Management of Articular Cartilage Injuries

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San Francisco
Why the Fuss?

- **Literature confirms:**
  - Approximately **60%** of all knee arthroscopies reveal articular cartilage damage\(^1\)
  - Significant defects in ~ **20%** of all knees\(^2\)

- **Articular cartilage:**
  - Poor intrinsic capacity for repair:
  - Avascular
  - Chondrocytes imbedded in matrix cannot migrate to area of repair

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Goals of Cartilage Repair

- Restore articular cartilage surface
- Relieve patient symptoms and improve function
- Match bio-mechanical properties of normal hyaline cartilage
- Prevent or slow progression of focal chondral injury to end stage arthritis
Articular Cartilage
Composition and Function

- **Chondrocytes (5 %)**
  - Create and maintain collagen and other matrix proteins
  - Only chondrocytes are genetically predisposed to this function
- **Proteoglycans (5-10 %)**
  - Bind water molecules and provide sheer strength
- **Type II Collagen**
  - Provide tensile strength
Hyaline Cartilage vs. Fibrocartilage

**Hyaline cartilage consists of:**
- Proteoglycan aggregate, Collagen Types: II, IX, XI
- Organized collagen fiber orientation
- Consistant proteoglycan staining (Safranin-O, red)

**Fibrocartilage consists of:**
- Proteoglycan, Collagen Type I
- Unorganized collagen fiber orientation
- Diffuse proteoglycan staining (Safranin-O, red)
Biological Resurfacing Options for Chondral Defects

- Regrow Fibrocartilage (bms)
  - Microfracture
- Regrow Hyaline-like Cartilage
  - ACI (Genzyme)
    - Periosteum
  - ACI 2\textsuperscript{nd} Generation (Matrix)
    - MACI, Hyalograft
- Transplant articular cartilage w/ bone
  - OC graft (auto, allo)
Size Matters
Large vs. Small:

< 2cm² vs. 2cm²

SIZE DOESN'T MATTER
Small Chondral Lesions

Lesion < 2 cm²

Primary Treatment
- Low-Demand
  - Debride
  - Microfx
- High-Demand
  - Microfx
  - Auto OCG

Secondary Treatment
- Low / High Demand
  - OCG for failed Micfx
  - ACI
Large Chondral Lesions

Lesion > 2 cm²

Primary Treatment
- Low-Demand
  - Debride
  - MicFx
- High-Demand
  - ACI
  - AutoOCG (Mosaicplasty)
  - Allograft

Secondary Treatment
- Low / High Demand
  - ACI
  - Allograft

Low-Demand vs. High-Demand

Low-Demand: Lesions ≤ 2 cm²
High-Demand: Lesions > 2 cm²

Low / High Demand: Lesions > 2 cm² with additional factors

Courtesy of Scott Gillogly, MD
Debridement & Lavage

- **Strengths:**
  - Arthroscopic
  - Does not violate sub-chondral bone
  - Stabilize edges of lesion
  - Temporary pain relief

- **Limitations:**
  - Lack of tissue fill / restoration
  - Low prospects for long term result
  - Progression of lesion
**MicroFracture:**

- **Strengths:**
  - Arthroscopic
  - Relatively simple procedure

- **Limitations:**
  - Creates fibro-cartilage / poor wear characteristics
  - More effective on smaller defects
  - 6-8 weeks non-weight-bearing and CPM required to optimize results
  - Results diminish over time

Courtesy of Brian Cole, MD
MICROFRACTURE RESULTS

- 11 yr Follow – up (7 – 17 yrs)
- 71 knees / avg age 30
- Lysh / Teg / SF – 36 / WOMAC
- Subjectively: 80% improved
- Functionally: 95% improved
- Excellent Survivorship

STEADMAN, ARTHROSCOPY, 2003
LEVEL 4 CASE SERIES
MICROFRACTURE RESULTS

- PROSP. COHORT Study of 48 MFx Pts
- Avg. Age 41 (16 – 60) / Avg Size 4.8cm²
- 56% Traumatic / 24 mos Minimum F/U
- OUTCOMES: IKDC / SF – 36 PCS
- Success: 67% G to E / 25% F / 8% POOR
- AC - Specific MRI in 24 cases
- 54% Good / 29% Moderate / 17% Poor
- Clinical = MRI Correlation
- Success: **BMI & Short Sx Duration** (<12 mos)

MITHOEFER, JBJS, 2005
LEVEL 4 STUDY
MFx in ACTIVE PATIENTS

- PROSP. COHORT Study of 32 Athletes
- Avg. Age 38 (16 – 54) / Avg Size 4.9cm²
- 59% Traumatic / 24 mos Minimum F/U
- OUTCOMES: Brittberg / Tegner / Marx
- Success: 66% G to E / 44% RTS at Hi Impact
- Activity Score Decline: 47%
- Success: Age < 40, Lesions < 200 mm²
  preop Sx < 12 mos & No prior Surgery

MITHOEFER, AJSM, 2006
MFx Results May Deteriorate

- PROSP. COHORT Study of 85 Patients
- Avg. Age 39 (19 – 55) / Avg Size 1 – 4 cm²
- 6 / 18 / 24 mos F/U
- OUTCOMES: Mod Cinci / ICRS Scores / MRI
- Clinical Success: Better in Pts < 40 yrs old
- Condyles > Trochlea
- Results Decline Between 18 and 36 months

Kreuz, Arthroscopy, 2006
LEVEL 4 CASE SERIES
OsteoChondral Autografting

**Strengths:**
- Single procedure
- May be performed arthroscopically
- Fills defect with native hyaline cartilage.

**Limitations:**
- Limited to smaller defects
- Donor site morbidity
- Make chondral defect into osteochondral defect
- Proud-tilted-recessed plug
- Congruity of joint difficult to reproduce with multiple plugs
- Cobblestone effect

*Barber/Chow 50% incongruence*
*(11/22) second looks*
*KJOC 12% proud/25% recessed/16% angled*
OATs vs. MFx: PRCC LEVEL 1 DATA (2.75cm²)

- 28 OATs vs. 29 MFx / All Comp. Athletes
- Avg Age 24 yrs (15 – 40) / Mean F/U 37m
- Overall Success: HSS / ICRS / Xray
  - OATs G/E: 96% vs. 52% for MFx
- Functional RTS: OATS 93% vs. 52% MFx
- MRI Tissue Fill: OATs 84% vs. 49% for MFx
- 58% Biopsied at 1 yr / ICRS Tissue Asses.
  - OATs G/E: 84% vs. 57% for MFx

GUDAS, Arthroscopy, 2005 LEVEL 1 RCT
OC Autograft – Donor Site Morbidity

- All donor sites demonstrated a significant contact pressure through 1-110 degrees of knee motion

Contact Pressures at Osteochondral Donor Sites in the Knee
- Simonian et al AJSM July 1998
OCG: Other Issues

- Incorporation
- Subchondral sclerosis
- Cysts/ Clefts
- Size of graft:
  - Larger is better (>6mm)
    - More hyaline tissue
    - Fewer technical steps
    - More robust grafts
    - Reduced concentrated loads
    - Improved pullout strength
    - But… more contouring challenges
  
- Position of graft:
  - Flush > recessed > proud

_HUANG, AJSM, 2004_
Osteochondral Allografts

**Strengths:**
- Bone fixation
- Hyaline cartilage

**Limitations:**
- Limited supply
- Disease transmission
- Viability of chondrocytes
  - > 21 DAY STORAGE: CC ABSENCE
  - (MALININ, JBJS, 2006)
- Non-union/ collapse
- Circular shaped lesions
OSTEOCHONDRAL ALLOGRAFTS

25 pts.
Fresh Cold- Stored OC Allografts (15 – 43d)
Consec. Case Series
F/U: 35 mons (24 – 67)
Sat: 84% / Fx: 79% / Rx: 88%
McCulloch, AJSM, 2007

19 pts.
Fresh Cold- Stored OC Allografts (17 – 42d)
Prosp. Case Series
F/U: 48 mons (21 – 68)
MRI: NL ctlg thick. in 18
Williams, JBJS, 2007
OBI:

4/23/07 FDA REGULATORY HOLD!

- Resorbable (6mo), porous scaffold, which allows the in-growth of new healing tissue.
- Synthetic (polylactide-co-glycolide + Ca Sulfate to enhance bone ingrowth)
- Easy to use
- FDA approved as bone void filler only – not for ctlg!
- No long term follow up or published studies
OBI: 10 month f/u

Courtesy of Don Rose MD
Autologous Chondrocyte Implantation

- **Strengths:**
  - Can produce hyaline-like cartilage in many patients
  - Can fill defects regardless of size/shape with functional repair tissue.
  - Moderate to large defects that have failed previous intervention

- **Limitations:**
  - Two procedures
  - More invasive
  - Expense
  - Longer recovery – return to sports
Carticel® History

- 1987: First patients treated in Sweden
- 1994: Pilot study (23 patients) published (Brittberg, et al. NEJM)
- 1995: Carticel® launched, first patient treated in US
- 1997: Genzyme receives biologic license (BLA) from FDA
- 2000: 1st major publication with long-term outcomes (Peterson, et al. CORR)
- 2004: 10,000th Carticel implant
- 2005: CPT Code: 27412 / 10th Year Anniversary
The repair of experimentally produced defects in rabbit articular cartilage by autologous chondrocyte transplantation.

Grande DA, Pitman MI, Peterson L, Menche D, Klein M.

Department of Bioengineering, Hospital for Joint Diseases Orthopaedic Institute, New York, J Orthop Res. 1989

82% fill vs. 18% fill
1994 Gothenberg

Dr Halbrecht with Dr Lars Peterson
Identifying a Carticel® Patient: Indications

Joint Factors:

- Moderate to large (> 2cm²) symptomatic cartilage defects on the distal femur (MFC / LFC / Trochlea)
  - (Patella) off label
- Either chondral or osteochondral (OCD)
- Relatively healthy joint
  - No OA
  - Stable
  - Alignment
  - Intact meniscus
Identifying a Carticel® Patient: Indications

Patient Factors:

- Younger patients - 16-55
  (avg. ~ 35 YO)
- Symptomatic:
  - Compromised activities of daily living
  - Refractory to treatment
- Localized lesion(s)
- Willing & capable of rehabilitation program
Surgical Technique

**Carticel™ Treatment**

1. Healthy cartilage biopsy taken from patient

2. Biopsy sent to Genzyme Tissue Repair for processing
   - Periosteal flap, taken from lower leg bone and sutured on top of defect

3. Cultured cells sent to surgeon

4. Cultured cartilage cells injected under periosteal flap
Biopsy Procurement

- Harvest from lesser or non-weight bearing surface
  - Superior medial or lateral femoral articular cartilage or intercondylar notch (preferred)
- Using a ring currette or notchplasty gouge
  - Obtain full-thickness biopsies down to subchondral bone (approx. size 200-300 mg)
Defect Preparation

- Excise all damaged or unhealthy cartilage from perimeter of the defect
- Leave sharp, vertical walls of healthy cartilage with smooth edges
- Avoid penetration of subchondral bone
- Bone bed should be intact and free of fibrous tissue and bleeding
Periosteum Procurement

- Measure defect and add 2mm to the margins for femoral condyle defects and 3mm for trochlea defects
- Obtain periosteum from proximal medial posterior cortex of the tibia
- Remove fascia layer over the periosteum
- Use periosteal elevator to carefully remove periosteum from bone
- Keep periosteum moist to reduce shrinkage
Periosteum Fixation

- Place periosteum over defect with cambium layer down
- Use 6.0 Vicryl suture on a P-1 cutting needle
- Space sutures 3-4mm apart to achieve a water tight seal
- Leave a superior opening for cell injection
Watertight Testing

- Inject sterile saline into defect
- Inspect for leakage
- Fibrin glue is used to assist in achieving watertightness
- Aspirate all remaining saline from under the periosteum
Cell Implantation

- Resuspend cells in vial with catheter
- Insert catheter tip through superior opening of periosteum
- Ensure even distribution of cells
- Close superior opening with additional sutures and fibrin glue
ACI: Technique Video
What happens once the chondrocytes are implanted?

- Animal studies have shown that chondrocytes attach to subchondral bone after implantation\(^1, 2\)
- Chondrocytes proliferate and increase in cell number
- Chondrocytes produce matrix
- Matrix matures
Histological Analysis

- The repair tissue resembles hyaline cartilage versus fibrocartilage \(^1,2,3,4,5\)
- The implant tissue continues to mature and remodel for up to two years\(^1,4\)
- Post ACI biopsy specimens show integration at the margins and integration to the subchondral bone \(^2,3\)
- Superficial fibrous surface area from periosteal remnant

Hyaline Repair Tissue > 2 year
Histology and Polarized Light
ACI: Case Example: Large Lesion

Chondrocyte Implantation (Pre-Surgery)

Chondrocyte Implantation (Post-Surgery)
Case Example: Small lesion

- A.Q.
  - 40 yo M
  - W.C.
  - Sxs 18 mo
  - Defect MFC 13mm x 7mm
Post Op MRI: A.Q.
Bone Scan

Pre-op

Post-op
1 Year F/U Arthroscopy: A.Q.
Remodeling Phases and Rehabilitation

The rate of progression may vary depending on the lesion location, size and concomitant procedures. If symptoms occur, patients should reduce activity to reduce pain and swelling. Individual results may vary and not all patients achieve full function.

**Proliferation Phase**
- Weeks 0-12
- Non-weight bearing
- 0-2 weeks
- Progressive weight bearing 3-12 weeks

**Matrix Remodeling**
- Weeks 13-36
- Low Impact Sports

**Maturation**
- Weeks 36-52
- High Impact Sports
Carticel: Post Op Management: Continued

- Unloader brace
  - Use for first 6 months
**Long-Term Swedish Experience**

**Isolated Femoral Condyle Demographics**

- Patients: 57
- Average age: 33 yrs
- Average size defect: 4.2 cm²
- Range: 1.6 to 12.0 cm²
- Average follow-up: 4 yrs

29 out of 57 patients had at least one prior procedure, 35% had two procedures.

**Femoral Condyle Clinical Assessment**

- 90% Successful Treatment

**Femoral Condyle Patient Assessment**

- Visual Analog Scale:
  - Excellent: 58%
  - Good: 32%
  - Fair: 6%
  - Poor: 4%

- Functional Activities:
  - Baseline: 5%
  - Strenuous Activities: 85%

AAOS, Orlando 2000
### ACI Swedish Durability Data

**Isolated Femoral Condyles**

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Avg. Age</th>
<th>Avg. Size</th>
<th>Clinical Assessment Excellent</th>
<th>Clinical Assessment Good</th>
<th>Clinical Assessment Failure</th>
<th>Modified Cincinnati</th>
<th>Tegner Wallgren</th>
<th>VAS</th>
<th>Patient Expectations</th>
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<td><strong>Pre-op Baseline</strong></td>
<td>19</td>
<td>30.4</td>
<td>4.0 cm²</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1.2</td>
<td>7</td>
<td>84.5</td>
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<tr>
<td><strong>2 Years</strong></td>
<td>19</td>
<td>32.4</td>
<td></td>
<td>12</td>
<td>5</td>
<td>2</td>
<td>8.9</td>
<td>9.5</td>
<td>14.2</td>
<td>89%</td>
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<tr>
<td><strong>7.5 years avg)</strong></td>
<td>18</td>
<td>40.5</td>
<td></td>
<td>11</td>
<td>5</td>
<td>2</td>
<td>9.2</td>
<td>9.8</td>
<td>12.2</td>
<td>88%</td>
</tr>
<tr>
<td><strong>Range 5-12 yrs</strong></td>
<td>18</td>
<td>94%</td>
<td></td>
<td></td>
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<td></td>
<td>+8</td>
<td>+2.8</td>
<td>+72.3</td>
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</table>

- **Pre-Value**
- **Post-Value**
ACI Swedish Durability Data:

All First Consecutive Patients Treated
(Femoral Condyle+Patella+OCD)

Patient Demographics

<table>
<thead>
<tr>
<th>Condition</th>
<th>Count</th>
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<td>Femoral condyles</td>
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<td>Patella</td>
<td>15</td>
</tr>
<tr>
<td>OCD</td>
<td>7</td>
</tr>
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</table>

Key Note: 97% durability. No evidence of clinical deterioration nor tissue breakdown with second look arthroscopes. 79% overall success rate.
## Osteochondritis Dissecans (OCD) Demographics

- **Patients**: 32
- **Average age**: 25 yrs
- **Average size defect**: 5.3 cm²
- **Range**: 1.5 to 16.0 cm²
- **Average follow-up**: 3.9 yrs

81 prior procedures performed in 32 patients, avg 2.5 previous procedures

## OCD Clinical Assessment

- **Excellent**: 56%
- **Good**: 28%
- **Fair**: 13%
- **Poor**: 3%

84% Successful Treatment

## OCD Patient Assessment Visual Analog Scale

- **Baseline**: 3%
- **Functional Activities**: 90%
- **Strenuous Activities**: 84%

AAOS, Orlando 2000
Long-Term Swedish Experience

Trochlea Demographics

- Patients: 15
- Average size defect: 5.2 cm²
- Average follow-up: 3.9 yrs

Trochlea Clinical Assessment

Pre Values
- Excellent/Good: 0%
- Fair: 30%
- Poor: 70%

Post Values
- Excellent/Good: 80%
- Fair/Poor: 20%

AAOS, Orlando 2000
Long-Term Swedish Experience

**Patella Demographics**

- **Patients**: 67
- **Average size defect**: 5.5 cm²
- **Average follow-up**: 4.5 yrs

**Patella Clinical Assessment**

**Pre Values**

- Excellent/Good: 90%
- Fair: 10%
- Poor: 0%

**Post Values**

- Excellent/Good: 75%
- Fair/Poor: 25%
Autologous Chondrocytes - Objective Analysis
Second look with matching histology

Patient #3
Arthro Assessment=12

Indentation
Normal 3.4 - Repair 3.7

2 years post implant

Courtesy of Lars Peterson
Autologous Chondrocytes - Objective Analysis
Second look with matching histology

Patient #6
Arthroscopic Assessment=10

Indentation
Normal 3.8-Repair Tissue 3.7

8 years post implant

Courtesy of Lars Peterson
Challenging patient population (36 patients)
- 64% failed previous treatment
- Mean defect size 6.1 cm\(^2\)
- Median age 36 years
- 38% worker’s compensation cases
- 80% of the patients improved
ACI Cartilage Registry: March 2001
Clinical Results: > 5 year F/U group

All Defect Locations

Clinician Evaluation
n = 28

Patient Evaluation
n = 36

Bx 60-M

0 2 4 6 8 10
Poor Fair Good Very Good Excellent

3.04 (SD=1.07) 7.21 (SD=3.08)
3.00 (SD=1.33) 6.75 (SD=2.70)
Carticel: Complications

- Repeat Arthroscopy
  10-25%
  - Periosteal hypertrophy
  - Fibrosis/ scar
  - Graft delamination
Improvement in Bone Homeostasis Following Autologous Chondrocyte Implantation of the Knee

Halbrecht J. et al Orthopedics 2004

This retrospective review and clinical follow-up demonstrates the effectiveness of autologous chondrocyte implantation of the knee. 24 patients with average follow-up of 26.5 months were evaluated. The mean Lysholm score improved from 43.58 before surgery to 71.42 at most recent follow-up, the modified Cincinnati knee score for overall clinician evaluation improved from 2.96 to 6.92, and the mean modified Cincinnati knee score for overall patient evaluation improved from 3.21 to 6.13 at \( P < 0.05 \). Seventy-nine percent of patients responded that they would have the same knee surgery again and 83% rated the results of their knee surgery as good to excellent. Limited radionuclide bone scans with single photon emission computed tomography were completed in 11 of the patients to assess the physiology and homeostasis of subchondral bone adjacent to treated articular cartilage defect(s).

**A trend was identified suggesting improvement in mean subchondral bone scores at a mean of 29.6-months follow-up compared to preoperative bone scan assessment.** There was also a trend towards greatest improvement correlating with the patients with the best clinical scores. The results of this study suggest that autologous chondrocyte implantation of the knee can be successful in improving pain and function in patients with articular cartilage...
Complex Cases:

Halbrecht J. et al  Orthopedics 2004

- 24 patients
- Avg. defect size 4.9cm
- 12/24 had associated surgery
  - Six Men allograft
  - Two HTO
  - Three ACL
  - One Fulkerson

<table>
<thead>
<tr>
<th>PATIENT NO</th>
<th>LOCATION OF TREATED DEFECT</th>
<th>SIZE OF DEFECT (cm²)</th>
<th>ASSOCIATED OPERATIONS</th>
<th>GRADE OF DEFECT (PRE-OP)</th>
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<tr>
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<td>CMA</td>
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## Clinical Results

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<th>Improved (%)</th>
<th>Same (%)</th>
<th>Declined (%)</th>
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<tr>
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<td>75</td>
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<tr>
<td><strong>Mod. Cincinnati</strong></td>
<td>79</td>
<td>8</td>
<td>13</td>
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**Patient Perception**

- 92% would probably or definitely have the ACI procedure repeated
- 83% rated the results of their surgery as good to excellent
Mean overall clinician and patient evaluation scores of the patient population at follow up compared to baseline at time of biopsy.

Modified Cincinnati Knee Score

<table>
<thead>
<tr>
<th>Overall Clinician Evaluation</th>
<th>Biopsy</th>
<th>Most Recent Follow-up</th>
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<tbody>
<tr>
<td>Overall Patient Evaluation</td>
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</tr>
<tr>
<td>Most Recent Follow-up</td>
<td>3.21</td>
<td>6.13</td>
</tr>
</tbody>
</table>
Mean scores of overall patient population at follow-up compared to baseline at time of biopsy.

![Graph showing Lysholm Score](image)
## Scoring system for assessing limited radionuclide Bone scan with SPECT.

<table>
<thead>
<tr>
<th>0 – Normal (n = 01, 0)</th>
<th>1 – Minor Changes (n = 2¹, 3²)</th>
<th>2 – Moderate Changes (n = 3¹, 5²)</th>
<th>3 – Severe Changes (n = 6¹, 3²)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Unicompartmental involvement</td>
<td>- 1-2 compartment involvement</td>
<td>- Multicompartmental involvement</td>
</tr>
<tr>
<td></td>
<td>- Increased uptake relative to normal</td>
<td>- Increased uptake relative to normal</td>
<td>- Increased uptake relative to normal</td>
</tr>
<tr>
<td></td>
<td>- &lt;30% of ipsilateral plateau/condyle</td>
<td>- 30-50% of ipsilateral plateau/condyle</td>
<td>- &gt;50% of ipsilateral plateau/condyle</td>
</tr>
</tbody>
</table>

¹ Number of patients preoperatively  
² Number of patients at most recent follow-up visit
Mean Spect Score Post op compared to Pre op

*Not statistically significant at a p-value of <0.05*
Mean Spect Score By Subgroup:

*Not statistically significant at a p-value of <0.05*
Case Example

Pre op

Post op
ACI: Comparison Results

- Most data on localized defects femoral condyle

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Peterson et al</td>
<td>30.4</td>
<td>4.0</td>
<td>43.5</td>
<td>1.2</td>
</tr>
<tr>
<td>Follow-up</td>
<td>84.7 (9.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>US - Carticel</td>
<td>38.0</td>
<td>6.2</td>
<td>n/a</td>
<td>3.0</td>
</tr>
<tr>
<td>Follow-up</td>
<td>n/a</td>
<td></td>
<td>6.0 (6.3)</td>
<td></td>
</tr>
<tr>
<td>Our Study</td>
<td>39.1</td>
<td>4.9</td>
<td>43.6</td>
<td>3.0</td>
</tr>
<tr>
<td>Follow-up</td>
<td>71.4</td>
<td></td>
<td>71.4</td>
<td>7.0</td>
</tr>
</tbody>
</table>

1 Scores from 2-year (7.5-year) follow-up
2 Scores from 2-year (4-year) follow-up
CONCLUSION

- ACI is successful in improving pain and function in patients with articular cartilage defects and may improve subchondral bone homeostasis based on bone scan evaluation.

- A larger patient population and longer follow-up are necessary to confirm statistical significance and determine the long term efficacy of this procedure in preventing progression of OA...
**Autologous Chondrocyte Implantation Compared with Microfracture in the Knee**

A Randomized Trial

By Gunnar Knutsen, MD, Lars Engbretsen, MD, PhD, Tom C. Ludvigsen, MD, Jon Olav Droget, MD, Torbjørn Grøntvedt, MD, PhD, Eirik Solheim, MD, PhD, Torbjørn Strand, MD, Sally Roberts, PhD, Vidar Isaksen, MD, and Oddmund Johansen, MD, PhD

- ACI = Microfx at 2 years
- Authors’ Conclusions:
  - Microfracture maybe more suitable for a primary procedure for a small local contained defect.
  - ACI may be a better option for patients who have failed microfracture or have larger non-contained defects.

- Critique:
  - Expect deterioration of Microfx results
Carticel Repair: Advanced Techniques

Complex Lesions and Combined Procedures

JEFFREY HALBRECHT MD
SAN FRANCISCO, CA
“Now, how can I be of assistance?”
Advanced Biological Resurfacing: Decisions Making

- Evaluate each case!
  - Single/ multiple lesions
  - Unipolar/Bipolar
  - Chondral/Osteochondral?
  - Deformity
  - Alignment
  - Meniscectomy
  - Stability
Minas - BWH Complex Cases

Total = 86
- FC + HTO/TTO = 42% (36)
- FC + ACL = 7% (6)
- Trochlea = 30% (26)
- Patella = 19% (16)
- Tibia = 5% (4)
- Multiple = 44% (38)

n.b. patients may appear in multiple categories

Knee Society Score

<table>
<thead>
<tr>
<th>Time</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>BL</td>
<td>58</td>
</tr>
<tr>
<td>12M</td>
<td>68</td>
</tr>
<tr>
<td>24M</td>
<td>72</td>
</tr>
<tr>
<td>36M</td>
<td>62</td>
</tr>
<tr>
<td>48M</td>
<td>87</td>
</tr>
</tbody>
</table>

p1=0.008  (12M compared to baseline)
p2=0.038  (24M compared to baseline)
p1=0.075  (36M compared to baseline)
p1=0.105  (48M compared to baseline)
Combined Procedures: Scott Gillogly - Atlanta

76 pts. (12 additional staged)

At ACI:

- ACL reconstruction 13 (8 allograft)
- PF Realignment 39 (AMTT)
- HTO 14 (8 staged)
- Meniscal Transplant 5
- Bone Graft (staged) 4
- Osteochondral Autograft 1

76
ACI Subgroup Clinical Results

### Modified Cincinnati Rating Scale
Minimum 2 year follow-up

#### ACI Subgroup Clinical Results

<table>
<thead>
<tr>
<th>Subgroup</th>
<th># Pts</th>
<th>MCRS Baseline</th>
<th>MCRS 2 Yrs.</th>
<th>Statistical Significance</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACI + Concomitant Procedure(s)</td>
<td>26</td>
<td>3.3</td>
<td>8.2</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td>ACI only</td>
<td>28</td>
<td>3.9</td>
<td>8.5</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td>Acute (&lt; 1 yr from injury or symptoms)</td>
<td>16</td>
<td>3.2</td>
<td>8.9</td>
<td>p &lt; .01</td>
<td>Knee Score p&lt;.01</td>
</tr>
<tr>
<td>Chronic (&gt; 1 yr from injury or symptoms)</td>
<td>38</td>
<td>3.8</td>
<td>8.1</td>
<td>yes</td>
<td>Sport Score p&lt;.001</td>
</tr>
<tr>
<td>Isolated defect</td>
<td>43</td>
<td>3.8</td>
<td>8.4</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td>Multiple defects</td>
<td>11</td>
<td>2.9</td>
<td>7.8</td>
<td>no</td>
<td></td>
</tr>
</tbody>
</table>

Also Not Significant: Gender (except Females on Sports Score p<.005), Age, Workers Comp, Size, Location (except Patella on Sports Score p<.05)
Advanced Biological Resurfacing
Combined Procedure:

**ACI + Meniscal Allograft**

- Chondral defect with absent meniscus
- Single or two stage
- Allograft first
Bipolar Lesions

- ACI for femoral condyle
- Microfracture for small tibial lesions
- Meniscal allograft
Bipolar Lesion

Video
Bipolar Lesion: Follow Up
Combined Procedures

- ACL
- Meniscal Allograft
- HTO
- Patella Realignment
ACL / ACI

- Often two stage by default
- If single stage:
  - ACL first
  - Be mindful of incisions/periosteum
  - Modify rehab
ACI/ HTO

- Minimal joint space narrowing
- Physiologic varus
- Single vs 2 stage
- Opening wedge
Patella Lesions

- Keys to success
  - Contained lesion
  - Complete debridement
  - Avoid bipolar
  - Correct alignment
Swedish Experience: Patella Defects Treated with Autologous Chondrocyte Implantation

67 Patients with 2-year follow-up

- Isolated Lesions with reconstruction extensor mech
  - Avg. 4.0 cm²
  - #7 (4/7)
  - 57% Good/Excellent
  - 43% Fair/Poor

- Isolated Lesions w/ reconstruction extensor mech plus other lesion
  - Avg. 5.3 cm²
  - #20 (17/20)
  - 85% Good/Excellent
  - 15% Fair/Poor

- Patella Trochlea Kissing Lesion w/ reconstruction extensor mech
  - Avg. 4.0 cm²
  - #20 (15/20)
  - 75% Good/Excellent
  - 25% Fair/Poor

- Patella Trochlea Kissing Lesion w/ reconstruction extensor mech
  - Avg. 6.8 cm²
  - #20 (11/20)
  - 55% Good/Excellent
  - 45% Fair/Poor
Patella Case Examples
Patella Case History

9 Months Lateral Facet
Patella Ridge Restored

9 Months Medial Facet

Courtesy T. Spalding
Bipolar Patella Defects

- Poor results
- Consider Microfx for smaller lesion
- Alignment

Lateral trochlea  Patella
Trochlea

- Re-establish contour
- Oversize periosteum
- Alternating sutures
- Avoid excess tension
- Alignment
- Post op rehab!
Isolated Trochlea Lesions in Knees Treated with Autologous Chondrocyte Implantation >Two Year

Swedish

<table>
<thead>
<tr>
<th>Pre</th>
<th>Post</th>
<th>Avg. Size 4.5cm²</th>
<th>12/15 Improved</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5</td>
<td>6.5</td>
<td></td>
<td>6/15 Improved</td>
</tr>
</tbody>
</table>

U.S

<table>
<thead>
<tr>
<th>Pre</th>
<th>Post</th>
<th>Avg. Size 5.2cm²</th>
<th>29/33 Improved</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.15</td>
<td>6.91</td>
<td></td>
<td>27/33 Improved</td>
</tr>
</tbody>
</table>

2- Significant limitations w/ADL, no sports

6- Some limitations with sports, but able to participate
Tibia

- Extensive exposure
- Medial: take down MCL, MM
- Lateral: take down LM (+/-LCL)
Multiple Lesions

- Ration cells!
- Sequential periosteal harvest
- Cells at conclusion of case
- Consider combined procedure (ACI / OCG)
Very Large Lesions

- Posterior access
- Alvarado Leg positioner
- Consider bone anchors posteriorly
- Avoid patch perforation
- Patch quilt
- 2 vials cells
Complex lesions

- Internal osteophyte
- “Skip “ lesions
- “Ovalize” irregular borders
Posterior Condyle Lesions

- Hyperflex/Alvarado
- Modify needle/anchors
ACI: Uncontained Defects

- Defect extending to intercondylar notch
- Defect extending to edge of condyle
ACI: Uncontained Defects

- Careful debridement to preserve margins
- Secure to periosteum, synovium, bone
Osteochondritis Dissecans
Deep Lesion

Stage Bone Procedure > 8mm Bony Involvement

Courtesy of T. Minas
Swedish Sandwich Technique

Deep Bony Involvement
1. Bone Graft
2. Periosteum cambium up
3. Secure with fibrin glue
4. Periosteum cambium down
5. Implant cells

1 yr. Follow-up MRI
Bone Reconstituted
Full Repair Tissue

Courtesy of M. Brittberg
Carticel Repair: Complex Lesions

Conclusions

- Salvage Cases
- Young patients
- Alignment, Stability, Meniscus for success
- Consider bipolar if tibial lesion small
- Patella, trochlea, OCD
- Results Promising
What’s New...
<table>
<thead>
<tr>
<th>Country</th>
<th>Company</th>
<th>Product</th>
<th>Scaffold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>IGOR</td>
<td>ACT/ MACT</td>
<td>Fibrin/collagen matrix</td>
</tr>
<tr>
<td>Austria/Italy</td>
<td>Arthrex</td>
<td>Arthromatrix</td>
<td>Collagen Scaffold</td>
</tr>
<tr>
<td>Germany</td>
<td>Co.don</td>
<td>Chondro-sphere</td>
<td>3-D sphere</td>
</tr>
<tr>
<td>Germany/USA</td>
<td>Verigen</td>
<td>MACI</td>
<td>Porcine Collagen</td>
</tr>
<tr>
<td>Germany/Italy</td>
<td>Biotissue Technologies</td>
<td>Bioseed-C</td>
<td>PGLA fleece</td>
</tr>
<tr>
<td>Holland</td>
<td>ISOTIS</td>
<td>Cell active</td>
<td>PEGly+ PB Terephtalate</td>
</tr>
<tr>
<td>Europe</td>
<td>Sulzer/Zimmer</td>
<td></td>
<td>Equine Collagen</td>
</tr>
<tr>
<td>Italy</td>
<td>FAB/Fidia Advanced Biopolymers</td>
<td>Hyalograft</td>
<td>Hyaluronan based 3-D scaffold</td>
</tr>
<tr>
<td>Switzerland</td>
<td>Geistlich</td>
<td>Chondroglide</td>
<td>Periosteal substitute</td>
</tr>
<tr>
<td>USA</td>
<td>Histogenics</td>
<td>NeoCart</td>
<td>Biodegradable Matrix</td>
</tr>
<tr>
<td>USA</td>
<td>Articular Engineering</td>
<td>ARC Cartilage</td>
<td>Stimulate chondrocytes to form in vitro ctg tissue</td>
</tr>
<tr>
<td>USA</td>
<td>BD Biosciences</td>
<td>OPLA</td>
<td>3D calcium+ collagen scaffold</td>
</tr>
</tbody>
</table>
MACI: Open

Courtesy of Dr Steven Abelow
M.A.C.I.

- **N= 50**
  - 42 knees
  - 8 ankles
- **78% male; 18% female**
- **Age: 14-48 years**
- **Size: 2.5-20 sq cm**
- **VAS**
  - Preop- 62% > 6
  - Postop-67% < 3
The Future:
Stem Cells – Growth Factors – Selected Chondrocytes

Chondrogen

Chondrogen Preclinical Data:

“Our research demonstrates that injection of adult stem cells promotes regeneration of the meniscus and protects the articular cartilage from degeneration leading to osteoarthritis.”
THANK YOU