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INTRODUCTION

Therapies currently available for the stimulation and improvement of tissue repair include the application of light and forms of phototherapy that utilize parts of the electromagnetic spectrum beyond the visible range. Used in addition to best clinical practice in the management of soft tissue injuries, there is considerable evidence that they can help improve tissue repair. The main types of phototherapy will be described, emphasizing the mechanisms by which they produce the effects. Evidence supporting their efficacy will be presented. The aim of this presentation is to provide the practitioner with sufficient knowledge to:

- Select appropriate treatments for different types of soft tissue injuries and
- Monitor their effectiveness non-invasively.

PHOTOTHERAPY

Electromagnetic radiation in the form of photons delivered in either laser or non-laser form has been applied to wounds as a means of stimulating healing for over 30 years. The technique is now often referred to as phototherapy, photon therapy or as photobiomodulation, the use of photons to modulate biological activity, these terms can be used interchangeably.

Light consists of those wavelengths of the electromagnetic spectrum that are visible to the human eye. This part of the spectrum extends flow violet to red. Infrared (IR) is beyond the visible range. The perceived colour depends on the wavelength. White light is a mixture of all the visible wavelengths. For photons to reach a wound all that is required is that the wound be either exposed to air, or bathed in sterile saline, or covered by a transparent dressing. Exposure to red light and/or infrared radiation can stimulate the healing of both chronic wounds (Mester et al 1985) and acute wounds (Dyson & Young 1986).

LASER is an acronym for Light Amplification by the Stimulated Emission of Radiation. The stimulated emission of radiation occurs when a photon interacts with an energized atom. When an atom is energized, for example by electricity, one of its electrons is excited, i.e. raised to a higher energy orbit than its orbit when in the resting state. If the energy of the incident photon is equal to the energy difference between the electron's excited and resting states, then stimulated emission of a photon occurs and the excited electron returns to its resting state. This photon has the same properties as the incident photon, which it also emitted. This process is repeated in the adjacent energized atoms, producing a laser beam). Unlike light from non-laser sources, this light is:

- Monochromatic, i.e. of a single wavelength
- Collimated, i.e. its rays are nondivergent
- Coherent, i.e. in phase, the troughs and peaks of the waves coinciding in time and space.

With regard to laser therapy, monochromaticity is its most important characteristic. To produce an effect, the light must be absorbed, and absorption is wavelength-specific. Different substances absorb light of different wavelengths. Mitochondria, present in all cells, contain cytochromes that absorb red light. Some cells absorb some wavelengths of infrared radiation, while other cell types absorb other IR wavelengths.

LILT is an acronym for **L**ow **I**ntensity **L**aser **T**herapy (Baxter 1994). It is synonymous with LLLT, the acronym for **L**ow **L**evel **L**aser **T**herapy. Unlike the high intensity medical lasers used to thermally cut and coagulate tissues, LILT involves the use of medical lasers that operate at intensities too low to damage living tissues. Their action is photobiomodulation; they can stimulate inactivated tissue components and inhibit activated components (Agaihy et al 1998; Dyson, Agaihy & Ghali 2002).

LEPT is an acronym for **L**ow **E**nergy **P**hoton **T**herapy (Gupta et al 1998). It includes LILT and is a form of phototherapy, photon therapy or photobiostimulation.

LILT equipment

This has three essential components:

- A lasing medium, which is capable of being energized sufficiently for lasing to occur
- A resonating cavity containing the lasing medium.
- A power source that transmits energy into the lasing medium.

This type of lasing medium used determines the wavelength, and therefore the colour of the laser beam. For example, a HeNe laser, in which the lasing medium is a mixture of helium and neon gases, produces red light with a wavelength of 632.8 nm. Gallium,

aluminum and arsenide, the lasing medium of GaAlAs semiconductor diodes, also produces monochromatic radiation, but the wavelength of this depends on the ratio of these three materials and is in the red-infrared range of the electromagnetic spectrum, typically 630-950 nm.

The resonating cavity containing the lasing medium has two parallel surfaces, one being totally reflecting, the other being only partially reflecting. Photons emitted from the lasing medium are reflected between these surfaces, some of them leaving through the partially reflecting surface as the laser beam. The cavity of a HeNe laser is many cms long, whereas that of a GaAlAs semiconductor diode is minute, the diode being the lasing medium and its polished ends the reflecting surfaces. Most LILT devices are currently of the GaAlAs type. Their treatment heads may contain either one or several diodes. Those with one diode resemble laser pointers and are designed to treat acupuncture and trigger points; they can also be used to treat small regions in and around wounds. Those with many diodes are generally called cluster probes and allow large areas to be treated rapidly. The diodes may be housed in a rigid head or in a flexible material. The latter can be applied around curved surfaces such as the shoulder. Cluster probes housing multiple diodes are available, emitting either one or several wavelengths in the red and infrared range. The red light targets all cells, while different wavelengths in the infrared range appear to target specific cell types. In cluster probes all, some or none of the diodes may produce coherent radiation, but all produce monochromatic radiation.

The power source for a LILT device may be either a battery or mains electricity. Many of the smaller, simpler, LILT devices are portable and battery powered. The main function of the power source is to energize the lasing medium.

Application of LILT to a soft tissue injury

When treating a closed lesion the LILT probe can be placed in direct contact with the skin. When treating an open wound LILT is usually applied through a transparent dressing via a cluster probe. This can either be placed in contact with the dressing or held above it if the wound is painful. Mester et al (1985) recommended the use of an energy density of 4 J/cm^2, Joules being calculated by multiplying the power density (in W/cm^2) by the irradiation time in seconds. In addition to treating the wound bed, Baxter (1996) recommends treating the intact skin around the wound with a single diode probe at points about 1-2 cm from the wound margin and about 2-3 cm apart. The probe should be pressed finnly onto the intact skin. This reduces attenuation by temporarily displacing erythrocytes that would absorb some of the incident energy. It is usually recommended that the energy density applied be no more than 10 J/cm^2.

When LILT is used to treat a patient the following treatment parameters should be recorded:

- Wavelength (in nm)
- Treatment duration (in min)
- Power output (in mW)
- Power density (in mW/cm^2). Calculated by dividing the power output by the irradiating area (or spot size) of the laser. The spot of a semiconductor diode is typically 0.1-0.125 cm^2. The number of diodes multiplies this when a cluster probe is used.
- Energy density (in J/cm^2). This is calculated by multiplying the power density by the irradiation time in seconds.
- If LILT is used in pulsed mode then the pulse repetition rate in Hz (i.e. number of pulses per second) should also he recorded.

Many of the early publications in the field of LILT were marred by incomplete description of the treatment parameters. This has, however, improved as understanding of the importance of the various treatment parameters has increased.

LILT Bioeffects

For LILT to be effective, the tissue targeted must absorb photons. Absorption is wavelength depended. Red light is absorbed by cytochromes in the mitochondria of all living cells, whereas certain wavelengths of IR may be absorbed by specific proteins of the cell membrane, these proteins varying according to the type of cell. Provided that appropriate wavelengths and energy densities are used, cell activity can be stimulated if it is suboptimal. Cells in which this has been investigated include mammalian keratinocytes, lymphocytes, macrophages, fibroblasts and endothelial cells, all cells of significance in tissue repair. Much of this work has been reviewed by Baxter (l994). Cells affected by LILT show a temporary increase in permeability of their cell membranes to calcium ions (Young et al 1990). This may be the mechanism by which LILT modulates cell activity, as has been shown to occur following US treatment. Other electrotherapeutic modalities may act in a similar fashion.

How LILT stimulates tissue repair

Mechanism

The triggering of cell activity by reversible changes in membrane permeability when photons are absorbed could be responsible for the stimulation of tissue repair (Young & Dyson 1993). Increase in calcium uptake by macrophages exposed to red light and IR in vitro has been shown to be wavelength and energy density dependent. Of the wavelengths tested, 660, 820 and 870 nm were effective; 880 nm was ineffective. These same wavelengths also affected growth factor production by the macrophages, 660, 820 and 870 nm being stimulatory, whereas 880 nm was not. Energy densities of 4 and 8 J/cm^2 were found to be effective; 2 and 19 J/cm^2 were not (Young et at 1990). Red light of 660 nm wavelength is absorbed by the cytochromes of mitochondria, where it stimulates ATP production and

increases cytoplasmic H+ concentration, which can affect cell membrane permeability (Karu 1988). IR radiation of 820 and 870 nm may be absorbed by components of the cell membrane and affect membrane permeability directly. Some of these components vary in different cell types, which may be why the IR wavelengths absorbed by cells differ according to the cell type. For example, 870 nm affects macrophages (Young et al 1990) but not mast cells (El Sayed & Dyson 1990). It maybe possible to selectively stimulate macrophages but not mast cells in vivo by exposure to an 870 nm probe; this remains to be investigated.

Cells differ in their sensitivity to LILT according to their environmental conditions. For example, mast cells in the environment of a tissue injury can be stimulated to degranulate by treatments that do not produce this effect in the mast cells of intact soft tissue (El Sayed & Dyson 1990).

Following a reversible change in membrane permeability to calcium ions, the cell responds by doing what it is designed to do. In the case of macrophages, this is to produce growth factors and to phagocytose debris whereas mast cells degranulate, releasing histamine amid other substances.

The molecular mechanisms by which LILT, affects cell activity begin with photoreception, when the photons are absorbed. This is followed by signal and growth factor transduction, amplification and a photo response, e.g. cell proliferation, protein synthesis production all of which may assist in tissue repair.

Membrane structure varies according to the cell type. The absorption of sonic wavelengths of IR by some cells but not by others may be due to differences in their membrane structure. Theoretically, it should be possible, by the judicious selection of IR wavelengths, to affect some cell types in vivo while leaving others unaffected. Red light, however, affects all cell types, being absorbed by the mitochondrial cytochromes present in all living cells.

The cellular effects of LILT relevant to tissue repair include the stimulation of

- Adenosine triphosphate (ATP) production
- Mast cell recruitment and degranulation
- Growth factor release by macrophages
- Keratinocyte proliferation
- Collagen synthesis
- Angiogenesis

At the tissue level there is an acceleration of the resolution of acute inflammation, resulting in the more rapid formation of granulation tissue and reepithelialisation than in sham-irradiated control tissue. Any or all of these effects could help to explain why wound healing can be stimulated by LILT.

CLINICAL POINTS

- Red light will affect all the cells involved in the healing process
- IR is more selective
- To stimulate macrophages while leaving mast cells unaffected, use 870nm, IR radiation
- Cells vary in their sensitivity to phototherapy according to their environmental conditions, those of injured tissue being more sensitive than those of intact tissue.

Effect of LILT on acute wounds

As with any other technique, the healing of acute wounds can only be stimulated by LILT if they are healing suboptimally. For example, if skin wounds are kept in a dry environment, their healing is delayed, and in such wounds LILT can stimulate granulation tissue and wound contraction (Dyson & Young 1986). The most effective energy density reported is 4 J/cm^2.

Effect of LILT on chronic wounds

In 1985 Mester et al surveyed the LILT treatment of over 1000 patients with chronic ulcers. Using an energy density of 4J/cm^2, they showed 50-100% healing, variation being related to the type of lesion and the clinical condition of the patient. It has been suggested that the induction of acute inflammation in chronic wounds permits the local release of factors stimulating tissue repair. The use of LILT and other forms of phototherapy can increase the rate of resolution of acute inflammation with the result that the entry of the injury into the proliferative phase of repair occurs more rapidly. Although there have been many reported studies on the effect of LILT on the healing of acute wounds many of them are flawed in that they provide insufficient information for them to be reproduced by others (Basford 1989). In recent years this situation has improved, see, for example the study by Gupta et al (1998) on the healing of venous ulcers.

The use of LILT to relieve pain and edema

In 1979 Zhukov et al demonstrated that red light produced by a HeNe laser could reduce post-thrombophlebetic edema and leg ulceration at intensities of only 0.1 J/cm^2. Reduction of edema would be expected to reduce ulcer-associated pain.

The use of high-resolution ultrasound imaging to monitor tissue repair

High-resolution diagnostic ultrasound is of considerable value in tissue repair as a means of assessing the extent of tissue damage and of monitoring its repair (Dyson et al 2003). In these days of evidence-based clinical practice it is essential that the effectiveness of treatment be monitored objectively. Ultrasound imaging permits this to be done non-invasively, rapidly and painlessly. Unlike surface photography, it allows tissue changes within, throughout and around the wound to be visualized in the manner of a biopsy, but without any damage to the patient. Magnified, high-resolution images of living tissue akin to, low power micrographs can be produced by using 20 MHz US; the technique is therefore often referred to as ultrasound biomicroscopy. The images obtained are digital, can be archived, and can be emailed to remote sites for analysis if this is required, an example of telemedicine in action.

Portable, user and patient-friendly high resolution scanners are now commercially available. It is recommended that soft tissue changes within and around the injury be recorded with a high resolution US scanner every time that the injury is treated. Taking these scans can be done by the physical therapist or other clinician treating the injury and adds only a few minutes to the time spent with each patient. A scanner operating at a frequency of 20 MHz can provide a vertical resolution of the order of 65 μ, and clear discrimination between acoustically different materials such as tissue fluid, debris, granulation tissue, scar tissue and the various layers of the epidermis, dermis and hypodermis. Changes in superficial tendons and ligaments can also be imaged (see www.longprotinc.com for further information). The software incorporated into some scanners allows linear and area measurements to be made from the scans. These are then stored, together with the scans and the patient's notes, in a secure, retrievable fashion.

High-resolution ultrasound scans should be taken before treatment is commenced and throughout the course of any treatment so that its effectiveness can be monitored and changes made if the response of the patient indicates this.

CONCLUSIONS

Light, including laser therapy and the other forms of phototherapy described above, can assist in wound healing if used in an appropriate manner. Most act by accelerating the resolution of inflammation so that the proliferative phase of healing begins earlier, leading to speedier tissue repair. Cell activity is jump-started by changes in membrane permeability. The cells then do what they are capable of doing. Macrophages, for example, phagocytose debris and secrete growth factors. These factors, which are angiogenic and mitogenic, stimulate time activity of fibroblasts, endothelial cells and other cells involved in the repair process so that healing is accelerated.

The clinician responsible for treating an injured patient is better equipped to select the most beneficial treatment for the patient if armed with an understanding of each therapy and of its mode of action.

The ultimate test of any treatment is the way in which the patient responds to it. Systemic changes in the patient should be documented and the injures imaged non-invasively throughout healing. Changes in soft tissue structure and physiology should be quantified where possible so that valid comparisons can be made. The sharing of findings via peer-reviewed journals and conference presentations will add to our understanding of these treatments and improve the lot of injured patients.

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