Meta Cell Technology

Photo Boosting

The LIGHT DOSE

It is well known that photobiomodulation (PBM) has biostimulatory action. However, these beneficial properties can only be achieved when using and applying PBM in a clever way. PBM converts light energy into metabolic and thus triggers multiple factors that contribute to several processes, such as the increase of ATP.[1,2] It is important to note that the effects are only possible within an ideal therapeutic window characterized by a specific response of each tissue and/or cell type.[3]

Currently, there is already pre-established knowledge that PBM therapy may present stimulatory and inhibitory results, as well as no effects at all, depending on the dose used, resulting in the so-called biphasic dose/response.[4] This curve was first identified and named in the late 19th century,[5] but it certainly offered another proof of the Arndt-Schultz Law. This rule, named after Hugo Schulz and Rudolf Arndt in 1888, basically states that, for every substance, small doses stimulate, moderate doses inhibit, and large doses kill. For an even older source, Paracelsus stands out with one of his famous phrases: “The dose makes the poison,” claiming that poison is in everything, and nothing is without poison: the dosage makes it either a poison or a remedy. The principles of biphasic response state that a very low dose of light has no effect, and a lightly higher dose generates a positive effect until a threshold is reached.[3] If the dose of light is increased beyond that point, the benefit progressively decreases until the baseline (no effect) is reached, and further increases will have detrimental effects on the tissue.[3-6] Variables can be analyzed in isolation, but the proper understanding of PBM parameters, as well as its application time, is more an integration exercise than a memorization one: this understanding is mandatory to achieve clinical results and biological benefits.

Some authors like to consider irradiation parameters as the “medicine” and irradiation time as the “dose”.[7] This is not the only approach. Besides, since it has been demonstrated that these are not necessarily reciprocal (e.g., if the power is doubled and the time is halved, then the same energy is delivered, but a different biological response is often observed[6]), it is probably an oversimplification of the matter. Still, it is useful to properly understand PBM parametrization.

The evaluation and knowledge of the dose/response curve can be of great value in the choice of protocols to be proposed and can be used in the scientific and clinical settings in different types of pathologies.[3] The “medicine” parameters—wavelength, irradiance, pulse structure, coherence, and polarization—are summarized in Table 1. The “dose” parameters—energy, energy density, irradiation time, and treatment interval—are summarized in Table 2.

Table 1. Irradiation parameters (the “medicine”)

Irradiation parameter	Unit of measurement	
Wavelength	nm	Light is packets of electromagnetic energy that also have a wave-like property. Wavelength is measure in nanometers (nm) and is visible in the 400–700 nm range. Wavelength determines which chromophores will absorb the light. LLLT devices are typically in the range 600–1000 nm as there are many peaks for cytochrome *c* oxidase in that range and clinical trials have been successful with them. There is some contention as wavelengths above 900 nm are probably more absorbed by water than CCO and excitation seems less likely so it introduces the possibility that maybe IR absorption by water in the phospholipid bilayers causes molecular vibration and rotation) sufficient to perturb ion channels alter cellular function
Irradiance	W/cm^2	Often called Power Density (technically incorrect) and is calculated as Power (W)/Area (cm^2) = Irradiance
Pulse structure	Peak power (W) Pulse freq (Hz) Pulse width (s) Duty cycle (%)	If the beam is pulsed then the Power reported should be the Average Power and calculated as follows: Peak Power (W) × pulse width (s) × pulse frequency (Hz) = Average Power (W). Pulses can be significantly more effective than CW[30] however, the optimal frequencies and pulse duration (or pulse intervals) remain to be determined
Coherence	Coherence length depends on spectral bandwidth	Coherent light produces laser speckle, which has been postulated to play a role in the photobiomodulation interaction with cells and sub-cellular organelles. The dimensions of speckle patterns coincide with the dimensions of organelles such as mitochondria. No definitive trials have been published to-date to confirm or refute this claim
Polarization	Linear polarized or zcircular polarized	Polarized light may have different effects than otherwise identical non-polarized light (or even 90° rotated polarized light). However, it is known that polarized light is rapidly scrambled in highly scattering media such as tissue (probably in the first few hundred μm). However, for the birefringent protein structures such as collagen the transmission of plane polarized light will depend on orientation. Several authors have demonstrated effects on wound healing and burns with polarized light[19,86,91]

Extracted from Chung et al.[14]

As with any other forms of technology-based treatment, there is a lot of physics behind PBM. Wavelength, for example, shows an effective optical window that runs from about 600 nm to 1200 nm, where tissue penetration of light is maximized. This is the reason why the use of PBM in animals and human beings involves red and infra-red lights almost exclusively.[8]

Table 2. Irradiation time/energy/fluence (the "dose")

Energy (Joules)	J	Calculated as: Power (W) × time (s) = Energy (Joules) This mixes medicine and dose into a single expression and ignores irradiance. Using Joules as an expression of dose is potentially unreliable as it assumes assumes a reciprocity relationship between irradiance and time[37,38]
Energy density	J/cm^2	Common expression of LLLT "dose" is Energy Density. This expression of dose again mixes medicine and dose into a single expression and is potentially unreliable as described above
Irradiation time	Seconds	Given the possible lack of reciprocity between irradiance and time[37,38] it is our view that the safest way to record and prescribe LLLT is to define the irradiation parameters ("the medicine") see Table 1, and then define the irradiation time (as the "dose").
Treatment interval	Hours, days or weeks	The effects of different treatment intervals is underexplored at this time though there is sufficient evidence to suggest that this is an important parameter. With the exception of some early treatment of acute injuries LLLT generally requires at least two treatments a week for several weeks to achieve clinical significance

Extracted from Chung et al.[14]

As regards the energy involved in PBM treatments, published articles applied diverse energy densities on cells, typically ranging from 0.1 J/cm^2 to 7.5 J/cm^2, with 1 J/cm^2 and 5 J/cm^2 sweet spots.[9] Power densities at the site normally range from 0, 1.67 mW/cm^2 to 12.5 mW/cm^2, since the energy is usually delivered in 10 minutes. In spite of these, some studies have examined power up to 1000 mW.[9] Results show that diverse cell types may respond differently to light and that their responses were dose dependent.[10]Again, the following must be taken under consideration: i) if doses are too low, they will not trigger the metabolic paths that will ultimately lead to PBM biological benefits,[11] and ii) very high doses will be harmful. Therefore, 5 J/cm^2 as a sweet spot was applied to different cell types.[12,13]

Dosimetry in PBM, laser and LLLT is highly complicated. Due to the large number of interrelated parameters, there are no comprehensive studies analyzing the change of effects when individual parameters are varied one by one, and it must be pointed out that it is unlikely that such a study will ever be carried out.[14] This considerable level of complexity means that the choice of parameters often depends on the experimenter's or the practitioner's personal preference or experience rather than on a consensus by an authoritative body.

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