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Autologous Chondrocyte Implantation Versus Microfracture of the Knee

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Articular cartilage is prone to damage from acute high-energy trauma and from repetitive shear and torsional forces applied to the superficial surface [1]. Therefore, chondral lesions are a common pathology of the knee joint; they have been found in 60% of knees undergoing arthroscopy [2]. Untreated full-thickness cartilage lesions (grade III or IV according to Outerbridge [3]) are usually associated with significant pain and swelling; furthermore they provoke an increased risk of subsequent osteoarthritis [4-8]. Due to the fact that individuals tend to remain active for longer the need for durable alternatives to arthroplasty increases. Reparative and restorative techniques are available to treat cartilage defects surgically; unfortunately, no treatment option has been identified as the gold standard yet [9,10].

In 2007, 2.7 million knee arthroscopies were performed in the United States and in Europe; they included 1.8 million cartilage procedures, among them 450,000 were Micro Fractures (MF) and 50,000 autologous chondrocyte implantations (ACI) [11]. Reparative Micro Fracture (MF), a single-stage arthroscopic technique developed by Steadman in 1980 [12], results in an intrinsic repair of the chondral lesion. Penetrating the sub-chondral bone plate enables bone marrow cells to migrate into the defect and to create a "super clot" that eventually matures into firm repair tissue. Due to its minimally invasive approach, technical simplicity, limited surgical morbidity and low costs [4] and because it does not prevent the application of other cartilage repair procedures that may be needed in the future [13], it is now a common first-line treatment [14,15] for full-thickness chondral defects of the knee. In 1987, the first ACI was performed by Brittberg [16]. This technique is a two-stage biological approach. In an initial arthroscopy a cartilage biopsy is harvested from a low-loadbearing area on the proximal part of the medial femoral condyle of the affected knee and sent for chondrocyte culturing. During an arthrotomy three to six weeks later the cartilage lesion is debrided. At present, many modifications exist. According to the original technique a watertight chamber is formed into which a suspension [17] with the expanded (characterized [18] or non-characterized) chondrocytes is injected; they start to fill out the lesion by producing a matrix. Finally, autologous periosteum [16-19] or a resorbable bi-layer collagen membrane is used to cover the watertight chamber [20]. To prevent uneven cell distribution and leakage of chondrocytes from the defect [17], the matrix-associated ACI was developed. The chondrocytes are immediately cultured in a three-dimensional biocompatible scaffold (collagen membrane, hyaluronic polymer, collagen gel [21-24]) which contains and stabilizes the chondrocytes; it is trimmed to exactly match the defect before it is implanted. [19,21,25].

However, up to now neither MF nor ACI has proven to be superior to the other in terms of efficacy and safety [9]. Both have shown to relieve symptoms and improve function significantly [26] and both provide better results in the treatment of defects in the femoral condyles rather than in the patellofemoral compartment [27]. Furthermore, younger and more active patients, with a shorter duration of preoperative symptoms, fewer surgical procedures prior to cartilage repair or restoration, and without concomitant ligamentous instability, meniscal deficiency, or femorotibial or patellofemoral malalignment can expect the best outcome regardless of the used technique [28]. Of interest, the situation looks quite different for the defect size. It does not have an impact on ACI [25,29,30], but it significantly influences the outcome after MF. Due to the fact that this technique is based on a sufficient pool formation in the bed of the lesion, the super clot has to be protected by a stable cartilage shoulder [31] which is normally provided by defects smaller than 200 mm^2 [32]. Whereas defects up to 500 mm^2 are surrounded by healthy tissue which does not break up under load, defects larger than 500 mm^2 do not have a mechanical environment that reduces shear and compressive forces [32]. Therefore, Microfracture is not effective for the treatment of large lesions [25,31,33,34]; significantly less improvement was achieved for lesions larger than 400 mm^2 [35] and 200 mm^2 [36-38], respectively as compared to smaller lesions.

Furthermore, the quality of the repair tissue plays an important role because good or excellent clinical outcomes are directly correlated with hyaline-like defect fill [39]. Microfracture induces the growth of a repair tissue that consists of type-I, type-II, and type-III collagen [40] and varies from fibrocartilage [38] alone to a mixture of fibrocartilage and hyaline-like cartilage [29,41-43]. Some researchers presume that the original defect fill will become stable and can take over the function of hyaline cartilage [33,35,42], others express the opinion that the hybrid tissue does not support weight bearing in the long-term [38,43] and therefore deteriorates in its function over time; a decrease in score values was observed after 18 [44,45] and 24 [29,34,41,46] months, respectively. In contrast, ACI can restore the integrity of damaged chondral areas with hyaline-like cartilage, a hybrid of fibrocartilage and hyaline-like tissue (with chondrocytes organized in isogeneic groups and with proteoglycans and glycosaminoglycans in the extracellular matrix) or with fibrocartilaginous material containing type-I and type-II collagen [16,20,39,47-49]. Several studies evaluated that ACI may offer good and stable clinical results up to 11 years [30,39,47,49-51]. Due to the fact that the final matrix remodeling phase starts approximately six months [1] after surgery and continues for two [20,39,52] to three years [1] the regenerated tissue progressively hardens resulting in further functional improvement over time. [30,39].

Undoubtedly, ACI is superior to MF with regard to the quality of the defect fill. Nevertheless, the available literature does not address the necessity for all chondral lesions to be filled with normal stratified hyaline cartilage; the concept of "Demand Matching" [53] (patient goals, compliance, expectations and perceptions as well as physical demands on the knee due to daily routine and recreational activities) should be applied when deciding on the appropriate technique for a particular lesion. Thereby the disadvantages of ACI must not be neglected. ACI is a technically demanding surgical procedure which

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requires an extensive and strenuous rehabilitation; achieving the ultimate clinical benefits may be delayed for at least six to 12 months in some patients [54]. On the contrary, MF involves less surgery, thus the rehabilitation is easier, allowing a faster recovery and enabling athletes a faster return to competition [55,56]. Finally, the cost factor has to be taken into consideration. The costs for ACI are approximately ten times as high as for MF, mainly caused by the chondrocyte cell cultivation. [57].

In conclusion, ACI and MF are complementary procedures. Decision-making has to take individual circumstances and personal preferences as well as patient- and defect-specific factors into consideration. For cost reasons and due to the fact that ACI is suggested to provoke a better outcome than MF only when treating defects larger than 400 mm^2 [28]. MF has to be considered indispensable for smaller lesions. Although, it may be appropriate for larger lesions too, it should not be applied routinely to them because ACI results in a less favorable and less predictable outcome when it is performed as second-line procedure after MF [58]. In larger defects and in high-demand patients ACI should be the treatment of choice because its hyaline-like defect fill will most likely enable potential long-term benefits whereas MF may not adequately relieve symptoms and restore function.

References

1. Jones DG, Peterson L (2006) Autologous chondrocyte implantation. J Bone Joint Surg Am 88: 2502-2520.
2. Widuchowski W, Widuchowski J, Trzaska T (2007) Articular cartilage defects: study of 25,124 knee arthroscopies. Knee 14: 177-182.
3. Outerbridge HK, Outerbridge AR, Outerbridge RE (1995) The use of a lateral patellar autologous graft for the repair of a large osteochondral defect in the knee. J Bone Joint Surg Am 77: 65-72.
4. Safran MR, Seiber K (2010) The evidence for surgical repair of articular cartilage in the knee. J Am Acad Orthop Surg 18: 259-266.
5. Buckwalter JA (2002) Articular cartilage injuries. Clin Orthop Relat Res 402: 21-37.
6. Curl WW, Krome J, Gordon ES, Rushing J, Smith PB, et al. (1997) Cartilage injuries: A review of 31,516 knee arthroscopies. Arthroscopy 13: 456-460.
7. Davies-Tuck ML, Wluka AE, Wang Y, Teichtahl AJ, Jones G, et al. (2008) The natural history of cartilage defects in people with knee osteoarthritis. Osteoarthritis Cartilage 16: 337-342.
8. Gelber AC, Hochberg MC, Mead LA, Wang NY, Wigley FM, et al. (2000) Joint injury in young adults and risk for subsequent knee and hip osteoarthritis. Ann Intern Med 133: 321-328.
9. Magnussen RA, Dunn WR, Carey JL, Spindler KP (2008) Treatment of focal articular cartilage defects in the knee: a systematic review. Clin Orthop Relat Res 466: 952-962.
10. Benthien JP, Schwaninger M, Behrens P (2011) We do not have evidence based methods for the treatment of cartilage defects in the knee. Knee Surg Sports Traumatol Arthrosc 19: 543-552.
11. http://www.odtmag.com/
12. Blevins FT, Steadman JR, Rodrigo JJ, Silliman J (1998) Treatment of articular cartilage defects in athletes: an analysis of functional outcome and lesion appearance. Orthopedics 21: 761-768.
13. Williams RJ 3rd, Harnly HW (2007) Microfracture: indications, technique, and results. Instr Course Lect 56: 419-428.
14. Bekkers JE, Inklaar M, Saris DB (2009) Treatment selection in articular cartilage lesions of the knee: a systematic review. Am J Sports Med 37: 148S-155S.
15. Strauss EJ, Barker JU, Kercher JS, Cole BJ, Mithoefer K (2010) Augmentation strategies following the microfracture technique for repair of focal chondral defects. Cartilage 1: 145-152.
16. Brittberg M, Lindahl A, Nilsson A, Ohlsson C, Isaksson O, et al. (1994) Treatment of deep cartilage defects in the knee with autologous chondrocyte transplantation. N Engl J Med 331: 889-895.
17. Marlovits S, Hombauer M, Truppe M, Vécsei V, Schlegel W (2004) Changes in the ratio of type-I and type-II collagen expression during monolayer culture of human chondrocytes. J Bone Joint Surg Br 86: 286-295.
18. Saris DB, Vanlauwe J, Victor J, Haspl M, Bohnsack M, et al. (2008) Characterized chondrocyte implantation resuts in better structural repair when treating symptomatic cartilage defects of the knee in a randomized controlled trial versus microfracture. Am J Sports Med 36: 235-246.
19. Brittberg M (2008) Autologous chondrocyte implantation-technique and long-term follow-up. Injury 39: S40-S49.
20. Bentley G, Biant LC, Carrington RW, Akmal M, Goldberg A, et al. (2003) A prospective, randomised comparison of autologous chondrocyte implantation versus mosaicplasty for osteochondral defects in the knee. J Bone Joint Surg Br 85: 223-230.
21. Marlovits S, Zeller P, Singer P, Resinger C, Vécsei V (2006) Cartilage repair: Generations of autologous chondrocyte transplantation. Eur J Radiol 57: 24-31.
22. Bartlett W, Gooding CR, Carrington RW, Skinner JA, Briggs TW, et al. (2005) Autologous chondrocyte implantation at the knee using a bilayer collagen membrane with bone graft. A preleiminary report. J Bone Joint Surg Br 87: 330-332.
23. Vasiliadis HS, Wasiak J (2010) Autologous chondrocyte implantation for full thickness articular cartilage defects of the knee. Cochrane Database Syst Rev CD003323.
24. Fuss M, Ehlers EM, Russlies M, Rohwedel J, Behrens P (2000) Characteristics of human chondrocytes, osteoblasts and fibroblasts seeded onto a type I/III collagen sponge under different culture conditions. A light scanning and transmission electron microscopy study. Ann Anat 182: 303-310.
25. Kon E, Gobbi A, Filardo G, Delcogliano M, Zaffagnini S, et al. (2009) Arthroscopic second-generation autologous chondrocyte implantation compared with microfracture for chondral lesions of the knee: prospective nonrandomized study at 5 years. Am J Sports Med 37: 33-41.
26. Henn RF, Gomoll AH (2011) A review of the evaluation and management of cartilage defects in the knee. Phys Sportsmed 39: 101-107.
27. Gomoll AH, Farr J, Gillogly SD, Kercher J, Minas T (2010) Surgical management of articular cartilage defects of the knee. J Bone Joint Surg Am 92: 2470-2490.
28. Harris JD, Siston RA, Pan X, Flanigan DC (2010) Autologous chondrocyte implantation: a systematic review. J Bone Joint Surg Am 92: 2220-2233.
29. Knutsen G, Engebretsen L, Ludvigsen TC, Drogset JO, Grøntvedt T, et al. (2004) Autologous chondrocyte implantation compared with microfracture in the knee. A randomized trial. J Bone Joint Surg Am 86: 455-464.
30. Filardo G, Kon E, Di Martino A, Iacono F, Marcacci M (2011) Arthroscopic second-generation autologous chondrocyte implantation: a prospective 7-year follow-up study. Am J Sports Med 39: 2153-2160.
31. Mithoefer K, Williams RJ 3rd, Warren RF, Potter HG, Spock CR, et al. (2006) Chondral resurfacing of articular cartilage defects in the knee with the microfracture technique. Surgical technique. J Bone Joint Surg Am 88: 294-304.
32. Erggelet C, Mandelbaum B, Lahm A (2000) Der Knorpelschaden als therapeutische Aufgabe - Klinische Grundlagen. Deutsche Zeitschrift für Sportmedizin 2: 48-54.
33. Steadman JR, Briggs KK, Rodrigo JJ, Kocher MS, Gill TJ, et al. (2003) Outcomes of microfracture for traumatic chondral defects of the knee: average 11-year follow-up. Arthroscopy 19: 477-484.
34. Mithoefer K, Williams RJ 3rd, Warren RF, Potter HG, Spock CR, et al. (2005) The microfracture technique for the treatment of articular cartilage lesions in the knee. A prospective cohort study. J Bone Joint Surg Am 87: 1911-1920.
35. Miller BS, Steadman JR, Briggs KK, Rodrigo J J, Rodkey WG (2004) Patient satisfaction and outcome after microfracture of the degenerative knee. J Knee Surg 17: 13-17.
36. Asik M, Ciftci F, Sen C, Erdil M, Atalar A (2008)The microfracture technique for the treatment of full-thickness articular cartilage lesions of the knee: midterm results. Arthroscopy 24: 1214-1220.
37. Gudas R, Kalesinskas RJ, Kimtys V, Stankevicius E, Toliusis V, et al. (2005)

A prospective randomized clinical study of mosaic osteochondral autologous transplantation versus microfracture for the treatment of osteochondral defects in the knee joint in young athletes. Arthroscopy 21: 1066-1075.

38. Gudas R, Stankevicius E, Monastyreckiene E, Pranys D, Kalesinskas RJ (2006) Osteochondral autologous transplantation versus microfracture for the treatment of articular cartilage defects in the knee joint in athletes. Knee Surg Sports Traumatol Arthrosc 14: 834-842.

39. Peterson L, Brittberg M, Kiviranta I, Akerlund EL, Lindahl A (2002) Autologous chondrocyte transplantation: Biomechanics and long-term durability. Am J Sports Med 30: 2-12.

40. Frisbie DD, Trotter GW, Powers BE, Steadman JR, Howard RD, et al. (1999) Arthroscopic subchondral bone plate microfracture technique augments healing of large chondral defects in the radial carpal bone and medial femoral condyle of horses. Vet Surg 28: 242-255.

41. Knutsen G, Drogset JO, Engebretsen L, Grøntvedt T, Isaksen V, et al. (2007) A randomized trial comparing autologous chondrocyte implantation with microfracture. Findings at five years. J Bone Joint Surg Am 89: 2105-2112.

42. Bae DK, Yoon KH, Song SJ (2006) Cartilage healing after microfracture in osteoarthritic knees. Arthroscopy 22: 367-374.

43. Gobbi A, Nunag P, Malinowski K (2005) Treatment of full thickness chondral lesions of the knee with microfracture in a group of athletes. Knee Surg Sports Traumatol Arthrosc 13: 213-221.

44. Kreuz PC, Erggelet C, Steinwachs MR, Krause SJ, Lahm A, et al. (2006) Is microfracture of chondral defects in the knee associated with different results in patients aged 40 years or younger? Arthroscopy 22: 1180-1186.

45. Kreuz PC, Steinwachs MR, Erggelet C, Krause SJ, Konrad G, et al. (2006) Results after microfracture of full-thickness chondral defects in different compartments in the knee. Osteoarthritis Cartilage 14: 1119-1125.

46. Mithoefer K, Williams RJ 3rd, Warren RF, Wickiewicz TL, Marx RG (2006) High-impact athletics after knee articular cartilage repair: A prospective evaluation of the microfracture technique. Am J Sports Med 34: 1413-1418.

47. Ferruzzi A, Buda R, Faldini C, Vannini F, Di Caprio F, et al. (2008) Autologous chondrocyte implantation in the knee joint: open compared with arthroscopic technique. Comparison at a minimum follow-up of five years. J Bone Joint Surg 90: 90-101.

48. Horas U, Pelinkovic D, Herr G, Aigner T, Schnettler R (2003) Autologous chondrocyte implantation and osteochondral cylinder transplantation in cartilage repair of the knee joint. A prospective, comparative trial. J Bone Joint Surg Am 85-A: 185-192.

49. Marcacci M, Berruto M, Brocchetta D, Delcogliano A, Ghinelli D, et al. (2005) Articular cartilage engineering with Hyalograft C: 3-year clinical results. Clin Orthop Relat Res 435: 96-105.

50. Moseley JB Jr, Anderson AF, Browne JE, Mandelbaum BR, Micheli LJ, et al. (2010) Long-term durability of autologous chondrocyte implantation: a multicenter, observational study in US patients. Am J Sports Med 38: 238-246.

51. Kreuz PC, Müller S, Ossendorf C, Kaps C, Erggelet C (2009) Treatment of focal degenerative cartilage defects with polymer-based autologous chondrocyte grafts: four-year clinical results. Arthritis Res Ther 11.

52. Gikas PD, Morris T, Carrington R, Skinner J, Bentley G, et al. (2009) A correlation between the timing of biopsy after autologous chondrocyte implantation and the histological appearance. J Bone Joint Surg Br 91: 1172-1177.

53. Farr J, Cole B, Dhawan A, Kercher J, Sherman S (2011) Clinical cartilage restoration: evolution and overview. Clin Orthop Relat Res 469: 2696-2705.

54. Batty L, Dance S, Bajaj S, Cole BJ (2011) Autologous chondrocyte implantation: an overview of technique and outcomes. ANZ J Surg 81: 18-25.

55. Kon E, Filardo G, Berruto M, Benazzo F, Zanon G, et al. (2011) Articular cartilage treatment in high-level male soccer players: a prospective comparative study of arthroscopic second-generation autologous chondrocyte implantation versus microfracture. Am J Sports Med 39: 2549-2557

56. Riyami M, Rolf C (2009) Evaluation of microfracture of traumatic chondral injuries to the knee in professional football and rugby players. J Orthop Surg Res 4: 13.

57. Cameron P, Wright C, Wale JMG, Hart J, Morgan DFN (2010) Matrix-induced autologous chondrocyte implantation (MACI) and autologous chondrocyte implantation (ACI). Edited by Ageing DoHa, Canberra, Medical Services Advisoty Committee.

58. Minas T, Gomoll AH, Rosenberger R, Royce RO, Bryant T (2009) Increased failure rate of autologous chondrocyte implantation after previous treatment with marrow stimulation techniques. Am J Sports Med 37: 902-908.