Can we Assess Ligamentization of ACL Grafts

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Val d'Isere 2014

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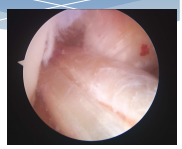
Ligamentization-overview



* What is ligamentization
* Structure of tendons and ligaments
* How can it be evaluated

  -Biopsy
  -MRI
* Does information from MRI match biopsy
* What is the relevance to clinical practice

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

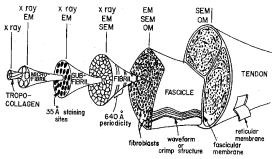
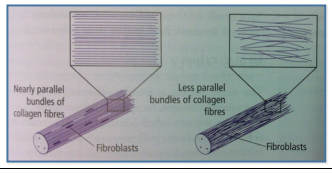


Fig: J. Kastelic, A. Galeski, and E. Baer", The Multicomposite Structure of Tendon", Connective Tissue Research, 1978, Vol 6, pp. 11-23.

Tendon Ligament

* Less metabolically active
* Collagen more parallel
* Flattened nuclei
* Less DNA content

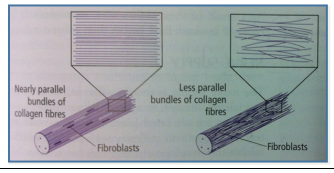
* More metabolically active
* Collagen less parallel
* More rounded nuclei
* Higher DNA content



Tendon Ligament

* Less type 3 collagen
* Less proteoglycans
* More total collagen

* More type 3 collagen
* More proteoglycans
* Less total collagen

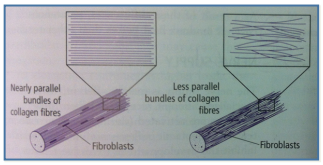


Ligament

Wavy pattern increasing capacity to absorb tension (crimping)

Handles large unidirectional tensile loads

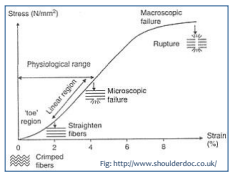
Tolerates smaller stresses on other directions



Load Elongation Curves

Anterior Cruciate Ligament

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



Ligamentization- Amiel et al

0363-5465/86/1400-0449$02.00/0
THE AMERICAN JOURNAL OF SPORTS MEDICINE, Vol. 14, No. 6
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winner of the basic science research award

The natural history of the anterior cruciate ligament autograft of patellar tendon origin*

DAVID AMIEL,† DIP ING, JEFFREY B. KLEINER, MD, AND WAYNE H. AKESON, MD

From the Division of Orthopaedics and Rehabilitation, University of California, San Diego, California

Ligamentization- Amiel et al


The natural history of the anterior cruciate ligament autograft of patellar tendon origin*

- 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%

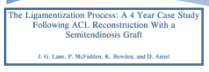
Driven by cells derived from outside the graft

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


The Ligamentization Process: A 4 Year Case Study Following ACL Reconstruction With a Semitendinosis Graft

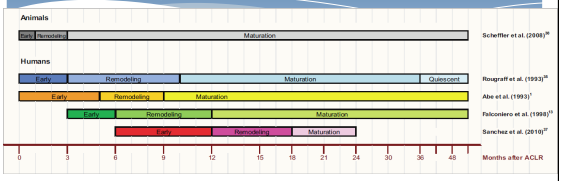
J. G. Lane, P. McFadden, K. Bowden, and D. Amiel

The Journal of Arthroscopic and Related Surgery 9(2): 149-153

Early human case report 1993

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

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

Ligamentization Claes et al

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

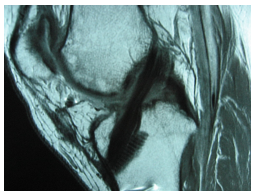
Histological Assessment
- Haematoxylin and Eosin

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

0363-5465/01/2929-0751$02.00/0
The American Journal of Sports Medicine, Vol. 29, No. 6
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Winner of the 2000 Excellence in Research Award

Biomechanical Properties and Vascularity of an Anterior Cruciate Ligament Graft Can Be Predicted by Contrast-Enhanced Magnetic Resonance Imaging

A Two-Year Study in Sheep*

Andreas Weiler,†‡ MD, Gunnar Peters,† CM, Jürgen Mäurer,§ MD, Frank N. Unterhauser,† MD, and Norbert P. Südkamp,† MD

From the †Trauma and Reconstructive Surgery, Sports Traumatology and Arthroscopy Service and §Department of Radiology, Charité, Campus Virchow-Clinic, Humboldt-University of Berlin, Germany

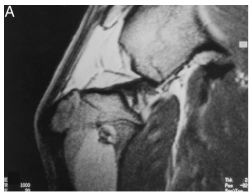
Ligamentization-Weiler et al

* 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

Weiler et al 2001 AJSM 29 (6)

Ligamentization-Weiler et al

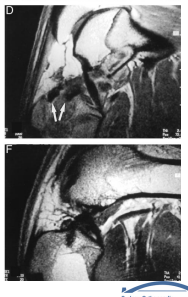
* MRI-1.5 Tesla proton density plain and gadolinium enhanced prior to sacrifice
* Signal/noise quotient measured for each graft
* Correlated with max load to failure, stiffness and tensile strength



Weiler et al 2001 AJSM 29 (6)

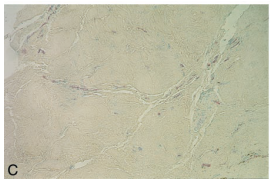
Ligamentization-Weiler et al

* 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

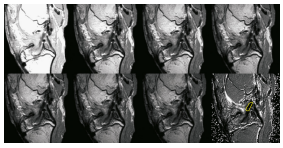
* Correlations for Gadolinium enhanced images were stronger than plain images
* Immunohistochemistry confirmed gadolinium enhancement reflected vascular status in early remodelling
* Signal intensity is a useful tool to follow graft maturation



Other MRI/Biopsy study

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



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

Ligamentization

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Thank you