Clinical Treatment Algorithms and Decision Making for Cartilage Repair

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DISCLOSURES

Industry:
- Genzyme: Consultant (payments to KMSF non for profit)
- Icartilage: Consultant $0
- Ceterix: Consultant (payments to KMSF non for profit)
- Smith&Nephew : Institutional Support

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Editorial Board / Board Memberships:
- OJSM, Cartilage, The Knee, Journal of Sports Rehabilitation
- Board Member ICRS,
- Scientific Review Cmte. AF (Great Lakes Chapter)

Reviewer for Journals:
- AJSM, CORR, JKS, O&O, Orthopaedics, Tissue Engineering

Incidence

- 136 surgeons over 4.3 years
- 31,516 arthroscopies
- 63% with Lesions (2.7/knee)
  - Grade III 41%
  - Grade IV 20%
  - Fracture 1.3%
  - OCD .7%

IV: < 40 y.o. = 5% (1,729 cases)

Curl et al.; Arthroscopy, 1997
Natural History
- 31 patients
- F/U: 14 years
- > 50% developed symptomatic joint space narrowing
- >25,000 scopes
- 60% chondral lesions
- 67% FCD's, 2% OCD's, 29% OA lesions
- 1,000 patients (age 39 ± 14)
- 58% MFC, 9% LFC, 6% trochlea
- ACL injuries have a high (84-100%) rate of chondral injuries of varying severity.

Nishimori et al. KSSTA 2008, Frobell et al. JBJS 2011, Potter et al. AJSM 2012,


| Table 1: Significant Predictors of Each Outcomes Scale at 6 Years (p values) |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Structure       | IKDC            | KOOS            | Marx            | Pain            | ADL             | Sports/Rec QOL  |
| Articular Cartilage |                |                 |                 |                 |                 |                 |
| MFC             | 0.012           | 0.017           | 0.002           | 0.05            |                 |                 |
| LFC             | 0.002           | 0.029           |                 |                 |                 |                 |
| MTP             | 0.002           | 0.033           | 0.024           | 0.02           | 0.029           |                 |
| LTP             | 0.037           |                 |                 |                 |                 |                 |
| Patella         |                 |                 |                 |                 |                 |                 |
| Trochlea        | 0.000           |                 |                 |                 |                 |                 |

Cohort f/u = 93% (1411/1512)

UK ACL Data:
- The young patients (under 20) make up the majority of ACL replacement patients
- Particularly concerning is that over 60% get diagnosed after 3 months or longer
- In the state of KY the age group under 25 has seen a 15% increase in ACL reconstructions performed between 2009 and 2011
IMAGING:

- Modalities:
  - Plain x-rays (bilat):
    - a/p + lateral
    - p/a flex weightbearing
    - PF sunrise / merchant
    - Long leg alignment
  - MRI:
    - T1+T2+PD Sag,Cor,Ax
    - Cartilage specific: DESS, FSPD etc
    - Cartilage Quantifying: DGEMRIC, T1rho, T2 mapping, Na+ scanning
  - Bone Scan:
    - Whole body, three-phase
  - CT:
    - PF alignment
    - contrast (intra-articular)

SCOPE:

- Part of the pre-operative workup:
  - Lesion location / size
  - "Character of the compartment"
  - Unexpected findings:
  - Technique choice

Caveat: do not rely on outside pictures only

ICRS Grading Scale ©

ICRS Grade 3 – severely abnormal
Cartilage defects extending down >50% of cartilage depth (A) as well as down to calcified layer (B) and down to but not through the subchondral bone (C). Blisters are included in the grade (D)

ICRS Grade 0 – normal

ICRS Grade 1 – nearly normal
Superficial lesions. Soft indentation (a) and/or superficial cracks or fissures

ICRS Grade 2 – abnormal
Lesion extending down to <50% of cartilage depth

ICRS Grade 4 – severely abnormal
Microfracture

OSTEOCHONDRAL AUTOGRRAFT
(MOSAIC/ OATS)
ARTICULAR CHONDROCYTE IMPLANTATION (ACI)

OSTEOCHONDRAL ALLOGRAFT
OSTEOCHONDRAL ALLOGRAFT

- Concept:
  - stored allograft
  - particulated juvenile allograft cartilage

- Advantage:
  - easy applicable
  - Easier to obtain than OC allograft
  - Marketed as off-the-shelf but really is not.

Clinical data:
- Bonner et al. JKS 2010
- Farr et al. ICRS 2010
- Thompkins M AOSSM 2012
- Post market study temp. stopped in 2012
- >4000 cases done to date (5.5 years)

Denovo NT (Zimmer)

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Currently available Treatment Options for Focal Chondral Defects

Osteochondral grafting:
- Autograft:
  - Mosaic 
  - OATS 
- Fresh OC Allograft

Marrow Stimulation:
- Microfracture 
- Antegrade drilling

Cell transplantation:
- Denovo NT (Zimmer)

Cell transplantation:
- ACI

Osteochondral grafting:
- Allograft: 
- Chondrofix (Zimmer)

= currently available with clinical data
= available with less than minimal data

Chondrofix (Zimmer):

Concept:
- Biphasic allograft plug (MMTG)

Advantage:
- Off the shelf availability
- Indications potentially the salvage patient that requires bridging (50 year old with isolated defect)

Clinical data:
- No published clinical data to date
- Post-market trial ongoing

BioCartilage (Arthrex):

Concept:
- Point-of care 
- Micronized Cartilage Matrix

Advantage:
- Off the shelf availability
- Easy application and use (microfracture)
- Cost (~$1,000) per defect

Experimental data:
- Fibrin glue retains grafts in goats Lewis PB et al JCRS 2009
- Allograft particles will heal defect in baboons Malissen et al ICBS 2009
- Increased repair tissue and improved MRI T2 mapping score in horses Fortier et al. JCRS 2010

Clinical data:
- None to date
- 1 month follow-up

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PRODUCTS THAT ARE ON THE MARKET AND HOW THEY ADD TO OR EXPAND THE OPTIONS:

- MACI:
  - Ease of application
  - Potential for arthroscopic procedure
  - Option for tibial defects

- DENOVO NT:
  - Availability
  - Ease of application
  - Potential for arthroscopic procedure
  - Option for tibial defects?

- BIOCARTILAGE:
  - Ease of application
  - Potential for arthroscopic procedure

- CHONDROFIX:
  - Availability
  - Ease of application
  - Potential for arthroscopic procedure

- SUBCHONDROPLASTY:
  - Addresses subchondral bony edema (bone bruise)
  - Potentially an option in early Osteoarthritis
  - Adjunct to chondral repair procedures

- CERULEAU Probe:
  - Novel concept to address early chondral changes
  - Possible adjunct treatment
  - Preventative?

- KINESPRING:
  - Early and established OA
  - Temporary unloading as way to TKA

Looking at the outcomes...

- 61/37 patients in a cartilage practice would have been enrollable as per clinical trial criteria
- High level clinical trial data guides our practice but reality often looks different.
DOES LOCATION HAVE AN EFFECT?

- **Location:**
  - **Microfracture:**
    - Femoral condyles: McIlhiney et al. AJSM 2006
    - Yes, central weight bearing portion of MFC: Kreuz et al. OC 2006
  - Trochlea: worse results than condyles
  - **Cell based techniques:**
    - Femoral condyles and trochlea have similar results
  - **Osteochondral allografts:**
    - Only small case series but primarily indicated for large defects in condyles
    - OC autograft / Mosaic: Smaller size defects only, >80 successful in TF joint, ~70% in PF joint Hangody et al. JBJS 2003, Nho 2010
  - **Donor site issues**

What about WC?

- **WC:** negative predictor for outcome:
  - 68% vs. 83% in ACI McIlhiney et al. AJSM 2006
  - 40% failure rate in WC patients over 40 McIlhiney et al. AJSM 2006
  - OC allografts worse results when WC Saeed et al. JBJS 1997
  - **Large effect for WC:**
    - Cannot be recommended as treatment if patient goes back to heavy physical labor work Lattermann et al. unpublished data
**Workman's Comp: ACI (20% Reduction in Outcome)**

- Major effect!

**Do Previous Procedures Have an Effect?**

- Previous procedures:
  - Re-MF: high failure rate
    - Mithoefer et al. AJSM 2009
  - Increased failure rate for cell based procedures
    - MF: 20%
    - Abrasion arthroplasty: 27%
    - Drilling: 28%
    - Roosbergen et al. AJSM 2009
  - N/A for OC allo/auto graft (area removed)
  - Unknown for Chondral allografts

**Subchondroplasty:**

- Concept:
  - Chronic subchondral bone bruises may represent chronic insufficiency fractures
  - Injection of calcium phosphate with a guide under arthroscopy

- Clinical data:
  - Small case series (60 patients with 11 that progressed towards TKA)

- Clinical Trials.gov:
  - Cohort study (n=760) safety trial
    - (≥20 points improvement in KOOS pain)
It may be a matter of size:

- 2cm² is considered the clinically relevant size based upon empiric and experimental data (1.6cm² (lateral) and 1.9cm² (medial) Flanigan DC et al. Arthroscopy 2010)

DOES SIZE HAVE AN EFFECT?

- Size:
  - Negative predictor for Microfracture
    - <4cm² non-athletes, 2cm² athletes
      - Mithoefer et al. AJSM 2006, 2009
  - No effect for cell based techniques:
  - Osteochondral allografts:
    - Only small case series but indicated for large defects in OCD lesions and AVN/Osteonecrosis;
      - Gatta et al. CORR 2010
      - Knutsen AJSM 2007
      - Kania J Knee 2005
  - OC autograft / Mosaic:
    - Larger sizes requiring more than 2 plugs increase failure rate
    - Donor site issues
Does size correlate with overall outcome:

- Prospective patient registry
- 57 ACI patients (65±7 yrs., 21 males), min 2 years f/u
- Patient Reported Outcomes completed pre-op and 3, 6, 12, and annually
  - IKDC
  - WOMAC
  - Lysholm
- Average follow-up: 2 ± 1 yrs.
- Raw defect size correlations (p<0.05)
  - Preoperative: WOMAC, r = 0.41
  - Postoperative: Lysholm, r = -0.30; WOMAC, r = 0.33
- Relative defect size correlations (p<0.05)
  - Preoperative: IKDC, r = -0.31; WOMAC, r = 0.43
  - Postoperative: IKDC, r = -0.29; Lysholm, r = -0.35; WOMAC, r = 0.33

Patients will improve regardless of their pre-operative score
- The pre-operative score, however, determines the post-operative score

Lower preop function scores associated with poorer outcomes:

- IKDC of <36
- 57 sensitivity and 0.83 specific for identifying those with poor (not meaningfully improved) outcome
- 72% Diagnostic Accuracy
- Relative risk of poor outcome is:
  - ODDS: 2.54
  - ICC: 1.39 to 4.12
UPDATE ARTICULAR CARTILAGE TREATMENT:
WHAT CHANGED MY PRACTICE:

- Length of symptoms has an effect on the outcome of cartilage procedures.

⇒ the earlier we identify these individuals, the better the outcome will be.
⇒ Need for better diagnostics!!

DOES ACTIVITY LEVEL HAVE AN EFFECT?

- Microfracture:
  - Defects < 2cm²: “work horse” (?)
  - 2-4cm²: “option”?  
  - 71% in NFL players RTP >4 seasons
  - results deteriorate after 2-3 years
  - < than 52% of high level athletes make it back to prev. level
  - 50% of all athletes make it back

Microfracture: Mithoefer et al. AJSM 2006,2009
Harrison et al. Arthroscopy 2010

- ACI:
  - Age and high level Soccer:
    - < 25-71% RTP
    - > 25 25% RTP
  - Sports activity (>1 time per week) improves outcome after ACI
  - Patient are more responsive to treatment if they participate in sports pre-operatively

ACI: Mithoefer et al. AJSM 2005
Kneus et al. AJSM 2007
Lattermann et al. unpublished data

ACTIVITY LEVEL:
ACTIVITY LEVEL: ACI

- Patients participating in sports are more responsive to treatment but:
  - Pietschmann et al. ICRS 2013: "resumption of high impact sports will lead to reduction in clinical outcomes"

What about weight?

- BMI 30-35 (obese):
  - Negative predictor for MF
    Mithoefer et al. AJSM 2009
  - No effect on ACI patients
    McNickle et al. AJSM 2009, Zaslav et al. AJSM 2009
  - BMI inversely correlated to post-op PRO scores
    Lattermann et al., unpublished data

DOES AGE HAVE AN EFFECT?

- Age:
  - Negative predictor for Microfracture
    Mithoefer et al. AJSM 2008, 2009
    Kreuz et al. Arthroscopy, 2006
    Gobbi et al. KSSTA 2005
  - Unclear for cell based techniques:
    - No effect: Boenberger et al. AJSM 2008
    - Maybe: McNickle et al. AJSM 2009
    - Yes: Knutsen et al. JBJS 2004
    - Yes in patients with unicompartmental OA and concomitant HTO
      Wood et al. Knee 2011
    - Basic Science: decreased synthetic ability of chondrocytes with increasing donor age
  - Age does not seem to have a significant correlation with outcome in patients <50 years
    Lattermann et al. unpublished data
What about the other 95% of the road to recovery?

- Significant deficits in knee extension strengths among all patients at 6 months and persisting among patellofemoral patients at 12 months

![Graph showing eccentric knee extension versus concentric knee extension](image)

**WHAT DO I FIND IMPORTANT**

- **Alignment:**
  - Any malalignment of more than 1-2 degrees requires a correction => increases magnitude of procedure
  - Less in PF joint as almost all of those procedures receive a TTT

- **Subchondral edema /bone loss on MRI:**
  - Large subchondral edema in a subacute or chronic setting indicates weakened subchondral bone => cell based chondral repair alone may not be sufficient
  - Bone loss >7mm may need to be addressed either changing the algorithm or requiring more extensive procedure (sandwich ACI)

- **Meniscal pathology:**
  - Lateral meniscus

**PEARLS for the Cartilage Guy:**

- **What is important:**
  - Know your patient population: follow-up
  - Manage expectations
    - Timeline: crutches, rehab
    - Cost
  - Beware of patients who:
    - Have a goal of return to high impact activities
    - History of non-compliance
    - Symptoms only with highest level activities
    - Unrealistic time constraints
    - "10/10 pain all the time"
    - WC?
Central Problem:

What have I learned?

- Specific indications for specific procedures are starting to emerge from the literature
  ⇒ No “one size fits all” strategy!
- Look at your patients using objective and subjective outcomes scores to determine your personal success with different techniques
- First order is: do no harm!
  ⇒ clinical studies need to guide our decision
- New technologies will not develop without physician support of clinical trials
  ⇒ consider taking part in these trials
- Do not take “gospels” at face value, be inquisitive and challenge the paradigm

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