Article

AO FAS AMERICAN ORTHOPAEDIC FOOT & ANKLE SOCIETY

Foot & Ankle International®
2018, Vol. 39(4) 393–405

DOI: 10.1177/1071100717746627
journals.sagepub.com/home/fai

Comparison of Juvenile Allogenous Articular Cartilage and Bone Marrow Aspirate Concentrate Versus Microfracture With and Without Bone Marrow Aspirate Concentrate in Arthroscopic Treatment of Talar Osteochondral Lesions

Sydney C. Karnovsky, BA[1], Bridget DeSandis, BA[1], Amgad M. Haleem, MD, PhD[2,3], Carolyn M. Sofka, MD[4], Martin O'Malley, MD[5], and Mark C. Drakos, MD[5]

Abstract

Background: The purpose of this study was to compare the functional and radiographic outcomes of patients who received juvenile allogenic chondrocyte implantation with autologous bone marrow aspirate (JACI-BMAC) for treatment of talar osteochondral lesions with those of patients who underwent microfracture (MF).

Methods: A total of 30 patients who underwent MF and 20 who received DeNovo NT for JACI-BMAC treatment between 2006 and 2014 were included. Additionally, 17 MF patients received supplemental BMAC treatment. Retrospective chart review was performed and functional outcomes were assessed pre- and postoperatively using the Foot and Ankle Outcome Score and Visual Analog pain scale. Postoperative magnetic resonance images were reviewed and evaluated using a modified Magnetic Resonance Observation of Cartilage Tissue (MOCART) score. Average follow-up for functional outcomes was 30.9 months (range, 12-79 months). Radiographically, average follow-up was 28.1 months (range, 12-97 months).

Results: Both the MF and JACI-BMAC showed significant pre- to postoperative improvements in all Foot and Ankle Outcome Score subscales. Visual Analog Scale scores also showed improvement in both groups, but only reached a level of statistical significance ($P < .05$) in the MF group. There were no significant differences in patient reported outcomes between groups. Average osteochondral lesion diameter was significantly larger in JACI-BMAC patients compared to MF patients, but size difference had no significant impact on outcomes. Both groups produced reparative tissue that exhibited a fibrocartilage composition. The JACI-BMAC group had more patients with hypertrophy exhibited on magnetic resonance imaging (MRI) than the MF group ($P = .009$).

Conclusion: JACI-BMAC and MF resulted in improved functional outcomes. However, while the majority of patients improved, functional outcomes and quality of repair tissue were still not normal. Based on our results, lesions repaired with DeNovo NT allograft still appeared fibrocartilaginous on MRI and did not result in significant functional gains as compared to MF.

Level of Evidence: Level III, comparative series.

Keywords: osteochondral lesions, juvenile articular cartilage, DeNovo Natural Tissue graft, microfracture, arthroscopic treatment

Osteochondral lesions (OCLs) of the talus are increasingly recognized injuries that are commonly associated with acute ankle sprains, fractures, and recurrent ankle instability. They present a challenging clinical problem due to the poor healing potential of articular hyaline cartilage. Conservative treatment is common in low-grade lesions but has a high failure rate, with larger lesions often requiring operative treatment.[8,47] Microfracture (MF) has been considered the primary treatment for symptomatic OCLs as it is a simple, single stage procedure that can be performed arthroscopically and has been shown to have good to excellent results in approximately 85% of patients.[48,49]

[1]Hospital for Special Surgery, New York, NY, USA
[2]Department of Orthopedic Surgery, Oklahoma University College of Medicine Health Sciences Center, Oklahoma City, OK, USA
[3]Department of Orthopedic Surgery, Kasr Al-Ainy College of Medicine, Cairo University, Cairo, Egypt
[4]Department of Radiology and Imaging, Hospital for Special Surgery, New York, NY, USA
[5]Department of Orthopedic Surgery, Foot and Ankle, Hospital for Special Surgery, New York, NY, USA

Corresponding Author:
Sydney C. Karnovsky, BA, Hospital for Special Surgery, 535 E 70th St, New York, NY 10021, USA.
Email: s.karnovsky@gmail.com

The procedure involves penetrating the subchondral bone to stimulate bleeding from the underlying bone and the migration of mesenchymal stem cells into the lesion site. These cells within the clotted blood may then remodel and become fibrocartilage in an attempt to fill the defect. However, fibrocartilage is biomechanically inferior compared to native hyaline cartilage and may degrade more quickly over time.[20] In addition, MF is less effective in treating larger lesions (>150 mm^2) and lesions on the shoulder of the talar dome. These lesions often require secondary procedures such as osteochondral allograft or autograft transplantation (OATs) or autologous chondrocyte implantation,[4,9,11,24,27,31,42] each of which has its own shortcomings including possible donor site morbidity, the potential need for an osteotomy, or necessity for multiple procedures.[6,36,40]

These limitations have led researchers to explore novel approaches to deliver cells and growth factors to an osteochondral defect to produce a more normal hyaline cartilage.[4] Juvenile allogenic chondrocyte implantation with bone marrow aspirate concentrate (JACI-BMAC) is an all-arthroscopic procedure that has the potential to reproduce hyaline cartilage without the morbidity and technical difficulties associated with other cartilage restorative techniques. DeNovo NT (Natural Tissue) graft (Zimmer Inc, Warsaw, IN) is a prepackaged particulated articular cartilage allograft derived from donors 2-12 years old. It contains immature juvenile chondrocytes with a high metabolic activity and the reported ability to regenerate hyaline-like cartilage.[1,22] The graft is implanted into the defect and secured with a fibrin sealant diluted with BMAC. The use of BMAC is indicated as it has been shown to improve the biomechanical and structural components of the reparative tissue.[13,24,28,43] There are few prior investigations that report the clinical and radiographic outcomes of this procedure in the ankle which have shown promising results and improved clinical outcome; however, they are Level IV studies without a comparison group, lack objective outcome measures and often have subjective outcome scores which are not validated.[12,36] To our knowledge, there are no comparative studies in the literature which meet those criteria. True comparisons between JACI-BMAC and existing cartilage repair techniques are needed to determine the role of DeNovo NT in relation to other cartilage resurfacing procedures, specifically MF, the current standard of care.

Our hypothesis was that the JACI-BMAC procedure would be superior to MF in treating osteochondral lesions of the talus. We thought patients undergoing JACI-BMAC would experience better functional improvement and possess higher quality repair tissue on magnetic resonance imaging (MRI) than MF patients. The purpose of this study was to assess the clinical and radiographic outcomes of patients who received JACI-BMAC for treatment of OCLs of the talus compared to those who received MF alone (13 patients) and MF supplemented with BMAC (17 patients). Our goal was to compare these groups' outcomes and to assess the site of cartilage repair using MRI with the previously described magnetic resonance observation of cartilage repair tissue (MOCART) semiquantitative grading system[36] to compare the quality of repair tissue produced by the two different procedures.

Methods

After approval was obtained from our institutional review board, the institution's foot and ankle registry was searched using relevant Current Procedural Terminology codes for all patients who underwent either MF or JACI-BMAC for an osteochondral lesion of the talus between 2006 and 2014. Patients were excluded if they were smokers, had rheumatoid or inflammatory joint disease, uncontrolled diabetes, an autoimmune disorder, or systemic inflammatory disease, or were immune suppressed. A total of 50 patients fit the inclusion criteria and composed the study cohort. Of these 50 patients, 30 had undergone arthroscopic MF treatment and 20 had received arthroscopic DeNovo NT for JACI-BMAC treatment. Within the arthroscopic MF treatment group, 17 patients received BMAC in addition to MF, based on surgeon preference. All patients had an MRI at least 1 year postoperatively. Patients with concurrent ankle instability were also identified, with ankle instability being defined on routine stress X-rays as a talar tilt of greater than 10 degrees varus or an anterior drawer of greater than or equal to 10 mm. For patients that presented with concurrent ankle instability, the instability was addressed by performing a lateral ankle stabilization procedure using either the Brostrom-Gould[15] or lateral ligament reconstruction, depending on the surgeon's preference. There were 7 patients who underwent procedures for instability in the MF group, with 4 receiving lateral ligament reconstructions and 3 receiving Brostrom stabilizations. In the DeNovo group, 4 patients underwent a procedure for instability, and all 4 had Brostrom-Gould type stabilizations (Table 1).

Retrospective chart review was performed and patient demographic information was recorded. There were 27 females and 23 males who composed the patient population overall, with an average age of 37.2 (range, 9 to 74) years. In the MF group, there were 15 females and 15 males, with an average age of 37.7 (range, 9 to 74) years, while there were 13 females and 7 males, with an average age of 36.6 (range, 16 to 52) years, in the JACI-BMAC group. Pre- and postoperative functional outcome scores were collected, including the Foot and Ankle Outcome Score (FAOS) and Visual Analog Scale (VAS) pain scale score. Size and location of the OCLs was collected from the operative notes. Lesion size was recorded as the largest diameter (mm) of the lesion as measured by the surgeon in the operating room. Lesion location on the talar surface was defined as either medial or lateral.

Table 1. Concurrent Procedures.

	Number of Patients
Microfracture Group	
Brostrom stabilization	4
Chrisman-Snook procedure	3
Hindfoot reconstruction	1
Ankle arthrotomy, tibial and medial malleolus ostectomy, removal of hardware	1
Talar/tibial exostectomy	5
JACI-BMAC Group	
Brostrom-Gould stabilization	4
Removal of hardware	2
Removal of loose body	2

Abbreviations: JACI-BMAC, juvenile allogenic chondrocyte implantation with autologous bone marrow aspirate.

Of the 50 patients in the study, 49 filled out FAOS and VAS pain scale surveys both preoperatively and postoperatively, 30 in the MF group and 19 in the JACI-BMAC group. The average follow-up was 30.9 (range, 12-97) months with the MF group having an average follow-up of 38.2 months (range, 12 to 97) and the JACI-BMAC group averaging a 19.4-month follow-up (range, 12 to 40).

MRI Assessment

All magnetic resonance (MR) images were reviewed by a radiologist fellowship trained in musculoskeletal radiology and were evaluated using the previously described modified MOCART score.[36] The MOCART system uses 9 parameters to evaluate the morphology and signal intensity of the repair tissue compared to native cartilage and has been shown to be a reliable method for assessing cartilage repair with low interobserver variability (Table 2).[36] All 50 patients included in the study underwent postoperative MRIs at a minimum at 12 months postoperatively that were scored using the MOCART system.

MR protocols differed within the study cohort since scans were performed across multiple institutions due to patient convenience in terms of location and insurance purposes. MR protocols included those performed at the primary institution (n = 30), those performed in the private radiology facility of 1 of the participating surgeons (n = 4), and those performed at outside facilities (n = 16).

All 50 patients received MRIs at a minimum of 12 months that were scored, with an average radiographic follow-up of 28.1 (range, 12-79) months. JACI-BMAC patients had postoperative MRIs with an average follow-up of 21.3 (range, 12.0 to 40) months, while MF patients had postoperative MRIs with an average follow-up of 32.5 (range, 12.0-78.6) months.

Table 2. MOCART Scoring System for the Evaluation of JACI-BMAC Using DeNovo NT Graft.[a]

Scoring Category and Variables (Score)	MRI Characteristics
1. Degree of Defect Infill	On a level with the adjacent cartilage
Complete	Over the level of the adjacent cartilage
Hypertrophy	Under the level of the adjacent cartilage; underfilling
Incomplete	
>50% of adjacent cartilage	
<50% of adjacent cartilage	
Subchondral bone exposed	
2. Integration to Border Zone	Complete integration with adjacent cartilage
Complete	Incomplete integration with adjacent cartilage; presence of fissure or defect
Hypertrophy	
Incomplete	
>50% of adjacent cartilage	
<50% of adjacent cartilage	
Subchondral bone exposed	
3. Surface of Repair Tissue	Lamina splendens intact
Surface intact	Fibrillations, fissures, and ulcerations
Surface damaged	
<50% of repair tissue depth	
>50% of repair tissue depth	
Degeneration	
4. Structure of Repair Tissue	
Homogenous	
Inhomogenous	
5. Signal Intensity of Repair Tissue	
Isointense	
Moderately hyperintense	
Markedly hyperintense	
6. Subchondral Lamina	
Intact	
Not intact	
7. Subchondral Bone	Edema, granulation tissue, cysts, sclerosis
Intact	
Not intact	
8. Adhesions	
Yes	
No	
9. Effusion	
Yes	
No	

Abbreviations: JACI-BMAC, juvenile allogenic chondrocyte implantation with autologous bone marrow aspirate; MOCART, Magnetic Resonance Observation of Cartilage Tissue score.
[a]Values between 0 and 100 represent the percentage of the total possible achievable score.

Operative Technique

The operative technique for MF has been described by various authors.[20] A thigh tourniquet was routinely used as well as standard anteromedial and anterolateral portals. The lesion was identified and debrided back to normal cartilage

Figure 1. Arthroscopic view of an osteochondral defect of the talus.

borders upon inspection and palpation with a probe. Once the base of the lesion was prepared to the level of the subchondral bone a small joint MF awl (Smith & Nephew, Jericho, NY) was used to perforate the subchondral plate with at least 3 mm of space in between holes to avoid fracture propagation of the underlying bone. The tourniquet was deflated to confirm that blood from the underlying bone was present through the holes.

The operative technique for JACI-BMAC was carried out arthroscopically as previously described by Drakos and Murphy.[19] Approximately 60 mL of bone marrow was aspirated from the anterior superior iliac crest and then concentrated in the Magellan Autologous Platelet Separator (Anteriocyte Medical Systems, Cleveland, OH), yielding about 3 mL of BMAC. The decision to use bone graft was made if there was a significant bone defect or void left by a subchondral cyst or necrotic bone. We defined this as a defect of approximately 1 cm in depth or greater. If bone grafting was necessary due to the presence of any bony defects below the articular cartilage in the talus, it was harvested at this time from either the iliac crest or the calcaneus depending on the size of the defect and extent of cystic change in the talus. Standard arthroscopy was performed and the area was debrided using a mechanical shaver to remove any scar tissue, osteophytes, and loose fragments (Figure 1). All fluid was then removed from the ankle using an epidural spinal needle and vacuum suction so that the remainder of the arthroscopy was performed dry. During this time, the DeNovo NT graft was prepared. Once the ankle was completely dry and all minor bleeds had ceased, the bone graft was placed into the defect using an arthroscopic cannula and packed down to form a stable bed using a Freer elevator. A fibrin glue sealant, Evicel (Ethicon, Rockville, MD), was layered over the bone graft. Then, DeNovo articular cartilage allograft was dispersed over the defect using an arthroscopic cannula. The cartilage graft was then covered with more Evicel for additional fixation. If no bone graft was used, the DeNovo was placed on the subchondral bone followed by Evicel and BMAC while the top layer of Evicel was still wet. The fibrin glue was allowed to set, which typically took 5 to 10 minutes.

Statistical Analysis

Descriptive statistics are presented as means and standard deviations for continuous variables and as frequencies and percentages for continuous variables. To look at pre- to postoperative clinical outcome scores for each individual cohort, the Wilcoxon signed rank test was used. To compare the MF and JACI-BMAC cohorts, univariate analyses were first conducted to compare patient and clinical characteristics. Continuous variables were assessed with the Wilcoxon rank sum test, while Fisher's exact test was used for categorical variables. Pre- to postoperative changes in outcomes scores were evaluated with the Wilcoxon signed rank test. Ordered logistic regression models were developed to evaluate the effect of procedure (MF vs JACI-BMAC) on MOCART outcomes adjusting for patient age and sex, instability, hypertrophy, and time to follow-up for MRI. A Spearman rank correlation test for the coefficients for outcome score was run for the continuous variables age, follow-up time, and lesion size. All analyses were performed with SAS Software version 9.3 (SAS Institute, Inc, Cary, NC, USA), with a level of significance of $\alpha = .05$. To compare JACI-BMAC patients with bone grafting to those without, Student's *t*-tests were performed with Microsoft Excel with a level of significance of $\alpha = .05$.

Results

Functional Outcomes

Both JACI-BMAC and MF groups had significant pre- to postoperative improvement in pain, activities, sports, and quality of life FAOS subscales with mean scores improving by 9.6 points, 7 points, 17.4 points, and 26.1 points for the MF group (Table 3) and 15.7 points, 19.4 points, 20.1 points, and 22.9 points for the JACI-BMAC group (Table 4). Postoperative VAS pain scale scores also improved for both groups (Tables 3-4). The MF group decreased by 2.3 points (indicating a decrease in pain). The JACI-BMAC group also showed improvement, decreasing by 1.9 points; however, this did not reach a level of statistical significance. When comparing the patient reported outcomes between the JACI-BMAC and MF groups, no significant differences between groups existed in postoperative scores (Table 5) or the pre- to postoperative change in scores (Table 6). When assessing differences in postoperative scores and the pre- to postoperative change in outcome scores between JACI-BMAC and MF groups while adjusting for potential confounders using a multivariate analysis, none of the differences in FAOS scores

Table 3. Overall Functional Outcome Scores for JACI-BMAC Patient Group.

Variable	Preop Mean	Postop Mean	Δ Pre- to Postop	*P* Value
VAS				
Pain scale	5.9 ± 3.3	4.3 ± 3.2	−1.9 ± 4.2	.082
FAOS Outcomes				
Pain	52.8 ± 23.5	67.6 ± 24.5	15.7 ± 20.4	.080
Symptoms	56.9 ± 25.4	64.7 ± 24.8	3.3 ± 26.4	.629
Daily activities	64.5 ± 23.4	74.1 ± 26.6	12.4 ± 19.4	.013
Sports activities	35.5 ± 21.4	48.9 ± 32.9	14.2 ± 20.1	.031
Quality of life	23.8 ± 19.8	43.1 ± 26.4	21.9 ± 22.9	.002

Abbreviations: FAOS, Foot and Ankle Outcome Score; JACI-BMAC, juvenile allogenic chondrocyte implantation with autologous bone marrow aspirate; VAS, Visual Analog Scale.

Table 4. Overall Functional Outcome Scores for Microfracture (MF) Patient Group.

Variable	Preop Mean	Postop Mean	Δ Pre- to Postop	*P* Value
VAS				
Pain scale	5.5 ± 2.7	3.9 ± 3.0	−2.3 ± 2.9	.006
FAOS Outcomes				
Pain	57.8 ± 20.8	68.1 ± 24.7	9.6 ± 23.0	.026
Symptoms	62.5 ± 17.9	55.7 ± 23.7	−6.2 ± 19.3	.186
Daily activities	71.7 ± 22.6	80.3 ± 24.8	7 ± 28.1	.010
Sports activities	35.4 ± 20.9	48.0 ± 31.4	17.4 ± 26.2	.016
Quality of life	24 ± 18.1	46.1 ± 31.5	26.1 ± 30.7	.008

Abbreviations: FAOS, Foot and Ankle Outcome Score; VAS, Visual Analog Scale.

Table 5. Comparison of Postoperative Outcome Scores Between JACI-BMAC and MF Patients.

Variable	DeNovo	Postop Mean	*P* Value
VAS			
Pain scale	No	3.9 ± 3.0	.891
	Yes	4.3 ± 3.2	
FAOS Outcomes			
Pain	No	68.1 ± 24.7	1
	Yes	67.6 ± 24.5	
Symptoms	No	55.7 ± 23.7	.177
	Yes	64.7 ± 24.8	
Daily activities	No	80.2 ± 24.8	.309
	Yes	74.0 ± 26.6	
Sports activities	No	48.0 ± 31.4	.93
	Yes	48.9 ± 32.9	
Quality of life	No	46.1 ± 31.5	.906
	Yes	43.1 ± 26.4	

Abbreviations: FAOS, Foot and Ankle Outcome Score; JACI-BMAC, juvenile allogenic chondrocyte implantation with autologous bone marrow aspirate; MF, microfracture; VAS, Visual Analog Scale.

Table 6. Comparison of Pre- to Postoperative Difference in Outcome Scores Between JACI-BMAC and MF Patients.

Variable	DeNovo	Δ Pre- to Postop	*P* Value
VAS			
Pain scale	No	−2.3 ± 2.9	.082
	Yes	−1.9 ± 4.2	
FAOS Outcomes			
Pain	No	9.6 ± 23	.59
	Yes	15.7 ± 20.4	
Symptoms	No	−6.2 ± 19.3	.317
	Yes	3.3 ± 26.4	
Daily activities	No	7.0 ± 28.1	.836
	Yes	12.4 ± 19.4	
Sports activities	No	17.4 ± 26.2	.443
	Yes	14.2 ± 20.1	
Quality of life	No	26.1 ± 30.7	.636
	Yes	21.6 ± 22.9	

Abbreviations: FAOS, Foot and Ankle Outcome Score; JACI-BMAC, juvenile allogenic chondrocyte implantation with autologous bone marrow aspirate; MF, microfracture; VAS, Visual Analog Scale.

between the groups achieved the minimal clinically important difference (~10 points). As a result, this suggests there may not be enough of a difference between these 2 treatments to distinguish them in terms of patient outcomes in the short term.

Relationships between outcomes and lesion location, lesion size, bone grafting, hypertrophy, and instability were assessed for both the JACI-BMAC and MF groups separately. In terms of lesion location, the JACI-BMAC group had 18 medial lesions and 2 lateral lesions versus 17 medial

lesions and 13 lateral lesions for the MF group. Location of the OCL (medial/lateral) was not associated with any outcomes pre- or postoperatively for either group. Patients who received JACI-BMAC had significantly larger lesions, with an average lesion size of 13.0 mm (range, 8.0-22.0 mm) compared to 7.4 mm (range, 2.0-15.0 mm) for MF patients ($P < .001$). Patients who received MF alone had an average lesion size of 9.2 mm while patients who received MF with BMAC had an average lesion size of 5.8 mm. The intergroup difference in lesion size showed no significant effect on FAOS, VAS, and MOCART scores in both an ordered logistic regression test as well as a Spearman rank correlation test. In the JACI-BMAC group, 4 patients required bone grafting due to defects one centimeter or greater. Within the JACI-BMAC group, there were no statistically significant differences between those patients that received bone grafting compared to those that did not in the post- to preoperative change in all FAOS subscales, SF-12 scores, and VAS pain scale scores. Furthermore, there were no significant differences between the groups in overall MOCART score and in the 9 MOCART subscales, significant differences were only found in the adhesions category ($P = .001$).

There was a significant difference in the percentage of patients that demonstrated hypertrophy postoperatively between the 2 groups with 70% (14 out of 20) of the JACI-BMAC patients and 30% (9 out of 30) of the MF patients demonstrating hypertrophy postoperatively. This had no significant effect on clinical outcomes but in a regression model showed a significant effect on the MOCART parameters degree of defect infill, integration to border zone, and surface of repair tissue, indicating that a significant portion of the DeNovo patients did worse in these subcategories than the MF patients.

A separate analysis was performed to test for differences within the MF group for patients who did and did not receive additional BMAC. We also looked at the differences between these groups (MF, MF-BMAC) and DeNovo using a single factor ANOVA test. The test showed that there was no significant difference in MOCART scores between the 3 groups ($F<F$ critical [$0.1016<3.1996$] and $P = .9036$) indicating that the addition of BMAC did not have a significant effect on the overall MOCART scores. The test also showed that there was no significant difference in overall FAOS scores between the 3 groups ($F<F$ critical [$1.61235<3.4668$] and $P = .22315$) indicating that the addition of BMAC did not have a significant effect on the overall FAOS scores.

There was no significant difference between the percentage of patients receiving concurrent instability procedures between the groups. In total, 20% (4 out of 20) of JACI-BMAC patients and 23.3% (7 out of 30) of MF patients had concurrent instability that was addressed simultaneously with the OCL. Presence of instability had no significant effect on clinical outcomes but in a regression model, showed a significant effect on the MOCART parameter subchondral lamina with patients in both groups being less likely to have an intact subchondral lamina.

Radiographic Outcomes

The average MOCART score for the JACI-BMAC group was 51.5 (range, 10.0-85.0) versus 53.3 (range, 10.0-95.0) for the MF group. Overall MOCART scores were not significantly different between groups ($P = .887$). When assessing the 9 MOCART parameters individually, both Degree of Defect Infill and Integration to Border Zone were significantly different between groups (Table 7). The JACI-BMAC group tended to have more patients with hypertrophy than the MF group with 70% of JACI-BMAC patients demonstrating overfill at the lesion site compared to 30% of MF patients (Figure 2). Comparatively, most MF patients demonstrated underfilling of the lesion, with 63.4% showing either an incomplete fill compared to the level of adjacent cartilage or the subchondral bone exposed (Figure 3). It was also found that the subchondral bone was not intact for the majority of patients in both groups (85% of JACI-BMAC patients and 86.7% of MF patients), with most patients showing persistent bone marrow edema postoperatively in both groups (Figure 4).

Differences in individual MOCART parameters did not result in significant differences of functional outcomes on the FAOS and VAS pain scale scores. Specifically, the degree of defect infill did not result in any differences in functional outcomes between patients with complete filling of the lesion, incomplete filling, or with hypertrophy, regardless of operative technique. There were also no differences in outcomes between patients in which the subchondral bone was intact versus not-intact. However, there was a significant negative correlation (–0.546) found between overall MOCART score and FAOS pre- to postoperative change in the pain subscale ($P = .002$) and the quality of life subscale ($P = .049$). It should be noted, though, overall MOCART score has little clinical meaning.

Complications

In total, 14 patients (14 out of 50, 28%) returned to the operating room for revision procedures due persistent symptoms over the course of 8 years (Table 8). Average time for return to the OR was 29.8 (range, 3 to 95) months and the average lesion size was 8.9 mm (range, 4 to 22 mm) at the time of these patients' initial surgery. Of the 30 patients who underwent MF, 9 were indicated for revision procedures (9/30, 30%). These patients had an average lesion size of 7.6 mm (range, 4 to 12 mm) at the time of their first surgery and an average lesion size of 7.6 mm (range, 3 to 12 mm) at the time of revision surgery. Of the 20 JACI-BMAC patients, 5 were indicated for revision procedures (5/20, 25%). Average lesion size for these patients at the time of initial surgery was 12 mm (range, 8 to 22 mm) and the average lesion size

Table 7. Difference in MOCART Parameter Results Between the JACI-BMAC and MF Groups.

	MF		JACI-BMAC		
MOCART Parameter	n	%	n	%	*P* Value
Degree of Defect Infill					
Complete	4	13.3	0	0	.003
Hypertrophy	7	23.3	13	65	
Incomplete	17	56.7	4	20	
Subchondral bone exposed	2	6.7	3	15	
Integration to Border Zone					
Complete	6	20	0	0	.014
Hypertrophy	0	0	3	15	
Incomplete	21	70	13	65	
Subchondral bone exposed	3	10	4	20	
Surface of Repair Tissue					
Surface intact	6	19.4	4	20	.964
Surface damaged	1	3.2	1	5	
<50% of repair tissue depth	16	51.6	11	55	
>50% of repair tissue degeneration	8	25.8	4	20	
Structure of Repair Tissue					
Inhomogenous	10	33.3	6	30	1
Homogenous	20	66.7	14	70	
Signal Intensity of Repair Tissue					
Isointense	12	40	9	45	.773
Moderately hyperintense	18	60	11	55	
Subchondral Lamina					
Intact	12	40	5	25	.373
Not intact	18	60	15	75	
Subchondral Bone					
Intact	4	13.3	3	15	1
Not intact	26	86.7	17	85	
Adhesions					
No	12	40	9	45	1
Yes	18	60	11	55	
Effusion					
No	25	83.4	16	80	.724
Yes	5	16.7	4	20	

Abbreviations: JACI-BMAC, juvenile allogenic chondrocyte implantation with autologous bone marrow aspirate; MF, microfracture; MOCART, Magnetic Resonance Observation of Cartilage Tissue score.

at the time of revision surgery was 12.3 mm (range, 10 to 15 mm). There were no infections or acute synovitis reactions. In each of the JACI-BMAC patients, there was reparative tissue present although the tactile stiffness and texture was clearly different from the surrounding normal cartilage.

Discussion

This study showed that both the MF technique and JACI-BMAC technique using DeNovo NT graft could result in significant pre- to postoperative improvements in clinical outcomes for patients undergoing treatment of osteochondral lesions of the talus. However, when comparing the 2 techniques, postoperative functional outcomes and the quality of repair tissue on MRI were similar with no significant differences in outcome scores and only differences in 2 out of the 9 radiographic parameters (degree of defect infill and integration to border zone) between the two groups. These findings contradict our hypotheses that JACI-BMAC procedure would be superior to MF in treating osteochondral lesions of the talus, showing better functional improvement and higher quality repair tissue on MRI than MF patients.

MF is typically recommended as the primary means of treating small to medium size OCLs of the talus because of its technical ease and favorable results. The success of the MF procedure has been systematically reviewed, with good to excellent outcomes observed in 80-85% of patients and a weighted mean AOFAS score of 86.8 points.[18,49] Although many authors have reported good results in the short-term, several have reported poorer outcomes. A study by Hunt

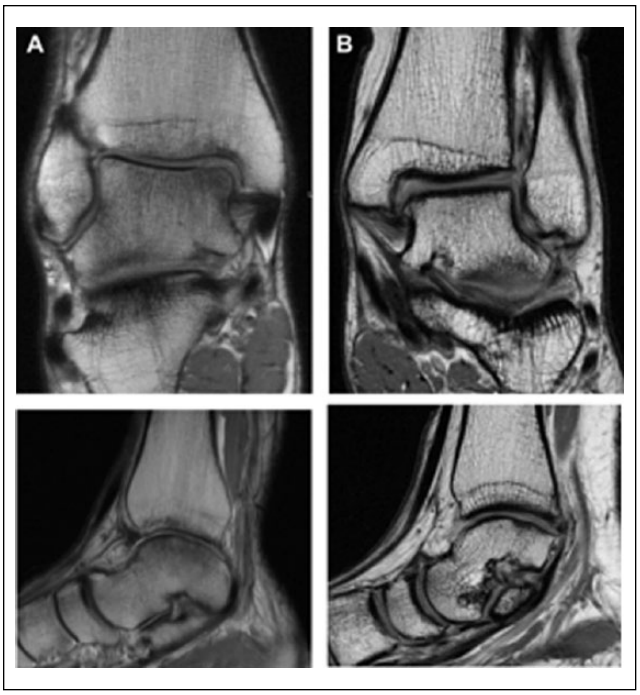

Figure 2. Repair cartilage showing persistent hypertrophy at (A) 14 months status post-JACI-BMAC and (B) 12.6 months status post-MF in the coronal (top) and sagittal (bottom) planes.

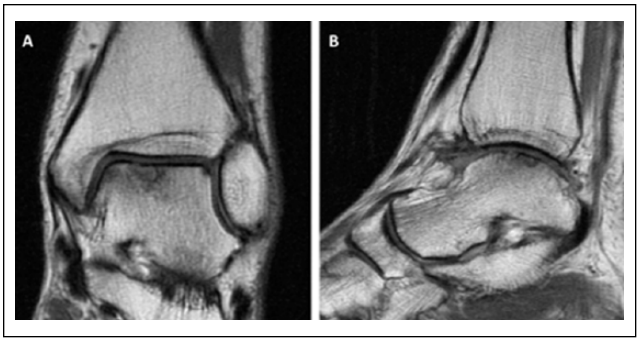

Figure 3. Patient 12.6 months status post-MF showing underfilling of the lesion, with repair cartilage fill reaching >50% the level of the adjacent cartilage in the (A) coronal and (B) sagittal planes.

Figure 4. Persistent edema present at (A) 14 months status post-JACI-BMAC and (B) 12.6 months status post-MF.

Table 8. Revision Procedures of Patients Who Needed to Return to the Operating Room.

Revision Procedure	Number of Patients
MF Group	
Debridement and MF with BMAC	4
Debridement, synovectomy and synovial hyperplasia resection, removal of loose body with BMAC	1
OATS	1
Debridement with DeNovo	2
Arthroscopic resection, tibial exostectomy, removal of loose bodies with BMAC	1
JACI-BMAC Group	
MF with BMAC	1
MF and debridement	1
OATS	3

Abbreviations: ACI, autologous chondrocyte implantation; JACI-BMAC, juvenile allogenic chondrocyte implantation with autologous bone marrow aspirate; MF, microfracture; OATS, XXX.

and Sherman[33] found only 46% of OCLs treated with MF had good or excellent outcomes at a mean follow-up of 66 (range, 6 to 169) months using the Berndt and Harty scale, and a recent prospective study by Goh et al[29] reported functional outcomes measured by the Ankle-Hindfoot Scale (AHS) were excellent for 49% of patients, good for 10%, fair for 30%, and poor for 11% of patients, with an average follow-up of 14.2 (range, 12 to 30) months.

The long-term effectiveness of MF has been questioned due to the resulting repair tissue consisting of fibrocartilage which has lower biomechanical strength compared to native hyaline cartilage and is likely to degenerate over time.[23,32,38] A study by Ferkel et al[20] is one of the only studies evaluating osteochondral lesions over more than 2 years after a MF procedure. When compared with their earlier findings, the authors' long-term outcomes deteriorated with time in 35% of cases over an average follow-up period of 5 years (based on the qualitative Weber evaluation). These results were based on the Alexander system and qualitative Weber evaluation. They suggest that because fibrocartilage is biomechanically inferior to hyaline cartilage, the tissue will continue to wear over time and longer term outcomes will be poorer. In addition, some studies have reported MF to be ineffective in treating larger lesions.[9,11,14,26,28] Chuckpaiwong et al[11] reported good to excellent results in 100% of patients with small to medium sized lesions (<15 mm in diameter) at 32 months follow-up; however, they found all but one patient with a large lesion (>15 mm in diameter) had poor outcomes. Choi et al[9] also found a correlation between lesion size and outcomes, finding 80% of patients with lesions >15 mm in diameter (>150 mm^2) had poor outcomes. Due to these shortcomings, many OCLs

treated with MF end up requiring secondary procedures such as osteochondral allograft, autograft, or autologous chondrocyte implantation (ACI).[4,25,27,31] There are a number of drawbacks to these secondary procedures including additional osteotomy to access the talar surface, donor site morbidity from a cartilage harvest site, or a staged type procedure which necessitates 2 procedures. Furthermore, insurance companies still consider OATS to be an experimental procedure putting an excessive financial burden on patients. These associated morbidities and technical difficulties have led surgeons to search for other ways to improve the quality of the reparative tissue through minimally invasive techniques with biologic adjuncts including growth factors, mesenchymal stem cells and minced allograft tissue.

JACI-BMAC is a relatively new all-arthroscopic procedure that uses juvenile chondrocytes implanted directly into the defect site to regenerate cartilage. The rationale with this technique is that using juvenile chondrocytes with a greater metabolic activity will result in a higher propensity to generate hyaline-like cartilage versus the mainly fibrocartilaginous repair tissue produced with MF and without the morbidity and technical difficulties associated with other restorative techniques such as OATs or ACI.[22,39] However, few studies exist that investigate the clinical and radiographic outcomes of this procedure and whether it is superior to MF. In our study, we chose to combine the JACI with BMAC. Our rationale for this approach was that most of the cartilage lesions were not simple shear injuries and had an underlying violation of the subchondral plate. As such, they tended to bleed from the subchondral bone. Multiple studies show that the quality of the reparative tissue can be improved with BMAC when compared to blood from the subchondral bone.[13,25,28,43] We used the BMAC to help the JACI incorporate with the surrounding native articular cartilage as well as improve the quality of the cartilage repair.

The first to report the use of arthroscopic juvenile chondrocyte implantation in the ankle was Kruse et al,[35] who presented the clinical results of a 30-year-old female who was found to be pain free with no activity limitations postoperatively. However, no outcome scores were collected and there was no radiographic assessment performed. A retrospective review of 23 patients by Coetzee et al[12] showed good pain and functional outcomes were observed in most patients who received juvenile allograft to treat talar OCLs according to AOFAS (85 ± 18, 78%), SF-12 (PCS: 46 ± 10, MCS: 55 ± 7.1), FAAM (daily living: 82 ± 14, sports: 63 ± 27), and VAS (24 ± 25 of 100) scores. However, only 3 ankles were treated arthroscopically, there were no preoperative scores for comparison, and there was no radiographic analysis performed to evaluate the quality of repair tissue. None of these studies had a comparison group or objectively quantified the state of the osteochondral lesion postoperatively.

MRI has become increasingly useful for the noninvasive evaluation of cartilage repair. Additional specialized semiquantitative techniques such as T2 mapping, delayed gadolinium-enhanced MRI, and diffusion-weighted imaging can provide information on the morphological appearance of the repair tissue as well as the cartilage structure and molecular composition.[3,37,47,49] However, there have been contrasting findings regarding the quality of repair tissue produced by MF using the aforementioned MRI techniques. Some have reported the tissue produced by MF has a similar collagen fiber network to adjacent tissue and shows complete integration, fill, and homogeneity.[17] In contrast, others have shown structural differences between repair and adjacent cartilage, suggesting the presence of fibrocartilage in the repair tissue, and have reported a much lower percentage of lesions showing complete integration, fill, homogeneity, and intact surfaces. It has also been reported that the majority of lesions have subchondral bone which is not intact.[3,6] Recent studies have used a MOCART scoring system and reported average MOCART scores of 59.5 ± 17.2 points[3] and 64 ± 14 points.[6]

The radiographic results obtained in our study are comparable to those previously reported, with repair tissue in the overall patient population (both MF and JACI-BMAC groups combined) showing structural and surface abnormalities consistent with fibrocartilage such as having a low percentage of integration (12.1%), surface continuity (19.6%), and homogenous structure (31.4%). Similar to previous reports, the subchondral bone was not intact for most lesions (86.3%). This is the first study to report radiographic outcomes following JACI-BMAC. Looking at the MRI results of the JACI-BMAC group, the MOCART scores were similar to those of the MF patients, with differences observed in only 2 individual parameters, degree of defect infill and integration to border zone, which were both greater for the MF patients. This was most likely due to most JACI-BMAC patients demonstrating persistent hypertrophy on their postoperative MRIs. Hypertrophy, such as that seen with ACI in the knee, tends to result in locking or catching, but its effects on the ankle have not been reported. Hypertrophy can occur for several reasons and can be easily seen on an MRI as a reparative cartilaginous scaffold that augments the native cartilage such that it produces the appearance of a little hill or bubble that is often higher than the native articular cartilage (Figure 5).[42] In our patients, the presence of hypertrophy was not found to affect clinical outcomes. The reparative tissue was distinctly different from the surrounding cartilage when evaluating the MOCART scores in both groups. This indicates that the JACI-BMAC technique does not consistently reproduce hyaline cartilage despite the presence of the juvenile chondrocytes.

One significant limitation to the study was the heterogeneity of MR scans performed across multiple institutions which may have affected MOCART scoring. The absence of high resolution fast spin echo proton density images in

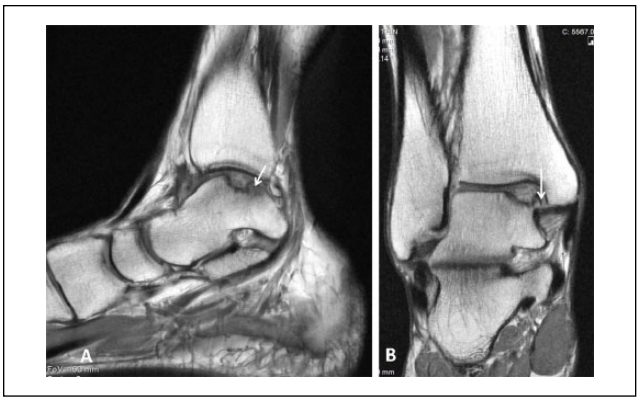

Figure 5. (A) Sagittal and (B) coronal fast spin echo images demonstrate hypertrophy of the reparative cartilaginous scaffold (arrows).

all patients resulted in greater difficulty in providing a detailed analysis of the morphology of the overlying reparative cartilage. In addition, varying magnetic field strength (0.3T, 1.5T, 3.0T) as well as pulse sequence parameters utilized may have affected not only the signal of articular cartilage, but its morphology and its ability to be visualized and analyzed. Specific pulse sequence parameters (specifically gradient echo imaging) can result in significant loss of signal from the deep layer of articular cartilage (the tidemark) which may underestimate cartilage thickness.[42] T2 values of soft tissues also decrease slightly with increasing field strength.[7] On the other hand, low field strength magnets often do not provide robust signal to noise resulting in the inability to clearly visualize small structures such as surface cartilage lesions or the integrity of the tidemark. Such heterogeneity of magnetic field strengths and pulse sequence parameters likely contribute to the inconsistency in MOCART scoring and clinical outcomes reported in the literature, at least in the setting of cartilage repair in the knee.[15] To account for this limitation, ordered logistic regression models were designed to help determine if MRI quality had a significant effect on outcome scores and MOCART scores and no significant effect was found.

There has been some variability in correlation of MOCART scores with clinical outcomes both in the evaluation of operatively treated osteochondral lesions in the knee as well as the ankle.[2,16,21,32,35,45,46] Marlovits et al[36] found a statistically significant correlation between the MOCART parameters and clinical outcomes 2 years after autologous chondrocyte transplantation (ACT) in the knee. Negative trends in MOCART scores have; however, also been documented in the setting of improved clinical outcomes status post-ACI in the knee in addition to no significant correlation.[2,16,45] In the ankle, positive trends in MOCART scores have been demonstrated with good clinical outcomes after autologous osteochondral transplantation (AOT) for treatment of osteochondral lesions of the talus;[21] however, a subgroup of the same authors performed a Level III study and found no significant difference in MOCART scores after AOT for operative treatment of osteochondral lesions of the talus in patients having a secondary procedure after failed MF.[46] The variability in the literature documenting positive outcomes with MOCART scores is likely due to the heterogeneity of MRI parameters utilized as well as different clinical outcomes scoring systems. Nevertheless, the MOCART scoring system remains the most accepted standardized semiquantitative method to evaluation operatively treated articular cartilage lesions with MRI.

Clinical limitations included the heterogeneity of the group, including those patients that had bone grafting or an ankle stabilization procedure, which does not allow for a pure group of OCLs to be analyzed. In addition, the lesion size differed between the JACI-BMAC and MF groups, and could have affected the success of the procedure, patient reported outcomes, as well as the degree to which the cartilage was repaired. Furthermore, the postoperative time to MRI varied between the groups (though all patients had MRIs at least 1 year postoperatively). This could have affected the MOCART parameters, as cartilage quality can change over time. To control for all of these factors, multiple logistic regressions were run, to analyze if each of these limitations had an effect on MOCART scores and clinical outcomes. The only significant factor found was presence of instability, which had no significant effect on clinical outcomes but did have an effect on the MOCART parameter subchondral lamina, with patients in both groups being less likely to have an intact subchondral lamina. There was no significant difference between the number of patients receiving concurrent instability procedures in the 2 groups, and the regression model also showed no significant effect of instability when comparing the 2 groups. We were not able to include bone grafting in any of the regression models because with of the small number of patients that had bone grafting (4 in the DeNovo group), the model would have not been able to reach statistical significance. In a separate comparison of post- to preoperative differences in all FAOS subscales, SF-12 scores, and VAS scores as well as overall MOCART scores and 8/9 subscales of MOCART, the only significant difference was found in "adhesions," suggesting that bone grafting did not change the measured results of the DeNovo patients and had a minimal effect on our overall comparison of MF and DeNovo. We chose to use BMAC based on the authors' positive early experience with BMAC and MF and the potential improvement of reparative tissue with mesenchymal stem cells which have the potential to differentiate into healthy chondrocytes.[13,25,28,44]

Conclusion

The current study sought to compare the outcomes of patients treated with JACI-BMAC to those who underwent

MF for talar OCLs to determine whether JACI-BMAC is superior to MF in producing better functional outcomes and more hyaline-like repair cartilage. To our knowledge, this is the first study to use validated outcome scores and an objective MOCART MR grading system to evaluate 2 different arthroscopic techniques for osteochondral lesions of the talus. The limitations of MF have been clearly documented with primarily Level IV data. However, the additional cost of newer techniques such as JACI-BMAC, BMAC or PRP must be thoroughly investigated to determine if such interventions justify the greater economic burden incurred. It is up to researchers to demonstrate the clinical benefit of more novel interventions with higher quality data to both the orthopedic community as well as the insurance companies who determine reimbursement. Our results for patients treated with MF, including treatment without supplemental BMAC in the case of larger lesions and with supplemental BMAC for smaller OCLs in accordance with surgeon preference, were similar to those previously mentioned. Functional outcomes significantly improved postoperatively. Patients who were treated with JACI-BMAC also saw significant improvement postoperatively. However, when comparing overall postoperative FAOS and VAS pain scale scores and MOCART scores as well as the change in FAOS and VAS pain scale scores pre- to postoperatively, there were no significant differences between the JACI-BMAC and MF groups, suggesting both repair techniques result in similar functional outcomes. Regression analysis based on OCL size revealed there was no difference in outcomes despite larger lesions sizes in patients treated with JACI-BMAC compared to those who received MF with and without BMAC. Furthermore MOCART scores were abnormal in both groups. This suggests that JACI-BMAC has no clear advantage over MF in the short and intermediate term. More studies must be done to investigate the long-term outcomes of the arthroscopic JACI-BMAC procedure.

Acknowledgments

The study took place at the Hospital for Special Surgery and was approved by the institution's Foot and Ankle Registry, which is approved by our Institutional Review Board. The study was presented in part at the American Orthopaedic Foot & Ankle Society Specialty Day Meeting, San Diego, CA, July 2016.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. ICMJE forms for all authors are available online.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Adkisson HD, Martin JA, Amendola RL, et al. The potential of human allogeneic juvenile chondrocytes for restoration of articular cartilage. *Am J Sports Med*. 2010;38(7):1324-1333. doi:10.1177/0363546510361950.
2. Aldrian S, Zak L, Wondrasch B, et al. Clinical and radiological long term outcomes after matrix induced autologous chondrocyte transplantation: a prospective follow up at a minimum of 10 years. *Am J Sports Med*. 2014;42(11):2680-2688. doi:10.1177/0363546514548160.
3. Apprich S, Trattnig S, Welsch, et al. Assessment of articular cartilage repair tissue after matrix-associated autologous chondrocyte transplantation or the microfracture technique in the ankle joint using diffusion-weighted imaging at 3 Tesla. *Osteoarthr Cartil*. 2012;20(7):703-711. doi:10.1016/j.joca.2012.03.008.
4. Aurich M, Bedi HS, Smith PJ, et al. Arthroscopic treatment of osteochondral lesions of the ankle with matrix-associated chondrocyte implantation: early clinical and magnetic resonance imaging results. *Am J Sports Med*. 2011;39(2):311-319. doi:10.1177/0363546510381575.
5. Becher C, Thermann H. Results of microfracture in the treatment of articular cartilage defects of the talus. *Foot Ankle Int*. 2005;26(8):583-589.
6. Becher C, Zuhlke D, Plaas C, et al. T2-mapping at 3T after microfracture in the treatment of osteochondral defects of the talus at an average follow-up of 8 years. *Knee Surg Sports Traumatal Arthrosc*. 2015;23(8):2406-2412. doi:10.1007/s00167-014-2913-9.
7. Bottomley PA, Foster TH, Argersinger RE, Pfeifer LM. A review of normal tissue hydrogen NMR relaxation times and relaxation mechanisms from 1-100 MHz: dependence on tissue type, NMR frequency, temperature, species, excision, and age. *Med Phys*. 1984;11(4):425-448.
8. Buckwalter JA, Mow VC, Ratcliffe A. Restoration of injured or degenerated articular cartilage. *J Am Acad Orthop Surg*. 1994;2(4):192-201.
9. Choi WJ, Park KK, Kim BS, Lee JW. Osteochondral lesion of the talus: is there a critical defect size for poor outcome? *Am J Sports Med*. 2009;37(10):1974-1980. doi:10.1177/0363546509335765.
10. Chrisman OD, Snook GA. Reconstruction of lateral ligament tears of the ankle. An experimental study and clinical evaluation of seven patients treated by a new modification of the Elmslie procedure. *J Bone Joint Surg Am*. 1969;51(5):904-912.
11. Chuckpaiwong B, Berkson EM, Theodore GH. Microfracture for osteochondral lesions of the ankle: outcome analysis and outcome predictors of 105 cases. *Arthroscopy*. 2008;24(1):106-112. doi:10.1016/j.arthro.2007.07.022.
12. Coetzee JC, Giza E, Schon LC, et al. Treatment of osteochondral lesions of the talus with particulated juvenile cartilage. *Foot Ankle Int*. 2013;34(9):1205-1211. doi:10.1177/1071100713485739.
13. Cooke ME, Allon AA, Cheng T, et al. Structured three-dimensional co-culture of mesenchymal stem cells with chondrocytes promotes chondrogenic differentiation without hypertrophy. *Osteoarthritis Cartilage*. 2001;19(10):1210-1218. doi:10.1016/j.joca.2011.07.005.

14. Cuttica DJ, Smith WB, Hyer CF, Philbin TM, Berlet GC. Osteochondral lesions of the talus: predictors of clinical outcome. *Foot Ankle Int*. 2011;32(11):1045-1051.
15. De Windt TS, Welsch GH, Brittberg M, et al. Is magnetic resonance imaging reliable in predicting clinical outcome after articular cartilage repair of the knee? A systematic review and meta-analysis. *Am J Sports Med*. 2013;41(7):1695-1702. doi:10.1177/0363546512473258.
16. Dhollander AA, Huysse WC, Verdonk PC, et al. MRI evaluation of a new scaffold based allogenic chondrocyte implantation for cartilage repair. *Eur J Radiol*. 2010;75(1):72-81. doi:10.1016/j.ejrad.2009.03.056.
17. Domayer SE, Welsch GH, Stelzeneder D, et al. Microfracture in the ankle: clinical results and MRI with T2-mapping at 3.0 T after 1 to 8 years. *Cartilage*. 2011;2(1):73-80. doi:10.1177/1947603510380901.
18. Donnenwerth MP, Roukis TS. Outcome of arthroscopic debridement and microfracture as the primary treatment for osteochondral lesions of the talar dome. *Arthroscopy*. 2012;28(12):1902-1907. doi:10.1016/j.arthro.2012.04.055.
19. Drakos MC, Murphy CI. Particulated juvenile articular cartilage allograft transplantation with bone marrow aspirate concentrate for treatment of talus osteochondral defects. *Tech Foot Ankle Surg*. 2015;24(2):88-93.
20. Ferkel RD, Zanotti RM, Komedna GA, et al. Arthroscopic treatment of chronic osteochondral lesions of the talus: longer-term results. *Am J Sports Med*. 2008;36(9):1750-1762. doi:10.1177/0363546508316773.
21. Flynn S, Ross KA, Hannon CP, et al. Autologous osteochondral transplantation for osteochondral lesions of the talus. *Foot Ankle Int*. 2016;37(4):363-372. doi:10.1177/1071100715620423.
22. Friel NA, Cole BJ. Sports medicine and translational research: solving clinical problems in shoulder and knee through basic science research. *Rush Orthopedics J*. 2009;5(9):8-11.
23. Furukawa T, Eyre DR, Koide S, Glimcher MJ. Biochemical studies on repair cartilage resurfacing experimental defects in rabbit knee. *J Bone Joint Surg Am*. 1980;62(1):79-89.
24. Giannini S, Buda R, Vannini F, DiCaprio F, Grigolo B. Arthroscopic autologous chondrocyte implantation in osteochondral lesions of the talus: surgical technique and results. *Am J Sports Med*. 2008;36(5):873-880. doi:10.1177/0363546507312644.
25. Giannini S, Ceccarelli F, Girolami M, Coppola G, Ferrari A. Biological osteosynthesis in osteochondral lesions of the talus. *Ital J Orthop Traumatol* 1989;15(4):425-432.
26. Giannini S, Buda R, Vannini F, Cavallo M, Grigolo B. One-step bone marrow-derived cell transplantation in talar osteochondral lesions. *Clin Orthop Relat Res*. 2009;467(12):3307-3320. doi:10.1007/s11999-009-0885-8.
27. Giza E, Sullivan M, Ocel D, et al. Matrix-induced autologous chondrocyte implantation of talus articular defects. *Foot Ankle Int*. 2010;31(9):747-753. doi:10.3113/FAI.2010.0747.
28. Gobbi A, Karnatzikos G, Scotti C, et al. One-step cartilage repair with bone marrow aspirate concentrated cells and collagen matrix in full-thickness knee cartilage lesions: results at 2-year follow-up. *Cartilage*. 2011;2(3):286-299. doi:10.1177/1947603510392023.
29. Goh GSH, Razak HRBA, Mitra AK. Outcomes are favorable after arthroscopic treatment of osteochondritis dissecans of the talus. *J Foot Ankle Surg*. 2015;54(1):57-60.
30. Hangody L. The mosaicplasty technique for osteochondral lesions of the talus. *Foot Ankle Clin*. 2003;8(2):259-273.
31. Hannon CP, Ross KA, Murawski CD, et al. Arthroscopic bone marrow stimulation and concentrated bone marrow aspirate for osteochondral lesions of the talus: a case control study of functional and magnetic resonance observation of cartilage repair tissue outcomes. *Arthroscopy*. 2016;32(2):339-347. doi:10.1016/j.arthro.2015.07.012.
32. Hannon CP, Smyth NA, Murawski CD, et al. Osteochondral lesions of the talus: aspects of current management. *Bone Joint J*. 2014;96-B(2):164-171. doi:10.1302/0301-620X.96B2.31637.
33. Hunt SA, Sherman O. Arthroscopic treatment of osteochondral lesions of the talus with correlation of outcome scoring systems. *Arthroscopy*. 2003;19(4):360-367.
34. Jurina A, Dimnjakovic D, Mustapic M, Smoljanovic T, Bojanic I.Clinical and MRI outcomes after surgical treatment of osteochondral lesions of the talus in skeletally immature children [published online ahead of print March 11, 2016]. *J Pediatr Orthop*.
35. Kruse DL, Ng A, Paden M, Stone PA. Arthroscopic DeNovo NT(®) juvenile allograft cartilage implantation in the talus: a case presentation. *J Foot Ankle Surg*. 2012;51(2):218-221. doi:10.1053/j.jfas.2011.10.027.
36. Marlovits S, Singer P, Zeller P, et al. Magnetic resonance observation of cartilage repair tissue (MOCART) for the evaluation of autologous chondrocyte transplantation: determination of interobserver variability and correlation to clinical outcome after 2 years. *Eur J Radiol*. 2006;57(1):16-23.
37. McGahan PJ, Pinney SJ. Current concept review: osteochondral lesions of the talus. *Foot Ankle Int*. 2010;31(1):90-101. doi:10.3113/FAI.2010.0090.
38. McNickle AG, Provencher MT, Cole BJ. Overview of existing cartilage repair technology. *Sports Med Arthrosc*. 2008;16(4):196-201. doi:10.1097/JSA.0b013e31818cdb82.
39. Mitchell ME, Giza E, Sullivan MR. Cartilage transplantation techniques for talar cartilage lesions. *J Am Acad Orthop Surg*. 2009;17(7):407-414.
40. Mosher TJ. Musculoskeletal imaging at 3T: current techniques and future applications. *Magn Reson Imaging Clin N Am*. 2006;14(1):63-76.
41. Niethammer RT, Pietschmann MF, Horng A, et al. Graft hypertrophy of matric-based autologous chondrocyte implantation: a two-year follow-up study of NOVOCART 3D implantation in the knee. *Knee Surg Sports Traumatol Arthrosc*. 2014;22:1329-1336.
42. O'Driscoll SW. The healing and regeneration of articular cartilage. *J Bone Joint Surg Am*. 1998;80(12):1795-1812.
43. Qing C, Wei-ding C, Wei-min F. Co-culture of chondrocytes and bone marrow mesenchymal stem cells in vitro enhances the expression of cartilaginous extracellular matrix components. *Braz J Med Biol Res*. 2011;44(4):303-310.
44. Rosa D, Balato G, Ciaramella G, et al. Long term clinical results and MRI changes after autologous chondrocyte

implantation in the knee of young and active middle aged patients. *J Orthop Traumatol*. 2016;17(1):55-62. doi:10.1007/s10195-015-0383-6.

45. Ross AW, Murawski CD, Fraser EJ, et al. Autologous osteochondral transplantation for osteochondral lesions of the talus: does previous bone marrow stimulation negatively affect clinical outcome? *Arthroscopy*. 2016;32(7):1377-1383. doi:10.1016/j.arthro.2016.01.036.
46. Trattnig S, Millington SA, Szomolanyi P, Marlovits S. MR imaging of osteochondral grafts and autologous chondrocyte implantation. *Eur Radiol*. 2007;17(1):103-118.
47. Verhagen RA, Struijs PA, Bossuyt PM, van Dijk CN. Systematic review of treatment strategies for osteochondral defects of the talar dome. *Foot Ankle Clin*. 2003;8(2):233-242, viii-ix.
48. Winalski CS, Minas T. Evaluation of chondral injuries by magnetic resonance imaging: repair assessments. *Op Tech Sports Med*. 2000;8(2):108-119. doi:10.1053/otsm.2000.6577.
49. Zengerink M, Struijs PAA, Tol JL, van Dijk CN. Treatment of osteochondral lesions of the talus: a systematic review. *Knee Surg Sports Traumatol Arthrosc*. 2010;18:238-246. doi:10.1007/s00167-009-0942-6.