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Light wavelengths and bioactivities.

Synopsis:

Light is a term for the visible and near-visible portions of electromagnetic radiation. It is composed of magnetic and electric oscillating sinusoidal waves perpendicular to each other and propagates in the same direction. Probably the single most defining characteristic of electromagnetic radiation is its wavelength. Electromagnetic radiation exists over a vast range of wavelengths, ranging in scale from picometers (one trillionth of a meter) to kilometres. This range of wavelengths is collectively referred to as the electromagnetic spectrum. Since the energy of a photon is inversely proportional to its wavelength. Among the broad spectrum of electromagnetic radiation, 'light' comprises the visible spectrum from violet/blue to near-infrared (NIR) and offers a distinct safety advantage with photon energy in the range of 0.5–3 eV.

Poly-chromatic light: The term polychromatic means having several colours. It is used to describe the light that exhibits more than one colour, which also means that it contains radiation of more than one wavelength.

Monochromatic light: The term monochromatic comes from the Greek word mono, meaning single, and chroma, meaning colour. So monochromatic light means light of one colour. In scientific terms, it means light of a single wavelength.

Conclusions:

Whilst being safe, this photonic energy can interact with organic molecules. It is emerging that various types of extra-ocular photoreceptors can absorb light of multiple wavelengths and trigger a variety of molecular cascades, culminating in altered cellular energy production and gene expression, a significant benefit for the energy demand of cells.

Indeed, polychromatic light might have multiple beneficial effects at the same time concerning a monochromatic light source.

FLE platform differs from other LED modalities since the photoconverter gel emits polychromatic fluorescent light covering the continuum of the visible spectrum (~415–610 nm).

The wavelength of light determines the depth of tissue penetration.

Table 1: Light bioactivities (nm).

Blue light	(415–500) nm has the shortest tissue penetration, reaching the stratum corneum and epidermis. It is used to treat acne vulgaris, it is also thought to have an anti-inflammatory effect regulating cytokines.
Green light	(500–570 nm) targets the epidermis and upper dermis to access fibroblasts and endothelial cells mediating proliferation and healing, the key elements in skin rejuvenation.
Yellow light	(570–590 nm) is indicated in wound healing by reaching the papillary dermal layer. It is used in post-laser recovery and is implicated in photoaging modulating ATP and fibroblast activity.
Orange and Red light	(590–760 nm) with the deepest skin penetration are noted for vascular activation, reducing inflammation, improving wound healing, and increasing collagen production.

Reference:
Edge, D. et al. 2020. Biophotonic Therapy Induced Photobiomodulation. In: Technology in Practical Dermatology. Springer, Cham.

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Benefits of pulsed light and evaluation of pulsed light versus continuous light.

Synopsis:

The concept of super-pulsing was originally developed for the carbon dioxide laser used in high-power tissue ablative procedures. The idea was that by generating relatively short pulses (?second) the laser media could be excited to higher levels than those normally allowed where heat dissipation constraints limit the maximum amounts of energy that can be used to excite the lasing media.

Pulsed light offers numerous potential benefits. Because there are "quench periods" (pulse OFF times) following the pulse ON times, pulsed light can generate less tissue heating. In instances where it is desirable to deliver light to deeper tissues increased powers are needed to provide adequate energy to the target tissue. This increased power can cause tissue heating at the surface layers and in this instance, pulsed light could be very useful.

Whereas continuous waves (CW) cause an increase in temperature of the intervening and target tissues or organ, pulsed light has been shown to cause no measurable change in the temperature of the irradiated area for the same delivered energy density.

Secondly, potassium and calcium ion channels in the mitochondria and the sarcolemma may be involved in the cellular response to LLLT.

Thirdly, by dissociating NO from CCO, an increased ATP production appears. If the light is pulsed multiple photodissociation events could occur, while in CW mode the number of dissociations may be much smaller.

Conclusion:

Overall pulsed light may be superior to continuous light due to the key points below:

- As pulsed light has 'quench periods', it can deliver energy to deep into the tissues while generating less heat at the surface layers;
- The logic in favour of pulsed light is that cells may need periods of rest, without which they can no longer be stimulated further;
- An increased ATP production may be stimulated by pulsed light.

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Cellular and tissutal mechanisms of LLLT.

LLLT has a wide range of effects at the molecular, cellular, and tissular levels. Within the cell, there is strong evidence to suggest that LLLT 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. These transcription factors then cause protein synthesis that triggers further effects down-stream, such as increased cell proliferation and migration, modulation in the levels of cytokines, growth factors and inflammatory mediators, and increased tissue oxygenation.

Immune cells appear to be strongly affected by LLLT. Mast cells, which play a crucial role in the movement of leukocytes, are of considerable importance in inflammation. Specific wavelengths of light can trigger mast cell degranulation which results in the release of the pro-inflammatory cytokine TNF-a from the cells. This leads to increased infiltration of the tissues by leukocytes.

LLLT 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 LLLT.

At the most basic level, LLLT acts by inducing a photochemical reaction in the cell, a process referred to as biostimulation or photobiomodulation. When a photon of light is absorbed by a chromophore in the treated cells, an electron in the chromophore can become excited and jump from a low-energy orbit to a higher-energy orbit. This stored energy can then be used by the system to perform various cellular tasks. There are several pieces of evidence that point to a chromophore within mitochondria being the initial target of LLLT.

Radiation of tissue with light causes an increase in mitochondrial products such as ATP, NADH, protein, and RNA, as well as a reciprocal augmentation in oxygen consumption, and various in vitro experiments have confirmed that cellular respiration is upregulated when mitochondria are exposed to a form of illumination.

Cytochrome c oxidase (CCO) is the crucial chromophore in the cellular response to LLLT. CCO is a large transmembrane protein complex, which is a component of the respiratory electron transport chain. The electron transport chain passes high-energy electrons from electron carriers through a series of transmembrane complexes (including CCO) to the final electron acceptor, generating a proton gradient that is used to produce ATP.

Thus, the application of light directly influences ATP production by affecting one of the transmembrane complexes in the chain: in particular, LLLT results in increased ATP production and electron transport.

The observation that NO is released from cells during LLLT has led to speculation that CCO and NO release are linked by two possible pathways. It is possible that LLLT may cause photodissociation of NO from CCO.

References:

Chung H, Dai T, Sharma SK, Huang YY, Carroll JD, Hamblin MR. The nuts and bolts of low-level laser (light) therapy. Ann Biomed Eng. 2012 Feb;40(2):516-33. doi: 10.1007/s10439-011-0454-7.

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Light and skin receptors: the role of Opsins.

Synopsis:

Life on earth depends on sunlight; it is a sine qua non condition for human survival. Skin, the largest organ of our body, is also constantly exposed to sunlight. Solar UV radiation is comprised of ~95% long wavelength UVA and ~5% short wavelength UVB, each activating distinct signaling pathways in the skin. UVB induces DNA damage, triggering the increase in pigmentation within many hours to days, while physiological doses of UVA trigger a retinal-dependent G-protein coupled signaling pathway causing immediate pigment darkening via activation of an unknown receptor (Olinki et al 2020).

Human skin is structured in layers: the uppermost layer, the epidermis, is comprised of keratinocytes surrounding a single basal layer of melanin-producing melanocytes; the dermis comprises a middle fibrous layer; and the subcutis is a cushioning layer upon which the epidermis and dermis rest. High energy UVA penetrates through both the epidermis and dermis, whereas UVB is primarily confined to the epidermis (Olinki et al 2020).

In the early 2000s, different wavelengths of light have different effects on human epidermal permeability were determined, indicating a potential array of spectrally distinct light receptors within the skin. Shortly thereafter, OPN1s and OPN2 were identified in human epidermal skin. (Olinki et al 2020).

Opsins are a large group of light-sensitive G protein–coupled receptors (GPCRs) that use retina as a ligand and trigger signaling cascades upon distinct wavelength of light. Opsins, primarily found in light-detecting cells such as the retinal photoreceptors, are widely known for their key role in visual transduction (Sadowska et al., 2021). Indeed, depending on location of the expression, there are different categories of opsins. OPN2, OPN3, and OPN4 are expressed in the epidermis (Olinki et al 2020).

The role of opsin is also investigated as they are activated by blue light (415 nm). Blue light can increase pigmentation in normal human melanocytes (NHMs) via OPN3 photoactivation. The opsin receptor is possibly excited by blue light, stimulating the transient receptor potential channels and then causing a flood of calcium, which triggers calcium/calmodulin-dependent protein kinase-II (CAMKII) and in the end causes gene transcription changes. OPN2 (Rhodopsin) and OPN3 (Panopsin, Encephalopsin) were found to be expressed not only in the skin, but also in the anagen hair follicle. Opsin's role has also been investigated in the modulation of pigmentation and melanogenesis, but only in the Fitzpatrick skin type III and higher (Sadowska et al., 2021). Downregulation of OPN3 reduces the expression of OPN1 and OPN5, suggesting a potential interaction between OPN3, OPN1 and OPN5 which could explain UVA-dependent responses. (Olinki et al., 2020).

Conclusions:

Several studies demonstrated that opsins modulate various physiological processes of the skin, including wound healing, melanogenesis, photoaging, and hair growth. Since each opsin has distinct absorption spectra and signaling transduction, the optimization of light therapy tailored to the features of each opsin will maximize the benefit that PBM can offer in the clinic. There has been a growing interest in the application of light therapy to clinical cases owing to the advantages of a cost-effective and non-invasive approach (Suh et al., 2020).

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Suh S, Choi EH, Atanaskova Mesinkovska N. The expression of opsins in the human skin and its implications for photobiomodulation: A Systematic Review. Photodermatol Photoimmunol Photomed. 2020 Sep;36(5):329-338. doi: 10.1111/phpp.12578.

Safety and efficacy of Energy Based Devices in combination with injectables.

Synopsis:
Combining aesthetic interventions to target ageing processes often leads to better results than a single treatment. Nevertheless, few guidelines using multiple interventions have been published to date. This review aims to summarize and critically appraise recent developments and clinical investigations on the safety and efficacy of combining Injectables and Energy Based Devices (EBD). A thorough analysis of the literature using PubMed and Scopus using the keywords; dermal filler, hyaluronic acid, Botox, BoNT (Botulinum neurotoxin), combination, LLLT (low level light therapy), light, energy based and LED was performed. A total of 9 clinical research articles were selected from the aforementioned databases. In these studies, the use of EBDs in combination with Fillers and/or BoNT included over 125 patients and 400 treatments in total.

Results and Discussion:

According to the Carruthers consensus study, BoNT often provides a synergistic effect, leading to superior results of greater duration when combined with fillers, lasers, light- or energy-based devices or surgical procedures. The consensus was defined as approval from 75% to 94% of all participants, whereas agreement of 95% denoted a strong consensus. For same-day treatments, BoNT and fillers may be performed together in either sequence, whereas micro-focused ultrasound with visualization (MFU-V) is recommended before injectable agents (Carruthers et al., 2016).

The concomitant use (same day) of laser and HA fillers for facial rejuvenation represents an effective and safe strategy which improves clinical results and patient satisfaction (Urdiales-Gàlvez et al., 2019) The panel recommendations are: If we want to perform a combined procedure on the same day (HA and light treatments), start always with the light treatments, avoiding skin manipulations after having injected.

Six studies by Cuerda-Galindo and co-workers (2015) documented no histological changes in fillers injected after applying radiofrequency, IPL or laser treatments and one study documented improvement in collagen after IPL treatment and toxin injection.

Akerman et al. (2022) successfully combined the non-ablative 1,540nm erbium with glass laser treatment followed by administering a highly purified hyaluronic acid injectable into the post-acne facial scars. The novel combination treatment overall demonstrated an average mild to moderate improvement in post-acne facial scars appearance, with high patient satisfaction three months after treatment and a good safety profile.

According to Wang et al. (2021) in 41 single-session treatments with fillers and EBDs, there were no documented adverse events related to the spreading of fillers or energy treatment of filled areas, including product migration, unexpected loss of filler volume, vascular occlusion, acute pain, cutaneous necrosis, blindness and cutaneous burn.

No histological changes in PMMA (polymethylmethacrylate) microspheres were observed in any treatment area. An expected lymphohistiocytic response was identified in all areas where PMMA microspheres were present. Laser, light, and ultrasound treatments can safely be administered following a PMMA-collagen injection (Wu et al., 2016).

Studies examining the efficacy and safety of intense pulsed light, ablative fractional lasers, nonablative fractional lasers, micro-focused ultrasound with visualization, thermistor-controlled subsurface monopolar radiofrequency, cryolipolysis, liposuction, laser lipolysis, neuromodulators, and hyaluronic acid dermal fillers in the neck were assessed. The authors' experience in clinical practice is that many neck rejuvenation techniques can be combined safely (Vanaman et al., 2016).

Using the review of the literature and clinical experience, Langelier and colleagues (2016) discuss our strategy for combining botulinum toxin, facial filler, ablative laser, intense pulsed light (IPL), micro-focused ultrasound, and microneedle fractional radiofrequency to treat aesthetic problems of the upper face. With attention to safety recommendations, injectable, light, laser, and energy-based treatments can be safely combined with experienced hands to provide enhanced outcomes.

Providing multiple treatments in 1 session improves patient satisfaction by producing greater improvements in a shorter amount of time and with less overall downtime than would be necessary with multiple office visits (Lengelier et al., 2016).

Most studies found no evidence of filler degradation, adverse events, or histologic changes after treatment with non-ablative lasers, IPL, or radiofrequency, even when administered immediately after filler implantation. It would be reasonable to suggest administering deeper lasers, if required, before soft-tissue augmentation.

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Fillers may be combined with lasers, IPL, or radiofrequency devices in any order on the same day without an increase in adverse effects or decrease in efficacy. Without the guiding evidence for the order or sequence of combination treatments, there is great variation in the pattern of practice (Humphrey et al., 2016).

FLE + Injectables | Protocol Recommendations:

Based on the scientific evidence, the following protocols can be recommended;

- Fluorescent Light Energy (FLE) can be used before a Filler injection
- Fluorescent Light Energy (FLE) can be used immediately prior (same session) to a Filler injection
- Fluorescent Light Energy (FLE) can be used two weeks post a Filler injection
- Fluorescent Light Energy (FLE) can be used before a BoNT injection
- Fluorescent Light Energy (FLE) can be used immediately prior (same session) to a BoNT injection
- Fluorescent Light Energy (FLE) can be used two weeks post a BoNT injection.

Conclusions:
The use of Energy Based Devices (including Fluorescent Light Energy, FLE) combined with an injectable dermal filler such as Botox and Hyaluronic Acid could be considered safe according to the literature data.
A review of the literature demonstrates the safety of same day combined treatments for rejuvenation (Cuerda-Galindo et al. 2015).
BoNT often provides a synergistic effect, leading to superior results of greater duration when combined with fillers, lasers, light- or energy-based devices or surgical procedures (Carruthers et al., 2016)
Providing multiple treatments in 1 session improves patient satisfaction by producing greater improvements in a shorter amount of time and with less overall downtime than would be necessary with multiple office visits (Lengelier et al., 2016).
A combination approach often produces the most optimal outcome for a patient seeking skin rejuvenation.
Procedures may vary across the clinics. Some physicians use energy-based therapies before the injection, others after the injection.
The physician's clinical evaluation should consider the patient's case by case needs. All the parameters involved in these procedures should be assessed along with the temperatures and the depth of both the energy based device and the fillers' chemical-physical properties.

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