Cartilage repair and regeneration.

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Disclosures: Kensey Nash Board of Scientific Advisors, Arthrex consultant

Goal?

• Repair, restore, regenerate cartilage
• Reduce pain
• Restore function

Cartilage Damage

• Pathophysiology of degeneration
  – The joint as an organ
  – Biomarkers for pain
• Injury
  – Biomarkers for those that lead to OA
• Widespread degenerative changes
  • Terminal repair

Available tools

• Microfracture
• ACI / MACI
• OATS
• OC allografts
• BMAC
• Synthetic scaffold

Damage to repair

• Chondromalacia
• Focal cartilage damage
• OCD
• Wide spread OA
• Co-morbidities
  – Meniscus, ACL
  – Terrible Triad
    • varus, MM deficient, MFC

Indications for surgery

- Pain
- Effusion
- Mal-alignment
- Instability

Microfracture

- Indicated in small full thickness defects
  - Not through subchondral bone
- Superclot = fibrin + growth factors + cells

Microfracture - evidence

- Horses, non-human primate, humans

- Increased fill in defect
- Diminished pain
- Return to function
- Durable?

Microfracture 8mo post-op. 3T MRI

- Moderate echo time FSE

When to microfracture?

- Lesions < 2.3 cm²
- Vertical wall and remove calcified cartilage
- Younger, lower BMI

Single stage cartilage repair

- Cartilage Autograft Implantation System (CAIS)
- DeNovo NT
- DeNovo ET
- Augmented microfracture
  - Bone marrow concentrate
  - BST CarGel
  - Cartilix
  - Calcitex
  - Geire C
  - AMIC (Autologous Matrix Induced Chondrogenesis)
BMC

• Bone marrow aspirate concentrate
  – Increases stem cells as compared to PRP
  – Fortier et. al. *JBJS*, in press.

3T MRI imaging

Second look arthroscopy at 12 weeks
- no biopsy
Return to exercise
Euthanasia 8 months post-operative:
- 3T MRI
- Gross score
- Histology: osteochondral, synovial membrane
- Multiphoton microscopy
- Synovial fluid and tissue for biochemistry

Single stage cartilage repair

• Scaffolds
  • TruFit (Smith and Nephew)
  • Osseofit (Biomet)
  • ChondroMimetic (OrthoMimetic)
  • KNC CRD (Kensey Nash)
Purpose of study

- Hypothesis: a biphasic graft (KNC CRD) would be safe and improve osteochondral repair compared to microfracture
  - KNC CRD (Kensey Nash Corporation Cartilage Repair Device)
- Bioresorbable biphasic scaffold
  - Collagen type I - β-TCP/PLA
  - Soak in bone marrow aspirate

Study design

- 12 horses (2-5 yrs)
  - GLP
  - PE, lameness evaluation, radiographs
- Lateral femoral trochlear ridge
  - 10 x 10 mm osteochondral defect
- KNC CRD
  - Soaked in bone marrow aspirate
  - Press fit into defect
  - ROM

Operative procedure

KNC CRD

Arthroscopic implantation

microfracture

Study design

- Patellofemoral joint radiographs
  - T = 0, post-op, 4, 12, 24 months
- Rehabilitation
  - Weekly lameness (pain on palpation, lameness, effusion, ROM)
  - Stall rest 6 wk, hand walk 10 wk, turn out (1/3 acre paddock)
- Second-look arthroscopy
  - 4 months, 12 months
  - Modified ICRS scoring system
- Euthanized 24 months

Results

- KNC CRD and microfracture
  - No pain on palpation, lameness, heat, soft tissue swelling, joint effusion, decreased ROM
Radiographs

Radiographic scores

LSM (SE): lysis, % replaced by bone, cyst formation, osteophyte formation, migration, peri-implant radiodensity.

(each subcategory: 0 = normal)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mean (SE) of difference</th>
<th>Significance of difference between two parameters</th>
<th>Coefficient of repeatability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sclerosis</td>
<td>0.19 (0.12)</td>
<td>0.005</td>
<td>2.62</td>
</tr>
<tr>
<td>Replaced With Bone</td>
<td>0.17 (0.13)</td>
<td>0.19</td>
<td>2.21</td>
</tr>
</tbody>
</table>

Second look arthroscopy

Second look arthroscopy statistics

- NSD by treatment or time for patella, color, surface area repaired, integration, surface, or total safety score.
- KNC CRD had better fill ($p<0.0001$), total efficacy ($p=0.0021$), and total arthroscopic scores ($p=0.0069$) at 4 months compared to control.
- Neither treatment changed from 4 to 12 months

Conclusions

- KNC CRD (12 month study)
  - Safety
    - no adverse reactions, no migration
  - Improved early repair compared to microfracture
    - defect fill
    - total efficacy score
    - overall gross cartilage repair score
  - Long term (24 month) efficacy and durability of repair presently being assessed.

Osteochondral autograft / allografts

- Cartilage replacement?
- Indications:
  - Larger, deeper lesions
  - OCD, post traumatic, failed prior tx
  - Use allografts <28 days, minimize bone, press fit
  - Autograft: OATS
Evolution of ACI Cell Therapy

- **CARTICEL®**
  - 1st described by Brittberg et al NEJM 1994
  - Autologous cultured chondrocytes in suspension
  - Implanted beneath surgically applied periosteal patch
  - On market in US since 1995

- **MACI®**
  - 3rd generation product, represents a significant improvement over traditional ACI
  - Autologous cultured chondrocytes on bio-compatible collagen membrane
  - Membrane fixed in place typically with fibrin sealant
  - On market since 1998: 18 countries in Europe, Middle East and Asia Pacific region.
  - Pivotal trial ongoing, will support basis for global registration

When to use ACI / MACI?

- Lesions >2cm²
- Femoral condyle, talus, patella

What strategy?

- Small: 0-1 cm
- Medium: 2-4 cm
- Large: >4 cm

- MACI
- BMAC
- Microfracture

- Check and correct alignment
- Rehabilitation