Marrow (MSC) Stimulation Techniques:
Microfracture/Microfracture Plus/Cartiform

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Cartilage Repair

Marrow Stimulation Procedure Frequency

- Non-Cartilage Procedures: 880,000
- Debridement Procedures: 1,341,100 (ICRS Grade 1)
- Grafts (Allo, Auto) Procedures: 32,000 (ICRS Grade 3/4)
- ACI/ACT Procedures: 20,000 (ICRS Grade 3/4)
- Microfracture Procedures: 427,000 (ICRS Grade 2/3)
Cartilage Repair Algorithm

Cartilage Lesion

Size < 3cm
- Deep (>1cm)
  - OATS
  - Mosaicplasty
- Superficial

Size > 3cm
- Superficial
  - Microfracture
- Deep (>1cm)
  - MACI
  - CACI
  - OC-Allograft
  - MACI
Cartilage Repair Algorithm

Cartilage Lesion

Size < 3cm
- Deep (>1cm)
  - OATS
  - Mosaicplasty
  - Synthetics +/- MSC
- Superficial
  - Microfracture
  - 2nd Gen Mfx
  - MSC
  - DeNovo

Size > 3cm
- Superficial
  - MACI
  - CACI
  - 4th Gen ACI
  - MASS
  - De Novo
- Deep (>1cm)
  - OC-Allograft
  - MACI
  - 4th Gen ACI
  - Synthetics
Microfracture

Steadman, *Operat Tech Orthop* 1997
Mithoefer and Steadman, *Tech Knee Surg* 2006
Microfracture
Repair Tissue

Microfracture

- Increased Repair Cartilage Volume
- Fibro-Hyaline Repair Cartilage Tissue
- Limited Type II Collagen Content
- Limited Aggrecan Content
**Microfracture**

**Clinical Results**

Review of 28 studies (3122 patients):

- Improvement <2yrs 75-100%
- Improvement >2 yrs 67-86%
- Functional Deterioration 47-80%

Limited Data on Patellofemoral Lesions
## Microfracture Outcomes

<table>
<thead>
<tr>
<th>Factors</th>
<th>Better Results With</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&lt; 40 Years</td>
</tr>
<tr>
<td>Duration of Symptoms</td>
<td>&lt;12 Months</td>
</tr>
<tr>
<td>Lesion Size</td>
<td>&lt;4cm²</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>&lt; 30kg/m²</td>
</tr>
<tr>
<td>Preoperative Activity Level</td>
<td>Tegner Score &gt;4</td>
</tr>
<tr>
<td>Prior Surgery</td>
<td>Primary Microfracture</td>
</tr>
<tr>
<td>Repair Cartilage Volume</td>
<td>Good Defect Fill (&gt;66%)</td>
</tr>
</tbody>
</table>

Mithoefer, AJSM 2009
Articular Cartilage Repair

Treatment Option - Microfracture

Return to Professional Sport: 67-100 %

Mithoefer and Steadman, Cartilage 2012
Steadman, J Knee Surg 2003
Return to Sport

Microfracture NBA-Study

- Professional Athletes
- 67% Full Return
- Return at 6-7 Months
- Limited Playing Time
- Lower Performance
- 17% Return < 2 Seasons
- 33% No Return (>30 years)
Microfracture

Athletic Population

- 7.5-15 years F/U
- Best results:
  - Defect Size < 2cm
  - Age <30 years
- Return to Sport 60-80%
- Same Level > 5yrs: 20-37%
- Failure rate 11-38%
- Decreasing Function after 2 years
- OA progression in 40-48%
  - Older patients, Large/Multple lesions

Gobbi KSSTA 2014
Mithoefer Cartilage 2010
Microfracture

Decrease of Function
Microfracture

MRI Findings

MRI Results

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

References:
- Mithoefer JBJS 2005
- Kreuz, Osteoarthritis Cartilage 2006
- Mithoefer, AJSM 2009
- Ramappa, J Knee Surg 2007
Microfracture
Fill Grade and Functional Score Decrease

*P<0.05

Fill Grade

Good
Moderate
Poor

Fill Grade
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

- Results at 10 years above Baseline
- 48% OA at 15 yrs

Knutsen JBJS 2016
Salzmann KSSTA 2012
Mithoefer AJSM 2009
Microfracture

Preop

6 months postop
Microfracture

Preop

6 months postop
Microfracture

Preop  6 months postop
Microfracture
Second Look

10 Months
Microfracture
Bone Overgrowth
Microfracture

Subchondral Bone Overgrowth

- Incidence: 63%

- Influencing Factors:
  1. Lesion Location
  2. BMI
  3. Surgical Technique

- Increased Failure Rate
  - 25% vs. 3%

Mithoefer AJSM 2016
Marrow Stimulation Complications:

- 2-7 Fold Higher Failure Rate for 2nd ACI
  - Marrow Stimulation Techniques 26%
  - Microfracture 20-25%
  - Control 4-8%

- Marrow stimulation should be used only for correct indications
Microfracture
Technique Modification

Microfracture Awl: “Sealing Effect”
Microfracture
Technique Evolution

Better Repair/MSC Recruitment

- Deeper marrow access
- Smaller awl diameter
- Microdrilling
- ↑ Number of Perforations

Zedde Joints 2016
Microfracture
Technical Evolution

Drilling and Nanofracture

- Drilling:
  - No Bone Compaction
  - No Fracture
  - No Sealing Effect
  - Less Necrosis

- Nanofracture:
  - Deeper Marrow Access
Microfracture Plus
Augmentation Strategies

Biologic Augmentation

- Hyaluronic Acid Injection
- LpPRP
- Growth Factor Augmentation
  - BMP-7
  - BMP-4
  - FGF-18
  - IGF-1
- Cytokine Modulation
MASS Technologies

Mesenchymal Augmentation Scaffold Stimulation

- Scaffold-Guided MSC-based Chondroinduction Techniques
- Applying novel tissue engineering techniques to address limitations of 1st generation MFx
Scaffold Augmentation (MASS)

- **Collagen Membrane**
  - Type I/III or Atelocollagen

- **Chitosan/Hydrogel**

- **Micronized Allograft (Chondrons)**
  - Chemotactic (MSC Recruitment)
  - MSC Differentiation
  - Clot Stabilization
  - Proanabolic Effect

- **Improved Quality/Quantity**
MASS
Autologous Matrix Induced Chondrogenesis (AMIC®)

(N)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

Gao AJSM 2019
Gille KSSTA 2010
Pascarella KSSTA 2010
Gille Acta Orthop Trauma Surg 2013
MASS
Autologous Matrix Induced Chondrogenesis (AMIC®)
AMIC Results (Registry/Systematic Review)

- Increased repair tissue quantity
- No effect on repair tissue quality
- No effect on biomechanical properties
- Subchondral bone effect
- Better 5-year Durability than Mfx (RCT)

Gao AJSM 2019
Volz Int J Orthop 2017
Anders Open J Orthop 2013
Pascarella KSSTA 2010
Gille Acta Orthop Trauma Surg 2013
Lee Cartilage 2014
MASS
Chitosan Scaffold (CarGel®)

- Chitosan (D-Glucosamin Polysaccharide)
- 3-D injectable liquid scaffold
- Increases chondrogenic differentiation
- Arthroscopic and mini-open technique
- Randomized Trial: ↑Fill and Quality
- Clinical Outcome similar at 60 Mo
- Modification with BMAC

Snow Cartilage 2018
Steinwachs Knee 2018
Method Cartilage 2016
Hoemann AJSM 2015
Stanish, JBJS 2013
Shive Cartilage 2015
MASS
BioCartilage® Scaffold

- Micronized allograft matrix (100-300 μm)
- Off the shelf (Shelf Life: 5-yrs), Low cost
- Porous, cartilage-derived scaffold (Col2, PGA), +/- PRP
- Promotes chondrogenic differentiation
- Minimally invasive technique
- Experimental: Hyaline-like cartilage
- Limited clinical data, Postmarket study

Shin Arthrosc Tech 2014
Hirohara Sports Med Arthrosc 2015
MASS
Biocartilage-Arthroscopic Implantation

Repair Cartilage Tissue
- ↑↑↑Histologic Quality
- ↑↑↑Tissue Volume

Fortier AJSM 2016
Carter JCOT 2018
5 years postop
MASS

Biocartilage: Tibial Defects

Wang Arthosc Tech 2017
**Chondral Allograft+Mfx**

**Cartiform**

**Combination Techniques**

- Perforated allograft cartilage
- Principle: Chondrons + MSC
  - Viable Cells
  - Chondrogenic Effect (TGF-β, IGF, BMPs)
- Basic Science Data, Case reports

Fortier 2011
Bekkers 2013
Woodmass 2017
Chondral Allograft and Mfx

Cartiform

- Postop MRI: 6 Months
Marrow Stimulation: BMAC

Autologous Bone Marrow Aspirate (MSC):

- MSC outperform Chondrocytes on extracellular matrix-derived scaffolds
- MSC Effects:
  - Progenitor Cell
  - Growth Factors
  - Anti-Inflammatory Effect
- Experimental Studies:
  - BMAC > MF
MSC: BMAC

Clinical Results:
- Significant Knee Function Score Improvement
- Better < 45 Years, Small, isolated defects
- Results comparable to MACI
- MRI 80% Complete Fill
- Hyaline Like Histology

Gobbi AJSM 2014
Gobbi KSSTA 2016
**Cartilage Resurfacing**

**Simultaneous Knee Pathology**

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**Coexisting Knee Pathology**

- **Importance of Correcting Pathology**
  - Malalignment
  - Meniscus Tear
  - Meniscal Deficiency
  - Maltracking Patella
  - Ligament Instability

- **Simultaneous or Staged**
- **No Negative Effect on Outcome/Return**

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Salzmann, AJSM 2016
Mithoefer AJSM 2005
Peterson AJSM 2002
Cartilage Rehabilitation

Rehabilitation Progress

- Technique-Specific
- Athlete-Specific
- Sport-Specific
- Accelerated Loading
- Phased Progression
- Biology-Based
- Neuromuscular Recovery
- Blood Flow Restriction

Mithoefer JOSPT 2012
Della Villa AJSM 2010
Schmitt JOSPT 2014
Wondrasch AJSM 2015
Summary

Conclusion

- Microfracture is effective first-line treatment of acute small articular cartilage defects in young patients.
- Limited repair tissue quality, quantity, and integration and subchondral bone changes may limit durability and success of 2nd repair procedures.
- Technique and Biological Innovation → 2nd Generation MASS can help to improve prior limitations and outcomes and may extend indications.