Cartilage has a very poor potential for healing and therefore surgical management is often warranted to treat osteochondral defects. First line treatment for osteochondral defects may be divided into two broad categories; an attempt to repair the lesion (microfracture) or replace it with viable tissue (osteochondral graft). Despite promising short to medium term clinical results, healing of the defect as assessed by arthroscopy and MRI shows reason for concern.

**Reasons for Concern**

**Microfracture**:

- At second look arthroscopy only 30% showed lesions had integrated at 12 months post operatively. [1]
- On MRI at 5 years post-op, 64% show incomplete integration of repair tissue and 100% had cracks and fissing. [2]
- At 3 ½ year follow-up, 48% had fair/poor clinical results. [3]
- 35% deterioration in outcome scores in patients seen 5 years prior. [4]

**Osteochondral Autograft Transplant**:

- Poor graft integration observed in animal models at cartilaginous interface [5,6].
- 25% cell death at the graft periphery and cyst formation in up to 75% of patients on MRI [7]

These problems have led to the implementation of biological adjuncts in order to improve healing.

**Platelet-Rich Plasma – Establishing proof of concept in vitro**:

- Culturing porcine chondrocytes in 10% PRP resulted in increased proteoglycan and collagen synthesis, as well as DNA content compared to fetal bovine serum and PPP. [8]
- PRP increased production of hyaluronic acid and hepatocyte growth factor by synoviocytes excised from arthritic patients. [9]
- PRP also acts as an anti-inflammatory. Inhibits NF-kappaB through hepatocyte growth factor in human chondrocytes cultures in PRP. [10]
- In human chondrocytes cultured in IL-1 beta to stimulate osteoarthritic environment, PRP decreased IL-1 beta mediated inhibition of COL2A1 and ACAN gene expression. Additionally, reduced IL-1 beta induced increase of ADAMTS4 and PTGS2 gene expression. [11] Confirmed by additional study culturing chondrocytes in IL-1beta and TNF-alpha with collagen matrix enhanced PRP – showing increased condrogenesis, collagen type II deposition and inhibition of IL-1beta and TNF-alpha. [12]

**Platelet-Rich Plasma – Establishing proof of concept in vivo**:

- PRP treated PLGA scaffold improved osteochondral lesion healing in a rabbit model when compared to OCLs treated with a PLGA scaffold alone. [13]
• PRP + microfracture in a rabbit model showed improved cell distribution ICRS score, however other features did not reach statistical significance. [14]
• In a sheep model, PRP and PRP + fibrin as an adjunct to microfracture for osteochondral defects improved cartilage healing when compared to microfracture alone. [15]
• PRP + nanocomposite scaffold showed worse cartilage and bone regeneration compared to scaffold alone. [16]

Bone Marrow Aspirate Concentrate – Establishing proof of concept in vivo

• In an equine model, microfracture when combined with BMAC demonstrated improved healing on ICRS score and MRI with T2 mapping when compared to microfracture alone. [17]
• Microfracture + HA + BMAC showed improved healing compared to HA + microfracture and microfracture alone in a goat model. [18]
• In a prospective clinical study, talar OCLs were treated with BMAC + collagen/HA composite. Mean pre-op AOFAS scores were 64.4, compared to 91.4 post-op. MRI and 2nd look arthroscopy with biopsy (5 pts) showed integration of regenerative tissue. [19]

Platelet-Rich Plasma + Bone Marrow Aspirate Concentrate – Establishing proof of concept in vitro

• Human MSCs cultured in 10% PRP had increased levels of DNA compared to FBS control. TGF-Beta1 concentration was most closely associated with increased DNA levels. [20]
• Human MSCs progenitors derived from sub chondral bone were stimulated to migrate by PRP at any concentration. Osteogenic and adipogenic differentiation not present, while chondrogenic differentiation was present. Furthermore, PRP increased type II collagen matrix formation. Particularly relevant for microfracture. [21] Confirmed by further studies showing the PRP increases MSCs proliferation while maintaining their chondrogenic differentiating capacity. [22,23]
• Human MSCs cultured in PRP show increased proliferation and increased mRNA expression of osteogenic and chondrogenic markers. [24]

Our Results of Bone Marrow Aspirate Concentrate with Autologous Osteochondral Graft

• 72 patients with mean 28 months follow-up. MRI T2 Mapping closely resembles native relaxation times

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<th>Pre-Operative Score</th>
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Different Formulations of Platelet-Rich Plasma

• Depending on concentration system used, may produce leukocyte-rich PRP or leukocyte-poor PRP. [25]
• Even if using the same system, there is both inter-personal and intra-personal variability. [26,27]
Take Home Points

Biological augmentation shows promise in both *in vivo* and *in vitro* models by addressing not only the anabolic deficiency of an OCL but also the chronic inflammatory environment. Clinical evidence is now needed in order to further substantiate the use of biological augmentation. Furthermore, the details of treatment have to be outlined, including the most optimal formulations, quantity, and frequency of use.

References


