeatal laser application and found a 48% improvement in tinnitus loudness and 58% improvement in duration.\textsuperscript{22} Further research is needed to assess therapeutic efficacy and the potential for application to medication-induced ototoxic tinnitus. In the meantime, laser therapy is a reasonable consideration for this patient population, given excellent safety and the limited availability of alternative treatments.

**Pain Management and Orthopedics**

Oncologic pain management involves a holistic perspective. While the acute pain crises may involve metastatic disease, co-morbid non-malignant conditions may contribute significantly to the overall pain burden. Improvement in pain associated with the co-morbid conditions can decrease pain medication use, decrease associated sedation and constipation, and enhance quality of life for oncology patients. Therefore, treating conditions such as osteoarthritis or tendinopathy can be an essential part of improving quality of life in patients with advanced cancer.

LLLT has demonstrated efficacy for multiple painful co-morbid conditions that affect this patient population. These include tendinopathies such as osteoarthritis,\textsuperscript{23,24} lateral epicondylitis,\textsuperscript{25-28} and Achilles tendinopathy,\textsuperscript{29} acute and chronic neck pain,\textsuperscript{30} tension and migraine headache,\textsuperscript{31} myofascial pain syndrome,\textsuperscript{32-33} knee pain,\textsuperscript{34} chronic low back pain,\textsuperscript{35,36} lumbar disc herniation,\textsuperscript{37} frozen shoulder,\textsuperscript{38} plantar fasciitis,\textsuperscript{39} and limb pain and swelling after ischemic stroke.\textsuperscript{40}

Carpal tunnel syndrome (CTS) can be a dose limiting side effect of aromatase inhibitors (AIs) used in breast cancer therapy. There are no clinical trials specifically assessing the use of LLLT for AI-induced carpal tunnel syndrome. However, LLLT is established as an effective treatment for CTS in 5 clinical trials.\textsuperscript{41-45}

A prospective randomized placebo controlled trial compared the efficacy of standard conservative management with splinting alone, LLLT or splinting plus LLLT in 45 patients with mild or moderate idiopathic CTS. The LLLT intervention involved 10 treatments over 3 months. Compared to the other two groups, the patients receiving LLLT plus splinting experienced a higher rate of full or partial recovery, improved EMG-measured median nerve conduction and increased grip strength.\textsuperscript{46} Based on the evidence from this and other studies, the FDA has approved CTS as an indication for certain LLLT lasers.

Temporomandibular joint dysfunction can develop as a complication of bulky tumor masses associated with lymphoma or head and neck cancer. This improves with tumor debulking via chemotherapy, radiation, surgery, or immune therapies. However, the interim period can be quite painful for the patient. Palliative treatment options include acupuncture and gentle physical medicine. In the dental literature, LLLT is being actively studied as a further potential treatment modality for TMJ in otherwise healthy patients. In double blind placebo controlled trials, LLLT has decreased subjective pain measured on a visual analog scale.\textsuperscript{47-52} Some studies found increases in joint mobility and chewing performance.\textsuperscript{53} It is reasonable to consider this therapy in the oncology patient population when TMJ arises.

**Fatigue and Exercise Tolerance**
Fatigue, muscle weakness, and decreased exercise tolerance are common quality of life concerns for patients with advanced cancer. Therapeutic exercise and l-carnitine can improve fatigue in oncology patients. However, poor patient performance status and/or limited oral intake can limit the application of these therapies.

LLLT offers an additional treatment option. In vitro studies show that LLLT supports energy metabolism via increasing adenosine triphosphate synthesis. This has been confirmed in multiple cell types including human red blood cells, lymphocytes, neurons, and adipose cells. In human monocytes, LLLT increases nitric oxide release while decreasing reactive oxygen species. LLLT increases activity of all enzymes of the electron transport chain. Furthermore, it increases mitochondrial membrane potential, ATP, and cAMP in hypoxic, anoxic, wounded cells.

So far, clinical studies on LLLT and fatigue have only assessed healthy and/or athletic patient populations. Lasers of 650 – 860 nm have been shown to increase muscle endurance. Some studies also find decreased post-exercise levels of serum lactate and c-reactive protein. The results were statistically significant in 1 study, while 2 other studies showed a non-significant trend in favor of increased exercise tolerance. The potential to increase exercise tolerance via laser therapy is an intriguing application that merits further research, both to clarify efficacy and to assess applications in chronically ill populations.

**Dermatology and Wound Care**

LLLT can address several dermatologic concerns of oncology patients, including the healing of wounds, dermal ulcers, and burns and the reduction of postoperative pain and swelling.

Oncology patients are often affected by dermal ulcers and wounds. This includes decubitus ulcers caused by immobility, wounds associated with infiltrating tumor or co-morbid diabetes, and post-operative conditions. In a clinical trial assessing chronic refractory wounds, LLLT increased heat shock protein expression in wounds and accelerated wound closure. A trial assessing chronic diabetic leg wounds found 56% more granulation tissue deposition and 79.2% acceleration of healing compared to placebo. The dental literature discusses the wound healing benefits of LLLT extensively, particularly in terms of improving post operative pain and swelling. Further research is needed to assess the efficacy of LLLT for post operative pain and swelling associated with general surgery and oncologic surgeries. In the meantime, LLLT is a reasonable thing to try.

Hospital-based burn units are adopting LLLT for healing and pain control. While I have not treated severe burns in the oncology population, I have cared for inpatients with Stevens Johnson syndrome who were later sent to a burn unit for further care. I wish that I had had access to LLLT in that setting to enhance care for those patients.

LLLT is being studied as a treatment for alopecia, primarily for alopecia areata and androgenetic alopecia. The FDA has approved one LLLT device specifically for androgenetic alopecia. Potential applications for chemotherapy-induced alopecia are intriguing and merit further study.

**Gastroenterology and Pulmonology**

In researching this article, I was surprised to find clinical trials regarding the use of LLLT for gastrointestinal and respiratory conditions. These include noncalculous cholecystitis, chronic gastritis, and both acute and chronic asthma.
Potentiation of Anti-cancer Therapies

LLLT may have benefit in potentiating other anti-cancer therapies though evidence has not reached the level of clinical trials. A June 2010 German paper reports ‘extraordinary’ levels of growth inhibition when HeLa cervical cancer cells were exposed to 670 nm red laser after pretreatment with green tea. There is also evidence for the potentiation of radiation therapy via local increases in ATP, which depletes tumor stores of reduced glutathione in mouse models. Similarly, increased ATP potentiated the effects of adriamycin on an ovarian cancer cell line in vitro.

Implementing Laser Therapy

There are multiple advantages to implementing LLLT in oncology practice. Foremost, patients appreciate having nothing to swallow. Because LLLT may also lower the need for pain medication, laser therapy may provide a number of benefits. Obviously LLLT will not cause the constipation that opioids do. Perhaps more importantly, LLLT does not have the sedating action of most pain medications, allowing for increased alert quality time with family, which is especially precious to patients with advanced cancers. LLLT has no interactions with other oncology treatments, so it can be used when other treatments are precluded by interaction concerns. Considering these benefits to oncology patients, we are currently exploring the addition of LLLT here at CTCA.

Properly-administered laser treatment is painless and does not damage the skin. Best results occur with multiple treatments. Insurance reimbursement in the range of $45 per treatment area may be available via category III CPT codes.

Most LLLT treatments in the United States last 2-5 minutes per treatment area, with some authors raising the theory that shorter treatments biostimulate while longer treatments suppress. The Arndt-Schulz rule and some clinical evidence suggest a biphasic dose-response curve favoring frequent, brief treatments, though the ideal treatment schedule has not been conclusively established.

When purchasing a laser therapy system, consider the FDA approval category and wavelength. FDA approval categories describe the laser’s documented mechanism of action. NHN approval indicates that a laser has been proven to biostimulate cells via increases in ATP production. Examples are the Erchonia and Microlight lasers. ILY approval indicates that the laser works via heating tissue, similar to that of a heating lamp. Regarding wavelength, individual research studies list the wavelength used. Overall, the 630 – 850 nm range is effective for the majority of applications.

Conclusion

LLLT offers a variety of benefits to the oncology patient and the naturopathic physician. Advantages include robust scientific evidence, brief treatment time, diverse clinical indications, and patient comfort.

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References


89 Huang YY, Chen AC, Carroll JD, Hamblin MR. Biphasic dose response in low level light therapy. Dose Response. 2009 Sep 1;7(4):358-83.