White Paper

July 2020

Multi Radiance Research Series: ACTIVet PRO 2.0 Laser

Moving forward and enhancing technology

Multi Radiance
Super Pulsed Lasers

ACTIVET PRO

The ACTIVet PRO 2.0 Laser White Paper

Moving forward and enhancing technology

Multi Radiance Research Series
July 2020

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Executive Summary:

The ACTIVet PRO, first introduced in 2016, launched a new era in veterinary laser therapy as the most powerful, ultra-portable super pulsed laser therapy device available. The first-in-class features included an expansion of the therapeutic window to include blue (465nm LED) for antimicrobial therapy, an optimized depth of penetration time profile of 39% (DPTP), and skin-safe thermal time profile (TTP).

The purpose of this white paper is to introduce the new features and benefits of the 2.0 upgrade and detail a new comparative study and case reports performed with the ACTIVet PRO. Several new modes, including a manual mode (where all parameters can be adjusted individually), Priority Principle Assist (including companion and equine presets), and energy delivered readout in Joules will be discussed.

Introduction:

Photobiomodulation (PBM) with super pulsed laser and LEDs has been used for nearly 2 decades to modulate pain, reduce inflammation, and promote healing. Several systematic reviews performed by experts in the field have identified strong evidence for tendinopathy,[1] chronic joint disorders,[2] acute pain,[3] osteoarthritis and rheumatoid arthritis[4], myofascial trigger points and myofascial pain syndrome[5], and pain relief effects by laser irradiation on joint areas.[6]

A Super Pulsed Laser (SPL) by Multi Radiance Medical works differently than traditional high-powered lasers. By producing a burst of highly-focused peak power light at just a billionth-of-second duration, it results in a low thermal influence on the skin and passes the dermis much more efficiently to reach deeper tissue. Cleared as a Class 1M laser (safest by FDA/OSHA), the non-thermal treatments deliver a beneficial phototherapeutic effect even when dealing with dark pigmented animal skins.

As the technology evolves and science unveils other mechanisms of action and biological effects, the use of SPL will continue to expand. New devices will continue to be introduced into the market. Today's technological advancements allow for the inclusion of new features and enhancements that are not possible in older systems.

The truth is that all technology will require an upgrade. Upgrades do not always require new hardware; creating new software can utilize the present hardware in novel and interesting configurations. Often this can unlock new usability features or settings that were previously unavailable.

Software upgrades can also include new or enhanced features, or better compatibility with different devices or applications. They can also improve software stability and remove outdated features. This means businesses using older technology will not have the functionality that could provide a competitive advantage.

Several new features of the upgrade will allow veterinarians more freedom and options to expand and improve their super pulsed laser therapy programs. The manual mode allows for new combinations or isolations of the four wavelengths to create new therapeutic effects. To ensure consistent and reliable outcomes, total delivered energy can be displayed on the screen to assist in documentation. Expanded frequencies and additional presets are updated to the latest available.

Wavelength, Depth of Penetration and Thermal Profile:

Current evidence suggests that the cascade of events leading to photobiomodulation effects by red to near-infrared (IR) illumination is initiated by the mitochondrial cytochrome c oxidase (CCO).[7] Respiration in the mitochondria can be inhibited by nitric oxide (NO) binding to CCO, which competitively displaces oxygen and affects cell metabolism. Excess NO binding is associated with inflammatory processes, cell damage, and apoptosis.[8] Light absorption dissociates NO, allowing cellular respiration to resume, normalizing cellular activity.

For this process to be effective, light must first be absorbed into the target cells by passing through the exterior layers of the skin. Therefore, adequate light penetration is the foundation of a beneficial treatment and is related to the depth of penetration, wavelength (nm) and energy (mW) delivered. Albuquerque-Pontes, et al.[9] evaluated the depth of penetration through the dorsal skin of rats to determine the effects of concurrent multiple wavelengths of 640nm red LED, 875nm IRED LED, and 905nm SPL with a total average of approximately 450 mW of power. There was 39% DPTP attributed to the higher efficacy of the new ultra-bright red and infrared LEDs of the ACTIVet PRO. The study concludes that a combination of multiple wavelengths creates a synergism that enhances each individual wavelength's ability to penetrate the skin.

The favorable DPTP, created by the core of multiple wavelengths, allows a greater percentage of light energy to penetrate beneath the skin and minimizes the amount of energy being transformed into heat. However, any decrease in the DPTP can contribute to an increase in skin surface temperature, which can lead to a reduction in the phototherapeutic effects and a dangerous rise in tissue temperature.

The North American Association for Photobiomodulation Therapy (NAALT) has recognized that photobiomodulation (PBM) is a non-thermal process. However, most continuous wave lasers/LEDs and all high-powered Class 4 lasers produce a considerable amount of unwanted heat that may limit the phototherapeutic response or cause tissue damage. Isman, et al.[10] found evidence that the increased heat accumulation from high-powered laser also stimulated apoptotic pathways of cell death. Apoptosis is normally mediated by caspases, which trigger cell death.[11] The damage was not induced by the heat alone. Khan, et al [12] established a correlation between a rise in surface temperature (> 45 °C) and phototoxic tissue damage. Therefore, it can be argued that a higher-powered laser that generates superficial tissue heating in the skin does not provide photobiomodulation as is currently understood, but rather triggers apoptotic pathways.

Vanin, et al. evaluated the thermal impact of the ACTIVet PRO (450 mW and 50 Hz frequency) on light, medium and dark skin. Skin temperatures were observed using a FLIR thermographic camera to monitor the delivery of 25 J, 80 J, and 133 J to the skin. No groups experienced excessive photothermal effects ($p>0.05$) that may affect patient safety and no threat or concern regarding cytotoxicity. The lack of accumulating skin temperature may be attributed to the ultra-short pulse structure related to the frequency of the super pulsed laser and pulsing of the LEDs and IREDs.

Light absorption is linked to the depth of penetration, the distance between the source of energy and the target tissue, the integrity or degree of damaged tissue, and

most importantly the wavelength. Luna, et al. [13] performed a comparative depth of penetration in equines with light and dark skin with the ACTIVet PRO and a Class 4 Laser (LiteCure). The ACTIVet PRO delivered more than ten times the energy under the skin than the Class 4 laser device. When both light and dark skin types were considered, the penetration was 17 (light skin) and 8 (dark skin) times greater, suggesting that a better effectiveness might be achieved by the ACTIVet PRO. The amount of light delivered to the target was achieved without clipping the hair of the horse to prevent damage to the show horse's coat.

The ACTIVet PRO produces 450 mW of total energy. This amount of power helps to shorten treatment times. However, a high dose given in a quick amount of time can yield photo-inhibitory or photothermal effects within the tissue. Unlike high-powered Class 4 lasers, the ACTIVet PRO increases power without the unwanted photothermal effect, avoiding the production of excessive reactive oxygen species (ROS) that can lead to photocytotoxicity and apoptosis. [14]

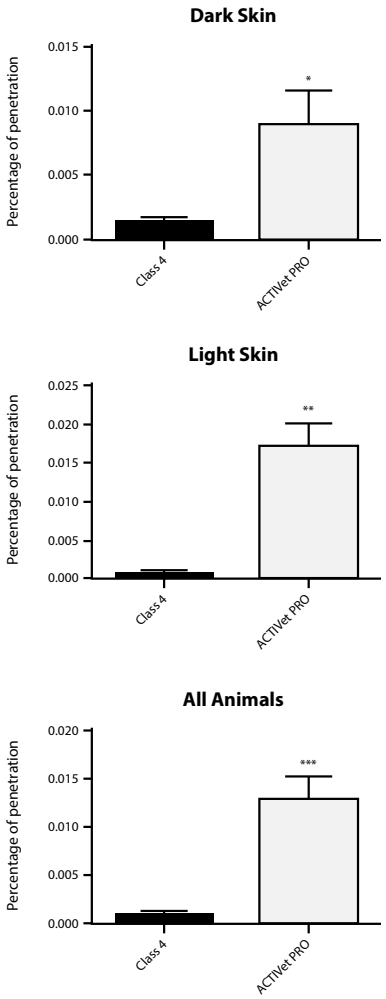


Fig. 2. Mean (SD) of percentage of light penetration of the Class IV versus ACTIVet PRO devices in dark skin, light skin, and both kinds of skins grouped. * P<.05; ** P<.01; and *** P<.001

Energy and Dose:

Dose is one of the most critical parameters in PBM and yet it is one of the most difficult to grasp. While it seems straightforward, understanding the amount of energy needed for each can vary greatly between devices and among studies. Light energy needs to be converted into biochemical energy through the process of oxidative phosphorylation. Then, dose is simply the amount of energy needed to stimulate or inhibit a photobiological response.

The dose or energy is the ability to perform work. Most research groups and many manufacturers recommend that the dose delivered to a patient during a treatment session should be based on the measure of dose expressed in Joules: the product of power (Watts) and duration (seconds). One Watt second = one Joule; 1 J = 1 Watt x 1 second. One of the most significant inhibitors to the more widespread adoption of laser therapy in the clinical environment relates to the difficulty in getting an effective laser dose to work on a variety of different machines. The debate is not yet resolved, and the energy density will be used here, mainly because the published research almost exclusively cites it, and therefore, it may be of more use when it comes to trying to replicate an evidence-based treatment dose.

It is particularly important to deliver an appropriate light dose within the acceptable thresholds for any application. Not all devices enable the practitioner to view the delivered dose. Some may provide basic parameters such as pulsing, power levels, and time. The dose should be adjusted from low dose, for small or superficial conditions/patients and acupuncture points, to high dose, to efficiently deliver enough energy (Joules) to saturate/stimulate large areas/patients as well as deep-seated and/or chronic musculoskeletal conditions. It is currently argued that Joules (i.e. Energy) may in fact be the most critical parameter.

The ACTIVet PRO 2.0 displays treatment progress in two ways. A countdown timer will keep track of the remaining treatment time; however, users can toggle between energy being delivered in Joules and time remaining. In many instances, a non-significant effect may be attributed to providing too much or too little energy; this new feature will assist in documenting and delivering adequate amounts of energy.

Wavelengths:

There is some degree of consensus as to the best wavelengths of light and acceptable dosages to be used. Wavelengths in the 600–700nm range are used to treat superficial tissue, and longer wavelengths in the 780–950nm range, which penetrate further, are used to treat deeper-seated tissues. [15] Wavelengths in the 405-480nm range have been found to have beneficial antimicrobial properties.

The ACTIVet PRO has four separate wavelengths that cover the entire therapeutic spectrum. The Pillars Paper (available from Multi Radiance) details the studies to validate the combined and individual effects of the various wavelengths. Combining wavelengths creates a different type of effect that is unique to that combination. Multi Radiance utilizes a proprietary core combination of 905nm, 640nm, and 850nm to create a synergistic effect that in turn activates mitochondrial function for over 24 hours.

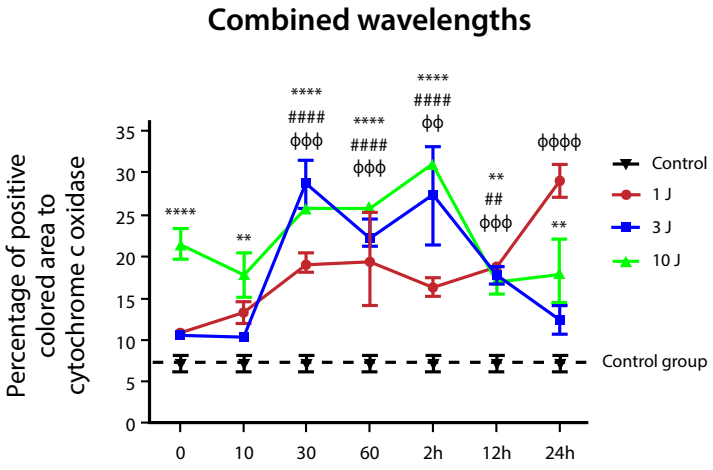
Blue light-emitting diodes are a newly emerging light source with a potential to replace the conventional chemical methods, mercury UV lamps, and xenon lamps in water disinfection. The 455nm blue LED light retains some of the antibacterial properties of UV light, but without the risks associated with UV over exposure.[16] Evidence supports the use of blue LED to kill acne, [17] MRSA, [18] and the bacteria that cause periodontal disease. [19]

Several meta analyses have demonstrated the ability of light to accelerate wound healing. [20, 21] While most studies have been performed using red or infrared light, Adamskaya, et al. [22] recently demonstrated the effect of blue light (470nm) significantly influences wound healing by affecting keratin expression via a photolytic release of NO from nitrosylated proteins. Non-coherent blue light penetrates rather poorly, due to the almost complete absorption in the superficial layers of the skin; however, that makes it ideally suited to treat conditions of the skin.

The ACTIVet PRO includes three ultra-bright, high-powered 455nm blue LEDs to supplement the wound healing ability of the red and infrared LEDs. This inclusion offers an entirely new approach to managing wounds by not only accelerating wound repair, but also reducing bacterial burdens of infected wounds.

Staphylococcus pseudintermedius is a common commensal and opportunistic pathogen of the skin of dogs and is the most common cause of bacterial skin infections. In recent years, meticillin-resistant S. pseudintermedius (MRSP) infections have become much more common. Schnedeker, et al. [23] measured the in vitro bactericidal activity of 465nm blue light on meticillin-susceptible Staphylococcus pseudintermedius (MSSP) and meticillin-resistant Staphylococcus pseudintermedius (MRSP). There was a significant decrease in colony count with blue light irradiation at all doses for MRSA (P = 0.0006).

Leal and Tomazoni [24] investigated the combined synergistic effects of three different wavelengths and three doses on cytochrome c oxidase activity in intact skeletal muscle. PBMT with the combination of super pulsed laser, red and infrared LEDs can increase cytochrome c oxidase activity in intact skeletal muscle, mainly with a 10 J dose fulfilling the time-response window from 5 minutes until 24 hours after irradiation.



Updated in the 2.0 software is the ability to mix wavelengths with the new Manual mode, allowing users to manually control selected wavelengths. Wavelengths can be used singularly or in any combination (up to four at one time) and this will change the desired therapeutic output. These five sub-menu settings work together to control which wavelengths are emitted and pulsing options. Users can also combine red and blue LED therapy in a single session, which allows for the red and blue LEDs (no IRED and SPL) to be pulsed in sequence or fired simultaneously to provide both antimicrobial and anti-inflammatory therapy concurrently to enhance wound healing.

There has been considerable research performed on single wavelengths. With the 2.0 upgrade, any wavelength may now be isolated to replicate and utilize single wavelength outcomes demonstrated in the literature. The isolated red light (continuous wave [CW] option) promotes proliferation of skin cells, especially those of fibroblasts, vascular endothelial cells, and epidermal cells, and, thereby, accelerated wound healing. [25] Isolated blue LED (CW) modulates inflammatory infiltrate and improves the healing of superficial wounds. [26] 904 nm super pulsed laser augments burn wound healing by reducing nitro-oxidative stress and the induction of endogenous antioxidants [27] and for laser acupuncture. [28]

The combinations are limitless and will allow for continued expansion of outcomes as new information regarding therapies and treatments emerge.

Wavelength Options:

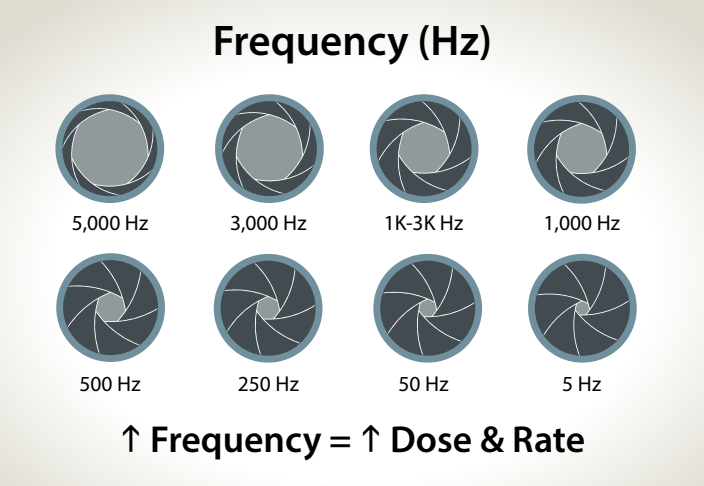
- Red (isolated): wound healing, upregulation of mitochondrial function, CW mode
- Blue (isolated): wound healing, antimicrobial effects, CW mode
- Infrared (isolated): pain relief, downregulation of mitochondrial activity
- SPL (isolated): laser acupuncture with photoprobes
- Infrared/SPL (combined): pain relief, activation of nervous system
- Red/Blue (pulsed wave) antimicrobial and anti-inflammatory therapy concurrently to enhance wound healing.

It is recommended to only mix wavelengths with evidence to support the method of action and treatment outcomes.

Frequency:

Light delivered in a continuous wave (CW) has been the most common way to deliver the light energy for PBM. However, research indicates that overall, pulsed light may be superior to CW light, with everything else being equal. This seems to be particularly true for neck, shoulder, and knee pain. [29] Short and intermittent light emission might enhance NO dissociation, therefore augmenting mitochondrial energy production and cellular activity. [30] Super pulsed laser (SPL) delivery might favorably enhance this cellular strategy. The nanosecond pulse duration of exceptionally large bursts of energy may provide periods of rest for cells, without which they can no longer be stimulated further and allow for thermal tissue relaxation (minimize the accumulation of heat).

The rate or frequency involves the generation of a dose-related response. The frequency of the stimulation (energy) is varied when the rate of energy delivered is changed. A faster or slower rate of delivery can activate different biological process through the biphasic dose response seen in PBM.



The Multi Radiance Super Pulsed Laser controls the rate and amount of light entering the tissue by the selection of preset frequencies. Lower frequencies (less than 500 Hz) tend to penetrate deeper into the body, activating tissues such as bone, muscle, tendons, and ligaments, and help to control inflammatory processes. Higher frequencies (greater than 500 Hz) penetrate less deeply into the body, delivering more energy superficially by overloading the upper layers of the skin and activating nerve endings for pain relief.

Based upon peer-reviewed and published research, the 2.0 upgrade includes six additional frequencies have been added to the original eight. These additions allow for greater control over the rate of dose delivery and provide specificity of the most effective dose for given symptoms. Of special interest is the 500-5000 Hz sweep for pain and the 500-1000 Hz for stimulating nerve regeneration.

There is value to both continuous wave and super pulsed laser for the various applications of PBM. [31] Red and blue LEDs that are in continuous mode can improve clinical outcomes when used in monotherapy. Red light, as discussed earlier, can have a strong impact on the inflammatory process. Blue light for the best antimicrobial effects needs energy delivered with higher densities that can be achieved fast with CW mode. A CW option has been added to the submenu to allow for switching between the two modes.

Protocols and Priority Principle

Protocols for PBM can greatly improve outcomes and reliability of any treatment procedure. This allows for reproducible results that have been established by studies or clinical practice. Standard protocols outline the correct way to approach clinical care, the order and procedure. If done on a consistent basis, this ensures clients are getting the best results possible. This can yield higher customer satisfaction rates, increased patronage, and extensive customer loyalty, all of which contribute to the bottom line of the practice.

While protocols can provide clear and detailed instructions for a specific condition and device, they offer little to no variability. Compounded by patient irregularity, there can be multiple variations in the severity of the disease or injury and symptoms presented. Multi Radiance developed the Priority Principle method of treating injuries and illnesses to solve this issue. First introduced in the ACTIVet PRO LaserShower, Priority Principle mode is available now on the ACTIVet PRO 2.0.

Common to all injuries and conditions are universal symptoms, including inflammation, swelling, pain, etc. The Priority Principle utilizes these basic symptoms to approach the current state of the patient's health at that moment. By understanding the basic parameters of each priority, the appropriate dose and technique will deliver the maximal phototherapeutic response.

Specific symptoms include acute and chronic injuries, the Pain Spasm Cycle (Swelling, Inflammation, Spasm and Pain), Tissue Repair, and Functional Activities (Range of Motion and Strength). Each of these specific symptoms are best treated with a specific dose and rate of energy. The ACTIVet PRO 2.0 now comes pre-programmed with Priority Principle for equine, small, and large companion animals. The adjustments to the dose are based on size and have been preset for each symptom. This allows for a more precise application while being more flexible than a limiting set of standard treatment protocols.

Conclusion

Updated to the 2.0 software, the ACTIVet PRO is unrivaled as the most powerful, ultra-portable super pulsed laser therapy device available. The new manual mode (where all parameters can be adjusted individually), Priority Principle Assist (including companion and equine presets), and energy delivered readout in Joules set a new standard for veterinary laser therapy.

About Multi Radiance Medical

Headquartered in Solon, Ohio, Multi Radiance Medical is a leading developer and manufacturer of FDA-cleared super pulsed laser therapy devices for pain management, wound healing, inflammation control, and more in veterinary medicine. For 10 years, Multi Radiance laser technology has offered veterinary professionals a safe, non-invasive, and drug-free alternative to prescription medications and surgery.

Multi Radiance Medical's Super Pulsed Laser Technology is in the safest classification of lasers and its efficacy has been validated in vitro, in vivo, in controlled laboratory experiments and in clinical practice. The company is currently involved with over 30 clinical studies worldwide and has over 35 published, peer-reviewed studies. Multi Radiance's mission is to investigate, validate and educate practitioners with the knowledge and clinical skills necessary to achieve the best possible outcomes.
Join the hundreds of professionals each month and thousands per year who choose Multi Radiance Super Pulsed Lasers. Visit multiradiance.com to explore products and learn about the technology.

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