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Am J Sports Med 2012 40: 2273 originally published online August 24, 2012
DOI: 10.1177/0363546512457008

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Clinical and Radiological Outcomes 5 Years After Matrix-Induced Autologous Chondrocyte Implantation in Patients With Symptomatic, Traumatic Chondral Defects

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Investigation performed at the Medical University of Vienna, Vienna, Austria

Background: To date, few studies have been published reporting the 5-year follow-up of clinical and radiological outcomes for chondral defects treated with matrix-induced autologous chondrocyte implantation (MACI).

Hypothesis: A significant improvement in clinical and radiological outcomes after treatment of symptomatic, traumatic chondral defects of the knee with the MACI implant will be maintained up to 5 years after surgery.

Study Design: Case series; Level of evidence, 4.

Methods: A prospective evaluation of the MACI procedure was performed in 21 patients with chondral defects of the knee. After the MACI procedure, patients were clinically assessed with the Knee injury and Osteoarthritis Outcome Score (KOOS), the Tegner-Lysholm score, the International Knee Documentation Committee (IKDC) Subjective Knee Form, and the modified Cincinnati score at years 1, 2, and 5. The quality of repair tissue was assessed by magnetic resonance imaging using the magnetic resonance observation of cartilage repair tissue (MOCART) score at months 3 and 6 and years 1, 2, and 5.

Results: Significant improvements ($P < .05$) were observed for all 5 KOOS subcategories at year 1 and were maintained through year 5 in 90.5% of patients (19/21). Treatment failure occurred in only 9.5% of patients (2/21). Significant improvements ($P < .05$) from baseline to year 5 were also observed for the IKDC score (30.1 to 74.3), the modified Cincinnati score (38.1 to 79.6), and the Tegner-Lysholm activity score (1.8 to 4.3). Similarly, the MOCART score significantly improved ($P < .001$) from baseline to year 5 (52.9 to 75.8). After 5 years, complete filling (83%) and integration (82%) of the graft were seen in the majority of patients. Signs of subchondral bone edema were still present in 47% of patients at 5 years. No product-specific adverse events were reported over the 5-year follow-up period.

Conclusion: Patients treated with a MACI implant demonstrated significant clinical improvement and good quality repair tissue 5 years after surgery. The MACI procedure was shown to be a safe and effective treatment for symptomatic, traumatic chondral knee defects in this study.

Keywords: cartilage repair; clinical outcomes; matrix-induced autologous chondrocyte implantation; MRI

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One or more of the authors has declared the following potential conflict of interest or source of funding: Dr Marlovits has received from Genzyme a reimbursement for attending a symposium and a consultant fee for speaking at and organizing a symposium. The other authors have no conflicts of interest. Genzyme Biosurgery provided funding to Precise Publications for medical writing support in article preparation.

Articular cartilage defects have a limited capacity for self-repair, as cartilage does not have access to the blood stream, which provides a pathway to nutrients and other cells and proteins that stimulate regeneration.³⁴ Trauma, knee instability, and abnormal loading are often associated with articular cartilage lesions, are common causes of disability, and are often associated with pain, reduction of joint mobility, and loss of function.¹⁷ Because cartilage defects may progress to osteoarthritis over time, early repair may be beneficial and could possibly slow down this progression.^{19,24}

Full-thickness articular cartilage defects can be repaired using a number of cartilage repair techniques that fall into 3 categories: bone marrow stimulation techniques (eg, microfracture),^{20,31} direct chondral replacement techniques (eg, osteochondral autograft transfer [OAT] and osteochondral allograft),¹⁶ and cell culture-based techniques (eg, autologous chondrocyte implantation [ACI] and matrix-induced autologous chondrocyte transplantation/

implantation [MACT/MACI]).^{4,10} The main advantage of cell-based techniques is the development of hyaline-like cartilage as opposed to bone marrow stimulation procedures, which most often produce fibrocartilage, a repair tissue found to be biomechanically inferior to normal hyaline cartilage.²⁵ Compared with osteochondral autografts or allografts, larger defects can be treated with cell-based techniques without increasing the prevalence of donor-site morbidity. Despite their unique morphological and biochemical advantages, the main disadvantage of osteochondral allografts is their lack of availability in some countries.

While in the ACI procedure autologous chondrocytes are directly injected into a defect covered with a periosteal flap fixed with stitches, in the MACI procedure the chondrocytes are cultured on a type I/III collagen membrane, which is then fitted to the defect and fixed with fibrin glue. The use of a solid collagen membrane is advantageous, as it slows down the dedifferentiation⁷ or induces redifferentiation during the culturing process and eliminates the need to collect periosteum.^{8,14,36}

Overall, reported results have demonstrated that MACI is a safe and clinically effective procedure for the treatment of moderate to large symptomatic full-thickness articular cartilage defects, with significant improvements in pain, function, and activity up to at least 5 years.^{**} The MACI procedure also results in good quality repair tissue that is firm with good fill, integration, attachment, and appearance^{3,4,8,11,23,33,36} and has chondrocytes that express type II collagen, proteoglycans, and chondroitin sulfate.^{11,36} Compared with microfracture, the MACI procedure resulted in significantly better improvements in Lysholm, Tegner activity, and International Cartilage Repair Society (ICRS) scores over time⁵ and better repair tissue by magnetic resonance imaging (MRI) analysis.² Additionally, a study comparing the MACI implant with OAT found similar clinical outcomes and reported that MACI repair tissue evaluated by MRI was similar to healthy cartilage but that OAT repair tissue was significantly different from healthy cartilage.²⁹

In this prospective cohort study, we report a 5-year follow-up for clinical and radiological outcomes in patients treated with the MACI procedure for symptomatic chondral defects of the knee.

MATERIALS AND METHODS

Study Design and Participants

For this prospective cohort study, patients were recruited between October 2000 and December 2004 for elective treatment of symptomatic traumatic defects of articular cartilage of the knee with the MACI procedure at a single academic clinical center. Ethical approval for the study was obtained from an institutional review board.

Study participants were men and women 19 to 50 years of age with a defect size $>2\text{ cm}^2$ and no knee instability or

malalignment (axis deviation $>5^\circ$). There were no restrictions on the upper limit of the defect size or number of defects. Patients were excluded from the study if they were obese ($>20\%$ of normal body mass index); had a total or subtotal resected meniscus (but not after partial meniscectomy), severe neurological disorders, metabolic arthritis, joint infections, tumors, psychiatric diseases, arthrofibrosis, or autoimmune diseases; or were pregnant. The morphological characteristics of the meniscus were evaluated with preoperative MRI. All patients provided written informed consent before study enrollment.

Graft Preparation

At the time of initial arthroscopy and grading of the defect, 200 to 300 mg of normal full-thickness hyaline cartilage was biopsied from a minimally weightbearing area of the intercondylar notch and then placed in transport medium. Subsequently, all cell and graft procedures were performed using Good Manufacturing Practices at Verigen Denmark (Copenhagen, Denmark) or Verigen Germany (Leverkusen, Germany). After removal of the extracellular matrix by enzymatic digestion, the chondrocytes were isolated and expanded in monolayer culture using serum taken from the patient at surgery. Once the cell number reached 15 to 20 million, usually within 3 to 4 weeks, the chondrocytes were seeded on a type I/III collagen bilayer membrane (Chondro-Gide, Geistlich, Wolhusen, Switzerland, or ACI-Maix, Matricel, Herzogenrath, Germany).

Surgical Technique

Through a mini-arthrotomy, the cartilage defect was prepared by curettage to remove any fissured and undermined cartilage. Debridement of the subchondral bone plate was performed with care to prevent perforation or subchondral bone bleeding. The dimensions of the defect were transferred to a template; the collagen membrane containing the seeded chondrocytes was trimmed to fit exactly into the defect and then implanted. Orientation of the graft was such that the cells were placed facing the subchondral bone. Fibrin glue (Tissucol, Baxter, Vienna, Austria) was applied on the edges to fix the graft; no periosteal cover or sutures were used. In some cases, 2 or 3 layers of collagen membrane were implanted to completely fill the defect. The joint was manipulated intraoperatively to ensure adherence and stability of the implant. At the conclusion of the procedure, the joint was wrapped in a compressive elastic bandage.

Postoperative Rehabilitation

Immediately after surgery, immobilization of the joint was recommended for 12 to 24 hours, followed by a standardized rehabilitation program. Early rehabilitation began on the second postoperative day with continuous passive motion for 6 to 8 hours per day and was continued for 6 weeks. Continuous passive motion was used to promote the healing process of the transplanted because it has been shown to increase the synthetic activity of the chondrocytes.

**References 8, 9, 12, 13, 15, 21, 23, 30.

Several studies have described that, compared with intermittent active motion, continuous passive motion produces more rapid metaplasia from undifferentiated mesenchymal tissue to hyaline articular cartilage within the healing tissue.^{28,35} In addition, patients were asked to perform isometric muscle contractions and circulation exercises for their lower limb.

Patients were instructed to use crutches immediately after the procedure to avoid full weightbearing. The increase in weightbearing and the restoration of range of motion (ROM) were dependent on the defect's location. Patients with defects in the tibiofemoral joint were allowed partial weightbearing (20% of their body weight) for 6 weeks, followed by a gradual increase. Full weightbearing was not allowed before the eighth postoperative week. The ROM was not restricted, and patients were encouraged to perform ROM exercises in a way that no pain and effusion occurred. Because the physiology of cartilage tissue requires the stimulus of movement and weightbearing to meet biomechanical demands, total immobilization with no weightbearing was avoided.¹ Full ROM and full weightbearing in the early postoperative phase were also avoided to not jeopardize the healing of the grafts, which are still immature at that time. Therefore, limitations on ROM and weightbearing were implemented to ensure optimal healing of the grafts.

If the defect was located in the patellofemoral joint, patients used a knee brace, allowing a ROM between 0° and 20° of knee flexion (S 0-0-20). Patients were allowed partial weightbearing (50% of their body weight) for the first 6 weeks. Full weightbearing with the brace locked at S 0-0-20 was allowed after 6 weeks. Active and passive movements in unloaded positions were restricted to an area of S 0-0-40 for the first 4 weeks. The ROM for active and passive movements in unloaded positions was then increased approximately 20° per week.

For strengthening, isometric, concentric, and eccentric exercises (open and closed kinetic chain) began in the first week after surgery. Neuromuscular exercises were also implemented to improve the dynamic stability of the knee. The increase and progression of the strengthening and neuromuscular exercises were individualized to each patient. Generally, patients underwent postoperative physical therapy 3 times a week from weeks 2 to 6 and then twice a week to 3 months postoperatively.

Clinical Outcomes

Four clinical scores with documented reliability and validity were used to assess outcomes. These included the Knee injury and Osteoarthritis Outcome Score (KOOS), which encompassed pain, symptoms, activities of daily living, function in sport and recreation, and knee-related quality of life.²⁷ Activity level was also evaluated with the Tegner-Lysholm score.³² The International Knee Documentation Committee (IKDC) Subjective Knee Form and the modified Cincinnati score were used to measure subjective symptoms, joint function, and sports activities.^{18,26} Postoperative assessments were performed at 1, 2, and 5 years.

High-Resolution MRI

Magnetic resonance imaging was performed at the beginning of the study on all patients using a 1.0-T MR System (Gyrosan Intera, Philips, Best, the Netherlands). A standard knee MRI protocol was used, including proton-density (PD) and T2-weighted fast spin echo (FSE) sequences for imaging of the cartilage. A circular polarized knee coil was used to apply the following sequences: sagittal T1 spin echo, sagittal dual turbo spin echo (TSE), coronal short T1 inversion recovery (STIR)-TSE, and 3-dimensional gradient echo sequence with fat suppression (3D-GRE-fs). High-resolution images were obtained by placing a flexible standard surface coil (Gyrosan Intera, Philips) with an inner diameter of 8 cm placed over the site of cartilage repair, and a sagittal or axial dual TSE sequence was applied.

The MRI protocol was identical for all patients after 5 years; all sequences were performed on a 3.0-T MR Unit (Tim Trio, Siemens Healthcare, Erlangen, Germany) in combination with a dedicated 8-channel knee coil (Invivo, Gainesville, Florida). The following sequences were performed: (1) a high-resolution PD-TSE sequence (repetition time [TR]/echo time [TE]: 2400/28 msec; flip angle: 160°; field of view [FOV]: 120 × 120 mm; matrix: 512 × 512; slice thickness: 2 mm; voxel size: 0.2 × 0.2 × 2 mm; bandwidth: 244 Hz/Px; number of slices: 32; scan time: 6 min 11 sec); (2) a T2-weighted dual FSE sequence (TR/TE: 5120/9.5 msec; inversion time [TI]: 124 msec; flip angle: 140°; FOV: 180 × 180 mm; matrix: 448 × 448; voxel size: 0.4 × 0.4 × 3 mm; bandwidth: 203 Hz/Px; number of slices: 30; scan time: 6 min 45 sec); (3) a T1-weighted turbo inversion recovery magnitude (TIRM) sequence (TR/TE: 7690/41 msec; TI: 220 msec; flip angle: 150°; FOV: 150 × 150 mm; matrix: 256 × 256; voxel size: 0.6 × 0.6 × 3 mm; bandwidth: 250 Hz/Px; number of slices: 36; scan time: 2 min 35 sec); and (4) an isotropic true fast imaging with steady-state precession (3D-TrueFISP) sequence (TR/TE: 8.9/3.8 msec; flip angle: 28°; FOV: 160 × 160 mm; matrix: 384 × 384; voxel size: 0.4 × 0.4 × 0.4 mm; bandwidth: 200 Hz/Px; number of slices: 320; scan time: 6 min 45 sec).

The MRI scans were evaluated using the magnetic resonance observation of cartilage repair tissue (MOCART) scoring system, a method developed for use after autologous chondrocyte transplantation in the knee,²² with the PD-TSE, the dual FSE, and the TIRM sequences. The TIRM sequence was used to assess the bone for fluid (bone bruise). Each patient was assessed at baseline, 3 and 6 months, and 1, 2, and 5 years. Scoring was recorded for 9 separate parameters of graft outcome: degree of the defect fill, integration with the border zone, condition of the repair tissue, signal intensity on 2 different sequences (PD-TSE and dual FSE; classified as normal, nearly normal, and abnormal, relating to signal alteration in comparison with the adjacent cartilage), integrity of the subchondral lamina and bone, and presence of adhesions and effusion. The total score ranges from 0 to 100. In more specific examinations, bone marrow edema was graded from 0 to 4 (normal, small, medium, large, or

diffuse, respectively), and joint effusion was graded from 0 to 3 (absent, small, medium, or large). The MRI scans were read by 2 independent readers experienced in musculoskeletal imaging and cartilage repair.

Safety

Adverse events included inflammation, elevation of body temperature, intra-articular hematoma, or swelling that resulted in readmission of the patient or further invasive procedures. Swelling and effusion were recorded as adverse events if flexion and extension of the knee were impaired and the postoperative aspiration of the knee joint revealed more than 30 mL of intra-articular fluid.

Statistical Analysis

The statistical analysis included a tabular description of the demographic data, the subjective clinical scores, and the MRI evaluation. For data analysis, a 1-way analysis of variance (ANOVA) with repeated measures was performed to compare the respective scores at the different time points, as the clinical outcome data approximately followed a normal distribution. Significance was reached at $P < .05$. Mean values and standard deviations were calculated for clinically meaningful changes in the KOOS, IKDC, modified Cincinnati, and Tegner-Lysholm scores.

RESULTS

Disposition and Demographics

Twenty-four MACI procedures were performed in 21 consecutive patients (Table 1). One patient had 2 grafts performed, while another had 3 grafts. Of the 21 patients enrolled in the study, 18 patients completed both the clinical and imaging section of the 5-year follow-up. Two patients did not complete the study because of treatment failure, and 1 patient did not have any imaging performed. None of the patients was lost to follow-up.

The mean age of patients at the time of implantation was 35.2 years (range, 20-48 years). Of the 24 chondral defects treated with the MACI implant, the mean defect size was 5.1 cm² (range, 2.4-9.9 cm²), and 13 were located on the medial femoral condyle, 4 on the lateral femoral condyle, and 7 on the patella. One patient had a diagnosed osteochondral defect, and the MACI procedure was combined with a bone graft. Before the MACI procedure, 16 patients (76.2%) had undergone procedures including meniscus and/or ligament surgery, patellofemoral surgery, osteotomy, debridement, or bone marrow stimulation.

Clinical Assessment

Overall, all patients showed significant improvement on all clinical outcomes. Specifically, significant improvements ($P < .05$) were observed for all 5 KOOS subcategories at year 1, and the improvements were maintained through year 5 (Figure 1), with 90.5% of patients (19/21)

TABLE 1
Demographics

Variable	Values
N	21
Grafts, n	24
Age, mean (range), y	35.2 (20.1-47.8)
Sex, n (%)	
Male	18 (86)
Female	3 (14)
Defect size, mean (range), cm ²	5.1 (2.4-9.9)
Defect location, n (%)	
Medial femoral condyle	13 (54)
Lateral femoral condyle	4 (17)
Patella	7 (29)
Prior procedure, n (%)	16 (76)

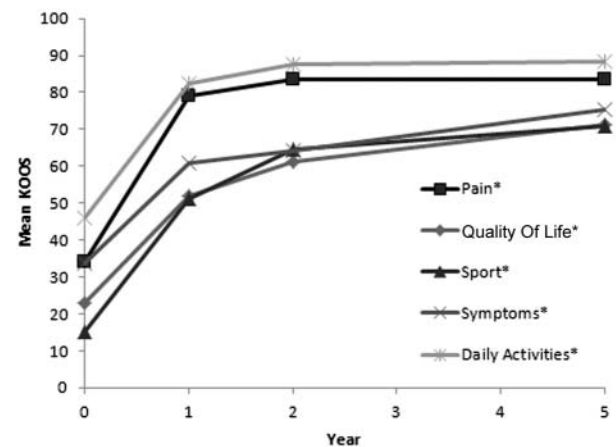


Figure 1. Mean scores for the Knee injury and Osteoarthritis Outcome Score (KOOS) subscales in patients treated with matrix-induced autologous chondrocyte implantation over time. * $P < .05$ for years 1, 2, and 5 compared with baseline.

improving over 5 years. The overall KOOS increased from 29.6 ± 9.15 to 77.7 ± 21.2 ($P < .05$). The mean IKDC score before surgery was 30.1 ± 6.6 , with symptoms including pain and effusion and a reduced knee function and inability to perform sport activities. The patients experienced the greatest improvements during the first year and reached a stable improvement 2 years postoperatively (Figure 2A). After 5 years, the IKDC score was 74.3 ± 20.4 ($P < .05$). In addition, the mean modified Cincinnati score (Figure 2B) and the mean Tegner-Lysholm activity score (Figure 2C) significantly improved from baseline to year 1 ($P < .05$), and all outcome scores maintained this improvement over 5 years.

MRI Assessment

At 60 months, the mean MOCART score significantly increased from 52.9 at baseline to 75.8 ± 18.0 ($P < .001$) (Figure 3 and Table 2). A significant improvement in the

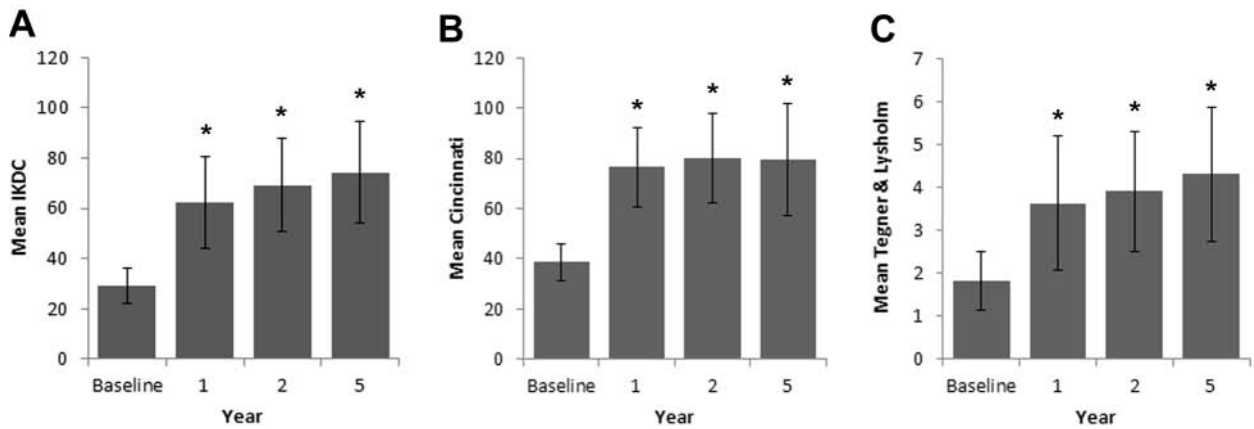


Figure 2. Mean (A) International Knee Documentation Committee (IKDC) scores, (B) modified Cincinnati scores, and (C) Tegner-Lysholm scores for patients treated with matrix-induced autologous chondrocyte implantation over time. * $P < .05$ for years 1, 2, and 5 compared with baseline.

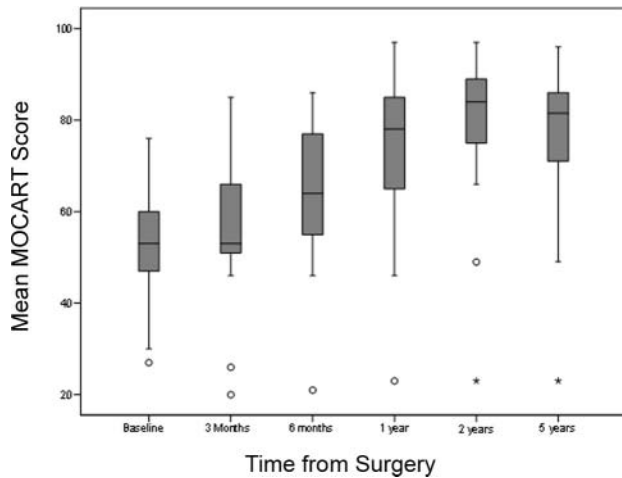


Figure 3. Box plot of the magnetic resonance observation of cartilage repair tissue (MOCART) score for magnetic resonance imaging assessment.

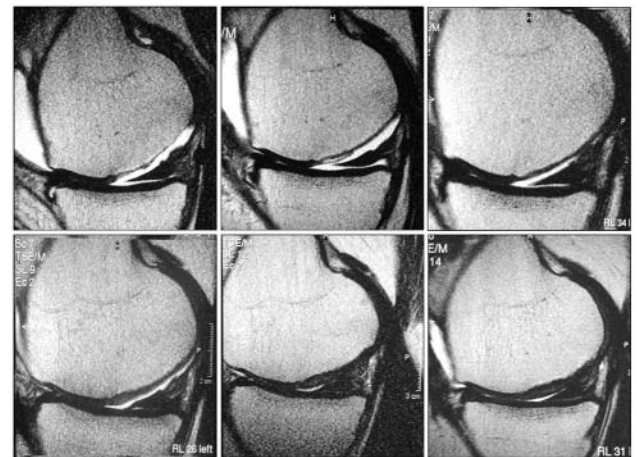


Figure 5. Development of the cartilage repair tissue of a medial femoral condyle defect treated with matrix-induced autologous chondrocyte implantation (sagittal dual T2-FSE) over time. From left to right: preoperative; 3-, 6-, and 12-month; and 2- and 5-year postoperative magnetic resonance imaging scans. By 2 years postoperatively, the defect was completely filled with good integration to the adjacent cartilage and subchondral bone.

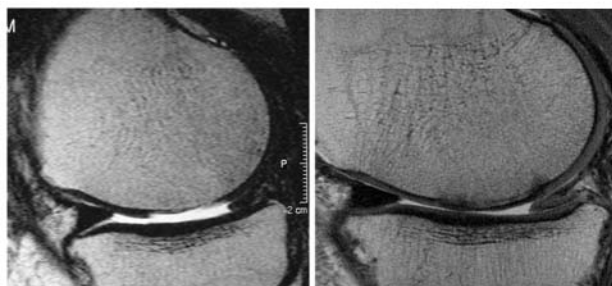


Figure 4. Complete filling and integration of the cartilage repair tissue on a medial femoral condyle 5 years after matrix-induced autologous chondrocyte implantation (sagittal dual T2-FSE). Left: preoperative magnetic resonance imaging (MRI) scan; right: 5-year MRI scan.

MOCART score was observed as early as 3 months ($P = .049$) and continued to increase and remain significantly higher relative to baseline throughout the study ($P < .001$) (Figure 3 and Table 2). At 5 years, complete filling of the defect was observed in 83.3% of cases (Figure 4). Development of cartilage repair tissue over time is shown in Figure 5.

The rate of subchondral bone edema peaked at 3 months (71% of cases). After 3 months and until the end of the follow-up period, there was a gradual persistent decline in the rate, with 47.4% (9/19) of the patients showing signs of subchondral bone edema at 5 years.

TABLE 2

Magnetic Resonance Imaging Assessment: Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) Score					
Time From Surgery	n	Minimum	Maximum	Mean \pm Standard Deviation	P Value ^a
Baseline	21	27	76	52.9 \pm 12.5	
3 months	21	20	85	56.9 \pm 15.2	.049
6 months	21	21	86	64.3 \pm 14.9	<.001
1 year	21	23	97	74.6 \pm 18.3	<.001
2 years	21	23	97	79.2 \pm 17.2	<.001
5 years	18	23	96	75.8 \pm 18.0	<.001

^aP value versus baseline.

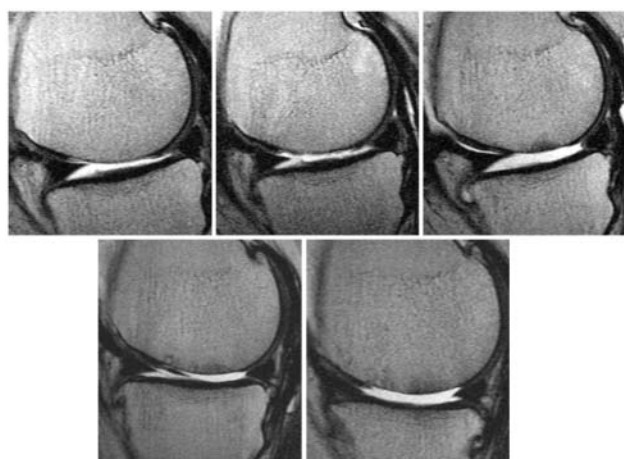


Figure 6. Failure of a matrix-induced autologous chondrocyte implantation graft on a medial femoral condyle defect (sagittal dual T2-FSE) over time. From left to right: preoperative; 3-, 6-, and 12-month; and 2-year postoperative magnetic resonance imaging scans.

Complete integration of the graft with the surrounding native cartilage occurred rapidly and at a high level, with 82% of patients appearing to have complete cartilage integration as soon as 3 months after surgery. Over the course of the follow-up period, 12 patients maintained their initial integration status, 3 patients showed signs of improved integration, and 2 patients showed deterioration from complete integration to partial integration.

Bone integration of the graft typically occurred by the 3-month scan. At 2 years postoperatively, complete bone integration had occurred in all graft sites (95%) except for 1, which initially showed no signs of bone integration but had partially integrated by 2 years. Furthermore, 1 graft deteriorated from fully integrated at 3 months to partially integrated at 12 months, but full integration recurred between 12 and 24 months. At 5 years postoperatively, 94% showed complete integration to the subchondral bone.

No adhesions were seen in the femoral condyle grafts, but 2 of the 7 patella grafts (29%) had adhesions. One patient with a patella graft who developed an adhesion was noted to have severe osteoarthritis on the 3-month MRI scan. Subchondral cysts were observed in 5 cartilage defects preoperatively, but all resolved after surgery. At

2 years, 1 of the subchondral cysts had recurred. No further change in subchondral bone cyst prevalence was observed 5 years postoperatively.

Volume filling of the defects was observed to be good at 2 years, with 83% of femoral grafts showing greater than 51% volume filling and 65% of grafts showing greater than 76% filling. One graft showed no signs of filling at 3 months but began to fill by 12 months. Throughout the follow-up period, there was a clear trend of a gradual increase in volume filling of the defects. After 5 years, 76% of the femoral grafts showed normal filling of the defect.

The PD-TSE and dual FSE sequences provided the most meaningful data with regard to signal intensity. The majority of grafts showed signal intensity equal to articular cartilage at the 5-year follow-up MRI, with more than 76% of the femoral condyle grafts showing signal intensity equal to the adjacent cartilage.

Complications and Failures

No product-specific adverse events were recorded for any of the 21 patients. Typical postoperative swelling and effusion resolved in all patients within 4 weeks of the MACI procedure and were not rated as product-specific adverse events. No postoperative fever, infection, or reoperation occurred. No serious adverse events were reported, and no deaths occurred. Graft hypertrophy of the medial femoral condyle was found in 2 cases, which both resolved after 2 years. There were no cases of graft hypertrophy in patients with patella grafts.

Two patients had a treatment failure between years 2 and 5 because of pain; 1 patient was treated with arthroscopy and debridement, and the other had a knee replacement. In the latter patient, delamination of the cartilage repair tissue occurred between 6 and 12 months, and the transplanted area was completely empty 2 years postoperatively (Figure 6).

DISCUSSION

This is the second largest study reporting 5-year clinical and imaging outcomes of patients treated with the MACI procedure for symptomatic, traumatic chondral defects. Overall, a significant improvement in all subscales of the KOOS and the modified Cincinnati, IKDC, and Tegner-Lysholm scores was demonstrated shortly after the 3-month

assessment period and was maintained through 5 years. Furthermore, the majority of patients showed good quality repair tissue on imaging, demonstrating complete integration of the graft as early as 3 months, which was also maintained through 5 years. The MACI procedure was successful in 90% of patients with a good safety-related profile.

Previously reported studies have also shown significant improvements in clinical scores up to 5 years in patients treated with the MACI procedure for chondral defects. Ebert and colleagues¹² found significant improvements in all subcategories of the KOOS as well as the physical component summary and mental component summary of the SF-36 survey in 35 patients with 46 lesions. Similarly, Bauer and colleagues⁶ found significant improvements for 18 patients in all KOOS subcategories for up to 5 years, although the improvement for the symptoms subcategory was significant only up to the 3-year time point. Furthermore, Behrens and colleagues⁸ found significant improvements from baseline in the ICRS score, the Lysholm-Gillquist score, and the Meyers score for the 11 patients assessed at 5 years. However, no significant improvement was observed in their Tegner-Lysholm score.

Ebert and colleagues¹² also found similar imaging results at their 5-year follow-up, with 89% of grafts having good to excellent filling of the graft defect, 72% of grafts with good to excellent subchondral bone, and 67% having good to excellent graft infill. In addition, Genovese et al¹³ showed similar results at their 5-year follow-up, with 73% of their cases having complete lining of the defect, 60% with complete integration to the border zone, and 73% having a homogeneous structure and regular surface of repair tissue. However, the study by Bauer and colleagues⁶ described a cohort with only 33% of patients with medial knee osteoarthritis showing good infill of the defect after 5 years. The authors reasoned that the discrepancy observed in their MRI outcomes compared with other more positive studies may have been because their patients had a relatively large lesion size and more previous operations and were older than 49 years of age.⁶

Generally, patients treated with a MACI implant appear to have a favorable safety profile. Although no adverse events were reported in our study, 2 cases of deep vein thrombosis had been reported in early postoperative stages of a previous study.¹² In our study, we observed a 10% treatment failure rate (2/21), which is close to other reported rates (2%-7%) for MACI-treated patients,^{12,13} although 1 study reported a graft failure rate as high as 47% (7/17).⁶ In the latter study, the authors speculated that advanced age (>49 years) in 6 of the 7 treatment failures and noncompliance with the rehabilitation regimen were the possible reasons for the high rate of graft failure observed.⁶ Previous studies have reported hypertrophic graft rates of 13% at 5 years,¹³ although in our study, only 2 cases of graft hypertrophy were observed, and both resolved within 2 years with no arthroscopic debridement required. Overall, the results of our study are consistent with those of a recent review by Brittberg,⁹ which reported that rates of postoperative complications and/or adverse events are low (0%-6.3%) with the MACI implant and can include tissue hypertrophy, infections, subsequent surgical procedures, and treatment failures.

The limitations of this study are that it was a prospective case series that lacked any comparative cohort or control. However, this is one of the few prospective MACI studies presenting both clinical and MRI analyses for up to 5 years.^{6,12,13} Another limitation of the study is that it has a relatively small cohort, although only 1 other study evaluated more patients at 5 years.¹² Finally, only imaging data were recorded, and no histological analyses were performed on the repair tissue because most patients did not want to undergo unnecessary further invasive surgery.

In summary, we have shown that patients treated with the MACI procedure demonstrate significant clinical improvement and good quality repair tissue at 5 years. In our study, the MACI procedure was shown to be a safe and effective treatment for symptomatic, traumatic chondral knee defects. Longer term follow-up studies with more patients are warranted to assess if the beneficial effect of MACI implants lasts through a longer assessment period.

ACKNOWLEDGMENT

The authors acknowledge Dominique Verlaan, PhD, from Precise Publications LLC for providing medical writing support.

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