# Osteochondral lesions under 15mm2 of the Talus; is iliac crest Bone marrow Aspirate Concentrate the Key to success?

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| **Ethical review** | Approved WMO |
| **Status** | Pending |
| **Health condition type** | Bone and joint therapeutic procedures |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON49126

**Source**
ToetsingOnline

**Brief title**
OUTBACK trial

### Condition

- Bone and joint therapeutic procedures

**Synonym**
cartilage damage of the ankle; osteochondral talar defect

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum
**Source(s) of monetary or material Support:** Arthrex,Arthrex Inc

## Intervention

**Keyword:** arthroscopic surgery, bone marrow apirate concentrate, Bone marrow stimulation, talar osteochondral defect

## Outcome measures

### Primary outcome

The primary outcome measure is the difference in pain during weight-bearing

between pre-operative and 24 months after surgery on a numeric rating scale

(NRS).

### Secondary outcome

Secondary parameters are:

- Questionnaires: EQ5D, AOFAS, FAOS, NRS (in rest, during running, during

stair-climbing, during performing sports), FAAM, SF-12, Ankle Activity Scale

(AAS), return to sports, return to work

- Radiological outcomes: CT-scan (depth, wide, length, joint space measurement)

and MRI scan (T2 relaxation times)

- Cost-effectiviness

- Cell-subset analysis

- Complications, Re-operations, Demographic data

# Study description

### Background summary

Osteochondral defects (OCDs) of the talus have a significant impact on the quality of life of patients. When OCDs are of small nature (up to 15 mm in diameter), and have failed conservative management, surgical intervention may

be necessary. For small cystic defects the current treatment is an arthroscopic bone marrow stimulation (BMS) procedure, during which the damaged cartilage is resected and the subchondral bone is microfractured (MF), in order to disrupt intraosseous blood vessels and thereby introduce blood and bone marrow cells into the debrided lesion, forming a microfracture fibrin clot, which contains a dilute stem cell population from the underlying bone marrow. This procedure has been reported to have a 75% successful long-term outcome. Recently, the additional use of biological adjuncts has become popular, one of them being bone marrow aspirate concentrate (BMAC) from the iliac crest. BMAC consists of mesenchymal stem cells, hematopoietic stem cells and growth factors, which may therefore theoretically improve the quality of subchondral plate and cartilage repair. The current evidence for treating talar OCDs with BMS plus BMAC is limited and heterogeneous. It is unclear to what extent the treatment of talar OCDs with BMS plus BMAC is beneficial in comparison to BMS alone.

**Study objective**

The main objective of the present study is to compare the clinical outcome of bone marrow stimulation alone versus bone marrow stimulation and bone marrow aspirate concentrate (BMAC) for small symptomatic osteochondral defects of the talus.

**Study design**

This study concerns a physician and patient-blinded multicenter randomized controlled trial with a 24-month follow-up period at the outpatient clinic. All patients that visit the outpatient clinic (in any of the participating centers) for small symptomatic talar OCDs up to 15 mm in depth and/or diameter - anteroposterior or mediolateral-, eligible for BMS surgery will be asked if they are willing to participate in the present study. If they are interested, patients will be informed about this study and are given two weeks to decide upon participation. In case patients provide their consent, they are screened for meeting the inclusion criteria, and are assessed pre-operatively by documenting a questionnaire containing the EQ5D, Numeric Rating Scale (NRS) of pain, the American Orthopaedic Foot and Ankle Hindfoot Score (AOFAS) Foot and Ankle Outcome Score (FAOS), Foot and Ankle Ability Measure (FAAM) and the Short-Form 12 (SF-12). As part of the standard AMC pre-operative protocol concerning talar OCDs, the patients will receive a preoperative dual energy computed tomography (CT) scan. Additionally, the patients will receive an Magnetic Resonance Imaging (MRI) scan pre-operatively. Subsequently after surgery, patients will be followed-up at 2 weeks, six weeks, three months, one-year and two years post-operatively. At two weeks post-operatively complication assessment will be performed as well as on 6 weeks.
Pre-operatively, at three months and at one-year and two years post-operatively outcome scores with the aforementioned scorews will be collected.
At these follow-up moments the patients will be requested to fill out

questionnaires and a physical examination will be performed. At one and two -year of follow-up, a CT-scan and a MRI-scan will be made to guide prognosis and judge the quality of the cartilage (the CT-scan is a standard follow-up procedure, also in other surgical treatments for this indication). Apart from the scores mentioned above in the pre-operative questionnaire, the post-operative questionnaires will contain scores assessing the resumption to sports, work, as well as maintenance of sport and work activities (Ankle Activity Scale (AAS)).
As the use of biological adjuncts supplemental to bone marrow stimulation is gaining popularity in the orthopaedic field, but has not yet been proven in clinical trials that were controlled, it is of clinical importance to assess the efficacy of the use of BMAC supplemental to BMS versus BMS alone. Bone marrow stimulation alone will function as the control group in the present study as this has been the conventional surgical method for small talar osteochondral defects that are small of nature for the past decades. A control group of untreated patients with persisting and disabling complaints of a talar osteochondral defect cannot be justified as this impedes quality of life and may have serious consequences.
The control group of the present study will receive arthroscopic bone marrow stimulation. Additionally, from this group will receive a 2mm Jamashidi needle puncture over the iliac crest. From this needle puncture, bone marrow aspirate will be harvested. This will then be concentrated to check for the cell characterization. The concentrated bone marrow will however not be implanted into the osteochondral talar lesion. The reasoning behind this is that we can check whether the cell characterization (average cell count and concentration) of the control group is similar to the experimental arm of the present RCT. This, as the BMAC cells will be sent for characterization for Colony Forming Unit Cell counts in order to ensure that there are no discrepancies between the experimental group and the control group with regards to BMAC quality. Also, by these means, the control group will be blinded for BMAC harvesting by means of the same 2mm puncture wound, in order to increase internal validity of the study.
The experimental group will also receive arthroscopic treatment of the talar OCD through bone marrow stimulation. Additionally this group will receive a harvesting procedure of BMAC through a 2mm Jamashidi needle puncture wound over the iliac crest, in the exact same manner as in the control group. 1mL of BMAC obtained after spinning the bone marrow aspirate will be sent for CFU characterization in order to compare with the control group. The BMAC that is left after concentrating the aspirate will be implanted into the defect which has undergone bone marrow stimulation by the orthopaedic surgeon. An interim analysis will be conducted at 12 months postoperatively, in order to assess short-term and mid-term results.

**Intervention**

Both groups of patients are surgically treated with arthroscopic bone marrow stimulation (BMS). The control group will receive BMS alone but with a

sham-treatment consisting of a Jamashidi (bone marrow aspiration) needle puncture of the iliac crest. The aspirated bone marrow concentrate will be collected and sent for cell characterisation but will not be inserted in the talar OCD.
The intervention group will also receive arthroscopic BMS. From this group, BMAC from the iliac crest will be taken by the same needle puncture. Part of this concentrate will be sent for cell characterisation. Another part will be implanted into the talar OCD.

**Study burden and risks**

Patient burden is mainly caused by the pre and postoperative questionnaires that need to be filled out.Preoperatively and postoperatively patients will not visit the outpatient clinical more frequently than standard care concerning regular check-ups. The risk of the investigational treatment, that is BMS with supplemental BMAC is equal to the standard risks associated with the control group (BMS and sham stab incision) for this indication. Risks or complications associated with ankle arthroscopy in general can be bleeding, infection, venous thrombosis and damage to superficial nerves. Pre- and post-operative radiology are not considered risks or extra burdens as these are part of standard care.

# Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

• Patients with a symptomatic OCL of the talus who are scheduled for arthroscopic debridement and microfracture
• OCL depth and/or diameter <= 15 mm on computed tomography medial-lateral and/or anterior-posterior
• Age 18 years or older
• Intact remaining articular cartilage of the joint Kellgren-Lawrence stage 0-1

## Exclusion criteria

• Concomitant OCL of the tibia
• Ankle osteoarthritis grade 2 or 3
• Ankle fracture < 6 months before scheduled arthroscopy
• Inflammatory arthropathy (e.g Rheumatoid arthritis)
• History of (or current) hemopoeitic disease or immunotherapy
• Acute or chronic instability of the ankle
• Use of prescribed orthopaedic shoewear
• Other concomitant painful or disabling disease of the lower limb
• Pregnancy
• Implanted pacemaker
• Participation in previous trials < 1 year, in which the subject has been exposed to radiation (radiographs or CT)
• Patients who are unable to fill out questionnaires and cannot have them filled out
• No informed consent
• HIV positive or hepatitis B or C infection (based on the anamnesis of the patient)

# Study design

## Design

Study type: Interventional

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| Intervention model: | Other |
| Allocation: | Randomized controlled trial |
| Masking: | Single blinded (masking used) |
| Control: | Active |
| Primary purpose: | Diagnostic |

### Recruitment

NL

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|---|---|
| Recruitment status: | Pending |
| Start date (anticipated): | 01-09-2020 |
| Enrollment: | 72 |
| Type: | Anticipated |

### Medical products/devices used

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|---|---|
| Generic name: | Arthrex Angel System |
| Registration: | Yes - CE intended use |

## Ethics review

Approved WMO

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| Date: | 20-10-2020 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |

## Study registrations

### Followed up by the following (possibly more current) registration

No registrations found.

### Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
| --- | --- |
| CCMO | NL67715.018.19 |