Analysis of Failed Fresh Osteochondral Allografts of the Talus

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Ryan Pomajzl, MD
My disclosure is in the Final AOFAS Mobile App. I have no potential conflicts with this presentation.

Paul Fortin, MD
My disclosure is in the final AOFAS Mobile App. I have a potential conflict with this presentation due to: Musculoskeletal Tissue Foundation
Introduction & Study Objective

• OC allografting in the **knee**
  – Satisfaction rates up to 86%\(^1\)
  – Failure rates 18%\(^1\)

• OC allografting in the **talus**
  – Studies showing statistically significant improvement in pain and outcome scores
  – Failure rates of up to 35%\(^2,3,4\)

• **Study Objective:**
  To investigate the *in vivo* failure of fresh osteochondral allografts of the talus using structural histology and immunohistochemistry coupled with radiographic analysis and chart review.
Materials and Methods

• HIC-approved (HIC# 2013-118) retrieval study
  – Focusing on failed osteochondral allografts of the talus
  – Implanted and removed by a single surgeon
  – Conducted at our institution between 2009 and 2013

• Retrieved allografts underwent decalcified histologic processing (HistoTox Laboratories, Boulder, CO). 5.0 μm thin sections underwent structural and immunohistochemical staining.

• Medical Records Review and Radiographic Analyses
  – Patient Demographic & Surgical Data
  – Radiographic Analysis
    • Alignment, Radiolucency, Graft Height, Density

• Histologic and Immunohistochemical Analyses
  – Safranin-O/Fast Green
  – IHC Staining: Osteocalcin, TNF-α, CD4, CD8, CD68
Results: Medical Records Review & Graft Height

8 allografts from 7 patients:
- 5 Female; 2 Male
- 5 Right; 3 Left
- Average ages at implant & revision
  - 39 (range, 16 - 50); 42 (range, 17 - 58)
- Average term of implantation
  - 35 months (range, 12 - 96)
- Reasons for implantation
  - Post-traumatic arthritis
  - Osteonecrosis
- Reasons for revision
  - Graft collapse
  - Nonunion
  - Progressive arthritis
  - Pain

<table>
<thead>
<tr>
<th>Graft Height</th>
<th>Post-Index (mm)</th>
<th>Revision of Post-Index (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average</td>
<td>10.65</td>
<td>7.92</td>
</tr>
<tr>
<td>SD</td>
<td>1.43</td>
<td>1.80</td>
</tr>
<tr>
<td>Range</td>
<td>8.24 - 12.85</td>
<td>5.50 - 10.07</td>
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</tbody>
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- Height Difference: - 2.73 mm
- On average, the graft decreased in height by ~25% (Range, 5 - 44%)
Results: Radiographic Analysis

Preoperative

- Collapse/Subchondral Lucencies
  - 100% exhibit collapse (8/8)

Early Postoperative

- Interface
  - Visible in 63% (5/8)
  - Not visible in 38% (3/8)

12 Months Post-Op/Failure

- Density
  - Increased in 88% (7/8)
  - Decreased in 13% (1/8)
• Empty lacunae in the bony aspect of the graft indicates large areas of necrotic bone.
• Agrees with radiographic density data.

• Minimal red-staining on a Safranin-O/Fast Green stained section indicates very little sulfated glycosaminoglycan (proteoglycan) content remains in the graft cartilage.
- **Osteocalcin** staining is associated with normal, healthy bone.
- Staining most intense at the center of graft, with little to no staining at graft periphery.
- Absence of staining at graft periphery is characteristic of non-viable bone.

- **CD68** staining is indicative of osteoclasts.
- Confined to the periphery of the graft in all 8 cases.
- May be responsible for normal remodeling or the mechanical failure observed on radiographs.
TNF-α

- **TNF-α** is a proinflammatory cytokine (adipokine).

- Demonstrated most intense staining in central portion of the graft.

- May indicate future immune/inflammatory cell infiltration.
CD4 & CD8 Staining

- **CD4** staining is indicative of Helper T-cells, Macrophages, or Monocytes.
- Found throughout graft, but most intense at graft-host interface.
- Helper T-cells promote maturation and activation of CD8+ lymphocytes, the main effectors of allograft rejection.

- **CD8** staining is indicative of Cytotoxic T-cells, and Natural Killer cells.
- Found in close proximity to CD4+ cells.
- Taken with CD4 staining may indicate immune-mediated graft rejection.
Discussion:

- Radiographic analysis demonstrated a substantial loss of graft height and joint space narrowing associated with failure of the osteochondral allografts.

- Structural stains indicated a loss of sulfated glycosaminoglycans within the allograft’s cartilage and osteoclast-mediated bony resorption—both of which were localized to the graft-host interface.

- Immunostaining, specifically CD4 and CD8 staining, suggests that graft failure may be related to host immune response to the allogenic tissue.

Future Work:

- Expand collection of failed osteochondral allografts to include retrievals from external sites.

- Characterize the immune-related allograft rejection pathway using advanced immunostaining techniques, including tissue microarrays.

- Examine effects of immune-modulating drugs on allograft incorporation in animal models of fresh osteochondral allografting of the talus.
References


