Scaffolds Based Therapy for Osteochondral Lesions of the Talus
A Systematic Review

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Disclosure

NO CONFLICT TO DISCLOSE

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Our disclosures are in the Final AOFAS Mobile App. We have no potential conflicts with this presentation.
Surgical strategies for OCL of the talus

1. **Reparative technique**
   - Bone marrow stimulation, ACI

2. **Replacement technique**
   - Osteochondral auto/allograft transplantation

- **Scaffold for cartilage regeneration**
  - Template, typically seeded with cells and occasionally growth factors
  - Basic Requirements
    - Biodegradable
    - Noncytotoxic
    - Mechanically competent/similar to surrounding tissue
    - Appropriate chemistry
    - Able to regulate cell activity
Scaffold-based therapy for OCL of the talus

- **2 step surgery**
  - MACI (Matrix-associated Autologous Chondrocyte Implantation)
- **1 step surgery**
  - AMIC (Autologous Matrix-Induced Chondrogenesis)
    - BMS + Bi-layer collagen I/III membrane
  - ACIC (Autologous Collagen-Induced Chondrogenesis)
    - BMS + collagen type I gel application
  - BMDCT (Bone marrow derived cells transplantation)
    - CBMA + type I/III collagen or HA scaffold
  - Cell free scaffold therapy
    - Biomimetic scaffolds, Cartilage Extracellular Matrix
  - Cartilage Extracellular Matrix and CBMA

What is evidence for scaffold-based therapy for OCL of the talus?

**Purpose**

*The purpose of the current systematic review is to clarify the effectiveness of scaffold-based therapy for OLT based on available clinical evidence*
Methods

Literature search PubMed/MEDLINE and EMBASE in January 2017 based on PRISMA guidelines
(cartilage OR cartilage injury OR cartilage damage OR cartilage repair OR cartilage defect OR osteochondral lesion OR osteochondral dissecans OR osteochondral defect OR osteochondral injury OR osteochondral fracture OR osteochondritis dissecans)
AND
(ankle OR talus OR tibia OR talocrural joint)
AND
(scaffold OR scaffold-based repair OR matrix-assisted chondrocyte implantation OR cartilage regeneration OR osteochondral repair).

• **Inclusion criteria**
  – Clinical studies evaluating the effect of scaffolds for ankle cartilage repair
  – All patients included had >6 months follow-up
  – Published in a peer review journal
  – Written in English

• **Exclusion criteria**
  – Review, Cadaveric study, Case report, Animal, In vivo
Methods

Examination of literature using 5 parameters

1. Level of evidence
   
   *based on JBJS from Marx RG et al*

2. Quality of evidence
   
   *Modified Coleman Methodology Score*

3. Variable reporting of outcome data

4. Clinical outcome

5. Return to sport at previous level

Variable reporting of outcome data

- Demographic information
- Sex
- Age (range)
- Patient history
- Duration of symptoms
- History of trauma
- Activities of daily living, including athletic participation
- Body mass index
- Study design
- Prospective/retrospective
- No. of patients
- Percentage of patients in follow-up
- Consecutive patients
- Follow-up time (range)
- Method of lesion size measurement
- Classification system used
- Details of surgical technique
- Clinical variables
  - Lesion size (length, width, and depth at deepest point)
  - Lesion location
  - Presence of cyst
  - Associated pathology
  - Concomitant procedures
  - Description of rehabilitation
- Imaging data
  - Imaging used to identify lesion
  - Imaging used at follow-up
- Patient-reported outcomes
  - Pain, function, and activity scale preoperatively
  - Pain, function, and activity scale at follow-up
Results

28 clinical studies
- Total 897 ankles
- Mean age 30.9 y.o.
- Mean follow-up 37.7 months
- Lesion size 215 mm²

Total 30 treatment groups
- MACI (13), BMDCT (9), AMIC (4), Cartilage ECM (2)
- ACIC (1), Cell-free scaffold (1)

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Total</th>
<th>MACT</th>
<th>BMDCT</th>
<th>AMIC</th>
<th>Cartilage ECM</th>
<th>ACIC</th>
<th>Cell-free scaffold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment groups, n</td>
<td>30</td>
<td>13</td>
<td>9</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Ankles, n</td>
<td>897</td>
<td>330</td>
<td>416</td>
<td>126</td>
<td>16</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Sex, male/female/unknown, n</td>
<td>501/322/72</td>
<td>174/111/45</td>
<td>238/153/22</td>
<td>79/47/0</td>
<td>7/9/0</td>
<td>3/2/0</td>
<td>-</td>
</tr>
<tr>
<td>Age, y, weighted mean (range)</td>
<td>30.9 (19-61)</td>
<td>30.1</td>
<td>30.2</td>
<td>34.9</td>
<td>42.7</td>
<td>25.6</td>
<td>-</td>
</tr>
<tr>
<td>Duration of symptoms, mo, weighted mean (range)</td>
<td>34.3 (6-216)</td>
<td>34.5</td>
<td>36.5</td>
<td>23.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Lesion size, mm², weighted mean (range)</td>
<td>215 (116-527)</td>
<td>171</td>
<td>248</td>
<td>240</td>
<td>130</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Follow-up, mo, weighted mean (range)</td>
<td>37.7 (6-87)</td>
<td>45.8</td>
<td>32.7</td>
<td>38.2</td>
<td>10.4</td>
<td>6</td>
<td>30</td>
</tr>
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Results

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<tr>
<th>Level of evidence</th>
<th>Quality of evidence</th>
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<tr>
<td>1</td>
<td>Excellent (MCMS&gt;84)</td>
</tr>
<tr>
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<th>AOFAS score is common (89%)</th>
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Variable reporting outcome data
- Demographic information: 93%
- Patients history: 30%
- Study design: 73%
- Clinical variables: 49%
- Imaging data: 73%
- Patient-reported outcomes: 85%

Clinical outcome scores
- 14 evaluation items
- AOFAS score is common (89%)

Quality of evidence
- Excellent (MCMS>84): 0
- Good (MCMS 70-84): 0
- Fair (MCMS 55-69): 7 (25.0%)
- Poor (MCMS <55): 21 (75.0%)

AOFAS score is not valid for OLT

Low quality
- Hard to reproduce
- Variability

Hospital for special surgery
Where the world comes to get back in the game
Results

• Clinical outcome (AOFAS score)
  MACT (12 groups 310 pts) : 59.1 -> 86.7
  BMDCT (9 groups 419 pts) : 61.1 -> 88.2
  AMIC (4 groups 126 pts) : 50.7 -> 82.3

• Return to sports
  – MACT; 1, AMIC; 2, BMDCT; 5 studies (only 8 studies)
  – Mean 68.3% of patients with lesion size 2.5 mm² returned to sports at previous level
Discussion

- 96% of included studies were of poor LOE
- No studies were of good or better methodological quality
- Low LOE and QOE studies are more likely to show overestimated outcomes compared to higher LOE and QOE studies. Careful attention should be paid when evaluating outcomes of scaffold-based therapy for OLT.
- Large variability and underreporting of clinical data between studies. Unable to compare the results across studies.
- The mean lesion size treated with scaffolds was 215 mm$^2$, which is much larger than traditional indication size for BMS. Suggesting that the use of scaffolds may further improve the potential of reparative techniques.
- 12 different scoring systems were used. 4 BMDCT groups showed that clinical outcome deteriorate after peaking at 2-3 year postoperatively.
Conclusions

• Scaffold-based therapy for OLT may produce favorable clinical outcome

• However, low LOE, poor QOE, and variability of the data have confounded the effectiveness of scaffold-based therapy

• Further, well-designed studies, are necessary to determine the effectiveness of the use of scaffold for OLT, especially when compared to available traditional treatments
References

- Schneider TE, Karaikudi S. Matrix-induced autologous chondrocyte implantation (MACI) grafting for osteochondral lesions of the talus. Foot Ankle Int 2009;30(9):810-4