

# CLINICAL AND RADIOGRAPHIC EVALUATION AFTER ACL RECONSTRUCTION WITH THE EMPHASIS ON SURGICAL TECHNIQUE AND TIME OF RECONSTRUCTION

Ioannis Karikis

Department of Orthopaedics  
Institute of Clinical Sciences  
Sahlgrenska Academy, University of Gothenburg  
Sweden



UNIVERSITY OF GOTHENBURG

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ioannis.karikis@vgregion.se

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## *To Marina and Afrodite*

Σα βγεις στον πηγαιμό για την Ιθάκη,  
να εύχεται νάναι μακρύς ο δρόμος,  
γεμάτος περιπέτειες, γεμάτος γνώσεις...  
...Κι αν πτωχική την βρεις, η Ιθάκη δεν σε γέλασε.  
Έτσι σοφός που έγινες, με τόση πείρα,  
ήδη θα το κατάλαβες η Ιθάκες τι σημαίνουν.  
(Ιθάκη, 1910, Κ.Π. Καβάφης)

As you set out for Ithaka  
hope your road is a long one,  
full of adventure, full of discovery...  
...And if you find her poor, Ithaka won't have fooled you.  
Wise as you will have become, so full of experience,  
you will have understood by then what these Ithakas mean.  
(Ithaka, 1910, C.P. Cavafy)

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# ABSTRACT

The overall purpose of this thesis was to assess the short-, mid- and long-term clinical and radiographic results after anterior cruciate ligament (ACL) reconstruction, in relation to different surgical techniques, such as the anatomic and non-anatomic single-bundle (SB) and anatomic double-bundle (DB) techniques. Furthermore, the aim was to evaluate the influence of the time between the injury and ACL reconstruction on the postoperative outcome. In Study I, the long-term clinical and radiographic outcomes were compared between patients undergoing either early surgery, at a median of three months after injury (30 patients), or late surgery, at a median of 30 months after the injury (31 patients). The early reconstruction group required significantly fewer meniscectomies at the index operation than the late reconstruction group and displayed significantly less medial compartmental osteoarthritis (OA), ten years after reconstruction. Study II was a prospective, randomised, controlled trial comprising 105 patients with the aim of comparing the outcome of the anatomic SB and the anatomic DB techniques. At the five-year follow-up, statistically significant differences could not be demonstrated between the SB and DB groups in terms of subjective and objective clinical outcomes, as well as in terms of knee laxity measure-

ments and the presence of OA. In Study III, the tibial tunnel was assessed up to five years after anatomic SB ACL reconstruction using hamstring tendon autografts and biocomposite interference screws in 51 patients. Standardised digital radiographs with weight-bearing anteroposterior and lateral views of the knee were obtained in the early postoperative period, at two and at five years postoperatively. In the majority of patients (83%), the width of the tibial tunnel had decreased on one or both radiographic views at five years compared with the early postoperative period. In Study IV, the clinical outcome after the anatomic DB (45 patients) and non-anatomic SB (49 patients) techniques was compared, in a prospective consecutive series. At the two-year follow-up, there were no significant differences between the groups in terms of subjective and objective assessments, including knee laxity measurements.

**Keywords:** Knee, Anterior Cruciate Ligament, Reconstruction, Double Bundle, Single Bundle, Biocomposite, Interference Screw, Osteoarthritis

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## SAMMANFATTNING PÅ SVENSKA

Syftet med avhandlingen var att undersöka det kliniska och radiologiska resultatet på kort, medellång och lång tid efter en främre korsbandsrekonstruktion avseende olika operationsmetoder såsom anatomisk och icke-anatomisk enkeltunnelteknik samt anatomisk dubbeltunnelteknik. Ett annat syfte var att utvärdera vilken betydelse som tid mellan korsbandsskada och operation har på det postoperativa utfallet. Studie I var en långtidsuppföljning (10 år) där patienter (n=30) som opererats för sin främre korsbandsskada inom median 3 månader jämfördes med patienter (n=31) som opererades först efter median 30 månader med avseende på det kliniska och radiologiska resultatet. Den tidiga gruppen uppvisade statistiskt signifikant färre resektionskrävande meniskskador i samband med operation, och hade statistiskt signifikant mindre artrosutveckling vid undersökningstillfället jämfört med den sena gruppen. Studie II var en prospektiv randomiserad studie som jämförde anatomisk enkeltunnelteknik (n=52) med anatomisk dubbeltunnelteknik (n=53) 5 år efter främre korsbandsrekonstruktion. Inga

statistiskt signifikanta skillnader kunde påvisas avseende kliniska resultat såsom knälaxitet, patientrapporterad knäfunktion eller graden av artrosutveckling. I Studie III undersöktes 51 patienter 5 år efter främre korsbandsrekonstruktion, operationen gjordes med anatomisk enkeltunnelteknik, hamstringsenegraft och fixation med resorberbar interferensskruv i tibia. Patienterna genomgick standardiserad belastad knäröntgen (anterio-posterior och lateral projektion) vid 3 tillfällen, kort tid efter operation, efter 2- och 5 år. Hos 83 procent av patienterna hade tunnelvidgningen i tibia minskat mellan första undersökningstillfället och 5 års undersökningen. I en prospektiv konsekutiv studiedesign jämfördes i Studie IV det kliniska resultatet 2 år efter främre korsbandsrekonstruktion mellan en grupp patienter (n=45) som opererats med anatomisk dubbeltunnelteknik och en grupp (n=49) som opererats med icke-anatomisk enkeltunnelteknik. Inga statistiskt signifikanta skillnader kunde påvisas avseende kliniska resultat såsom knälaxitet och patientrapporterad knäfunktion.

## ΠΕΡΙΛΗΨΗ ΣΤΑ ΕΛΛΗΝΙΚΑ

Ο σκοπός της παρούσας εργασίας ήταν να μελετήσει και να συγκρίνει τα κλινικά και ακτινολογικά μικρο-, μέσο- και μακρο-πρόθεσμα αποτελέσματα μετά από τη χειρουργική αποκατάσταση ρήξης του πρόσθιου χιαστού συνδέσμου (ΠΧΣ), μεταξύ διαφορετικών τεχνικών όπως η ανατομική ή μη ανατομική τεχνική της μονής δέσμης (ΜΔ) μοσχεύματος και η ανατομική τεχνική της διπλής δέσμης (ΔΔ) μοσχεύματος. Επιπρόσθετα, μελετήθηκε και η επίδραση του χρόνου αναμονής μεταξύ της ρήξης του ΠΧΣ και της χειρουργικής αποκατάστασης στο μετεγχειρητικό αποτέλεσμα. Η Μελέτη I σύγκρινε τα μακροπρόθεσμα κλινικά και ακτινολογικά αποτελέσματα μεταξύ ασθενών που υποβλήθηκαν σε πρόωρη χειρουργική αποκατάσταση μετά τον τραυματισμό (Ομάδα Α, 30 ασθενείς), με διάμεση τιμή τους 3 μήνες μετά τον τραυματισμό και αυτών που υποβλήθηκαν σε καθυστερημένη χειρουργική αποκατάσταση μετά τον τραυματισμό (Ομάδα Β, 31 ασθενείς), με διάμεση τιμή τους 30 μήνες μετά τον τραυματισμό. Η ομάδα της πρόωρης αποκατάστασης υποβλήθηκε σε στατιστικώς λιγότερες μνησκειομένες σε σχέση με την ομάδα της καθυστερημένης αποκατάστασης, στη στιγμή της επέμβασης, καθώς επίσης παρουσίασε στατιστικώς μικρότερο βαθμό οστεοαρθρίτιδας στο έσω μεσάρθριο διάστημα, 10 έτη μετεγχειρητικά. Η Μελέτη II ήταν μια προοπτική τυχαίοποιημένη ελεγχόμενη μελέτη που συμπεριέλαβε 105 ασθενείς με σκοπό να συγκρίνει τα

αποτελέσματα μεταξύ της ανατομικής τεχνικής ΜΔ και της ανατομικής τεχνικής ΔΔ. Δεν παρατηρήθηκαν στατιστικώς σημαντικές διαφορές μεταξύ των δύο τεχνικών, 5 έτη μετεγχειρητικά, όσον αφορά στις δοκιμασίες σταθερότητας του γόνατος, στα υπόλοιπα υποκειμενικά κι αντικειμενικά κλινικά αποτελέσματα καθώς επίσης και στα ακτινολογικά ευρήματα οστεοαρθρίτιδας. Η Μελέτη III εκτίμησε το μέγεθος της σήραγγας στην κνήμη 51 ασθενών, έως και 5 έτη μετά την αποκατάσταση του ΠΧΣ με την ανατομική τεχνική της ΜΔ χρησιμοποιώντας αυτομόσχευμα από τους τένοντες των οπίσθιων μηριαίων μυών και βιοαπορροφήσιμες βίδες. Ψηφιακές προσθιοπίσθιες και πλαγιοπλάγιες ακτινογραφίες με φόρτιση του μέλους πραγματοποιήθηκαν στην πρόωρη μετεγχειρητική περίοδο, στα 2 και 5 έτη μετεγχειρητικά. Η πλειοψηφία των ασθενών (83%), εμφάνισε μείωση του εύρους της κνημιαίας σήραγγας σε μία ή και στις δύο ακτινογραφικές προβολές στα 5 έτη μετεγχειρητικά σε σύγκριση με την πρόωρη μετεγχειρητική περίοδο. Η Μελέτη IV σύγκρινε τα κλινικά αποτελέσματα μεταξύ της ανατομικής τεχνικής ΔΔ (45 ασθενείς) και της μη ανατομικής τεχνικής ΜΔ (49 ασθενείς), σε δύο προοπτικές διαδοχικές σειρές ασθενών. Δεν παρατηρήθηκαν στατιστικώς σημαντικές διαφορές μεταξύ των δύο τεχνικών όσον αφορά στις δοκιμασίες σταθερότητας του γόνατος καθώς και στα υπόλοιπα υποκειμενικά κι αντικειμενικά κλινικά αποτελέσματα, 2 έτη μετεγχειρητικά.



# LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

- I. The long-term outcome after early and late anterior cruciate ligament reconstruction**  
Karikis I, Åhlén M, Sernert N, Ejerhed L, Rostgård-Christensen L, Kartus J  
*Arthroscopy*. 2018 March 6; e-published ahead of print
- II. Comparison of anatomic double- and single-bundle techniques for anterior cruciate ligament reconstruction using hamstring tendon autografts: a prospective randomized study with 5-year clinical and radiographic follow-up**  
Karikis I, Desai N, Sernert N, Rostgard-Christensen L, Kartus J  
*Am J Sports Med*. 2016 May;44(5):1225-36
- III. Radiographic tibial tunnel assessment after anterior cruciate ligament reconstruction using hamstring tendon autografts and biocomposite screws: a prospective study with 5-year follow-up**  
Karikis I, Ejerhed L, Sernert N, Rostgård-Christensen L, Kartus J  
*Arthroscopy*. 2017 Dec;33(12):2184-2194
- IV. Comparison of outcome after anatomic double-bundle and antero-medial portal non-anatomic single-bundle reconstruction in ACL-injured patients**  
Karikis I, Ahldén M, Casut A, Sernert N, Kartus J  
*Knee Surg Sports Traumatol Arthrosc*. 2017 Apr;25(4):1307-1315

# ABBREVIATIONS

<b>ACL</b>	Anterior Cruciate Ligament
<b>ADL</b>	Activity of Daily Living
<b>AM</b>	Anteromedial
<b>AP</b>	Antero-posterior
<b>β-TCP</b>	beta-Tricalcium Phosphate
<b>BMI</b>	Body Mass Index
<b>BPTB</b>	Bone-Patellar Tendon-Bone
<b>CT</b>	Computed Tomography
<b>DB</b>	Double-Bundle
<b>G</b>	Gracilis
<b>HA</b>	Hydroxyapatite
<b>IKDC</b>	International Knee Documentation Committee
<b>KOOS</b>	Knee Osteoarthritis and Outcome Score
<b>LSI</b>	Leg Symmetry Index
<b>MMT</b>	Maximum Manual Test
<b>MRI</b>	Magnetic Resonance Imaging
<b>OA</b>	Osteoarthritis
<b>OARSI</b>	Osteoarthritis Research Society International
<b>PCL</b>	Posterior Cruciate Ligament
<b>PDLA</b>	Poly-D-Lactic Acid
<b>PGA</b>	Polyglycolic Acid
<b>PGA/PLA</b>	Polyglycolic Acid/Polylactic Acid
<b>PL</b>	Posterolateral
<b>PLLA</b>	Poly-L-Lactic Acid
<b>PROM(s)</b>	Patient Reported Outcome Measurement(s)
<b>PTOA</b>	Post-Traumatic Osteoarthritis
<b>QoL</b>	Quality of Life
<b>RCT</b>	Randomised Clinical Trial
<b>ROM</b>	Range Of Motion
<b>SB</b>	Single-Bundle
<b>ST</b>	Semitendinosus

## DEFINITIONS IN SHORT

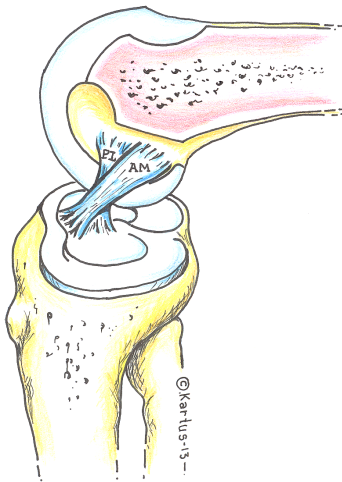
<b>ACL reconstruction</b>	Reconstruction of the native ACL using a graft
<b>Autograft</b>	Tissue from a part of an individual's own body that is transplanted into another part
<b>Instability</b>	A symptom that a patient reports; the sensation of shifting, buckling or giving-way of the knee
<b>Laxity</b>	An objective finding of passive motion in the knee joint
<b>Non-parametric statistics</b>	Statistical methods in which the data are not required to fit a normal distribution
<b>Null hypothesis</b>	The type of hypothesis used in statistics that proposes that no statistical significance exists in a set of given observations
<b>Parametric statistics</b>	Statistical methods for analysing data from a population that follows a probability distribution based on a fixed set of parameters
<b>P-value</b>	The probability, under the null hypothesis, of obtaining a result equal to or more extreme than what was actually observed
<b>Power</b>	The probability of finding a significant association when one truly exists
<b>Sensitivity</b>	Percentage of patients with a condition who are classified as having positive results
<b>Specificity</b>	Percentage of patients without a condition who are classified as having negative results
<b>Type I error</b>	Incorrect rejection of a true null hypothesis ("false positive")
<b>Type II error</b>	Incorrect acceptance of a false null hypothesis ("false negative"), often because of a lack of power frequently due to too few studied patients

# 01 INTRODUCTION

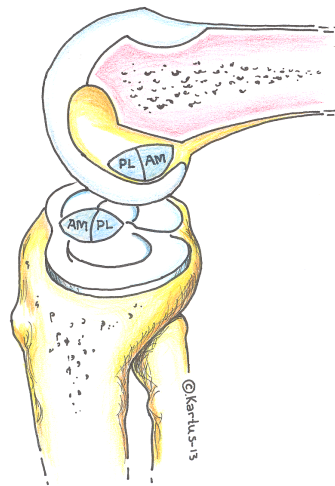
## 1.1 ANTERIOR CRUCIATE LIGAMENT ANATOMY

The length of the anterior cruciate ligament (ACL) ranges from 22 mm to 41 mm, with a mean of 32 mm. The origin of the ACL is on the posteromedial surface of the lateral femoral condyle and the insertion between the intercondylar eminences on the anterior tibia. The femoral footprint has an oval shape, with a diameter of about 18 mm in length and 11 mm in width [102]. The tibial insertion site has been described as a “duck’s foot” insertion pattern [12]. Functionally, the ACL consists of at least two bundles which have different characteristics. The bundles are called the anteromedial (AM)

and the posterolateral (PL) bundle, according to their tibial origins. The AM bundle is tightened during knee flexion, especially at 45–60 degrees, and the PL bundle is tightened when the knee is extended. Accordingly, the AM bundle contributes to knee stability in knee flexion, providing anteroposterior (AP) stability, while the PM bundle plays an important role when the knee is near extension, providing rotational stability. In conclusion, both bundles are important but during different parts of the range of motion (ROM) [62,218].



**Figure 1.** Schematic drawing of the double-bundle ACL anatomy. AM = anteromedial bundle, PL = posterolateral bundle.  
© C. Kartus



**Figure 2.** Schematic drawing of the femoral and tibial ACL footprints. AM = anteromedial bundle, PL = posterolateral bundle.  
© C. Kartus

## 1.2 ACL INJURY

According to the last report from the Swedish National Knee Ligament Register, the annual incidence of ACL injury in Sweden is estimated at approximately 80/100,000 inhabitants, which corresponds to about 6,000 injuries per year. Soccer is the most common activity associated with

ACL injury for both genders [200]. The injury mechanism usually involves valgus in light flexion, combined with rotation, or hyperextension with rotation, both with and without body contact in contact sports [30,149].



**Figure 3.** Image showing the common injury mechanism leading to non-contact ACL injury. © C. Kartus

### 1.3 KNEE LAXITY

---

#### **Static laxity**

ACL injury results in a disturbance of the primary function of the ACL, which is the stability of the tibia in relation to the femur in the anterior direction. The AP translation in an injured knee is assessed by the Lachman manual test and/or by instrumented laxity systems such as the KT-1000 arthrometer [52,202].

#### **Dynamic laxity**

A patient with an ACL injury experiences an unstable knee, particularly in sporting activities, i.e. “giving-way” symptoms. This dynamic laxity can be identified by using the pivot-shift test [73] or by different rotational laxity instruments [2].

### 1.4 PATIENT-REPORTED OUTCOME MEASUREMENTS

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Patient-reported outcome measurements (PROMs) are patients’ subjective reports related to their function or health and are used in order to evaluate a treatment or a condition. They take the form of, for example, self-completion questionnaires, diaries,

interviews or web-based forms. PROMs therefore add further information from the patients’ viewpoint and supplement objective assessments and examiner-performed evaluations of a treatment [153].

### 1.5 TIMING OF ACL RECONSTRUCTION

---

ACL injury is a major knee injury and ACL reconstruction is a common surgical procedure in orthopaedics [92,130]. According to the Swedish ACL Register, approximately half these individuals undergo surgery involving a subsequent ACL reconstruction. The initial routine treatment for ACL injury that is implemented in Sweden involves a conservative rehabilitation treatment algorithm. If this algorithm results in an unsatisfactory outcome, ACL reconstruction followed by rehabilitation is recommended, especially in young patients and patients engaged in recreational sports and heavy physical work. In Sweden, the average time between injury and surgery has historically been more than one year. This could be explained by the initial conservative algorithm, as well as by a delay in diagnosis before the treatment of an ACL injury is initiated [200].

Back in the 1990s, the landmark study by Shelbourne et al. suggested that early ACL reconstruction jeopardises the knee and

makes it vulnerable to arthrofibrosis [179]. Further studies have subsequently agreed with these findings [72,177,207]. On the other hand, late reconstruction has been considered to result in a delayed return to work and sports due to muscle atrophy and loss of strength, as well as more cartilage and meniscal damage [90,93,178]. The review by Beynon et al. reported that the time interval between index injury and surgery is not as important as the condition of the knee at index surgery, i.e. not swollen and without ROM deficits [27]. Patients should undergo modern rehabilitation pre-operatively in order to reduce swelling and regain ROM and muscle strength [109]. However, there is no consensus on the ideal timing for ACL reconstruction [59,114,184]. Recent studies have reported that a delay in surgery of more than five months after the index injury increases the risk of meniscal and chondral lesions [42,53,104,186]. Concomitant meniscal and chondral injuries have been shown to

lead to further degenerative changes in the knee joint compared with isolated ACL injuries [145,164]. In the meta-analysis by Smith et al., there was no significant difference between early and delayed reconstruction in terms of the Lysholm knee score or Tegner activity level, as well as the incidence of arthrofibrosis, chondral injuries, patellofemoral pain or meniscal lesions [184]. In addition, in the systematic review by Andernord et al. including Level I and II studies, few or no differences in objective

and subjective outcomes related to the timing of surgery were reported. Nonetheless, these reviews show heterogeneity between the included studies in defining early or late reconstruction, as they range from two days to seven months and three weeks to 24 years respectively [13,184]. In addition, the included studies vary in terms of surgical techniques, graft and outcome measurements. A comparison between these studies is therefore difficult to make.

## 1.6 SURGICAL TECHNIQUE

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Arthroscopically assisted ACL reconstruction was introduced in 1982 by David Dandy [50] using a two-incision technique (“outside-in” or “rear-entry” technique). One incision was made on the tibial side for graft harvesting and tibial drilling, while the other incision was made in the lateral femoral condyle for femoral drilling. In the 1990s, the development of arthroscopic instruments led to the use of a one-incision technique and transtibial femoral drilling (“all-inside” technique). This technique

became popular because of the shorter surgery time and improved cosmetic outcome compared with the two-incision technique. Despite the fact that the placement of the ACL graft was isometric and thus non-anatomic, studies at that time reported no significant differences between these two techniques [35,67]. In the late 1990s and the early 2000s, there was a shift towards anatomic placement of the ACL graft and the use of the transportal technique.

### 1.6.1 NON-ANATOMIC ACL RECONSTRUCTION

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#### **Isometry – transtibial technique**

Isometric placement of the ACL graft means that the distance between the graft origin and insertion is the same during flexion and extension of the knee joint.

With this placement, it was believed that elongation of the graft would be avoided [223]. Isometric placement of the graft was achieved, using the transtibial technique, by drilling the femoral tunnel high and deep in the intercondylar notch close to the posterior limit of Blumensaat’s line and drilling the tibial tunnel more posteriorly. However, the graft was placed non-anatomically in a more vertical position and biomechanical and clinical studies have shown poor results in restoring knee kinematics and rotatory

laxity [113,134]. Moreover, notchplasty was performed routinely, in conjunction with the transtibial technique, as it was regarded as a useful step in the visualisation of the femur. Notchplasty involves removing bone from the medial wall of the lateral femoral condyle in the intercondylar notch in order to avoid impingement by the graft. Studies have shown that notchplasty may have a negative effect on knee kinematics [95]. Nowadays, notchplasty is only performed in cases where there are anatomical reasons, such as notch narrowing or osteophyte formation or during additional surgeries in order to manage arthrofibrosis and revision surgery [161].

### O'clock position

This method has been used in order to drill the femoral tunnel with reference to a particular o'clock position in the lateral femoral condyle in the intercondylar notch. This method has several limitations because the depth of the notch and other anatomic landmarks are not taken into consideration. The orientation of the clock also varies during knee flexion and the method is therefore not easy to reproduce [204].

### Transportal technique

For the past decade, there has been a trend

towards an anatomic approach in ACL reconstruction. To achieve more "independent" femoral drilling, the transportal technique, i.e. drilling the femoral tunnel through the anteromedial (AM) portal, has been introduced. Using the AM portal, the surgeon has improved visualisation of the anatomic landmarks of the native ACL, as well as the advantage of obtaining a more accurate, anatomic horizontal placement of the femoral tunnel compared with the transtibial technique [38,165]. Corry et al. were early advocates of the advantages of the transportal technique [46].

## 1.6.2 ANATOMIC ACL RECONSTRUCTION

---

During the past decade, efforts have been made to develop techniques for reconstructing the AM and PL bundles separately, the double-bundle (DB) technique [204,218]. The aim is to mimic the native ACL patterns, as the two bundles can be tensioned separately. This introduced the term "anatomic" reconstruction and the DB surgical technique [205]. However, the use of two separate bundles in the DB technique does not mean that the reconstruction is anatomic [129]. Anatomic ACL reconstruction can be performed by

using either the DB or single-bundle (SB) technique, with graft placement within the native ACL femoral and tibial footprints. Anatomic ACL reconstruction is defined as the functional restoration of the native ACL in terms of dimension, collagen fibre directions and places of attachment, even if a complete restoration is not possible [205]. The clinical outcome after ACL reconstruction can be the same for the SB and DB techniques, if the reconstruction is individualised according to the size and anatomy of the native ACL [82].

## 1.7 KNEE STABILITY AND ACL RECONSTRUCTION

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Despite having a stable knee at clinical examination, many patients describe a feeling of instability or insecurity [216]. As the PL bundle primarily controls rotational laxity, it has been suggested that DB ACL reconstruction more effectively restores the kinematics compared with only reconstructing the AM bundle and the AP laxity [11]. This has been confirmed in several biomechanical and randomised

clinical trials (RCTs) showing superior results for the DB technique in terms of the pivot-shift test [83,88,99,100,181,191]. On the other hand, other clinical studies with a short- to mid-term follow-up report no or only a few potential benefits of DB reconstruction over SB reconstruction in terms of laxity restoration or subjective PROMs [3,82,171,190,215].



## 1.8 POST-TRAUMATIC OSTEOARTHRITIS

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ACL injury is associated with the development of post-traumatic knee osteoarthritis (PTOA) [8,145]. The aetiology of PTOA development is multifactorial and has not yet been clearly defined. Concomitant intra-articular lesions, instability, changes in gait and knee biomechanics after ACL injury, as well as cartilage degradation depending on the inflammatory process, change the homeostasis of the knee joint and may lead to PTOA [14,44,124]. It has been reported that patients with ACL-deficient knees who develop PTOA are about 10-15 years younger than patients who develop primary OA [169].

Regardless of conservative or surgical treatment, 50% of patients with an ACL injury develop PTOA 10-20 years after injury [121]. Reports in the literature after ACL reconstruction have revealed a varying incidence in the development of radiographic PTOA from 0-100% and this can be explained not only by the type of injury, i.e.

isolated ACL rupture or with concomitant lesions, but also by the many different radiographic classification systems [8,15,23,145]. The most commonly used classification systems assessing tibiofemoral OA are the Kellgren-Lawrence [96], the Fairbank [60], the Ahlbäck [1], the International Knee Documentation Committee (IKDC) form [73] and the Osteoarthritis Research Society International (OARSI) [10]. Furthermore, the cause of PTOA after ACL reconstruction could be influenced by graft choice, patient age and gender, activity level and body mass index (BMI), as well as detectable bone bruises in magnetic resonance imaging (MRI) [7,8,147,157,159]. Another aspect that is interesting is that there is no strong correlation between radiographically evident OA and clinical symptoms [137,140,147,148,157,164]. The distinction of radiographic signs and symptoms should therefore be taken into consideration.

## 1.9 BONE TUNNEL ENLARGEMENT AND BIOCOMPOSITE INTERFERENCE SCREWS

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Bone tunnel enlargement following ACL reconstruction is a well-known phenomenon and several theories about the cause have been discussed. The true aetiology is unknown, but it involves mechanical, chemical and biological factors. Factors that have been mentioned include heat necrosis during drilling, a foreign-body inflammatory response and a chemical response to absorbable implants, graft-tunnel motion and aggressive rehabilitation [79,85,188,189,210].

ACL reconstruction using interference screws and autologous hamstring tendon grafts is a commonly performed surgical procedure [32,156]. Metallic interference screws have been a traditional fixation method that provides stable fixation [188].

Nevertheless, disadvantages, such as laceration of the graft during screw insertion, artefacts during subsequent MRI and complicated revision surgery, have been reported [16,180,222]. Biodegradable and, more recently, biocomposite interference screws have been developed in order to overcome these disadvantages [20,21,58,110].

Biodegradable screws consist of substances such as polyglycolic acid (PGA), poly-p-dioxanone and copolymers of polyglycolic acid/polylactic acid (PGA/PLA), as well as polymers like poly-L-lactic acid (PLLA) and poly-D-lactic acid (PDLA) [128,209]. Apart from the comparable pull-out force and stiffness associated with the metallic screw, biodegradable screws were supposed to degrade and be replaced in the long term

by bone tissue [110]. However, biodegradable screws have some disadvantages. Screw breakage during insertion, soft-tissue reactions, the absence of osteoconductivity and bone tunnel enlargement have been reported [16,110]. In the past decade, in order to increase the osteoconductive properties of the implants, biocomposite materials have been introduced. Beta-tricalcium phosphate ( $\beta$ -TCP) has, for example, been added to biodegradable polymers. Biocomposite implants are supposed to degrade over time, but more rapidly than biodegradable

implants, and, due to their osteoconductivity, result in faster graft incorporation, bone tissue formation in the tunnel and subsequently reduced tunnel width [20,21,58,143]. However, the role of biocomposite screws in tunnel enlargement or narrowing is not clear, as reports in the literature are conflicting [189]. Some studies have reported tunnel narrowing and signs of screw incorporation, but other studies report no tunnel narrowing and the presence of screw remnants several years after the surgical procedure [16,20,49,120,136,166].

# 02 AIMS

## **Study I**

To compare the long-term clinical and radiographic outcomes between patients who underwent surgery within five months (early) after ACL injury and those who waited at least two years (late) for the operation. The hypothesis was that early ACL reconstruction would render fewer associated intra-articular injuries at the index operation and result in a better clinical and radiographic outcome compared with late ACL reconstruction.

## **Study II**

To compare the outcomes between the anatomic DB and anatomic SB techniques five years after the reconstruction, especially in terms of the pivot-shift test but also regarding other clinical measurements and radiographic assessments of OA development. The hypothesis was that the anatomic DB ACL reconstruction would result in a better outcome in terms of the pivot-shift test compared with the anatomic SB reconstruction.

## **Study III**

To evaluate the tibial tunnel radiographically five years after ACL reconstruction using hamstring tendon autografts and bio-composite interference screws. The hypothesis was that no tibial tunnel enlargement would be found five years after ACL reconstruction.

## **Study IV**

To investigate whether the anatomic DB ACL reconstruction has a better clinical outcome at a two-year follow-up compared with non-anatomic SB reconstruction. The hypothesis was that the anatomic DB technique results in less rotatory and AP laxity compared with the non-anatomic SB technique.

# 03 PATIENTS

Table A *Patients*

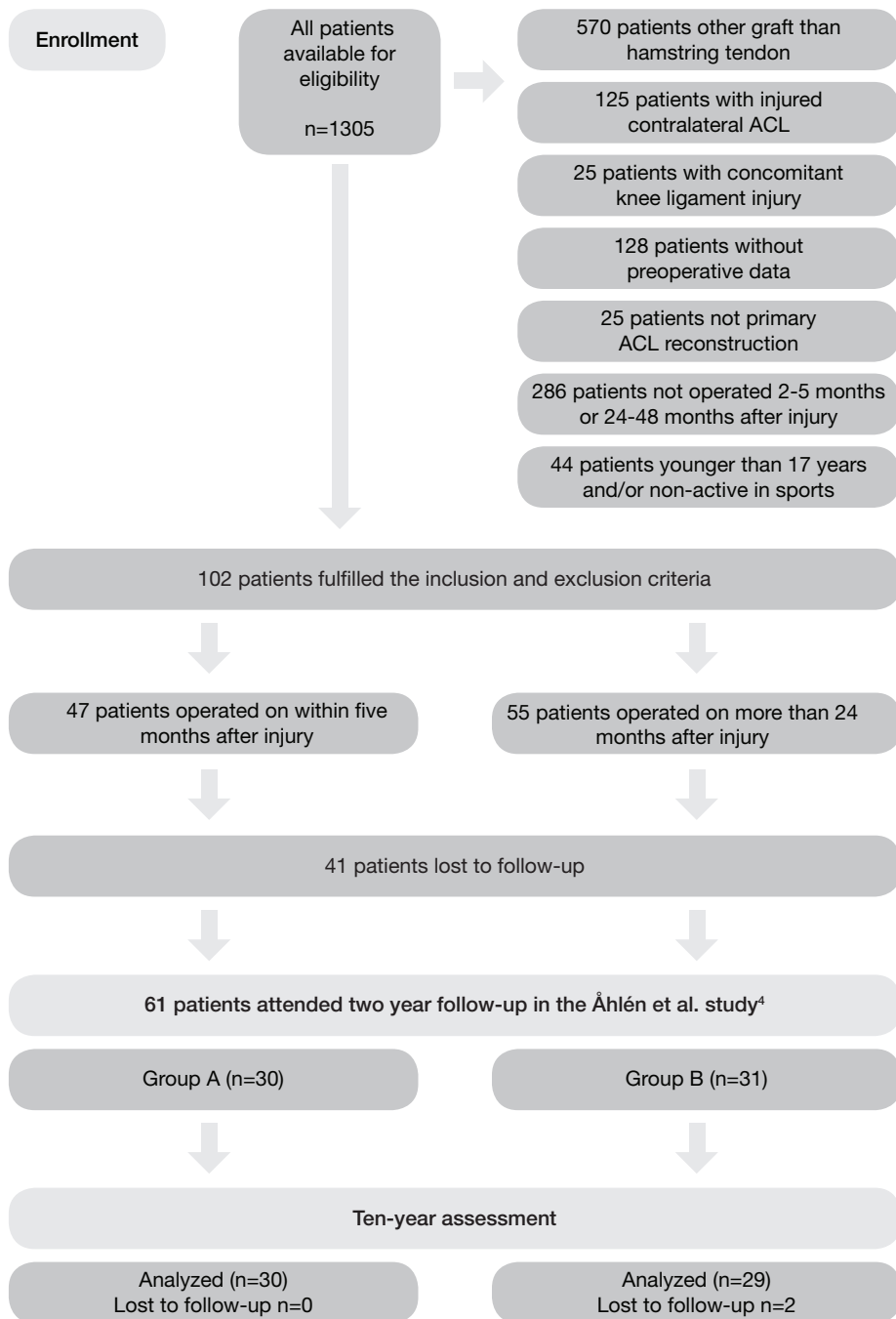
	Total number	Age at operation (years) Mean (SD)	Women/men	Allocation of patients
Study I	N=61 Group A n=30 Group B n=31	Group A 26 (9.1) Group B 27 (6.5)	Group A 15/15 Group B 12/19	
Study II	N=105 SB group n=52 DB group n=53	SB group 28 (8.5) DB group 30 (9.2)	SB group 15/37 DB group 18/35	All patients in the SB group included in Study III 45 patients in the DB group included in Study IV
Study III	N=52	28 (8.5)	15/37	All patients included in Study II
Study IV	N=94 SB group n=49 DB group n=45	SB group 32 (8.8) DB group 29.6 (8.4)	SB group 18/31 DB group 13/32	45 patients included in Study II

The inclusion and exclusion criteria were the same in all the studies. The **inclusion criteria** were unilateral ACL rupture and primary reconstruction using semitendinosus (ST) or semitendinosus and gracilis (ST/G) tendon autografts. ACL rupture was determined by either clinical and/or MRI examinations. The **exclusion criteria** were a concomitant posterior cruciate ligament (PCL) injury, medial or lateral collateral ligament laxity greater than 1+, previous major knee surgery, or a contralateral ACL injury before the date of the index operation.

## Study I

Study I is a long-term follow-up of patients previously reported on in a short-term follow-up study [4]. The study includes a retrospectively generated hypothesis on prospectively collected data. The reconstructions were performed between April

1996 and November 2005 and all the data derive from three different hospitals in Sweden. The study comprised two groups. In Group A, the patients (n = 30) were operated on within five months (median, 3; range 2-5 months) and, in Group B (n = 31), the patients were operated on more than 24 months (median, 30; range 24-48 months) after the injury. Two patients from the original study in Group B were lost to follow-up. One patient declined participation during the follow-up and the other moved to another country (Figure 4). The demographics of the study are presented in Table 1 in Paper I, page 4. There were no significant differences between the groups in terms of age at index operation, gender, injured side and pre-injury Tegner activity scale. The mean time for follow-up was 123 months in Group A and 128 months in Group B (p=0.44).



*Group A, early reconstruction group*  
*Group B, late reconstruction group*

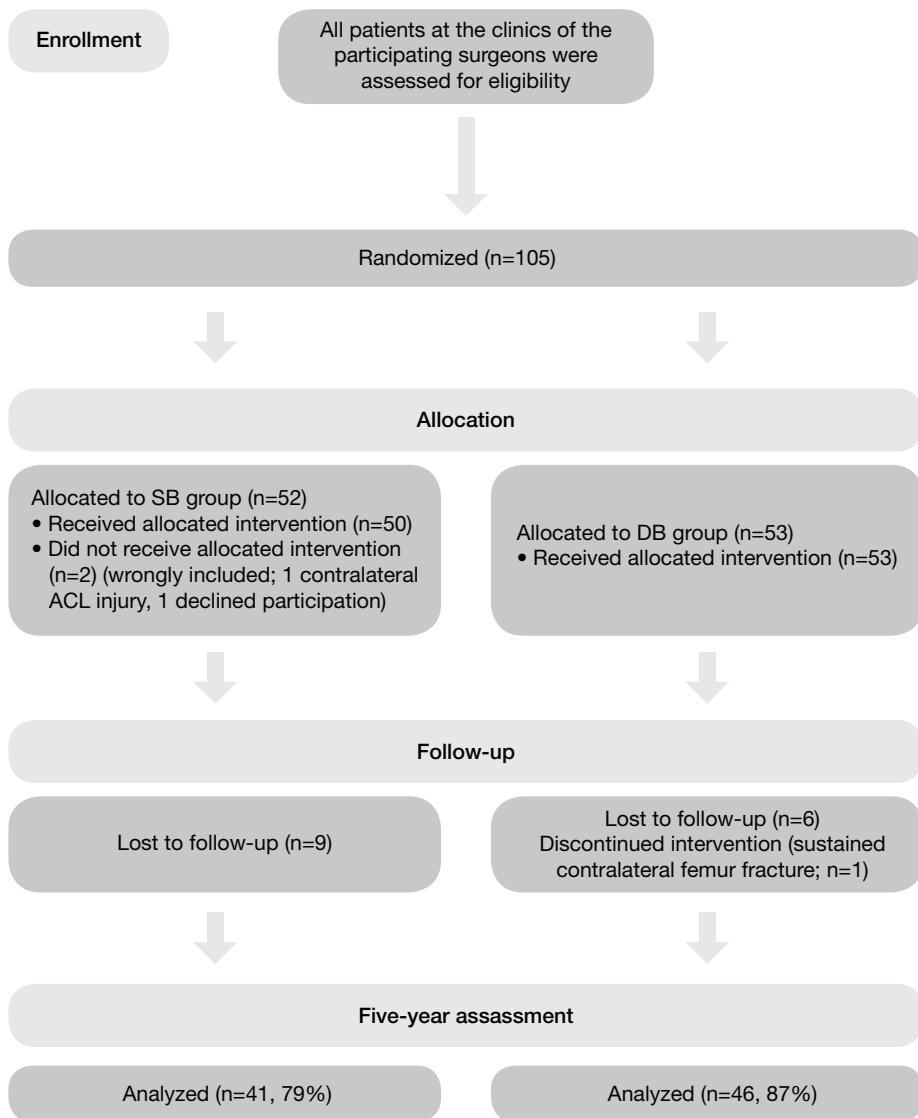
**Figure 4.** Flowchart of patients included in Study I.

## Study II

Study II is a mid-term follow-up of a previously reported cohort [3]. The participants were recruited from two hospitals ( $n = 31$  and  $n = 74$  respectively). The original cohort was an unselected group of patients without regard to age (if  $>18$  years), gender, or activity level. Patients fulfilling the inclusion criteria were consecutively asked to participate in the study. The indication for surgery was failed non-surgical treatment or participation in pivoting sports in which non-surgical treatment was regarded as an inferior treatment option. The participants were then randomised to undergo surgery using either the anatomic SB ( $n=52$ ) or anatomic DB ( $n=53$ ) technique. Randomisation took place using sealed envelopes administered by the study co-ordinator, who drew them from a box with an equal number of envelopes for both study groups (Figure 5). Moreover, all the envelopes were sealed and opened just before the operation when the patients were anaesthetised.

Between March 2008 and September 2009, a total of 105 patients were randomised and they underwent surgery in either the SB group or the DB group. Two patients did not receive the allocated intervention, because they were incorrectly included in the study; one patient discontinued the intervention during the follow-up because of a contralateral femoral fracture; and 15 patients were lost to follow-up. The five-year follow-up examinations were performed on 87 patients (83%; SB:  $n = 41$ ; DB:  $n = 46$ ), (Figure 5).

The demographics of the study groups are presented in Table 1 in Paper II, page 1,229. The pre-injury Tegner activity level was significantly lower in the DB group (SB group: mean,  $7.8 \pm 1.3$ ; DB group: mean,  $7.3 \pm 1.5$ ,  $p=0.02$ ). Preoperatively, there were no significant differences between the study groups in terms of the preoperative Tegner activity level, Lysholm knee score, the one-leg-hop test, extension or flexion deficit of the knee, the KOOS, the side-to-side knee laxity tests and the pivot-shift test.



*SB, anatomic single-bundle ACL reconstruction*  
*DB, anatomic double-bundle ACL reconstruction*

**Figure 5.** *Flowchart of patients included in Study II.*

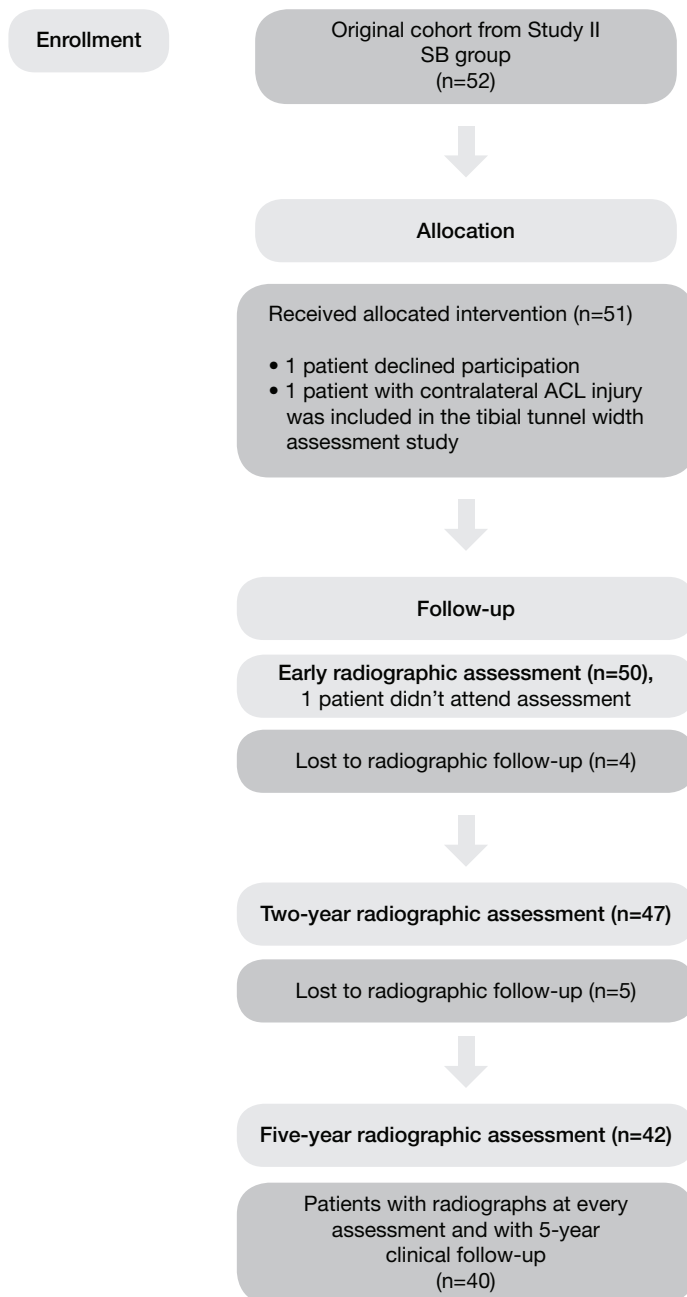
### Study III

The patients in Study III were a subset from Study II. The patients in the SB group (n=52) in Study II were included in Study III and were followed up prospectively with radiographs directed at the tibial tunnel, until five years after surgery. As a result, 51 patients were included in Study III (Figure 6). The radiographs were obtained on three occasions; in the early postoperative period (mean, 5 months  $\pm$  2.3 months), after two years and after five years. One patient who sustained a contralateral ACL injury before the date of the index operation, but after the

preoperative clinical tests, was kept in the radiographic part of the study but not in the side-to-side clinical assessments. Patients fulfilling the inclusion criteria were asked consecutively to participate in the study.

The demographic characteristics of the study group are presented in Table 1, Paper III, page 2,189. The mean follow-up period was 65 months ( $\pm$ 3.9 months). Of 51 patients, 40 (78%) had radiographs taken at all three radiographic assessments and underwent clinical examinations preoperatively and at the five-year follow-up (Figure 6).





*SB, single-bundle*

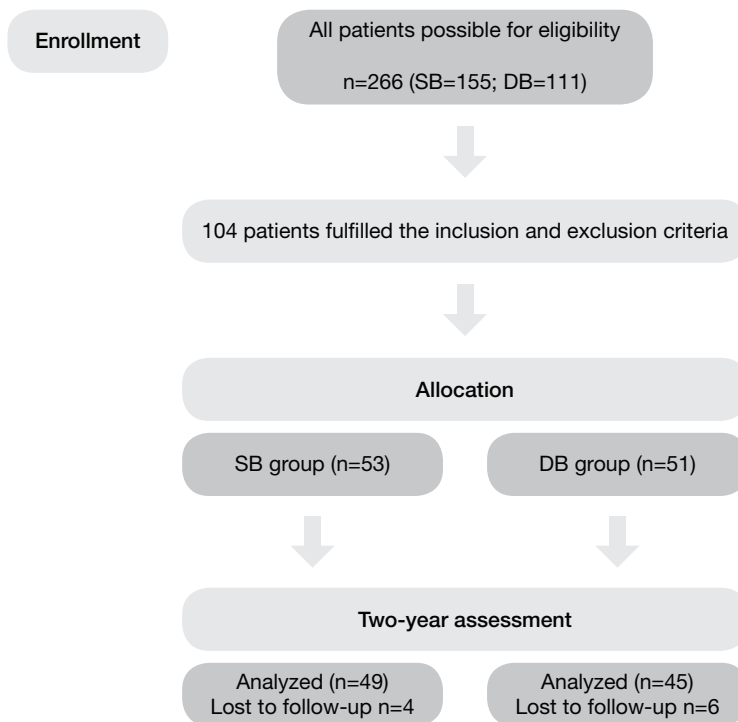
**Figure 6.** *Flowchart of patients included in Study III.*

### Study IV

In a prospective consecutive series, 45 patients underwent ACL reconstruction using the anatomic double-bundle technique (DB group). These patients were a subset from a previous study by Ahldén et al. [3]. In another prospective consecutive series, 49 patients underwent ACL reconstruction using the non-anatomic single-bundle technique (SB group), (Figure 7). The study involves prospectively collected data; however, the hypothesis was implemented retrospectively. The study groups consisted

of unselected patients without regard to age (if >18 years), gender, activity level, weight and height. All the operations were performed in two hospitals in the same region of Sweden.

The demographics of the study groups are presented in Table 1, Paper IV, page 1,309. There were no significant differences between the two groups preoperatively, in terms of age, gender, time between injury and operation and associated injuries at the time of the index operation. The follow-up period was two years.



*SB, non-anatomic single-bundle ACL reconstruction*  
*DB, anatomic double-bundle ACL reconstruction*

**Figure 7.** Flowchart of patients included in Study IV.

# 04 METHODS

## 4.1 SURGICAL TECHNIQUES

### Graft Harvesting

At the index operation, the ST or ST/G autografts were harvested through a 3-cm oblique or longitudinal skin incision over the pes anserinus on the anteromedial aspect of the proximal tibia. The sartorius fascia was incised parallel to the fibres of the fascia just above the thicker and more distally inserted

ST tendon. After the vinculae had been cut under visual control, the full length of the tendons was harvested with a semi-blunt, semi-circular open tendon stripper (Acufex, Microsurgical Inc., Mansfield, MA, USA). A harvest-site drain was not used and the wound was only closed with skin sutures.

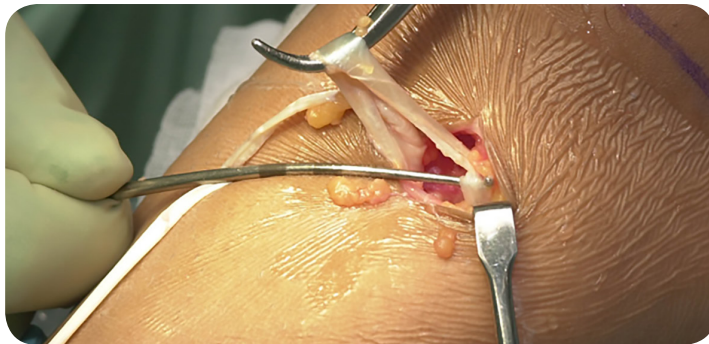


Figure 8a. *The vinculae are exposed and cut under visual control.* © J. Kartus

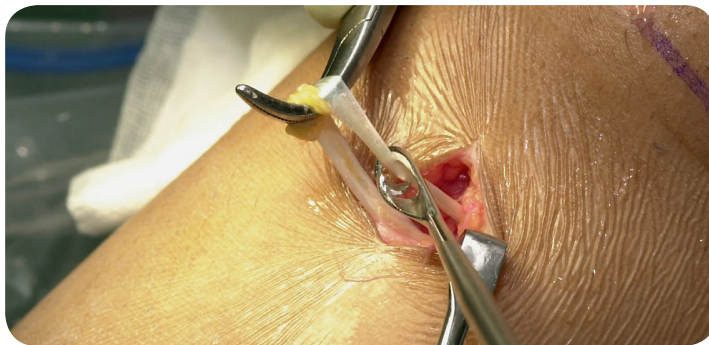
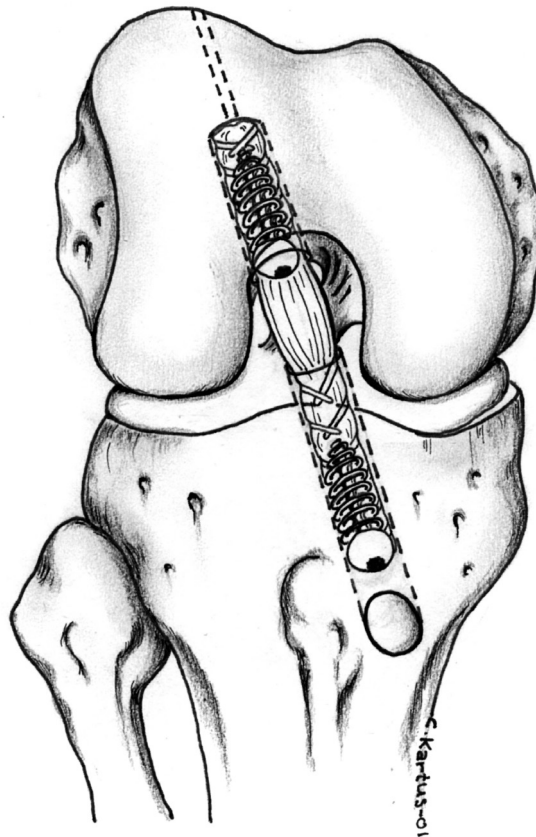


Figure 8b. *Tendon harvesting with a tendon stripper.* © J. Kartus

### Study I (non-anatomic SB technique)

Three senior surgeons performed the reconstructions using hamstring tendon autografts according to previously established and described principles [118]. Specifically, the ST or ST/G autograft was harvested through an oblique skin incision, as described previously. Associated intra-articular injuries, such as meniscal ruptures and chondral lesions, were addressed at the time of the index operation. Small meniscal tears were debrided and larger tears were resected or sutured. The femoral drilling was performed using a fluted reamer either through

the anteromedial portal (n=45) or using the transtibial approach (n=16). Tibial drilling was performed using a tibial elbow aimer and a fluted reamer. All the bone tunnels were drilled to approximately 0.5 mm above the diameters of the respective grafts. Metallic interference screws (RCI®, Smith and Nephew, Andover, MA, USA) were used for graft fixation on both sides, with a size of 7 mm on the femoral side and 7 to 9 mm on the tibial side. The anatomic principles in terms of ACL reconstruction technique had not yet been established when the operations were performed.



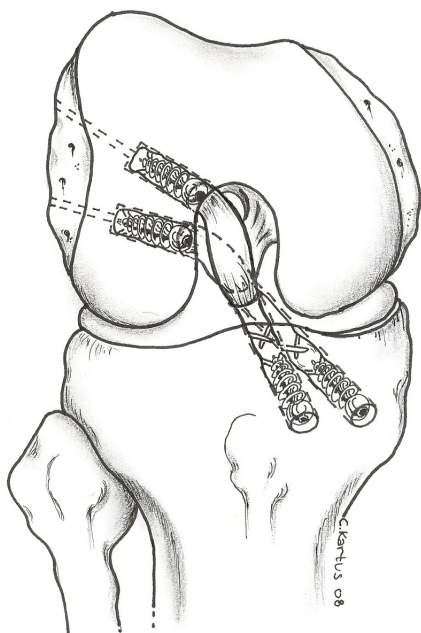
**Figure 9.** Non-anatomic placement of the graft.  
*Note that the graft has a more vertical orientation.*  
© C. Kartus

## Study II (anatomic DB and SB techniques)

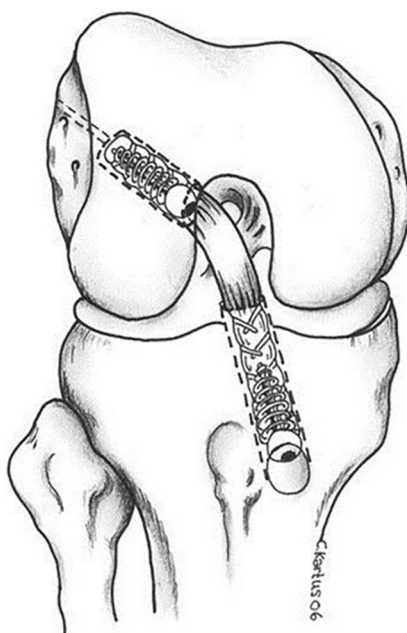
Four senior surgeons performed all the reconstructions. Standard anterolateral and AM portals were established peri-operatively. Associated intra-articular injuries, such as meniscal ruptures and chondral lesions, were addressed at the time of the index operation. Femoral and tibial ACL footprints were identified, in addition to the lateral intercondylar and bifurcate ridges. ACL remnants were resected. The ST

and G tendons were harvested through a longitudinal skin incision, as described previously. Femoral drilling was performed through the AM portal. The tibial tunnels were drilled using a tibial elbow aimer and a fluted reamer.

In both techniques, all the tunnels were placed anatomically in accordance with the knowledge of anatomic ACL reconstruction available in 2008–2009 when the surgeries were performed.



**Figure 10a.**  
*Anatomic DB ACL reconstruction.*  
© C. Kartus



**Figure 10b.**  
*Anatomic SB ACL reconstruction.*  
© C. Kartus

### Anatomic DB technique

For the DB technique, both the femoral and tibial remnants of AM and PL bundles were identified with the knee in 90° of flexion. The femoral tunnels were addressed first. The femoral insertion sites of the AM and PL bundles were identified and marked with an awl. The AM tunnel was drilled

first just deep to the bifurcate ridge, followed by the PL tunnel just shallow to the bifurcate ridge in 39 of the patients using a free-hand technique and in 14 patients using a DB femoral guide (Acufex anatomic ACL guide system, Smith & Nephew, Andover, MA, USA). The tibial tunnels were drilled in the centre of the footprint

of the AM and PL bundles; the AM tunnel was placed in line with the anterior horn of the lateral meniscus and the PL tunnel in front of the PCL. All the drill holes had a diameter 0.5 mm larger than the graft diameters. On the femoral and the tibial sides, the drill holes were between 6.5 and 7 mm for the AM bundle and 6 mm for the PL bundle. Metal interference screws 6 x 20 mm (RCI®, Smith & Nephew, Andover, MA, USA) were used on the femoral side in

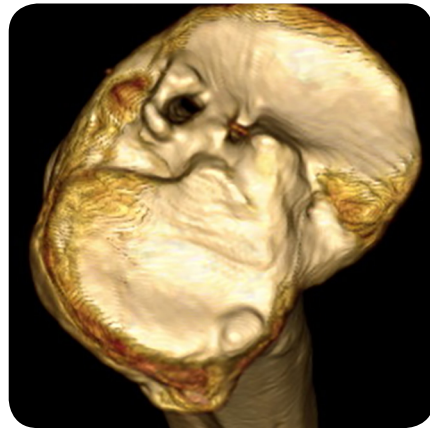
both tunnels and biocomposite screws, either 7.3 x 20 mm or 7.3 x 25 mm (Matryx®, ConMed Linvatec, Largo, FL, USA) were inserted well inside the cortical bone on the tibial side. The AM graft consisted of a double ST tendon and the PL graft consisted of a double or triple G tendon. Tibial fixation was performed at 5° to 10° of knee flexion for the PL bundle and at 40° to 60° of knee flexion for the AM bundle [3].



**Figure 11a.**

*Figures 11a–b. Three-dimensional (3D) computed tomography (CT) images showing the placement of the femoral (11a) and the tibial (11b) tunnels after anatomic DB reconstruction.*

© M. Ahldén



**Figure 11b.**

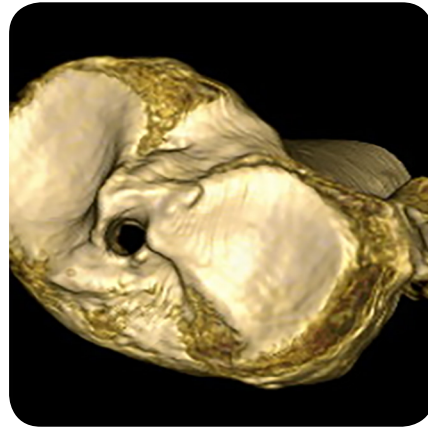
### Anatomic SB technique

The femoral tunnel was addressed first. The femoral ACL insertion site was marked with an awl in the shallow aspect of the AM bundle insertion site, near the centre of the ACL footprint to place the centre of the tunnel just deep to the bifurcate ridge about 8–10 mm from the posterior cartilage at 3 or 9 o'clock in the notch orientation, with the knee in 90° of flexion. The femoral tunnel was predrilled using a 4.0-mm sharp non-cannulated drill or a guide wire before the final tunnel, determined by the size of the graft, was drilled. On the tibial side, the

centre of the tunnel was placed in line with the anterior horn of the lateral meniscus. All the bone tunnels were drilled 0.5 mm larger than the diameter of the respective grafts, which were between 7.5 and 8.5 mm. Metal interference screws, 7 x 25mm (RCI®), were used on the femoral side and biocomposite screws, 9 x 25 mm (Matryx®), were inserted well inside the cortical bone on the tibial side. The ACL graft consisted of four- or five-stranded ST/G tendons. Tibial fixation was performed at 10° to 20° of knee flexion [3].



**Figure 12a.**



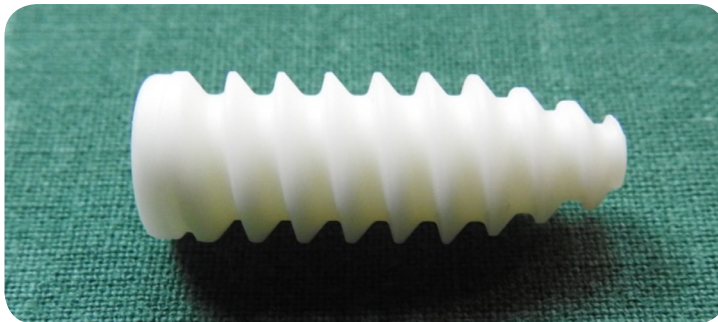
**Figure 12b.**

*Figures 12a-b. 3D CT images showing the placement of the femoral (12a) and the tibial (12b) tunnels after anatomic SB reconstruction. © M. Ahldén*

### **Study III (anatomic SB technique)**

Study III used the same surgical principles in terms of the SB ACL reconstruction technique as Study II, as the patients in Study III were a subset from Study II (SB group). In terms of the fixation device on the tibial

side, biocomposite interference screws, 9 x 25 mm (Matryx®), were used. Specifically, these screws were made of self-reinforced poly-levo (96%)/dextro (4%)-lactide/ $\beta$ -TCP [SR-PL(96)/D(4)LA/ $\beta$ -TCP] (77% PLDLA and 23%  $\beta$ -TCP).



**Figure 13.** *Image showing the biocomposite interference screw (Matryx®) used in Studies II and III and in the DB group in Study IV. © I. Karikis*

#### **Study IV (anatomic DB technique and non-anatomic SB technique)**

Three senior surgeons performed the reconstructions. Standard anterolateral and AM portals were established. Associated intra-articular injuries, such as meniscal ruptures and chondral lesions, were addressed at the time of the index operation. The ST and G tendons were harvested through a 3-cm longitudinal skin incision, as described previously. All femoral drillings were performed using a fluted reamer through the anteromedial portal. All tibial drillings were performed using a tibial elbow aimer and a fluted reamer. All bone tunnels were drilled to approximately 0.5 mm above the diameters of the respective grafts.

##### **Anatomic DB technique**

The surgical technique in terms of anatomic

DB reconstruction was the same as that described above in Study II.

##### **Non-anatomic single-bundle technique**

In the non-anatomic single-bundle group, the hamstring tendons were prepared for a quadruple graft with a diameter usually between 7 and 8.5 mm. The femoral tunnel was placed approximately at the 10.30 or 01.30 o'clock position in a right or a left knee respectively, with the knee flexed at 90°. The tibial tunnel was placed anterior to the normal posterior cruciate ligament through the remnant of the native ACL. A 7 mm metal interference screw (RCI®, Smith & Nephew, Andover, MA, USA) was used on the femoral side, while a 9 mm RCI® screw was used on the tibial side. After the femoral screw had been inserted, firm traction was applied to the graft during the insertion of the tibial screw, with the knee in full extension.

## 4.2 REHABILITATION

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All the patients underwent rehabilitation according to the same guidelines, under the supervision of their local physiotherapists, permitting immediate full weight-bearing, full ROM including full hyperextension and without the use of a brace [28,211]. Closed kinetic chain exercises were started immediately postoperatively [213]. Running was permitted at three months

and contact sports at the earliest six months postoperatively, provided that the patient had regained full functional stability in terms of strength, co-ordination and balance, as compared with the contralateral leg. It was not uncommon for full functional stability not to be achieved until 9-12 months postoperatively.

## 4.3 CLINICAL EXAMINATIONS

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### **Examiners**

In Study I, all the preoperative and final follow-up examinations were performed by physiotherapists who were not involved in the rehabilitation. Preoperatively, multiple physiotherapists were involved, but the final follow-up was performed by only one physiotherapist.

In Study II, a single, independent physiotherapist, who was not involved in the re-

habilitation, performed all the pre- and postoperative follow-up clinical assessments. The physiotherapist was blinded to the surgical technique to which the patient had been randomised but not to the aim of the study at the time of the examination.

In Study III, all the preoperative and final follow-up examinations were performed by the same physiotherapist as in Study II.

In Study IV, one physiotherapist, who was



not involved in the rehabilitation, performed all the pre- and postoperative follow-up examinations. The physiotherapist was blinded to the type of surgical technique that was used.

#### **Manual Lachman test (Studies I and II)**

The manual Lachman test is regarded as the most sensitive clinical test for diagnosing an acute complete ACL tear [26,112,160]. The test is performed with the patient in the supine position and the knee flexed at about 20° to 30°. The examiner stabilises the femur

with one hand and firm pressure is applied to the proximal tibia with the other hand in order to translate the tibia anteriorly. In cases of ACL deficiency, increased translation and a “soft end-point” is felt, while a sufficient ACL prevents anterior translation and a “firm end-point” is felt.

The manual Lachman test was estimated by the examiner as the amount of anterior or drawer movement of the tibia and was graded as 0, + (<5 mm), ++ (5-10 mm), or +++ (>10 mm), compared with the uninjured contralateral knee [202].



**Figure 14.** *The manual Lachman test assesses the anteroposterior laxity of the knee. © I. Karikis*

#### **KT-1000 instrumental laxity (Studies I, II, III and IV)**

The instrumented KT-1000 arthrometer (MEDmetric®Corp, San Diego, CA, USA) was used to evaluate the anterior displacement of the tibia in relation to the femur. The patients were in the supine position during the examination and both legs were placed on a thigh support with 30° of knee flexion [77]. A foot-rest and a strap around the thighs kept the legs in a neutral position [63,81]. After calibrating the instrument to zero before the test, at least three measurements were made on each knee and the

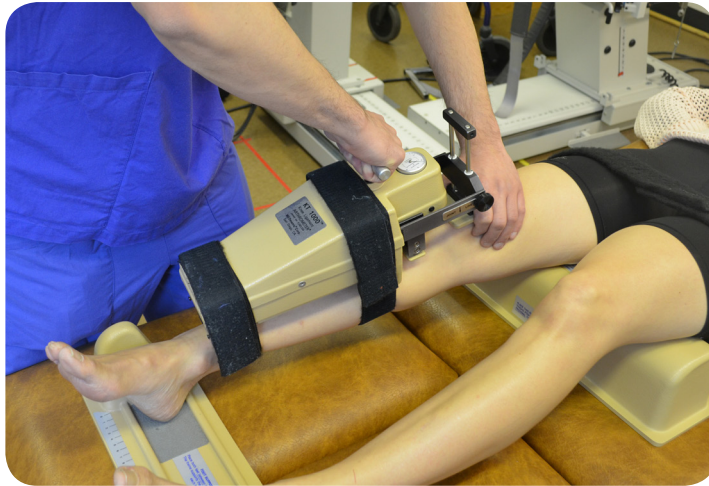
average value was registered. The amount of displacement was interpreted to the nearest 0.5 mm and a side-to-side difference was calculated [52]. The uninjured knee was always examined first.

The reproducibility of this test has been reported as good [51,187,214]. Furthermore, all KT-1000 arthrometer assessments – apart from the preoperative assessments in Study I – were performed by one examiner, as suggested by Sernert et al. [173].

In Study I, a force of 89 Newtons (N) was used preoperatively and a force of 134 N and the maximum manual test (MMT) were

used at the follow-up. In Studies II and III, a force of 134 N and the MMT were used both preoperatively and at the follow-up. In

Study IV, a force of 134 N was used both preoperatively and at the follow-up.



**Figure 15.** *The KT-1000 arthrometer quantifies the anteroposterior knee laxity. © I. Karikis*

#### **Pivot-shift test (Studies I, II, III and IV)**

The pivot-shift test is regarded as the most specific test for diagnosing ACL tears [26,112,160]. This test is dynamic and evaluates a combination of rotational and translational laxity and closely mimics the subluxation that patients experience after ACL injury. The pivot-shift test is performed with the patient in the supine position, the hip in 30° of flexion and the knee in full extension. The examiner applies a valgus strain and slightly rotates the

tibia internally. In this position, the lateral tibial plateau subluxates anteriorly in cases of ACL deficiency. The knee is then flexed slowly and the subluxated lateral compartment of the knee relocates. The relocation of the tibia occurs at about 30° of knee flexion and can be experienced by the examiner, indicating a positive result for the test.

The pivot-shift test was graded clinically using grades 0 to III, according to IKDC guidelines [73].



**Figure 16.** Image showing the execution of the pivot-shift test.  
© I. Karikis

#### Range of motion (ROM) (Studies I, II, III and IV)

The ROM was measured with the patient in the supine position using a hand-held goniometer and was recorded to the nearest 5° [37]. The uninjured leg was always tested first. Full active range of extension and flexion were measured and cases of

hyperextension were also noted. The side-to-side differences were calculated and, if the measurements displayed a side-to-side difference of  $\geq 5^\circ$  in either extension or flexion, the patients were dichotomously distributed as having or not having an extension or flexion deficit.



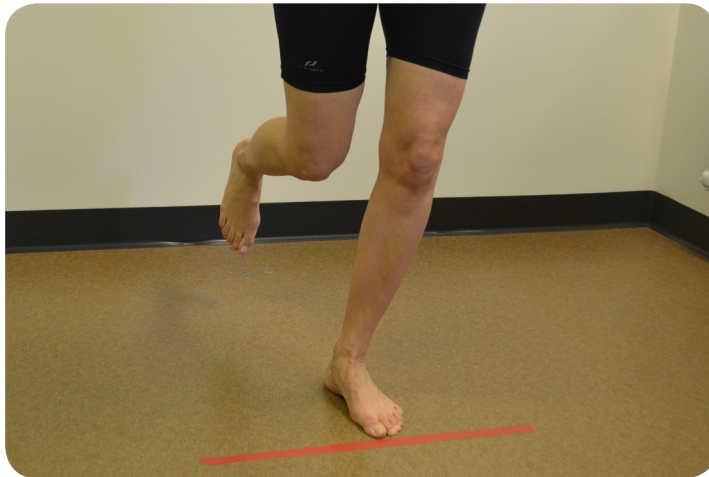
**Figure 17.** A hand-held goniometer was used to measure the ROM.  
© I. Karikis

#### 4.4 FUNCTIONAL PERFORMANCE TESTS

##### **The one-leg-hop test (Studies I, II and IV)**

The one-leg-hop test was performed by jumping and landing on the same foot holding the hands behind the back. The non-injured leg was always tested first.

Three attempts were allowed for each leg and the longest hop was registered for each leg separately. A quotient (%) between the index and non-injured leg was calculated [199].

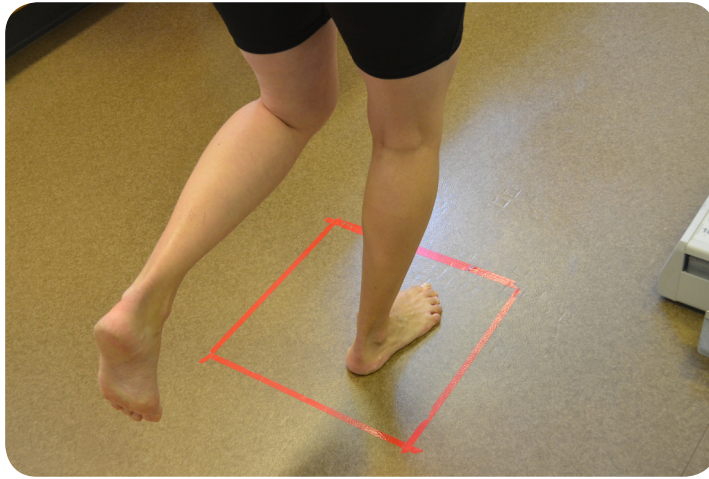


**Figure 18.** *The one-leg-hop test.* © I. Karikis

##### **The square-hop test (Study II)**

The square-hop test was performed by standing on the leg to be tested outside a 40 x 40 cm square marked with tape on the floor. For the right leg, the patients were instructed to jump clockwise in and out of the square as many times as possible during a period of 30 seconds. For the left leg, the patient performed the test in a counter-clockwise direction. The test was

video-recorded and assessed by the same blinded physiotherapist and both the total number of jumps and the number of successful jumps (i.e. without touching the taped square) were counted. A quotient (%) between the index and non-injured leg was calculated. This test was modified from the one previously described by Östenberg et al. [150].

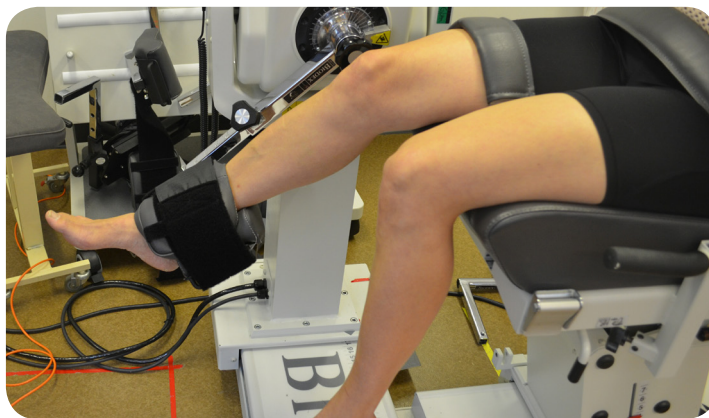


**Figure 19.** *The square-hop test.* © I. Karikis

#### **Isokinetic muscle strength assessment (Study I)**

The Biodex strength-testing machine was used for isokinetic strength testing (Biodex Multi-Joint System 4 Pro, Biodex Medical Systems Inc, Shirley, NY, USA). The patients warmed up by cycling on a stationary bicycle for five minutes. The non-operated side was always tested first. The isokinetic peak torque measurements for knee flexion and extension were measured at 60° and

180°/sec (five and 10 repetitions respectively). The patients were in the prone position with their hips in extension when measuring strength in knee flexion, as suggested by Tashiro et al. [197]. To determine the deep knee flexion strength, the torques at 90° of knee flexion were obtained from the torque curves at 60°/sec and at 180°/sec. The Limb Symmetry Index (LSI) was calculated as the quotient (%) between the index and non-injured leg in all measurements.



**Figure 20.** *Image showing the Biodex machine (Biodex Multi-Joint System 4 Pro, Biodex Medical Systems Inc, Shirley, NY, USA) that was used to assess muscle strength.* © I. Karikis

## 4.5 FUNCTIONAL SCORES

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### **Lysholm knee scoring scale (Studies I, II, III and IV)**

The modified Lysholm knee scoring scale was assessed by the patient using a self-administered questionnaire [36,198]. The questionnaire did not show the scores for the alternative answers to the patient, as described by Höher et al. [78]. The score consists of eight items; Limp (5 points), Support (5 points), Locking (15 points), Instability (25 points), Pain (25 points), Swelling (10 points), Stair Climbing (10 points) and Squatting (5 points).

### **Tegner activity scale (Studies I, II, III and IV)**

The Tegner activity scale was developed to complement the Lysholm knee scoring scale. The score was assessed by the examiner during the course of the examination preoperatively and at the follow-ups. The score is graded between 0-10, where grades

0-4 cover activities of daily living and work and grades 5-10 represent recreational or competitive sport activities [198].

### **The Knee injury and Osteoarthritis Outcome Score (KOOS) (Studies I, II and IV)**

The KOOS was originally developed to assess patients with OA. It has been validated for ACL reconstruction in both the short and long term [167,168]. It is a self-administered PROM and consists of 42 questions distributed in five separately scored subscales; Pain (9 questions), Symptoms (7 questions), Function in Daily Living (ADL) (17 questions), Function in Sports and Recreation (Sports/Rec) (5 questions) and Knee-related Quality of Life (QoL) (4 questions). All questions are graded from zero to four points. For each subscale, the score is normalised to a 0-100 scale. A higher score represents better function.

## 4.6 RADIOGRAPHIC ASSESSMENTS

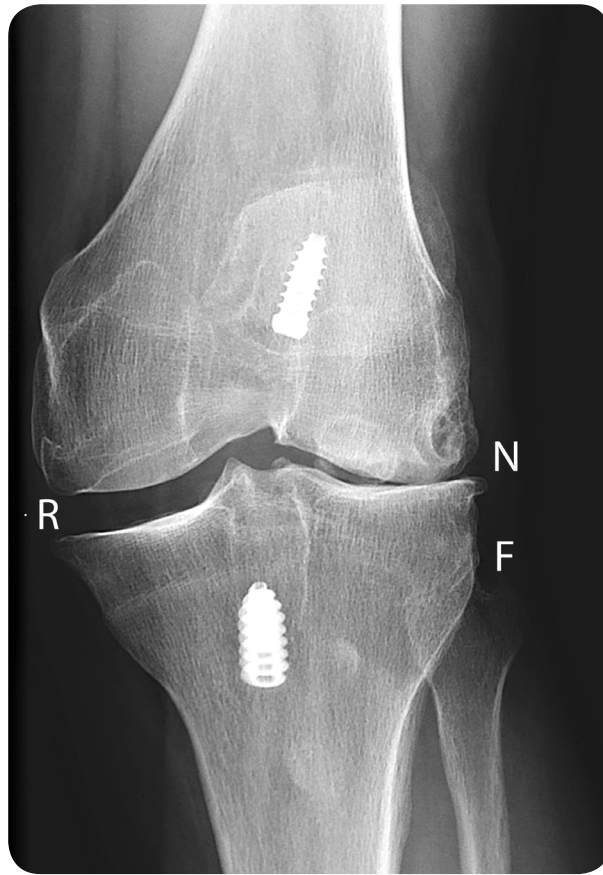
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### **Osteoarthritis (OA) evaluation (Studies I and II)**

In Study I, standard digital radiographs with the knee in 30° of flexion and weight-bearing AP and lateral views of both the index and contralateral knees were obtained at follow-up. In Study II, standard digital radiographs of the index knee were obtained on two occasions; in the early postoperative period (at approximately six weeks) and at the five-year follow-up.

An independent musculoskeletal radiologist interpreted the radiographs and assessed them according to the grading systems of Ahlbäck and Kellgren-Lawrence

[1,96]. Moreover, the Fairbank system, originally designed to detect minor changes after meniscectomy, was used [60]. For the Fairbank system, the cumulative number of positive findings, from 0 to 6, was calculated for each patient, as previously described by Lidén et al. [118]. Furthermore, in Study II, patellofemoral OA was classified as “none”, “minor”, “moderate”, or “severe” and the presence of patellofemoral osteophytes as “none”, “minor”, “moderate”, or “large”. The radiologist has previously been analysed for reproducibility for OA classifications of the knee, with kappa values between 0.55 and 1.00 [118].



**Figure 21.** Image showing a standard weight-bearing radiograph in the AP view according to the Fairbank classification system (F, flattening; N, narrowing; R, ridging). © J. Kartus

### Tibial tunnel enlargement (Study III)

The enrolled patients underwent unilateral standard digital radiographs of the index knee, as described above. The radiographic assessments were performed in the early postoperative period (mean, 5 months  $\pm$  2.3 months), after two years and after five years. The same radiologist as above interpreted the radiographs and assessed the tibial bone tunnels. The tunnels were determined by using the sclerotic margins as landmarks. The measurements were obtained with the digital measurement function in the software. At three points perpendicular to the length axis of the tunnel, one at each end

and one in the centre of the tunnel, on both the AP and lateral views, the width was measured. The mean value of the three measurements on each projection was calculated and defined as the width of the tunnel. The inter-rater and intra-rater test-retest reliability of this procedure has been considered good, with interclass correlation coefficient values of between 0.84 and 0.97 for the tibial measurements [111]. To obtain reliable tibial tunnel measurements regardless of the magnification factor, the head of the metallic femoral RCI<sup>®</sup> screw was used as a reference. As a result, the diameter of the head of the femoral screw was

measured on both the AP and lateral views on all radiographs for each patient. Using the knowledge of the true diameter of the head of the RCI® screw, a calculation of the true tibial tunnel measurement was made

according to the formulas: (1) true femoral screw head/measured femoral screw head = magnification factor and (2) tibial tunnel measurement x magnification factor = true tibial tunnel measurement.

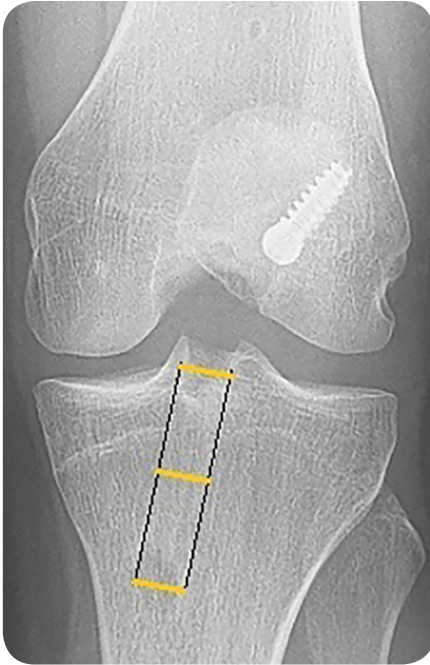


Figure 22a.

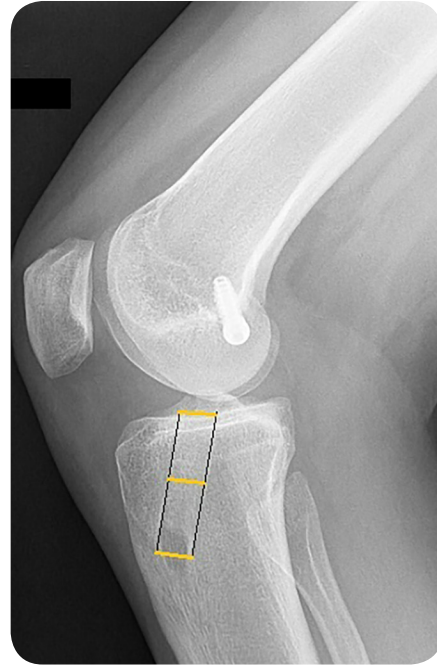


Figure 22b.

*Images showing the points of measurement of the tibial tunnel width in the anteroposterior view (22a) and in the lateral view (22b). Reprinted with kind permission from Elsevier Publications.*

## 4.7 STATISTICAL METHODS

### Study I

Mean ( $\pm$  standard deviation) and median (range) values are presented when applicable. For comparisons of dichotomous variables between the groups, the chi-square test or Fisher's exact test was used. For comparisons of both continuous and non-continuous variables, the Mann-Whitney *U* test was used. Wilcoxon's signed-rank test was used for comparisons of the preoperative and postoperative data within the study groups. The paired *t*-test was used for the statistical analysis of muscle strength

measurements. A *p*-value of  $< 0.05$  was considered statistically significant.

In the statistical analysis of the follow-up data, patients who sustained a contralateral ACL injury were excluded when the side-to-side difference-based variables were analysed.

The primary variable in the study was the presence of OA in the index knee at the long-term follow-up. The power analysis was based on the need for meniscal resection at the index operation and the assumption that at least these patients would



develop OA in the long term. Specifically, if the patients in Group A had a 25% prevalence of OA, while the patients in Group B had a prevalence of 60%, then 30 patients were required in each group at the long-term follow-up to reach a power of 80% with a p-value of  $< 0.05$ .

### Study II

Mean ( $\pm$  standard deviation) and median (range) values are presented when applicable. For comparisons of dichotomous variables between the groups, the chi-square test was used. When comparisons of continuous and non-continuous variables were required, the Mann-Whitney *U* test was used. Wilcoxon's signed-rank test was used for comparisons of the pre- and postoperative data and for comparisons between six-week and five-year radiographic assessments within the study groups. Spearman's test was used for correlation analysis between the cumulative Fairbank score and BMI. Statistical significance was set at a p value of  $< 0.05$ .

Patients who sustained a contralateral ACL injury were excluded when the side-to-side difference-based variables were analysed at the five-year follow-up.

The primary variable in the study was the pivot-shift test. The study was powered to reveal a difference of 1 grade on the pivot-shift test between the study groups, with a power of 80%. It was assumed that a difference of 1 grade in the pivot-shift test was clinically important; the standard deviation of the pivot-shift test was estimated to be 1.5 grades. To reach a power of 80%, 36 patients were thus needed in each group. To increase the power of the study and to allow for dropouts, 105 patients were initially randomised.

### Study III

Mean ( $\pm$  standard deviation) and median (range) values are presented when

applicable. Wilcoxon's signed-rank test was used for comparisons of the preoperative and five-year follow-up clinical assessment data. A statistical comparison of the means over time was performed with one-way repeated-measures analysis of variance, whereas the Bonferroni test was used for the post-hoc analyses. Spearman's test was used for correlation analysis between the KT-1000 arthrometer laxity measurements, the Lysholm knee score and the Tegner activity level and the diameter of the tibial tunnels at the five-year follow-up. Statistical significance was set at a p value of  $< 0.05$ .

To be able to detect a decrease in the tunnel width of 1 mm, with a standard deviation of 2 mm, a power of 80% and a  $p < 0.05$ , 33 patients were required. To increase the power of the study and to allow for missing values, just over 50 patients were included in the study.

### Study IV

Mean ( $\pm$  standard deviation) and median (range) values are presented when applicable. For comparisons of dichotomous variables between the groups, the chi-square test or Fisher's exact test was used. In terms of comparisons of both continuous and non-continuous variables, the Mann-Whitney *U* test was used. Wilcoxon's signed-rank test was used for comparisons of the preoperative and postoperative data within the study groups. A p value of  $< 0.05$  was considered statistically significant.

The primary variable in the study was the pivot-shift test. It was estimated that 90% of the patients would have a negative pivot-shift test in the anatomic DB group and that the corresponding percentage would be 60% in the non-anatomic SB group. To reach a power of 80%, the required sample size would be just over 30 patients in each group. To increase the power of the study, the aim was to include 50 patients in each group.

## 4.8 ETHICS

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### **Study I**

The Regional Ethical Review Board at the University of Gothenburg approved the study (approval no. 2009-12-21/575-09/Gothenburg). The participants received oral and written information about the study, after which written consent was obtained.

### **Study II**

The Regional Ethical Review Board at the University of Gothenburg approved the study (approval no. 2008-05-08/157-08/Gothenburg). The participants received oral and written information about the study, after which written consent was obtained.

### **Study III**

The Regional Ethical Review Board at the University of Gothenburg approved the study (approval no. 2008-05-08/157-08/Gothenburg). The participants received oral and written information about the study, after which written consent was obtained.

### **Study IV**

The Regional Ethical Review Boards at the Universities of Gothenburg and Stockholm approved the study (approval no. 2008-05-08/157-08/Gothenburg; 2011-04-15/2011/337-31/3/Stockholm).

# 05 RESULTS

## 5.1 STUDY I

The mean follow-up period was 123 months in Group A and 128 months for Group B (n.s.). There was no significant difference between the groups in terms of the prevalence of meniscal or chondral lesions at the index operation (Table 1, Paper I, page 4). However, the frequency of meniscectomy was significantly lower in Group A; six of 30 patients (20%) in Group A (four medial menisci) and 16 of 31 (52%) in Group B (13 medial menisci) required resection of the damaged meniscus ( $p=0.01$ ). Three patients in Group A (1 medial meniscus and 2 lateral menisci) and two patients in Group B (medial meniscus) underwent meniscal sutures (Table 2, Paper I, page 5). Four patients in Group A (one patient was operated twice due to a medial meniscal suture rupture) and three patients in Group B underwent additional meniscal surgery. Five patients in Group A and one patient in Group B sustained a contralateral ACL injury in the period leading to the follow-up (n.s.), (Table 1, Paper I, page 4).

Preoperatively and at the follow-up, significant differences could not be demonstrated between the groups in terms of the Tegner activity scale, the Lysholm knee score and the one-leg-hop test. Moreover, both groups improved significantly over time (Table 3, Paper I, page 5). Three patients in

each group (10%) had returned to the same or a higher Tegner activity level compared with their preinjury level. Additionally, 16 patients (55%) in Group A and 21 patients (72%) in Group B ( $p=0.19$ ) had returned to a Tegner activity level higher than 4 (participation in recreational or competitive sports) at follow-up.

There were no statistically significant differences between the groups in terms of the ROM, knee laxity tests and muscle strength measurements in terms of LSI between the groups at the follow-up (Tables 3, 5, 7, Paper I, pages 5, 7, 9 respectively). The contralateral knee in both groups had significantly better flexion peak torque values at 60°/sec, as well as flexion torque values at 90° at both 60 and 180°/sec velocities (Table 7, Paper I, page 9). The KOOS revealed a statistically higher score in Group A compared with Group B in terms of the subscore for QoL but not for the other subscales (Table 4, Paper I, page 6).

The radiographic assessments at follow-up revealed significantly more medial compartmental OA in Group B compared with Group A in terms of the Ahlbäck classification ( $p=0.037$ ). The index knee displayed significantly more OA than the contralateral knee in both groups (Table 6, Paper I, page 8).

**Table B** *The table shows the meniscal incidence and index procedure at the index operation, as well as the OA evaluation of the index knee at follow-up.*

	Group A (n=30)	Group B (n=31)	Significance (p value)
<b>Meniscal lesions at index operation, n</b>			
No meniscal lesion	14	11	n.s. (0.38)
Medial meniscus	5	13	
Lateral meniscus	9	3	
Bilateral menisci	2	4	
<b>Meniscal lesions – index procedure</b>			
Partial meniscectomy, n (%)	6 (20%)	16 (52%)	<b>p=0.01</b>
<b>Radiographic OA evaluation according to Ahlbäck classification, index knee, at follow-up</b>			
Lost to follow-up	-	2	
<b>Medial tibiofemoral compartment, n (%)</b>			
0	27 (93)	21 (73)	p=0.037
I	2 (7)	7 (24)	
II	-	1 (3)	
Missing values	1	-	
<b>Lateral tibiofemoral compartment, n (%)</b>			
0	22 (76)	24 (83)	n.s. (0.61)
I	5 (17)	2 (7)	
II	2 (7)	3 (10)	
Missing values	1	-	

*OA, osteoarthritis; n.s., not significant  
significant p values in bold*

## 5.2 STUDY II

Preoperatively and at the five-year follow-up, no significant differences could be demonstrated between the study groups in terms of the Tegner activity level, Lysholm knee score, one-leg-hop test, KOOS and ROM deficits. The square-hop test revealed no significant differences between the groups at follow-up (Tables 2 and 3, Paper II, pages 1230-31). The pivot-shift test and the other knee laxity tests revealed no significant differences between the groups both preoperatively and at follow-up. Furthermore, 89% of patients in the SB group and 84% in the DB group had a negative (grade 0) pivot-shift test at follow-up

(n.s.) (Table 4, Paper II, page 1,232).

Both groups improved significantly between the preoperative and five-year follow-up assessments in terms of all variables, except for the range of extension (extension deficit) in the SB group and the range of flexion (flexion deficit) in the DB group. Moreover, the range of flexion (flexion deficit) was significantly poorer at the follow-up than preoperatively in the SB group (p=0.03) (Tables 2, 3 and 4, Paper II, pages 1,230-32). Additionally, seven patients in the SB group (17%) and 11 (24%) in the DB group (n.s.) returned to the same or higher Tegner activity level when compared

with the preinjury level at the five-year follow-up.

During the follow-up period, no patient underwent revision ACL reconstruction. Thirteen patients, nine in the SB group and four in the DB group, underwent second-look arthroscopic surgery (n.s.) (Table 1, Paper II, page 1,229). Five patients in the SB group and one patient in the DB group sustained a contralateral ACL injury (n.s.). No significant differences could be shown between the study groups in terms of the presence of OA early in the postoperative period or at the five-year follow-up, apart from the significantly greater lateral compartmental OA according to the Ahlbäck classification in the early postoperative period in the SB group ( $p=0.01$ ), (Table 5, Paper II, page 1,233). In the DB group, there was a significant increase in the development of OA between the early postoperative period and five-year follow-up

according to the Ahlbäck classification regarding the lateral compartment, the cumulative Fairbank score and the Kellgren-Lawrence classification. In the SB group, a significant increase in the presence of patellofemoral osteophytes was seen. Moreover, the cumulative Fairbank score, at the five-year follow-up, was significantly higher for patients with concomitant injuries in the whole cohort (with concomitant injuries: mean, 1.35 [range, 0-6]; without: mean, 0.35 [range, 0-2]; ( $p=0.01$ ) and in the SB group (with concomitant injuries: mean, 1.32 [range, 0-6]; without: mean, 0.11 [range, 0-1];  $p=0.046$ ) but not in the DB group (with concomitant injuries: mean, 1.38 [range, 0-5]; without: mean, 0.47 [range, 0-2];  $p=0.08$  n.s.). No correlation was found between the cumulative Fairbank score at the five-year follow-up and BMI in either group.

**Table C** *The pivot-shift test and the instrumental KT-1000 laxity assessments in the study groups.*

		Preoperative		Significance (p value)	Five-year follow-up		Significance (p value)
		SB (n=50)	DB (n=53)		SB (n=36)	DB (n=45)	
Pivot-shift test	0	-	-	n.s. (0.68)	89%	84%	n.s. (0.56)
	1	2%	2%		11%	16%	
	2	92%	94%				
	3	6%	4%				
KT-1000 anterior MMT side-to-side difference, mm				n.s. (0.72)			n.s. (0.72)
Median (range)		6.0 (0-11)	6.0 (-2-12)		2.0 (-4-8)	2.0 (-7-8.5)	
Mean (SD)		5.6 (2.7)	5.4 (3.0)		2.3 (2.7)	2.2 (2.7)	
Missing values		-	1		-	-	
KT-1000 anterior 134 N side-to-side difference, mm				n.s. (0.85)			n.s. (0.68)
Median (range)		5.0 (-1-11)	5.3 (-4-15)		2.3 (-4-11)	2.5 (-3-10)	
Mean (SD)		5.2 (2.4)	5.2 (3.2)		2.8 (3.1)	2.6 (3.0)	
Missing values		-	1		-	-	

*MMT, maximum manual test; SD, standard deviation; n.s., not significant*

*Both groups improved significantly at follow-up in terms of the laxity assessments compared with the preoperative measurements ( $p<0.001$ ).*

*Patients with a reconstructed or injured ACL on the contralateral side were excluded when the side-to-side difference-based variables were analysed.*

### 5.3 STUDY III

No significant decrease in tibial tunnel width on the AP view was found between the early postoperative period and the two-year assessment (n.s.) or between the early postoperative period and the five-year assessment (n.s.). On the lateral view, a significant decrease in tunnel width was found between the early postoperative period and the five-year assessment ( $p=0.014$ ). In six of 40 patients (15%), the width of the tunnel was larger at five years than in the early postoperative period on both the AP and lateral projections. In 15 patients (38%), the tunnel diameter increased on one projection and decreased or remained unchanged on the other, while in 18 patients (45%) the tunnel diameter decreased on both projections. One patient did not have an AP-view

radiograph at five years and was registered as having a missing value. As a result, in 83% of the patients, the tunnel diameter decreased on one or both projections. There was no correlation between the tibial tunnel width and the KT-1000 arthrometer measurements, Lysholm knee score and Tegner activity level at the five-year follow-up (Table 5, Paper III, page 2,191).

One male patient developed a ganglion cyst on the tibia at the location of the screw and underwent successful debridement and curettage surgery, 42 months after the primary ACL reconstruction. Other additional procedures in the study group after the index operations are presented in Table 1, Paper III, page 2,189.

**Table D** Tibial tunnel mean diameters as seen on the radiographs at the early postoperative assessment, at two years and five years postoperatively.

	Early post-op (n=40)	Two years (n=40)	Five years (n=40)	Early post-op vs two years (p value)	Early post-op vs five years (p value)	Two years vs five years (p value)
AP view, mean diameter, mm						
Median (range)	9.6 (6.0 – 13.3)	9.1 (5.5 – 12.2)	9.2 (5.1 – 13.7)	n.s. (0.18)	n.s. (0.64)	n.s. (>0.99)
Mean (SD)	9.4 (1.4)	9.1 (1.4)	9.2 (1.5)			
Missing values	-	-	1			
Lateral view, mean diameter, mm						
Median (range)	9.7 (6.0 – 13.2)	9.3 (6.3 – 12.2)	9.1 (5.8 – 11.8)	n.s. (0.19)	<b>p=0.014</b>	n.s. (0.26)
Mean (SD)	9.6 (1.5)	9.3 (1.5)	9.0 (1.4)			
Missing values	-	-	-			

*AP, anteroposterior; n.s., not significant; postop, postoperative period; SD, standard deviation significant p value in bold*

## 5.4 STUDY IV

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The mean follow-up period was 24.7 months in the SB Group and 26.1 months for the DB Group ( $p=0.005$ ).

No significant difference was found between the study groups in terms of the pivot-shift test both preoperatively and at follow-up (n.s.). At follow-up, a negative pivot-shift test (grade 0) was found in 78% in the DB group and 74% in the SB group (n.s.). Preoperatively, the KT-1000 knee laxity measurement at 134 N was significantly higher in the DB group ( $p = 0.02$ ) but not at follow-up (n.s.) (Table 4, Paper IV, page 1,311).

Preoperatively, no significant difference was found between the study groups in terms of the knee extension deficit (n.s.). At follow-up, the extension deficit was

significantly larger in the DB group than in the SB group ( $p = 0.001$ ). In terms of flexion deficits, no significant differences were found between the groups either before reconstruction or at follow-up (n.s.) (Table 3, Paper IV, page 1,311).

The study groups were comparable in terms of PROMs, apart from the fact that the DB group had a significantly higher Tegner activity level both preoperatively and at follow-up compared with the SB group ( $p = 0.03$  and  $p = 0.004$  respectively), (Tables 5 and 6, Paper IV, page 1,312). Both groups had improved in most clinical assessments at the two-year follow-up compared with the preoperative findings (Tables 3, 4, 5, Paper IV, pages 1,311-1,312).

# 06 DISCUSSION

## 6.1 TIMING OF ACL RECONSTRUCTION

The most important finding in Study I was that meniscal lesions requiring resection at the index operation were significantly more frequent in the patients that underwent surgery late after ACL injury than in the patients that underwent surgery early after injury. The association between delaying the ACL reconstruction and subsequent meniscal and cartilage lesions due to knee instability is well established [34,42,57,69]. Lateral meniscal lesions are associated more with the acute setting of ACL injury, while medial meniscal tears increase as the time from ACL injury passes [42,45,53,97,176]. This can probably be explained by the fact that the medial meniscus also performs a counteracting function against anterior displacement of the tibia [9,115]. Church and Keating found a significantly higher incidence of meniscal tears – particularly the medial meniscus – and chondral lesions in patients undergoing surgery more than 12 months after injury compared with those undergoing surgery earlier than 12 months, in a retrospective study comprising 183 patients [45]. Sri-Ram et al. reviewed 5,086 patients and reported that the risk of requiring medial meniscal surgery was doubled, if the ACL reconstruction was delayed by five months, and increased by a factor of six, if the reconstruction was delayed for more than one year [186]. Another issue that is of clinical importance is how the time of reconstruction is related to the reparability of the meniscus. Chhadia et al. found that the repair rate for medial meniscus lesions during ACL reconstruction decreased with

increasing time to surgery, especially one year after the injury [42]. In a recent study, Krutsch et al. recommended reconstruction within six months after primary ACL injury due to the higher rate of reparable meniscal tears [104]. In Study I, the rate of meniscectomy at index operation was significantly higher in the late reconstruction group, which is in line with the literature. The incidence of meniscectomy, moreover, occurred mostly on the medial side.

In terms of cartilage pathology, Granan et al. reviewed 3,475 patients from the Norwegian National Knee Ligament Registry and found that the odds of cartilage lesions increased by about 1% for each month elapsing from the injury, while the odds of the cartilage lesions were almost twice as high if a meniscal tear was present [69]. Additionally, Brambilla et al. concluded that ACL reconstruction within 12 months can significantly reduce the risk of chondral and meniscal lesions [34]. Despite the fact that the meniscectomies were more frequent in the late group in Study I, the overall incidence of concomitant meniscal and cartilage pathology revealed no significant differences between the groups. This can probably be explained by the small numbers of patients in the groups.

Moreover, at the long-term follow-up, the patients in Study I demonstrated a significantly increased prevalence of medial compartmental knee PTOA grade I in the index knee in the late group compared with in the early group, in terms of the Ahlbäck classification system. The other



classification systems used in the study were unable to reveal any significant difference between the groups. This could be related to a potentially underpowered study. Oiestad et al. and Risberg et al. followed the same study group both at 10-15 and at 20 years respectively. They found significant PTOA development in patients that underwent surgery late after ACL injury. The late-reconstructed group thus comprised patients with associated meniscal and chondral lesions, while the early group comprised isolated ACL injuries [146,164]. However, it is clear that the more pronounced associated injuries were probably caused by the delay in the intervention.

Another aspect that has been debated is the development of postoperative arthrofibrosis in cases of early ACL reconstruction. In the early 1990s, it was suggested that delayed reconstruction would reduce the risk of knee stiffness [47,179,207]. According to Beynon et al., the condition of the knee at the index operation is more important than the time between injury and operation [27]. The RCTs by Raviraj et al. and Bottoni et al., during the past decade, found that early reconstruction does not jeopardise the knee [31,162]. The meta-analysis by Kwok et al., including Level I and II studies, focused in particular on the risk of postoperative stiffness and revealed that, if a modern surgical technique and an accelerated rehabilitation algorithm are applied, there is no increased risk of stiffness, if an ACL reconstruction is performed as early as one week after injury [109]. A recent prospective study by Herbst et al. compared patients who underwent surgery within 48 hours after injury with patients who underwent surgery during the

inflammation-free interval (mean 53.9 days after injury). At 24 months after surgery, the ROM was comparable between the groups [76].

In Study I, there were no significant differences between the two groups in terms of ROM deficits.

Furthermore, there is no consensus in the literature in terms of the optimal time between injury and ACL reconstruction. Andernord et al. included 22 at least Level II studies in their systematic review and concluded that there were few or no differences in subjective and objective outcomes related to the timing of ACL surgery. However, the definition of early and late reconstruction revealed large-scale heterogeneity between the included studies [13]. A more recent meta-analysis by Lee et al. only assessed studies in which the timing of reconstruction was the primary variable and a pooled analysis was performed between RCTs. The authors reported no significant differences between early and late ACL reconstruction in terms of the KT-1000 knee laxity test and the Lysholm knee score, which is in line with Study I. For this reason, the risk of meniscal and cartilage lesions was not evaluated in this meta-analysis [114].

There is therefore no clear consensus on when to perform ACL reconstruction. However, minimising the risk of meniscal and chondral pathology due to recurrent knee instability appears to be of major importance. Young patients with a high activity level involving cutting and pivoting activities should undergo ACL reconstruction early after ACL injury, together with a modern postoperative rehabilitation programme [103,206,212].

## 6.2 PROMs AND ACTIVITY LEVEL AFTER ACL RECONSTRUCTION

All the studies included in this thesis assessed PROMs commonly used to evaluate the outcome after ACL reconstruction. Apart from the objective clinical assessments, e.g. knee laxity tests, it is important

to know how the patients report their function and satisfaction after surgery. The KOOS is a site-specific instrument that was developed and validated with the aim of evaluating the short- and long-term

symptoms and function in patients with knee injuries, including ACL injuries, that could result in future OA [168]. However, there are inherent weaknesses in its use, as the KOOS is based on an extension of the disease-specific Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) [24]. Hambly et al. suggested that the KOOS subscales of “Sport/Rec” and “QoL” correlated best with the subjective outcome after primary ACL reconstruction [71]. In Study II, the KOOS was assessed in both groups (anatomic SB and anatomic DB groups) both preoperatively and at the five-year follow-up. Study II revealed a statistical improvement in each group at follow-up in terms of all the KOOS subscales. However, the greatest improvement was found in the subscales of “Sport/Rec” and “QoL”, which demonstrates the importance of these subscales for the evaluation after ACL reconstruction. Furthermore, caution should be taken when using the KOOS as an indicator of success or lack of success after ACL reconstruction, as the thresholds for functional recovery, treatment success and failure vary in the literature [22,48,65,70,122] and the KOOS should therefore be regarded as a supplement for evaluation of the outcome after ACL reconstruction.

Another PROM that was used in this thesis is the Lysholm knee score. The Lysholm knee score was originally designed to assess function after knee ligament injury [123]. In 1985, the Lysholm score was modified for the evaluation of meniscal injuries and, as a complement to the Lysholm knee score, the Tegner activity scale was developed

[198]. However, Risberg et al. found that the Lysholm knee score was not accurate in identifying functional problems during strenuous activities [163]. Additionally, Bengtsson et al. reported that the Lysholm knee score had better sensitivity for the outcome related to meniscal tears, patellofemoral pain syndrome and lateral ankle sprain, rather than ACL injuries [25]. Nonetheless, in the study by Briggs et al., the Lysholm knee score and the Tegner activity scale were re-evaluated 25 years after their introduction. The authors concluded that the Lysholm knee score and the Tegner activity scale provide a comprehensive outcome assessment with acceptable responsiveness for patients with ACL injuries [36].

Studies I, II and IV revealed a statistically significant improvement in terms of the Tegner activity scale between preoperative and postoperative assessments. However, the patient groups did not return to their preinjury Tegner activity levels. Ardern et al. reviewed more than 7,000 patients and reported a low return to preinjury activity levels after ACL reconstruction, especially among patients participating in competitive sports [18]. Jerre et al. also found a significant decrease in activity level among competitive athletes [89]. Psychological factors are strongly correlated with returning or not returning to previous activities [17,107,108]. Additionally, the activity level has a tendency to decrease over time. Moreover, other long-term follow-up studies after ACL reconstruction have reported a value of about four in the Tegner activity level (non-recreational and non-competitive sports) [23,147,164].

### 6.3 POST-TRAUMATIC OSTEOARTHRITIS (PTOA)

ACL reconstruction appears not to protect the knee from the development of PTOA [23,66]. A recent review and meta-analysis showed, however, that ACL reconstruction could reduce the risk of developing degenerative changes at 10 years

[8]. Additionally, the reported prevalence of radiographic PTOA after ACL injury and ACL reconstruction shows a wide range in the literature and this could be explained by heterogeneity in the population, activity levels, BMI, treatment choice, time between

injury and reconstruction and associated injuries, i.e. isolated ACL injuries and/or with combined injuries (chondral and meniscal lesions) [7,8,13,69,156]. Furthermore, the use of various classification systems, as well as differences in the interpretation of these systems, could probably affect the reported rate of PTOA [8,140,172].

In Study I, ACL-reconstructed knees in each group and in the whole cohort demonstrated a higher prevalence of PTOA compared with the contralateral uninjured knee, 10 years after the intervention. This is in line with other studies with a long-term follow-up, showing that ACL reconstruction is unable to protect the knee from developing PTOA [8,23,164]. In Study II, a pooled analysis including all patients, i.e. both SB and DB groups, revealed that the cumulative Fairbank score on the radiographs was significantly poorer at the five-year follow-up compared with the early postoperative findings, in patients with concomitant meniscal and/or chondral lesions.

In Study II, there were no differences in OA changes between the groups at the five-year follow-up. The RCTs by Suomalainen et al. and Song et al. were unable to reveal significant differences between SB and DB reconstructions in terms of OA at their mid-term follow-ups at about five years [185,192]. Recently, Järvelä et al. reported similar OA rates between the SB and DB techniques

in an RCT after a ten-year follow-up [86]. Both Song et al. and Järvelä et al. found more OA in patients who underwent meniscectomies at the index operation. This is in line with Study II, in which patients with concomitant meniscal and cartilage lesions had significantly more OA.

Furthermore, the term “pre-osteoarthritic” disease after ACL injury has been introduced to describe conditions that alter the homeostasis of the knee joint [44]. These conditions involve the inflammatory response after the injury, structural concomitant pathologies (cartilage and meniscal lesions) and biomechanical changes due to the kinematic alteration. The inflammatory response is high in the acute phase after ACL injury [6,194,195], but it can remain high long after ACL injury [124]. The large majority of patients (>80%) with an acute ACL injury have damage to the subchondral bone, i.e. bone-marrow oedema [64,84]. Potter et al. found that all ACL-injured patients sustained an MRI-detectable chondral injury at the acute onset, in a study comprising 42 patients [159]. Finally, ACL deficiency changes the static and dynamic bearing of the knee, leading to loads on the cartilage [41,44,119]. How to address these factors and identify which are reversible in order to modify and reduce PTOA development remains unclear.

## 6.4 SINGLE-BUNDLE VERSUS DOUBLE-BUNDLE ACL RECONSTRUCTION

### Rotational knee laxity

The theoretical advantage of DB ACL reconstruction is that the two bundles are able to mimic the native ACL function better than a single bundle. The AM bundle stabilises the knee in the AP direction and the PL bundle provides rotational support [11]. In Study II, the anatomic DB reconstruction was not superior to the anatomic SB reconstruction in terms of residual rotational

knee laxity (pivot-shift test), five years after the index operation. Additionally, in Study IV, the non-anatomic SB reconstruction produced results similar to those of the anatomic DB reconstruction in terms of the pivot-shift test, in the short term postoperatively. Furthermore, in both studies, the majority of patients had a negative pivot-shift test at the follow-ups, independent of the surgical technique that had been employed.

Several RCTs have reported that DB reconstruction renders a better outcome in terms of the pivot-shift test than SB reconstruction [83,88,100,181,191,217]. Hussein et al. compared three groups and reported a significantly better outcome in terms of rotational knee laxity in the DB group than in the anatomic SB and non-anatomic SB groups, three to five years postoperatively [83]. In contrast, other RCTs were unable to demonstrate that the DB technique was superior [3,91,171,185,190,215]. Furthermore, a recent RCT with a long-term follow-up reported no significant difference in terms of the pivot-shift test between the DB and SB techniques [86].

The systematic review by Samuelsson et al. from 2009 comprising eight RCTs reported that DB reconstruction produces less rotatory knee laxity, but there were no significant differences in the clinical outcome between the SB and DB techniques. On the other hand, whether or not SB reconstructions were performed using an anatomic technique was not clearly described [170]. Furthermore, a systematic review by Suomalainen et al. reported that the DB technique produced better results in terms of rotational stability, as measured by the pivot-shift test [193]. The meta-analysis by Kongtharvonskul et al. showed that the probability of obtaining normal pivot shift was four times higher after DB reconstruction compared with SB reconstruction. However, the included studies demonstrated large heterogeneity [101].

The comprehensive systematic review by Björnsson et al. compared the DB and SB techniques based on current evidence. The review revealed that the DB reconstruction produced less AP and rotatory knee laxity than the SB technique. On the other hand, no differences were found in the short-term PROMs and other objective assessments [29]. Lastly, a recent meta-analysis of Level I and II studies with short- to mid-term follow-ups showed that anatomic DB reconstruction was superior to anatomic

(independent femoral drilling technique) SB reconstruction in terms of the pivot-shift test but not in terms of functional recovery [224].

An issue that is of clinical importance when assessing rotational knee laxity is the accuracy of the pivot-shift test. The pivot-shift test has very high specificity in diagnosing ACL injury but low sensitivity [26,112,160]. However, the pivot-shift test exhibits moderate levels of inter- and intra-observer reliability [105,106,155]. Moreover, there is no consensus on the optimal technique for executing the pivot-shift test and the clinical assessment and grading vary between examiners [133]. Efforts have been made to develop instruments to quantify the pivot-shift test and several devices have been introduced [80,106,132,219,220]. Nonetheless, the wide-scale implementation of these modalities in clinical practice is still questionable.

#### **AP knee laxity**

Studies II and IV did not find significant differences between the ACL reconstruction techniques at the follow-ups and all the groups improved significantly over time in terms of the AP knee laxity assessment, which is in line with other studies [86,190,192,216]. The meta-analysis by Li et al. reported no significant difference in terms of KT-1000 arthrometer assessments [117]. In a meta-analysis, Desai et al. demonstrated that the anatomic DB technique is superior to the anatomic SB technique, primarily in terms of AP laxity. Despite this, the authors concluded that it remains uncertain whether these findings in favour of the DB technique are of clinical importance in the long term [54]. This is in line with a recent review of overlapping meta-analyses which reports that most studies show a significant favourable outcome from using the DB reconstruction in terms of knee laxity assessments but not in subjective outcome scores such as the Tegner activity scale and Lysholm knee scores [126].

### Other clinical outcomes

In addition to knee laxity assessments, Studies II and IV were unable to reveal any significant differences between the respective groups in terms of functional performance tests, activity level and PROMs, apart from the Tegner activity level in Study IV that was significantly higher in the anatomic DB group than the non-anatomic SB group both preoperatively and at the two-year follow-up. No similar difference could be demonstrated in Study II. Moreover, in Study II, the anatomic SB group revealed a significantly poorer outcome at follow-up than preoperatively in terms of knee flexion within the study group, but there were no significant differences between the two groups. In Study IV, the DB group showed a significantly greater extension deficit than the non-anatomic SB group. This could be explained by the fact that the time between

injury and operation in the non-anatomic SB group was longer than in the DB group, even though it was not statistically significant. Despite this statistical significance in terms of ROM deficits in Studies II and IV, the loss of motion was small and probably not clinically important. The meta-analysis by Li et al. reported a smaller knee extension deficit in favour of the DB technique, while van Eck et al. found no significant differences [116,203]. In the comprehensive review by Björnsson et al., the majority of included studies revealed no significant differences between SB and DB reconstruction in terms of the Tegner activity level, Lysholm knee score, KOOS and ROM [29]. Mascarenas et al. reported no significant differences between the DB and SB techniques in terms of subjective outcome [126].

## 6.5 TUNNEL ENLARGEMENT

Biodegradable interference screws have been introduced in order to overcome the disadvantages of metal screws, especially during revision surgery. Another theoretical advantage is their potential to integrate in bone over time during their resorption [58,110]. Studies have, however, shown that the outcome in terms of biodegradation, integration and tunnel enlargement was not as good as expected. Laxdal et al. and Stener et al. found that PLLA screws caused larger tunnel diameters than metal screws, two and eight years respectively after ACL reconstruction, demonstrating the absence of ossification when using the PLLA screw [111,188]. Another RCT with two years of follow-up reported more tunnel enlargement in the femur in the biodegradable group compared with the metal group [128]. A recent study with two- and five-year postoperative MRI assessments after DB reconstruction revealed tunnel narrowing but also a high rate of fluid-filled cysts in the location of the biodegradable screws

[98]. In the meta-analysis by Emond et al., the authors found that knees undergoing surgery using biodegradable screws had a higher rate of effusion than patients undergoing surgery with metal screws; however, it was not possible to perform a meta-analysis of the included studies in terms of tunnel enlargement [58]. Furthermore, the meta-analysis by Laupattarakasem et al. demonstrated a similar clinical outcome between biodegradable screws and metallic screws, despite the fact that biodegradable screws showed larger tunnel enlargement and higher rates of effusion and screw breakage [110].

In order to increase the osteoconductivity of biodegradable screws and reduce the risk of hydrolysis, manufacturers have added materials such as  $\beta$ -TCP or hydroxyapatite to polymers like PLLA [21]. Reports in the literature on tunnel narrowing and, consequently, the ossification properties of the biocomposite screws vary. Arama et al. assessed the tunnels with MRIs five years

after ACL reconstruction after using a bio-composite screw composed of PLLA-HA. This screw showed partial resorption and incomplete ossification [16]. In the RCT by Bourke et al., two different bio-composite screws were assessed in terms of tunnel expansion and osseointegration two years after ACL reconstruction using hamstring tendon autografts. Both groups showed no signs of ossification or tunnel narrowing. Moreover, in one group, the incidence of tibial cysts was 88% [33]. In Study III, most patients revealed no tibial tunnel enlargement in either one or both radiographic views, five years postoperatively. Barber et al. assessed the osteoconductive behaviour of the same screw as in Study III with computed tomography (CT) four years postoperatively and concluded that the screw showed full resorption and satisfactory ossification. However, they used a

bone-patellar tendon-bone (BPTB) graft [20]. A recent study assessed two bio-composite screws composed of  $\beta$ -TCP-PLLA with different concentrations for reconstructions using BPTB or hamstring tendon autografts respectively. Both screws revealed no case of tunnel enlargement and considerable osteoconductivity at a mean follow-up of three years [143].

The clinical outcome in Study III was satisfactory with a significant improvement in both objective and subjective assessments, as well as no correlation between tibial tunnel enlargement and AP knee laxity, which is in line with previous studies [16,33,136,143,188]. On the other hand, Järvelä et al. and Moisala et al. have claimed that tunnel enlargement in the tibia was associated with increased knee laxity [87,128].

## 6.6 HAMSTRING MUSCLE STRENGTH DEFICIT AFTER ACL RECONSTRUCTION

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Several studies have shown that most patients who undergo ACL reconstruction using hamstring tendon autografts have persistent weakness in deep knee flexion after harvesting of the tendons [5,43,139,197]. Although hamstring tendons are able to regenerate, there are still deficits in deep knee flexion [5,43,138,196]. There is little evidence in terms of the timing of ACL reconstruction using hamstring tendon autografts and subsequent muscle-strength outcome. In the 1990s, Wasilewski et al. reported no significant differences between patients who underwent surgery within a month versus at least six months after injury, with regard to isokinetic quadriceps and hamstring muscle strength in the index knee, 18 months after the reconstruction [207]. The early (reconstruction within two weeks) and delayed (within eight to 12

weeks) groups in an RCT showed no significant differences in terms of hamstring isokinetic muscle strength, one year after surgery [127]. In another study, significant differences between acute and chronic reconstructions could not be revealed in knee extension and flexion strength, two to six years after the reconstruction [68]. Study I presented long-term results after early and late ACL reconstructions, without significant differences in terms of isokinetic muscle strength between the groups. However, Study I revealed a statistically significant difference between the contralateral uninjured knee and the index knee in both groups with regard to isokinetic deep knee flexion strength, which was in favour of the contralateral knee, which is in line with previous studies [142,152,175].

# 07 STRENGTHS AND LIMITATIONS

## Study I

The main strength is the long-term follow-up, including radiographic assessments evaluated by one independent radiologist. Moreover, both groups were comparable in terms of demographics and pre-injury Tegner activity scale and underwent surgery using the same type of graft and fixation device.

The main limitation of the study is the retrospective implementation of the hypothesis, although the data were collected prospectively. The study might be underpowered because of the lack of randomisation and the fact that the power calculation was based on the knowledge of meniscectomies in the study groups. Moreover, the exclusion of some patients with a contralateral ACL injury in the statistical analysis of side-to-side difference-based variables and the presence of missing values in the muscle strength assessments could render low statistical power. Another limitation is that this study only includes patients in the late group seeking medical attention due to subsequent knee instability and it is not known how many patients never came back for surgery.

## Study II

The main strength of this study is its randomised design, with more than 80% follow-up five years postoperatively, including a radiographic assessment. Moreover, all clinical and radiographic assessments were performed by unbiased, experienced investigators and all the reconstructions were performed by experienced senior surgeons using standardised surgical procedures.

There are a number of limitations to Study II. First, the primary outcome of the study, the pivot-shift test, exhibits moderate levels of inter- and intra-observer reliability. Second, it was not known exactly when the patients returned to activity, because they were rehabilitated by their local physiotherapist due to the large geographical catchment area. Third, the development of OA was assessed on radiographic findings instead of MRI. Moreover, the integrity of the graft was only assessed by clinical tests and not by other means. Lastly, an individualised surgical approach to each patient, in terms of the anatomic ACL reconstruction concept, was not possible, as the study was randomised.

## Study III

The strengths of this study are its prospective design, the mid-term follow-up with consecutive clinical and radiographic follow-ups and the fact that all clinical and radiographic assessments were performed by unbiased, experienced investigators.

The limitations are, however, that the study was neither randomised nor had a control group. The use of biocomposite screws only in the tibia and metallic screws in the femur could be another limitation. However, the main reason for this choice was the need for a reference measurement. Lastly, the use of radiographs in order to assess the tunnel size and consequently the osteoconductive behaviour of the biocomposite screw may be a weakness of the study. Scores that quantify ossification and screw resorption using CT and MRI have been reported [19,56]. However, even though standard

radiographs only measure the diameter, they have been shown to be comparable to CT and MRI in defining bone tunnel enlargement, according to the studies by Webster et al. and Buelow et al. [39,208].

#### **Study IV**

The strengths include the use of the AM portal for femoral drilling in both groups and the fact that the rehabilitation and examination protocols were the same for both groups. Furthermore, one independent physiotherapist made all the preoperative

and postoperative assessments.

The main limitation is that the study was not randomised. The fact that the patients originate from two different series might involve inclusion bias. Furthermore, the type of tibial interference screw was not identical in the study groups. Lastly, MRI or arthroscopy was not performed as part of the follow-up and it was therefore not possible to define true graft failure in addition to the laxity assessment and also not possible to evaluate cartilage status.



# 08 CONCLUSIONS

## Study I

Patients who underwent early ACL reconstruction required significantly fewer meniscectomies at the index operation than patients who underwent late reconstruction and revealed significantly less OA on the medial side of the knee 10 years after reconstruction. However, no significant differences were found between the groups in terms of clinical assessments.

## Study II

At the five-year follow-up of an unselected group of patients, anatomic DB reconstruction was not superior to anatomic SB reconstruction in terms of the pivot-shift test, AP knee laxity, PROMs and functional outcome. No significant differences between the two techniques in terms of OA development could be seen.

## Study III

In 83% of patients, the width of the tibial tunnel had decreased on one or both radiographic views at five years compared with the early postoperative period after ACL reconstruction using biocomposite interference screws. Moreover, the clinical outcome at follow-up was satisfactory.

## Study IV

In an unselected group of patients, anatomic DB ACL reconstruction did not result in a superior clinical outcome, including rotatory and AP knee laxity, compared with the non-anatomic SB reconstruction at the two-year follow-up.

# 09 FINAL CONSIDERATIONS - FUTURE PERSPECTIVES

## **Timing of ACL reconstruction**

Early or late ACL reconstruction? It is generally agreed by surgeons that surgery should be performed before additional meniscal and/or chondral lesions occur. However, the definition of early ACL reconstruction is difficult to establish. High-quality RCTs are a way of evaluating the impact of timing on the outcome. Nonetheless, ethical considerations arise, because delaying the reconstruction increases the risk of more knee pathology. Large-scale register studies could perhaps provide more information on this issue.

## **PTOA**

OA after ACL injury still remains an issue of research. Why is there a weak association between radiographically evident OA and symptoms? Why do patients who manage to cope with their ACL injury and never undergo surgery not develop cartilage degeneration [141]? Recent studies have focused on the early diagnosis of acute cartilage pathologies in conjunction with an ACL injury using quantitative MRI mapping [151,201]. Together with the biomechanical analysis of ACL-deficient knees, this could help us understand factors that influence the early onset of PTOA and thus develop and implement early intervention strategies [44].

## **Surgical technique**

This thesis shows that, if a standardised SB ACL reconstruction technique is used, the short- and mid-term outcome is equal to that produced by DB reconstruction in unselected patients. Based on the fact that the

majority of surgeons in Sweden perform fewer than 30 ACL reconstructions every year, it appears reasonable to implement an easy, secure and standardised surgical protocol such as the SB technique [200]. The DB technique is technically demanding, with a longer surgical time, and more expensive to perform than the SB technique [144,154]. Moreover, the anatomic placement of ACL grafts should be the aim of every surgeon. Apart from this, knee geography, such as size and depth, activity level, occupation, expectations and lifestyle, should be taken into consideration in the diagnosis, treatment and rehabilitation of each individual separately in order to achieve the optimal outcome.

Recently, the role of the anterolateral complex in ACL injury and surgical treatment has been debated and interest in extra-articular tenodesis has grown, especially in knees with excessive rotational instability [61,74,75,94,131,135,174,221]. Moreover, recent studies have added new information about the anatomy of the ACL. The anatomic appearance of the ACL is more flat and ribbon-like than previously reported [182,183]. In the future, it will be interesting to see how these factors affect the choice and evolution of surgical techniques in ACL reconstruction.

## **Pivot-shift test**

In terms of rotational knee laxity, the interpretation of the pivot-shift test that is used globally depends on the examiner. It is crucial to recognise knees with complicated and altered kinematics after ACL injury, as well as to assess objectively the outcome of

reconstruction over time. The development of tools that quantify the pivot-shift test is therefore important. Several instruments have been introduced and tested, but their widespread use in clinical practice has not yet been established.

#### **Biocomposite interference screws**

This thesis reveals that the use of a biocomposite interference screw allows for at least partial ossification and renders satisfactory mid-term results after ACL reconstruction. One question is raised here; how reliable are biocomposite screws in terms of osteoconductivity? The answer is complicated. A mid-term follow-up might not be long enough to show the osteoconductivity properties. Several types of biocomposite screw have been evaluated using different surgical techniques and different types of ACL graft. As a result, it is difficult to draw any clear conclusion. The use of register studies would probably assist in evaluating the osteoconductivity of biocomposite implants due to the large population, but, for ethical reasons, it is not feasible to obtain

radiographs to such an extent. Finally, the use of another implant composition, such as non-reactive plastic like polyether ether ketone (PEEK) or the addition of true osteoinductive materials or true bone autografts, could be considered in the future [40,55,125,158].

**Taken as a whole,** ACL rupture is a common injury among young active individuals and athletes. The challenge is to find a surgical method that offers optimal results in terms of knee laxity, function and the opportunity to return to the previous level of activity. It is also important to follow patients over long time periods and analyse the results when the consequences, such as impaired function, pain or OA, become apparent after a number of years. Continuously evaluating and comparing different surgical techniques is an important step in assuring the quality of care and offering patients the best possible treatment. Last but not least, the prevention of ACL injury should be another major point of focus.

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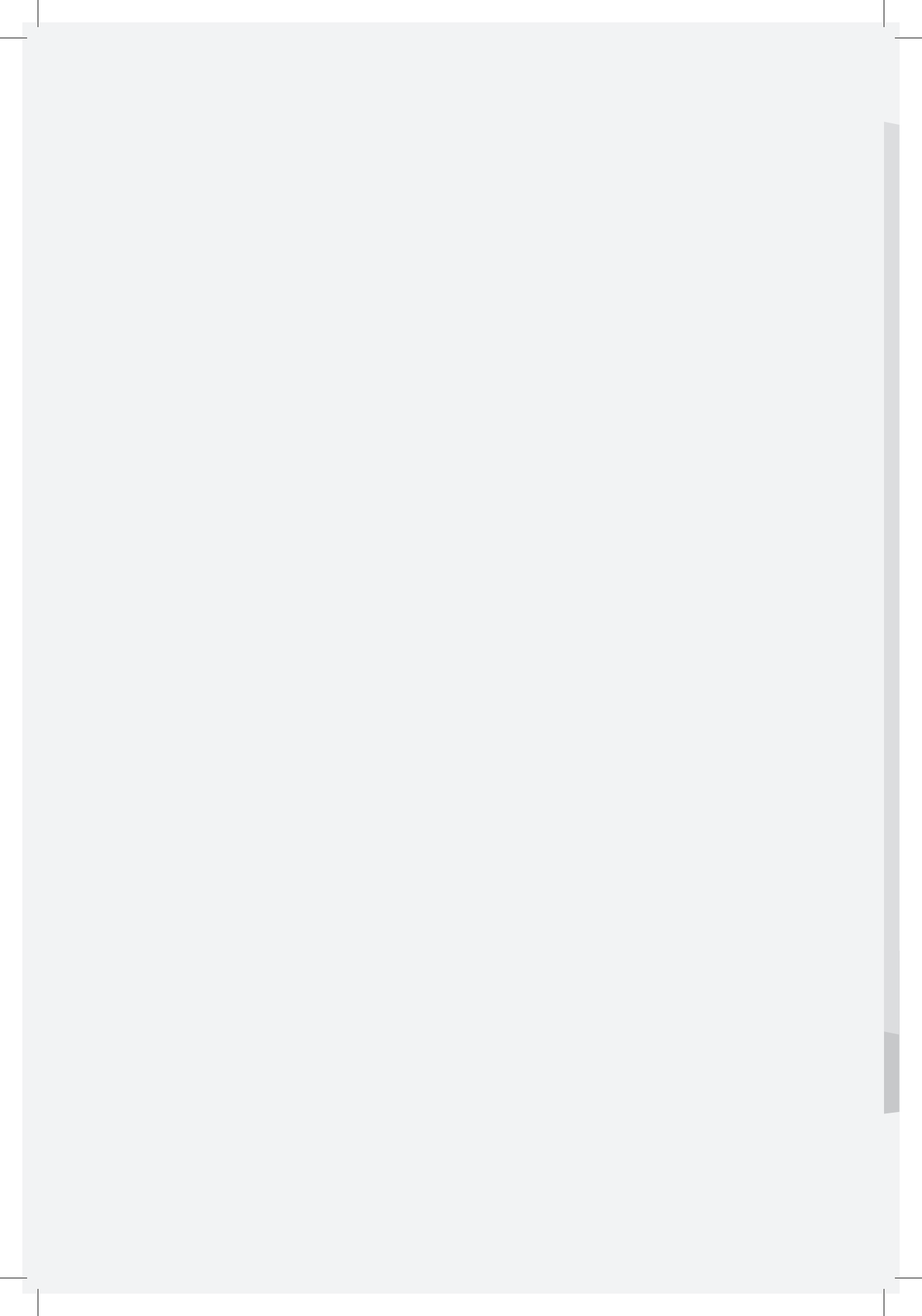


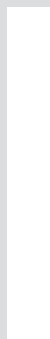
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PAPERS I-IV

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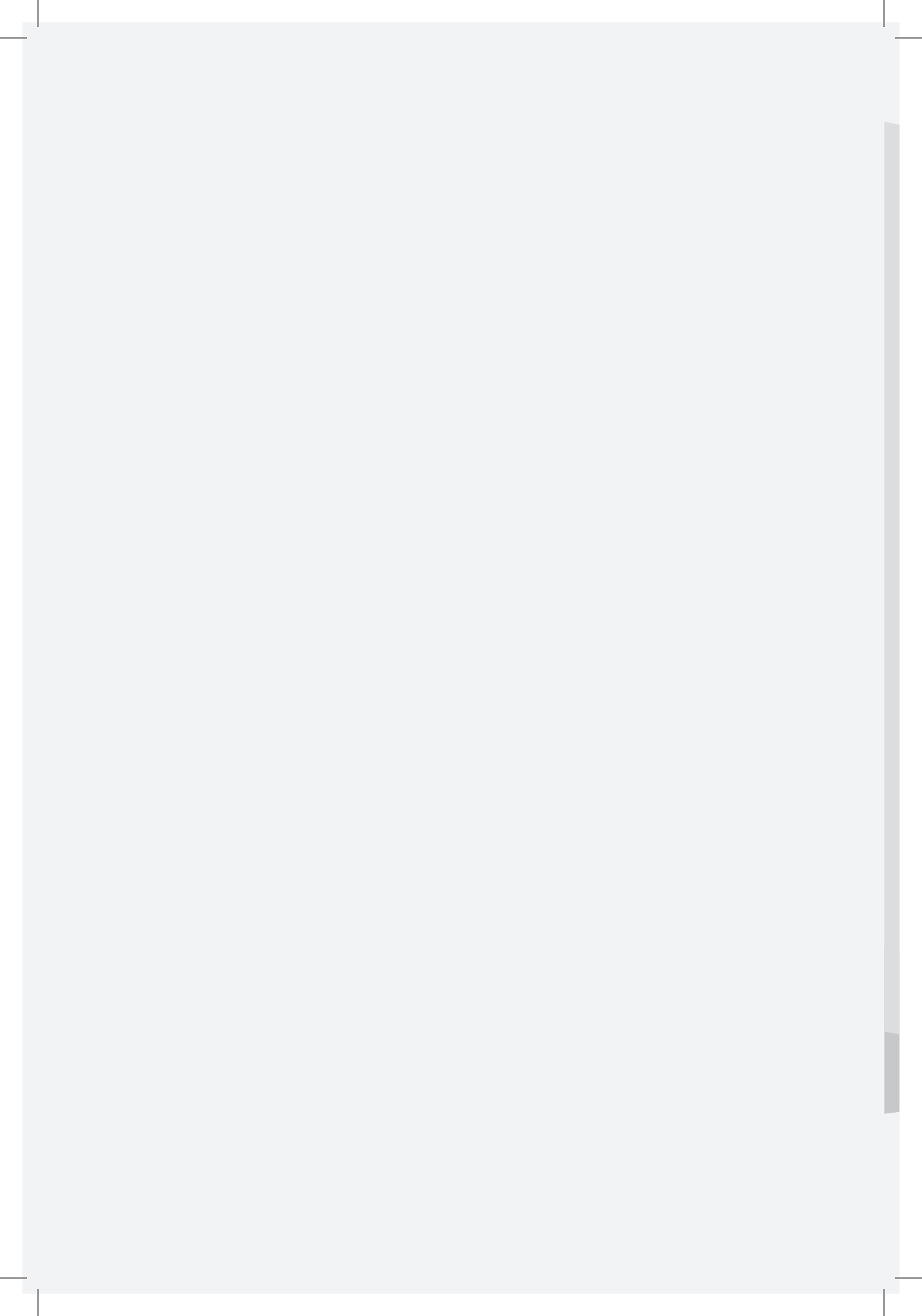
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**The long-term outcome after early and late anterior cruciate ligament reconstruction**

Karikis I, Åhlén M, Sernert N, Ejerhed L, Rostgård-Christensen L, Kartus J

*Arthroscopy. 2018 March 6; e-published ahead of print*

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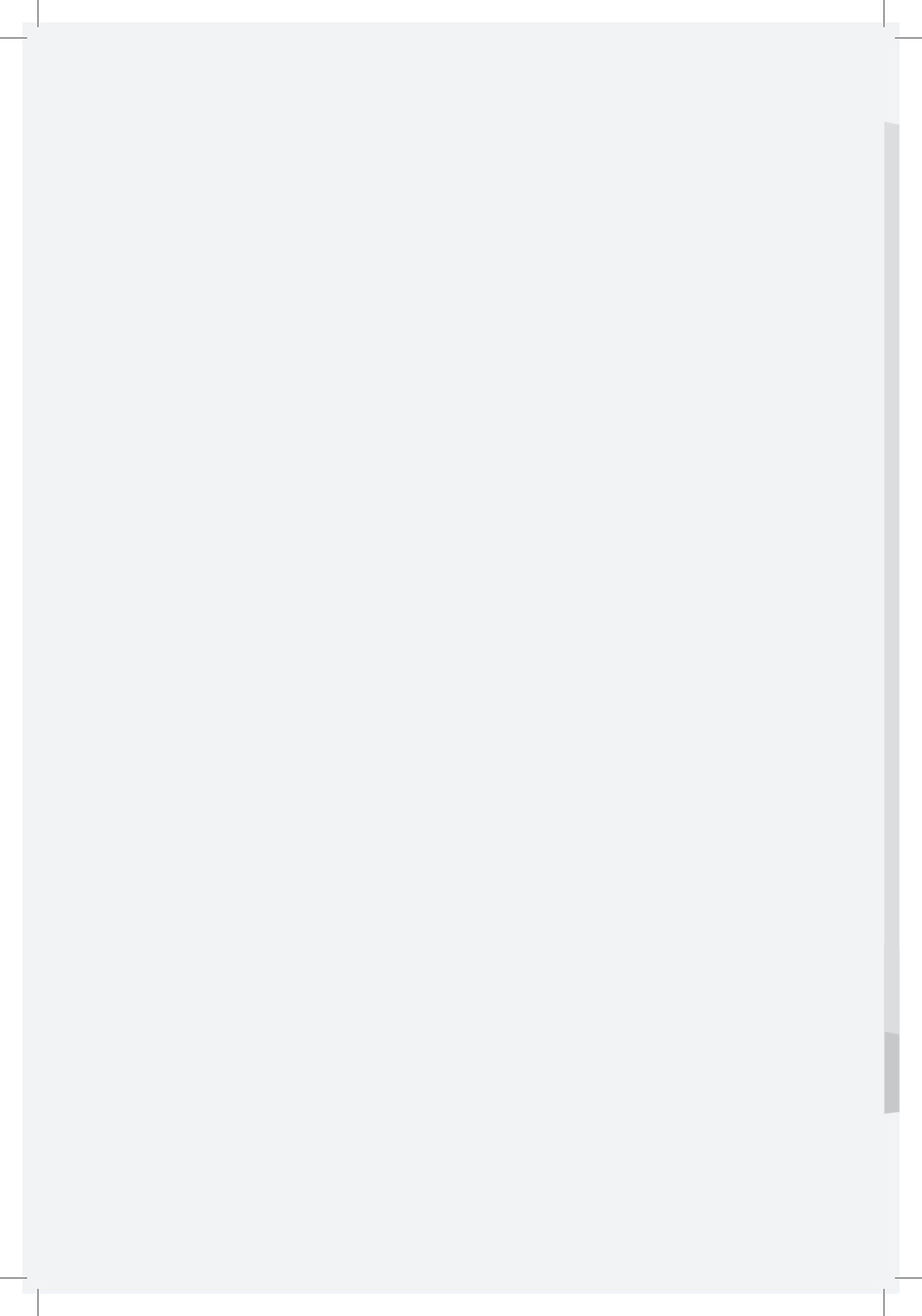


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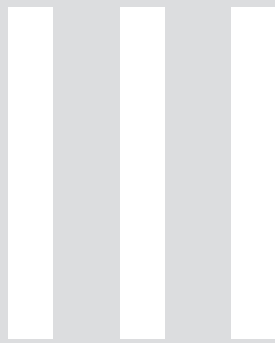
**Comparison of anatomic double- and single-bundle techniques for anterior cruciate ligament reconstruction using hamstring tendon autografts: a prospective randomized study with 5-year clinical and radiographic follow-up**

Karikis I, Desai N, Sernert N, Rostgard-Christensen L, Kartus J  
*Am J Sports Med.* 2016 May;44(5):1225-36

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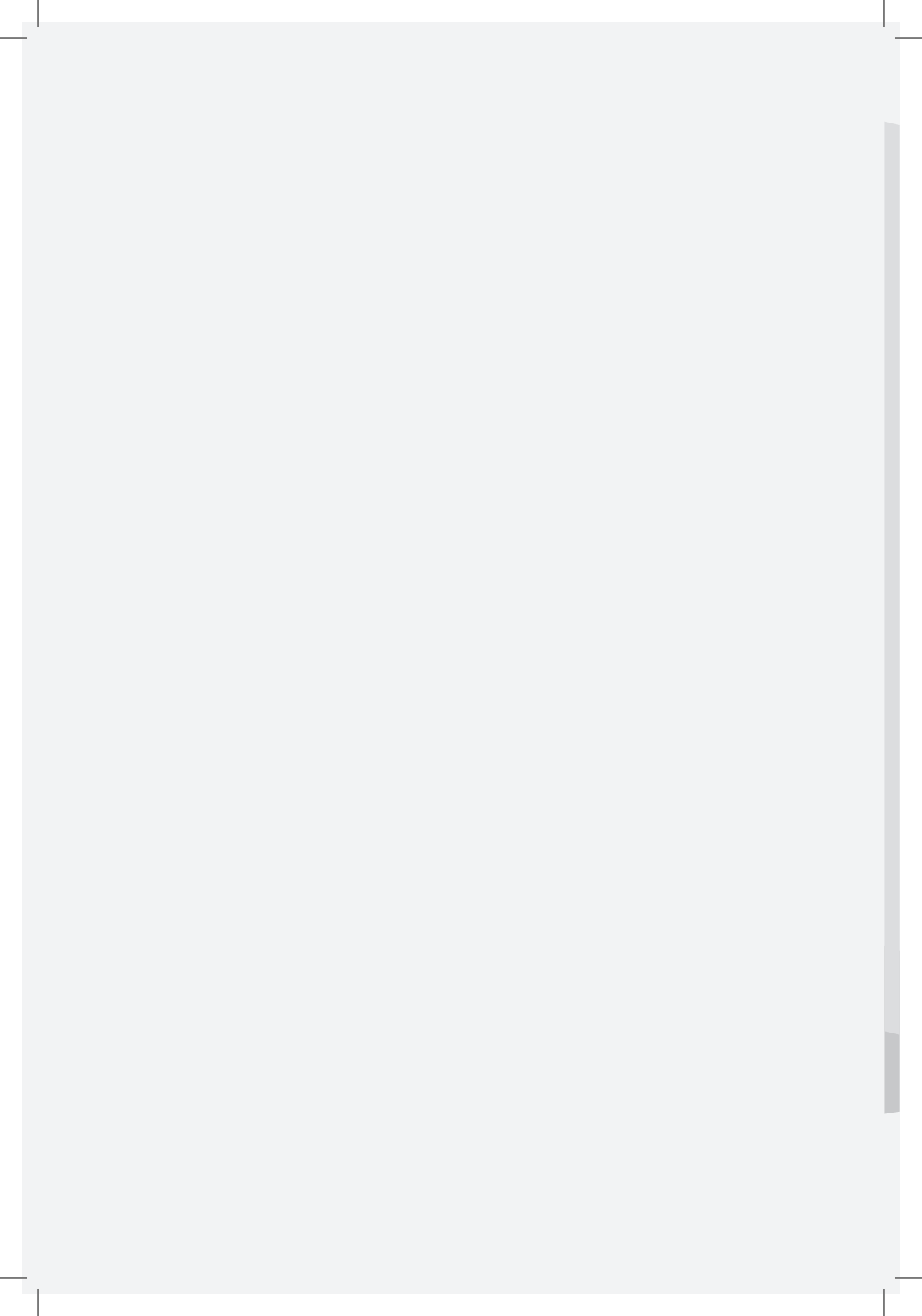


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**Radiographic tibial tunnel assessment after anterior cruciate ligament reconstruction using hamstring tendon autografts and biocomposite screws: a prospective study with 5-year follow-up**

Karikis I, Ejerhed L, Sernert N, Rostgård-Christensen L, Kartus J  
*Arthroscopy. 2017 Dec;33(12):2184-2194*

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# IV

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**Comparison of outcome after anatomic double-bundle and antero-medial portal non-anatomic single-bundle reconstruction in ACL-injured patients**

Karikis I, Ahldén M, Casut A, Sernert N, Kartus J

*Knee Surg Sports Traumatol Arthrosc.* 2017 Apr;25(4):1307-1315

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