Evaluation of Transduction Efficiency of Self-complementary Adeno-associated Virus Vector Serotypes in Canine Joint Cell Culture: Development of a New Strategy for the Treatment of Canine Osteoarthritis

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Osteoarthritis is a leading cause of chronic disability in dogs. Current treatments are of limited success and therefore new biotechnological therapeutic methods such as gene transfer are being investigated. Intra-articular gene transfer enables genetic modifications of joint cells for therapeutic purposes while minimizing systemic effects. Self-complementary adeno-associated virus (scAAV) vector delivery has been shown as an effective and safe method for transducing joint tissues with low immunogenicity and high efficiency in horses and humans. The objective of this research was to determine the most suitable scAAV vector serotype to maximize transduction efficiencies in canine monolayer culture model (chondrocytes, synoviocytes, and mesenchymal stem cells). Transduction efficiency of scAAV vectors serotypes was compared using green fluorescent protein (GFP) encoded scAAV and fluorescent microscopy. Flow cytometry was used for objective quantification of transduction efficiency and identification of the optimal scAAV serotype. Serotype 2 and 2.5 revealed excellent transduction efficiency for all three cell types. Further studies should investigate potential immune responses with certain serotypes, such as neutralizing antibody, before *in vivo* application in clinical trials.

Underwater kinematic analysis of the fore- and hindlimbs during straight line free swimming in horses

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Introduction: Swimming is used for rehabilitation and conditioning of horses. Underwater limb biomechanics have not previously been described in horses.

Hypothesis/Objectives: The goals were to analyze two-dimensional kinematics data of front and hindlimb joints during swimming by 1-Calculating and comparing angles and range of motion (ROM) of the joints during swimming against a reference; 2-Calculating angular velocity during a swimming stride cycle; 3-Comparing joints angular velocity during protraction and retraction.

Methods: Underwater videos were recorded from eleven endurance horses swimming in a straight-line pool (75m long). Markers located on each joint enabled the calculation of the extrema and ROM of the

joints. Swimming ROM data were also compared to overground passive mobilization. Angular velocities and protraction-retraction angles were also calculated during swimming. Differences between angles, ROMs, and angular velocities were compared using one-way ANOVAs. A paired t-test was used to compare values between protraction and retraction.

Results: Tarsus ROM was similar but fore/ hind fetlock, carpus and stifle ROMs were significantly greater during passive mobilization compared to swimming. The carpus showed the greatest ROM and angular velocity in the forelimbs. In the hindlimbs, stifle and tarsus had the greatest angular velocity. For all joints, the angular velocity was greater during the retraction phase.

Conclusions: Swimming exercise could be beneficial for rehabilitation when greater ROM than obtained in the water-treadmill with limited joint loading is desirable. Furthermore, the lower ROM of front- and hindlimb fetlock during swimming could be beneficial for rehabilitation of suspensory apparatus and superficial digital flexor tendon.

Systematic Review of Postoperative Rehabilitation Interventions after Cranial Cruciate Ligament Repair

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Cranial cruciate ligament disease (CCLD) is the leading cause of hindlimb lameness and stifle osteoarthritis in dogs. Postoperative rehabilitation for CCLD is among the most common reasons for veterinary rehabilitation referral. The objective of the current study was to systematically review the evidence for rehabilitation following surgical correction of CCLD. Google Scholar and Pubmed databases were searched for studies evaluating postoperative rehabilitation interventions for dogs with CCLD per the international Prospective Register of Systematic Reviews (PROSPERO). Studies were assigned Level of Evidence (I-IV) and Risk of Bias (RoB) by 2 reviewers; a third reviewer was enlisted when consensus could not be reached. Nineteen studies met inclusion criteria. Twelve were level II, 6 level III, and 1 level IV. RoB was high for 9, high-moderate 2, low-moderate 1, and low 7. Therapeutic exercise had the greatest number of studies (7), but all had high RoB. Cold compression therapy resulted in 3 level II and 1 level III (2 high RoB; 2 low RoB). Low-level light therapy resulted in 3 level II studies; all with low RoB. Extracorporeal shockwave had 3 level II studies (low to high-moderate RoB). There was 1 paper each on low-intensity pulsed ultrasound (level II; low RoB) and electrical stimulation (level III; high-moderate RoB).

Conclusion: Systematic review supports rehabilitation interventions in recovery of post-operative CCLD in dogs; however, many studies had high risk of bias. Based on existing evidence, exercise-based rather than modalities-based therapy should be prioritized for CCLD rehabilitation.

Efficacy of a commercial dry sleeve cryotherapy system for cooling the equine metacarpus

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Cryotherapy is a common rehabilitation method used in horses and is recommended in the acute phase of injury to minimize inflammation. A commercial cryotherapy system (Game Ready®) is used to apply cryotherapy and compression to the distal limb of horses. This system has been evaluated over 60 minutes, however compliance with longer treatments may be difficult. In people, cooling of muscle is greater with compression compared to cryotherapy alone. Knowledge regarding the effect of shorter treatments and compression is essential when designing rehabilitation plans. The objective was to evaluate cooling of the metacarpal subcutaneous tissue and the SDFT using this cryotherapy system. We hypothesized metacarpal subcutaneous and SDFT temperatures would decrease to between 10-19°C in healthy horses and that cooling/compression would result in greater decreases in temperatures compared to cooling alone. Thermocouples were implanted into the metacarpal subcutaneous tissues and the SDFT of five horses. Treatments (cryotherapy, cryotherapy/compression) were randomly assigned to forelimbs and performed for 20 minutes and temperatures recorded. No limbs in the cryotherapy group and one limb in the cryotherapy/compression group achieved temperatures between 10-19°C. The mean max change in temperature for the subcutaneous tissue with cryotherapy was 2.7°C and 7.1°C for cryotherapy/compression. For the SDFT, the mean max change in temperature with cryotherapy was 1.5°C and 10.1°C with cryotherapy/compression. When using the Game Ready® system, compression should be used to provide a greater decrease in temperature, however a longer treatment period or greater compression may be required to attain temperatures within the therapeutic range (10-19°C).

Nonsurgical Rehabilitation in Dachshunds with T3-L3 Myelopathy: Prognosis and Rates of Recurrence

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Dachshunds are at significant risk of experiencing thoracolumbar intervertebral disk herniation during their lifetimes. In cases of significant neurologic deficits or refractory pain, current standard of care includes advanced imaging, surgical intervention, and postoperative rehabilitation. Although conservative management is commonly recommended for cases where standard of care is declined, little is known on the prognosis of treatment with conservative management and rehabilitation (nonsurgical rehabilitation). This retrospective cohort study assessed 12-week functional outcome and recurrence of clinical signs in 40 dachshunds with T3-L3 myelopathy treated with nonsurgical rehabilitation. Overall prognosis was good with 34 of 40 (85.0%, 95%CI 70.2 – 94.2) dachshunds achieving functional pet status by 12 weeks post-injury. Modified Frankel Score (MFS) at presentation was significantly ($P<0.001$) higher in dogs with a positive 12-week outcome compared to dogs that did not recover by 12 weeks. All dogs with motor function at presentation (MFS ≥3b) had a positive outcome, where no dogs lacking deep nociception (MFS 0) had a positive outcome. Among 27 dogs with a positive 12-week outcome for whom follow-up was available, the 1- and 2-year recurrence rates for T3-L3 myelopathy were 5% and 11%, respectively. Nonsurgical rehabilitation should be considered in dachshunds with mild to moderate T3-L3 myelopathy or in severe cases when advanced imaging and surgical intervention are not possible.

Multifidus muscle activation in response to therapeutic exercises in horses

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Thoracolumbar pain has been identified in both human and equine patients. Equine exercise programs routinely incorporate ground poles and training devices to increase spinal stability. The multifidus muscle has been an area of focus due to atrophy associated with spinal disease. Our objectives were to use electromyography to determine the average work performed and peak muscle activity of the multifidus in horses trotting over ground poles and while wearing a resistance band based training device. We hypothesized that ground poles and the training device would each increase average work performed and peak multifidus muscle activity.

Cranial thoracic locations showed significantly increased muscle work and peak activation when horses were trotted over ground poles. The peak activation was significantly greater in horses trotting over poles in both lumbar regions. When the influence of the training device was investigated without ground poles, left caudal thoracic muscle work and peak activity, and right lumbar muscle work were significantly lower when using the training device. When the training device was combined with trotting over ground poles, both left and right caudal thoracic regions showed significantly lower muscle work and peak activity.

In conclusion, implementing ground poles can be an effective strategy to increase the activation of the multifidus muscle, however, caution should be taken when incorporating the use of a resistance band training device as muscle work and peak activation were significantly reduced in most locations. Further study should be performed in regards to the training device to determine its effects on epaxial musculature.