The Veterinary Pillars Paper

Validating Multi Radiance Laser Technology

Exposing the Facts and Fallacies of Class IV Laser Therapy

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Exposing the Facts and Fallacies of Class IV Laser Therapy

Class IV Laser Therapy is not Photobiomodulation. A review of the evidence proves that it operates on a much different pathway.

A New Paradigm: Blue Light for Anti-Microbial Control

New peer reviewed study shows the correct dose of Blue Light to kill MRSA.

Safety and Efficacy for Home Use Laser Therapy

Extending veterinary care into the home with safe, over the counter cleared Class 1M Super Pulsed Laser Technology

Foreword

I began integrating low level, cold laser therapy into my veterinary practice thirty-five years ago for a simple reason. I was interested in doing whatever I could to help animals heal. At the beginning of my veterinary career I chose to live the "James Herriott" experience, practicing with all animals great and small in a mixed animal practice in the bucolic mountains of New England. Each day, I was not sure if I would be delivering a calf, treating a lame horse, operating on a fracture on a dog hit by a car or suturing a wound on an alpaca. At that time, veterinary medicine was primarily limited to medications and surgery. After a few years I found that my deepest passion in veterinary medicine was to explore new approaches to help the animals heal that either did not respond to conventional medical and surgical therapies or where they were having side effects or were simply not indicated for surgery. I began that search by studying the scientific basis of acupuncture and its clinical applications.

I had my first experience with low level laser therapy during an acupuncture certification course when a colleague saw me limping. I explained that I had been kicked by a young heifer during my senior year at Cornell and the orthopedist diagnosed me with a vascular injury to my patella, decreasing circulation to it and simply said "get used to limping when you overdo it". I had hoped for a better solution. This colleague then showed me the "cold" laser he was using on acupuncture points and said he had used it to increase microcirculation and relieve pain and inflammation as well. I was open minded enough to considering the possibility and he showed me how to treat my knee. I was amazed to experience such instantaneous pain relief. By the next day I was no longer limping on it. It continued to heal and it resolved the problem. That was my first exposure to laser therapy and stimulated my interest in exploring its potential application in veterinary care. I would often joke that I would only use something on the animals after experiencing it on myself and seeing if it helped. Shortly thereafter I purchased my first low level, veterinary laser and began helping animals to relieve pain, inflammation and accelerate healing.

As I continued to explore natural, nontoxic approaches to help animals heal, combining my scientific training with my deep compassion for animals, I would use three criteria to evaluate whether I felt a particular therapy might be beneficial to integrate into my evolving integrative veterinary program. I would simply ask myself: 1. Does this therapy work? 2. Is the therapy safe? 3. Are the results reproducible? If I found it efficacious, safe and reproducible, I would begin to incorporate it into my practice.

In almost four decades of very active practice since graduating Cornell, receiving my master's degree in neurophysiology and behavior and teaching as a clinical assistant professor at both Colorado State University and Tufts University veterinary schools, I have always felt compelled to explore further and deeper. Too often, cases would present for which we lacked answers using the tools and drugs available. Compassion runs deep in veterinarians, but diagnoses are tougher when we have to rely on nonverbal communications, come up with novel ways of understanding how to go beyond treating symptoms and get at the root cause of the disease or the underlying issue that's preventing treatments from producing a fully healed recovery.

After studying and integrating acupuncture and other complementary therapies into a more expansive approach to veterinary medicine, I edited the textbooks "Veterinary Acupuncture, Ancient Art to Modern Medicine" (Mosby/Elsevier) and co-edited "Complementary and Alternative Veterinary Medicine, Principles and Practice" (Mosby/Elvsevier). Both textbooks included sections on veterinary laser therapy. If we are open, insights and technology sometimes converge to allow us to break through "conventional thinking" and truly innovate. That, is how it was for me as the science and the evidence began to reveal how acupuncture worked, physiologically. Acupuncture needles often gave me better outcomes when other available treatments failed. Not only could I use acupuncture safely for consistent results, but over time even some of its loudest critics crossed over, got certified and reproduced these results. And today, it's widely accepted. It was partly due to these pioneering efforts and contributions that I was honored to be named as one of the 15 most influential veterinarians by my peers.

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Laser therapy, is similar. It was a breakthrough for surgery, providing much needed control and precision for resecting tumors and preserving healthy tissues. It was then adapted for therapeutic purposes with new claims that in some cases worked for me and in others not enough. Intuitively, I had some hesitation and concern regarding Class IV laser's hazard designation with the attendant clinician/patient safety requirements. Wavelengths specifically suited for precise shallow ablation did not seem to deliver the promised depth of penetration required for my high level horse's soft tissue injuries to ligaments and tendons. Subsequent research only confirmed that heat was never intrinsic to the mechanisms of action. In fact, it was the nonthermal photochemical and photophysical effects that explained laser therapy's improvements in blood flow and tissue repair, even the inhibitory applications for pain relief.

Thirty years later, following my introduction to Multi Radiance Medical's super pulsed cold lasers, I realized that this was a very significant, positive evolution of laser technology and was offering the next level of therapeutic healing. Today, I am pleased to enthusiastically write the foreword to the following Veterinary Pillars Paper because it appears that the research demonstrates that the fundamental criteria of efficacy, safety and reproducibility of effects have been satisfied. By shortening pulse widths to nanoseconds, heat side effects are gone. Simple physics dictates that thermal issues do not surface until millionth of second durations or longer. Super pulsing has become synonymous with safety, but the term is only applicable to these nanosecond pulses, not by addition of a simple gate for on, off.

Laser therapy's mechanisms, now explained and accepted as nonthermal, plus the comparative safety of super pulsing, makes for a modality I enthusiastically support. The following newest addition to Multi Radiance's research, the Veterinary Pillars Paper, continues their commitment to exploration and pushing our understandings of light and frequencies. This also makes great sense since at the quantum level we are all fundamentally light waves and particles. Practitioners in both human and veterinary are finding that heat-free super pulsed lasers offer very reproducible outcomes, lessening our dependence on medications with potentially detrimental side effects. In addition, the blue wavelengths provided with these lasers also seem to be effectively fighting a scourge of our time: drug resistant bacteria. The patented combining of multiple synergistic wavelengths, plus blue light in one highly portable device offers the opportunity to help heal a wider array of conditions in veterinary medicine.

After nearly forty years of a very busy veterinary career of practice, teaching, writing and research, retirement from active practice finds me eternally grateful to all my teachers, colleagues, clients and patients, two-legged, four-legged and winged, for their help and support. May we all be blessed to continue exploring and expanding healing approaches together for the benefit of all beings!

Allen M. Schoen, DVM,MS, PhD (hon.)
Editor, Veterinary Acupuncture, Ancient Art to Modern Medicine
Co-editor, Complementary and Alternative Veterinary Medicine
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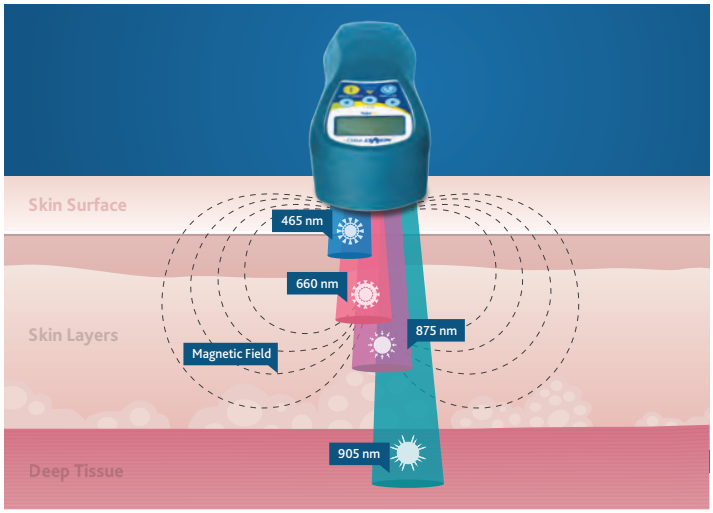
Introduction

When exploring the truth, seek first to identify what is not true

Photobiomodulation (PBM) therapy, also known as low level laser therapy (LLLT), continues to be widely used for injury management and pain relief in a wide variety of species. Its popularity as one of the most exciting and novel innovations in veterinary medicine today has expanded its use in prophylactic care as well as the improvement of sports performance by equestrian and canine athletes. The use of LLLT for the reduction and resolution of infection is also rapidly gaining traction in veterinary medicine.



While an impressive body of evidence to categorically support PBM exists, confounding bias, inaccurate claims and scientific fallacies continue to create confusion among clinicians. There are many different "views" on what constitutes the best available device. It is not always the one with the best price, the most features, or most futuristic design. When separating fact from fiction, the best device not only combines consistent, successful, clinical outcomes but undergoes a rigorous scientific proof of concept (POC).

The intention of this document is to explore the science of light-based therapies through the available peer-reviewed evidence and dispel confusion surrounding light therapy. Additionally, a glimpse of the clinical utility of PBM is discussed for veterinarians and owners to better understand the potential value of the therapeutic lasers.

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The Clinical Use of Photobiomodulation (PBM)

Pain is a problem for veterinary patients; as the signs are often hard to detect, this can often delay the diagnosis and treatment of the underlying cause. Chronic pain tends to be very subtle – owners report their animals are "slowing down", have less interest in activities they used to enjoy, don't jump on furniture as frequently, are grumpier than normal, and withdraw from normal interactions.

The application of light-based modalities has proven to be an excellent means of reducing pain, either as a complementary modality or as a standalone treatment. There are virtually no known side effects, no long-term safety concerns as can occur with medications, and it is simple to administer. PBM can be used to treat a wide variety of conditions in dogs, cats, horses, and exotics.

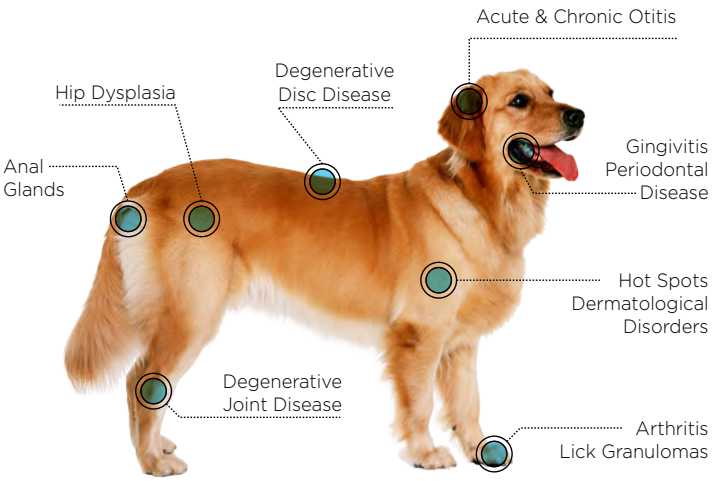
Most commonly, PBM is used to treat pain and inflammation associated with soft tissue injuries, such as sprains, strains, tendonitis (inflammation of tendons, which connect muscle to bone), and desmitis (inflammation of ligaments, which connect two bones or cartilage). These injuries occur commonly in 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. Practitioners often find the reduction of inflammation, the relaxation of muscles and the control of pain are maximized when PBM is used in conjunction with other rehabilitation therapy modalities, including massage, chiropractic adjustments, balance and strengthening exercises, an underwater treadmill, and acupuncture.

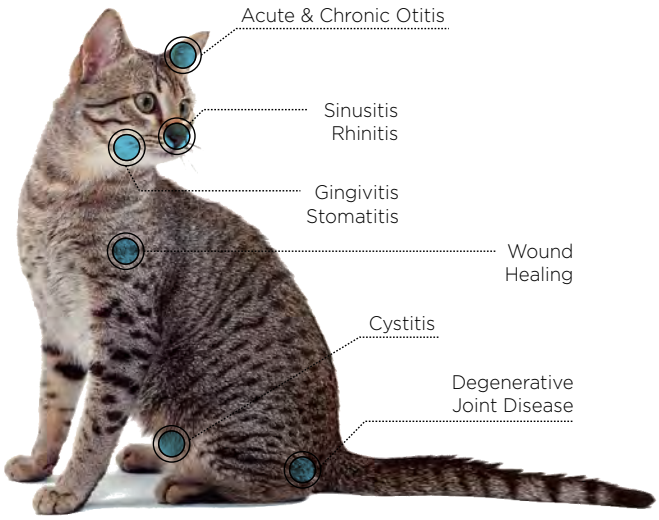
Veterinarians frequently prescribe non-steroidal anti-inflammatory drugs (NSAIDs) in addition to rehabilitation therapy for patients. Therapists anecdotally report that using PBM prior to performance can help minimize the risk of these injuries.

Regardless of species, osteoarthritis (OA) is a common cause of pain. Much like soft tissue sprains and strains, PBM can be a central component of a multimodal approach to treating OA.

PBM can be particularly helpful in reducing pain, and enabling arthritic animals to be more active. Increased activity can facilitate weight loss, which further reduces strain on joints and the clinical signs of OA.

PBM is beneficial in managing wounds and dermatologic abnormalities, including hot spots, lick granulomas, otitis externa, pyoderma (infection of the skin), and healing of surgical incisions. 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 with these conditions, reduce bacterial load (especially if blue light settings are used), and promote blood flow to the affected areas.





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Changing the Status Quo:

Evidence Based and Translational Research for Veterinary Laser Therapy

Confusion about best wavelengths, dose, and power remain a major source of concern and uncertainty among clinicians. Dogma, often perpertrated by the opinions of self-appointed experts in the field, continues to muddle the greater scientific understanding of clinical veternary laser therapy. For years, companies have sold devices that have been too low in power, too high in power, generated too much heat, etc. 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 largest offenders are companies that sell very high powered, defocused surgical lasers as "therapeutic" modalities.

Six examples have been identified that are scientifically provable but challenge currently held beliefs:

1) Class IV lasers are NOT the most advanced devices currently available.
2) More (often excessive) power DOES NOT equate with better outcomes.
3) The resulting heat from high powered laser is NOT beneficial.
4) Larger doses are NOT necessary to derive clinical benefits.
5) The mechanism of action behind high powered laser is NOT photobiomodulation.
6) Clinical and laboratory research DOES NOT support the use of high powered lasers in therapy.

Class IV lasers are often promoted as being the latest and greatest in laser technology, but were in fact investigated in the 1990s and found to be very inefficient. Jan Tunér, a clinician and early adopter of PBM contends, "There is no specific 'technology' that enables a manufacturer to choose a laser diode that produces more than 500 mW, thus the term "Class IV technology" is simply used to infer a differential benefit that does not exist. Apart from power, the only differences between Class IIIB and IV lasers are the potential hazards and, usually, the price."[1] Some laser companies claim that a Class IV laser 'by default' is better than any other classification of laser available. This is simply not true. The classification of lasers is designed to keep users and patients safe. This certainly has nothing to do with efficacy.

The North American Association for Photobiomodulation Therapy (NAALT) has recognized that photobiomodulation (PBM) is a nonthermal process.[2] The primary effects of the PBM are based on photochemical and photophysical changes and not the result of thermal influence in tissue.[3,4] However, most continuous wave lasers/LEDs and all high powered Class IV lasers produce a considerable amount of unwanted heat that may limit the phototherapeutic response or result in tissue damage. Joenson et al. demonstrated the thermal effects of low level light devices as recommended in the World Association for Laser Therapy (WALT) guidelines for musculoskeletal and inflammatory conditions are negligible (<1.5°C) in light, medium, and dark skin.

Mantineo et al.[5] notes that the temperature increases are more pronounced for 980 nm Class IV than any other wavelengths. Khan et al.[6] established a correlation between a rise in surface temperature (> 45 °C) and phototoxic tissue damage. There are no guidelines for treatment for high powered devices. Higher doses delivered with a strong IIIB laser (200 mW) are capable of increasing skin temperature significantly and these photothermal effects may produce punctuate erythema (first-degree superficial burns) or exceed the thermal pain threshold.[7]

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 clinicians. However, light absorption creates heat as an unwanted, inefficient and potentially dangerous byproduct. Laser, like ultrasound, at low levels, can stimulate while at higher levels it becomes destructive.[8] Heat becomes a compounding limitation in achieving optimal phototherapeutic effects. Depending on the intensity of the light, the PBM effect can quickly degrade into a photothermal overload. The rule of reciprocity is not valid.

Isman et al.[9] found evidence that the increased heat accumulation from high powered laser also stimulated apoptotic pathways of cell death. Reactive oxygen

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species (ROS) are an unavoidable byproduct of oxygen metabolism and their cellular concentrations are determined by the balance between their rates of production and their rates of clearance by various antioxidant compounds and enzymes. Low ROS concentrations exert beneficial effects regulating cell signaling cascades.[10]

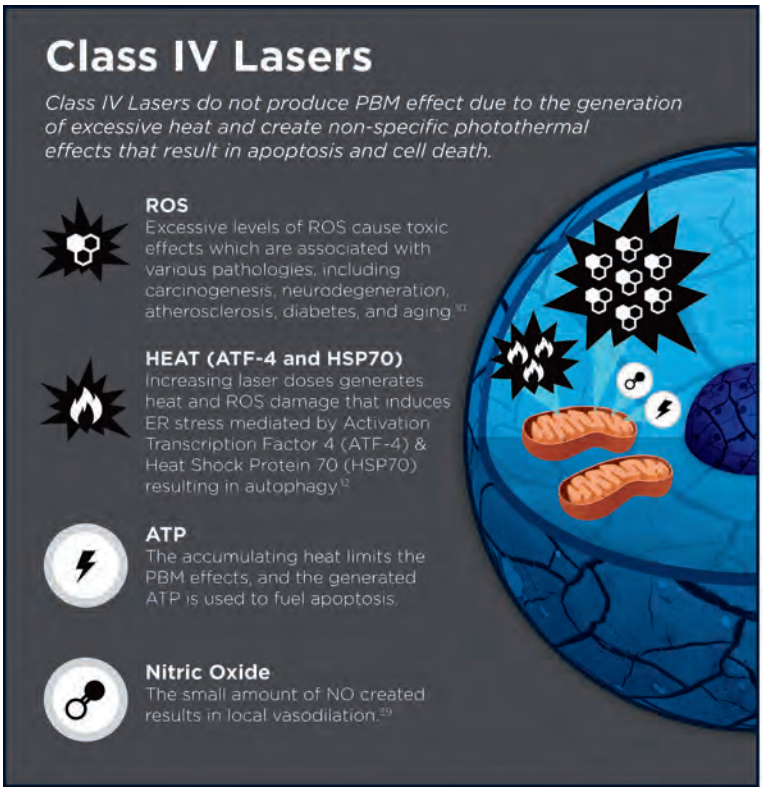
Apoptosis is normally mediated by caspases, which trigger cell death.[11] However, the damage was not induced by the heat alone. Khan et al.[12] observed that the larger doses provided by high powered lasers also generates ROS that when combined with accumulating heat in the skin resulted in phototoxic tissue damage. Laser doses from Class IV lasers generate heat and ROS damage that induce cell membrane stress mediated by Activation Transcription Factor 4 (ATF-4) and Heat Shock Protein 70 (HSP70). This results in autophagy. Therefore, it can be argued that a higher powered laser that generates superficial tissue heating in the skin doesn't provide PBM as we currently understand it, but rather trigger apoptotic pathways.

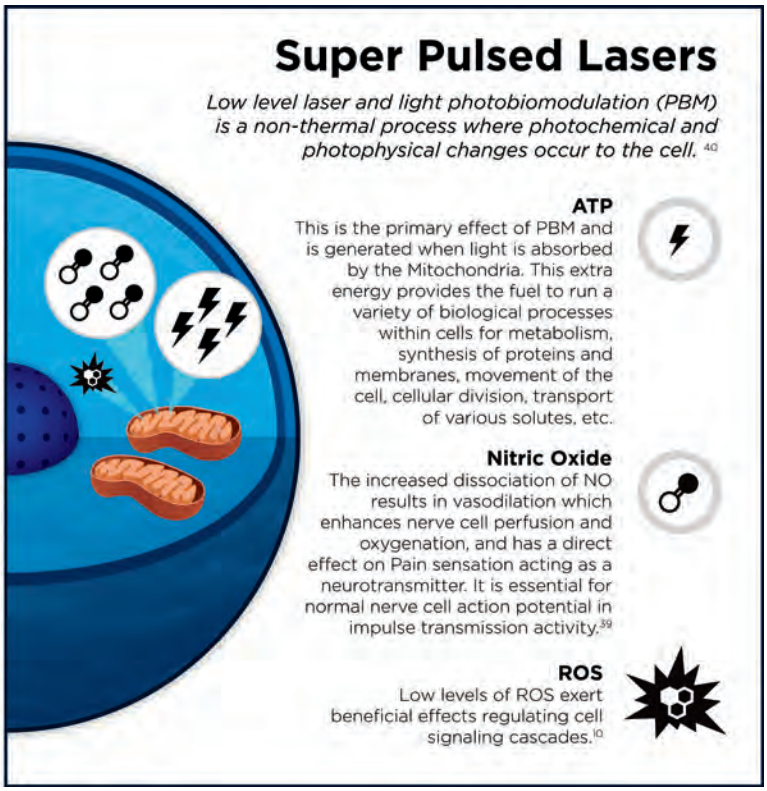
The effects of high powered laser are more likely to be related to photothermal effects rather than photochemical or photophysical. This newly identified mechanism may be more related to the apoptosis pathway rather than the stimulation of CCO and ATP production described by photobiomodulation. The term "therapy" may not be the best suited for high powered laser application.

Khan et al.[13] have suggested by cooling target site prior to high powered laser would neutralize laser phototoxicity. However, de Paiva[14] et evaluated the effect of "pre-cooling" tissue following exercise induced muscle damage and found cryotherapy prior to laser therapy significantly negated the phototherapeutic benefits seen in the "laser only" group. Therefore, the idea of using a cold therapy prior to the administration of high powered laser to negate the effect of photothermal issues is not clinically valid or indicated, since the beneficial effect of the light is absent.

While a demonstration of a high powered laser that can deliver hundreds of joules in a very short time can be an impressive feat, the downside is that the needed reduction of an inflammatory process is blocked and the body's ability to heal itself, disabled. "The greater the power, the better the overall outcome" is an often used and scientifically inappropriate statement.

Since "Class IV" or high powered lasers are not truly PBM, none of the research done on PBM should be cited to demonstrate their efficacy. Quite to the contrary, nearly all positive PBM studies have been done with the use of low powered lasers. Studies done with high powered lasers failed to demonstrate superior results (or even results on par) when compared to lower-powered devices. A lower treatment effect at 980 nm seems to result from specific absorption properties of the chromophores. [15]





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It should be noted, that due to the extreme heat generated with high powered lasers, it would be nearly impossible to perform a true randomized, double-blind study.

With virtually no side effects and minimal contraindications, low level laser and LED Laser therapy treatments are considered safe to use in almost all clinical situations and patient populations. High-powered lasers cannot claim the same safety, effectiveness or scientific validation other than for their original intended use as a surgical tool.

Efficacy and Effectiveness

Clinicians should not confuse the efficacy of a technology with the effectiveness of a product or device. Marketing hype stretches the truth to highlight the "potential" benefits of these devices while failing to mention the drawbacks. Multi Radiance Medical (MRM) embarked on the proof of concept (POC) in early 2012 that identify the basic mechanisms of action of different light sources (laser and LEDs). (Refer to Appendix "A" for a more complete scientific review of the POC and an independent comparison of Multi Radiance Super Pulsed Laser Technology results to both Class IIIB and Class IV lasers.)

All light, whether laser or ordinary, is part of the electromagnetic spectrum of energy and composed of photons, or "packets" of energy. Albuquerque-Pontes et al.[16] identified the optimal dose of several different wavelengths and light sources to optimally enhance ATP production. Friedmann et al.[17] utilized the identified best dose and wavelength to confirm that a synergy exists between the pulsed low level laser and light emitting diodes in Multi Radiance Medical devices.

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 is necessary to understand how light enters the body. Researchers have recently 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.

Despite claims to the contrary, increased power does not improve the penetrative quality of the light. Advocates of high powered devices claim, in trade journals, that high powered lasers have a better tissue penetration than any low level laser. Sangkwan and Jong-In[18] 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.[19] found that 808 nm of light penetrates as much as 54% deeper than 980 nm light. The poor penetration of 980 nm is likely due to absorption by water and why it is likely to produce more tissue heating than photochemical effects.[20] Simply put, penetrating the skin barrier cannot be compensated by a higher power output, as it will cause light to be absorbed superficially, more quickly, leading to greater heat generation.[21]

Work by Anders et al.[22] with high powered Class IV lasers with 1 and 4 W outputs confirms the poor penetration of the 980 nm wavelength. The percentage of light penetrating through the skin barrier was measured at 33% for the 1 W output and decreased to 30% with the 4 W. While this appears to be adequate penetration, the amount of energy being absorbed in the superficial layers of the skin was measured at 1.2 W/cm2 for the 1 W output and a whopping 4.9 W/cm^2 for the 4 W output. This yielded only 2.45% of penetration of the high powered laser into deeper tissues. This is hardly efficient, considering the amount of energy necessary at the surface, which can potentially create tissue damage, and affect patient comfort levels. The Anders et al. experiment was conducted with New Zealand white rabbits, which have a genetic deviation called albinism.[23] The actual penetration of the Class IV light into the tissue is likely even less if pigment is present in the skin samples.

Vanin et al. evaluated the effect of high powered laser on three experimental groups stratified per skin pigmentation (light, medium, and dark pigmented skin according Von Luschan's chromatic scale). A significant increase in skin temperature and discomfort during high powered laser irradiation was reported especially in dark pigmented skin. Clinicians should be cautious when using these high powered lasers to avoid clinical situations where heat may not be indicated including wounds, acute injuries, and areas of paresthesia. The risks of possible tissue overheating, retinal damage or increases in discomfort do not outweigh the novelty of using a higher-powered device.

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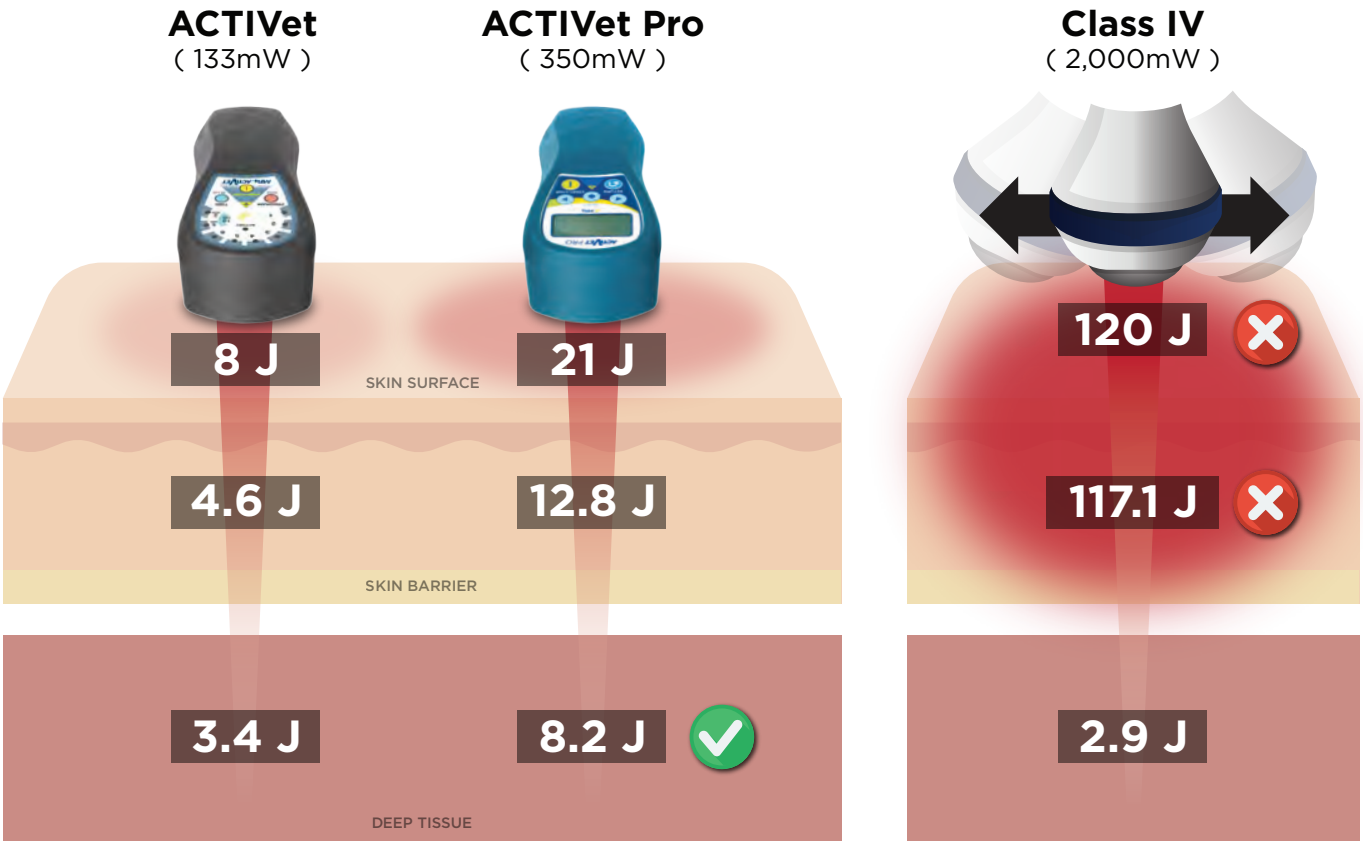
There is a baseline and upper limit for the necessary power and energy density required for a desired response. Basically, this is a measure of how much light or how tightly packed the photons are in the beam. An irradiance that is too low will fail to stimulate the tissue, give lackluster clinical results and be no more effective than ordinary light. A high powered continuous wave laser, rather than transforming all photons into biochemical energy, will convert more energy into heat. This creates a compromise between power and heat.

It has been suggested in the literature that other modes, such as super pulsing, may have different skin penetration time profiles. Super pulsed lasers (SPL) produce 'bursts' of light energy at a higher peak power with a lower thermal influence and have been suggested to prevent the conversion of photons from light to heat.[24] Biological tissue is "aware" of incident energy pulses, only if they are over one millisecond in width.[25]

Brondon et al.[26] found super-pulsing better able to penetrate through melanin fibers and Joensen et al.[27] evaluated and found super pulsed 904 nm LLLT energy penetrated 2-3 easier through the rat skin barrier than a continuous wave device (CW) of 810 nm. Anders et al.[28] attempted to replicate the study but failed to observe any effect due to use of a non-standardized power meter to measure light through the tissue.

Joensen et al.[29] measured a significant increase in skin temperature, as much as 22.3°C, while administering higher doses of light with both CW and SPL devices. Vanin et al.[30] replicated a study by Grandinétti et al.[31] 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 (350 mW and 50 Hz frequency).

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 ultrashort pulse structure related to the frequency of the super pulsed laser and pulsing of the LEDs and IREDs. Pulsing and super pulsing, by nature, have a clear distinctive advantage; their operation, by design, is to minimize heat.



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Super pulsed laser creates the desired higher peak power, however due to the ultrashort pulses, there is little resulting heat accumulating within the target tissue. To work in concert with the super pulsing laser, both IREDs and LEDs are pulsed to reduce photothermal effects on tissue. The patented combination of wavelengths in the Multi Radiance Medical device helps to improve the percentage of available light at greater tissue depths. This resolves any issues with the inefficient use of higher-powered outputs in continuous wave devices and a poor penetration profile. Leal-Junior and Albuquerque-Pontes[32] evaluated the depth of penetration time profile (DPTP) of the original ACTIVet and Albuquerque-Pontes et al.[33] performed the same study with the ACTIVet PRO to determine the effects of concurrent multiple wavelengths of 660n m Red LED, 875 nm IRED and 905 nm SPL.

Each individual wavelength was tested separately with and without the tissue skin flaps to establish the percentage of energy penetration. Data observed also confirmed what Joenson et al. found regarding the pattern of linearly increasing penetration of the light over time by the super pulsed laser. 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 suggests and demonstrates a pattern of linearly increasing penetration of the light over time with a 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 the 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 when the power is doubled compared to original and a 357% increase when the power is doubled again. This can be attributed to 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 increase by a factor of 4.

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.

All Multi Radiance Veterinary devices have a Class 1 laser classification, which puts into the safest category of therapeutic lasers. Unlike a Class IV laser, a lower powered laser can also be applied in contact with the skin directly over the pathological tissue and held stationary for the necessary time to deliver the appropriate amount of energy. This is significantly more efficient, accurate, predictable and safe.

A New Paradigm: Blue Light for Anti-Microbial Control

Blue light, particularly in the wavelengths between 405–470 nm, has attracted increasing attention due to its intrinsic antimicrobial effect. Commonly accepted to be less detrimental to mammalian cells than ultraviolet (UV) irradiation, non-coherent blue light penetrates rather poorly, due to the almost complete absorption in the superficial layers of the skin, making it ideally suited to treat conditions of the skin.

Per the American Society for Microbiology, such infections are the second most commonly-encountered type in private practice, and the most common type presented in 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 Staphylococcus aureus, MRSA[34] 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

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following blue light exposure may explain the mechanism of blue light inactivation of wound pathogens.

470 nm Blue LED light retains some of the antibacterial properties of UV light, but without the risks associated with UV overexposure[35] and the effects seen with blue LEDs are equal and on par with results seen with higher powered blue lasers.[36] 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.[37] 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.[38] replicated the previous study by the Enwemeka group to test the bactericidal activity of blue light (465-nm) with the ACTIVet PRO on meticillin-susceptible and meticillin-resistant Staphylococcus pseudintermedius. 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

MSSP: Meticillin-Susceptible Staphylococcus pseudintermedius
MRSP: Meticillin-Resistant Staphylococcus pseudintermedius
MRSA: Meticillin-Resistant Staphylococcus aureus
CC: median colony counts | NC: negative control (not irradiated)
TG: treatment group | % Red: percent reduction

Safety and Efficacy for Home Use Laser Therapy

Despite the well-documented effectiveness of light therapy, many veterinary practices are not able to fully utilize the modality for their patients' most amenable conditions such as pain management, inflammation and wound healing. Elder dog and cat populations have grown significantly because of improved care and diet. But as a result, osteoarthritis with its attendant pain and stiffness is generally now the most prevalent condition 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 of pain and stiffness and to upregulate metabolic processes at the cellular level in the respiratory chain of mitochondria.

Laser therapy continues to grow due in part to more clients' concern over both short and long term effects from prolonged use of anti-inflammatory and pain medications. Conversely, laser therapy has no known side effects, only restricted during pregnancy or in the presence of cancer.

There are many lasers on the market that are currently used for administering laser therapy. However, all Class IV and IIIB lasers are required by OSHA regulations to install safety measures such as blacked out windows in dedicated treatment rooms with inadvertent entry alarm systems on their doors and laser devices and of course protective eyewear. Ultimately, Class 1M laser devices are cleared as equivalent to 'over-the-counter safe'. This is due to their extremely high power peak, but very short pulse durations measured in nanoseconds. No special hazard precautions are required for use of these devices.

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Conclusion

Class IV is not a technology or a measure of efficacy; it is a hazard classification, as defined by FDA. Class IV lasers do not work on the same pathways that low level laser and photobiomodulation work. In addition, a Class IV laser is not qualified to be termed as photobiomodulation because it is a thermal modality. Laser therapy as it relates to pain management and physical rehabilitation, is not a thermal modality, and it has never relied on heat to be efficacious. Heat in general can be therapeutic, but heat from a laser is not. Heat from a laser is an unwanted, inefficient and potentially dangerous side effect of a laser's wavelength being unable to penetrate the skin barrier. Class IV lasers elevate skin temperatures quickly, but studies show heat from laser also produces excessive reactive oxygen species, which has been proven to be cytotoxic. The excessive doses needed to get light to the target tissue, may well be creating this heat, unknown and undetectable by physician or patient, unless there is a cross-over from warmth to discomfort. The apoptosis pathway is triggered never the less as temperatures approach 42° C. Finally, Class IV laser research lacks inclusion in any systematic review with meta-analysis, the highest level of research, because it produces heat and cannot be sufficiently blinded for double-blinded, placebo-controlled randomized clinical trials.

Multi Radiance is an innovative and impressive technology, designed specifically for laser therapy and thoroughly validated and optimized (see Appendix A). The technology is a combination of super pulsed laser (GaAs 905 nm), infrared and red LEDs (875 nm and 660 nm) for enhancing ATP production, stimulating NO release and activating ROS as validated by the Pillars "Proof of Concept" studies completed during 2012-2014. Each wavelength and light source creates a synergistic effect when combined, for a summated effect greater than any of them separately. The concurrent multiple wavelengths span the entire therapeutic light spectrum to reach varying depths of penetration while creating the first unique nonthermal 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.

Practitioners and clinicians are invited to review not only the text of this paper, but also the graphs and especially the research study references from which it is derived. The true efficacy and outcomes, positive and negative produced by the use of laser and LEDs are better understood as a consequence of recent and repeatedly confirmed research. Historically, established paradigms are often dismantled in the face of overwhelming evidence as research improves. This Veterinary Pillars Paper is an invitation to all to investigate, corroborate and compare laser classifications based on the highest levels of evidence: peer-reviewed published studies. It represents a sincere effort to separate hyperbole and anecdotal from evidence based conclusions.

Multi Radiance is a global leader in therapeutic lasers, selling thousands of units each year. Our goal is to set new standards for the industry by expanding research, education and the understanding of light-based therapies in new and novel areas of medicine where adequate treatments may not exist. Extensively tried and tested over 20 years, the MR4 and TQ product lines deliver the most reliable and clinically significant results available. Multi Radiance is peer-reviewed and practice proven.

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Jennifer Kasten, DVM
Jennifer Kasten, DVM obtained her veterinary degree from The Ohio State University. She completed a rotating internship at Peterson and Smith Equine Hospital in Ocala, Florida, and additional training in veterinary anesthesia and analgesia at North Carolina State University. Her research has focused on anesthesia and sedation, and canine infectious disease prevention. She currently works as an Interactive Medical Editor for Brief Media, the publisher of Clinician's Brief, and as consultant for Multi Radiance Medical. Dr. Kasten is an active alumna volunteer at Ohio State's College of Veterinary Medicine and a member of the scholarship committee of the American Veterinary Medical Foundation.

Douglas Johnson, ATC, EES, CLS
Doug Johnson is a certified athletic trainer with over 20 years of clinical/industrial experience. 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. He is the Senior Vice President, Clinical and Scientific Affairs at Multi Radiance Medical and is involved in numerous research studies on the effects of super pulsed laser in sports performance and recovery, neuromuscular conditions, ophthalmology, and veterinary science. He is the clinical advisor to Laser Therapy U and elected to the Board of Directors of the North American Association for Light Therapy (NAALT).

Ernesto Cesar Pinto Leal-Junior, Prof. Ph.D., M.Sc., PT
Ernesto Cesar Pinto Leal-Junior, PT, PhD has a bachelor's degree in Physical Therapy from 2002 in Brazil. In 2004 he got received 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 at 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 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 and he acts as area editor of Brazilian Journal of Physical Therapy.

His 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.

Currently Dr. Leal-Junior has almost 100 scientific papers published, more than 70 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.

Since January 2015, Dr. Leal-Junior is a recipient of the Research Productivity Award given by Brazilian Council of Research and Development. He has been granted by Brazilian research agencies and by private companies with more than $1,000,000 USD in grants and scholarships.

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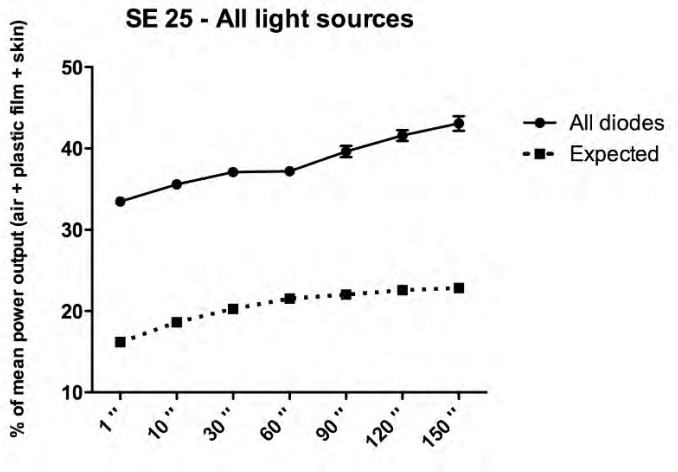
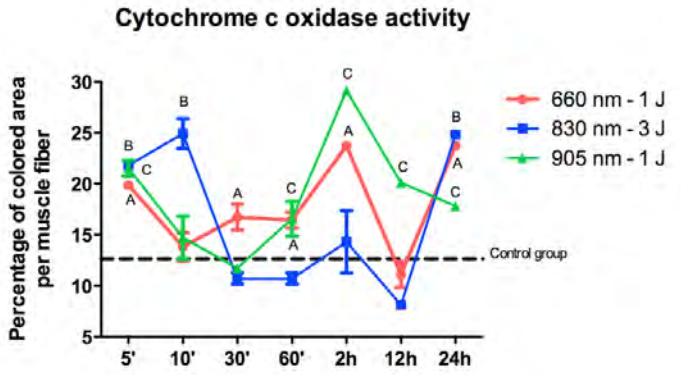
Appendix A

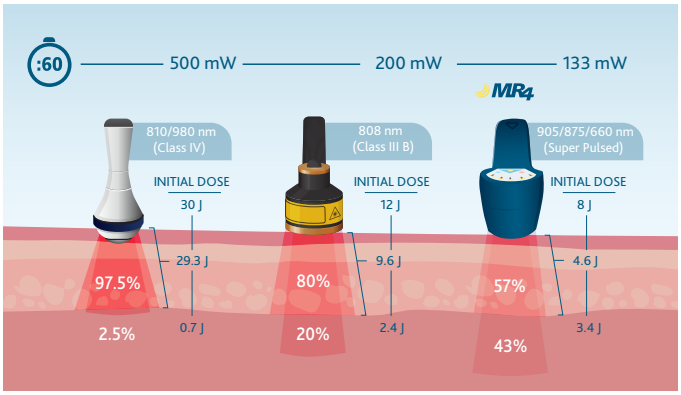
Proof of Concept and Review of the Pillars Paper and Comparative Pillars Paper



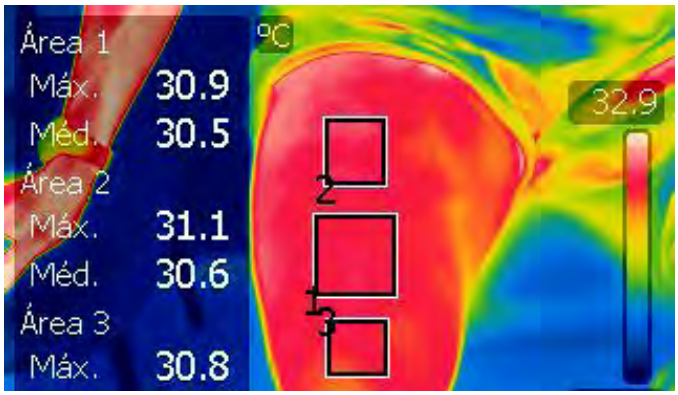
Leal-Junior et al. studied the effects of depth of penetration with multiple wavelengths to establish how various wavelengths and light sources interact when applied concurrently through the skin. They found when multiple wavelengths are combined, there Is a 100% increase in the available light below the skin and confirms the presence of synchronicity between wavelengths or the "Triple Cascade Effect"



Albuquerque-Pontes et al. investigated the effect of different wavelengths on Cytochrome C Oxidase and demonstrated that multiple wavelengths can prolong the time profile Activation of CCO with much smaller doses delivered across many different wavelengths with much lower average powers than one single wavelength of higher power



Simply penetrating the skin barrier cannot be compensated by a higher power output, it will just cause light to be absorbed superficially more quickly, leading to greater heat generation, especially if the wavelength selected possesses a weak penetration profile. Here, there is 5 times the light reaching deeper target tissue with 75% less power at the surface. The depth of penetration depicted here are based on research studies: Anders et al., Joenson et al., and Leal-Junior et al.



Grandinetti et al. concluded that the concurrent use and combination of super pulsed lasers, and red and infrared LEDs is safe and can be used regardless of degree of skin pigmentation without concern of damaging thermal effects to the skin. The researchers concluded also that the effectiveness seen in the three prior clinical trials tested with the same device and parameters is the result of a desirable photobiomodulatory effect and not related to superficial tissue heating.

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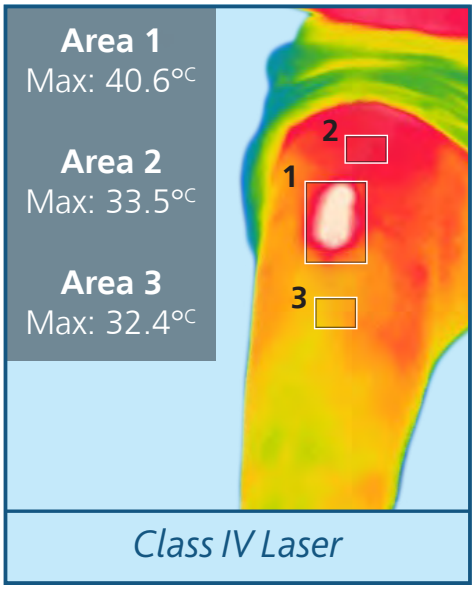
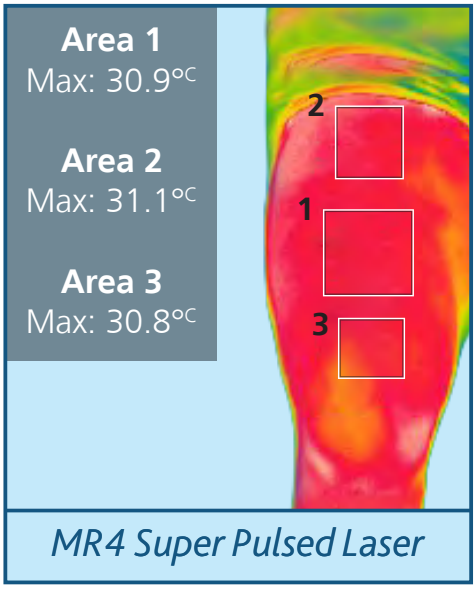
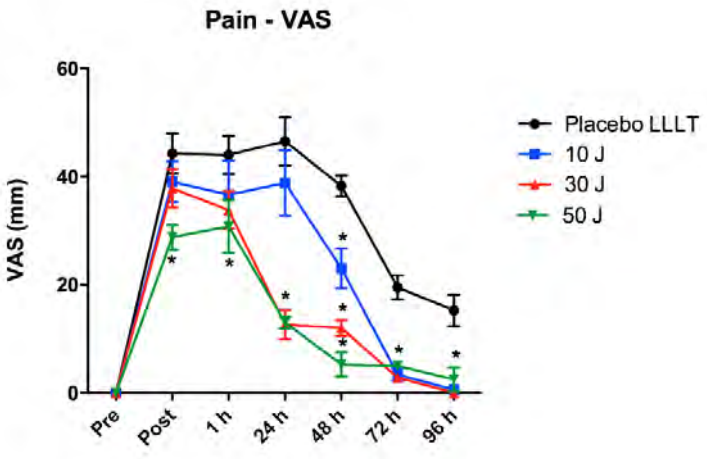
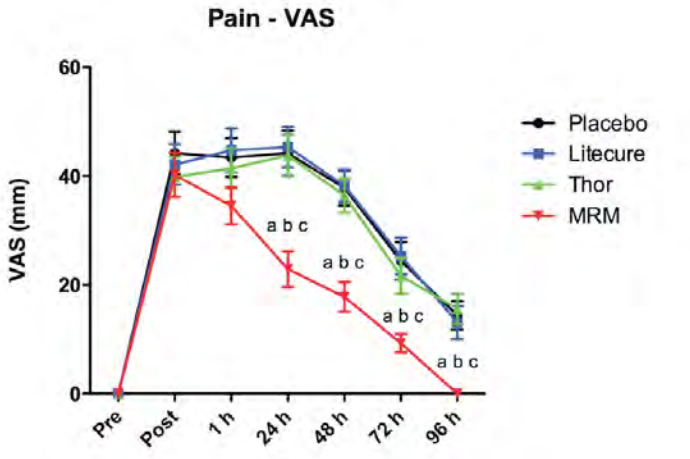




Grandinetti et al. performed a thermal profile on the Multi Radiance LaserShower LS50. At all doses, the MR4 Laser did NOT increase the skin temperature to the same levels reported in prior studies that could affect patient safety and comfort. Depicted here on the right is the homogenous nature of the Multi Radiance Laser and on the left the raised skin temperature and creation of "Hot Spots" in the tissue treated with Class IV Laser. These pictures were taken with a FLIR thermographic camera in the Laboratory of Phototherapy in Sports and Exercise in 2015





On the left, Leal-Junior et al. validated the proper dose to control VAS (Pain) Levels. While all doses controlled VAS better than placebo, the 50J was determined best.

On the right, an independent study by De Marchi et al. validated Multi Radiance Laser Technology for controlling VAS and also compared it to a Class IIIB (Thor Photomedicine) and Class IV (LiteCure). The MRM technology outperformed both Class IIIB and Class IV lasers in controlling VAS pain levels.

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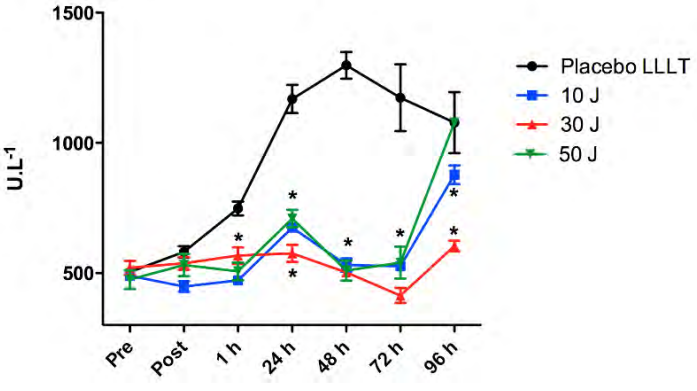
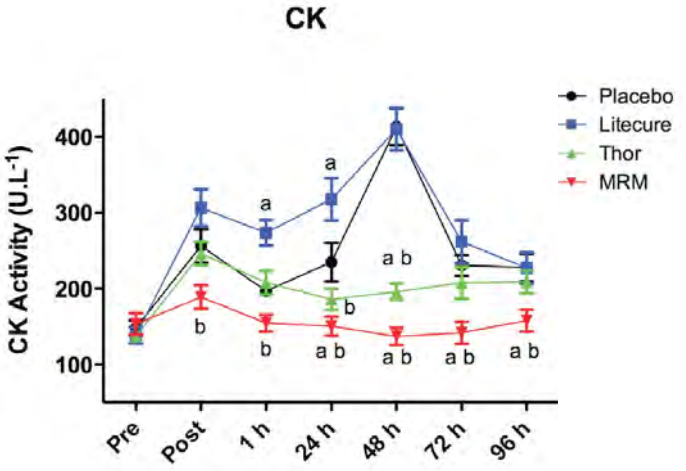
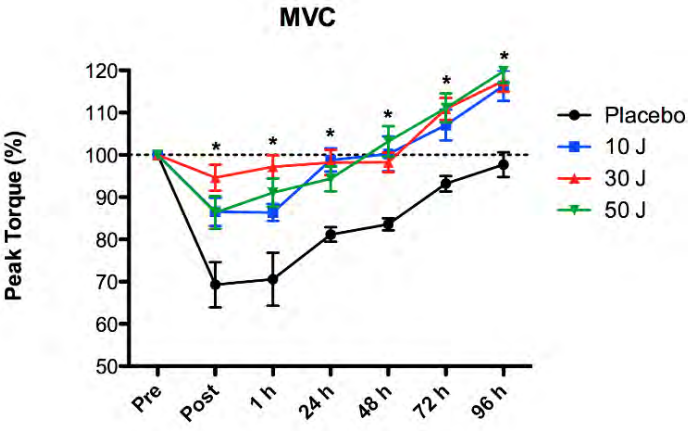
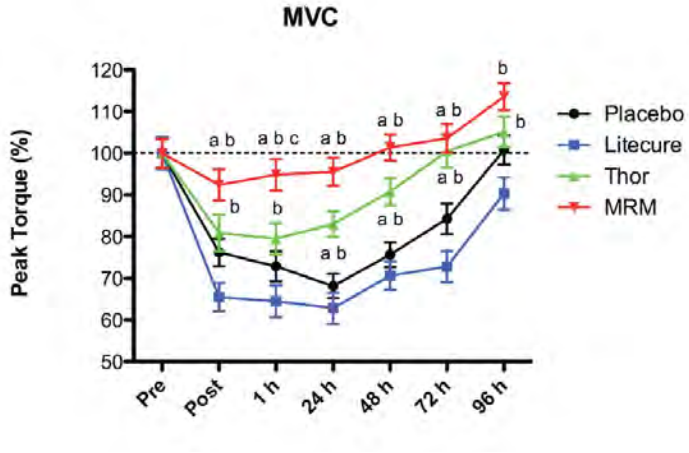




On the left, Leal-Junior et al. validated the proper dose to control Creatine Kinase (CK) Levels. These are biomarkers that indicate muscle damage (and inflammation for Veterinary). While all doses controlled CK better than placebo, the 30J was determined best.

On the right, an independent study by De Marchi et al. both validated Multi Radiance Laser Technology for controlling CK levels but compared it to a Class IIIB (Thor Photomedicine) and Class IV (LiteCure). Not only did MRM technology outperform Class IIIB and Class IV lasers in controlling CK levels, the Class IV LiteCure Laser performed worse than the placebo. This indicated that the Laser induced muscle damage and the authors called for more research in this area to determine why applying Class IV laser did more damage than doing no treatment at all.





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 IIIB (Thor Photomedicine) and Class IV (LiteCure). The MRM technology outperformed both Class IIIB and Class IV lasers in controlling MVC Peak Torque %. As with CK levels, MVC Peak Torque % using a Class IV LiteCure Laser performed worse than placebo.

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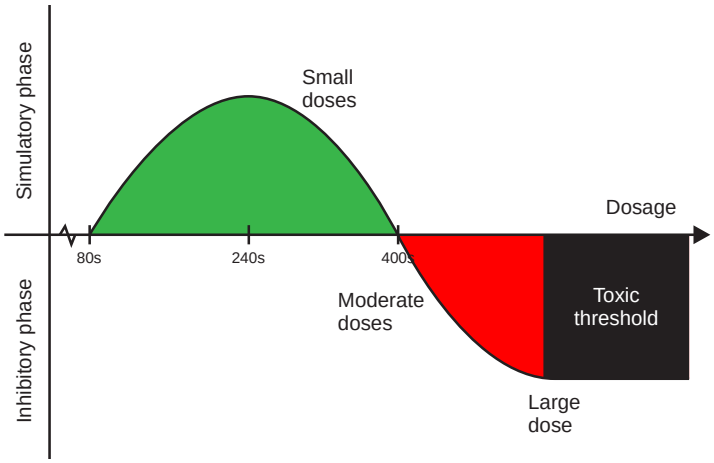
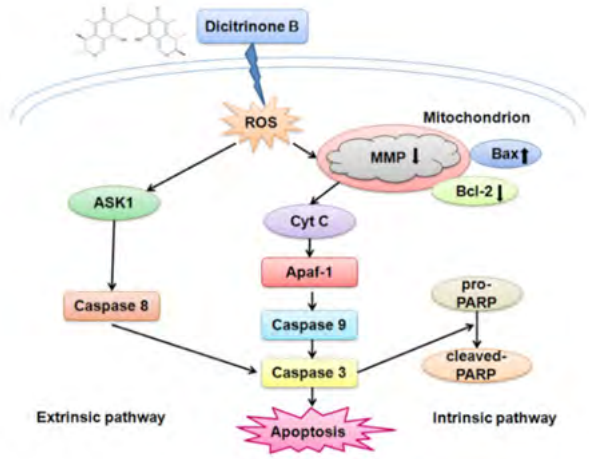
Appendix A

Proof of Concept and Review of the Pillars Paper and Comparative Pillars Paper



Leal-Junior et al. validated the dosimetry curve of a Multi Radiance LS50 LaserShower at 250 Hz. For the first 80s, there is no response. From 80s to 400s the response is stimulatory until after 400s when it becomes inhibitory. It is important to note that the LS50 cannnot achieve the Toxic Threshold of Photocytotoxicity, but Khan et al. determined that Class IV lasers can and do as part of the ATF4 apoptosis pathway. The authors found "we noted that surface temperature (45 °C) and treatment time (30 sec) correlated with significant skin irrespective of skin color and conventional laser treatment parameters namely, damage irradiance and fluence."



Isman et al., found evidence that the use of 980nm Diode laser caused increased expression of TRPM4 and TRPM7 which are responsible for stimulation of apoptotic pathways of cell death. Khan et al., observed that the larger doses provided by Class IV lasers generates heat and ROS damage induced ER stress-mediated by Activation Transcription Factor 4 (ATF-4) and Heat Shock Protein 70 (HSP70) resulting in autophagy. These observations suggest Laser-generated heat (upstream) inactivates ROS scavengers that act along with dose-dependent ROS (effector) generation to result in phototoxic tissue damage.

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