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# Laser therapy (photobiomodulation): An integral part of wound management

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he "flight response" of our equine patients predisposes them to traumatic injury. Patients frequently present with a wide variety of wounds: simple lacerations, penetrating and contaminated, degloving distal limb catastrophes, and those lesions that not only involve the dermis but also involve the tendinous, other soft tissue structures, the joints, and bone. The goal in the management of these wounds is to restore these traumatized tissues to normal anatomical activity while leaving as little evidence as possible that they even occurred.

An essential part of any wound management program is the application of laser, photobiomodulation therapy (PBMT). This provides a relief of pain, a modulation to the inflammatory response, and an increase in circulation through physiological and biochemical reactions that result in an accelerated healing process.

### Basic mechanisms of action that allow PBMT to accelerate the healing process

Our patients have a natural response to repair any traumatic insult.<sup>1</sup> This localized and systemic response is divided into four overlapping phases: hemostasis (clotting), inflammation, tissue growth (proliferation), and maturation.<sup>2</sup> The scientific evidence is now understood how PBMT influences each of these phases, in either a supporting or augmented role, or in allowing an acceleration of the healing process.

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### Hemostasis

Never apply PBMT during the initial active hemorrhaging. PBMT results in vasodilation of the vasculature, which may accelerate the hemorrhaging and negate normal clot formation.<sup>3</sup> In an average wound, the initial vasoconstriction only lasts 5 to 10 minutes. This is immediately followed by histamine-induced vasodilation of the vasculature<sup>4</sup> (Stadelmann et al. 1998). Under the influence of histamine, the vasculature also becomes more porous.

Research has shown that laser-irradiated RBL-2H3 mast cells released histamine.<sup>5</sup> The photo-acceptor, cytochrome C oxidase, within the membrane of the mitochondria, absorbs photonic energy, provided by deep penetrating irradiation and initiates mitochondrial signaling. These signals then result in a cytosolic alkalization which causes openings of Ca (2+) channels on the membrane, the transient receptor potential vanilloid (TRPV), and therefore and increased increment of Ca (2+). This increased Ca (2+) consequently facilitates an enhanced histamine release.<sup>6</sup> This porous condition of the vasculature and concurrent release of chemokines by platelet activation attracts and facilitates the entry of inflammatory cells and leukocytes into the wound site, leading to the next phase in the healing process.<sup>7</sup>

### Inflammatory phase

This phase is a complex sequence of biochemical and physiological events. PBMT modulates this phase to prevent suppuration, chronic prolonged inflammation, and excessive fibrosis. PBMT modulates the inflammatory phase through:

- An increased production and release of nitric oxide: a potent vasodilator.<sup>8</sup> This, in conjunction with histamine, increases the porousness of the blood vessels, which facilitates the entry of leukocytes and macrophages into the wound site.
- When immune cells are irradiated with certain wavelengths of light, inflammatory mediators, such as cytokines and chemokines, are released. These mediators regulate the immunological process of inflammation using complex signaling mechanisms.<sup>9</sup>
- Irradiation modulates the inflammatory process by decreasing the levels of inflammatory cytokine IL-1 $\beta$ .<sup>10</sup>

### Proliferative phase

This phase is marked by the formation of fleshy granulation tissue, which includes inflammatory cells, fibroblasts, and neovasculature in a matrix of fibronectin, collagen, glycosaminoglycans, and proteoglycans.<sup>11</sup> During this phase, angiogenesis, fibroplasia (collagen deposition and granulation tissue formation), epithelialization, and wound contraction occur.<sup>12</sup>

Numerous studies have proven PBMT promotes angiogenesis:

- The beneficial effects of nitric oxide to include pain relief, resolution of edema, improved lymphatic drainage, and improved wound healing via angiogenesis.<sup>13</sup>
- Promotion of cardio-protection and angiogenesis following heart attacks in mice.<sup>14</sup>
- An induction of angiogenesis and an improvement in ischemic wound healing. 15
- A determination of a therapeutic dose range to increase blood flow to the biceps brachii muscle of the forearm.<sup>16</sup>

PBMT has a proliferative effect on fibroblasts, keratinocytes, endothelial cells, lymphocytes, muscle cells, and stem cells.<sup>17,18,19</sup> Irradiation of these results in a release reactive oxygen species, culminating in the expression of transcription factors such as NF-KB, which then activate a form of nitric oxide synthase, which leads to proliferation.<sup>20, 21, 22</sup>

PBMT improved the remodeling of the extracellular matrix (ECM) during the healing process in tendons through activation of MMP-2 and stimulation of collagen synthesis.<sup>23</sup> Irradiation maintained human fibroblast viability and increased collagen synthesis *in vitro* utilizing human fibroblast (HS68) cultures.<sup>24</sup>

PBMT aids in the proliferation of epithelial cells during re-epithelialization of the dermis. In a single case study, a patient suffering from thalassemia intermedia with a non-healing ulcer on the ankle was irradiated with a dosage of 17.3 J/cm² daily for two weeks, followed by an average dosage of 6.5 J/cm² for another two-week period. There was immediate re-epithelization and no recurrence in a follow-up six months later.<sup>25</sup>

Wound contraction results from the proliferation and action of differentiated fibroblasts, myofibroblasts, in the granulation tissue, which contain filaments of smooth muscle actin. These filaments in the fibroblasts connect to other fibroblasts and the ECM and contract; pulling the wound margins toward the center. FBMT increases the transformation and proliferation of fibroblasts into myofibroblasts, accelerating wound contraction. This contraction determines the speed of second intention wound healing in addition to the cosmetic appearance of the scar.

### Maturation and remodeling

During maturation, the type III collagen that is prevalent during proliferation is replaced by type I collagen.<sup>27</sup> Originally disorganized collagen fibers are rearranged, cross-linked, and aligned along tension lines.<sup>28</sup> Collagen provides the tensile strength of the wound, and although this period corresponds to the most rapid gain in strength, only 20 percent of the final strength of the wound is achieved in these first three weeks of repair.<sup>29</sup> At this point, collagen synthesis is balanced by collagen lysis; this prevents the accumulation of excessive amounts of collagen and formation of scar tissue.

### Dosing

The anatomical area, the tissues involved, the distance to the target tissues, the age of the wound, the category (opened or closed), and the presence or absence of infection or contamination are unique to each patient and must be considered when determining a therapeutic dose. Therefore, there are no universal dosages. Always treat to effect. There is a wide margin of safety; if too little is administered, there will be no clinical benefit to treatment. The dosages on the following table are only guidelines and each case should be considered individually.<sup>30</sup>

WOUND TYPE	DOSE J/cm²
Superficial: Abrasion, contusion, incision	4 ± 2
Laceration: Sutured	4 ± 6
Laceration: Open	8 ± 12
Laceration: Involving muscle and/or tendon and/or hoof	10 ± 12
Puncture: Superficial, not infected	6 ± 8
Puncture: Infected, muscle, tendon involved	8 ± 12
Chronic or profuse granulation tissue:	10 ± 14

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### Frequency of treatment

Ideally, acute wounds should receive PBMT daily. Once a visible clinical response is noted, therapy sessions will then be spaced out with a day or more between sessions until the wound is completely resolved.

The clinical results achieved through PBMT are cumulative in effect. Progress should be witnessed with each therapy session. If there isn't a clinical response after the second treatment, insure your diagnosis and increase the dosage in small increments to assure a sufficient dosage is reaching the target tissue.

Initially chronic wounds should be treated daily for two to three sessions. These sessions are then spaced out as needed to achieve constant clinical progress. Chronic wounds often receive an initial debridement, which then reclassifies them as an acute wound. The goal for the treatment of these chronic injuries is always complete resolution.

### **Case examples**

#### Case 1

**Presentation:** A 8-year-old warmblood show jumper. Acutely lame after competition.

**Dx:** Core lesion within superficial digital flexor tendon. **PBMT:** 15 J/cm² daily on-contact during Passive range of motion exercises (PROM) for six days. Every other day for another 18 therapy sessions. Hand walking beginning after 6th session. PROM exercises and massage twice/day on most days. Support wrap.

**Recheck, 45 days:** Note normal tissue replacement and lack of any scar tissue.

**Recommendations:** Begin light work. Progress carefully. **Resolution:** At 12 weeks, returned to jumping. At 16 weeks, competed at previous level before injury.

### Case 2

**Presentation:** A 19-year-old trail horse open contaminated laceration that involved the tendon sheaths but not the tendons or joint capsule.

Rx: Standard of care antibiotics, phenylbutazone, tetanus antitoxin. Cleaned, lavaged with sterile saline, and wrapped using a commercial, semi-occlusive, multilayered hydrophilic-gel wound product. PBMT therapy at 12 J/cm² off-contact with a scanning technique encompassing the entire wound including a 3-cm. border along the epithelial margins was initiated on Day 8. PBMT was administered on Days 9, 10, 12, 14, 15, 17, 21, 24, 26, 31, 33, 38, and 43. On Day 12, the saline lavage was replaced by hydrotherapy from the garden hose. Wound was never scrubbed after the initial cleaning and never required debridement.

**Resolution:** On Day 43, the animal was sound with normal range of motion and he resumed his career as a trail horse in the western Canadian Rocky Mountains within one month.

### Conclusion

PBMT is a scientifically proven therapy for accelerating wound healing in any type of equine wound. The addition of PBMT to the standard of care use of antibiotics, lavage, topicals, pain management, drainage, and debridement will return the traumatized area to function faster with less cosmetic disfigurements. •

### REFERENCES

To view references to this article, visit veterinary practicenews.com/ November-2017-Education-Center-Companion-Animal-Health/.

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Post 12 photobiomodulation therapy sessions.



Post five photobiomodulation therapy sessions.



Post 15 photobiomodulation therapy sessions.