What is the future of ACL reconstruction?

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Clinical question

• Do patients with an injury of their ACL have alternate options beyond conventional surgery?
ACL reconstruction surgery

- Highly successful operation
  - 90-95% good to excellent results
  - Same day surgery
  - Return to unrestricted sports participation at all levels
How well are we doing?
How well are we doing?

- ACL surgery does not guarantee return to previous level of participation
- ACL surgery does not eliminate pivot shift
- ACL surgery does not prevent radiographic osteoarthritis
Return to High School– and College-Level Football After Anterior Cruciate Ligament Reconstruction: A Multicenter Orthopaedic Outcomes Network (MOON) Cohort Study
Potential failure sites

- Early post-op
  - Graft fixation
    - 400-700N
    - Cyclic loading
- 2-3 mos post-op
  - Graft strength decreased 50%
- >6 mos post-op
  - Graft failures

Graft Strength Over Time

![Graft Strength Chart](chart.png)
Why not repair?

- Preserve insertion sites
- Preserve proprioception
- Preserve cells

- Poor surgical outcomes
  - Synovial fluid prevents fibrin clot
  - Fibroblast apoptosis
  - Collagen breakdown
Enhanced repair

- ACL fibroblasts enhanced by TGF B2, FGF2
- FGF2 improved healing of ACL laceration
- HGF improved ACL recon in rabbits
Bio-enhanced repair

- Immediate ACL repair
  - Collagen scaffold
  - PRP
  - Suture stent
  - Joint preservation at one year
- Delayed ACL repair
  - Not as successful
  - Alteration of synovial environment?

Proffen, et al Arthroscopy 2014
Bio-enhanced repair

- Mesenchymal stem cells injected into partial transection of ACL - Rat model
  - Better strength
  - Better histology

Kanaya, et al Arthroscopy 2007
Bridge enhanced ACL repair

Fig. 1: Torn ACL

Fig. 2: Place BEAR™ implant between torn ACL ends. Add blood.

Fig. 3: Pull torn ACL ends into implant with stitches.

Fig. 4: Healing ACL tissue replaces BEAR™ implant.
What is wrong with autografts?
What are the problems with current graft options?

<table>
<thead>
<tr>
<th>Autografts</th>
<th>Allografts</th>
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<tr>
<td>• Donor site morbidity</td>
<td>• Higher failure rate in collegiate athletes</td>
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<td>• Risk of patella fx</td>
<td>• Risk of disease transmission</td>
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<td>• Impact on hamstring strength</td>
<td>• Slower incorporation</td>
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<td>• Harvest increases surgical time</td>
<td>• Does not replicate ACL anatomy</td>
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Tissue Engineering Strategy for ACL Regeneration

- TGF
- IGF
- FGF
- BMP

- Resorbable scaffold

- Femur
- Tibia

- Neoligament
Biodegradable scaffold

- Withstand mechanical loads
- Degrade
- Promote cell attachment
- Deliver cell signals

![Graph showing the changes in Net breaking load, Fibrous scaffold loses strength, and Neoligament gains strength over time post-implantation.](image)
Stem cell derived multiphasic ACL graft

- Sheep model
- BMSCs
  - Bone culture
  - Ligament culture
- At six months mechanical properties comparable to adult ACL

Ma, et al. Tissue Eng Pt A 2012
Silk-collagen scaffold

- Rabbit model
  - 18 mos
  - Regenerate functional ACL tissue
  - Prevent degenerative arthritis

Shen et al. Biomaterials 2014
Biodegradable polymer scaffolds

- pDTD-DD – collagen scaffold
- Sheep model
- Intact at 12 wks
- Good cartilage preservation

Recommendations/Conclusions

- Alternatives to conventional surgical reconstruction are in the process of being developed. Use of biologics, stem cells, scaffolds and tissue engineering offer potential alternatives once they have been fully tested and refined. To date, these options are not yet available for human ACL reconstruction.
References

• Vavken P, Triton-X is most effective among three decellularization agents for ACL tissue Engineering. J Ortho Research 2009,
• Gilbert TW, “Decellularization of tissues and organs. Biomaterials 2006; 27:3675-3683
• Badylak SF, “Xenogeneric extracellular matrix as a scaffold for tissue reconstruction” Transpl Immunol 12:367-377
Summary

- Tissue engineering applications in ACL surgery
- A significant challenge
  - Biocompatible
  - Withstand physiologic loads
  - Functional tissue regeneration
  - Promote joint preservation
- Should be the future!
Thank you