Emerging Options for Cartilage Repair

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Articular Cartilage Injury

Epidemiology

Athletic Cartilage Injury

- Prevalence:
  - Athletes 36%
  - General Population 16%
- 86% of Athletic Cartilage Injury Symptomatic

Associated Injuries:
- Meniscus tear: 47%
- ACL Tear: 30%
- Collateral Ligament Tear: 14%

Flanigan, Med Sci Sports Exerc 2010

Articular Cartilage Injury

Natural History

Untreated Cartilage Defects in Athletes

- 75% Initial Return to Sports
- Significant Reduction at 12-15 years
- Decline in Competitive Sports
- Decline in Team Sports
- Decreased Pivoting Sports and Jogging
- Limitation of Lifestyle in 41-90%
- Swelling and Pain
- 57-80% Radiographic Signs of OA

Heir AJSM 2010

Cartilage Repair Algorithm

Cartilage Repair Procedure

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

Microfracture Efficacy
- Gudas AJSM 2012
- Mithoefer, AJSM 2009

Cartilage Repair Procedure Frequency

Life Science Intelligence Market Report, 2009
Microfracture

MRI Findings

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

Microfracture

Complications/ Failures

Failure/Revision
- <2 years 2.5%
- 2-10 years 238%
- Higher Failure Rate with:
  - Lower Repair Tissue Quality
  - Lower Repair Tissue Quantity
  - Smoking
  - Longer Duration of Symptoms
- 45% Kiellgren Grade I at 10 yrs

Microfracture

Decrease of Function

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

Microfracture

Fill Grade and Functional Score Decrease

Fill Grade
Good
Moderate
Poor

P<0.05

Microfracture

Complications/Failures

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• <2 years 2.5%
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Microfracture

Subchondral Bone Overgrowth
- Incidence: 63%
- Influencing Factors:
  1. Lesion Location
  2. BMI
  3. Surgical Technique
- Increased Failure Rate
  • 25% vs. 3%
Microfracture Technique Modification

Microfracture Awl: “Sealing Effect”

Microfracture Innovation

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

MASS Technology

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

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

AMIC Results (Registry/Systematic Review)
- Increased repair tissue quantity
- No effect on repair tissue quality
- No effect on biomechanical properties
- Subchondral bone overgrowth
- Clinical Results similar to (M)ACI
- Better Durability

MASS
Autologous Matrix Induced Chondrogenesis (AMIC®)
MASS Chitosan Scaffold (BST-CarGel®)

- Chitosan (D-Glucosamin Polysaccharide)
- 3-D injectable liquid scaffold
- Increases chondrogenic differentiation
- Basic Science: ↑Fill and Quality
- Increased Type 2 collagen and GAG content
- Arthroscopic and mini-open technique

Hoemann JBU 2005
Strauss, Cartilage 2010

MASS Chitosan-Scaffold (BST-CarGel®)

Randomized Multicenter Trial (80 pts)
- Control Microfracture
- Results at 60 months
- Improved Repair Cartilage Volume
- Better ICRS Histology Scores (P<0.05)
- Better T2 Mapping values
- Similar Clinical Outcomes

Stanish, JBU 2013
Shive, Cartilage 2015

MASS Biocartilage

- Arthroscopic Implantation

Shin Arthrosc Tech 2014
Hirohara Sports Med Arthrosc 2015

MASS Biocartilage

- Arthroscopic Implantation

Chondral Allograft+Mfx

Combination Techniques
- 2 cm perforated allograft cartilage
- Combined with Microfracture
- Principle: Chondrons + MSC
- Viable Cells
- Chondrogenic Effect (TGF-β, IGF, BMPs)
- Minimally Invasive Technique
- Single-step Procedure
- 2-year shelf life

Fortier 2011
Bekkers 2013

Chondral Allograft+MSC

Cartiform
Osteochondral Autograft

Repair Techniques
Mosaicplasty

Clinical Results
- Hyaline Cartilage
- Fibrocartilage Fill of Donor Site
- Donor Site Morbidity 3-36%
- Hemarthrosis up to 30%
- Limited Plug availability
- Good/Excellent Results 79-92%
- Good durability 10-20 yrs
- Short Rehabilitation

Biphasic-Scaffolds
Trufit®/Porous Tissue Matrix ™

Clinical Results:
- Knee Function Scores ↑
- Return to Sport worse than OATS
- Limitations:
  - Fibro-Hyaline repair tissue
  - Slow Incorporation/Bone restoration
  - Persistent Effusion
  - 20% Revision Rate
  - 70% Failure Patella
  - BMAC Augmentation !

Osteochondral Allograft

Results:
- Survival: 96%(5y)→82%(10y)→74%(15y)→66%(20y)
- Return to sport 76%
- Reoperations 47%
- Limited Fresh Graft Availability
- Bony Incorporation: Shell Grafts
- Better Long-Term Outcome:
  - Unipolar Lesions
  - Age <30yrs

Osteochondral Allograft

Chondrofix
- Limited Fresh Allograft
- Human OC-Allograft
- Decellularized, Sterile
- Off Shelf Use
- Intact Mechanical Properties
- Early Loading
- Failure Rate 72% at 2 years !!

Carmont A 2009
Hindle 2013
Bekkers 2013
Joshi 2012
Krych 2015

BMAC Augmentation!
**Biomimetic OC-Scaffold**
- 3 Layers: (type1 Col —Mg-Hydroxyapatite)
- One step, Off shelf
- Biointegration+ OC-Restoration
- 2-5yrs: Scores↑, 70% Integration, 78% Fill

**Chondral Allograft**
- Juvenile Minced Cartilage
- Single Stage/Off Shelf
- Superior Cell Activity
- 100x Faster Matrix Production
- Femur and Patellar Defects
- KOOS improvement @ 2 years
- MRI-T2 similar to normal cartilage
- Fibrohyaline Tissue, High Col-II
- 30% Overgrowth
- Graft Delamination

**Autologous Chondrocyte Transplantation**
- Juvenile Minced Cartilage
- Single Stage/Off Shelf
- Superior Cell Activity
- 100x Faster Matrix Production
- Femur and Patellar Defects
- KOOS improvement @ 2 years
- MRI-T2 similar to normal cartilage
- Fibrohyaline Tissue, High Col-II
- 30% Overgrowth
- Graft Delamination

**Autologous Cell Implantation**
- Clinical Results
  - Functional Improvement 67-96%
    - Adolescents 96-100%
    - Age > 45 Years 78%
    - Femoral Condyle 80-82%
    - Trochlea/Patella 67-92% *
    - OCD Lesions 89-91%
    - Athletes 66-96%
    - Salvage Procedure 76-80%
  - * Improved results with Fulkerson Osteotomy

**Autologous Chondrocytes**
- Failure Rate
  - Primary ACI
  - After Previous Failed Procedure

**Chondrocyte Implantation Complications**
- Hypertrophy
- Limited Integration
- Limited Fill
- Delamination
Autologous Cell Transplantation

- **ACI**: Autologous Chondrocytes and Periosteum
- **CACI**: Autologous Chondrocytes and Collagen Membrane
- **MACI**: Matrix Seeded Autologous Chondrocyte Implantation

### Complications

<table>
<thead>
<tr>
<th></th>
<th>ACI</th>
<th>CACI</th>
<th>MACI</th>
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<tbody>
<tr>
<td>Hypertrophy</td>
<td>26%</td>
<td>5%</td>
<td>5%</td>
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<tr>
<td>Delamination</td>
<td>8%</td>
<td>3%</td>
<td>5%</td>
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<tr>
<td>Limited Integration</td>
<td>0%</td>
<td>4%</td>
<td>5%</td>
</tr>
<tr>
<td>Limited Neocartilage</td>
<td>4%</td>
<td>2%</td>
<td>4%</td>
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<tr>
<td>Revision Rate</td>
<td>25%</td>
<td>12%</td>
<td>15%</td>
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**Gomoll, AJSM 2009**

**Complications**

**ACI/CACI/MACI**

**Niemeyer, AJSM 2008**

**4th Generation Technique**

**NeoCartilage Implantation**

1. 2-Stage Autologous Technique
2. Cell 3D Culture on Collagen Matrix
3. Implantation of Cartilage Disk
4. Clinical Results up to 60 Months
5. Phase II-RCT
6. Better Response than Mfx

**Fortier, JBJS 2010**

**Stem Cells**

**Stem Cells: BMAC**

- MSC Effects:
  - Progenitor Cell
  - Growth Factors
  - Anti-Inflammatory Effect

- Experimental Studies:
  - BMAC > MF
Stem Cells: 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

Stem Cells: Allogenic

Cartilage Rehabilitation

Rehabilitation Progress
- Technique-Specific
- Athlete-Specific
- Sport-Specific
- Accelerated Loading
- Phased Progression
- Biology-Based
- Neuromuscular Recovery

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

Summary

Emerging Cartilage Technologies
- High Clinical Demand
- Further Clinical Improvement Needed
- Extensive Scientific Growth
- Evolving Cartilage Restoration Technologies
- Increasing Cartilage Quality+Quantity
- Promise for Further Clinical Improvement

Future of Cartilage Repair

Thank You!