The Veterinary Pillars Paper

Validating Multi Radiance Laser Technology

Iker Asteinza Castro, MVZ, MSc Dipl.
Ernesto Leal-Junior PhD, PT
Douglas S. Johnson, ATC, EES, CLS

Photoceutical vs. Photobiomodulation Therapy

Optimized dose of light energy and frequency of exposure, that significantly impacts treatment, improves quality of life, and supports the veterinary continuum of care.

Light Therapy in Dental and Perioperative Care

Blue light exposure can act as an extension of the asepsis seen after surgery, and an integral part of protocols for all dental procedures.

Safe and Effective Home Laser Therapy

Extending the Continuum of Care into the home with safe, over the counter cleared, advanced laser technology.

About the Authors:

Iker Asteinza Castro, MVZ, MSc, Dipl

Iker Asteinza, Doctor of Veterinary Medicine, has more than 20 years in private veterinary practice. He owns two reference veterinary hospitals for small animals with veterinary specialties. Dr. Iker is a graduate of Master of Science in Veterinary Medicine Faculty and Biomedical Research Institute and Medicine and Surgery of Dogs and Cats Diploma in the National Autonomous University of Mexico (UNAM), and he has been an Associate Professor in the small animal department at Universidad Del Valle de México since 2014. Dr. Asteinza is a member of the board of the Mexican Association of Veterinary Hospitals (AHMVET), responsible for developing the content and platform for the certification of continuing education for associate veterinarians. He is also a lecturer for Laser therapy in international congresses, and he has worked developing protocols and spreading the news of laser therapy in everyday practice, including perioperative care.

Douglas Johnson, ATC, EES, CLS

Douglas Johnson is a certified athletic trainer with over 25 years in clinical practice and serves as the Senior Vice President, Clinical and Scientific Affairs at Multi Radiance Medical. He is also Chief Science Officer at PhotoOpTx. He attended Wayne State University and The University of Detroit-Mercy where he earned a Summa Cum Laude Bachelor of Science degree in Sports Medicine in 1994. Mr. Johnson is involved in numerous research studies involving photobiomodulation that focus on human performance enhancement and rehabilitation. His present area of research involves evaluating the effects of photobiomodulation on degenerative diseases and diabetes. Mr. Johnson is currently a fellow of the Laboratory of Phototherapy and Innovative Technology, Sao Paulo, Brazil.

Ernesto Cesar Pinto Leal-Junior, Prof. PhD, M.Sc., PT

Ernesto Cesar Pinto Leal-Junior, PT, PhD earned a Bachelor of Science degree in Physical Therapy in 2002 in Brazil. In 2004 he got his Master´s Degree in Biomedical Engineering at University of Vale do Paraiba (Univap) in Brazil, and he defended his PhD thesis in 2010 at University of Bergen - Norway (Section of Physiotherapy Science, Department of Public Health and Primary Health Care, Faculty of Medicine and Dentistry). In 2012 he finished his post-Doctoral appointment at the Department of Pharmacology of University of Sao Paulo.

His current position is as Full Professor at Nove Julho University in Sao Paulo - Brazil, where he is the head of the Laboratory of Phototherapy in Sports and Exercise and supervises several post-doctoral fellows, Ph.D. candidates, and master's degree students. He is also a reviewer of several international peer-review journals, specifically in the photobiomodulation and sports science fields. Since 2014 he has been a member of the editorial board of Photomedicine and Laser Surgery, and since 2015 he acts as area editor of the Brazilian Journal of Physical Therapy.

Dr. Leal's research expertise is photobiomodulation therapy in skeletal muscle disorders. A special interest has been developed in photobiomodulation research (low-level laser therapy and light emitting diode therapy) for skeletal muscle fatigue delaying, performance enhancement, injury prevention and recovery after strenuous physical activity, and more recently in progression delaying of muscular dystrophies.

According to Google Scholar, Dr. Leal-Junior has 191 scientific papers published, more than 130 of them in international peer-reviewed journals (indexed by Pubmed/Medline). He has presented more than 40 scientific papers at national and international congresses and in September 2011, Dr. Leal-Junior was awarded by NAALT with the Young Clinical Research Award in Phototherapy. He is a recipient of the Research Productivity Award given by the Brazilian Council of Research and Development. Currently he sits on the board of WALT – World Association for Laser Therapy as their Scientific Director.

The Veterinary Pillars Paper

Validating Multi Radiance Laser Technology

Authors:
Iker Asteinza Castro, MVZ, MSc, Dipl
Douglas Johnson, ATC, EES, CLS
Ernesto Leal Junior, PhD, PT

Introduction:

Veterinary medicine has changed dramatically over the years in unexpected, never-seen-before ways. The importance of pets in the daily life of families has increased the demand for animal care and the veterinary marketing is growing rapidly. Private practices are consolidating, with corporations now owning 80% of the veterinary market. The increase in curbside treatments caused many clinics to adapt to new protocols and find alternatives to traditional care. Novel therapies are often sought to improve the well-being and quality of life in support of care provided by medications and surgery.

Super pulsed laser therapy (SPLT), a form of low-level laser therapy (LLLT), continues to be widely utilized for soft tissue repair and pain relief in veterinary medicine. New studies and publications have validated the effects of light to manage chronic arthritis, improve post-surgical healing, promote osteosynthesis, and repair tendon and ligamentous injuries. No longer considered an alternative or complementary therapy, the application of light energy has moved to mainstream adaptation in veterinary rehabilitation. Even more recently, SPLT has expanded into preventative and dental care. Perioperatively, light therapy is now associated with surgical procedures to reduce wound dehiscence and reduce the necessity of rescue analgesics with pre-surgery application in dogs and cats; during the operation to modulate the inflammatory process; and post-operatively to reduce recovery time and modulate pain.

The intention of this scientific monograph is to explore the benefits of SPLT, to understand the peer-reviewed evidence, and dispel confusion surrounding the available products. Additionally, a glimpse into new utilities for SPLT are included to better understand the clinical use and value of the therapeutic laser.

Pain management is central to veterinary practice, not adjunctive. Alleviating pain is not only a professional obligation, but also a key contributor to successful case outcomes and enhancement of the veterinarian-client-patient relationship. A commitment to pain management identifies a practice as one that is committed to compassionate care, optimum recovery from illness, injury, or surgery, and enhanced quality of life.

> In dogs, signs of acute pain can include anorexia, depression, vocalization, gait, or posture changes, panting, chewing, licking, biting, or general agitation.
>
> Cats tend to hide, stop eating, avoid human contact, squint, lick, or bite when they are experiencing acute pain.
>
> As horses are a prey species, signs of pain, especially of musculoskeletal origin, are as equally subtle as they are in small animals. Most commonly, pain results in gait or behavioral abnormalities, many of which can only be identified by owners or under specific conditions (work under saddle, jogging on a hard surface, tight circles in one direction, etc.).

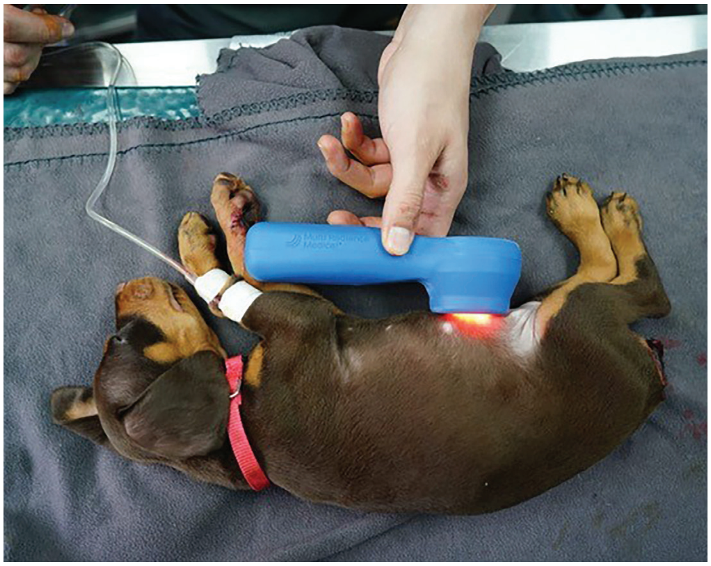


Photo credit. Animal Home Veterinary Hospital, MX.

The signs of pain can often be hard to detect, especially in progressive chronic pain, thus delaying the diagnosis and treatment of the underlying cause. Chronic pain tends to be very subtle – owners report pets' depression, having less interest in activities they used to enjoy, avoiding jumping on furniture as frequently, acting grumpier than normal, and withdrawing from normal interaction. Veterinarians frequently prescribe non-steroidal anti-inflammatory drugs (NSAIDs) in addition to rehabilitation therapy for patients as a first approach.

Classic veterinary medical education places a strong emphasis on treatment of disease through pharmacology and surgery. Increasingly, evidence-based data and experience justify a strong role for nonpharmacologic modalities for pain management. The addition of light-based modalities, such as SPLT, should be considered an integral part of a balanced, individualized treatment plan.[1] SPLT has proven to be an excellent means of managing and reducing pain, either as a complementary modality or as a standalone treatment. There are no known side effects, no long-term safety concerns that can occur with medications, and SPLT is relatively easy to administer.

The Science Behind Laser Therapy

Differing from other veterinary procedures, the information known about veterinary laser therapy comes from translating research and therapies from human medicine. In 2010, Multi Radiance Medical, a laser therapy company known for peer-reviewed studies and safe high-powered lasers, launched the first veterinary SPLT device to manage chronic pain,[2] inflammation,[3] and arthritic [4] conditions based upon results validated in human medicine scientific articles.

SPLT, a therapeutic modality that specifically utilizes non-thermal lasers, has gained recognition in veterinary medicine due in part to its profound biological effects on tissue, including increased cell proliferation,[5] accelerating the healing process, promoting tissue regeneration, preventing cell death,[6] pain relief,[7] and anti-inflammatory activity.[8] Unlike other medical laser procedures (surgical laser, for example), it is understood that any form of low level laser therapy is considered a non-thermal process. The absorption of light creates a chemical change that affects the healing rate of injured tissue and provides effective analgesia for both acute and chronic pain.

Energy from the SPL is emitted in the form of photons – packets of light energy. When a photon is absorbed by an endogenous chromophore (a molecule that absorbs light, such as a mitochondrion of a cell), an electron in the chromophore is excited and jumps from a low-energy orbit to a higher-energy orbit. This stored energy fuels the acceleration of the electron transport chain and reestablishes oxidative phosphorylation. This in turn induces a complex chain of physiological reactions in diseased and damaged tissues that increases ATP production, modulates the release of reactive oxygen species, and signals the release of transcription factors.

Understanding the Parameters of Super Pulsed Laser Therapy

For years, companies have sold devices that are too low in power with inefficient skin penetration, or too high in power and generate heat, while being hailed as the newest or most advanced. The blurring of the available science is often done to sell devices without the proper validation and optimization necessary to realize maximum clinical benefit. The key to eliciting a phototherapeutic response is the proper selection of device parameters. While there may be a considerable difference among devices, successful outcomes are based on two main considerations: the wavelength (identified in nanometers, nm, and denotes the color) and the power (energy, measured in watts or milliwatts).

Wavelength Selection

Therapeutic lasers use light of a specific wavelength to either stimulate or inhibit biological function. It is understood that the desired biological effect is associated with the wavelength. There is some degree of consensus as to the best wavelengths of light and what acceptable dosages are to be used.

Despite claims to the contrary, increased power does not improve the penetrative quality of the light. Sangkwan and Jong-In[9] demonstrated that depth of penetration is wavelength-specific, and the 830 nm wavelength was able to penetrate deeper into the body than 655 nm, 980 nm, and 1064 nm. Hudson et al.[10] found that 808 nm light penetrates as much as 54% deeper than 980 nm light. The penetration of 980 nm is likely limited due to absorption by water and produces more tissue heating.[11] Simply put, penetrating the skin barrier cannot be compensated solely by a higher power output; superficial absorption in the upper layers of the skin will more quickly lead to heat generation.[12]

All therapeutic devices will utilize either single or multiple wavelengths from red (630 nm to 750 nm), near infrared (750 nm to 980 nm), or blue wavelengths (455 nm to 470 nm). Red wavelengths tend to activate photochemical effects in the body like reducing inflammation and promoting healing and are used to treat superficial tissue due to the poor penetration into the body. Infrared (IR) wavelengths in the 780–980 nm range produce greater photophysical changes that affect nerve conduction in peripheral nerves and inhibit nociceptors to mitigate pain. IR wavelengths penetrate deeper in the body and are used to treat deeper-seated tissues.[13]

Blue light-emitting diodes (LED) are a newly emerging light therapy source with potential to replace conventional chemical methods, mercury ultraviolet (UV) lamps, and xenon lamps in water disinfection. A 455 nm blue LED retains some of the antibacterial properties of UV light, but without the risks associated with UV overexposure.[14] Evidence supports the use of blue LED to kill acne,[15] MRSA,[16] and the bacteria that cause periodontal disease.[17] Blue wavelengths in the 455-470 nm range have been found to have beneficial anti-microbial properties and are becoming more popular for treatment of infections, dermatological issues, and for use during dental procedures.[18]

A review of the available literature has demonstrated that depth of penetration is directly related to the wavelength, and actual measurements of the skin penetration by light over time are necessary to understand how light enters the body. Researchers have been studying the effects of depth of penetration by testing various wavelengths and powers to determine which are better suited for deeper or superficial applications.

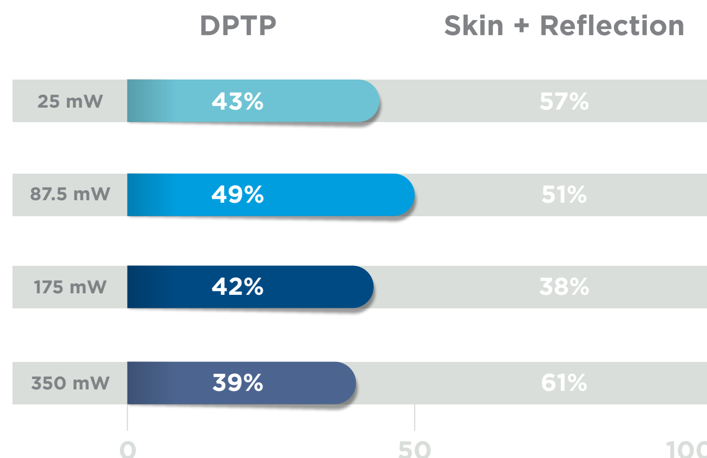


Figure 1: The data suggest and demonstrate a pattern of linearly increasing penetration of the light over time with 43% of the available light from the ACTIVet and 49% of the ACTIVet PRO penetrating beyond the skin, representing a 15% improvement over the original.

Leal-Junior and Albuquerque-Pontes[19] evaluated the depth of penetration time profile (DPTP) of the original ACTIVet and Albuquerque-Pontes, et al.[20] performed the same study with the ACTIVet PRO to determine the effects of concurrent multiple wavelengths of 660 nm Red LED, 875 nm IR LED and 905 nm Super Pulsed Laser (SPL). Each individual wavelength was tested separately with and without the tissue skin flaps to establish the percentage of energy penetration. The data also confirmed what Joenson, et al.[21] found regarding the pattern of linearly increasing penetration of the light over time by the SPL. The individual wavelength penetration profiles provided a predicted measurement (summated total of each individual wavelength) to compare with an actual reading of the combined wavelength time profile.

The data suggest and demonstrate a pattern of linearly increasing penetration of the light over time with 43% of the available light from the ACTIVet and 49% of the ACTIVet PRO penetrating beyond the skin, representing a 15% improvement over the original. This improved skin penetration time profile allows for a greater proportion of the available light energy to penetrate beneath the skin. By improving the efficiency of penetration, the necessary energy provided at the surface is significantly less, reduces conversion into heat, and avoids a dangerous rise in tissue temperature.

These studies conclude that a combination of multiple wavelengths creates a "synergism" that enhances each individual wavelength's ability to penetrate the skin. While not surprising, there was an expected linear decrease in DPTP when the mean output of power was increased. A 57% increase in the loss of light occurs when the power is doubled compared to the original and a 357% increase occurs when the power is doubled again. This can be attributed to a greater amount of light scattering at the surface and an increase in the absorption of light in the superficial layers of the skin. However, there is a net increase in the amount of light delivered below the surface of 135% when the power is doubled and over 215% when the power is increased by a factor of four.

It appears that a synergistic combination of pulsed multi wavelengths (including a super pulsed one) provides the most efficient means of increasing the penetration time profile. 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.

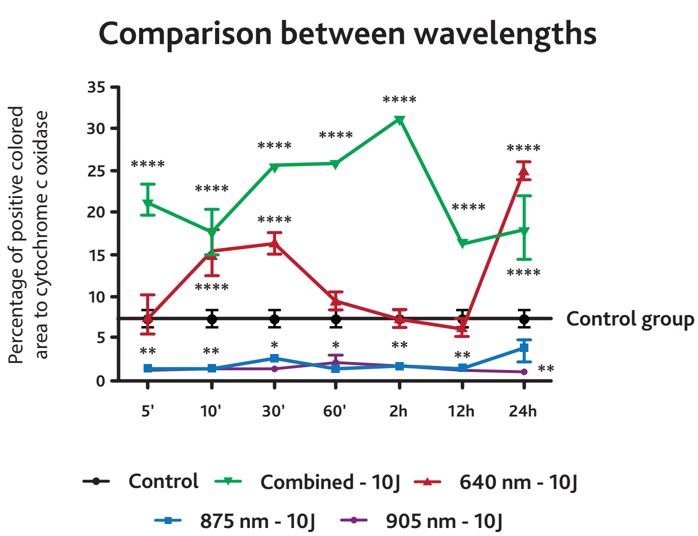


Figure 2: Cytochrome c oxidase activity through immunohistochemistry. * indicates statistically significant difference ($p<0.05$) compared to the placebo-control group. ** indicates statistically significant difference ($p<0.01$) compared to the placebo-control group. **** indicates statistically significant difference ($p<0.0001$) compared to the placebo-control group.

The ACTIVet PRO Series utilizes four separate wavelengths to cover the entire therapeutic spectrum. The Pillars Paper (available from Multi Radiance Medical --www. multiradiance.com--) details the studies that validate the combined and individual effects of the various wavelengths. Multi Radiance Medical utilizes a proprietary core combination of 905 nm, 660 nm, and 860 nm wavelengths to create a synergistic effect that is unique to that combination. Albuquerque-Pontes et al.[22] identified the optimal dose of several different wavelengths and light sources to optimally enhance ATP production. Friedmann et al.[23] utilized the identified best dose and wavelength to confirm that a synergy exists between the pulsed low-level laser and LEDs in Multi Radiance Medical devices.

Leal and Tomazoni[24] investigated the ACTIVet PRO to evaluate the synergistic effects of the unique combination of different wavelengths and doses on cytochrome c oxidase activity in intact skeletal muscle.

The researchers discovered the combined wavelengths created a beneficial positive effect greater than any of the individual wavelengths. While individual wavelengths are capable of modulating CCO function for brief durations, it was only the combined wavelengths that could sustain mitochondrial activity for a full 24 hours following a single exposure to the super pulsed device. The increase in energy in the form of adenosine triphosphate (ATP) can be used by the living system to perform various tasks, such as cellular metabolism, microcirculation, promoting oxygen availability, and modulation of the inflammatory process.

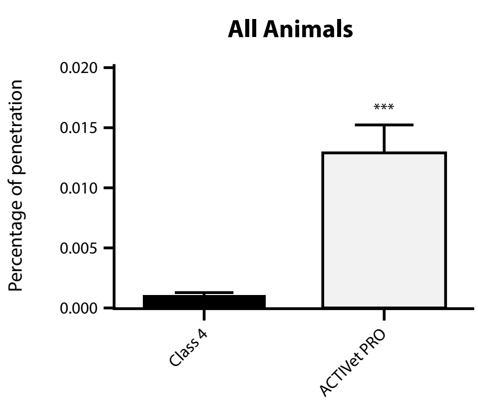
When and Why Power Matters

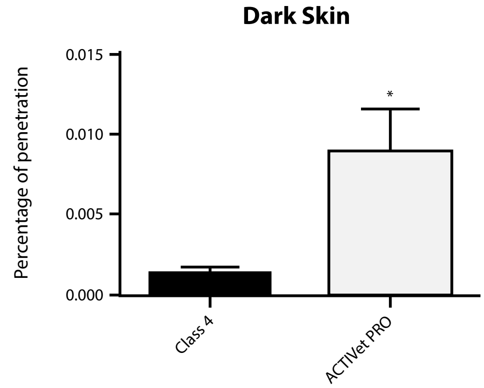
Beneficial and successful laser therapy outcomes are based upon delivering the correct dose of light energy. Typically, a higher output of power means that a certain desired dose (measured in joules) is delivered more quickly. On the surface, this may seem logical and beneficial considering the availability of direct patient care time continues to be a constraint for many veterinarians. It has been found that greater doses of light are not related to the capacity of penetration as it was assumed years ago and the dose at the surface does not equate to the dose that reaches a target inside the body. The rule of reciprocity is not valid.

Confusion sets in when determining how much power is necessary. The amount of light that penetrates the skin is dependent upon the characteristics of the wavelength and not the power driving it. So, while hundreds of joules may be exposed to the skin, only a fraction of that energy may penetrate beyond it. This in turn may not shorten the treatment time, as the dose at the target still needs to be sufficient.

The type of response (tissue repair or pain relief as controlled by the biphasic dose response) depends primarily on the wavelength of light, which controls the penetration depth, and secondly on the amount of energy or power of the device. That is, the light must be able to penetrate the skin and an adequate amount of energy must be absorbed to have an effect. Therefore, wavelength and power are related.

A dose response has been frequently observed where low levels of light have an improved ability to stimulate and repair tissues and higher levels can modulate pain responses by inhibition. The result seen is often puzzling because a biphasic dose response has a dual action. Subsequently, adequate accumulation of energy is needed to trigger the desired biological reaction. The abundance of “positive” doses can be attributed to the fact that a range exists for both stimulation and inhibition that are influenced by power output, thermal profile, and depth of penetration. If the device emits too little power, it could take an impossibly long time to reach the necessary dose. Conversely, greatly increasing the power may increase the risk – eye and skin safety, device regulatory controls – or create an unwanted thermal effect. Simply put, penetrating the skin barrier cannot be compensated by a higher power output; a balance of power as it relates to the wavelength is needed. Typical outputs seen in devices range from 100 milliwatts to several watts.





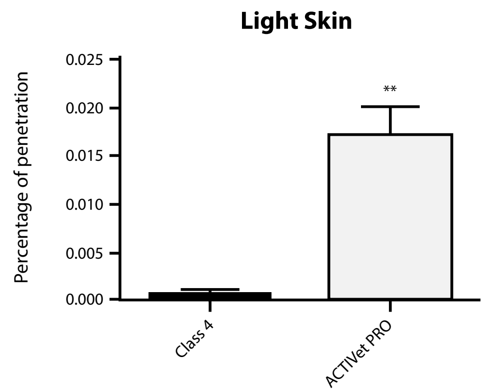
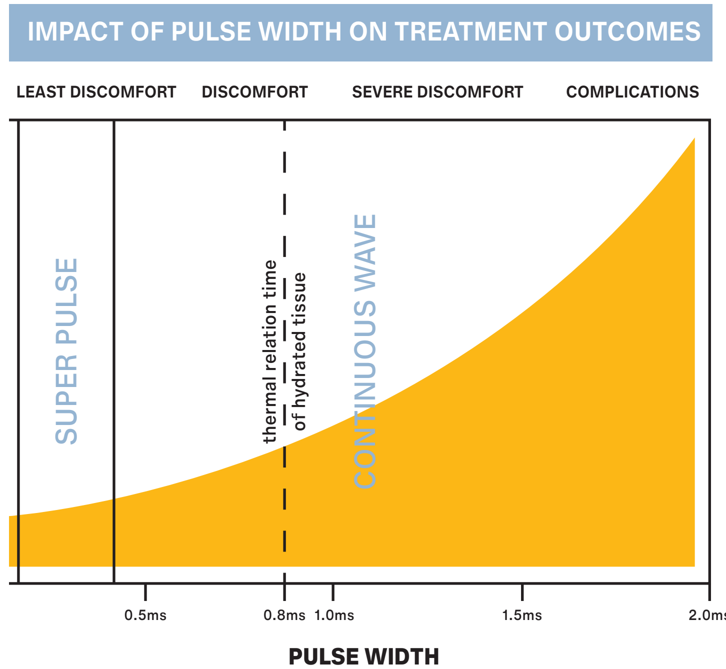


Figure 3: Mean (SD) of percentage of light penetration of the class IV versus ACTIVet PRO devices in dark skin, light skin, and both kinds of skins grouped. *P<.05; *P<.01; and ***P<.001

Light energy absorption creates heat as an unwanted byproduct that reduces the phototherapeutic efficacy. Khan, et al.[25] established a correlation between a rise in surface temperature (> 45 °C) and phototoxic tissue damage. As Joenson, et al.[26] described, the thermal effects of LLLT at doses recommended by the World Association of Laser Therapy (WALT) guidelines for musculoskeletal and inflammatory conditions are negligible (<1.5°C) in light, medium, and dark skin. Accumulating heat can be an issue with high-powered devices. Laser, like ultrasound, at low levels can stimulate while at higher levels it becomes destructive.[27] Heat becomes a compounding limitation in achieving optimal phototherapeutic effects but can be minimized by scanning. This can make dosing complicated due to energy lost from distance reflection and changes in spot size and treatment areas that reduce light intensity. Choosing appropriate wavelengths based upon the ideal target selection can deliver a greater proportion of the light into the body resulting in less heat.

It has been suggested in the literature that other modes, such as super pulsing, may have different skin penetration time profiles. SPL works differently than traditional pulsed high-powered lasers. By generating extremely high-powered bursts of light at billionths-of-seconds durations, a super pulsed laser's energy passes the dermis much more efficiently to reach deeper tissue, preventing the conversion to heat.[28]

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.[29], 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.



Brondon, et al.[30] found super pulsing better able to penetrate through melanin fibers and Joensen et al.[31] evaluated and found super pulsed 904 nm LLLT energy penetrated two to three times easier through the rat skin barrier than a continuous wave (CW) device of 810 nm. Vanin, et al. replicated a study by Grandinétti, et al.[33] that evaluated the thermal impact of the ACTIVet PRO on light, medium and dark skin. Baseline measurements were taken prior to the start and skin temperatures were measured using a FLIR thermographic camera. Four doses were applied: placebo, 25 J, 80 J, and 133 J to the skin. The ACTIVet PRO was set to full power (450 mW and 50 Hz frequency).

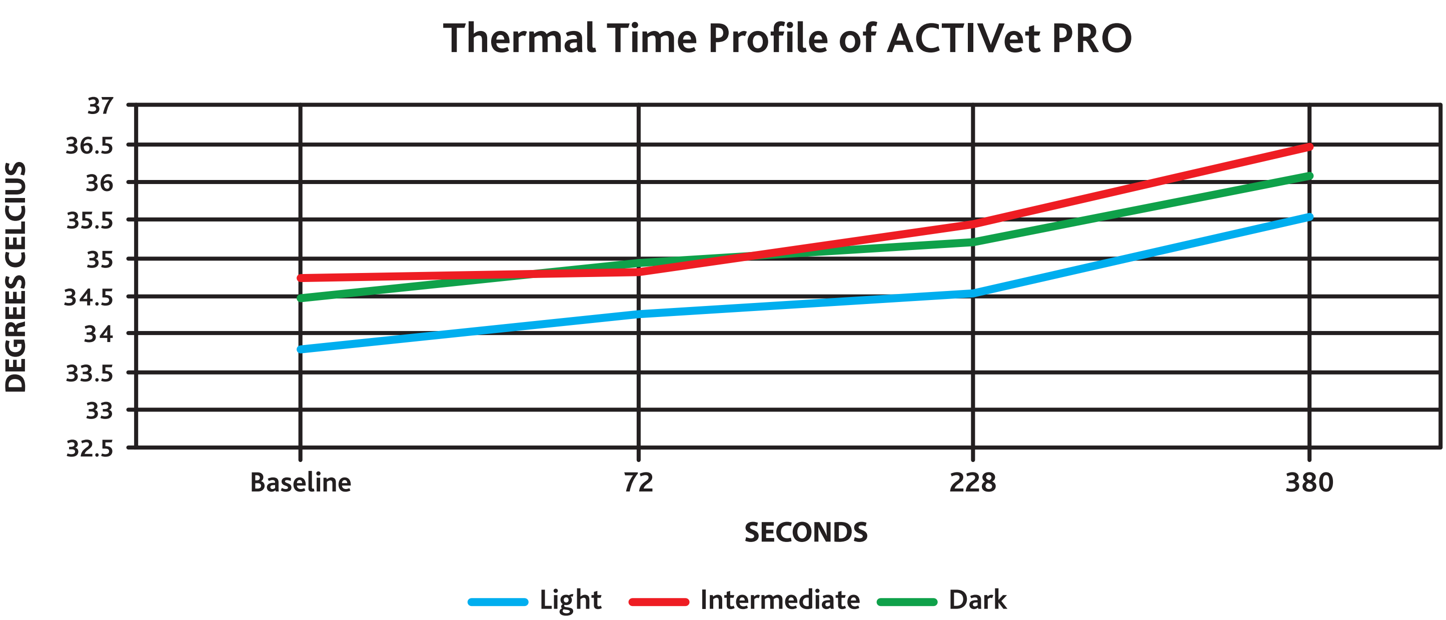


Figure 4: There was a non-significant increase ($p>0.05$) in all skin types and with all doses. No groups experienced excessive photothermal effects that may affect patient safety and no threat or concern regarding cytotoxicity in clinical practice exists

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. Biological tissue is "aware" of incident energy pulses only if they are over one millisecond in width.[34] This means that the device can be held in direct contact with the skin without worry of excessive heating, even when dealing with dark-pigmented animal skins. This type of laser has the safest FDA and Occupational Safety and Health Administration (OSHA) classification and is also eye safe, so both the pet and the operator are not required to wear safety goggles.

❶ Photobiomodulation (PBM) is a non-thermal process.[35]

❷ The primary effects of PBM are based on photochemical and photophysical changes and not the result of thermal influence in tissue.[36,37]

❸ Larger doses are NOT necessary to derive clinical benefits.

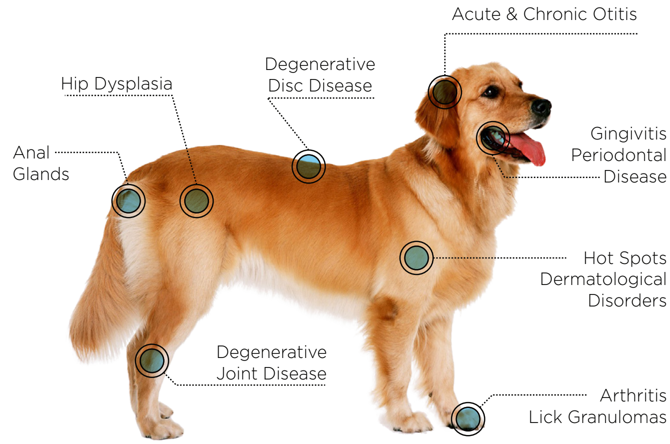
❹ Beneficial and successful laser therapy outcomes are based upon delivering the correct dose of light energy.

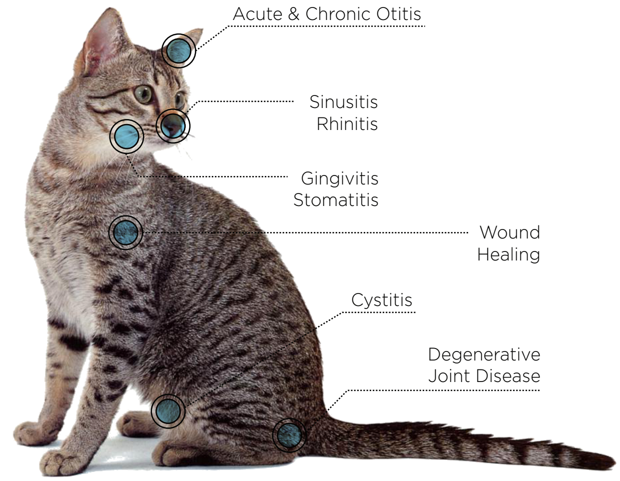
❺ Super pulsed laser's energy passes the dermis much more efficiently to reach deeper tissue, preventing the conversion to heat.

❻ A positive synergistic effect exists when multiple wavelengths are applied concurrently.[38]

Clinical Use of Super Pulsed Laser Therapy

For over fifty years, PBM has been shown to reduce inflammation and edema, induce analgesia, and promote healing in a range of musculoskeletal pathologies. The popularity of laser therapy has grown and transcended into a multidisciplinary scientific approach across many fields. In general, laser therapy has been studied more deeply in human medicine with positive outcomes in rehabilitation, dentistry, ophthalmology, and athletic performance. With virtually no side effects and minimal contraindications, SPLT is considered safe to use in almost all clinical situations and patient populations. More veterinarians are recommending laser therapy as a part of a regular treatment for common diseases: osteoarthritis, otitis, stomatitis,[39] wounds,[40] ligament injuries in small animals and horses[41] and corneal ulcers,[42] just to mention a few.





Relieving pain

PBM, especially when performed with SPL, is beneficial for pain relief and can accelerate the body's ability to heal itself. SPLT has a long history of strong scientific evidence, which supports its use in pain management.

Pain has an unpleasant sensory and emotional experience associated with or resembling actual or potential tissue damage.[43] Most pain will resolve when the noxious stimulus is removed, inflammation has resolved, or the body has healed itself. However, pain may persist even after the resolute removal of the provoking stimulus and the apparent healing of the injury.

The direct effect of laser therapy at the peripheral nerve endings of nociceptors prevents the nerve from reaching thresholds, similarly to opioids causing postsynaptic inhibition. This inhibitory effect can create analgesia in as little as 10 to 20 minutes following a treatment.[44] Therefore, it can be helpful in managing fractures, post-operative pain,[45] ligament sprains, and muscle strains. Laser therapy also encourages vasodilation and activation of the lymphatic drainage system, thus reducing swelling.

Controlling inflammation

Although the standard of care for many inflammatory diseases is immunosuppressive agents, such as corticosteroids with undesirable toxicities, SPLT offers a unique approach by being noninvasive and incurring minimal side effects. These anti-inflammatory mechanisms and the noninvasive nature of laser therapy suggest that it would be used effectively for animals suffering from chronic disorders such as osteoarthritis[46] and inflammatory diseases[47] such as otitis, stomatitis, or dermatitis.

Osteoarthritis (OA) is a common cause of pain for many different species. SPLT can be a central component of a multimodal approach to treating OA. By reducing pain, arthritic animals can be more active and facilitate weight loss that reduces strain on joints.

Healing wounds

In general, wounds heal in an orderly complex process consisting of three overlapping phases: inflammatory reaction, proliferation, and remodeling. Recent studies in veterinary medicine show the potential benefit of wound healing using laser therapy, including accelerated wound healing.[48,49] Early use of the laser is associated with reduced inflammatory infiltration intensity and increased proliferation and early epithelialization.

Veterinarians find SPLT to be beneficial in helping the management of wounds and dermatologic abnormalities, including hot spots, lick granulomas, otitis externa, superficial pyodermas, and healing of surgical incisions.

Antimicrobial blue light has been the subject of several clinical wound trials, the results of which could demonstrate the viability of this technology as a clinical treatment to reduce different multi-resistant bacteria.[50,51] Several meta-analyses have demonstrated the ability of light to accelerate wound healing.[52,53] While most studies have been performed using red or infrared light, Adamskaya et al.[54] recently demonstrated the effect of blue light (470 nm) significantly influences wound healing by affecting keratin expression via a photolytic release of nitric oxide (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 skin conditions such as superficial pyodermas and dermatophytosis.

Photo credit. Animal Home Veterinary Hospital, MX.

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, Methicillin-resistant staphylococcus pseudintermedius (MRSP) infections have become much more common. Schnedeker, et al.[55] measured the in vitro bactericidal activity of 465 nm blue light on meticillin-susceptible Staphylococcus pseudintermedius (MSSP), Methicillin-resistant Staphylococcus aureus (MRSA) and MRSP. There was a significant decrease in colony count with blue light irradiation at all doses for MRSA ($P = 0.0006$).

Commonly accepted to be less detrimental to mammalian cells than UV irradiation, blue light, particularly in the wavelengths between 405 and 470 nm, has attracted increasing attention due to its intrinsic antimicrobial effect. Per the American Society for Microbiology, such infections are the second most encountered type in private practice, and the most common type presented in medical emergency rooms. Unfortunately, as bacterial resistance to antibiotics grows, other means of stopping these infections are increasingly needed. Studies on blue light inactivation of important wound pathogenic bacteria, including MRSA[56] and Pseudomonas aeruginosa have also been reported. At higher radiant exposures, blue light exhibits a broad-spectrum antimicrobial effect against both Gram-positive and Gram-negative bacteria. The subsequent production of cytotoxic reactive oxygen species following blue light exposure may explain the mechanism of blue light inactivation of wound pathogens.

Blue LED (470 nm) light retains some of the antibacterial properties of UV light, but without the risks associated with UV overexposure[57] and the effects seen with blue LEDs is equal and on par with results seen with higher powered blue lasers.[58] Currently, microbial resistance to blue light does not exist. Therefore, blue light can provide an easily applicable, safe, and cost-effective treatment for the enhancement of wound healing and antimicrobial action.

Enwemeka, et al.[59] suggest 470 nm blue light kills HA-MRSA and CA-MRSA in vitro. The higher the dose, the more bacteria were killed, but the effect was not linear, and was more impressive at lower doses than at higher doses. Schnedeker, et al.[60] replicated the previous study by the Enwemeka group to test the bactericidal activity of blue light (465 nm) with the ACTIVet PRO on MSSP and MRSP. There was a significant decrease in colony count for all doses for MRSA (P=0.0006) but no statistical difference for MSSP or MRSP. However, there was a non-significant reduction in both MSSP of 11.7% and 21.2% of MRSP with the 225 J/cm^2 doses. These strains likely would require more than a single dose, given subsequently, to eradicate the colonies.

Table 1: Median Colony Counts and Percent Reduction for Negative Control and Treatment Groups [Meticillin-Susceptible Staphylococcus pseudintermedius, Meticillin-Resistant Staphylococcus pseudintermedius and Positive Control (Meticillin-Resistant Staphylococcus aureus)] after irradiation with 465-nm Blue Light

	MSSP			MRSP			MRSA		
Blue Light Dose	CC (#colonies)			CC (#colonies)			CC (#colonies)		
	NC	TG	%Red	NC	TG	%Red	NC	TG	%Red
56.25 J cm^{-2}	29	27	6.9	23	25	-8.7	67	4.5	93.3
112.5 J cm^{-2}	31	28	9.7	29.5	29.5	0	72.5	0	100
225 J cm^{-2}	38.5	34	11.7	26	20.5	21.2	90.5	0	100

Figure 5: MSS P = Meticillin-Susceptible Staphylococcus pseudintermedius, MRSP = Meticillin-Resistance Staphylococcus pseudintermedius, MRSA = Meticillin-Resistance Staphylococcus aureus, CC = Median colony counts, NC = negative control (not irradiated), TG = treatment group, % Red = percent reduction

If there is infection or concern of infection present, blue light therapy can be used to reduce the bacterial load and minimize the need for antimicrobial therapy. PBM can speed healing by decreasing pain and inflammation, reducing bacterial load, and promoting blood flow to the affected areas.

Dental care

Blue light is used with good results in dermatological problems, specifically in pyodermas, where the bacterial load is high, reducing the resolution to less than half the time compared to standard treatment,[61] and blue light should be considered as a regular tool during oral cavity procedures. Several epidemiological studies have suggested that oral infection, especially marginal and apical periodontitis, may be a risk factor for systemic infection/septicemia.[62] In humans where oral cleaning is much more widespread than pets, bacteremia was observed in 100% of the human patients after dental extraction, in 70% after dental scaling, in 55% after third-molar surgery, in 20% after endodontic treatment, and in 55% after bilateral tonsillectomy.[63]

Figure 4 Feline patient (8yo), Receiving Blue Light therapy after Dental scaling Periodontal disease grade IV. Photo credit. Animal Home Veterinary Hospital, MX.

The efficacy of blue light to eliminate pathogens associated with oral diseases has been established with pathogens such as Staphylococcus aureus, Streptococcus spp,[64] Pseudomonas aeruginosa, Porphyromonas gingivalis, among others, as well as in the reduction or elimination of biofilm.[65,66,67,68] Blue light can become an integral part of protocols for dental cleanings, teeth scalers, dental extractions, abscess debridement, and all procedures in the oral cavity, to work together with red, infrared, and SPLT, which has shown to reduce pain,[69] swelling, edema and trismus after extractions[70,71] and managing recurrent intra-oral ulcers.[72]

Perioperative care

Most dental and surgical procedures, especially neuters or spays, create some degree of acute inflammation, followed by a tissue repair phase and the need for post-procedure pain management. Several studies suggest that pretreatment of the surgical site can improve post-operative outcomes, especially scar formation[73] when applied prior to the procedure to help minimize post-procedure pain.[74] However, the use of therapeutic laser as a perioperative adjunct remains unexplored despite reported positive results in human medicine. The main benefits described following the application of laser therapy include pain management, inflammation reduction, risk reduction of wound infections, and acceleration of tissue repair.[75] All veterinary doctors will agree that less pain, reduced use of anti-inflammatories or pain medication, accelerated healing in muscle, bone or skin, and diminished infections that delay the healing of patients will help further improve surgical outcomes.

Super pulsed laser can

- Accelerate scar formation at the site of a healing wound
- Reduce pain pre- and post-surgery
- Manage inflammation: lasing pre-, during and post-surgery
- Kill pathogens with blue (465-470 nm) light
- Improve bone healing and regeneration
- Assist in rehabilitation to improve functional outcomes

A single application of SPLT at the conclusion of a surgical procedure can enhance the fibrous tissue formation by fibroblasts at the incision site. An ideal scar is one that is largely undetectable, at the same level as the adjacent tissue, and with the same coloration as the surrounding skin. When SPLT is utilized to increase wound healing and decrease scar formation, the final appearance is improved along with the speed of healing in humans[76] and in dogs that received laser therapy after hemilaminectomies with better incision appearance and faster healing.[77]

Pain management has long been established as one of the best effects of light energy. By lasing specific acupuncture points prior to performing ovarian hysterectomies, an analgesic effect lasted for over 24 hours with a single treatment application. The effect of laser therapy can be effective enough to eliminate the need for rescue medication in the first 24 hours post-surgery in felines and canines. Low level laser also manages to reduce, or even eliminate, the need for the administration of rescue medications in the first 24 hours after surgery in cats[78] and dogs.[79]

The American Animal Hospital Association[80] and the American Association of Feline Practitioners[81] have both suggested the use of laser therapy for analgesia, especially for cats, for whom only a few pain-control medications are approved. However, as technology evolves, the areas of laser as an analgesic have spread to such traumatic surgeries as hip arthroplasty, where a triple-blinded clinical trial reported reduction of inflammation and pain when standard pain management is complemented with the use of SPLT, decreasing the need to use analgesics, and providing greater comfort to patients.[82]

Laser therapy can up-regulate antioxidant protections and decrease oxidative stress. One of the most reproducible effects is an overall reduction in inflammation, which is particularly important for disorders of the joints. Research groups have reported the anti-inflammatory benefit in molar extractions performing laser therapy before[83] and/or immediately post-surgery[84] with positive significant differences for the patients.

Blue light exposure can act as an extension of the asepsis typically seen in the first three days after surgery. Its antimicrobial use is helpful in treating pathogens such as the normal flora of the skin or recurrent contaminants such as Escherichia coli, Pseudomonas, Staphylococci spp, Streptococci, multi drug-resistant pathogens, among others. All of these are susceptible to being eliminated with blue light,[85] which must be considered since together with the presence of blood as a culture medium in any surgery wound, it could complicate the recovery.

Therapeutic laser for surgery is also known to promote angiogenesis, improvement of blood flow, release of ATP, stimulation of growth factors, fibroblasts, and biomarkers. These are natural promoters of regeneration in muscle tissue, bone, and deep tissue, in addition to promoting cell differentiation in bone formation.[86] This leads to considering the use of SPL for orthopedic surgeries that require bone formation such as osteosynthesis for fractures, tibial tuberosity advancement (TTA), triple pelvic osteotomy (TPO), and tibial plateau leveling osteotomy (TPLO); SPLT is free of thermal effects and totally safe, allowing use even with metal implants. In neurological surgeries, such as hemilaminectomy in patients with compression due to intervertebral disk disease (IVDD), the use of laser therapy has shown a quicker recovery. This was achieved by ambulation three to four times faster than the control group; this is more advantageous because ambulatory dogs have a lower incidence of urinary tract infections, pneumonia, disease muscle atrophy, and decubital ulcers.[87]

After surgery, specifically orthopedic, laser therapy has shown great benefits to control pain, tissue regeneration, and strengthening tissues such as muscles and ligaments.[88] In the first three to five days after surgery, the focus is on reducing inflammation and pain as well as stimulating vascularization and healing. Applying laser therapy to painful joints and muscles before and sometimes after therapeutic exercise can help to minimize discomfort during and after exercise.

After healing is achieved, it is recommended to regain movement functions through strengthening of muscles, ligaments, and joints.[89] Therefore, a surgical candidate should be treated up to one hour before surgery (to avoid the vasodilation caused by the laser), possibly during the procedure with antimicrobial blue light, and postoperatively. The neural blockage that occurs 20 minutes following the procedure will remain present at the time of the surgery and recovery. Laser therapy can be a great adjunct to a comprehensive rehabilitation program.[90] Compared to many other modalities, it can be easily integrated into the plan of care. A vital component and goal of rehabilitation programs is the proper management of pain; if pain is under control, the patient will be able to return to function by building strength and range of motion.

Laser therapy should be considered in conjunction with operative procedures such as:

- dental cleanings
- skin incisions
- wounds
- routine surgeries such as sterilizations
- biopsies
- orthopedic surgeries with osteotomies that require healing of bone, muscle, and skin, inflammation that delays recovery for several weeks

Performance

Most commonly, low level laser is used to treat pain and inflammation associated with soft tissue injuries, such as sprains, strains, tendonitis (inflammation of tendons, which connect muscle to bone), and desmitis (inflammation of ligaments, which connect two bones or cartilage). These injuries occur commonly in high-performance canine and equine athletes, and are caused by indirect trauma, overexertion, overloading, and fatigue. Poor conditioning prior to athletic performance may also contribute to these types of injuries.

Achieving optimal athletic performance is the desire of all athletes from the recreational to the professional. Performance is influenced by a combination of physiological factors. Injury rates increase following muscular fatigue[91,92] and fatigue has been identified as a limiting factor in performance in almost every individual in every sport.

The positive evidence for the role of SPLT in improving exercise performance and markers related to exercise recovery has expanded its use to address fatigue-related injuries. Administered immediately before resistance exercise,[93] pre-exercise exposure with SPLT protects exposed muscles from exercise-induced damage and speeds recovery. Competitive sports such as dog agility, show jumping, eventing, flat racing, polo, barrel racing, cutting, reining, and roping are all experiencing rapid growth for use of SPLT due to the accumulation of favorable outcomes published in journals, increased regulatory pressure for reducing side effect producing drugs, and the general increase in awareness of its benefits. With the current focus on preventive measures to reduce the risk of injuries in sports, SPLT offers a unique, noninvasive, nonpharmacologic means of reducing muscular fatigue.

Enhancing at-home laser therapy for pets: At-home care provides same results with less stress for pets and owners

Despite the well-documented effectiveness of light therapy, many veterinary practices are not able to fully utilize the modality for patients' most amenable conditions such as pain management, inflammation, and wound healing. Aging dog and cat populations have grown significantly because of improved care and diet. But as a result, osteoarthritis pain and stiffness is one of the most prevalent conditions in any companion animal practice. These conditions often reach chronic levels before getting proper attention and require a series of treatments to administer a "loading dose" for relief and to upregulate metabolic processes at the cellular level in the respiratory chain of mitochondria.

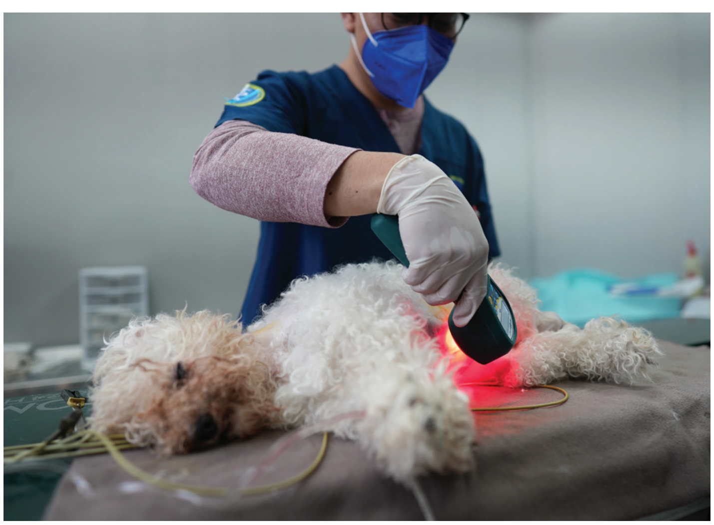


Photo credit. Animal Home Veterinary Hospital, MX.

However, for many pet owners this course of treatments in the early stages is problematic considering busy schedules and the stress it imposes on dogs and especially cats who are not keen on being placed into transport carriers. Veterinarians and technicians are familiar with highly stressed cats requiring arm's length protective leather gloves to safely handle these patients. All too frequently, appointments are cancelled or rescheduled because of convenience issues or pet owners are reluctant to stress their pets with more frequent office visits. Either way, the patient can suffer because conditions persist without adequate remedial treatments.

The My Pet Laser program has been shown to greatly improve patient outcomes for arthritis, inflammatory processes, and post-operative wound healing by providing veterinarian-prescribed clinical strength SPLT to clients at home Multi Radiance Medical's My Pet Laser is super pulsed and cleared as equivalent to 'over-the-counter safe.' This is due to its extremely high peak power, but very short pulse durations, measured in nanoseconds. No special hazard precautions are required for use of these devices. My Pet Laser devices can provide needed frequencies of treatment for a variety of clinical conditions with zero pet stress or liability.

The portability, safety, ease of use, and effectiveness of the My Pet Laser make it ideal for a laser therapy rental program. The veterinarian creates a custom treatment plan for the pet, then rents the laser device to the pet owner for a weekly fee. The pet owner then administers the laser therapy to the pet in the comfort of home. Rental intervals are followed up with visits scheduled to document the patient's progress. Pets continue to receive therapy and heal without stress, and the veterinarian generates passive income on the rentals – a win-win-win situation for all involved. The benefits of home treatment have resulted in accelerated injury recovery, reduced pet anxiety from car travel, decreased time pets are in pain, and fewer medications needed to manage pain.

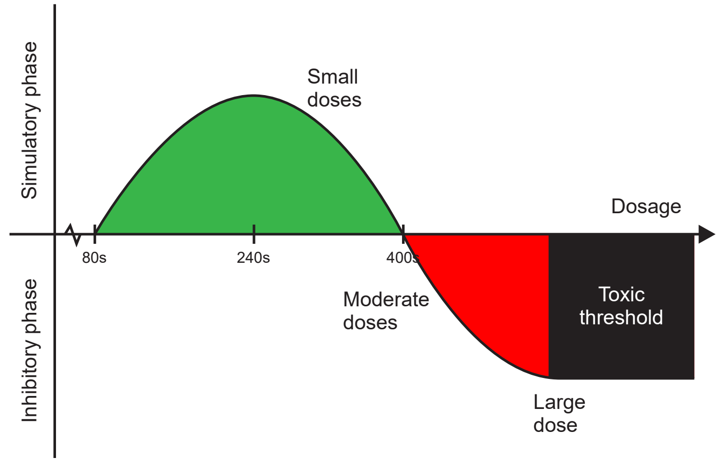
Evidence Based and Translational Research for Veterinary Laser Therapy

As more studies continue to be published, laser therapy continues to support procedures such as surgeries, pain management, osteoarthritis, ligament rupture, and wound management.[94] Because of its three main effects – pain relief, anti-inflammation, and wound healing – laser therapy should be considered a necessary tool in everyday practice.

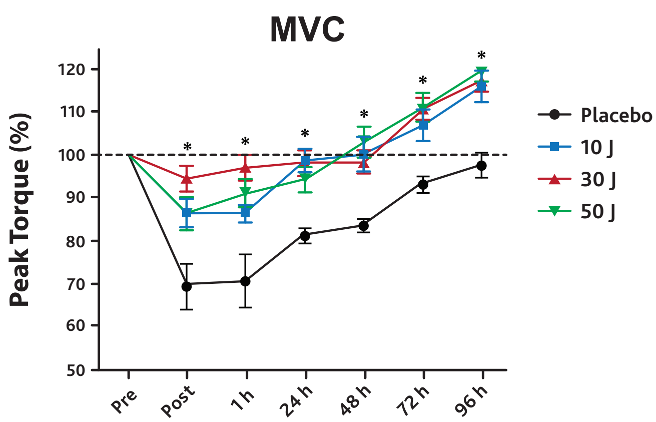
For laser therapy to be effective, the treatment needs to be applied several times (between 1 and 10 treatment sessions) at intervals ranging from twice a day to three times weekly. If the wrong irradiation parameters or time are utilized, the treatment will be ineffective and unlikely to have a significant effect.

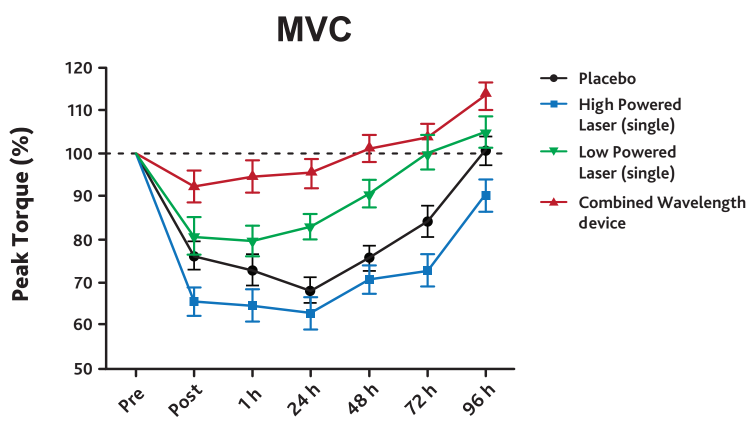
Treating Light as a Photoceutical

PBM is a form of medicine that applies non-thermal forms of light energy to activate beneficial therapeutic outcomes. The dose or energy required to produce the phototherapeutic effect is one of the most crucial parameters in PBM to optimize. A dose refers to a specified amount of light energy expressed in joules delivered at a single time. By contrast, the dosage is the recommended administration of a specific amount, number, and frequency of doses over a specific period.



We often think of PBM as being either stimulatory (repair) or inhibitory (pain relief); this is defined as a biphasic dose. These effects are the direct result of the delivered dose. If an optimization study is not performed, the selection of doses in larger clinical trials can be nothing short of a random guess and may account for many of the unsuccessful outcomes in the literature and the very wide range of suggested doses from the World Association for Laser Therapy (WALT).[95]





On the left, Leal Junior et al. validated the proper dose to control Peak Torque %. While all doses controlled MVC better than placebo, the 30J dose was determined best. On the right, an independent study by De Marchi et al. validated Multi Radiance Laser Technology for controlling MVC and also compared it to a Class 3B (Thor Photomedicine) and Class IV (LiteCure). The MRM technology outperformed both Class 3B and Class IV lasers in controlling MVC Peak Torque %. As with CK levels, MVC Peak Torque % using a LiteCure Laser performed worse than placebo.

Hampering the widespread adoption of PBM is the lack of consistent reliable doses due to device wavelength and power variability. There appears to be a range of doses that are influenced by power output, thermal profile, and depth of penetration. Understanding the dose response of each device studied allows for the design of larger, translational clinical trials that utilize the identified optimal parameters (wavelength, dose, treatment interval, etc.) to validate PBM for specific indications.

Multi Radiance Medical optimized the dose response for the combination of super pulsed laser, pulsing red and infrared LEDs, and static magnetic field from 2012-2014. The studies have since been peer-reviewed and published and a summary called The Pillars Paper and is currently available from Multi Radiance Medical.

Conclusion

With virtually no side effects and minimal contraindications, low-level laser therapy treatments are gaining recognition and popularity in veterinary medicine. Studies show promise in assisting with the most common ailments and procedures seen in the veterinary clinic, including managing pain, reducing inflammation, healing wounds, in post-operative and rehabilitation settings, and more. The simplicity and safety of this modality offers an additional benefit of at-home treatments for pets. Laser therapy promises veterinarians a new tool to provide safe, noninvasive care to keep pets healthy and put pet parents at ease.

Photo credit. Animal Home Veterinary Hospital, MX.

Multi Radiance Medical laser therapy technology combines super pulsed laser (GaAs 905 nm) and infrared and red LEDs (875 nm and 660 nm) for enhancing ATP production, stimulating NO release, and activating ROS. Each wavelength and light source create a synergistic effect, combining with the others, to summate greater than each individual effect.[96] The concurrent multiple wavelengths span the entire therapeutic light spectrum to reach varying depths of penetration while creating the first unique non-thermal synergy that improves overall penetration by 100%. This, in turn, creates an optimal mix of the available parameters to maximize therapeutic outcomes in the clinic for consistent and reliable results.

In addition to wavelength, a device's power also determines a dose response of either tissue repair or pain relief. Multi Radiance Medical's super pulsing technology emits light in extremely high-powered bursts of light at billionths-of-seconds durations, allowing the laser energy to pass through the skin more efficiently to reach deeper target tissue without generating excessive heat. Accumulating heat – and possible tissue damage – can be an issue with traditional high-powered continuous wave laser therapy devices.

There are many peer-reviewed, published studies documenting the positive clinical effects of super pulsed laser therapy in the areas of pain relief, inflammation reduction, healing wounds with antimicrobial blue light, dental care, perioperative care, bone healing and regeneration, rehabilitation, and sports performance. With a product line including in-clinic and at-home laser therapy devices, veterinarians can provide pets with the best outcomes utilizing Multi Radiance Medical technology.

Multi Radiance Medical is a global leader in therapeutic lasers, selling thousands of units each year. The company's goal is to set new standards for the industry by expanding research, education, and the understanding of light-based therapies in new areas of medicine where adequate treatments may not exist. Extensively tried and tested, Multi Radiance Medical's veterinary product line delivers the most reliable and clinically significant results available. Multi Radiance Medical is peer-reviewed, and practice proven.

References:

[1] Epstein, M., Rodan, I., Griffenhagen, G., Kadrlik, J., Petty, M., Robertson, S., & Simpson, W. (2015). 2015 AAHA/AAFP pain management guidelines for dogs and cats. Journal of the American Animal Hospital Association, 51(2), 67-84.
[2] Leal-Junior EC, Johnson DS, Saltmarche A, Demchak T. Adjunctive use of combination of super-pulsed laser and light-emitting diodes phototherapy on nonspecific knee pain: double-blinded randomized placebo-controlled trial. Lasers Med Sci. 2014;29(6):1839-1847. doi:10.1007/s10103-014-1592-6
[3] Tomazoni SS, Costa LOP, Joensen J, Stausholm MB, Naterstad IF, Ernberg M, Leal-Junior ECP, Bjordal JM. Photobiomodulation Therapy is Able to Modulate PGE2 Levels in Patients With Chronic Non-Specific Low Back Pain: A Randomized Placebo-Controlled Trial. Lasers Surg Med. 2020 Apr 24. doi: 10.1002/lsm.23255. Epub ahead of print. PMID: 32330315.
[4] Vassão, P. G., Parisi, J., Penha, T. F. C., Balão, A. B., Renno, A. C. M., & Avila, M. A. (2021). Association of photobiomodulation therapy (PBMT) and exercises programs in pain and functional capacity of patients with knee osteoarthritis (KOA): a systematic review of randomized trials. Lasers in Medical Science, 1-13.
[5] Fekrazad, R., Asefi, S., Allahdadi, M., & Kalhori, K. A. (2016). Effect of photobiomodulation on mesenchymal stem cells. Photomedicine and laser surgery, 34(11), 533-542.
[6] Eells, J. T., Gopalakrishnan, S., & Valter, K. (2016). Near-infrared photobiomodulation in retinal injury and disease. In Retinal Degenerative Diseases (pp. 437-441). Springer, Cham.
[7] Chow, R. T., & Armati, P. J. (2016). Photobiomodulation: implications for anesthesia and pain relief. Photomedicine and laser surgery, 34(12), 599-609.
[8] Hamblin, M. R. (2017). Mechanisms and applications of the anti-inflammatory effects of photobiomodulation. AIMS biophysics, 4(3), 337.
[9] Sangkwan Lee and Jong-In Youn; Evaluation of Diffuse Reflectance in Multi-layered Tissue for High Intensity Laser Therapy; Journal of the Optical Society of Korea, Vol. 17, Issue 2, pp. 205-212 (2013); http://www.opticsinfobase.org/josk/abstract.cfm?uri=josk-17-2-205
[10] Hudson DE, Hudson DO, Wininger JM, Richardson BD. Penetration of laser light at 808 and 980 nm in bovine tissue samples. Photomed Laser Surg. 2013 Apr;31(4):163-8. doi: 10.1089/pho.2012.3284. Epub 2013 Feb 26.
[11] Mantineo, M., Pinheiro, J. P., & Morgado, A. M. (2014, February). Evaluation of low level laser therapy irradiation parameters on rat muscle inflammation through systemic blood cytokines. In SPIE BiOS (pp. 89320M-89320M). International Society for Optics and Photonics. Chicago
[12] Tunér, J. (2014). No Cure from LiteCure. Annals of Laser Therapy Research, Annals Issue 1 2014. http://www.laserannals.com/2014/03/22/no-cure-from-litecure/
[13] Chung, Hoon et al. "The nuts and bolts of low-level laser (light) therapy." Annals of biomedical engineering vol. 40,2 (2012): 516-33. doi:10.1007/s10439-011-0454-7
[14] Kleinpenning, M. M., Smits, T., Frunt, M. H., Van Erp, P. E., Van De Kerkhof, P., & Gerritsen, R. M. (2010). Clinical and histological effects of blue light on normal skin. Photodermatology, photoimmunology & photomedicine, 26(1), 16-21.
[15] Morton, C. A., Scholefield, R. D., Whitehurst, C., & Birch, J. (2005). An open study to determine the efficacy of blue light in the treatment of mild to moderate acne. Journal of dermatological treatment, 16(4), 219-223.
[16] Enwemeka, C. S., Williams, D., Enwemeka, S. K., Hollosi, S., & Yens, D. (2009). Blue 470-nm light kills methicillin-resistant Staphylococcus aureus (MRSA) in vitro. Photomedicine and laser surgery, 27(2), 221-226.
[17] Chui, C., Hiratsuka, K., Aoki, A., Takeuchi, Y., Abiko, Y., & Izumi, Y. (2012). Blue LED inhibits the growth of Porphyromonas gingivalis by suppressing the expression of genes associated with DNA replication and cell division. Lasers in surgery and medicine, 44(10), 856-864.
[18] Watson, A. (2020). Gingival Photobiomodulation Therapy in Canines Following Dental Procedure (Doctoral dissertation, California State Polytechnic University, Pomona).
[19] Leal-Junior EC, Albuquerque-Pontes GM. Depth penetration profile of phototherapy with combination of super-pulsed laser, red and infrared LEDs on human skin. Lasers Med Sci [in preparation]
[20] Albuquerque-Pontes GM, Johnson DS, Leal-Junior EC. Depth penetration of different settings of photobiomodulation therapy (PBMT) with combination of super-pulsed laser, red and infrared LEDs. [article in preparation
[21] Joensen, J., Øvsthus, K., Reed, R. K., Hummelsund, S., Iversen, V. V., Lopes-Martins, R. Á. B., & Bjordal, J. M. (2012). Skin penetration time-profiles for continuous 810 nm and Superpulsed 904 nm lasers in a rat model. Photomedicine and laser surgery, 30(12), 688-694.
[22] Albuquerque-Pontes GM, Leal-Junior EC, et al. Effect of different doses, wavelengths and application intervals of low-level laser therapy on cytochrome c-oxidase activity in intact skeletal muscle in rats. Lasers Med Sci June, 2014 Epub ahead of print]
[23] Friedmann H, Lipovsky A, Nitzan Y, Lubart R. Combined magnetic and pulsed laser fields produce synergistic acceleration of cellular electron transfer. Laser Therapy, 2009, 18(3): 137-141
[24] Leal-Junior, E. C. P., & da Silva Tomazoni, S. (2019, June). Synergistic effects of combination of three wavelengths and different light sources in cytochrome c oxidase activity in intact skeletal muscle of rats. In European Conference on Biomedical Optics (p. 11079_50). Optical Society of America.
[25] Arany, P. Exploring Photobiomodulation Dose Regimens Via Preclinical In Vitro and Animal Models. Optical Society Of America (OSA) Incubator Low Level Laser Therapy: The Path Forward, August, 2014, Washington, DC, USA.
[26] Joensen J, Ovsthus K, Reed RK, Hummelsund S, Iversen VV, Lopes-Martins RÁ, Bjordal JM.; Skin penetration time-profiles for continuous 810 nm and Superpulsed 904 nm lasers in a rat model.; Photomed Laser Surg. 2012 Dec;30(12):688-94. doi: 10.1089/pho.2012.3306. Epub 2012 Oct 1.Source
[27] "Effects of Power Densities, Continuous and Pulse Frequencies, and Number of Session of Low Level Laser Therapy on Intact Rat Brain" by Ilic, S., Leichliter, S., Streeter, J., Oron, A., DeTaboada, L., Oron, U. Photomed Laser Surg, 2006 Augu;24(4):458-66.
[28] Hashmi, J. T., Huang, Y. Y., Sharma, S. K., Kurup, D. B., De Taboada, L., Carroll, J. D., & Hamblin, M. R. (2010). Effect of pulsing in low-level light therapy. Lasers in surgery and medicine, 42(6), 450-466.
[29] Luna, S. P. L., Schoen, A., Trindade, P. H. E., & da Rocha, P. B. (2020). Penetration Profiles of a Class IV Therapeutic Laser and a Photobiomodulation Therapy Device in Equine Skin. Journal of Equine Veterinary Science, 85, 102846.
[30] Brondon P, Stadler I, Lanzafame RJ. Pulsing influences photoradiation outcomes in cell culture. Lasers Surg Med. 2009;41(3):222–226. [PubMed]
[31] Joensen J, Ovsthus K, Reed RK, Hummelsund S, Iversen VV, Lopes-Martins RÁ, Bjordal JM.; Skin penetration time-profiles for continuous 810 nm and Superpulsed 904 nm lasers in a rat model.; Photomed Laser Surg. 2012 Dec;30(12):688-94. doi: 10.1089/pho.2012.3306. Epub 2012 Oct 1.Source
[32] Vanin AA, Grandinetti VS, Johnson DS, Leal-Junior EC. Thermal impact of a photobiomodulation therapy (PBMT) portable device with combination of super-pulsed laser, red and infrared LEDs in human skin. [article in preparation]
[33] dos Santos Grandinétti, V., Miranda, E. F., Johnson, D. S., de Paiva, P. R. V., Tomazoni, S. S., Vanin, A. A., ... & Leal-Junior, E. C. P. (2015). The thermal impact of phototherapy with concurrent super-pulsed lasers and red and infrared LEDs on human skin. Lasers in medical science, 1-7.
[34] Oshiro T. Low-Reactive Laser Therapy: Practical Applications. 1991, ISBN 0471928453, John Wiley and Sons Publisher.
[35] Anders, Juanita, J., J. Lanzafame, Raymond, and R. Arany, Praveen. "Low-Level Light/Laser Therapy Versus Photobiomodulation Therapy." Photomedicine and laser surgery (2015).
[36] Dyson M. "Primary, secondary and tertiary effects of phototherapy: a review". Abstract from the 7th Congress of North American Association for Laser Therapy, Toronto, Canada, June, 2006
[37] Lanzafame R et al. "Temperature-controlled 830-nm low-level laser therapy of experimental pressure ulcers." Photomedicine and Laser Therapy 22.6 (2004): 483-488.
[38] Friedmann H, Lipovsky A, Nitzan Y, Lubart R. Combined magnetic and pulsed laser fields produce synergistic acceleration of cellular electron transfer. Laser Therapy, 2009, 18(3): 137-141
[39] Ahmed, M. K., Jafer, M., Nayeem, M., Moafa, I. H., Quadri, M. F. A., Gopalaiah, H., & Quadri, M. F. A. (2020). Low-level laser therapy and topical medications for treating aphthous ulcers: A systematic review. Journal of Multidisciplinary Healthcare, 13, 1595.
[40] Evans, D. H., & Abrahamse, H. (2008). Efficacy of three different laser wavelengths for in vitro wound healing. Photodermatology, photoimmunology & photomedicine, 24(4), 199-210.
[41] Zielińska, P., Nicpoń, J., Kiełbowicz, Z., Soroko, M., Dudek, K., & Zaborski, D. (2020). Effects of high intensity laser therapy in the treatment of tendon and ligament injuries in performance horses. Animals, 10(8), 1327.

[42] Rhee, Y. H., Cho, K. J., Ahn, J. C., & Chung, P. S. (2017). Effect of photobiomodulation on wound healing of the corneal epithelium through Rho-GTPase. Medical Lasers, 6(2), 67-76.
[43] Raja, Srinivasa N.; Carr, Daniel B.; Cohen, Milton; Finnerup, Nanna B.; Flor, Herta; Gibson, Stephen; Keefe, Francis J.; Mogil, Jeffrey S.; Ringkamp, Matthias; Sluka, Kathleen A.; Song, Xue-Jun (21 July 2020). "The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises". PAIN. Articles in Press. doi:10.1097/j.pain.0000000000001939. ISSN 0304-3959.
[44] Bashiri H. Evaluation of low level laser therapy in reducing diabetic polyneuropathy related pain and sensorimotor disorders. Acta Med Iran. 2013;51(8):543–547.
[45] Langella LG, Casalechi HL, Tomazoni SS, et al. Photobiomodulation therapy (PBMT) on acute pain and inflammation in patients who underwent total hip arthroplasty-a randomized, triple-blind, placebo-controlled clinical trial. Lasers Med Sci. 2018;33(9):1933-1940. doi:10.1007/s10103-018-2558-x
[46] Looney, A. L., Huntingford, J. L., Blaeser, L. L., & Mann, S. (2018). A randomized blind placebo-controlled trial investigating the effects of photobiomodulation therapy (PBMT) on canine elbow osteoarthritis. The Canadian Veterinary Journal, 59(9), 959.
[47] Bartels KE. Lasers in medicine and surgery. Vet Clin Small Anim. (2002) 32:495–515. doi: 10.1016/S0195-5616(02)00002-5
[48] Peplow, P. V., Chung, T. Y., & Baxter, G. D. (2010). Laser photobiomodulation of wound healing: a review of experimental studies in mouse and rat animal models. Photomedicine and laser surgery, 28(3), 291-325.
[49] Kuffler, D. P. (2016). Photobiomodulation in promoting wound healing: a review. Regenerative medicine, 11(1), 107-122.
[50] Enwemeka, C. S., Williams, D., Enwemeka, S. K., Hollosi, S., & Yens, D. (2009). Blue 470-nm light kills methicillin-resistant Staphylococcus aureus (MRSA) in vitro. Photomedicine and laser surgery, 27(2), 221-226.
[51] Schnedeker AH, Cole LK, Lorch G, Diaz SF, Bonagura J, Daniels JB. In vitro bactericidal activity of blue light (465 nm) phototherapy on meticillin-susceptible and meticillin-resistant Staphylococcus pseudintermedius. Vet Dermatol. 2017 Oct;28(5):463-e106. doi: 10.1111/vde.12451. Epub 2017 May 22. PMID: 28543810.
[52] Woodruff, L. D., Bounkeo, J. M., Brannon, W. M., Dawes, K. S., Barham, C. D., Waddell, D. L., & Enwemeka, C. S. (2004). The efficacy of laser therapy in wound repair: a meta-analysis of the literature. Photomedicine and laser surgery, 22(3), 241-247.
[53] Enwemeka, C. S., Parker, J. C., Dowdy, D. S., Harkness, E. E., Harkness, L. E., & Woodruff, L. D. (2004). The efficacy of low-power lasers in tissue repair and pain control: a meta-analysis study. Photomedicine and Laser Therapy, 22(4), 323-329.
[54] Adamskaya, N., Dungel, P., Mittermayr, R., Hartinger, J., Feichtinger, G., Wassermann, K., ... & van Griensven, M. (2011). Light therapy by blue LED improves wound healing in an excision model in rats. Injury, 42(9), 917-921.
[55] Schnedeker AH, Cole LK, Lorch G, Diaz SF, Bonagura J, Daniels JB. In vitro bactericidal activity of blue light (465 nm) phototherapy on meticillin-susceptible and meticillin-resistant Staphylococcus pseudintermedius. Vet Dermatol. 2017;28(5):463-e106. doi:10.1111/vde.12451
[56] Enwemeka, C. S., Williams, D., Enwemeka, S. K., Hollosi, S., & Yens, D. (2009). Blue 470-nm light kills methicillin-resistant Staphylococcus aureus (MRSA) in vitro. Photomedicine and laser surgery, 27(2), 221-226.
[57] Kleinpenning, M. M., Smits, T., Frunt, M. H., Van Erp, P. E., Van De Kerkhof, P., & Gerritsen, R. M. (2010). Clinical and histological effects of blue light on normal skin. Photodermatology, photoimmunology & photomedicine, 26(1), 16-21.
[58] Masson-Meyers, D. S., Bumah, V. V., Biener, G., Raicu, V., & Enwemeka, C. S. (2015). The relative antimicrobial effect of blue 405 nm LED and blue 405 nm laser on methicillin-resistant Staphylococcus aureus in vitro. Lasers in medical science, 30(9), 2265-2271.
[59] Enwemeka, C. S., Williams, D., Enwemeka, S. K., Hollosi, S., & Yens, D. (2009). Blue 470-nm light kills methicillin-resistant Staphylococcus aureus (MRSA) in vitro. Photomedicine and laser surgery, 27(2), 221-226.
[60] Schnedeker A, Cole L, Lorch G, Diaz S, Bonagura J, Daniels J (2017) In vitro bactericidal activity of blue light (465-nm) phototherapy on meticillin-susceptible and meticillin-resistant Staphylococcus pseudintermedius (Manuscript in preparation)
[61] Marchegiani, A., Spaterna, A., Cerquetella, M., Tambella, A. M., Fruganti, A., & Paterson, S. (2019). Fluorescence biomodulation in the management of canine interdigital pyoderma cases: a prospective, single-blinded, randomized and controlled clinical study. Veterinary dermatology, 30(5), 371-e109.
[62] Li, X., Kolltveit, K. M., Tronstad, L., & Olsen, I. (2000). Systemic diseases caused by oral infection. Clinical microbiology reviews, 13(4), 547-558.
[63] Xiaojing Li, K. M. (2000). Systemic Diseases Caused by Oral Infection. Oct(547–558).
[64] Gomez, G. F., Huang, R., MacPherson, M., Zandona, A. G. F., & Gregory, R. L. (2016). Photo inactivation of Streptococcus mutans biofilm by violet-blue light. Current microbiology, 73(3), 426-433.
[65] De Lucca, A. J., Carter-Wientjes, C., Williams, K. A., & Bhatnagar, D. (2012). Blue light (470 nm) effectively inhibits bacterial and fungal growth. Letters in applied microbiology, 55(6), 460-466.
[66] Shany-Kdoshim, S., Polak, D., Houri-Haddad, Y., & Feuerstein, O. (2019). Killing mechanism of bacteria within multi-species biofilm by blue light. Journal of oral microbiology, 11(1), 1628577.
[67] Vaknin, M., Steinberg, D., Featherstone, J. D., & Feuerstein, O. (2020). Exposure of Streptococcus mutans and Streptococcus sanguinis to blue light in an oral biofilm model. Lasers in medical science, 35(3), 709-718.
[68] Josewin, S. W., Kim, M. J., & Yuk, H. G. (2018). Inactivation of Listeria monocytogenes and Salmonella spp. on cantaloupe rinds by blue light emitting diodes (LEDs). Food microbiology, 76, 219-225.
[69] Tanboga, I., Eren, F., Altınok, B., Peker, S., & Ertugral, F. (2011). The effect of low level laser therapy on pain during dental tooth-cavity preparation in children. European Archives of Paediatric Dentistry, 12(2), 93-95.
[70] Raiesian, S., Khani, M., Khiabani, K., Hemmati, E., & Pouretezad, M. (2017). Assessment of low-level laser therapy effects after extraction of impacted lower third molar surgery. Journal of lasers in medical sciences, 8(1), 42.
[71] Eroglu, C. N., & Keskin Tunc, S. (2016). Effectiveness of single session of low-level laser therapy with a 940 nm wavelength diode laser on pain, swelling, and trismus after impacted third molar surgery. Photomedicine and laser surgery, 34(9), 406-410.
[72] Vale, F. A., Moreira, M. S., Almeida, F. C. S. D., & Ramalho, K. M. (2015). Low-level laser therapy in the treatment of recurrent aphthous ulcers: a systematic review. The Scientific World Journal, 2015.
[73] Ramos, Renato Matta, Marion Burland, Jefferson Braga Silva, Lauren Marquardt Burman, Marco Smiderle Gelain, Leticia Manoel Debom, Jean Michel Bec, Mohsen Alirezai, Carlos Oscar Uebel, and Jean Valmier. "Photobiomodulation improved the first stages of wound healing process after Abdominoplasty: an experimental, double-blinded, non-randomized clinical trial." Aesthetic plastic surgery 43, no. 1 (2019): 147-154.
[74] Ezzati K, Fekrazad R, Raoufi Z. The Effects of Photobiomodulation Therapy on Post-Surgical Pain. J Lasers Med Sci. 2019;10(2):79-85. doi:10.15171/jlms.2019.13
[75] Hochman, L. (2018). Photobiomodulation therapy in veterinary medicine: a review. Topics in companion animal medicine, 33(3), 83-88.
[76] Friedman, O., Gofstein, D., Arad, E., Gur, E., Sprecher, E., & Artzi, O. (2020). Laser pretreatment for the attenuation of planned surgical scars: A randomized self-controlled hemi-scar pilot study. Journal of Plastic, Reconstructive & Aesthetic Surgery, 73(5), 893-898.
[77] Wardlaw, J. L., Gazzola, K. M., Wagoner, A., Brinkman, E., Burt, J., Butler, R., ... & Senter, L. H. (2019). Laser therapy for incision healing in 9 dogs. Frontiers in veterinary science, 5, 349.
[78] Nascimento, F. F., Marques, V. I., Crociolli, G. C., Nicacio, G. M., Nicacio, I. P., & Cassu, R. N. (2019). Analgesic efficacy of laser acupuncture and electroacupuncture in cats undergoing ovariohysterectomy. Journal of Veterinary Medical Science, 18-0744.
[79] Tomacheuski, R. M., Taffarel, M. O., Cardoso, G. S., Derussi, A. A., Ferrante, M., Volpato, R., & Luna, S. P. (2020). Postoperative Analgesic Effects of Laserpuncture and Meloxicam in Bitches Submitted to Ovariohysterectomy. Veterinary Sciences, 7(3), 94.
[80] https://www.aaha.org/your-pet/pet-owner-education/ask-aaha/laser-therapy/
[81] https://journals.sagepub.com/doi/pdf/10.1177/1098612X15572062
[82] Langella, L. G., Casalechi, H. L., Tomazoni, S. S., Johnson, D. S., Albertini, R., Pallotta, R. C., ... & Leal-Junior, E. C. P. (2018). Photobiomodulation therapy (PBMT) on acute pain and inflammation in patients who underwent total hip arthroplasty—a randomized, triple-blind, placebo-controlled clinical trial. Lasers in medical science, 33(9), 1933-1940.
[83] Petrini, M., Ferrante, M., Trentini, P., Perfetti, G., & Spoto, G. (2017). Effect of pre-operatory low-level laser therapy on pain, swelling, and trismus associated with third-molar surgery. Medicina oral, patologia oral y cirugia bucal, 22(4), e467.
[84] Eroglu, C. N., & Keskin Tunc, S. (2016). Effectiveness of single session of low-level laser therapy with a 940 nm wavelength diode laser on pain, swelling, and trismus after impacted third molar surgery. Photomedicine and laser surgery, 34(9), 406-410.

[85] Wang, Y., Wang, Y., Wang, Y., Murray, C. K., Hamblin, M. R., Hooper, D. C., & Dai, T. (2017). Antimicrobial blue light inactivation of pathogenic microbes: State of the art. Drug Resistance Updates, 33, 1-22.
[86] Amid, R., Kadkhodazadeh, M., Ahsaie, M. G., & Hakakzadeh, A. (2014). Effect of low level laser therapy on proliferation and differentiation of the cells contributing in bone regeneration. Journal of lasers in medical sciences, 5(4), 163.
[87] Draper, W. E., Schubert, T. A., Clemmons, R. M., & Miles, S. A. (2012). Low-level laser therapy reduces time to ambulation in dogs after hemilaminectomy: a preliminary study. Journal of Small Animal Practice, 53(8), 465-469.
[88] Flaherty, M. J. (2019). Rehabilitation therapy in perioperative pain management. Veterinary Clinics: Small Animal Practice, 49(6), 1143-1156.
[89] Baltzer, W. I. (2020). Rehabilitation of companion animals following orthopaedic surgery. New Zealand veterinary journal, 68(3), 157-167.
[90] Photobiomodulation, P. Retrospective Observational Study and Analysis of Two Different Photobiomodulation Therapy Protocols Combined with Rehabilitation Therapy as Therapeutic Interventions for Canine Degenerative Myelopathy.
[91] Montgomery PG, Pyne DB, Hopkins WG, Dorman JC, Cook K, Minahan CL. . The effect of recovery strategies on physical performance and cumulative fatigue in competitive basketball. J Sports Sci. 2008; 26 11: 1135– 1145.
[92] Girard O, Lattier G, Micallef J, Millet G. . Changes in exercise characteristics, maximal voluntary contraction, and explosive strength during prolonged tennis playing. Br J Sports Med. 2006; 40 6: 521– 526.
[93] Antonialli FC, De Marchi T, Tomazoni SS, et al. Phototherapy in skeletal muscle performance and recovery after exercise: effect of combination of super-pulsed laser and light-emitting diodes. Lasers Med Sci. 2014;29(6):1967-1976. doi:10.1007/s10103-014-1611-7
[94] Hochman, L. (2018). Photobiomodulation therapy in veterinary medicine: a review. Topics in companion animal medicine, 33(3), 83-88.
[95] Bjordal, J. M. (2012). Low level laser therapy (LLLT) and World Association for Laser Therapy (WALT) dosage recommendations. Photomedicine and laser surgery, 30(2), 61-62.
[96] Friedmann H, Lipovsky A, Nitzan Y, Lubart R. Combined magnetic and pulsed laser fields produce synergistic acceleration of cellular electron transfer. Laser Therapy, 2009, 18(3): 137-141

Scientific Monograph Series Laser Therapy University
www.lasertherapyu.org