Articular Cartilage Injury in Athletes

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Articular Cartilage Injury in Athletes

Timothy R. McAdams¹, Kai Mithoefer², Jason M. Scopp³, and Bert R. Mandelbaum⁴

Abstract

Articular cartilage lesions in the athletic population are observed with increasing frequency and, due to limited intrinsic healing capacity, can lead to progressive pain and functional limitation over time. If left untreated, isolated cartilage lesions can lead to progressive chondropenia or global cartilage loss over time. A chondropenia curve is described to help predict the outcome of cartilage injury based on different lesion and patient characteristics. Nutriceuticals and chondroprotective agents are being investigated as tools to slow the development of chondropenia. Several operative techniques have been described for articular cartilage repair or replacement and, more recently, cartilage regeneration. Rehabilitation guidelines are being developed to meet the needs of these new techniques. Next-generation techniques are currently evaluated to optimize articular cartilage repair biology and to provide a repair cartilage tissue that can withstand the high mechanical loads experienced by the athlete with consistent long-term durability.

Keywords
microfracture, cartilage repair, sports injury

Introduction

Articular cartilage defects of the knee are frequently observed. Curl and coworkers described 53,569 hyaline cartilage lesions in 19,827 patients undergoing knee arthroscopy.²⁴ Similarly, a recent prospective survey of 993 consecutive knee arthroscopies demonstrated evidence of articular cartilage pathology in 66%.⁵ Most lesions are single high-grade lesions located on the femur. Levy and coworkers have noted an increasing frequency of chondral injuries in collegiate, professional, and world-class athletes.²¹ Besides this rising incidence in high-level competitive sports, increasing participation in organized recreational sports such as soccer, basketball, and football has been associated with a growing incidence of sports-related articular cartilage injuries.⁴,⁵⁹,⁹⁵ Articular cartilage lesions frequently result in association with acute ligament or meniscal injuries, traumatic patellar dislocations, and osteochondral injuries or may develop from chronic ligamentous instability or malalignment.⁴,⁹⁶,¹²⁵ Articular cartilage defects of the femoral condyles have been observed in up to 50% of athletes undergoing anterior cruciate ligament (ACL) reconstruction with an increased propensity in female athletes.¹⁹,¹¹⁰ These injuries often limit participation in athletic activity while predisposing the athlete to early joint degeneration.³²,⁶⁹

Due to their documented poor spontaneous repair potential, injuries to the articular cartilage surfaces present a therapeutic challenge particularly in young and active individuals.¹⁸,¹⁹,⁵⁷ Recent development of new surgical techniques has incited considerable clinical and scientific interest in articular cartilage repair, replacement, and most recently, regeneration.²,³,¹⁶,⁴³,⁹⁸,¹³⁰ Because injuries to the articular cartilage of the knee have been shown to present one of the most common causes of permanent disability in athletes,²⁸,³⁰ management of articular cartilage in this high-demand population has important long-term implications.¹¹⁸,¹¹⁹ Due to the documented detrimental effect of excessive joint loading and articular impaction,¹⁸,⁵⁷ articular cartilage repair in the athletic population requires cartilage surface restoration that can withstand the significant mechanical joint stresses generated during high-impact, pivoting sports. Besides reducing pain, increasing mobility, and improving functional outcome scores, the ability to return to sport and to continue to perform at the preinjury level presents a therapeutic challenge.

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athletic level is the most important parameter for outcome evaluation from articular cartilage restoration in this challenging population.

Natural History

The limited ability of articular cartilage for spontaneous repair has been well documented. Following the acute injury and resultant tissue necrosis, the lack of vascularization of articular cartilage prevents the physiological inflammatory response to tissue injury. The absent potential for replication and repair by the intrinsic mature chondrocytes and lack of recruitment of extrinsic undifferentiated repair cells results in a qualitatively and quantitatively insufficient repair cartilage. Repetitive loading of the injured articular cartilage results in further cellular degeneration with accumulation of degradative enzymes and cytokines, disruption of collagen ultrastructure, increased hydration, and fissuring of the articular surface. These biochemical and metabolic changes mimic the early changes seen in osteoarthritis.

While much knowledge has been gained from laboratory studies about the progression from cartilage injury to osteoarthritis, prospective clinical information about the natural history of articular cartilage lesions is still rare, particularly in athletes. This lack of long-term data can be largely attributed to the previous inability to accurately diagnose and follow chondral lesions by noninvasive techniques. One study demonstrated that hyaline cartilage defects cause pain and swelling and predict severe changes in lifestyle and athletic activity in patients with ACL injuries. Other authors have shown that untreated articular cartilage defects in patients with ACL deficiency resulted in significantly worse outcome scores up to 19 years after the original injury. Nebelung reported 68% of ACL-deficient East German Olympic athletes had grade 4 chondral lesions 20 years after injury. Importantly, a Swedish study reported on the long-term results in 28 athletes with isolated, severe chondral damage in the weightbearing condyles. While 75% of athletes returned to their sport initially, a significant decline of athletic activity was observed 14 years after the initial injury with radiographic evidence of osteoarthritis in 57% of these athletes. Similarly, a prospective study of osteochondral lesions reported poor results with strenuous athletic activity in 38% and moderate to severe radiographic evidence of osteoarthritis in 45% at an average of 34 years. This is consistent with the findings of a National Institutes of Health (NIH) consensus conference on osteoarthritis, which demonstrated a relative risk of 4.4 to 5.3 for knee osteoarthritis in high-demand, pivoting athletes. Church found an increased risk of degenerative change in patients who delayed ACL reconstruction to more than 1 year after injury compared to patients who were reconstructed within 1 year. This increased risk for arthritic joint degeneration is felt to result from the high joint stresses associated with the repetitive joint impact and torsional loading seen with the rapid deceleration motions, frequent pivoting, and player contact in high-impact sports.

Chondropenia

The increased risk for development of knee osteoarthritis in athletes is well documented, particularly at the elite level. Intact articular cartilage possesses optimal load-bearing characteristics and adjusts to the level of activity. Increasing weightbearing activity in athletes and adolescents has been shown to increase the volume and thickness of articular cartilage and to increase knee cartilage glycosaminoglycan content. In the healthy athlete, a positive, linear dose-response relationship exists for repetitive loading activities and articular cartilage function. However, studies indicate that this dose-response curve reaches a threshold and that activity beyond this threshold can result in maladaptation and injury of articular cartilage. If the integrity of the functional weightbearing unit is lost, either through acute injury or chronic microtrauma in the high-impact athlete, a chondropenic response is initiated that can include loss of articular cartilage volume and stiffness, elevation of contact pressures, and development or progression of articular cartilage defects. Concomitant pathological factors such as ligamentous instability, malalignment, and meniscal injury or deficiency can further support progression of the chondropenic cascade. Without intervention, chondropenia leads to progressive deterioration.
of articular cartilage function and may ultimately progress to osteoarthritis.

Commonly used classification systems for cartilage injury include the Outerbridge and International Cartilage Repair Society (ICRS).16,105 These classification systems are based on size and depth of the articular cartilage lesion. We propose a new cartilage score, the “chondropenia severity score” (CSS), which includes consideration of the chondropenia curve. The CSS gives objective scores to each anatomical location and also considers meniscal injury (Table I). Based on the CSS, a young athlete with an isolated grade III lesion would have a better prognosis than an older individual with degenerative medial and lateral meniscal tears and a diffuse grade II chondral injury. The senior author (B.R.M.) has been using the CSS in all arthroscopies over the last 2 years, and studies are ongoing to see how the CSS relates to prognosis for different age groups, body mass index, and gender.

**Nutritional Supplements and Viscosupplementation**

Nutritional supplements have received much recent interest as both a way to prevent cartilage injury and limit its progression.23,41 However, most of the literature on nutritional supplements involves their role in general osteoarthritis, and very little is known about how it may affect athletes at different stages of the chondropenia curve. Regardless, the sports physician should have a basic understanding of the common supplements as they will undoubtedly continue to increase as investigators search for a way to slow joint destruction.

**Glucosamine and Chondroitin**

After publication of The Arthritis Cure in 1997, glucosamine has been the center of much attention and controversy.133 Glucosamine has been found to be safe and effective in meta-analysis studies88,135 but definitive conclusions were difficult due to possible commercial bias and different methodologies. In 2006, the NIH sponsored the GAIT (Glucosamine/chondroitin Arthritis Intervention), which compared glucosamine, chondroitin, glucosamine/chondroitin combination, celecoxib, and placebo in 1,583 patients with knee arthritis. The glucosamine/chondroitin sulfate combination had a rate of response 6.5% greater than placebo, but this was not statistically significant. Other nutritional supplements, including methylsulfonylmethane (MSM),61 S-adenosylmethionine,99 and collagen hydrolysate,23 are all being studied as potential supplements to limit arthritis pain.

Viscosupplementation, like nutritional supplements, has become a popular treatment option for osteoarthritis of the knee. A series of 3 to 5 injections of hyaluronic acid, hylan, or hyaluronan may be done in an effort to decrease pain and improve function. Much discrepancy exists between the studies of viscosupplementation. Campbell compared meta-analyses on hyaluronate efficacy and safety and found moderate evidence to support the benefit of hyaluronate with respect to pain reduction and functional improvement with a low risk of harm.20 Likewise, a meta-analysis by Wang et al. found hyaluronate injections can reduce pain from arthritis of the knee with few adverse effects.138 Although not commonly used in the younger athlete, viscosupplementation can be helpful for recreational athletes who are lower on the chondropenic curve. Further study is needed to determine what, if any, chondroprotective role glucosamine/chondroitin, other nutritional supplements, and viscosupplementation have in athletes with articular cartilage injury.
Table 1. Chondropenia Severity Score (CSS) is Graded 0 to 100 and Involves Assessment of Meniscus Injury as well as Size and Number of Cartilage Lesions

<table>
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<th>LATERAL COMPARTMENT</th>
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</tr>
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<td>Grade IA 8</td>
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<tr>
<td>Grade IB</td>
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<td>Grade IB 6</td>
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<tr>
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<td>Grade IIA 5</td>
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<td>&lt;1/3 remaining</td>
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SUMS:
TOTAL CSS:

Patient Name: ________________________  Index Knee: ____________________

Dob: ___________________________
Treatment

Historically, surgical attempts at cartilage repair involved stimulation of mesenchymal stem cell metaplasia to form fibrocartilage. This is done by lavage, debridement, drilling, or microfracture, all in an attempt to repair a cartilage defect through marrow stimulation. In an attempt to improve the quality of the cartilage, investigators devised methods to replace rather than repair a cartilage defect. This involves allografts or autografts that fill the defect through a variety of techniques. Most recently, biologic autologous chondrocyte culture techniques have emerged in an effort to regenerate hyaline cartilage. The treatment algorithm for articular cartilage defects depends on both the size and depth of the lesion (Fig. 2).

![Figure 2. Clinical algorithm for management of articular lesions in athletes.](image)

![Figure 3. Microfracture technique for articular cartilage repair with debridement of cartilage margins (A), removal of calcified cartilage (B), and systematic distribution of microfractures of the subchondral bone (C), resulting in formation of a pluripotent mesenchymal clot in the cartilage defect that is well anchored in the microfracture holes (D).](image)

**Cartilage Repair: Mesenchymal Stem Cell Stimulation**

Reports of mesenchymal stem cell stimulation first occurred in 1946 when Magnusson described debridement of injured hyaline cartilage. Subsequent reports described abrasion, drilling, and microfracture. In 1994, Rodrigo described the use of an “ice pick,” or small surgical awls, to create microfractures, the technique commonly used today for marrow stimulation.

The microfracture technique has been well described and involves debridement through the calcified cartilage layer followed by perforation of the subchondral bone with arthroscopic surgical awls (Fig. 3). In an equine study, Frisbie demonstrated the importance of removal of the calcified cartilage layer in order to maximize the amount of repair tissue. The subchondral bone perforations are generally between 2 to 4 mm apart, depending on the size of the lesion. Steadman emphasizes early motion protocols with continuous passive motion (CPM) and limited weight-bearing for 8 weeks in order to optimize long-term functional outcome. However, Marder found no difference in the clinical result of microfracture between patients who were nonweightbearing with CPM versus patients allowed weightbearing as tolerated without CPM.

Initial studies showed good early clinical results that tended to deteriorate with time. Recently, Steadman measured functional outcomes in 71 knees after microfracture, and clinical improvement persisted 7 years after surgery in 80%. Mithoefer prospectively studied 48 patients who underwent microfracture and found 67% good to excellent results at 2-year minimum follow-up. Suboptimal results were correlated with high body mass index and poor fill grades on MRI. Mithoefer also prospectively evaluated the results of microfracture technique in high-impact athletes and found 66% good to excellent results. In this high activity group, 47% had a decrease in Tegner activity scores after an initial increase.

Microfracture is an appealing option in the treatment of articular cartilage injury because it is relatively simple with minimal morbidity. It appears best suited for young patients with acute, smaller contained lesions. Potential deterioration of clinical results over time may be related to defect repair with “hyaline-like” rather than true hyaline cartilage, with resultant compromise in wear characteristics. This has prompted investigation toward replacement and remodeling techniques.

**Cartilage Replacement: Substitution**

**Replacement Options**

Segmental fresh allograft replacement of osteochondral defects was first reported by Lexar in 1908. Additional studies showed good to excellent results in 75% to 86% of patients, but the risk of disease transmission and difficulties with procurement of fresh, unirradiated grafts have limited widespread use of this technique.

More recently, osteochondral autograft transplantation surgery (OATS), or “mosaicplasty,” has been utilized for small, 1- to 2-cm lesions. In this technique, the osteochondral autograft cylindrical plugs are harvested from an area of the distal femur that experiences the lowest contact pressures, most commonly the superomedial and superolateral trochlea. The donor site can be “back-filled” by bone graft substitute if desired, but donor-site morbidity can be significant. Peripheral chondrocyte death from mechanical
The surgical technique was described by Hangody and can be accomplished through a miniarthrotomy or arthroscopically. Good to excellent results were reported in a 2005 study by Gudos, which showed 83% patient satisfaction and 88% radiographic availability. In a prospective study in 2007, McCulloch and colleagues reported 84% patient satisfaction with 88% radiographic availability. In a larger group of patients to determine if the duration of allograft storage affects the clinical results in the treatment of distal femur osteochondral defects.

Options for cartilage transplantation in larger defects include cartilage slurry and osteochondral allograft transplantation. Stone reported significant improvement in pain and function after articular cartilage paste grafting for an average defect size of 28.6 cm². There were 83% of competitive-level soccer players who returned to play. Results in adolescent athletes were even better with a 96% return to high-impact sports. ACI also appears effective for trochlear lesions. In 2007, Mandelbaum evaluated 40 trochlear lesions (mean size, 4.5 cm²) treated with ACI and found a statistically significant increase in Cincinnati Knee Score at an average follow-up of 59 months. Long-term durability of ACI was reported by Petersen in 2002, with 82% good to excellent results at 2 years and 83% good to excellent results at 5 to 11 years after ACI. Sports participation appears to improve the long-term results of ACI.
ACI has recently been compared to both debridement and mosaicplasty. Fu compared ACI to debridement in 2005.\textsuperscript{36} In this study, patients who underwent ACI obtained higher levels of knee function and had greater pain relief than those who underwent debridement, with a minimum follow-up of 3 years. In 2003, Bentley prospectively compared ACI versus mosaicplasty in 100 randomized patients.\textsuperscript{12} Good to excellent results were seen in 88\% of the ACI group compared with 69\% in the mosaicplasty group. Repeat arthroscopy at 1 year showed good to excellent repair in 82\% of the ACI group and only 34\% in the mosaicplasty group. Mean defect size was 4.66 cm\(^2\), and mean follow-up was 19 months (minimum, 1 year). Horas also compared ACI to mosaicplasty but found equally good results after 2 years in 40 patients.\textsuperscript{53}

ACI provides an autologous source of hyaline-like tissue and can be used in larger lesions with no donor-site morbidity. The stiffness of ACI hyaline-like tissue (2.77 N) more closely approximates hyaline cartilage (3.07 N) than fibrocartilage seen after microfracture (1.27 N).\textsuperscript{108} This is important because reduced stiffness leads to fissures in tissue texture and progressive degradation.\textsuperscript{38}

The negative aspects of ACI include technical difficulty, requires a staged procedure, and potential cost/reimbursement issues. One of the main technical challenges is the periosteal flap, and problems with periosteal hypertrophy may necessitate debridement in 18\% to 31\% of patients.\textsuperscript{50,142} When human chondrocytes are cultured and multiplied, they lose their ability to produce type II cartilage matrix and begin producing type I collagen as part of the dedifferentiation process. Once implanted and covered by the periosteum, the chondrocytes redifferentiate in response to local biochemical factors. However, this redifferentiation can be hypertrophic, which can be a clinical problem. Researchers are studying culture techniques that would limit the amount of redifferentiation.\textsuperscript{75}

In an attempt to limit the hypertrophy that occurs during redifferentiation, alternatives to the periosteal flap have evolved. In this way, no incision is necessary to harvest the periosteum, and the procedure can sometimes be done arthroscopically.\textsuperscript{31,109} Gooding\textsuperscript{40} found that a porcine type I/III collagen membrane showed no improvement over a periosteal membrane.

Rather than simply altering the cultured chondrocyte cover, the latest techniques involve a biodegradable matrix seeded with chondrocytes to cover the defect (“matrix articular cartilage implantation,” or MACI). The biological matrix can be composed of a porcine type I/III collagen membrane, polydioxanone/polyglactin, or other material. The matrix should be resorbable, able to be seeded with cultured chondrocytes, and provide a 3-dimensional scaffold that limits chondrocyte hypertrophy. Promising results have been seen in Europe and Australia, where these techniques are most popular.\textsuperscript{8,11,66,84,102,131,135} Ossendorf reported on 40 patients who underwent ACI with a polyglactin/polydioxanone matrix scaffold.\textsuperscript{104} Cincinnati, Lysholm, Knee Injury and Osteoarthritis Outcome Score (KOOS), and SF-36 knee scores showed significant improvement at 2-year follow-up. Biopsy specimens in 4 patients at 9 and

Figure 5. Technique of mosaicplasty using osteochondral cylinder harvest from the peripheral trochlea (A) and press-fit insertion into the cartilage defect in a mosaic pattern with recreation of the condylar convexity (B).

Figure 6. Case study of a high-impact athlete treated with autologous chondrocyte transplantation (A). Image taken 4 months after injury for a full-thickness lesion of the weightbearing femoral condyle (B). Second-look arthroscopy at 1 year demonstrated complete restoration of the articular cartilage surface (C). After returning to high-impact sports at the preinjury level, magnetic resonance imaging evaluation 4 years postoperatively showed a maintained repair cartilage while continuing to participate in high-impact athletics (D).

Source: 6A reproduced with permission from Genzyme Biosurgery, Cambridge, MA.
12 months showed evidence of hyaline-like tissue, but this was not quantified. MRI at 6 and 12 months showed good defect filling.

Bartlett compared porcine collagen membrane–ACI to porcine collagen biomatrix–ACI. In 91 patients, both groups showed improvement in Cincinnati Knee Score at 1 year. The 2 techniques showed comparable amounts of hyaline cartilage and graft hypertrophy at 1 year. Although a biomatrix seeded with chondrocytes has the theoretical advantages of less chondrocyte leakage, less graft hypertrophy, and a more even chondrocyte distribution, this has not yet been shown clinically. At the time of this publication, membrane ACI (MACI) techniques are not available for use in the United States.

Rehabilitation after Cartilage Reconstitution Procedures
Little is known about the optimal rehabilitation protocols after cartilage reconstitution procedures. The phases of rehabilitation in cartilage reconstitution are proliferative, transitional, remodeling, and maturation. Although early motion with progression to closed chain rehabilitation is standard, recommendation regarding the timing of progression can vary greatly due to the significant variation in techniques. Hambly recently reviewed rehabilitation protocols and noted the deficiency in evidence-based evaluations. The ICRS recently met in Zurich, Switzerland, to develop a consensus statement regarding rehabilitation after cartilage reconstitution. Until specific guidelines are developed, it is critical for the surgeon and therapist to communicate regarding the durability of the surgical technique, size and location of the lesion, and specific restrictions for the chosen procedure.

Future Directions
The future of articular cartilage reconstitution lies in regeneration of tissue. At this time, regeneration involves collecting and culturing chondrocytes with subsequent reimplantation, using a variety of carriers and membranes. Even when successful, chondrocyte implantation results in “hyaline-like” tissue rather than true hyaline tissue, and glycosaminoglycan profiles of the implanted cartilage differ from that of native hyaline tissue. In addition, apoptotic cell death may contribute to delamination of the graft in the setting of chondrocyte implantation. Based on currently available repair technologies, new approaches are being evaluated that may help to improve quality and quantity of the repair cartilage tissue and overcome the current technical and biologic limitations. Second-generation microfracture techniques may improve stabilization and adhesion of the microfracture clot by using different thrombogenic and adhesive polymers that also increase mesenchymal cell recruitment and 3-dimensional organization. Third-generation ACI techniques have been developed that use implantation of 3-dimensional neocartilage generated from autologous chondrocytes in bioreactors. These techniques can be performed less invasively and may help to accelerate the prolonged postoperative recovery after ACI. Implanting highly productive, selected autologous chondrocytes may help to further increase repair cartilage quality and quantity. In addition, single-step cartilage autograft implantation onto a bioabsorbable scaffold is being evaluated.

Stem cells have the potential to differentiate into chondrocytes under appropriate conditions, potentially with improved cell viability, and are at the forefront of articular cartilage regeneration investigations. Specifically, mesenchymal stem cells (MSCs), found in bone marrow, skin, and adipose tissue, are capable of differentiating into articular cartilage as well as other cells of mesenchymal origin. Hui et al. compared MSC transplants to cultured chondrocytes, osteochondral autograft, and periosteal grafts in animal models of osteochondritis dissecans. Based on histological and biomechanical evaluation, the authors found the MSC transplants to be comparable to cultured chondrocytes and superior to periosteum and osteochondral autograft in their ability to repair chondral defects. Another study found MSCs to be superior to cultured chondrocytes in a rabbit model. Dragoon found that MSCs derived from adipose tissue predictably healed chondral defects in a rat model. MSCs can be easily obtained and provide significant promise in the future of cartilage tissue engineering.

Concomitant Procedures
Combined pathology is frequently encountered by the surgeon treating articular cartilage defects in the athletic knee. Malalignment, ligamentous instability, or meniscal injury and deficiency are known to contribute to the development of articular cartilage lesions, and surgically addressing these concomitant pathologies is critical for an effective and durable articular cartilage repair. A recent study demonstrated that isolated or combined adjuvant procedures including ACL reconstruction, high tibial osteotomy, or meniscal allograft and repair did not negatively affect the ability to return to athletics after autologous chondrocyte transplantation. Similarly, treatment of associated injuries of menisci or ACL did not influence the recovery time or level of athletic activity after mosaicplasty, and better outcomes have been demonstrated with microfracture in patients who undergo simultaneous ACL reconstruction.
because performing simultaneous adjuvant procedures in the athletic population avoids the prolonged rehabilitation and absence from competition associated with staged procedures, which has been shown to limit the athlete’s ability to return to demanding athletic activity.\textsuperscript{14,95}

**Summary**

Articular cartilage repair in athletes is aimed at returning the athlete to the preinjury level of athletic participation without increased risk for long-term arthritic degeneration. Nutritional supplements may play a role in both the prevention and treatment of articular cartilage injury. Several surgical techniques have been shown to improve function and athletic activity after articular cartilage reconstitution in this population. The rate of improvement and ability to return to athletic activity is dependent on age, length of the preoperative intervals, lesion size, and activity level. Proper rehabilitation is critical to the success of the current surgical techniques. Each technique is associated with specific advantages and limitations, and second-generation techniques are being developed to improve the current shortcomings. Adjuvant procedures to correct concomitant pathology are critical for the success of the articular cartilage repair and do not seem to negatively affect the ability to return to demanding sports. Future directions include regeneration through gene therapy utilizing stem cells. Long-term studies in this population will determine the efficacy of articular cartilage repair to slow or reverse chondropenia and to prevent the development of secondary arthritic degeneration.

**Declaration of Conflicting Interests**

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