An Introduction to Modern Anterior Cruciate Ligament Repair

Thesis submitted for the degree of doctor of medical sciences at the University of Antwerp to be defended by

Christiaan Heusdens

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Faculteit Geneeskunde en Gezondheidswetenchappen
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Content

Chapter 1 Introduction

1.1 Anterior cruciate ligament anatomy

The anterior cruciate ligament (ACL) is a key structure in the knee joint. Together with the posterior cruciate ligament (PCL) they form an X as they cross each other, hence they are called cruciate ligaments. The ACL is situated in the middle of the knee joint. The ACL originates at the posterior part of the inner surface of the lateral femoral condyle. From its origin, the ACL runs anteriorly of the PCL towards its insertion at the anterior central part of the tibia. The ACL has a mean length of 32 mm and a width of 7-12 mm in extension. The ACL is a band of dense connective tissue. It has a microstructure of collagen bundles of multiple types (mostly type I) and a matrix made of a network of proteins, glycoproteins, elastic systems, and glycosaminoglycans with multiple functional interactions. The complex ultrastructural organization and abundant elastic system of the ACL allows it to withstand multiaxial stresses and varying tensile strains [1]. Proprioceptors make out 2.5% of the ACL. A proprioceptor is a sensory receptor which receives stimuli from within the body, especially one that responds to position and movement and gives feedback to the brain and spinal cord [2, 3]. These proprioceptors play a role in defining and controlling normal joint movement [4]. Abnormal range or speed movements of the joint will trigger the brain to stimulate appropriate musculature to stabilize the joint.

The ACL is innervated by posterior articular branches of the tibial nerve. The major supplying arterial vessel of the ACL is the middle genicular artery (Figure 1.1). A small amount of blood comes to the lower portion of the anterior cruciate ligament from the synovial network supplying the fat pad and the anterior horns of the menisci. Both the femoral and tibial attachments are deprived of vascular penetration from the underlying bone.

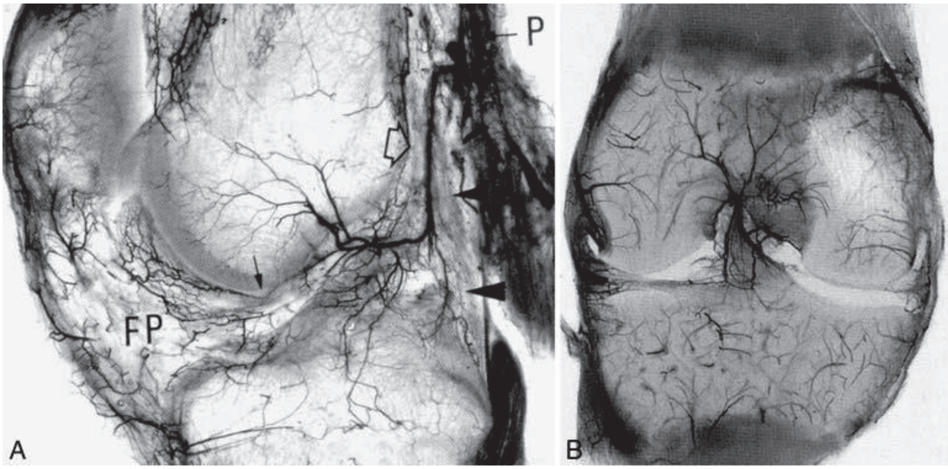


Figure 1.1 Knee vasculature. Right knee. The left sagittal section (a) shows the origin of the middle genicular artery (MGA) at a right angle (open arrow) to the popliteal artery (P), its almost vertical crossing of the posterior capsule (arrowheads), and its intra-articular osseous and soft tissue distribution. The descending branches for the cruciate ligaments are clearly visible. The small arrow in front of the ACL indicates some arterioles within the ligamentum mucosum, apparently anastomosing with the intercondylar descending branches of the MGA. FP refers to infrapatellar fat pad. The coronal section (b) shows the fan-like intra-epiphyseal distribution of the branches of the roof of the intercondylar notch of the femur (intercondylar radiate arteries) and also the arteries descending along the ACL. [1] This image was reproduced with permission from Duthon et al.

The ACL is an important stabilizer of the knee. The ACL consist of two non-isometric bundles, the anteromedial bundle and the posterolateral bundle. The anteromedial bundle is the main resistor for anterior tibial translation and the posterolateral bundle provides constraint to tibial internal rotation [1, 5]. The double bundle description of the ACL has been questioned by Śmigielski et al. with the introduction of the flat ribbon concept in 2016 [6]. They describe an ACL which does not consists of two separate bundles, but can be compared with a flat ribbon with different parts of the ACL/ribbon under tension during the extension-flexion phases of the knee. The discussion on the double bundle or flat ribbon ACL anatomy is ongoing. In summary, the complex structural organization, the varied orientation of the two bundles or ribbon of the ACL, and the abundant elastic system makes the ACL different from other ligaments and tendons. The ACL is a unique and complex structure able to withstand multiaxial stresses and varying tensile strains. This specificity and complexity may explain the difficulty in reproducing the original ACL following surgical reconstruction [1].

1.2 ACL rupture risk factors and incidence

Injury to the ACL is the most common ligament injury of the knee joint. An ACL injury typically occurs when the foot touches the ground, the knee is close to full extension and a landing manoeuvre, lateral cutting manoeuvre or a sudden deceleration is performed. Forty percent up to more than 70 % of the ACL injuries are attributed to noncontact mechanisms, involving pivoting, cutting, or jumping [7, 8]. Several intrinsic risk factors of ACL injury have been found. The two most established intrinsic risk factors are increased tibial plateau slope and a narrow intercondylar notch. Many other potential intrinsic factors have been noted such as joint laxity, familial predisposition and BMI [9]. There are often associated injuries with the ACL rupture. The most frequent associated injuries are the medial collateral ligament (19 to 38%) and lateral (20 to 45%) or medial (0 to 28%) meniscal ruptures [7].

Ruptures of the ACL mainly occur in younger active people. In a nationwide study on ACL ruptures in Iceland, the average age was 33.9 years. For males the peak incidence was in their early twenties. Females showed two peaks, one in their teens and another in their forties resulting in an older average age at rupture compared to males (35 ± 16 vs 33 ± 13, $p = 0.06$) [10]. Male athletes have a greater incidence of ACL injuries based on increased exposure to higher risk sports. High-level sport athletes, specifically those involved in in the following pivoting sports; football, basketball, soccer, rugby, skiing, handball, volleyball and dancers, have a greater risk of ACL injury. This is likely attributed to increased exposure to intense training and more frequent competition [11]. Females have a 3-fold greater risk of ACL rupture than males participating in the same sport. It is likely that genetic predisposition, hormone levels, narrower notch width, and differences in cutting and landing biomechanics increased the risk for females on an ACL rupture [9, 12]. There was no sex-based difference in the risk of ACL injury in Alpine skiers. However, recreational Alpine skiers demonstrated a greater incidence of ACL injury, with the lowest incidence occurring in expert skiers [9].

Each year 0.03 to 1.62% of non-high-level sport athletes and 0.15 to 3.67% of high-level sport athletes are affected. [11] More than 200,000 people in the United States each year suffer from an ACL rupture, with direct and indirect costs greater than $7 billion annually [7]. For Belgium, there is no literature available on the ACL rupture incidence, but an estimation can be made of 9,000-12,000 ACL ruptures annually as 6,745 cruciate ligament surgeries were performed in 2017 (according to RIZIV/INAMI, Belgian National Sickness and Invalidity Insurance Institute). The socio-economic burden is considerable as the majority of ACL injuries occur in people of working age. The indirect costs related to absence from work, school or university are in addition to costs borne by the healthcare system [13].

1.3 MRI

If there is a suspicion of a ruptured ACL after anamnestic and clinical examination, magnetic resonance imaging (MRI) is the established non-invasive imaging test for confirmation of a ruptured ACL. On MRI an intact ACL appears as a continuous linear structure, with low signal intensity, extending from the central anterior side of the tibial plateau to the medial aspect of the lateral femoral condyle (Figure 1.2A). An acute ruptured ACL is characterized on MRI as an amorphous cloud-like appearance of high signal intensity at the rupture site due to the edema and hemorrhagic areas. There is a loss of continuity or an abnormal intra-substance signal of the ligament with fibers that do not run parallel to the intercondylar roof (Figure 1.2C). In a chronic ACL rupture, the ACL origin side can be found reattached to the PCL or more anteriorly on the lateral femoral condyle or there is an empty notch sign: the ACL is retracted and there is an absence of the proximal ACL (Figure 1.2B). According to the guidelines of American Academy of Orthopedic Surgeons, strong evidence supports that MRI can provide confirmation of ACL injury, and assist in identifying concomitant knee pathology such as other ligament, meniscal, or articular cartilage injury [14]. Meta-analyses on diagnosing ACL tears on MRI resulted in a sensitivity and specificity of 87-92% and 93-99% respectively [15, 16]. A higher magnetic field strength of 3 Tesla did not improve the diagnostic performance for evaluating knee menisci and ACL compared to 1.5 Tesla [16, 17]. MRI is also valuable after surgical ACL reconstruction, as it is able to identify a number of aspects and situations that could suggest potential problems. Graft signal and integrity, correct tunnel placement, tunnel widening, arthrofibrosis and problems with fixation devices or the donor site could all compromise the surgical outcomes and potentially predict the failure of the ACL reconstruction [18]. In contrast to MRI after ACL reconstruction, MRI data after ACL repair is scarce. MRI could provide important information on the location of the ACL rupture pre-operative (although this can be complicated due to the edema and hemorrhage in the acute phase) and post-operative on the possible complications as well as the ACL healing process.

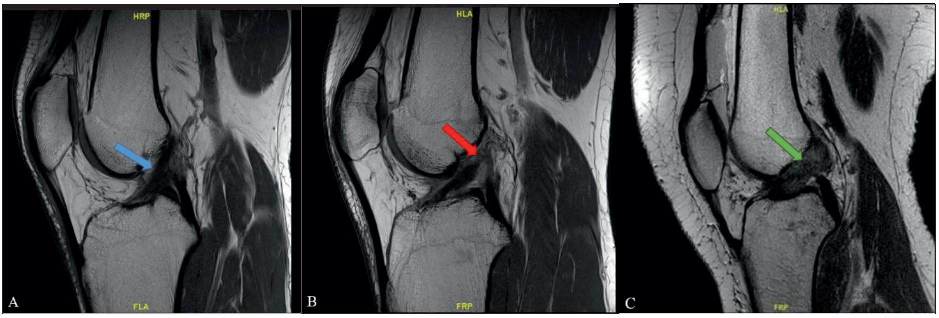


Figure 1.2 Sagittal proton density weighted MR images of the knee showing A: an intact anterior cruciate ligament (ACL, blue arrow); B a proximal chronic ruptured ACL (red arrow) and C: an acute ruptured ACL, note the broadening of the ACL (green arrow) due to the edema and hemorrhage.

1.4 Non-operative ACL rupture treatment

Patients with a ruptured ACL can be treated non-operatively with physiotherapy and operatively; tendon graft reconstruction is the gold standard. Functional braces have not been shown to provide adequate restoration of stability [7]. Non-operative therapy involves three months of supervised physiotherapy; range of motion training, gradual strengthening of the quadriceps, hamstrings, hip abductors, core muscles and a progressive return to activity [7]. After three months the patient has a re-evaluation. If the patient has no instability complaints in its activities of daily living and sports, the patient is advised to continue the exercises on its own [14]. Muaidi et al. found a good short- to mid-term prognosis in terms of self-reported knee function and functional performance after conservatively managed ACL-deficient knees [19]. However, subjects reduced their activity levels on average by 21% following injury. Fifty percent of the patients will still experience instability complaints after non-operative rehabilitation and are advised to have an ACL reconstruction.

Although reviews do not support operative treatment above non-operative treatment, operative treatment is advised to prevent further damage in the knee. A critical review (2012) stated that there are no evidence-based arguments to recommend a systematic surgical reconstruction to any patient who ruptured his ACL [20]. Knee stability can be improved not only by surgery but also by neuromuscular rehabilitation. Whatever the treatment, fully normal knee kinematics are not restored. While the patients wish to go back to their sport and want everything possible done to prolong their ability to perform these activities, they should be informed that the risk of further knee lesions and osteoarthritis remains high, whatever the treatment, surgical or conservative.

The Cochrane library published in 2016 a review and concluded (low-quality evidence) that there was no difference between surgical management (ACL reconstruction followed by structured rehabilitation) and conservative treatment (structured rehabilitation only) in patient-reported outcome measures (PROMs) of knee function at two and five years after injury. However, these findings need to be viewed in the context that many participants with an ACL rupture remained symptomatic following rehabilitation and later opted for ACL reconstruction surgery [21]. The Dutch ACL guidelines published in 2012 state there seems no difference in outcome on the long-term between non-operative and operative ACL treatment [22].

1.5 ACL reconstruction

Uncontrolled manoeuvres in unstable knees can cause meniscal or cartilage lesions. To prevent future degenerative changes, patients performing pivoting sports and patients with persistent instability complaints after conservative treatment are advised to be treated with a surgical ACL reconstruction. Since the mid-eighties the gold standard for an operative treatment of an ACL rupture is reconstruction with a tendon graft. The ligament is often replaced with (an) autograft donor tendon(s). Until the nineties most ACL reconstructions were performed with a bone-patellar tendon-bone graft in Europe. At the moment, most ACL reconstructions are performed with the semitendinosus hamstrings tendon. Numerous studies have compared bone-patellar tendon-bone autograft versus hamstrings autograft and found no difference in clinical knee scores and risk of failure [9]. Recently the quadriceps tendon as a graft for ACL reconstruction is more popularized [23]. ACL reconstruction surgery starts with removing the graft tendon with or without the connecting bone block from the same knee. Subsequently an arthroscopy of the knee is performed. Meniscal or cartilage procedures are undertaken, if necessary. The ruptured ACL remnants are removed, including its proprioceptors. Bone tunnels, of the same diameter as the graft, are drilled at the origin and insertion of the ACL. The graft is passed through the bone tunnels and fixed in the femur with a button or screw. In full extension the graft is fixed in the tibia with a button or a screw (Figure 1.4 A). The patient is discharged at the day of surgery or the day after and advised to walk with crutches for three to six weeks. Intensive rehabilitation is started post-surgery with a physiotherapist. On average, most patients finish the rehabilitation after 9-12 months and can restart with pivoting sports. Other ACL graft options are allografts or synthetic grafts. As these grafts have their own technical difficulties, higher costs and higher risks of graft failure compared to autograft reconstructions, they are not widely used in Europe [24]. With the description of the anterolateral ligament, Steven Claes et al. started the discussion on anterolateral stability [25]. The anterolateral complex provides anterolateral rotatory stability and acts as a secondary stabilizer to the ACL [26]. Several novel lateral extra-articular procedures have been described as an augmentation to ACL reconstruction [27-29], but clinical evidence is currently lacking to support clear indications.

Although ACL reconstruction is the gold standard for surgical treatment of the ruptured ACL, there are a number of problems related to this surgery. Graft harvesting is associated with a degree of morbidity from tissue loss. More than 20% of the patella tendon graft patients experience anterior knee pain and 15% experience kneeling pain [30]. Hamstrings muscle weakness following harvesting averages 10% [31]. After ACL reconstruction the anteroposterior (AP) stability is often restored. The rotatory stabilizing component of the ACL is more difficult to restore, 24% of ACL reconstructed patients have a positive Pivot shift sign [32]. During the harvesting of the graft, its native vascularization is destroyed, the graft is a “dead ligament”.

Revascularization of the graft takes 6–12 months. The ingrowth of the graft in the bone takes up to two years [33]. Most of the re-ruptures of ACL reconstructed grafts occur in the first two years after surgery. Nagelli et al. and Hewett et al. advocate a delay in returning to sports for the first two years, instead of 9-12 months, as this would significantly reduce the incidence of re-ruptures [34]. Another disadvantage of conventional ACL reconstruction is the extensive rehabilitation period. A successful recovery encompasses intensive physiotherapy and requires a lot of effort, dedication, time and perseverance [35]. "The physiotherapist becomes the patient's best friend for the next 9-12 months." On average, patients return to their work after 11 weeks and are allowed to return to sports after 9-12 months; ACL reconstruction has a huge socio-economic impact [7, 35]. According to Ardern et al., the return to competitive sports after ACL reconstruction is only 44 to 55% [36]. In another study, Biau et al. found that only 40% of patients gain full functional recovery [32]. The two most common reasons for not returning to sport are fear of re-injury and functional problems of the reconstructed knee. Another problem after ACL reconstruction is rupture of the ACL graft. In a review with more than 10 years of clinical follow-up, the reported ACL graft rupture risk was 6.2% (range, 0% to 13.4%) and clinical failure occurred in approximately 10.3% (range, 1.9% to 25.6%). Graft rupture risks up to 28% are reported in high-risk populations [37, 38]. Rousseau et al. describe in their group of 958 patients with two years of follow-up, a re-rupture risk of 3.1% for the bone-patellar tendon-bone group and 7% in the hamstrings group [30]. In a systematic review with a minimum of five years of follow-up after ACL reconstruction, the risk of ACL rupture in the contralateral knee (11.8%) is double the risk of ACL graft rupture in the ipsilateral knee (5.8%) [39]. To reduce the risk of re-rupture, return to sport (RTS) criteria have been described. Grindem et al. describe a re-rupture risk of 38.2% of those who failed RTS criteria versus 5.6% of those who passed the RTS criteria [40]. Another problem are the re-operations for non-graft rupture related indications. For example arthrofibrosis, pain due to the hardware, secondary meniscal or cartilage lesions, infection, etc., which are reported in 24% of ACL reconstructed knees [30]. Although one of the mean reasons of performing ACL reconstructions is the prevention of degenerative changes, ACL reconstruction does not prevent the development of osteoarthritis. Reconstructed knees and non-operatively treated knees demonstrated a risk of 4.71 times and 2.41 times, respectively, for development of moderate to severe arthritis compared with controls. The risk of developing arthritis after ACL reconstruction with concomitant partial meniscectomy was 3.5 to 5 times greater than without meniscectomy in 2 studies [9]. In a prospective study of 958 patients treated with bone-patellar tendon-bone or hamstring tendon graft, the total risk of complications was 39% [30]. Given the limitations and risks associated with the current gold standard treatment of an ACL rupture, there is room for improvement.

1.6 ACL repair

ACL repair could be a promising surgical technique with theoretically advantages over ACL reconstruction. Modern ACL repair techniques are less invasive compared to ACL reconstruction. Bone tunnels drilled for the repair techniques are less than half the size of the bone tunnels needed for ACL reconstruction. There is no graft harvesting morbidity, as no graft is needed. Preservation of the native ACL ligament with its proprioceptors contributes in the feedback on position and dynamic stability of the knee, which could reduce the rehabilitation period and therefore the economic burden [41]. ACL repair has the potential to preserve the native insertion site as well, which may in turn lead to more normal joint mechanics and decreased risk of post-traumatic osteoarthritis [42]. Another advantage is that in the event of a re-rupture, a standard ACL reconstruction can be performed. "No bridges are burned."

The first documented ACL repair was performed by AW Robson, consulting surgeon in 1895 in Leeds, United Kingdom. A 41 year old miner ruptured both his cruciate ligaments from their upper attachments, 39 weeks after the trauma both ligaments were repaired. The ends of the cruciate ligaments were in "a somewhat shreddy condition". The ACL and PCL were stitched in position by means of catgut ligatures, to the synovial membrane of the femoral condyles. Six years later this patient was re-examined. He was able to run and returned to his mining job, without missing a day on account of his knee since the operation [43]. The historic technique used for ACL repair consisted of an arthrotomy, suturing of the ACL with drill holes in the femur and cast immobilization for 4-6 weeks and was in use up to the mid 80´s of the 20th century [44]. Excellent short-term outcomes on open ACL repair were reported [45], however high risks of failure were reported after mid-term follow-up [46-49]. ACL repair was abandoned in favor of ACL reconstruction, which became the gold standard for surgical ACL treatment. Historically, proximal, mid- and distal ACL bundle ruptures were repaired. The proximal part of the ACL is better vascularized, which could explain why a subset of ACL repair patients did report good to excellent outcomes even after mid-term follow-up [50].

'Unlike other ligaments in our body, the ACL does not heal after a complete rupture' was the paradigm up till the last decade [51]. Costa-Paz et al. reported in 2012 a clinical and MRI study which showed that an acutely injured ACL may eventually spontaneously heal, allowing return to athletic activity [51]. In the same year, Steadman et al. described the healing response technique [52]. By performing microfracturing, a blood clot is formed next to the proximal ruptured ACL, which enhances the ACL to heal. This allowed the patients to return to high levels of recreational activity and to restore knee function to normal levels. In a select group of mature patients with acute proximal ACL ruptures, the healing response procedure was an effective ACL repair technique treatment.

Other studies compared ACL fibroblasts with those obtained from the medial collateral ligament (MCL), an extra-articular ligament that has no difficulty healing with conservative "non-surgical" treatment. It was found that MCL and ACL cells within injured ligaments have comparable rates of proliferation, and that each ligament is able to revascularize after rupture. A comparable collagen production within the ligaments was observed [53]. What could be the reason for the poor healing response of the intra-articular ruptured ACL?

Murray et al. published in 2013 a potential explanation [42, 53]. The ACL is surrounded by synovial fluid, whereas the MCL and all other extra articular ligaments are not. Although the ACL has to heal in a hostile environment, the ACL has a healing capacity. It is essential that a stable fibrin–platelet clot between the ruptured ends of the ACL is formed, which can transform in stable scar tissue. The continuous flow of the synovial fluid in the knee hampers the formation of this clot (Figure 1.3). As a solution, they advocated bio-enhanced repair using a collagen-based scaffold and autologous blood as promising results are obtained from in vitro and in vivo animal studies, but further well-controlled human trials are needed to assure the ultimate efficacy of these novel ACL repair approaches.

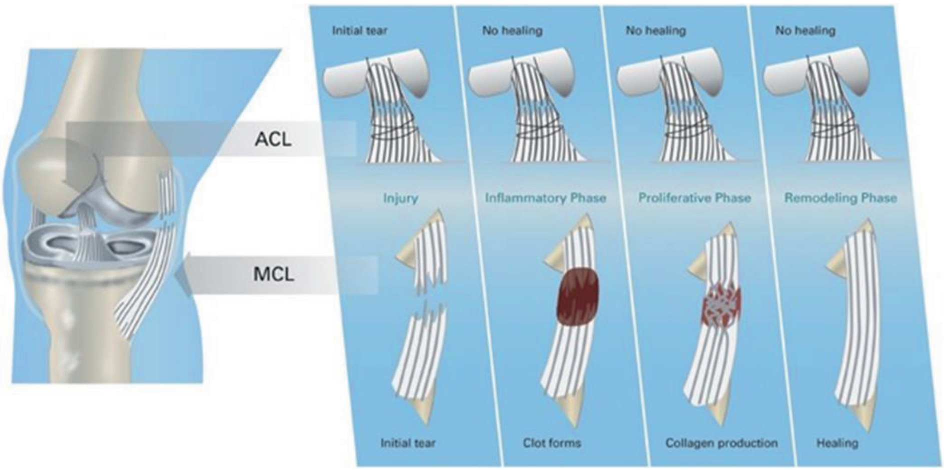


Figure 1.3 Differences in the intrinsic healing response of the ACL (bottom row) and medial collateral ligament of the knee (MCL, top row). The ACL is injured, but no blood clot forms in the injury site, likely due to the synovial fluid which bathes the ligament washing the clot out. In contrast, in the MCL, blood clot forms at the site of the tear and stabilizes the two ligament ends. The MCL tissue can then grow into this provisional scaffold and the defect can be healed. The loss of the provisional scaffold in the ACL is likely the key mechanism behind its failure to heal [1]. This image was reproduced with permission from Murray et al.

1.6.1 Dynamic intraligamentary stabilization

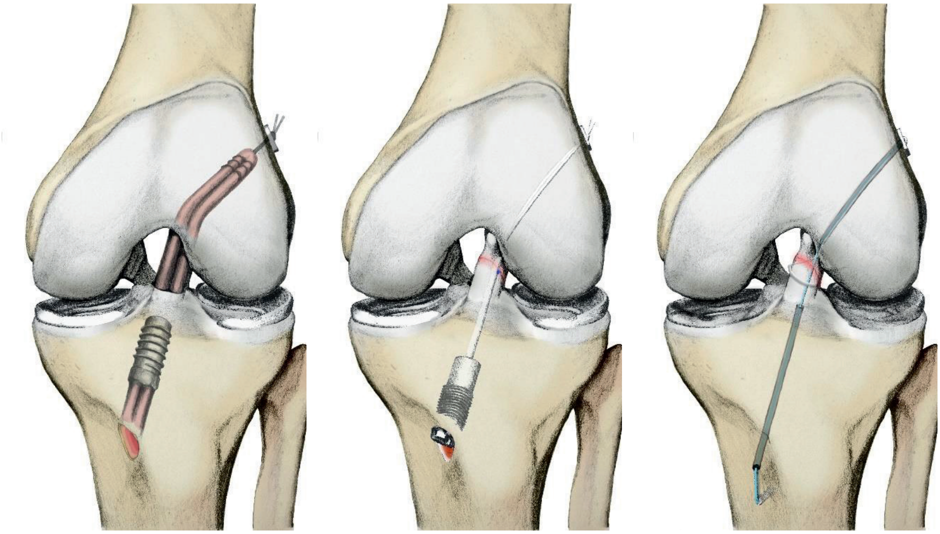
In 2012 Sandro Kohl et al. published an animal study of a new technique, dynamic intraligamentary stabilization (DIS) that utilizes biological self-healing for repair of acute ACL ruptures [54]. The ruptured ACL is brought back to its origin with polydioxanone (PDS) sutures and the knee is stabilized with a strong suture alongside the ACL which is fixed in the tibia with a spring-screw system (Figure 1.4 B). The DIS technique successfully induced self-healing of ruptured ACL in a sheep model. Knee joints remained stable during the healing period allowing free range of motion and full weight bearing, and no signs of osteoarthritis or other intra-articular damage in the three months follow-up were observed. In 2013 Sandro Kohl et al. published "A novel technique, dynamic intraligamentary stabilization creates optimal conditions for primary ACL healing: A preliminary biomechanical study" [55]. In this study they describe a potential biomechanical solution for the ACL repair failures in the past. A rigid fixation was used to repair the ACL, which failed upon cyclic loading. By creating a dynamic fixation, that restored AP stability and could withstand the repetitive cyclic forces, a biomechanically stable environment was created in which the ACL could heal.

The next year, the results of the first 10 patients treated with DIS (Ligamys, Mathys Ltd., Bettlach, Switzerland) with a 2-year follow-up were reported [56]. This treatment resulted in stable clinical and radiological healing of the ruptured ACL in all but one patient of this first series. They attained normal knee scores, reported excellent satisfaction and could return to their previous levels of sporting activity. A case series of 278 patients treated with DIS for an acute ACL rupture with a mean follow-up of 14 months showed non inferior PROMs compared to pre-operatively, stable anterior-posterior knees and a re-rupture risk of 2.9% [57]. In summary, promising results of a novel treatment for acute ACL repair were presented by the developers of the DIS technique at the end of 2014/ early 2015.

1.6.2 Suture tape augmentation/ InternalBracing augmentation technique

The suture tape augmentation technique (STA), also called suture tape reinforcement or Internal Bracing Ligament Augmentation Technique (InternalBrace™, Arthrex GmbH, Naples, Florida) is a repair technique for several ligaments and can be used for all knee ligaments, as well as the ruptured ACL [27, 58-61]. The ruptured parts of the ACL are brought together with a lasso suture and are protected with a 2 mm high-strength tape which acts as an internal brace, to provide an environment in which the ACL can heal (Figure 1.4 C). This technique reinforces the ligament as a secondary stabilizer, encouraging natural healing of the ligament by protecting it during the healing phase and supporting early mobilization. Heitmann et al. published in 2014 a biomechanical study on porcine [62]. In this study the augmented suture repair of the ACL provides significantly higher stability compared with isolated suture repair or reconstruction with hamstring tendons. He concluded that the concept of ligament bracing could be a promising future treatment option in acute knee dislocations.

In the same period Professor Gordon MacKay popularized the STA technique. On congresses he showed videos of patients who recovered rapidly after acute ligament repair, among which acute ACL repair, with the STA technique. MacKay et al. published in 2015 a review of ligament augmentation with the internal brace. Lateral ankle and acute ACL repair with the STA technique are explained in particular. The 1-year follow-up results of 68 patients are presented [63]. The results of this study suggest that at short-term follow-up, repair with the STA technique is at least as effective in restoring stability and function to the knee as traditional ACL reconstruction surgery.



A **B** **C**

Figure 1.4 Operation techniques for anterior cruciate ligament (ACL) rupture. Left knee. (A) The ruptured ACL has been removed and reconstructed with a hamstrings tendon, fixed in the tibia and femur with a screw and button. (B) Left knee. The ruptured ACL is repaired with the dynamic intraligamentary stabilization (DIS). [50] (C) Left knee. The ruptured ACL is repaired with the suture tape augmentation technique (STA).

1.6.3 Starting up ACL repair at the Antwerp University Hospital

In 2014, the author started as a consultant orthopedic surgeon, specialized in knee surgery at the Antwerp University Hospital (UZA). A special interest in ACL surgery grew. In that period, ACL repair as an alternative operative treatment for the acute ruptured ACL showed promising results and had the potential to be an improvement of the gold standard, ACL reconstruction. Together with dr. Lieven Dossche, orthopedic surgeon at UZA as well, a training led by Professor Stefan Eggli, the developer of DIS, was followed. The development and biomechanics of DIS were further explained and a sawbone DIS training was undertaken. During a visit to Munster and Ghent tips and tricks were given during real life DIS surgery. The first DIS surgery at UZA was undertaken under supervision of an experienced DIS surgeon, after which dr. Dossche and the author assisted each other for the first DIS procedures at UZA.

A similar procedure was undertaken before patients were treated at UZA with the STA technique. An instructional course and cadaver training by Professor Gordon MacKay, developer of STA technique was followed. During a visit to Professor Gordon MacKay in Glasgow, tips and tricks were given during real life STA surgery. The first STA surgery was undertaken by dr. Dossche and the author together and they assisted each other for the first STA procedures at UZA.

1.7 Aim

In 2015, proof of concept for the DIS and STA ACL repair techniques was given, but the literature on these novel repair techniques was scarce. As early adaptors of these new techniques, we felt that we could contribute to the discussion whether these novel repair techniques could be a treatment option for the acute ruptured ACL. For this thesis, several studies have been conducted which led to further insight in modern acute ACL repair with the STA and DIS technique, which was still in ‘its child´s shoes’ (translation of Dutch proverb) in 2015.

The aim of this thesis is to contribute to the discussion whether these novel repair techniques could be a treatment option for the acute proximal ACL rupture. By describing the ACL STA surgical technique (Chapter 2) step by step and sharing tips and tricks for the DIS repair technique (Chapter 5), orthopedic surgeons could get more acquainted with these novel techniques. Three case series with 2-year follow-up results after ACL repair (Chapter 3-5) are presented, as well as MRI findings after ACL repair (Chapter 6). The call for more data on ACL repair, especially RCTs, is underwritten in the LIBRƎ study protocol (Chapter 7). A critical appraisal on four different modern ACL repair techniques is presented (Chapter 8).

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Chapter 2 Anterior Cruciate Ligament Repair Using Independent Suture Tape Reinforcement

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2.1 Abstract

Recently there has been renewed interest in primary repair of the anterior cruciate ligament (ACL). Repair of the acute proximal ruptured ACL can be achieved with the independent suture tape reinforcement ACL repair technique. The independent suture tape reinforcement technique reinforces the ligament as a secondary stabilizer, encouraging natural healing of the ligament by protecting it during the healing phase and supporting early mobilization. The purpose of this article is to describe, with video illustration, this ACL repair technique.

2.2 Introduction

Anterior cruciate ligament (ACL) rupture is a common sport-related injury. ACL reconstruction has been the gold standard for the operative treatment of an ACL rupture for many years. However, only 63% to 65 % of the patients return to their pre-injury sport level and 10.3% have a graft failure after 10 years [1]. Moreover, ACL reconstruction does not protect patients from developing osteoarthritis. Therefore, there has been renewed interest in primary repair of the ACL [2].

The independent suture tape reinforcement (ISTR) technique for ACL repair consists of an ultra-high-strength 2 mm wide tape that bridges the ligament and is fixed on the femur with a button and a knotless bone anchor on the tibia. A looped suture holds the distal ACL stump to its femoral attachment. This technique reinforces the ligament as a secondary stabilizer, encouraging natural healing of the ligament by protecting it during the healing phase and supporting early mobilization [3].

2.3 Indication

In the case of an acute (within 3 months) ruptured ACL, we start with an arthroscopic inspection of the ruptured ACL. If the ACL is ruptured proximally and the tissue is not retracted and of good quality, the ISTR ACL repair is performed. Otherwise, the procedure is intra-operatively converted to a standard ACL reconstruction.

2.4 Positioning

The patient is placed in the supine position, and a tourniquet is placed on the upper thigh. The injured leg is prepared and draped in the surgeon’s preferred position similar to the ACL reconstruction procedure.

2.5 Surgical technique

2.5.1 ACL inspection

Standard anterolateral and anteromedial portals are created, and arthroscopic inspection of the knee is performed. A PassPort cannula (Arthrex, Naples, FL) is placed in the anteromedial portal, to facilitate the suture management and prevent interposing tissue. If necessary, meniscal or cartilage surgery is performed. The ACL is inspected. Proximal ruptures of the ACL are repaired with the ISTR technique. The ACL remnant is left intact and not shaved. If the rupture is mid-substance or distal, or the ACL remnant is retracted or of poor quality, a standard ACL reconstruction is performed (Figure 2.1).

Figure 2.1 Placing of the flexible arthroscopic cannula for anterior cruciate ligament repair using the independent suture tape reinforcement technique. Left knee, frontal view. Standard anterolateral and anteromedial portals are created, and arthroscopic inspection of the knee is performed. If necessary, meniscal or cartilage surgery is undertaken. Proximal ruptures of the anterior cruciate ligament are repaired with the independent suture tape reinforcement technique. The anterior cruciate ligament remnant is left intact and not shaved. A flexible arthroscopic cannula (*) is placed in the anteromedial portal to facilitate the suture management and prevent interposing tissue. This image provided courtesy of Arthrex, Inc. © 2018.

2.5.2 Tibial tunnel

A standard tibial ACL guide is placed at 60° at the center of the ACL footprint. A skin incision is made above the pes anserinus, and a 3.5 mm tibial tunnel is drilled, just passing through the tibial cortex at the ACL footprint. To prepare the tract through the ACL for the high-strength tape, the drill is manually advanced (not drilled) through the distal part of the center of the ACL stump (Figure 2.2). The drill sleeve is tapped in the anterior tibial cortex, and the drill is switched for a tubed shuttle suture (FiberStick; Arthrex). The shuttle suture is grasped out of the tube with a suture grasper. The tube is left in place until the shuttle suture is brought through the medial portal, taking care to prevent the shuttle suture from cutting through the ACL stump (Figure 2.3).

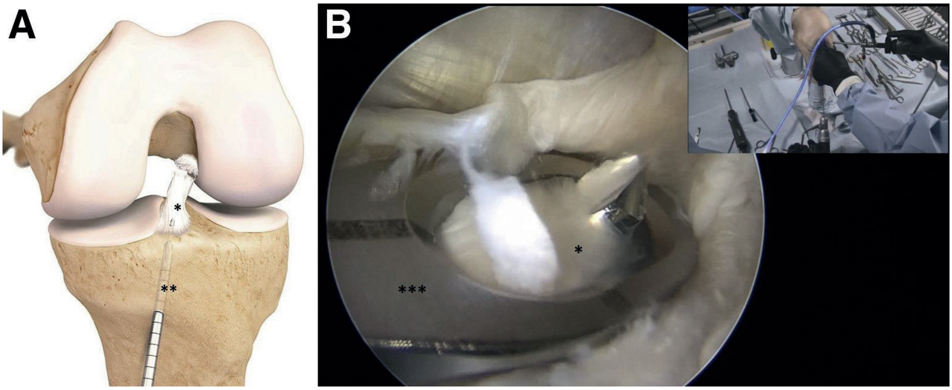

Figure 2.2 Drilling of the tibial tunnel for anterior cruciate ligament repair using the independent suture tape reinforcement technique. (A) Left knee frontal view. This image provided courtesy of Arthrex, Inc. © 2018. (B) Left cadaver knee, intra-articular view on the anterior cruciate ligament (ACL) stump. At the center of the ACL footprint (*), a standard tibial ACL guide (***) is placed at 60_ and the tibial tunnel (**) is drilled. The drill is manually advanced (not drilled) through the distal part of the center of the ACL stump.

Figure 2.3 Placement of shuttle sutures for anterior cruciate ligament repair using the independent suture tape reinforcement technique. Left knee frontal view. A tubed shuttle suture (*) to advance a single shuttle suture (**) is placed through the tibia tunnel and through the anterior cruciate ligament stump. The tubed shuttle suture is left in this position to prevent the shuttle suture cutting through the anterior cruciate ligament stump. This image provided courtesy of Arthrex, Inc. © 2018.

2.5.3 ACL suture

The lasso end of a looped suture (FiberLink; Arthrex) is placed over the end of a suture passer (Scorpion; Arthrex) and loaded on the suture passer. The looped suture is passed through the mid-substance of the ACL stump (Figure 2.4). Care is taken not to capture the tubed shuttle suture (which is still in the ACL tissue). The looped suture is retracted through the medial portal, forming a lasso around the distal ACL stump (Figure 2.5). A second looped suture can be placed if there is doubt about the grip on the distal stump or in case of a multibundle rupture.

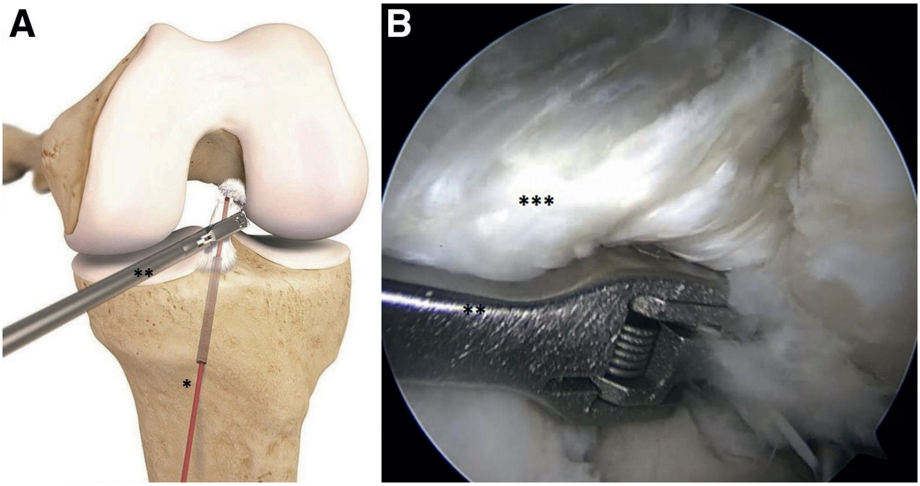

Figure 2.4 Suture passer used for anterior cruciate ligament repair with the independent suture tape reinforcement technique. (A) Left knee frontal view. This image provided courtesy of Arthrex, Inc. © 2018. (B) Left cadaver knee, intra-articular view on the anterior cruciate ligament (ACL) stump and the suture passer. After placing the tubed shuttle suture (*) through the tibia tunnel and the ACL stump (***), a looped suture is passed through the mid-substance of the ACL stump with a suture passer (**), forming a lasso around the distal ACL stump. Care is taken not to capture the tubed shuttle suture (which is still in the ACL tissue).

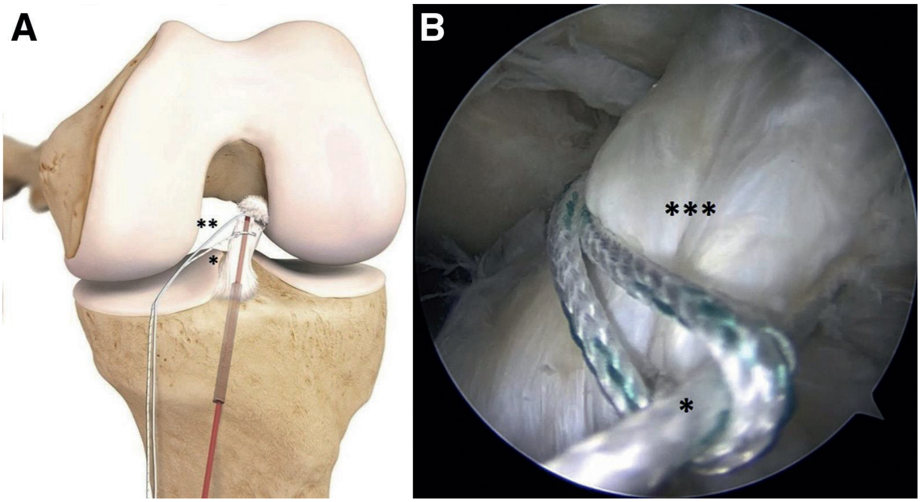

Figure 2.5 Looped suture used in anterior cruciate ligament repair using the independent suture tape reinforcement technique. (A) Left knee frontal view. This image provided courtesy of Arthrex, Inc. © 2018. (B) Left cadaver knee, intra-articular view on the anterior cruciate ligament stump and the looped suture. The looped suture (*), forming a lasso around the anterior cruciate ligament stump (***), is retracted through the medial portal. The shuttle suture (**) is taken from the tube and retracted through the medial portal as well.

2.5.4 Femoral tunnel

At the femoral attachment, microfracturing is performed (Figure 2.6). With a 3.5 mm drill (Drill Tip Guide Pin; Arthrex), the femoral tunnel is drilled from the center of the femoral footprint inside out, with the knee fully flexed (Figure 2.7). A stab incision is made through the skin at the drill exit point, along the drill onto the femoral cortex, which facilitates tying the sutures on the femoral button later in the procedure. The end of the looped suture and the shuttle suture are placed through the eyelid at the end of the drill and passed through the joint, the femoral tunnel, and the skin. By pulling gently on the looped suture, the distal ACL stump is repositioned against the femoral attachment (Figure 2.8). The shuttle suture is going to be the lead suture for the ISTR (*Internal*Brace ligament augmentation repair; Arthrex).

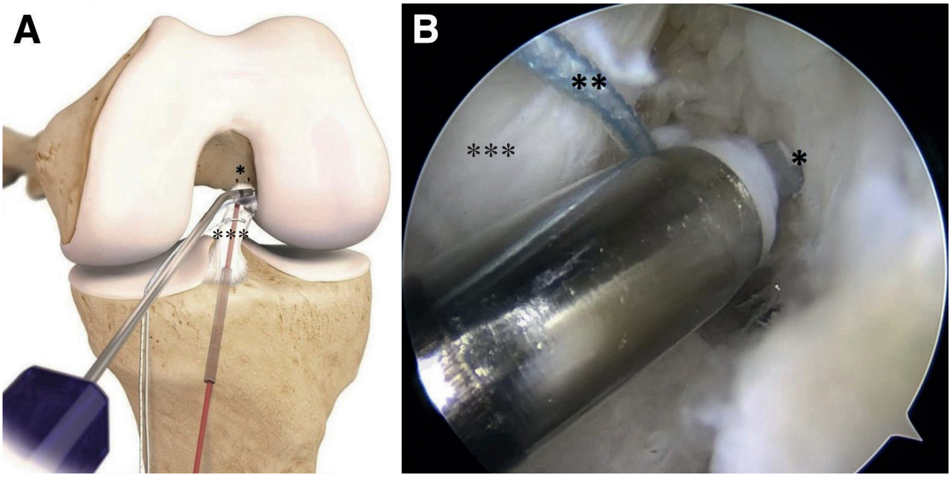

Figure 2.6 Microfracturing during anterior cruciate ligament repair using the independent suture tape reinforcement technique. (A) Left knee frontal view. This image provided courtesy of Arthrex, Inc. © 2018. (B) Left cadaver knee, intra-articular view in the notch. Microfracturing (*) at the femoral attachment of the ACL (***) is performed to improve the healing potential. Care is taken not to damage the shuttle suture (**).

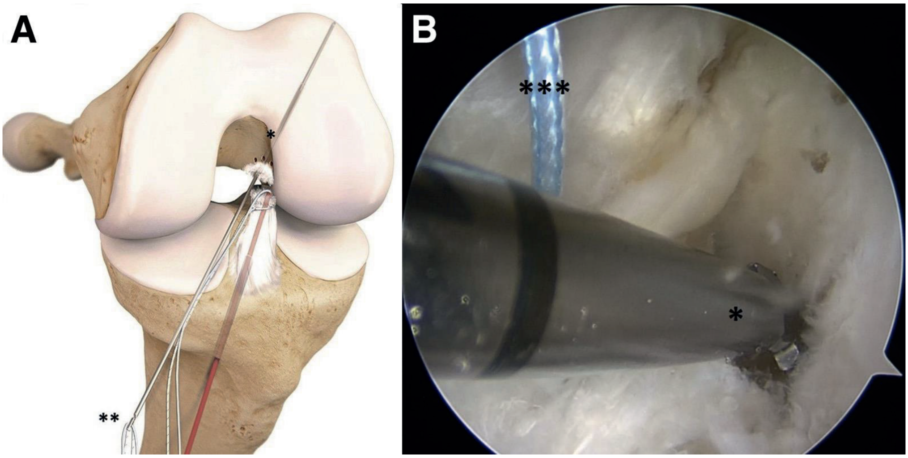

Figure 2.7 Drilling of the femoral tunnel during anterior cruciate ligament repair using the independent suture tape reinforcement technique. (A) Left knee frontal view. This image provided courtesy of Arthrex, Inc. © 2018. (B) Left cadaver knee, intra-articular view on the center of the femoral footprint; the starting point of the drill for the femoral tunnel. With a 3.5 mm drill (*), the femoral tunnel is drilled from the center of the femoral footprint inside out, with the knee fully flexed. The looped suture and the shuttle suture (***) will be passed through the femoral tunnel with the end of the drill (**).

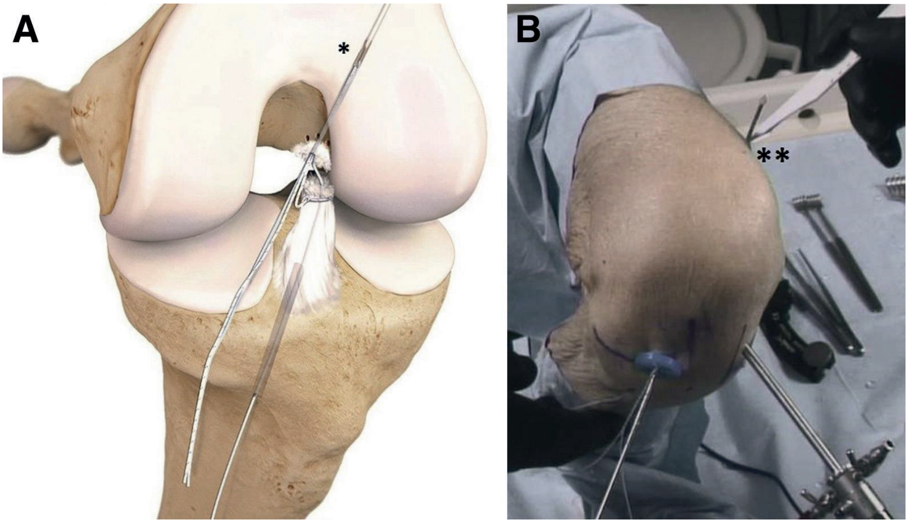

Figure 2.8 Placement of the repair knot during anterior cruciate ligament repair using the independent suture tape reinforcement technique. (A) Left knee frontal view. This image provided courtesy of Arthrex, Inc. © 2018. (B) Left cadaver knee, external frontal view. It is important to mobilize the tractus at the lateral femur just along the drill pin down to the lateral cortex with a stab incision (**). Splitting the iliotibial band allows proper placement of the repair knot. The looped suture and the shuttle suture are passed from the anteromedial portal through the femoral tunnel with the end of the drill (*). The tube from the shuttle suture is removed from the tibial tunnel.

2.5.5 Independent suture tape reinforcement

A femoral button (Retrobutton/TightRope RT; Arthrex) loaded with a high-strength tape is transported proximally by the tibial end of the shuttle suture, through the tibial tunnel, the center of the ACL, and the femoral tunnel. The high-strength tape (FiberTape; Arthrex) is an ultra-high-strength 2 mm wide tape consisting of a long-chain ultra-high molecular weight polyethylene core with a braided jacket of polyester and ultra-high molecular weight polyethylene. The button is flipped on the femoral cortex, and the high-strength tape is advanced in the femoral tunnel by pulling the 2 tensioning strands, one at a time (Figure 2.9). The high-strength tape is kept on a slight tension until it is fixed, just below the tibial tunnel. After predrilling with a 4.5 mm drill and a 20 mm drill stop, followed by tapping, a 4.75 mm bone anchor (SwiveLock; Arthrex) loaded with both ends of the high-strength tape is placed with the knee in full extension (Figure 2.3). To avoid overtightening, the high-strength tape is marked at the beginning of the screw of the bone anchor and repositioned in the eye of the bone anchor at the marked level, and finally the bone anchor is placed in the drill hole (Figure 2.10). Care is taken not to damage the hamstrings. The tibial drill hole is kept under direct vision to avoid superficial placement of the bone anchor in the bone or losing the position of the drill hole.

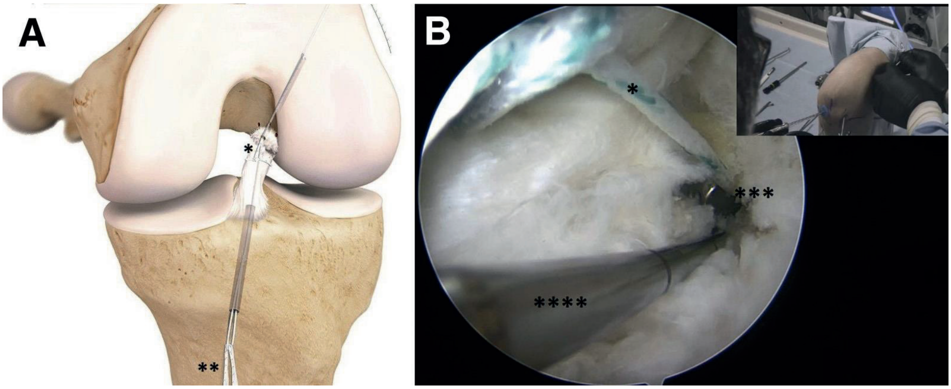

Figure 2.9 Repositioning of the anterior cruciate ligament (ACL) stump during ACL repair using the independent suture tape reinforcement technique. (A) Left knee frontal view. This image provided courtesy of Arthrex, Inc. © 2018. (B) Left cadaver knee, intra-articular view of the femur button at the starting point of the femoral tunnel. By pulling gently on the looped suture (*), the distal anterior cruciate ligament stump is repositioned against the femoral attachment. The shuttle suture (**) is going to be the lead suture for the independent suture tape reinforcement. A femoral button (***) loaded with a high-strength tape is transported proximally by the tibial end of the shuttle suture, through the tibial tunnel, the center of the ACL, and the femoral tunnel. A probe (****) can be used to facilitate the passing of the button in the femoral tunnel.

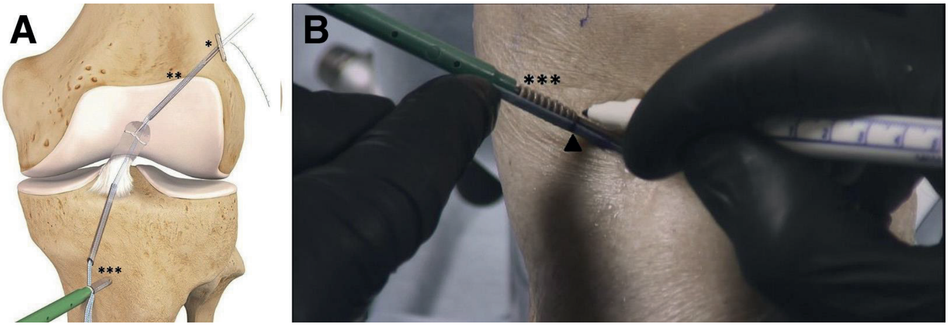

Figure 2.10 Placement of the high-strength tape during anterior cruciate ligament (ACL) repair using the independent suture tape reinforcement technique. (A) Left knee frontal view. This image provided courtesy of, Inc. 2018. (B) Left cadaver knee, external frontal view, marking of the high-strength tape. The button is flipped on the femoral cortex (*), and the high-strength tape (**) is advanced in the femoral tunnel by pulling the 2 tensioning strands, one at a time. The high-strength tape is being kept on a slight tension until it is fixed just below the tibial tunnel. A bone anchor (***) loaded with both ends of the high-strength tape is placed with the knee in full extension. To avoid overtightening, the high-strength tape is marked at the beginning of the screw of the bone anchor (:) and repositioned in the eye of the bone anchor at the marked level, and finally the bone anchor is placed in the drill hole. Care is taken not to damage the hamstrings.

2.5.6 ACL repair

With the ISTR completed, we now focus on the ACL repair. The knee is positioned in 90° of flexion. The ruptured ACL fibers are gently tensioned with the looped suture to approximate the distal stump to the femoral footprint. It is important for the distal stump to be in contact with the proximal stump; a gap is not acceptable. The looped suture is tied with the 2 tensioning strands on the femoral button with the appropriate tension on the ACL. The remnants of the looped suture, tensioning strands, and high-strength tape are cut and removed (Figure 2.11). Video 1 (https://www.arthroscopytechniques.org/article/S2212-6287(18)30042-2/fulltext) shows the ACL ISTR repair technique on a left cadaver knee.

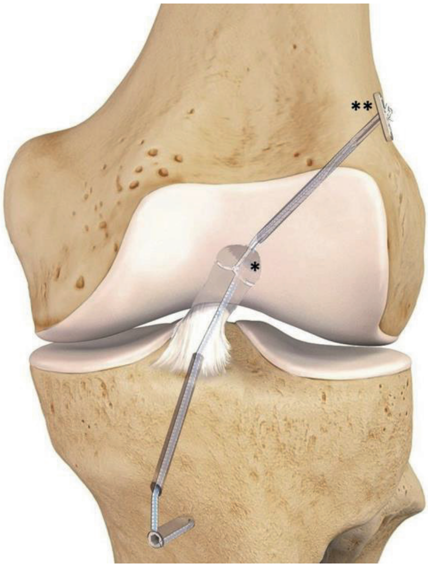

Figure 2.11 Tensioning of the looped sutures in anterior cruciate ligament repair using the independent suture tape reinforcement technique. Left knee frontal view. The ruptured ACL fibers are gently tensioned with the looped suture (*) to approximate the distal stump to the femoral footprint with the knee in 90° of flexion. The looped suture is tied with the 2 tensioning strands on the femoral button (**) with the appropriate tension on the anterior cruciate ligament. The remnants of the looped suture, tensioning strands, and high-strength tape are cut and removed. This image provided courtesy of Arthrex, Inc. © 2018.

2.6 Rehabilitation

The rehabilitation protocol can be compared with an accelerated ACL reconstruction protocol. The patients were allowed to fully weight bear with crutches as required during the first weeks. Physical therapy focuses on early range of motion, muscle control, and restoration of function. This approach is facilitated by the limited pain and swelling, allowing accelerated early-phase rehabilitation. Patients were allowed to perform pivoting sports if the neuromuscular function had recovered; for most patients, this happened within 5 months. No brace was required.

2.7 Discussion

Compared with other ACL repair techniques, one of the key features of the ISTR technique is the secondary stabilizer. The ISTR reinforces the ACL and acts as a safety belt, encouraging natural healing of the ligament by protecting it during the healing phase and supporting early mobilization [3]. The ISTR technique is less invasive than ACL reconstruction; the 3.5 mm bone tunnels are about half the size of the reconstruction bone tunnels. In the case of a re-rupture, a standard ACL reconstruction can still be performed as “no bridges are burned.” The native ACL is spared, which could lead to a preservation of its proprioceptive properties and contribute to a shorter rehabilitation period. Furthermore, there is no hamstring or patella tendon harvesting comorbidity as no graft is needed (Table 2.1). In a 1-year follow-up case series of 68 patients treated with the ISTR technique for an acute ruptured ACL, Mackay et al. describe comparable findings with early results from ACL reconstruction, with the greatest improvements seen in return to sporting activity [3].

Advantages	Disadvantages
The native ACL is spared, providing proprioceptive properties and enhancing the revalidation.	Not all ACL ruptures can be repaired.
No donor harvesting morbidity.	Synthetic augmentation.
The independent suture tape reinforcement technique is less invasive than ACL reconstruction.	
In case of re-rupture, a standard ACL reconstruction can be performed.	

Table 2.1 Advantages and Disadvantages of Anterior Cruciate Ligament (ACL) Repair Using Independent Suture Tape Reinforcement

One limitation is that not all ACL ruptures can be repaired (Table 2.2). If there is a gap between the ruptured ends, the continuous flow of the synovial fluid hampers the formation of a stable fibrin-platelet clot between the ruptured ends of the ACL in which stable scar tissue can form. Over time the distal stump can retract, which makes it impossible to repair without leaving a gap between the bundles [4]. If the stump is not retracted during this time, it can be found reattached on the posterior cruciate ligament or more anterior to the femoral origin. If the distal stump can be mobilized and brought back to its femoral origin and the tissue quality is sufficient, a repair can still be performed. The outcome of mid-substance (25%-75%) ACL repairs is significantly worse than that of proximal ruptures.

Proximal ACL ruptures, with sufficient tissue quality and good contact between the ruptured ends, have the best outcomes [5]. In the case of an acute (within 3 months) ruptured ACL, we start with an arthroscopic inspection of the ruptured ACL. If the rupture is not repairable, a graft is harvested and a standard ACL reconstruction is performed. Otherwise, the ISTR ACL repair is performed, which provides an environment in which the ruptured ACL can heal.

Limitations of Anterior Cruciate Ligament Repair Using the Independent Suture Tape Reinforcement Technique
There is a time limit of approximately 3 months post-rupture for the surgery.
The ACL stump has to be of good tissue quality and not retracted.
No gap between the ruptured ends is allowed after the repair.
Outcome of mid-substance (25% - 75%) ACL repairs are significantly worse.
No mid- to long-term follow-up results are published.

Table 2.2 Limitations of Anterior Cruciate Ligament (ACL) Repair Using the Independent Suture Tape Reinforcement Technique

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Chapter 3 Anterior Cruciate Ligament Repair with Independent Suture Tape Reinforcement: a Case Series with 2-year Follow-up

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3.1 Abstract

Purpose The treatment of acute anterior cruciate ligament (ACL) ruptures with a repair technique has recently regained interest. A novel ACL repair technique was described using Independent Suture Tape Reinforcement with 2-year follow-up results.

Methods Forty-two consecutive patients with an acute ACL rupture undergoing repair using this technique were followed up for a minimum of 2 years. Patients with mid-substance, distal ACL ruptures, poor ACL tissue quality or retracted ACL remnants as well as patients with multi-ligament injuries were excluded. Knee Injury and Osteoarthritis Outcome Score (KOOS), Visual Analogue Pain Scale (VAS-pain), Veterans RAND 12 Item Health Survey (VR-12) and the Marx Activity scale were collected by online questionnaires. Two year post-operative patients were asked by telephone if they had experienced a re-rupture.

Results All the KOOS subscales improved significantly in comparison to the pre-operative score. The largest improvement of all scores was seen at 3 months post-operatively which is significant in all cases. The KOOS sport and recreation showed a meaningful change and the largest improvement of the KOOS subscales at 3 months post-operatively, as well as the highest total improvement at 1 year post-operatively compared to pre-operatively. The VAS-pain and VR-12 physical score improved significantly, however the Marx activity scale decreased significantly in comparison to pre-operative scores. Two patients reported a re-rupture (4.8%, CI 1.7–11.2%).

Conclusions This is the first case series that described the 2-year follow-up results of patients with an acute, proximal ACL rupture, treated with the Independent Suture Tape Reinforcement repair technique. A meaningful KOOS sport and recreation change and significant improvements in the KOOS, VAS-pain and VR-12 physical scores as well as a significant decrease of the Marx activity scale in comparison to pre-operative scores are demonstrated. Two of the 42 patients (4.8%) reported an ACL re-rupture. Repair with this technique could be clinically relevant as a treatment option for patients with an acute, proximal ACL rupture which is not retracted and of good tissue quality.

3.2 Introduction

Anterior cruciate ligament (ACL) rupture is a common lesion in active adolescents and young adults. ACL insufficiency can lead to symptomatic instability, secondary meniscal pathologies and degenerative changes [2, 3]. ACL reconstruction has been the gold standard for the operative treatment of an ACL rupture for many years. ACL reconstruction results have been widely studied and techniques have improved over time [4]. Nevertheless only 63-65 % of the patients return to their pre-injury sport level and 10.3% have a graft failure after 10 years [5]. Furthermore, ACL reconstruction does not protect patients from developing osteoarthritis [3, 5]. As a result, there has been renewed interest in primary repair of the ACL [6-8].

Historically, primary repair of the ACL had moderate mid-term results in the 1970's and 1980's [9] and the growing success of ACL reconstruction led to its demise [8]. However, the historic technique used for ACL repair consisted of an arthrotomy, suturing of the ACL with drill holes in the femur and cast immobilization [9]. In 2014 Heitmann et al. [10] showed in a biomechanical study on porcine knee joints with multi-ligamentary lesions, a significantly higher stability on ACL augmented suture repair compared with isolated suture repair or reconstruction with hamstring tendons. He concluded that the concept of ligament bracing could be a promising future treatment option in acute knee dislocations. Most recently, several new arthroscopic techniques have been developed and good short-term results (≤2 years) are reported [11-17]. Eggli et al. [14] report a 5-year survival rate of 80% and excellent clinical outcomes with a dynamic intraligamentary stabilization ACL repair technique.

Although the ACL has to heal in a hostile environment [18], recent studies show the healing capacity of the repaired ACL [11-16]. Murray et al. [18] describes the necessity of a stable fibrin-platelet clot between the ruptured ends of the ACL in which stable scar tissue can form. The continuous flow of the synovial fluid hampers the formation of this clot. The independent suture tape reinforcement for ACL repair consists of an ultra-high strength biocompatible 2 mm width tape which bridges the ligament and is fixed on the femur with a button and a knotless bone anchor on the tibia.

By bringing the distal ACL end in touch with the proximal end with a looped suture, the gap between the two ends should be reduced as far as possible. The 2 mm high-strength tape provides stability and could act as a scaffold, together with the looped sutures, to keep the clot between the ruptured ends. Combined with the healing response technique described by Steadman et al. [19] the independent suture tape reinforcement repair technique provides an environment in which the ACL can heal [17]. This technique reinforces the ligament as a secondary stabilizer, encouraging natural healing of the ligament by protecting it during the healing phase and supporting early mobilization.

The purpose of this study is to describe the 2-year follow-up results of a novel ACL repair technique using the independent suture tape reinforcement. As far as we know, this will be the first case series that describes the 2-year follow-up results of this novel ACL repair technique. These results could support the growing evidence that ACL repair could earn a place as a treatment option for the acute, proximal ACL rupture and therefore, be clinically relevant. It was hypothesized that patients treated with this technique for an acute, proximal rupture of the ACL would demonstrate significant improvements in patient reported outcome measures (PROMs) over time.

3.3 Materials and methods

The patient cohort consisted of patients operated from 2011 until 2014, who underwent repair of the ACL using the independent suture tape reinforcement for a clinically and radiologically (MRI) proven acute, proximal ACL rupture (<12 weeks). Patients participated in a prospectively used web-based tool to collect questionnaires. Exclusion criteria were patients with multi-ligament injuries, mid-substance or distal ACL ruptures or a retracted ACL remnant as well as poor ACL tissue quality. The excluded patients were treated with an ACL reconstruction. There were no age restrictions.

Forty-three patients were included in the study. One patient was lost to follow-up within 3 months post-operatively leaving 42 patients in this study. Eighteen patients were female (42.9%) and 24 were male (57.1%). Mean (SD) age at time of operation was 33 (14.5) years (range 14-60 years). All of the patients were evaluated by online questionnaires and also contacted by telephone to collect data regarding ACL re-rupture. In the same study time period 55 patients were treated with an ACL reconstruction (Figure 3.1). All surgical procedures were performed by the senior author.

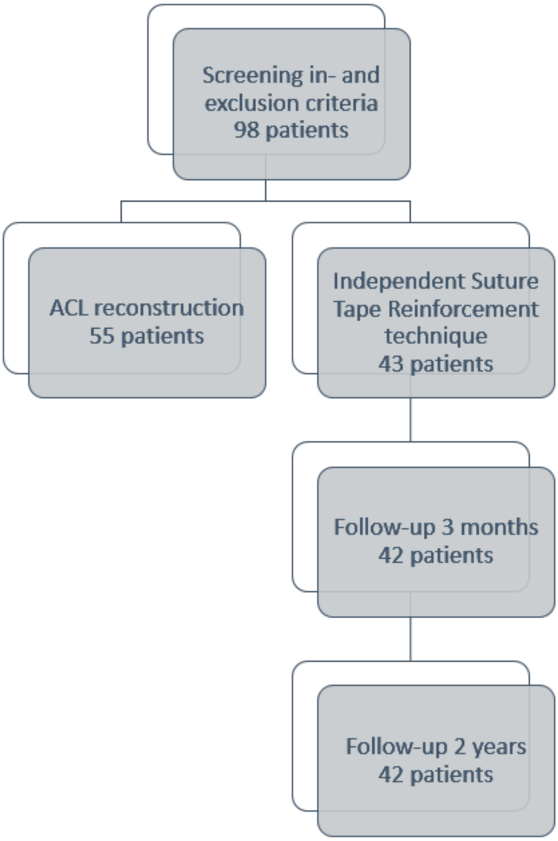

Figure 3.1 Flowchart of patient enrollment

3.3.1 Surgical technique

Proximal ruptures of the ACL, less than three months old (Figure 3.2), were repaired with the independent suture tape reinforcement (InternalBrace™ Ligament Augmentation Repair, Arthrex, Inc., Naples, FL). If the rupture was mid-substance or distal or the ACL remnant was retracted or of poor tissue quality, an ACL reconstruction was performed. A 3.5 mm tibial tunnel is drilled, ending at the center of the ACL footprint. A looped suture (FiberLink®, Arthrex Inc., Naples, FL) is placed through the mid-substance of the ACL stump (Figure 3.3). At the femoral attachment microfracturing is performed. The femoral tunnel is drilled from the center of the femoral footprint inside out, with the knee fully flexed. A shuttle suture and the looped suture are passed through the femoral tunnel. A femoral button, loaded with a high-strength tape (FiberTape®, Arthrex, Inc., Naples, FL), is flipped on the femoral cortex and the high-strength tape is advanced in the femoral tunnel. The high-strength tape is fixed in extension in the tibia with a bone anchor (SwiveLock®, Arthrex Inc., Naples, FL). The ruptured ACL fibres are gently tensioned with the looped suture to approximate the distal stump to the femoral footprint with the knee in 90° of flexion. The looped suture is tied on the femoral button with the appropriate tension on the ACL (Figure 3.4).

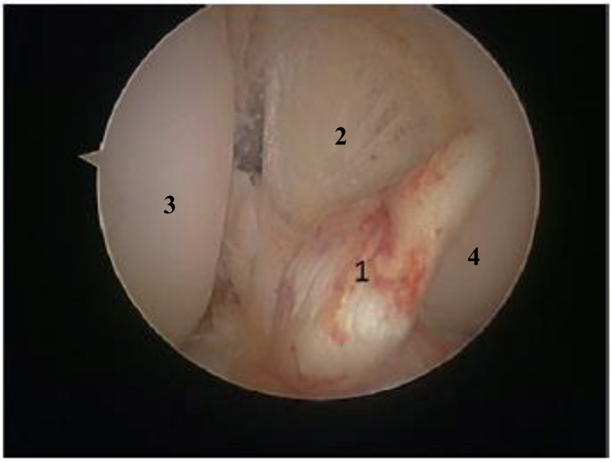

Figure 3.2 Anterior cruciate ligament rupture of 5 weeks old. Right knee, intra-articular view through the anterolateral portal. A 5-week-old proximal anterior cruciate ligament rupture (1). The synovium is still intact, the tissue is of good quality and not retracted. (1) anterior cruciate ligament, (2) posterior cruciate ligament, (3) lateral femoral condyle, (4) medial femoral condyle

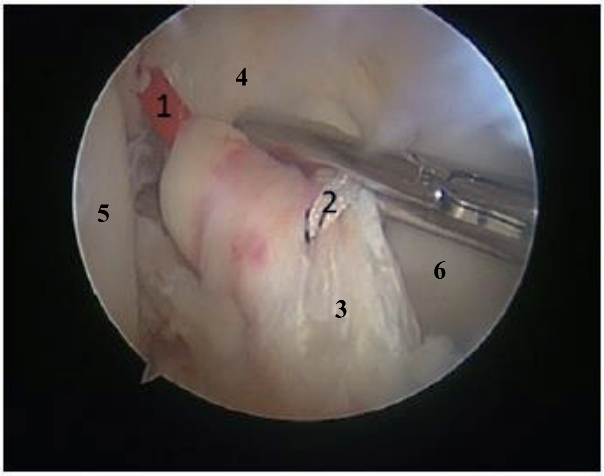

Figure 3.3 Placement of shuttle suture during anterior cruciate ligament repair using the independent suture tape reinforcement technique. Right knee, intra-articular view through the anterolateral portal. A tubed shuttle suture (1) has been passed through the tibial tunnel and the center of the ACL footprint. A looped suture (2) is placed through the mid-substance of the ACL stump. (3) anterior cruciate ligament, (4) posterior cruciate ligament, (5) lateral femoral condyle, (6) medial femoral condyle

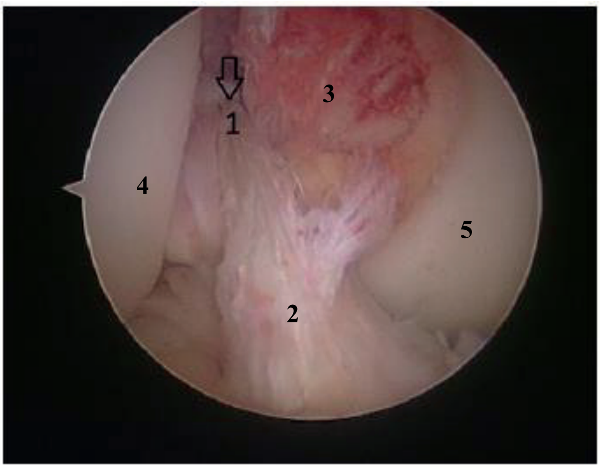

Figure 3.4 Retensioning of the anterior cruciate ligament (ACL) during ACL repair using the independent suture tape reinforcement technique. Right knee, intra-articular view through the anterolateral portal. The tape was passed through the center of the ACL and is, therefore, not visible. The looped suture (1), seen in Figure 3.2 in the mid-bundle position, is now visible more proximally (arrow) on the retensioned ACL. (2) anterior cruciate ligament, (3) posterior cruciate ligament, (4) lateral femur condyle, (5) medial femur condyle

The post-operative rehabilitation protocol could be compared to an accelerated ACL reconstruction protocol. Patients were allowed full weight bearing with crutches as required during the first weeks. Physical therapy focuses on early range of motion, muscle control and restoration of function. This is facilitated by the limited pain and swelling, allowing accelerated early phase rehabilitation. Patients were allowed to perform pivoting sports if the neuromuscular function had recovered, for the most patients this was within 5 months. No brace was required.

3.3.2 Clinical and functional evaluation

Patients were evaluated prospectively with the Surgical Outcome System (SOS, Arthrex, Naples, Fl, USA). SOS is a web-based tool which sends questionnaires and PROMs by e-mail at pre-scheduled timepoints, after informed consent was given by the patient. The collected PROMs were the Knee Injury and Osteoarthritis Outcome Score [20] (KOOS), Visual Analog Pain Scale (VAS-pain), Veterans RAND 12 Item Health Survey [21] (VR-12) and the Marx Activity Scale [22]. These data were collected pre-surgery and at 3, 6, 12 and 24 months post-operatively, except for VR-12 (no 3-month measurement) and Marx Activity Scale (no 3- and 6-month measurement). All the patients were contacted by telephone at 24 months post-operatively to collect data about ACL re-rupture. Before analyzing the anonymous data retrospectively in a different center, this study has been deliberated with the local Belgian ethical committee. They stated that under the Belgian law no IRB approval is needed if the anonymous data are analyzed retrospectively.

3.3.3 Statistical analysis

KOOS subscales, VAS-pain, VR-12 subscales and Marx activity scales were presented as means with standard errors (SEs) at each available timepoint. A linear mixed model with time as fixed effect and individual as random intercept was fitted for each of the outcomes. The significance of the main effect of time allowed us to evaluate if there was an overall change of the scores over time. In case of significance, post hoc testing was done comparing the consecutive timepoints using the estimates from the mixed model with Bonferroni-Holm correction for multiple testing. Mean difference between the outcomes at consecutive timepoints with SE estimated using the mixed model are reported. The ACL re-rupture risk was expressed as a proportion with confidence interval. Results were considered significant if $p < 0.05$. All analyses were performed with SPSS statistics (IBM, version 21) except the mixed model which was done in SAS 9.4 (SAS Institute, Cary NC). A post hoc sample size calculation was performed.

3.4 Results

Thirty-two patients (76%) filled in the patient questionnaires pre-operative and 37 patients (88%) 24 months post-operatively. Mean and SE of the different scales (KOOS, VAS-pain, VR-12 and Marx Activity scale) pre-operative, 3-, 6-, 12- and 24-month post-operative (when available) are reported in Table 3.1. Table 3.2 and 3.3 report the mean difference (SE) in outcome for these scales between two consecutive time points as estimated by the linear mixed model. All of the KOOS scores show a significant evolution over time.

Scale	Pre-operative (n=32)	3 months (n=30)	6 months (n=24)	12 months (n=34)	24 months (n=37)
KOOS pain	65.5 (3.1)	85.3 (2.2)	89.1 (2.3)	93.5 (1.2)	87.9 (2.6)
KOOS symptoms	51.8 (3.3)	78.8 (3.2)	84.7 (3.1)	86.9 (1.9)	84.5 (2.5)
KOOS ADL	73.0 (3.3)	91.0 (1.6)	95.6 (1.8)	98.2 (0.5)	93.2 (2.0)
KOOS sport/recreation	26.6 (3.9)	64.2 (3.6)	75.8 (4.0)	86.2 (2.2)	76.6 (4.8)
KOOS QOL	25.6 (2.8)	55.8 (3.7)	63.0 (3.5)	76.1 (2.8)	70.8 (4.3)
VAS-pain	2.7 (0.4)	1.0 (0.3)	0.4 (0.1)	0.7 (0.2)	1.3 (0.3)
VR-12 Physical	35.9 (1.6)		51.3 (1.3)	54.0 (0.6)	50.3 (1.3)
VR-12 Mental	53.4 (1.6)		56.8 (1.4)	56.3 (1.1)	54.9 (1.5)
Marx scale	12.3 (0.6)			8.2 (0.9)	8.3 (1.0)

Table 3.1 Overview of scores at different time points. Mean (SE) of Knee Injury and Osteoarthritis Outcome Score (KOOS), Visual Analogue Pain Scale (VAS-pain), Veterans RAND 12 Item Health Survey (VR-12) and the Marx Activity scale pre-operative and at 3, 6, 12 and 24 months

Scale	3-month pre-operative	6-3 months	12-6 months	24-12 months	P value time
KOOS pain difference	20.3 (3.0) **P < 0.0001**	4.0 (3.3) P=0.442 (n.s.)	3.4 (3.2) P=0.442 (n.s.)	-5.3 (2.8) P=0.191 (n.s.)	**P < 0.0001**
KOOS symptoms difference	27.5 (3.0) **P < 0.0001**	6.3 (3.3) P=0.167 (n.s.)	1.3 (3.2) P=0.807 (n.s.)	-2.3 (2.8) P=0.807 (n.s.)	**P < 0.0001**
KOOS ADL difference	18.4 (2.8) **P < 0.0001**	4.7 (3.0) P=0.243 (n.s.)	1.8 (2.9) P=0.543 (n.s.)	-4.6 (2.6) P=0.239 (n.s.)	**P < 0.0001**
KOOS sport/recreation difference	37.9 (5.3) **P < 0.0001**	12.4 (5.7) P=0.090 (n.s.)	8.7 (5.5) P=0.132 (n.s.)	-9.0 (4.9) P=0.132 (n.s.)	**P < 0.0001**
KOOS QOL difference	31.6 (4.2) **P < 0.0001**	9.0 (4.5) P=0.099 (n.s.)	9.5 (4.4) P=0.099 (n.s.)	-4.5 (3.8) P=0.244 (n.s.)	**P < 0.0001**
VAS-pain difference	-1.7 (0.4) **P < 0.0001**	-0.5 (0.4) P=0.362 (n.s.)	0.3 (0.4) P=0.437 (n.s.)	0.5 (0.3) P=0.362 (n.s.)	**P < 0.0001**

Table 3.2 Linear mixed model outcome. Table reports the mean difference (SE) in outcome (KOOS and VAS-pain) between two consecutive time points as estimated by the linear mixed model. P value time gives the P value for the overall time effect. P values of two-by two comparisons of consecutive time points are given per comparison. Significant p values are in bold

Scale	6-month pre-operative	12-6 months	24-12 months	P value time
VR-12 physical difference	15.7 (1.8) **P < 0.0001**	2.6 (1.8) P=0.141 (n.s.)	-3.8 (1.6) **P=0.033**	**P < 0.0001**
VR-12 mental difference	3.6 (1.8)	-1.2 (1.8)	-0.9 (1.5)	P=0.215 (n.s.)
		12-month pre-operative	**24-12 months**	**P value time**
Marx difference		-4.5 (0.9) **P < 0.0001**	0.7 (0.8) P=0.421 (n.s.)	**P < 0.0001**

Table 3.3 Linear mixed model outcome. Table reports the mean difference (SE) in outcome (VR-12 and Marx activity scale) between two consecutive time points as estimated by the linear mixed mode P value time gives the p value for the overall time effect. P values of two-by two comparisons of consecutive time points are given per comparison. Significant P values are in bold

The largest improvement of all the scores is seen at 3 months post-operatively which is significant in all cases. The highest scores are reached 1 year post-operatively, except for the VAS-pain. At 2 years post-operatively the scores decrease slightly compared to 1 year post-operatively. The KOOS sport and recreation scores show the largest improvement of the KOOS subscales at 3 months post-operatively and the highest total improvement at 1 year post-operatively compared to pre-operatively (Figure 3.5). According to Ingelsrud et al. [23] a change of 12.1 points on the KOOS sport and recreation is a minimal important change after undergoing ACL reconstruction. We found in our study a mean change of 37 points between 3 months and pre-operative KOOS sport and recreation with a SD of 24 points, using this SD we calculated that 34 patients were sufficient to have 80% power to detect an effect of 12 assuming a significance level of 5%. The VAS-pain and VR-12 physical score improved significantly; however, the Marx activity scale decreased significantly compared to the pre-operative scores. The VR-12 mental score showed no significant evolution over time.

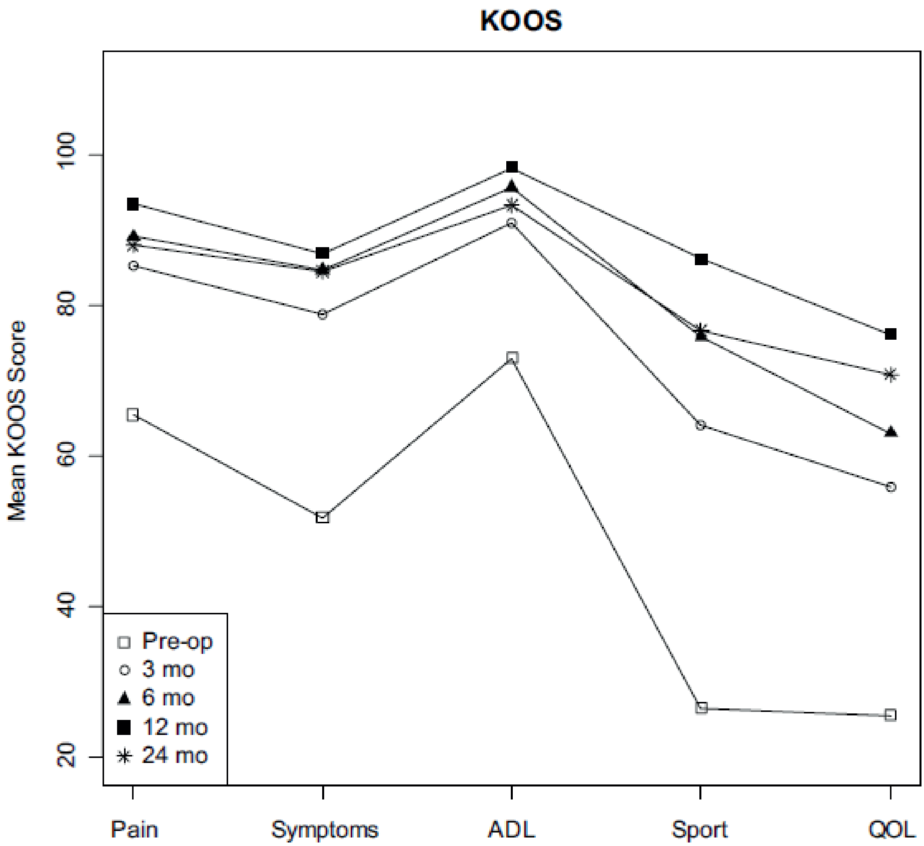

Figure 3.5 Knee Injury and Osteoarthritis Outcome Score Subscales at different time points. Mean Knee Injury and Osteoarthritis Outcome Score Subscales at different time points

Two re-ruptures (4.8%, CI -1.7 -11.2%) were reported. One patient had a re-rupture at 5 months when he landed in valgus after a mid-air collision playing soccer. The other re-rupture occurred when the patient was playing soccer 15 months after the ACL repair. Both patients were treated with an ACL reconstruction without complications.

3.5 Discussion

The most important findings of the present study are the meaningful KOOS sport and recreation change and the significantly improved PROMs at 2-year follow-up using an independent suture tape reinforcement repair technique for an acute, proximal ACL rupture in comparison to pre-operative scores. All post-operative KOOS, VAS-pain and VR-12 physical scores show significant improvement compared to pre-operative scores. However, there is a decrease of the mean Marx activity scale (SE), from 12.3 (0.6) pre-injury to 8.3 (1.0) 2 years post-operatively. A decrease of the Marx activity scale is described as well post-operatively after ACL reconstruction. Spindler et al. describe in their multicenter unilateral ACL reconstruction cohort group of 448 patients, a pre-operative median Marx activity scale of 12, which lowers to 9 at 2-year post-operative and to 7 at 6-year post-operative [24]. Nwachukwu et al. describe in their competitive athlete cohort with an ACL reconstruction a mean drop from 15.8 at baseline to 11.9 2-year post-operative [25]. The reported re-rupture risk of 4.8% within 2 years is acceptable for a new ACL repair technique. Eggli et al. [13] describe one rupture (10%) in 10 patients with a 2-year follow-up and Henle et al. [15] describe 8 re-ruptures (2.9%) in 278 patients at an average of 338 days post-operatively with a dynamic intraligamentary stabilization technique. DiFelice et al. [16] report one re-rupture (9%) in 11 patients within 2 years with a novel arthroscopic technique for suture anchor repair. Achtnich et al. [12] describe a re-rupture risk of 15% at a mean follow-up of 28 months with a proximal re-fixation technique using knotless anchors and microfracturing. The two previous mentioned anchor repair techniques are lacking a secondary stabilizer which is one of the key features of the independent suture tape reinforcement we have described. This technique reinforces the ACL as a secondary stabilizer, encouraging natural healing of the ligament by protecting it during the healing phase and supporting early mobilization [11].

Csintalan et al. report a mean age (SD) of 29.8 (10.0) years on 4485 ACL reconstructions and Yasen et al. 30.9 (range 15-61) years on the anatomic all-inside ACL reconstruction [26, 27]. Although the mean age in our patient group is higher at 33 (14.5) years, a higher mean age is also described in other ACL repair techniques. The mean age of the 11 patients treated with suture anchor primary anterior cruciate ligament repair is 37 (13) and for the 278 patients treated with a dynamic intraligamentary stabilization ACL repair technique 32.4 (11.4) [15, 16]. As the ACL repair techniques are less invasive compared to the ACL reconstruction, the threshold to perform an ACL repair surgery could be lower compared to ACL reconstruction, which could lead to a higher mean age. Another explanation could be that the injury pattern of the ACL is different and that more proximal ACL ruptures, which are not retracted and of good quality, are seen with a higher age.

Patients younger than 20 years who undergo ACL reconstruction are at significantly increased risk for both graft rupture and contralateral ACL injury [28]. Whether age per se is a risk factor or age represents a proxy for other factors remains to be determined. The higher mean age 33 (14.5) and the lower Marx activity scale could be of influence on the reported re-rupture risk (4.8%) in our study cohort.

Kiapour et al. describe several potential advantages of ACL repair as an alternative to the current surgical reconstruction [29]. ACL repair has the potential to preserve the native insertion site and proprioceptive function, which may in turn lead to more normal joint mechanics and decreased risk of post-traumatic osteoarthritis. Long-term follow-up and further research will have to show if these potential advantages are applicable to the technique we have described. One of the perceived advantages of the independent suture tape reinforcement ACL repair technique compared to ACL reconstruction is that no hamstring or patella tendon harvesting comorbidity is expected as no graft is needed. By drilling 3.5 mm bone tunnels, about half the size of the reconstruction bone tunnels and saving the native ACL, with its mechanoreceptors [30], the Independent Suture Tape Reinforcement repair technique is less invasive compared to ACL reconstruction. In the event of a re-rupture, a standard ACL reconstruction can be performed.

There are several limitations associated with this study. Firstly, only the Marx activity scale, which questions the highest activity levels of last year, compares the pre-rupture level with the post-operative level. The other patient questionnaires are pre-operative data, instead of pre-rupture data, which makes it difficult to compare the pre-injury level and post-operative level. Secondly, there are no objective clinical outcome data with 2-year follow-up, such as post-operative radiographic evaluation to confirm the healing of the ACL. As this is a patient case series, no comparison can be made to the gold standard ACL reconstruction. A randomized trial between ACL reconstruction and ACL repair with independent suture tape reinforcement could focus on the difference in rehabilitation time, re-rupture risk and PROMs. Mid- to long-term follow-up will have to show if the re-rupture risk will not increase with this repair technique.

Several new arthroscopic ACL repair techniques have been developed and good short-term results (≤2 years) are reported. Theoretically spoken ACL repair could have an advantage over ACL reconstruction; by preserving your own ligament and its proprioceptors the revalidation could be quicker and there is no comorbidity of harvesting the donor graft. This article contributes to the increasing evidence that with the novel ACL repair techniques and stricter indications, ACL repair could earn a place as a treatment option for the acute, proximal ACL rupture [11-17], but further research is necessary.

3.6 Conclusions

This is the first case series that described the 2-year follow-up results of patients with an acute, proximal ACL rupture treated with an independent suture tape reinforcement repair technique. A meaningful KOOS sport and recreation change and significant improvements in the KOOS, VAS-pain and VR-12 physical scores as well as a significant decrease of the Marx activity scale in comparison to pre-operative scores are demonstrated. Two of the 42 patients (4.8%) reported an ACL re-rupture. Repair with this technique could be clinically relevant as a treatment option for patients with an acute, proximal ACL rupture which is not retracted and of good tissue quality.

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Chapter 4 Suture Tape Augmentation ACL Repair; Stable Knee and Favorable PROMs, but a Re-rupture Rate of 11% within Two Years

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Suture Tape Augmentation ACL Repair, Stable Knee, and Favorable PROMs, but a Re-rupture Rate of 11% within Two Years.

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4.1 Abstract

Purpose The aim of this study is to investigate clinical and magnetic resonance imaging (MRI) outcomes after anterior cruciate ligament (ACL) repair using the suture tape augmentation (STA) technique.

Methods This prospective interventional case series included 35 patients who underwent STA ACL repair and were all followed up for two years. The ACL rupture was between 4 and 12 weeks old and per-operatively confirmed repairable. The International Knee Documentation Committee (IKDC), Lysholm and Tegner scores were collected together with return to work (RTW), return to sport (RTS), re-rupture and re-intervention rate. Lachman testing was performed and ACL healing was evaluated on MRI using a grading scale based on the ACL's morphology and signal intensity with grade 1 representing good ACL healing and grade 3 representing poor ACL healing.

Results The number of patients who returned to their pre-rupture level for IKDC, Lysholm and Tegner scores at two years of follow-up are 17/26 (65.4%), 13/25 (52.0%) and 18/27 (66.7%) patients, respectively. Median RTW and RTS periods were 5.5 weeks (range 0 to 32 weeks) and 6 months (range 2 to 22 months), respectively. The Lachman side-to-side difference decreased significantly ($P < 0.001$) to less than 3 mm after surgery and remained stable. Four patients (11.4%, 95% CI [3.2, 26.7]) suffered from a re-rupture and three other patients (8.6%, 95% CI [1.8, 23.1]) needed a re-intervention for another reason than re-rupture. MRI follow-up of 31 patients showed overall grade 1 ACL healing in 14 (45.2%) patients, grade 2 ACL healing in 11 (35.5%) patients and grade 3 ACL healing in 6 (19.4%) patients. A higher risk of re-rupture was associated with grade 3 ACL healing at 6 months post-operatively and a pre-operative Tegner score of ≥ 7.

Conclusion This study shows that treatment of the acute, repairable ACL with the STA technique leads to a stable knee and favorable patient-reported outcome measures (PROMs). However, the re-rupture rate of 11.4% within the 2-year follow-up is a concern.

4.2 Introduction

In the 1970's and 80's, repair techniques were performed to treat anterior cruciate ligament (ACL) ruptures. These open repair techniques were abandoned after disappointing five year follow-up outcomes and ACL reconstruction became the gold standard treatment [1, 2]. The introduction of several novel ACL repair techniques in the last decade has led to renewed interest in acute primary ACL repair [2-5].

Van der List et al. reported that arthroscopic ACL repair techniques were safe, with failure rates of 7 – 11%, no complications and functional outcome scores of > 85% of maximum scores [2]. Bucci et al. also reported that current literature on ACL repair reports better outcomes than in the past and subjective patient-reported outcome measures (PROMs) following ACL repair are not inferior to PROMs after ACL reconstruction [6].

One of the most published ACL repair techniques is the dynamic intraligamentary stabilization (DIS) technique. The first publications by the DIS developer group confirm the healing capacity of the ACL and report excellent patient satisfaction and re-rupture rates of 2.9% and 10% [3, 7]. More recent publications from independent researchers show re-rupture rates up to 20% at 2-year follow-up and failure rates of 30% at five year follow-up [8, 9].

The suture tape augmentation (STA) technique is a repair technique that preserves the native ACL and provides a secondary stabilizer to reinforce the repaired ACL during the healing phase [10, 11]. Preservation of the native ligament and its proprioceptors contributes to the feedback on position and dynamic stability of the knee, which improves rehabilitation after surgery [5, 10, 12, 13]. The STA technique is less invasive compared to ACL reconstruction as graft harvesting morbidity is avoided, and the 3.5 mm bone tunnels drilled for the STA technique are less than half the size of bone tunnels needed for ACL reconstruction [2, 10, 13].

Currently, literature on STA ACL repair is not extensive. Two STA ACL case series report promising results in terms of an increase in PROMs and re-rupture rates of 4.8% and 1.5%. However, both studies do not compare post-operative data with pre-rupture data and lack a clinical as well as magnetic resonance imaging (MRI) follow-up [4, 10]. A retrospective study by Ortmaier et al. on sports activity, states that short-term outcomes after STA ACL repair and ACL reconstruction are comparable, and that STA treatment enables sports activity and provides a sense of well-being similar to that of classic ACL reconstruction [14].

To the best of our knowledge, no independent prospective clinical results, longitudinal MRI follow-up or risk factors for re-rupture on STA ACL repair have been reported yet.

The purpose of this study was to investigate clinical results, re-rupture risk factors and MRI outcomes, two years after primary ACL repair with the STA technique. The hypothesis was that STA ACL repair would lead to an acceptable re-rupture rate around 6% and good clinical outcomes in terms of PROMs and knee stability.

4.3 Material & methods

4.3.1 Patient recruitment

This prospective case series was approved by the institutional review board of the Antwerp University Hospital (B300201525523) and written informed consent was obtained from all study participants. Patients with a proximal or mid-substance bundle ACL rupture between 4 and 12 weeks old at the moment of surgery were recruited for treatment with the STA technique. Patients with an acute ACL rupture of less than four weeks old were recruited for treatment with DIS in a different study. Per-operative evaluation of good ACL tissue quality and sufficient contact between the stumps were vital inclusion criteria and determined whether the ACL was suitable for repair. Patients who were not active in sports and therefore could be treated with a conservative treatment, or patients who had multi-ligament injuries, excluding medial collateral ligament or anterolateral ligament lesions, or fractures that could compromise rehabilitation were not included.

Seventy-two patients presented at the Antwerp University Hospital between 2015 and 2017 with an acute ruptured ACL of less than 12 weeks old. Thirteen patients were pre-operatively excluded for not meeting in- and exclusion criteria. Fifteen patients were treated within 4 weeks with DIS and 44 patients were allocated to be treated with the STA technique. Seven of these 44 patients were per-operatively excluded due to a non-repairable ACL rupture and two patients refused to be followed up. This prospective case series thus includes the first 35 consecutive patients treated with the STA technique at the Antwerp University Hospital who were all followed up for two years. (Figure 4.1)

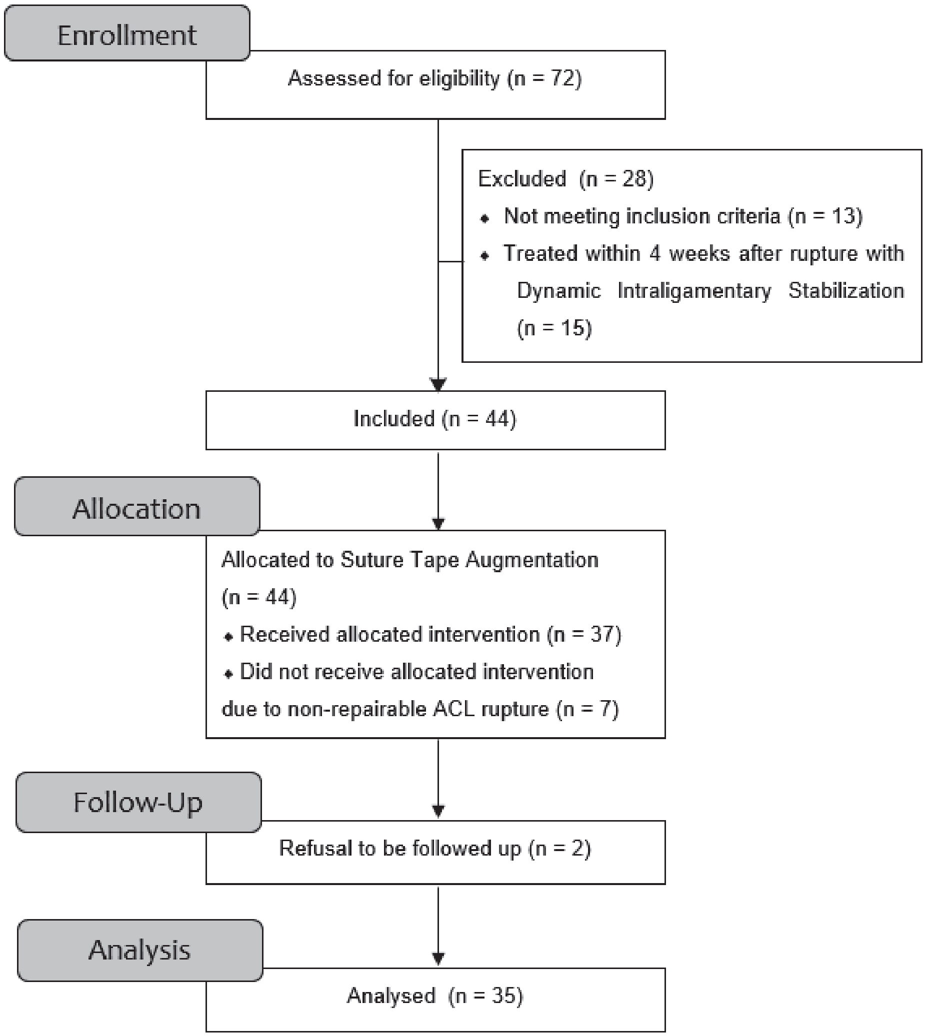

Figure 4.1 CONSORT flow diagram.

The mean age (standard deviation; SD) of the study population was 32.8 (9.7) years old and ranged from 18 to 54 years, 18 (51.4%) patients were female.

4.3.2 Study design

Pre-rupture and post-operative PROMs after 6, 12 and 24 months were collected via questionnaires completed during consultation. The International Knee Documentation Committee (IKDC), Lysholm, Tegner and Visual Analogue Scale (VAS) satisfaction scores were collected [15, 16]. Time between the surgery and return to work (RTW), time between the surgery and return to sport (RTS), re-intervention and re-rupture data were collected as well. Patients who suffered from re-rupture were subsequently treated with ACL reconstruction and further excluded from analysis of study results. Lachman testing was performed using a Rolimeter (Aircast, Neubeuern, Germany) to measure the anterior-posterior knee laxity difference between the injured and contralateral knee [17]. Clinical failure was defined as Lachman test of >3 mm difference between the injured and contralateral knee in combination with a subjective feeling of instability. All patients were asked to undergo MRI follow-up at 6, 12 and 24 months post-operatively. Imaging was performed on a commercially available, clinical whole-body 3-T MRI system (Magnetom Prisma Fit, Siemens Healthcare, Erlangen, Germany). A dedicated phased-array knee-coil with 15 receiver channels and 1 transmission channel (Quality Electrodynamics, Mayfield Village, OH, USA) was used. A radiologist with 20 years of experience in musculoskeletal radiology interpreted all images, blinded to the patient's clinical information. ACL healing on MRI was evaluated and categorized based on the ACL's morphology and signal intensity, as follows: grade 1: well-defined, straight, continuous, normal-sized ACL with signal intensity similar to or only slightly higher than that of the posterior cruciate ligament (PCL); grade 2: normal sized (or slightly thickened) continuous, straight ACL demonstrating a high signal compared to that of the PCL; and grade 3: an ill-defined, irregular ACL that is thinned or not discernible [18, 19]. The ACL healing grade was defined per time point and an overall healing grade was determined for each patient with two or three post-operative MRI images based on the evolution of the ACL's healing process over time during follow-up. For the test-retest reliability we calculated a weighted kappa and found a very good reliability of 0.85 (95% CI [0.71, 0.98]) [20].

4.3.3 Surgical technique

The surgical technique has previously been described by Heusdens et al. [10]. Proximal and mid-bundle ACL ruptures were repaired using the STA technique (InternalBraceTM Ligament Augmentation Repair, Arthrex Inc., Naples, FL). After inspection of the ACL stump, a 3.5 mm tibial tunnel was drilled, ending at the center of the ACL footprint. A looped suture (FiberLink®, Arthrex Inc., Naples, FL) was placed through the distal ACL stump. At the femoral attachment, two to four microfracturing holes were made to enhance healing of the ACL. The femoral tunnel was drilled from the center of the femoral footprint inside out, with the knee fully flexed. A suture shuttle and the looped suture were passed through the femoral tunnel. A femoral button, loaded with a high-strength tape (FiberTape®, Arthrex Inc., Naples, FL), was flipped on the femoral cortex and the high-strength tape was advanced in the femoral tunnel.

The high-strength tape was fixed in extension in the tibia with a bone anchor (SwiveLock®, Arthrex Inc., Naples, FL). The ruptured ACL fibers were gently tensioned with the looped suture to approximate the distal stump to the femoral footprint with the knee in 90° of flexion. The looped suture was tied on the femoral button with appropriate tension on the ACL (Figure 4.2).

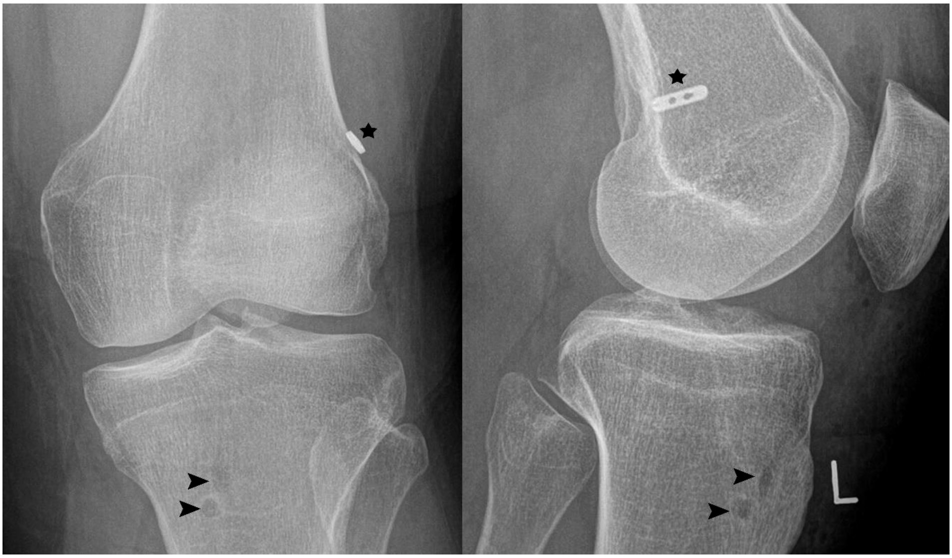

Figure 4.2 Radiographic findings of the left knee after suture tape augmentation. At the end of the small tibial bone tunnel, the high-strength tape is fixed with a bone anchor (arrowheads).The proximal fixation is with a femoral button, parallel to the distal femoral cortex (asterisk).

4.3.4 Post-operative rehabilitation

The post-operative rehabilitation protocol could be compared to an accelerated ACL reconstruction protocol. Patients were allowed full weight-bearing with crutches as required during the first weeks. Physical therapy focused on early range of motion, muscle control and restoration of function. This was facilitated by the limited pain and swelling, allowing accelerated early-phase rehabilitation. Patients were allowed to perform pivoting sports if the knee had a full range of motion, no effusion, upper leg muscular circumference > 90% and a single leg hop test > 90% [10].

4.3.5 Statistical analyses

A post-hoc sample size calculation was performed, indicating that to obtain a 95% confidence interval of width 16% around the acceptable re-rupture rate of 6%, a total of 34 patients was needed. The goal of this study was to recruit all possible patients during a 2-year period and explore the findings. IKDC, Lysholm, VAS satisfaction scores and the Lachman difference were presented as mean with SD and Tegner score as median with range at the different time points. A linear mixed model including time (categorical variable) as a fixed effect and individual as a random intercept was fitted for each of the outcomes. In case of a significant time effect, post-hoc testing was done comparing each of the considered time points to the pre-rupture (pre-operative) values on the one hand, and the consecutive time points on the other. Raw and corrected P values using the Bonferroni-Holm correction for multiple testing were reported. The mixed model was corrected for age and gender by adding these factors, one by one, to the model. Return to pre-rupture level was defined respectively for the IKDC, Lysholm and Tegner scores. A return to pre-rupture level was considered for the IKDC score if the current score was higher than or equal to the IKDC score pre-rupture minus 10 points [21]. A return to pre-rupture level was considered for the Lysholm score if the current score lay within the same range or a higher range as the pre-rupture score, assuming the following ranges: < 65 poor, 65 – 83 fair, 84 – 90 good, > 90 excellent [16, 22]. For the Tegner score, a return to pre-rupture level was considered when the current score was the same as or higher than the pre-rupture score [16, 21]. Median times to reach the pre-rupture level were calculated for each of these scores with 95% confidence intervals. For RTW and RTS, Kaplan-Meier curves were produced and median RTW and RTS with 95% confidence intervals were reported. For each time point during follow-up, the proportion of patients with different grades of ACL healing on MRI were reported. The ACL re-rupture rate was expressed as a proportion with 95% confidence interval (using exact Clopper-Pearson method).

The association between the occurrence of re-rupture and the type of rupture, grade of ACL healing on MRI 6 months post-operative, pre-operative Tegner score (< 7 versus ≥ 7) and age (< 25 versus ≥ 25) on re-rupture was evaluated using a Fisher's exact test. Results were considered significant if $P < 0.05$. All analyses were performed with SPSS statistics (IBM, version 21) and R 3.5.2 (R core team, 2018) except the mixed model, which was done in SAS 9.4 (SAS Institute, Cary NC).

4.4 Results

4.4.1 Patient and surgical characteristics

The patient population of this study consists of non-high-level sport athletes from various sport levels, with pre-rupture Tegner scores ranging from 1 to 9, and a median Tegner score of 6. Pre-rupture, 9/33 (27.3%) patients were performing heavy physical work, 10/33 (30.3%) patients light physical work and 14/33 (42.4%) patients sedentary work, the working category of the two remaining patients is unknown.

Additional Procedure	Number of Patients
Medial Meniscus Suture	9
Lateral Meniscus Suture	7
Partial Medial Meniscus Resection	5
Partial Lateral Meniscus Resection	2
Medial Collateral Ligament Repair	4
Anterolateral Ligament Repair	1

Table 4.1 Additional Procedures During Primary Surgery

Twenty-two (62.9%) patients had one or more additional procedures together with the STA surgery. (Table 4.1) The overall mean (SD) surgery time was 91 (21) minutes. The mean (SD) surgery time of the patient group (n = 22) that underwent additional procedures during primary intervention was 102 (18) minutes and of the patient group (n = 13) without additional procedures was 73 (11) minutes.

4.4.2 Clinical outcomes during 2-year follow-up

Scale	Pre-rupture [d]	Pre-operative	6 months	12 months	24 months
Lachman difference (mm) [b]		3.7 (2.1)	0.7 (1.7)	0.7 (1.1)	1.0 (1.2)
IKDC [c]	94.8 (9.2)		75.0 (13.8)	81.6 (12.1)	85.3 (13.2)
Lysholm	93 (14)		85 (12)	85 (11)	86 (10)
Tegner	6 (1 - 9)		4.5 (2 - 8)	5 (1 - 8)	6 (1 - 9)
VAS Satisfaction	-	-	8 (1)	8 (2)	9 (1)

Table 4.2 Outcome Measures at Different Time Points During Follow-up [a]

[a] *Lachman difference, IKDC score, Lysholm score and VAS satisfaction score are reported as mean (SD). Tegner score is reported as median (range).*
[b] *Lachman testing was performed using a Rolimeter. Measured side-to-side differences are reported in mm.*
[c] *IKDC; International Knee Documentation Committee Score.*
[d] *Pre-rupture data were collected via questionnaires during pre-operative consultation.*

Mean scores (SD) of IKDC, Lysholm and VAS satisfaction at different time points during follow-up are reported in Table 4.2 together with the mean (SD) Lachman side-to-side difference in millimeters and median Tegner (range). The Lachman side-to-side difference remained < 3 mm post-operatively for all patients and no clinical failure was observed, except for those suffering from re-rupture. A linear mixed model with time as fixed effect showed significant effects over time for all these measurements ($P < 0.001$), except for VAS satisfaction (n.s.) which can be expected since there are no pre-operative data available about patient satisfaction. Comparing the two-sided 95% CI for the difference between IKDC score at 24 months post-operatively and pre-rupture [15.1, -4.7] to a non-inferiority margin of 10 IKDC points, showed no non-inferiority after 24 months compared to the pre-rupture level. When correcting the linear mixed model for age and gender we found a significant effect of these variables on the reported Tegner scores ($P = 0.012$ and $P = 0.041$, respectively). On average there is a decrease in Tegner score of 1 point per 10 years (95% CI [-1, -0.2]) and on average this score is 1 point (95% CI [-2, -0.04]) lower for women compared to men (time estimates were similar in the unadjusted and adjusted models). (Supplementary table 4.1)

The proportions of patients who returned to their pre-rupture level for IKDC, Lysholm and Tegner scores at different time points during follow-up are reported in Table 4.3. The median times to return to the pre-rupture level were 24 months (95% CI [17.8, 30.2]), 6 months (95% CI [3.2, 8.8]) and 12 months (95% CI [5.6, 18.4]) for the IKDC, Lysholm and Tegner score, respectively. The median RTW period was 5.5 weeks (95% CI [4.4, 6.6]), ranging from 0 to 32 weeks, and is represented in Figure 4.3. The median RTS period was 6 months (95% CI [4.6, 7.4]), ranging from 2 to 22 months, and is represented in Figure 4.4.

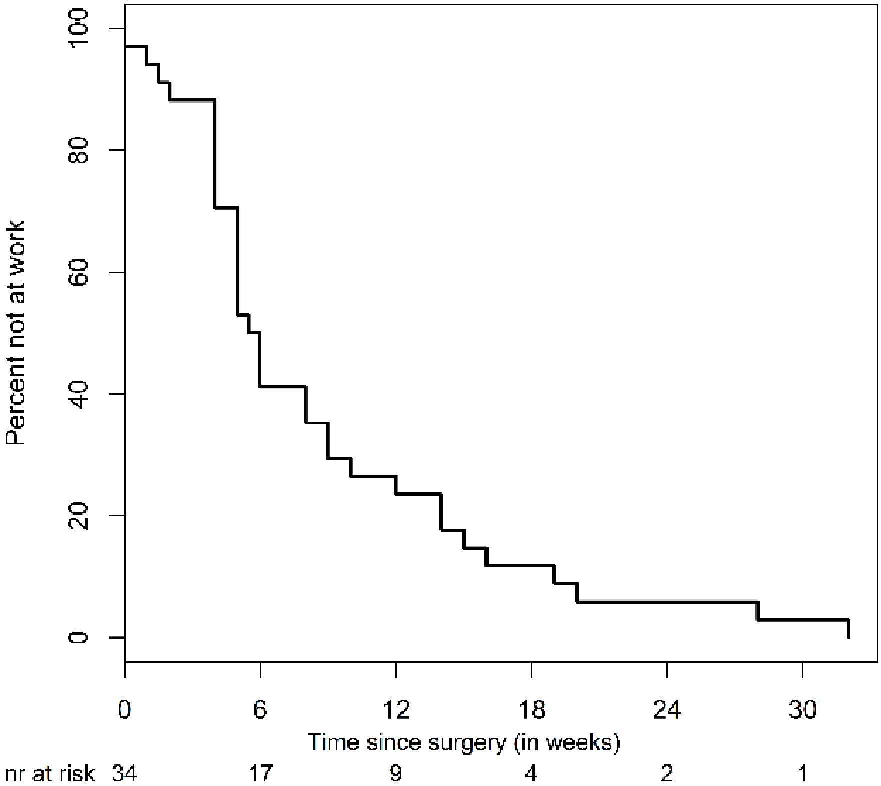

Figure 4.3 Kaplan-Meier curve of the time to event with the return to work as event and time of surgery as time 0. Number (nr) at risk below the figure is the number of patients not at work at the given time points.

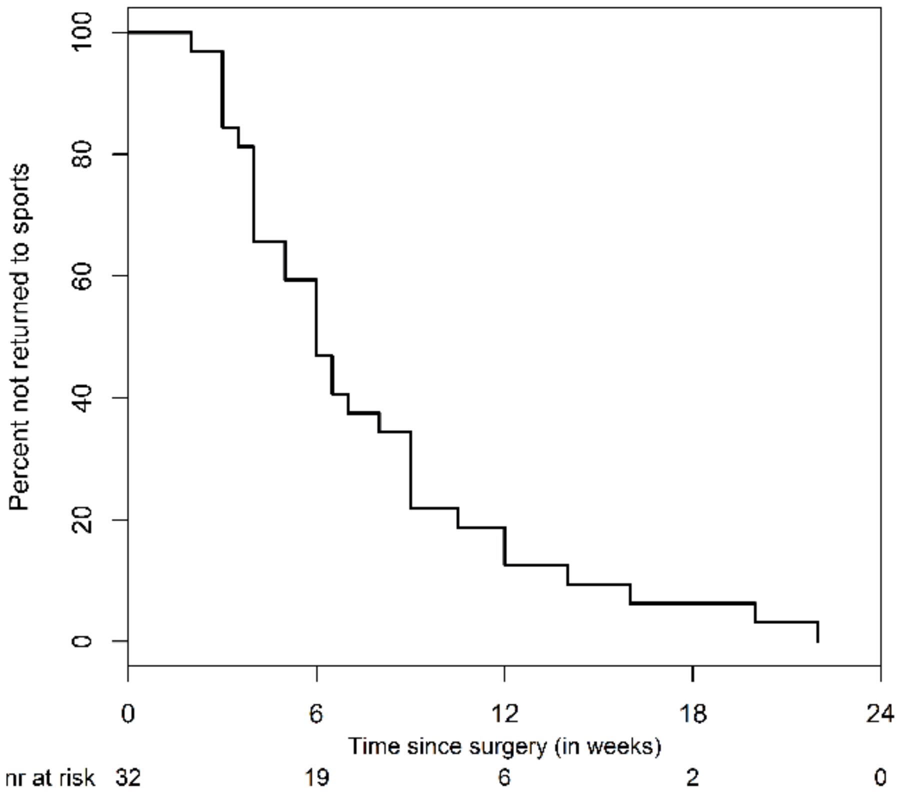

Figure 4.4 Kaplan-Meier curve of the time to event with the return to sports as event and time of surgery as time 0. Number (nr) at risk below the figure is the number of patients not returned to sports at the given time points.

Outcome	6 months	12 months	24 months
IKDC [a]	6/ 31 (19.4%)	11/25 (44.0%)	17/26 (65.4%)
Lysholm	13/27 (48.1%)	13/26 (50.0%)	13/25 (52.0%)
Tegner	11/32 (34.4%)	11/27 (40.7%)	18/27 (66.7%)

Table 4.3 Proportion of Patients Who Returned to Their Pre-rupture Level at Different Time Points During Follow-up

[a] IKDC; International Knee Documentation Committee Score.

4.4.3 MRI, re-intervention and re-rupture

The proportion of patients for the different grades of ACL healing per time point are presented in Table 4.4. Cross tabulation of the ACL healing grades showed that ACL healing grade did not change between one and two years of follow-up for the 20 patients who fully completed their MRI follow-up.

	6 months	12 months	24 months	Overall
Patients	35	28	23	31
Grade 1	0 (0.0%)	11 (39.3%)	13 (56.5%)	14 (45.2%)
Grade 2	30 (85.7%)	11 (39.3%)	7 (30.4%)	11 (35.5%)
Grade 3	5 (14.3%)	6 (21.4%)	3 (13.0%)	6 (19.4%)

Table 4.4 Number of Patients with Different Grades of ACL Healing on MRI at Different Time Points During Follow-up [a]

[a] Data are reported as number (percentage)

Three (8.6%) patients had a re-surgery. One patient was treated for a medial meniscus rupture in combination with arthrofibrosis. The second patient suffered from arthrofibrosis and a cyclops lesion. The third patient was treated for an extension deficit that was caused by an overly tight FiberTape® (Arthrex, Inc., Naples, FL). These problems were solved after re-surgery.

Four other patients (11.4%) suffered from re-rupture. One patient had a motorcycle accident 7 months post-operatively which resulted in an ACL re-rupture. Two patients experienced the re-rupture while playing soccer at 9 and 13 months post-operatively and one patient while dancing 22 months post-operatively. These patients were subsequently treated with an ACL reconstruction and further excluded from analysis of study results. Significance between type of rupture (proximal or mid-bundle), age, pre-operative Tegner score, and grade of ACL healing on MRI six months post-operatively and re-rupture are reported in Table 4.5.

	No Re-rupture	Re-rupture	% Re-rupture Within Group	P Value Fisher's Exact Test
Proximal rupture	26	3	10.3	0.546
Mid-bundle rupture	5	1	16.7	
Grade 1 healing	0	0	0.0	0.006 [a]
Grade 2 healing	29	1	3.3	
Grade 3 healing	2	3	60.0	
Age < 25	7	3	30.0	0.061
Age ≥ 25	24	1	4.0	
Tegner pre-op < 7	19	0	0.0	0.035 [a]
Tegner pre-op ≥ 7	12	4	25.0	

Table 4.5 Association Between Type of Rupture, ACL Healing on MRI 6 Months Post-operatively, Age, Pre- operative Tegner Score and Occurrence of Re-rupture

[a] $P < 0.05$.

4.5 Discussion

The most important findings of this study are that treatment with the STA ACL repair technique leads to a stable knee and favorable PROMs. However, four (11.4%) patients of our study cohort experienced a re-rupture within the 2-year follow-up. Analysis of risk factors for re-rupture showed that patients with a pre-operative Tegner score of ≥ 7 and with grade 3 ACL healing on MRI 6 months post-operatively have a higher chance of re-rupture.

Longitudinal MRI follow-up shows healing of the ACL between 6 and 12 months. The healing status remained unchanged between 12 and 24 months post-operatively in our study, suggesting that the repaired ACL does not further heal after one year post-operatively. Similar findings have been described in a study after ACL repair with DIS [23]. However, in a non-longitudinal MRI study, van der List et al. describe different results after ACL repair with a hyper-intense repaired ligament within one year, and a signal similar to that of the intact PCL only after two years [24]. Van Dyck et al. performed a diffusion tensor imaging (DTI) MRI study on 14 patients treated with the STA technique. DTI results are different from conventional MRI, as DTI provides information about tissue microstructure and its degree of organization by quantifying water diffusion. Their findings suggest that healing of the ACL is incomplete at 24 months post-operatively [25]. We observed overall poor ACL healing on MRI in six (19.4%) of our study patients during the 2-year follow-up. Mid- to long-term MRI follow-up could contribute in determining the ACL repair healing time and potential clinical consequences.

In addition, we observed a significant association between grade 3 ACL healing at six months post-operatively on MRI and re-rupture ($P = 0.006$). Post-operative MRI grading as a possible predictor for re-rupture after ACL repair has not been described before and needs to be further investigated.

Only two other STA ACL repair case series on adults, from the developer of the STA technique, have been published. They reported re-rupture rates of 1.5% and 4.5% [4, 10]. The re-rupture rate of 11.4% in this case series is rather high. The learning curve that comes with new techniques could be a possible explanation for this re-rupture rate. Also, patient selection could have influenced the re-rupture rate as patients with proximal and mid-bundle ruptures were included while recent literature on other ACL repair techniques states that mid-substance ruptures are less suitable for repair and have a higher complication rate [26-29]. Achtnich et al. and Jonkergouw et al. found similar results regarding failure after ACL repair using suture anchors with failure rates of 15% and 10.7%, respectively [12, 30]. Ahmad et al. conclude that there is evidence for the potential space of ACL repair in the decision tree for individualized treatment, and the best outcome will be in hands of the best patient selectors [31].

A quick rehabilitation was observed in this case series with a median RTW of 5.5 weeks (range 0 to 32 weeks) and median RTS of 6 months (range 2 to 22 months). Patients were only allowed to return to their pivoting sports if the knee had a full range of motion, no effusion, upper leg muscular circumference > 90% and a single leg hop test > 90% [10]. Groot et al. describe a general RTW of 11 weeks after ACL reconstruction [32]. Lai et al. report that most high-level sport athletes RTS between 6 and 13 months after ACL reconstruction, which is less time than reported for non-high-level sport athletes [33]. The healing phases of the repaired ACL differs from the ACL reconstruction ligamentization phases and therefore the rehabilitation period could be different as well [19]. The quick rehabilitation in our study could be explained by the less-invasive STA technique and the preservation of the native ACL with its proprioceptors. ACL reconstruction does not preserve the native ligament with its proprioceptors which could lead to overloading of the ACL graft or loss of confidence in the knee [4, 13, 34, 35]. Kiapour et al. state that preservation of the native ACL with its proprioceptors may lead to more normal joint mechanics and a decreased risk for post-traumatic osteoarthritis [13].

The proportion of study patients who returned to their pre-rupture level for IKDC, Lysholm and Tegner score increased over time to 65.4%, 52.0% and 66.7%, respectively, but it needs to be noted that some patients who reached their pre-rupture level within one year lost this level again at two years. This is also observed after ACL reconstruction [21]. Ardern et al. report that less than 50% of patients RTS at their pre-rupture level after ACL reconstruction [34]. Ohsawa et al. on the other hand report that 64.6% of patients return to their pre-rupture level of Tegner score after ACL reconstruction, which is similar to the proportion observed in this study [36].

Risk factors for a re-rupture with the STA technique have not previously been described for adults. For DIS repair, young age and a high level of sport activity have been found to influence the risk of failure [8, 31, 37-39]. This case series with four patients who experienced a re-rupture, suggests a higher risk on re-rupture for patients with a pre-operative Tegner ≥ 7 ($P = 0.035$) and for patients with grade 3 ACL healing on MRI at 6 months post-operatively ($P = 0.006$). A trend towards significance ($P = 0.061$) for the effect of young age, below 25 years, for a re-rupture was observed. As patient selection is emphasized for ACL repair further investigation is needed [31].

The re-surgery rate of 20% in this STA ACL repair cohort study is similar to the resurgery rate reported in other studies. Rousseau et al. observed a surgical re-surgery rate of 28% in their cohort of 958 ACL reconstruction patients [40]. Two randomized controlled trials comparing ACL DIS repair versus ACL reconstruction, report an overall re-surgery rate of 25.6% and 29.5% in the ACL DIS repair groups versus 22.5% and 33.3% in the ACL reconstruction groups [21, 38].

This study has several limitations. First, the sample size is relatively small, as the goal of this study was to recruit all possible patients during a 2-year period and explore the findings. We realize that a sample of 35 patients is not adequate to prove non-inferiority of 24 months to pre-rupture or the estimate percentage returned to pre-rupture level in a very precise way due to lack of power. Also the results on the effect of patient characteristics on the clinical outcomes or the analysis of the risk factors for re-ruptures are only explorative in this relative small sample and need further investigation. However results in this study can serve as a pilot to guide future sample size calculations. Secondly, as this study is a case series, no direct comparison can be made between the STA technique and reconstruction surgery or other repair techniques. Hence, high-quality large randomized clinical trials with longer follow-up comparing ACL repair techniques and ACL reconstruction are needed [41, 42]. Third, patients were recruited at one center, which could bias the representativeness of our study population. Fourth, a learning curve could have influenced the results as patients included in this case series are the first patients who have been treated with the STA technique by two surgeons.

To the best of our knowledge, this is the first case series which presents independent prospective clinical results, longitudinal MRI follow-up and risk factors for re-rupture on STA ACL repair. Patients with Tegner ≥ 7 have a higher chance on re-rupture. A strict patient selection could contribute in decreasing the re-rupture rate. Further studies with a long-term follow-up will have to show if modern ACL repair can be a “game changer” or if history will repeat itself [1].

4.6 Conclusion

This study shows that treatment of the acute, repairable ACL with the STA technique leads to a stable knee and favorable PROMs. However, the re-rupture rate of 11.4% within the 2-year follow-up is a concern.

	Comparison	Estimate	Lower	Upper	Raw P Value	Corrected P Value
Lachman						
	6m-Pre-op	-3.0	-3.5	-2.4	< 0.001[b]	< 0.001[b]
	12m-Pre-op	-2.9	-3.5	-2.3	< 0.001[b]	< 0.001[b]
	24m-Pre-op	-2.7	-3.4	-2.1	< 0.001[b]	< 0.001[b]
	12m - 6m	0.03	-0.6	0.7	(n.s.)	(n.s.)
	24m - 12m	0.2	-0.5	0.9	(n.s.)	(n.s.)
IKDC[a]						
	6m-Pre-rupture	-20.6	-25.5	-15.7	< 0.001[b]	< 0.001[b]
	12m-Pre-rupture	-12.6	-17.9	-7.3	< 0.001[b]	< 0.001[b]
	24m-Pre-rupture	-9.9	-15.1	-4.7	< 0.001[b]	0.001[b]
	12m - 6m	8.0	2.6	13.4	0.004[b]	0.008[b]
	24m - 12m	2.6	-2.9	8.2	(n.s.)	(n.s.)
Lysholm						
	6m-Pre-rupture	-9	-14.6	-3.7	0.001[b]	0.007[b]
	12m-Pre-rupture	-7	-12.5	-1.4	0.014[b]	(n.s.)
	24m-Pre-rupture	-7	-12.5	-1.3	0.016[b]	(n.s.)
	12m - 6m	2	-3.5	7.9	(n.s.)	(n.s.)
	24m - 12m	0.1	-5.8	5.9	(n.s.)	(n.s.)
Tegner						
	6m-Pre-rupture	-1	-1.9	-0.7	< 0.001[b]	< 0.001[b]
	12m-Pre-rupture	-1	-1.7	-0.4	0.002[b]	0.010[b]
	24m-Pre-rupture	-0.3	-1.0	0.3	(n.s.)	(n.s.)
	12m - 6m	0.3	-0.4	1.0	(n.s.)	(n.s.)
	24m - 12m	0.7	0.0	1.4	0.045[b]	(n.s.)

Supplementary table 4.1 Post-hoc Comparisons of the Different Time Points Using the Linear Mixed Model

[a] IKDC; International Knee Documentation Committee Score.

[b] $P < 0.05$.

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Chapter 5 Tips and Tricks to Optimize Surgical Outcomes After ACL Repair Using Dynamic Intraligamentary Stabilization

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5.1 Abstract

Purpose This paper describes technical difficulties and outcomes for the first 15 patients treated with Dynamic Intraligamentary Stabilization (DIS) for anterior cruciate ligament (ACL) repair.

Methods The first 15 patients treated with DIS were included. To optimize the inclusion process, a new pre-operative pathway was developed. All intra-operative technical problems were recorded. During the 2-year follow-up period, patient-reported outcome measures (PROMs), return to work (RTW), anterior-posterior (AP) knee laxity using a Rolimeter and ACL healing as revealed by MRI follow-up scans were recorded.

Results During 11 DIS procedures, 15 technical problems were encountered. Six were surgeon-related and 9 were material-related. All problems were resolved intra-operatively. Re-surgery was performed in 4 patients due to arthrofibrosis and in 1 due to a cyclops lesion. The DIS implant was removed in all 5 patients. According to the Tegner score, 7 of 10 (70%) patients returned to the pre-injury level of sporting activity within 6 months. The mean return to work time was 5.4 (standard deviation; SD 3.6) weeks. On MRI, 10 patients showed normal ACL healing (Grade 1) and 3 showed a high repair signal intensity (Grade 2). Although 2 patients showed no signs of ACL healing on MRI (Grade 3), no instability was reported or measured post-operatively or after the DIS implant was removed.

Conclusion All intra-operative technical problems were resolved and did not lead to conversion to ACL reconstruction. We share tips and tricks that could assist surgeons who are just starting to use the DIS technique.

5.2 Introduction

Anterior cruciate ligament (ACL) rupture is a common injury in active adolescents and young adults. ACL insufficiency can lead to symptomatic instability, secondary meniscal pathologies and degenerative changes [1].

Surgical treatment with arthroscopic reconstruction of the injured ACL is the gold standard. The overall rate of return to the pre-injury level of sporting activity at 2 years after ACL reconstruction is 63-65%. Although this technique provides satisfactory functional results according to the International Knee Documentation Committee (IKDC) and Lysholm scores, and stability with high levels of patient satisfaction, medium- and long-term results are associated with an increased risk of osteoarthritis and a graft failure risk of 10.3% [1].

Several studies support the hypothesis that the ruptured ACL possesses capacity for biological healing [2-4]. The healing response of ligamentous tissue after injury is well documented in other human ligaments [5, 6]. Several factors compromise the self-healing capacity of the ruptured ligament, such as a hostile synovial fluid environment, lack of blood supply and post-injury instability due to separation of the ligament stumps [2, 7-10].

The Dynamic Intraligamentary Stabilization (DIS) technique was developed for the treatment of acute ACL ruptures. The DIS device combines an internal dynamic spring-screw mechanism with a 1.8 mm braided polyethylene anchoring suture to provide continuous stability of the ACL during the self-healing period. [11] Henle et al. reported a case series of 278 patients treated with DIS; 8 patients experienced ACL re-rupture and 3 had insufficient subjective stability of the knee [12]. They concluded that anatomical repositioning, along with DIS and microfracturing, leads to clinically stable healing of the ruptured ACL in a large majority of patients. Most patients exhibited almost normal knee function, reported excellent satisfaction, and were able to return to their previous levels of sporting activity.

Post-operative MRI can be used to assess ACL healing. De Smet et al. and van der List et al. described the use of post-operative MRIs after ACL repair, but there have been no reports of longitudinal MRI follow-up after DIS [13, 14].

Orthopedic surgeons are familiar with the concept of a learning curve when a new surgical procedure is introduced. When a new surgical technique is introduced in a structured manner, such as by following training courses and performing the surgery on cadavers with the assistance of expert practitioners, this learning curve can be reduced [15]. To date, no previous study has presented tips and tricks for the DIS technique to help reduce the learning curve.

The objective of this paper is to present our technical difficulties and outcomes to help reduce the learning curve and assist surgeons who are starting to use the DIS ACL-preserving technique.

5.3 Materials and methods

5.3.1 Study design

Over a 2-year period, the first 15 patients treated with DIS were included. To optimize the inclusion process, a new pre-operative pathway was developed. All intra-operative technical problems were recorded. During 2 years of follow-up, patient-reported outcome measures (PROMs), return to work (RTW), anterior-posterior (AP) knee laxity using a Rolimeter and ACL healing on follow-up MRI scans were recorded.

A limit of 3 weeks (21 days) after the rupture has been proposed for carrying out ACL DIS repair [12]. This changes ACL management from a chronic to a (sub)acute problem. A new pathway for patients with a suspected acute ACL rupture had to be developed to enable diagnostic work-up and treatment to take place within 3 weeks after ACL injury. To create awareness of urgent referral, information and lectures were given to the emergency department, general practitioners, physiotherapists and sports physicians. At the appointment desk, a consultation within 2 days was arranged if there was a suspicion of an acute ACL rupture. Cooperation with the radiology department was essential: 1 MRI slot per week was reserved for suspected acute ACL rupture.

Inclusion criteria included an ACL rupture less than 3 weeks old, confirmed on MRI. The study participants had to be between 18 and 60 years old. Exclusion criteria were as follows: posterior cruciate ligament (PCL) injury, lateral collateral ligament (LCL) or grade 2-3 posterolateral corner injury, a fracture that could influence rehabilitation and a non-repairable ACL rupture (intra-operative confirmation). For this study a repairable ACL was defined as a proximal or mid-substance rupture (according to a 3-digit ACL rupture classification; Figure 5.1 [12]) with good tissue quality and with no gap between the proximal and distal stump after the repair, all confirmed intra-operatively. Before inclusion in the trial, written informed consent was obtained from each study participant, in accordance with ICH-GCP guidelines. The study was approved by the Ethics Committee of Antwerp University Hospital (B300201525523).

The pre-, intra- and post-operative problems encountered were recorded. Pre-injury and post-operative PROMs (Tegner, Lysholm and IKDC scores) were recorded [16, 17]. Patient satisfaction using a visual analogue scale (VAS) and return to work and sporting activity were also recorded. Anterior-posterior (AP) knee laxity in 30° flexion (Lachman test) was measured using a Rolimeter [18]. Patients were assessed at 3, 6, 12 and 24 months post-operatively.

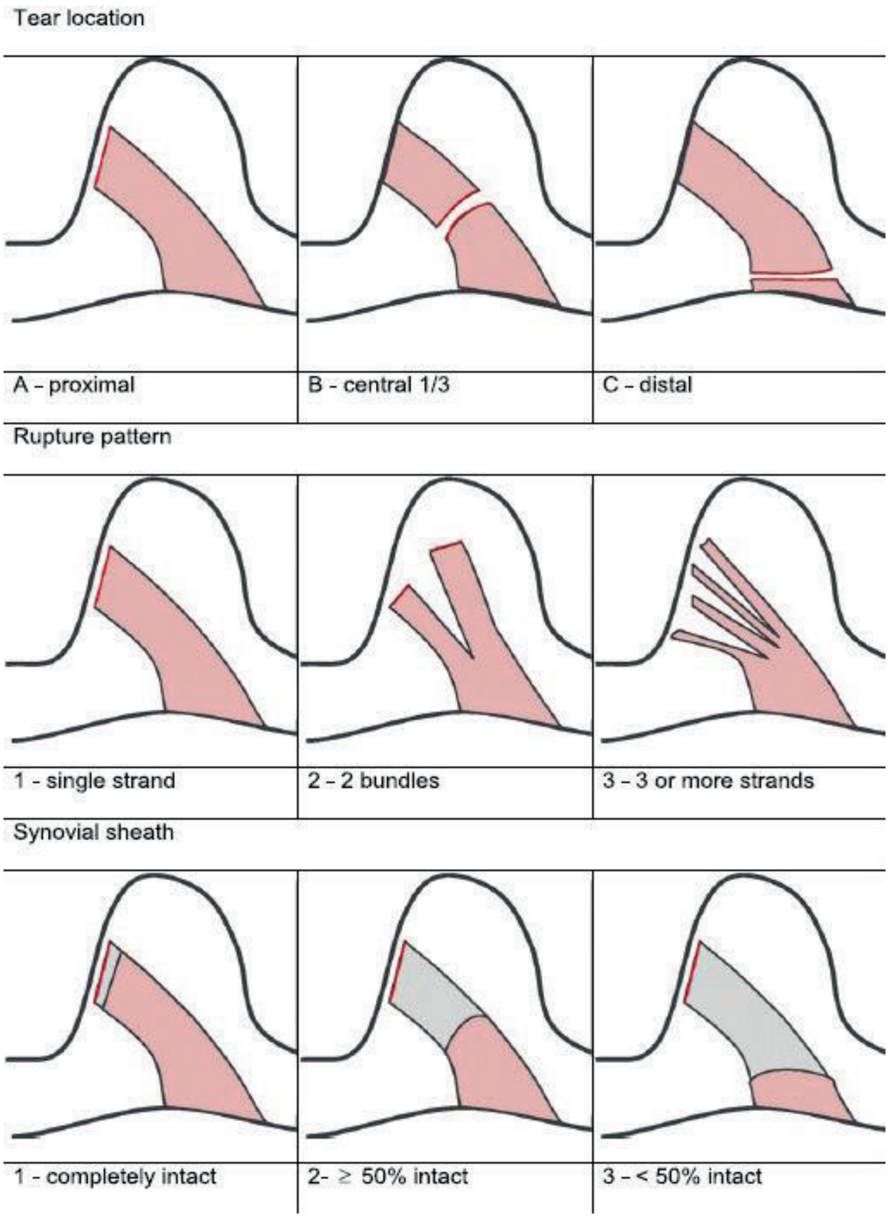

Figure 5.1 Three-digit ACL rupture classification. Anterior intercondylar view of the right knee. The ACL is drawn in pink, the upper curved black line represents the femur and lower curved line represents the tibia. The first digit describes the ACL rupture location: 'A' for proximal third, 'B' for central third and 'C' for distal third. The second digit is the ACL rupture status: '1' for 1 bundle, '2' for 2 bundles and '3' for multilacerated. The third digit describes the ACL synovial tube: '1' for completely intact, '2' for ≥50% intact and '3' for < 50% intact [12]

All patients were invited to undergo MRI follow-up scans at 3, 6, 12 and 24 months post-operatively. Imaging was performed with a 1.5-T MRI system (Magnetom Aera Tim, Siemens Healthcare, Munich, Germany). Slice encoding for metal artifact reduction (SEMAC) was used to reduce image distortion resulting from the tibial implant [19]. The MRI protocol included the following sequences: sagittal PD-weighted TSE with SEMAC; axial, sagittal, and coronal STIR SEMAC; and coronal T1-weighted TSE sequence with SEMAC. Conventional 1.5- or 3-T MRI was performed if the DIS device had been removed. The MRI scans were assessed by consensus between a radiologist (PVD, with 20 years of experience in musculoskeletal radiology) and an orthopedic surgeon (CH, with 10 years of experience in knee surgery). All images were interpreted with the reviewers blinded to the patient's clinical information. The morphology (position, straight band, and size) and repair signal intensity were assessed on MRI and the ACL repair was graded as follows: [20] Grade 1, well-defined, straight, continuous, normal-sized ACL with signal intensity similar to or only slightly higher than that of the PCL; Grade 2, normal-sized (or slightly thickened) continuous, straight ACL showing a high signal compared to that of the PCL; and Grade 3, an ill-defined, irregular ACL that is thinned or not discernible.

5.3.2 Surgical technique

The following steps were undertaken to reduce the steepness of the learning curve:

- The orthopedic surgeons (CH and LD) followed a training course organized by the manufacturer of the DIS implant (Mathys Ltd Bettlach, Bettlach, Switzerland)
- The first operation was assisted by an orthopedic surgeon who was experienced with the DIS technique.
- For subsequent operations, the surgeons (CH and LD) assisted each other.

A standard anterolateral portal and a slightly larger anteromedial portal were created, followed by a comprehensive examination of the knee joint. Concomitant injuries were treated and the morphology of the ACL rupture was evaluated. The ACL rupture type was classified by rupture localization, rupture pattern and synovial sheet evaluation (Figure 5.1) [12]. The surgical technique for DIS was described by Eggli et al. [21] Briefly, the tibial stump of the ACL is positioned against the femoral stump using transosseous PDS 2-0 sutures, thereby restoring the anatomical position of the ACL. Intra-operatively, a knot-pusher through the PDS retaining sutures can be used to check if the distal stump is fully reduced to the proximal stump. If the ACL is not repairable, the operation can be converted to reconstruction during the same procedure. In addition to the technique described by Eggli et al., we used lasso sutures (FiberLinkTM, Arthrex®, Naples, FL) on a suture-passer (Scorpion, Arthrex®) [22] to reduce the ACL stump in case of a multiple or mid-bundle rupture. A maximum of 3 lasso sutures fit in the femoral tunnel. At the femoral footprint, microfracturing was carried out. A tibial tunnel was drilled, exiting posterolateral to the tibial footprint to prevent damage to the ACL's blood and nerve supply.

The spring-screw implant (Ligamys®, Mathys Ltd Bettlach, Bettlach, Switzerland) was placed in the tibial tunnel. The femoral tunnel was drilled at the origin of the ACL. The ACL was reinforced with a strong polyethylene cord which was fixed on the femoral side with a button. With the knee in extension, the reinforcement cord was fixed on the tibial side in the spring-screw implant with a force of 50-80 N, depending on the sex of the patient.

Post-operative treatment consisted of a schematic training plan with a physiotherapist, following the Ligamys® protocol [23].

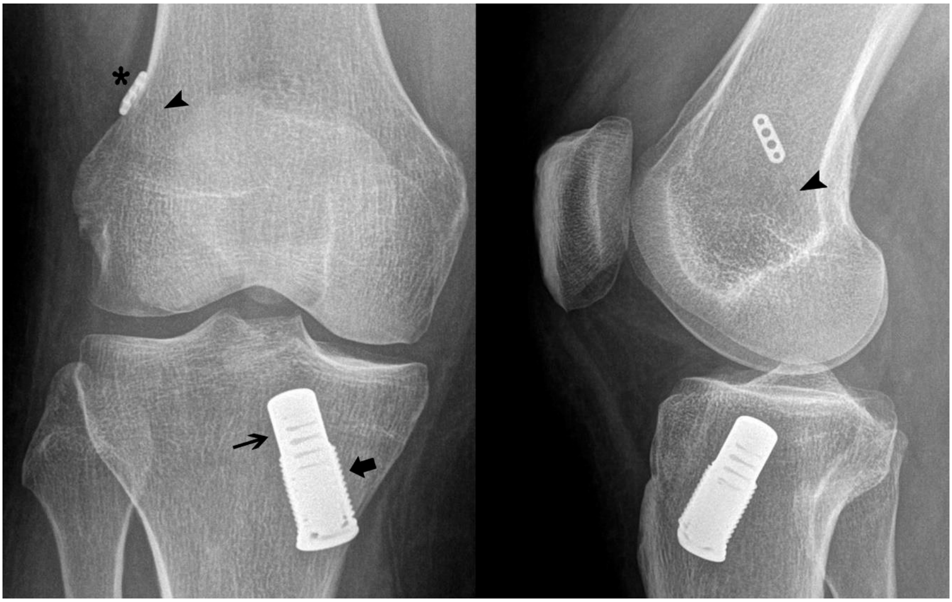

Figure 5.2 Radiographic findings of the right knee after Dynamic Intraligamentary Stabilization. The tibial implant consists of a spring (thin arrow) and screw (thick arrow)-mechanism. Note small femoral bone tunnel (arrowhead) and proximal fixation with a femoral button (asterisk).

5.4 Results

5.4.1 Demographics of the study population

Two surgeons (CH and LD) performed the DIS operation in 15 patients between October 7, 2014, and September 21, 2016. The male-to-female ratio was 6:9. The mean (SD) age was 32.8 (9) years. The right-to-left knee ratio was 6:9. The mean (SD) injury-to-surgery interval was 17 (2) days. Eight patients showed additional lesions of the injured knee. Eight patients had medial collateral ligament (MCL) lesions, and 3 of them were treated with InternalBrace™ (Arthrex) [24]. One patient had a type 1 strain of the LCL which was treated conservatively. In 2 patients, the lateral meniscus was sutured and in 1 patient the medial meniscus was partially resected. In 11 of the 15 patients, no additional procedures were performed.

5.4.2 Rupture classification

Seven patients (46.7%) had an A.1.1 rupture (proximal third, single strand, completely intact synovial sheath), 1 (6.7%) had an A.1.3 rupture (proximal third, single strand, <50% intact synovial sheath), 4 (26.7%) had an A.2.1 rupture (proximal third, 2 bundles, completely intact synovial sheath), 1 (6.7%) had an A.3.1 rupture (proximal third, 3 or more strands, completely intact synovial sheath) and 2 (13.3%) had a B.3.1 rupture (central third, 3 or more strands, completely intact synovial sheath) (Figure 5.1) [25]. Lasso sutures were used for the B.3.1. ruptures and for an A.2.1. rupture, after the PDS sutures broke out.

5.4.3 Post-operative data

Clinical scores (Tegner, Lysholm and IKDC scores), the AP difference between healthy and injured knees, and patient satisfaction (VAS) were recorded. Patients were asked what the score was before injury and after 3, 6, 12 and 24 months (Table 5.1). With the Tegner score as a guide, 7 of 10 patients (70%) returned to the pre-injury level of sporting activity after 6 months, 10 of 13 patients (76.9%) after 1 year and 11 of 14 (78.6%) after 2 years. The mean (SD) return to work time was 5.4 weeks (3.6).

Outcome measure	Pre-injury	Pre-operative	3 months	6 months	12 months	24 months
Tegner score	4.9 (2.7)		3.1 (2.1)	5.4 (2.6)	4.9 (2.6)	5.1 (2.5)
Lysholm score	96.3 (11.6)		66 (21.8)	88.7 (7.4)	94.1 (7.5)	96.1 (5.0)
IKDC score	99.0 (1.8)		0.2 (2.0)	79.4 (15.7)	88.4 (9.7)	93.9 (4.4)
Lachman difference (mm)		4 (2.4)	0.2 (2.0)	0.7 (1.4)	0 (1.5)	0.4 (1.7)
Satisfaction (VAS)			8.4 (1.6)	8.4 (1.4)	9.2 (0.47)	9.3 (0.8)

Table 5.1 Clinical scores, Lachman anterior-posterior difference (mm) between the DIS repair and the contralateral knee, and patient satisfaction. Values represent means (standard deviation). DIS, Dynamic Intraligamentary Stabilization; IKDC, International Knee Documentation Committee; VAS, Visual Analogue Scale

5.4.4 Problems encountered intra-operatively

During 11 DIS procedures, 15 technical problems were encountered. Six were surgeon-related and 9 were material-related. All problems were solved intra-operatively.

During 5 procedures, we experienced a malfunction of the suturing forceps and were not able to pass the resorbable PDS 2-0 sutures through the ACL stump. These problems were not encountered with second-generation suturing forceps.

In 2 procedures, the shuttle suture broke while the polyethylene cord was being passed through the femoral tunnel. The broken shuttle suture was replaced with a stronger shuttle suture.

During 1 procedure, the spring-screw implant fell apart while the guide suture was being retrieved. A new implant was placed, but this also fell apart. We put the spring back in the second implant and it did not fall apart again. The manufacturer of the implant addressed this problem as a production error. We did not encounter this problem subsequently.

Leading the polyethylene cord distally caused problems during 2 procedures at the ACL stump site. The polyethylene cord became entangled with the ACL stump or the PDS 2-0 sutures. A new shuttle suture was tied to 1 of the shuttle suture ends distally and passed proximally through the femoral tunnel, after which the polyethylene cord was transported distally with no problems.

During 1 of the procedures, the clamping cone broke off while it was being secured to the spring-screw implant. Afterwards, we noticed that we had not placed the clamping cone in-line with the spring-screw implant. It is important to place the clamping cone exactly in-line with the spring-screw implant.

We also would like to emphasize the importance of maintaining adequate tension on the PDS retaining sutures while the polyethylene cord is passed through the femoral tunnel and fixated. After the procedure was finished, the final arthroscopic check showed an attenuated ACL; the PDS sutures were not properly tensioned and therefore the ACL stump was not tight to its origin. We had to loosen the clamping cone and the femoral button with the polyethylene cord to be able to tension the retaining sutures adequately. With this maneuver, we achieved adequate tension on the ACL. During re-fixation with the clamping cone, the polyethylene cord broke. While a new polyethylene cord was being transported through the femoral tunnel, the PDS sutures in the ACL stump broke out. When we replaced the PDS retaining sutures in the ACL stump, the sutures did not have enough grip to reduce the stump. Through the use of lasso sutures, we managed to reduce the ACL stump to its origin at the correct tension.

To prevent interposing tissue or tissue bridges from the medial arthroscopic portal between the different sutures, we make a larger medial arthroscopic portal, place the suturing forceps around the threads outside the portal, and pass it through the portal intra-articularly. No interposing tissue should be encountered (Figure 5.3). Tips and tricks are summarized in Table 5.2.

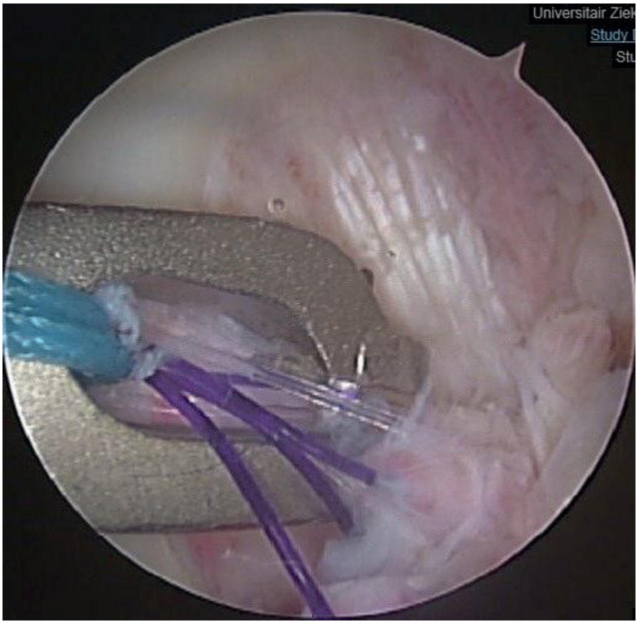

Figure 5.3 Suture management during anterior cruciate ligament repair using dynamic intraligamentary stabilization. Arthroscopical intercondylar view from the lateral portal of the left knee. Suture management with the sutures through the suturing forceps from the medial portal: no interposing tissue between the different sutures

Tips and tricks	
Pre-operative	Develop a pre-operative patient pathway to enable a diagnostic work-up and treatment within three weeks after the ACL injury.
ACL stump	Using a knot-pusher through the PDS retaining sutures, check whether the distal stump is fully reduced to the proximal stump (Figure 5.4). If the ACL stump cannot be properly reduced using the PDS 2.0 sutures, or if it is a multilacerated rupture, lasso sutures can be used.
Suture management	Make a larger medial arthroscopic portal and check with the suturing forceps around the threads through the medial portal for interposing tissue or tissue bridges (Figure 5.3).
Shuttle sutures	Use strong shuttle sutures to prevent breakage of the shuttle suture in the femoral tunnel.
Implant tension	Do not exceed 60 N tension on the spring-screw implant for women; we aim for 50 N in slender or smaller women.
MRI	Absence of healing on MRI should be interpreted with caution, and correlation with clinical findings is necessary.

Table 5.2 Tips and tricks for surgeons who are starting with DIS. ACL, anterior cruciate ligament; PDS, polydioxanone suture

5.4.5 Problems encountered post-operatively

Post-operatively, 4 (26.7%) patients developed a jumper's knee within the first 3 months during rehabilitation. Adaptation of physiotherapy and anti-inflammatory drugs resolved these problems, and a normal rehabilitation program could be resumed thereafter.

Four patients (26.7%) developed arthrofibrosis, confirmed on MRI. They underwent arthrofibrolysis and DIS removal at, respectively, 2, 4, 6 and 8 months post-operatively. All 4 patients were women, and 2 of these 4 patients were slender. They both felt immediate relief after arthrofibrolysis and removal of the DIS, and stated that they had regained their "natural knee movement", which they had lost since the primary DIS procedure.

One patient (6.7%) developed a cyclops lesion. Arthroscopy showed an intact ACL and the cyclops lesion, which was removed.

In all 5 patients who had a re-surgery, the DIS implant was removed as well. AP knee laxity did not increase after the implant was removed.

There were no ACL re-ruptures after a 2-year follow-up. No patients reported instability post-operatively, including the patients who underwent removal of the DIS implant.

5.4.6 MRI

A total of 47 MRI studies for the 15 patients were available for review (3 months, n=8; 6 months, n=12; 12 months, n=13; and 24 months, n=14). Thirty-eight MRI examinations were performed using the SEMAC MRI protocol at 1.5-T and 8 examinations were performed using a conventional protocol at 3-T if the spring-screw implant had been removed.

At 24 months post-operatively, 9 patients showed normal ACL healing (Grade 1) and 3 showed persistent high repair signal intensity (Grade 2) on MRI. Two patients showed no signs of ACL healing on MRI (Grade 3). One patient refused to undergo MRI follow-up at 24 months, but demonstrated a healed ACL repair at 12 months. Based on the MRI findings, remodeling of the ACL repair was most evident between 6 and 12 months post-operatively. The healing status remained unchanged between 12 and 24 months post-operatively, except for 1 patient. Findings are summarized in Table 5.3.

Patient No.	ACL rupture type	Post-operative ACL healing on MRI			
	Intra-operative	3 months	6 months	12 months	24 months
1	A.1.1.	3	3	3	3
2	A.1.3.		2	2	2
3	A.1.1.		2	1	1
4	A.1.1.	2		1	1
5	A.3.1.	2		2	2
6	A.1.1.	3	2	1	1
7	A.2.1.			3	3
8	A.1.1.		2	1	1
9	A.2.1.		2	1	1
10	B.3.1.	3	2	2	1
11	A.2.1.		2		2
12	A.1.1.	2	2	1	1
13	B.3.1.	2	2	1	
14	A.1.1.				1
15	A.1.1.	2	1	1	1

Table 5.3 Intra-operative ACL rupture type [12] and post-operative ACL healing on MRI was graded as follows: [20] Grade 1, well-defined, straight, continuous, normal-sized ACL with signal intensity similar to or only slightly higher than that of the PCL; Grade 2, normal-sized (or slightly thickened) continuous, straight ACL showing a high signal compared to that of the PCL; and Grade 3, an ill-defined, irregular ACL that is thinned or not discernible. ACL, anterior cruciate ligament; PCL, posterior cruciate ligament

5.5 Discussion

We present the technical difficulties and outcomes for the first 15 patients treated with DIS with follow-up over 2 years, as well as tips and tricks to optimize the surgical outcomes of ACL repair using the DIS technique.

Starting a new technique involves “start-up problems”. Organizing a new patient pathway, dealing with “new” arthroscopic instruments and suture management, post-operative problems and MRI interpretation after ACL repair are examples of the issues we encountered. This paper provides tips and tricks that could assist surgeons who are just starting to use this ACL-preserving technique.

Setting up a new pathway for patients with a suspected acute ACL rupture to allow diagnostic work-up and treatment to take place within 3 weeks after the injury is important when introducing DIS. Making specific agreements with the outpatient clinic, radiology department and operation theatre is key to enable surgery to take place within 3 weeks after injury. General practitioners, physiotherapists and emergency physicians should be informed, as the management of a ruptured ACL is changing from a chronic lesion to a sub-acute lesion. Referred patients with suspected acute ACL rupture were evaluated in our outpatient clinic within 2 days. To ensure rapid access to an MRI, a weekly slot was made available to evaluate acute ACL ruptures.

With these prior arrangements, we managed to treat acute ACL ruptures within 3 weeks of injury, but were not able to treat most ACL ruptures within this time-frame. Patient delay and delay by referring doctors were among the reasons why most ACL ruptures were treated after 3 weeks.

Murray et al. reported the necessity of a stable fibrin-platelet clot between the ruptured ends of the ACL within which stable scar tissue can form [26]. If the distal stump is not fully in contact with its proximal counterpart, the synovial fluid will wash out the fibrin-platelet clot and the ACL will not heal. Intra-operatively, a knot-pusher through the PDS retaining sutures can be used to check whether the distal stump is fully reduced to the proximal stump (Figure 5.4). It is advisable to perform this maneuver before the 10 mm DIS tibial tunnel is created. If the stump cannot be reduced properly, the operation can be converted to reconstruction during the same procedure and the tibial tunnel can be adjusted to the correct size for reconstruction.

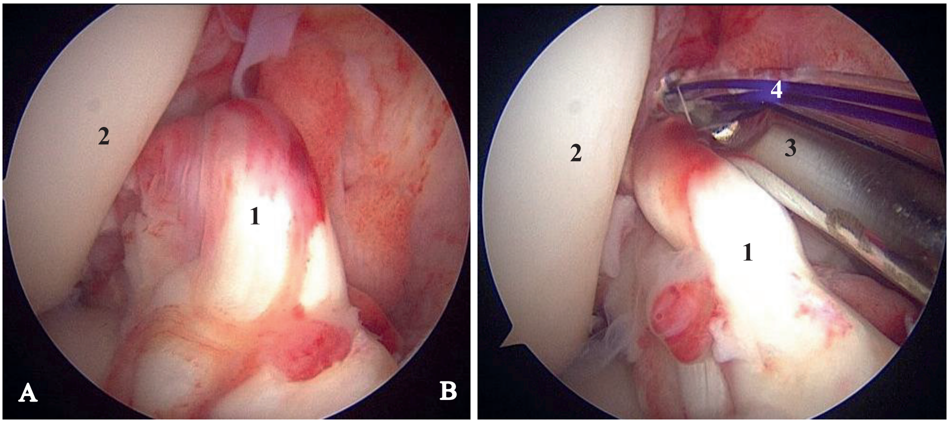

Figure 5.4 Anterior cruciate ligament (ACL) repair using dynamic intraligamentary stabilization. (A) Right knee, arthroscopic view of the ruptured anterior cruciate ligament (ACL). The distal bundle is not in contact with the proximal bundle. (B) Right knee, arthroscopic view of the ruptured anterior cruciate ligament (ACL). With a knot-pusher through the polydioxanone retaining sutures, the reduction of the ACL stump can be assessed. A gap between the proximal and distal stump should not be accepted. (1) anterior cruciate ligament, (2) lateral femoral condyle, (3) knot pusher, (4) PDS sutures

In addition to the standard DIS technique, we used lasso sutures (FiberLinkTM, Arthrex®) on a suture-passer (Scorpion, Arthrex®) [22] if the PDS sutures could not fully reduce the ACL. With the lasso sutures, more traction can be applied to the ACL stump and, in the case of a multiple-bundle rupture, the lasso can reduce several bundles, whereas the PDS sutures can break out of smaller bundles.

One of the problems encountered intra-operatively was entangling of the 4 to 6 sutures from the arthroscopic portal due to a tissue bridge. Shoulder surgeons are already more familiar with suture management; for most knee surgeons, this is a new action that has to be performed to prevent tissue bridges between the different sutures (Figure 5.3).

A delay of 3 weeks (21 days) between the rupture and DIS surgery has been proposed [12]. In other ACL repair techniques, [27, 28] the ACL can be repaired up to 3 months after the rupture. Van der List et al. reported that primary repair was more likely to be possible in older patients and patients with a lower BMI, and when surgery was performed within 4 weeks of injury [29].

Nowadays, we perform DIS up to 4 weeks after rupture. We believe that this period can be even longer, as long as the ACL stump is ruptured proximally, shows good tissue quality and is able to make full contact with the proximal stump.

In this study, 2 patients with a mid-bundle rupture were treated with DIS. One of these patients developed arthrofibrosis and an arthroscopic arthrofibrolysis was performed.

Evangelopoulos et al. [30] reported high complication risks (78.8%) for mid-substance ACL ruptures treated with DIS. However, the 2 patients with a mid-bundle rupture in this study showed a healed (grade 1) ACL on MRI (Table 5.3). Mid-substance ACL ruptures and a high pre-injury sporting activity level have been reported to be predictors of an inferior outcome [31]. Therefore, we now no longer perform DIS on mid-bundle ruptures.

Overall complication risks of up to 57.8% [32] have been reported with the DIS procedure. Haberli et al. [33] reported a re-surgery risk of 48.2% in 190 patients after DIS ACL repair. Of these re-surgeries, 5.8% were scar tissue debridement with hardware removal due to range of motion deficits. In this study, 5 of the 15 patients had a re-surgery within the 2-year follow-up period. All the patients who developed decreased knee function and arthrofibrosis were women. Two of these 4 patients felt immediate relief after arthrofibrolysis combined with removal of the DIS implant and expressed that they had regained their “natural knee movement”. We believe that, especially for slender women, extra attention should be given to the tension on the DIS implant. The DIS manufacturer recommends that the tension on the DIS implant should not exceed 60 N for women, while for slender women we prefer not to exceed 50 N. Patients should be informed pre-operatively about the possibility of re-surgery.

The literature on RTW after ACL reconstruction or repair is not extensive. Bieri et al. [33], in a matched study between DIS and reconstruction, reported that DIS patients benefited from a reduction in absence from work of almost 1 month compared with ACL reconstruction patients. This difference is probably related to the early timing of surgery that is recommended for DIS. In this study, the mean (SD) RTW time was 5.4 (3.6) weeks. Compared to reconstruction, there is no comorbidity due to graft harvest and since the proprioceptors of the ACL are also preserved, this could hypothetically lead to a faster rehabilitation and RTW.

On MRI, the healing process of the repaired ACL is different compared to the “ligamentization” phase of ACL reconstruction. Van der List et al. reported that post-operative MRI accurately predicted re-rupture of ACLs that had undergone a primary repair. Furthermore, the repaired ligament can be expected to be hyper-intense within the first year, while the signal becomes similar to that of an intact PCL after two years [14]. Based on the MRI findings in this study, remodeling of the ACL repair was most evident between 6 and 12 months post-operatively. The healing status remained unchanged between 12 and 24 months post-operatively, except for one patient.

Although patients may demonstrate signs of ACL healing on MRI following repair, persistently high repair signal intensity can be seen for more than 12 months post-operatively in clinically stable knees. Absence of healing on MRI should be interpreted with caution, and correlation with clinical findings is necessary [34].

A systematic review of DIS concludes that there is sufficient evidence to support DIS repair as possibly an effective modality for the treatment of acute proximal ruptures of the ACL. Overall, there is evidence to suggest that ACL repair should be included in the decision tree for individualized treatment planning. The best outcomes will be achieved with the selection of suitable patients [35].

5.6 Conclusion

In our experience with dynamic intraligamentary stabilisation (DIS) for ACL repair, all intra-operative technical problems were resolved and did not require conversion to ACL reconstruction. The tips and tricks presented in this manuscript could assist surgeons who are just starting to use the DIS technique.

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Chapter 6 MRI Following Primary Repair of the Anterior Cruciate Ligament

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MRI Following Primary Repair of the Anterior Cruciate Ligament

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6.1 Abstract

Primary repair of the anterior cruciate ligament (ACL) is being performed increasingly in the treatment of acute proximal ACL ruptures. Advantages of ACL repair over surgical reconstruction have been discussed in previous chapters of this thesis. Given this evolution of ACL surgical treatment, radiologists and orthopedic surgeons should be familiar with the new repair techniques and their appearances on post-operative imaging. In this article, we describe two different surgical techniques for primary ACL repair, Dynamic Intraligamentary Stabilization and Internal Brace Ligament Augmentation, and provide an overview of the normal and abnormal appearances after this type of repair at magnetic resonance imaging (MRI) follow-up.

6.2 Introduction

Although it was abandoned in the past after arthroscopic ACL reconstruction became popular in the early 1990's, there has been a renewed interest in primary ACL repair over the past decade [1]. This is due to a combination of improved knowledge of the basic biology of human ACL healing, [2, 3] and the recent availability of new ACL repair techniques [4-6]. Although the intra-articular ACL fails to heal after complete rupture due to the lack of stable blood clot formation in the gap between the ruptured ends of the ligament, recent studies have shown that the proximal ACL has a surprisingly productive response to injury [7, 8]. Murray et al. reported histologically different zones in the human ACL, with a higher cellular and vascular density in the proximal part of the ligament compared to the distal part [7]. Nguyen et al. studied human biopsy samples from ACLs that were scarred to the posterior cruciate ligament at the time of reconstruction [8]. These authors showed that the proximal ACL has an intrinsic healing response with typical characteristics similar to the medial collateral ligament that can heal spontaneously [8]. Consequently, new ACL repair techniques are being developed with focus on the repair of proximal ACL ruptures [4, 6, 9, 10]. The first clinical results of primary ACL repair are promising [4, 6, 9, 10]. Published studies have confirmed a definite trend towards improved outcomes in patients with acute proximal ACL rupture, possibly because this group could have better tissue quality [2, 6, 9]. In contrast, poor tissue quality is typical for mid-substance and chronic ACL ruptures, and a repair of these injuries have a higher failure rate [11, 12]. Few studies published in the orthopedic literature have included MRI in the follow-up of patients after primary ACL repair [13, 14]. However, these studies were primarily concerned with the functional outcomes of the ACL repair, and the MRI findings were not discussed in detail. In particular, longitudinal assessment with MRI of ACL healing following repair with an internal brace has not been well documented.

In this article, we provide an overview of the normal and abnormal findings after such repair at MRI follow-up. MRI data were collected as part of a pilot study performed prior to an ongoing multicenter, randomized controlled trial in our institution comparing ACL repair and conventional ACL reconstruction for relative clinical efficacy and economic benefit. Our Institutional Review Board approved this study and written informed consent was obtained from all participants.

6.3 Surgical techniques

The goal of primary ACL repair is to re-approximate the proximally ruptured ACL to the lateral femoral condyle and use the proximal part of the ligament's healing capacity [4-6]. The surgical techniques are discussed in other chapters of this thesis. Although there is no consensus regarding the single best technique for primary ACL repair, there are indications that some form of internal bracing, with either non-absorbable suture, scaffolds or a graft, can increase the success rate of the repair procedure [6]. Two ACL repair techniques facilitating ACL healing, both with a different form of an internal brace, have recently become available for clinical use, namely, InternalBrace™ Ligament Augmentation (IBLA, also known as Independent Suture Tape Reinforcement or Suture Tape Augmentation, Arthrex, Naples, Florida, USA) [15, 16] and Dynamic Intraligamentary Stabilization (DIS or also known as Ligamys™, Mathys Ltd Bettlach, Switzerland) [13]. The IBLA procedure can be carried out up to 12 weeks and the DIS procedure up to 3 weeks following rupture, depending on the ACL rupture location, remnant length and tissue quality. The first clinical results obtained with these techniques are promising [17-20].

6.4 MRI of ACL healing after repair with IBLA and DIS

The MRI appearance of the healing ACL after repair with an internal brace is variable and changes with time. In the first 3 months post-operatively, the ligament has an edematous aspect due to the previous trauma as well as the surgical intervention (Figures 6.1 and 6.2). Between 3 and 6 months after surgery, a gradual decrease of the signal intensity and swelling of the ACL over time occurs, resulting in a normal-sized ACL having low signal intensity within one year after surgery. This time course of MRI changes of the ACL following primary repair with an internal brace can most commonly be observed in patients with a clinically stable knee. This suggests that stability of the knee at this early stage is being maintained not only by the internal brace, but also, at least in part, by the healing of the repaired tissue [14, 21]. Moreover, any case of non-healing would gradually become clinically apparent within the first post-operative year, as there is a gradual loss of the device tension within the first 6 post-operative months [21]. Therefore, internal bracing techniques rely on healing of the ACL to be effective. Typically, the healing status on MRI remains unchanged between 12 and 24 months post-operatively.

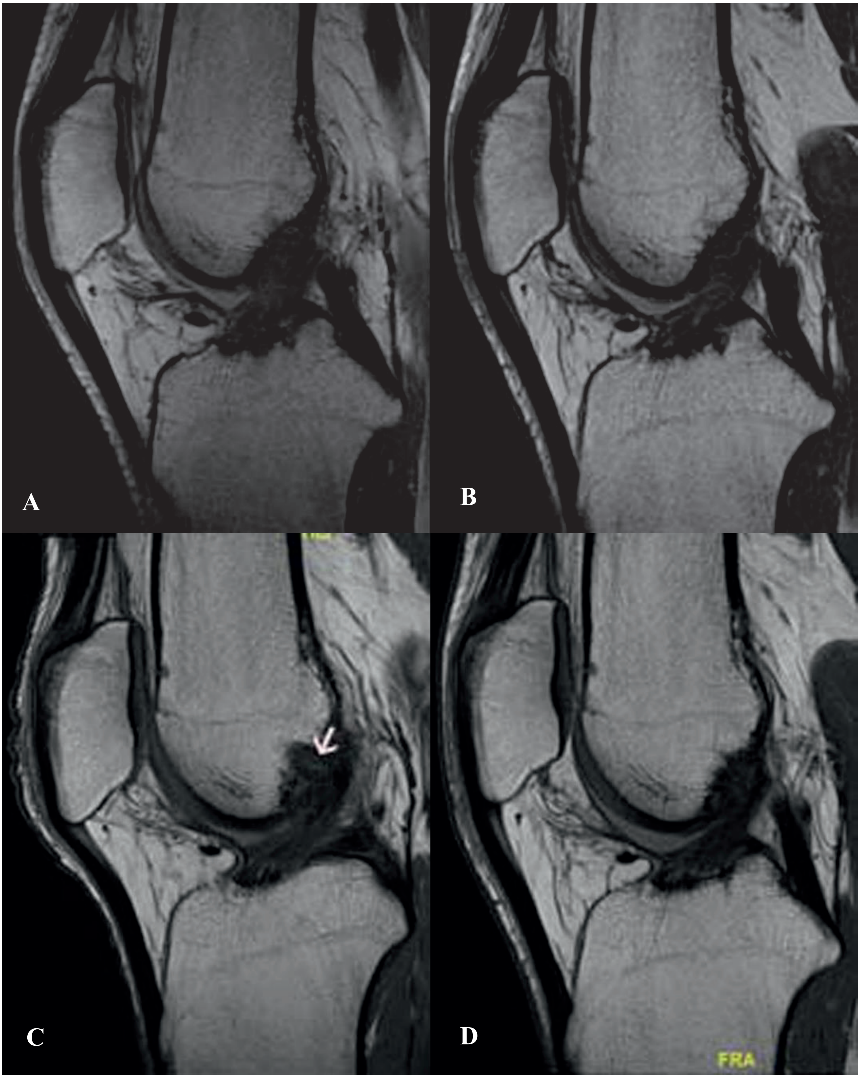

Figure 6.1 Normal ACL healing after primary repair with InternalBrace™ Ligament Augmentation, as seen on sagittal proton density weighted MR images. At 3 months (A), ACL repair is slightly thickened and hyperintense and has indistinct margins due to post-operative edema. At 6 months (B), decrease in signal intensity and remodeling are seen. Further remodeling takes place between 12 (C) and 24 (D) months post-operatively. At 24 months, a completely healed ACL is seen. Note FiberTape running through the center of the femoral footprint (arrow). Patient had a clinically stable ACL at all time points.

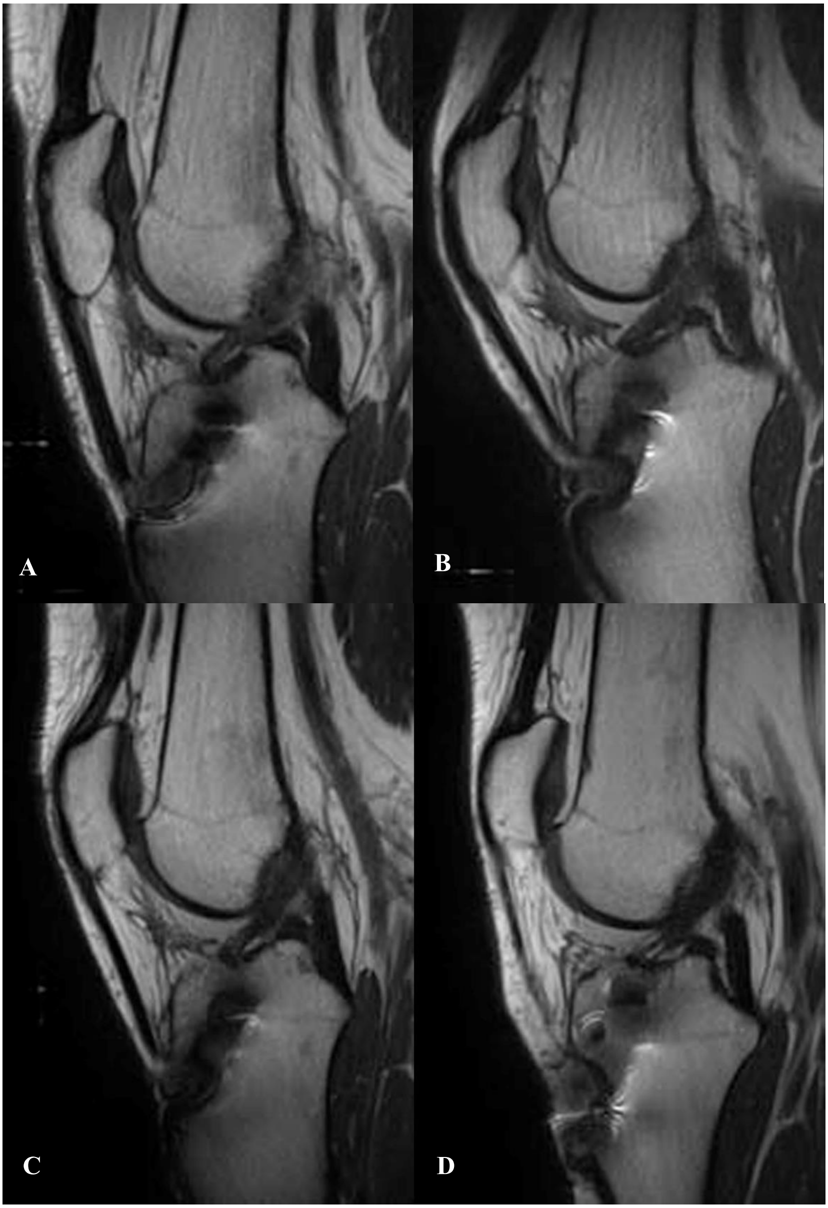

Figure 6.2 Clinically stable ACL healing after primary repair with Dynamic Intraligamentary Stabilization, as seen on sagittal proton density weighted MR images with use of slice encoding for metal artifact reduction (SEMAC).27 At 3 months (A), ACL repair is hyperintense due to post-operative edema. Note large joint effusion. MR at 6 months post-operatively (B) shows normal ACL healing exhibiting gradual decrease in the repair's signal intensity. Follow-up MR images at 12 (C) and 24 (D) months post-operatively show further gradual decrease in signal intensity with normal continuity of ACL fibers.

The time course of changes of the ACL repair contrasts with that commonly observed after standard ACL reconstructions, in which the signal intensity of the ACL graft gradually increases in the early postoperative period, peaks at 4 to 8 months after surgery, and then decreases with further graft maturation (a process referred to as ‘ligamentization’) [22]. MRI findings indicate that the healing process of the repaired ACL is different and does not involve such “ligamentization” phase.

Occasionally, high signal intensity of the ACL repair can be seen persisting for up to 12 months or even longer after surgery (Figure 6.3). A possible explanation for this observation is the so-called “windshield-wiper effect” [23]. This phenomenon, described in conventional ACL reconstruction, is caused by (sagittal) graft motion with flexion and extension of the knee, which may lead to bone tunnel widening. Similarly, it might be that the internal brace acts as a healing obstacle, resulting in a longer healing process [14]. Therefore, we suggest that it is not prudent in the first post-operative year to consider the repair to have failed based on increased signal intensity after this type of repair.

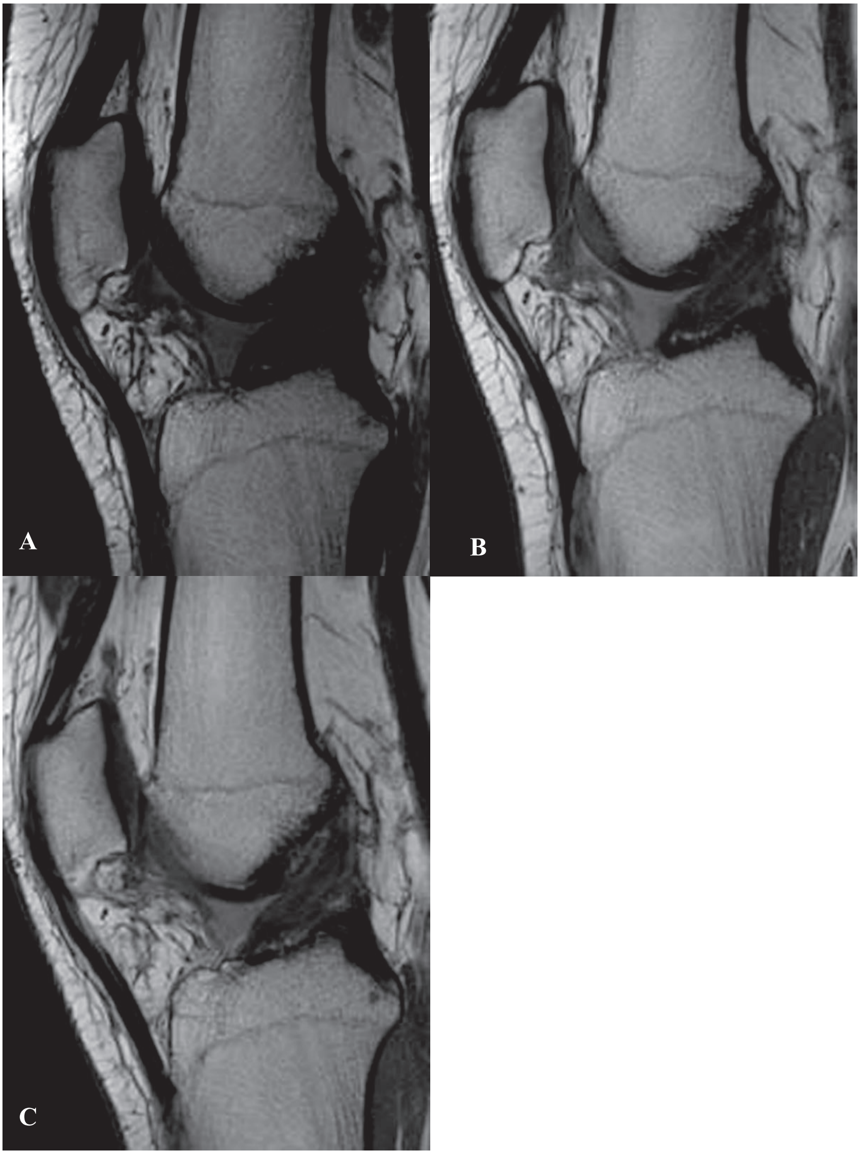

Figure 6.3 Persistent high signal in the ACL after primary repair with InternalBrace™ Ligament Augmentation, as seen on sagittal proton density weighted MR images. A, At 6 months, ACL repair is hyperintense due to post-operative edema. High signal intensity of the repair persists at 12 (B) and 24 (C) months post-operatively.

6.5 Complications

The most frequently encountered complications after primary ACL repair with internal bracing include absence of healing, arthrofibrosis and re-rupture of the ACL repair.

Over time, the ACL can be partially replaced by irregular strands of fibrous tissue bridging between the femur and tibia with extensive scarring of the notch (Figure 6.4). Typically, these findings show little evolution over time and may be visible on MRI up to 24 months after surgery. It is important to note that absence of healing on MRI is not always accompanied by instability of the knee. This discrepancy between clinical and imaging findings may be explained by both restoration of the ACL's integrity and scar tissue formation, and clinical recovery of ACL function is resultant to both of them [14].

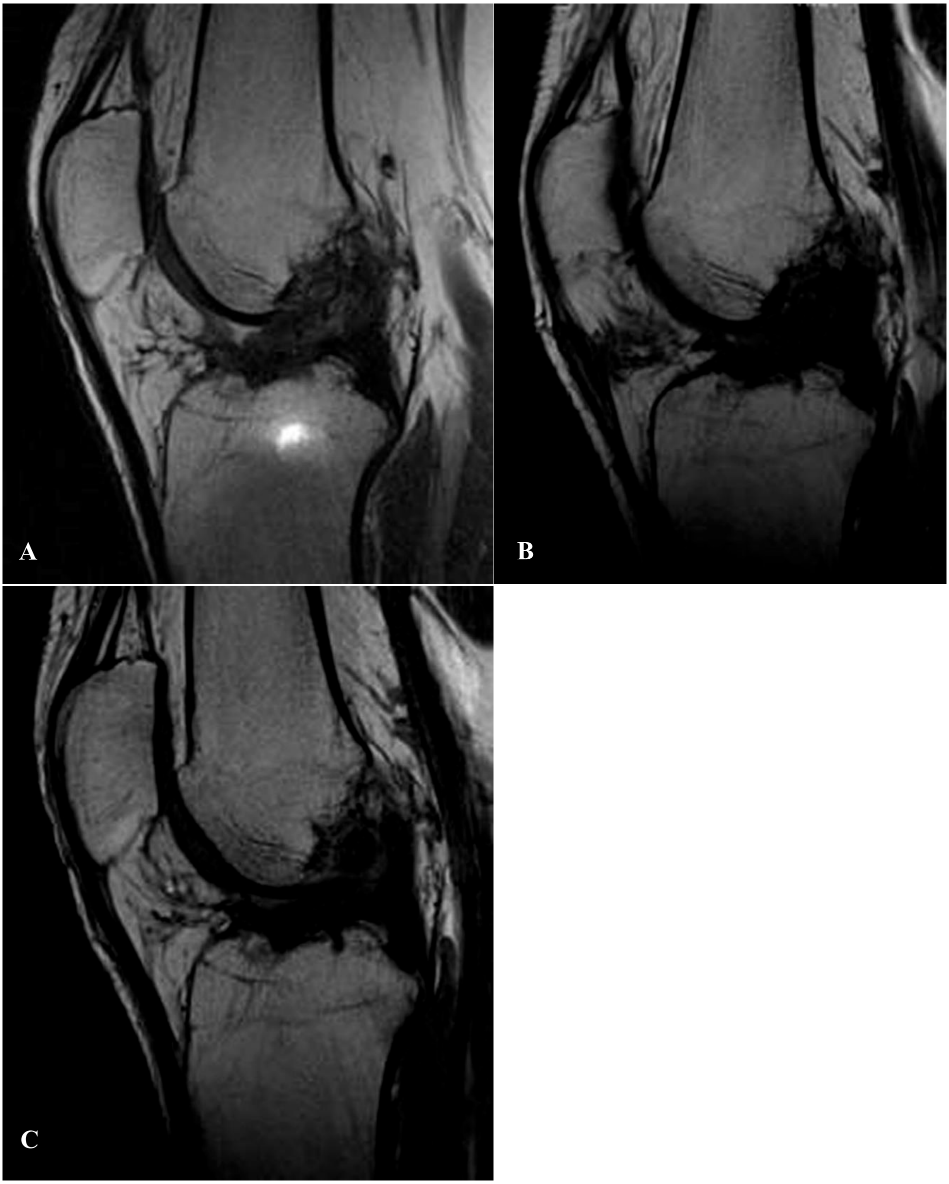

Figure 6.4 Clinically stable ACL after primary repair with Dynamic Intraligamentary Stabilization without signs of healing on MRI. Sagittal proton density weighted MR image at 6 months (A) post-operatively shows irregular appearance of the ACL with abnormal ligament strands and extensive fibrosis at the intercondylar notch. Follow-up MRI assessments at 12 (B) and 24 (C) months post-operatively remain unchanged.

Arthrofibrosis is a common complication after ACL repair (Figure 6.5). It is defined as the presence of excessive scar tissue in the (knee) joint, leading to symptoms of joint stiffness and a painful restriction of motion [24]. Although the risk factors remain unclear, the timing of surgery is generally considered an important predictor of arthrofibrosis with an increased incidence if surgery is performed within the first four weeks following trauma [24, 25]. As primary repair is performed in acute settings to prevent ligament retraction, arthrofibrosis can be expected a common finding after ACL repair, especially in the case of DIS repair, which is performed within 3 weeks after injury. In addition, microfracturing at the femoral footprint during the ACL repair may also contribute to (excessive) scar tissue formation. Interestingly, local arthrofibrosis (so called 'cyclops lesion'), most commonly attributed to incorrect positioning of the tibial tunnel in conventional ACL reconstruction, can also be seen after primary (anatomical) repair of the ACL (Figure 6.6). In patients with symptomatic limitation in the ROM, early arthroscopic arthrolysis (<1year) is needed to improve outcome [25]. The use of novel biological/tissue engineering techniques, including growth factors, stem cells and bio-scaffolds, has been the focus of current research in ACL healing and repair [3]. Future studies should assess how to guide the biological healing response optimally, as excessive biological activity may lead to hypertrophic scar tissue formation whereas lack of a biological response leads to failure of the ACL repair procedure [2, 3, 14].

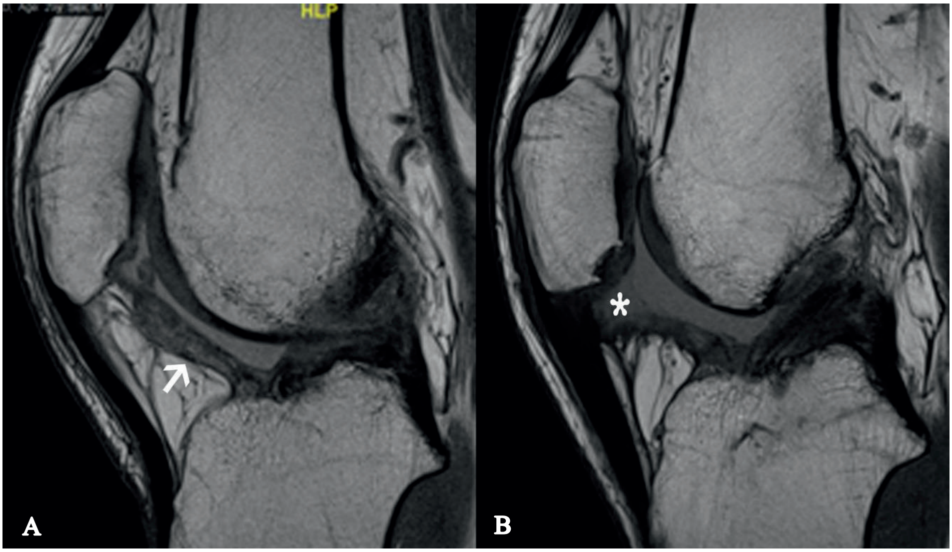

Figure 6.5 Decreased ROM after Dynamic Intraligamentary Stabilization repair due to arthrofibrosis. Sagittal proton density weighted MR images at 12 months post-operatively (A) show extensive fibrosis in Hoffa's fat pad (arrow). Follow-up MRI assessment at 24 months post-operatively (B) shows status after arthroscopic arthrolysis with resection (asterisk) of Hoffa's fat pad. Note normal healing of the ACL repair.

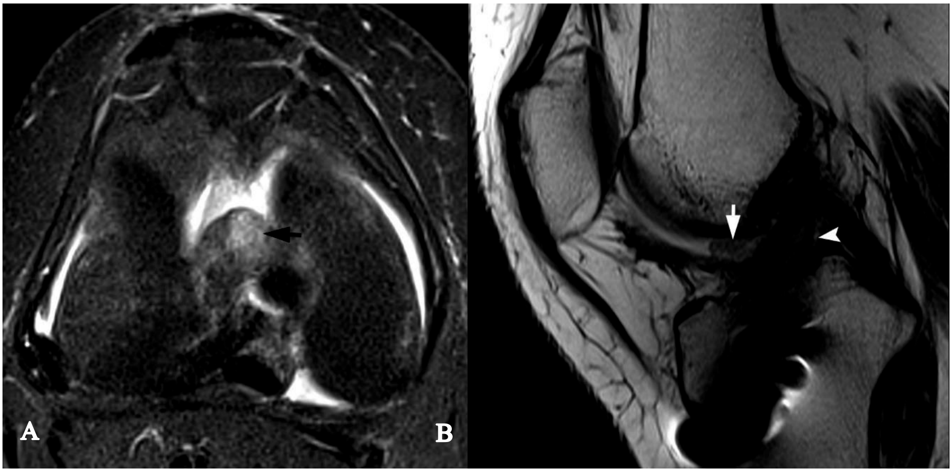

Figure 6.6 Cyclops lesion after Dynamic Intraligamentary Stabilization repair. Axial T2 weighted image with fat suppression (A) and sagittal proton density weighted image (B) reveal a small, oval mass anterior to the ACL repair (arrow) in keeping with localized fibrosis/cyclops lesion. Also note the augmentation wire posterior of the tibial ACL footprint (arrowhead).

Re-rupture of the ACL repair typically occurs between 8 and 12 months post-operatively, in patients performing highly competitive sports. MRI findings of complete re-rupture include complete discontinuity of the repair with absence of intact ACL fibers, T2-hyperintense fluid in the gap and horizontal fiber orientation or laxity of the ACL (Figure 6.7). Hydrops may be present in case of an acute rupture. Clinically, this is accompanied by signs of instability (anterior drawer, Lachman and pivot shift test). Partial rupture of the ACL repair may be more difficult to diagnose as high signal intensity may be present due to prolonged healing. We suggest that any new high MRI signal within the repair should be carefully correlated with the clinical findings. In the case of a repair rupture, a standard ACL reconstruction can still be performed as “no bridges are burned” after primary repair [4, 12].

A well-known late complication of standard ACL reconstruction is the formation of ganglion cysts within the bone tunnels due to degeneration of the tendon graft [26]. Cystic fluid collections can extend proximally through the tibial tunnel into the joint space or distally into the soft tissues anterior to the tibial tubercle. Although cyst formation in the graft is generally not associated with graft failure, it can cause pain and limitation of motion. In our experience, ganglion cysts are not encountered after primary ACL repair as only a 2 mm internal brace fiber tape is passed through small (3.5 mm) bone tunnels. Similarly, complications associated with graft harvesting can be avoided with the new ACL repair procedures [2, 4].

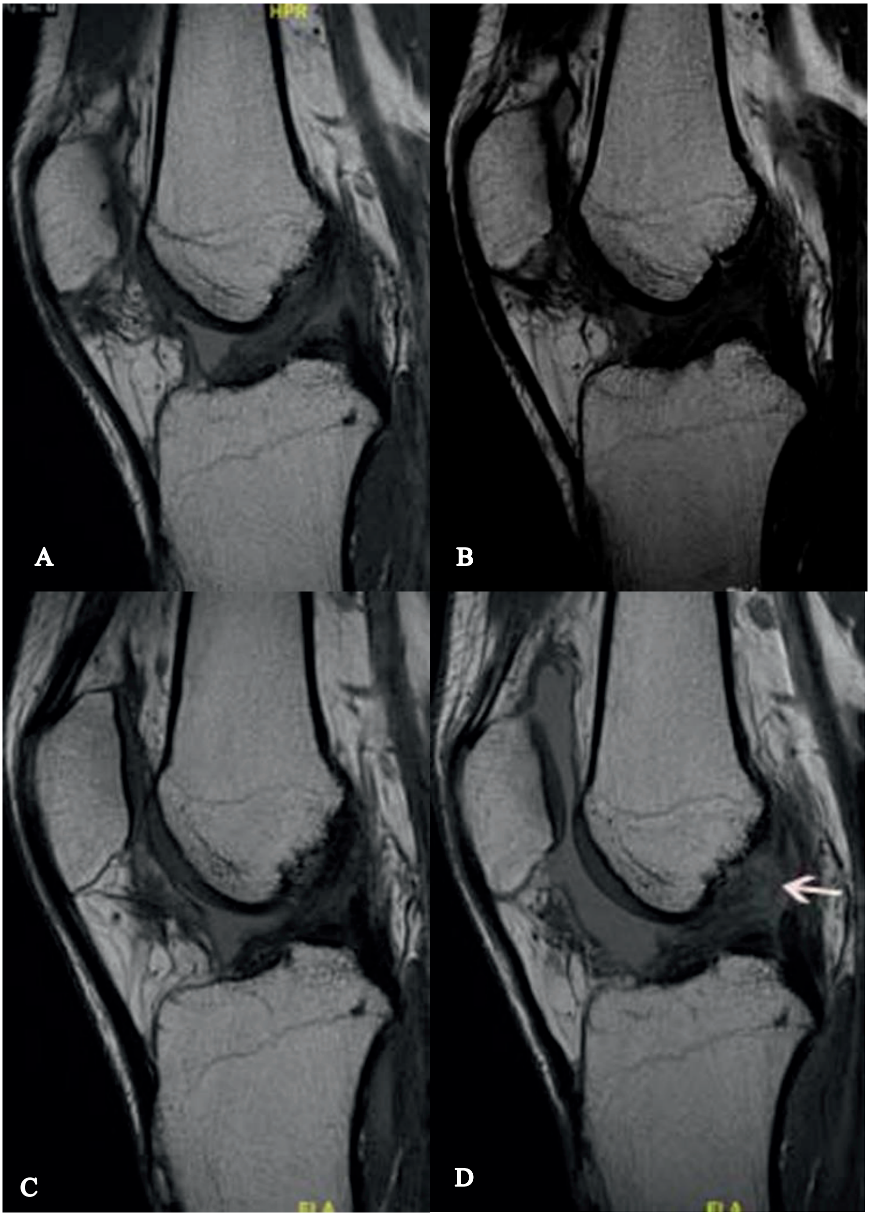

Figure 6.7 Re-rupture of the ACL after repair with InternalBrace™ Ligament Augmentation, as seen on sagittal proton density weighted MR images. Follow-up MR images at 3 (A), 6 (B) and 12 (C) months post-operatively show healing with continuity of the ACL and slightly high signal persisting over time. Two weeks later, patient had a traumatic re-rupture of the ACL repair. New high signal (arrow) is seen in the proximal third of the repaired ligament below the repair construct (D). Also note large joint effusion due to new trauma.

6.6 Conclusions

Primary repair of the ACL with internal bracing is being performed increasingly for the treatment of acute proximal ACL ruptures. In this article, we have reviewed the normal appearance of the repaired ACL on MRI after ACL repair as well as the possible complications of these techniques. The healing process of the repaired ACL is different compared to ACL reconstruction, without a “ligamentization” phase. Although patients may demonstrate signs of ACL healing on MRI following repair, persistent high signal intensity within the repair can be seen for more than 12 months post-operatively in clinically stable knees. Absence of healing on MRI should be interpreted with caution, and correlation with clinical findings is necessary. It is important for the radiologist and orthopedic surgeon to be familiar with the normal MRI appearance of ACL healing after repair, and its potential complications in order to avoid misinterpretation and subsequent unnecessary or delayed surgical intervention.

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Chapter 7 Study Protocol: a Single-blind, Multi-center, Randomized Controlled Trial Comparing Dynamic Intraligamentary Stabilization, Internal Brace Ligament Augmentation and Reconstruction in Individuals with an Acute Anterior Cruciate Ligament Rupture: LIBRƎ study

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7.1 Abstract

Background The current gold standard for the treatment of an anterior cruciate ligament (ACL) rupture is reconstruction with tendon graft. Recently, two surgical ACL repair techniques have been developed for treating an acute ACL rupture: Dynamic Intraligamentary Stabilization (DIS, Ligamys®) and Internal Brace Ligament Augmentation (IBLA, InternalBraceTM). We will conduct a single-blind, multi-center, randomized controlled trial which compares DIS, IBLA and reconstruction for relative clinical efficacy and economic benefit.

Methods Subjects, aged 18-50 years, with a proximal, primary and repairable ACL rupture will be included. DIS is preferably performed within 4 weeks post-rupture, IBLA within 12 weeks and reconstruction after 4 weeks post-rupture. Patients are included in study 1 if they present within 0-4 weeks post-rupture and surgery is feasible within 4 weeks post-rupture. Patients of study 1 will be randomized to either DIS or IBLA. Patients are included in study 2 if they present after 4 weeks post-rupture and surgery is feasible between 5-12 weeks post-rupture. Patients of study 2 will be randomized to either IBLA or reconstruction. A total of 96 patients will be included, with 48 patients per study and 24 patients per study arm. Patients will be followed up for 2 years.

The primary outcome is change from baseline (pre-rupture) in International Knee Documentation Committee score to 6 months post-operatively. The main secondary outcomes are the EQ-5D-5L, Tegner score, Lysholm score, Lachman test, isokinetic and proprioceptive measurements, magnetic resonance imaging outcome, return to work and sports, and re-rupture/failure risks. The statistical analysis will be based on the intention-to-treat principle. The economic impact of the surgery techniques will be evaluated by the cost-utility analysis. The LIBRƎ study is to be conducted between 2018 and 2022. Due to a delayed inclusion and covid-19 regulations, the inclusion period will be prolonged for at least two more years.

Discussion This LIBRƎ study protocol is the first study to compare DIS, IBLA and ACL reconstruction for relative clinical efficacy and economic benefit. The outcomes of this study will provide data which could aid orthopedic surgeons to choose between the different treatment options for the surgical treatment of an acute ACL rupture.

7.2 Background

The anterior cruciate ligament (ACL) is an important stabilizer of the knee. The ACL prevents anterior tibial translation and provides constraint to tibial internal rotation [1]. 2.5% of the ACL consists of proprioceptors [2, 3], which give feedback to the brain and spinal cord about the positioning of the knee joint. These proprioceptors play a role in defining and controlling normal joint movement [4]. Abnormal range or speed movements of the joint will trigger the brain to stimulate appropriate musculature to stabilize the joint.

Injury to the ACL is the most common ligament injury of the knee joint. Ruptures of the ACL mainly occur in young people (aged 16-40 years) performing pivoting sports like football, hockey, basketball and skiing. Each year 0.03% to 1.62% of non-high-level sport athletes and 0.15% to 3.67% of high-level sport athletes are affected [5]. In Belgium, 6.745 cruciate ligament surgeries were performed in 2017 (according to RIZIV/INAMI, Belgian National Sickness and Invalidity Insurance Institute). The socio-economic burden is considerable as the majority of ACL injuries occur in people of working age. The indirect costs related to absence from work, school or university are in addition to costs borne by the healthcare system [6].

Since the mid-eighties the gold standard for an operative treatment of an ACL rupture is reconstruction with a tendon graft. This involves removing native ACL tissue including its proprioceptors. The ligament is often replaced with autograft donor tendon(s), such as a hamstrings tendon or a part of the patellar tendon. A number of problems have been identified as graft harvest is associated with a degree of morbidity from tissue loss. Hamstrings muscle weakness following harvesting averages 10% in most studies [7]. Revascularization of the graft takes 6-12 months and ingrowth of the graft in the bone takes up to 2 years [8]. Another disadvantage of conventional ACL reconstruction is the rather long period of revalidation associated with a huge socio-economic burden.

A successful recovery from an ACL reconstruction encompasses intensive physiotherapy and requires a lot of effort, dedication, time and perseverance. According to Ardern et al. [9], the return to competitive sports after ACL reconstruction is only 44 to 55%. In another study, Biau et al. [10] found that only 40% of patients gain full functional recovery. Nagelli and Hewett postulated that delay in returning to sports for the first 2 years will significantly reduce the incidence of second ACL injuries [11]. Given the limitations and risks associated with the current gold standard treatment of an ACL rupture, there is room for improvement.

The last few years there is a renewed interest in ACL repair as an alternative operative treatment for the acute ruptured ACL. Two novel surgical ACL repair techniques have been developed and proof of concept has been established for treating an acute ACL rupture: Dynamic Intraligamentary Stabilization (DIS, also known as Ligamys®, Mathys Ltd, Bettlach, Switzerland) and Internal Brace Ligament Augmentation (IBLA, InternalBrace™, also known as Independent Suture Tape Reinforcement or Suture Tape Augmentation, Arthrex GmbH, Naples, Florida) repair techniques [12, 13].

The DIS technique has been shown to successfully induce self-healing of a ruptured ACL in animal models. Biomechanical studies in human cadaveric knees have shown that DIS restores knee joint kinematics comparable to that of an ACL-intact knee and provide further evidence that DIS is capable of providing knee joint stability during ACL healing [14-16]. A clinical experience of the first 3 years after DIS in a large case series was reported by Henle et al. [17]. They found that anatomical repositioning, along with DIS and microfracturing, leads to clinically stable healing of the ruptured ACL in 96% of patients. In their study, most patients exhibited a normal knee function, reported excellent satisfaction, and were able to return to their previous levels of sports activities. The same group also presented excellent outcomes and satisfaction with regards to the treatment result of all the patients with a functionally healed ACL with a 5-year follow-up [18]. Factors influencing the success of ACL repair with DIS were described by Krismer et al. and focus on patient selection [19]. In general, a higher percentage of successful outcomes after ACL repair are seen in patients with an acute, proximal ACL rupture because these tend to have better healing capacity and tissue quality. Although no significant differences were found in treatment costs and revision risks, patients treated by DIS benefited from nearly one month shorter absence from work as compared to patients treated by conventional ACL reconstruction. This was possibly due to the fact that the DIS procedure is recommended up to the first 21 days after ACL injury. For an ACL reconstruction there is no time limit [20].

Relatively little data is available in the literature on the IBLA technique. The proof of concept was provided by Mackay et al. [21]. They reported clinical outcomes at a minimum of 1-year follow-up, and found that IBLA is at least as effective in restoring stability and function of the knee as the conventional ACL reconstruction, with the greatest improvements seen in the decreased time of recovery. The same group also presented good functional outcomes along with radiographic and arthroscopic evidence of a healed ACL, in one of the first patients treated with IBLA [22].

In a 2-year follow-up of 42 patients treated with the IBLA technique, two patients (4.8%) reported an ACL re-rupture. Heusdens et al. conclude that repair with this technique could be clinically relevant as a treatment option for patients with an acute, proximal ACL rupture which is not retracted and of good tissue quality [23]. In addition, Smith et al. demonstrated the potential for excellent outcomes for pediatric ACL repair with temporary IBLA as an attractive alternative to ACL reconstruction [24].

To our knowledge, there is only one randomized controlled trial (RCT) published comparing an ACL repair technique with the conventional ACL reconstruction [25]. Hoogeslag et al. concluded that DIS is not inferior to ACL reconstruction in terms of subjective patient-reported outcome measures (PROMs) 2 years post-operatively, but for reasons other than revision ACL surgery due to re-rupture a higher number of related adverse events were seen in the DIS group [25].

Furthermore, there are no RCTs published comparing different ACL repair techniques with each other. Because of the lack of RCTs orthopedic surgeons are careful in adapting these new repair techniques. This clinical trial was designed in order to provide more scientific evidence on which of the three surgery techniques could possibly be the most clinically and economically effective for treating an acute ACL rupture.

7.3 Methods

7.3.1 Study objectives

7.3.1.1 *Primary objective*

To determine the clinical efficacy of two alternative techniques DIS and IBLA in comparison to the conventional ACL reconstruction for treating an acute ACL rupture. We are interested in the three pairwise comparisons between the techniques: DIS versus ACL reconstruction, IBLA versus ACL reconstruction and DIS versus IBLA.

7.3.1.2 *Secondary objectives*

- To assess whether DIS and IBLA offer an improvement in quality of life (QOL), patient satisfaction and functioning of the patient compared to conventional ACL reconstruction.
- To assess whether DIS and IBLA result in a shorter recovery period compared to conventional ACL reconstruction in terms of the mobilization period with crutches after the surgery, and return to work (RTW) and sports (RTS) period.
- To assess whether there is a difference between DIS and IBLA versus conventional ACL reconstruction in terms of pain and complications during and after surgery.
- To assess whether there is a difference between DIS and IBLA versus conventional ACL reconstruction in terms of ACL re-ruptures/failures.
- To determine the economic benefit of the two alternative techniques DIS and IBLA in comparison to the conventional ACL reconstruction for treating an acute ACL rupture.
- For all of these objectives also the mutual comparison between DIS and IBLA will be considered.

7.3.2 Study design

The LIBRƎ trial is a single-blind, multi-center, prospective, RCT comparing Ligamys® ACL repair, InternalBrace™ ACL repair and conventional ACL reconstruction for relative clinical efficacy and economic benefit.

Patients admitted for an acute traumatic knee sprain needing ACL surgery will be recruited at the Antwerp University Hospital, University Hospital Brussels and Onze Lieve Vrouw Hospital, Belgium between February 2018 and the end of 2022.

The LIBRƎ study is single-blind, meaning that the patient and the physiotherapist are blinded to the performed surgical technique, but they are aware in which part of the study the patient participates (study 1 or study 2). Patient's physiotherapist will follow a study-specific rehabilitation protocol (identical for the three treatment arms), depending on the readiness of the patient for a next phase and not restricted to a predefined time line.

In the study design, the time-dependent nature of ACL repair surgeries has been taken into account. The company Mathys Ltd advices DIS to be performed within 3 weeks after the ACL rupture. Previous ACL repair surgery experience from the authors (CH and LD) led to a prolonged DIS ACL repair period within 4 weeks post-rupture. IBLA can be performed up to 12 weeks after the ACL rupture. ACL reconstruction is preferably performed when the knee has regained its function. This is commonly after 4 weeks post-rupture and can be performed up to many years later. Taken into account these time limits there will be two parallel studies (Figure 7.1).

- Study 1 (RCT 1) with a time frame 0-4 weeks post-rupture: patients are randomized 1:1 to DIS or IBLA
- Study 2 (RCT 2) with a time frame 5-12 weeks post-rupture: patients are randomized 1:1 to IBLA or conventional ACL reconstruction.

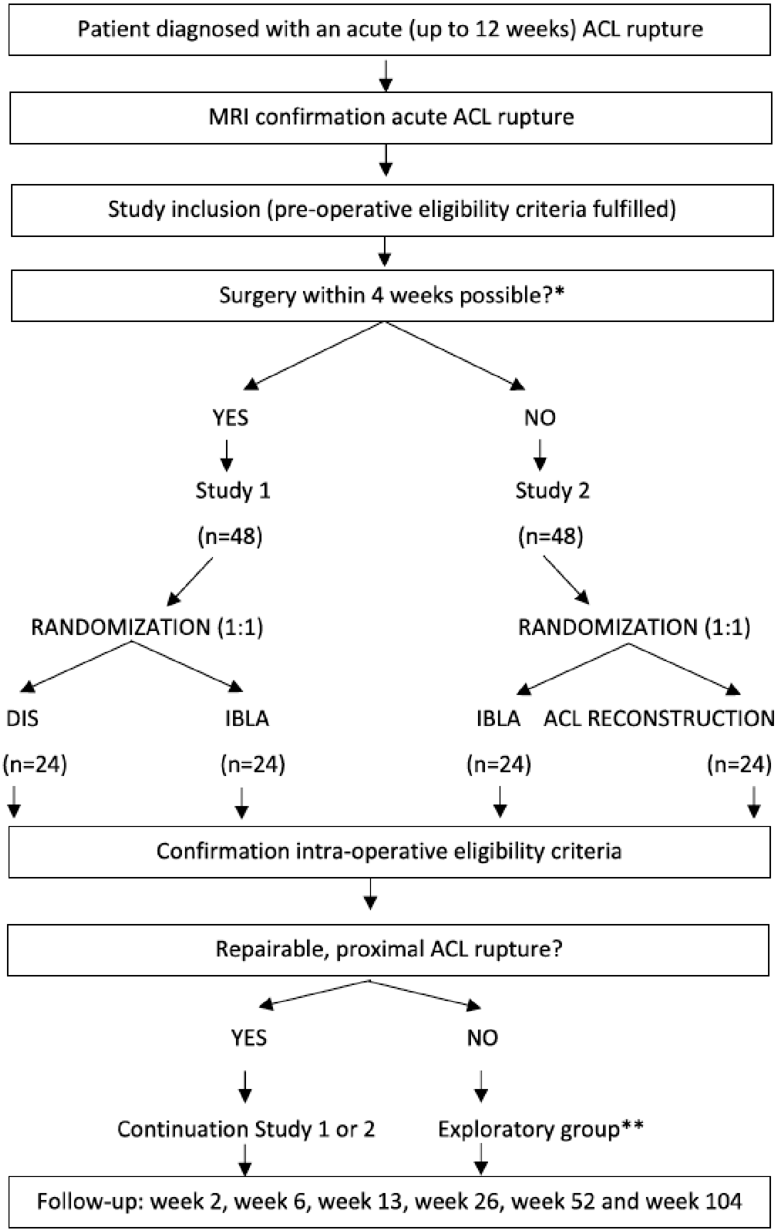

*Figure 7.1 Study flow diagram: screening, inclusion, surgery and follow-up. *Depends on when the patient presents at the consultation desk after the ACL rupture. **Patients in the exploratory group will be replaced, but are still part of the study. ACL = Anterior Cruciate Ligament, DIS = Dynamic Intraligamentary Stabilization, IBLA = Internal Brace Ligament Augmentation, MRI = Magnetic Resonance Imaging*

Allocation to either study 1 or study 2 depends on the patient's admission time point after ACL injury and if it is practically feasible to perform ACL surgery within 4 weeks. There is a patient and referral delay, a magnetic resonance imaging (MRI) needs to be performed to confirm the ACL rupture and the surgery has to be planned. On the other hand, inclusion and surgery between week 5-12 after injury is expected to be more manageable to plan. There will be an intra-operative confirmation in study 1 and study 2 of the ACL's eligibility for repair. If the proximal ACL rupture is not suitable for repair, ACL reconstruction will be performed. To keep the three arms (DIS, IBLA and the conventional reconstruction arm) comparable, patients with a non-repairable proximal ACL rupture will be replaced by a new patient even if they were randomized to the conventional ACL reconstruction. These patients will be seen as excluded from the randomized medical device (but not excluded from the study) and will undergo a conventional ACL reconstruction (exploratory group). These patients will be treated as a sub-population and will not be included in the primary analysis.

7.3.3 Study population

7.3.3.1 *Inclusion criteria*

- Primary acute proximal ACL rupture: 3-digit ACL rupture classification, type A (MRI and intra-operative confirmation) [2] (Figure 7.2).
- Age: 18-50 years.
- Presented and planned surgery within 4 weeks after the ACL rupture (Study 1).
- Presented and planned surgery between 5-12 weeks after the ACL rupture (Study 2).
- The ACL remnant is suitable for repair in the three treatment arms: at least 75% of the distal ACL remnant must be in contact with the proximal remnant/femoral condyle (intra-operative confirmation).
- Mentally and verbally capable of participating in the study.
- Written informed consent (according to the ICH-GCP Guidelines).

7.3.3.2 *Exclusion criteria*

- Posterior cruciate ligament injury and/or posterolateral ligamentous complex grade 3 injury, lateral collateral ligament grade 3 injury or medial collateral ligament grade 3 injury.
- Osseous fractures or trauma that could impair rehabilitation and/or ACL repair.
- Neurological disorder or systemic disease.
- Inflammatory disease, rheumatoid arthritis, spondyloarthropathy or active malignancy
- Non-sportive: Tegner score of less than 3.
- Not suited for intervention due to lack of mobility, meaning not achieving 90° of flexion before surgery.

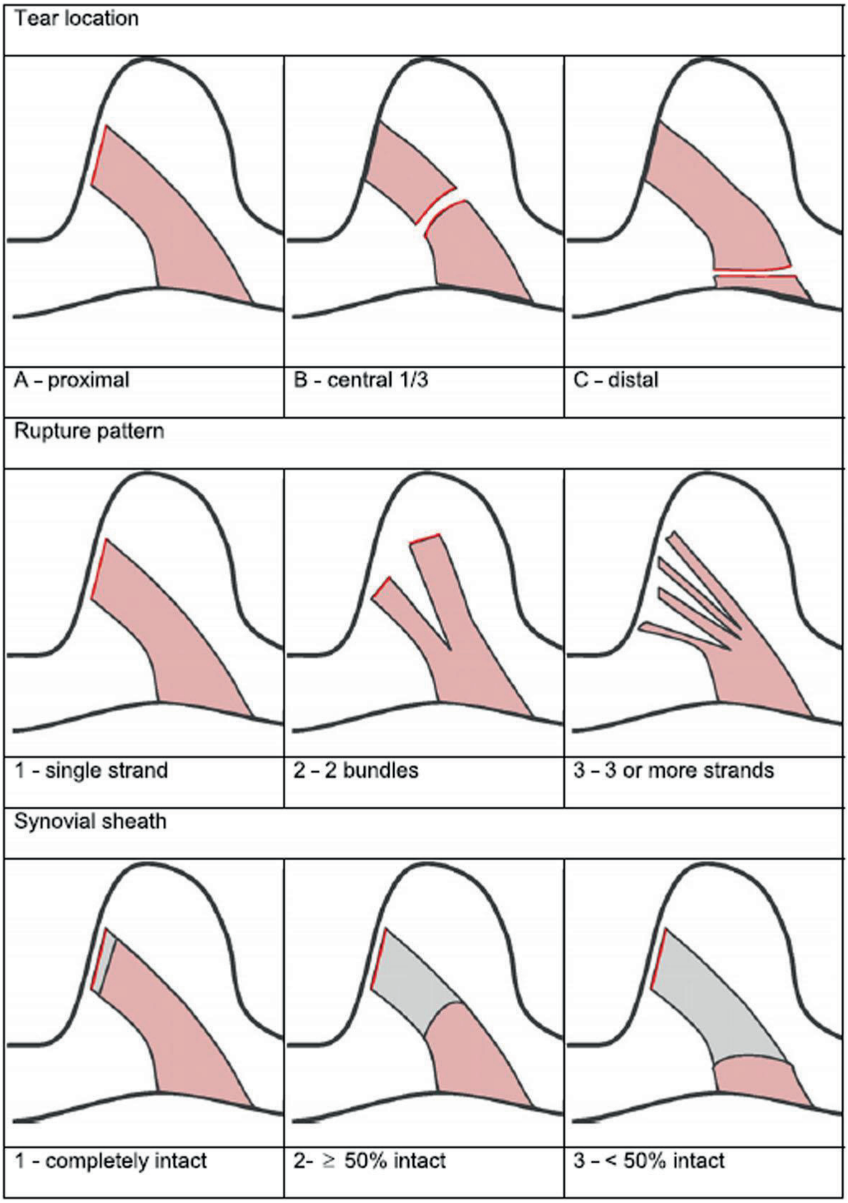

Figure 7.2 Three-digit ACL rupture classification. Anterior intercondylar view of the right knee. The ACL is drawn in pink, the upper curved black line represents the femur and lower curved line represents the tibia. The first digit describes the ACL rupture location: 'A' for proximal third, 'B' for central third and 'C' for distal third. The second digit is the ACL rupture status: '1' for 1 bundle, '2' for 2 bundles and '3' for multilacerated. The third digit describes the ACL synovial tube: '1' for completely intact, '2' for ≥50% intact and '3' for < 50% intact [17]

7.3.4 Study intervention

7.3.4.1 *Conventional ACL reconstruction*

ACL reconstruction involves replacing the ruptured ligament with a harvested graft (quadrupled semitendinosus) taken from the patient's ipsilateral knee [26]. This arthroscopic procedure involves harvesting the hamstrings tendon graft, removing the ruptured ACL and drilling tunnels in the femur and tibia to place the graft in the same anatomical position as the native ACL. The graft is fixed on the femur with an adjustable suture button, and on the tibia with a post- and interference screw.

7.3.4.2 *Dynamic intraligamentary stabilization*

The DIS repair technique was described by Eggli et al. [12]. The tibial stump of the ACL is reduced to the femoral footprint by transosseous sutures thereby restoring the anatomical position of the ACL [15]. Additional to the technique described by Eggli et al., lasso sutures will be used to reduce the tibial stump, if the stump cannot be reduced with PDS sutures. With this adaption, multi-bundle ruptures can be repaired. The knee is stabilized with a strong polyethylene cord which is passed on the tibial side behind the tibial footprint to prevent damage to the ACL tibial blood and nerve supply. At the femoral side the cord is passed through the anatomical footprint after carrying out microfracturing at this site. Using a dynamic spring-screw implant, the cord is brought under tension on the anteromedial aspect of the tibia just above the pes anserinus insertion. The proximal tibia is hereby pulled in a constant posterior drawer position with a force of 50-80 Newton depending on the sex of the patient. It is hypothesized that DIS repair continually stabilizes the knee and therefore can enable mechanically stable ACL healing [12].

7.3.4.3 *InternalBrace ligament augmentation*

The IBLA repair technique involves repair of the ACL as well [13, 27]. The proximal end of the ACL stump is re-approximated against the medial wall of the lateral femoral condyle or the proximal remnant with a lasso suture. The knee is stabilized with a high-strength tape, fixed on the femur with a femoral button, passing besides or through the ACL from the femoral footprint to the tibial footprint and fixed on the tibia with a bone anchor. The InternalBrace™ reinforces the ligament as a secondary static stabilizer, encouraging natural healing of the ligament by protecting it during the healing phase and supporting early mobilization.

The three surgical techniques will be performed in Antwerp University Hospital, University Hospital Brussels and Onze Lieve Vrouw Hospital using similar surgical protocols. No additional anterolateral procedure will be performed. In case of a non-repairable ACL rupture, a conventional ACL reconstruction will be performed. In case of failure/re-rupture of the repaired ACL (DIS/IBLA technique) a conventional ACL reconstruction can be performed. In case of failure/re-rupture of the reconstructed ACL, a revision of the reconstruction can be performed.

7.3.5 Study endpoints

7.3.5.1 *Primary endpoints*

The primary endpoint is change in International Knee Documentation Committee (IKDC) from baseline (pre-rupture) to 6 months post-operatively. The difference in IKDC score between the reconstruction technique and the repair techniques (DIS/IBLA) is expected to be the largest at 6 months post-operatively, due to the proprioceptive conservation with the repair techniques.

The IKDC is a commonly used instrument to determine the outcome following various knee procedures, including ACL reconstructions [28]. In essence, it is a subjective well-known tool that provides patients with an overall function score (range 0-100). The score is interpreted as a measure of function with higher scores representing higher levels of function. The questionnaire addresses three categories: symptoms (pain, swelling, stiffness, etc.), activity (rising from chair, going up and down stairs, jumping, squatting, etc.) and knee function [29].

7.3.5.2 *Secondary endpoints*

- Pain experienced by the patients as measured by visual analogue scale (VAS) pain score [30, 31].
- Overall functioning by the patient, related to the knee, as measured by Tegner and Lysholm score [32].
- Health-related quality of life (HRQoL) as measured by EQ-5D-5L [33, 34].
- Time to recovery as measured by mobilization with crutches, RTW and RTS.
- Patient satisfaction towards the surgery and revalidation level as measured by VAS satisfaction.
- Mechanic functioning of the knee as measured by Lachman test; single leg hop, triple leg hop, triple crossover hop and drop jump test; proprioceptive measurement; isokinetic measurement; and knee function [35-42].
- Intra- and post-operative complications: adverse device effects (ADEs) and serious adverse events (SAEs).
- Success of the operation techniques defined as the number of non-failures.
    - A failure is defined as:
        - A re-rupture of the graft or the repaired ACL: clinically and MRI-confirmed
        - Instability complaints: AP translation difference of more than 3 mm (Lachman test) between the injured knee and the contralateral knee, and subjective instability complaints [17].
- The number of physiotherapy and (extra) orthopedic surgeon consults.
- ACL healing will be evaluated with MRI [43].

7.3.6 Study procedures

Table 7.1 gives an overview of the clinical and radiological evaluations the patient will encounter following written informed consent. The physiotherapy will be performed by the patient's physiotherapist according to the study-specific rehabilitation protocol. This physiotherapy protocol is based on five phases. Proceeding to the next phase depends on the patient's rehabilitation progress and not on the post-operative time.

Timepoint	Clinical and radiological evaluations
Pre-operative	Pre-rupture; Tegner score, Lysholm score and IKDC score Post-rupture; VAS pain, knee function, Lachman test, EQ-5D-5L, isokinetic and proprioceptive measurement, MRI
Intra-operative	Knee function, pivot shift test, surgery time, complications
Post-operative	
Day 1	VAS pain, RTW, rupture-surgery interval, EQ-5D-5L, complications
Week 2	VAS pain, RTW, knee function, EQ-5D-5L, complications
Week 6	VAS pain, VAS satisfaction, mobilization with crutches, RTW, RTS, knee function, Lachman test, EQ-5D-5L, complications, X-ray
Week 13 (3 months)	VAS pain, VAS satisfaction, mobilization with crutches, RTW, RTS, knee function, Lachman test, EQ-5D-5L, Tegner score, Lysholm score, IKDC score, complications, isokinetic and proprioceptive measurement
Week 26 (6 months)	VAS pain, VAS satisfaction, RTW, RTS, knee function, Lachman test, EQ-5D-5L, Tegner score, Lysholm score, IKDC score, complications, number of physiotherapy and orthopedic surgeon consults, single leg and triple leg hop test, triple crossover hop test, isokinetic and proprioceptive measurement, MRI
Week 52 (12 months)	VAS pain, VAS satisfaction, RTW, RTS, knee function, Lachman test, EQ-5D-5L, Tegner score, Lysholm score, IKDC score, complications, number of physiotherapy and orthopedic surgeon consults, single leg and triple leg hop test, triple crossover hop and drop jump test, isokinetic and proprioceptive measurement, MRI
Week 104 (24 months)	VAS pain, VAS satisfaction, RTW, RTS, knee function, Lachman test, EQ-5D-5L, Tegner score, Lysholm score, IKDC score, complications, number of physiotherapy and orthopedic surgeon consults, MRI

Table 7.1 Pre-, intra- and post-operative clinical and radiological evaluations

IKDC International Knee Documentation Committee, MRI magnetic resonance imaging, RTW return to work, RTS return to sports, VAS visual analogue scale

MRI is performed on a 3-T system (Magnetom Prisma Tim, Siemens, Erlangen, Germany) for IBLA and ACL reconstruction arms. For patients treated by DIS, a 1.5-T system (Magnetom Aera Tim, Siemens, Erlangen, Germany) with metal artefact reduction sequences will be used. The 4-level Howell classification, originally proposed for grading ACL graft, is adapted for evaluating the repaired ligaments [44]. The morphology and signal intensity of the ACL graft or repair will be subjectively assessed on conventional MRI [45].

When re-surgery is needed or a failure occurs, the patient is not excluded from the study and the follow-up will continue according to this protocol. Under re-surgery, we consider all surgeries a patient undergoes on the side of the injured knee affecting his/her mobility. Re-surgery following re-rupture will be considered as a failure.

If the proximal ACL rupture is not suitable for repair, the patient will undergo an ACL reconstruction (exploratory group). These patients will be followed according to this protocol except for the post-operative MRI measurements on week 52 and 104, and the post-operative isokinetic measurements on week 13, 26 and 52 as these measurements are study-specific and not standard of care.

7.3.7 Study duration

The start date of inclusion is February 2018, expected end date of inclusion is June 2020. The follow-up duration is 2 years. Last patient follow-up visit is expected in June 2022. Due to a delayed inclusion as a result of the covid-19 regulations, the inclusion period will be prolonged for at least two more years.

7.3.8 Sample size

The primary outcome is change in IKDC score from baseline (pre-rupture) to 6 months post-operatively. A difference in IKDC change score of 13 points between the treatment arms is considered clinically meaningful as described by Irrgang et al. and Collins et al. [46, 47]. In order to detect an effect of 13 IKDC points with 80% statistical power between any of the two treatment arms using an independent samples t-test in which alpha is 0.025 (alpha corrected for the fact that per study data set 2 tests will be performed), assuming a standard deviation of 13 on the change in IKDC score per arm (SD found in pilot study), we need 21 patients per arm. Taking into account a drop out of 10%, we need 24 patients per arm or 48 patients in total which have to be randomized.

In study 1, 24 patients per arm (DIS and IBLA) will be included and in study 2, 24 patients per arm (IBLA and ACL reconstruction) will be included. The total number of patients to be included is 96. We expect that the total number of addressed patients will range from 96 to 106, as we expect that about 10% of the patients will not have a repairable, proximal ACL rupture. They will not be eligible (any more) after the intra-operative confirmation and these patients (exploratory group) will not contribute the number of 96 patients needed for inclusion.

7.3.9 Randomization and blinding

Randomization will take place when the patient is diagnosed with an acute ACL rupture, which is MRI confirmed, fits all the in- and exclusion criteria (expect for the two inclusion criteria which are intra-operatively confirmed: proximal and repairable ACL rupture), and when the patient has signed the informed consent. The randomization procedure will be generated in Castor Electronic Data Capture software (Castor EDC, Amsterdam, the Netherlands). Castor uses stratified block randomization. Randomization will be stratified according to center. Per center a permuted block randomization with variable block size will be used.

The LIBRƎ study is a single-blind study meaning that the treating physicians (principal and sub-investigators) and the study coordinator are not blinded. The patient and the patient's physiotherapist are blinded.

7.3.10 Statistical methods

7.3.10.1 *Data management and analysis software*

Castor EDC software will be used for data management. This ICH-GCP compliant web-based software covers all aspects of data management, data collection, ADE/SAE reporting, randomization, patient surveys and monitoring in multi-center studies. Patients will receive an e-mail via Castor with a request to fill-in the questionnaires.

All data is gathered from study 1 and 2 for data collection and cleaning via direct entry in Castor EDC (electronic case report forms (eCRF)). The eCRF data in the Castor EDC are stored on an accredited data center hosting in the Netherlands (accreditations: ISO 27001:2013, ISO 9001 and NEN7510). Data can be retrieved from this data center at any point in time to perform the required statistical patient data analyses led by Antwerp University Hospital. Full audit trail is available to log every change to the trial's data as well as which user made the change.

All statistical analyses will be performed in SAS version 9.4 or higher, R version 3.3.2 or higher, or SPSS 24.

7.3.11 Statistical analyses

7.3.11.1 *Analysis of the primary outcome*

To answer the research question comparing the three treatment arms the research question is split up in three separate questions:

- Is there a difference between DIS and IBLA (≤4 weeks)?

Results from study 1 will be used in a linear regression model with IKDC at 6 months as outcome and treatment, and IKDC at baseline as predictors. This linear regression model will allow correction for possible confounders like age, gender and working category.

- Is there a difference between IBLA (5-12 weeks) and conventional ACL reconstruction?

Results from study 2 will be used in a linear regression model with IKDC at 6 months as outcome and treatment, and IKDC at baseline as predictors. This linear regression model will allow correction for possible confounders like age, gender and working category.

- Is there a difference between DIS and conventional ACL reconstruction?

Results from study 1 and study 2 will be compared using a linear regression model with IKDC at 6 months as outcome and treatment, and IKDC at baseline as predictors. As this is a non-randomized comparison this model will correct for possible confounders like age, gender and working category.

For the primary analysis all patients that didn't have a repairable, proximal ACL rupture will be excluded from the analysis (exploratory group). Patients with a failure or re-surgery will be included in the primary analysis.

7.3.11.2 *Analysis of the secondary outcomes*

- To evaluate robustness of the results a sensitivity analysis of the primary outcome will be done using different analysis sets.
    - Analysis set without failures: patients that have a failure within the 6 months of follow-up are excluded from this analysis
    - Analysis set without re-surgeries: patients that have a re-surgery within the 6 months of follow-up are excluded from this analysis
- In case we are not able to show superiority between the arms, we will consider non-inferiority between the arms. To this end we will choose 10 IKDC points as non-inferiority margin (see Hoogeslag et al. [25]). Non-inferiority will be considered in the different analysis sets and only be concluded if they give similar findings. The analysis sets considered here are intention-to-treat, the analysis set without failures and the analysis set without re-surgeries.
- As the IKDC scores are measured at many different time points during the patient's follow-up we can compare the evolution over time between the treatment arms using a linear mixed model. Also here we will consider the effect of failure and re-surgery through inclusion and exclusion of the results after failure.
- Linear regression will be performed on the changes from baseline to 24 months in the continuous outcomes like VAS pain, VAS satisfaction, Tegner score, Lysholm score, EQ-5D-5L, Lachman test, single leg and triple leg hop test, triple crossover hop and drop jump test, isokinetic and proprioceptive measurement and knee function. The evolution over time of these continuous outcomes will be compared between the different treatments using a linear mixed model.
- A survival analysis with log-rank test will be used to compare the time to RTW and time to RTS between the different treatment arms. The time from the surgery until the patient is mobile without crutches will be analyzed in the same way.
- The number of physiotherapy/orthopedic surgeon consults will be compared between the different treatment arms using linear regression.
- The morphology and signal intensity of the ACL will be assessed with MRI and compared between the different treatments using a Chi-square test at the different time points.

In all the analyses there will be appropriately corrected for possible confounders (age, gender, working category, Tegner score of more than 7) especially in the analysis where the ACL reconstruction arm is compared to the DIS arm as this is a non-randomized comparison. As the sample size is small mainly ANCOVA models where only one covariate is added will be explored. As the sample size will not allow to combine all covariates in the model any conclusion for the non-randomized comparison will be carefully stated.

7.3.11.3 *Analysis of safety endpoints*

- The number of patients with SAEs will be reported per treatment arm.
- The proportion of patients having complications will be compared between the different treatments using a Chi-square test.

7.3.11.4 *Exploratory analyses*

- The IBLA arm (0-4 weeks) will be compared to the IBLA arm (5-12 weeks) to assess the optimal time frame for surgery.
- To identify if the patients that are intra-operatively confirmed of having an unrepairable and/or non-proximal, primary ACL rupture have certain characteristics in common and as such are an identifiable sub-population.

7.3.12 Cost-utility analysis

The health economic evaluation will possibly demonstrate the improved economic impact on the healthcare system of the new ACL repair techniques compared to the conventional ACL reconstruction. In addition, a second analysis will possibly determine which of the two ACL repair techniques, DIS or IBLA, provides the best economic benefits also depending on the given clinical time frame. A cost-utility analysis will be used for the economic evaluations, since the main objective is the impact on HRQoL.

The result of the cost-utility analysis will be the Incremental Cost-Utility Ratio (ICUR) [33, 34]. In order to calculate the ICUR, we need to calculate the cost and the Quality-Adjusted Life Year (QALY), since ICUR = cost/QALY.

7.3.12.1 *Cost*

Healthcare costs need to be evaluated from the perspective of the healthcare payer. This includes payments out of the federal government's and the communities' healthcare budget as well as patients' co-payments. The reference case analysis includes only the direct healthcare costs. These costs are directly related to the treatment of the disease (health services, hospitalization, etc.) as well as direct healthcare costs related to the disease in life years gained (e.g. occurring ADEs in the mid-term).

The productivity losses are indirect non-healthcare costs and will be presented in a separate, complementary analysis. These losses result from impairment of capacity to work. Short-term losses of productivity during paid work will be quantified by the human capital approach, i.e. the period-related income of the patient arm concerned. Productivity costs in the human capital approach are calculated by multiplying the total number of days of work absenteeism by the national average labour cost per day. Labour costs include employee wages and/or salaries and employer's social security contributions. The Belgian average labour cost per working day is estimated at €257.

7.3.12.2 *Utility*

A cost-utility analysis includes a HRQoL measurement in the assessment of treatment outcome. One of the trial's aims is to calculate the intervention's cost-utility to support a reimbursement request. To measure the impact on HRQoL we will use the EQ-5D-5L generic instrument, as recommended by the Belgian guidelines [33]. By using a generic utility instrument the comparability of the outcomes of these analyses may be improved. This generic instrument will be used to calculate the reference case and in a sub-analysis the disease specific instrument, the IKDC score, will complement this analysis.

The utility values which correspond to the EQ-5D-5L health states range from 0-1, where 0 is the value of death and 1 is the value of perfect health. These index values (utility values) will be calculated by using the value set of United Kingdom, since the Belgian value set is not (yet) available. QALYs will be used as an outcome measure which combines HRQoL and survival. QALYs are preferred for cost-utility analysis because of their clarity, simplicity, ease of application, and face validity [33, 34]. Additionally, sensitivity analyses will be performed to examine the effect of uncertainty about the utility values.

In the final report the conclusions drawn in the clinical study analysis will be combined with the outcomes of the cost-utility analysis.

7.4 Discussion

This LIBRƎ (Ligamys®, InternalBraceTM, REconstruction) study protocol is the first to compare DIS, IBLA and the gold standard ACL reconstruction for relative clinical efficacy and economic benefit. In this 2-year follow-up study subjective, objective and functional outcomes will be compared in patients treated with DIS, IBLA or ACL reconstruction. The hypothesis of this study is that DIS and IBLA will prove to be more effective than the conventional ACL reconstruction 6 months post-operatively, based on the IKDC score.

There are several cohort studies on the short- and mid-long-term result on ACL repair, providing a proof of concept and justifying further research. The theoretical advantages of primary ACL repair compared to reconstruction include preservation of the native ACL, its proprioceptive function, and avoidance of morbidity associated with graft harvesting. The preservation of the proprioceptors could attribute to a reduced recovery time and consequently a reduced need for costly physiotherapy and faster RTW and RTS [17, 20, and 21]. So far, only one study has been published which compared DIS with the ACL reconstruction [25]. In contrast to the study of Hoogeslag et al. [25], our study is single-blind which means that the patients and the physiotherapists were blinded in order to reduce bias. In addition, we explicitly asked the patients to think about the pre-rupture situation when filling-in the pre-operative IKDC score so there would not be misinterpretation. Another strength of this study is the standardised rehabilitation protocol for the physiotherapists.

Longitudinal MRI follow-up after ACL repair could give additional information on the healing of the ACL and potential failures. The longitudinal isokinetic and proprioceptive measurements will give feedback on the rehabilitation period and the claim that by maintaining your own ACL, the proprioceptors are maintained as well [48]. In addition to the clinical effectiveness analysis, a cost-utility analysis will be performed to provide economic support for the most indicated surgery technique after an acute ACL rupture.

The ideal scenario would have been to include the ACL reconstruction group in Study 1 and defer the ALC reconstruction until 5 weeks post-injury, but this is a design choice we did not make for several reasons. The DIS technique has to be performed within four weeks post ACL rupture and ACL reconstruction after the knee has regained its function, often after four weeks post ACL rupture. IBLA can be performed up to 12 weeks post ACL rupture. If ACL reconstruction would be performed within the four weeks this would not be according to clinical practice. If the patients in Study 1 would have to be recruited in a 3 instead of 2 arms comparison, 78 patients would have to be recruited within the 4 weeks after ACL rupture. Due to patient and doctors referral delay, many of the patients with a ruptured ACL report to our orthopedic departments after 4 weeks and therefore could not be included in the 3 arm comparison. We expected the early patient group (0-4 weeks) to be more challenging to recruit compared to the 5-12 weeks post-rupture group; 78 patients within 0-4 weeks would substantially prolong the inclusion period. Patient blinding would be more difficult as patients can easier guess which treatment they received depending on the rupture-surgery time. For both the 0-4 and 5-12 weeks groups, after inclusion a date of surgery will be chosen, afterwards the randomization will be performed. If first the randomization will be performed and afterwards the date of surgery is chosen with the patients, it could give a clue which type of surgery the patient will receive. Hence, we decided to organize our study according to the principle: randomize each patient to the possible treatment options at the time of presentation post-rupture, corresponding with common clinical practice.

Ahmad et al. conclude in their systematic review paper that there is sufficient evidence to support that DIS repair may be an effective modality for the treatment of acute proximal ruptures of the ACL [49]. However, comparative studies are lacking. Upcoming studies should compare the technique to ACL reconstruction with failure as an endpoint. Comparison to rigid methods of proximal fixation is also necessary to justify the need for dynamic fixation. In the LIBRƎ study, the aforementioned points are compared. Overall, there is evidence to suggest the potential space for ACL repair in the decision tree for individualized treatment planning.

7.5 Conclusions

This LIBRƎ study protocol is the first study to compare DIS, IBLA and ACL reconstruction for relative clinical efficacy and economic benefit. The outcomes of this study will provide data which could aid orthopedic surgeons to choose between the different treatment options for the surgical treatment of an acute ACL rupture.

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Chapter 8 ACL Repair: A Game Changer or Will History Repeat Itself? A Critical Appraisal

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ACL Repair: A Game Changer of Will History Repeat Itself? A Critical Appraisal.

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To prevent overlap with other chapters, a few adjustments concerning the original publication have been made for this chapter.

8.1 Abstract

Until the past decade the common thought was that the anterior cruciate ligament (ACL) was not able to heal and restore knee stability. In this manuscript a brief review of studies of the developers and the early adaptors of four different modern ACL repair techniques are presented. After promising short- to mid-term ACL healing results by the developers, the results of the early adaptors show more variety in terms of re-rupture and re-surgery for other reasons. Risk factors for failure are a young age, high pre-injury sports activity level, mid-substance ruptures and impaired integrity of the ACL bundles and the synovial sheath. There is a call for more clinical data and randomized clinical trials.

Conclusion: an important finding of the past decade is that the ACL is able to heal and subsequently re-stabilize the knee. Patient selection is emphasized: the ideal patient is a non-high athlete older than 25 and has an acute proximal one bundle ACL rupture. Further research will have to show if ACL repair could be a game changer or if history will repeat itself.

8.2 Introduction

Anterior cruciate ligament (ACL) repair returned to the spotlight with the introduction of modern ACL repair techniques. Although initially good short-term results after open ACL repair were presented in the 1970's, mid-term results deteriorated. Feagin et al. reported a significant re-injury risk after repair of the ACL in 17 out of 32 patients treated with an open repair and five-year follow-up [1]. The technique used for open ACL repair consisted of an arthrotomy, suturing of the ACL with drill holes in the femur and cast immobilization for 4–6 weeks [2]. This open repair technique was replaced by arthroscopic ACL reconstruction in the 1980s.

ACL reconstruction is the gold standard for surgical treatment of the ruptured ACL despite a number of problems related to this surgery: anterior knee pain (20%), kneeling pain (15%), hamstring muscle weakness following harvesting (10%), rotatory instability with a positive pivot shift (24%), re-rupture (6%, up to 28% in high-risk populations), and clinical failure (10%), and only 50% to 65% of non-high-level sport athletes return to their preinjury level of sports [3–5]. Another disadvantage of conventional ACL reconstruction is the extensive rehabilitation period. On average, patients return to their work after 11 weeks and are allowed to return to sports after 9–12 months [6]. ACL reconstruction has a huge socio-economic impact, as the majority of ACL injuries occur in people of working age [6,7]. ACL reconstructed knees and non-operatively treated knees demonstrated a risk of 4.71 times and 2.41 times, respectively, for development of moderate to severe arthritis compared with controls [8].

In a prospective study of 958 patients treated with bone–patellar tendon–bone or hamstring–tendon graft ACL reconstruction with two years of follow-up, the total risk of complications was 39% and the surgical revision risk for any reason was 28% [3]. Given the limitations and risks associated with the current gold standard treatment of an ACL rupture, there is room for improvement.

It was common thought that the ACL was not able to heal and restore knee stability, until Costa-Paz et al. and Steadman et al. documented the healing of the ACL in 2012 [9,10]. In the past decade, four different modern ACL repair techniques have been introduced. ACL repair could be a promising surgical technique with theoretical advantages over ACL reconstruction. Modern ACL repair techniques are less invasive compared to ACL reconstruction. If bone tunnels are drilled for the repair techniques, they are less than half the size of the bone tunnels needed for ACL reconstruction. There is no graft harvesting morbidity as no graft is needed. Preservation of the native ACL ligament and its proprioceptors contributes in the feedback on position and dynamic stability of the knee, which could reduce the rehabilitation period and therefore the economic burden [11]. ACL repair has the potential to preserve the native insertion site as well, which may in turn lead to more normal joint mechanics and decreased risk of post-traumatic osteoarthritis [12]. Another advantage is that in the event of a re-rupture, a standard ACL reconstruction can be performed. “No bridges are burned.” The author started with ACL repair in 2014 as an early adaptor and has performed more than 130 ACL repairs with three of the four ACL repair techniques. In this manuscript, a brief review of studies of the developers and the early adaptors of four different modern ACL repair techniques are presented. The present status and considerations for the future of ACL repair and its research are shared.

8.3 Literature by the developers

8.3.1 Dynamic intraligamentary stabilization

In 2012, Sandro Kohl et al. published an animal study of a new ACL repair technique, dynamic intraligamentary stabilization (DIS, also known as Ligamys, Mathys Ltd., Bettlach, Switzerland) [13]. The ruptured ACL is brought back to its origin with polydioxanone sutures (PDS) and the knee is stabilized with a strong suture alongside the ACL, which is fixed in the tibia with a spring–screw system (Figure 8.1). In 2014, Sandro Kohl et al. describe a potential biomechanical solution for the ACL repair failures in the past [14]. A rigid fixation was used to repair the ACL, which failed upon cyclic loading. By creating a dynamic fixation that restored anteroposterior (AP) stability and could withstand the repetitive cyclic forces, a biomechanically stable environment was created in which the ACL could heal [14]. The next year, the results of the first 10 patients treated with DIS with a 2-year follow-up were reported [15]. This treatment resulted in stable clinical and radiological healing of the torn ACL in all but one patient of this first series. They attained normal knee scores, reported excellent satisfaction and could return to their previous level of sporting activity.

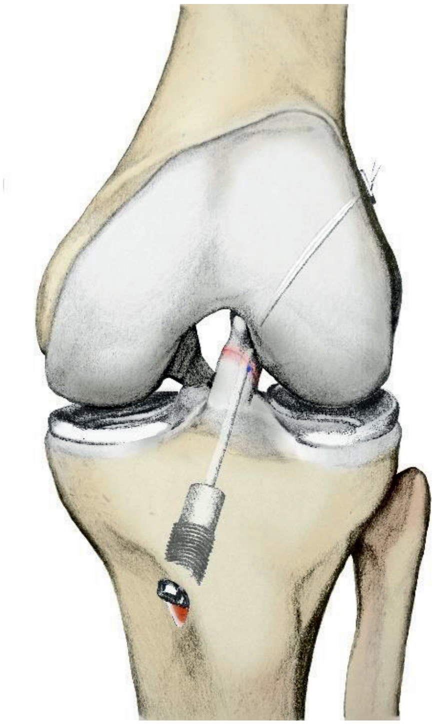

Figure 8.1 Left knee, frontal view. Anterior cruciate ligament (ACL) repair using dynamic intraligamentary stabilization.

A case series of 278 patients treated with DIS for an acute ACL rupture with a mean follow-up of 14 months showed non-inferior patient-reported outcome measures (PROMs) compared to preoperatively, stable AP knees and a re-rupture risk of 2.9% [16]. In summary, promising results of a novel treatment for acute ACL repair were presented by the developers of the DIS technique at the end of 2014. In 2016, Kohl et al. reported a high risk of secondary interventions in a group of 50 patients with a 2-year follow-up. In this group, 10% developed instability, 10% needed an arthrofibrolysis, and 60% required removal of the tibial screw [17].

8.3.2 Suture tape augmentation/ InternalBrace ligament augmentation

The suture tape augmentation (STA) technique, also called independent suture tape reinforcement or internal bracing ligament augmentation technique (InternalBrace, Arthrex GmbH, Naples, FL, USA) is a repair technique that can be used for all knee ligaments, including the ACL, and for ankle, elbow and shoulder ligaments as well. The ruptured parts of the ACL are brought together with a lasso suture and protected with a 2 mm wide high-strength tape that acts as an internal brace to provide an environment in which the ACL can heal (Figure 8.2) [18].

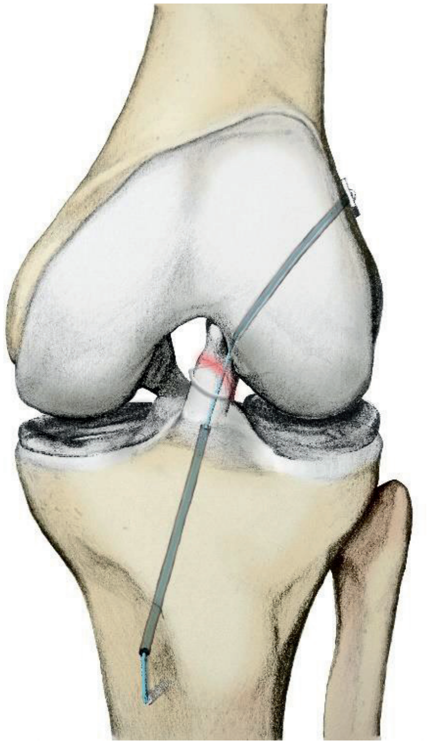

Figure 8.2 Left knee, frontal view. Anterior cruciate ligament (ACL) repair using suture tape augmentation.

This internal brace reinforces the ligament as a secondary stabilizer, encouraging natural healing of the ligament by protecting it during the healing phase and supporting early mobilization. Heitmann et al. published in 2014 a biomechanical study on porcine. In this study, the augmented suture repair of the ACL provides significantly higher stability compared with isolated suture repair or reconstruction with hamstring tendons [19]. MacKay et al. published in 2015 a review on ligament augmentation with the internal bracing technique containing the one-year follow-up results of 68 patients [20]. The results of this study suggest that at short-term follow-up, repair with the STA technique is at least as effective in restoring stability and function to the knee as traditional ACL reconstruction surgery. Two-year follow-up results of 42 patients treated with the STA technique by the developer showed that a meaningful Knee Injury and Osteoarthritis Outcome Score (KOOS) sport and recreation change and significant improvements in the KOOS Visual Analogue Pain Scale (VAS pain), Veterans RAND 12-item health survey (VR-12) physical scores as well as a significant decrease of the Marx activity scale in comparison to preoperative scores are demonstrated [21]. Two of the 42 patients (4.8%) reported an ACL re-rupture. They conclude that repair with this technique could be clinically relevant as a treatment option for patients with an acute, proximal ACL rupture that is not retracted and is of good tissue quality.

8.3.3 Suture anchor primary ACL repair

Difelice et al. published in 2015 the results of an early follow-up of 11 consecutive cases treated with suture anchor primary repair (SAPR) of the ACL with a mean follow-up of 3.5 years [23]. For the SAPR technique, the ruptured ACL was sutured starting at the intact distal end of the ligament and advanced in an alternating, locking Bunnell-type pattern up to the avulsed end for both the anteromedial and posterolateral bundle. Sutures were fixed with a suture anchor at the anteromedial and posterolateral femoral origin site of the ACL (Figure 8.3). In their study, one patient had a re-rupture and one patient had a KT-1000 AP laxity side-to-side difference of 6 mm. They concluded that this technique can achieve short-term clinical success in a carefully selected subset of patients with proximal avulsion tears and excellent tissue quality [23]. These clinical outcomes were maintained at a mean follow-up of 6.0 ± 1.5 years [24]. In the following years, Difelice and van der List have performed extensive work on modern ACL repair. They proposed a treatment algorithm for ACL injuries that is based on tear location and tissue quality [25,26]. A retrospective study on 52 repairs and 90 reconstructions showed that following primary repair, patients had better range of motion and trends towards fewer complications than with reconstruction [27].

In a cohort study, 56 consecutive patients underwent arthroscopic ACL SAPR, of which the latter 27 patients (48.2%) received internal bracing in addition to ACL SAPR. They reported good objective and subjective outcomes at a 3.2-year follow-up in a carefully selected population, with a failure risk of 7.4% for patients treated with ACL SAPR with internal bracing and 13.8% for patients without internal bracing. There were no statistically significant or clinically relevant differences in subjective outcomes [28]. In a large cohort study, it was noted that 44% of patients with an ACL rupture had repairable ACL tears. Primary repair was more likely to be possible in older patients, patients with lower BMI and when surgery was performed within four weeks of injury [29]. Treatment failure was found to be significantly higher in the age group <22 years (37.0%) as compared to the 22–35 years (4.2%) and the >35 years (3.2%) groups [30]. Different studies showed that tear location and tissue quality on preoperative MRI can predict eligibility for arthroscopic primary ACL repair, and postoperative MRI was found to accurately predict the chance of re-rupture of the primarily repaired ACL [30–32].

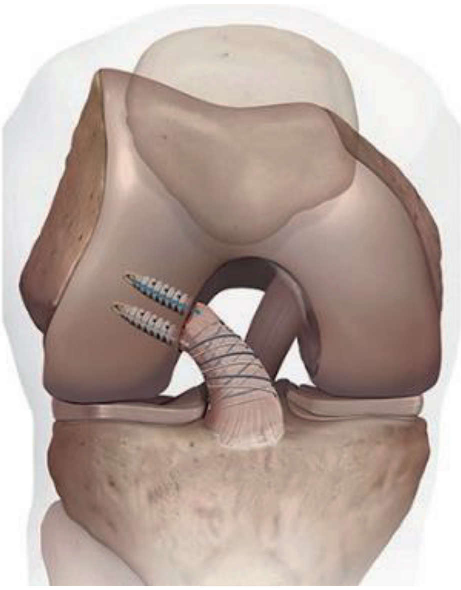

Figure 8.3 Right knee, frontal view. Anterior cruciate ligament (ACL) repair using suture anchors.. This image can be found in the 'ACL Primary Repair Surgical Technique' brochure, Arthrex GmbH [21].© Reprinted with permission of Arthrex GmbH

8.3.4 Bridge-enhanced ACL repair

Compared to the previously mentioned repair techniques, extensive fundamental research and animal studies have been published on the bridge-enhanced ACL repair (BEAR) technique [22,33–38]. The BEAR technique involves suture repair of the ligament combined with a bioactive scaffold to bridge the gap between the torn ligament ends (Figure 8.4). This blood-laden scaffold implant prevents the synovial fluid to "wash out" the regenerative cells and provides a structure and environment which facilitates the ACL healing. In 2016, the first-in-human cohort study compared BEAR with ACL reconstruction, and outcomes were assessed three months postoperatively. The results of this study suggested that the BEAR procedure had a risk of adverse reactions low enough to warrant a study of efficacy in a larger group of patients [39]. Within the 2 year follow-up, there were no graft or repair failures, and BEAR produced similar outcomes to ACL reconstruction with a hamstring autograft [40]. A randomized controlled trial (RCT) of 65 BEAR versus 35 ACL reconstruction patients showed similar outcomes in both treatment groups for PROMs and AP knee laxity two years postoperatively in a young and active cohort [34]. Re-injuries that required a second ipsilateral ACL surgical procedure occurred in 14% of the BEAR group and 6% of the ACL reconstruction group. Eight of the patients that converted from BEAR to ACL reconstruction in the study period had similar primary outcomes to patients who had a single ipsilateral ACL procedure [34].

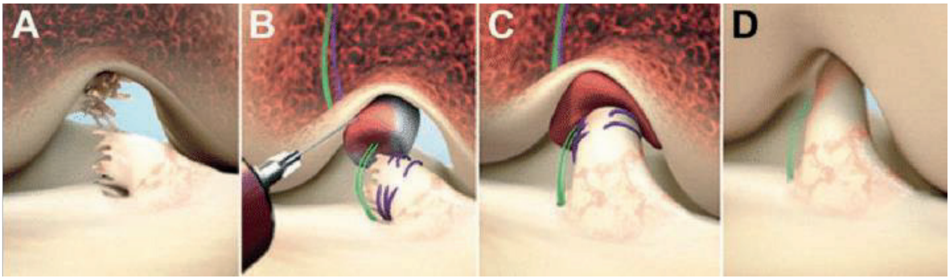

Figure 8.4 Right knee, frontal view. Anterior cruciate ligament (ACL) repair using bridge-enhancement. Bridge-enhanced anterior cruciate ligament (ACL) repair, frontal view right knee: (a) Ruptured ACL; (b) The scaffold is saturated with the patient's blood; (c) The tibial stump is pulled up into the saturated scaffold; (d) Healing of the ACL [32]

8.4 Early adaptors

8.4.1 Dynamic intraligamentary stabilization

Most ACL repair studies by early adaptors have been published on DIS. After promising short- to mid-term results by the developers, the DIS results by the early adaptors show more variety. Five year follow-up has been reported by Kösters et al. on 65 patients treated with DIS [41]. Eight patients (12.3%) had a re-rupture, and four (6.2%) patients had to be revised performing an arthrolysis due to extension deficit. Ahmad et al. report a minimum five years' survival rate after primary ACL DIS repair of 70% [42]. This value dropped to 56% in highly active patients performing competitive sports. Patients not suffering failure of repair demonstrated adequate restoration of knee laxity and high satisfaction.

Several short-term case reports showed a failure risk of 15% or more and a high re-surgery risk for other reasons than revision [43–47]. Other short-term case reports confirm the positive results of the developers group with an ACL failure of less than 10% and a low re-surgery risk for other reasons than revision [46,48,49]. Ateschrang et al. performed an arthroscopy on 47 patients treated with DIS after a minimum postoperative interval of six months for semiquantitative evaluation of ACL integrity, function and scar-tissue formation [50]. Full restoration of the ACL volume was affirmed in 30 (63.8%) patients and two-thirds restoration in 13 (27.7%). Hypertrophic scar formation was observed in 23 (48.9%) patients. Deficient ACL recovery was noted in four patients (8.5%), of which no one required secondary reconstruction surgery.

Two RCTs have been published. Hoogeslag et al. randomized 48 patients who underwent DIS (24 patients) or ACL reconstruction (24 patients) [51]. In the DIS group, 8.7% experienced a re-rupture and 20.8% were treated with repeat surgeries versus 19% re-ruptures and 12.5% repeat surgeries in the ACL reconstruction group. DIS was not inferior in terms of an International Knee Documentation Committee (IKDC) subjective score two years postoperatively. Kösters et al. randomized 85 patients between DIS (43 patients) and ACL reconstruction (42 patients) [52]. A total of seven patients (16.3%) in the DIS group experienced clinical failure and underwent single-stage revision. In the ACL reconstruction group, five patients (12.5%) experienced failure of the reconstruction procedure; four (10%) of these patients required 2-stage revision. Anterior tibial translation measured by Rolimeter testing was significantly increased after ACL repair with DIS, whereas clinical failure was similar to that after ACL reconstruction. In addition, functional results after ACL repair with DIS for acute tears were comparable with those after ACL reconstruction.

Risk factors described for failure after DIS repair are: young age, high pre-injury sports activity level, high knee laxity, mid-substance ruptures, and impaired integrity of the ACL bundles and the synovial sheath [45,53].

8.4.2 Suture tape augmentation/ InternalBrace ligament augmentation

In a cohort study of adolescent patients (7–18 years old), 22 patients treated with STA were compared with 157 reconstruction patients [54]. The cumulative incidence of graft failure in the first three years after surgery was 48.8% (95% CI, 28.9–73.1%) in the STA group, as opposed to 4.7% (2.1–10.3%) in the reconstruction group. There was no difference in return to sports between the groups. Among individuals who did not re-rupture their ACL, the PROMs as well as the range of motion were comparable between both groups. These results led to the conclusion that the high risk of failure for the STA group in this short-term follow-up should be considered when selecting the treatment for adolescent patients with an ACL injury. Ortmaier et al. matched 24 patients treated with STA with 25 hamstring and 20 quadriceps tendon reconstruction patients with a minimum follow-up of 12 months [55]. Overall, the return to sports rate was 91.3%. There were no significant differences in the number of sport disciplines and the return to sports time within or among the groups. Re-rupture or re-surgery risks are not mentioned. In a retrospective study of 27 patients with a mean age of 27.4 ± 8.6 years and a minimum of 2 year follow-up (range 2.0–3.8 years), a graft failure risk of 15% was reported [56]. Schneider et al. reported a re-surgery risk of 3% in a group of 88 STA patients with a mean age of 42 ± 13 years and a mean follow-up of 21 months. Patients' age (>40 years), BMI (>30) and coexisting ligament or meniscal injuries did not seem to influence postoperative functional results [57]. Heusdens et al. published a prospective case report on their first 35 patients treated with STA with a 2 year follow-up. Four patients (11.4%) suffered from a re-rupture and three other patients (8.6%) needed a re-intervention for another reason than re-rupture. A pre-operative Tegner score of ≥ 7 and grade 3 ACL healing on MRI at six months postoperatively were associated with a higher risk of re-rupture [58].

8.4.3 Suture anchor primary ACL repair

No results have been published yet by early adaptors of the SAPR technique. Achtnich et al. and Hoffmann et al. have performed ACL proximal repair with a comparable technique to the SAPR technique, but there are some differences [59,60]. Instead of two separate bundles, the ruptured ACL is reattached as one bundle and microfracturing is performed. Achtnich et al. describe in their case-control study comparable functional outcomes between 20 patients treated with proximal re-fixation of the ACL using knotless suture anchors and microfracturing versus 20 patients in the control group treated with single-bundle ACL reconstruction [59]. Although the failure risk was 15% in the ACL re-fixation group and 0% in the reconstruction group, they suggest that re-fixation of the ACL is a feasible treatment option in carefully selected patients. Hoffmann et al. describe in their retrospective study on 12 patients with five year follow-up good to excellent clinical mid-term outcomes in 75% of the patients [60]. Three patients (25%) experienced a failure. In cases of additional serious damage to extensor structures or systemic rheumatic disease, loss of function and unsatisfying clinical results occurred.

8.4.4 Bridge-enhanced ACL repair

No results have been published yet by early adaptors of the BEAR technique.

8.5 Conclusions

ACL repair could be a promising surgical technique with previously mentioned theoretical advantages over ACL reconstruction. The question remains whether these advantages can be demonstrated in clinical practice and whether the mid-term results will not deteriorate, as in the 1970's with the old ACL repair techniques. The four previously described ACL repair techniques show promising short term results published by the developers, which encouraged further research. Through time, clinical results of early adaptors of the ACL repair techniques were published and the discussion became more diverse. Compared to the developers' results, there seemed to be an overall higher re-rupture risk and re-surgery risk for other reasons than revision. Currently the debate on ACL repair is continuing. The publications of the past few years taught us that the ruptured ACL is able to heal, but patient selection is critical. Future research will have to show if ACL repair could be a game changer or if history will repeat itself.

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Chapter 9 General Conclusion and Future Perspectives

9.1 General conclusion

Anterior cruciate ligament (ACL) repair returned in the spotlight with the introduction of modern ACL repair techniques. In 2015, proof of concept for the Dynamic Intraligamentary Stabilization (DIS) and Suture Tape Augmentation (STA) ACL repair techniques was given, but the literature on these novel repair techniques was scarce. As early adaptors of these new techniques, we felt that we could contribute to the discussion whether these novel repair techniques could be a treatment option for the acute ruptured ACL. For this thesis, several studies have been conducted which led to further insight in modern acute ACL repair with the STA and DIS technique. The aim of this thesis is to contribute to the discussion whether these novel repair techniques could be a treatment option for the acute proximal ACL rupture.

Previously it was common thought that the ruptured ACL responds differently than the other knee ligaments and that the ACL is not able to heal [1]. The continuous flow of synovial fluid in the knee hampers the formation of a stable fibrin–platelet clot between the ruptured ends of the ACL, which prevents the formation of stable scar tissue [2]. By bringing the ruptured ACL ends tight against each other, the synovial fluid does not prevent the formation of stable scar tissue and the ACL should be able to heal.

Our studies confirm the ability of the ACL to heal with the DIS and STA technique and subsequently re-stabilize the knee [3-5]. The post-operative antero-posterior (AP) knee laxity which was measured with the Rolimeter, does not show a significant side to side difference up to two years postoperative. Longitudinal conventional MRI follow-up shows healing of the ACL between 6 and 12 months. This status remained unchanged between 12 and 24 months post-operatively.

An important result after ACL repair is the re-rupture risk. The re-rupture risk was high (> 50%) at mid-term follow up in the 70´s with the classical ACL repair technique. This led to abandonment of ACL repair in favor of ACL reconstruction. ACL reconstruction has nowadays a commonly accepted re-rupture risk between 3 and 7 % within 2 year follow-up [6]. In this thesis the re-rupture risk results of three case series with 2 year follow-up are presented. The STA re-rupture risk was 4.8% in the case series which presented the data of the developer of the STA technique. In our early adaptor STA patient group from Antwerp the re-rupture risk was 11.4%. A similar lower re-rupture risk in the developer data groups, compared to the early adaptor groups is described for DIS as well. In contrast to our smaller DIS case series with a re-rupture risk of 0%, several short-term early adaptor DIS case series showed a failure risk of 15% or more [7]. In an early adaptor study of 57 patients with 5 year follow-up, the survival rate after primary ACL repair with DIS technique was 70%. This value dropped to 56% in highly active patients performing competitive sports [8]. The higher re-rupture risks was not reflected in the three RCTs that have been published so far [9-11]. The two DIS versus ACL reconstruction and the BEAR versus ACL reconstruction RCTs with a 2 year follow-up did not show a significant re-rupture risk difference. These three RCTs reported a non-inferiority or comparable results for the PROMs as well. The re-rupture risk after modern ACL repair is a focus of discussion and more RCTs, as we undescribed in the LIBRƎ study protocol, are needed.

To reduce the re-rupture risk after ACL repair, risk factors should identified. Risk factors for failure after DIS ACL repair have been described: young age, high pre-injury sports activity level, high knee laxity, mid-substance ruptures, impaired integrity of the ACL bundles and the synovial sheath [12, 13]. Risk factors for a re-rupture with the STA technique have not previously been described for adults. Our early adaptor STA case series with four patients who experienced a re-rupture suggests a higher risk on re-rupture for patients with a pre-operative Tegner ≥ 7 and for patients with grade 3 ACL healing on MRI at 6 months post-operatively. A trend towards significance ($P = 0.061$) for the effect of young age, below 25 years, for a re-rupture was observed. In a five-year follow-up study with 57 DIS patients Ahmad et al. underlined the potential of ACL repair, but also highlighted the danger of the procedure if strict patient selection is not appreciated [8]. Patient selection could be an important factor to reduce the re-rupture risk.

One of the supposed advantages of ACL repair is the reduced rehabilitation period and therefore economic burden. Compared to reconstruction, the ACL repair techniques are less invasive and the preservation of the native ACL ligament and its proprioceptors could contribute in the feedback on position and stability of the knee. This reduced rehabilitation period should be reflected in the return to sports (RTS) and return to work (RTW) time span data. Data on the time span for RTS and RTW after ACL repair and even after reconstruction are not extensive. A quick rehabilitation was observed in our STA and DIS case series with a median postoperative RTW of respectively 5.5 and 5.4 weeks. A median postoperative RTW of 11 weeks after ACL reconstruction has been described by Groot et al. [14]. In a matched study between DIS and reconstruction, the postoperative RTW time span was similar for both groups [15]. The DIS patients did benefit from a reduction in absence from work of almost 1 month, related to the earlier timing of surgery for DIS. The median RTS, after fulfilling the return to sports criteria, in our early adaptor STA case series was 6 months. RTS time span data for ACL reconstruction is scarce as RTS is often depicted as a percentage of the group at one or two years postoperative. Even if the ACL reconstruction patient has fulfilled the return to sports criteria, a time span of 9-12 months is considered as a minimum for RTS, due to the ligamentization phases of the ACL graft. More RTW and RTS data is needed to prove the supposed advantage of a reduced rehabilitation period after ACL repair.

A higher risk of secondary interventions (for re-rupture as well as other complications) has been reported after DIS [7]. This is not confirmed in our case reports. We believe that the 20% secondary interventions in our STA group and the 33.3% in our DIS group is similar to the re-surgery rate reported in other ACL reconstruction studies. Rousseau et al. observed a re-surgery rate of 28% in their cohort of 958 ACL reconstruction patients [6]. Two randomized controlled trials comparing ACL DIS repair versus ACL reconstruction, report an overall re-surgery rate of 25.6% and 29.5% in the ACL DIS repair groups versus 22.5% and 33.3% in the ACL reconstruction groups [10, 11].

Modern ACL repair was still in its infancy when we started in 2014. Starting a new technique involves “start-up problems”. To help other orthopedic surgeons to get acquainted with ACL repair, we have performed two studies in which we share our experience. Our step by step description of the STA ACL repair technique gives guidance how this surgery can be performed. We advise to perform STA ACL repair on proximal ruptures. The ACL stump should be of good tissue quality and not retracted. No gap between the rupture ends is allowed after the repair. In the event of a re-rupture, a standard ACL reconstruction can be performed, “no bridges are burned”. A time limit of approximately three months post-rupture is suggested for this surgery [16]. In the second study we present the technical difficulties and outcomes of our first 15 patients treated with DIS with 2 year follow-up, as well as tips and tricks to optimize the surgical outcomes of ACL repair using the DIS technique [4]. The manufacturer of the DIS implants advises to treat the patients within 3 weeks after the ACL rupture. This changes the time-management of an ACL rupture from a chronic injury to a sub-acute injury, a new pathway is needed to treat these patients in time. With these prior arrangements, we managed to treat acute ACL ruptures within 3 weeks of injury, but were not able to treat most ACL ruptures within this time-frame. Patient delay and delay by referring doctors were among the reasons why most ACL ruptures were treated after 3 weeks. Nowadays we perform a DIS ACL repair up to 4 weeks post rupture. We believe that this period can be even longer, as long as the ACL stump is ruptured proximally, shows good tissue quality and is able to make full contact with the proximal stump.

Hoogeslag et al. have performed a biomechanical study on the intact ACL, the ruptured ACL, DIS repaired and STA repaired knee [17]. They conclude that only the DIS repaired knee resulted in restoration of anterior tibia translation values similar to the ACL-intact knee. In their study the anterior tibia translation after DIS is even less compared to the intact ACL. The anterior tibia translation after STA is more compared to the intact ACL. We believe that DIS repair has a higher chance of over-constraining the knee, which can lead in a “not natural” feeling in the knee and arthrofibrosis. This could explain why we had several DIS patients, especially slender women, who regained their natural knee movement after removal of the DIS. We therefore prefer not to exceed 50 N on the DIS implant for slender women instead of the advised 60 N [4].

The question has been raised whether MRI could be useful in the assessment pre- and postoperative ACL repair. If MRI could facilitate in differentiating between a proximal and mid-bundle rupture, this could assist in the preoperative planning and patient information. Van der List et al. concluded that their MRI classification system for different tear types was reliable in assessing tear location in acute ACL injuries [18]. In our experience grading the ACL location on MRI is difficult. ACL ruptures can be partial, oblique, retracted and can even be at different locations in the ruptured ACL [19, 20]. In acute ACL injuries, the presence of edema and hemorrhage impede the exact demarcation and location of the ACL rupture. A definitive indication for repair will therefore be made during the arthroscopy. We advise to explain these circumstances to the patient preoperatively and start the ACL surgical procedure with an arthroscopy if the rupture location on MRI is within the proximal 50%. During the arthroscopy the ruptured ACL can be assessed directly: if repairable (proximal rupture, good tissue quality and not retracted) the repair procedure can continue, otherwise a reconstruction should be performed. The most frequent complications we encountered on MRI after primary ACL repair include absence of healing, arthrofibrosis and re-rupture of the ACL repair. The healing process of the repaired ACL is different compared to ACL reconstruction, without a "ligamentization" phase. An overall normal ACL healing on MRI was observed in our STA and DIS groups in respectively 45% and 67%, no healing was observed in respectively 19 and 13%. It is important to note that absence of healing on MRI is not always accompanied by instability of the knee, persistent high signal intensity within the repair can be seen for more than 12 months postoperatively in clinically stable knees. This discrepancy between clinical and imaging findings may be explained by both restoration of the ACL's integrity and scar tissue formation, and clinical recovery of ACL function could be a resultant to both of them [21]. Absence of healing on MRI should be interpreted with caution, and correlation with clinical findings is necessary.

The number of reviews on ACL repair is remarkable. In the last four years, 12 reviews have been published on ACL repair. Two reviews favor ACL reconstruction over ACL repair. Three reviews address the poor amount of high-quality evidence, which makes it difficult to establish the role of ACL repair. The seven other reviews highlight the promising results or describe ACL repair as a (safe) treatment option for the acute ruptured ACL [7]. The overall consensus in these reviews is that prospective studies comparing different ACL repair techniques with ACL reconstruction with sufficient follow-up are needed. We have underwritten this call and started the LIBRƎ study, sponsored by the research foundation Flanders (FWO Vlaanderen, Belgium). This study compares DIS (Ligamys) with STA (Internal Bracing) and Reconstruction [22]. The future outcomes of this study will provide data which could aid orthopedic surgeons to choose between the different treatment options for the surgical treatment of an acute ACL rupture.

In conclusion: this thesis "An Introduction to Modern Anterior Cruciate Ligament Repair" contributes to the discussion whether these novel repair techniques could be a treatment option for the acute proximal ACL rupture. The ability of the ACL to heal and subsequently re-stabilize the knee with the DIS and the STA repair techniques is confirmed. A step by step description of the ACL STA surgical technique as well as tips and tricks for the DIS repair technique are shared. The healing of the ACL can be monitored with MRI, but correlation with clinical findings is necessary. Based on the two case-series on acute ACL repair with the STA technique it seems that this technique could be clinically relevant as a treatment option for patients with an acute, proximal ACL rupture. A careful patient selection is advised. To reduce the risk on a re-rupture, the ideal patient would be a non-high level athlete (Tegner score of < 7) and older than 25 years with an acute proximal ACL rupture of good tissue quality which is not retracted. The call for more data on ACL repair, especially RCTs, is underwritten in the LIBRƎ study protocol and considerations for the future of ACL repair research are given.

9.2 Future perspectives

There are several issues that should be addressed in future ACL repair research. High-quality large RCTs between ACL reconstruction and ACL repair, as well as between the different ACL repair techniques are needed. PROMs, RTW, RTS, instrumented knee laxity measurements, MRI outcome, cost-utility analysis, re-surgeries for another reason than re-rupture, re-rupture and failure risks and their risk factors should be addressed in these studies. As young patients (below the age of 25) and high-level sport athletes seem to have a higher risk on re-rupture following ACL repair, possibly this subgroup is better treated with ACL reconstruction. Although these groups have a higher risk on failure after ACL reconstruction as well, the reported failure chance in the ACL repair case reports are higher (up to 44% at 5-year follow-up) [12].

The reported average age for an ACL rupture varies between 29.1 and 33.9 years, not only young and highly active teenagers rupture their ACL. In addition, proximal ACL ruptures are to occur more in the age group of 25 years and older. Several publications emphasize patient selection criteria of patients older than 25 years and the non high-level sport athletes with an acute proximal bundle ACL rupture. These patients could be the ideal candidate for ACL repair. That raises the question whether ACL repair is needed altogether for this group. Conservative treatment, rehabilitation under supervision of a dedicated physiotherapist is an underestimated treatment. RCTs between conservative management, ACL repair and ACL reconstruction could provide an answer for the patient group older than 25 year olds and non-high-level sport athletes. A downside for conservative ACL treated patients with persistent instability, is the diminished possibility for a successful ACL repair after 3-6 months [7].

One of the major problems of ACL repair is the higher re-rupture risk reported in several early adaptor case series. This should be reduced before ACL repair will be accepted by the orthopedic community as a viable alternative for ACL reconstruction. Another interesting development of the past decade, is the improved understanding in the anterolateral complex. ACL repair together with an anterolateral extra-articular procedure could reduce the re-rupture risk. This could be especially interesting for patients younger than 25 years and high-level sport athletes. As the anterolateral extra-articular procedure is a relative simple procedure which can be performed together with ACL repair, this could be an improvement that can already be implemented [7].

Another option to reduce the re-rupture risk could be to improve the ACL healing. Ateschrang et al. describes an arthroscopically confirmed complete restoration of the DIS repaired ACL in 64% after a minimum post-operative interval of 6 months [21]. Hypertrophic scar formation was observed in 49% of the patients. In our DIS and STA case series, we describe a respectively 67 % and 45% grade 1 healed ACL on MRI [23]. To improve the healing of the ACL, ACL healing stimulating factors could be introduced. But which ACL healing stimulating factors, how to deliver them and maintain these factors within the ACL wound site, surrounded by the “hostile” synovial fluid? Collagen application has already been described to provide healing benefits with superior clinical outcome after DIS ACL repair [24]. With the promising introduction of the bridge-enhanced ACL repair (BEAR) technique, which uses a bio-active scaffold to stimulate the ACL healing a further step could have been made to improve the ACL healing [9]. Future studies in this area could bring ACL repair to “the next level”.

New developments in quantitative MRI (qMRI) can play an important role in ACL repair research. qMRI can, in a non-invasive way, provide information on ACL microstructure and its degree of organization by measuring tissue biophysical properties, e.g. diffusion, T2*. Recent studies have shown that DTI and UTE T2* are promising biomarkers for monitoring ACL healing following surgery [25, 26].

ACL reconstructed knees and non-operatively treated knees with an ACL rupture demonstrated a 4.71 times and 2.41 times risk, respectively, for development of moderate to severe arthritis compared to controls. ACL repair preserves the native insertion site as well as the native ACL proprioceptors, which may in turn lead to more normal joint mechanics and decreased risk of post-traumatic osteoarthritis. Long-term follow-up has to show if, in contrast to ACL reconstruction or conservative treatment, modern ACL repair protects against the increased risk of post traumatic osteoarthritis [7].

ACL reconstruction still remains the gold standard, until more ACL repair data can prove otherwise. Therefore all ACL repair patients should be closely monitored and followed-up, preferably in high-quality large RCTs [7].

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Chapter 10 Summary

Modern anterior cruciate ligament (ACL) repair was still in “it’s child´s shoes” (translation of Dutch proverb) in 2015. In the following years it became a hot topic in the orthopedic community.

Excellent short-term outcomes on open ACL repair were reported in the ´70s with open ACL repair, however high risks of failure were reported after mid-term follow-up. ACL repair was abandoned in favor of ACL reconstruction, which became the gold standard for surgical ACL treatment in the ´80s of the last century. Given the limitations and risks associated with the current gold standard treatment of an ACL rupture, there is room for improvement. Modern ACL repair has theoretically several advantages compared to ACL reconstruction. Modern ACL repair techniques are less invasive and there is no graft harvesting morbidity. Preservation of the native ACL ligament and its proprioceptors contributes in the feedback on position and dynamic stability of the knee, which could reduce the rehabilitation period and decrease the risk of post-traumatic osteoarthritis. Due to the high failure risk of open ACL repair in the past, the orthopedic community is reluctant to start with ACL repair. Data on the modern ACL repair techniques will have to show if the theoretical advantages can be proven in daily practice or if history will repeat itself.

Novel ACL repair techniques have been introduced this last decade. The aim of this PhD is to contribute to the discussion if these novel repair techniques could be a treatment option for the acute proximal ACL rupture.

If a surgeon would like to start with a new technique, the surgeon prepares him or herself by getting familiar with the surgical technique. In this thesis, the suture tape augmentation (STA) surgical technique is described in detail (Chapter 2). Drawings, pictures and a video have been made to explain the surgical technique, step by step. The indication for STA ACL repair and the rehabilitation protocol as well as the advantages, disadvantages, including the limitations are given. Chapter 2 could contribute in the knowledge of STA ACL repair surgical technique.

ACL repair data on the STA ACL repair technique was and still is not extensive. Only one case series of 68 patients with one year follow-up, treated by the developer of the STA technique, was published in 2015. In chapter 3 the results of 42 patients who have been treated by the developer of the STA technique are described. This is the first case series with a 2 year follow-up of the STA ACL repair technique. Several patient reported outcome measures (PROMs) showed a meaningful and or significant improvement (KOOS sport and recreation change, VAS-pain and VR-12 physical scores) in comparison to pre-operative. The Marx activity scale demonstrated a significant decrease in comparison to pre-operative. Two of the 42 patients (4.8%) reported an ACL re-rupture. The conclusion of this study is that repair with the STA technique could be clinically relevant as a treatment option for patients with an acute, proximal ACL rupture which is not retracted and of good tissue quality.

Chapter 4 reports on our own data of 35 patients who have been treated with the STA ACL repair technique at the Antwerp University hospital. This is the first prospective case-series with independent data of the STA ACL repair on adults. The clinical results, re-rupture risk factors and magnetic resonance imaging (MRI) outcomes with a 2 year follow-up after STA ACL repair are reported. This case series shows that STA ACL repair leads to a stable knee, favorable patient-reported outcome measures (PROMs) and quick rehabilitation after surgery, with a median return to work (RTW) period of 5.5 weeks and a return to sports (RTS) period of 6 months. The re-rupture risk is 11.4% and the re-surgery for another reason than re-rupture is 8.6%. A pre-operative Tegner score (activity score) of ≥ 7 was associated with a higher risk on re-rupture. Another significant association was observed between the grade of ACL healing on MRI six months post-operatively and re-rupture ($P = .006$). When analyzing the effect of age (< 25 versus ≥ 25) on re-rupture, a trend towards significance was observed ($P = .061$). This study shows that treatment of the acute, repairable ACL with the STA technique leads to a stable knee and favorable PROMs. However, the re-rupture risk of 11% within the 2-year follow-up is a concern.

A different ACL repair technique is the dynamic intraligamentary stabilization (DIS) technique. In contrast with the STA technique, the internal brace of the DIS system is dynamic due to the distal fixation in a spring-screw system. This should lead to a more biomechanically stable environment of the knee. The manufacturer of the DIS system advices to repair the ACL within 3 weeks after the rupture, whereas for the STA technique the advised maximum is 3 months. For ACL reconstruction there is no time limit. This changes the management of the ruptured ACL for the DIS technique in a semi-acute trauma. In chapter 5, our experience with the first DIS ACL repairs at the Antwerp University Hospital is described. Starting a new technique involves 'start-up problems'. Organizing a new patient pathway to treat the patients within 3 weeks after the trauma, dealing with 'new' arthroscopic instruments and suture management, post-operative problems and MRI interpretation after ACL repair are examples of the issues we encountered. In two years, 15 patients have been treated with this novel ACL repair technique. From the beginning we meticulously recorded the pre-operative, intra-operative and post-operative problems and our solutions. Tips and tricks that could assist surgeons who are starting with the DIS technique are shared.

MRI can be used to evaluate the (repaired) ACL. It is important for the radiologist and orthopedic surgeon to get familiar with the normal MRI appearance of ACL healing after repair, and its potential complications in order to avoid misinterpretation and subsequent unnecessary or delayed surgical intervention. In chapter 6, we have described the normal appearance of the repaired ACL on MRI as well as the possible complications of these techniques. The healing process of the repaired ACL is different compared to ACL reconstruction, without the "ligamentization" phase. Although patients may demonstrate signs of ACL healing on MRI following repair, absence of healing on MRI within the repair can be seen for more than 12 months postoperatively in some patients with clinically stable knees. MRIs after ACL repair should therefore be interpreted with caution, and correlation with clinical findings is necessary.

Multiple reviews on ACL repair have been written on a relatively small amount of case-series the last few years. All these reviews conclude that there is an urge for more data on ACL repair. Long-term follow-up and especially randomized controlled trials between ACL reconstruction, the gold standard and the new ACL repair techniques as well as between the different ACL repair techniques are needed. In 2017, the application for the LIBRƎ study, a multi-center prospective RCT comparing DIS, STA and reconstruction in individuals with an acute ACL rupture was granted by the FWO (Research Foundation Flanders) for the TBM (Applied Biomedical Research with a Primary Social finality) project. With the author as principal investigator, the study started in 2018. The protocol of the LIBRƎ study has been published (Chapter 7). The validated PROMS, clinical, proprioceptive and isokinetic measurements and MRI to determine the clinical efficacy of two alternative techniques, DIS and STA, in comparison to the conventional ACL reconstruction for treating an acute ACL rupture will supply a large data pool in which several different aspects of ACL repair versus reconstruction can be compared. The LIBRƎ study is being conducted and could lead to a better comparison between the DIS and STA ACL repair techniques and the gold standard ACL reconstruction.

Four different ACL repair techniques have dominated the ACL repair discussion. In chapter 8, a narrative review and critical appraisal of the four different ACL repair techniques, studies by the developers and the early adaptors and the present status is given. After promising short- to mid-term results by the developers, the results of the early adaptors show more variety in terms of re-rupture and re-surgery for other reasons, which led to a more varicolored discussion. Risk factors for failure are described. There is a call for more clinical data and RCTs. Future research could include conservative management versus ACL repair and reconstruction, as well as the risk on osteoarthritis. ACL repair combined with an anterolateral extra-articular procedure could reduce the re-rupture risk, which could be interesting especially for the high-risk groups. One of the most important findings of the last decade is that the ACL is able to heal and subsequently stabilize the knee again. Patient selection is emphasized: the ideal patient is a non-high level athlete older than 25 years with an acute proximal ACL rupture. Further research will have to show if ACL repair could be a game changer or if history will repeat itself.

In conclusion: this thesis "An Introduction to Modern Anterior Cruciate Ligament Repair" contributes to the discussion whether these novel repair techniques could be a treatment option for the acute proximal ACL rupture. The ability of the ACL to heal and subsequently re-stabilize the knee with the DIS and the STA repair techniques is confirmed. A step by step description of the ACL STA surgical technique is presented. Our first results and tips and tricks for the DIS repair technique are shared. The healing of the ACL can be monitored with MRI, but correlation with clinical findings is necessary. Based on the two case-series on acute ACL repair with the STA technique it seems that this technique could be clinically relevant as a treatment option for patients with an acute, proximal ACL rupture. A careful patient selection is advised. To reduce the risk on a re-rupture, the ideal patient would be a non-high level athlete (Tegner score of < 7) and older than 25 years with an acute proximal ACL rupture of good tissue quality which is not retracted. The call for more data on ACL repair, especially RCTs, is underwritten in the LIBRƎ study protocol and considerations for the future of ACL repair research are given.

Chapter 11 Samenvatting

De voorste kruisband (VKB) is een belangrijke stabilisator in de knie. De VKB voorkomt het te ver naar voren bewegen van het onderbeen (tibia) en draagt ook bij aan de rotatoire stabiliteit van de knie. VKB rupturen zijn de meest voorkomende band letsels van de knie. De gemiddelde leeftijd waarop iemand zijn VKB scheurt is ongeveer 34 jaar. Een gescheurde VKB kan op drie manieren behandeld worden. Ten eerste conservatief: met behulp van een kinesist (fysiotherapeut) worden de spieren en stabiliteit van de knie opgetraind, waarna 50% van de patiënten geen instabiliteitsklachten ervaart. De andere 50% met blijvende instabiliteitsklachten, evenals sporters die veel draai (rotatoire) bewegingen maken, zullen met een operatie behandeld worden. Ten tweede, met de klassieke operatieve behandeling; de reconstructie. Hierbij wordt een hamstringpees (andere pezen zijn ook mogelijk) uit dezelfde knie 'geoogst' en teruggeplaatst op de plaats van de gescheurde VKB. Ten derde is het operatief ook mogelijk om de VKB te hechten/ herstellen. Voor deze techniek is geen andere pees nodig. Het onderste deel van de gescheurde VKB wordt tegen het bovenste deel gespannen met een hechting. Naast de gehechte VKB wordt een 'veiligheidsgordel' gespannen, die gedurende de genezingsperiode van de VKB, de gehechte VKB beschermt als er te veel kracht op komt te staan.

VKB herstel operaties werden in de jaren '70 al uitgevoerd, alleen de resultaten bleken destijds tegen te vallen. De VKB reconstructie werd de standaard operatieve behandeling van een gescheurde VKB. VKB reconstructie is een goede operatieve behandeling, echter er kleven ook nadelen aan. Enkele voorbeelden; 39% van de patiënten krijgt een complicatie, binnen 2 jaar heeft 6% een re-ruptuur (in hoog risico groepen zelfs 28%), patiënten ervaren nog pijn rond de knieschijf (20%) en bij knielen (15%), geen goede rotatoire stabiliteit (24%), de revalidatie duurt 9-12 maanden en maar 50-65% van de amateur sporters haalt zijn oude niveau weer en er blijft een verhoogde kans op artrose (slijtage). Er is ruimte voor verbetering.

Recent zijn moderne VKB herstel operatietechnieken geïntroduceerd. De theoretische voordelen hiervan zijn; de operatie is minder invasief, het behouden van de eigen VKB met de zenuwcellen (proprioreceptoren) die bijdragen aan de stabiliteit waardoor de revalidatieperiode verkort kan worden, er hoeft geen pees 'geoogst' te worden, mogelijk beschermt het tegen de verhoogde kans op artrose en indien een re-ruptuur optreedt kan een klassieke VKB reconstructie worden uitgevoerd ('no bridges are burned').

De bedoeling van deze thesis is om een bijdrage te leveren aan de discussie of deze moderne VKB herstel technieken een behandelingsoptie kunnen zijn voor patiënten met een acuut gescheurde VKB.

In hoofdstuk 2 wordt beschreven hoe een VKB herstel operatie uitgevoerd kan worden met de ‘Suture Tape Augmentation’ (STA) techniek. Samen met de ontwikkelaar van deze techniek, professor Gordon MacKay, hebben we de STA techniek uitgelegd met begeleidende foto’s, tekeningen en video. De voor- en nadelen, evenals adviezen worden gegeven. Deze beschrijving helpt andere orthopedisch chirurgen als zij met de nieuwe STA techniek willen starten.

De resultaten van professor Gordon MacKay zijn eerste 42 patiënten die hij behandeld heeft met de STA VKB techniek worden beschreven in hoofdstuk 3. Dit artikel is de eerste studie waarin de resultaten van patiënten met de STA VKB techniek met een twee jaar opvolging beschreven worden. De patiënten hebben een betekenisvolle verbetering op verschillende kniescores en 4.8 % heeft een re-ruptuur. Uit deze studie blijkt dat STA VKB herstel techniek klinisch relevant kan zijn voor patiënten met een acute, niet verschrompelde en uit goed weefsel bestaande VKB ruptuur.

In hoofdstuk 4 beschrijven we de resultaten van de eerste 35 patiënten die we zelf in het Universitair Ziekenhuis Antwerpen (UZA) hebben behandeld met de STA VKB herstel techniek met twee jaar opvolging. In deze studie beschrijven we dat de patiënten weer een stabiele knie hebben gekregen (gemeten met de rolimeter), de patiënten hebben gunstige kniescores, 50% is na 5.5 week weer aan het werk en 50% is binnen 6 maanden weer aan het sporten. Een re-ruptuur kwam voor in 11.4% van de patiënten en 8.6% kreeg een heroperatie voor een andere reden dan re-ruptuur. Patiënten met een hoog sportniveau (Tegner ≥ 7) en patiënten die op de MRI na 6 maanden geen goede genezing tonen (‘grade 3 ACL healing’) hebben een verhoogde kans op een re-ruptuur. Met deze kennis kan in de toekomst beter patiënten geselecteerd worden die in aanmerking komen voor de STA VKB herstel techniek. Concluderend toont deze studie aan dat de behandeling van de acute, herstelbare VKB ruptuur met de STA techniek leidt tot een stabiele knie, gunstige kniescores, echter het re-ruptuur risico van 11% is een zorg.

De dynamische intraligamentaire stabilisatie (DIS) techniek is een andere moderne VKB herstel techniek. In 2014 hebben we deze techniek voor het eerst toegepast in het UZA. Als een arts met een nieuwe techniek begint, zijn er vaak “opstart problemen”. In hoofdstuk 5 worden de ervaringen en resultaten van onze eerste DIS patiënten beschreven. We hebben een nieuwe patiëntenstroom moeten ontwikkelen, aangezien deze patiënten binnen 3 weken na de ruptuur geopereerd moesten worden. Het nieuwe instrumentarium, hechtdraden management, postoperatieve problemen en MRI interpretatie zijn voorbeelden van ‘problemen’ waarmee we ervaring hebben opgedaan. ‘Tips and Tricks’ worden gedeeld, die andere orthopedisch chirurgen kunnen helpen die met de DIS techniek starten.

Om de (herstelde) VKB te beoordelen kan gebruik worden gemaakt van MRI. In hoofdstuk 6 wordt een overzicht van MRI beelden gegeven van de DIS en STA techniek, uitleg en mogelijke complicaties, zodat radiologen en orthopedisch chirurgen bekend worden met de beelden van deze nieuwe techniek. Hiermee neemt hopelijk de kans op een misinterpratie af, waardoor patiënten sneller de juiste behandeling krijgen. Het genezingsproces van de VKB op de MRI geeft andere beelden dan het reeds bekende ‘ligamentisatie proces’ na een VKB reconstructie. Indien een patiënt 1 jaar na VKB herstel op MRI nog geen genezing vertoont, kan de knie klinisch wel stabiel zijn. MRI’s na VKB herstel dienen behoedzaam beoordeeld te worden en dienen gecorreleerd te worden met de klinische bevindingen.

In 2017 is door het Fonds Wetenschappelijk Onderzoek (FWO) Vlaanderen het onderzoeksvoorstel van de LIBRƎ studie gehonoreerd. De LIBRƎ studie vergelijkt twee verschillende herstel technieken (DIS en STA) en de klassieke VKB reconstructie en wordt uitgevoerd in meerdere ziekenhuizen (multicenter RCT). In 2018 is de studie gestart met de auteur als hoofdonderzoeker (principal investigator). Voor een degelijke studie dient vooraf veel tijd en energie gestoken te worden in de te selecteren (hoofd)uitkomsten en statische berekeningen. Het protocol voor de LIBRƎ studie, bestaande uit gevalideerde (knie) patiënten vragenlijsten, klinische onderzoek, positiezin en krachtmetingen, MRI en begeleidende statistiek is beschreven in hoofdstuk 7.

Naast de DIS en STA VKB herstel techniek, zijn er nog 2 andere herstel technieken recent ontwikkeld, namelijk ‘suture anchor primary repair’ (SAPR) en ‘bridge-enhanced ACL repair’ (BEAR) techniek. In hoofdstuk 8 wordt de bestaande literatuur kritisch besproken. Hierbij wordt een indeling gemaakt in de studies die gepubliceerd zijn door ontwikkelaars van de technieken en de onafhankelijke eerste gebruikers (‘early adaptors’). De goede tot uitstekende resultaten van de ontwikkelaars wordt niet door alle eerste gebruikers gehaald. Met name het percentage op re-rupturen en heroperaties voor andere redenen ligt hoger, wat leidt tot een genuanceerdere discussie. Toekomstig onderzoek zou zich kunnen richten, naast de vergelijking van VKB herstel en reconstructie, ook op de vergelijking met de conservatie behandelde VKB ruptuur. Daarnaast biedt de nieuwe ontwikkeling en kennis van de anterolaterale versteviging procedures een mogelijkheid om het re-ruptuur percentage omlaag te brengen. Dit kan met name voor de hoog risicogroepen interessant zijn. Een van de belangrijkste conclusies is dat de VKB wel in staat is om te genezen, dit in tegenstelling tot wat er nog tot 10 jaar geleden gedacht werd. Patiënten selectie wordt benadrukt: de ideale patiënt voor een VKB herstel operatie is ouder dan 25 jaar, sport niet op een hoog niveau (Tegner < 7) en heeft een acuut gescheurde VKB die bestaat uit één bundel van goed weefsel kwaliteit. Toekomstig onderzoek zal moeten aantonen of VKB herstel een ‘game changer’ zal zijn, of dat de geschiedenis zich zal herhalen.

Conclusie:

Dit proefschrift “Een introductie in moderne voorste kruisband herstel technieken” draagt bij aan de discussie of VKB herstel een behandeloptie zou kunnen zijn voor patiënten met een acuut gescheurde VKB. De mogelijkheid van de VKB om te genezen met de DIS en STA techniek wordt bevestigd. Een stap voor stap beschrijving van de VKB STA techniek wordt gegeven. Resultaten van en ‘tips and tricks’ voor de DIS techniek worden beschreven. Het genezingsproces van de herstelde VKB kan gemonitord worden met MRI, echter correlatie met de klinische bevinden zijn noodzakelijk. Gebaseerd op de twee VKB STA patiënten studies, lijkt het dat VKB herstel met de STA techniek een klinisch relevante behandeling kan zijn voor patiënten met een acute VKB ruptuur. Een strikte patiënten selectie wordt hierbij geadviseerd: de ideale patiënt voor een VKB herstel operatie is ouder dan 25 jaar, sport niet op een hoog niveau (Tegner < 7) en heeft een recente, in het bovenste gedeelte, gescheurde VKB van goed weefsel kwaliteit. Tenslotte, wordt de vraag naar meer onderzoek, in het bijzonder gerandomiseerde studies, onderschreven in het LIBRƎ protocol en worden overwegingen voor toekomstig VKB herstel onderzoek gegeven.

Curriculum Vitae

Christiaan Hendrik Willem (Krik) Heusdens was born on 27th of April 1978 in Zwolle, the Netherlands. After finishing secondary school (V.W.O., R.S.G. in Steenwijk) he studied medicine at Erasmus University Rotterdam as of 1996. He graduated as medical doctor in 2004 and has been working as a resident at Rijnland Ziekenhuis (Leiderdorp) and HagaZiekenhuis (The Hague). He was trained as an orthopedic surgeon at HagaZiekenhuis, Medisch Centrum Haaglanden (The Hague) and Leids Universitair Medisch Centrum (Leiden), under supervision of prof. dr. Rob Nelissen. He completed this training in 2013. From 2014 up to the present moment he is a staff member of the orthopedic surgery and traumatology department at Antwerp University Hospital, with a special interest in knee and sports surgery. For the first half year he combined this with a part-time knee-fellowship at Monica Hospital (Antwerp), under supervision of prof. dr. Peter Verdonk. Prof. dr. Johan Somville and prof. dr. Jef Michielsen, the former and present chairman of the orthopedic surgery and traumatology department at Antwerp University Hospital have played an important role by guiding and encouraging his clinical and scientific career. At Antwerp University Hospital he started a knee ligament research project, together with dr. Lieven Dossche and prof. dr. Pieter Van Dyck. In 2017 he received a FWO TBM (Research Foundation – Flanders, Applied Biomedical Research with a Primary Social finality) grant and became the Principal Investigator of the LIBRƎ study (chapter 7, this thesis). Krik Heusdens has an interest in knee surgery innovations. He has started and cooperated in multiple (international) studies, among which knee joint distraction, arterial embolization as a treatment for osteoarthritis or total knee arthroplasty pain and augmented reality knee arthroplasty. He lectures at Antwerp University (faculties of Medicine and Health Sciences and Rehabilitation Sciences and Physiotherapy) and supervised five master theses in the past five years. He also lectured and presented abstracts at multiple national and international scientific meetings and organized several cadaver clinics. In 2020 he became a member of the Belgian governmental committee on reimbursement for implants and invasive medical devices. He is married to his amazing wife Andrea and they are blessed with three beautiful children: Olivier, IJsbrand and Leonore.

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Team UZA orthopedie

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List of Abbreviations

ACL	Anterior cruciate ligament
ADE	Adverse device effect
AP	Anteroposterior
BEAR	Bridge-enhanced ACL repair
CI	Confidence interval
DIS	Dynamic intraligamentary stabilization
DTI	Diffusion tensor imaging
eCRF	Electronic case report form
EDC	Electronic data capture
FP	Infrapatellar fat pad
FWO	Fonds wetenschappelijk onderzoek
HR QoL	Health-related quality of life
ICUR	Incremental cost-utility ratio
IBLA	Internal bracing ligament augmentation
IKDC	International knee documentation committee
ISTR	Independent suture tape reinforcement
KOOS	Knee injury and osteoarthritis outcome score
LCL	Lateral collateral ligament
MCL	Medial collateral ligamnet
MGA	Middle genicular artery
MRI	Magnetic resonance imaging
PCL	Posterior cruciate ligament
PDS	Polydioxanone suture
PROM	Patient-reported outcome measure
PT	Patellar tendon
QALY	Quality-adjusted life year
QED	Quality electrodynamics
qMRI	Quantitative magntic resonance imaging
QoL	Quality of life
RCT	Randomized controlled trial
ROM	Range of motion
RTS	Return to sports
RTW	Rterun to work
SAE	Serious adverse event
SAPR	Suture anchor primary repair
SD	Standard deviation
SE	Standard error

SEMAC	Slice encoding for metal artifact reduction
SI	Signal intensity
SOS	Surgical outcome system
ST	Semitendinosus tendon
STA	Suture tape augmentation
TBM	Applied biomedical research with a primary social finality
UZA	Antwerp university hospital
VAS-pain	Visual analogue pain scale
VAS-satisfaction	Visual analogue satisfaction scale
VR-12	Veterans RAND 12 items health survey

Anatomic Structures

English	**Dutch**	**Terminologia Anatomica**
Anterior cruciate ligament	Voorste kruisband	Ligamantum cruciatum anterius
Anterolateral ligament	Anterolaterale ligament	Ligamentum anterolaterale
Femur	Dijbeen	Femur
Fibula	Kuitbeen	Fibula
Fibular collateral ligament	Buitenste knieband	Ligamentum collaterale fibulare
Hamstrings	Hamstrings	
Iliotibial band	Tractus iliotibialis	Tractus iliotibialis
Infrapatellar fat pad	Hoffa´s vetlichaam	Corpus adiposum infrapatellare
Knee	Knie	Genu
Lateral femoral condyle	Buitenste gewrichtsknobbel van het dijbeen	Condylus lateralis femoris
Lateral meniscus	Buitenste meniscus	Meniscus lateralis
Ligamentum mucosum/ Infrapatellar plica	Ligamentum mucosum	Plica synovialis infrapatellaris
Medial meniscus	Binnenste mensicus	Meniscus medialis
Middle genicular artery	Middelste geniculare arterie	Arteria media genus
Patella	Knieschijf	Patella
Patellar ligament	Kniepees	Ligamentum patellae
Pes anserinus	Ganzenpoot aanhechting	
Popliteal artery	Knieslagader	Arteria poplitea
Posterior cruciate ligament	Achterste kruisband	Ligamentum cruciatum posterius
Quadriceps	Quadriceps	Musculus quadriceps
Quadriceps tendon	Quadriceps pees	
Semitendinosus	Halfpeesachtige spier	Musculus semitendinosus
Spinal cord	Ruggenmerg	Medulla spinalis
Tibia	Scheenbeen	Tibia
Tibial collateral ligament	Binnenste knieband	Ligamentum collaterale tibiale
Tibial nerve	Scheenbeen zenuw	Nervus tibialis
Tibial plateau	Plateau van de knie	

‘Se vogliamo che tutto rimanga come è, bisogna che tutto cambi.’

-‘Als we willen dat alles blijft zoals het is, moet alles veranderen.’-

‘Il Gattopardo / De tijgerkat’ ,

Giuseppe Tomasi di Lampedusa