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# Does the Autologous Matrix-Induced Chondrogenesis (AMIC®) technique result in positive outcomes for the repair of cartilage lesions in the kneein adolescent patients? Preliminary results at 2,6 years average follow-up

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**Chondral and osteochondral lesions of the knee in skeletally immature patients, can result in serious long-term sequelae, such as early knee arthrosis. While there is an abundance of studies concerning chondral repair techniques, there have been relatively few studies that have examined outcomes following cartilage repair in skeletally immature patients. Therefore, we planned to answer the following question: does the AMIC® technique result in positive outcomes for the repair of cartilage lesions in the knee in adolescent patients ? Our hypothesis was that the AMIC® technique improves outcomes for skeletally immature patients with an ICRS stage III or IV osteochondral lesion two year after the surgery. This was an European retrospective, multicenter study, including 27 patients aged from 12 to 19 years. We included adolescents with open epiphysis on x-ray, with an ICRS stage III or IV symptomatic lesion of the knee. The average defect size was 2.3 cm2. All patients had been treated with the surgical technique AMIC®. Post-operative outcomes were assessed by the Knee injury and Osteoarthritis Outcome Score (KOOS). Results showed a significant improvement at a mean follow-up of 2.6 years (min 2; max 6 years) across all KOOS domains: 55 vs. 69% (p<0.001) on symptoms, 58 vs. 87% (p<0.001) on pain, 31 vs. 71% (p<0.001) on quality of life, 29 vs. 73% (p<0.001) on sports and leisure activities, and 67 vs. 90% (p<0.001) on activities of daily life. AMIC® technique performed for the repair of stage III or IV ICRS articular cartilage lesions in the knees of adolescent patients, provides clinical improvements 2.6 years after surgery, but results are not perfect with adolescents who may still symptomatic.**

## INTRODUCTION

Chondral and osteochondral lesions of the knee, whether caused by osteochondritis dissecans or trauma, are pathologies that particularly affects adolescents[1]. Among adolescents who have undergone ACL reconstruction, it was noted that up to 50% of these patients have had lesions of the articular cartilage[2]. In the long term, such untreated lesions are likely to progress to arthrosis or residual knee pain in adulthood[3]. As hyaline cartilage does not have a good capacity for spontaneous regeneration, correct management of the cartilage lesions can be seen as essential in order to prevent the progression of degenerative joint conditions[4].

If orthopaedic treatment is admitted for non-displaced osteochondral lesion, at times the free fragment is still re-insertable and thus can be fixed to its original site[5]. However when the situation is not favourable for fixation of the fragments or a non-surgical treatment, there are still a variety of surgical techniques which can be performed[6,7]. Among these are osteochondral autograft transplantation (OAT)[8], autologous chondrocyte implantation (ACI)[9], bone marrow stimulation (BMS) which is also referred to as microfracture (MFx)[10]. In addition, the BMS technique can be augmented with the application of an acellular scaffold. This is the autologous matrix-induced chondrogenesis (AMIC®) technique[11]. AMIC® is a matrix-assisted bone marrow stimulation technique combining microfracture with the use of a type I/III porcine collagen matrix (Chondro-Gide®

(Geistlich®, Wolhusen, Switzerland)). The matrix is able to stabilize and protect the bone marrow clot produced from the microfracture that the allows the migration of mesenchymal stem cells[12,13]. The goal of this technique is to create a de novo cartilage within the lesion which has mechanical qualities very close to native hyaline cartilage[14].

The positive outcomes following AMIC® in the knee have been documented in the literature[15-17]. However, the data is generally focused on adults, with a poor documentation concerning younger patients[7,18]. Regarding skeletally immature patients, the outcomes data on cartilage repair are limited.

The aim of this study was to assess AMIC® technique outcomes for the repair of cartilage lesions in the knee in adolescent patients two years after the surgery.

Our hypothesis was that the AMIC® technique improves outcomes for skeletally immature patients with an osteochondral lesion two years after the surgery.

## MATERIAL AND METHODS

We conducted a retrospective multicenter study including 7 centers in 3 countries (France, Switzerland, and Germany) and involved 7 orthopedic surgeon who all had a specialization in pediatrics. All pre-operative data for patient outcomes measures (PROM) was collected prospectively and then post-operatively for this study.

Inclusion criteria were patients with a radiologically immature skeleton (open epiphyses) who had been operated on for an ICRS (International Cartilage Repair and preservation Society) stage III or IV lesion of the knee by the AMIC® method (Figure 1)[18]. The diagnosis was made on the preoperative MRI or CT arthrography. The size of the defect was measured per-operatively and the surgeon ensured that the fragment was not fixable before doing AMIC®. We excluded patients with a limb axis defect more than 5° or requiring osteotomy, uncorrected laxity of the knee (central shift or untreated patellar instability) and patients for whom we did not have enough data (Figure 2). All preoperative radiographs were analyzed and those of patients with closed physis were excluded.

The surgical technique was similar to that described by Benthien and Behrens[19]. Three different surgical approaches were noted :

The technique could be performed by arthrotomy: the patient was installed in the supine position with a wedge to place the knee at 90° flexion, medial or lateral parapatellar arthrotomy (depending on the location of the defect on the imaging) was performed. Any cartilaginous debris was resected, then the lesion was debrided (until appearance of subchondral bone), multiple perforations were then made in the focus using a 1.2 mm pin until bleeding from subchondral bone was obtained. Once the bleeding had occurred (if a tourniquet was employed, it was deflated just after pinning), the defect was filled and covered with the ChondroGide® (Geistlich®, Wolhusen, CH) collagen membrane which was fixed using either PDS 5-0 or biological glue.

Or the technique could be done by an arthroscopy followed by an arthrotomy : with the same installation

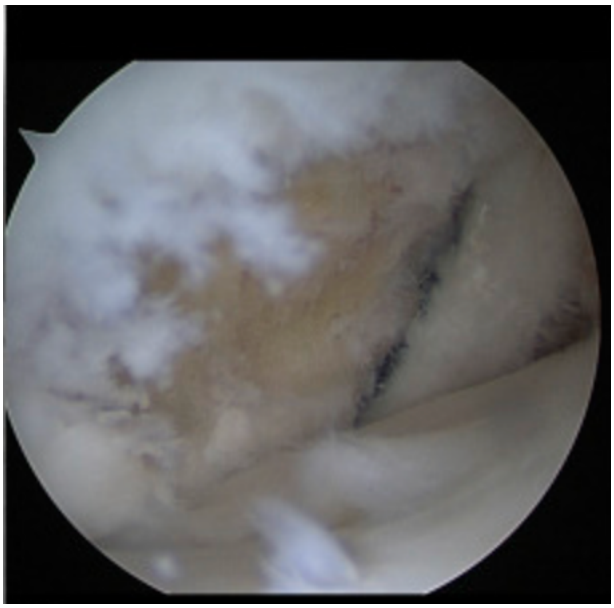

*Fig. 1 — Arthroscopic view of a lateral condyle osteochondral lesion (Stage IV ICRS classification).*

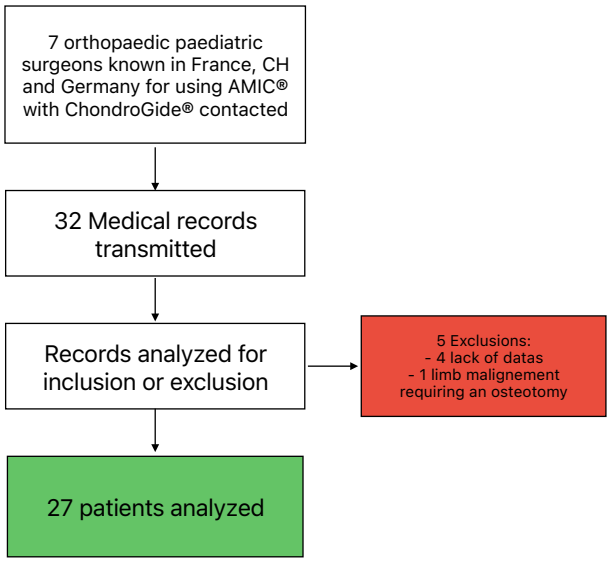


*Fig. 2 — Flow chart.*

an arthroscopy with a 30° optic lens was performed first in order to locate the lesion and remove any cartilaginous foreign body. The lesion was debrided using a shaver, then the perforations were made. The arthrotomy was then performed to fill and cover the lesion with the ChondroGide® membrane which was fixed as described above.

Or the entire technique (freshening and filling of the lesion) were performed under arthroscopy with a 30° arthroscope.

Postoperative care was identical in the 3 techniques. The treated limb was placed in an articulated splint, with passive and active mobilization of the knee authorized from the outset. However, weight bearing was prohibited in the first postoperative month. Muscle strengthening was also not allowed during the first postoperative month. Prophylaxis of thromboembolic disease was determined according to the pubertal stage.

The PROM used in this study as the Knee injury and Osteoarthritis Outcome Score (KOOS) (20). It was collected prospectively during the pre and post-operative consultation. If the etiology was trauma, we ensured to be far from the acute episode to not underestimate the pre-operative KOOS.

Informed consent wasn't necessary regarding the French legislation (observational and retrospective study).

## RESULTS

### *Patients*

A total of 27 patients with a maximum age of 19 years were identified as having had surgery to repair chondral or osteochondral defects via the AMIC® technique between July 2013 and January 2020. Among the mechanisms of injury, the traumatic episodes were most often a lateral dislocation of the patella. 4 patients had a previous surgery (2 ablations of osteochondral flap, 1 fixation with screw of an osteochondritis and 1 patellar stabilization by an isolate MPFL reconstruction). The baseline characteristics of patients are provided in Table I. The technique was performed by arthrotomy on 17 patients, 7 patients underwent an arthroscopy followed by an arthrotomy, and 5 patients had the entire procedure under arthroscopy. No patient had any extra concomitant surgery. The average follow-up was 2.6 years (range 2 to 6 years).

No postoperative complication was reported. A recurrence of osteochondritis dissecans was found in one patient (suspected due to persistent pain and diagnosed after a post-operative MRI) at 2 years after the surgery. He has been re-operated with OAT.

### *Statistics*

Statistical analyses were performed using Medcalc® (version 18, MedCalc Software®, Ostend, Belgium). Normality of the data was determined via a Shapiro-Wilk test, data to compare pre and post-operative scores for each domain of the KOOS were assessed using a Friedman's test due to the relatively small sample size as well as a non-normal distribution of the post-operative scores. The significance level was set at $p<0,05$.

### *Patient Reported Outcome Mesure (PROM)*

We noted a significant improvement in all the domains of the KOOS. Results are presented in the Table II. The minimally clinically important change score

**Table I.** — Baseline characteristics.

| | |
|---|---|
| Sex (n) | |
| Male | 15 |
| Female | 12 |
| ICRS lesion stage (n) | |
| III | 6 |
| IV | 21 |
| Lesion cause (n) | |
| OCD | 13 |
| Acute Trauma | 13 |
| Not recorded | 1 |
| Localisation (n) | |
| medial condyle | 2 |
| lateral condyle | 5 |
| trochlea | 3 |
| patella | 17 |
| Defect Size ($cm^2$) | |
| Mean | 2,3 ± 0.7 |
| Range | 1,5 - 4,0 |
| Age (years) | |
| Mean | 15,5 ± 1,7 |
| Range | 12 - 19 |

**Table II.** — Pre and Post-Operative KOOS domains.

| KOOS Domain | Pre-Operative % (min; max) | Post-Operative % (min; max) | p |
|---|---|---|---|
| Symptoms | 55 (36; 71) | 69 (39; 94) | 0,007 |
| Pain | 58 (28; 86) | 87 (53; 100) | <0,0001 |
| Quality of life | 31 (0; 56) | 71 (31; 100) | <0,0001 |
| Sports and leisure | 29 (0; 70) | 73 (25; 100) | <0,0001 |
| Activity of daily life | 67 (35; 96) | 90 (31; 100) | <0,0001 |

(MCID) was defined as an improvement of 10% for each KOOS domain, except for the sport and leisure domain where it was an improvement of at least 12%, in accordance with the recommendations of the ICRS[3], according this criteria 20 patients (74%) has an clinically relevant improvement of the KOOS.

## DISCUSSION

After analysing our results, our hypothesis was verified AMIC® technique provides clinical improvement 2.6 years after surgery in adolescents with a stage III or IV lesion of articular cartilage. However, if we analyse the post-operative domains of the KOOS we can observe that the results are not perfect with average scores between 70 and 90%, and a MCID for only 74% of patients.

To our knowledge, this is the first multicentre study that has evaluated clinical outcome following the AMIC® technique in adolescent patients.

Demographics of the patients included in our study matched those of the other studies of cartilage lesion in adolescents[21]. However, one notable difference from the other patient populations was the location of the defects. While the medial condyle has been noted as the most common site of a chondral lesion[22], this was not the case in our series, with only 2 patients (7%) presenting with medial condyle lesions, we have not found an explanation for this. Nevertheless, our results are consistent with a recent meta-analysis published in 2021 which had noted an improvement in all KOOS domains, with an average follow-up of 3,77 years with patients mean age of 35,6 years[17]. The clinical results are good but not perfect, as Murray et al point out, there is currently no cartilage restoration technique giving results with a vast majority of asymptomatic patients[23].

Optimal surgical technique is also a point of interest to any surgeon, and in this study, there were 3 different techniques used. Unfortunately, we did not have enough patients to provide a meaningful comparison of the results between arthroscopic techniques and open surgery and fixation with glue or suture. In the literature there does not seem to be any

difference in outcomes relative to different surgical techniques for AMIC®[24], and fixation method[25,26].

Compared to other techniques currently indicated for treating moderate-sized chondral or osteochondral lesions in adolescents, the AMIC® method has several advantages, in particular its doesn't need to take a graft of cartilage and it is done in one procedure. A systematic review on outcomes following cartilage repair in adolescents had noted that OAT (2 studies), Autologous Cell Implantation (ACI) (7 studies) and Micro-fracturing (MFx) (4 studies) all had comparable positive outcomes in adolescent patients[6]. ACI requires surgery in 2 stages, thus more logistical resources are required, resulting in extra costs for results that are not necessarily better[27,28]. While it was noted that MFx did result in positive outcomes, the durability of this repair has lately been called into question. A randomized controlled trial (RCT) showed MFx patient's outcomes tending towards baseline after 2 years while AMIC® patients maintained the positive results at 5 years follow-up[25]. Additionally, a Bayesian network meta-analysis noted that the AMIC® procedure for focal chondral defects of the knee performed better overall (in comparison to other knee cartilage repair techniques) at approximately 3 years follow-up[15]. OAT has shown very good long-term results with 82% of adults satisfied after 8 years[29]. But presents the risk of a non-geometric filling of the osteochondral defect with possibly an area not covered by the cartilage graft, pain from donor site is reported in 10 to 40% of cases. Furthermore the rate of reoperation after OAT is relatively high in paediatric population, in 2022 Hall et al. found a rate of 25,5% of reoperation at a median of 6,6 months after surgery[30].

Our study had several limitations. It was a retrospective study with a selection bias (only 7 selected surgeons participated to the study), Recruitment was carried out over 7 years with heterogeneous follow-up durations and few data collected by surgeon. Furthermore, we did not make a comparison with another surgical technique of microfracture without using a membrane or with a control group. It is accepted that in the paediatric population the osteochondral lesions can evolve favourably without treatment[22], which could have been the case for some of our patients in the serie. For patients with a traumatic lesion, we didn't have the time from injury to surgery. We couldn't make multivariate analyses to know if a concomitant femero-patellar joint stabilisation could have an influence on our results because of the small number of patients. We also didn't perform postoperative imaging in order to control the filling of the defect objectively. Lastly, the use of a child-specific validated outcome score may be beneficial to younger patients. While there is a KOOS specific to children, there is no specified cut-off age for which the KOOS adult should be used, while the authors stated that comprehension was limited in younger children[31]. Considering that our mean age was almost 16 years, the KOOS we used to be likely a valid PROM. Although our data only included 27 adolescent patients, this is actually the higher cohort of patients on this topic to our knowledge[5,22,33,34]. Larger sample sizes may offer more applicable data, as randomized studies with other surgical techniques to find the place of AMIC® for skeletally immature patients presenting a cartilaginous lesion of the knee.

We can conclude that AMIC® technique performed for the repair of stage III or IV ICRS articular cartilage lesions in the knees of adolescent patients, provides clinical improvements 2.6 years after surgery, but results are not perfect with adolescents who may still symptomatic.

## CONCLUSIONS

Humeral shaft fractures in adult polytraumatized patients were most often AO-type A (66%) and treated operatively (90%). High rates of radial nerve palsy at presentation (20%) and nonunion (27%) were found. Approximately five years post trauma, patients reported levels of quality-of-life comparable to the population norms and standardized combined scores, but still experienced upper extremity disability.

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