

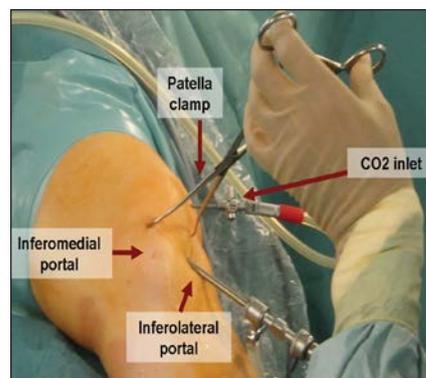
# Autologous Collagen-induced Chondrogenesis: Single-stage Arthroscopic Cartilage Repair Technique

Asode AnAnthrAm Shetty, md; seok Jung kim, md; PrAveen BilAgi, md; dAvid stelzeneder, md

## abstract

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Autologous collagen-induced chondrogenesis is a novel, single-staged arthroscopic cartilage repair technique using microdrilling and atelocollagen or fibrin gel application under carbon dioxide insufflation. Atelocollagen is a highly purified type I collagen obtained following the treatment of skin dermis with pepsin and telopeptide removal, making it nonimmunogenic. In this procedure, atelocollagen mixed with fibrinogen and thrombin in a 2-way syringe can maintain the shape of the articular surface approximately 5 minutes after application due to the reaction between the thrombin and fibrinogen. Carbon dioxide insufflation facilitates the application of the gel under dry conditions. Ten patients (mean age, 38 years) with symptomatic chondral defects in the knee who were treated arthroscopically with microdrilling and atelocollagen application were retrospectively analyzed. All defects were International Cartilage Repair Society grade III or IV and were 2 to 8 cm<sup>2</sup> in size intraoperatively. For the clinical assessment, Lysholm score was assessed preoperatively and at 2-year follow-up. All patients underwent morphological magnetic resonance imaging at 1.5-Tesla at 1-year follow-up. Mean Magnetic Resonance Imaging Observation of Cartilage Repair Tissue score at 1-year follow-up was 70.4±20.2 (range, 15-95). The Magnetic Resonance Imaging Observation of Cartilage Repair Tissue score for patellar lesions was similar to that of lesions in other locations: 73.3±11.7 vs 68.1±25.5, respectively. This technique had encouraging clinical results at 2-year follow-up. Morphological magnetic resonance imaging shows good cartilage defect filling, and the biochemical magnetic resonance imaging suggests hyaline-like repair tissue.



**Figure:** Intraoperative photograph showing the instrument setup during arthroscopic cartilage repair using the autologous collagen-induced chondrogenesis technique.

*The authors are from the Kent Knee Unit (AAS, SJK, PB, DS), Spire Alexandra Hospital, Chatham; the Faculty of Health and Social Sciences (AAS), Canterbury Christ Church University, Chatham Maritime; Medway Maritime Hospital (PB), Gillingham, Kent, United Kingdom; the Department of Orthopedic Surgery (SJK), Uijeongbu St Mary's Hospital, The Catholic University of Korea, Kumoh-dong, Uijeongbu City, Gyeonggi-do, Korea; and the Department of Orthopaedics (DS), Medical University of Vienna, Vienna, Austria.*

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*Correspondence should be addressed to: Seok Jung Kim, MD, Department of Orthopedic Surgery, Uijeongbu, St Mary's Hospital, The Catholic University of Korea, Kumoh-dong, Uijeongbu City, Gyeonggi-do, 480-717, Korea (peter@catholic.ac.kr).*

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Chondral defects in young to middle-aged patients are commonly seen in clinical practice.<sup>1,2</sup> Although several treatments designed to regenerate cartilage have had encouraging results, none have proved to be simple and effective. Microfracture predominantly produces fibrocartilage.<sup>3</sup> Autologous chondrocyte implantation is considered an effective procedure to produce hyaline-like cartilage.<sup>4,5</sup> However, it is expensive and involves 2-stage surgical procedures, with the associated morbidity of arthroscopy and harvesting a small portion of normal articular cartilage.

Cell-free collagen type I gels or scaffolds combined with marrow stimulation techniques have been used successfully for cartilage repair.<sup>6-12</sup> Atelocollagen is a highly purified type I collagen obtained following the treatment of skin dermis with pepsin and telopeptide removal, which makes it nonimmunogenic. It is used in medical, cosmetic, and research fields. Its physical properties are virtually identical to natural, nonsoluble collagen. Therefore, it is used as a collagen scaffold in tissue regeneration.

This article describes a novel arthroscopic surgical technique that can be performed using microdrilling and atelocollagen gel. Patients can be discharged the same day as their surgery. The hypothesis was that this technique would provide cartilage regeneration and improve symptoms in patients with isolated cartilage defects of the knee.

## Materials and Methods

### Patients

This was a retrospective study consisting of symptomatic patients with isolated full-thickness (International Cartilage Repair Society/Outerbridge grade III/IV) cartilage lesions. The defect sizes were 2 to 8 cm<sup>2</sup>. Mean±SD patient age was 44.9±11.2 years (range, 26-63 years). Patients with generalized osteoarthritis, more than 5° of malalignment, and an age older than 65 years were excluded

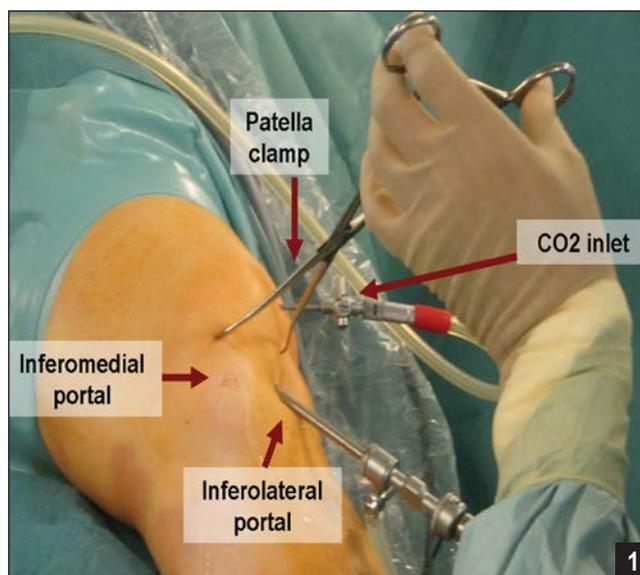
from undergoing autologous collagen-induced chondrogenesis (ACIC). All patients undergoing ACIC between April 2009 and December 2009 were included in the study. All patients gave informed consent to undergo the procedure.

### Surgical Technique

All procedures were performed under general anesthesia. The standard anterolateral and anteromedial arthroscopic portals were used to evaluate the knee using normal saline under pressure (approximately systolic blood pressure). After assessing the defects, the lesions were debrided down to the subchondral bone using a curette and shaver. A stable shoulder was established at the margin of the defect. Microdrilling was performed using the 45° angled drill (Powerpick drill; Arthrex Ltd, Sheffield, United Kingdom). Drill holes were made at 3-mm intervals to a depth of 6 mm (Figures 1-3).

The second part of the procedure was performed under dry arthroscopic conditions using carbon dioxide (CO<sub>2</sub>) insufflation. Carbon dioxide was introduced at 20 mm Hg pressure with a flow rate of 20 L/min using a Wolf cannula (Karl Storz GmbH, Tuttlingen, Germany) and disposable tubing with a filter (Insufflation tubing with Wolf adaptor; Leonhard Lang UK Ltd, Stroud, United Kingdom) through a superolateral portal.

To make the joint completely dry, residual normal saline in the joint was aspirated using gentle suction with a 20-mL syringe and an angled suction tube (Exmoor, Taunton, United Kingdom). The lesions



**Figure 1:** Intraoperative photograph showing the instrument setup during arthroscopic cartilage repair using the autologous collagen-induced chondrogenesis technique.

were dried using cotton buds, which were introduced through the joint using plastic tubing. For patellar and trochlear lesions, a patellar clamp (AO or Lewin bone clamp [DePuy Synthes Ltd, Hertfordshire, United Kingdom]) was applied to lift the patella and further open the joint.

Under arthroscopic vision, the gel was applied into the defect. The CO<sub>2</sub> pressure and the adhesiveness of the gel allowed attachment even against gravity, especially to patellar defects. Once the first layer of gel was applied and after a delay of 1 to 2 minutes, the gel was injected under the first layer to achieve full defect filling. The gel usually hardened within 5 minutes, and then it was shaped in situ using a McDonalds dissector [Bolton Surgical Ltd, Sheffield, United Kingdom] (Figure 3).

Once this was established, the CO<sub>2</sub> was switched off, and the knee was insufflated with normal saline under pressure. The stability of the graft was further ascertained by moving the knee through a full range of motion several times followed by visual inspection. The skin was closed with sutures or steri-strips.

### Rehabilitation

All patients underwent a standardized rehabilitation protocol. Patients were ad-

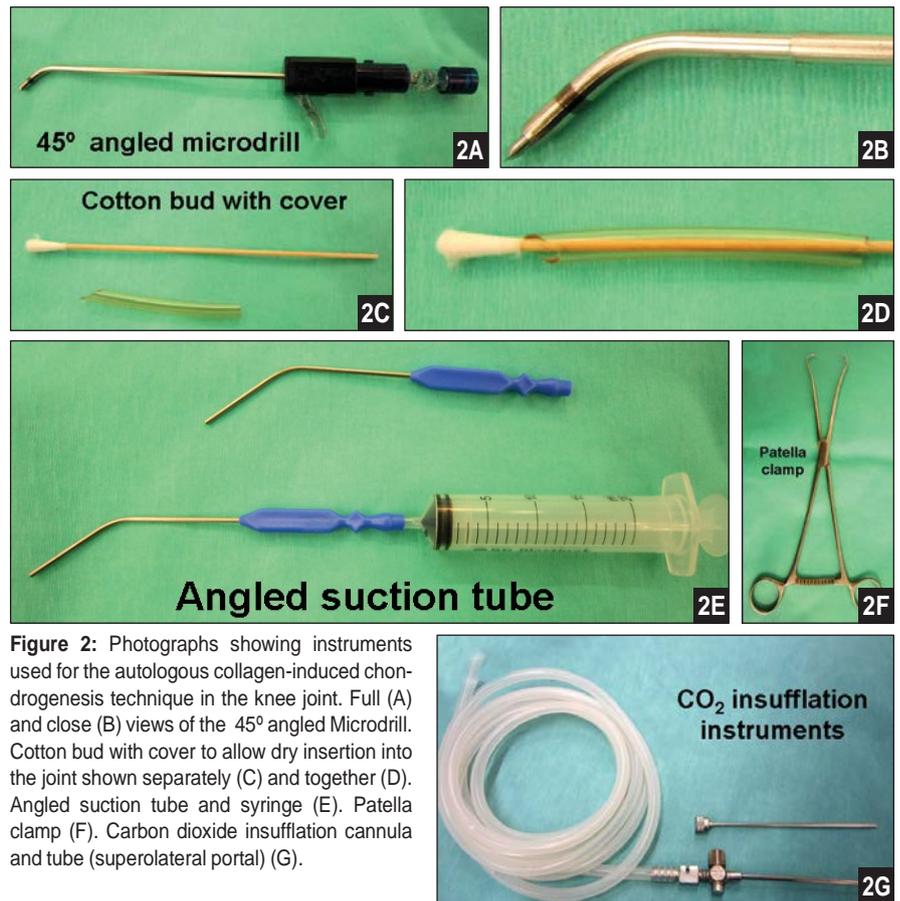
for 6 weeks postoperatively. Gradually, increased loads were applied during the first 6 weeks. Flexion was only restricted in patients with patellofemoral defects. In these patients, flexion to 30° was allowed within the first 2 weeks and was gradually increased to 90° at 6 weeks postoperatively. After that, the full range of motion was approached.

### Clinical Assessment

All patients were assessed using the Lysholm score preoperatively and at 2-year follow-up.

### Magnetic Resonance Imaging Assessment

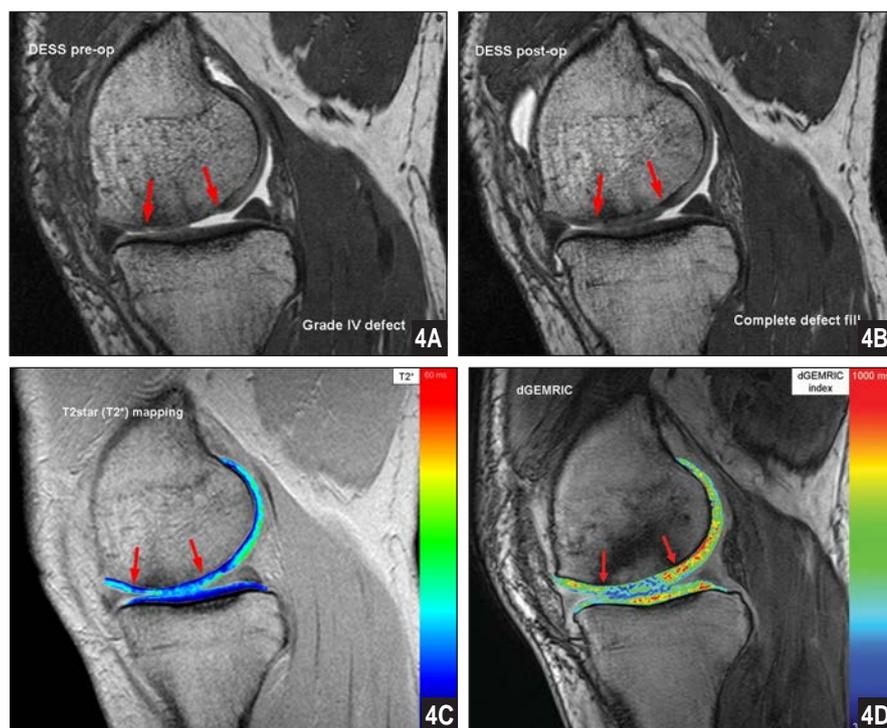
Every patient was assessed using a specific cartilage magnetic resonance imaging (MRI) protocol using fast spin-echo and double-echo steady-state sequences preoperatively and at 1-year follow up. A 1.5-Tesla MRI unit (Siemens Avanto; Siemens Healthcare, Inc, Erlangen, Germany) and a dedicated multichannel knee coil were used. High field strength MRI (1.5- or 3.0-Tesla) has yielded high resolution images that identify most cartilage lesions.<sup>13,14</sup> For a structured morphological assessment, the MRI observation of cartilage repair tissue (MOCART) score was used postoperatively.<sup>15</sup> A MOCART



**Figure 2:** Photographs showing instruments used for the autologous collagen-induced chondrogenesis technique in the knee joint. Full (A) and close (B) views of the 45° angled Microdrill. Cotton bud with cover to allow dry insertion into the joint shown separately (C) and together (D). Angled suction tube and syringe (E). Patella clamp (F). Carbon dioxide insufflation cannula and tube (superolateral portal) (G).



**Figure 3:** Arthroscopic images showing the steps of autologous collagen-induced chondrogenesis. Debridement with curette and shaver is followed by microdrilling. Under carbon dioxide insufflation of the joint, the defect is dried using a suction tube and cotton swabs. The application of the collagen/fibrinogen/thrombin gel using a 2-way syringe is followed by contouring the gel scaffold with a McDonalds dissector. After 5 minutes of scaffold hardening, graft stability is assessed by moving the knee through a full range of motion under saline insufflation.



**Figure 4:** A 51-year-old man undergoing autologous collagen-induced chondrogenesis. Three-dimensional double-echo steady-state magnetic resonance image showing the preoperative International Cartilage Repair Society grade IV defect on the medial femoral condyle (arrows) (A), which was filled with repair tissue (arrows) 12 months after arthroscopic autologous collagen-induced chondrogenesis (B). Similar T2 values can be observed on the T2 map in the cartilage repair tissue (34±6 ms) compared with the surrounding weight-bearing native cartilage (arrows) (36±6 ms) (C). A delayed gadolinium-enhanced magnetic resonance image of cartilage scan of the same patient at 2.5-year follow-up showing T1-gadolinium values of 505±147 ms for the repair tissue and 560±120 ms for the surrounding native cartilage in the weight-bearing area, which suggests hyaline-like repair tissue (arrows) composition with near to normal proteoglycan content (D).

score of 0 represents the worst possible result, and 100 represents the best possible MRI outcome.

**Statistics**

Descriptive statistics are presented as mean±SD. A paired 2-tailed *t* test was performed to compare pre- and postoperative Lysholm scores. An alpha level of 0.05 was considered statistically significant.

**results**

The lesions were located on the patella in 6 patients, medial femoral condyle in 5, lateral femoral condyle in 1, and trochlea in 2 (4 patients had 2 lesions).

Mean±SD Lysholm score improved from 51.7±27.1 preoperatively to 81.3±24.6 at 2-year follow-up (*P* .05),

which is consistent with a marked clinical improvement.

Postoperative MRIs showed good results in most patients. Mean±SD MOCART score at 1-year follow-up was (range, 15-95). The MOCART score for patellar lesions was similar to lesions in other locations: 73.3±11.7 vs 68.1±25.5, respectively. Figure 4 shows examples of MRI outcomes.

**discussion**

To the authors’ knowledge, this is the first report of an arthroscopic single-stage method using CO<sub>2</sub> insufflation and atelocollagen gel for cartilage repair (ACIC). The authors demonstrated good clinical results at 2-year follow-up after ACIC. Many authors have reported successful

cartilage repair using collagen gel or collagen scaffolds in the knee.<sup>6-12</sup>

The current results are comparable with those of Gille et al,<sup>11</sup> who reported a mean 2-year Lysholm score of 76. The results of Kusano et al,<sup>12</sup> with Lysholm scores of 76 to 94, are in the range of the current 2-year results. Piontek et al<sup>16</sup> and Marcacci et al<sup>17</sup> reported the feasibility of all arthroscopic autologous chondrocyte transplantation and arthroscopic single-stage autologous matrix-induced chondrogenesis procedure. However, Piontek et al<sup>16</sup> have not provided clinical results.

The current approach differs from their technique in that CO<sub>2</sub> is used for insufflation instead of normal air. Carbon dioxide can be insufflated under pressure to slightly inflate the joint and facilitate intra-articular procedures. Carbon dioxide has an excel-

lence in articular surgery.<sup>18-20</sup> Animal studies have shown that continuous venous infusion of CO<sub>2</sub> resulted in no adverse events.<sup>21</sup>

For procedures in which a collagen membrane is transplanted to the cartilage defect, the depth of the defect area should be relatively greater, and the press fit should be created accordingly. In patients in whom the depths of the defect areas are shallower, the scaffold needs to be maintained with sutures at the transplantation site. Atelocollagen and fibrin mixture do not need this process. According to the coagulation cascades, they can be maintained at the sites where a defect is shallow. Collagen is the connective tissue protein that plays a key role in maintaining the tissue morphology, and atelocollagen is a highly purified type I collagen that was obtained following the treatment of pepsin from the skin dermis. Currently, collagen is obtained from animal tissues, and the atelocollagen for this surgical technique was obtained from porcine skin. This atelocollagen is obtained following the removal of telopeptide, which is immunologically problematic, and is used for various things, such as wound healing, vessel prosthesis, bone substitute, and hemostatic agent.

The current authors do not use a circular punch or large-diameter drill to debride the defect. The surrounding native cartilage tissue can be adequately preserved by using a curette and shaver for defect debridement. In particular, for noncircular-shaped defects, the current technique gives more flexibility to the surgeon without the necessity for going too far into the healthy native tissue.

In this procedure, the fibrin can maintain the shape of the articulation approximately 5 minutes after injection due to the reaction between the thrombin and fibrinogen in the 2-way syringe. Therefore, even if a defect exists along the chondral margin, fibrin helps maintain the shape of the graft according to the articulation. Fibrin gel has recently attracted attention as a good material for cartilage reconstruction.<sup>22,23</sup>

Microdrilling was preferred to microfracture due to the former benefitting from better channels to bone marrow stroma, which would facilitate stem cell recruitment.<sup>24</sup> These channels also serve an important function by increasing the adhesive force of the graft to the defect during knee range of motion. However the results of the rabbit study reported by Chen et al<sup>24</sup> have to be confirmed by clinical human studies.

Morphological MRI demonstrated good cartilage growth, and the 1-year MOCART results are comparable with those of other studies.<sup>6,25,26</sup> A quantitative MRI evaluation with T2-mapping and delayed gadolinium enhanced MRI of cartilage was only available in 1 patient but demonstrated promising results with good repair tissue quality (Figure 4).

## Conclusion

A single-stage arthroscopic procedure using microdrilling combined with ACIC appears to be an effective cartilage regeneration method. 

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