Articular Cartilage Lesions: Current Treatment Options

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Cartilage Transplantation

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Case Example

- 22 y/o female s/p lateral meniscectomy

Articular Cartilage

• “troublesome thing and once destroyed, it is not repaired”
  Hunter W. On the structure and diseases of articulating cartilage, 1743

Articular Cartilage

- Highly organized, complex structure and function
- Decreases impact of mechanical load
- Decreases friction
- Degeneration leads to pain, loss of motion → arthritis

Immunohistochemical Section Through the Joint

Articular Cartilage

- Poor Capacity for Intrinsic Repair
  - Avascular
    - Lacks inflammatory phase
  - Chondrocytes protected in a thick extracellular matrix
  - Chondrocytes unable to migrate from uninjured matrix to zone of injury
Causes of Chondral Injury

• Cyclic loading > 25 N/mm²
• Direct blow causing > 40% strain
• Twisting injury e.g. ACL tear
  – Chondral delamination
  – “Bone bruises” not all benign!
• Repetitive microtrauma in skeletally immature
  – Osteochondritis Dissecans
• Trauma

Symptoms of Chondral Injury

• Pain with weight bearing / activities
  – No pain unless subchondral bone involved
• Mechanical symptoms
  – Locking, catching, grinding
• Swelling

Prevalence of Chondral Injuries

• Review of 31,516 knee arthroscopies
  – Grade III Lesions → 41%
  – Grade IV lesions → 19.2%
  – Grade IV, in pts < 40 years old → 5%
  [Curl (Arthroscopy, 1997)]
• Review of 1,000 knee arthroscopies
  – Isolated Grade III or IV defects > 1 cm² in pts < 40 → 5.6%
  [Hjelle (Arthroscopy, 2002)]

Goals of Cartilage Repair

• Restore articular cartilage surface
• Match biochemical and biomechanical properties of normal hyaline cartilage
• Improve symptoms and function
• Prevent or slow progression of focal chondral injury to end stage arthritis

Decision Making Options Overlap

• Patient-specific variables
  – Age
  – Demand level
  – Response to previous tx
  – Patient preference
    • Auto vs Allograft tissue
• Malalignment
  • Corrective osteotomy
• Post-menisectomy
  • Meniscal transplantation
• Instability
  • Ligament Reconstruction
Decision Making
Options Overlap

- Defect-specific variables
  - Size
  - Depth
  - Location
  - Number
  - Geometry
  - Containment

Size Matters!

Smaller lesions are well shouldered and protected.

Goal of Surgery:
To produce a durable repair tissue able to withstand increased mechanical forces.

Cartilage Injury

- Treatment options
  - Chondroplasty (debridement)
  - Bone Marrow Stimulating Techniques
    - Microfracture
  - Osteochondral Autograft (OATS)
  - Osteochondral Allograft (Allograft OATS)
  - Autologous Cartilage Implantation (ACI)

Treatment Algorithm for Chondral Lesions

Deciding which treatment option to use...

Lesions <2cm
- Arthroscopic Debridement
- Marrow Stimulating Technique
- Osteochondral Autograft
- Autologous Chondrocyte Implantation

Primary Treatment
- Low Demand
- High Demand

Secondary Treatment
- Low/High Demand

Lesions > 2 cm
- Arthroscopic Debridement
- Marrow Stimulating Technique
- Osteochondral Autograft
- Autologous Chondrocyte Implantation

Primary Treatment
- Low Demand
- High Demand
- Low/High Demand

Secondary Treatment
Debridement / RF-Energy
Lesions < 2cm², Contained and Shouldered

• Advantages
  – Single-stage / arthroscopic
  – Cost-effective
  – Reduced mechanical symptoms
    • Jackson (1992) -- 3 yr f/u
    • Hubbard (1996) -- 5 yr f/u

• Disadvantages
  – No resurfacing of the lesion (Buckwalter, 1988)
  – Inadequate for athletic / active patients (Levy 1996)
  – Risk of thermal injury with coblation
    • Andrews (AJSM, 2004) → shoulder

Radiofrequency Energy
Bovine Femoral Cartilage

Oratec  Mitek  Arthrocare
Green - Live chondrocytes
Red - Dead chondrocytes

Bone Marrow Stimulation
Lesions < 2 cm², Contained

• Advantages
  – Quick and easy
  – Single-stage / arthroscopic
  – Cost-effective
  – Successful results esp. in younger pts, traumatic defects
    • Steadman (Orthopedics, 1998)
    • Gill (Oper Tech Orthop, 2001)
    • Knutsen et al (JBJS, 2004)

• Disadvantages
  – Rehab not easy (CPM, crutches x 6-8 wks)
  – Breach the subchondral bone
    • Compromises other options e.g. ACI (Minas, 2009)
    • Intra-lesional osteophytes (Radin, 1986)
  – Unpredictable results with larger lesions
    • Bert (1989), Rodrigo (1996)
  – Durability of fibrocartilage?
Hyaline Cartilage vs. Fibrocartilage

- **Hyaline cartilage**
  - Type II Collagen
  - Organized collagen fiber orientation
  - Durable

- **Fibrocartilage**
  - Type I Collagen
  - Unorganized collagen fiber orientation
  - Less Durable

Bone Marrow Stimulation

**Microfracture**

- Tissue breakdown following microfracture

Osteochondral Autograft

**Lesions < 2 cm²**

- **Advantages**
  - Single-stage / arthroscopic procedure
  - Cost-effective
  - Single unit of mature cartilage and bone
  - Quicker recovery time than ACI / Allograft
  - Autogenous
  - 79 – 92% successful for femoral condyle lesions

  - Morgan, Bobic, Carter (1998)
  - Long, Gambardella (ICS, 2000)

- **Disadvantages**
  - Donor site morbidity (lesions >2 cm²)
  - No cartilage is completely non-weightbearing (Simonian, 1998)
  - Technically demanding
    - Plugs must be flush! (Koh, AJSM, 2004)
    - Impact loading during insertion
      - Can damage cartilage (Whiteside, JBJS-B, 2005)
  - Complications increase with larger lesions (Hangody, 1999)
Osteochondral Autograft

Plugs must be perpendicular and flush.

Osteochondral Allograft
Lesions > 2cm²

• Advantages
  – Single unit of mature cartilage and bone
  – Larger lesions possible
  – Lesions with bone loss possible
    • OCD, trauma, failed OATS, etc.
  – Good to excellent results long-term

Toronto Group, JBJS-B, 1997 → 84% at 7.5 yrs
Garrett, ICL, 1998 → 84% at 52 mos
UCSD group, Clin Sports Med, 1999 → 91% at 1-18 yrs
Williams et al, JBJS-A, 2007
Emmerson et al, AJSM, 2007 → 70% at 7.7 yrs

Osteochondral Allograft
Lesions > 2cm²

• Disadvantages
  – Procurement / availability
  – Sizing issues / technically demanding
  – Open procedure
  – Cartilage viability declines with time
    • Fresh → 1-7 days
    • Cryopreserved → < 20 days

Malinin et al, JBJS-A, 2006

Osteochondral Allograft
Lesions > 2cm²

• Disadvantages
  – Removes bone (burns bridges)
  – Expensive
  – Disease transmission (know your source)
    • Can’t sterilize like other allografts
    • Risk of viral transmission low (1 in 2 million)
    • Risk of bacterial transmission???
  – Immune response / Delayed healing

Williams et al, AJSM, 2007

Osteoarticular Allograft for OCD

Retrograde Allograft OATS for Tibial Lesion
Allograft OATS for Bipolar Lesions

Autologous Chondrocyte Culture and Reimplantation

First described by Peterson in 1987
Use of tissue engineering to treat cartilage injury

Autologous Chondrocyte Implantation
Lesions > 2cm²

Advantages
– Autologous chondrocytes
– “Hyaline-like” repair tissue
– Treatment of larger lesions and PF lesions
– Does not burn bridges
  • Maintains subchondral bone
– Good to excellent results in 80-90% for femoral condyle lesions


Disadvantages
– Two step / staged procedure
– Arthrotomy required
– Meticulous, time consuming
– Expensive
– Prolonged rehabilitation (1 year)
– Re-operation rate (21-36%)
  • Patch hypertrophy / delamination

Henderson et al, Arthroscopy, 2006
Gooding et al, Knee, 2006

Autologous Chondrocyte Implantation
Indications

• Focal, full-thickness chondral defects
  – Femoral Condyles and Trochlea
  – Not FDA approved for Patella
    • Difficult to get approved!
• Osteochondritis dissecans (OCD)
  – < 8 mm bone loss
  – Fresh allograft OATs is my preference
• Ages: 15 to 50 years
  – 40 years for me

Femoral Condyle Trochlea OCD
Autologous Chondrocyte Implantation

**Indications**

- Focal defects with normal surrounding articular cartilage

*Not indicated for osteoarthritis*

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**ACI Procedure**

**MFC Lesion**

- Prepare Defect
- Periosteum Procurement

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**Chondral Biopsy**

- Assessing Chondral Defect
- Harvesting the Biopsy
- Preparing for Transport

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**ACI Procedure**

**MFC Lesion**

- Prepare Defect
- Periosteum Procurement

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**ACI Procedure**

**MFC Lesion**

- Suture Patch
- Periosteal Patch

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ACI Procedure
MFC Lesion

- Fibrin glue to seal periosteum
- Cell implantation
- Suture and re-seal with fibrin glue

Autologous Chondrocyte Implantation
Treatment of the Complex Knee

- Patellofemoral lesions
  - Difficult to treat with other methods
  - Results improved with tibial tubercle osteotomy
    Henderson and Lavigne, Knee, 2006
    Mandelbaum et al, AJSM, 2007
    Farr, CORR, 2007
- Multiple Defects
  - MFC
  - LFC
  - Trochlea

Autologous Chondrocyte Implantation
Time Course of Healing

<table>
<thead>
<tr>
<th>Stage</th>
<th>Time</th>
<th>Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proliferation</td>
<td>0 – 6 weeks</td>
<td>Soft, primitive repair tissue</td>
</tr>
<tr>
<td>Transition</td>
<td>7 wks – 6 mths</td>
<td>Expansion of matrix putty-like consistency</td>
</tr>
<tr>
<td>Remodeling</td>
<td>6 – 18 mths. (up to 3 yrs. changes can occur)</td>
<td>Matrix remodeling, tissue stiffens to normal hardness</td>
</tr>
</tbody>
</table>

Quality of cartilage studies

An Analysis of the Quality of Cartilage Repair Studies
By David R. Jackson, Louis Echternacht, MD, PhD, and James H. Blum, MD, PhD

"generally low methodological quality studies"
"caution is required when interpreting results after surgical cartilage repair"

Jakobsen et al, JBJS, 2005

Results
Prospective Randomized Studies

- ACI versus OATS
  - 100 pts, mean defect size 4.66 cm²
  - Mean follow-up 19 months
  - ACI → 88% good / excellent results
  - Mosaicplasty → 69% good / excellent results
  - Good / excellent repairs at repeat arthroscopy
    - ACI → 82%
    - Mosaicplasty → 34%

Results
Prospective Randomized Studies

• ACI versus OATS
  – 40 pts, 2 year follow-up
  – Equal clinical results but slower recovery after ACI
    • Lysholm, Meyers, Tegner
  – Repair tissue mostly fibrocartilage with some hyaline-like tissue in ACI group
  – Normal hyaline cartilage in OATS group
  Horas et al (JBJS, 2003)

• ACI versus OATS
  – 47 pts, no previous surgery
  – 32% improved after debridement alone
  – 16% lost to f/u
  – 23 pts underwent ACI or OATS
    • ACI  68% G / E results
    • OATS  88% G / E results
  Dozin et al, Clin J Sport Med, 2005

• ACI versus Microfracture
  – 80 pts, 2 year follow-up
  – Good results in both groups
  – No statistically significant differences
    • Knee scores (ICRS, Lysholm, Tegner)
    • Histology
  – More improvement in SF-36 physical component in microfracture group
  Knutsen et al (JBJS, 2004)

Results
Biopsy Studies

• 1 year s/p ACI vs. native cartilage
• Less GAG concentration
• Inferior to healthy cartilage
  – Histology
  – Immunohistochemistry
  – MRI

Results
Biopsy Studies

• 57 patients s/p ACI
• 32 / 55 (58%) grossly abnormal at second look
  – Only 28% hyaline or hyaline-like cartilage
• 23 / 55 (42%) normal-looking at second look
  – 65% hyaline or hyaline-like cartilage
  Henderson et al, CORR, 2007

Questions remain…

• Does ACI really produce more durable hyaline-like repair tissue?
• Which technique is really the best long-term???
**Summary**

- Cartilage has poor healing potential
- Overlapping spectrum of options available
- Challenge is to duplicate normal cartilage

**Smaller lesions (< 2 cm²)**
- Low-demand → Debridement
- High-demand → Microfracture, OATS

**Larger lesions, Revisions (> 2 cm²)**
- ACI, osteochondral allograft

**The Future…**

- Next generation ACI
  - Collagen scaffold seeded with autologous chondrocytes
    - Matrix-induced ACI (MACI)
      - JBU-S-8, 2005
      - Promising results in multi-center European studies
      - Not available in U.S. yet
    - Select better subset of chondrocytes for culture
      - “Characterized” ACI (Chondroselect)
      - Better results vs. microfx (AJSM, 2008)

- Expose chondrocytes to pressure loads during culture + collagen matrix
  - Neocart

- Expose chondrocytes to growth factor (FGF-2) during culture + HA / fibrin matrix
  - Biocart II

**Artificial cartilage substitutes**

- Potential “off the shelf” solution for cartilage lesions
- Resorbable scaffolds
  - OBI plugs (Smith Nephews)
  - Truefit plugs (Biomet)
  - Bioactive matrices
- Hydrogel implants
- No good clinical studies
  - “Off label” indication for cartilage repair
  - My experience limited to backfilling OATS donor sites

**The Future…**

- Allograft Juvenile Cartilage
  - DeNovo NT / ET
  - Juvenile cartilage cells better at repairing defects
  - No bone so no immune response and no bridges burned
  - Minimal published data on NT
  - Prospective studies in progress
- Gene therapy to enhance cartilage repair
  - FGF-2 (J Gene Med, 2005)
  - IGF-1 (Gene Ther, 2005)
  - TGF-beta 1 (Tiss Eng, 2005)
THANK YOU!