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# Augmenting Osteochondral Autograft Transplantation and Bone Marrow Aspirate Concentrate with Particulate Cartilage Extracellular Matrix Is Associated With Improved Outcomes

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## Abstract

**Background:** Osteochondral autograft transplant (OAT) is often used to treat large osteochondral lesions of the talus and is generally associated with good outcomes. The addition of adjuncts such as cartilage extracellular matrix with bone marrow aspirate concentrate (ECM-BMAC) may further improve the OAT procedure but have not been thoroughly studied. We hypothesized that the placement of ECM-BMAC around the OAT graft would improve radiographic and patient-reported outcomes following OAT.
**Methods:** Patients who received OAT, with ECM-BMAC or BMAC alone, were screened and their charts were reviewed. For patients who did receive ECM-BMAC, the mixture was spread around the edges of the OAT plug and into any surrounding areas of cartilage damage. Survey and radiographic data were collected. Average follow-up in both groups was over 2 years. Magnetic resonance imaging scans were scored using the Magnetic Resonance Observation of Cartilage Tissue (MOCART) system. Outcomes were compared statistically between groups.
**Results:** Patients treated with ECM-BMAC (n = 34) demonstrated significantly greater improvement of scores in the FAOS categories Symptoms (17 vs −3; $P = .02$) and Sports Activities (40 vs 7; $P = .02$), and the MOCART category Subchondral Lamina ($P = .008$) compared to those treated with BMAC alone (n = 30). They also experienced significantly lower rates of postoperative cysts (53% vs 18%, $P = .04$) and edema (94% vs 59%, $P = .02$).
**Conclusion:** The addition of ECM-BMAC to OAT was associated with improved imaging and clinical outcomes compared to OAT with BMAC alone.
**Level of Evidence:** Level III, retrospective cohort study.

**Keywords:** osteochondral lesion of the talus, allogenic cartilage extracellular matrix, osteochondral autograft transplantation, bone marrow aspirate concentrate

## Introduction

Osteochondral lesions of the talus (OLTs) represent a unique challenge for clinicians and their patients because of the limited healing ability of articular cartilage. Although conservative treatment is common in smaller lesions, it has a high failure rate, and larger lesions tend to require operative intervention.[5,42] Microfracture, historically the standard of care for symptomatic OLTs, is not particularly effective for

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the treatment of lesions larger than 150 $mm^2$ or for those on the shoulder of the talar dome.[6,7] Expert consensus has suggested an upper limit for microfracture of 100 $mm^2$, although the evidence in support of this is currently considered to be low quality.[24] Lesions of this size often require a revision procedure after treatment with microfracture, which could include osteochondral allograft or autograft transplantation or autologous chondrocyte implantation.[4,6,7,18,20,25,30] Osteochondral autograft transplantation (OAT) in particular, whether used as a primary or secondary procedure, has proven to be effective in treating larger lesions that are not suited to microfracture.[6,7] Treatment with OAT has demonstrated good to excellent outcomes in patients with large, cystic lesions of the talus.[2,17,22,28,32,36,37] One systematic review reported a success rate of up to 87.4% at medium-term follow-up for OAT with at least 1 individual report achieving up to 94% good to excellent outcomes.[22,37] Although long-term follow-up results are lacking for the talus, treatment with osteochondral autograft has demonstrated long-term success when used for knee injuries.[23,31]

OAT is a mosaicplasty technique designed to replace the damaged articular cartilage within the ankle with normal, hyaline articular cartilage harvested from another site in the patient's body. The autograft for the OAT procedure can be obtained from multiple sites, with the lateral minimally weightbearing zone of the patient's ipsilateral femoral condyle among the most common. An osteotomy or arthrotomy is then required to access the lesion site for repair. Use of an autograft is thought to reduce the rate of failure compared to the use of a cadaveric allograft.[38] Despite reports of good to excellent outcomes, OAT is not without its potential complications and disadvantages. Concerns have been raised over the potential for donor site morbidity in the knee, nonunion following osteotomy, and postoperative cyst formation.[34,35,41] Donor site morbidity is one of the most common postoperative complications following OAT, with a systematic review of 11 studies reporting on 500 ankles reporting a 3.6% rate of donor site morbidity.[37] Such morbidity may commonly include pain or swelling during physical activity.[17] Furthermore, many large OLTs present as amorphous, irregular shapes that create additional challenges during treatment using OAT, which routinely uses cylindrically shaped plugs. Knee cartilage is also thicker than ankle cartilage, which can pose additional challenges when seeking to obtain a level fit.

Recent research examines the efficacy of biologic adjuncts as potential solutions to these challenges. Prior evidence suggests that these adjuvant therapies may have the ability to further improve the quality of cartilage repair tissue following OAT.[9,14,21,33,38,40] Bone marrow aspirate concentrate (BMAC) is one such adjunct that contains mesenchymal stem cells and growth factors important for cartilage repair.[15] Evidence suggests that BMAC, when used to coat the osteochondral plug or when placed at the base of the lesion prior to inserting the graft, may help improve integration at the lesion site and reduce the rate of postoperative cyst formation.[39] Micronized allogenic cartilage extracellular matrix (ECM) is another biologic that may help to relieve the challenges associated with OAT. BioCartilage Extracellular Matrix (Arthrex, Naples, FL) is derived from allograft cartilage and consists of the extracellular components native to articular cartilage such as type II collagen, proteoglycans, and other cartilaginous growth factors. Used alongside OAT, it has the potential to improve reparative tissue and the integration of the autograft plug.[12] When mixed with BMAC consisting of mesenchymal stem cells, the ECM product is intended to serve as a scaffold, delivering important growth factor and cellular components to help promote autologous cell interactions and repair. Thus, the goal of using ECM-BMAC with OAT is to improve the integration of the autograft plug as well as the degree of infill and quality of tissue at the repair site (Figure 1).

The existing literature on ECM is relatively sparse. A prior biological study using an animal model indicated that allogenic ECM is safe to use and resulted in better integration of repair tissue and production of desired type II collagen when compared to repairs following microfracture.[16] A few prior reports also evaluated the use of ECM during treatment of smaller OLTs and documented increases in patient-reported outcome measures following the use of ECM combined with BMAC. Unfortunately, these studies did not report on objective radiographic outcomes regarding the structural quality of the repairs and are limited because of small cohort sizes.[8,11] Another recent study evaluated clinical and radiographic outcomes, reporting a 96.7% success rate in which clinical and/or radiographic healing was achieved in patients after using ECM to treat smaller OLTs.[1] However, to our knowledge there is no study examining the effect of ECM-BMAC on OAT outcomes for the treatment of large OLTs.

The purpose of this study was to compare the clinical and radiographic outcomes of cases during which ECM-BMAC was used to augment the standard OAT procedure for the treatment of OLTs to those during which BMAC alone was used. We hypothesized that patients treated with ECM-BMAC would experience better functional improvement, possess higher-quality repair tissue on postoperative MRI, and would exhibit lower rates of postoperative cysts and edema compared to patients treated using OAT with BMAC alone.

## Methods

### Study Population and Design

After approval was obtained from our IRB, relevant Current Procedural Terminology codes were used to identify patients who were treated by one of 4 surgeons for a talar

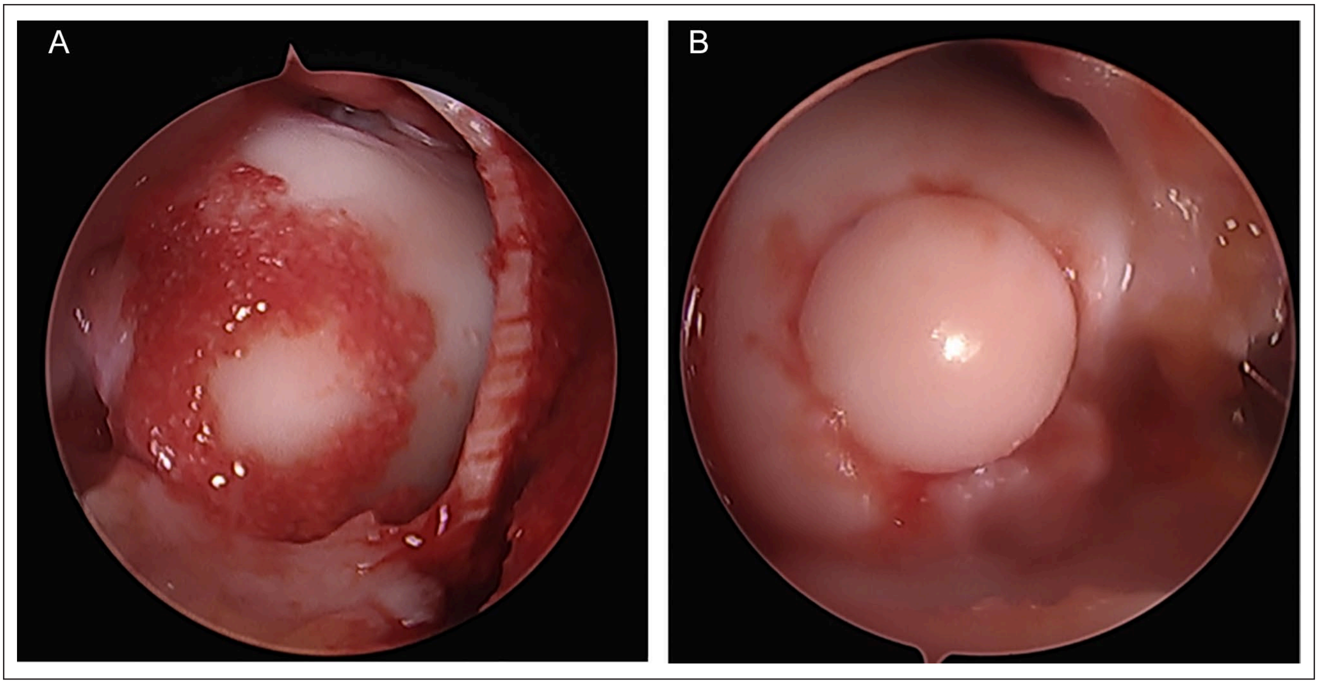


**Figure 1.** Insertion of OAT plug. (A) OAT plug with ECM-BMAC, which is used as a mortar to surround the graft. (B) OAT plug without ECM-BMAC. (ECM-BMAC, extracellular matrix with bone marrow aspirate concentrate; OAT, osteochondral autograft transplant)

osteochondral lesion using OAT between 2009 and 2018. Retrospective chart review was used for each patient to determine whether or not OAT was augmented with an adjuvant mixture of ECM-BMAC. Every time ECM was used, it was mixed with BMAC prior to being placed around the OAT graft. BMAC was also used to augment the OAT procedure in every patient treated without ECM. Decisions regarding treatment method were based on surgeons' preferences and biologic adjuncts available for use at the time of each procedure. ECM was added in all cases from 2016 or later, and all cases from 2015 or earlier did not involve ECM. One surgeon was responsible for the majority of the cases without ECM and a few of the ECM cases. Another surgeon was responsible for the majority of the ECM cases. The other 2 surgeons completed several cases each.

Patients with concurrent ankle instability were also identified. Ankle instability was defined as a talar tilt of greater than 10 degrees varus or an anterior drawer of greater than or equal to 10 mm on routine stress x-rays performed in the clinic.[27] For patients who presented with concurrent ankle instability, the instability was addressed by performing a lateral ankle stabilization procedure using either the Brostrom-Gould method or lateral ligament reconstruction, depending on the surgeon's preference.

Retrospective chart review was performed. Patients with bipolar lesions or evidence of arthritic progression were excluded. Pre- and postoperative functional outcome scores, including the Foot and Ankle Outcome Score (FAOS) and Patient-Reported Outcomes Measurement Information System (PROMIS) Physical Function, Pain Interference, Global Physical Health, and Pain Intensity domains, were collected prospectively through the foot and ankle registry database at our institution. Postoperative functional outcomes were collected at a minimum of approximately 12-month follow-up. Size and location of the OCLs were collected from operative notes. Lesion size was recorded in square millimeters. Lesion location was also defined as medial, posteromedial, anteromedial, lateral, posterolateral, anterolateral, or central to the talar surface. Some patients required 2 OAT plugs to repair their lesion, and this was recorded during chart review. It was also noted whether or not patients required hardware removal. All other postoperative complications were also noted including infection, malleolar nonunion, and knee morbidity.

## *MRI Assessment*

Postoperative MRIs were collected for research purposes. Patients were asked to return for imaging postoperatively at no specified time point. All magnetic resonance (MR) images were reviewed by a radiologist fellowship trained in musculoskeletal radiology and were evaluated using the modified Magnetic Resonance Observation of Cartilage Tissue (MOCART) score.[1] The radiologist was not told which patients had received the ECM-BMAC treatment. The MOCART system uses 9 parameters to evaluate the morphology and signal intensity of the repair tissue compared with native cartilage and has been shown to be a reliable method for assessing cartilage repair with low interobserver variability.[29] In addition, the radiologist indicated whether or not an adjacent cyst or signs of edema were present on patients' postoperative MRIs. MR protocols were not standardized within the study cohort because scans were performed across multiple institutions. However, each MRI was evaluated by the same board-certified radiologist who has completed a fellowship in musculoskeletal disease.

### Surgical Technique

OAT is a technique that has been previously described by various authors.[23,28,41] Our specific technique has previously been described in detail,[26] so only certain portions will be covered here. First, bone marrow is aspirated and concentrated, yielding about 3 mL of BMAC. Dissection and osteotomy are carried out to allow access to the ankle joint and visualization of the osteochondral lesion. The lesion is identified, reamed, and any cysts are removed. Autografts are procured from the ipsilateral knee. One to 2 grafts that are 10 mm in diameter and 10 to 12 mm deep are then removed from the lateral aspect of the trochlea in accordance with the size of the lesion. The plug is shaped and then soaked in BMAC previously taken from the iliac crest. The hole created in the trochlea is backfilled with an allograft plug consisting of a cancellous scaffold and cartilage scaffold (Arthrex). Attention is then turned back to the ankle.

Bone graft, obtained from the talus when the recipient site is prepared, can be placed in the base of the lesion. This is done based on surgeon discretion and the bone graft is obtained from the talus after the diseased OLT is cored out. The autograft is soaked in BMAC and then tapped into place within the lesion so that it is contoured perfectly level with the talar dome. In cases utilizing adjunctive ECM-BMAC, BMAC is mixed with the ECM and this mixture is placed around the OAT plug and in any other areas of cartilage damage within the ankle using an arthroscopic cannula. A freer elevator is then used to spread the ECM-BMAC over the entire defect and ensure the border between the OAT plug and native talus is adequately covered (Figure 1). Once excellent fill of the defect is achieved, a layer of fibrin glue sealant Evicel (Ethicon, Rockville, MD) is placed over the repair, and this is allowed to dry for 10 minutes.

Finally, the medial malleolar osteotomy is repaired using Kirschner wire, 2.0-mm plates, and multiple 2.4-mm screws. All wounds are irrigated and incisions repaired in both the ankle and knee prior to placing the patients in a nonweightbearing splint for 2 weeks. Patients begin to work on range of motion 2 weeks after surgery. Partial weightbearing and physical therapy is initiated at 6 weeks. Return to sports usually occurs at 6-9 months postoperatively.

### Statistical Analysis

Descriptive statistics are presented as means and standard deviations whereas categorical variables are reported as frequencies or percentages. Pre- and postoperative functional outcome scores in each cohort, OAT plus ECM-BMAC and OAT without ECM, were compared using Wilcoxon rank sum tests. To assess differences based on the inclusion of adjunctive ECM-BMAC during OAT, Wilcoxon rank sum tests and 2-group $t$ tests were used to compare postoperative FAOS scores, pre- to postoperative change in FAOS, and total MOCART scores. These tests were also used to compare age, BMI, and lesion size. Chi-square or Fisher exact tests were used to compare lesion location, the rate of postoperative cyst formation, rate of postoperative edema, rate of double plug use, failure rate, use of bone grafting, and differences in individual MOCART characteristics between the 2 groups. Failure was defined by the persistence of symptoms unable to be managed conservatively, leading to recommendation for revision surgery. Wilcoxon rank sum tests were also used for subgroup analyses comparing outcome scores with and without cysts. The influence of concurrent bone grafting or ankle stabilization procedures on radiographic and patient-reported outcomes were analyzed using Wilcoxon rank-sum tests. Finally, simple linear regression was used to assess the relationship between MRI follow-up time and total MOCART score for the entire cohort. All analyses were run with a significance level $\alpha$ of .05.

## Results

Sixty patients (64 ankles) were identified at a mean clinical follow-up of 31.5 months (range: 12.5-73.0 months). Of these cases, 34 were treated with OAT augmented by an ECM-BMAC mixture and 30 were treated with OAT and BMAC alone. One patient was treated for bilateral OLTs using OAT augmented by ECM-BMAC with 5 months between procedures. Two patients were also treated bilaterally using OAT without ECM, with 8 and 15 months between these procedures. Finally, one patient was treated using OAT without ECM on the right ankle and then was treated using OAT augmented by ECM-BMAC on the left ankle 6 years later.

Nine patients (26%) in the ECM-BMAC group received 2 plugs, compared with 6 patients (20%) in the group without ECM. This difference was not statistically significant ($P$ = .57). Nineteen patients in total had painful hardware removed, and there was no difference in rates of hardware removal between groups ($P$ = .99).

**Table 1.** Lesion Location in OAT Patients Treated With and Without ECM-BMAC.

| | Number of Lesions in this Location, n/n (%) | | |
|---|---|---|---|
| Location | No ECM | With ECM | *P* Value[a] |
| Medial | 20/30 (67)[b] | 25/34 (74)[c] | .42 |
| Lateral | 9/30 (30)[b] | 9/34 (26)[c] | .60 |
| Central | 1/30 (3) | 0/34 (0) | .45 |

Abbreviations: ECM-BMAC, extracellular matrix with bone marrow aspirate concentrate; OAT, osteochondral autograft transplant.
[a]*P* values represent the significance of any difference in percentages.
[b]Four posteromedial; 1 posterolateral in the BMAC group.
[c]Two posteromedial; 2 anteromedial; and 1 anterolateral in the ECM-BMAC group.

There were no failures in the group treated with ECM-BMAC. Three cases in the group treated without ECM were deemed failures. Two of these underwent revision surgery involving microfracture with biologics around the original talar lesion. The third was indicated for ankle fusion but did not return to our institution for treatment. The difference in failure rates between groups was not statistically significant (0% vs 10%; $P = .08$). No patient experienced postoperative infection or malleolar nonunion. There were 4 instances of postoperative knee pain for which all patients were managed conservatively. Three of these were in the group treated with ECM.

## *Demographics*

In total, 26 patients were female and 34 were male. Patients in the ECM-BMAC group had an average age at surgery of 42.6 years compared to an average of 33.2 years for the group treated without ECM ($P = .007$). No significant difference was observed in the distribution of BMI values between groups ($P = .55$). The average clinical follow-up for OAT+ECM-BMAC cases was 25.4 months (range: 13-47 months), whereas the average follow-up for cases without ECM was 38.4 months (range: 12.5-73 months). These average clinical follow-up times were significantly different ($P < .01$). There were 7 patients who underwent procedures for instability in the ECM-BMAC group and 2 patients in the control group.

## *Lesion Size and Location*

No significant differences were observed in either lesion size ($P = .23$) or location between groups. The average lesion size of the entire cohort was 145 $mm^2$. The relative numbers of patients in each group with medial, lateral, and central lesions were comparable (Table 1).

## *Functional Outcomes*

Patients were asked to complete either FAOS or PROMIS preoperatively and 1 or both surveys postoperatively. Our institution began prospectively administering PROMIS in March 2016 and as a result, only ECM-BMAC patients were asked to complete PROMIS domains. ECM-BMAC patients treated before March 2016 took FAOS preoperatively, and as a result all patients were asked to take FAOS postoperatively.

Twenty-five ECM-BMAC patients completed postoperative surveys. Average FAOS follow-up in the OAT+ECM-BMAC group was 25.34 months (range, 11.47-41.13 months). Twenty patients treated without ECM completed postoperative FAOS surveys with an average follow-up of 32.87 months (range, 6.53-73.3 months). Average time to FAOS survey follow-up was not significantly different between the groups ($P = .15$).

Functional outcome scores significantly improved pre- to postoperatively for the OAT+ ECM-BMAC group for all FAOS subscales and for the overall FAOS score, obtained by taking the average of all 5 subcategories (Table 2). FAOS functional outcome scores significantly increased in the Pain and Quality of Life subscales for the OAT control group treated without ECM, as did the overall FAOS score. However, increases of 4.39 and 6.79 points in FAOS Activities of Daily Living and Sports subcategories were not statistically significant for this group (Table 3). FAOS Symptoms decreased by an average of 2.51 points, which also was not a statistically significant change.

Postoperative FAOS scores and pre- to postoperative change in FAOS scores were compared between patients who received adjunctive ECM-BMAC and those who did not. The average postoperative FAOS Symptoms and Quality of Life subscale scores were significantly greater for the OAT+ECM-BMAC group ($P = .04$ and $P = .05$, respectively). In addition, the average pre- to postoperative change in score was significantly greater for OAT+ECM-BMAC cases in the FAOS Symptoms ($P = .02$), Activities of Daily Living ($P = .05$), and Sports ($P = .02$) subscales. Significant differences were not found for the other comparisons (Table 4).

A subgroup analysis compared functional outcome scores for patients with and without cysts, regardless of treatment group. FAOS scores were used for this comparison. Patients with a cyst had an average total FAOS score of 56.4 at an average follow-up of 31 months. Patients without

**Table 2.** Overall Functional Outcome Scores for OAT+ECM-BMAC Patient Group.

| Variable | Preop., Mean ± SD | Postop., Mean ± SD | Δ Preop. to Postop., Mean ± SD | *P* Value[a] |
|---|---|---|---|---|
| FAOS outcomes | | | | |
| Sample size, n | 11 | 16 | | |
| Pain | 58.84 ± 13.71 | 81.77 ± 18.51 | 23.15 ± 25.31 | .03 |
| Symptoms | 58.12 ± 12.28 | 77.01 ± 15.37 | 17.06 ± 22.50 | .05 |
| Daily Activities | 70 ± 12.29 | 87.26 ± 16.94 | 15.62 ± 15.58 | .03 |
| Sports Activities | 27.22 ± 16.60 | 58.64 ± 28.74 | 39.76 ± 27.89 | .009 |
| Quality of Life | 25.57 ± 16.35 | 64.06 ± 25.36 | 36.11 ± 32.64 | .01 |
| Overall | 48.66 ± 9.80 | 73.49 ± 19.33 | 22.98 ± 24.85 | .02 |
| PROMIS outcomes | | | | |
| Sample size, n | 13 | 25 | | |
| Physical Function | 42.1 ± 4.35 | 49.41 ± 9.40 | 7.46 ± 9.28 | .01 |
| Pain Interference | 58.98 ± 5.43 | 49.93 ± 10.21 | –7.94 ± 10.78 | .001 |
| Pain Intensity | 51.28 ± 8.30 | 38.99 ± 8.14 | –6.88 ± 13.29 | .02 |
| Global Physical Health | 47.32 ± 6.43 | 52.87 ± 8.97 | 5.90 ± 9.67 | .009 |

Abbreviations: ECM-BMAC, extracellular matrix with bone marrow aspirate concentrate; FAOS, Foot and Ankle Outcome Score; OAT, osteochondral autograft transplant; Postop., postoperative; Preop., preoperative; PROMIS, Patient-Reported Outcomes Measurement Information System.
[a]*P* Values represent the significance of pre- to postoperative change in scores.

**Table 3.** Overall Functional Ankle Outcome Scores for OAT without ECM-BMAC Patient Group.[a]

| FAOS Outcomes | Preop., Mean ± SD (n = 20) | Postop., Mean ± SD (n = 20) | Δ Preop. to Postop., Mean ± SD (n = 16) | *P* Value |
|---|---|---|---|---|
| Pain | 60.57 ± 21.06 | 75.56 ± 19.47 | 14.74 ± 19.94 | .01 |
| Symptoms | 64.12 ± 22.02 | 64.58 ± 19.92 | –2.51 ± 18.03 | .61 |
| Daily Activities | 76.78 ± 17.38 | 81.47 ± 17.46 | 4.39 ± 11.40 | .14 |
| Sports Activities | 45.39 ± 30.92 | 51.51 ± 27.05 | 6.79 ± 28.17 | .40 |
| Quality of Life | 20.63 ± 21.94 | 45.52 ± 28.88 | 27.99 ± 26.17 | <.01 |
| Overall | 53.48 ± 18.35 | 63.80 ± 19.99 | 10.68 ± 16.52 | .02 |

Abbreviations: ECM-BMAC, extracellular matrix with bone marrow aspirate concentrate; FAOS, Foot and Ankle Outcome Score; OAT, osteochondral autograft transplant; Postop., postoperative; Preop., preoperative.
[a]These patients did not receive PROMIS surveys. *P* values represent significance of pre- to postoperative change.

cysts had a significantly higher average total FAOS score of 80.2 at an average follow-up of 29 months ($P$ = .002). Preoperative FAOS scores were not significantly different between these groups ($P$ = .75), nor were average follow-up times ($P$ = .78).

Average PROMIS follow-up was 22.01 months for patients treated with ECM-BMAC (range, 11.63-38.76 months). Functional outcome scores significantly improved pre- to postoperatively for the OAT+ ECM-BMAC group in PROMIS Physical Function, Pain Interference, and Global Physical Health (Table 2).

## *Radiographic Outcomes*

Twenty-two OAT+ECM-BMAC cases had postoperative MRIs. Average radiographic follow-up was 14.18 months (range, 4.34-38.77 months). Seventeen cases where ECM was not used had postoperative MRIs with an average radiographic follow-up time of 18.80 months (range, 2.1-50.37 months). These follow-up times were not significantly different ($P$ = .21). In total, 24 MRIs were performed at the primary institution and 15 were performed at outside facilities. The average total MOCART score was greater for the OAT+ECM-BMAC compared to the average total MOCART score for OAT cases without ECM. However, there was no statistically significant difference between the 2 averages (Table 5).

When analyzing individual MOCART parameters, 1 statistically significant difference was detected. For cases in which ECM-BMAC was used, a significantly greater proportion of repairs exhibited intact subchondral lamina (55% vs 12%; $P$ = .008). Two other categories demonstrated trends that favored ECM-BMAC but were not statistically significant. These were Structure (64% homogeneous with

**Table 4.** Comparison of Postoperative Outcome Scores for OAT With and Without ECM-BMAC.

| Variable | Postop. Mean | | | Δ Pre- to Postop. Mean | | |
|---|---|---|---|---|---|---|
| | No ECM | With ECM | *P* Value | No ECM | With ECM | *P* Value[a] |
| FAOS outcomes | | | | | | |
| Pain | 75.56 ± 19.47 | 81.77 ± 18.51 | .35 | 14.74 ± 19.94 | 23.15 ± 25.31 | .37 |
| Symptoms | 64.58 ± 19.92 | 77.01 ± 15.37 | .04 | –2.51 ± 18.03 | 17.06 ± 22.50 | .02 |
| Daily Activities | 81.47 ± 17.46 | 87.26 ± 16.94 | .25 | 4.39 ± 11.40 | 15.62 ± 15.58 | .056 |
| Sports Activities | 51.51 ± 27.05 | 58.64 ± 28.74 | .46 | 6.79 ± 28.17 | 39.76 ± 27.89 | .02 |
| Quality of Life | 45.52 ± 28.88 | 64.06 ± 25.36 | .05 | 27.99 ± 26.17 | 36.11 ± 32.64 | .50 |
| Overall | 63.80 ± 19.99 | 73.49 ± 19.33 | .15 | 10.68 ± 16.52 | 22.98 ± 24.85 | .27 |

Abbreviations: ECM-BMAC, extracellular matrix with bone marrow aspirate concentrate; FAOS, Foot and Ankle Outcome Score; OAT, osteochondral autograft transplant; Postop., postoperative; Preop., preoperative.
[a]*P* values represent significance of between-group differences.

**Table 5.** Comparison of Postoperative Radiographic Outcomes With and Without ECM-BMAC.

| Variable | Score or Percentage Rate | | |
|---|---|---|---|
| | No ECM | With ECM | *P* Value[a] |
| Total MOCART score, mean ± SD | 62.94± 25.68 | 68.86 ± 16.97 | .42 |
| Postoperative cysts, % | 52.94 | 18.18 | .039 |
| Postoperative edema, % | 94.12 | 59.09 | .024 |

Abbreviations: ECM-BMAC, extracellular matrix with bone marrow aspirate concentrate; MOCART, Magnetic Resonance Observation of Cartilage Tissue.
[a]*P* values represent the significance of differences between groups.

ECM, 30% without; $P = .054$) and Subchondral Bone (36% intact with ECM, 6% without; $P = .052$). Linear regression analysis of total MOCART score and follow-up time to MRI failed to detect a significant relationship between these variables when the data from both groups were combined ($P = .125$).

The rates of postoperative cysts and edema were compared on MRI for cases with radiographic follow-up. The rates of adjacent postoperative cysts and postoperative edema were significantly lower in cases where ECM-BMAC was used compared to those without ECM (Table 5).

### *Bone Grafting and Ankle Stabilization*

Twenty-six of 34 (76.5%) patients in the OAT+ECM-BMAC group were treated with bone grafting, compared with 24 of the 30 patients (80%) in the OAT without ECM group ($P = .77$). Total MOCART ($P = .034$) varied significantly across patients with bone grafting (average total MOCART 60.9) vs patients without bone grafting (average total MOCART 76.5). Difference in pre- to postoperative change in PROMIS scores ($P > .05$ for all domains) and postoperative FAOS ($P = .860$) scores did not vary significantly across patients who did or did not undergo concurrent bone grafting. Total MOCART ($P = .694$), difference in pre- to postoperative change in PROMIS scores ($P > .05$ for all domains), and postoperative FAOS ($P = .113$) scores did not vary significantly across patients who did or did not undergo concurrent ankle stabilization.

## Discussion

Significant improvement in FAOS and PROMIS outcome scores pre- to postoperatively indicated achievement of good patient-reported outcomes following the treatment of large OLTs using OAT supplemented by adjunctive ECM-BMAC. Furthermore, significantly greater pre- to postoperative change in FAOS Symptoms, Daily Activities, and Sports categories following treatment with OAT+ECM-BMAC compared to cases where OAT was used without ECM may also suggest that better clinical and functional outcomes can be achieved through the addition of ECM-BMAC during an OAT procedure. This is further supported by significantly increased mean postoperative FAOS scores for the Symptoms and Quality of Life categories when ECM was used relative to when it was not. Although baseline preoperative FAOS scores were generally higher in the OAT group treated without ECM-BMAC, the difference was not statistically significant. Therefore, this likely had minimal effect on the differences detected in outcomes.

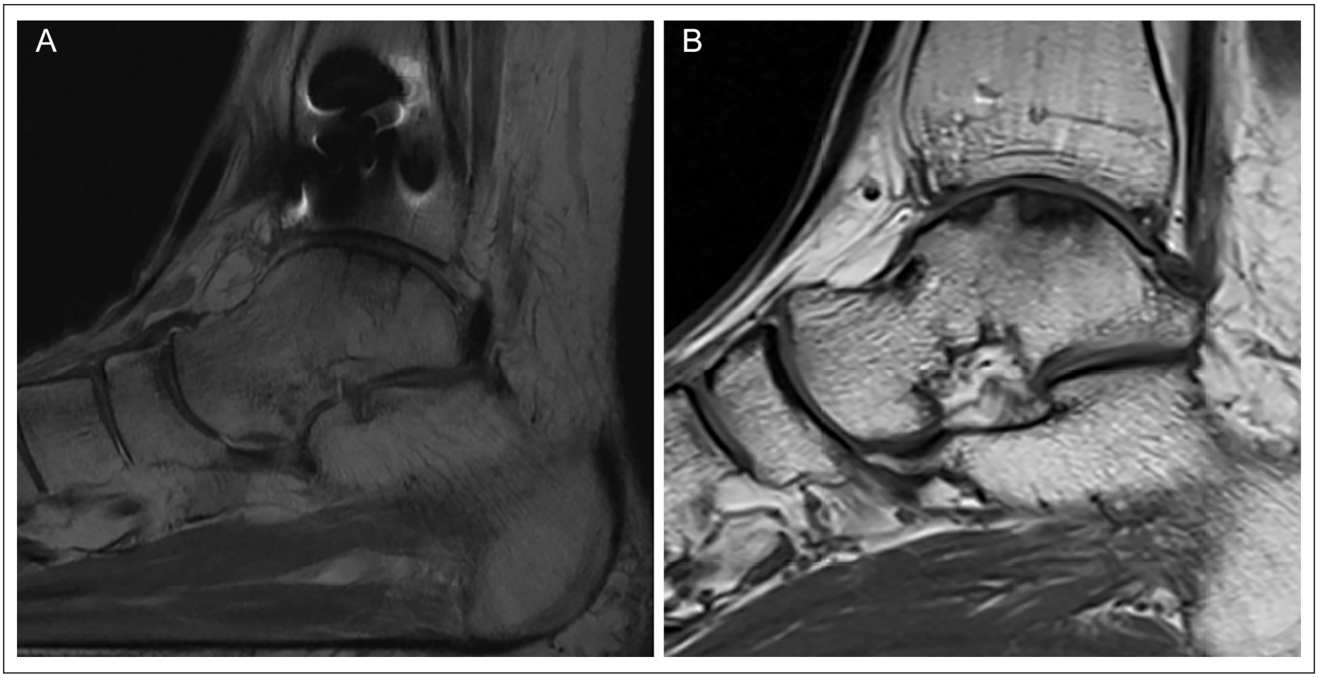


**Figure 2.** (A) Postoperative MRI demonstrating intact subchondral lamina. (B) Postoperative MRI demonstrating compromised subchondral lamina. (MRI, magnetic resonance imaging)

No statistically significant difference was detectable in the overall MOCART score between OAT cohorts treated with and without ECM-BMAC. Although this finding suggests the addition of ECM did not improve the overall structural integrity of the reparative tissue formed following OAT, some differences were observed between groups in the individual MOCART categories, with subchondral lamina found to be intact significantly more often in cases where ECM-BMAC was used (Figure 2). Furthermore, rates of postoperative cyst formation and postoperative edema were significantly lower in ECM-BMAC cases (Figure 3). Considered collectively, clinical and radiographic findings suggest that the addition of ECM mixed with BMAC during OAT may reduce the chances of adjacent cysts and edema forming postoperatively, and furthermore, this reduction may impact clinical outcomes resulting in better outcomes than when OAT is performed with BMAC alone.

OAT is generally associated with good outcomes, though it can be accompanied by drawbacks such as postoperative cyst formation. According to a position statement put forth by the American Orthopaedic Foot & Ankle Society (AOFAS) in 2018, OAT is considered an endorsed, nonexperimental treatment for larger OLTs.[3] Multiple studies report good to excellent clinical outcomes, observing success rates as high as 93% to 94% and significant improvement in postoperative functional outcome scores at short-term and long-term follow-up.[2,17,22,23,28,32,36,37] Particularly, Hangody et al demonstrated a 93% success rate for talar OAT in 98 patients at medium-term follow-up.[23] However, other studies have raised concerns about associated comorbidities of OAT such as high rates of postoperative cysts.[35,41] Subchondral cysts are thought to form because of synovial fluid entering the space created at the interface between the osteochondral plug and the native articular surface and subchondral bone during an OAT procedure.[28,39] Buildup and pressure of the synovial fluid is thought to contribute to the formation of cyst and potentially the degradation of subchondral bone over time.[28,39] This can also contribute to intraosseous edema, which may lead to persistent symptoms.

Additionally, large OLTs can often take amorphous, noncircular shapes, which can further increase the potential for postoperative cysts to form. When osteochondral grafts do not match the exact shape of the lesion they are intended to fill, surrounding areas of degenerative cartilage and spaces created at the graft-host interface can become larger, thus increasing the likelihood of synovial fluid buildup and eventual subchondral cyst formation. This presents a challenge as the OAT plugs and instrumentation are circular, potentially leading to mismatch. Use of a nesting technique can help, but may not always be adequate depending on the lesion's shape. Evidence suggests cystic development may compromise the OAT graft, thereby affecting long-term structural survival, and potentially clinical outcomes.[7,13,19]

One previous study indicated that using BMAC alone as an adjunctive therapy might reduce the rate of postoperative cysts formed following OAT.[39] Patients treated with OAT

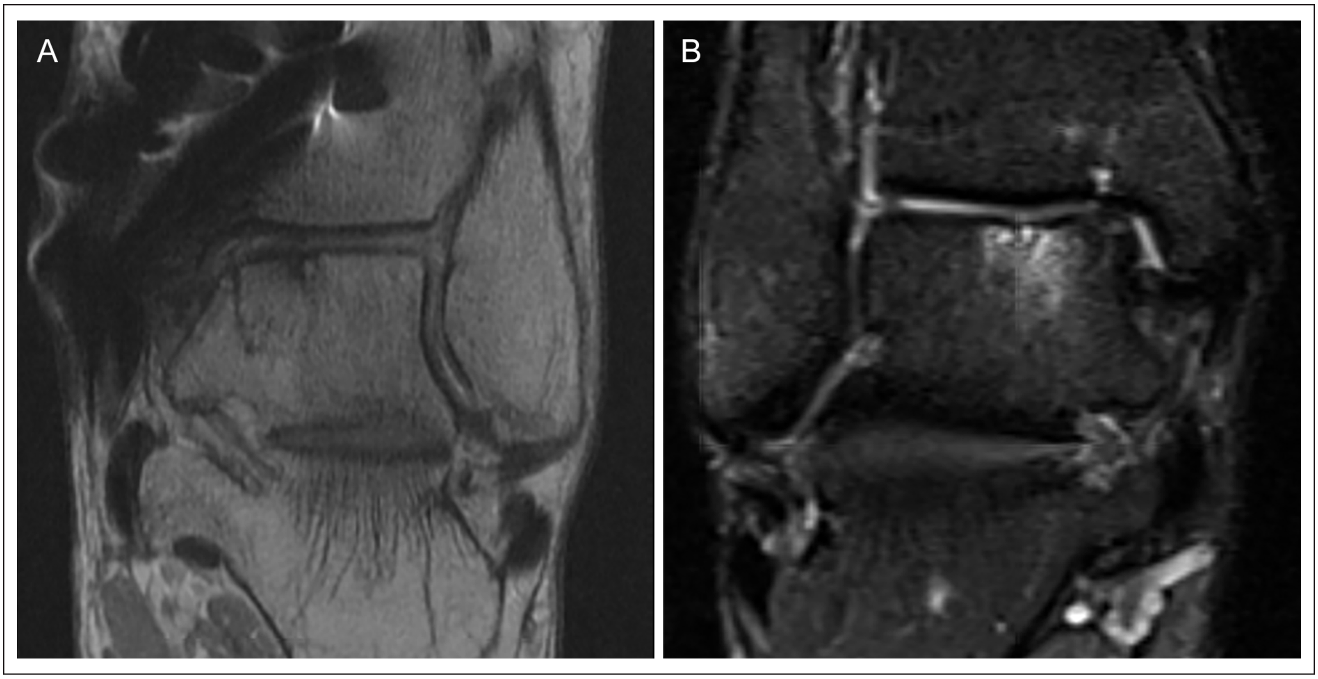


**Figure 3.** (A) Postoperative MRI without cyst formation or widespread edema. (B) Postoperative MRI with notable cyst formation and edema. (MRI, magnetic resonance imaging)

were compared to patients treated with OAT and BMAC injected into the base of the lesion and throughout the ankle joint following implantation of the graft. The rate of postoperative cysts was significantly lower in the patient cohort who received adjuvant BMAC (76.9% vs 46.4%; $P = .02$); however, there were no statistically significant differences observed in postoperative FAOS or SF-12 outcomes.[39] Taken in consideration with prior evidence showing that BMAC generally improves the quality of reparative tissue, this result suggests that adjunctive therapy may improve the quality of repair achieved by OAT.[9,14,21,33,38,39] Combining ECM and BMAC created a particularly beneficial adjunctive option for application. When applied around the OAT plug, ECM-BMAC seems to act as a mortar that fills in the crevices that can exist around the graft-host interface owing to the amorphous shape of the lesion or additional areas of degenerative cartilage. In this way, the addition of ECM-BMAC might further improve the OAT repair and decrease the rate of postoperative cyst formation by preventing synovial fluid from entering these spaces and compromising the structure of the subchondral bone.

In this study, our postoperative cyst rate for the OAT+ECM-BMAC cohort was significantly lower in comparison to the cyst rate found following OAT without adjunctive ECM, and at 18.18%, it was also lower than the cyst rate of 46.4% observed by Shimozono et al[39] when BMAC alone was used as an adjunct. The postoperative cyst rate of 53% observed in cases treated with BMAC alone was similar to those reported in past studies of OAT without ECM.[35,41]

The clinical significance of the lower postoperative cyst rate associated with use of ECM-BMAC in this study has yet to be definitively determined. Prior literature on the clinical impact of postoperative cysts following cartilage injury and repair is inconclusive. At least 1 study found postoperative cysts were asymptomatic and did not correlate significantly with short-term postoperative outcomes following OAT.[35] Meanwhile, the results of other studies have provided reason for concern over the formation of postoperative cysts because of negative effects in both short- and mid-term outcomes.[7,13,19] Our own subgroup analysis also suggested that presence of cysts was clinically relevant, as reflected by lower functional outcome scores. When comparing all patients with cysts to those without, significantly higher postoperative FAOS outcome scores were observed in the group without cysts. This suggests that the presence of cysts around an OAT graft may be associated with poorer patient-reported outcomes. Since ECM-BMAC was observed to reduce the rate of cysts, this finding offers a possible mechanism by which ECM-BMAC may improve functional outcomes. Of note, further exploration of the specific location of lesions with regard to synovial fluid entrance and cyst formation is warranted.

Finally, previous findings on postoperative edema point to the potential clinical significance of the lower observed rate of edema with the use of ECM-BMAC. Cuttica et al[10] found a significant correlation between the presence of edema detected on MRI and clinical outcomes following microfracture. Specifically, "poor" clinical outcomes were 7 to 8 times more likely when either "moderate" or "severe" edema was present compared to when either "low" or "no edema" was present. Although the majority of patients treated in our study do exhibit postoperative edema, this percentage was significantly lower in cases supplemented with ECM-BMAC. We did not perform a subgroup analysis comparing outcomes with and without edema because there were very few patients in the no-edema group who had complete survey data. Nevertheless, the findings of Cuttica et al[10] serve as additional evidence that the radiographic improvements observed with ECM-BMAC could correspond to significantly better clinical outcomes for this cohort of patients.

Limitations in our study included the heterogeneity of the group. For example, patients that also had bone grafting or an ankle stabilization procedure were included, adding a degree of variability into our analyses. Total MOCART scores varied significantly across patients with and without bone grafting, suggesting that the impact of bone grafting or its indications warrants further consideration. Additionally, 4 cases of bilateral osteochondral lesions were included, which may have unpredictably influenced patient-reported outcome measures. The inclusion of cases from 4 surgeons added to the heterogeneity of the study sample. One surgeon performed the majority of cases for the ECM group and another surgeon performed the majority of cases for the comparison group. This may have introduced variation in surgical skill or technique that could not be included in our analysis.

Average clinical follow-up time was significantly different between groups. The average time to clinical follow-up was significantly longer in the BMAC control group, which may lead to inferior radiographic and patient-reported outcomes in that group. However, average time to FAOS follow-up survey was not significantly different. Average time to postoperative MRI, the basis of our most meaningful results, was longer in the BMAC control group, though this difference was not statistically significant either. Additionally, age at the time of surgery was greater in the group that received ECM-BMAC compared with the group that did not. It is possible that differences in functional demands related to age could influence patient-reported and radiographic outcomes.

This was not a randomized study, and treatment was based on surgeon preference and the biological adjuncts available at the time of surgery. This lack of randomization may introduce confounding variables. In particular, OAT is associated with variation in the quality of the transplantation, both in terms of indications and technical elements such as fit, curvature, depth, and thoroughness of removal of antigenic material. These differences depend on the surgeon and may have a confounding effect of the outcomes measured. A study comparing randomized treatment groups with equally represented surgeons would provide higher level evidence but was not feasible in this context. Further, the present study did not evaluate preoperative MRIs. This decision was made based on the utility of the MOCART scoring system in evaluating cartilage repairs, rather than preoperative MRIs before undergoing repair. This area could be explored in future studies.

This study does face additional limitations related to MRI results. The large range of MRI follow-up times means that our radiographic data were somewhat heterogeneous. Lastly, the fact that MRIs were performed at multiple institutions could affect radiographic outcomes, particularly MOCART scoring, because of differences in imaging protocols and quality. A board-certified musculoskeletal radiologist determined that each of the included MRIs was of adequate quality for scoring.

## Conclusion

This study sought to evaluate functional and radiographic outcomes following the use of OAT augmented by adjunctive ECM-BMAC for the treatment of large OLTs by comparing these outcomes to OAT patients treated with BMAC but without ECM. In this group of patients we found significant improvements in several FAOS functional outcomes and lower rates of postoperative cysts and edema associated with the use of adjuvant ECM.

### Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Mark C. Drakos, MD, reports personal fees from Arthrex, outside the submitted work. Jonathan T. Deland, MD, reports personal fees from Arthrex, outside the submitted work. ICMJE forms for all authors are available online.

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