Is Microfracture a thing of the past?
Augmentation Approaches
“MFX 2.0”
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CONCACAF Medical Committee
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Team Physician US Soccer, LA Galaxy, Pepperdine University

Microfracture
Background

Microfracture Utilization:
• European Survey: Microfracture most frequent technique (76%)
• Microfracture most frequent treatment method in NFL (43%)

Cartilage Repair
Procedure Frequency
Cartilage Repair Algorithm

- **Cartilage Lesion**
  - Size < 2cm
    - Deep (>1cm)
  - Size > 2cm
    - Deep (>1cm)
    - Superficial

- **OATS/Mosaicoplasty**
- **Microfracture**
- **Chondrocyte Transplant**
- **OC-Allagraft ACT**
- **OATS/ACT**
- **Redo-AC**
- **ACT**
- **Arthroplasty**

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Microfracture

**Surgical Technique**

Hybrid Fibro-Hyaline Repair Tissue with Limited Col-II and Aggrecan Content

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Microfracture Clinical Efficacy

- **Microfracture Efficacy**
  - Improvement <2yrs: 75-100%
  - Improvement >2 yrs: 67-86%
  - Functional Deterioration: 47-80%
  - Improvement over Baseline at 10 yrs

Gudas AJSM 2012
Mithoefer AJSM 2009
Microfracture
Clinical Efficacy

Factors
Better Results with

Age
- <40 years old

Duration of Symptoms
- <12 Months

Lesion Size
- <3.4cm²

Body Mass Index
- <30kg/m²

Preoperative Activity Level
- Tegner Score >4

Prior Surgery
- Primary Microfracture

Repair Cartilage Volume
- Good Defect Fill (>66%)

Microfracture
Athletic Population

Microfracture
Systematic Review: 821 Athletes
67% Good/Excellent Results
KOOS Sports: 21 Pts
Tegner Increase in 76%
Score Decrease >2 yrs (42%)
Return to Sport 44-100% (2-16 mo)
Pre-injury Level 67% (50-100%)
Continued Sport at 2-10 years 49% (18-71%)

Return to Professional Sport: 67-100%
**Microfracture**
Decrease of Function

![Microfracture Decrease of Function Graph](image)

Kun, AJSM 2009-2011

**Fill Grade and Functional Score Decrease**

![Fill Grade and Functional Score Decrease Graph](image)

Blevins Orthopedics 1999
Mithoefer, JBJS 2005

**Microfracture MRI Findings**

- Complete Fill 18-95%
- Poor Fill 17-57%
- Complete Integration 4-8%
- Function Correlates with Fill

Mithoefer, JLG 2006
Kraus, Osteoarthritis Cartilage 2009
Mithoefer, AJSM 2009
Ramappa, J Knee Surg 2007
Microfracture
Complications/Failures

Failure/Revision
- <2 years  2.5%
- 2-10 years  2-38%
- Higher Failure Rate with:
  - Lower Repair Tissue Quality
  - Lower Repair Tissue Quantity
  - Smoking
  - Longer Duration of Symptoms
- 46% Kellgren Grade I at 10 yrs

Salman KESSA 2012
Sailer AJSM 2012
Mithoefer AJSM 2009

Microfracture
Revision

Effect on Revision:
- 2.5-Fold Increased Failure Rate for Second Procedure
  - Marrow Stimulation Techniques 26%
  - Microfracture 20%
  - Control 8%
- Marrow stimulation should be used only for correct indications

Mithoefer AJSM 2009
Jungermann AJSM 2012

Microfracture
Subchondral Bone Overgrowth

- Incidence: 33-45%
- Influencing Factors:
  1. Lesion Location
  2. Meniscal Status
  3. Surgical Technique
- Effect On Function?

Mithoefer ICRS 2012
Microfracture
Bone Overgrowth

Indications and Contraindications

**Indications**
- Grade 3-4 Defects
- Lesions ≤ 2 cm²
- Acute Lesions
- Age < 40 years
- Incidental Lesions
- No Prior Surgery

**Contraindications**
- Degenerative Defects
- Uncontained Lesions
- BMI > 30 kg/m²
- Defects > 2 cm²
- Multiple Defects
- Revision Surgery

Strengths and Weaknesses

**Strengths**
- Minimally Invasive
- Low Morbidity
- Technically Simple
- Cost Effective
- Short Rehabilitation
- Incidental Defects
- Fast Improvement

**Limitations**
- Fibro-Hyaline Repair
- Small Defects Only
- Unpredictable Fill
- Limited Integration
- Bone Overgrowth
- Decreasing Function
Microfracture Technique Modification

Microfracture “Sealing Effect”

Chen J Orthop Res 2009

Microfracture 2.0

Innovation

Drilling and Nanofracture

• Drilling:
  – No Bone Compaction
  – No Fracture
  – No Sealing Effect
  – Less Necrosis
• Nanofracture:
  – Deeper Marrow Access

MASS Technology 2.0

“The Only Constant is change”

Mesenchymal Augmentation Scaffold Stimulation

• Scaffold-Guided MSC-based Chondroinduction Techniques
• Applying novel tissue engineering techniques
to address limitations of 1st generation MFx
Microfracture Plus 2.0
Second Generation Technologies
Marrow Augmentations and Scaffold Stimulation (MASS)

- Clinical and Trials
  - AMIC (Collagen Matrix)
  - Biocartilage
  - BST CarGel (Chitosan)
  - PEG Hydrogel
    - CS Adhesive
    - Fibrinogen
    - PRP

BioCartilage™ Arthrex
Micronized Cartilage Matrix

- Does MFx “plus” work with allograft tissue? In vivo supportive evidence:
  - Medial femoral condyle defects created within a rabbit model
  - Control group = microfracture performed
  - Treatment group = MFx plus lyophilized cartilage fragments formed into a scaffold
  - Treatment group had persistent upregulation of cartilage phenotypic markers: Type II Collagen and Aggrecan

The Use of Micronized Allograft Articular Cartilage (BioCartilage) and Platelet Rich Plasma to Augment Marrow Stimulation in an Equine Model of Articular Cartilage Defects
Cole, Fortier et al 2015
Case Biocartilage
22 y/o female soccer player

Does the principle of MFx “plus” work?

- BST CarGel (Piramal Healthcare)
  - Chitosan based scaffold mixed with blood
    - Shrimp exoskeleton
  - Received CE mark approval April 2012
  - Conducting randomized pivotal trial in Canada

BST CarGel
Hoemann JBJS 2005
Strauss, Cartilage 2010

Chitosan + Blood

Gross – 6 months

Histo – 6 month

Novel Scaffold-Based BST-CarGel Treatment Results in Superior Cartilage Repair Compared with Microfracture in a Randomized Controlled Trial

William D. Safran, MB; Robert McCormack, MD; Reena Upreti, MD; Nicholas Malzey, MD; Robert Callahan, MD; JBJS

Objective: To determine whether novel scaffold treatments improved repair outcomes as compared with microfracture.

Methods: A total of 20 patients with a full-thickness cartilage defect in the knee were randomized to receive microfracture therapy or implantation of scaffold and autologous chondrocytes developed from a harvested minced cartilage. Repairs were retrieved at the time of arthroscopy at 9 months of follow-up and were assessed histologically.

Results: The scaffold group had significantly higher repair tissue quality compared with microfracture, and superior repair tissue quality compared with microfracture was associated with a significantly higher repair tissue repair area. There was no difference in repair tissue repair area between groups.

Conclusions: The scaffold and microfracture repair areas were comparable, and scaffold therapy resulted in significantly higher repair tissue quality than microfracture.

Level of Evidence: Therapeutic Level I. See Instructions for Authors for a complete description of levels of evidence.
Co-Primary Endpoint Met MRI:
Quantity of Repair Tissue by Lesion % Fill at 12 months

<table>
<thead>
<tr>
<th>Lesion % Fill</th>
<th>BST-CarGel</th>
<th>MFX</th>
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<td>92.81</td>
<td>p=0.0105</td>
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* Means adjusted for lesion volume+SE
BST-CarGel, n = 41; MFX, n= 37

MASS
Autologous Matrix Induced Chondrogenesis (AMIC®)

AMIC
- Single stage procedure
- Bilayer Membrane (Type I/III or II ovine Collagen)
- Facilitates cell migration and adhesion
- Stimulates Chondrogenic Differentiation
- Stabilizes MSC clot
- Fibrin Glue Fixation
- +/- PRP Augmentation
- High tensile strength
- Membrane resorbes

Gille KSSTA 2010
Pascarella KSSTA 2010
Gille Acta Orthop Trauma Surg 2013
Fuss 1999
MASS
Autologous Matrix Induced Chondrogenesis (AMIC®)

AMIC Results/Registry
• Increased repair tissue quantity
• No effect on repair tissue quality
• No effect on biomechanical properties
• Subchondral bone overgrowth

Gille KSSTA 2010
Pascarella KSSTA 2010
Gille Acta Orthop Trauma Surg 2013

MASS
PEG-Scaffold (Chondux®)

• Microfracture-Based (MSC)
• Chondroitin Sulfate Adhesive
• Liquid 3-D PEGDA-Hydrogel Scaffold

MASS
PEG-Scaffold (Chondux®)
MASS
PEG-Scaffold (Chondux®)

Advantages
- Adaptation to Defect Geometry
- Immediate Complete Defect Fill
- Adhesive—Integration ↑
- Ingrowth/Migration of MSC
- MSC Stimulation (↑GAG, ↓ Col 1)
- Stimulation of intact Chondrocytes
- Limitation of Fibroblast Growth

Clinical Results:
European Cohort Study (30 pts) vs Mfx (12 Mo):
- Improved Repair Cartilage Volume (MRI)
- Better T2 Relaxation Values
- Improved Histology (Hyaline-like)
- Improved Biomechanics
- 100% Integration grade 1-2
- No Bony Overgrowth

MASS
PEG-Fibrinogen (Gelrin C®)

Procedure
- One-step procedure (Microfracture)
- Injectable hydrogel conforms to defect
- UV-Polymerization in situ (90 sec)
- Chemotactic scaffold (cell invasion)

Advantages
- Off-the-shelf
- Minimally Invasive
- Applicable to all lesion geometries
- Immediate Implant Stability
- Tight integration
- Controlled biodegradation (enhancing)
EFFECTS OF PLATELET-RICH PLASMA ON TISSUE ENGINEERED CARTILAGE

Massimo Petrera*, MD - J. N. Amritha De Croos°, PhD - Jonathan Iu*, BSc - Mark Hurtig§, DVM - Rita A. Kandel°, MD - John S. Theodoropoulos*, MD

University of Toronto Orthopaedic Sports Medicine 
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§ Department of Biomedical Sciences, University of Guelph

Formation of Articular Cartilage in vitro

EFFECTS OF PLATELET-RICH PLASMA ON TISSUE ENGINEERED CARTILAGE

Intact cartilage layer and increased extracellular matrix in constructs cultured with 20% PRP

Samples cultured in Ham's F-12 supplemented with 20% PRP had significantly thicker tissue

Intact cartilage layer and increased extracellular matrix in constructs cultured with 20% PRP

Immunostaining: prevalence of type II collagen
Results

Mechanical testing

Tissue engineered cartilage cultured with 20% PRP showed superior compressive mechanical properties with an equilibrium modulus of 38.1±3.6 kPa versus 15.6±1.5 kPa for 20% PPP (p=0.0002) and 20.4±3.5 kPa for 20% FBS (p=0.007).

Biochemistry

Proteoglycan

Samples supplemented with 20% PRP had significantly higher GAG content (176.1±18.8 µg GAG/mg dry wt) compared to those supplemented with 20% FBS (112±10.6 µg GAG/mg dry wt, p=0.01) or 20% PPP (131.5±14.8 µg GAG/mg dry wt, p=0.11).

Conclusions

- The presence of PRP in the culture media enhances the in vitro formation of cartilage with increased ECM and greater compressive mechanical properties, while maintaining features of hyaline phenotype.
- This treatment may be a way to generate better tissue suitable to use for cartilage repair.
- Further study to evaluate this tissue in vivo is required.

Enhance reparative response of microfractures in the treatment of chondral defects of the knee: An experimental study in an animal model


- Repeated platelet concentrate injections 5 injections of ACP post microfracture macroscopically, histologically, and biomechanically superior to microfracture alone after 3, 6, and 12 months.
PRP improves healing of Microfracture of Articular Cartilage defect

- 36 pts
- 2 groups MFX vs MFX + 6 ACP injections
- WOMAC, Tegner, IKDC, Cincinnati score all significantly better of MFX+ACP
- No adverse events related to this application were noted during the procedure
- The results of our study showed that periodical intra-articular injections of autologous conditioned plasma after cartilage repair with microfracture improve cartilage regeneration and may prevent further degenerative changes

Microfracture

Conclusions
- Microfracture is effective first-line treatment of acute small articular cartilage defects in young patients in short term.
- Limited repair tissue quality, quantity, and integration and subchondral bone changes may limit durability and success of 2nd repair procedures
- Correct indications for microfracture help to optimize outcome after articular cartilage repair
- 2nd Generation MASS Technology seems to improve prior limitations and outcome 2.0

Microfracture Improvement

Augmentation Strategies
- Hyaluronic Acid Injection
- PRP
- Growth Factor Augmentation
  - Factors: BMP-2, BMP-7, BMP-4, FGF-18, IGF-1
  - Stimulation of: MSC Differentiation, Proliferation, Metabolism
- Cytokine Modulation
  - IL-1Ra + IGF-1
  - Inhibition of Inflammatory Response