Received: 26 February 2024 | Accepted: 11 July 2024

DOI: 10.1002/ksa.12387

Autologous matrix-induced chondrogenesis provides better outcomes in comparison to autologous minced cartilage implantation in the repair of knee chondral defects

Peter Behrendt[1,2] | **Lena Eggeling**[3] | **Anja Lindner**[4] | **Fidelius von Rehlingen-Prinz**[5] | **Matthias Krause**[5] | **Michael Hoffmann**[4] | **Karl-Heinz Frosch**[5] | **Ralph Akoto**[3] | **Justus Gille**[6]

[1]Department of Orthopaedics and Traumatology, University Medical Center Schleswig-Holstein, Campus Kiel, Kiel, Germany

[2]Department of Anatomy, Christian-Albrechts-University, Kiel, Germany

[3]Department of Trauma Surgery, Orthopaedics and Sports Traumatology, BG Hospital Hamburg, Hamburg, Germany

[4]Department of Trauma Surgery, Orthopedics and Sportsorthopedics, Asklepios St. Georg, Hamburg, Germany

[5]Department of Trauma and Orthopaedic Surgery, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

[6]Department of Orthopaedic and Trauma Surgery, Regio Kliniken, Hamburg, Germany

Correspondence

Peter Behrendt, Department of Orthopaedics and Traumatology, University Medical Center Schleswig-Holstein, Campus Kiel, Kiel, Germany.
Email: peter.behrendt.kiel@gmail.com

Abstract

Purpose: In symptomatic mid-sized focal chondral defects, autologous matrix-induced chondrogenesis (AMIC) and minced cartilage implantation (MCI) offer two versatile treatment options. This study aimed to conduct a matched-patient analysis of patient-reported outcome measures to compare these two surgical treatment methods for focal chondral defects.

Methods: At the first centre, patients underwent a single-stage procedure in which autologous cartilage was hand-minced, implanted into the defect and fixed with fibrin glue. At the second centre, patients underwent AMIC, which was fixed in place with fibrin glue. All patients were seen 2–4 years postoperatively. Postoperative outcomes were assessed using the visual analogue scale for pain (VAS), the Lysholm score and the five domains of the knee osteoarthritis outcome score (KOOS). Patients from each surgical centre were matched by age, sex, defect size and defect localisation.

Results: In total, 48 patients from two surgical centres (24 from each site) were matched for sex, age (MCI 30.3 ± 14.9 years vs. AMIC 30.8 ± 13.7 years) and defect size (MCI 2.49 ± 1.5 cm^2 vs. AMIC 2.65 ± 1.1 cm^2). Significantly better scores in the AMIC cohort were noted for VAS ($p = 0.004$), Lysholm ($p = 0.043$) and the KOOS subscales for pain ($p = 0.016$) and quality of life ($p = 0.036$). There was a significantly greater proportion of positive responders for Lysholm in the AMIC group (92%) compared with the MCI group (64%).

Conclusions: The AMIC procedure delivers superior patient outcomes compared with hand-minced autologous cartilage implantation. These are mid-term outcomes, with follow-up between 2 and 4 years.

Level of Evidence: Level III.

Abbreviations: AMIC, autologous matrix-induced chondrogenesis; BMS, bone marrow stimulation; KOOS, knee injury and osteoarthritis outcome score; MCI, minced cartilage implantation; MSC, mesenchymal stromal cells; PASS, patient acceptable symptom state; PROM, patient-reported outcome measures; RCT, randomised control trial; VAS, visual analogue scale.

KEYWORDS
AMIC, articular cartilage, autologous matrix-induced chondrogenesis, chondral, minced cartilage

INTRODUCTION

While the health benefits of remaining physically active are apparent, this may be associated with an increasing prevalence of focal chondral defects [5]. Importantly, chondral lesions present a challenging clinical scenario due to the avascular and aneural nature of articular cartilage. Unfortunately, as noted in the first anatomical description of articular cartilage by Wiliam Hunter in 1743, an observation which continues to hold true today, cartilage lesions do not heal. Consequently, a longer-term sequela of focal chondral defects is the progression of cartilage damage leading to osteoarthritis and, eventually, knee arthroplasty [14]. Thus, there is a clear need to treat chondral defects.

To date, several options are available for the repair of chondral lesions [7, 21]. While bone marrow stimulation (BMS) in various forms has been used for over 30 years in the treatment of chondral lesions, the sustainability of the technique has been called into question [26]. Owing to the apparent limitations, a variety of devices and techniques have been developed in attempts at improving the technique. Among the treatments are two-stage procedures, such as autologous chondrocyte implantation (ACI) and single-stage procedures, including a variety of techniques, such as osteochondral and chondral allografts, minced cartilage and scaffolds. However, while there are a plethora of options, there is also a notable difference in the quantity and quality of the clinical data regarding each treatment [21].

Although several surgical options exist in clinical use, there is a distinct paucity of direct comparisons of treatments regarding patient outcomes. Among comparative studies, a randomised controlled trial (RCT) that had compared BMS with autologous matrix-induced chondrogenesis (AMIC), which, similar to BMS is a single-stage procedure, had shown that BMS patients experienced a worsening of patient outcomes as soon as 2 years after surgery, whereas the patients in the AMIC cohort exhibited positive outcomes for 10 years [26]. Another RCT demonstrated positive results up to 10 years status post for patients who had undergone the AMIC procedure for repair of chondral lesions of the knee, whereas those undergoing microfracture alone saw a worsening of scores [26]. Besides AMIC, another surgical intervention for focal chondral defects is the use of minced autologous cartilage, which is placed at the site of a treated defect. In this technique, viable chondrocytes are brought into the defect, which is theorised to promote the outgrowth of embedded chondrocytes from tissue fragmentation [20]. Promising results in a recent case series have also shown that this is a viable treatment option [24].

With increasing interest in evidence-based medicine, it seems in the patients' best interests that clinical decisions be based on the best possible outcomes. There are very few comparative studies of the outcomes of different surgical techniques for the repair of focal chondral defects. It was hypothesised that scaffold cover over the repair site would provide a superior clinical outcome, as measured by common patient-reported outcome measures (PROMs). Therefore, to provide clinical evidence, a matched-patient analysis of PROMs was conducted, comparing two surgical treatments for focal chondral defects: autologous minced cartilage implantation (MCI) and AMIC.

MATERIALS AND METHODS

The study was conducted in accordance with the ethical standards enumerated in the 1964 Declaration of Helsinki and its later amendments. Ethical approval for the AMIC registry and the MCI was obtained from the ethics review boards of the University of Lübeck (No. 19-178) and the University of Hamburg (2021-10417-BO-ff), respectively.

Data from two surgical sites were used for this analysis, with three senior orthopaedic surgeons primarily responsible for the AMIC (J. G.) and MCI (P. B., R. A.) procedures. All patients who underwent primary surgeries were seen between 2 and 4 years postoperatively as part of the standard of care. Patients of the MCI cohort were matched as pairs with patients who were treated with AMIC (1:1 matched pair analysis) in terms of age, sex, defect size and defect localisation. The data for the AMIC cohort were obtained from the AMIC knee registry, which is an ongoing, multicentre database for recording changes in knee function and symptoms over time. In the registry, the Lysholm score, the knee injury and osteoarthritis outcome score (KOOS) and the visual analogue scale (VAS) for pain were recorded. Documentation was made on electronic case report forms, with surgeons having access to the registry via a web interface.

Patients

All 48 patients included in this study (24 in each treatment group) were seen for initial treatment of a

chondral lesion; hence, there were no revision surgeries. Chronic cases were treated conservatively for at least 6 months before surgery, whereas acute injuries were seen as close as possible to the date of the initial trauma.

Treatment

MCI

At one surgical site (surgeons responsible: P. B., R. A.), all patients were treated with a one-stage procedure in which autologous cartilage, which was recovered during the debridement and preparation of the defect site before BMS, was hand minced and then implanted at the defect site. During this procedure, the defect was debrided of all damaged or unstable cartilage until a healthy surrounding cartilage wall was achieved. The cartilage retrieved from the treated areas or from a low-weight-bearing region was then minced into fragments of ≤1 mm size until a paste-like appearance was achieved. The minced cartilage was then placed in the defect, which was stabilised by covering the treated defect site with fibrin glue (Tisseel, Baxter).

AMIC

At the second surgical site (surgeons responsible: J. G.), patients who had undergone surgery for full-thickness chondral or osteochondral lesions in the knee were included in the study. The index procedure followed the manufacturer's instructions for use and was performed using a mini-open approach. After debridement, a 1.2-mm drill was used to perforate the subchondral bone plate to a depth of 1 cm, thereby mobilising bone marrow stem cells into the defect. Care was taken to leave areas of the subchondral bone plate between the drillholes intact. A bilayer type I/III collagen membrane (Chondro-Gide®, Geistlich Pharma AG) was placed over the treated area and fixed in place with a fibrin sealant (Tisseel, Baxter).

Rehabilitation

Although the patients were treated at two centres, the rehabilitation protocols adhered to the clinical standards following cartilage repair surgery. In fact, both study centres used identical rehabilitation protocols. These follow progressive weight-bearing over several weeks, along with recovery of range of motion and restoration of strength before progression to functional exercises [15].

Outcomes assessment

All patients in these two cohorts had a follow-up visit between 2 and 4 years status post. Therapeutic outcomes were assessed based on three scores: VAS, Lysholm and KOOS. Patients rated their pain using the VAS, with 0 indicating no pain and 10 indicating the worst pain the patient had known. Functional outcomes were assessed using Lysholm and KOOS scores because these are the well-validated functional scores [3].

Statistical analysis

To detect differences between the two treatment groups, using $\alpha = 0.05$ and $\beta = 0.8$, the a priori power analysis was based on the published outcomes for the minced cartilage [24] and data on the AMIC published by a co-author [13]. The analysis indicated that it was necessary to collect data from a minimum of 46 patients. The Lysholm, VAS and KOOS domains were compared with a paired t test; a p value of 0.05 was considered statistically significant. Positive treatment responders in terms of the patient acceptable symptomatic state (PASS) were defined by a Lysholm score >70 according to previously published data [2] and were analysed with a Fisher's exact test. The analysis was performed using GraphPad Prism 8 (San Diego). Based on the VAS values, post hoc power analysis revealed 0.89, with α set to 0.05.

RESULTS

Patient demographics are shown in Table 1. There were no significant differences in age or defect size.

When the PROMs were compared, the patients who were treated with AMIC exhibited significantly superior scores in VAS and Lysholm than patients treated with MCI. For the KOOS domains, pain and quality of life showed significantly higher scores than in the MCI cohort, whereas two other domains (activities of daily living and symptoms) showed a trend towards better outcomes in the AMIC cohort. In terms of positive responders [6], 92% of AMIC-treated patients exceeded the PASS value at the time of follow-up, as compared with 67% of MCI patients, which was significantly different ($p = 0.033$) (Table 2).

Specific to the KOOS, Figure 1 depicts the difference in outcome scores for each domain of the KOOS. Of these domains, AMIC demonstrated significantly higher scores in two domains (pain and quality of life) but no significant differences in the domains of symptoms (n.s.) and activities of daily life (n.s.). Also, sport and recreation showed no significant difference between the surgical techniques.

TABLE 1 Patient demographics.

	MCI	AMIC	*p* Value
Age, mean (range) (year)	29.2 ± 14.1 (14–58)	30.4 ± 13.5 (14–62)	n.s.
Follow-up (month)	32.2 ± 7.9	37.0 ± 8.8	n.s.
Defect size, mean (cm^2)	2.6 ± 1.5	2.65 ± 1.1	n.s.
Defect location (*n*)			
Patellofemoral	13	13	
Medial femoral condyle	8	8	
Lateral femoral condyle	3	3	
Sex			
Female	11	11	
Male	13	13	
Lesion classification			
ICRS 4	6		
ICRS 4a	13		
ICRS 4b	3		
Outerbridge 4		24	

Abbreviations: AMIC, autologous matrix-induced chondrogenesis; ICRS, International Cartilage Repair Society; MCI, minced cartilage implantation.

TABLE 2 Comparison of patient outcomes.

	MCI	AMIC	*p* Value
VAS	4.1 ± 2.7	1.9 ± 1.9	0.004
Lysholm	70.1 ± 25.7	83.1 ± 13.9	0.043
KOOS			
Pain	72.8 ± 26.5	88.3 ± 11.7	0.016
Quality of life	50.4 ± 22.3	65.6 ± 24.4	0.036
Function in daily living	82.6 ± 22.9	92.9 ± 8.2	n.s.
Symptoms	77.2 ± 21.4	86.7 ± 12.2	n.s.
Sports	60.4 ± 28.5	64.5 ± 34.1	n.s.
Positive responders	67%	92%	0.033

Abbreviations: AMIC, autologous matrix-induced chondrogenesis; KOOS, knee injury and osteoarthritis outcome score; MCI, minced cartilage implantation; VA, visual analogue scale.

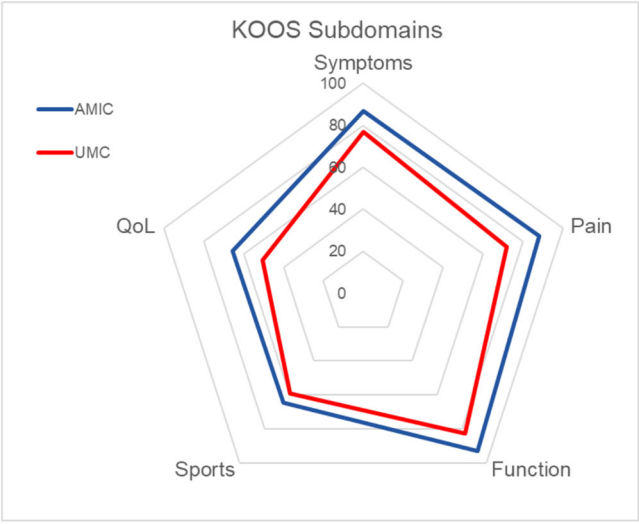

FIGURE 1 Knee injury and osteoarthritis outcome score (KOOS) scores for the two cohorts. AMIC, autologous matrix-induced chondrogenesis; UMC, uncovered minced cartilage.

In addition to the overall cohort, the outcomes in the subset of patients who had a patellofemoral lesion were compared (Figure 2). Like the outcomes in the entire patient group, the AMIC patients had better scores for VAS ($p = 0.004$), Lysholm ($p = 0.026$) and three of the five KOOS domains. Although the KOOS domains for symptoms ($p = 0.028$), pain ($p = 0.049$) and quality of life ($p = 0.011$) were significantly different, neither function (n.s.) nor sport (n.s.) were different when compared between the two treatment groups.

DISCUSSION

The most important results of this study are that the PROMs for Lysholm, VAS and two of the KOOS domains were significantly better among the AMIC-treated patients. In contrast, two of the remaining KOOS domains showed a trend towards better outcomes than MCI. Furthermore, the positive response rate among the AMIC patients was 92%,

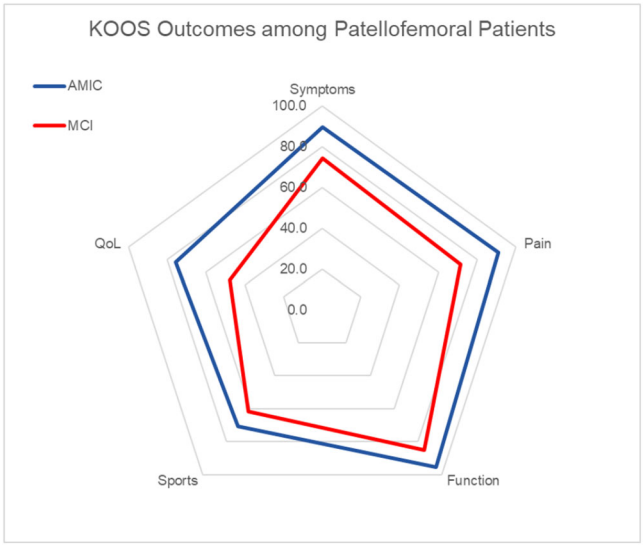

FIGURE 2 Knee injury and osteoarthritis outcome score (KOOS) scores for the patellofemoral patients. AMIC, autologous matrix-induced chondrogenesis.

whereas among the MCI cohort, it was 64%. These results indicate that the AMIC procedure delivers better patient outcomes than the MCI. Importantly, this comparison of techniques was matched by age, defect size and defect location. Therefore, while the variability between patient cohorts was limited as much as possible, the results demonstrated more favourable, robust outcomes for the AMIC procedure.

In the treatment of chondral lesions, BMS, for example, microfracture, microdrilling or abrasion chondroplasty, has long been considered a first-line treatment for focal chondral defects due to its ease of use and low cost, as well as positive short-term outcomes. BMS achieves these results by penetrating the subchondral bone, allowing the migration of mesenchymal stromal cells (MSCs) and growth factors into the cartilage defect, resulting in a superclot that is rich in MSC that can differentiate into chondrocytes [26]. However, the clot itself is essentially fragile, which may have been a disadvantage, particularly, for patellofemoral lesions. Before the differentiation of MSC and subsequent formation of cartilage, the clot is exposed to significant shearing force, which may displace the superclot. Furthermore, synovial fluid pressure variations may stimulate repair tissue to differentiate more rapidly, resulting in fibrous tissue [11]. As a result, data concerning microfracture in the knee have shown a tendency to offer initial positive results, but it also has the highest risk of conversion to total knee arthroplasty [9].

As an improvement on simple BMS, the application of a bilayer type I/III collagen membrane as part of an AMIC procedure offers a way to contain the superclot. This resulted in a biological chambre that protects and contains the MSC as it differentiates into chondrocytes, eventually regenerating healthy cartilage [17]. Based on MRI analysis, the AMIC procedure has resulted in the formation of hyaline-like cartilage [27], a substantial improvement over the fibrocartilage that is typically formed after microfracture. As a result, long-term follow-up shows robust, sustained and positive outcomes [6, 16]. The data from this study seem representative of larger studies using the AMIC technique in the tibiofemoral and patellofemoral compartments [12, 13]. However, the data for minced cartilage are sparse. While an RCT has shown that the technique is superior to microfracture [4], few subsequent studies have confirmed these outcomes.

A case series of 27 patients presented positive outcomes over a 2-year follow-up [18]. However, a recent meta-analysis included only three papers, and the authors of that study stated that the most recent evidence is scarce and relied only on the results of 2 years after surgery [10]. Interestingly, of the patients who had been enroled in the case series [18], 19 of the surgeries used Chondro-Gide® to cover the site after the autologous minced cartilage had been placed. Similarly, the presentation of the 5-year follow-up also stated that the minced cartilage, which had been placed into the defect, was sealed with fibrin glue or a combination of fibrin glue and Chondro-Gide® membrane, although the exact numbers were not specified in that paper [24]. Cell–biomaterial interactions play a significant role in the remodelling of various cartilage regenerative procedures and could therefore explain the differences between MCI and techniques that use a membrane or scaffold, such as AMIC.

It is not clear why the results for MCI presented here were not equivalent to those for AMIC. While a case series had shown positive outcomes, surgeons in that case had covered the minced cartilage with Chondro-Gide® when the defect site was patellofemoral [18]. The most recent case series for minced cartilage also demonstrated positive outcomes, with 69% of patients exceeding the PASS value for Lysholm [24]. However, it should be noted that their proportion was similar to the proportion that we reported (64%) in our study. The mechanism for this is unclear. The shear forces in the knee could displace the cartilage fragments, which is why covering the treatment site has been suggested [23]. In addition, different techniques of mincing cartilage have been introduced, indicating that the size of cartilage fragments may influence regenerative capacity [22]. Although there is no clinical evidence for this hypothesis, it has been suggested that different types of minced cartilage techniques must be evaluated separately.

In the treatment of focal cartilage defects, the results in the peer-reviewed literature offer a variety of methods, with most outcomes generally positive. In contrast, a recent meta-analysis reported few

differences in outcomes when comparing BMS and BMS augmented with a scaffold [8]. Importantly, in that meta-analysis, most of the follow-up (11 of 14 studies) was for only 2 years, as previously noted, and is the expected time for which BMS will provide positive outcomes. In contrast to these short-term results, a Bayesian network analysis assessed 36 studies involving 2179 patients, among six surgical procedures with follow-up extending to 124 months and a mean defect size of $3.7 \pm 1.2\,cm^2$. The authors reported better outcomes and lower rates of revisions and failure in the AMIC-treated patients [19]. Notably, this meta-analysis included only comparative studies, either RCT or case–control.

Among the treatments for focal cartilage defects, the surgeons' choice considers the surgical procedure, whether fully arthroscopic or mini-open and data has shown that these two procedures deliver equivalent results in the treatment of focal chondral defects in the knee [25]. There is also a major differentiation in surgical approaches with regard to one-stage (e.g., BMS, AMIC, MCI) or two-stage procedures (e.g., ACI technique). Among single-stage procedures, BMS as a stand-alone therapy has not shown good long-term outcomes, with outcomes deteriorating as soon as 2 years status post [26]. Autologous MCI has shown positive results, although the peer-reviewed literature is sparse [4, 24]. ACI has a significant history of clinical use, dating back 25 years. The use of a collagen I/III membrane instead of a periosteal flap in ACI has a comparably long history. While there is substantial evidence to support its role in the treatment of focal chondral defects, ACI procedures are conducted in two stages, with an attendant increase in surgical risks and expense [13].

Regarding comparisons of surgical treatments, whether AMIC or MCI, further investigation is necessary to examine the differences in outcomes. As noted, the defect sites are exposed to notable shearing forces in the knee; thus, it is possible that the cartilage particles did not remain in place during the post-operative and rehabilitation phases of the patients' recovery. If that is the case, covering the treated defect with a matrix would seem a prudent step, adding minimal time to surgery while enhancing the likelihood of a positive outcome for the patient. Longer follow-up for these patients is needed to assess the stability of these positive outcomes. Patients would also benefit from studies that position the various treatments, whether MCI, AMIC or ACI, among others, in terms of their relative effectiveness, although such an undertaking would be resource-intensive.

Although the AMIC registry collects preoperative data in addition to follow-up, the cohort of MCI patients had only postoperative data due to the retrospective study design. This is certainly the major limitation of our study. Therefore, it was not possible to determine changes in these patients' scores and whether they exceeded the minimal clinically significant difference. Future studies should regard preoperative scores as essential for evaluating the utility of a treatment.

In addition to the lack of preoperative scores, concomitant surgeries were not captured in the registry. This is a shortcoming that should be remedied moving forward. Another limitation is the length of follow-up, between 2 and 4 years status post, which are short-term outcomes. However, other published data for AMIC in the knee indicate that these positive outcomes are likely to continue in the long term [6, 16]. Therefore, a longer follow-up of these matched patients will provide useful clinical data to surgeons who treat focal chondral defects. A longer follow-up period would also allow for the collection of data concerning revisions or treatment failures.

Finally, radiological outcomes were not available. However, considering the data indicating that MOCART scores do not correlate to the patient-reported outcomes [1], it is unlikely that this diminishes the results of the study. The data obtained in this study are clinically relevant to surgeons, as patients were shown to have better outcomes with AMIC compared with MCI. Therefore, it may be advisable to include the placement of a scaffold or membrane, in addition to BMS, as part of the surgical planning for the repair of focal chondral defects of the knee.

CONCLUSIONS

While the treatment of chondral and osteochondral defects remains a clinical challenge, the two single-stage techniques both provide benefits to the patients in terms of pain and function. At short-term follow-up, AMIC demonstrated better scores and a higher responder rate than fibrin glue fixed autologous MCI in most of the assessed outcomes.

AUTHOR CONTRIBUTIONS

Peter Behrendt: Conceptualisation; methodology; validation; formal analysis; writing—original draft preparation; writing—review and editing; visualisation. **Lena Eggeling**: Formal analysis; Investigation; writing—review and editing; visualisation. **Anja Lindner**: Validation; Formal analysis; investigation; writing—review and editing; visualisation. **Fidelius von Rehlingen-Prinz**: Formal analysis; investigation; writing—review and editing. **Matthias Krause**: Validation; writing—review and editing. **Michael Hoffmann**: Formal analysis; investigation; writing—review and editing. **Karl-Heinz Frosch**: Conceptualisation; validation; writing—review and editing. **Ralph Akoto**: Conceptualisation; writing—review and editing. **Justus Gille**: Conceptualisation; methodology; validation; formal analysis; investigation; writing—original draft preparation; writing—review and editing;

visualisation; supervision; project administration. All authors have read and agreed to the final version of this manuscript.

ACKNOWLEDGEMENTS

The authors have no funding to report. Open Access funding enabled and organized by Projekt DEAL.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Primary data are available from the corresponding author by reasonable request.

ETHICS STATEMENT

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the institutional Ethics Committee of the University of Hamburg (2021-10417-BO-ff) and the University of Lübeck (No. 19-178). Informed consent was obtained from each patient prior to the study.

ORCID

Peter Behrendt https://orcid.org/0000-0002-5282-0233

REFERENCES

1. Casari, F.A., Germann, C., Weigelt, L., Wirth, S., Viehöfer, A. & Ackermann, J. (2021) The role of magnetic resonance imaging in autologous matrix-induced chondrogenesis for osteochondral lesions of the talus: analyzing MOCART 1 and 2.0. *Cartilage*, 13, 639S–645S. Available from: https://doi.org/10.1177/1947603520946382
2. Chahal, J., Lansdown, D.A., Davey, A., Davis, A.M. & Cole, B.J. (2021) The clinically important difference and patient acceptable symptomatic state for commonly used patient-reported outcomes after knee cartilage repair. *The American Journal of Sports Medicine*, 49(1), 193–199. Available from: https://doi.org/10.1177/0363546520969883
3. Chamorro-Moriana, G., Perez-Cabezas, V., Espuny-Ruiz, F., Torres-Enamorado, D. & Ridao-Fernández, C. (2022) Assessing knee functionality: systematic review of validated outcome measures. *Annals of Physical and Rehabilitation Medicine*, 65(6), 101608. Available from: https://doi.org/10.1016/j.rehab.2021.101608.
4. Cole, B.J., Farr, J., Winalski, C.S., Hosea, T., Richmond, J., Mandelbaum, B. et al. (2011) Outcomes after a single-stage procedure for cell-based cartilage repair. *The American Journal of Sports Medicine*, 39(6), 1170–1179. Available from: https://doi.org/10.1177/0363546511399382
5. Curl, W.W., Krome, J., Gordon, E.S., Rushing, J., Smith, B.P. & Poehling, G.G. (1997) Cartilage injuries: a review of 31,516 knee arthroscopies. *Arthroscopy: The Journal of Arthroscopic & Related Surgery*, 13(4), 456–460. Available from: https://doi.org/10.1016/s0749-8063(97)90124-9
6. deGirolamo, L., Schönhuber, H., Viganò, M., Bait, C., Quaglia, A., Thiebat, G. et al. (2019) Autologous matrix-induced chondrogenesis (AMIC) and AMIC enhanced by autologous concentrated bone marrow aspirate (BMAC) allow for stable clinical and functional improvements at up to 9 years follow-up: results from a Randomized Controlled Study. *Journal of Clinical Medicine*, 8(3), 392. Available from: https://doi.org/10.3390/jcm8030392
7. Filardo, G., Andriolo, L., Angele, P., Berruto, M., Brittberg, M., Condello, V. et al. (2020) Scaffolds for knee chondral and osteochondral defects: indications for different clinical scenarios. A consensus statement. *Cartilage*, 13(1_supplement), 1036S–1046S. Available from: https://doi.org/10.1177/1947603519894729
8. Fortier, L.M., Knapik, D.M., Dasari, S.P., Polce, E.M., Familiari, F., Gursoy, S. et al. (2022) Clinical and magnetic resonance imaging outcomes after microfracture treatment with and without augmentation for focal chondral lesions in the knee: a systematic review and meta-analysis. *The American Journal of Sports Medicine*, 51(8), 2193–2206. Available from: https://doi.org/10.1177/03635465221087365
9. Frank, R.M., McCormick, F., Rosas, S., Amoo-Achampong, K., Erickson, B., Bach, B.R. et al. (2018) Reoperation rates after cartilage restoration procedures in the knee: analysis of a large US commercial database. *The American Journal of Orthopedics*, 47(6), 1–15. Available from: https://doi.org/10.12788/ajo.2018.0040
10. Frodl, A., Siegel, M., Fuchs, A., Wagner, F.C., Schmal, H., Izadpanah, K. et al. (2022) Minced cartilage is a one-step cartilage repair procedure for small defects in the knee—a systematic-review and meta-analysis. *Journal of Personalized Medicine*, 12(11), 1923. Available from: https://doi.org/10.3390/jpm12111923
11. Gill, T.J., Asnis, P.D. & Berkson, E.M. (2006) The treatment of articular cartilage defects using the microfracture technique. *Journal of Orthopaedic & Sports Physical Therapy*, 36(10), 728–738. Available from: https://doi.org/10.2519/jospt.2006.2444
12. Gille, J., Reiss, E., Behrens, P., Jakob, R.P. & Piontek, T. (2023) Positive outcomes following autologous matrix-induced chondrogenesis (AMIC) in the treatment of retropatellar chondral lesions: a retrospective analysis of a patient registry. *BMC Musculoskeletal Disorders*, 24(1), 964. Available from: https://doi.org/10.1186/s12891-023-06923-8
13. Gille, J., Reiss, E., Freitag, M., Schagemann, J., Steinwachs, M., Piontek, T. et al. (2021) Autologous matrix-induced chondrogenesis for treatment of focal cartilage defects in the knee: a follow-up study. *Orthopaedic Journal of Sports Medicine*, 9, 2325967120981872. Available from: https://doi.org/10.1177/2325967120981872.
14. Houck, D.A., Kraeutler, M.J., Belk, J.W., Frank, R.M., McCarty, E.C. & Bravman, J.T. (2018) Do focal chondral defects of the knee increase the risk for progression to osteoarthritis? a review of the literature. *Orthopaedic Journal of Sports Medicine*, 6, 2325967118801931. Available from: https://doi.org/10.1177/2325967118801931.
15. Hurley, E.T., Davey, M.S., Jamal, M.S., Manjunath, A.K., Alaia, M.J. & Strauss, E.J. (2021) Return-to-play and rehabilitation protocols following cartilage restoration procedures of the knee: a systematic review. *Cartilage*, 13(1_supplement), 907S–914S. Available from: https://doi.org/10.1177/1947603519894733
16. Kaiser, N., Jakob, R.P., Pagenstert, G., Tannast, M. & Petek, D. (2021) Stable clinical long-term results after AMIC in the aligned knee. *Archives of Orthopaedic and Trauma Surgery*, 141, 1845–1854. Available from: https://doi.org/10.1007/s00402-020-03564-7
17. Kim, B.S., Na, Y. & Jang, D.S. (2022) Outcomes of bone marrow aspirate concentrate and matrix-induced chondrogenesis (BMIC) for treatment of osteochondral lesions of the talus. *Foot and Ankle Surgery*, 28(7), 944–949. Available from: https://doi.org/10.1016/j.fas.2022.01.005
18. Massen, F.K., Inauen, C.R., Harder, L.P., Runer, A., Preiss, S. & Salzmann, G.M. (2019) One-step autologous minced cartilage

procedure for the treatment of knee joint chondral and osteochondral lesions: a series of 27 patients with 2-year follow-up. *Orthopaedic Journal of Sports Medicine*, 7(6), 2325967119853773. Available from: https://doi.org/10.1177/2325967119853773.

19. Migliorini, F., Eschweiler, J., Schenker, H., Baroncini, A., Tingart, M. & Maffulli, N. (2021) Surgical management of focal chondral defects of the knee: a Bayesian network meta-analysis. *Journal of Orthopaedic Surgery and Research*, 16, 543. Available from: https://doi.org/10.1186/s13018-021-02684-z
20. Moser, L.B., Bauer, C., Otahal, A., Kern, D., Dammerer, D., Zantop, T. et al. (2023) Mincing bovine articular cartilage with commercially available shavers reduces the viability of chondrocytes compared to scalpel mincing. *Journal of Experimental Orthopaedics*, 10(1), 97. Available from: https://doi.org/10.1186/s40634-023-00661-5
21. Niemeyer, P., Albrecht, D., Aurich, M., Becher, C., Behrens, P., Bichmann, P. et al. (2023) Empfehlungen der AG Klinische Geweberegeneration zur Behandlung von Knorpelschäden am Kniegelenk. *Zeitschrift fur Orthopadie und Unfallchirurgie*, 161(1), 57–64. Available from: https://doi.org/10.1055/a-1663-6807
22. Ossendorff, R., Walter, S.G., Schildberg, F.A., Spang, J., Obudzinski, S., Preiss, S. et al. (2023) Biologic principles of minced cartilage implantation: a narrative review. *Archives of Orthopaedic and Trauma Surgery*, 143(6), 3259–3269. Available from: https://doi.org/10.1007/s00402-022-04692-y
23. Riboh, J.C., Cole, B.J. & Farr, J. (2015) Particulated articular cartilage for symptomatic chondral defects of the knee. *Current Reviews in Musculoskeletal Medicine*, 8, 429–435. Available from: https://doi.org/10.1007/s12178-015-9300-0
24. Runer, A., Ossendorff, R., Öttl, F., Stadelmann, V.A., Schneider, S., Preiss, S. et al. (2023) Autologous minced cartilage repair for chondral and osteochondral lesions of the knee joint demonstrates good postoperative outcomes and low reoperation rates at minimum five-year follow-up. *Knee Surgery, Sports Traumatology, Arthroscopy*, 31, 4977–4987. Available from: https://doi.org/10.1007/s00167-023-07546-1
25. Tan, C.H.B., Huang, X.O., Tay, Z.Q. & Bin Abd Razak, H.R. (2024) Arthroscopic and open approaches for autologous matrix-induced chondrogenesis repair of the knee have similar results: a meta-analysis. *Journal of ISAKOS*, 9(2), 192–204. Available from: https://doi.org/10.1016/j.jisako.2023.10.003
26. Volz, M., Schaumburger, J., Gellißen, J., Grifka, J. & Anders, S. (2024) A randomized controlled trial demonstrating sustained benefit of autologous matrix-induced chondrogenesis (AMIC®) over microfracture: 10-year follow-up. *European Journal of Orthopaedic Surgery & Traumatology*. Available from: https://doi.org/10.1007/s00590-024-03948-0
27. Wiewiorski, M., Miska, M., Kretzschmar, M., Studler, U., Bieri, O., Valderrabano, V. (2013) Delayed gadolinium-enhanced MRI of cartilage of the ankle joint: results after autologous matrix-induced chondrogenesis (AMIC)-aided reconstruction of osteochondral lesions of the talus. *Clinical Radiology*, 68(10), 1031–1038. Available from: https://doi.org/10.1016/j.crad.2013.04.016

How to cite this article: Behrendt, P., Eggeling, L., Lindner, A., von Rehlingen-Prinz, F., Krause, M., Hoffmann, M. et al. (2024) Autologous matrix-induced chondrogenesis provides better outcomes in comparison to autologous minced cartilage implantation in the repair of knee chondral defects. *Knee Surgery, Sports Traumatology, Arthroscopy*, 1–8. https://doi.org/10.1002/ksa.12387