Arthroscopic Autologous Minced Cartilage Implantation of Cartilage Defects in the Knee

A 2-Year Follow-up of 62 Patients

Stefan Schneider,[*] MD, Robert Ossendorff,[†‡] MD, Sebastian G. Walter,[§] MD, Moritz Berger,[‖] PhD, Christoph Endler,[¶] MD, René Kaiser,[*] MA, Ansgar Ilg,[*] MD, Gian M. Salzmann,[#**] MD, and Johannes Holz,[*††] MD
Investigation performed at OrthoCentrum Hamburg, Hamburg, Germany

Background: Symptomatic cartilage defects of the knee joint are frequently diagnosed and can be treated with different available surgical methods. Nevertheless, there is currently no gold standard treatment for all indications. Minced cartilage implantation is increasingly coming into focus as a refined surgical technique.

Purpose: To investigate the 2-year clinical and radiological outcomes of arthroscopic autologous minced cartilage repair with the standardized commercial implantation system AutoCart.

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

Methods: A total of 62 consecutive patients were included and prospectively evaluated preoperatively and at 3, 6, 12, and 24 months postoperatively. Outcomes were assessed using the Knee injury and Osteoarthritis Outcome Score (KOOS), visual analog scale (VAS) for pain, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Single Assessment Numeric Evaluation (SANE), and Tegner activity scale at all follow-up time points. The examination of preoperative magnetic resonance imaging (MRI) was performed using the Area Measurement and Depth and Underlying Structures (AMADEUS) score, and the examination of MRI at 24 months was performed using the Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) 2.0 score.

Results: There were 34 male and 28 female patients (mean age, 38.79 $\pm$ 10.78 years) with symptomatic cartilage lesions with a mean defect size of 2.53 $\pm$ 1.24 cm^2. Lesions were predominantly International Cartilage Repair Society grade 3 located in the region of the femoral condyles. Concomitant surgery was performed in 40.3% of patients. The total KOOS score significantly improved from 62.4 $\pm$ 13.1 at baseline to 74.4 $\pm$ 15.9 at 24 months ($P < .001$). The secondary outcome measures of the VAS, WOMAC, and SANE showed a similar pattern, with score improvements in the follow-up period compared to baseline. The mean AMADEUS score was 64.75 $\pm$ 13.87, while the mean MOCART 2.0 score was 62.88 $\pm$ 9.86, among 20 available patients. The revision surgery rate was 8.1% mainly because of hypertrophy (6.5%).

Conclusion: Among this cohort of patients, minced cartilage implantation demonstrated satisfying 2-year outcomes with increased patient-reported outcome measure scores from 3 to 24 months postoperatively. Regenerated tissue quality on MRI was comparable to that using other cartilage repair methods and showed no associations with patient characteristics or patient-reported outcome measures. Larger cohorts, longer postoperative intervals, and comparable trials are needed to further evaluate the role of this technique in treating cartilage defects.

Keywords: knee; articular cartilage; articular cartilage resurfacing; biological healing enhancement; minced cartilage; particulated cartilage; patient-reported outcome measures

Osteochondral lesions across the knee joint are frequent and display premature osteoarthritis. Typical clinical symptoms are swelling, pain, and loss of function.[10] The

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primary goal of every cartilage repair procedure is to generate the highest possible repair tissue quality, as this is related to a good clinical outcome, return to sports, and long-term durability. Several different techniques have been presented to repair these lesions.[5] Autologous chondrocyte implantation (ACI) has clearly evolved as a frequently used technique with a robust track record and long-term data.[29] Yet, several drawbacks are evident: 2-stage costly procedure, donor site morbidity in the non-weightbearing area of the harvested osteochondral cylinders, dedifferentiation of expanded cells, and regulatory burdens. Fresh osteochondral allograft transplantation represents an attractive 1-stage procedure with a rather quick time to return to sports.[35] However, it is not available in every country. Minced cartilage implantation is a single-stage surgical procedure, which has recently gained interest. The surgical technique was first introduced by Albrecht et al[1] in 1983. In this 1-step procedure, cartilage tissue is removed from the defect's edge and reimplanted.[37] Reimplanted tissue is thus differentiated according to location. Sharp cutting (removal with a shaver, by hand, or with a scalpel) activates the cartilage cells, allowing them to redifferentiate. The technique described here is performed arthroscopically, with platelet-rich plasma (PRP) enhancement.[2] Fixation is performed using autologous thrombin or fibrin, which is produced from PRP.[40] There is currently limited evidence, but the first 5-year results of the open approach have recently been published with satisfactory pain reduction and increased activity levels.[36] The biological background of the technique has also been previously published.[31,38] The present study aimed to report the 2-year clinical and radiological outcomes of arthroscopic minced cartilage implantation utilizing a shaver, tissue collector, and preparation system.

METHODS

This study was approved by the local ethical committee (2021-10018-BO-ff) before study initiation. Informed consent forms were signed by all patients.

Surgical Procedure

The indications for the surgical procedure were symptomatic cartilage defects or osteochondral defects of the knee joint, as previously described in detail.[40] Kissing lesions and advanced osteoarthritis were a contraindication of this procedure. All surgical interventions were performed by 2 senior orthopaedic surgeons (S.S., and J.H.). All patients underwent preoperative magnetic resonance imaging (MRI) and standard radiography (not included in this study). In the case of coexisting abnormalities (eg, ligamentous instability, mechanical axis malalignment, meniscal injury, or patellar instability), further appropriate interventions were carried out. Malalignment of >3° varus or valgus with cartilage defects in the overloaded compartment necessitated osteotomy. Patients with indications for osteotomy were excluded for a better analysis of the procedure described. Minced cartilage implantation was performed during routine diagnostic arthroscopic surgery. The plastic spongiosa technique was performed in cases of osteochondral lesions. Cancellous bone from the iliac crest was harvested and filled in the defect, which was combined with minced cartilage implantation as a sandwich procedure. In all cases, the arthroscopic minced cartilage implantation technique was performed with the AutoCart system (Arthrex) as described previously.[40] In short, cartilage was harvested from the defect with minimal enlargement of the defect after preparation with a 3.0-mm soft tissue shaver (Arthrex). An autologous tissue collector (GraftNet; Arthrex) was connected to the shaver for harvesting. The calcified layer was removed. No subchondral drilling was performed. Cartilage was minced into small fragments (paste-like appearance) and collected at once. Minced cartilage was subsequently mixed with autologous leukocyte-poor PRP in a ratio of 1:3. An applicator (obturator) was loaded with the chips/PRP mixture. An additional 3 mL of PRP was inserted into a specific device (Thrombinator; Arthrex) to generate autologous thrombin. After the joint dried, the defect was refilled up to 50% to 80% with the mixture of cartilage and PRP using an applicator. After adjusting tissue into the defect, a few drops of autologous fibrin as a final layer were applied to the defect for fixation. After a short waiting period (5 minutes), the joint was moved to confirm that the graft was sufficiently fixed.

Rehabilitation

A standardized postoperative rehabilitation protocol was used for all patients. Immediately postoperatively, the

‡Address correspondence to Robert Ossendorff, MD, Department of Orthopaedics and Trauma Surgery, University Hospital Bonn, Venusberg Campus 1, 53127 Bonn, Germany (email: robert.ossendorff@ukbonn.de).
*OrthoCentrum Hamburg, Hamburg, Germany.
†Department of Orthopaedics and Trauma Surgery, University Hospital Bonn, Bonn, Germany.
§Department of Orthopaedics and Trauma Surgery, University Hospital Cologne, Cologne, Germany.
||Institute of Medical Biometry, Informatics and Epidemiology, Faculty of Medicine, University of Bonn, Bonn, Germany.
¶Department of Diagnostic and Interventional Radiology, University Hospital Bonn, Bonn, Germany.
#Gelenkzentrum Rhein-Main, Hochheim am Main, Germany.
**Schulthess Klinik, Zurich, Switzerland.
††MSH Medical School Hamburg, University of Applied Sciences and Medical University, Hamburg, Germany.
S.S. and R.O. contributed equally to this article.
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Ethical approval for this study was obtained from OrthoCentrum Hamburg (2021-10018-BO-ff).

knee joints were immobilized in a straight brace. On the first postoperative day, continuous passive motion was started. If the medial or lateral femoral condyle had been treated, there was a period of nonweightbearing up to 6 weeks. If the trochlea or patella had been treated, the joint needed to be nonweightbearing for 2 weeks. After that, weightbearing increased to full weightbearing. With patellofemoral transplantation, flexion was limited to 40° for the initial 2 weeks, 60° for weeks 3 and 4, and 90° for weeks 5 and 6.

Patient-Reported Outcome Measures

All patients were assessed using a digital outcome reporting system (Surgical Outcomes System; Arthrex). The use of this outcome reporting system was approved by the local ethical committee previously. Emails with a link were sent to the patients at defined time points, redirecting them to the questionnaires. Patient-reported outcome measure (PROM) scores were collected before surgery and at the 3-, 6-, 12-, and 24-month follow-up time points. The primary PROM was the Knee injury and Osteoarthritis Outcome Score (KOOS) with its specific subscales of Pain, Symptoms, Activities of Daily Living, Sports, and Quality of Life. Secondary complementary PROMs included the visual analog scale (VAS) for pain; Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) for pain, stiffness, and function; Single Assessment Numeric Evaluation (SANE); and Tegner activity scale. The VAS for pain scores ranged from 0 (indicating no pain or best function) to 10 (indicating worst pain or worst function). Additionally, any postoperative complications and reoperations were diligently documented.

Radiological Examination

Preoperative and 24-month postoperative 3-T MRI was performed, and scans were evaluated by 2 independent blinded examiners (a radiologist specializing in musculoskeletal imaging with 7 years of experience [C.E.] and an orthopaedic surgeon with 5 years of experience [S.G.W.]). The Area Measurement and Depth and Underlying Structures (AMADEUS)[17] score was used to preoperatively assess the severity of chondral and osteochondral defects. Intraoperative classification of the defect was performed with the International Cartilage Repair Society (ICRS) grading system. The transplant quality after minced cartilage implantation was evaluated by the Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) 2.0 score, with 100 as the best score and 0 as the worst score, at 24 months after surgery. MRI scans were only obtained if patients had ongoing symptoms, if they had a traumatic episode, or before revision surgery. The reliability of the MOCART score has previously been proven.[41] For this study, the interrater reliability of the 2 examiners was 0.704 for the MOCART 2.0 score and 0.968 for the AMADEUS score; the mean score of both assessments was used.

Statistical Analysis

Statistical analysis was performed using R (Version 4.1.1; R Foundation) by an independent statistical examiner (M.B.). Descriptive analyses included the calculation of means, standard deviations, and ranges for continuous variables and frequencies (absolute and relative) for categorical variables. Linear mixed regression models were used to compare the outcome scores over time. Post hoc pairwise comparisons with the Tukey method were used to compare different time points separately for each outcome. Additionally, multivariable regression models were fitted to adjust for potential risk factors (regression coefficient β). Clinical outcome scores at 24 months were compared to MRI results (MOCART and AMADEUS) using the Spearman rank correlation coefficient (r_s). An r_s of 1 indicates a perfect positive association of ranks, an r_s of 0 indicates no association between ranks, and an r_s of -1 indicates a perfect negative association of ranks. Correlations of r_s between 0.29 and 0.00 or -0.29 and 0.00 were defined as low, 0.30 to 0.65 or -0.30 to -0.65 as medium, and >0.65 or <-0.65 as high. Statistical significance was defined as $P < .05$. Graphical analysis was performed using GraphPad Prism (Version 9; GraphPad Software).

RESULTS

Patient Characteristics

A total of 62 consecutive patients were included in this study with a follow-up of 24 months. The cohort comprised 54.8% of men and 45.2% of women. The mean age was 38.79 ± 10.78 years (range, 14-61 years). The mean body mass index (BMI) was 26.95 ± 5.15 kg/m^2, which is in range with the German population. Overall, 16.1% were active smokers. Additionally, 29 patients (46.8%) reported undergoing at least 1 prior surgery of the knee joint. Concomitant surgery was performed in 25 (40.3%) of the patients, predominantly meniscal resection (n = 17), meniscal refixation (n = 9), and ligament surgery (n = 4 for anterior cruciate ligament reconstruction, n = 2 for medial patellofemoral ligament reconstruction). Detailed patient data are shown in Table 1.

Defect characteristics are displayed in Table 2. In all, 43 patients had a single defect, while 19 patients had 2 or 3 defects. Most of the defects were located in the medial femoral condyle (n = 23), followed by the lateral femoral condyle (n = 13) and patella (n = 12). The remaining defects were located in the trochlea (n = 8), tibia (n = 1), or combined regions (n = 5). The ICRS grade was 3 in 60 patients. However, 2 patients with osteochondritis dissecans showed ICRS grade 4. The cause of the lesion was in most cases focal degenerative (77.4%), whereas 19.4% had traumatic causes. As mentioned, 2 cases were caused by osteochondritis dissecans. The mean lesion size was 2.53 ± 1.24 cm^2, with a range between 0.25 and 6.00 cm^2.

TABLE 1
Patient Characteristics (n = 62)

	Mean ± SD (Range) or n (%)
Sex	
Male	34 (54.84)
Female	28 (45.16)
Age, y	38.79 ± 10.78 (14-61)
Body mass index, kg/m^2	26.95 ± 5.15 (19.00-43.75)
Smoking status	
Yes	10 (16.13)
No	52 (83.87)
At least 1 prior surgical procedure	29 (46.77)
Arthroscopic surgery (including meniscal surgery)	13 (20.97)
Anterior cruciate ligament reconstruction	12 (19.35)
Autologous chondrocyte implantation	2 (3.23)
Medial patellofemoral ligament reconstruction	1 (1.61)
Other	1 (1.61)
Concomitant surgery	25 (40.32)
1 procedure	17 (27.42)
≥2 procedures	8 (12.90)
Type of concomitant surgery	
Ligament reconstruction	6 (16.22)
Meniscal repair	9 (24.32)
Meniscal resection	17 (45.95)
Other soft tissue procedure	4 (10.81)
Other osteochondral procedure	1 (2.70)

TABLE 2
Cartilage Defect Characteristics (n = 62)

	Mean ± SD (Range) or n (%)
No. of defects per patient	
1	43 (69.35)
2	10 (16.13)
3	9 (14.52)
Defect location	
Medial femoral condyle	23 (37.10)
Lateral femoral condyle	13 (20.97)
Trochlea	8 (12.90)
Patella	12 (19.35)
Tibia	1 (1.61)
Combined	5 (8.06)
International Cartilage Repair Society classification	
Grade 3	60 (96.77)
Grade 4	2 (3.23)
Cause of lesion	
Traumatic	12 (19.35)
Osteochondritis dissecans	2 (3.23)
Focal degenerative	48 (77.42)
Lesion size, cm^2	2.53 ± 1.24 (0.25-6.00)
>3	18 (29.03)
2-3	15 (24.19)
1-2	20 (32.26)
<1	9 (14.52)

PROM Scores

The mean total KOOS score was 62.4 ± 13.1 at baseline (preoperatively), with a statistically significant improvement from 6 to 24 months' follow-up (6 months: 72.3 ± 14.0 [$P < .001$]; 12 months: 73.3 ± 14.5 [$P < .001$]; 24 months: 74.4 ± 15.9 [$P < .001$]) (Figure 1). The same pattern was also detected in all subscores. The KOOS Pain, Symptoms, and Quality of Life subscores were significantly increased from baseline to 3 months postoperatively (Pain: 63.8 ± 17.1 vs 71.3 ± 17.3, respectively [$P = .002$]; Symptoms: 49.1 ± 11.5 vs 55.8 ± 11.5, respectively [$P = .001$]; Quality of Life: 31.4 ± 14.9 vs 40.1 ± 19.8, respectively [$P = .009$]). Compared to baseline, the KOOS Activities of Daily Living and Sports subscores were significantly higher at 6 months (Activities of Daily Living: 72.5 ± 19.1 vs 84.2 ± 14.6, respectively [$P < .001$]; Sports: 37.8 ± 24.5 vs 49.8 ± 26.2, respectively [$P = .021$]). None of the KOOS subscores showed a deterioration over the 2-year period.

The mean VAS for pain score was 3.86 ± 2.22 preoperatively and significantly reduced from 3 to 24 months' follow-up (Table 3). The WOMAC pain score showed a similar trend, with improved scores from 3 months' follow-up. The WOMAC stiffness score showed a significant improvement at final follow-up (24 months). The WOMAC function and SANE scores improved from 6 to 24 months' follow-up compared to baseline. Of note, the Tegner score was reduced at 3 and 6 months postoperatively and reached preoperative levels at 12 and 24 months' follow-up.

Multivariable regression analysis investigated the effect of the potential risk factors of age, sex, BMI, smoking status, and lesion size. Detailed findings are summarized in Table 4. BMI was negatively associated with the total KOOS, WOMAC pain and function, KOOS Pain, Symptoms, and Activities of Daily Living and VAS for pain scores. Age, smoking status, and lesion size did not show statistically significant associations. Furthermore, the number of defects, cause of the lesion (traumatic vs degenerative), defect location, and concomitant surgery were not associated with any PROM scores.

MRI Results

Data sets from 20 patients were available for MRI analysis at 2 years' follow-up. There were 42 patients not available for the radiological assessment. The mean preoperative AMADEUS score of these 20 patients was 64.75 ± 13.87. The mean overall MOCART 2.0 score among 20 patients was 62.88 ± 9.86 (Figure 2). For the MOCART 2.0 subscores, there was generally a good fill and integration of repair tissue, but the surface and structure of repair tissue were only fair/poor. Details on the different subscores are displayed in Table 5.

Regression analysis between the MOCART 2.0 score and age, sex, BMI, smoking status, and lesion size did not result in statistically significant differences. The number of defects, cause of the lesion (traumatic vs

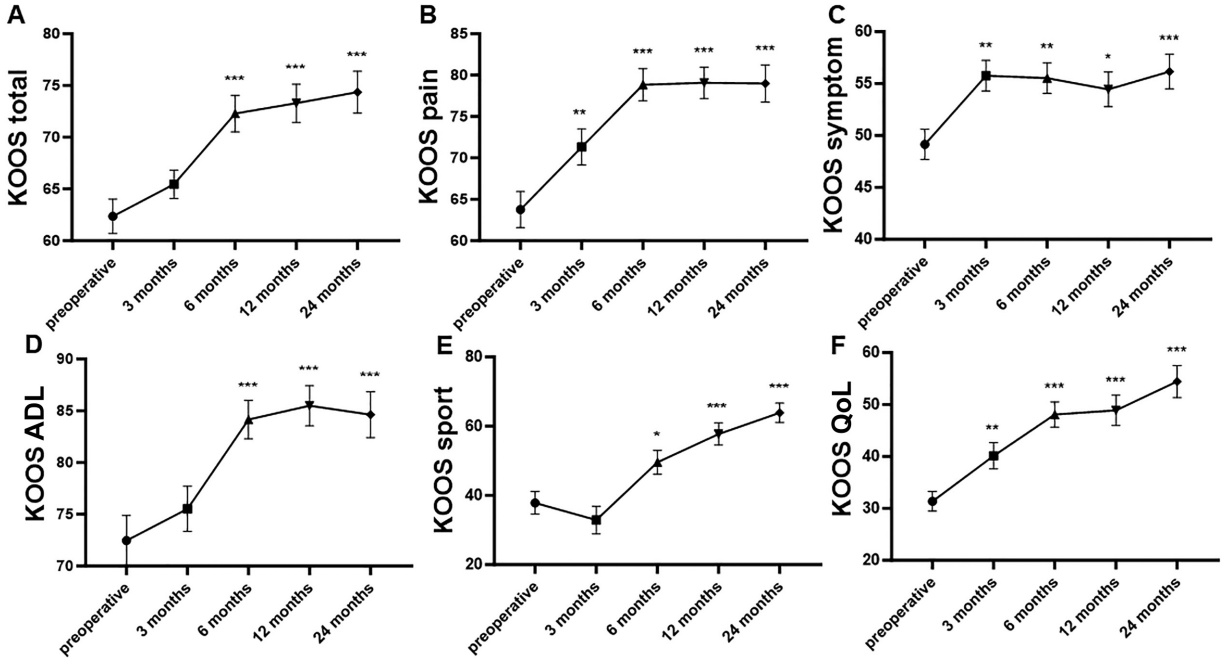

Figure 1. Primary outcome measure of the Knee injury and Osteoarthritis Outcome Score (KOOS). (A) Total KOOS score, (B) KOOS Pain subscore, (C) KOOS Symptoms subscore, (D) KOOS Activities of Daily Living (ADL) subscore, (E) KOOS Sports subscore, and (F) KOOS Quality of Life (QoL) subscore at 3, 6, 12, and 24 months' follow-up compared to preoperatively. *$P < .05$, **$P < .01$, and ***$P < .001$. Values are displayed as mean ± standard deviation.

TABLE 3
Secondary PROM Scores[a]

	Preoperative	3 mo	6 mo	12 mo	24 mo
VAS pain					
Mean ± SD	3.86 ± 2.22	2.23 ± 1.95	2.09 ± 1.82	2.20 ± 1.98	2.50 ± 2.26
P		**<.001**[b]	**<.001**[b]	**<.001**[b]	**<.001**[b]
WOMAC pain					
Mean ± SD	71.2 ± 17.7	78.6 ± 17.4	85.5 ± 13.9	86.1 ± 14.0	83.6 ± 18.3
P		**.002**[c]	**<.001**[b]	**<.001**[b]	**<.001**[b]
WOMAC stiffness					
Mean ± SD	64.5 ± 27.7	64.1 ± 23.6	71.0 ± 25.9	73.2 ± 23.7	74.6 ± 26.1
P		>.999	.382	.117	**.044**[d]
WOMAC function					
Mean ± SD	72.5 ± 19.1	75.5 ± 17.3	84.2 ± 14.6	85.5 ± 15.2	84.6 ± 17.4
P		.563	**<.001**[b]	**<.001**[b]	**<.001**[b]
SANE					
Mean ± SD	45.3 ± 18.3	53.5 ± 22.6	65.7 ± 20.4	65.5 ± 20.5	67.1 ± 23.2
P		.085	**<.001**[b]	**<.001**[b]	**<.001**[b]
Tegner					
Mean ± SD	4.29 ± 2.49	2.52 ± 1.68	3.35 ± 1.38	3.73 ± 1.78	3.84 ± 1.69
P		**<.001**[b]	**.005**[c]	.219	.993

[a]PROM, patient-reported outcome measure; SANE, Single Assessment Numeric Evaluation; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.
[b]Bolded values indicate statistical significance: $P < .001$.
[c]Bolded values indicate statistical significance: $P < .01$.
[d]Bolded values indicate statistical significance: $P < .05$.

TABLE 4
Regression Analysis of Risk Factors[a]

	Age		Sex		BMI		Smoking Status		Lesion Size	
	β	*P*	β	*P*	β	*P*	β	*P*	β	*P*
KOOS										
Total	–0.126	.477	–4.631	.126	–0.808	**.014**[b]	0.189	.962	–0.881	.471
Pain	–0.203	.295	–8.286	**.014**[b]	–1.030	**.005**[c]	–1.185	.784	–1.003	.453
Symptoms	0.224	.108	–2.741	.242	–0.835	**.001**[c]	3.165	.307	–1.546	.108
Activities of Daily Living	–0.137	.493	–6.230	.071	–1.037	**.006**[c]	0.867	.847	–0.519	.708
Sports	–0.316	.235	–12.827	**.006**[c]	–0.922	.058	1.963	.739	–1.406	.439
Quality of Life	–0.358	.163	–5.387	.215	–0.359	.434	2.901	.612	1.459	.408
VAS pain	0.004	.888	0.756	.057	0.109	**.011**[b]	–0.109	.833	0.074	.640
WOMAC										
Pain	–0.152	.415	–6.162	.055	–1.165	**.001**[c]	–0.244	.953	–0.954	.459
Function	–0.137	.493	–6.230	.071	–1.037	**.006**[c]	0.867	.847	–0.519	.708
Stiffness	0.130	.676	–5.654	.287	–0.957	.092	–1.820	.794	–3.776	.084
SANE	–0.096	.670	–3.477	.366	–0.339	.406	2.768	.586	0.769	.623
Tegner	–0.032	.136	–0.545	.114	–0.062	.090	–0.131	.771	0.051	.713

[a]BMI, body mass index; KOOS, Knee injury and Osteoarthritis Outcome Score; SANE, Single Assessment Numeric Evaluation; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.
[b]Bolded values indicate statistical significance: $P < .05$.
[c]Bolded values indicate statistical significance: $P < .01$.

TABLE 5
MOCART 2.0 and AMADEUS Scores[a]

	Mean ± SD	Possible Range
MOCART 2.0		
Overall	62.875 ± 9.864	0-100
Volume fill of cartilage defect	14.500 ± 3.890	0-20
Integration into adjacent cartilage	11.625 ± 3.649	0-15
Surface of repair tissue	5.375 ± 2.862	0-10
Structure of repair tissue	1.375 ± 3.395	0-10
Signal intensity of repair tissue	9.625 ± 3.078	0-15
Bony defect or bony outgrowth	5.750 ± 3.111	0-10
Subchondral changes	14.625 ± 4.442	0-20
AMADEUS		
Overall	64.750 ± 13.865	0-100
Area	28.625 ± 6.886	0-40
Depth	6.375 ± 7.249	0-20
Underlying structures	25.750 ± 5.006	0-30
Addendum	4.000 ± 4.961	0-10

[a]AMADEUS, Area Measurement and Depth and Underlying Structures; MOCART, Magnetic Resonance Observation of Cartilage Repair Tissue.

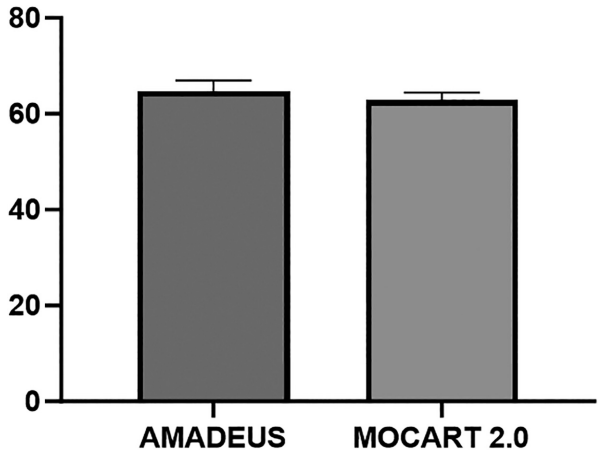

Figure 2. Qualitative evaluation of the cartilage defect preoperatively by the Area Measurement and Depth and Underlying Structures (AMADEUS) score and of resulting repair tissue by the Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) 2.0 score at 24 months' follow-up after minced cartilage implantation. Values (n = 20) are displayed as mean ± standard deviation.

degenerative), defect location, and concomitant surgery were also not associated with the MOCART 2.0 score. Associations between clinical scores and MOCART 2.0 and AMADEUS scores are presented in Table 6. A trend of positive association with the MOCART 2.0 score was only significant for the KOOS Sports subscore. The Tegner score was significantly associated with higher MOCART 2.0 scores. No statistically different associations were detected for the AMADEUS score.

Adverse Events

Adverse events were assessed in the cohort of 62 patients (Table 7). A total of 5 (8.1%) patients needed revision surgery. The most common adverse event related to surgery was hypertrophy. Patients returned to work at a mean of 64.18 ± 54.42 days after surgery.

TABLE 6
Associations of MOCART 2.0 and AMADEUS Scores to Clinical Scores[a]

	MOCART 2.0 Score at 24 mo		AMADEUS Score Preoperatively	
	β	*P*	β	*P*
KOOS				
Total	0.262	.081	–0.065	.783
Pain	0.202	.146	–0.061	.780
Symptoms	0.164	.307	–0.313	.195
Activities of Daily Living	0.096	.603	0.023	.934
Sports	0.184	**.044**[b]	–0.050	.733
Quality of Life	0.124	.116	–0.039	.754
VAS pain	–0.928	.243	–0.195	.511
WOMAC				
Pain	0.098	.522	0.020	.933
Function	0.096	.603	0.023	.934
Stiffness	0.127	.143	–0.186	.158
SANE	0.190	.083	–0.091	.599
Tegner	2.198	**.017**[b]	0.087	.954

[a]AMADEUS, Area Measurement and Depth and Underlying Structures; KOOS, Knee injury and Osteoarthritis Outcome Score; MOCART, Magnetic Resonance Observation of Cartilage Repair Tissue; SANE, Single Assessment Numeric Evaluation; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.
[b]Bolded values indicate statistical significance: $P < .05$.

TABLE 7
Adverse Events

	Mean ± SD (Range) or n (%)
Revision surgery	5 (8.06)
Hypertrophy resection	4 (6.45)
Implantation of mini-endoprosthesis	1 (1.61)
Time to return to work, d	64.18 ± 54.42 (10-227)

DISCUSSION

The main finding of our study is that arthroscopic minced cartilage implantation for the treatment of cartilage lesions of the knee was an effective and safe procedure. The 2-year data of 62 patients showed an improvement on all PROMs. The results were clinically relevant and comparable with those of other currently used cartilage restoration methods.[34]

Clinical Outcomes and Comparison With Other Cartilage Repair Techniques

There are various methods to regenerate or treat damaged articular cartilage. One method is to stimulate bone marrow to build and repair cartilaginous tissue (eg, microfracture or autologous matrix-induced chondrogenesis). The clinical results for microfracture are rather poor because of the lower quality of fibrocartilaginous regenerated tissue (low quantity of collagen type 2).[11,35] Nevertheless, long-term clinical results for the combination of a membrane with microfracture (autologous matrix-induced chondrogenesis) are satisfactory.[18]

Another technique includes osteochondral transplantation with allografts or autografts. Limiting factors are a lack of congruence or limited donor site availability and high costs. Nevertheless, this technique shows good long-term results.[16,32]

Good long-term results are also described for ACI. Brittberg et al[4] conducted a prospective randomized trial of matrix-induced ACI versus microfracture. They detected a superior clinical outcome in patients with a defect size of >3 cm^2 after 5-year follow-up. In a prospective multicenter phase 3 trial of hydrogel-based arthroscopic ACI in patients with large cartilage defects (4-12 cm^2), Niemeyer et al[27] reported an increase in the overall KOOS score from 39.8 points at baseline to 86.1 points at 2 years' follow-up, which is a stronger improvement compared to our study. However, the baseline score in our study was higher, which makes a comparison difficult. Significant disadvantages of ACI are the high costs for general health services and that it is a 2-stage procedure.[25]

The data available for minced cartilage implantation remain limited, although the technique was already described in the 1980s. Runer at al[36] published satisfactory 5-year results with few complications utilizing an open technique. In the current study, the mean VAS for pain score was 3.86 preoperatively, with a significant improvement to a score of 2.50 at 24 months. In comparison to other studies, patients reported decreased pain at baseline. Additionally, Runer et al[36] reported a preoperative numeric rating scale score of about 7, with a decrease to a score of 2 at 2 years' follow-up. Consequently, their 34 patients reported a higher preoperative pain level but a similar follow-up result compared to our study. Other

publications with this technique have included only a few patients and reported on data at 1-year follow-up.[6,12,44] Saris et al[39] reported clinical outcomes at 5 years' follow-up after 1-step cell-based cartilage repair using recycled autologous chondrons and allogeneic mesenchymal stem cells. A combination of 10% autologous chondrons recycled from debrided defect tissue and 90% allogeneic bone marrow–derived mesenchymal stem cells was used to treat symptomatic cartilage defects on the femoral condyle or trochlear groove in 35 patients. The overall KOOS score significantly improved from 57.9 ± 16.3 at baseline to 78.9 ± 17.7 at 5 years' follow-up. The VAS for pain score also showed a significant improvement. Cugat et al[9] used an autologous matrix with hyaline cartilage chips and platelet-rich growth factors for the treatment of full-thickness cartilage or osteochondral defects in a preliminary study of 15 patients. Their mean follow-up was 15.9 months. The PROMs including the VAS for pain, WOMAC pain and stiffness, Lequesne index, and 12-item Short Form Health Survey physical component summary showed significant improvements from baseline. Interestingly, both studies exclusively utilized cartilage from the debrided lesion rim. Other studies have reported good clinical outcomes when using healthy cartilage from non-weightbearing regions or combining cartilage from the defect site with healthy cartilage.[22,42]

MRI Findings

The MOCART 2.0 score showed comparable results to previously published results of minced cartilage implantation.[36] Runer et al[36] also analyzed unscheduled MRI scans from 19 patients who had symptoms, had trauma, or needed revision surgery in a total series of 28 patients. Their mean follow-up was 41.8 ± 2.2 months after the surgical intervention, with a mean overall MOCART 2.0 score of 62.3 ± 17.4. Interestingly, our 2-year results for 20 patients treated with this standardized technique were lower compared to those treated with the ACI technique.[27,28] Niemeyer et al[27] reported a mean MOCART 2.0 score of 80 points for all included patients (n =25) and 92.1 points for patients with lesions <5 cm^2 (n = 7) after treating large cartilage defects with hydrogel-based ACI. Interestingly, longer follow-up studies of first-generation ACI and microfracture showed worse MRI findings, with a mean MOCART score of 54.1 for microfracture versus 49.8 for ACI, without statistical differences between these techniques after 10 years' follow-up.[30] Consequently, it remains unclear if newer ACI techniques show the long-term durability of high regenerated tissue quality. Interestingly, in our study, the MOCART 2.0 subscores showed a good fill, but poor surface and structural subscores were detected. Nevertheless, the qualitative assessment of repair tissue (MOCART 2.0) did not show significant correlations to PROM scores. Lower regenerated tissue quality did not result in lower PROM scores or greater revision rates at 24 months' follow-up. This was also reported previously for other cartilage repair techniques.[21,23] Therefore, the value of the MOCART 2.0 score for assessing treatment success remains unclear. Moreover, only 20 MRI scans in the cohort of 62 patients were available. This is because of the limited availability of MRI scans, with imaging only performed in selected patients with acute symptoms after trauma or existing pain, which might affect the outcome. It can be hypothesized that the MOCART 2.0 score would be even higher for the 42 patients without symptoms. Wodzig et al[44] published a 12-month follow-up of 14 patients showing satisfactory cartilage coverage, as measured by the MOCART 2.0 score, along with clinically and statistically significant functional improvements, consistent with the findings of our study.

Minced Cartilage Implantation Techniques and Combined Procedures

There are several options to process cartilage with different techniques. This includes enzymatically processed cartilage and mechanically minced cartilage. Typically, the enzymatic process is performed with ACI. The aim of the minced cartilage implantation technique, as with other cartilage procedures, is to form hyaline or hyaline-like tissue. Cell outgrowth, proliferation, and differentiation are fundamental for the formation of cartilage. A major step in implementing this is the sharp fragmentation of cartilage tissue. This was demonstrated by Lu et al[20] as a prerequisite for the formation of "neo-cartilage."

The use of fragmented chondrocytes has been described previously with different techniques, which makes a comparison between the studies difficult. Previous studies of the minced cartilage implantation technique with 2- and 5-year outcomes included the use of a collagen membrane in combination with fibrin glue. Cole et al[8] used a combination of fibrin glue and a synthetic scaffold and a specific mincing device (Cartilage Autograft Implantation System). Christensen et al[7] performed the technique with fibrin glue only. The mincing process was performed by hand with a scalpel. In the current study, we present a standardized procedure with a commercial product and a larger cohort.

Fragmentation leads to the production and proliferation of chondrocytes in the extracellular matrix. The extracellular matrix serves as the microenvironment for chondrocytes and is fundamental for stable cartilage regeneration. To preserve the stable cellular phenotype, chondrocytes rely on their interaction with the pericellular matrix.[14] The pericellular matrix lies between the plasma membrane and the extracellular matrix. Its existence at the interface between the cell and its microenvironment allows it to exert a profound impact on cell function.[24]

Some studies have examined the type of cartilage mincing by different instruments and have come to different conclusions. Mincing with a scalpel or curette was compared with mincing with a shaver. As shown above, the functionality of mincing with a scalpel was proven with the transplantation of larger cartilage fragments at 5 years.[36] It is debatable whether mincing with a shaver also produces a cell-active mass that can lead to proliferation. Gebhardt et al[13] were able to show that viability and proliferation are maintained when the fragments are

removed with a shaver. They compared harvesting with a curette, with a shaver, and with a shaver followed by PRP. The addition of PRP to shaver-minced cartilage resulted in increased proteoglycan production by chondrogenic spheroids in vitro. This suggests progress toward the creation of a cartilage-specific extracellular matrix.

A study by Moser et al[26] showed that the vitality of bovine chondrocytes was reduced after cultivation for 7 days in comparison with shaver harvesting. The use of the selected shaver is critical in this study. There were 3 different sizes of the same shaver type used here. A shaver is a device that has a sharp serrated edge. The size of the tissue fragments produced by the serrated instruments is significantly smaller than that obtained with the 3.0-mm shavers used in technical studies, so that the transplantation of intact pericellular and extracellular tissue components described here is significantly reduced.[40] Furthermore, we point out that cartilage tissue from slaughtered bovine knee joints was used in the aforementioned study, which could differ in its functional phenotype compared to human cartilage tissue.

The reaction of cartilage to external stimuli such as pressure or sharp cutting has been previously described.[33] Furthermore, it has also already been shown in vitro that the extent of cartilage fragmentation has a noteworthy impact on extracellular matrix production in vitro. Bonasia et al[3] were able to show that the use of a pasty mass is advantageous. They reported increased outgrowth with enhanced extracellular matrix production with a higher degree of chondral fragmentation in an in vitro study with human cartilage.

In the technique used here, PRP was added to harvested cartilage. The positive effect of PRP on the proliferation and viability of isolated chondrocytes has been demonstrated.[15] As mentioned above, Gebhardt et al[13] showed that tissue obtained and enhanced with PRP led to increased proteoglycan production in vitro. The addition of PRP to shaved minced cartilage tissue had no effect on cell growth, cell viability, or proliferation capacity. However, compared to chondrocytes isolated from cartilage repair tissue without the addition of PRP, it resulted in significantly greater normalized proteoglycan content. This observation suggests that the addition of PRP may improve the ability to form a cartilage-specific extracellular matrix. However, further fundamental investigations are still pending.

The biological background of the technique has been investigated in various in vitro and in vivo studies.[31] The compound of the pericellular matrix and chondrocytes is called the chondron. Although fragmentation reduces the size of cartilage tissue, many of these connections remain. Studies have shown that these appear to have a beneficial chondrogenic effect, even in comparison to first-generation ACI, and studies in comparison with third-generation ACI are pending.[43,45]

Adverse Events

In the present study, 4 patients had to undergo revision surgery because of hypertrophy. As these patients underwent surgery at the beginning of recruitment for this study, this can be attributed to the learning curve of the surgeons regarding filling of the defect with autologous cartilage tissue. Initially, the defects were filled up to the surrounding native cartilage level. In the experience of the senior author (G.M.S.) over the past 5 years, this is not necessary. Only 50% to 80% of the defect needs to be filled. The hypertrophy found, however, confirms a chondroinductive effect and the proliferative properties of tissue.

Hypertrophy is also found in a similar way in ACI. Various possible causes are also being discussed, such as the influence of static compressive stress on the proliferation of chondrocytes. These reasons can presumably be attributed to the minced cartilage implantation technique.[19]

Analogous to all other cartilage therapies, concomitant abnormalities must be addressed. For example, meniscal injuries were included in this study. However, major osseous interventions such as osteotomy were excluded to reduce the impact on the PROM scores.

Limitations

This study has some limitations. A multicenter randomized controlled trial with a comparative group would be the gold standard for the highest evidence. Future studies could explore this concept. Moreover, only MRI data of selected patients (n = 20) were available. The focus of this study was primarily the clinical outcomes (PROM scores) of 62 patients. Future studies should focus on MRI evaluations to confirm the preliminary results reported here. Furthermore, a large number of concomitant surgical procedures may influence the outcomes. Osteotomy procedures were excluded, which are often performed concomitantly with cartilage repair techniques. Future studies with a greater number of patients can address these concerns.

CONCLUSION

Our study first showed the clinical and radiological 2-year results of standardized minced cartilage implantation with a commercially available system. Overall, the procedure was safe with good clinical outcomes on all examined PROMs. Clinical and radiological outcomes were comparable to those of other frequently used cartilage repair techniques. Additional long-term and comparison studies are needed.

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