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Case Report

# Meniscal Allograft Transplantation Combined with Cartilage Repair in the Treatment of Large Cartilage Defects of the Meniscectomized Knee Joint: A Case Report and Literature Review

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#### **Abstract**

Meniscal substitution by meniscal allograft transplantation (MAT) has been thought to be a better alternative treatment option for painful meniscectomized knees in young people. Although MAT have shown good short-term results regarding healing of the allograft to the joint capsule and symptomatic relief, it is still uncertain that MAT is able to re-establish the normal load distribution function as the native meniscus and prevent osteoarthritis (OA) progression. Meniscectomized knees with a large cartilage defect in the femorotibial joint and general cartilage degeneration are usually contra-indications of MAT. We present a case of large cartilage defects both in the lateral femorotibial joint and the patella at 25 years after subtotal meniscectomy. A 36-year-old woman complained her left knee pain and click, presenting an antalgic limping with a cane for over 5 years. Her preoperative range of motion (ROM) of the knee joint was quite limited (-15° of extension and 90° of flexion). The patient was treated with MAT on a simultaneous third-generation autologous chondrocyte implantation (ACI) into the cartilage defects both in the femorotibial compartment and the patella and an osteochondral autograft transplantation (OAT) in the lateral plateau. After 6 months of follow-up, she had neither pain nor click in the left knee joint and walked without a cane. The post-operative ROM was -10° of extension and 110° of flexion. MRI demonstrated a good healing of both the grafted meniscus and tissue-engineered cartilage of the lateral femorotibial joint and the patella. Cartilage repair must be complementarily attributed to restore the normal load distribution function of the grafted allogenic meniscus. We believe that a simultaneous ACI with or without OAT on MAT might be a promising procedure for large cartilage defects of knee joint after subtotal or total meniscectomy for young people, preventing progression of OA for a long time.

Keywords: meniscus, allograft, transplantation, knee, autologous chondrocyte implantation

### Introduction

The menisci of the knee joint play important roles of load distribution, stress reduction, joint lubrication, proprioception, joint congruity, and knee stabilization [1.2]. Based on several biomechanical and clinical studies, preservation of torn menisci such as meniscal repair is a consensus to prevent osteoarthritis (OA) progression,

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especially in young patients [3]. The Japanese National Database showed that 69,310 patients underwent meniscectomy, 13,416 underwent meniscus repair and 379 underwent both in a single admission between 2007 and 2015 [4]. The characteristic trends where the popularity of meniscal repair increased rapidly at the expense of meniscectomy in Japan, and the proportion of meniscal repair exceeded that of meniscectomy in those younger than 30 years in 2015 [4]. However, subtotal or total meniscectomy is not sometimes avoided for the treatment in the cases with the complex tears of degenerated discoid menisci. Even partial meniscectomy decreased clinical outcome scores over time in patients treated arthroscopically for symptomatic discoid meniscus [5].

Meniscal substitution by meniscal allograft transplantation (MAT) has been thought to be a better alternative treatment option for painful meniscectomized knees in young people [6,7]. Although MAT have shown good short-term results regarding healing of the allograft to the joint capsule and symptomatic relief, it is still uncertain that MAT is able to re-establish the normal load distribution function as the native meniscus and prevent OA progression. Obesity (BMI>35) and systemic diseases (e.g. infection, collagen diseases, synovial chondromatosis) deteriorate the outcomes of MAT [7]. Young patients with open physis should not undergo MAT which damages the epiphysial plate. Besides axial mal-alignment of the lower extremity, and/or unstable knees, a large cartilage defect in the femorotibial joint and general cartilage degeneration are usually contra-indications of MAT [7]. By contrast, Frank et al. analyzed 100 knees to determine clinical outcomes for patients undergoing osteochondral allograft (OCA) with MAT as compared with a matched cohort of patients undergoing isolated OCA with a minimum 2 years follow-up, demonstrating that there were no significant differences in patient-reported clinical outcome scores and failure rate between OCA with MAT and without MAT [8]. However, it is not clarified what size of cartilage defect is limited to get good outcomes for OCA.

Autologous chondrocyte implantation (ACI) was developed by Brittberg et al. [9] in 1994 and is a promising treatment to repair cartilage defects; expanded chondrocytes harvested from a non-weight-bearing area are cultured in a monolayer culture system and injected. This cell-based method is representative of first-generation ACI, which has shown excellent clinical results and long-term durability [10]. However, it has some disadvantages of dedifferentiation of the expanded chondrocytes, leakage of grafted cells from the defect, and uneven distribution of cells in the defect. To resolve these problems, Ochi et al. developed tissue-engineered cartilage, containing not only cells but also matrix, i.e., third -generation matrix-associated ACI, in which cultured cells are embedded in Atelocollagen gel and cartilage-like tissue is produced ex vivo [11]. Experimental studies have demonstrated that the phenotype of the cultured chondrocytes maintained and enables even distribution of cells in the transplanted tissue with a lower risk of chondrocytes leakage from the grafted site [12,13]. Clinical studies have shown good outcomes and long-term durability [14,15].

Ogura et al. analyzed data from 17 symptomatic patients (18 knees) who underwent ACI combined with MAT for concomitant cartilage lesions and meniscal deficiency. Their results showed a 75% survival rate at both 5 and 10 years [16]. However, their ACI was a conventional cell-based ACI, i.e., first-generation ACI. In this paper, we report a case of large cartilage defects both in the lateral femorotibial joint and the patella at 25 years after subtotal meniscectomy, treating a simultaneous third-generation ACI with an osteochondral autograft transplantation (OAT) on MAT.

#### **Case Report**

A 36-year-old woman who underwent subtotal meniscectomy for the symptomatic lateral discoid meniscus complained her left knee pain and click, presenting an antalgic limping with a cane for over 5 years. Orthopedic examination revealed swelling and ballottement of the left knee joint, and meniscus sign and tenderness at the lateral

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compartment. Her preoperative ROM was -15° of extension and 90° of flexion. The radiographic Kellgren–Lawrence classification was Grade 2 and the standing femorotibial angle (FTA) was 175° (Figure 1), and the Rosenberg's view showed the diminished joint space of the lateral compartment. Preoperative proton density magnetic resonance imaging (MRI) showed the lateral meniscus diminished by subtotal meniscectomy and a focal cartilage defect in the lateral femoral condyle and the lateral tibial plateau (Figures 2A-2C). Degenerated cartilage was noted in the patella in the axial view of MRI (Figure 2D).



Figure 1. Preoperative radiographs (A) weight-bearing anteroposterior view, and (B) lateral view.



Figure 2: Preoperative proton density MRI (A) the lateral meniscus diminished by subtotal meniscectomy (arrow) in the coronal view, (B) and a focal cartilage defect (\*) of the lateral femoral condyle and tibial plateau (†) in the sagittal view, (C) A partial anterior segment of the lateral meniscus remains after subtotal meniscectomy (white arrow) in the axial view, and (D) cartilage degeneration (††) in the patella in the axial view.

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The Japanese Orthopaedic Association (JOA) and Lysholm scores were 37 and 19 points, respectively. Upon diagnosis of a painful subtotally-meniscectomized knee with concomitant focal cartilage defects of the lateral femoral condyle and the patella, we had minutely planned MAT combined with ACI. Then we negotiated perseveringly about this MAT plan with the Tokai Reginal Tissue Bank (Nagoya, Japan), that has supplied allografts such as bone-patellar tendons for allogenic anterior cruciate ligament reconstruction and bone allografts for revision arthroplasties in more than 10,000 cases for over 10 years. The protocol of MAT was approved of the Ethical Committee of Shimane University School of Medicine and the operation was permitted by the Chugoku Regional Bureau of Health and Welfare in Japan.

At the first surgery, arthroscopy was performed to evaluate lesions and harvest cartilage slices under general anesthesia. Arthroscopy revealed that the lateral meniscus was sub totally absent and focal cartilage defects were noted both in the lateral condyle ( $20 \times 34$  mm) and patella ( $17 \times 19$  mm in the medial facet,  $23 \times 18$  mm in the lateral facet) (Figures 3A & 3B). Then, according to the ACI procedure described by Ochi et al. [11], 420 mg of cartilage tissue was harvested arthroscopically from the non-weight-bearing areas of the left knee. The cartilage tissue was subjected to enzymatic digestion, the extracellular matrix was removed, and the chondrocytes were isolated [11]. These chondrocytes were embedded in a three-dimensional culture using Atelocollagen gel (Koken Atelocollagen Implant, Koken Co., Ltd., Tokyo, Japan) for 4 weeks.

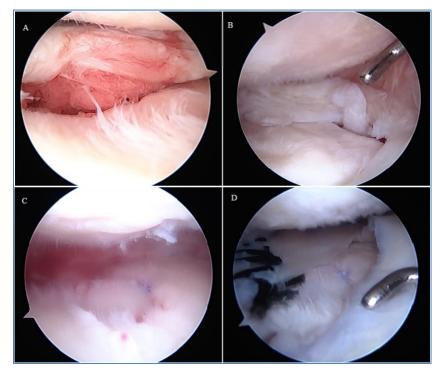


Figure 3: Arthroscopic findings (A) the lateral meniscus diminished by subtotal meniscectomy in the lateral compartment and cartilage degeneration in the lateral tibial plateau, (B) a focal defect of the cartilage of the lateral femoral condyle, (C) an osteochondral autograft was transplanted in the lateral tibial plateau, and (D) meniscus allograft was sutured in the lateral compartment.

At the second surgery, under general anesthesia, an osteochondral autograft (8.5 mm in diameter) taken from the non-weight bearing area of the lateral femoral condyle was transplanted into the lateral tibial plateau under arthroscopy (Figure 3C). Next, a deepfrozen meniscal allograft with bone supplied by the Tokai Reginal Tissue Bank (Nagoya, Japan) was applied to the lateral compartment modifying the method by Farr et al., and was sutured to the

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peripheral capsule by three sutures of FastFix meniscal repair system (Smith & Nephew, Tokyo, Japan) and three sutures by all-inside technique using the Knee ScorpionTM suture passer (Arthrex Inc., München, Germany; Figures 3D & 4A). Then, ACI was performed according to the method of Ochi et al. [9]. The cultured chondrocytes embedded in Atelocollagen were transplanted into cartilage defects beneath periosteal patches from the left tibia. Finally, the patch was sutured (Figures 4B & 4C).

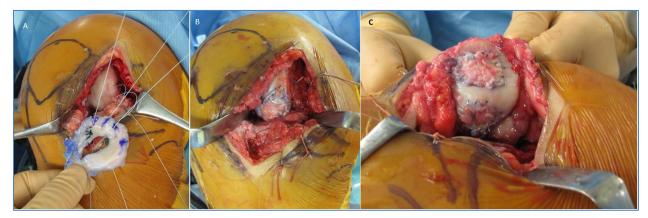
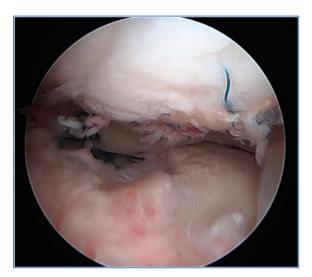


Figure 4: Surgical procedure (A) meniscal allograft transplantation in the lateral compartment, (B) autologous chondrocyte implantation in the lateral femoral condyle, and (C) autologous chondrocyte transplantation in the patella.

ROM exercise started two weeks after surgery, partial and full weight bearing walking started at 4weeks, and 6 weeks after surgery, respectively. At 3 months post-operatively, she underwent arthroscopic debridement for the knee contracture. Arthroscopy showed the fixation of the allogenic meniscus and the ACI implant (Figure 5). At 6 months later, she complained neither pain nor click and could walk without giving way. Physical examination demonstrated neither swelling nor ballottement of the left knee joint, improving the ROM (-10°-110°) without any meniscus signs. She had no allergic symptoms and normal data on her blood-chemical tests. The JOA and Lysholm scores at 6 months after operation were 81 and 86, respectively. Radiographs and MRI showed that lateral joint space was maintained, the meniscal allograft was fixed good in the lateral compartment and the ACI (Figures 6 &7). She was satisfied very much with the outcome of MAT combined with ACI and OAT.



**Figure 5:** Arthroscopic finding at 3 months after surgery: transplanted meniscal allograft in the lateral compartment, ACI in the lateral femoral condyle, and an osteochondral autograft, all were biologically fixed.

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Figure 6: Postoperative radiographs at 6 months after surgery (A) weight-bearing anteroposterior view, and (B) lateral view.



Figure 7: Postoperative proton density MRI at 6 months after surgery (A) the fixed meniscal allograft in the lateral compartment (white arrow), ACI in the lateral femoral condyle (\*), and an osteochondral autograft (OAT: arrow) in the coronal view, (B) in the sagittal view. Arrow in the non-weight bearing area of the lateral femoral condyle shows the donor site of OAT, and (C) the ACI (†) in the patella in the transverse view.

## Discussion

This is the first report of MAT with a simultaneous third-generation ACI and OAT into the cartilage defects in the meniscectomized knee joint. Because both cartilage and menisci play biomechanical roles in the knee joint complementarily, patients who have large cartilage defects or general cartilage degeneration after subtotal or total meniscectomy are contra-indications of MAT or ACI in isolation [8]. Although several clinical studies demonstrated good results of MAT or ACI performed in isolation [10,17-20], the clinical data concerning MAT combined with ACI are limited. A pilot study of a simultaneous ACI on MAT by Bhosale et al. demonstrated that six out of eight patients improved post-operatively in terms of pain relief and increased activity at one year, with five showing continued

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improvement at mid-term (3.2 years) [21]. Both Farr et al. and Rue et al. analyzed 29 and 31 patients with a minimum of 2-year follow-up, respectively, suggesting that MAT in combination with ACI demonstrated improvement in both symptoms and knee function and offered a safe alternative option for the patients [22,23]. However, the improvements were less than literature-reported outcomes of either procedure performed in isolation. Although Ogura et al. showed a 75% survival rate at both 5 and 10 years, 7 knees (58%) required subsequent surgical procedures due to arthrofibrosis in 5 knees, followed by ACI graft hypertrophy [16].

To improve the clinical results and reduce the adverse effects, we have decided to treat a simultaneous third generation-ACI on MAT. Several systematic reviews demonstrated complication rates were higher with first-generation ACI [24,25]. Indeed, this report is a pilot study of MAT combined with 3<sup>rd</sup>-generation ACI, i.e., implantation of tissue-engineered cartilage-like tissue, however, we believe that biological reconstruction for symptomatic meniscectomized knees with large cartilage defects by using MAT, ACI, and/or OAT might provide better clinical outcomes for young patients. A long-term follow-up should clarify the benefits and risks of this combined procedure and the chondroprotective effect preventing OA progression.

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