LASER THERAPY: AN OVERVIEW

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Summary:
This tutorial lecture will cover:

- The medical uses of laser therapy
- The clinical role of laser therapy in the stimulation of tissue repair and regeneration, using wound healing as an example
- The stages involved in these processes, concentrating on the cellular changes which result in healing
- The effects of laser therapy on cells necessary for successful healing
- The cellular mechanisms producing these effects.

Laser therapy can involve the use of either high or low power lasers. High power lasers produce clinically significant thermal changes in biological tissue; in contrast, the action of low power lasers is predominantly nonthermal.

The devices used in what is generally, though not always accurately, described as low power laser therapy, also known as low level laser therapy (LLLT), low intensity laser therapy (LILT) and low energy photon therapy (LEPT), operate at the milliwatt level. They utilize either single or cluster probes, and can be used in continuous or pulsed mode. They have been used successfully for over 30 years in Europe and Asia to aid tissue repair and to relieve pain. Unfortunately many of the early published studies on the effectiveness of laser LLLT are marred by incomplete description of treatment parameters, poor experimental design such as lack of controls, and inadequate blinding.
The LILT output information that should be recorded is as follows:

- Wavelength
- Power density
- Energy density
- Pulse duration
- Pulse repetition rate
- Total irradiation time.

The biological target should also be adequately described, and suitable inclusion and exclusion criteria specified. In clinical investigations into the healing of previously chronic wounds, use of non-invasive, and thus non-damaging, quantitative techniques of digital photography and ultrasound biomicroscopy is recommended. Digital photography provides a record of colour, shape and surface area changes. Ultrasound biomicroscopy allows the visualisation, recording and quantification of microscopic changes throughout the full depth of the wound and in the intact tissues adjacent to it. There is an urgent need for publication, after peer review, of more double blind, placebo controlled, clinical trials using non-invasive quantitative techniques that provide clinically relevant data rapidly and safely.

For laser therapy to progress as a clinical science it is essential that its mode of action be studied. Much has been revealed about this from experimental work carried out using animals *in vivo* and cells *in vitro*. It has been demonstrated in animals that dry wounds in which healing is delayed can heal faster when treated with LLLT. The acute inflammatory phase of a repair is accelerated and, possibly as a consequence of the more rapid release of growth factors during this phase, granulation

and re-epithelialization begin more quickly. Acute inflammation is an essential part of repair because angiogenic and mitogenic growth factors are produced during it from a variety of cell types including mast cells and macrophages.

Mast cells synthesize and secrete chemicals that assist in the initiation of inflammation and stimulate various aspects of repair, including angiogenesis. These chemicals are released into the extracellular matrix when the mast cells degranulate in response to membrane permeability changes. In intact skin, exposure *in vivo* to red light (660 nm) and to some wavelengths of infrared *in vivo* (820, 940 or 950 nm) was followed by an increase in mast cell numbers in comparison with sham-irradiated controls. 870 and 880 nm were not effective, possibly because the cells did not absorb them. There was no increase in degranulation. In contrast, in partial thickness wounds there was an increase in degranulation as well as in cell number. This suggests an increase in the sensitivity of mast cells to degranulating stimuli following tissue damage.

Another cellular effect of laser therapy is enhanced growth factor release by macrophages. In an *in vitro* study it was found that of the wavelengths examined 660, 820 and 870 nm were stimulatory, but 880 was not. It may be possible to selectively stimulate macrophages but not mast cells *in vivo* by exposure to an 870 nm probe; this remains to be investigated.

The enhanced secretion of growth factors may be triggered by membrane permeability changes to calcium ions. This permeability change could be initiated in some cases by the light-induced production of free radicals. The stimulated cell then responds by doing what it is designed to do. In the case of macrophages, this is to secrete growth factors and phagocytose debris. Wavelengths which stimulate macrophages to release growth factors also stimulate calcium uptake temporarily, as do specific energy densities. In designing a clinical trial, it is important to use an appropriate wavelength and an effective energy density; this should be determined in a pilot study.

The molecular mechanisms by which LLLT affects cell activity begin with photoreception followed by signal transduction and amplification, and then by a photoresponse, e.g. cell proliferation or secretion, leading to the stimulation of tissue repair. Membrane structure differs according to the cell type, which may explain why some cells absorb some IR wavelengths, whereas other cells absorb other IR wavelengths. In theory, it should therefore be possible by the judicious selection of infrared wavelength to affect some cell types while leaving others unaffected. Red light lacks this selectivity, being absorbed by the mitochondrial cytochromes present in all cell types.

The cellular effects of laser therapy relevant to tissue repair are reversible membrane permeability changes, which stimulate a range of cellular events including:

- Mast cell recruitment and degranulation.
- Growth factor release by macrophages
- Angiogenesis
- Keratinocyte proliferation

At the tissue level, there is an acceleration of the resolution of acute inflammation, with the result that granulation tissue formation and re-epithelialisation occur more rapidly than in sham-irradiated controls. Any or all of these effects could help to explain why delayed wound healing can be stimulated by LLLT.