Scientific Evidence Base for Cartilage Injury and Repair in the Athlete

M.R. Steinwachs¹, L. Engebretsen², and R.H. Brophy³

Abstract
Soccer players and athletes in high-impact sports are frequently affected by knee injuries. Injuries to the anterior cruciate ligament and menisci are frequently observed in soccer players and may increase the risk of developing an articular cartilage lesion. In high-level athletes, the overall prevalence of knee articular cartilage lesions has been reported to be 36% to 38%. The treatment for athletic patients with articular cartilage lesions is often challenging because of the high demands placed on the repair tissue by impact sports. Cartilage defects in athletes can be treated with microfracture, osteochondral grafting, and autologous chondrocyte implantation. There is increasing scientific evidence for cartilage repair in athletes, with more extensive information available for microfracture and autologous chondrocyte implantation than for osteochondral grafting. The reported rates and times to return to sport at the preinjury level are variable in recreational players, with the best results seen in younger and high-level athletes. Better return to sport is consistently observed for all repair techniques with early cartilage repair. Besides minimizing sensorimotor deficits and addressing accompanying pathologies, the quality of the repair tissue may be a significant factor for the return to sport.

Keywords
articular cartilage injury, cartilage repair, sports injury knee, return to sports, athletes, scientific evidence

Introduction
Defects of the joint cartilage have a very limited healing capacity. Therefore, injuries resulting from trauma or repetitive loading can lead to osteoarthritis over time. Soccer players and athletes in high-impact sports are particularly susceptible to knee injuries (Figure 1A, B). Up to 60% of patients demonstrate significant cartilage damage on arthroscopic evaluation.¹,²,³ In more than half of these patients, additional damage to the ligaments and menisci is present.⁴,⁵,⁶ The patella (Figure 1B) and the femur condyle are most often affected, followed by injury to the tibial plateau.⁷,⁸ ACL ruptures, which occur with up to a 3-fold higher probability in female athletes,⁹ have a 20% to 60% rate of chondral and osteochondral defects, increasing the risk for osteoarthritis up to 12 times in high-demand and pivoting athletes.¹⁰ The early diagnosis and treatment of cartilage and associate injuries is a key element to allow for a return to sports after injury in athletes. Besides the reconstruction of ligaments and menisci, addressing the cartilage lesions seems to be the most crucial point in avoiding the progression of a sustained cartilage defect to osteoarthritis.⁸,¹¹,¹² Persistent ligamentous instability and loss of meniscal tissue lead to dramatic changes in biomechanics. Together with high loads and shear forces exerted in impact sports, they are strong negative predictive factors for cartilage repair and return to sports after an injury. Age, gender, BMI, duration of symptoms, defect location and size, number of previous interventions, and sensorimotor capability are additional important factors affecting return to sports.¹³,¹⁴

Cartilage Injury in Athletes
The prevalence of articular cartilage defects in athletes has not been well studied in the literature. Given the demands placed on the lower extremity during typical sports training and competition, these defects are likely to be symptomatic and potentially career threatening for most athletes. Some studies have investigated this issue in the knee but there is little evidence for the hip or ankle.

¹Department of Orthobiology & Cartilage Repair, Schulthess Klinik Zurich, Switzerland
²Oslo Sports Trauma Research Center, Norwegian School of Sports Science and Department of Orthopaedic Surgery, Oslo University Hospital, Oslo, Norway
³Department of Orthopaedic Surgery, Washington University School of Medicine, St. Louis, Missouri, USA

Corresponding Author:
M. R. Steinwachs, Department of Orthobiology and Cartilage Regeneration, Schulthess Clinic, Lenggstrasse 2, 8008 Zurich, Switzerland
Email: matthias.steinwachs@kws.ch
A recent systematic review of the prevalence of chondral defects in the athletes’ knees provides an overview of the literature to date on this topic. This review of 11 studies including 931 athletes from American football, basketball, and endurance running recorded the overall prevalence of knee articular cartilage lesions to be 36%. The most common location was patellofemoral (37%), followed by the femoral condyle (35%) and tibial plateau (25%). Among patellofemoral lesions, the patella was more commonly involved (64%) than the trochlea (36%). Tibiofemoral lesions more commonly involved the medial compartment (68%) than the lateral compartment (32%). Fourteen percent of the athletes, all of whom were basketball players or endurance runners, were asymptomatic at the time of diagnosis. Among these athletes, the overall prevalence of knee articular cartilage lesions was 59% (reported range 18%–63%).

A very recent study of elite American football athletes reported an incidence of 38.2% among those who underwent magnetic resonance imaging (MRI) at the National Football League combine. Only 53% of athletes at the combine underwent MRI imaging, so the overall reported prevalence was 20.1%, but this assumes there were no lesions in the 47% of athletes who were not imaged. Given the demands of American football on the knee joint, it is likely that at least some of these athletes had asymptomatic cartilage defects that were not imaged.

Although there has been one study reporting outcomes after surgical treatment for articular cartilage injury to the knee in soccer players, there is little data on the incidence or prevalence of such lesions in this population. Articular cartilage injury is likely to be common in this population for a number of reasons, including the demands placed on the knee joint by soccer (football), the high incidence of knee injury in soccer (football), and the increased risk for knee osteoarthritis in former elite soccer players. The association of articular cartilage injuries with other injuries to the knee such as ACL or meniscal tears has been well established in the literature for athletes and the general population but is not a focus of this review. There is no published data on the epidemiology of hip and ankle focal articular cartilage lesions in athletes.

The limited evidence to date suggests there is a high prevalence of focal chondral defects in the knee even in the asymptomatic athlete. Because the natural history of these lesions is not known, the management of such lesions in asymptomatic athletes is challenging. If these lesions are or become symptomatic, the evolving treatment options for articular cartilage defects may be applied as indicated below. More studies are needed to better define the incidence and prevalence of full-thickness cartilage defects in the knee, hip, and ankle of athletes.

**Cartilage Repair in Athletes**

In recent years, a number of surgical approaches, including microfracture (MF), autologous chondrocyte implantation (ACI), and osteochondral transplantation (OATS) have been developed for the repair of cartilage defects. The evidence for these different treatment modalities has been widely published. In the recent literature, 2 independent systematic reviews, one with 1400 athletes in 20 clinical trials (787 undergoing MF, 362 ACI, 261 OATS) and the other with 730 athletes in 11 trials (447 MF, 183 ACI, 28 OATS), have been published. The studies were homogeneous in respect to study quality according to the Coleman methodology score (average 69.8 points) in all the parameters evaluated. The outcome parameter investigated was “return to sports on preinjury level” of the 3 above-mentioned cartilage...
repair techniques in the treatment of International Cartilage Repair Society (ICRS) grade III/IV defects in athletes’ knee joints. Additional interventions, mostly ACL and meniscal surgery, were noted in 50% of the patients in the review by Mithoefer et al.\textsuperscript{31} compared with 32% of the cartilage repairs in the review by Harris et al.\textsuperscript{32} The femoral condyles and the patellofemoral joint were the most commonly treated locations in both publications.

**Microfracture**

This method is one of the arthroscopic marrow stimulation techniques (Figure 2A) forming a clot of fibrin and precursor cells from the bone marrow.\textsuperscript{28} Fibrous tissue with a histologic range from primitive scar tissue to fibrous–hyaline mixed cartilage tissue is generated under local biochemical and biomechanical factors.\textsuperscript{33,34} The advantage of this technique is the minimally invasive approach, which is easily executed in combination with the arthroscopic treatment of collateral injuries. Drawbacks of the technique are the inferior mechanical tissue properties,\textsuperscript{35} and the formation of intralesional osteophytes,\textsuperscript{27,36} limiting midterm tissue durability.\textsuperscript{10,34,36,37} Active patients younger than 40 years with small defects, low body mass index, and a short duration of preoperative symptoms show the best results.\textsuperscript{27,33,38,41}

Mithoefer and coworkers\textsuperscript{31} evaluated the outcome of 787 patients with microfracture in 12 clinical trials. The mean Coleman methodology score in these studies equaled 65 (0–100) points. At a mean follow-up of 42 months and with a mean defect size of 3.6 cm\textsuperscript{2}, an average of 66% (519 of 787) of the patients were able to participate in sports activities 8 months after surgery, 45% (353 of 787) of them at the preinjury level (Figure 2B). Harris and colleagues\textsuperscript{32} in their review of 8 comparable publications with microfracture in 447 athletes arrive at slightly superior results, with 59% of the patients returning to their preinjury level of sports 17 months postoperatively (Figure 2B). Onset of symptoms of less than 12 months before surgery was associated with a significantly higher return to sports rate (67%) compared with a longer history of more than 12 months (14%).\textsuperscript{10} The operative technique, follow-up, and patient’s characteristics as well as the rehabilitation protocols were comparable in both publications.

**Autologous Chondrocyte Implantation**

The technique developed by Lars Peterson\textsuperscript{29} is based on tissue regeneration by isolated autologous chondrocytes. The native chondrocytes are harvested arthroscopically and cultured under standardized conditions.\textsuperscript{42} During a second, open procedure, the cell suspension is implanted under a peristeum flap or a collagen membrane (Figure 3A).\textsuperscript{29,43,44} After a phase of adherence to the defect ground and proliferation of the cells, a primary tissue evolves that, during approximately 2 years, matures to histologically superior repair cartilage under the local biochemical and biomechanical conditions.\textsuperscript{45-47} Tissue specimens harvested from the regenerated areas demonstrate a histologic range from fibrous–hyaline mixed to hyaline-like repair tissue.\textsuperscript{33,34,38} More hyaline-like histologic quality seems to be essential for long-term durability of the tissue.\textsuperscript{34,35,48,49} Different modifications (ACT-P, ACT-C, MACT, etc.) of the original technique have been developed and evaluated short-term. The regeneration of the cartilage tissue can be described in 3 phases: I, Proliferation; II, Transition; III,
Remodelling and Maturation. The rehabilitation process is adapted to this long process of tissue maturation, with impact sports being prohibited for 12–18 months after surgery.\textsuperscript{50,51} The advantage of this technique, besides the potential for histologically superior and stable repair tissue, is the capacity to address larger defects of more than 2 cm\textsuperscript{2}. Disadvantages are the long rehabilitation process, high costs, and multiple procedures.

In the systematic review of Mithoefer et al.,\textsuperscript{31} 7 ACI trials with 362 athletes and an overall mean follow-up of 42 months were identified. The mean Coleman methodology score was 77 points (0–100 points). Given an average defect size of 5.1 cm\textsuperscript{2}, 67% (242 of 362) of the patients were able to return to sports at 18 months, 64% (232 of 362) of them at the preinjury level (Figure 3B). Concomitant procedures were performed in 57% of the patients. The best durability of 96% (continued sport participation) was reported after ACI.

Harris and colleagues\textsuperscript{32} analyzed 3 ACI trials with 183 athletes in their systematic review. An average of 78% (142 of 183) of the patients was able to participate in sports at their preinjury level 25 months postoperatively (Figure 3B). A short duration of symptoms (less than 1 year) and no previous interventions were associated with a significantly higher return to sports ratio.\textsuperscript{40,52}

Osteochondral Transplantation

This technique uses osteochondral cylinders of 5 to 12 mm diameter and 15 to 20 mm length, harvested from low-stress areas of the joint to address small- and medium-sized chondral and osteochondral defects in a press-fit technique.\textsuperscript{53,54} The cartilage in this technique consists of hyaline tissue (Figure 4A). In contrast to the cell-based methods like microfracture and ACI, no maturation process of the tissue is required for establishing mechanical competence. After implantation, the transplanted tissue adapts structurally to the surrounding biomechanics.\textsuperscript{55} As the osseous part of the cylinder has to be integrated, the rehabilitation protocol is similar to that established in fracture healing. For athletes, the advantages of this technique are the high tissue quality and the highly predictable integration of the cylinders besides a relatively short rehabilitation and limited costs.\textsuperscript{54} Of disadvantage is the donor site morbidity, leading to complaints depending on the size and number of cylinders transplanted as well as the sometimes insufficient vertical integration of the cartilaginous component of the graft and the necessity for an open procedure.\textsuperscript{56} Because of the limited number of available cylinders, this technique is suitable for defect sizes of less than 3 cm\textsuperscript{2}.

Mithoefer and coworkers\textsuperscript{31} analyzed 6 trials dealing with the OATS technique comprising 261 athletes with a follow-up of 42 months in their review. The Coleman methodology score equaled 71 points. Given a mean defect size of 2.4 cm\textsuperscript{2}, 91% of the patients (238 of 261) were able to practice sports within 7 months of the operation, 64% (167 of 261) of them at the preinjury level (Figure 4B). The review of Harris et al.\textsuperscript{32} comprises only 1 OATS trial that was evaluated in the Mithoefer et al. study.

Conclusion

Soccer players and athletes from other high-impact, pivoting sports are at risk for complex injuries involving the articular cartilage, ligaments, and menisci. Without differentiation by sport, the overall prevalence of knee articular cartilage lesions in professional athletes is estimated to be 36%. In athletes, the treatment of articular cartilage lesions is often challenging and associated with some limitations so that
45% to 78% of the athletes are able to return to sport at the preinjury level over a variable time period (7–25 months). The levels of evidence for ACI (mean Coleman methodology score 77 points), osteochondral transplantation (mean Coleman methodology score 71 points), and microfracture (mean Coleman methodology score 65 points) were acceptable, though limited for the autologous osteochondral grafting. The best evaluated technique is the microfracture (787 and 447 athletes), followed by the ACI (362 and 183 athletes) and the OATS (261 athletes). Superior results were found for ACI (64%–78% RTSPL), with the best durability but the longest mean time to return to sport (18 month), followed by OATS (64% RTSPL) and Microfracture (45%–67% RTSPL). The time from injury to surgery, the number of procedures and the quality of the repair tissue, as well as the successful treatment of accompanying pathologies, appears to be a significant factor influencing return to sport.

Acknowledgment and Funding
The authors received no financial support for the research, authorship, and/or publication of this article.

Declaration of Conflicting Interests
The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References
1. Curl WW, Krome J, Gordon ES, Rushing J, Smith BP, Poehling GG. Cartilage injuries: a review of 31,516 knee arthroscopies. Arthroscopy. 1997;13(4):456-60.
2. Levy AS, Lohnes J, Sculley S, LeCroy M, Garrett W. Chondral delamination of the knee in soccer players. Am J Sports Med. 1996;24(5):634-9.
3. Widuchowski W, Widuchowski J, Trzaska T. Articular cartilage defects: study of 25,124 knee arthroscopies. Knee. 2007;14(3):177-82.
4. Agel J, Arendt EA, Bershadsky B. Anterior cruciate ligament injury in national collegiate athletic association basketball and soccer: a 13-year review. Am J Sports Med. 2005;33(4):524-30.
5. Griffin LY, Agel J, Albohm MJ, Arendt EA, Dick RW, Garrett WE, et al. Noncontact anterior cruciate ligament injuries: risk factors and prevention strategies. J Am Acad Orthop Surg. 2000;8(3):141-50.
6. Piasecki DP, Spindler KP, Warren TA, Andrish JT, Parker RD. Intraarticular injuries associated with anterior cruciate ligament tear: findings at ligament reconstruction in high school and recreational athletes. Am J Sports Med. 2003;31(4):601-5.
7. Arøen A, Løken S, Heir S, Alvik E, Ekeland A, Granlund OG, et al. Articular cartilage lesions in 993 consecutive knee arthroscopies. Am J Sports Med. 2004;32(1):211-5.
8. Flanigan DC, Harris JD, Trinh TQ, Siston RA, Brophy RH. Prevalence of chondral defects in athletes’ knees: a systematic review. Med Sci Sports Exerc. 2010;42(10):1795-801.
9. Prodromos CC, Han Y, Rogowski J, Joyce B, Shi K. A meta-analysis of the incidence of anterior cruciate ligament tears as a function of gender, sport, and a knee injury reduced regime. Arthroscopy. 2007;23:1320-5.
10. Mithoefer K, McAdams T, Williams RJ, Kreuz PC, Mandelbaum BR. Clinical efficacy of the microfracture technique for articular cartilage repair in the knee: an evidence-based systematic analysis. Am J Sports Med. 2009;37(10):2053-63.
11. Mandelbaum BR, Browne JE, Fu F, Micheli L, Mosely JB Jr, Erggelet C, et al. Articular cartilage lesions of the knee. Am J Sports Med. 1998;26(6):853-61.
12. Shelbourne KD, Jari S, Gray T. Outcome of untreated traumatic articular cartilage defects of the knee: a natural history study. J Bone Joint Surg Am. 2003;85-A(Suppl 2):8-16.

13. Myer GD, Paterno MV, Ford KR, Quatman CE, Hewett TE. Rehabilitation after anterior cruciate ligament reconstruction: criteria-based progression through the return-to-sport phase. J Orthop Sports Phys Ther 2006;36(6):385-99.

14. Wilk KE, Bremik K, Reinold MM, Devine KM, Dugas JR, Andrews JR. Rehabilitation of articular lesions in the athlete’s knee. J Orthop Sports Phys Ther. 2006;36(10):815-27.

15. Bachmann G, Basad E, Rauber K, Damian M, Rau W. Degenerative joint disease on MRI and physical activity: a clinical study of the knee joint in 320 patients. Eur Radiol. 1999;9(1):145-52.

16. Bradley J, Honkamp N, Jost P, West R, Norwig J, Kaplan L. Incidence and variance of knee injuries in elite college football players. Am J Orthop. 2008;37(6):310-4.

17. Kaplan L, Schurhoff M, Selesnick H, Thorpe M, Uribe J. MRI of the knee in asymptomatic professional basketball players. Arthroscopy. 2005;21(5):557-61.

18. Krampla W, Mayrhofer R, Malcher J, Kristen K, Urban M, Hruby W. MR imaging of the knee in marathon runners before and after competition. Skeletal Radiol. 2001;30(2):72-6.

19. Major N, Helms C. MR imaging of the knee: findings in asymptomatic collegiate basketball players. Am J Roentgenol. 2002;179(3):641-4.

20. Marans H, Kennedy D, Kavanagh G, Wright T. A review of intra-articular knee injuries in racquet sports diagnosed by arthroscopy. Can J Surg. 1998;31(3):199-201.

21. Schueller-Weidekamm C, Schueller G, Uffmann M, Bader T. Does marathon running cause acute lesions of the knee? Evaluation with magnetic resonance imaging. Eur Radiol. 2006;16(10):2179-85.

22. Schueller-Weidekamm C, Schueller G, Uffmann M, Bader T. Incidence of chronic knee lesions in long-distance runners based on training level. Eur J Radiol. 2006;58(2):286-93.

23. Shellock F, Miller W, Douglas B, Ainge G, Brown D, Dierenfield L. Knees of Ironman triathletes: magnetic resonance imaging assessment of older (>35 years old) competitors. J Magn Reson Imaging. 2003;17(1):122-30.

24. Stahl R, Luke A, Ma C, Krug R, Steinbach L, Majumdar S, et al. Prevalence of pathologic findings in asymptomatic knees of marathon runners before and after a competition in comparison with physically active subjects—a 3.0 T magnetic resonance imaging study. Skeletal Radiol. 2008;37(7):627-38.

25. Walczak B, McCulloch P, Kang R, Zelazny A, Tedeschi F, Cole B. Abnormal findings on knee magnetic resonance imaging in asymptomatic NBA players. J Knee Surg. 2008;21(1):27-33.

26. Hirshorn KC, Cates T, Gillogly S. Magnetic resonance imaging documented chondral injuries about the knee in collegiate football players: 3-year National Football League combine data. Arthroscopy. 2010;26(9):1237-40.
41. Mithoefer K, Williams RJ 3rd, Warren RF, Wickiewicz TL, Marx RG. High-impact athletics after knee articular cartilage repair: a prospective evaluation of the microfracture technique. Am J Sports Med. 2006;34(9):1413-8.

42. Niemeyer P, Pestka JM, Kreuz PC, Salzmann GM, Köstler W, Südkaempf NP, et al. Standardized cartilage biopsies from the intercondylar notch for autologous chondrocyte implantation (ACI). Knee Surg Sports Traumatol Arthrosc. 2010;18(8):1122-7.

43. Steinwachs M, Kreuz PC. Autologous chondrocyte implantation in chondral defects of the knee with a type I/III collagen membrane: a prospective study with a 3-year follow-up. Arthroscopy. 2007;23(4):381-7.

44. Steinwachs M. New technique for cell-seeded collagen-matrix-supported autologous chondrocyte transplantation. Arthroscopy. 2009;25(2):208-11.

45. Trattnig S, Pinker K, Krestan C, Plank C, Millington S, Marlovits S. Matrix-based autologous chondrocyte implantation for cartilage repair with Hyalograft C: two-year follow-up by magnetic resonance imaging. Eur J Radiol. 2006;57(1):9-15.

46. Wada Y, Watanabe A, Yamashita T, Isobe T, Moriya H. Evaluation of articular cartilage with 3D-SPGR MRI after autologous chondrocyte implantation. J Orthop Sci. 2003;8(4):514-7.

47. Watanabe A, Wada Y, Obata T, Sasho T, Ueda T, Tamura M, et al. Time course evaluation of reparative cartilage with MR imaging after autologous chondrocyte implantation. Cell Transplant. 2005;14(9):695-700.

48. Peterson L, Vasiliadis HS, Brittberg M, Lindahl A. Autologous chondrocyte implantation: a long-term follow-up. Am J Sports Med. 2010;38:1117-24.

49. Vasara AI, Nieminen MT, Jurvelin JS, Peterson L, Lindahl A, Kivistö I. Indentation stiffness of repair tissue after autologous chondrocyte transplantation. Clin Orthop Relat Res. 2005;(433):233-42.

50. Hambly K, Bobic V, Wondrasch B, Van Assche D, Marlovits S. Autologous chondrocyte implantation postoperative care and rehabilitation: science and practice. Am J Sports Med. 2006;34(6):1020-38.

51. Kreuz PC, Steinwachs M, Erggelet C, Lahm A, Krause S, Ossendorf C, et al. Importance of sports in cartilage regeneration after autologous chondrocyte implantation: a prospective study with a 3-year follow-up. Am J Sports Med. 2007;35(8):1261-8.

52. Mithöfer K, Peterson L, Mandelbaum BR, Minas T. Articular cartilage repair in soccer players with autologous chondrocyte transplantation: functional outcome and return to competition. Am J Sports Med. 2005;33(11):1639-46.

53. Bobić V. Arthroscopic osteochondral autograft transplantation in anterior cruciate ligament reconstruction: a preliminary clinical study. Knee Surg Sports Traumatol Arthrosc. 1996;3(4):262-4.

54. Hangody L, Dobos J, Baló E, Pánics G, Hangody LR, Berkes I. Clinical experiences with autologous osteochondral mosaicplasty in an athletic population: a 17-year prospective multicenter study. Am J Sports Med. 2010;38(6):1125-33.

55. Hangody L, Fules P. Autologous osteochondral mosaicplasty for the treatment of full-thickness defects of weight-bearing joints: ten years of experimental and clinical experience. J Bone Joint Surg Am. 2003;85(90002):25-32.

56. Matricali GA, Dereymaeker GP, Luyten FP. Donor site morbidity after articular cartilage repair procedures: a review. Acta Orthop Belg. 2010;76(5):669-74.