

## Photo-Thermal Boosting

### Introduction

Autologous preparations are products that are often used in regenerative medicine treatments. From a biological perspective, they are extremely useful because they are rich in cells and in multiple bioactive components, such as growth factors. For this reason, said preparations are used in all types of pathologies to support and optimize physiological processes, such as wound healing or tissue regeneration.

Several types of autologous materials exist, such as cell concentrates or blood derivatives, just to name a couple of examples. Of these, platelet-rich plasma (PRP) is undoubtedly the most popular. As is well known, millions of PRP treatments have been performed worldwide in the last decade. To obtain it, there are well-defined and studied protocols,<sup>1,2,3</sup> although their variability is too significant not to be considered. Key steps will determine the maximum biological potential of PRP products. Traditionally, these steps are: preservation of platelet viability and its activation method.<sup>4</sup>

Platelet activation is the mechanism that leads to its degranulation and, consequently, the release of bioactive molecules stored in its granules into the medium. These molecules have different chemical constitution, although, so far, interest has been mostly focused on growth factors (GFs). When released in the targeted area, GFs support all types of physiological processes. Historically, calcium gluconate or calcium chloride have been used to activate platelets, but modern trends advocate for the use of natural products and the avoidance of unnecessary chemical substances.

In this context, photobiomodulation (PBM) has made great progress, being a safe, non-toxic, effective way to get the same, or better, results. PBM is a non-invasive, non-toxic light therapy, mainly applied within the range of 600 nm-1,000 nm. Its biological effect is usually attributed to light absorption by a photoreceptor of the cellular respiratory chain<sup>5</sup> through cytochrome C oxidase (COX) or Complex IV, although two hypotheses currently predominate: i) the mitochondrial hypothesis, which suggests that mitochondria absorb photons and increase ATP synthesis,<sup>6</sup> and ii) the ionic channel hypothesis, which attributes the effect of PBM to a higher calcium entry into the cell due to an increase in light sensitivity of its ionic channels.<sup>7</sup>

Scientific research on PBM started about 50 years ago.<sup>8,9</sup> To date, the beneficial effects of PBM have been verified in a variety of diseases and physiological processes, in which the reduction of inflammation or the stimulation of lesion repair has been observed in vivo and in vitro,<sup>10</sup> as well as other effects, such as the reduction of hypoxic damage.<sup>11</sup> PBM can stimulate some cellular metabolic pathways, which will impact their viability, differentiation, proliferation, or migration. This will ultimately lead to a potential improvement of cell regeneration ability<sup>12</sup> and the achievement of beneficial effects in the treatment of several diseases, conditions, and physiological processes, such as wound healing, reduction of inflammation, or

stimulation of lesion repair.<sup>13</sup> Light is a booster for cellular activity. Photo Boosted Platelet-Rich Plasma is the most significant advance in PRP treatments in the last decade.<sup>14</sup>

Light in the near-infrared region of the spectrum induces the release of PDGF, FGF and TGF- $\beta$  from platelets in a higher amount and for a longer time than that obtained with activation of calcium chloride.<sup>15</sup> Photon absorption by COX leads to the acceleration of electron transfer reactions and ATP production,<sup>16,17</sup> and limits terminal phosphorylation in the mitochondrial respiratory chain.<sup>15</sup> Irradiation: i) increases the activity of Complexes I, II, III, IV and of succinate dehydrogenase in the electron transport chain; ii) stimulates the NADH dehydrogenase and cytochrome C oxidase; and iii) increases ATP synthesis and the level of nitric oxide (NO).<sup>18</sup> Furthermore, red and near-infrared lights stimulate the proliferation of stem cells derived from human adipose tissue.<sup>19</sup> On the other hand, after 24 hours, photoactivation increases the amount of ATP<sup>15</sup> and, in some entities, it decreases pain.<sup>20</sup>

Besides photoboosting, photoconditioning, photoactivation, and photomodulation,<sup>3,14</sup> there is another physical technique that can improve the clinical capabilities and healing potential of PRP: thermal biomodulation (TBM).<sup>21</sup> This is another way to increase the amounts of GFs in PRP. Cold can alter the concentration of GFs found in PRP based on variables such as time or temperature of exposure.<sup>22</sup> It also improves GFs release kinetics, increasing the sustain and total amount of GFs released during the days after the application. Cold has a positive effect on PRP,<sup>23</sup> a fact that has been observed in several protocols, such as in samples conditioned for 10 minutes at 4°C (pre-TC vs. post-TC measurements for EGF, FGFb, VEGF [ $p < 0.001$ ],<sup>24</sup> or for 30 minutes.<sup>23</sup>

MCT<sup>®</sup> is a system specially designed to ensure the effective and safe delivery of photo and thermal boosting stimuli to biological tissues during a medical consultation. The MCT Kit<sup>®</sup> can hold any fluid tissue (blood, plasma, sera, purified tissues, cellular solutions, etc.) to be boosted with light and temperature, either separately or simultaneously. The MCT Kit<sup>®</sup> was built with medical grade materials with excellent thermal conductivity and optical properties. Its constituent polymers can withstand thermal fluctuations between -3°C and +50°C, and they ensure that the mechanical fluctuations of the materials don't compromise air tightness, or any characteristic of the tissue held inside.

The MCT<sup>®</sup> system can stimulate tissues with temperature and/or electromagnetic energy from the visible spectrum, and/or infrared regions. For this purpose, MCT<sup>®</sup> carried out studies quantifying the passage and losses of all the waves that it emits. These facts are highly significant because they are closely related with the concept of "dosage" and have enabled MCT<sup>®</sup> to become the first scientific effective system of platelet and cellular photothermal boosting. Among other factors, MCT<sup>®</sup> controls: i) regular transmittance, ii) diffuse transmittance, iii) reflectance, iv) reflection, v) scattering, and vi) losses in the different media through which energy passes. Some of these parameters are inherent to each material, such as the refractive index of a polymer, but others may vary based on how each piece is built. Aside from the right choice of materials, the structure of the MCT Kit<sup>®</sup> takes into account several matters that are purely physical, such as wall thickness, volume of the cavity, or light and thermal interfaces. Even the way in which MCT<sup>®</sup> manufactures each piece has been decisive, since, during the injection of a polymer, there may be internal flows or deposits determining faceted processes inside the material that can alter the way in which waves travel through it.

MCT<sup>®</sup> can apply reproducible (scientific) treatment protocols because it can ensure the stimulus that each tissue receives. The MCT Kit<sup>®</sup> is a single-use device, marketed in sterile conditions.

The MCT Unit<sup>®</sup> includes two pre-programmed protocols. The first protocol is useful to increase ATP synthesis in any type of live cells or in cells with mitochondria. The second protocol is useful to increase platelet degranulation, increase the amount of GFs in PRP and generate a more physiological, sustained and powerful release. This protocol was updated in 2022, since in 2021, photo-thermal boosting was performed serially instead of simultaneously. The MCT Unit<sup>®</sup> is ready to easily upgrade any protocol (as scientific evidence progresses) using an USB port.

MCT<sup>®</sup> also has a custom protocol that allow users to use the temperature and light the way they want. Specifically, up to 12 J/min can be delivered with each wavelength, although MCT<sup>®</sup> delivers as dictated by scientific evidence worldwide. Furthermore, the MCT Unit<sup>®</sup> can emit infrared, amber, green and blue lights, if the MCT<sup>®</sup> R&D department or other researchers can account for its use with scientific evidence.<sup>25</sup> Regarding thermal boosting, the MCT Unit<sup>®</sup> has the capacity to stimulate autologous materials with temperatures ranging from 4°C to 42°C. The possibilities offered by the MCT<sup>®</sup> technology are almost endless.

## References

1. Emer J. Platelet-Rich Plasma (PRP): Current Applications in Dermatology. *Skin Therapy Lett.* 2019;24(5):1–6.
2. Lansdown DA, Fortier LA. Platelet-Rich Plasma: Formulations, Preparations, Constituents, and Their Effects. *Oper Tech Sports Med.* 2017;25(1):7–12.
3. Weibrich G, Kleis WKG, Hafner G, Hitzler WE. Growth factor levels in platelet-rich plasma and correlations with donor age, sex, and platelet count. *J Cranio-Maxillofacial Surg.* 2002;30(2):97–102.
4. Amin I, Gellhorn AC. Platelet-Rich Plasma Use in Musculoskeletal Disorders: Are the Factors Important in Standardization Well Understood? *Phys Med Rehabil Clin N Am.* 2019;30(2):439–49.
5. Ahrabi B, Tavirani MR, Khoramgah MS, Noroozian M, Darabi S, Khoshsirat S, et al. The effect of photobiomodulation therapy on the differentiation, proliferation, and migration of the mesenchymal stem cell: A review. *J Lasers Med Sci.* 2019;10(4):S96–103.
6. Han B, Fan J, Liu L, Tian J, Gan C, Yang Z, et al. Adipose-derived mesenchymal stem cells treatments for fibroblasts of fibrotic scar via downregulating TGF- $\beta$ 1 and Notch-1 expression enhanced by photobiomodulation therapy. *Lasers Med Sci.* 2019;34(1).
7. Fallahnezhad S, Jajarmi V, Shahnavaz S, Amini A, Ghoreishi SK, Kazemi M, et al. Improvement in viability and mineralization of osteoporotic bone marrow mesenchymal stem cell through combined application of photobiomodulation therapy and oxytocin. *Lasers Med Sci.* 2019;35(3):557–66.
8. Heiskanen V, Hamblin MR. Photobiomodulation: Lasers: vs. light emitting diodes? *Photochem Photobiol Sci.* 2018;17(8):1003–17.
9. DeLong JM, Russell RP, Mazzocca AD. Platelet-rich plasma: The PAW classification system. *Arthrosc - J Arthrosc Relat Surg.* 2012;28(7):998–1009.
10. Samadi P, Sheykhhasan M, Khoshinani HM. The Use of Platelet-Rich Plasma in Aesthetic and Regenerative Medicine: A Comprehensive Review. *Aesthetic Plast Surg.* 2019;43(3):803–14.
11. Weibrich G, Kleis WKG, Hafner G, Hitzler WE. Growth factor levels in platelet-rich plasma and correlations with donor age, sex, and platelet count. *J Cranio-Maxillofacial Surg.* 2002;30(2):97–102.
12. Pinto H, Goñi Oliver P, Sánchez-Vizcaino Mengual E. The Effect of Photobiomodulation on Human Mesenchymal Cells: A Literature Review. *Aesthetic Plast Surg.* 2021 Aug;45(4):1826–42.
13. Kouhkeheil R, Fridoni M, Abdollahifar MA, Amini A, Bayat S, Ghoreishi SK, et al. Impact of Photobiomodulation and Condition Medium on Mast Cell Counts, Degranulation, and Wound Strength in Infected Skin Wound Healing of Diabetic Rats. *Photobiomodulation, Photomedicine, Laser Surg.* 2019;37(11):706–14.
14. Freitag J, Barnard A, Rotstein A. Photoactivated platelet-rich plasma therapy for a traumatic knee chondral lesion. *BMJ Case Rep.* 2012;15:1–4.

15. Irmak G, Demirtaş TT, Gümüşderelioglu M. Sustained release of growth factors from photoactivated platelet rich plasma (PRP). *Eur J Pharm Biopharm.* 2020;148:67–76.
16. Karu TI. Multiple roles of cytochrome C oxidase in mammalian cells under action of red and IR-A radiation. *IUBMB Life.* 2010;62(8):607–10.
17. Hamblin MR. Mechanisms and Mitochondrial Redox Signaling in Photobiomodulation. *Photochem Photobiol.* 2018;94(2):199–212.
18. Yu W, Naim JO, McGowan M, Ippolito K, Lanzafame RJ. Photomodulation of Oxidative Metabolism and Electron Chain Enzymes in Rat Liver Mitochondria. *Photochem Photobiol.* 1997;66(6):866–71.
19. Wang Y, Huang YY, Wang Y, Lyu P, Hamblin MR. Red (660 nm) or near-infrared (810 nm) photobiomodulation stimulates, while blue (415 nm), green (540 nm) light inhibits proliferation in human adipose-derived stem cells. *Sci Rep.* 2017;7(1):1–10.
20. AKM M, P L, KN C, BU S. Clinical outcome of photoactivated platelet-rich plasma in the treatment of knee osteoarthritis. *Rheumatol Orthop Med.* 2019;4(1):1–4.
21. Du L, Miao Y, Li X, Shi P, Hu Z. A novel and convenient method for the preparation and activation of PRP without any additives: temperature controlled PRP. *Biomed Res Intl* 2018;doi:10.1122/2018/1761865
22. Wen YH, Lin WY, Lin CJ, Sun YC, Chang PY, Wang HY, et al. Sustained or higher levels of growth factors in platelet-rich plasma during 7-day storage. *Clin Chim Acta.* 2018 Aug 1;483:89–93.
23. Etulain J, Mena HA, Meiss RP, Frechtel G, Gutt S, Negrotto S, et al. An optimised protocol for platelet-rich plasma preparation to improve its angiogenic and regenerative properties. *Sci Rep.* 2018;8(1):1–15.
24. Pinto H, Melamed G. Thermal conditioning: improving PRP Growth Factor content. *Prime.* 2020june; 3-5
25. Gresner P, Watała C, Sikurová L. The effect of green laser light irradiation on whole blood platelets. *J Photochem Photobiol B.* 2005 Apr 4;79(1):43-50.