HISTORY OF ARTIFICIAL LIGAMENTS

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Who are we?

Movmedix®, formerly L.A.R.S (Laboratoire d'Application et de Recherche Scientifique) is a company founded in 1992 by J-P Laboureau, in Arc-sur-Tille, France.

The company designs, develops, and manufactures artificial ligaments for Sports Medicine, orthopaedic and trauma applications.

LARS™ product range offers a large portfolio broadening the treatment options for multiple soft tissues injuries. Movmedix® sells its products through a distribution network of 25 countries around the world.

INTRODUCTION

The tear and rupture of the Anterior cruciate ligament (ACL) is the most frequent knee injury, with around 100,000 and 250,000 lesions occurring in the US each year[1,2]. ACL tears have poor healing ability, forcing patients to undergo reconstructive surgery. There has been ample research to find safe and clinically effective treatments. Among these, autografts are nowadays considered the gold standard for ACL reconstruction procedures.

The drawback, however, of harvesting the tissue from elsewhere in the body is the significantly increased patient morbidity. Allografts are another option, eliminating the necessity of harvesting tissue. Although this modern tissue treatment indeed mitigates the potential risk of disease transmission and graft rejection, it is not available in every country, and when available, the graft may not correspond to the desired size.

In addition, the quality of the tissue may vary depending on where it is harvested from or how it was prepared. Lastly, artificial (or synthetic) ligaments have existed for a long time, and many surgeons recognize them as excellent alternative treatments. Nonetheless, the clinical results of most devices launched on the market did not meet surgeons' expectations. As a result, only a few ACL reconstruction devices exist, including the LARS, which has been on the market for the last 30 years.

Unfortunately, despite publications describing positive short and medium-term clinical outcomes, these devices remain associated with previous generations of artificial ligaments.

The question that may come to mind is, "Why be so persistent in researching and developing a technology and a product to replace grafts?". Although clinical results related to graft treatments are usually positive, artificial ligaments are a means of overcoming grafts' limitations. In addition, when artificial ligaments are implanted, patients suffer neither short nor mid-term morbidities; long-term physical deficiencies are also avoided thanks to the fact that no tissue was harvested from elsewhere in the body.

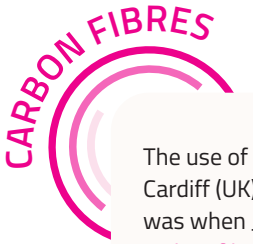
Furthermore, the need to wait for graft maturation or "ligamentization" is eliminated, so that recovery may be faster than in the case of a graft reconstruction procedure. It is always available off the shelf, ready to be used. It has predetermined dimensions and mechanical properties, and the surgeon implants it with a fixation system that guarantees a stable initial fixation.

In the document below, the first section will trace the history of artificial ligaments in order to understand the main characteristics of the devices that preceded the LARS and the causes of their clinical failures. Then, it will explain what makes LARS different from the other implants.

Why are artificial ligaments of interest?

- Availability
- Strong mechanical properties
- Prevention of graft harvesting and morbidities
- Predetermined dimensions
- Easier and shorter operations
- Sterile

THE FIRST GENERATION



The use of artificial ligaments increased in the second half of the 20th century. Cardiff (UK) researchers in the 1970s worked on a ligament prototype[1]. This was when Jenkins and his team designed a new device composed of braided carbon fibres, expected to act as a 3D scaffold and induce tissue ingrowth[3].

As animal studies had shown positive results, clinical trials on humans were started. However, Rushton et al. reported worrying outcomes, with 25% of the patients complaining of discomfort and knee pain[4] . In addition, arthroscopic control confirmed synovitis, identifying black-stained synovium due to abrasion between fibres, leading to carbon debris. In some patients, this debris was even found in the lymph nodes[4].

Following these catastrophic results, systems like the Integraft System (Osteonics, Livermore, CA) coated the carbon fibre implants with polylactic acid[5] . Engineers hoped the coating would protect the fibres from excessive-wear debris. However, despite the efforts made to improve the device, mechanical failures - such as ruptures due to weak torsion resistance - were observed.

Thus, the clinical studies came to a unanimous conclusion: the coated ligament was unsuitable for clinical use[1,5,6]. In the same decade, several other devices were put on the market, such as the Proplast ligament (Vitex-Inc, Houston, TX, USA), made of polytetrafluoroethylene (PTFE) and carbon oxide, all without success[5].

> *"Since a high proportion of our tissues is composed of carbon compounds, it would not perhaps be surprising that implants of the pure elements should be well tolerated by these tissues."*
> *- Jenkins[7], 1977*

COMPOSITE LIGAMENT

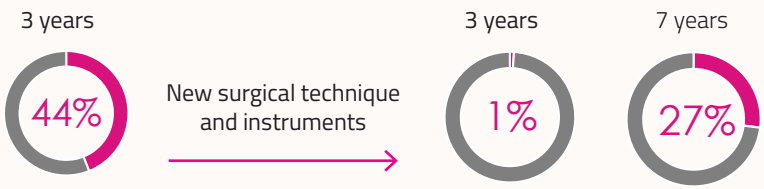
In 1985, another approach emerged with the release of the ABC ligament (Surgicraft Redditch, UK). The ABC ligament was a composite device made of carbon fibre and polyethylene terephthalate (PET) braided in a zigzag pattern[8].

The first clinical results were poor, with many failures and notably an abnormal laxity shown at 34-month follow-ups[9]. In 1992, the surgical technique was modified, and new instrumentation was developed by introducing a tibial jig to simplify the bone tunnel position[8].

Such innovations lead to a substantial improvement in ABC short-term results[8]. Nevertheless, medium-term results were disappointing.

Over time, this device, too, fell out of use[10].

ABC failure rate[7]



The first generation in brief

- Unacceptable failure rate
- Shearing forces between crossing fibres lead to substantial amounts of carbon debris and rupture[10]
- Inadequate mechanical properties (unnecessary stiffness, low torsion, and poor elongation resistance)[1,5]

THE SECOND GENERATION

	Gore-Tex	Dacron	KLAD	Leeds-Keio
Company	WL Gore	Stryker	3M	Neoligaments
Type	Prosthesis	Prosthesis	Scaffold/ reinforcement	Scaffold/ reinforcement
Release-removal	1986-1993	1989-1994	1987-2000	1982-2003
Design	Tightly braided	Tightly knitted, with a loosely porous sheath	Diamond braided	Woven structure with longitudinal bundles and transverse bundles
Material	PTFE*	PET**	PP***	PET
Ultimate tensile load	5300 N	3630 N	1500 N	2000N
Stiffness	270 N/mm	420 N/mm	56 N/mm	200 N/mm

**Polytetrafluoroethylene ; **Polyethylene terephthalate ; ***Polypropylene*

> *"The fatigue of the implant leads to axial breaking and fibres fraying." - Laflamme et al.*

	Advantages	Reasons of failures
Gore-Tex (W.L Gore)	High mechanical properties	Excessive abrasion in bone tunnels, loosening, synovitis, high failure rate
Dacron (Stryker)	High mechanical properties, design supposed to reduce abrasion	Excessive abrasion in bone tunnels, synovitis, high failure rate
KLAD (3M)	Protect autograft from excessive stress	Synovitis, delayed autograft maturation, not better than autograft alone
LK (Neoligaments)	Scaffold and augmentation device, mechanical properties close to native ACL	Long-term results not satisfying, tissue maybe not functional (fibrous)

Common reasons for failures

- Poor design (shape, orientation of the fibres)
- Excessive abrasion:
  - to the bone tunnels edges
  - between fibres
- Inadequate mechanical properties (torsion, elongation...)
- Biocompatibility (not systematic tissue ingrowth, synovitis...)
- Surgical techniques (arthrotomy, tunnel placement...)

THE SECOND GENERATION

POLYMER ERA

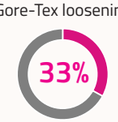
The new devices developed in the '80s were all composed of artificial polymers to avoid the issues generated by carbon fibres. The most frequently implanted devices were: Gore-Tex, Dacron, Kennedy Ligament Augmentation Device, and Leeds-Keio.

Gore-Tex

The Gore-Tex (W.L Gore, Flagstaff, AR, USA) ligament was designed to be implanted in replacement of the ACL using the "over-the-top" technique. However, worrying medium-term clinical results were reported. Several scientific publications highlighted complications such as loosening of the ligament in a third of patients at 4 years follow-up[12], a 17% revision rate at 18 months[14], and a 29% rupture rate at five years[13], while a meta-analysis also found a 26,6% rate of synovitis[15].

Moreover, wear particles were found in the lymph nodes of patients who had received the implant[13]. In a longer follow-up, osteoarthritis symptoms were also observed in 62% of patients[16]. The Gore-Tex graft was withdrawn from the market in 1993[13]. Retrospectively, a study deemed the device too large, with dimensions preventing a correct positioning in the intra-articular space[17].

Gore-Tex loosening



Dacron

The Dacron (Stryker Corp, Kalamazoo, MI, USA) was designed as a scaffold for ACL replacements, but without functional tissue ingrowth, it acted instead like a prosthesis[18]. The device was designed to be implanted either with an "over-the-top" technique or with traditional bone tunnels. Early clinical results were catastrophic, with rupture rates reaching up to 40% at 18 months[13,19].

On longer-term follow-ups, 80% of patients developed osteoarthritis symptoms[1,20], and 84% suffered from unacceptable anteroposterior knee stability[18]. Excessive abrasion on bone tunnels' edges was the main reason for early failure[1,6]. The Dacron device was withdrawn from the market in 1994[11].

LK, Leeds-Keio

British and Japanese researchers initially developed the LK (Neoligaments, Leeds, England) implant. The ligament was fixed with staples and bone plugs using a porous intra-articular segment, allowing tissue ingrowth[1,21].

The first clinical publications about the LK were contradictory: some mentioned functional tissue on the LK implant at a 1 year follow up[22], while others did not find new tissue but instead reported synovial inflammation[23]. On a longer-term overview (13.3 years), a rupture rate of 28% and an increased laxity rate of 56% were observed[24]. As a result of such clinical results, the LK ligament was no longer seen as a viable device for ACL reconstruction[5,25]. In 2003, the Leeds-Keio II was put on the market: a radio frequency-generated glow discharge procedure was added to the manufacturing process of the ligament, resulting in a more hydrophilic implant[11].

A few studies showed this ligament to be promising; however, some authors thought it was not supported by enough clinical results to be used in ACL replacement[15,26]. Nevertheless, the LK implant showed encouraging results for other applications, such as extensor mechanism deficiencies[11].

Thus, the LK technology evolved into Poly-Tapes (Neoligaments, Leeds UK), a band made to «treat soft tissue approximation and reconstruction of ligaments and tendons,» as described on Neoligaments' website.

LK – Laxity at 13 years

Kennedy LAD

The Kennedy LAD or KLAD (3M, St Paul, MN, USA) was different from previous devices as it was designed to reinforce autografts. Initially, it was promoted only for the Marshall-MacIntosh technique, but it was later used for all types of grafts[1,5].

The clinical results of the KLAD are mixed. On the one hand, only 1.9% of ruptures were brought to light[13], and other authors reported moderate residual laxity[27]. On the other hand, Kdolsky et al. observed a failure rate of 19.3% at five years[28]. The suture interface between the graft and the LAD was eventually identified as the weakest point of the system[5]. Moreover, yarn-yarn and yarn-bone abrasion induced inflammatory response and synovitis, delaying the maturation of the autograft[6,25].

None of the studies was able to show that using the KLAD as a reinforcement of the autograft yielded better results than the simple autograft. The device was finally removed from the market in 2000.

THE THIRD GENERATION

Inspired by its predecessors while representing at the same time a breakthrough device in several aspects, the Ligament Advanced Reinforcement System™ or LARS™ was designed by professor J-P Laboureau and has been marketed since 1992. This ligament is made of PET and is considered the «third generation" of artificial ligaments.

WHY LARS IS DIFFERENT?

1 Specific design

The device innovates in its intra-articular segment, with free longitudinal fibres in two bundles. The LARS mimics the native ligament and is resistant to torsion and elongation.

In addition, free fibres allow for cell adhesion and proliferation[1]. The ligament is composed of two intraosseous segments (warp-knitted fibres).

This pattern is non-deformable and resistant to stretching, unlike some braided or woven ligaments[1,29].

2 Versatile

The LARS ligament can be either used for reconstruction, allowing for preservation of ligament stumps, or as a graft reinforcement if the stumps are resorbed.

Native ACL stumps are not only essential for the cell colonisation of the device, but they also allow the preservation of mechanoreceptors[29], which are essential for the patient's sensory perception.

3 A 'savoir-faire' made in France

A high-performance cleaning process ensures the removal of the additives used during the manufacturing process of PET fibres, thus offering superior biocompatibility.

4 Precise technique

Emphasis is also put on the correct isometric position of the bone tunnels. Improper placement can lead to several complications (impingement, over-tension, abrasion, debris ...).

5 Experience

LARS has been on the market for 30 years and has shown better results than all previous devices, with the lowest rates of synovitis (0.2%), failure (2.6%), and revision (2.6%) in the meta-analysis of Batty et al.[15].

What is more, LARS has had good clinical results in the short and medium-term compared to autograft[30–33]. Studies with longer follow-ups have also shown the positive clinical results of LARS, highlighting its clinical scores (Lysholm, Tegner, IKDC) as superior to autograft techniques[33–35].

CONCLUSION

As ligament tears have become increasingly prevalent over the past years, many companies have searched for a durable alternative to the gold standards of autografts and allografts. Unfortunately, the first artificial ligament trials in the '80s and '90s resulted in poor clinical results, meeting neither surgeons' nor patients' expectations. Also, the materials' inadequate mechanical properties, combined with inadequate designs and surgical techniques, turned the initial excitement into disillusion.

Many devices, therefore, fell out of use or were withdrawn from the market in the '90s. Despite these failures, surgeons and engineers did not give up on the dream of developing a safe implant available off the shelf, which would allow patients to recover as fast as possible without suffering from additional morbidities.
Third-generation LARS is often mistakenly associated with first & second-generation artificial ligament devices. However, armed with a better understanding of the failures of previous generations of devices, Movmedix® has paved the way for the rehabilitation of artificial ligaments and their vast potential.

In 1992, the next breakthrough was reached by LARS with the launch of the 3rd generation of artificial ligaments. This new generation has demonstrated significant results, thanks to its free fibres section and a superior cleaning process. LARS has now been on the market for 30 years, with 15 years of documented clinical data[1]. Its use for ACL reconstruction[36] has slowly but surely expanded to include a good number of countries around the world, with few ruptures or synovitis being reported[15,30–35].

"History suggests that when past surgical practices have failed, their 'rediscovery' was consistently associated with a better understanding of the vital interdependence between ACL anatomy, tissue composition, biomechanics, and healing processes"
- Martin et al .

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