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ORIGINAL STUDY

Treatment of Patellofemoral Cartilage Defects in the Knee by Autologous Matrix-Induced Chondrogenesis (AMIC)

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This study presents the prospective two-year clinical and MRI outcome of autologous matrix-induced chondrogenesis (AMIC) for the treatment of patellofemoral cartilage defects in the knee. Ten patients were clinically prospectively evaluated during 2 years. MRI data were analysed based on the original and modified MOCART (Magnetic Resonance Observation of Cartilage Repair Tissue) scoring system. A satisfying clinical improvement became apparent during the 24 months of follow-up. The MOCART scoring system revealed a slight tendency to deterioration on MRI between one and 2 years of follow-up. However, the difference was not statistical significant. All cases showed subchondral lamina changes. The formation of intralesional osteophytes was observed in 3 of the 10 patients (30%). In conclusion, AMIC is safe and feasible for the treatment of symptomatic patellofemoral cartilage defects and resulted in a clinical improvement. However, the favourable clinical outcome of the AMIC technique was not confirmed by the MRI findings.

INTRODUCTION

Cartilage lesions of the knee are commonly found during routine arthroscopy. A review of 31 516 knee arthroscopies noted a 63% prevalence of chondral lesions, in which 19% had grade IV chondromalacia, with the patella as the most common location (*9,49*). These lesions may cause pain, swelling, mechanical symptoms, and functional impairment. In addition to the problem of avascularity of articular cartilage and its limited capacity for self-repair, the complexity of the patellofemoral joint with its high axial and shearing forces makes treatment very challenging (*31*). Furthermore, this type of defects are often associated with abnormal patellofemoral pressure, such as lateral compression or excessive lateral position of the patella on the trochlea, which can result in cartilage damage (*35,37*). All these facts together may explain only 70 % good or very good results on the patellofemoral joint using classical or membrane-covered autologous condrocyte implantation (ACI) (*20,31,35*) compared with 90 % on femoral condyles (*33,39*). Hence, the therapeutic state of the art for patellofemoral lesions has yet to be determined. ACI has been suggested as a second-line treatment option only, following failed microfracture (*25,37,46*).

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Microfracture techniques are directed at the recruitment of bone marrow cells and have been widely used to treat local cartilage defects. In this type of procedures, mesenchymal stem cells (MSCs) migrate in the fibrin network of the blood clot (*8*). However, the fibrin clot is not mechanically stable to withstand the tangential forces (*15*). As described by Gille *et al* (*19*), an implanted exogenous scaffold (e.g. a collagen matrix) may improve the mechanical stability and durability for endogenous cells and may provide a proper stimulus for chondrogenic differentiation and cartilage regeneration. The AMIC (autologous matrix-induced chondrogenesis) procedure provides two major advantages ; on the one hand, it is a one-step procedure with no need of cartilage harvesting potentially leading to donor site morbidity, and on the other hand, it is cost-effective with no need of in vitro cell expansion (*5*). Results of the AMIC technique and several modifications have already been published by others (*4,6,10,11,19,28,36,40,45*). However, currently still little is known about the outcome of the AMIC technique in the patellofemoral joint. The goal of the presented pilot study was to determine the prospective clinical and MRI outcome of the AMIC technique for the treatment of patellofemoral cartilage defects in the knee. It was hypothesized that all patients treated with this technique would improve clinically and that this procedure would fill the cartilage defects completely with tissue with a signal similar to cartilage on MRI.

MATERIALS AND METHODS

Study population

Patients with focal cartilage defects involving the patella or trochlea and with clinical symptoms (pain, swelling, locking and ''giving away'') were eligible for treatment. Exclusion criteria were age under 18 and over 50 years, untreatable tibiofemoral or patellofemoral malalignment or instability, diffuse osteoarthritis or bipolar ''kissing'' lesions, major meniscal deficiency and other general medical conditions such as diabetes or rheumatoid arthritis. Clinical experimentation was approved by the Hospital Ethics Committee. Informed consent to participate in the study and to comply with the postoperative regimen was obtained from all patients. The patients included in this pilot study were treated between April 2009 and May 2011.

Ten patients (8 men and 2 women) were treated consecutively and followed prospectively for 2 years. The right-to-left side ratio was 4:6. The lesions were focal in all cases. Eight cartilage defects were located on the patella and two on the trochlea. All lesions were International Cartilage Repair Society (ICRS) grade III-IV (*23*) and had a mean size of 4.2 ± 1.9 cm^2. The cause of injury was traumatic in 4 cases and focal nontraumatic (focal degenerative lesions) in 6 cases. The mean age of the patients was 37.2 ± 7.1 years. The mean duration of symptoms before surgery was 24.9 ± 38.9 months.

Previous surgery in 4 of the 10 patients included 2 partial meniscectomies, 1 ACL (anterior cruciate ligament) reconstructions and 1 debridement of the chondral lesion. Associated procedures were performed in three patients : 2 Fulkerson osteotomies and one patient underwent a medial patellofemoral ligament reconstrution and a fulkerson osteotomy at the same time.

Surgical technique

A miniarthrotomy in a tourniquet-controlled bloodless surgical field was performed to allow access to the defect. The lesion was measured after the bottom of the cartilage defect was freshened, and the edges of the defect were trimmed back to stable walls of healthy cartilage. Microfracturing is performed with slow speed drilling (drill bit diameter 1.2 mm). When the size of the defect is evaluated, the collagen membrane is measured. The collagen I/III membrane (Chondro-Gide®) should be slightly undersized to avoid dislocation after movement and was fixated with sutures (Vicryl 6/0). The joint was then gently moved intraoperatively to evaluate whether the membrane remained in place.

The postoperative regimen was as follows : non-weightbearing during 2 weeks. Achieving a normal gait pattern was advised at 10 weeks postoperatively. An extension brace was prescribed for the first 4 weeks after surgery. Maximum active flexion did not exceed 15° for the first 2 weeks of rehabilitation. Full range of motion was allowed 8 weeks postoperatively. Isometric quadriceps training, straight length raising and hamstrings isometrics were advised during the first 2 weeks. Return to low impact sports was allowed 12 months after surgery.

Clinical evaluation

All 10 patients were clinically prospectively evaluated with use of the Knee injury and Osteoarthritis Outcome

Score (KOOS) (*3,41-43*), the Tegner activity scale (*47, 48*), Kujala patellofemoral score (*27*) and the visual analogue scale (VAS) (*7,17*) for pain preoperatively and at 6, 12 and 24 months of follow-up.

MRI technique

All MRI examinations at 12 and 24 months of follow-up were performed on a 1.5-T or a 3-T MR unit (either a Magnetom Avanto, a Magnetom Symphony Tim or Magnetom Trio, Siemens Medical Solutions, Erlangen, Germany). All ten patients had consented to follow the postoperative MRI evaluation protocol. We performed a standard knee MRI protocol including proton-density- and T2-weighted turbo spin echo (TSE) acquisitions using a dedicated send-receive eight channel knee coil. Imaging parameters of the sequences were the same as published previously (Fig. 1.) (*11,13,14*).

Original and modified MOCART system

For the description of the repair tissue, we used the original MOCART system previously published by Marlovits *et al* (*29,30*). Besides the original MOCART system, we also used a modification of this system previously published by Dhollander *et al* (*11-14*). Both morphological MRI classification systems were applied to the MRI images taken at 12 and 24 months of follow-up. All MR images were evaluated by one independent reviewer. Both the original and modified MOCART scores were expressed as a percentage of the maximum score (*11-14*).

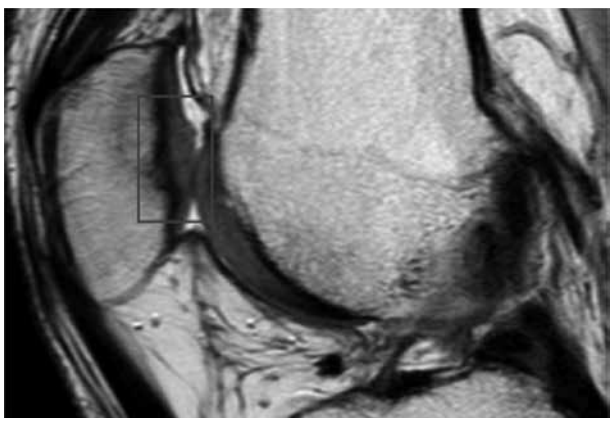

Fig. 1. — Sagittal proton-density- and T2-weighted turbo spin echo (TSE) image on 1.5 T MR unit. The black square shows an irregular subchondral bone plate with a hypertrophic aspect of the repair tissue.

Statistical analysis

All data are expressed in terms of means and standard deviations. The Wilcoxon test was used to analyse statistical differences between the preoperative and follow-up KOOS, Tegner, Kujala and VAS for pain scores, between the postoperative values of the original MOCART system and between the postoperative values of the modified MOCART system. For all tests $P < 0.05$ was considered significant. Statistical analysis was performed using SPSS statistics 21 (SPSS Inc, Chicago, IL).

RESULTS

During the follow-up period the VAS scores for pain indicated by the patients improved significantly (Fig. 2.). The differences between the preoperative and postoperative values (6, 12 and 24 months) were statistically significant ($P < .05$). According to the Tegner activity scale, a significant improvement became apparent at 12-months of follow-up ($P < .05$). The differences before and 6 months after the operation were not yet statistically significant (n.s.). Kujala patellofemoral scores revealed a significant improvement between pre-

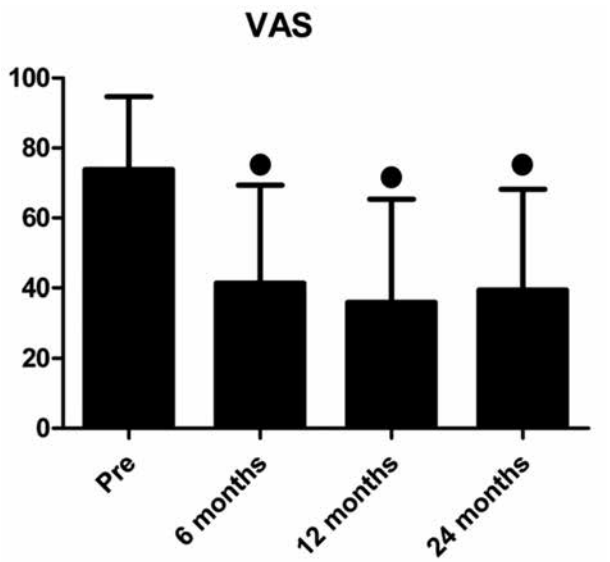

Fig. 2. — Mean values and standard deviations of the Visual Analogue Scale (VAS) for pain (N=10) : preoperative (Pre) and postoperative : 6 months, 12 months and 24 months. Values are expressed in millimetres. The black dots indicate statistically significant differences ($P < .05$) between the preoperative and postoperative values.

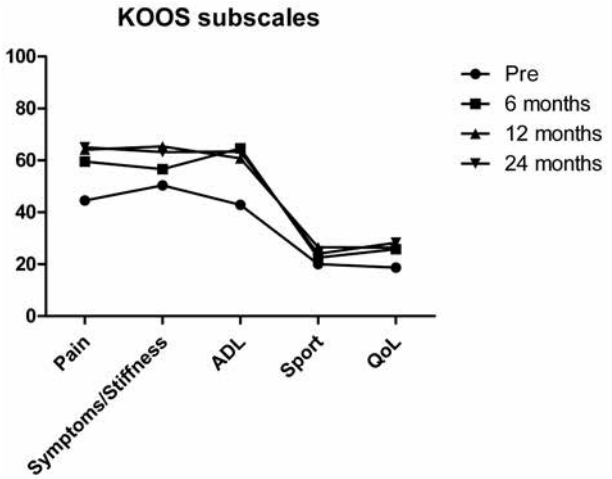

Fig. 3. — Mean values of the KOOS subscales (Pain, Symptoms/Stiffness, ADL (activities of daily living), Sport and Quality of Life (QoL)) (N=10) : preoperative (Pre) and postoperative : 6 months, 12 months and 24 months.

operative and 12 and 24 months of follow-up ($P < .05$). The mean total KOOS scores also improved statistically significantly when pre- and postoperative values (12 and 24 months) were compared ($P < .05$). Again, the differences before and 6 months after the operation were not statistically significant (n.s.). In general, all KOOS subdomains improved in the postoperative period, but only two KOOS subscale scores (pain and ADL (activities of daily living)) improved significantly during the 24 months of follow-up (Fig. 3.). The other 3 KOOS subdomains (symptoms/stiffness, sport and QoL (quality of life)) revealed no statistically significant differences (n.s.).

The exact mean values and standard deviations of the total KOOS scores, individual KOOS sub-domain scores, Tegner activity levels, Kujala patellofemoral scores and VAS for pain scores and *P* values of the comparison between preoperative scores and scores at 6, 12 and 24 months of follow-up are given in table I.

No infections occurred in the postoperative period. Two patients (20%) underwent a second-look arthroscopy because of catching, revealing hypertrophy of the regenerated tissue, which was adequately treated by shaving.

Table I. — Mean values and standard deviations of total KOOS, individual KOOS subdomains, Kujala patellofemoral scores, VAS for pain scores and Tegner activity levels (N=10) : preoperative and postoperative : 6 months, 12 months and 24 months. *P* values of the comparison between preoperative scores and scores at 6, 12 and 24 months of follow-up are also given. The VAS for pain scores are expressed in mm.

KOOS and Subdomains	**Pre**	**6 months**	**12 months**	**24 months**
Koos total	176.5 ± 83.2	229.0 ± 82.6 (n.s.)	243.2 ± 100.0 (*P = 0.047*)	243.9 ± 85.9 (*P = 0.047*)
Pain	44.5 ± 17.5	59.5 ± 22.2 (n.s.)	64.1 ± 20.7 (n.s.)	65.0 ± 23.3 (*P = 0.025*)
Symptoms/Stiffness	50.4 ± 18.3	56.6 ± 16.9 (n.s.)	65.4 ± 19.1 (n.s.)	63.2 ± 18.8 (n.s.)
ADL	42.9 ± 25.6	64.6 ± 22.7 (n.s.)	60.8 ± 23.5 (*P = 0.022*)	63.4 ± 20.8 (*P = 0.028*)
Sport	20.0 ± 20.3	22.5 ± 23.9 (n.s.)	26.5 ± 29.9 (n.s.)	24.0 ± 19.7 (n.s.)
QoL	18.7 ± 16.9	25.8 ± 11.4 (n.s.)	26.4 ± 18.6 (n.s.)	28.3 ± 14.8 (n.s.)
Vas for pain	73.9 ± 20.8	41.4 ± 28.0 (*P = 0.005*)	36.0 ± 29.4 (*P = 0.005*)	39.4 ± 28.8 (*P = 0.008*)
Tegner	1.5 ± 1.4	2.1 ± 1.4 (n.s.)	2.6 ± 1.4 (*P = 0.016*)	2.5 ± 1.5 (*P = 0.047*)
Kujala	41.9 ± 15.1	53.7 ± 24.3 (n.s.)	58.2 ± 20.7 (*P = 0.038*)	59.8 ± 21.2 (*P = 0.049*)

Twenty-four month longitudinal follow-up of the repair tissue with the original and MOCART system

During the 24-month follow-up period, it was shown that the original MOCART scores slightly decreased over time (Fig. 4a). The same was true for the modified MOCART scores. These percentages also slightly decreased over time (Fig. 4b). In other words, a slight tendency of deterioration of the repair tissue was observed on MRI during the 24 months postoperative period. However, the differences of both MOCART scores between 12 and 24 months of follow-up were not statistically significant (n.s.).

MRI data evaluated with the original MOCART system at 12 and 24 months of follow-up

At 12 and 24 months after the AMIC technique the MRI data were analysed according to the original MOCART system (Table II) (*11-14,30*). MRI data of all patients were available at 12 and 24 months of follow-up.

Briefly, hypertrophic filling of the defect was found in ten cases (20%) at 24 months of follow-up. Bone marrow changes were observed in 4 patients (40%) at the same evaluation point. The formation of intralesional osteophytes was observed in 3 of the 10 patients (30%).

DISCUSSION

The most important finding of the present study is that the AMIC procedure is safe and feasible for the treatment of patellofemoral cartilage defects in the knee. The overall clinical outcome is satisfying. However, the favourable clinical outcome was not confirmed by the MRI data. All cases showed subchondral lamina changes. Moreover, the formation of intralesional osteophytes was observed in 3 of the 10 patients (30%).

The AMIC (Autologous Matrix-Induced Chondrogenesis) technique was first described in 2003 by Behrens *et al* and at present it is widely used on the one hand in its original form and on the other hand with further developments (*2,6,11*). Although AMIC is a well-established treatment in cartilage

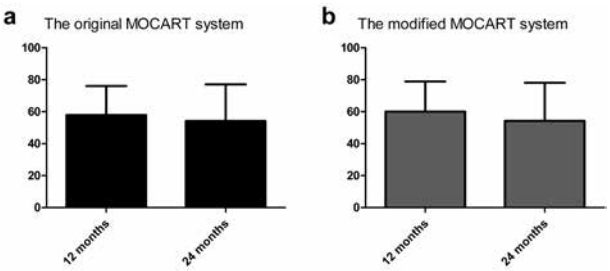

Fig. 4. — a. Mean values and SD of the original MOCART scores expressed in percentages : postoperative (N=10) : 12 months (57.9 ± 18.2) and 24 months (54.2 ± 22.9 ; 12 months - 24 months : n.s.) ***b.*** Mean values and SD of the modified MOCART scores : postoperative (N=10) : 12 months (60.0 ± 18.9) and 24 months (54.3 ± 23.9 ; 6 months - 24 months : n.s.).

defect therapy, the published evidence found in the literature is still limited (*19,28,45*). This is even more true for the outcome of this technique for the treatment of patellofemoral cartilage lesions.

In general, bone marrow stimulation techniques produce similar results in comparison with autologous chondrocyte implantation (*24*). Although the treatment of patellofemoral chondral lesions seems uncommon in some countries such as the United States, using cartilage repair techniques for patellofemoral lesions has become more and more accepted (*16*). This is represented by some studies exclusively dealing with the issue of Autologous Chondrocyte Implantation (ACI) for patellofemoral defects (*20,31,35*). Nevertheless, clinical results still seem inferior to those of defects located on the femoral condyles (*26,35,38,44*).

We report in this pilot study, the clinical results obtained of ten patients treated with the AMIC technique for patellofemoral cartilage lesions. The patients who participated in this study showed a statisfying clinical improvement after surgery. No decline in clinical outcome was observed. The clinical results are similar to those of other techniques, taking into account this small and challenging patient cohort (*19,37*).

In the present study, both the original and the modified MOCART system were used in a longitudinal fashion to evaluate the repair tissue. The modified MOCART system was developed by giving more weight to certain variables in an attempt to increase the prognostic value of the scoring system

Table II. — MRI evaluation of the repair tissue at 6 and 12 months after AMIC in terms of number and percentage (N=10).

Cartilage repair tissue grading scale (MOCART)				
Variables	12 months (*N*=10)		24 months (*N*=10)	
1. Degree of defect repair and filling of the defect				
Complete (on a level with adjacent cartilage)	3	30%	2	20%
Hypertrophy (over the level of the adjacent cartilage)	1	10%	2	20%
Incomplete (under the level of the adjacent carilage; underfilling)				
>50% of the adjacent cartilage	4	40%	4	40%
<50% of the adjacent cartilage	2	20%	2	20%
Subchondral bone exposed	0	0%	0	0%
(complete delamination or dislocation and/or loose body)				
2. Integration to border zone				
Complete (complete integration with adjacent cartilage)	4	40%	4	40%
Incomplete (incomplete integration with adjacent cartilage)				
Demarcating border visible (split-like)	3	30%	2	20%
Defect visible				
< 50% of the length of the repair tissue	2	20%	2	20%
> 50% of the length of the repair tissue	1	10%	2	20%
3. Surface of the repair tissue				
Surface intact (lamina splendens intact)	4	40%	3	30%
Surface damaged (fibrillations, fissures and ulcerations)				
<50% of repair tissue depth	4	40%	4	40%
>50% of repair tisue depth or total degeneration	2	20%	3	30%
4. Structure of the repair tissue				
Homogenous	4	40%	4	40%
Inhomogenous or cleft formation	6	60%	6	60%
5. Signal intensity of the repair tissue				
Dual T2-FSE				
Isointense	0	0%	1	10%
Moderately hyperintense	8	80%	6	60%
Markedly hyperintense	2	20%	3	30%
3D-GE-FS				
Isointense	0	0%	1	10%
Moderately hypointense	8	80%	6	60%
Markedly hypointense	2	20%	3	30%
6. Subchondral lamina				
Intact	1	10%	0	0%
Not intact	9	90%	10	100%
7. Subchondral bone				
Intact	7	70%	6	60%
Non-intact (edema, granulation tissue, cysts, sclerosis)	3	30%	4	40%
8. Adhesions				
No	10	100%	10	100%
Yes	0	0%	0	0%
9. Effusion				
No	5	50%	7	70%
Yes	5	50%	3	30%

and should be considered as an incentive for further research to develop a true prognostic and valid MRI scoring system (*12*). In general, both scores were moderate and slightly decreased over time. In other words, a slight tendency of deterioration of the repair tissue was observed on MRI during the 24 months postoperative period. However, the differences of both MOCART scores between 6 and 12 months of follow-up were not statistically significant (n.s.). Longer follow-up data are needed

to see whether the appearance of the repair tissue improves or not.

The percentages of original MOCART scores presented in this study at 24 months of follow-up (original MOCART : ± 54%) are similar to those published concerning the AMIC *plus* technique (original MOCART : ± 53%) (*11*). The AMIC *plus* technique combines autologous matrix-induced chondrogenesis (AMIC) with platelet-rich plasma gel (PRP) and was also used for the treament of patellar cartilage defects (*11*). From this comparison of MOCART percentages, no obvious beneficial effect of adding PRP to the AMIC technique is noticeable in the treatment of patellofemoral cartilage defects on MRI. More research on this interesting topic is needed.

Based on the original MOCART system, we analysed our patient group 12 and 24 months after the AMIC procedure. The majority of the chondral repair tissue filled the defect depth sufficiently. In contrast to the findings of Gille *et al* (*19*), we observed an irregular surface of the repair tissue in most of the cases and neither was the repair tissue isointense to the surrounding cartilage. We found subchondral lamina changes in all patients at 24 months of follow-up. Moreover, the formation of intralesional osteophytes was observed in 3 of the 10 patients (30%). However, in comparison with the AMIC *plus* technique (60% of the patients developed intralesional osteophytes), the original AMIC technique has a tendency to develop less intralesional osteophytes (*11*).

Two patients (20%) developed hypertrophy of the repair tissue observed on MRI and both of them underwent a second-look arthroscopy because of catching due to this finding. These findings were similar to those published concerning the AMIC *plus* technique (*11*). Niemeyer *et al* observed also a higher incidence of hypertrophic repair tissue (8.1%) in patients treated with ACI for patellofemoral cartilage defects (*34*). A possible explanation for these findings could be that higher shear forces in the patellofemoral joint provide stimuli for hypertrophy (*21,22,34*).

In contrast to other cartilage repair procedures, the AMIC procedure is quite easy to handle and can be done in a one-step surgery. There is no need for harvesting autologous cartilage. In this way, in vitro propagation of chondrocytes and the concomitant dedifferentiation issues are avoided. Therefore, this technique is less expensive, less time intensive and offers availability to all patients (*11*). In the original AMIC procedure published by Benthien *et al*, the collagen membrane is fixed with commercial fibrin glue (*5*). In the series published by Gille *et al*, a semiautologous fibrin glue was used (*19*). This type of fibrin glue is believed to offer superior properties than the commercial fibrin glue (*18*). We used sutures for the fixation of the collagen membrane to ensure a secure fixation. We did not observe transplant loosening, debonding of the graft or ablation and in turn clinical complications and reoperations. These observations are similar to those published by others (*1,11*).

It must be emphasized that only a small number of study objects were presented in this study, that the follow-up period was limited to 24 months and that all MRI images were evaluated by only one independent observer. Another important drawback of this pilot study population is the fact that associated procedures were performed in 3 patients. These limitations do not allow a broad generalization of the findings observed in this pilot study, but can be seen as an incentive for future research under the same theme.

CONCLUSION

In this study the AMIC technique was used for the treatment of patellofemoral cartilage lesions in the knee. The 2-year clincal and MRI outcome are discussed and now serves as control for future studies with modified protocols. The most important finding of the present study is that the AMIC procedure is safe and feasible for the treatment of patellofemoral cartilage defects in the knee. The overall clinical outcome is satisfying. However, the favourable clinical outcome was not confirmed by the MRI data. All cases showed subchondral lamina changes. Moreover, the formation of intralesional osteophytes was observed in 3 of the 10 patients (30%). Long-term and randomized controlled studies are mandatory to confirm the initial results and the reliability of this procedure.

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