


# Do we rebuild a real ligament?



Advanced Course on  
Knee Surgery  
January 19<sup>th</sup> - 22<sup>nd</sup> 2010

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## Ligamentization


- Still a matter of debate

## Ligamentization

- Does the ligamentization process result in the restoration of the original ligament?
- Does this ligamentization process restore the "double/triple" bundles organization?

## Basic science

- Graft healing
- Inflammatory phase
- Proliferative phase (4-12<sup>th</sup> wk.)
- Ligamentization phase (12- ...<sup>th</sup> wk.)

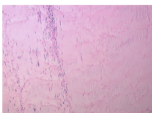


Amiel et al J Orthop Res 1986

## Basic science

- Early healing phase
  - Central acellularity and necrosis
  - Influx of host cells
    - Inflammatory cells
    - Fibroblasts
  - Complete replacement of viable graft cells by hosts cells around 2-4 weeks in animal models
 

Kleiner et al J Orthop Res 1986  
Kobayashi et al Trans Orthop Res 2005
  - No revascularization



## Basic science

- Proliferation phase (4-12 wks)
  - Increased cellularity with proliferation of fibroblast - myofibroblasts
  - Loss and reformation of collagen crimp
  - Revascularization

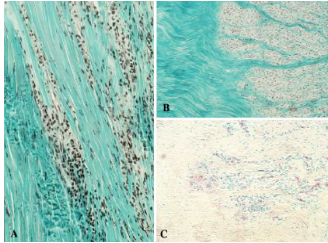
proliferative

  - Increased collagen type III / fibronectin
  - Increase smaller diameter collagen fibrils
  - Increased GAG content

reparative

## Basic science proliferation phase (4-12<sup>th</sup> wks)

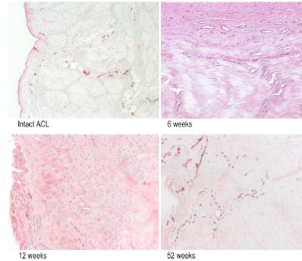
### Recellularization (4-12 wks)



Scheffler et al *Knee Surg Sports Traumatol Arthrosc* 2008

## Basic science proliferation phase (4-12<sup>th</sup> wks)

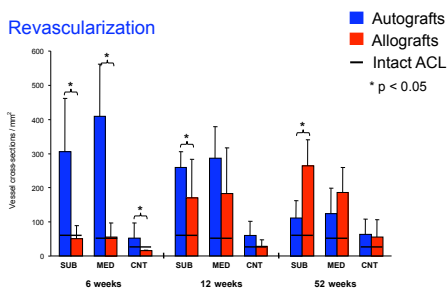
### Revascularization (4-12 wks)



Scheffler et al *Knee Surg Sports Traumatol Arthrosc* 2008

## Basic science: Proliferation phase (4-12 wks)

### Revascularization



Courtesy of Scheffler et al. *Arthroscopy*, Richard O'Connor Award 2007

## Basic science

### Ligamentization phase (12-... wks)

#### Remodeling phase:

- Structural and mechanical adaptation
- Increased in collagen content
- Non-reducible/reducible cross-link ratio increase

Maeda et al *Clin Orthop Res* 1997  
 Jackson et al *Am J Sports Med* 1993  
 Kirkpatrick et al *J South Orthop Assoc* 1996  
 Nikolaou et al *Am J Sports Med* 1986  
 Arnoczky et al *J Bone Joint Surg* 1986  
 Shino et al *J Bone Joint Surg* 1984  
 Scheffler et al *Arthroscopy* 2008

## Biology

- Favorable vascularization
- Cellular repopulation
- Matrix remodeling
- The ultimate small diameter collagen fibril orientation
- Final cross-sectional area of the graft

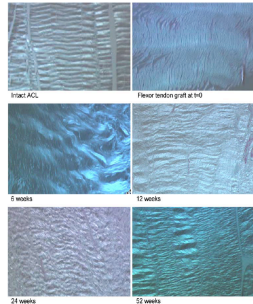
## Original ACL versus graft

- Similar macro-morphology within 6 to 12 months
- More type III collagen in the graft
- Unimodal pattern of small collagen fibers
- Crimp frequency remain increased in the graft
- In animal model, graft strength could never surpass 50-60% of the intact ACL

Abe et al *Arthroscopy* 1993  
 Jackson Am J Sports Med 1993  
 Liu et al *CORR* 1995  
 Weller et al *J Orthop Res* 2002  
 Weller et al *Am J Sports Med* 2004  
 Scheffler et al *KSSTA* 2008

## Original ACL versus graft

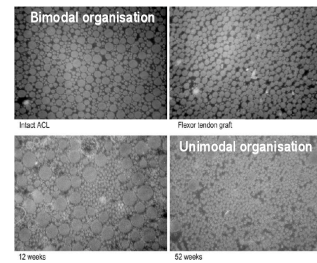
- Collagen crimp pattern a sheep model
- Polarized light microscopy x200



Scheffler et al Knee Surg Sports Traumatol Arthrosc 2008

## Original ACL versus graft

- Collagen remodeling sheep model



Scheffler et al Knee Surg Sports Traumatol Arthrosc 2008

## In human

- Same healing phases:
  - Graft necrosis, recellularisation, revascularization, ligamentization
- Remodeling is reduced
- Less necrosis (no more than 30%)
- Not all intrinsic grafts cells replaced by extrinsic cells
- Large area of normal collagen alignment and crimp pattern
- No excessive revascularization

Johnson Arthroscopy 1993  
Rougraff et al KSSSTA 1999

## Biological process

- In animal models, the graft undergoes a process of adaptation rather than full restoration of the intact ACL's biological properties.

« Law of functional adaptation »

Wilhem Roux

An organ will adapt itself structurally to an alteration, quantitatively and qualitatively in function

## What we know !

- MECHANICAL ENVIRONMENT
  - Placement of the graft
  - Tensioning
- Rehabilitation
- Patient compliance
- It takes time...

## How about "bundles"

- V. H. basketball player 29 y old  
ACL BPTB



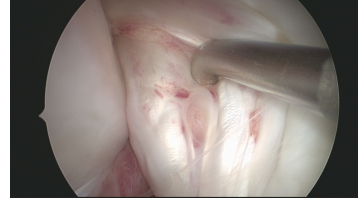
## How about "bundles"

- V. H. basketball player 29 y old  
ACL BPTB, 5 years post-ACLrec



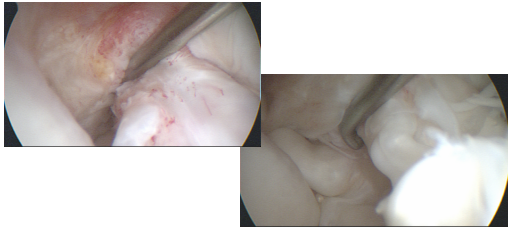
## How about "bundles"

- V. H. basketball player 29 y old  
ACL BPTB, 5 years post-ACLrec



## How about "bundles"

- V. J. 38 y old capoeira, 4 years  
post ACL-rec, partial ACL rupture



## In summary

- The ligamentization process is an adaptative transformation of the graft which **does not** lead to a full restoration of the intact ACL's biological properties.

## In summary

- Biological response is related to the **biomechanical** and biochemical environment into which the graft is placed

Surgeon  
PT

## In summary

- Biological response is related to the **biomechanical** and **biochemical** environment into which the graft is placed

Surgeon  
PT

Patient



## Epidemiology

- 1 ACL reconstruction/2000 inhabitants in US
- 200'000 ACL rupture/year in US
- 120'000 TKR/year

Steinert et al *Orthop Res Society San Francisco* 2008

- 31'000 ACL reconstructions/year in France

Symposium *French Society of Arthroscopy Lyon* 2007

## ACL failure

- Functional instability with sports or activities of daily living
- Increased pain
- Loss of motion
- Recurrent episodes of giving way
- SSD diff. > 5 mm, Lachman et pivot positive

## Graft necrosis

- Released of cytokines
  - Matrix.-metalloproteinase (MMP-3)
  - Tissue inhibitor metalloproteinase-1 (TIMP)-1
  - Interleukin-6 and 8 (IL-6, IL-8)
  - Tumor necrosis factor alpha (TNF-a)
  - IL-1
- Extended necrosis
- Collagen disturbance
- Myxoid degeneration
- Interfering process of revascularization

Cameron et al *Am J Sports Med* 1997  
Higuchi *Int Orthop* 2006

## Vascularization

- Overtensioning of the graft
- Patients habits:
  - Smoking, cocaine consumption
- Diabetes
- Choice of the graft
- Hypoxia
  - Period of avascular necrosis - decrease in VEGF expression

## Cells repopulation

- Vascularization
- GF cascade: TGF- $\beta_1$ , b-FGF, PDGF
- Age ?
- Genetic background ?
  - Fast healer ?
  - Slow healer ?

Kuroda et al *KSSSTA* 2000

## Matrix remodeling

- GF cascade: TGF- $\beta_1$ , b-FGF, PDGF
- Vascularization
- Cell repopulation
- Age ?
- Genetic background ?
  - Fast healer ?
  - Slow healer ?

Kuroda et al KSSTA 2000