Clinica Ortopedica e
Traumatologica
Università degli Studi di Pavia

Fondazione
IRCCS Policlinico
San Matteo

Chairman: Prof. F. Benazzo

New interest in synthetic ligaments ?

F. Benazzo

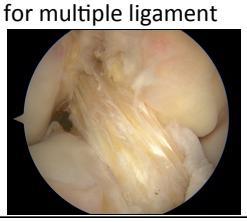
5th Advanced Course on Knee Surgery

Key Points

- Options for ACL reconstructions
- Reasons for scaffold
- The history: carbon fibers, gore-tex, dacron, Kennedy LAD, Leeds-Keio, others
- What we have to know: the rationale and the science behind
- Indications for use
- Conclusions

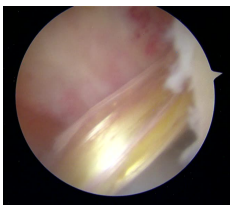
The gold standard: autologous grafts (>90% of ACL R)

- Harvest site morbidity
- Slow rehabilitation (revascularisation and collagenisation)
- Insufficient graft material for multiple ligament reconstructions
- One option surgery



Allograft (<5%)

- Limited availability
- Costs
- Potential for disease transmission
- Longer to incorporate
- Slight increase in laxity over time?
- Short operating time
- No harvest site morbidity



Ancient interest in synthetic graft

- To avoid donor-site morbidity
- To reduce operating time
- To have a faster rehab
- To have a graft infinitely available

The beginning: carbon fibres

- 1970s: Proplast (Vitex-Inc, USA) made of Teflon and carbon; Polyflex (Richard, USA) made of polypropylene; Intergraft (Osteonics Biomaterials, USA), made of carbon.
- Initially employed in tendon, then in ligaments.
- In 1981 first implant with an arthroscopic procedure

Dandy DJ et al, Clin Orthop Relat Res 1982

The beginning: carbon fibres

- Preliminary encouraging results
- Poor resistance to torsio… rupture
- Inflamma… …he knee joint
- C… …the liver

WITHDRAWN

…ushton N. et al, J Bone Joint Surg 1983

Gore-Tex

- 1986: polytetrafluorethylene (PTFE) (Gore-Tex, USA) approved by the Food and Drug Administration (FDA) for revision autologous ACL reconstructions.
- The highest ultimate tensile strength (5300 N); stiffness of 322 N/mm
- Excellent postoperative stability, early load-bearing capacity: encouraging short-term results.

Ahlfeld SK et al, Am J Sports Med 1987
Glousman R et al, Am J Sports Med 1988
Friedman MJ et al, Techniques Orthop 1988

- At a longer follow-up: worsening in knee stability
- Lack of tissue ingrowth and wear.

Gore-Tex

- 10/21 (47%) ruptured or partially damaged a… 11 months

Ferkel RD et a… 9

- Complication rate of 76% in … reconstruction followe… …J Sports Med 1992
- Rupture ra… …ears.

…edge SL et al, Am J Knee Surg 1992

- … …n 15 of 17 patients after 15 years …wide!)

Muren O et al, Acta Orthop 2005

- Inguinal limphoadenopathy

Wilson AG et al, AM J Sports Med 1998

WITHDRAWN IN 1993

Dacron

- 1989: Dacron ligament (Meadox Medicals, USA; Stryker Corp, USA) approved by the FDA
- Made of polyester, composed of an 8-mm diameter sleeve of loosely woven velour with a central core made of four tightly woven tapes.
- Encouraging results in the short term. Lachman and pivot shift negative in 75% of patients after 18 months

Lukianov AV et al, Am J Sports Med 1998

Dacron

However..

- 40% rupture rate in 57 patients after 18 months

Arnauw G et al, Acta Orthop Belg 1991

- 20% failure rate in 84 patients after 2 years, 35.7% after 5 years

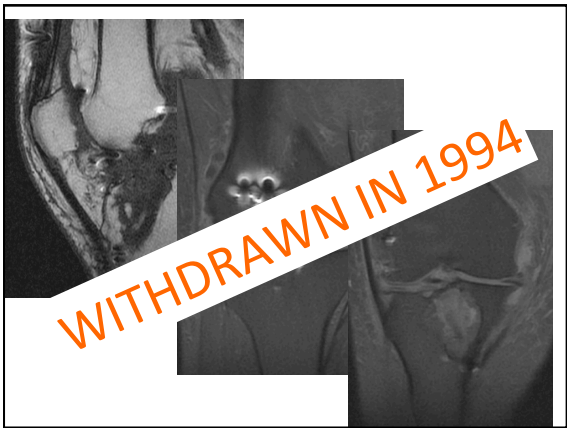
Wilk RM et al, Am J Sports Med 1993

- 30% complication rate in 110 patients at 2-5 years

Noble CA, AM J Sports Med 1989

- 44% rupture, 83% documented OA and only 14% acceptable stability and knee function after 9 years

Gillquist J et al, Am J Sports Med 1997



Kennedy LAD

- 1975: polypropylene made Ligament Augmentation Device (LAD) (3M, USA) introduced by Dr. John Kennedy
- Utilised as augmentation in addition to an autologous ACL reconstruction or after ACL primary repair
- Designed to transfer loads during initial healing process and to protect the autologous implant during its early phase

Kennedy LAD

- 48 Marshall-MacIntosh procedures reinf d with LAD followed for 50 months. P results in subjective questio examination and radiol an nonaugmented p
- 1.4% er 3 years
- incidence of reactive synovitis, decline of the Marshall-MacIntosh transfer

ABANDONED

al, Am J Sports Med 1985

U.S. Kennedy LAD clinical experience 1989

Leeds-Keio

- 1982: Leeds-Keio (Neoligaments Ltd, UK), woven polyester fibers porous coated.
- Scaffold: acts as an inducer for tissue ingrowth and promotes the formation of a neo-ligament on the intra-articular portion
- Over 50,000 LK grafts implanted worldwide.

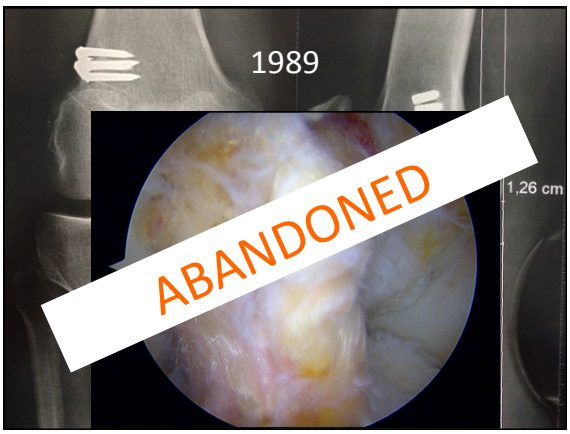
Leeds-Keio

- 15 te co
- 24 ur
- M Bl
- A 10

Others PET ligaments

- 51 patients with PET ligaments (Trevira, Proflex, Pro-Pivot) followed for 18-21 years
- Failure rate: 27%
- Normal or nearly normal IKDC grade in 24%
- Positive Lachman test in 75%
- OA on radiographs in 100%

Ventura A et al, The Knee 2010



Mechanical properties

Properties	Natural ligament	Carbon fibre	Gore-Tex	Dacron	Kennedy-LAD	Trevira	Leeds-Keio
Ultimate tensile strength (N)	1730	660	5300	3631	1500	1866	2000
Stiffness (N/mm)	182	$230x10^9$	322	420	280	68.3	270

Legnani C, Ventura A et al, Int Orthop 2010

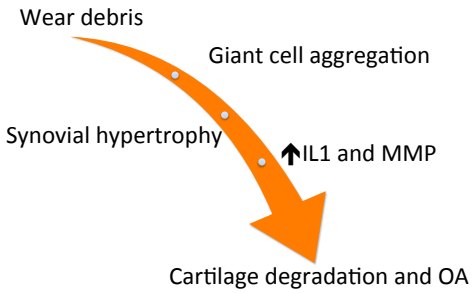
Late 1990s

Loss of trust in artificial ligaments: impaired tissue ingrowth and remodeling, breakage, wear debris, synovitis, recurrent instability, osteolysis.

"…artificial ligaments could induce osteoarthritis in the knee joint instead of preventing it."

Olson EJ, FU FH et al, Am J Sports Med 1988

OA developement



The late 1980s: the "golden age"

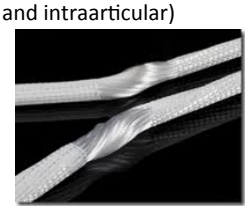
In 1990 in the USA:

- 250000 ACL reconstruction, of which:
  - 16000 Gore-Tex
  - 25000 LADs
  - 14000 Leeds-Keio

Friedman, 1990

The 2000s: LARS

Ligament Advanced Reinforcement System, France). Made of polyethylene terephtalate (PET), 2 parts (intraosseous and intraarticular)



Good clinical results at short follow up

Newman SD et al. Int Orthop 2012

LARS

- 159 patients followed for 3-5 years. 7 failures (4.4%), postoperative Lysholm score of 95, normal or nearly normal IKDC grade in 92%.

Gao et al, Arthroscopy 2010

- Compared to BPTB: better subjective and objective outcomes for LARS during the initial years, no difference after 24 months.

Nau T et al, J Bone Joint Surg [Br] 2002

- Compared to HT: higher knee stability in the LARS group after 4 years.

Liu ZT et al, Int Orthop 2009

- 24/28 (92%) good or optimal KOOS results at a mean of 7.9 years, 1 graft failure, no synovitis

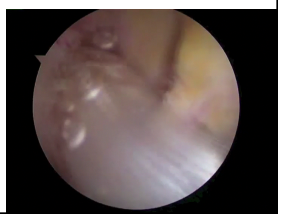
Parchi PD et al, Int Orthop 2013

The ideal patient…

- Middle aged active subjects with laxity/ disturbing instability not deserving TKA
- Athlete seeking for a fast recovery
- High-level athlete who injured his ACL at the nearly end of his career and/or is willing to be back to active sport
- Multiligament injuries (post-traumatic)

My approach

- Transtibial
- Transcondilar fixation on the femur
- Metallic screw on the tibia
- No specific rehab



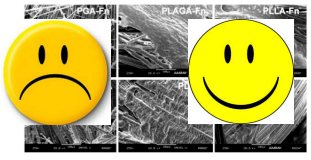
…the ideal artificial ligament

- Biocompatibility
- Mechanical characteristics similar to the native ligament

- SCAFFOLD: capable to allow immediate load bearing post-implantation and degrade at a rate comparable with that of developing cellular and tissue ingrowth.

Materials

- In vitro study on 3D braided scaffolds of PGA, PLGA, and poly(L-lactic acid) (PLLA) filaments
- Rabbit ACL fibroblasts seeded on PLGA and PLLA produce most matrix. PGA is detrimental (reduce cells number)



Lu HH et al, Biomaterials 2005
Kuo et al, 2010

Natural fibers

- Syntetic polymers lack functional chemical groups for cellular binding and may release acidic byproducts or polyesters during degradation.
- So.. interest in the application of natural, protein-based fiber materials as scaffold
- Collagen I (most prevalent in ligaments): not still possible to recreate cross-links → currently too weak

Nirmalanandhan VS et al, J Biomech 2008

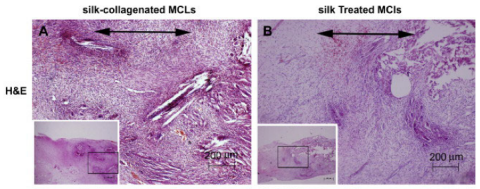
Silk

- Remarkable tensile strength and toughness, unmatched for natural proteins
- Displays surface amino acids for cell adhesion
- Remains structurally whole in aqueous solutions
- Degrades slowly (months) in vivo
- Can be fabricated into gels, films, braided fibers or nanofibers
- Waiting for long-term animal trials and clinical studies.

Functionalizing the graft

- Merging one scaffold with another to combining mechanical properties with integrin binding capability

Chen X et al, Biomat 2008



Growth factors

- Specific dose-response relationships of each growth factor
- bFGF led to an increased cell proliferation and production of collagen types I and III

Sahoo S et al, Differentiation 2010

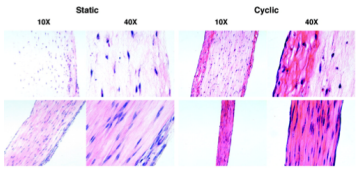
- TGFβ-1 led to an increased cell population, collagen and smooth muscle actin production in human ACL cells

Kuo CK et al, Dev Dyn 2008

Cyclic strains

- The application of cyclic strain (tensile and torsional strains) in stem cell based bioreactor systems promotes cell proliferation, cell alignment, and ligament-marker expression

Garvin J et al, Tissue Eng 2003



Key question: ligament-bone interface

- Enables the transfer of loads between distinct tissues
- Minimizes the formation of stress concentrations
- Supports the communication among multiple cell types necessary for interface function and homeostasis
- Research has to focus on it

Zhang X et al, J Shoulder Elbow Surg 2012

Prosthesis	Advantages	Disadvantages
Carbon	Reduction and even distribution of stress between graft and soft tissue attachment Polylactic acid coat protects graft during implantation Encourages ingrowth of collagen into implant	Migration of carbon wear particles Unacceptable incidence of implant stretching and rupture led to poor long-term functional outcomes
Gore-Tex	Tensile strength 3X native human ACL	Progressive long-term loosening
Dacron	Polyester coating serves to protect implant from abrasion	Poor long-term stability
Leeds-Keio Artificial Ligament	Acts as a scaffold for soft tissue ingrowth Excellent max. tensile strength which exceeds that of native ACL	Acts as more of a load-bearing prosthesis, allowing for fibrous tissue ingrowth Large number of long-term graft ruptures
Kennedy Ligament Augmentation Device	Protects autogenous graft from excessive stresses	Weak implant-graft interface Propensity to cause intra-articular inflam. response and resulting synovitis and effusions
LARS Ligament	Mimics natural ACL structure and orientation Reduces shearing forces on the implant Porosity encourages tissue ingrowth	Residual post-operative laxity still present No long-term follow-up studies yet
Tissue-engineered Scaffolds	Duplicate mechanical & structural properties of native ACL Restoration of normal knee joint kinematics Implant can resemble normal ACL over time	Loses strength over time Allogenecity of collagen scaffolds can lead to rejection Consistent reprod. difficult due to batch-to-batch variability Collagen not as modifiable as biodegradable polymers

Conclusions

- Too many times in the past we have been driven by the enthusiasm for what appeared to be the Holy Graal
- Do not be the first, do not be the last
- Cautions , ethical considerations
- Discussion with the patient
- Scientific interest in the basic science and in the research: the correct approach