Third-Generation Autologous Chondrocyte Implantation at the Knee Joint Using the Igor Scaffold

A Case Series With 2-Year Follow-up

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Background: For large, locally restricted cartilage defects in young patients, third-generation matrix-supported autologous chondrocyte implantation (ACI) with a variety of scaffolds has shown good mid- to long-term results.

Purpose/Hypothesis: This study aimed to monitor the clinical and radiological outcomes of patients who received ACI at the knee joint using the Igor scaffold (IGOR–Institute for Tissue and Organ Reconstruction) at 2-year follow-up. Our hypothesis was that there would be improvements in postoperative subjective scores and cartilage repair tissue quality.

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

Methods: A total of 21 patients (12 male and 9 female) were available for 2-year follow-up after third-generation ACI using the Igor scaffold. All were clinically assessed using the Knee injury and Osteoarthritis Outcome Score (KOOS), Tegner Activity Scale, Brittberg score, International Knee Documentation Committee (IKDC) Subjective Knee Form, Noyes Sports Activity Rating Scale, and visual analog scale for pain. For morphological evaluation, the magnetic resonance observation of cartilage repair tissue (MOCART) and MOCART 2.0 scores were calculated using 3-T magnetic resonance imaging performed at 3, 6, 12, and 24 months postoperatively. Results were compared between baseline and 24 months postoperatively.

Results: After 2 years, the clinical and radiological scores showed good to excellent results in the majority of patients. On the IKDC, 10 patients were graded as excellent, 4 as good, 5 as fair, and 2 as severe; on the KOOS, 7 patients were graded as excellent, 8 as good, 4 as fair, and 2 as severe. From baseline to latest follow-up, visual analog scale pain scores decreased from 5.6 ± 3.2 (mean $\pm$ SD) to 1.5 ± 2; KOOS results increased from 51 ± 20.7 to 75.2 ± 15.4; and the Tegner score improved from 2.2 ± 1.8 to 4.3 ± 1.3. The MOCART and MOCART 2.0 scores were comparable at 2-year follow-up, with mean values of 74 ± 10 and 78 ± 13, respectively. Satisfactory filling and integration were found in 90.5%. Overall, 16 of 21 patients (76.1%) were satisfied with the surgery and would undergo the procedure again.

Conclusion: Third-generation ACI using the Igor scaffold showed improvements in clinical and radiological results that were comparable with other scaffolds for patients with large traumatic or degenerative cartilage defects. Patients reported a decrease in pain and an increase in activity, with the majority reporting good results.

Keywords: Igor; cartilage repair; autologous chondrocyte transplantation; MOCART; MRI

Since the emergence of matrix-associated third-generation autologous chondrocyte implantation (ACI) >20 years ago, various scaffolds have been introduced. Today this technique is a well-established procedure for the treatment of large, full-thickness chondral defects, which may change the progression of early osteoarthritis at the knee joint.[16] It shows good mid- to long-term clinical and radiological results, [2,9,17,18] albeit not statistically significant as compared with the microfracture technique.[8]

Radiological and clinical results in the first 10 to 15 years show a peak at 2 years, with a steady state at 5 years and a slight impairment after 10 to 15 years,[1,2,4,5,40] indicating that 2-year results serve as an excellent predictive parameter for radiological and clinical development. At this time point, patients start to participate in their previous sports activities and increase their activities of daily living.

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For cartilage repair imaging, magnetic resonance imaging (MRI) is considered the gold standard.[19] Schreiner et al[32] mentioned that imaging studies for the assessment of knee cartilage and cartilage repair should contain the following set of sequences: 1 sagittal non–fat saturated high-resolution proton density–weighted turbo spin echo (PDw TSE), 1 sagittal fat-saturated PDw TSE, 1 sagittal T1-weighted TSE, and 1 coronal fat-saturated PDw TSE. For patellofemoral lesions, the imaging protocol should as well include an axial version of the fat-saturated PDw TSE sequence. The magnetic resonance observation of cartilage repair tissue (MOCART) score[21] is an excellent tool to evaluate the state and development of repair tissue and presents practical tools for systematic assessment.[19] It was recently revised with a new version and published as the MOCART 2.0,[32] which adapted new sequences and new requirements for cartilage repair tissue.

In the current study, we evaluated the Igor scaffold (provided by IGOR–Institute for Tissue and Organ Reconstruction), a cell-fibrin-collagen construct, for third-generation ACI. The study aims were to show midterm results of a consecutively treated patient population and to compare those with other published 2-year results. Objective and subjective clinical outcomes were assessed during clinical routine follow-ups at the same time point as MRI examination and as compared with different ACI scaffolds.

METHODS

Between 2013 and 2017, a total of 28 consecutive patients were treated at a single academic center with third-generation ACI using the Igor scaffold, a collagen matrix seeded with cultured autologous chondrocytes. The treatment was approved by the local ethics board, and patient consent was given.

The inclusion criteria for performing ACI were set according to the recommendations of the German working group Tissue Regeneration and Tissue Substitutes.[23] Thus, indications for ACI in this study were symptomatic chondral or osteochondral defects of articular cartilage of the knee joint with a defect size >2 cm^2. We excluded patients per the following criteria: age >55 years, osteoarthritis, uncorrected coronal axis deviation $>5^\circ$ or knee instability, total or subtotal meniscal resection, pregnancy, severe neurological disorders, metabolic arthritis, joint infections, tumors, psychiatric disease, arthrofibrosis, and autoimmune diseases. There was no restriction in the number of defects.

Study Patients

Of the 28 patients, 7 had to be excluded for incomplete examinations and data: 1 patient moved abroad, 3 were lost to follow-up, and 3 refused to participate in follow-up. In 1 patient, 3- and 6-month follow-up MRI was missing after metal implantation for valgus-producing high tibial osteotomy, which was removed before the 12-month examination, and in 3 patients, 3-month MRI was missing for other reasons. Ultimately, 21 patients were included in this retrospective study (Figure 1).

A total of 25 cartilage defects were treated (a combined treatment of 2 locations was indicated in 4 patients). Cartilage defects occurred in 12 cases after trauma, in 4 cases attributed to osteochondritis dissecans, and in 5 cases because of local degenerative events. We combined matrix-supported ACI with autologous cancellous grafts in 6 cases, a high tibial osteotomy for deformity correction in 1 case, and a duplication of the medial retinaculum in 2 cases. The patient characteristics are presented in Table 1.

Surgical Technique

For presurgical planning, a clinical evaluation, radiographs in 2 planes, and standing long-leg radiographs are essential and were performed in addition to MRI to assess alignment and grade of osteoarthritis. After arthroscopic defect evaluation, cell harvesting was performed by taking 2 to 4 cartilage samples the size of a grain of rice, using an arthroscopic rongeur or forceps, depending on the defect size. Cartilage and blood samples were sent to IGOR, which specializes in the production of autologous cell cultures.

The cells were cultivated on the basis of the patient's serum and synthetic cell culture media, until 20 to 30 million cells were counted, which usually took 3 to 4 weeks. A lower cell number is an indication for a second biopsy, which was not necessary in our patient population. IGOR offers the opportunity to freeze the cells and to reactivate them within 1 year. In a second surgical procedure, a mini-arthrotomy was set, and the defect area was prepared by curettes to achieve a stable edge to the healthy cartilage. A cell-fibrin solution containing the cultivated chondrocytes was injected with needles into a collagen fleece (Figure 2), which was cut exactly to the size of the defect and placed into it. The scaffold was covered with thrombin solution and fixed to the healthy cartilage with 4 to 8 stitches using a nonresorbable USP 6-0 suture.

We addressed comorbidities as follows: meniscal ruptures by partial meniscectomy (according to the inclusion and exclusion criteria); malalignment with proximal tibial or tibial tubercle osteotomy (depending on the origin of

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Ethical approval for this study was obtained from the Medical University of Vienna.

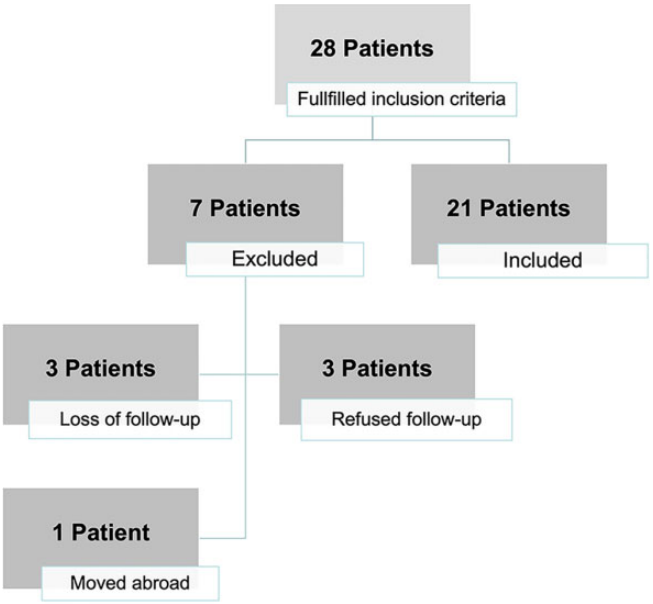

Figure 1. Patient flowchart.

deformity); and anterior-posterior instability, valgus or varus instability, or patellar instability with ligament reconstruction to avoid cartilage compromise.

Postoperative Rehabilitation

All patients in this study underwent the same standardized postoperative rehabilitation protocol, as published in a previous study.[39] This protocol differed according to the location of the treated defect, either the tibiofemoral joint (TFJ) or the patellofemoral joint (PFJ), and was adapted with the patient's rehabilitation progress. Transplants located at the PFJ were allowed earlier full weightbearing (FWB) in comparison with those at the TFJ, which were allowed a wider range of motion, as set through the use of an orthopaedic brace. Patients treated at the PFJ and TFJ followed an individualized program. In both groups, early rehabilitation began on the second postoperative day with continuous passive motion. In the TFJ group, increasing range of motion started with S 0-0-30° (neutral zero method in the sagittal plane, flexion until 30°) to S 0-0-90° (flexion until 90°) in phase 1 and progressed to full range of motion between weeks 4 and 8. For nonweightbearing and partial weightbearing, patients were instructed to use crutches immediately after surgery. Toe-touch weightbearing was permitted for the first 4 weeks (phase 1), followed by partial weightbearing of 50% body weight (up to week 8; phase 2) and progressing to FWB by 8 weeks (up to week 10; phase 3). Patients performed isometric muscle contractions and circulation exercises for the lower limb. In the PFJ group, partial weightbearing with half the body weight in combination with a brace fixed at S 0-0-20° was permitted in phase 1, with a gradual increase to FWB in phase 2, as supported by a brace and with increased range of motion at S 0-0-40° until the fourth week and S 0-0-60° until the sixth week. In phase 3, patients were allowed FWB without a brace. The program included the increase and expansion of isometric, concentric, and eccentric muscle exercises (open and closed kinetic chain) combined with neuromuscular exercises to improve the dynamic stability of the knee. Depending on the progression of the muscular and sensorimotor situation and the transplant location, patients started to train on a stationary bicycle after 6 to 8 weeks, started running after 8 to 12 weeks, and were allowed to perform high-impact sports after 12 to 18 weeks.[39]

TABLE 1
Patient Characteristics (N = 21)[a]

	Mean ± SD (Range) or No.
Demographic	
Age, y	31 ± 11.6 (18-49)
Male:female	12:9
Baseline characteristics	
Knee, right:left	7:14
Defect location	
MFC	6
LFC	5
Trochlea	3
Patella	3
MFC + trochlea	1
MFC + patella	3
Defect size, cm^2	4.8 ± 2.0 (1.8-10)

[a]LFC, lateral femoral condyle; MFC, medial femoral condyle.

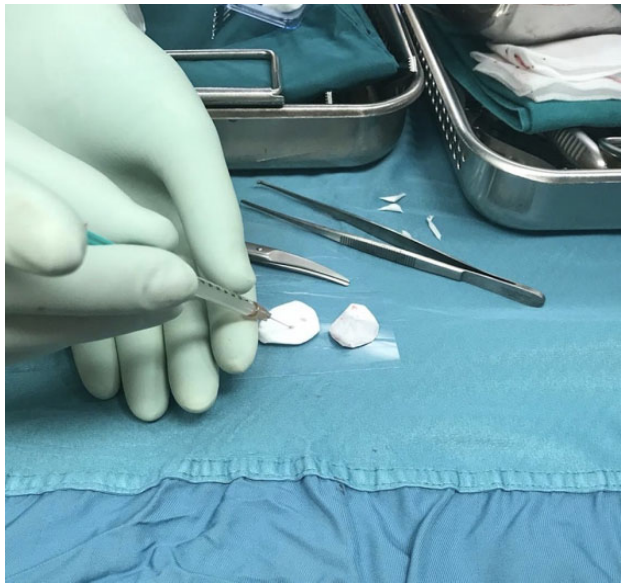

Figure 2. Injection of the cell-fibrin solution into a collagen scaffold.

MRI Evaluation

MRI evaluation included measurements during clinical routine follow-up at 3, 6, 12, and 24 months postoperatively. All

TABLE 2
Magnetic Resonance Imaging Protocol[a]

Sequence	PD/T2 TSE, sag	T1 SE, sag	PD TSE FS, cor	PD TSE, ax
FOV, mm × mm	150 × 150	150 × 150	150 × 132	150 × 150
No. of slices	29	29	26	32
Slice thickness	3	3	3	3
Slice gap, mm	0.3	0.3	0.3	0.3
No. of averages	1	1	2	1
TR, ms	6280	774	3680	4730
TE, ms	14/108	14	30	30
Flip angle, deg	180	90	180	180
Fat suppression	No	No	FS	FS
Pixel bandwidth, Hz/pix	142	120	140	140
MR acquisition type	2D TSE	2D SE	2D TSE	2D TSE
Voxel sizes, mm	0.2 × 0.2 × 3.0	0.2 × 0.2 × 3.0	0.1 × 0.1 × 3.0	0.1 × 0.1 × 3.0
Total acquisition time, min/s	4:06	3:40	03:50	03:39

[a]2D, 2-dimensional; ax, axial; cor, coronal; FOV, field of view; FS, fat saturation; MR, magnetic resonance; PD, proton density; sag, sagittal; SE, spin echo; TE, echo time; TR, repetition time; TSE, turbo spin echo.

scans were performed on 3-T MRI systems (Magnetom Prisma, Magnetom Prisma Fit; SIEMENS Healthineers). Patients were placed in a supine position with the knee extended in the center of a dedicated knee coil. The assessed MRI examinations were measured during routine clinical follow-up in predetermined time intervals. The complete MRI protocol is shown in Table 2. The evaluation of the MOCART and the MOCART 2.0 was performed by an experienced and an inexperienced reader according to the instructions published by Marlovits et al[21] and Schreiner et al.[32]

Clinical Evaluation

All patients were clinically evaluated preoperatively and at 3, 6, 12, and 24 months after surgery. Besides the clinical examination, the following outcome measures were included in a single questionnaire provided at the mentioned fixed periods: the Brittberg score,[7] International Knee Documentation Committee (IKDC) Subjective Knee Form,[3] Knee injury and Osteoarthritis Outcome Score (KOOS),[30] Noyes Sports Activity Rating Scale,[27] Tegner Activity Scale,[35] and visual analog scale for pain.[14] We classified the results of the IKDC, KOOS, Noyes, and 2 MOCART scores into excellent (85-100), good (70-84), fair (55-69), and severe (0-54).

Statistical Analysis

Statistical analysis was performed with the Wilcoxon rank-sum test for comparison of 2 time points and the Spearman test for correlation ($P < .05$, significant; $P < .01$, highly significant). We applied all tests with the SPSS software (Version 24.0; IBM).

RESULTS

Participants

No product-specific adverse events were recorded in our patient cohort. Typical postoperative swelling and effusion decreased in all patients within 4 weeks after implantation. Neither postoperative fever nor infection was observed, and no detachment of the transplants was seen in our patients. However, revision surgery was necessary within the time of observation for a male patient who experienced increased pain during walking after 2-year follow-up. The MRI showed a subchondral cyst, developed from a subchondral bone marrow edema–like signal in the area of the ACI. Arthroscopy showed a perfect transplant. The area of the bone marrow edema–like signal was drilled with wires. He was 1 of our 2 unsatisfied patients at the 24-month time point. The patient is now satisfied with the clinical outcomes. The second patient who was unsatisfied experienced intermittent pain during work as a police officer. She was treated at 2 locations and also had low back pain at the 2-year follow-up. In the meantime, she was treated with lumbar spine discectomy surgery and is still working in the field. These are 2 of 21 (9.5%) patients who were disappointed about their outcome or the complexity of the procedure at 2-year follow-up. Overall, 3 patients had a neutral opinion about the procedure, whereas 16 of 21 (76.1%) were satisfied with the surgery and would undergo the procedure again if necessary.

Clinical Assessment

At the clinical examination at 24 months postoperatively, range of motion was measured with full flexion and complete extension in all treated knee joints, with no restrictions as compared with the presurgical examination. According to the inclusion criteria, the collateral ligaments and cruciate ligaments were stable, with <5 mm of laxity in all cases.

All patients showed significant improvement in all evaluated clinical scores between the preoperative and 24-month postoperative time points. The Brittberg score increased from fair with moderate pain and occasional swelling to at least good with mild aching (Table 3); the IKDC, from 43.6 to 76.5 (Figure 3); the overall KOOS, from

TABLE 3
Clinical Results[a]

	Preoperative	Follow-up			
		3 mo	6 mo	12 mo	24 mo
Brittberg	2.9 ± 0.8	2.8 ± 0.8	2.2 ± 1.0	1.9 ± 0.9	1.9 ± 0.9
IKDC	43.6 ± 24.3	47.4 ± 15.6	66.3 ± 17.6	75.3 ± 17.0	76.5 ± 19.7
Noyes	42.4 ± 31.8	58.1 ± 25.3	16.7 ± 10.7	73.3 ± 18.6	76.9 ± 11.1
Tegner	2.2 ± 1.8	2.0 ± 1.2	3.2 ± 1.4	4.1 ± 1.5	4.3 ± 1.3
VAS pain	5.6 ± 3.2	2.6 ± 2.2	1.9 ± 2.2	1.6 ± 2.0	1.5 ± 2.0
KOOS					
QoL	36.6 ± 25.7	41.4 ± 21.9	52.4 ± 23.2	60.7 ± 21.8	64.9 ± 25.6
Pain	62.3 ± 25.2	70.9 ± 20.2	83.1 ± 17.6	86.2 ± 13.6	86.0 ± 16.2
Sport	35.7 ± 32.0	27.1 ± 17.4	56.7 ± 24.7	70.5 ± 23.0	71.0 ± 24.6
Symptoms	53.0 ± 11.9	58.8 ± 14.2	60.7 ± 12.3	60.5 ± 9.4	61.6 ± 9.1
ADL	67.2 ± 27.9	71.2 ± 25.1	87.1 ± 14.9	92.1 ± 10.6	92.6 ± 12.4
Overall	51.0 ± 20.8	53.9 ± 15.0	68.0 ± 15.7	74.0 ± 14.0	75.2 ± 15.4

[a]Values are presented as mean ± SD. ADL, Activities of Daily Living; IKDC, International Knee Documentation Committee Subjective Knee Form; KOOS, Knee injury and Osteoarthritis Outcome Score; QoL, Quality of Life; VAS, visual analog scale.

51 to 75.2 (subscales presented in Figure 4); the Noyes, from 42.4 to 76.9; the Tegner, from 2.2 to 4.3 with at least moderate-heavy labor and recreational sports; and the visual analog scale for pain, from 5.6 to 1.6. For the IKDC, 10 patients were graded as excellent, 4 as good, 5 as fair, and 2 as severe; for the overall KOOS, 7 as excellent, 8 as good, 4 as fair, and 2 as severe; and for the Noyes, 4 as excellent, 14 as good, and 3 as fair.

MRI Evaluation

In the MRI evaluation, the original MOCART increased from 58 to 74 ± 10 (range 55-95) between postoperative months 3 and 24 and the MOCART 2.0 from 65 to 78 ± 13 (range 45-100) (Figure 5). In particular, we found 3 excellent, 17 good, and 5 fair results in the MOCART and 8 excellent, 13 good, 3 fair, and 1 severe result in the MOCART 2.0. However, there was no statistically significant correlation between the results of clinical scores and either MOCART score. We found sufficient defect fill (>50%) as well as sufficient integration in 19 of 20 patients (90.5%). Two patients (9.5%) had cartilage filling <50% and 3 (14.3%) between 50% and 75%. In 3 (14%) and 4 (19%) patients, the MOCART and MOCART 2.0 decreased by 5 to 10 points between 12 and 24 months, respectively. In the MOCART 2.0, this was caused by decreasing defect fill and increasing subchondral changes in 2 cases, development of a subchondral bone marrow edema–like signal in 1 case, and inhomogeneity of the structure in 1 case. All other patients had increased or steady MOCART scores.

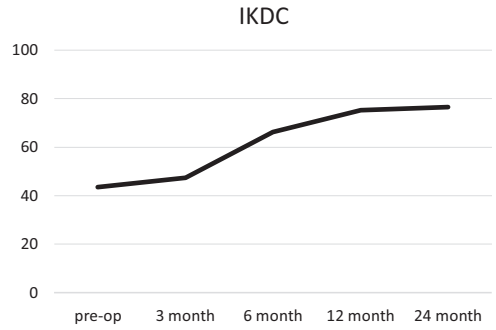

Figure 3. Results and course of the International Knee Documentation Committee (IKDC).

DISCUSSION

Various studies have presented promising midterm results of different scaffolds used for third-generation ACI.[39] The current study is the first to present results of the Igor scaffold, showing good to excellent outcomes in all clinical and radiological evaluations with improvements during treatment. The majority of the radiological results were graded as good on the MOCART and MOCART 2.0, with a lack of excellent results on the MOCART. For the Noyes Sports Activity Rating Scale there were mainly good results, for the overall KOOS, excellent and good results were equally represented, and for the IKDC, nearly half of patients showed excellent results.

Two years seems to mark a critical threshold in the matrix-associated ACI (MACI) technique, as in MRI follow-up examinations, the development of the transplant shows completion of graft maturation in T2 sequences at this time point.[25] The patients have already started to perform in their previous sports and have reduced their commitment to specific physiotherapy exercises. In the literature, the published 2-year results are usually observed clinically and radiologically, and the tendency seems to be that if the results are good at 2 years, they remain good at 10, 15, and 20 years postoperatively.[2,4,5] However, as revision surgery is frequent in long-term follow-up studies,[24] long-term results from randomized controlled trials including third-generation ACI are needed.

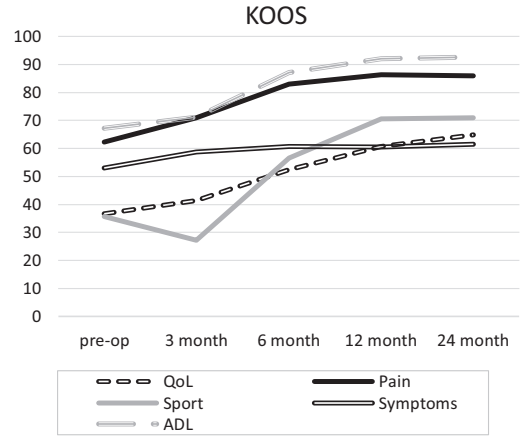

Figure 4. Results and course of the KOOS subscales. ADL, Activities of Daily Living; KOOS, Knee injury and Osteoarthritis Outcome Score; QoL, Quality of Life.

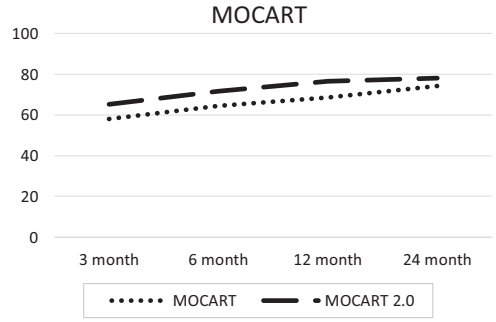

Figure 5. Results and course of the MOCART and the MOCART 2.0. There was no statistically significant correlation between clinical and radiological results in this examination. The MOCART and MOCART 2.0 scores were comparable at 24-month follow-up, with mean values of 74 ± 10 and 78 ± 13, respectively. MOCART, magnetic resonance observation of cartilage repair tissue.

In 2006, Marlovits et al[22] presented various cell biomaterials used as scaffolds, such as hyaluronan polymer (Hyalograft; Fidia Advanced Biopolymers Laboratories), collagen gel (CaRes; Arthro Kinetics AG), collagen membrane (ArthroMatrix [Arthrex/Orthogen]; MACI [Verigen/Genzyme]; matrix-associated autologous chondrocyte transplantation [IGOR/André]), and polymer matrices (BioSeed-C [BioTissue]; Novocart 3D [TeTeC Tissue Engineering Technologies AG]). In 2013, Stein et al[34] published a review of scaffolds that showed not only superiority to microfracture but also patient improvement on clinical scores: a fibrin-hyaluronan matrix (BioCart II; Histogenics Corp), a purified and cell-free porcine collagen I/III membrane (Matrix-Induced ACI; Sanofi US), an agarose-alginate hydrogel (Cartipatch; Tissue Bank of France), a Hyaff 11 matrix (Hyalograft C Autograft; Anika Therapeutics), and a bovine type I collagen 3-dimensional honeycomb matrix (NeoCart; Histogenics Corp).

Table 4 includes studies available on PubMed of third-generation ACI that included clinical and radiological results after 2 years. Results for the following scaffolds were available: the bilayer MACI technique,[6,32] the Novocart 3D,[25,39] the type I/III collagen membrane MACI (ACI-Maix),[11,20] the arthroscopic gel type ACI technique,[37] the cell-seeded ACI (which was compared with the second-generation collagen ACI),[15] the collagen-based CaReS scaffold,[36] the arthroscopically implanted chondrosphere,[33] a type I/III collagen membrane,[29] the 2-component gel-polymer scaffold BioSeed-C,[28] and the Hyalograft C.[17,36,38]

They are, in general, good to excellent results, with some exceptions in the KOOS subscores, but the scores are comparable or similar among the different scaffolds. The MOCART score shows values between 70 and 85, all graded as "good," except in the study by Siebold et al[33] (score of 60), who used spheres instead of a matrix. They seemed to differ in MRI appearance but showed equal or better clinical results as compared with the matrices. In the radiological and clinical scores, the Igor scaffold ranks in the middle field. The majority of studies comprised a small number of patients, between 8 and 72, except the study by Ebert et al,[11] which included 194 patients with treatment at the PFJ and TFJ, making comparison difficult. Furthermore, most of the studies lacked a control group, and randomized studies are needed to compare matrices.

In our measurements, we found no statistically significant correlation between the radiological and clinical scores. This is in accordance with former publications; Ebert et al[12] found no correlations except an association between the MRI parameter effusion and some KOOS subgroups. In the evaluated cohort, we saw a few cases with low radiological scores but subjective clinical satisfaction as well as highly scored transplants in MRI with pain and limited treatment success, indicating that there is a considerable reliance on functional requirements and clinical demands. Predictive factors for ACI outcome and for the likelihood of total knee replacement are age, sex, location and number of defects, number of previous operations, and Lysholm score before surgery.[10]

Superior improvement in patient-reported outcome scores have been reported for ACI, with no increased risk of clinical failure.[13] No transplant failure was seen in our patients. However, in a few cases, the defect fill of the transplant decreased, and the appearance of subchondral bone changes increased between 12 and 24 months, with the risk of transplant failures in the future. In 1 case with the development of a small subchondral cyst between 1- and 2-year follow-up beneath a nearly perfect transplant, drilling of the cyst was necessary, and in 1 case with a neuroma of the medial patellar nerve after a mini-arthrotomy approach, revision surgery was performed.

Limitations of the study are the low number of patients with treatment at the PFJ and TFJ, including concomitant procedures in some patients. The study had a retrospective design and did not include a control group, which also applies to the majority of articles presenting short- to medium-term outcomes offering 1 specific scaffold. Furthermore, 7 of 28 patients were excluded from the study because of metal implants or incomplete follow-up.

TABLE 4
Comparison of 2-Year Results in Studies of Third-Generation Autologous Chondrocyte Implantation[a]

	Zak (Current) Igor (N = 21)	Zak (2014)[39] Novocart 3D (N = 23)	Gomoll (2017)[15] cs-ACI (N = 39)	Siebold (2018)[33] Chondrosphere (N = 30)	Marlovits (2012)[20] ACI-Maix (N = 21)	Yoon (2020)[37] GACI (N = 10)	Bozkurt (2018)[6] Bilayer MACI (N = 8)	Welsch (2010)[36]	
								CaReS (n = 10)	Hyalograft C (n = 10)
MOCART	74 ± 10	70 ± 19	75.1	60.3 ± 21.8	79.2 ± 17.2	85 ± 8	79	76.5 ± 12.7	70 ± 9.4
MOCART 2.0	78 ± 13	–	–	–	–	–	–	–	–
KOOS	75.2 ± 15.4; △25	–	–	–	–	–	–	–	–
QoL	64.9 ± 23.6; △28	51.6 ± 21.2; △23.5	59.5; △28	72.3 ± 16.9; △27	61.5; △38	55; △18	–	–	–
Pain	86 ± 16.2; △24	86.5 ± 13.9; △26	84.7; △18	82.2 ± 16.1; △41	81; △47	82; △18	–	–	–
Sport	71 ± 24.6; △35	54.5 ± 23.6; △36.5	61.2; △25	71.0 ± 16.0; △29	64; △49	65; △28	–	–	–
Symptoms	61.6 ± 9.1; △9	65 ± 8; △10	55.6; △5	81.7 ± 12.1; △40	64; △31	68; △10	–	–	–
ADL	92.6 ± 12.4; △25	91.5 ± 10.6; △33	89.7; △15	86.3 ± 15.6; △41	87.5; △41	86; △14	–	–	–
IKDC	76.5 ± 20; △33	70 ± 15; △34	68.0; △22	84.2 ± 5.6; △38	68.5; △30	–	–	–	–

	Saris (2014)[31] Bilayer MACI (N = 72)	Ebert (2017)[11] ACI-Maix; TF (n = 127)	Ebert (2017)[11] ACI-Maix; PF (n = 67)	Ossendorf (2007)[28] BioSeed-C (N = 40)	Robertson (2007)[29] CACI (N = 41)	Zaffagnini (2019)[38] Hyalograft C (N = 34)	Kon (2016)[17] Hyalograft C (N = 32)	Niethammer (2014)[26] Novocart 3D (N = 41)
KOOS	56.2 ± 23.9; △37	31.3 ± 19.8	23.4 ± 16.7	52.9; △25	48.2 ± 21.6; △25	–	–	–
Pain	82.5 ± 16.2; △46	65.2 ± 17.6	61.8 ± 15.4	78.2; △14	77 ± 16; △26	–	–	–
Sport	60.9 ± 27.8; △46	26.0 ± 23.7	26.3 ± 20.7	45.7; △20	38 ± 31.6; △29	–	–	–
Symptoms	83.7 ± 14.0; △35	68.1 ± 17.5	65.7 ± 16.9	78.9; △11	76.0 ± 18.4; △27	–	–	–
ADL	87.2 ± 16.5; △44	76.3 ± 17.9	70.2 ± 15.9	80.6; △13	83.4 ± 16; △22	–	–	–
IKDC	65.7 ± 18.5; △33	–	–	–	–	89.5 ± 11.3; △49	77.1 ± 17.4; △31	68.6 ± 21.8

[a]Values are presented as mean or mean ± SD; delta (△) indicates difference vs baseline. Blank cells indicate *not applicable*. Products/procedures (manufacturers) included the following: ACI-Maix (Matricel GmbH); bilayer MACI (matrix autologous chondrocyte implantation; Genzyme Biosurgery); BioSeed-C (BioTissue SA); CACI, collagen membrane autologous chondrocyte implantation; CaReS (Cartilage Regeneration System; Arthro Kinetics AG); chondrosphere (co.don AG); cs-ACI, cell-seeded autologous chondrocyte implantation; GACI, gel-type autologous chondrocyte implantation; Hyalograft C (Fidia Advanced Biopolymers Laboratories); Igor (IGOR–Institute for Tissue and Organ Reconstruction GesmbH); Novocart 3D (TeTeC Tissue Engineering Technologies AG). ADL, Activities of Daily Living; IKDC, International Knee Documentation Committee Subjective Knee Form; KOOS, Knee injury and Osteoarthritis Outcome Score; MOCART, magnetic resonance observation of cartilage repair tissue; PF, patellofemoral joint; TF, tibiofemoral joint.

However, none of these patients had, to our knowledge, any troubles, implant failures, or severe clinical abnormalities regarding the procedure.

CONCLUSION

Third-generation ACI using the Igor scaffold showed improvements in clinical and radiological results for patients with large traumatic or degenerative cartilage defects, which is comparable with other scaffolds. Patients noted a decrease in pain and an increase in activity, with high satisfaction with the 2-year results. The majority of patients remained in the "good" category; few achieved "excellent" results. Satisfactory filling and integration were found in 90.5%. Overall, 16 of 21 patients (76.1%) were satisfied with the surgery and would undergo the procedure again if necessary.

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