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Contraindications, Special Considerations, and Precautions

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Introduction

Since Endre Mester and his colleagues first reported what we now know as photobiomodulation (PBM) in 1968 (Mester *et al.*, 1968), those using lasers for therapeutic purposes have sought to use them safely. Researchers, industry, and laser therapists have published contraindications for laser therapy in an effort to "do no harm." Texts and journal articles have published lengthy lists of contraindications (Houghton *et al.*, 2010; Navratil and Kymplova, 2002; Tuner and Hode, 2010), some of which have been reproduced in veterinary therapy laser user manuals.

Significant inconsistency remains among the recommendations in publications, texts, and user manuals. The historical contraindications for PBM have been not been appropriately re-evaluated in light of the significant number of publications that have appeared as laser therapy has become more widely used and analyzed in numerous bench-top studies, animal-model studies, and clinical trials. Some conditions originally considered contraindication for PBM now require special consideration before treatment. Some simply require precaution when treating. Other conditions are no longer contraindications.

Proper training is a requirement for treating veterinary patients with a therapy laser. Only with proper training and knowledge can contraindications, special considerations, and precautions be evaluated and appropriately applied in each patient's treatment.

Contraindications

The list of absolute contraindications for exposure to therapeutic laser light is remarkably short, with only one item (Box 7.1).

Eye Exposure

The one absolute clinical contraindication for laser therapy is direct or reflected exposure through the pupil on to the retina. The hazards inherent in laser interaction with ocular structures are the historical basis for laser classifications by regulatory bodies, and present the greatest threat to the laser therapist, support staff, patient, and those who accompany the patient.

As is well addressed in Chapter 4 and in international and national safety standards (ANSI, 2011; IEC, 2014; OSHA, n.d.; Standards Australia, 2004), it is mandatory that eyes be protected by wavelength-specific safety eyewear or other shielding devices. Safety eyewear for humans will be supplied by any responsible veterinary therapy laser manufacturer. The patient's eyes can be protected by wavelength-specific goggles made for animals, dark soft Elizabethan collars, or covering with a dark cloth or a hand. The patient should not be allowed to investigate the target area while the treatment is being administered. Food treats or attention should be used to distract the patient, or restraint, when required.

One can adapt the environment in which the therapy laser is used to reduce the possibility of direct or reflected accidental laser beam exposure of eyes. Reflective surfaces, like stainless steel veterinary treatment tables, should be covered with patient-comfortable, non-reflective material. Mirrors, jewelry, and other potential sources of reflected laser energy must also be evaluated for potential harm.

Optical exposure is a stringent contraindication. The hazard comes from the therapy laser beam penetrating the cornea and pupil, and being focused by the lens on the retina. Scattered photons reaching the retina after transmission through other tissues do not pose an optical hazard. Thus, careful laser therapy application to

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Box 7.1 Laser therapy contraindications, special considerations, and precautions.

Absolute Contraindication

- Eye exposure

Special Considerations

- Locally injected medication
- Malignancy
- Pregnancy

Precautions

- Active epiphyses
- Hemorrhage
- Testicles
- Thyroid gland

False Contraindications

- Hyperpigmentation and tattoos
- Implants
- Microbial infection
- Photosensitizing medications

periorbital tissues is possible, as long as direct or reflected beam penetration through the pupil is avoided.

Special Considerations

Historically, a lack of knowledge and a healthy dose of prudence resulted in a long list of conditions being considered contraindications to laser therapy. Increased knowledge of the mechanisms of PBM brings an increased understanding that most of those conditions are not absolute contraindications. Rather, some are conditions that merit special consideration before being treated (see Box 7.1).

Patients with special consideration conditions will most often not be appropriate candidates for therapy. These are patients with conditions for which the risk of laser therapy, or the perceived risk, outweighs the benefit. Properly trained and knowledgeable veterinary laser therapists will evaluate each patient, communicate the special considerations to the patient's owner, obtain owner consent, and then deliver laser therapy treatment only when appropriate.

Locally Injected Medication

Laser therapy should not be applied over local vaccine or medication injection sites until sufficient time has passed for the injected substance to be absorbed and translocated from the site. Laser-induced vasodilation may alter pharmacologically ideal absorption and translocation rates, and no information exists about how various wavelengths of light might interact with vaccine components or medications.

If an injection is going to be made, and the area is going to be treated with laser therapy, first treat with laser therapy, and then administer the injection.

A good understanding of the pharmacodynamics of any vaccine or medication will help the veterinarian properly schedule therapy laser treatments. If, for example, a medication administered by intramuscular injection induces a myositis, and if that medication is renally cleared in 24 hours, then laser therapy of the myositis is appropriate after 24 hours.

Malignancy

A significant number of contradictory data exist concerning the effect of laser therapy on malignant tissue.

Most of the data come from *in vitro* studies using malignant human cell lines.

Using various wavelengths and parameters, laser application has been demonstrated to induce increased proliferation in human leukemic cells (Dastanpour *et al.*, 2015) and increased proliferation and invasion in human oral squamous cell carcinoma (SCC) cells (Gomes *et al.*, 2014). Seemingly contradictory is the demonstration of laser application having no significant effect on human breast adenocarcinoma cells (Cialdai *et al.*, 2015) and having a selective cytotoxic effect on human oral cancer cells (Liang *et al.*, 2015). A recent study analyzed the effect of PBM on the modulation of the osteoclastogenic potential of a cell line derived from human lingual SCC (Dias Schalch *et al.*, 2016). Using parameters for mucositis treatment, the study demonstrated a reduced osteoclastogenic effect on the tumor cells and suggested that PBM might represent a potential useful side effect while treating mucositis.

To date, no similar studies have been conducted using malignant cells from animal models. The effect of laser therapy on the malignant tissue of veterinary patients is not known. Until data specific to veterinary species are available, laser therapy should not be applied over a malignancy or the surgical site from which a malignancy has been removed.

Special consideration should be given to a surgical site from which a malignancy has been removed and surgical margins have been submitted for histopathological review. A positive margin report is an obvious contraindication for laser therapy and an indication for further surgical resection. Less obvious is whether laser therapy is appropriate after a negative or clear margin report. In generating negative margin reports,

pathologists look at a very small percentage of the entire margin, and there is often not a standard definition of how wide a negative margin has to be. Thus, even with a negative margin report, a possibility remains that some malignant cells have not been removed. That possibility should be discussed with the owner before instituting laser therapy.

Consideration must also be given to the safety of treating sites in close proximity or distant to a malignancy. A pilot study indicated an improved quality of life when PBM was used in the management of radiation dermatitis in human breast cancer patients (Censabella *et al.*, 2016). Though PBM does result in some systemic effects, current data indicate it is safe to apply laser therapy to veterinary patients in areas distant to known malignancies. The safety of treating at a distant site is illustrated by the use of laser therapy to treat chemotherapy-induced oral mucositis in human cancer patients (Ottaviani *et al.*, 2013).

Another special consideration regarding laser therapy and malignancy exists for terminal veterinary patients. PBM can be effective in reducing the pain and inflammation in tissue around a malignancy, so it should be considered a part of hospice management for terminal cancer patients. Owners should be involved in the decision to add laser therapy for pain management in terminal malignancies, after being informed about the potential effect on the malignancy. Anecdotal reports from practitioners support the concept that laser therapy can increase the duration and quality of the lives of veterinary hospice patients with terminal malignancy.

The special considerations required for the application of PBM in the presence of malignancy are very likely to change as further evidence emerges. A 2012 systematic literature review presented existing data on the potential application of PBM in the treatment of solid tumors (Santana-Blank *et al.*, 2012a). This review proposed that PBM might help restore homeostasis and homeokinesis in cancer patients. It suggested that by re-establishing physiological rhythms and inducing physiologically reparative effects for disease reversal in cancer and other complex diseases, PBM might, with minimal or no adverse effects, provide significant improvements in quality of life, even in patients with advanced neoplasms.

In a more recent publication, Santana-Blank *et al.* (2016) described what has been a paradigm shift or "quantum leap" in the understanding and use of light. Based on existing evidence, they argued that PBM can raise the standard of care and improve the quality of life of patients with cancer and other complex diseases. They noted strong arguments made within the past few years for a new understanding of the role of PBM in the treatment of cancer (Karu, 2010; Lanzafame, 2011; Santana-Blank *et al.*, 2012b).

Pregnancy

Applying laser therapy over a gravid uterus is almost always listed as a contraindication. The historical basis for pregnancy being a contraindication is lack of knowledge of the potential effect on the fetus, in addition to studies demonstrating changes in chicken embryo tissue after application of visible red laser wavelengths through a window opened in the eggshell (Avila *et al.*, 1999).

A rational analysis would indicate that fetal tissue within a gravid uterus will not be harmed by visible or near-infrared light photons. These wavelengths lack any mutagenic or teratogenic effect. Further, the fetus is well protected from exposure to photons, being surrounded by a significant thickness of tissues rich in the chromophores that most readily absorb the wavelengths being used.

Yet, despite evidence to the contrary, unless a special consideration exists that warrants direct treatment over a gravid uterus, the prudent veterinary laser therapist will avoid such treatment. As with some other modalities used during pregnancy, no proof exists of potential harm to the fetus. But, no proof exists that there is not a potential harm. Absence of proof does not legally constitute proof of absence. Thus, if laser therapy is applied over the gravid uterus, and an unrelated pregnancy complication or fetal deformity occurs, the burden of proof will be on the veterinarian to demonstrate that laser therapy did not cause the complication (Tuner and Hode, 2010).

A valid consideration is whether pregnant veterinary laser therapists (or other pregnant females present during treatment) are at risk. Clothing reflects, scatters, and absorbs visible and infrared photons, significantly reducing the number reaching underlying skin. Thus, clothing gives an additional layer that blocks photons from reaching the fetus. There is no evidence that the well-protected fetus of a pregnant and clothed female is at risk during a veterinary therapy laser application.

Precautions

Veterinary patients often present with conditions mentioned as contraindications for laser therapy for which strong evidence now indicates the risk, or the perceived risk, is significantly outweighed by the benefits of therapy. These conditions require precautions in prescribing and administering laser therapy (see Box 7.1).

Active Epiphyses

Epiphyses and open fontanels have been listed as contraindications because these are areas of rapid growth, with rapidly dividing cells. The reasoning has been that if

metabolic rate is increased by laser therapy, and osteogenesis is stimulated, then perhaps premature closure or asynchronous bone growth might occur.

Dozens of studies demonstrate that laser light has a stimulatory effect on osteogenesis (Jawad *et al.*, 2013; Son *et al.*, 2012). Yet, confusing data exist about the effect of laser therapy on active epiphyses. Studies have demonstrated different effects depending on wavelength and different treatment parameters in animals.

Daily application for 21 days of 10 J/cm^2 of 830 nm laser light to the distal epiphysis of rat femurs negatively influenced growth plates and reduced longitudinal length (Oliveira *et al.*, 2012). Application every other day for 20 days of 5 and 15 J/cm^2 of 830 nm laser light induced changes in epiphyseal cartilage, and increased the number of chondrocytes present, but the changes were insufficient to induce changes in bone length (Cressoni *et al.*, 2010). Daily application for 10 days of 4, 8, and 16 J/cm^2 of 670 nm laser light induced no changes in the epiphyseal cartilage or final bone length of rat tibias (de Andrade *et al.*, 2012).

Common to these studies is multiple applications of laser light over a period of several weeks. What these studies do not suggest is that application of laser therapy over a few days, for acute conditions in the area of active epiphyses, will induce the same negative consequences.

Prudent application of laser therapy, several times over 3–4 days, to an acute epiphysitis would be below the parameters used in the studies mentioned, and is indicated. Prolonged and repeated treatment over multiple weeks is not indicated.

Another consideration is the possible effect that laser therapy will have on an epiphysis if applied in close proximity. Though systemic effects are noted with laser therapy, animal studies indicate that while there is a local biostimulative effect on bone in the area being treated, the effect is not observed distant to the treated area (Batista *et al.*, 2015).

Hemorrhage

It has been clearly demonstrated, using a variety of wavelengths, energy densities, and delivery modes, that laser therapy induces a transient vasodilation (Chung *et al.*, 2012; Larkin *et al.*, 2012; Maegawa *et al.*, 2000). Since any induced vasodilation is unwanted during active hemorrhage, laser therapy should not be applied to tissue that is bleeding.

This precaution does not apply to tissue in which active hemorrhage is no longer present. No data suggest laser therapy will reactivate hemorrhage. Anecdotal reports from veterinary practices using laser therapy during and after invasive procedures, and for treatment of wounds, confirm that hemorrhage is not reactivated once hemostasis has been achieved.

Testicles

Though application of laser therapy to the testes has been listed as a possible contraindication in some sources, treatment in the area of the testes and of scrotal skin should be considered safe. The wavelengths of light used for veterinary laser therapy are not mutagenic.

In vitro studies have demonstrated increased motility in human sperm after irradiation with 830 and 905 nm laser light (Firestone *et al.*, 2012; Salman *et al.*, 2014). In an *in vivo* study using an animal model, a cumulative dose of approximately 28 J/cm^2 of 830 nm laser light over 15 days resulted in increased spermatogenesis, while a cumulative dose of approximately 47 J/cm^2 over the same time had a destructive effect on the seminiferous epithelium (Taha and Valojerdi, 2004).

These studies suggest that normally recommended doses of laser therapy light applied to the skin of the scrotum or the tissues around the testicles will, at worst, increase spermatogenesis and sperm motility. They also suggest that excessively high doses should not be applied directly into the testicle.

Thyroid Gland

Early animal studies on the effect of laser irradiation of the thyroid gland demonstrated increased mitotic activity of follicular cells and changes in the thyroid parenchyma (Parrado *et al.*, 1990, 1999). Using 904 nm laser light, these studies delivered cumulative doses of up to 140 J/cm^2 over 10 sessions. Understandably, reports like these suggest that laser therapy application over the thyroid glands should be contraindicated.

Subsequent studies indicated that lower total doses, delivered with fewer applications, result in no histological changes in the thyroid parenchyma. Three daily applications of 780 nm laser light at 4 J/cm^2 produced no morphological alteration in the thyroid glands of mice (Azevedo *et al.*, 2005). This study also demonstrated that irradiation of the thyroid has a stimulatory effect on thyroid hormone levels.

Even more recent studies suggest that laser therapy can be used for chronic autoimmune thyroiditis in humans, reducing dependence on medication (Höfling *et al.*, 2010, 2013).

An objective analysis indicates that repetitive, high-dose treatment directly over the glands should be avoided. It also indicates that occasional inadvertent exposure of the thyroid glands when treating nearby tissue is not contraindicated.

As more is learned about dosing, frequency of treatment, and effect on the thyroid gland in animal-model studies, it is possible that laser therapy may be indicated for veterinary species that experience reduced thyroid function.

False Contraindications

Conditions once thought to be contraindications for laser therapy that have been clearly disproved are false contraindications (see Box 7.1). Veterinary laser therapists should be able to explain to patients' owners why these conditions are no longer contraindicated.

Hyperpigmentation and Tattoos

Increased presence of pigments in the form of melanin or tattoo pigment is not a contraindication for laser therapy. Increased pigments will result in more superficial photon absorption, so when pigments are increased, treatment parameters need to be adjusted accordingly (Anderson and Parrish, 1981).

Patients with darker skin and hair coats should be treated with longer wavelengths in the therapeutic spectrum when possible, and the total dose conditions are treated with should be increased to ensure proper dosing for deep-tissue conditions. When using higher power density, monitoring the patient's skin temperature with a trailing finger is good practice. If a temperature other than a pleasant, gentle warming is detected, the speed of movement of the handpiece should be increased. Faster movement of the laser beam across the surface of the tissue can help avoid accumulation of unpleasant warmth, even when using veterinary therapy lasers that deliver a higher power-density laser beam.

Implants

Therapy laser wavelengths do not have a detrimental effect on metal or synthetic implants, suture material, or tissue adhesives used in veterinary medicine. Use when implants are present is not contraindicated.

PBM has been demonstrated to improve the health of soft tissue around implants in a number of animal models and in human dental patients (Aoki *et al.*, 2015; Tang and Arany, 2013). Since implant success is dependent on the health of the surrounding soft tissue, laser therapy may actually improve the chances of implant success.

The presence of a reflective metal implant does change the recommended parameters of treatment when the implant is only covered by a thin layer of tissue. Since the implant will reflect photons back into the overlying tissue, any dose delivered to the overlying tissue should be reduced. In most cases, this is accomplished simply by delivering only a small amount of the entire laser treatment over the implant.

Microbial Infection

In vitro, some wavelengths of light have been shown to stimulate the growth of cultures of some bacterial species and to inhibit others (Nussbaum *et al.*, 2003). Reliance on this information would indicate that microbial infection is a contraindication for laser therapy. On the contrary, however, other studies indicate that laser therapy, when applied *in vivo*, has a variety of immune-stimulating responses that help overcome microbial infection.

An animal-model investigation into the PBM effects of 1072 nm light on the immune response involved in antibacterial and wound-healing processes (Lee *et al.*, 2011) demonstrated enhancement of cutaneous immune response and higher vascular endothelial growth factor (VEGF) levels associated with more favorable clinical outcomes.

A study involving human patients showed the positive fungicidal effects of 830 nm laser light on oral stomatitis in a clinical setting (Maver-Biscanin *et al.*, 2004). Following laser irradiation at both 685 and 830 nm, statistically significant effects were observed *in vitro* on the turbidimetric growth kinetics of *Candida albicans* cultures and *in vivo* on the survival rate of infected mice (Seyedmousavi *et al.*, 2014).

In an animal-model study to see whether 780 nm laser light would stimulate host immunity in fighting fungal infection, neutrophils from mice that received laser therapy were more active metabolically and had higher fungicidal activity (Burger *et al.*, 2015).

A study to investigate the effects of laser therapy on a rat model of mastitis demonstrated that the number of polymorphonuclear cells in the mammary alveolus and the myeloperoxidase activity (an indicator of mastitis in dairy cattle) were decreased after therapy. The authors suggested that laser therapy might be beneficial in decreasing the somatic cell count and improving milk nutritional quality in cows with an intramammary infection (Wang *et al.*, 2014).

In vivo, PBM produces a complex, immune-enhancing effect that improves response to microbial infection. Laser therapy is indicated in microbial infections in veterinary patients.

Photosensitizing Medications

Numerous medications, both topical and systemic, are reported as being photosensitizers. A photosensitivity occurs when a chemical in a medication is photoactivated by light and a cutaneous manifestation arises. It has been suggested that photosensitization might be possible with the wavelengths and treatment parameters used in laser therapy, and thus treatment of both human and veterinary patients on these medications has historically been contraindicated.

In 2014, a review of publications for any report of adverse effects from laser therapy in patients on photosensitizing medication was conducted (Kerstein *et al.*, 2014). Only four publications linked the search term

"laser therapy" with multiple terms for photosensitive reactions. No adverse effects were reported.

In the absence of any published evidence that laser therapy-induced photosensitization occurs in veterinary patients, this should be considered a false contraindication.

Conclusion

The historical contraindications for laser therapy are inconsistent, inaccurate, and outdated. Knowledge from 5 decades of research and clinical application has rewritten the recommendations against using laser therapy on many conditions and anatomical sites once thought to be contraindicated. Direct eye exposure remains an absolute contraindication for all veterinary providers, patients, and owners. Some historical contraindications now require special consideration before treatment can be indicated, others simply require precaution when treating, and still others have been demonstrated to be false. Practitioners are encouraged to update their use of laser PBM with current knowledge about contraindications, special considerations, and precautions.

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