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August 10, 2020

College of Veterinarians of Ontario
2106 Gordon Street
Guelph, Ontario N1L 1G6

To:
Jan Robinson, Registrar & CEO: jrobinson@cvo.org
Sarah Kirby, Policy & Project Specialist: skirby@cvo.org

Follow-Up Regarding: CVO Policy and Position Statements on Forms of Energy

Dear Jan & Sarah,

I would like to thank you for hosting and inviting me to participate in the virtual meeting regarding Forms of Energy on July 30th, 2020. The Animal Rehab Division appreciates the opportunity to provide both written and verbal feedback on the Policy and Position Statements.

Further to the discussion on July 30th in regard to animal-specific literature as it pertains to the safety of therapeutic laser and radial shockwave, I have conducted an additional literature search specific to the concerns highlighted in the meeting. As well, I have highlighted the animal-specific literature that was already presented in my first letter as Appendix 1 and 2, and have included them here again for your perusal.

The new **Addendum** to Appendix 1 & 2 that I have provided covers the topic of laser therapy and the concern of an underlying cancer. According to the literature it would appear that laser is safe to use over cancerous lesions. Furthermore, laser therapy may have a beneficial effect on shrinking cancerous lesions. In regard to the literature on *radial* shockwave, I have provided links to two review papers that cite both animal and human literature that facilitate a better understanding of this modality. In Appendix 2 (SHOCKWAVE Safety), I had previously included references for shockwave and it's use in fractures (Wang CJ et al & Wang L et al). These citations are now highlighted for easier reference. Literature in the new Addendum provides additional animal studies regarding radial shockwave and fracture healing. The literature suggests that radial shockwave is not a concern in bone fractures, but rather may be of benefit. Three studies were found that commented specifically on the safety of radial shockwave in animal models. Four studies on radial shockwave were identified that discussed minor adverse events that occurred within their studies as well as tolerance to treatment. There is also a relevant concluding statement regarding use of shockwave before equine competition events.

In regard to the comfort of radial shockwave, please refer to a compilation of videos here included from various canine rehab practitioners across North America to show how un-sedated animals respond to this therapeutic tool.
*** https://youtu.be/rnuUcAwd6Ps***

We believe that 'evidence-informed' practice should be the goal in clinical practice as well as in the creation of policy. In areas where species-specific literature is non-existent, it is prudent to utilize non-species-specific literature or fundamental research as the best 'available evidence' to guide practice and policy. Unreasonably strict adherence to the 'evidence-based' concept would result in may animals (or humans) not being treated at all.

Thank you once again for taking the time to meet with me and other non-veterinarians who practice animal rehabilitation on the matter of forms of energy in animal care.

I look forward to further engagement with the CVO. Please direct your correspondence to me at physio@fourleg.com.

Sincerely,

L Edge Hughes

Laurie Edge-Hughes, BScPT, MAnimSt (Animal Physiotherapy), CAFCI, CCRT
Advocacy Lead,
The Animal Rehab Division of the Canadian Physiotherapy Association

c.c.
Dr. Susan Warren, President & Council: president@cvo.org

ADDENDUM

Laurie Edge-Hughes, BScPT, MAnimSt (Animal Physiotherapy), CAFCI, CCRT
Created for the Animal Rehab Division of the Canadian Physiotherapy Association

Low Level Laser Therapy / Photobiomodulation & Safety re: Cancer

Animal-specific literature

1. Hamblin MR, Nelson ST, Strahan JR. Photobiomodulation and Cancer: What Is the Truth?. *Photomed Laser Surg*. 2018;36(5):241-245. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5946726/

   "Although there are a few articles [of low quality] suggesting that photobiomodulation (PBM) therapy can be detrimental in animal models of tumors, there are also many articles that suggest the opposite and that light can directly damage the tumor, can potentiate other cancer therapies, and can stimulate the host immune system. Moreover, there are two clinical trials showing increased survival in cancer patients who received PBM therapy."

2. Petrellis MC, Frigo L, Marcos RL, et al. Laser photobiomodulation of pro-inflammatory mediators on Walker Tumor 256 induced rats. *J Photochem Photobiol B*. 2017;177:69-75. doi:10.1016/j.jphotobiol.2017.09.011

   "Our results suggest the evidence 1J-35,7J/cm2 treatment was able to produce cytotoxic effects by generation of ROS [reactive oxygen species] causing acute inflammation and thus may be employed as the best energy dose associated with Photodynamic Therapy."

3. Barasch A, Li H, Rajasekhar VK, et al. Photobiomodulation effects on head and neck squamous cell carcinoma (HNSCC) in an orthotopic animal model. Support Care Cancer. 2020;28(6):2721-2727. doi:10.1007/s00520-019-05060-0

   "Our results suggest that photobiomodulation at the utilized parameters does not provide protection to the tumor from the killing effects of radiation therapy."

Human

4. de Pauli Paglioni M, Araújo ALD, Arboleda LPA, et al. Tumor safety and side effects of photobiomodulation therapy used for prevention and management of cancer treatment toxicities. A systematic review. Oral Oncol. 2019;93:21-28.

   "Most studies showed that no side effects were observed with the use of PBMT. The results of this systematic review, based on current literature, suggest that the use of PBMT in the prevention and management of cancer treatment toxicities does not lead to the development of tumor safety issues."

5. Kiro NE, Hamblin MR, Abrahamse H. Photobiomodulation of breast and cervical cancer stem cells using low-intensity laser irradiation. *Tumour Biol*. 2017;39(6):1010428317706913. doi:10.1177/1010428317706913

   "Unlike chemotherapy, photodynamic therapy (PDT) offers a better post-therapeutic life quality without any known side effects. Low-intensity laser irradiation (LILI) and PDT could be used as adjuvant therapy to chemotherapy, radiotherapy, and surgery. It is worth to consider that LILI treatment might have a bioinhibitory effect on breast and cervical cancer stem cells."

6. Brandão TB, Morais-Faria K, Ribeiro ACP, et al. Locally advanced oral squamous cell carcinoma patients treated with photobiomodulation for prevention of oral mucositis: retrospective outcomes and safety analyses. Support Care Cancer. 2018;26(7):2417-2423. doi:10.1007/s00520-018-4046-z

   "This study suggests that photobiolomodulation therapy is a safe clinical modality for prevention of oral mucositis in oral squamous cell carcinoma patients."

Research & arguments for use of photobiomodulation as a treatment for cancer

7. Santana-Blank LA, Castes M, Rojas ME, Vargas F, Scott-Algara D. Evaluation of serum levels of tumour necrosis factor-alpha (TNF-alpha) and soluble IL-2 receptor (sIL-2R) and CD4, CD8 and natural killer (NK) populations during infrared pulsed laser device (IPLD) treatment. *Clin Exp Immunol*. 1992;90(1):43-48. doi:10.1111/j.1365-2249.1992.tb05829.x

8. Santana-Blank LA, Rodríguez-Santana E, Vargas F, Santana-Rodríguez KE. Photo-induced cytomorphologic changes in an advanced cancer phase I clinical trial. Lasers Surg Med. 2002;30(1):18-25. doi:10.1002/lsm.10017

9. Santana-Blank LA, Castes M, Rojas ME, Vargas F, Scott-Algara D. Evaluation of serum levels of tumour necrosis factor-alpha (TNF-alpha) and soluble IL-2 receptor (sIL-2R) and CD4, CD8 and natural killer (NK) populations during infrared pulsed laser device (IPLD) treatment. Clin Exp Immunol. 1992;90(1):43-48. doi:10.1111/j.1365-2249.1992.tb05829.x

10. Santana-Blank LA, Reyes H, Rodríguez-Santana E, Santana-Rodríguez KE. Microdensitometry of T2-weighted magnetic resonance (MR) images from patients with advanced neoplasias in a phase I clinical trial of an infrared pulsed laser device (IPLD). Lasers Surg Med. 2004;34(5):398-406. doi:10.1002/lsm.20068

11. Santana-Blank L, Rodríguez-Santana E, Santana-Rodríguez JA, Santana-Rodríguez KE. Solid tumors and photobiomodulation: a novel approach to induce physiologically reparative homeostasis/homeokinesis-review. J Solid Tumors 2012;2:23–35

12. Tanaka Y, Matsuo K, Yuzuriha S, Yan H, Nakayama J. Non-thermal cytocidal effect of infrared irradiation on cultured cancer cells using specialized device. Cancer Sci. 2010;101(6):1396-1402. doi:10.1111/j.1349-7006.2010.01548.x

13. Zimin AA, Zhevago NA, Buĭniakova AI, Samoĭlova KA. Vopr Kurortol Fizioter Lech Fiz Kult. 2009;(6):49-52.

14. Myakishev-Rempel M, Stadler I, Brondon P, et al. A preliminary study of the safety of red light phototherapy of tissues harboring cancer. Photomed Laser Surg. 2012;30(9):551-558. doi:10.1089/pho.2011.3186

Shock Wave Therapy – review papers, use in fractures, safety, adverse events, & useful commentary

Full Text reviews for reference

1. Wang CJ. Extracorporeal shockwave therapy in musculoskeletal disorders. J Orthop Surg Res. 2012;7:11. Published 2012 Mar 20. doi:10.1186/1749-799X-7-11 https://pubmed.ncbi.nlm.nih.gov/22433113/

2. Lohrer H, Nauck T, Korakakis V, Malliaropoulos N. Historical ESWT Paradigms Are Overcome: A Narrative Review. *Biomed Res Int*. 2016;2016:3850461. doi:10.1155/2016/3850461 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4967434/pdf/BMRI2016-3850461.pdf

Animal studies re: fractures

3. Gollwitzer H, Gloeck T, Roessner M, et al. Radial extracorporeal shock wave therapy (rESWT) induces new bone formation in vivo: results of an animal study in rabbits. *Ultrasound Med Biol*. 2013;39(1):126-133. doi:10.1016/j.ultrasmedbio.2012.08.026

   "This is the first study demonstrating low-energy radial shock waves to induce new bone formation in vivo."

4. Lyon R, Liu XC, Kubin M, Schwab J. Does extracorporeal shock wave therapy enhance healing of osteochondritis dissecans of the rabbit knee?: a pilot study. *Clin Orthop Relat Res*. 2013;471(4):1159-1165. doi:10.1007/s11999-012-2410-8

   "(Low dose) ESWT accelerated the healing rate and improved cartilage and subchondral bone quality in the OCD rabbit model."

5. Schnurrer-Luke-Vrbanić T, Avancini-Dobrović V, Sosa I, Cvijanovic O, Bobinac D. Effect of radial shock wave therapy on long bone fracture repair. *J Biol Regul Homeost Agents*. 2018;32(4):875-879.

   "Conclusively, long bone fracture repair is enhanced by RPWT, suggesting that it strongly stimulates the processes of callus ossification."

6. Buarque de Gusmão CV, Batista NA, Vidotto Lemes VT, et al. Effect of Low-Intensity Pulsed Ultrasound Stimulation, Extracorporeal Shockwaves and Radial Pressure Waves on Akt, BMP-2, ERK-2, FAK and TGF-β1 During Bone Healing in Rat Tibial Defects. *Ultrasound Med Biol*. 2019;45(8):2140-2161. doi:10.1016/j.ultrasmedbio.2019.04.011

"In conclusion, the protocols employed for ESWT and RPWT modulated distinct signaling pathways during fracture healing"

Shockwave and fracture healing (previously presented references) – Animal Models

- Wang CJ, Huang HY, Chen HH, Pai CH, Yang KD. Effect of shock wave therapy on acute fractures of the tibia: a study in a dog model. Clin Orthop Relat Res. 2001;(387):112-118.
- Wang CJ, Huang HY, Pai CH. Shock wave-enhanced neovascularization at the tendon-bone junction: an experiment in dogs. J Foot Ankle Surg. 2002 Jan-Feb;41(1):16-22.
- Wang CJ, Wang FS, Huang CC, et al. Treatment for osteonecrosis of the femoral head: comparison of extracorporeal shock waves with core decompression and bone-grafting. J Bone Joint Surg Am 2005;87:2380–7.
- Wang CJ et al. Extracorporeal shockwave shows regression of osteoarthritis of the knee in rats. J Surg Res 2010, 171(2): 601-608.
- Wang CJ et al. Extracorporeal shockwave shows chondroprotective effects in osteoarthritic rat knee. Arch Orthop Trauma Surg 2011, 131(8): 1547 – 1553.
- Wang CJ et al. Extracorporeal shockwave therapy shows time-dependent chondroprotective effects in osteoarthritis of the knee in rats. J Surg Res 2012, 178(1): 196 – 205.
- Wang L et al. Extracorporeal shock wave therapy in treatment of delayed bone-tendon healing. Am J Sport Med 2008, 36(2): 340 – 347.

Animal studies that comment on SAFETY of RADIAL Shockwave

7. Fu M, Cheng H, Li D, Yu X, Ji N, Luo F. Radial shock wave therapy in the treatment of chronic constriction injury model in rats: a preliminary study. Chin Med J (Engl). 2014;127(5):830-834.

"We observe the effects of RSWT on a NP model induced by chronic constriction injury (CCI) in rats. The safety was assessed through calculating sciatic functional index (SFI). No significant changes of SFI were observed in any groups after repeated sessions of RSWT and no increased pain or other side effects in any animals."

8. Facon-Poroszewska M, Kiełbowicz Z, Prządka P. Systemic inflammatory response to the Radial Pressure Wave Therapy (RPWT) in collagenase-induced Achilles tendinopathy

treated with Adipose Derived Stem Cells or Platelet Rich Plasma. Pol J Vet Sci. 2019;22(4):735-742. doi:10.24425/pjvs.2019.131403

"In conclusion, addition of RPWT to growth factors injections in the treatment of iatrogenic Achilles tendinopathy in sheep did not induce systemic inflammatory response."

9. Abed JM, McClure SR, Yaeger MJ, Evans RB. Immunohistochemical evaluation of substance P and calcitonin gene-related peptide in skin and periosteum after extracorporeal shock wave therapy and radial pressure wave therapy in sheep. Am J Vet Res. 2007;68(3):323-328. doi:10.2460/ajvr.68.3.323

   "To evaluate the effect of focused extracorporeal shock wave therapy (ESWT) and radial pressure wave therapy (RPWT) on immunohistochemical staining for substance P and calcitonin gene-related peptide (CGRP) in the skin and periosteum of sheep. Substance P- and CGRP-containing nerve fibers are not disrupted by EWST or RPWT."

Additional animal studies on RADIAL Shockwave re: efficacy, adverse effects, & relevant comments.

10. Crowe OM, Dyson SJ, Wright IM, Schramme MC, Smith RK. Treatment of chronic or recurrent proximal suspensory desmitis using radial pressure wave therapy in the horse. Equine Vet J. 2004;36(4):313-316. doi:10.2746/0425164044890562

    "Radial pressure wave therapy (RPWT) is a useful treatment modality for chronic or recurrent proximal suspensory desmitis (PSD) when combined with controlled exercise.

    The only adverse effects noted were occasional excoriation of the skin along the line of application of the handpiece and the development of small circular areas of hair loss and subsequent development of white hairs after treatment. These circular areas were often slightly removed from the actual area of treatment. None of the horses deteriorated clinically or ultrasonographically during the trial."

11. Brown KE, Nickels FA, Caron JP, Mullineaux DR, Clayton HM. Investigation of the immediate analgesic effects of extracorporeal shock wave therapy for treatment of navicular disease in horses. Vet Surg. 2005;34(6):554-558. doi:10.1111/j.1532-950X.2005.00087.x

    "To measure the acute analgesic properties of extracorporeal shock wave therapy (ESWT) in horses with navicular disease using objective ground reaction forces (GRF). Single ESWT treatment applied in this manner does not influence lameness in horses with navicular disease.

Clinical relevance: Although many equine regulatory commissions currently ban the use of ESWT before competition, our results suggest that such regulations may be unfounded."

12. Souza AN, Ferreira MP, Hagen SC, Patrício GC, Matera JM. Radial shock wave therapy in dogs with hip osteoarthritis. Vet Comp Orthop Traumatol. 2016;29(2):108-114. doi:10.3415/VCOT-15-01-0017

    "All dogs (n=30) completed the treatment protocol. Six patients had petechiae at the treatment site, but no signs of pain were reported by the operator immediately after treatment. Blind assessment (7 days after the last session) did not reveal superficial signs."

13. Mueller M, Bockstahler B, Skalicky M, Mlacnik E, Lorinson D. Effects of radial shockwave therapy on the limb function of dogs with hip osteoarthritis. Vet Rec. 2007;160(22):762-765. doi:10.1136/vr.160.22.762

    "All the dogs tolerated the treatment well and they did not need to be sedated."

APPENDIX 1

Safety of Laser Therapy

Laurie Edge-Hughes, BScPT, MAnimSt (Animal Physiotherapy), CAFCI, CCRT
Created for the Animal Rehab Division of the Canadian Physiotherapy Association

Background

Low Level Laser Therapy (LLLT), now being termed as photobiomodulation (PBM) is the mechanism by which nonionizing optical radiation from lasers and noncoherent sources in the visible and near-infrared spectral range are absorbed by endogenous chromophores to elicit photophysical and photochemical events at various biological scales, leading to physiological changes and therapeutic effects.(Anders et al 2015) The clinical applications for this tool have evolved tremendously in a number of important areas over the 50+ years since its inception.

Classes of Laser Therapy (Riegel & Godbold 2017)

There are 4 classes of Laser therapy units based on the power of the machine, and more specifically the need for protection to the eyes or skin.

Class 1/ 1M (<0.5 mW)

- Visible & Non-visible
- No eye or skin danger
- Examples: Some pointers, car entry remotes and grocery store scanners for example
- No heating & No healing

Class 2 / 2M (< 1mW)

- Visible
- Safe for short periods of time on eyes and for extended periods of time on the skin
- Examples: Some pointers, grocery store scanners and some measuring devices

Class 3 (1mW – 500mW)

3A /3R <5mW

- Visible & Non-visible
- Pointer lasers

3B >5mW lasers

- Visible & Invisible
- Hazardous to eye (with direct viewing or ‘mirror viewing’)
- Minimal hazard to skin (<1 degree C.)
- Examples: Therapeutic lasers
- Eye goggles recommended

Class 4 (> 500mW)

- **4a (Therapeutic lasers) / 4b (Surgical) *Note, the classifications of 4a and 4b are not ‘officially’ recognized but are ‘clinically’ significant in regards to application & purpose of the two distinctly different class 4 laser units.**
- Increases tissue temperature
- Hazardous to eye (direct, indirect, diffuse or scattered reflection)

  - Fire Hazard (may ignite combustible material)
  - Eye goggles and scanning method required for application

Contraindications (Godbold & Riegel 2017, Houghton et al 2010 – unless otherwise noted)

- Over the Eye
  - Do not aim laser beams into the eyes and everyone present should wear appropriate safety spectacles. (Cotler et al 2015)
- Locally Injected medications
  - Simply wait for it to be absorbed & translocated
  - Laser induced vasodilation may alter pharmodynamics
- Active haemmorhaging
- Over malignancy (conflicting evidence)
  - For safety – no lasering over malignancy or margins
  - *Might* be okay if tumour has been removed and margins are clear
  - Current data says "Okay to laser at sites distant to the tumour"
  - Considered useful for pain and inflammation in terminal patients
    - Owner involvement in decision to use laser is imperative!
  - *In vitro* studies show that laser might stimulate a tumour
  - *In vivo* studies have actually shown it might be beneficial
  - *(Ottaviani et al 2013, Santana-Black et al 2012(a), (b), Santana-Black et al 2016, Karu 2010, Lanzafame 2011)*

Precautions (Godbold & Riegel 2017)
- Active Epiphysis / Open Fontanel
  - Rodent studies have conflicting results
    - Daily laser x 21 days, changed bone length (Oliveira et al 2012)
    - Lasering every 2nd day x 21 day, changed cartilage, but not bone length (Cressoni et al 2010)
  - Clinical uses (as you would use laser normally) is likely okay
- Over the Thyroid
  - High doses (i.e. 140J/cm2) causes thyroid changes. (Parrado et al 2010)
  - Therapeutic doses (i.e. 4J/cm2) did not. (Azevado et 2005)
- Pregnancy
  - There are no randomized controlled trials on this subject.
  - One review paper concluded, "The available evidence, limited to low evidence level case reports and series, indicates cutaneous laser treatment during pregnancy is safe for both mother and fetus." (Wilkerson 2019)

Safety
In 2010, the Canadian Physiotherapy Association published 'ELECTROPHYSICAL AGENTS Contraindications and Precautions: An Evidence-Based Approach to Clinical Decision Making in

Physical Therapy'. According to this document, LLLT/non-coherent light is considered to be safe to use on tissues infected with non-virulent bacteria, areas with impaired circulation, areas of impaired sensation that prevents patients from giving accurate and timely feedback, areas overlying regenerating nerves, persons with hypertension or cardiac failure, areas overlying electronic devices, intact skin overlying implants composed of metal, plastic, or cement, tissues inflamed as result of recent injury or exacerbation of chronic inflammatory condition, areas of damaged or ''at risk'' skin, areas affected by skin diseases, and chronic wounds, and skin overlying active epiphysis." To my knowledge, this is the first – and, possibly, only – formal guidance document of this type to address the safety of Low Level Laser Therapy/Photobiomodulation in an evidence-based manner. The recommendations for physiotherapists were, accurate and well-founded in regards to the available research at the time.

Reviews and meta-analyses of laser therapy osteoarthritis, lateral elbow tendinopathy, non-specific low back pain and other musculoskeletal disorders have demonstrated the effectiveness of this modality with no reports of adverse events or serious side effects (Stausholm et al 2019, Bjordal et al 2008, Yousefi-Nooraie 2007, Gendron & Hamblin 2019). One review paper even stated, "The adverse effects of LLLT have been reported to be no different from those reported by patients exposed to placebo devices in trials." (Cotler et al 2015)

Musculoskeletal Applications for Selected Rehabilitative Conditions

- Tendinopathy Lesions (Tumilty et al 2010, Bordvick et al 2017, Tumilty et al 2016, Haslerud et al 2017)
- Tendinopathy lesions in combination with PRP (Allahverdi et al 2015, Barbosa et al 2013, de Carvalho et al 2016)
- Wound healing (Peplow et al 2010)
- Muscle strains / Myofascial trigger points (Hsieh et al 2015, Ramos et al 2018)
- Neck Pain / Musculoskeletal Pain (Chow et al 2009, Bjordal et al 2006)
- Osteoarthritis (Stausholm et al 2019, Soleimanpour et al 2014; Alghadir et al 2014; Glazov et al 2016; Madani et al 2014, Looney et al 2018)
- Bone Healing (Rogatko et al 2017, Gomes et al 2015; Briteño-Vázquez et al 2015; Batista et al 2015)
- Nerve healing / regeneration (Shamir et al 2001; Rochkind et al 2007 a, b: Rochkind et al 2001; Barbosa et al 2010; Anders et al 2014)
- Spinal Cord Injury (Byrnes et al 2005; Wu et al 2009, Rochkind et al 2002, Draper et al 2012)
- Brain injury / degeneration (Tedford et al 2015; Ando et al 2010; Godine 2017; Quihe et al 2012; Xuan et al 2013; Oron et al 2012; Naeser et al 2011)

Laser therapy is beneficial for pain relief and can accelerate the body's ability to heal itself. Laser has a long history and strong basic science evidence, which supports its use in pain management. It has few side effects and is well tolerated. It is clear that laser therapy is a safe and effective tool, and a valuable adjunct to rehabilitation practice.

Animal research is highlighted yellow. Mix of animal & human reviews are highlighted blue.

References:

1. Allahverdi A, Sharifi D, Takhtfooladi MA, Hesaraki S, Khansari M, Dorbeh SS. Evaluation of low-level laser therapy, platelet-rich plasma, and their combination on the healing of Achilles tendon in rabbits. Lasers Med Sci. 2015 May;30(4):1305-13.
2. Alghadir A, Omar MT, Al-Askar AB, Al-Muteri NK. Effect of low-level laser therapy in patients with chronic knee osteoarthritis: a single-blinded randomized clinical study. Lasers Med Sci. 2014 Mar;29(2):749-55.
3. Anders JJ et al. In vitro and in vivo optimization of infrared laser treatment for injured peripheral nerves. Lasers Med Surg. 2014 46(1): 34-45.
4. Anders JJ, Lanzafame RJ, Arany PR. Low-level light/laser therapy versus photobiomodulation therapy. Photomed Laser Surg 2015;33:183–184.
5. Ando T et al. Comparison of therapeutic effects between pulsed and continuous wave 810nm wavelength laser irradiation for traumatic brain injury in mice. Laser Med Surg. 2010 42(6): 450 – 466.
6. Azevado LH, et al. Evaluation of low intensity laser effects on the thyroid gland of male mice. Photomed Laser Surg. 2005, 23(6):567-570.
7. Barbosa D, de Souza RA, de Carvalho WR, Xavier M, de Carvalho PK, Cunha TC, Arisawa EÂ, Silveira L Jr, Villaverde AB. Low-level laser therapy combined with platelet-rich plasma on the healing calcaneal tendon: a histological study in a rat model. Lasers Med Sci. 2013 Nov;28(6):1489-94.
8. Barbosa RI, Marcolino AM, de Jesus Guirro RR, Mazzer N, Barbieri CH, de Cássia Registro Fonseca M. Comparative effects of wavelengths of low-power laser in regeneration of sciatic nerve in rats following crushing lesion. Lasers Med Sci. 2010 May;25(3):423-30.
9. Batista JD, Sargenti-Neto S, Dechichi P, Rocha FS, Pagnoncelli RM. Low-level laser therapy on bone repair: is there any effect outside the irradiated field?. *Lasers Med Sci*. 2015;30(5):1569-1574.
10. Bjordal JM, Johnson MI, Iversen V, Aimbire F, Lopes-Martins RA. Low-level laser therapy in acute pain: a systematic review of possible mechanisms of action and clinical effects in randomized placebo-controlled trials. Photomed Laser Surg. 2006 Apr;24(2):158-68.
11. Bjordal JM, Lopes-Martins RA, Joensen J, et al. A systematic review with procedural assessments and meta-analysis of low level laser therapy in lateral elbow tendinopathy (tennis elbow). *BMC Musculoskelet Disord*. 2008;9:75. Published 2008 May 29.
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14. Byrnes KR, Waynant RW, Ilev IK et al. (2005) 'Light promotes regeneration and functional recovery and alters the immune response after spinal cord injury.' Lasers Surg Med. 36: 171 – 185.
15. Chow RT, Johnson MI, Lopes-Martins RA, Bjordal JM. Efficacy of low-level laser therapy in the management of neck pain: a systematic review and meta-analysis of randomised placebo or active-treatment controlled trials. Lancet. 2009 Dec 5;374(9705):1897-908.
16. Cotler HB, Chow RT, Hamblin MR, Carroll J. The Use of Low Level Laser Therapy (LLLT) For Musculoskeletal Pain. *MOJ Orthop Rheumatol*. 2015;2(5):00068.
17. Cressoni MD, Giusti HH, Pião AC, et al. Effect of GaAlAs laser irradiation on the epiphyseal cartilage of rats. Photomed Laser Surg. 2010 Aug;28(4):527-32.
18. de Carvalho PK, Silveira L Jr, Barbosa D, Munin E, Salgado MA, Villaverde AB. Analysis of experimental tendinitis in rats treated with laser and platelet-rich plasma therapies by Raman spectroscopy and histometry. Lasers Med Sci. 2016 Jan;31(1):19-26.
19. Draper, W.E., Schubert, T.A., Clemmons, R.M., Miles, S.A., Low-level laser therapy reduces time to ambulation in dogs after hemilaminectomy: a preliminary study. Journal of Small Animal Practice. 2012 vol. 53: 465-469.

20. Gendron DJ, Hamblin MR. Applications of Photobiomodulation Therapy to Musculoskeletal Disorders and Osteoarthritis with Particular Relevance to Canada. *Photobiomodul Photomed Laser Surg*. 2019;37(7):408-420.
21. Glazov G, Yelland M, Emery J. Low-level laser therapy for chronic non-specific low back pain: a meta-analysis of randomised controlled trials. Acupunct Med. 2016 Oct;34(5):328-341.
22. Godbold & Riegel. Laser Therapy in Veterinary Medicine: Photobiomodulation. Wiley Blackwell, Iowa, 2017.
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Safety of SHOCKWAVE Therapy

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BACKGROUND

Shockwave originated in the 1960's and 70's for non-invasive treatment of kidney stones and gallstones (lithotripsy). Human and animal studies in the 1980's incidentally observed osteoblastic response patterns that generated an interest in additional therapeutic uses. Since that time, it has been used successfully for over 20 years to manage a variety of orthopedic conditions (Schmitz et al 2015).

TYPES OF SHOCKWAVE (Van der Worp et al 2013, Cleveland et al 2007, Furia et al 2010, Schmitz et al 2015)

Additional information sources:

- Shockwave therapy BC - http://www.shockwavetherapy.ca/about_eswt.htm - What is ESWT0 Accessed Dec 15, 2014.
- Shockwave therapy - http://www.shockwavetherapy.eu/ Accessed Dec 15, 2014.
- Shockwave Training – www.shockwavetraining.ca (Calgary, AB, Canada – March 17, 2019.)
- Shockwave theory - http://www.shockwavetherapy.education/index.php/theory/types-of-shockwave Accessed March 27, 2019.
- Electrotherapy on the Web: http://www.electrotherapy.org/modality/shockwave-therapies - Accessed March 25, 2019.
- Prouza O. 2013. Shockwave therapy in musculoskeletal treatment. http://skanlab.no/wp-content/uploads/2013/10/swt_part_1.pdf (accessed Mar 27, 2019).

There are two types of shockwave therapy. Focused shockwave therapy (FSWT) and radial shockwave therapy (RSWT).

FSWT

A pressure field is generated that converges in the adjustable focus at a selected depth in the body tissues, where the maximal pressure is reached. There are three methods for generation of a focused shockwave: electrohydraulic, electromagnetic and piezoelectric. All of these waves are generated in water (inside of the applicator), which allows for a more natural transference of the waves into the body, with limited reflection.

Electrohydraulic shockwaves are high-energy acoustic waves created by the underwater explosion with high-voltage electrode spark discharge. The waves are then focused with a reflector and targeted at the diseased area. It is a true shock wave at all settings.

Electromagnetic shockwaves are created by an electric current passing through a coil to produce a strong magnetic field. A lens is used to focus the waves, and the focal therapeutic point being defined by the length of the focus lens. The amplitude of the focused waves increases when the acoustic wave propagates towards the focal point. It is a true shock wave at high settings only.

Piezoelectric shockwaves involve a large number of piezocrystals mounted in a sphere that receives a rapid electrical discharge that induces a pressure pulse in the surrounding water that leads to a shockwave. The arrangement of the crystals causes self-focusing of the waves towards the target centre, which leads to a precise focusing and high-energy within a defined field. It is a true shock wave at high-energy settings only.

RSWT

Radial shock waves are produced by more recently developed pneumatic devices. The term 'radial' refers to the diverging pressure field of the RSWT devices, which reach a maximal pressure at the source of generation (as compared to a focal point away from the applicator). Accelerating a projectile, using compressed air through a tube on the end of which an applicator is placed, generates radial shockwaves. The projectile hits the applicator, which transmits the generated pressure wave into the body. (These waves are NOT generated in water).

INDICATIONS

Shockwave has been shown to be effective for the following select musculoskeletal disorders:

- Calcific tendons & tendinopathies (Kim et al 2014, Verstrelen et al 2014, Gerdesmeyer et al 2003, Cacchio et al 2006, Malliaropoulos et al 2017, Becker et al 2015, Gallagher et al 2012, Wang et al 2002, van der Worp et al 2014, Dedes et al 2018, Cacchio et al 2011, Ilieva et al 2012)
- Plantarfasciitis (Chang et al 2012, Crecco et al 2013, Ilieva 2013, Ibrahim et al 2010)
- Non—Union fractures (Birnbaum et al 2002, Furia et al 2010)
- Stress fractures (Moretti et al 2009, Rompe et al 2010))
- Osteoarthritis (Zhao et al 2012, Frisbie et al 2009, Kawcak et al 2011, Wang et al 2010, 2011, 2012, Dahlberg et al 2005, Mueller et al 2007, Souza et al 2016)
- Low back pain (Noarnicola et al 2018, Nedelka et al 2014)
- Sacroiliac joint pain (Moon et al 2017)
- Coccydynia (Marwan et al 2017)
- Myofascial trigger points (Ramon et al 2015, Walsh et al 2019)
- Necrosis of the femoral head (Wang CJ et al 2005, Wang L et al 2008)

CONTRAINDICATIONS

- Circulatory disorders where bleeding may be a concern (Desai et al 2017).
- Over malignant tumours. However, cancer itself in a removed area is not a contraindication (Crevenna et al 2019), and newer research is pointing towards shockwave as being an adjunct to cancer care due to its role in permeabilization of mammalian cell membranes (Lopez-Marin et al 2018). However, for now it remains a standard contraindication.

- Presence of infection – (Newer research however, is showing that shockwave may be helpful to reduce inflection in chronic wound cases – Zhang et al 2018).
- Shockwave is not generally applied to areas or locations overlying the abdomen or chest (where gas or air is present in the body) (Desai et al 2017, Sistermann & Kathagen 1998).
- Over the abdomen or lumbar spine in pregnant patients (Desai et al 2017).

Manufacturer-Promoted Contraindications without backing or contradiction in the literature

- Metabolic conditions whereby the bone may be fragile.
- Over major blood or nerve vessels too close to a treatment areas.
- Within 4 weeks of a cortisone injection to the area being treated. (The concern is that increased circulation may flush out the injected medication – No studies can be found to validate this contraindication)

Previously thought to be contraindications

- Nerve disorders - Shockwave is now being shown to be harmless to nerve and may improve nerve regeneration (Wu et al 2007, Mense & Hoheisel 2013)
- Over epiphyses in young patients - Newer reviews have stated that it is now considered safe (Lohrer et al 2016)
- Over metal implants – In the case of plated fractures, shockwave is still beneficial, with no adverse events related to the presence of a metal plate. (Wang et al 2001)
- In conjunction with corticosteroid treatment – Topic cortisone in conjunction with shockwave enhanced the effectiveness for plantar fasciitis. (Vahdatpour et al 2018) No studies could be found that compared effectiveness of shockwave therapy in conjunction with a corticosteroid injection.

ADVERSE EVENTS

Redness of the skin, bruising, petechiae, hematoma, and transient discomfort with treatment. (Bannuru et al 2014, Schmitz et al 2015)

CONCLUSIONS from a systematic review on efficacy and safety of Extracorporeal Shockwave Therapy (ESWT) (Schmitz et al 2015)

- ESWT is effective.
  88.5% of the RCTs (randomized controlled trials) on rESWT (radial) and 81.5% of all RCTs on fESWT (focused) had positive outcomes.
- ESWT is safe.
  There were no reports of serious adverse events in any of the studies included in this analysis
- For certain orthopedic conditions, RCTs on ESWT were the predominant type of RCT listed in the PEDro database and/or obtained the highest PEDro scores among all investigated treatment modalities.
  Type of RCT and highest PEDro scores (as compared to all other treatment modalities) were fulfilled for plantafasciopathy, non-calcific supraspinatus tendinopathy, and calcific tendonitis of the shoulder. RCTs for Achilles tendinopathy and lateral epicondylitis also

ranked high. There were not enough RCTs for ESWT to draw meaningful conclusions regarding greater trochanteric pain syndrome, patellar tendinopathy, knee osteoarthritis, long bone fracture, osteonecrosis of the femoral head, proximal hamstring tendinopathy, long bicipital tenosynovitis, myofascial pain syndrome, myogelosis of the masseter muscle, and spasticity.

- There was no difference in the 'quality' of RCTs on ESWT in PEDro with positive or negative outcomes.
- Application of local anesthesia adversely affects outcome of ESWT.
  The molecular mechanisms underlying this phenomenon are not yet fully understood, but substantial evidence points to a central role of the peripheral nervous system in mediating molecular and cellular effects of shock waves applied to the musculoskeletal system. These effects could be blocked by local anesthesia. Thus, it is now generally recommended to apply shock waves without local anesthesia to the musculoskeletal system.
- Application of insufficient energy adversely affects outcome of ESWT.
  RCTs that showed positive outcomes for rESWT & fESWT for calcifying tendonitis of the shoulder used 2.6x more energy flux density (EFD) than studies that showed a negative outcome. For plantarfasciopathy, positive studies used two times the EFD as negative RCTs. A similar finding was also made when comparing studies for Achilles tendinopathy.
  There is no scientific evidence in favour of either rESWT or fESWT with respect to treatment outcome.
  It appears that success is more dependent upon sufficient EFD (energy flux density – i.e. power) than with the type of ESWT.
- The distinction between radial ESWT as 'low-energy ESWT' and focused ESWT as 'high-energy ESWT' is not correct and should be abandoned.
  Different authors have used different thresholds for categorizing 'high' and 'low' energy. Because there is no consensus in the literature, this distinction appears arbitrary and should be abandoned.
- There is no evidence that a certain fESWT technology is superior to other technologies.
  Focused shock waves can be produced by electrohydraulic, electromagnetic, and piezoelectric shock wave generators. The RCTs on fESWT in PEDro do no indicate an advantage of a certain fESWT technology over other technologies.
- An optimum treatment protocol for ESWT appears to be three treatment sessions at 1-week intervals, with 2000 impulses per session and the highest EFD that can be applied. This recommendation is based on the average number of treatment sessions and the average interval between treatment sessions among all RCTs on ESWT in PEDro. With respect to the EFD of the impulses (to be as high as possible, i.e. what can be tolerated by the individual patient without application of local anesthesia), this recommendation is based on findings of one study on rESWT for plantar fasciopathy with positive outcome and another study on fESWT for calcifying tendonitis of the shoulder with positive outcome that 'more is better'. There is not a single RCT on ESWT in PEDro, contradicting this 'more is better' recommendation.

APPENDIX 2

SAFETY

Several review papers, meta-analyses, or randomized-controlled trials conclude that shockwave therapy is a safe modality for orthopedic conditions (Schmitz et al 2015), tendinopathies (Dedes et al 2018, Li et al 2017, Cacchio et al 2006), plantarfasciitis (Roerdink et al 2017), and osteoarthritis (Wang TS et al 2020).

Animal research is highlighted yellow. Mix of animal & human reviews are highlighted blue.

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