Investigating Bridge-Enhanced ACL Repair (BEAR) and the Viability over Typical Graft Reconstructions

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Background of ACL Tears

Anterior Cruciate Ligament (ACL) is a knee stabilizing ligament that is ruptured on average of around 150,000 times per year in the US.

- 43% of these knee injuries are strains or sprains => third most prevalent form of lower extremity injury
- Majority of these injuries occur during non-contact motions

Primary function is to control anterior translation and rotation of the tibia

- 2 bundles: one that handles flexion and one that handles extension

Surgeries of this injury vary in terms of graft locations, but present limitations

Limitations of Graft Reconstruction

Variety of autografts through use of quadricep, hamstring, or patellar tendons

- Variety of opinions as to which is superior
- Successful but consequences arise for graft use
  - ~15% require secondary surgery later on
  - May increase risk of re-injuring or even injuring the healthy knee
- Major increase in likelihood of developing Osteoarthritis

Requires extensive rehabilitation

- May begin the day after surgery and last many months
- Postoperative rehabilitation essential to regain gait biomechanics and weight distribution

What is BEAR?

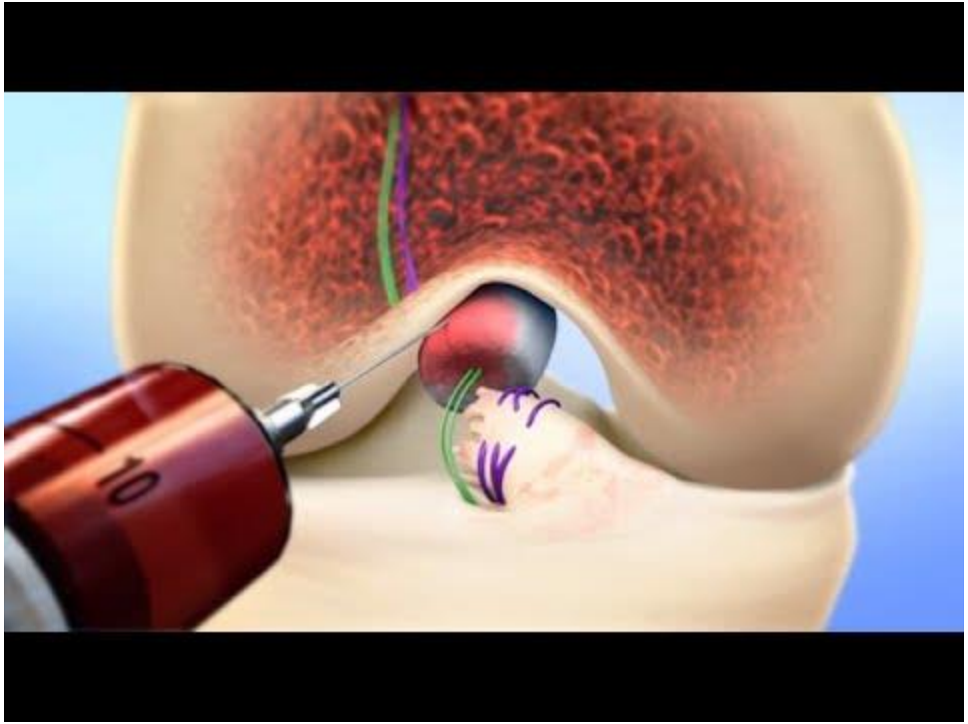
"Bridge-Enhanced ACL Repair" that uses tissue engineering to bridge together the ruptured ligament

- Removes need for traditional graft approach
- Theory of BEAR is to repair the native ACL instead of introducing bone tunneling

The procedure includes placing sutures at each torn end of the ACL and inserting a sponge in-between

- 8-12 week process to allow the body to replace the sponge with a new, natural ligament
- Can preserve nerve fibers at ligament insertion sites
    - Pivotal for knee biomechanics conservation

BEAR Video (52)



Hypothesis

BEAR will increase the biomechanical properties of the knee as well as minimize postoperative complications associated with graft reconstruction

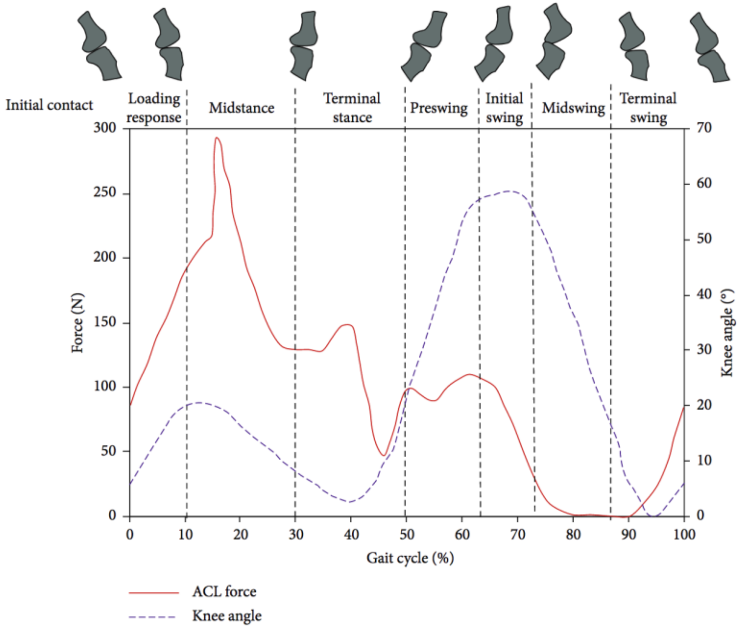
Will better restore biomechanics and weight distribution throughout the knee

- Less rehabilitation, less pain

Previous Studies in ACL Biomechanics

Pattern of Anterior Cruciate Ligament Force in Normal Walking

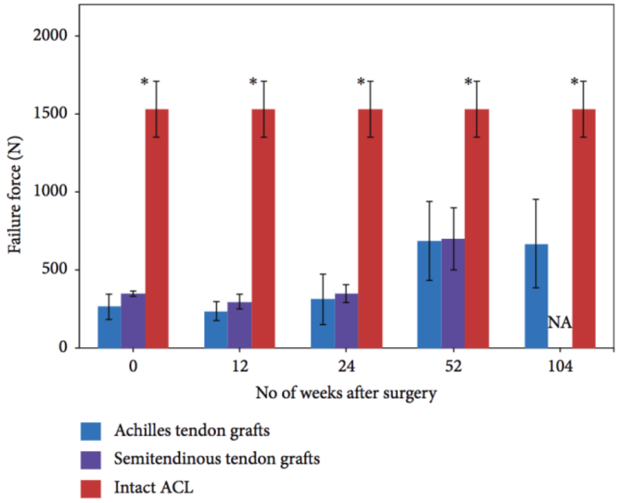
- 3-D Whole Body Model with Dynamic Optimization Theory for single gait cycle
- Joint angles/forces applied to 3-D Lower Extremity Model
- Peak ACL Force (anterior shearing force at knee) found to be 303 N during midstance



Previous Studies into ACL Reconstruction

A Review on Biomechanics of Anterior Cruciate Ligament and Materials for Reconstruction

- Tensile Tests of Femur-ACL-Tibia Complex
- Compared ACL to Tendon Materials used for graft replacement (Patellar Tendon = PT, etc.)
    - PT: higher loads, shorter elongation
    - Showed significantly lower failure loads



Previous Studies into ACL Reconstruction

Differences in Tibial Rotation <u>during Walking</u> in ACL Reconstructed and Healthy Contralateral Knees

- Walking exhibits offset external tibial rotation in stance phase
- Changes in tibial rotation contribute to knee osteoarthritis

Dynamic Function of the ACL-Reconstructed Knee <u>during Running</u>

- Knee kinematics of ACL Reconstructed Knee (PT or Quad Tendon) during downhill running found using stereoradiographic system
- Reconstructed knees exhibit increased anterior tibial translation and external rotation in stance phase
- These changes in rotational knee kinematics during functional loading may contribute to long-term joint-degradation and osteoarthritis

Previous Studies in the Development of BEAR

Bridge-Enhanced ACL Repair: A Review of the Science and the Pathway Through FDA Investigational Device Approval

- Cell seeding of fibroblasts on scaffold in rabbit knees were viable after 6 weeks (10x more collagen) but several risks (time, contamination risk, etc)
- Growth Factors (EGF, FGF, PDGF, etc) improve collagen synthesis and cell proliferation
  - Platelet-Rich Plasma (PRP)
- Collagen-PRP Scaffolds have been shown to heal ACL tear as well as ACL Reconstruction when compared to suture repair in large animal models
  - Significantly less osteoarthritis and maintains proprioception of ACL (knee stabilization)

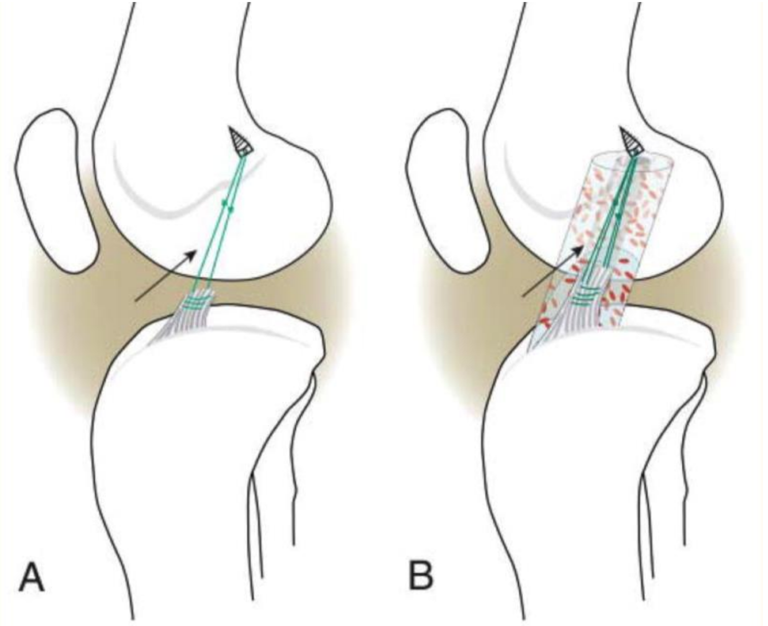
Previous Studies in the Development of BEAR

Collagen-Platelet Composites Improve the Biomechanical Properties of Healing Anterior Cruciate Ligament Grafts in a Porcine Model

- AP Laxity reduced 28% and 57% at 60° and 90° of knee flexion with CPC

Collagen-Platelet Composite Enhances Biomechanical and Histological Healing of the Porcine Anterior Cruciate Ligament

- Use of CPC in suture repair improved 3-month healing both mechanically both yield and stiffness



Previous Studies in the Development of BEAR

Collagen-Platelet Rich Plasma Hydrogel Enhances Primary Repair of the Porcine Anterior Cruciate Ligament

- Significant tensile mechanical improvements (yield and max loads, stiffness) at 4 weeks
- Needs more long-term testing

Biomechanical Outcomes of Bridge-enhanced Anterior Cruciate Ligament Repair are Influenced by Sex in a Clinical Model

- Improvement in healing and biomechanics when BEAR used compared to suture repair
- The differences in biomechanics depended heavily on sex
    - Females showed significantly less improvement due to BEAR when absorbable sutures used
    - Nonabsorbable sutures appeared to counteract this disparity in healing

Proposed Clinical Research Study for BEAR

The goal is to compare the calculated and observed biomechanical disparities caused by ACL repair surgery (BEAR vs. graft reconstruction) with an intact ACL (healthy contralateral knee)

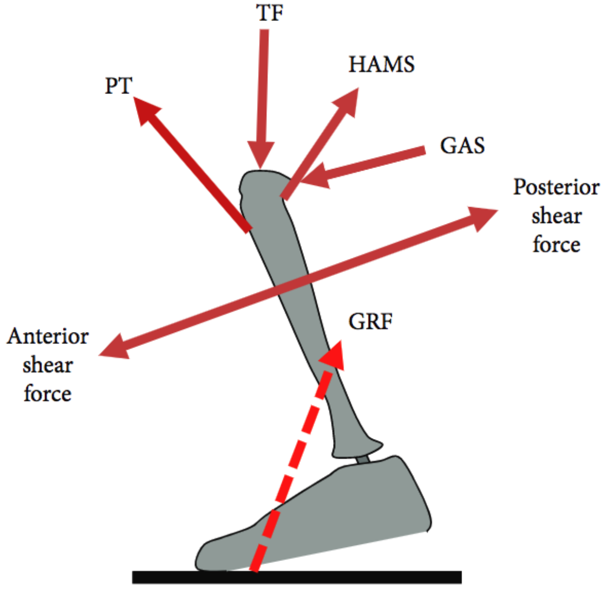
- 30 subjects (15 men, 15 women) in the age range of 16-50 (mean age around 35) undergoing unilateral, arthroscopic ACL Reconstruction
  - Minimum time of 1 month from injury to surgery (mean of roughly 10 months)
  - Exclusion: Substantial damage to contralateral knee as well as other structures of ACL-injured knee
- For both men and women, 5 will each undergo BEAR, patellar tendon graft, and quadricep tendon graft reconstructions
  - Comparisons of healing between surgery type and between sex can be observed
- 5 and 12 month biomechanical testing can provide insight into the potential benefits of BEAR over the accepted ACL graft reconstructions

Proposed Study (1) Measure *in vivo* ACL Loading

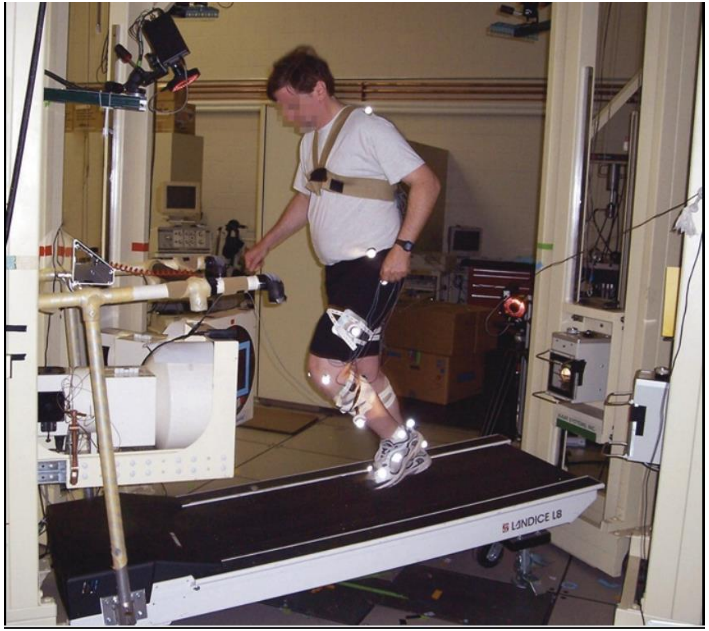
- Specific Aim 1: Using a 3D computational model to calculate *in vivo* ACL loading of both BEAR-treated and ACL-reconstructed knees during a phase of normal walking and comparing the differences to the estimated loading of an intact ACL.
    - Video Motion Imaging, Ground Reaction Forces (GRF), and Knee Forces measured and applied to a 3-D model of a knee
    - Image Capture with 3-D Model of knee estimates ACL loading

$$F_{\mathrm{ACL}} = F_{\mathrm{ACL}}^{\mathrm{sag}} + F_{\mathrm{ACL}}^{\mathrm{front}} + F_{\mathrm{ACL}}^{\mathrm{trans}} + \sum_j \mathrm{CT}_j$$

    - Model uses measured anterior shear force and resulting moments (adduction/abduction and internal/external rotation) and would provide confirmation of any resulting changes in ACL loading due in the various



Proposed Study (2) in Motion-Capture Imaging



- Specific Aim 2: Observing the biomechanical differences between patients of BEAR treated ACL surgeries in comparison with graft reconstructions through Motion-Capture Imaging
    - Propose a downhill movement simulation
    - Compare BEAR patients to graft patients
    - More stressful on ACL compared to level-ground running
        - Increase mechanical stresses
        - Eliminates double-support stance
- Use Dynamic RSA in assessment of knee kinematics
    - Study flexion, adduction, and rotation from initial foot

Future Directions

- FDA Device Approval requires demonstrations of safety, consistency, sterility, and biocompatibility of collagen scaffold
    - Further Requirements for devices incorporating biological elements
    - Minimizing contamination, proof that cells will remain in place, and assurance that growth factors target only desired cells
- Increase the number of subjects as well as begin targeting specific population groups (athletes, etc)
- Perform long-term studies to verify if biomechanical properties are maintained and ensure degradation of repaired ACL is less than that of graft reconstructions
- Improve the delivery of biological elements including growth factors and cellular material

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Questions?