



# Cartilage Therapy and Repair in Equine Athletes<sup>☆</sup>

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The status of articular cartilage often defines the level, progression, and subsequent prognosis of joint disease in both human and equine athletes. Although methods to diagnose equine cartilage defects have significantly improved over the past decade, articular cartilage damage and ensuing osteoarthritis remain a challenge to treat. The following 2 categories of surgical options for cartilage repair in the horse are typically considered: palliative and reparative or restorative. Palliative surgical care consists of arthroscopic debridement and lavage, whereas reparative options involve the use of marrow stimulation techniques. Restorative or reparative surgical options are an area of active research, including the use of osteochondral grafting, autologous chondrocyte implantation (ACI), and augmentation with mesenchymal stem cells (MSCs). Subchondral bone microfracture coupled with intra-articular stem cell injection is currently considered to be the optimal treatment combination for equine patients with articular cartilage defects. Following arthroscopic surgery, the rehabilitative goals are to provide support to the affected limb, restore joint flexibility, stability, and manage perioperative pain. In addition, biologic therapy for the treatment of equine joint disease continues to be clinically employed and of investigational interest. With the large amount of ongoing *in vitro* research in bioprinted osteochondral constructs and potential extracellular matrix components, and the advantages of the *in vivo* equine model of articular cartilage repair as well as naturally occurring disease, it seems inevitable that the horse would be used to develop these novel techniques. *Oper Tech Orthop* 26:155-165 © 2016 Published by Elsevier Inc.

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## Introduction

The past decade of equine orthopaedic research has been characterized by significant advancements in the understanding of the pathophysiology of joint disease through the use of more sophisticated imaging modalities combined with novel surgical techniques and improved surgical equipment. Although the interplay of all joint components including subchondral bone, synovial membrane, joint capsule, and

stabilizing ligamentous structures remains integral to overall joint health, it is the status of the articular cartilage that often still defines the level, progression, and prognosis of joint disease in both human and equine athletes.

Articular cartilage damage is common in performance horses, and has historically been described into the following 2 forms: chronic degeneration or acute or posttraumatic damage. Similar to human orthopaedic classifications, acute lesions are typically characterized by focal areas of cartilage loss that are best treated with joint resurfacing techniques, whereas chronic lesions remain challenging to address because of the presence of generalized pathologic change that comprises widespread osteoarthritis (OA). Reparative mechanisms of articular cartilage have traditionally been described as either intrinsic or extrinsic. Small articular cartilage defects (<5-7 mm) appear to heal intrinsically, or from within the cartilage, whereas larger lesions require the use of interventional (surgical) or extrinsic repair.

Clinical joint disease of equine athletes, similar to their human counterparts, often cannot usually be classified into discrete categories. This article aims to first summarize recent

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advancements in equine diagnostic imaging related to joint disease monitoring, then describe applied equine models of articular cartilage repair, and lastly summarize current surgical and biologic joint therapy usage in the horse with an emphasis on future and ongoing investigational directions in cartilage repair.

## Diagnosing Equine Joint Disease and Cartilage Injury

The level of sophistication and general knowledge in equine imaging has greatly increased in the past decade, making joint ultrasonography for articular cartilage assessment more routine. Specific to the equine stifle was a description of the simultaneous arthroscopic vs ultrasonographic boundaries of the femorotibial joints, with benefits and limitations of each modality also being described.<sup>1</sup> Overall, the combined efforts of diagnostic imaging with diagnostic arthroscopy resulted in a more global evaluation of the stifle because of the limitations of arthroscopy in the horse to access the central portion of the meniscus. When ultrasound was subsequently compared with arthroscopy for the evaluation of pathologic change within the equine stifle, it was confirmed that articular cartilage defects were best detected with arthroscopy, whereas periarticular osteophytes of the medial femoral condyle and lesions of the medial meniscus were best detected with ultrasonography.<sup>2</sup> With an increased understanding of how various modalities can be used in conjunction to optimize diagnoses and monitor healing, preoperative and postoperative ultrasonographic evaluations are becoming more commonplace in cases of equine cartilage damage with secondary soft tissue injury. Recently, contrast-enhanced ultrasonography has been shown to be a safe and feasible method for the evaluation of musculoskeletal structures of the equine distal limb, although its clinical usefulness in the evaluation of articular cartilage has yet to be fully explored.<sup>3</sup>

Likewise, with increased knowledge of normal equine anatomy and increased availability of equine-dedicated magnetic resonance imaging (MRI) units, magnetic resonance examinations are becoming commonplace in equine practice. Multiple quantitative MRI techniques that have been developed in human medicine to noninvasively evaluate and detect early chondral injury such as delayed gadolinium-enhanced imaging, T1rho and T2 mapping<sup>4,5</sup> have not yet surfaced for clinical use in the horse; however, it is likely that these techniques would soon be used in translational research.

Similar to MRI, equine applications of computed tomographic arthrography (CTA) that are able to provide a volumetric assessment of the joint and have been used to diagnose human knee injuries, have been a source of diagnostic investigation. The equine application of CTA was reported in Warmblood horses with stifle lameness,<sup>6</sup> and recently the use of CTA as it compares with other commonly used equine diagnostic methods was described in 24 horses with lameness localized to the femorotibial joints.<sup>7</sup> In this study, when CTA was compared with radiography, ultrasonography, and arthroscopy for the diagnosis of femorotibial

joint disease, the use of CTA detected more lesions in the cruciate ligaments, femoral and tibial condyles, and ligament entheses than the other diagnostic methods, but was not reliable for detection of articular cartilage damage on the medial femoral condyle. Tears of the cranio-lateral (axial) border of the medial meniscus were detected on arthroscopy and CTA, but not on ultrasonography. Although new diagnostic modalities continue to be explored, a strategic multimodality approach is currently used to assess equine cartilage health and monitor subsequent OA.

Of recent interest diagnostically has been the use of non-destructive cartilage or subchondral bone assessment techniques that are used in conjunction with direct visual arthroscopic assessment. Near-infrared (NIR) spectroscopy uses NIR light to generate spectral feedback when the NIR light is applied to a sample via a probe.<sup>8</sup> This method has been shown to provide valuable information at both a microscopic and macroscopic level beyond full-depth articular cartilage thickness in the rat.<sup>8,9</sup> Although it is not yet clinically available for use in the horse, it shows great potential because of its depth penetration and capacity to assess cartilage and subchondral bone simultaneously.

Optical coherence tomography (OCT) is an imaging modality that has recently been investigated to diagnostically assess equine articular cartilage.<sup>10,11</sup> Through the measurement of reflection and backscattering of NIR light, cross-sectional digital images have been produced during arthroscopy with resolutions comparable to that of low-power microscopy.<sup>12</sup> When compared with conventional arthroscopy alone, OCT provided additional detailed and quantitative information about the morphology of articular cartilage lesions including cavitation, fibrillation, superficial clefts, and fragmentation that were previously only partially detected.<sup>11</sup> The small diameter of the OCT probe has also been shown to make previously arthroscopically inaccessible areas reachable, making it an especially exciting modality for the early detection of equine cartilage lesions.<sup>11</sup>

## Applied Equine Models of Articular Cartilage Repair

The horse has been identified as potentially one of the best translatable species for novel cartilage repair studies for several reasons.<sup>13</sup> Of all the veterinary species used for translational cartilage research, equine articular cartilage is most similar to that of human cartilage.<sup>14</sup> A similar articular environment exists, and the surgical equipment used in equine orthopaedics is also similar, if not the same as that used in human orthopaedics. In addition, equine diagnostic capabilities through the use of similar imaging modalities has led to interpretations of experimental disease being correlated to clinical disease findings. These features, in addition to the availability of long-term follow-up and longitudinal biopsies in light of controlled exercise programs, have solidified the horse as a reliable surgical model for human and equine-focused studies of articular cartilage regeneration.<sup>15</sup>

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