



Low-level laser therapy

Low-level laser therapy (LLLT), **cold laser therapy**, **photobiomodulation** (PBM)^{[1][2][3][4]} or **red light therapy**^[5] is a form of medicine that applies low-level (low-power) lasers or light-emitting diodes (LEDs) to the surface of the body. Whereas high-power lasers are used in laser medicine to cut or destroy tissue, it is claimed that application of low-power lasers relieves pain or stimulates and enhances cell function. The effects appear to be limited to a specified set of wavelengths and new research has demonstrated effectiveness at myopia control.^[6] Several such devices are cleared by the United States Food and Drug Administration (FDA), and research shows potential for treating a range of medical problems including rheumatoid arthritis^[7] and oral mucositis.^[8]

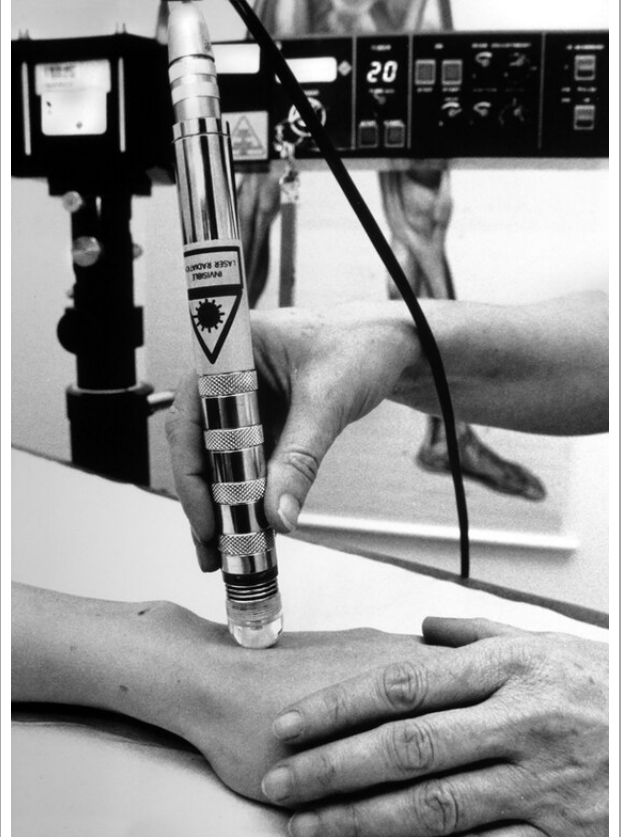
Mechanism

Research is ongoing about the mechanism of LLLT. The effects of LLLT appear to be limited to a specified set of wavelengths of laser,^[9] and administering LLLT below the dose range does not appear to be effective.^[10] Photochemical reactions are well known in biological research, and LLLT make use of the first law in photochemistry (Grotthuss-Draper law): light must be absorbed by a chemical substance in order for a photochemical reaction to take place. In LLLT that chemical substance is represented by the respiratory enzyme cytochrome c oxidase which is involved in the electron transport chain in mitochondria,^{[11][12]} which is the generally accepted theory.

Medical uses

Various LLLT devices have been promoted for use in treatment of several musculoskeletal conditions including carpal tunnel syndrome (CTS), fibromyalgia, osteoarthritis, and rheumatoid arthritis. They have also been promoted for temporomandibular joint disorders, wound healing, smoking cessation, and tuberculosis. LLLT appears to be effective for preventing oral mucositis in

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LLLT being applied for rheumatism in Sweden

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recipients of a stem cell transplant with chemotherapy.^{[8][13]} In other areas, evidence for LLLT remains conflicted. Some studies suggest that LLLT may be modestly effective in relieving short-term pain for rheumatoid arthritis,^[7] osteoarthritis,^[14] chronic low back pain,^[15] acute and chronic neck pain,^[16] tendinopathy,^{[9][17]} and chronic joint disorders.^[10] The evidence for LLLT being useful in dentistry,^{[18][19]} and in the treatment of wound healing^[20] is unclear.

Concerns have been raised in the literature about brain stimulation techniques that rely upon low-level (low-power) lasers and light-emitting diodes (LEDs). The transcranial photobiomodulation or transcranial low level light therapy is limited in neuromodulation due to several reasons:

- An excessive dose of radiation can be harmful.^[21] Therefore, at adequate doses of light there may be stimulation of growth, but at high doses excessive singlet oxygen may be produced and its chemical action may be harmful to cells.^{[22][21]}
- Regarding LED light therapy, this neurostimulation method based on the light-emitting diodes stimulation cannot pass through the skin, only laser can penetrate deeper tissues and stimulate brain areas accordingly. The penetration depth of white light and LED light into the skin increases with increasing wavelength from the UV to the visible light range, and then decreases again in the IR range depending on the selected optical properties. This depth further increases if the thickness of the stratum corneum decreases.^[23] Broadband polychromatic light (white light) and LED radiation can only penetrate 0.0017 mm to 5 mm of tissue.^[24] For example, research shows that at wavelengths of 450 nm and 650 nm only 1% of the light reaches approximately 1.6 mm and very little reaches 5 mm.^{[25][26]} Only laser radiation can propagate into deeper tissues.
- Since the action spectrum for tissue regeneration and repair consist of more than one wavelength,^{[27][21]} laser and LED light sources may offer some disadvantages,^[28] destroying healthy cells.^[21] We still lack knowledge of mental processes at the cellular level. The link between neuronal activity and mental processes is still an intriguing research question and a problem in treatment targeting. Therefore, no one can be sure whether the laser beam only reaches the neuronal structures in the brain that need treatment. An undetermined dose of radiation and the target of radiation can destroy healthy cells during the treatment procedure.^[21]

Veterinary use

Veterinary clinics use cold laser devices to treat a wide variety of ailments, from arthritis to wounds, on dogs and cats.^{[29][30]} Very little research has been done on the effects of this treatment on animals. Brennen McKenzie, president of the Evidence-Based Veterinary Medicine Association, has stated that "research into cold laser in dogs and cats is sparse and generally low quality. Most studies are small and have minimal or uncertain controls for bias and error".^{[31][32]} While allowing that some studies show promising results, he reports that others do not. While believing that there is enough evidence to warrant further study, he concludes that there is not enough evidence to support routine clinical use of cold laser in animals.

Society and culture

History

Faroese physician Niels Finsen is believed to be the father of modern light therapy.^[33] He used red light to treat smallpox lesions. He received the Nobel Prize in Physiology or Medicine in 1903.^[34] Scientific evidence for some of his treatments is lacking, and later eradication of smallpox and development of antibiotics for tuberculosis rendered light therapy obsolete for these diseases.^[35]

Hungarian physician and surgeon Endre Mester (1903–1984) is credited with the discovery of the biological effects of low power lasers,^[36] which occurred a few years after the 1960 invention of the ruby laser and the 1961 invention of the helium–neon (HeNe) laser.^[11] Mester accidentally discovered that low-level ruby laser light could regrow hair during an attempt to replicate an experiment that showed that such lasers could reduce tumors in mice. The laser he was using was faulty and wasn't as powerful as he thought. It failed to affect the tumors, but he noticed that in the places where he had shaved the mice in order to do the experiments, the hair grew back more quickly on the treated mice than on those among the control group.^[2] He published those results in 1967.^[11] He went on to show that low level HeNe light could accelerate wound healing in mice.^[11]

By the 1970s, he was applying low level laser light to treat people with skin ulcers.^[11] In 1974, he founded the Laser Research Center at the Semmelweis Medical University in Budapest, and continued working there for the remainder of his life.^[37] His sons carried on his work and brought it to the United States.^[36] By 1987, companies selling lasers were claiming that they could treat pain, accelerate healing of sports injuries, and treat arthritis, but there was little evidence for this at that time.^[36] Mester originally called this approach "laser biostimulation", but it soon became known as "low-level laser therapy" and with the adaptation of light emitting diodes by those studying this approach, it became known as "low-level light therapy", and to resolve confusion around the exact meaning of "low level", the term "photobiomodulation" arose.^[2]

Names

The following terms are accepted as alternatives of *low level light therapy* term: LLLT, laser biostimulation, laser phototherapy, low-level laser therapy, low-power laser irradiation, low-power laser therapy, and photobiomodulation therapy. The term *photobiomodulation therapy* is considered the preferred term by industry professionals.^{[3][4]} However LLLT has been marketed and researched under a number of other terms, including red light therapy,^[38] low-power laser therapy (LPLT), soft laser therapy, low-intensity laser therapy, low-energy laser therapy, cold laser therapy, bio-stimulation laser therapy, photo-biotherapy, therapeutic laser, and monochromatic infrared light energy (MIRE) therapy.^[39] More specific applications sometimes have their own

terms, for example when administered to acupuncture points, the procedure is called laser acupuncture. When applied to the head, LLLT may be known as transcranial photobiomodulation, transcranial near-infrared laser therapy (NILT),^[40] or transcranial low level light therapy.

Government action

The FDA filed a complaint for injunction in 2014, alleging that company QLasers PMA were marketing their devices as being able to treat “over 200 different diseases and disorders,” including cancer, cardiac arrest, deafness, diabetes, HIV/AIDS, macular degeneration, and venereal disease. This case resulted in a permanent injunction against the manufacture, marketing, sale, and distribution of those devices in 2015.^[41]

In 2017, the owner of QLasers, Robert Lytle, and two of QLasers's distributors were charged with a criminal conspiracy to commit fraud. Lytle pleaded guilty to one count of conspiracy to introduce misbranded medical devices into interstate commerce with the intent to defraud and mislead, and one count of criminal contempt in January 2018. Lytle was sentenced to serve 12 years in prison and made an initial restitution payment of \$637,000. Lytle's conspirators were sentenced to 24 months and 15 months, respectively.^{[42][43]}

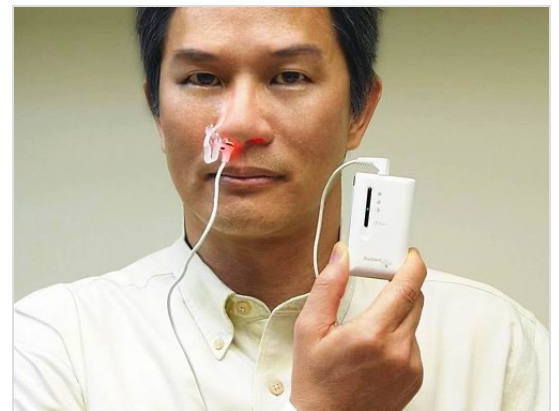
Reimbursement

Blue Cross Blue Shield Association and Aetna provide coverage for the prevention of oral mucositis, but not any other reason.^{[44][45]} The Centers for Medicare and Medicaid Services does not provide coverage for LLLT.^[46] Cigna lists LLLT as "experimental, investigational, or unproven for any indication" and provides literature review summaries for a number of conditions.^[47]

Research

Musculoskeletal

Evidence does not support a benefit in delayed-onset muscle soreness.^[48] It may be useful for muscle pain and injuries.^[49] A 2008 Cochrane Library review concluded that LLLT has insufficient evidence for treatment of nonspecific low back pain,^[50] a finding echoed in a 2010 review of chronic low back pain.^[51] A 2015 review found benefit in nonspecific chronic low-back pain.^[15] LLLT may be useful in the treatment of both acute and chronic neck pain.^[16] In 2013, however, a systematic review and meta-analysis of LLLT for neck pain indicated that the benefit was not of significant importance and that the evidence had a high risk of bias.^[52] In a study testing the efficacy of low-level laser therapy treating plantar



Demonstration of LLLT with intranasal irradiation

fasciitis found that LLLT significantly reduces pain in lower extremity tendinopathy and plantar fasciitis in the short and medium terms.^[53] The same study also stated that while comparing the effect of LLLT to that of therapeutic ultrasound in persons with patellar tendinopathy, and they found a statistically significant effect in favour of LLLT, both on pain reduction and function.^[54]

There are tentative data that LLLT is useful in the short-term treatment of pain caused by rheumatoid arthritis,^[7] and possibly chronic joint disorders.^[10] Research that compared the effects of LLLT against other treatments, sham treatments, or no treatment at all, and randomized adult patients with rheumatoid arthritis to receive it were considered. These outcomes included pain, functional capacity, adverse events, inflammation, disease activity, range of motion, stiffness in the morning, muscle strength, and quality of life.^[55] The findings indicate that the differences between utilizing a sham and an infrared laser may be negligible or nonexistent in terms of pain, stiffness in the morning, grip strength, functional ability, inflammation, range of motion, disease activity, and side events. We also discovered that the data about the effects of laser acupuncture against reflexology in terms of functional ability, quality of life, and inflammation is quite hazy, and about the effects of red laser versus sham in terms of pain, morning stiffness, and side events.^[56] The usefulness of red laser, laser acupuncture, and reflexology in the treatment of RA patients is not well enough demonstrated.^[57] A 2019 systematic review and meta-analysis found evidence for pain reduction in osteoarthritis.^[14] While it does not appear to improve pain in temporomandibular disorders, it may improve function.^[58]

There is tentative evidence of benefit in tendinopathy.^{[9][17]} A 2014 review found benefit in shoulder tendinopathy.^[59] A 2014 Cochrane review found tentative evidence that it may help in frozen shoulders.^[60]

Mouth

Similarly, the use of lasers to treat chronic periodontitis^[18] and to speed healing of infections around dental implants^[19] is suggested, but there is insufficient evidence to indicate a use superior to traditional practices.^[61] There is tentative evidence for dentin hypersensitivity.^[62] It does not appear to be useful for orthodontic pain^{[63][64]} LLLT might be useful for wisdom tooth extraction (complications).^[65]

Hair loss

LLLT has been studied as a treatment for hair loss; a review in 2012 found little evidence to support the use of lasers to treat hair loss.^[66] A 2014 review found tentative evidence for benefit for lasers,^[67] while another 2014 review concluded that the results were mixed, had a high risk of bias, and that its effectiveness was unclear.^[68] A 2015 review found tentative evidence of benefit.^[69] Additionally, a 2017 review of clinical trials found 10 of 11 trials reviewed "demonstrated significant improvement of androgenic alopecia in comparison to baseline or controls when treated with LLLT."^[70]

LLLT is shown to increase hair density and growth in both genders. The types of devices (hat, comb, helmet) and duration did not alter the effectiveness,^[71] with more emphasis to be placed on lasers compared to LEDs.^[72] Ultraviolet and infrared light are more effective for alopecia areata, while red light and infrared light is more effective for androgenetic alopecia.^[73]

Medical reviews suggest that LLLT is as effective or potentially more than other non invasive and traditional therapies like minoxidil and finasteride but further studies such as RCTs, long term follow up studies, and larger double blinded trials need to be conducted to confirm the initial findings.^{[74][75][76]}

Brain injuries

LLLT has been studied for traumatic brain injury (TBI) and stroke among other conditions.^[11] When applied to the head it is known as transcranial photobiomodulation or transcranial low level light therapy.

Cancer treatment side effects

LLLT has been studied as a way to reduce pain and swelling in breast-cancer related lymphedema.^{[77][20]} The 2015 systematic review & meta-analysis by Smoot, Chiavola-Larson, et al found: “Moderate-strength evidence supports LLLT in the management of [breast cancer related lymphoedema], with [...] reductions in volume and pain immediately after conclusion of LLLT treatments. Greater reductions in volume [of lymph nodes or surrounding tissues] were found with the use of LLLT than in treatments without it.”^[78]

Stem cells

An ongoing area of research is the application of LLLT for increasing cell proliferation, including stem cells.^[79]

Wound healing

Low level laser therapy has been studied as a potential treatment for chronic wounds, and higher-power lasers have sometimes been successfully used to close acute wounds as an alternative to stitching.^[80] However, as of 2012 and due to inconsistent results and the low quality of extant research, reviews in the scientific literature have not supported its widespread application.^{[80][81]}

See also

- Photomedicine
- Light therapy
- Blood irradiation therapy

- Photorejuvenation

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