# Bone Marrow Aspirate Concentrate for Bone Healing in Foot and Ankle Surgery

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**KEYWORDS**

• Bone marrow aspirate • Concentrate • BMAC • Cartilage • Bone

**KEY POINTS**

- Bone marrow aspirate concentrate (BMAC) contains mesenchymal stem cells, hematopoietic stem cells, other progenitor cells, bone morphogenetic proteins, and growth factors essential for bone healing.
- Strong animal evidence exists to support the use of BMAC for bone healing.
- Human data on the use of BMAC are promising but lack scientific rigor to validate its efficacy.

## INTRODUCTION

Arthrodesis remains the gold standard treatment of end-stage arthritis of the joints of the foot and ankle. Unfortunately, many patients have comorbidities that portend to an increase risk of nonunion, including smoking, diabetes, and avascular necrosis, among others. In various ways, all of these comorbidities compromise vascularity and, in turn, the delivery of nutrients and host reparative cells to the arthrodesis site. Attempting arthrodesis in these high-risk patients has led to nonunion rates as high as 40%, which can lead to persistent pain and debilitation.[1–4] Therefore, a need exists to find adjuncts to achieve union in foot and ankle arthrodesis procedures.

Autologous bone marrow aspirate concentrate (BMAC) has been successfully used for bone and soft-tissue healing.[5–8] The proposed benefit is the collection and transplantation of live cells and growth factors. BMAC contains mesenchymal stem cells (MSCs), hematopoietic stem cells (HSCs), endothelial progenitor cells, and other progenitor cells, in addition to growth factors, including bone morphogenetic proteins,

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platelet-derived growth factor, transforming growth factor-β, vascular endothelial growth factor, interleukin-8, and interleukin-1 receptor antagonist. It must be noted that the term *MSC* is not universally accepted and some investigators favor connective tissue progenitors (CTPs) or mesenchymal stromal cells (also MSCs).

Although unconcentrated bone marrow aspirate contains all of these same elements, concentration has been shown to significantly improve healing because a theoretic critical number of certain cellular elements, rather than the total cell count, has been shown to be more important.[9,10] Moreover, in foot and ankle surgeries, limited amounts of physical space exist for biologics implantation; therefore, concentration may be beneficial.

Both the MSCs and HSCs have the potential to differentiate into osteogenic progenitors. This differentiation can occur with the assistance of growth factors and induction proteins either locally (where the BMAC is transplanted to) or through these agents that are contained within the BMAC. Moreover, these cells have a paracrine effect to recruit additional host cells to the delivery site and enhance additional growth factor protein production in paracrine fashion.

Despite the theoretic advantages of BMAC, the level 1 clinical evidence for its use is minimal. In this article, the authors review the orthopedic literature and, more specifically, the foot and ankle literature for the use of BMAC for bone healing.

## ANIMAL EVIDENCE

Several animal studies exist demonstrating solid evidence for its use in aiding bone healing. Gianakos and colleagues[11] performed a review of all of the available evidence regarding long-bone healing in animals. They found overwhelmingly positive evidence for BMAC, with more than 35 articles included in that review. Of the studies reporting statistics, 100% showed a significant increase in bone formation in the BMAC groups compared with controls. Radiographic and micro–computed tomography (CT) imaging from these studies demonstrated a significant increase in bone volume, callus formation, woven bone formation, and union. Histology studies corroborated radiographic findings of significant or semiquantitative improvement in osteocyte number and bone formation.

However, the evidence is not always positive in favor of BMAC and seems to be less promising in metaphyseal defects. In a study of tibial metaphyseal bone healing in mini-pigs, Jungbluth and colleagues[12] compared the use of autograft, BMAC, and calcium phosphate. The BMAC group demonstrated significantly more bone formation compared with the calcium phosphate group, but the autograft group demonstrated significantly more bone formation than the BMAC group. Another study compared BMAC with platelet-rich plasma (PRP) on metaphyseal defects in rabbit tibiae.[13] CT and histomorphometry data demonstrated greater cortical bone and greater consolidation in the PRP group at 4 weeks.

## CLINICAL REPORTS

### *Non–Foot and Ankle Studies*

Several studies are reported describing use of BMAC for bone healing outside of the foot and ankle. Most of these studies have focused on osteonecrosis of the femoral head or tibia fracture nonunions.

Pepke and colleagues[14] performed a prospective randomized trial of 24 patients with osteonecrosis of the femoral head. Patients were randomized to core decompression only versus core decompression and BMAC. All patients were followed for 2 years after surgery. There was no significant difference in clinical outcome or femoral