Keys to Effective Low Level Light Therapy (LLLT)

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Low-level light therapy (LLLT) has vast potential in numerous therapeutic areas. However despite a large body of evidence, LLLT has yet to receive wide acceptance in the scientific community. Some of the primary reasons for this reluctance is the multitude of operating parameters that may be applied clinically, the difficulty in reproducing settings used by other investigators, as well as understanding how to select an effective light energy device. While finding the appropriate settings and device may seem overwhelming it doesn't have to be. The key to achieving effective clinical outcomes using LLLT is knowing what makes a safe and effective light energy device.

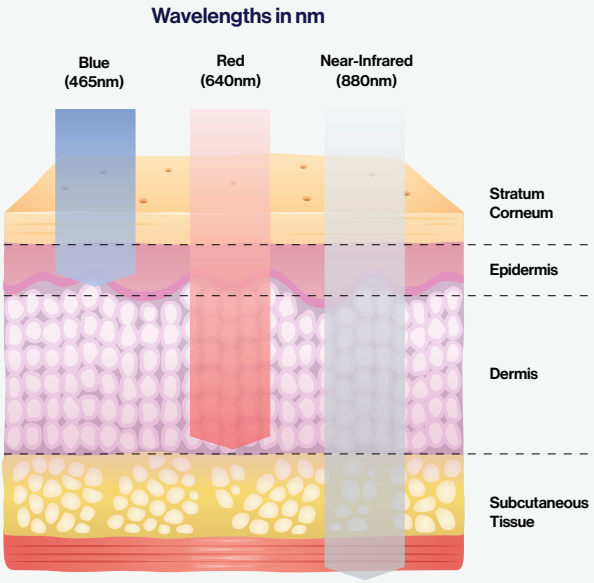
There are a number of products on the market which provide various ranges of power output, wavelength, pulse frequencies, and which deliver light energy in both short and longer time periods. In order to understand how to use this technology effectively, it is helpful to understand the fundamentals of how light therapy works. It is well known that the beneficial effects resulting from LLLT exhibit a biphasic dose response [1, 2]. This means that there is indeed a threshold at the upper and lower limit of LLLT leading to either a positive biological response, no response, or a negative response. This being said, there is no known finite set of parameters for effective LLLT dosimetry, but rather a range of effective parameters. Nevertheless, a sufficient amount of light energy must reach the target tissue in order for positive clinical outcomes to occur. Thus, in order to achieve clinical efficacy an understanding of the mechanisms involved should be considered.

The multimolecular complexes of the electron transport system have been postulated as the light receptors and increased mitochondrial activity of complexes I, II, III and IV have been observed [3, 4]. Cytochrome C oxidase, part of complex IV, generally is accepted as the primary photo-accepting molecule [3, 5, 6]. The absorption of this light energy then results in changes in reactive oxygen species (ROS) [7-9] as well as increased ATP production [10-15]. Increases of intracellular ROS and ATP activate transcription factors, which lead to activation of downstream signaling cascades resulting in the beneficial effects observed [1]. These signaling cascades most notably activate factors known to promote anti-aging, enhance wound healing, reduce pain and improve acne, as well as other clinical benefits. While these areas of research are still actively under investigation they are relatively well characterized.

There are multiple critical parameters that promote the biological responses described, however the most critical are wavelength, energy density and duration of treatment. The wavelength is of particular importance, because it needs to match the absorbance of the desired photoaccepting molecule, but will also determine the penetration depth of the light being delivered **(figure 1)**, regardless of the device that produces the light energy. The energy density will need to be high enough to elicit the desired effect, but low enough not to induce toxic or adverse effects. Generally, the clinical literature demonstrates that treatments delivered multiple times a week over several

weeks result in greater efficacy. However, these parameters will vary depending on the desired application.

Figure 1



The wavelength of light used determines the penetration depth through tissue. Human skin is comprised of multiple layers ranging from the superficial stratum corneum to the deeper subcutaneous tissue. Different wavelengths will have different penetration depths through tissue. Three effective wavelengths of light the Celluma delivers are 465 nm blue, 640 nm red and 880 nm near-infrared. Each wavelength is associated with particular beneficial effects and the penetration depth through the tissue is depicted.

Other additional considerations are the pulse frequency and the technological source of the light energy. Currently, there are no well-accepted or established effective pulse frequencies for given clinical applications [16, 17]. However, the pulsing of light is known to increase penetration depth and has been shown, in some cases, to have additional benefit in comparison to continuous light delivery. Moreover, when comparing laser and LED sources, both have demonstrated similar efficacy when optical parameters were closely matched [18]. Thus, at the energy levels commonly used for LLLT, laser and LED sources could be used interchangeably and achieve similar if not identical efficacy. All of these factors should be considered for then selecting an appropriate light delivery device.

One such device that has been designed to address all of these key factors is the Celluma from BioPhotas. The Celluma is a safe, affordable and easy to use flexible LED array. In contrast to other devices, it comes programmed with multiple operating modes for each clinical application, so the user requires no special training. The simplicity of the Celluma allows for easy operation at the push of a single button without the complication of adjusting multiple settings as required by most laser setups.

The Celluma has been approved by the FDA for multiple indications including: arthritis, muscle spasm, muscle and joint pain, muscle tissue tension, joint and muscle stiffness, diminished local circulation and inflammatory acne vulgaris, which gives further evidence of the safety of this device. The LED array is also light and portable removing the need for cumbersome bulky hardware as associated with other similar devices. The Celluma has 345 light emitting diodes that emit light energy at blue (465 nm), red (640 nm) and ear-infrared (880 nm) wavelengths with frequencies of 80 Hz, 680 Hz and 800 Hz respectively for a duration of 30 minutes per treatment.

Figure 2

The distance between the light source and treatment area is critical component of successful clinical outcomes. The Celluma can be placed above the treatment area or mounted to target the desired treatment area as shown. The flexibility of the device allows for optimal fitting of the contours of the body. This allows for even light delivery to a given location on the body, which represents a distinct advantage over similar, more rigid light delivery devices.

Two key clinical advantages of the Celluma are that it offers longer treatment duration and superior adaptation for fitting the contours of the body **(figure 2)**. A longer treatment time allows the body more time to respond to the therapeutic effect of LLLT. In addition, properly fitting the contours of the body is key to optimal energy absorption. The inverse square law states that the intensity of light administered to

the body will decrease as the square of the distance from the light source. Said another way, as the distance between a light source and a surface of absorption doubles, the amount of energy available for absorption decreases by four times. Accordingly, the Celluma conforming to a constant distance from the body for the duration of the treatment, will result in more optimal energy delivery which is a distinct advantage over rigid LED panels where the distance between the light source and subject changes, leading to inconsistent light delivery.

In conclusion, it is clear that there is a broad range of optical parameters reported to induce specific biological responses resulting in improved therapeutic outcomes. Here some of the key parameters leading to effective LLLT have been discussed and the Celluma has been introduced as a light delivery device, which has been developed according to these key parameters. There is a large body of evidence in the scientific literature describing the beneficial effect of LLLT, which are operating under similar optical parameters as the Celluma.

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