Lesson 2
Terminology & Mechanisms
Some names in use for the machines

Soft laser
Low level laser
Low intensity level
Low power laser
Low energy laser
…and others
Names in use for the therapy

Laser therapy
Low level laser therapy (LLLT)
Low intensity level therapy
Low power therapy
Low energy laser therapy
Cold laser therapy
…and others
Suggested for the therapy

PhotoBioModulation (PBM)

Formerly: Low Level Laser Therapy (LLLT)
Definition

Photobiomodulation (PBM): An event in which nonionizing optical radiation in the visible and near-infrared (NIR) spectral range is absorbed by endogenous chromophores to elicit photophysical and photo-chemical events at various biological scales. Photobiomodulation therapy (PBMT) is a form of light therapy based on the concepts of PBM and uses light in the visible and NIR spectra to cause physiological changes and clinical benefits.
My suggested for the unit:

THERAPEUTIC LASER
Suggested for in vitro: Low Level Laser Irradiation (no ”therapy” in vitro)

PMB includes:

- Lasers
- LEDs
- Broadband incoherent light
- Broadband polarized light
- And others

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Some lasers for PBM

- KTP 554 nm (green)
- HeNe 632.8 nm (red)
- InGaAlP 630-690 nm (red)
- GaAlAs 700-980 nm (partly invisible)
- GaAs 904/905 nm (invisible)
- Nd:YAG 1064 nm (invisible)
Some mechanisms
The first law of photochemistry (Grotthus–Draper Law) states that light must be absorbed by a molecule before photochemistry can occur. If a sample absorbs no light, there can be no photochemical effect. One of the key questions in low level laser therapy is the determination of photo-absorbing molecules which are responsible for photo-biological effects (photo-acceptors).
Red and near-IR light is thought to be primarily absorbed by cytochrome c oxidase, which is unit four in the mitochondrial respiratory chain. Since the recent discovery of mitochondrial nitric oxide synthase, it has been realized that nitric oxide produced in the mitochondria can inhibit respiration by binding to cytochrome c oxidase and competitively displacing oxygen, especially in stressed or hypoxic cells. Light absorption displaces or photo-dissociates the nitric oxide and thus allowed the cytochrome c oxidase to recover and cellular respiration to resume.
Nitric oxide is believed to be involved in the radiation-induced mesenteric arteriolar vasodilatation and subsequent increase in the microcirculatory blood flow.
Photoreceptors (1)

- **Cytochrome C Oxidase (CCO)**
  - terminal enzyme of the mitochondrial respiratory chain
  - ATP producer
Photoreceptors (2)

NADH-dehydrogenase
- flavoprotein
- NADH dehydrogenase is the first enzyme within the mitochondrial electron transport chain.

ATP producer
Photoreceptors (3)

• Some human photochemically reactive proteins:
  • Encephalopsin in the brain
  • Pinopsin in the pineal gland
• Prokaryotic and eukaryotic cells:
  • More than 500
Photoreceptors (4)

- Endogenous porphyrines
- (compare PhotoDynamic Therapy)
CELLULAR AND TISSULAR MECHANISMS OF PBM

The precise biochemical mechanism underlying the therapeutic effects of PBM are not yet well-established. From observation, it appears that PBM has a wide range of effects at the molecular, cellular, and tissular levels. In addition, its specific modes of action may vary among different applications. Within the cell, there is strong evidence to suggest that PBM acts on the mitochondria to increase adenosine triphosphate (ATP) production, modulation of reactive oxygen species (ROS), and the induction of transcription factors. Several transcription factors are regulated by changes in cellular redox state. Among them redox factor-1 dependent activator protein-1 (AP-1) (a heterodimer of c-Fos and c-Jun), nuclear factor kappa B (NF-κB), p53, activating transcription factor/cAMP-response element–binding protein (ATF/CREB), hypoxia-inducible factor (HIF)-1, and HIF-like factor. These transcription factors then cause protein synthesis that triggers further effects downstream, such as increased cell proliferation and migration, modulation in the levels of cytokines, growth factors and inflammatory mediators, and increased tissue oxygenation. The absorption of red or near infrared (NIR) light occurs through specific cellular chromophores or photoacceptors localized in the mitochondrial. During this process in mitochondria respiration chain ATP production is increased.
Immune cells, in particular, appear to be strongly affected by PBM. Mast cells, which play a crucial role in the movement of leukocytes, are of considerable importance in inflammation. Specific wavelengths of light are able to trigger mast cell degranulation, which results in the release of the pro-inflammatory cytokine TNF-α from the cells. This leads to increased infiltration of the tissues by leukocytes. PBM also enhances the proliferation, maturation, and motility of fibroblasts, and increases the production of basic fibroblast growth factor. Lymphocytes become activated and proliferate more rapidly, and epithelial cells become more motile, allowing wound sites to close more quickly. The ability of macrophages to act as phagocytes is also enhanced under the application of PBM.

More of this:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3288797/
Hamblin et al.
Laserlessons.info

The resultant nitric oxide has an important biological role, so ....... Laserlessons.info
Telomeres and life

Phototherapy works best on cells in a reduced redox situation


Luciana Almeida-Lopes

Fibroblasts before and after PBM. Note the parallel orientation if the cells. Important for cosmetics.

Laserlessons.info
cDNA microarray analysis of gene expression profiles in human fibroblasts HS27

(Zhang et al., J. Invest. Dermatol. 120:849, 2003)

$\lambda = 628 \text{ nm}$
$0.88 \text{ J/cm}^2$

9982 genes studied:

111 genes of 10 categories were affected by irradiation

- proliferation
- antioxidant
- metabolism
- membrane potential
- cytoskeleton
- DNA synthesis
- transcription factors
- immune/inflammation
- cytokines

PBM affects gene expressions

Laserlessons.info
Alexandratou et al. 2002. pH change in single fibroblast
Is it only a heat effect?


This experiment showed that the minute heat produced by a PBM device had no role for the stimulating effect.
Healthy cells do not respond much to PBM. The best effects are found in cells with a low redox potential.
Recommended reading

Ten Lectures on Basic Science of Laser Phototherapy

Tiina Karu

www.prima-books.com
50 years of use
No serious adverse effects discovered