

# A prospective evaluation of bone marrow aspirate concentrate and microfracture in the treatment of osteochondral lesions of the talus

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## ABSTRACT

**Background:** The term osteochondral lesion (OCL) refers to a defect involving the chondral surface and or subchondral bone. These lesions are associated with ankle injuries with bony and soft tissue and cause pain, decreased range of motion, swelling and impact adversely on quality of life. To date the standard treatment has been isolated microfracture (BMS). The aim of this study was to compare the outcomes of BMS alone to BMS augmented with bone marrow aspirate concentrate (BMAC) in the treatment of ankle OCLs.

**Methods:** This study was a prospective cohort study carried out from 2010–2015 in a single surgeon's practice. Patients from 2010–2012 were treated with microfracture alone while patients from 2013–2015 were treated with micro fracture augmented with bone marrow aspirate concentrate and fibrin glue. Self-reported patient outcome measures were measured. Complications, revision rates, and visual analogue pain scores were compared.

**Results:** 101 patients were included in the study. 52 patients were in the microfracture group while 49 patients were in the microfracture/BMAC group. The minimum follow-up for both groups was 36 months. Both groups had a statistically significant improvement in pain scores, quality of life scores, participation in sport and activities of daily living. The revision rate was 28.8% in the microfracture group versus 12.2% in the microfracture/BMAC group, which was statistically significant,  $p=0.0145$ . The majority of the lesions were less than 1.5 cm<sup>2</sup> in diameter in both cohorts.

**Conclusions:** Microfracture and bone marrow aspirate concentrate appears to be a safe and effective treatment option for osteochondral lesions of the talus. The addition of bone marrow aspirate concentrate does not result in any increase in ankle or donor site morbidity. It is a well-tolerated therapy which decreases revision rates for treatment of the osteochondral lesions when compared to microfracture alone.

**Level of evidence:** Level III.

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## 1. Introduction

Ankle sprains are an extremely common injury; approximately 27,000 ankle sprains occur per day in America. Osteochondral lesions of the talus refer to a chondral or subchondral defect of the articular cartilage and potentially the underlying bone [1,2].

These lesions may become symptomatic and lead to a variety of complaints. Common complaints include deep ankle pain, catching/locking symptoms, instability, swelling, decreased range of motion or stiffness. Treatment strategies for osteochondral lesions (OCLs) include both non-surgical and surgical options.

Success has been reported in up to 55% of conservatively treated OCL lesions in some series [3–5]. Surgical options are largely broken down into two groups, namely reparative or regenerative treatments. The reparative techniques include debridement and bone marrow stimulation techniques such as microdrilling and microfracture [3–6].

Regenerative techniques include autologous osteochondral transplants, autologous chondrocyte implantation (ACI), matrix induced autologous chondrocyte implantation (MACI), autologous matrix induced chondrogenesis (AMIC) and matrix-associated stem cell transplantation (MAST) [5,6]. The technique for ACI has been reported in the ankle for talar OCLs. It involves two stages; the first involves an arthroscopic biopsy of healthy cartilage. The second stage involves the ex vivo culture and replant of chondrocytes into the lesion, usually through a medial malleolar osteotomy. Cost has been cited as a prohibitive issue with this

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technique [5–7]. At a mean of 45 months, Petersen et al. [5] found that 11 of 14 patients had good or excellent results following ACI. Niemeyer et al. [8] performed a meta-analysis examining the use of ACI for the management of talar OCLs. 213 patients in 16 studies were analyzed. Although observing that good results have been reported, the analyzed studies were all level IV evidence, and included 9 different outcome measures. Further different indications and techniques were described. The authors conclude that superiority or inferiority to alternative surgical strategies could not be determined on this basis. MACI is a modification of ACI where the chondrocytes are embedded into a matrix scaffold, which is then fixed to the articular surface using fibrin glue [9,10]. The addition of a matrix scaffold to retain the chondrocytes in the defect in reality has made ACI all but obsolete [9–11]. Giannini et al. [12] reported their experience of MACI for talar OCLs in 46 patients followed for a mean of 87.2 months. At final follow-up, mean AOFAS score was 92, which had actually improved significantly over the studied period ( $p=0.0005$ ). AMIC involves clot stabilization following bone marrow stimulation through the use of a collagen scaffold. It is a single stage technique that involves microfracture done in the usual fashion with fibrin glue to fix the matrix [13]. AMIC has produced good results, with Valderrabano et al. [14] reporting an increase in AOFAS score from 60 to 89.

Matrix-associated stem cell transplantation (MAST) is a more recent modification of AMIC described by Richter and Zech [15]. In this single stage technique, autologous pluripotent stem cells are harvested from the iliac crest and concentrated with a centrifuge. The supernatant is then implanted into a type I/III collagen scaffold, which is then laid over the defect and fixed using fibrin glue. In 25 patients undergoing 26 MAST procedures, Richter and Zech [15] reported improved mean post-operative Visual Analogue Score Foot and Ankle (VAS FA) from 49.2 to 94.5, with 89% of patients returning to sporting activity.

However there are disadvantages in terms of donor site morbidity and the development of subchondral bone cysts over time [16–18].

Bone marrow aspirate concentrate (BMAC) is a biologic adjunct. The bone marrow is comprised of both hematopoietic and mesenchymal stem cells. Mesenchymal stem cells (MSCs) have the ability to differentiate into both chondrogenic and osteogenic progenitor cells. Hematopoietic cells can differentiate into platelets, which together can induce a favorable environment for the repair and laying down of new cartilage. This new cartilage is more similar to hyaline cartilage than the cartilage generated with microfracture alone [19–21].

Failure of microfracture of OCLs is becoming more recognised as an entity in chronic post-operative ankle pain and the need for a more durable treatment is clear [20,22,23]. In this regard BMAC augmented microfracture has been suggested as a credible therapeutic option [22].

This purpose of this study was to compare a cohort of patients who were treated with arthroscopic microfracture alone for symptomatic OCL lesions with a matched cohort treated with bone marrow aspirate concentrate (BMAC) and microfracture, to determine outcomes and revision rates. The hypothesis of this study was to demonstrate that the addition of BMAC to microfracture led to an improvement in outcomes and that the revision rates in the cohort were lower. This would imply a more durable treatment.

## 2. Methods

### 2.1. Study design

A prospective cohort study was carried out from 2010 to 2015 in a single surgeon's practice. Patients from 2010 to 2012 were treated

with arthroscopic microfracture alone without biologic adjuncts. These patients were followed prospectively. Patients from 2013 to 2015 were treated with BMAC and microfracture and followed accordingly.

### 2.2. Instruments used

Patient reported outcome measures were recorded both pre-operatively and post-operatively visits using the Foot and Ankle Outcome Score (FAOS) validated questionnaire. Complications including adverse events, re-operation for any reason and pain scores were recorded. The FAOS questionnaire is a validated questionnaire that has five domains looking at the burden of foot and ankle symptoms [24]. A score from 1 to 100 is possible with a score of 100 indicating no symptoms and a score of 1 indicating extreme disability. Visual analogue pain scores were recorded on a scale of one to ten as well.

### 2.3. Sample

The cohorts were age and sex matched for comparison. All patients completed questionnaires at routine office visits. The diagnosis was established using history, clinical examination, plain radiographs and confirmed by magnetic resonance imaging to characterize the location and size of the OCL. The radiographs were weight bearing.

The defects were characterized according to size and location (Table 1). Specifically the size was measured on a pre-operative MRI in diameter and correlated with intra-operative findings using Hepple criteria [25]. The size was greater than 1.5 cm<sup>2</sup> in five patients in cohort, and four patients in cohort 2. The final size was taken as the intra-operative measurement.

A chart review and telephone follow up was conducted on all patients to capture complications, adverse events and subsequent/revision surgeries. Patients who had additional procedures like concomitant stabilization procedures or malalignment were also recorded. No patients had a malalignment procedure at the same time as the microfracture procedures. If a patient had a stabilization procedure performed at the same time as the OCL this was recorded. However a specific documentation of instability was not recorded in all instances (Fig. 1).

#### 2.3.1. Inclusion criteria

- Patients aged over 18.
- Patients with osteochondral lesions of talus proven by MRI.
- Patients who were not candidates for treatment with autologous matrix induced chondrogenesis (AMIC) or osteochondral autologous cartilage transfer system.

#### 2.3.2. Exclusion criteria

- Patients less than 18 years of age.
- Patients who had additional treatment contemporaneously like OATS (osteochondral autologous cartilage transfer system) or MACI (matrix-induced autologous chondrocyte implantation).

There were 52 patients in the 2010–2012 group and 49 in the 2013–2015 group. The patients in the arthroscopic microfracture group were followed up for a minimum of 4.5 years with a mean of 58 months. The patients in the 2013–2015 group were followed up for a minimum of 2.5 years with a mean of 40 months.

### 2.4. Surgical technique/procedure

Patients from 2010–2012 had microfracture alone. The patient was positioned supine with the leg on a knee rest under general or

**Table 1**  
Demographics for groups.

	Group 1: microfracture N = 52			Group 2: BMAC and microfracture N = 49			P value
Gender: male	41			39			
Female	11			10			
	Total: 52			Total: 49			
Revision rate:	N = 15/52 28.8%			N = 6/49 12.2%			
Smoker:	9.5%			10.5%			
Age:	Mean	Min-max	Std. dev	Mean	Min-max	Std. dev	
	39.7	22–60	10.78	34.6	18–64	11.81	
Lesion distribution:	47% medial talar dome 53% lateral talar dome			55% medial talar dome 45% lateral talar dome			
Lesion size:	N = 5 > 1.5 cm <sup>2</sup> (9%) N = 47 >0.7 cm <sup>2</sup> < 1.5 cm <sup>2</sup> (91%)			N = 4 > 1.5 cm <sup>2</sup> (8%) N = 46 >0.7 cm <sup>2</sup> < 1.5 cm <sup>2</sup> (92%)			
Pre-op VAS Pain score (1–10)	Mean		Std. dev	Mean		Std. dev	
	7.34		1.49	6.82		1.67	
Post-op VAS Pain score (1–10)	Mean		Std. dev	Mean		Std. dev	
	4.30		2.1	3.38		1.8	
Improvement in VAS Pain score (1–10)	Mean		Std. error	Mean		Std. error	P < 0.05
	3.04		0.53	3.44		0.18	
Pre-op Symptoms score (FAOS questionnaire)	Mean		Std. error	Mean		Std. error	
	47.06		4.2	55.2		3.37	
Post-op Symptoms score (FAOS questionnaire)	Mean		Std. error	Mean		Std. error	
	68.87		3.5	75.6		2.85	
Pre-op Pain score (FAOS questionnaire)	Mean		Std. error	Mean		Std. error	
	59.74		4.6	62.3		3.01	
Post-op Pain score (FAOS questionnaire)	Mean		Std. error	Mean		Std. error	
	76.96		4.2	82.3		2.12	
Pre-op Sports score (FAOS questionnaire)	Mean		Std. error	Mean		Std. error	
	47.1		6.8	43.69		4.0	
Post-op Sports score (FAOS questionnaire)	Mean		Std. error	Mean		Std. error	
	70.5		5.1	70.85		3.3	
Pre-op QOL score (FAOS questionnaire)	Mean		Std. error	Mean		Std. error	
	44.36		7.3	31.06		2.8	
Post-op QOL score (FAOS questionnaire)	Mean		Std. error	Mean		Std. error	
	68.13		5.8	64.45		2.8	
Pre-op ADL score (FAOS questionnaire)	Mean		Std. error	Mean		Std. error	
	63.34		3.8	69.02		3.04	
Post-op ADL score (FAOS questionnaire)	Mean		Std. error	Mean		Std. error	
	72.9		3.2	84.59		2.20	

spinal anesthetic. A thigh tourniquet was routinely used and an ankle stirrup was applied for traction/distraction. Arthroscopy of the entire ankle was carried out. The initial cap of degenerative or loose cartilage was removed with a curette. A shaver was then utilized. The edges and floor must be debrided to bleeding bone. An awl is used for microfractures. The holes are placed from the periphery towards the center of the lesion, roughly three to four mm apart to fracture the subchondral plate. These patients had a washout of the ankle with normal saline 0.9%. Local anaesthetic infiltration was applied to the skin wounds which were closed with 3–0 monocryl<sup>®</sup> sutures and steri-strips. The patient was placed in an immobilizer boot. For the first 10 days post-operatively the boot is worn 24 h a day. After patients were instructed to commence unloaded active ankle ROM exercises. At 4 weeks the patients were instructed to begin weight bearing. The boot was removed at 6 weeks.

#### 2.4.1. Surgical technique for BMAC and microfracture

These patients had a full ankle arthroscopy prior to having the microfracture. If necessary, cheilectomy or soft tissue releases were completed prior to the microfracture, lest they disrupt the formation of the fibrin clot.

The anterior iliac crest was used as the donor site for harvesting the BMAC. 30mls were aspirated and concentrated using the Harvest<sup>®</sup> BMAC Cellular Therapy system<sup>®</sup> by CelgenTek Limited. This produces 2–4ml of mesenchymal stem cells typically. This procedure can take 20 min so it was routinely performed at the start of the procedure.

To insert the BMAC, the saline was aspirated from the joint and a “dry scope” was performed. The BMAC was injected into the surgical defect using a syringe and needle under arthroscopic control. It was applied in layers. The first layer covered the entire defect and was 2 mm–4 mm deep. A layer of Tisseel<sup>®</sup> was then applied onto the layer

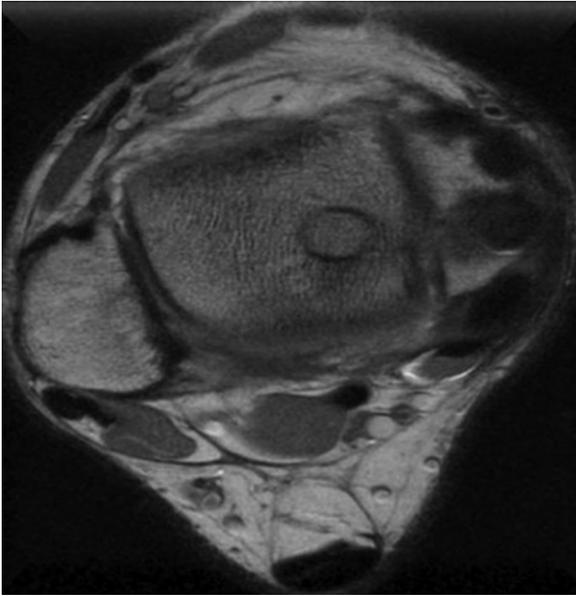


Fig. 1. Osteochondral lesión.

of BMAC. Tisseel<sup>®</sup> is a mixture of fibrin and thrombin and acts as a sealant [26]. This ensures the BMAC stays in place and does not wash out of the lesion, it also protects the MSCs from synovial fluid which may be toxic to these cells. Further layers of BMAC were then applied and covered until the defect was filled. The remaining BMAC was injected intra-articularly to enhance the healing response.

### 2.5. After-care

Patients in the BMAC group were asked not to move their ankle for first 10 days to prevent the clot from being dislodged. They wore an immobilizer boot similar to the first group and followed the same standard protocol (Fig. 2).

### 2.6. Statistical analysis

Statistical analysis was conducted using SPSS version 24. Both cohorts were matched in terms of age and gender. The mean ages of both were compared. The Shapiro–Wilk test was conducted to test for normality. This was not normally distributed. The independent samples t-test was conducted to identify any

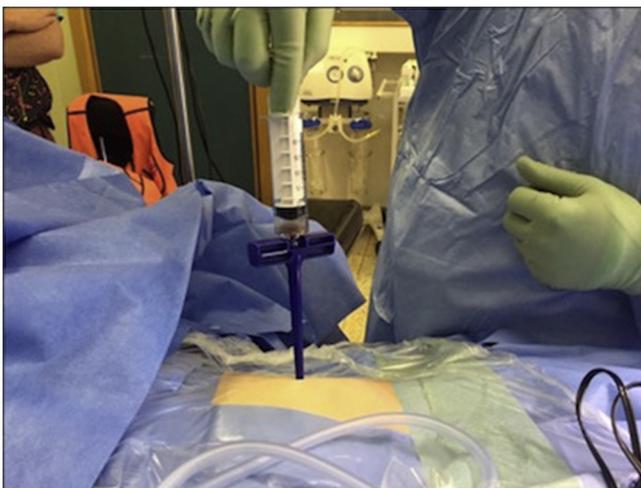


Fig. 2. Bone marrow aspirate concentrate harvest.

statistical differences in age between both groups as well as proportions for gender. The paired samples t-test were used to compare the pre intervention and post intervention FAOS scores. The Mann–Whitney U test was conducted to determine if there was any statistical significance between the two groups for revision rates.

## 3. Results

101 patients were identified for inclusion in this study. 52 patients were treated with microfracture from 2010 to 2012 (Group 1). 49 patients were treated with BMAC and microfracture from 2013 to 2015 (Group 2). The majority of these lesions were between 0.7 cm<sup>2</sup> and 1.5 cm<sup>2</sup> in size. A combination of medial and lateral talar dome lesions were treated with success. Patients experienced significant improvements in terms of self reported outcomes. Pain scores improved a mean of 3.44 points on the VAS scale (decreased from 7 to 3.3). Patients improved in terms of self reported quality of life, burden of symptoms and return to both sport and activities of daily living. Group 1 (Microfracture alone) had mean improvement of 21.8 for symptoms, 17.2 for pain, 9.56 for ADLs, 23.4 for sports and 23.7 for QOL in FAOS scores. These results were statistically significant  $P < 0.05$ . Group 2 (BMAC and microfracture) had a mean improvement of 20.38 for symptoms, 19.89 for pain, 15.69 for ADLs, 27.5 for sports and 33.41 for QOL in FAOS scores. These results were statistically significant  $P < 0.05$ . Revision rates for Group 1 were 28.8% and for Group 2 were 12%. There was a statistically significant difference between both groups,  $P = 0.015$ . The improvements were durable and sustained. There were little adverse events in this cohort. The revision rate was low in this cohort (6/49).

### 3.1. Cohort demographics

Both cohort groups were matched in terms of distribution of gender and age. The test of normality for age was carried out using the Shapiro–Wilk test. Age was not normally distributed. The Independent T samples test was carried out between the two groups. Equal variances were assumed as Levene's test for equality of variances was  $p = 0.93$ . There was no statistical difference between age in the two groups  $p = 0.63$ . There was no statistical difference between gender spread in the groups with a  $p = 0.08$ .

The mean age of the overall cohort was 36.26 with a standard deviation of 11.809 [18–64] (Table 1). 10% of the overall cohort were smokers.

In Group 1 the gender distribution was 20.8% females and 79.2% males. 9.5% of this cohort smoked. In group 2 the gender distribution was 23.1% female and 76.9% males. 10.5% of this cohort smoked.

### 3.2. Microfracture alone group (Group 1)

The mean follow up for this cohort was 58 months. One patient was lost to follow up due to migration.

The re-operation rate for this cohort for all reasons was 16/52 patients when followed up over a five year period. 15/52 (28.8%) were felt to be directly related to failure of the initial microfracture. One patient had a lateral ligament complex repaired at a later stage. 15 patients had subsequent surgery for their OCL. 13 patients had failure within 18 to 24 months with two within 12 months. These patients were re-imaged prior to repeat surgery. The mode of failure was fissuring of the fibrocartilage with residual oedema. There were no documented nerve injuries or thrombosis in this cohort. One patient had a superficial wound infection which resolved with a short course of oral antibiotics.

This group had a mean improvement of 21 points in terms of symptoms, 17 points in terms of pain, 9.5 points in terms of

**Table 2**

Group 1 FAOS questionnaire post treatment scores.

Δ = Change in scores	Mean	Std. dev	Std. error mean	95% CI: lower	95% CI: upper	t	Sig (2-tailed)
Δ Symptoms	21.81	16.97	3.5	29.15	14.47	6.16	0.000
Δ Pain	17.22	18.76	3.91	25.33	9.11	4.4	0.000
Δ ADL	9.56	15.046	3.13	16.07	3.06	3.049	0.006
Δ Sports	23.41	23.93	4.99	33.77	13.06	4.69	0.000
Δ QOL	23.76	24.46	5.10	34.35	12.17	4.65	0.000

**Table 3**

Group 2 FAOS questionnaire post treatment scores.

Δ = Change in scores	Mean	Std. dev	Std. error mean	95% CI: lower	95% CI: upper	t	Sig (2-tailed)
Δ Symptoms	20.38	23.04	3.36	27.14	13.61	6.02	0.000
Δ Pain	19.897	21.06	3.07	26.08	13.71	6.47	0.000
Δ ADL	15.649	20.58	3.00	21.69	9.60	5.21	0.000
Δ Sports	27.15	25.77	3.76	34.72	19.58	7.22	0.000
Δ QOL	33.41	28.24	4.12	41.70	25.12	8.11	0.000

**Table 4**

Improvement in Vas scores post treatment per group.

Scale: 1–10	Mean improvement in group	Std. error	Significance
Group 1: microfracture	3.04	0.53	P < 0.05
Group 2: BMAC and microfracture	3.44	0.18	P < 0.05

activities of daily living, 23.4 in terms of sports and 23.76 in terms of quality of life. These improvements were found to be statistically significant ( $P < 0.05$ ) (Table 2).

### 3.3. BMAC and microfracture group (Group 2)

The mean follow up for this cohort was 40 months. 6/49 (12.2%) patients have had a further surgery. Three patients went on to have AMIC procedure, two had repeated microfracture/BMAC and one had OATS procedure. There were 3 adverse events noted in this treatment group. One patient developed a deep vein thrombosis (DVT), one patient developed pain at the hip site post BMAC aspiration and one patient was treated for erythema around a portal site. The patient with hip pain post BMAC aspiration underwent plain film and MRI evaluation. Infection, collections, nerve injury and stress cortical injuries were excluded. The pain settled with simple analgesia after seven weeks.

This group had a mean improvement of 20.3 points in terms of symptoms, 19.8 points in terms of pain, 15.64 points in terms of activities of daily living, 27.15 in terms of sports and 33.4 in terms of quality of life. These improvements were found to be statistically significant,  $P < 0.05$  (Table 3).

ANOVA analysis was conducted to test if there was a statistical significance between the pre-operative and post-operative FAOS scores between groups. Each group had an independent statistically significant improvement in outcomes. There was a statistical difference in terms of ADL  $p = 0.03$  in the BMAC group however there was not a difference between groups in terms of pain, QOL, sports and symptoms.

### 3.4. Pain VAS scores

There was a mean improvement of 3.04 (std. error of 0.535) for Group 1,  $p = 0.023$ . There was a mean improvement of 3.43 (std. error of 0.183) for Group 2  $p = 0.018$ . However there was not a statistically significant difference detected comparing both groups ( $P = 0.63$ ) (Tables 4 and 5).

### 3.5. Revision rates

A comparison of the revision rates between both cohorts was analysed. The Shapiro–Wilk test was conducted to test distribution and non parametric analysis was used. A Mann–Whitney test was conducted which reached statistical significance;  $p = 0.015$ . The mean rank for group 1 was 41.1. The mean rank for group 2 was 32.72 (Tables 6–8).

## 4. Discussion

Osteochondral lesions are a cause of ongoing ankle pain after injury. Conservative treatment has a demonstrated success rate in 55% of cases, however careful lesion selection is required [4,27–30]. Microfracture and mosaicplasty produces fibrocartilage which is rich in type 1 cartilage, however, inferior in structure to the normal joint composition [31–33].

Current treatment limitations include durability of the repair, and quality of the repaired or regenerated cartilage. Traditional reparative strategies such as microfracture or micropicking stimulate bone marrow by penetrating the underlying subchondral bone and creating an inflammatory response, which in turn lays down fibrocartilage to fill the defect. The subchondral bone is stimulated to allow mesenchymal stem cells to exit and access the focal chondral defect to aid healing. Replacement techniques use autologous graft as a substitute to fill the deficient cartilage. Saxena and Eakin [1] have reported 96% success in high demand athletes at two to eight years following surgery for talar injuries which

**Table 5**

Non-parametric analysis between groups for VAS scores.

	Difference_VAS_Pain
Mann–Whitney U	508.00
Wilcoxon	1636.00
Z	–0.417
Asymp. Sig (2-tailed)	0.63

**Table 6**  
Revisions required per group.

Revision required for OCL:	Group 1: microfracture	Group 2: BMAC and microfracture
No	38	43
Yes	14	6
Total	52	49

**Table 7**  
Mann–Whitney test for revision rates comparison between two groups.

Revision required for OCL			
Group	N	Mean rank	Sum of ranks
Microfracture	52	41.17	947.00
BMAC and microfracture	49	32.72	1538.00
Total	101		

Revision required for OCL	
Mann–Whitney U	410.00
Wilcoxon W	1538.00
Z	−2.422
Asymp. Sig (2-tailed)	0.015

included microfracture and bone grafting. In a systemic review, Zengerink et al. reported 85% success with marrow stimulation [4,28]. The quality of the repair, however, has not been tested in the long term. Ferkel et al. [32] noted a 25% decrease in outcome scores when patients were reviewed five years later post microfracture. Hunt and Sherman [33] had 54% poor or fair follow-up results at 66 months post-procedure, and 61% of these patients still had pain. Kennedy et al. [36] reviewed microfracture success rates with OATS procedures 87% and 85% respectively, but OATS procedures was associated with 36% morbidity from the knee donor site. OATS or mosaicplasty is reserved for larger lesions and is an invasive procedure having multiple complications beyond knee pain including issues with the medial malleolar osteotomy and matching the graft to the talar surface [36]. Furthermore the

**Table 8**  
Results summary.

Results highlights	Group 1 (microfracture alone) N = 52	Group 2(BMAC/ microfracture) N = 49
Mean improvement Symptoms	21.8	20.38
Mean improvement Pain	17.2	19.89
Mean improvement ADLs	9.56	15.69
Mean improvement Sports	23.4	27.5
Mean improvement QOL	23.7	33.41
Revision rates	28.8%	12.2%

grafts will incur 25% cell death around the periphery and cysts form over time in up to 75% of cases [17,18].

BMAC is comprised of platelets and growth factors but in lower concentration than PRP [18]. It also contains multipotent mesenchymal stem cells (MSCs). When BMAC is used an adjunct to bone marrow stimulation; the stem cells are capable of differentiating into osteoblasts and chondrocytes. The differentiation of MSCs found in bone marrow into osteogenic and chondrogenic progeny has been acknowledged since the 1960s when Friedenstein et al. [35] reported on this.

Aspiration of bone marrow is usually performed intra-operatively. The iliac crest is a common site, the tibia and calcaneus can also be used [21,34–37].

Evidence supporting the use of BMAC to enhance cartilage repair is growing [19,37–39]. Kennedy et al. utilised BMAC as an adjunct to autologous osteochondral transplantation in the management of talar OCLs [36,37,40].

MSCs are multipotent progenitor cells which have the potential to differentiate into many connective tissue cell types like tenocytes, adipocytes, chondrocytes, myocytes and osteocytes [44–46]. MSCs have important paracrine effects to alter their local microenvironment to make conditions more favourable for healing, repair, and regeneration. MSCs are involved in modulating all the stages of the normal wound healing response [32,33,42,43]. This is due to downregulation of the inflammatory cytokines.

Hyaline cartilage is designed to resist repetitive loading of the joint and to allow low friction articulation. Chondrocytes surround an extracellular matrix with water, proteoglycans, and collagen [44–46]. The orientation of the fibers contributes to the ability of the cartilage to resist forces. The superficial horizontal fibres help resist shear forces while the deeper vertically orientated fibers resist compressive forces through the joint [22,47]. Hyaline articular cartilage relies on diffusion from the synovial fluid for nutrition and has poor regenerative capacity [27]. Cartilage is avascular, so even small cartilage lesions can remain and worsen due to increased loading of particular points. Fibrocartilage can occasionally form due to increased stimulation of underlying subchondral blood flow. The fibrocartilage may slow degeneration, but it is inferior biomechanically to hyaline cartilage [42,45].

Microfracture is thought to release MSCs and local growth factors into the environment [27]. This generates a fibrin clot which leads to fibrocartilaginous infill. This, however, is mainly composed of type 1 collagen. The native collagen is type-II collagen so the repaired cartilage has different biomechanical properties and can degenerate over time.

TISSEEL<sup>®</sup> was utilized as a technique to increase retention of the bone marrow aspirate concentrate in the defect. TISSEEL<sup>®</sup> is a combination of fibrin glue and sealant. It prevents early dispersal of the BMAC, allowing time for the fibrin super-clot to form and thus for the reparative process to begin. The sealer protein solution contains human fibrinogen and a synthetic fibrinolysis inhibitor which prevents premature degradation of the fibrin clot [26]. We believe the addition of BMAC with TISSEEL<sup>®</sup> prevents synovial fluid ingress into the super clot preserving more MSCs for longer in the defect. Together the two components combine and mimic the clotting cascade in its final stages to form a rubber-like mass that adheres to the BMAC and seals it in.

Without the application of TISSEEL<sup>®</sup> it can be difficult to ensure that a generous quantity of the BMAC stays within the microfractured lesion. If the BMAC is dispersed in the ankle joint without staying within the lesion then the clot is of limited size. This may then limit the amount of fibrocartilagenous repair occurring.

We also theorise that BMAC creates a favourable environment in the joint for ongoing cartilage repair as well as local healing when it is injected intra-articularly at the end of the procedure.

Good short- and medium-term results have been reported in the literature. Lee et al. [29] reported improvement in AOFAS scores from 63 to 90 in 35 patients followed for 33 months following arthroscopic microfracture. Chuckpaiwong et al. [49] found that patients with lesions <15 mm diameter fared much better than those with larger lesions >15 mm in size. Choi et al. [50] similarly found that patients with lesion sizes >15 mm did poorer. At longer follow-up, Van Bergen et al. [51] reported on 50 patients undergoing arthroscopic microfracture. They had a mean follow-up of 12 years (range 8–20 years). Median AOFAS scores for the group were 88. Polat et al. [52] conducted a review with minimum 5 year follow up. 88 patients were included and only 35 patients had no symptoms. Of the small number of studies examining cartilage repair that are available for scrutiny, 54% do not report lesion size as a variable and most are of poor quality or methodology.

The results for microfracture have not been universally good. Conflicting studies exist. Hunt and Sherman [33] found that less than half of 28 patients followed for a mean of 66 months reported good or excellent results. Becher et al. [39] indicated that 100% of 25 patients at 3.6–9.6 years following microfracture demonstrated chondral fibrillation and fissuring on MRI. Ferkel et al. [32] also observed that over a five-year period, 35% of fifty patients showed clinical deterioration from their initial result following microfracture.

#### 4.1. Strengths and limitations

As with all single surgeon series limitations exist. Potential confounding factors include the length of follow up in both groups. However a minimum of 2.5 years has been achieved in both groups. Most failures occurred within the first 12–18 months in the microfracture group alone. We postulate this follow up will have captured most of the patients. Only two patients were not available for follow up. A further potential limitation of this study is the lack of post-operative imaging to confirm lesion integration. Post-operative MRIs were not routinely carried out unless patients required it to investigate a pain source. This is due to budgetary constraints in the environment which the study was being performed. It is not standard practice to perform MRIs in a post operative setting unless there is a direct clinical requirement.

Further RCTs with longer follow up are needed to assess the durability the effect of augmentation with BMAC on the microfracture process.

Strengths of this study include the long follow up, the relatively large cohort of patients of a homogenous cohort. All but two patients were included in the follow up for this study. The complication rate was extremely low in the total study cohort. The revision rate/failure rate has been low overall in both cohorts but particularly in the augmented. Pain scores have been reduced and patient self-reported outcomes have been favourable.

## 5. Conclusion

Continued follow up is necessary to monitor the durability of treatment for these patient cohort groups. Larger randomized control trials comparing the various modalities of treatment for OCLs is necessary. It is necessary to attempt to develop a standard treatment protocol for OCLs based on age, patient profile and size and consistency of the lesion.

Based on the results of this study to date BMAC and microfracture are a credible treatment option for OCLs. It has yet to be seen how this treatment, specifically BMAC and microfracture will fair with larger lesions >3 cm<sup>2</sup>. There is little in the way of the donor site morbidity which can occur with OATS. This treatment is less expensive and time consuming than OATS procedure.

Microfracture does not preclude further treatment in the form of mosaicplasty.

Patients who have symptomatic OCLs may benefit from treatment with bone marrow aspirate concentrate and microfracture based on the results of this cohort study. Diagnostic imaging has dramatically improved over the last two decades and the ability to diagnose OCLs has improved in line with this. OCLs are becoming more recognized as an entity in chronic ankle pain and the demand for a durable treatment is ever present. The desire to stave off definitive joint replacement or arthrodesis exists and BMAC with microfracture offers a credible therapy option.

## Conflict of interest statement

This is to declare there are no existing conflicts of interesting from all the authors involved in this study.

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