

# Histological analysis of ACL reconstruction failures due to synthetic-ACL (LARS) ruptures

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**Summary.** *Introduction:* Anterior Cruciate Ligament (ACL) reconstruction is an established surgical procedure. Synthetic ligaments represent an option for ACL reconstruction. Their popularity declined for the raising concerns due to re-ruptures, knee synovitis and early arthritis related to I and II generation artificial ligaments. The introduction of a III generation synthetic ligament (Ligament Advanced Reinforcement System-LARS) permitted renewed interest in the adoption of this kind of graft. Main purpose of our study was to describe the histological findings on samples obtained from a consecutive series of ACL revision surgeries due to LARS ACL reconstruction failures. Secondary aim was to determine the reason for LARS rupture. *Methods:* In a period between 2016 and 2018 eleven patients underwent ACL revision surgery due to LARS ACL reconstruction failure. At the time of the arthroscopic procedure, samples of synovial membrane and remnants of the torn LARS were sent to the Pathological-Anatomy Institute of our Hospital for a histological analysis. *Results:* Histological analysis of the synovial tissues confirmed the arthroscopic evidence of synovitis mainly characterized by chronic inflammation with predominance of multinucleated giant cells. The adoption of polarized light microscopy revealed the presence of brightly bi-refractive material (LARS wear particles) in the synovial tissue; at higher magnification wear debris were detected inside the cytoplasm of multi nucleated cells. The histological analysis of the removed LARS revealed a surrounding typical foreign body reaction with poor signs of fibrovascular ingrowth of the synthetic ligament. *Conclusions:* Our findings could not clearly advocate a unique mechanism of LARS-ACL reconstruction failure: biologic issues (poor tissue ingrowth) and mechanical issues (fibers properties and tunnel position) probably concur in a multi factorial manner. ACL reconstruction using artificial ligaments can not be considered a simple surgery. Artificial augments require some expertise and could therefore achieve better results if used by skilled sport surgeons other than trainees or low volume surgeons. The Authors believe that ACL reconstruction with synthetic devices still have restricted indications for selected patients (e.g. elderly patients who require a fast recovery, professional athlete, autologous tendons not available and/or refusing donor tendons). Our study arises additional suspicion on the unresponsiveness of synthetic fibers and claim some concern in the implantation of synthetic devices. ([www.actabiomedica.it](http://www.actabiomedica.it))

**Key words:** anterior cruciate ligament, synthetic ligament, reconstruction, histology, failure

## Introduction

Anterior Cruciate Ligament (ACL) reconstruction is an established surgical procedure performed to restore knee stability that can achieve optimal results in terms of both patients related outcomes (symptoms, return to pre-injury level) and objective clinical assessment (knee stability assessed by instrumentations) (23).

Several surgical techniques have been described and it has been postulated that the best option should be tailored on patients' characteristics and expectations (22).

A crucial aspect regarding ACL reconstruction is the selection of the graft since each of the different possibilities have relative advantages and disadvantages. Autologous tendons harvested from a donor site (hamstring, patellar, quadriceps tendons) represent the graft of choice for many authors and the gold standard for younger patients (<40 years) (24). Allograft tendons (quadriceps, Achilles tendon, hamstring, patellar, anterior and posterior tibialis tendons and the fascia lata) represent an option in primary ACL reconstruction for older patients and in revision ACL surgery (21,24).

A third graft option for ACL reconstruction are synthetic ligaments. Supporters of artificial grafts advocate relative advantages compared to autografts and allografts: a quicker surgery in absence of donor site morbidity and a faster rehabilitation compared to autograft and the absence of potential disease transmission compared to allograft (21). Furthermore, the sterilization process and irradiation may contribute to the weakening of the allograft (26).

Despite the above assumptions, several failures in the early 80's and 90's - re-ruptures of the ligament, knee synovitis, clinical instability and early arthritis (1,2) - with I and II generation synthetic ligaments (1) lead to a progressive concern and their popularity declined.

The introduction on the market of a 3<sup>rd</sup> generation synthetic ligament (Ligament Advanced Reinforcement System-LARS) made of Polyethylene Terephthalate (PET) permitted renewed interest in the choice of this graft for primary (and revision) ACL reconstruction. The microscopic structure of the LARS and a particular purification mechanism of the fibers

should lead to a better soft tissue ingrowth and reduce the risk of synovitis (3). Furthermore, the fibers of the synthetic ligament present two different arrangement: in the intraarticular portion, the ligament consists of longitudinal fibers that are twisted at 90° angles without transverse fibers while in the extra articular part the LARS is waved by longitudinal and transverse fibers (21). These peculiar issues of the LARS should minimize the shear stress to the device thus leading to a better ingrowth of tissues with an inferior risk of wearing, less spreading debris particles and, therefore, a minor risk of synovitis and other complications advocated to older synthetic devices (1,14).

Despite very satisfying results on short to mid-term follow-up (15,16,21) a recent study by Tulloch et al (20), reported a LARS-ACL reconstruction failure rate of 33.3% at a minimum of 6 year of follow-up and concluded that the LARS should not be considered as a graft option for primary ACL reconstruction.

Main purpose of our study was to describe the histological findings on samples obtained from a consecutive series of ACL revision surgeries due to synthetic (LARS) ACL reconstruction failures.

Secondary aim was to determine the cause of failure of LARS ACL reconstructions.

## Materials and methods

In a period between 2016 and 2018 eleven patients (10 male, 1 female), mean age of 41 years-old (ranging from 24 to 49), presented at our Institution complaining for knee instability after ACL reconstruction performed with a synthetic ligament (LARS). All the patients had the primary ACL reconstruction in other hospitals and came at our clinics at a mean of 3 years (minimum 9 months, maximum 5 years) after the index surgery. All the patients were clinically tested (anterior drawer, Lachman and pivot shift test) and imaging investigations (X-Rays and MRI) were evaluated (Figure A-B-C).

All the eleven patients were treated due to the failure (rupture) of the LARS-ACL reconstruction determining clinical instability; none of the patients were treated due other symptoms potentially related to the artificial ligament (e.g. swelling or synovitis) or

associated lesions (e.g. meniscal tears, cartilage lesions, associated ligamentous injuries).

ACL revision surgeries were guided by the RE-*WISE* ACL classification (25) and in all the eleven patients we were able to perform a one-stage ACL revision surgery since previous tunnels well acceptable (7/11 revisions) or grossly malpositioned (4/11 revisions) such that they could be avoided during the drilling of new tunnels (26). In accordance with Di Benedetto et al (27), our preference in ACL revision surgery was towards allograft tendons – cryopreserved gracilis and semitendinosus - associated with a transtibial technique. In all the patients we utilized a femoral suspension system (Top Traction System-TTS) (28) (Figure D). At the time of the arthroscopic procedure, we withdrew samples of periarticular tissues (synovial membrane) and remnants of the torn LARS

(Figure E-F); when possible, the LARS stump was removed “en bloc”. Both the samples were sent to the Pathological-Anatomy Institute of our Hospital where the specimens were prepared on tissue slide sections and processed on Hematoxylin-Eosin staining. A histological analysis was performed on optical and polarized light microscopy at different magnification.

## Results

At the time of the ACL revision surgery we documented the arthroscopic findings in all the patients.

In eleven revision surgery (100% of the patients) the clinical diagnosis of rupture of the synthetic ACL reconstruction was confirmed intra operatively and in seven of the eleven patients we were able to remove “en



**Figure A-B-C-D.** X-Rays showing fixation methods in primary ACL reconstruction (A-B). MRI demonstrating the rupture of the ACL (C). Allograft hamstring tendons quadruplicated and prepared with a TTS screw (D).

bloc” one of the two stumps of the LARS, usually on the proximal (femoral) side (Figure G-H).

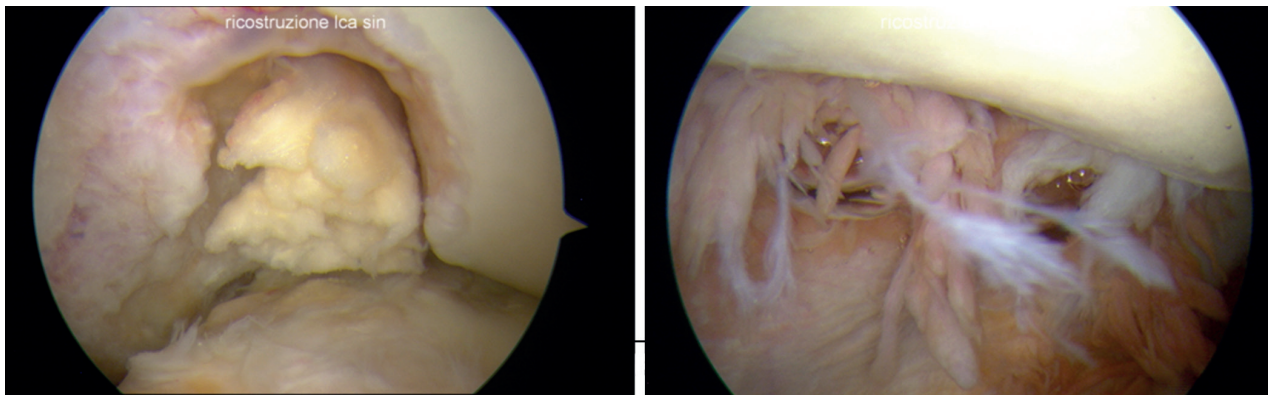
As expected, the removal of the LARS remnant showed the absence of macroscopic integration of the ligament at the bone-ligament interface; according to other authors (20,21), in all the eleven revision surgeries we have not found signs of osteolysis and/or widening of the tibial or femoral tunnels. Furthermore, in six of the eleven patients (54.5%) we found a wrong position of the tunnel and in 5 of them, according to Samitier et al and recent literature (26,29,30), the misplaced tunnel was more often on the femoral side and usually in a too vertical and anterior position. The roughly malposition of the tunnel led us to drill a new tunnel without a coalescence or weakening of the bone (Figure X-Y). In all the 11 revision surgeries we were able to perform a one-stage procedure without the need of staged procedure.

In all the patients we found severe widespread villonodular synovitis to every compartment of the knee joint. The synovitis was macroscopically characterized by evident hyperemic and redundant intra-articular tissue (Figure I-J).

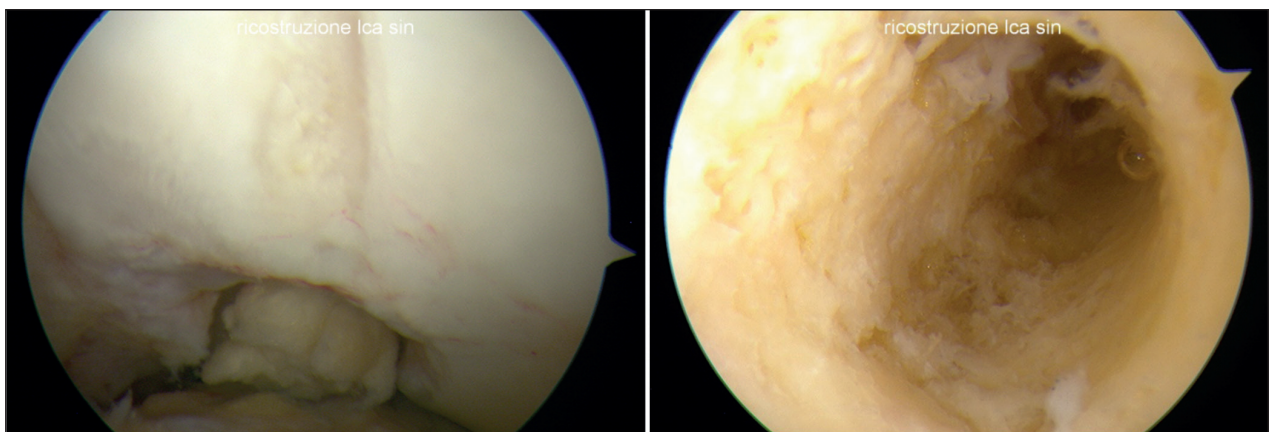
During the ACL revision surgeries we removed arthroscopically the failed LARS and we took samples of synovial tissue; both the specimens were preserved in formalin and sent to the pathological-anatomy institute for the analysis.

In all the patients a partial synovectomy rather than a radical synovectomy was performed in order to limit post-operative bleeding and swelling of the knees thus to facilitate an early rehabilitation protocol.

Histological analysis of the synovial tissue confirmed the arthroscopic evidence of synovitis; confocal microscopy revealed at different magnification the



**Figure E-F.** Arthroscopic findings. Femoral-side LARS stump with intercondylar and medial condyle signs of cartilage damage (E). Intra-articular tissues demonstrating villonodular synovitis (F).



**Figure G-H.** Rupture of the LARS at the opening of the femoral tunnel (G). (H) Femoral Tunnel after the removal of the LARS. Figure H demonstrates the absence of macroscopic signs of ligament bone ingrowth

hyperplasia and the hypertrophy of the synovial tissue characterized by a typical cellularity of chronic inflammation with predominance of multinucleated giant cells typical of foreign body reaction (Figure K-L).

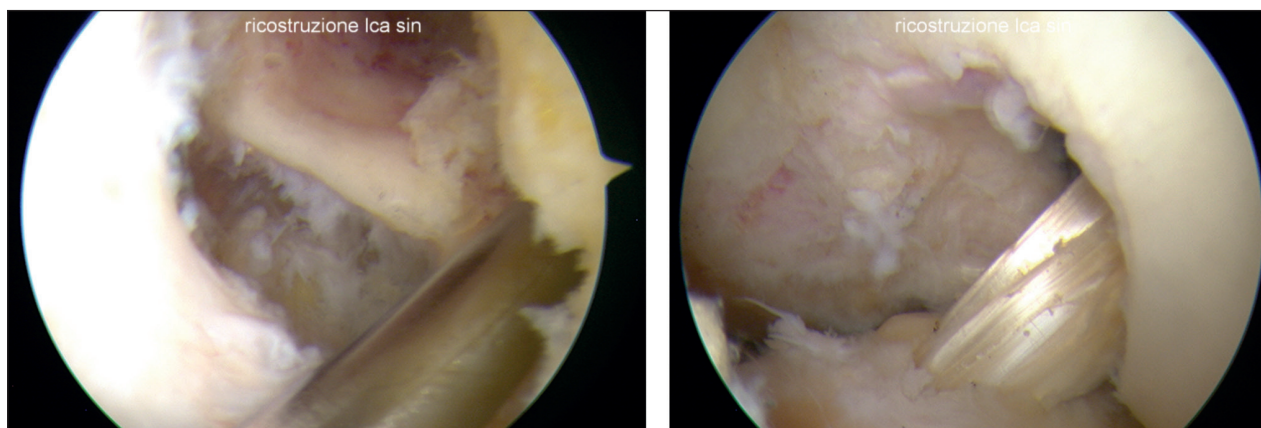
The adoption of polarized light microscopy - on the same histological slide - revealed at 2X magnification microscopy the presence of brightly polarizable - bi-refractive - material spread in the synovial tissue; at higher magnification (40X) polarized light microscopy detected the bi-refractive material inside the cytoplasm of multi nucleated cells (Figure M-N).

Assuming that bi-refractivity under polarized light is a characteristic of the synthetic fibers - poly ethylene terephthalate (PET) - we were able to demonstrate the widespread diffusion of wear particles in the synovial tissue and the consequent reaction of the organism.

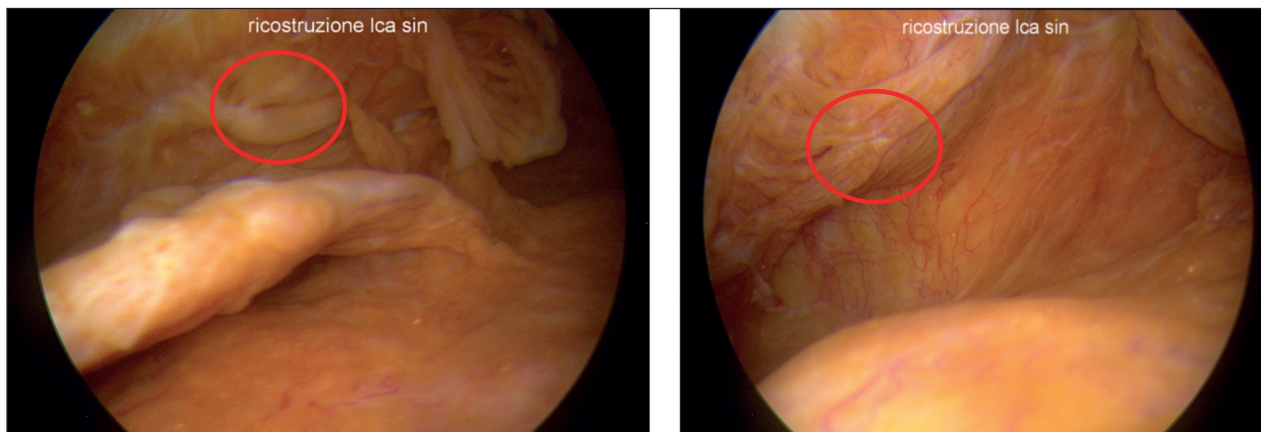
None of the synovial tissue samples presented signs of malignancy or local aggressivity. The same histological analysis was performed on sections of the stump or sections of the remnant of the ligament prepared on hematoxylin-eosin staining.

Light microscopy at different magnification well documented the arrangement of synthetic fibers disposed in a parallel and regular layout surrounded by a poor, dense fibrous - scar-like - tissue with multinucleated giant cell interposed (Figure N-O). Furthermore, the histological description made on the LARS revealed a typical foreign body reaction with poor signs of fibrovascular ingrowth of the synthetic ligament.

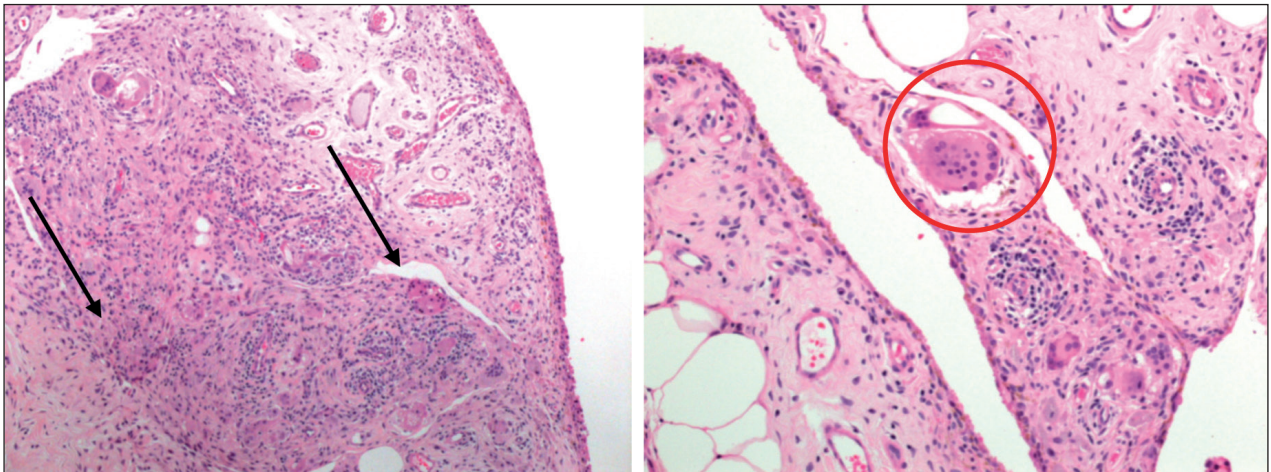
Polarized light microscopy applied on LARS sections (Figure P-Q) confirmed the brightly polarizable aspect of the synthetic PET fibers thus to confirm the



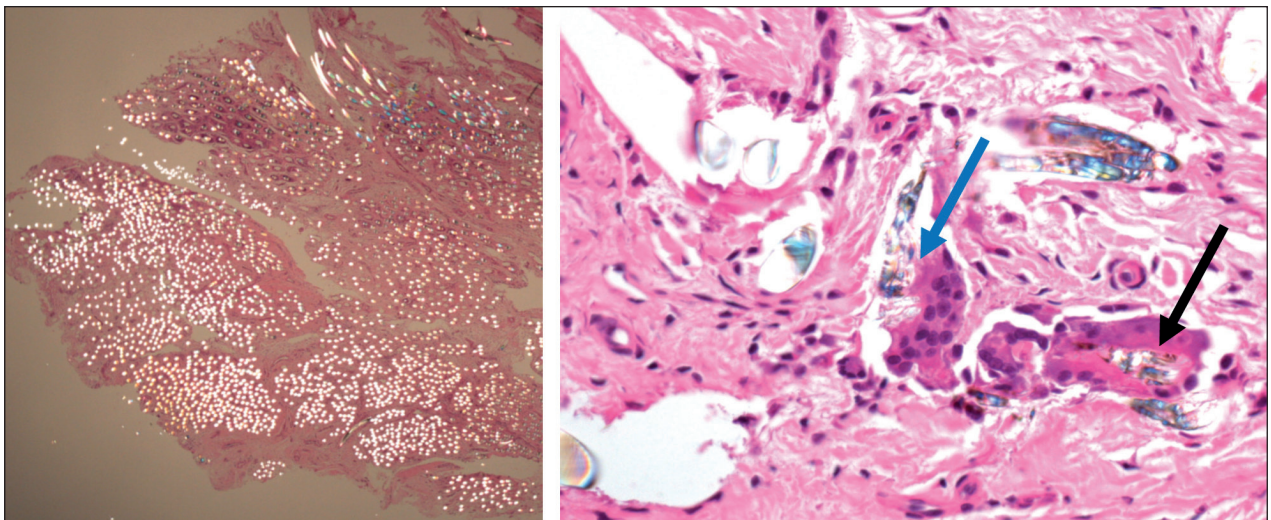
**Figure X-Y.** The examination tool show the direction of the new femoral tunnel without interfering with the previous anterior tunnel (X). Allograft hamstring ACL reconstruction in situ. The previous tunnel is still visible (Y).



**Figure I-J.** Severe widespread synovitis with hyperemic and hypertrophic tissues of the knee. Roughly PET debris are visible (red circles).



**Figure K-L.** Hematoxylin-Eosin staining of Synovial Tissue. 2X magnification microscopy demonstrate multiple multi-nucleated giant cells (black arrows) (H). 40X magnification shows a macrophage cell close to a foreign body (red circle) (I).



**Figure L-M.** Polarized light microscopy. 2X magnification showing spread debris in the synovial tissue (J). 40X magnification keeping a minimal polarization: black arrows on the right shows PET debris of the LARS inside the cytoplasm of a multinucleated cell. Blue arrow indicates a macrophage in the act of phagocytosing a PET particle (K).

nature of the wear particles demonstrated in the synovial tissue and inside the cytoplasm of multi nucleated cells.

Histological analysis performed both on the synovial tissues and on the synthetic ligament did not show any suspect cellularity for knee infection.

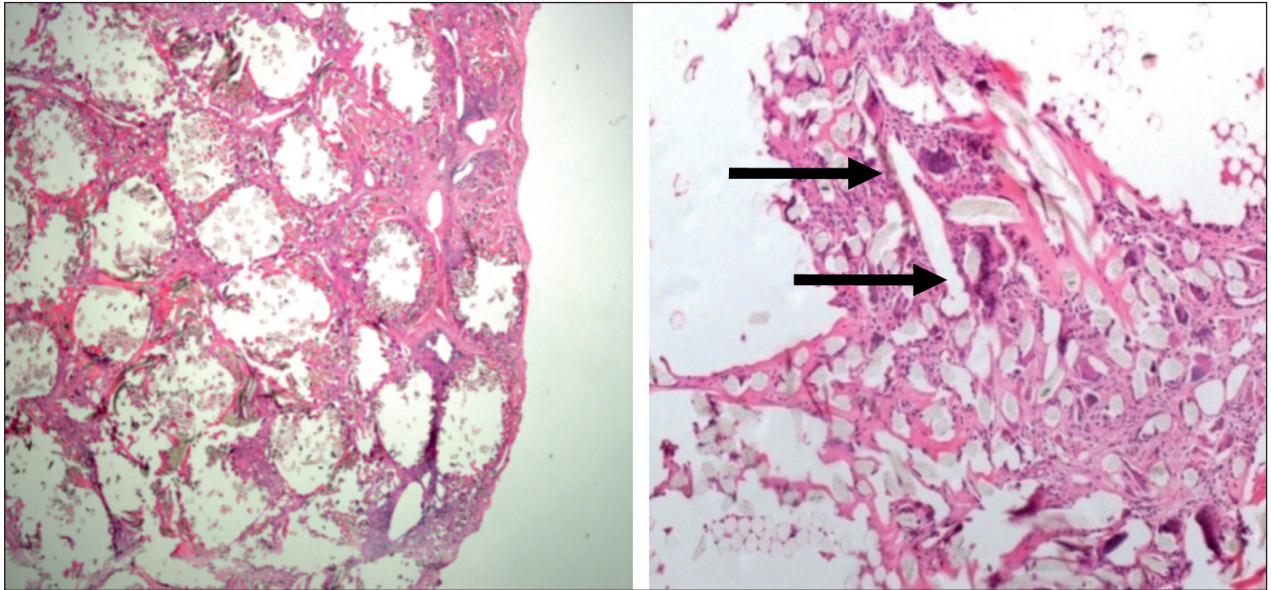
**Discussion**

ACL reconstruction is the gold standard to treat knee instability and to prevent meniscal tears and

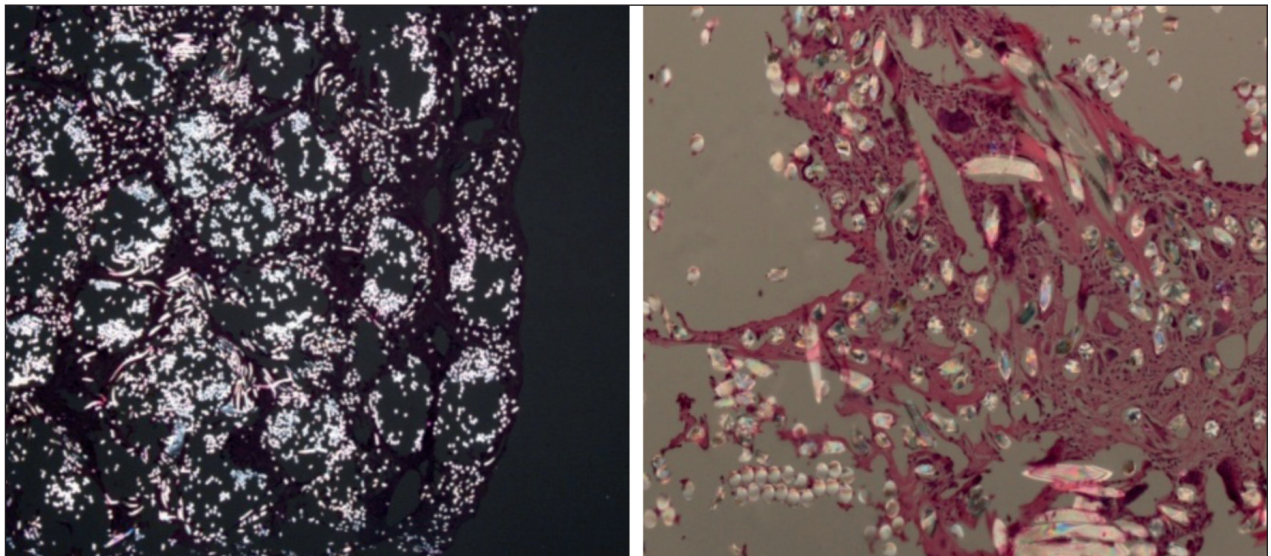
cartilage damage after an ACL injury: autograft tendons appear the graft of choice especially in young patients (4, 5).

Early artificial ligaments yielded poor results in terms of clinical outcomes and incidence of complications including mechanical failures, synovitis and early arthritis thus the majority of the orthopedic community ceased this graft option till the early 90's (12).

The introduction of LARS as a possible device for ACL reconstruction gained renewed interest among synthetic devices. Bianchi et al compared the LARS to



**Figure N-O.** Section of the LARS specimen demonstrates the regular arrangement of the fibers of the ligament with multinucleated giant cells (arrows) interspersed between the fibers.



**Figure P-Q.** same sections of picture L and M on polarizable light microscopy. LARS fibers show the typical bi refractivity.

hamstring tendon autograft in a 8 years follow-up concluding that both the grafts dramatically improved the knee functional outcome with LARS being superior in terms of achieved joint stability (14). In contrast Jia et al compared the LARS and autograft ACL reconstruction in a large meta-analysis and concluded that the two grafts are not different in terms of patient-oriented outcomes and complications but instrumented

knee laxity was more evident after synthetic ligaments, especially for early generation devices (14).

Jia demonstrated a low failure rate at a mid-term follow-up (seven years) with an incidence of 4.4% confirming an overall failure incidence of 4.75% in all the studies with a mean follow-up longer than 3 years (15).

Despite good mid-term results in the cited studies (12-15), no authors postulated LARS as the graft

of choice and still recommended caution in its use: some surgeons advocated the LARS as a suitable option for faster recovery after ACL reconstruction (15), others indicate LARS as an alternative for carefully selected cases, especially in older patients (12-16).

Tiefenbok, in contrast, after a minimum follow-up of 10 years, concluded that LARS system should not be currently suggested as a potential graft for primary ACL reconstruction due to a re-rupture failure rate of 27.8% and a low percentage of patient satisfaction (55.6%)( 17). Furthermore, Li et al reported the case of a 26 years-old patient with rare severe knee synovitis 3 years after the operation (18); some concerns arise from the young age of the patient, probably not respecting the correct indications for ACL reconstruction previously mentioned. Same author during revision arthroscopy observed a large amount of synovial hyperplasia in the knee joint and found the femoral tunnel placed too anteriorly. Moreover, the author performed a histological analysis of the LARS and detached a thick fibrous scar tissue around the graft and a poorly organized fibrous scar tissue infiltrated into the graft fibers (18).

Although these results came from a single patient case report, the histological analysis completely agree with our findings on eleven consecutive patients thus to supporting the hypothesis that without an appropriate tissue ingrowth, the LARS could progressively lose its structural integrity with an eventual graft fatigue failure.

Similar findings were reported by Norsworthy: the author during "second-look" surgeries after LARS ACL reconstruction demonstrated variable fibrous tissue incorporation with the LARS device (only 1 of the 21 patients) and frequent chronic synovitis with giant cell foreign body reaction (9 of the 21 patients) (1).

Recently Tulloch et al (19) took 12 second-look arthroscopies after primary LARS-ACL reconstruction due to mechanical symptoms (meniscal tears, cyclops lesions, cartilage damage) and/or knee instability: as described in our series, none of the patients underwent surgery for symptomatic synovitis. Interestingly the Author histologically demonstrated the presence of a hypertrophic synovial tissue more often than the arthroscopic appearance of synovitis among patient with a ruptured LARS; moreover, the author demonstrated

the presence of synovitis also in one of the six patients with an entire LARS and this is in accordance also with previous studies (7). The population enrolled in our study consisted only of patient with a rupture LARS and could therefore represent a bias: the confirmation of synovial tissue inflammation with an entire LARS or even in patients with normal arthroscopic intra-articular tissue aspect, reinforce the importance of our findings.

Tulloch et al in another paper (20) reported an elevated LARS ACL reconstruction failure rate of 33.3% at a median of 3.9 years after reconstruction: the reported data is high end unexpected for the Author himself. Several key points are in common between our findings and this study: the failure of the LARS mainly on the opening of the femoral tunnel, the absence of evidence of tunnel widening and the detection of frequent synovitis.

Whilst our results cannot conclude on a direct relation between LARS failure and the development of synovitis, our study supports previous research about the risk to expose the knee to synthetic material due to the risk of developing a foreign body reaction.

Although these objective considerations, our study has several limitations.

First, a low number of enrolled patients.

We don't use synthetic ligaments neither for primary and revision ACL surgery; all the patients had primary ACL reconstruction in other hospitals and the use of synthetic ligaments still has few indications compared to autologous and heterologous tendons.

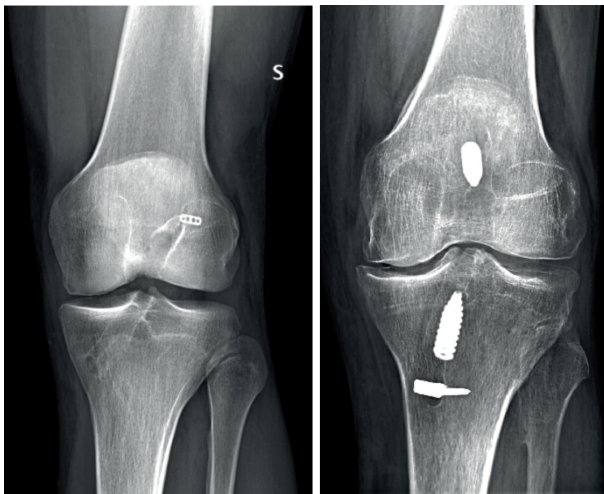
Second, the lack of a control group.

Our study only had a descriptive purpose of the histological findings on cases of LARS-ACL reconstruction failure (rupture of the ligament); in the period of the study we did not have any patients who underwent to a second-look arthroscopy in presence of an intact LARS neo-ACL so it was not possible to provide a control group.

Third, all the primary ACL reconstruction were performed in other hospitals.

Preoperative (X-Rays) and intraoperative findings demonstrated in several patients a wrong position of the synthetic ligament as shown in Figure R-S: this issue is detrimental for the synthetic ligament (8,9) due to the impingement in the intercondylar notch





**Figure R-S.** Pre operative X-Rays show two cases of failed ACL reconstructions using the LARS: both cases demonstrate a vertical ligament in the intercondylar notch.

and the consequent weakening of the fibers (mechanical failure?). Furthermore, some essential key point (8,9) in the use of the LARS at the time of the primary reconstruction (e.g. ACL stumps preserve) could not be evaluated.

Fourth, the histological analysis were performed only on patients with a rupture LARS.

Although we demonstrated a poor ingrowth inside the LARS, the isthopathological findings could be influenced by the spreading of the synthetic particles inside the knee joint (6) due to the rupture of the ligament and so our results are not definitive to advocate a biological failure of the graft.

## Conclusions

Despite objective results of our study (histologic analysis) we cannot clearly advocate a unique mechanism of LARS-ACL reconstruction failures: biologic issues (poor tissue ingrowth) and mechanical issues (fibers properties and tunnel position) probably concur in a multi factorial manner.

Although synthetic devices have some advantages compared to other grafts, ACL reconstruction using artificial ligaments cannot be considered a straightforward surgery. Artificial augments require some

expertise in ligament reconstruction surgery and is therefore a demanding procedure that can achieve better results in skilled sport surgeon hands other than trainees or low volume surgeon.

The Authors continue not to use synthetic ligaments for primary (or revision) ACL reconstruction and believe that ACL reconstruction with synthetic devices still have restricted indications in selected patients (e.g. elderly patients who require a fast recovery, professional athlete, autologous tendons not available and/or refusing donor tendons).

Our study arises additional suspicion on the unresponsiveness of synthetic fibers and even if the results cannot support a definitive relation between LARS failure and synovitis, we claim some concerns to expose the knee to artificial ligament implantation.

**Conflict of interest:** Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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