Can we Assess Ligamentization of ACL Grafts
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Ligamentization
- Morphological adaptation in the graft as a result of the functional demands
- Biopsy: Biochemical and histological changes in the graft tissue from tendinous to ligament
- Wolff’s Law of bone-laid down on lines of stress
- 1986 “Ligamentization” - Amiel, Kleiner & Akeson

Structure
Ligament and tendon have similar hierarchical structure.
Type 1 collagen – 90%
Type 3 collagen – 10%
Type 4 collagen
Hydrogen Cross-Linking

Tendon
- Less metabolically active
- Collagen more parallel
- Flattened nuclei
- Less DNA content

Ligament
- More metabolically active
- Collagen less parallel
- More rounded nuclei
- Higher DNA content

Tendon
- Less type 3 collagen
- Less proteoglycans
- More total collagen

Ligament
- More type 3 collagen
- More proteoglycans
- Less total collagen
Ligament

Wavy pattern increasing capacity to absorb tension (crimping)
Handles large unidirectional tensile loads
Tolerates smaller stresses on other directions

Load Elongation Curves

Anterior Cruciate Ligament

- Ultimate tensile load: 2160 N
- Stiffness: 242 N/mm
- Strain tolerance: 20%

Ligamentization - Amiel et al

- Coined term ligamentization
- Rabbit study: PT ACL reconstruction
- Continuous development of graft tissue
- Described histological changes over 30 weeks
- Mirrored by biochemical changes: Collagen cross link PT to ACL
  - GAGS: Absent to ACL levels
  - Type 3 collagen: 0% to 10%
- Driven by cells derived from outside the graft

Ligamentization

- Tendon Specific Biological Features
- Ligament Specific Biological Features

Continuous Biological Process
Three phases: early; remodelling; maturation
Graft response to neovascularisation and mechanical stress
Never achieve biomechanical properties of ACL
Remains distinguishable with electron microscopy

Ligamentization

- Early human case report 1993
  - Harvested 4 year old hamstring ACL graft
  - Compared to another patients ACL harvested during TKR
  - Harvesting as baseline
  - Similar crimp pattern, cell type, GAG composition & collagen cross linking in graft & ACL
  - Human studies reflected animal models

Fig: http://www.shoulderdoc.co.uk/
Ligamentization - systematic review

Claes et al. 2011 - systematic review

- Level 3 and 4 studies
- Variable time lines
- Graft is viable at all times in humans
- Gradual biological process of maturation

Not agreed upon

- Best animal model to study - dogs, goats, sheep, rabbits, monkeys
- Whether animal timelines are transferable to humans
- Limited number of human studies
- Sampling errors likely

More research is required

Assessment of Ligamentization

- Histological Assessment
  - Haematoxylin and Eosin
- Biochemical Assessment
  - Total Collagen and type
  - Total Glycosaminoglycan (GAG)
  - Reducible Collagen Crosslinks
- Biomechanical assessment
  - Stiffness
  - Load to failure

MRI Assessment

- Non invasive
- No risk of damage to graft
- Does it yield same information as biopsy

MRI Biomechanical and Histological Assessment

Ligamentization - Weiler et al.

- Correlation of biomechanical, histological and MRI assessment
- Compared signal intensity and morphology on MRI with biomechanics & histology
- Sheep model
- Not possible to do in humans
Ligamentization-Weiler et al

- MRI-1.5 Tesla proton density plain and gadolinium enhanced prior to sacrifice
- Signal/noise quotient measured for each graft
- Correlated with max load to failure, stiffness and tensile strength

Ligamentization-Weiler et al

- High signal intensity correlated with decreased mechanical properties during early remodelling
- Significant negative linear correlation between signal/noise quotient and load to failure, stiffness and tensile strength

Ligamentization-Weiler et al

- Correlations for Gadolinium enhanced images were stronger than plain images
- Immunohistochemistry confirmed gadolinium enhancement reflected vascular status in early remodelling
- Signal intensity is a useful tool to follow graft maturation

Fleming et al J Biomech 2011

- 6 week PT goat study
- 3T MRI
- T2 relaxation time and volumetric analysis correlated with graft stiffness & failure load

Other MRI/Biopsy study

Ligamentization-Summary

- We can assess ACL graft ligamentisation with MRI
- Histological and biochemical analysis are the gold standard
- Invasive and must partially damage the graft
- Only justified in the research setting

Ligamentization-Summary

- Animal studies show correlation between MRI and histologic/biochemical/biomechanical analysis
- Stronger with Gadolinium
- Not currently utilized in clinical practice to determine RTP
- May become more generalized with further work
Ligamentization
Unanswered questions

Does ligamentization always occur?
Does speed and extent correlate with improved outcomes?
Does ligamentization reflect the quality of the surgery?
Is ligamentization useful in varying rehabilitation protocols?
Is ligamentization assessment useful in determining return to play?

Ligamentization
Criteria for Return to Sports

* Joint has recovered-swelling/pain/ range of motion
* Neuromuscular recovery
* Psychologically ready
* Graft is strong enough
* All of the above

Thank you