Is Microfracture a thing of the past?
Augmentation Approaches
"MFX 2.0"

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KERLAN-JOBE INSTITUTE

Microfracture

Background

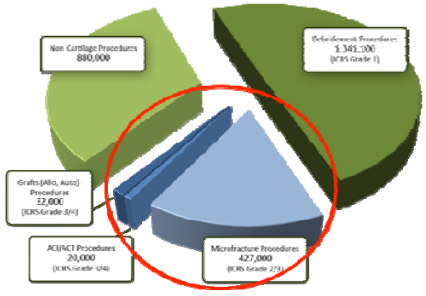
Microfracture Utilization:

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

Salzmann, Arch Orthop Trauma Surg 2010
Brophy J Knee Surg 2009

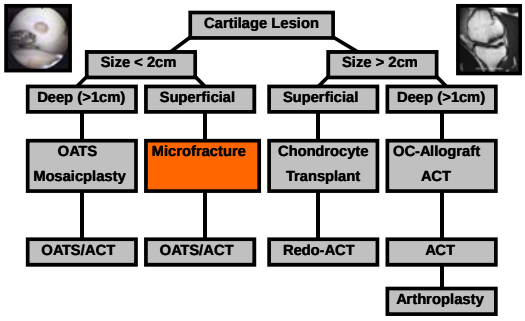
Cartilage Repair

Procedure Frequency



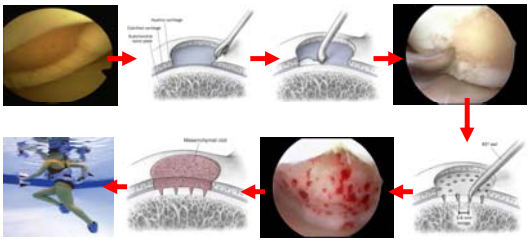
Life Science Intelligence Market Report, 2009

Cartilage Repair Algorithm



Microfracture

Surgical Technique



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

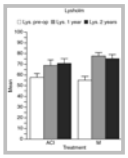
Microfracture

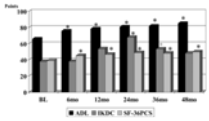
Clinical Efficacy

Gudas AJSM 2012
Mithoefer, AJSM 2009

Microfracture Efficacy

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





Microfracture

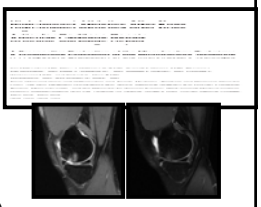
Clinical Efficacy

Factors	Better Results with
Age	• **<40 years old**
Duration of Symptoms	• **<12 Months**
Lesion Size	• **<2-4cm²**
Body Mass Index	• **< 30kg/m²**
Preoperative Activity Level	• **Tegner Score >4**
Prior Surgery	• **Primary Microfracture**
Repair Cartilage Volume	• **Good Defect Fill (>66%)**

Mithoefer, AJSM 2009

Microfracture

Athletic Population



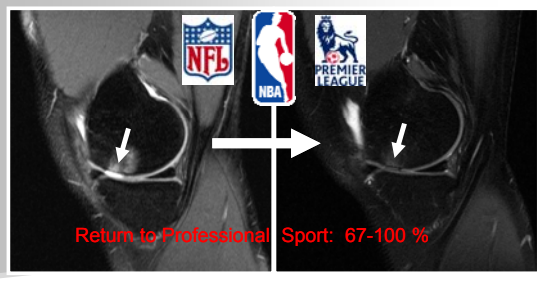
Microfracture

- 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%)**

Mithoefer Cartilage 2010
Namdari AJSM 2009
Riyami, J Ortho Surg Res 2009
Gobbi KSSTA 2006
Mithoefer AJSM 2006
Gudas, Arthroscopy 2005
Steadman J Knee Surg 2003
Blevins Orthopedics 1999

Microfracture

Athletic Population

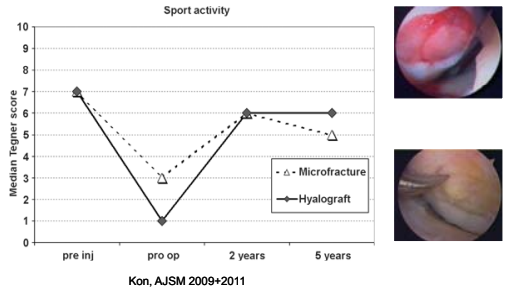


Mithoefer and Steadman, *Cartilage* 2012
Namdari, AJSM 2009

Steadman, J Knee Surg 2003
Riyami, J Othop Surg Res 2009

Microfracture

Decrease of Function

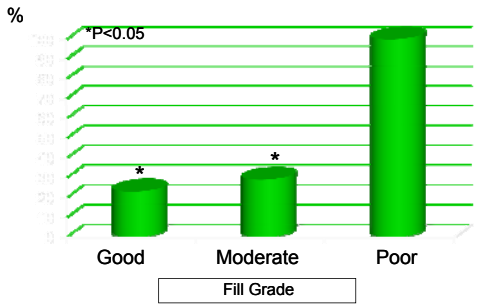


Kon, AJSM 2009+2011

Microfracture

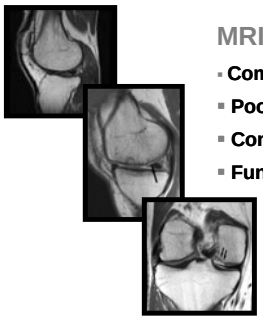
Blevins *Orthopedics* 1999
Mithoefer *JBJS* 2005

Fill Grade and Functional Score Decrease



Microfracture

MRI Findings



MRI Results

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

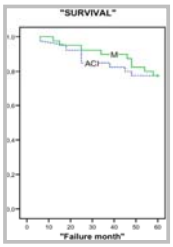
Mithoefer *JBJS* 2005
Kreuz, Osteoarthritis Cartilage 2006
Mithoefer, AJSM 2009
Ramappa, J Knee Surg 2007

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
- **48% Kellgren Grade I at 10 yrs**



Salzmann KSSTA 2012
Gudas AJSM 2012
Mithoefer, AJSM 2009

Microfracture

Revision

Effect on Revision:

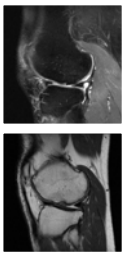
- **2.5-Fold Increased Failure Rate for Second Procedure**
  - Marrow Stimulation Techniques 26%
  - Microfracture 20%
  - Control 8%
- Marrow stimulation should be used only for correct indications

Minas AJSM 2009
Jungermann AJSM 2012

Microfracture

Subchondral Bone Overgrowth

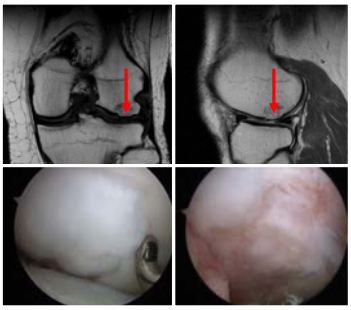
- Incidence: 33-45%
- Influencing Factors:
  1. Lesion Location
  2. Meniscal Status
  3. Surgical Technique
- Effect On Function ?



Mithoefer ICRS 2012

Microfracture

Bone Overgrowth



Microfracture

Indications and Contraindications

Indications

Grade 3-4 Defects
Lesions ≤ 2 cm^2
Acute Lesions
Age < 40 years
Incidental Lesions
No Prior Surgery

Contraindications

Degenerative Defects
Uncontained Lesions
BMI> 30 kg/m^2
Defects > 2 cm^2
Multiple Defects
Revision Surgery

Microfracture

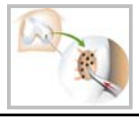
Strengths and Weaknesses

Strengths

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

Limitations

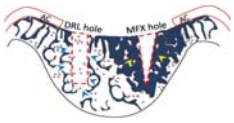
Fibro-Hyaline Repair
Small Defects Only
Unpredictable Fill
Limited Integration
Bone Overgrowth
Decreasing Function

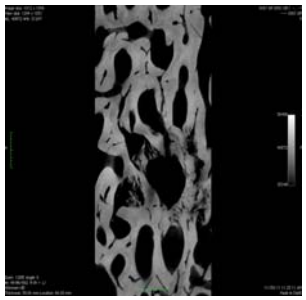


Microfracture
Technique Modification

Microfracture "Sealing Effect"

Chen J Orthop Res 2009

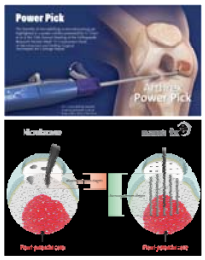




Microfracture 2.0
Innovation

Drilling and Nanofracture

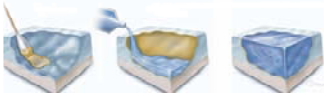
- Drilling:
  - No Bone Compaction
  - No Fracture
  - No Sealing Effect
  - Less Necrosis
- Nanofracture:
  - Deeper Marrow Access



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

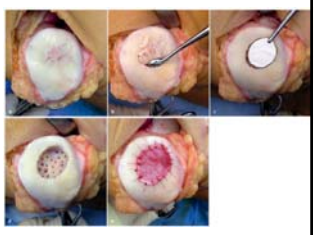


Microfracture Plus 2.0

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

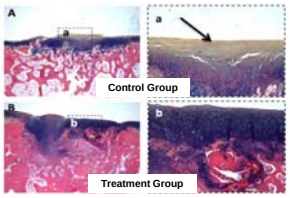


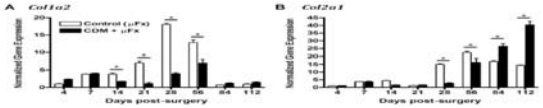
BioCartilage™ Arthrex

Micronized Cartilage Matrix

Chadha N et al. Porous Cartilage-Derived Matrix Scaffolds for Repair of Articular Cartilage Defects. ORS 2012; Poster No. 0735.

- **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 fagments formed into a scaffold**
  - **Treatment group had persistent upregulation of cartilage phenotypic markers: Type II Collagen and Aggrecan**

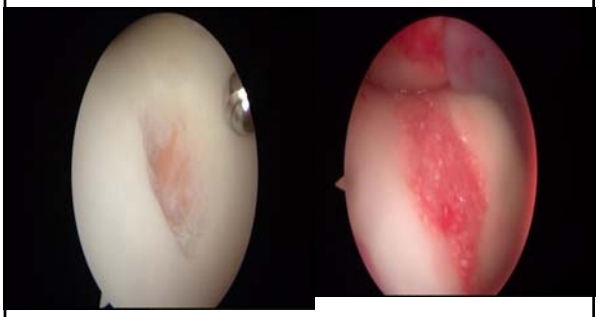




The Use of Micronized Allograft Articular Cartilage (BioCartilage) and Platelet Rich Plasma to Augment Marrow Stimulation in an Equine Model of Articular Cartilage Defects

Cole, Fortier et al 2015

Case Biocartilage
22 y/o female soccer player



BST CarGel

Hoemann JBJS 2005
Strauss, Cartilage 2010

- 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

JBJS

1640

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

William D. Stanish, MD, Robert McCormack, MD, Francisco Forriol, MD, Nicholas Mohtadi, MD, Stéphane Pelet, MD, PhD, Jacques Desnoyers, MD, Alberto Restrepo, MD, and Matthew S. Shive, PhD

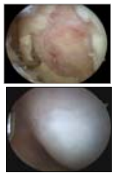
Investigation performed at twenty-six clinical sites in Canada, Spain, and South Korea

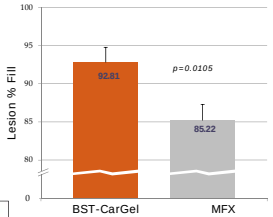
Conclusions: At twelve months, BST-CarGel treatment resulted in greater lesion filling and superior repair tissue quality compared with microfracture treatment alone. Clinical benefit was equivalent between groups at twelve months, and safety was similar.

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





JB&JS

* Means adjusted for lesion volume+SE
BST-CarGel®; n = 41; MFX, n= 37

MASS

Autologous Matrix Induced Chondrogenesis (AMIC®)

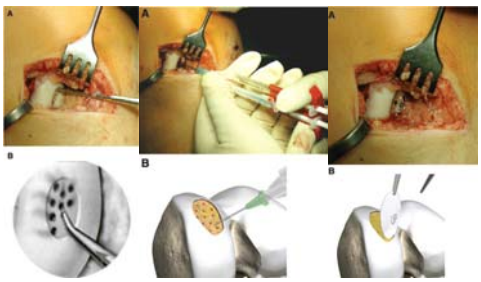
AMIC

- 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®)



MASS

Autologous Matrix Induced Chondrogenesis (AMIC®)

AMIC Results/Registry

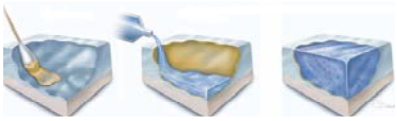
- Increased repair tissue quantity
- No effect on repair tissue quality
- No effect on biomechanical properties
- Subchondral bone overgrowth

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

MASS

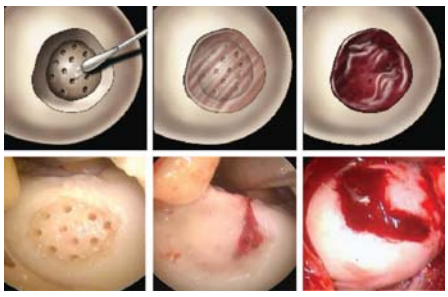
PEG-Scaffold (Chondux®)

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



MASS

PEG-Scaffold (Chondux®)

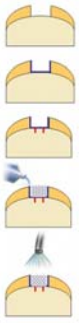


MASS

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



MASS

PEG-Scaffold (Chondux®)

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)

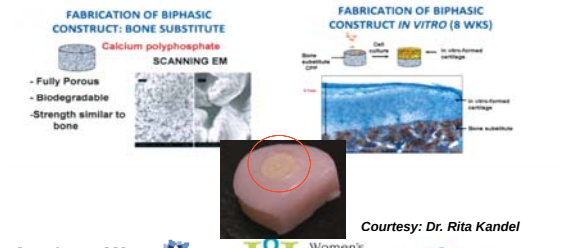
EFFECTS OF PLATELET-RICH PLASMA ON TISSUE ENGINEERED CARTILAGE

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
° Department of Pathology and Laboratory Medicine, CIHR-Bio Engineering of Skeletal Tissues Team, Mount Sinai Hospital, University of Toronto
§ Department of Biomedical Sciences, University of Guelph

EFFECTS OF PLATELET-RICH PLASMA ON TISSUE ENGINEERED CARTILAGE

Formation of Articular Cartilage *in vitro*



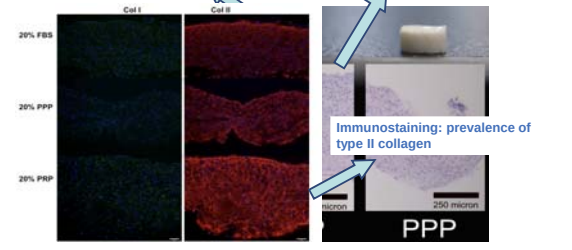
Courtesy: Dr. Rita Kandel

EFFECTS OF PLATELET-RICH PLASMA ON TISSUE ENGINEERED CARTILAGE

Results

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



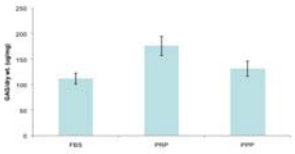
EFFECTS OF PLATELET-RICH PLASMA ON TISSUE ENGINEERED CARTILAGE

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±1.5kPa for 20% PPP (p=0.0002) and 20.4±3.5 kPa for 20% FBS (p=0.007)**

Biochemistry - Proteoglican



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

EFFECTS OF PLATELET-RICH PLASMA ON TISSUE ENGINEERED CARTILAGE

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

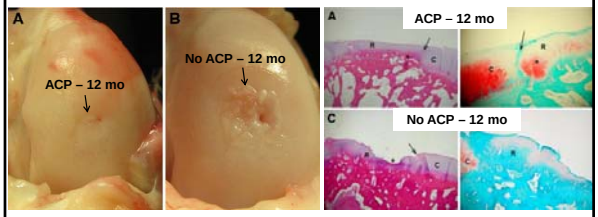
Women's College Hospital

University of Toronto Orthopaedic Sports Medicine

Enhance reparative response of microfractures in the treatment of chondral defects of the knee: An experimental study in an animal model
Milano et al. Arthroscopy. 2012.

ARTHROSCOPY
THE JOURNAL OF ARTHROSCOPIC AND RELATED SURGERY

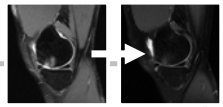
- Repeated platelet concentrate injections 5 injections of ACP post microfx: macroscopically, histologically, and biomechanically superior to microfx alone after 3, 6, and 12 months



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-Ira + IGF-1
  - Inhibition of Inflammatory Response

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