

**The effect of an Anatomic Double-bundle surgical technique on the
outcome of Anterior Cruciate Ligament Reconstructions**

PhD Thesis
Cathrine Aga



Department of orthopaedic surgery
Martina Hansens Hospital

Faculty of Medicine
University of Oslo
2018

© Cathrine Aga, 2019

*Series of dissertations submitted to the
Faculty of Medicine, University of Oslo*

ISBN 978-82-8377-359-0

All rights reserved. No part of this publication may be
reproduced or transmitted, in any form or by any means, without permission.

Photo cover: Stina Glømme

Cover: Hanne Baadsgaard Utigard.
Print production: Reprosentralen, University of Oslo.

“If it works, it's out of date.”

– **David Bowie**

Contents

Acknowledgements	6
List of papers	9
Abbreviations	10
Introduction	12
ACL injury	13
<i>Epidemiology</i>	13
<i>Risk factors</i>	14
Extrinsic factors	14
Intrinsic factors	14
<i>Injury mechanism</i>	15
<i>Diagnosis</i>	15
Specific tests	16
Imaging	16
ACL ligament	17
<i>Anatomy of the ACL</i>	17
Anatomy of the anteromedial and posterolateral bundles	19
<i>Biomechanics of the ACL</i>	19
Biomechanical properties of the ACL	20
Biomechanical studies of the two bundles	20
Biomechanical studies of the double-bundle reconstruction	21
Biomechanical studies of the anatomic reconstruction technique	22
ACL treatment	23
<i>Surgical treatment</i>	23
<i>ACL reconstruction techniques</i>	24
ACL grafts	24
Anatomic reconstruction techniques using Hamstring graft	25
Outcome measurements	27
<i>Patient-reported outcomes (PROs)</i>	27
KOOS	27
IKCD 2000 subjective scale	28
<i>Activity scales</i>	28
Tegner activity scale	28
<i>Physical examination and functional performance assessments</i>	28
Lachman's test	28
Pivot shift test	29
KT-1000	29
ROM	29
Functional performance tests	29
<i>Definition of failure after ACL surgery</i>	30
Graft failure	30
Treatment failure	30
Revision ACL	31
Results of Double-bundle ACL reconstructions	32
<i>Patient-reported outcomes</i>	32
<i>Knee laxity measures</i>	32

Knee register studies	33
Biomechanical testing of graft fixation devices	34
Tunnel widening	35
The aims of the thesis:	36
Summary of papers	37
<i>Paper 1:</i>	37
<i>Paper 2:</i>	38
<i>Paper 3:</i>	39
<i>Paper 4:</i>	40
General discussion	42
<i>Ethics</i>	42
Paper 1 and 4	42
Paper 2	42
Paper 3	42
<i>Design</i>	42
Paper 1	42
Paper 2	43
Paper 3	43
Paper 4	43
<i>Material</i>	43
Paper 1 and 4	43
Paper 2	44
Paper 3	44
<i>Baseline demographics and patient characteristics</i>	45
Paper 1 and 4	45
Paper 2	46
<i>Discussion of Methods</i>	46
Paper 1	46
Patient-reported outcome	46
Clinical assessment of knee laxity	47
Functional tests	47
Activity level	47
Tunnel positioning	48
Paper 2	48
Register studies	48
Paper 3	49
Biomechanical testing	49
Paper 4	50
Measurements of the tunnel widening	50
<i>Statistics</i>	52
Paper 1	52
Paper 2	52
Paper 3	53
Paper 4	53
<i>Discussion of Results</i>	54
Clinical outcome of double-bundle ACL reconstructions	54
Activity level	56
Positioning	56
Graft failures and revision outcome	58
Graft fixation	60
Tunnel widening	61

Conclusions	62
Future research	63
References	64

Acknowledgements

The following work was accomplished in collaboration with the following institutions: Martina Hansens Hospital (MHH), Oslo University Hospital (OUS), Steadman Philippon Research Institute (SPRI), Oslo Sports Trauma Research Centre (OSTRC) and the Norwegian National Knee Ligament Register.

There are so many people I have to thank for their contribution: Patients, colleges, friends, and family have all been more or less involved in this project during the last six years. I would like to express my sincere gratitude to the following:

To my advisor Lars Engebretsen: You have been amazing throughout my Ph.D. period. Always available, protecting the study at all times, being positive to new ideas and having faith in your Ph.D. students. Your advices and opinions have been essential for this thesis, yet you still let us "run our own business." You always stepped in and continued the follow-up of the patients if necessary. Thanks to you, this thesis could be accomplished. Because of your impressive network I was assured a phantastic team of researchers around me both national and international. We can only admire how you always put other researchers in front, being generous, and inspiring us all to do our best.

To my co-advisors May Arna Risberg and Stig Heir: To have such excellent researchers as co-advisors has been nothing else than inspiring. You have come up with essential inputs to the studies. To have your encouraging feedback and support have been of great help for this thesis to be accomplished.

To Arne Ekeland and Tor Kjetil Nerhus as chiefs of the Orthopaedic Department at Martina Hansen Hospital during this period of time. Only with your goodwill and help, this research project could be implemented in the clinic at MHH. Kjetil, your "tips and tricks" and always positive attitude towards this thesis definitely made the world of research easier for me.

To my great co-workers Ingrid Trøan and Steinar Johansen: Together with Lars, you were the most important persons for the primary study. The study was carried out over several years, but you always participated when needed and were determined to accomplish the work. Thank you for never giving up on the study. And thanks to Lars Bjune who started this study and included the first patients together with you.

To my roommate Nina Kise: Thank you for the inspiring talks and your continuous support and believe in the project.

To my colleges at the Knee Shoulder Department, Geir Solberg, Stefan Moosmayer and Ingerid Baksaa Aasen and many of my other colleges at MHH: I would like to thank you all for being such a wonderful team to work with, always positive and helpful.

My orthopedic friends that I have (mis)used for all kinds of discussions, research or not, throughout the period of my Ph.D.: Annette, Marianne, Ingebjørg, and Kjersti. I really appreciate your feedback and support.

A special thank to Robert LaPrade, my co-advisor during my visits to Vail. To perform research at the SPRI was an experience of a lifetime. Thank you for your guidance and support.

To Coen Wijdicks and my other co-workers from SPRI: Matt, Sean, Kyle, Grant, Bernardo, and Katherine. Thank you so much for your patience with me as a new researcher, and for the effort, you put into the studies we performed.

Also thanks to John Feagin who gave me inspiring thoughts about the project and learned me never to forget the history of the ACL-surgery.

Thanks to the staff at the Norwegian Knee Ligament Register, especially Stein Håkon Låstad Lygre. You saved me for hours of work and made a fantastic effort to get the statistical analysis finished on time.

To my coauthors from the Danish and Swedish Knee Ligament Registers, Martin Lind and Jüri Kartus: Thank you for your considerable help in providing data and editing the manuscript of this study.

Thanks to Morten Fagerland who made the statistical analysis for the main study. Your expertise was an important and valuable contribution to the study.

To the doctors at Oslo Kommunale Legevakt: Thank you for helping us to include the patients, your work was essential for this study to be completed.

Thanks to the Radiographic Department at Legevakten and your contribution to the study, performing all the radiographic examinations of the patients.

Thanks to the staff at the operating theatres of MHH and OUS for your considerable contribution to the study and the patients through all of those years.

I would also like to thank the OSTRC and the Orthopaedic Department at OUS. Through you, I was ensured to be a part of a high-level research environment.

I am lucky to have a fantastic family, family in law and many good friends around me. Thank you so much for your support throughout this period. I would also like to thank my parents who inspired me for doing things I believe in.

Finally, this work could not have been performed without support from my nearest family. To my dear husband Fredrik, and my beloved children Silke and Filip: Thank you for your patience with your mother and wife, I know it hasn't been easy.

“Walk On, Walk on
with hope in your hearts
And You'll Never Walk Alone....”

— **Gerry and the Pacemakers & Liverpool FC**

List of papers

C Aga, MA Risberg, M Fagerland, S Johansen, S Heir, I Trøan, L Engebretsen. No difference in the KOOS Quality of Life between anatomic Double-bundle and anatomic Single-bundle Anterior Cruciate Ligament reconstruction of the knee; a Prospective, Randomised, Controlled Trial. (*Accepted for publication in The American Journal of Sports Medicine*)

C Aga, JT Kartus, M Lind, SH Låstad Lygre, LP Granan, L Engebretsen. Risk of Revision Was Not Reduced by a Double-bundle ACL Reconstruction Technique: Results From the Scandinavian Registers. *Clin Orthop Relat Res.* 2017 Oct;475(10):2503-2512. doi: 10.1007/s11999-017-5409-3.

C Aga, M T Rasmussen, SD Smith, KD Jansson, RF LaPrade, L Engebretsen, CA Wijdicks. Biomechanical comparison of Interference screws and Combination screw and sheath devices for soft tissue Anterior Cruciate Ligament reconstruction on the tibial side. *The American Journal of Sports Medicine.* 2013 Apr;41(4):841-8. doi: 10.1177/0363546512474968. Epub 2013 Feb 12.

C Aga, KJ Wilson, S Johansen, G Dornan, RF LaPrade, L Engebretsen. Tunnel widening in single-versus double-bundle anterior cruciate ligament reconstructed knees. *Knee Surg Sports Traumatol Arthrosc.* 2017 Apr;25(4):1316-1327. doi: 10.1007/s00167-016-4204-0. Epub 2016 Jun 21.

Abbreviations

ACL	anterior cruciate ligament
ADL	activity of daily living
AM	anteromedial
AMB	anteromedial bundle
ANOVA	analysis of variance
AVE	advanced video extensometer
BPTB	bone-patellar tendon-bone
BMD	bone mineral density
CI	confidence interval
CONSORT	Consolidated standards of reporting trials
CT	computer tomography
DEXA	dual x-ray absorptiometry
3D CT	three-dimensional computer tomography
HR	hazard ratio
ICC	intra/inter class correlation coefficient
IKDC	International Knee Documentation Committee
KOOS	Knee injury and Osteoarthritis Outcome score
LCL	lateral collateral ligament
MARS	Multicenter ACL Revision Study
MCL	medial collateral ligament
MIC	minimal important change
MCID	minimal clinical important difference
mm	millimeter
MOON	Multicenter Orthopaedic Outcomes Score
MRI	magnetic resonance imaging
N	Newton
PCL	posterior cruciate ligament
PEEK	polyether-ether-ketone
PL	posterolateral
PLB	posterolateral bundle
PRO	patient reported outcome
PTS	posterior tibial slope
ROM	range of motion

RTS	return to sports
QoL	quality of life
RCT	randomized controlled trial
SD	standard deviation
STROBE	Strengthening the reporting of observational studies
TT	transtibial
UFS	universal force-moment sensor
US	United States

Introduction

The anterior cruciate ligament (ACL) reconstruction is one of the most common orthopedic procedures performed among young, active and healthy individuals. In the United States (US) more than 130,000 procedures are performed each year.^{145, 104} However, reports state that there is a subset of reconstructed patients who are still clinically unstable or unable to regain their prior function.^{10, 43} Further, long-term clinical studies have detected degenerative changes in up to 50% of the ACL injured patients irrespective of whether the patients were reconstructed or not.^{122, 136}

It is generally accepted that the ACL consists of two functional bundles named after their tibial attachment sites, the anteromedial (AM) and posterolateral (PL) bundle.¹³⁰ Biomechanical studies have demonstrated that each bundle is important for the knee stability.¹⁴³ The AM bundle is the main contributor to anteroposterior stability, whereas the PL bundle contributes to the rotational stability of the knee close to the extension.⁴⁷ The conventional single-bundle technique (non-anatomic) has been insufficient in restoring the original rotational laxity of the tibia.¹⁷⁸ Hence, the double-bundle technique was introduced to improve the outcome of the ACL reconstructions and thereby reduce the development of osteoarthritis.^{24, 175}

The anatomic single-bundle reconstruction technique, more closely resembling the anatomy and biomechanics of the native ACL, was developed parallel to the double-bundle technique.^{179, 180} The placement of the tunnels guided by anatomic landmarks with the free-hand drilling of the femoral tunnel through an accessory anteromedial portal has gradually replaced the non-anatomic, transtibial drilling technique with offset guides and o'clock positioning of the tunnels.⁶³

The initial biomechanical studies reported the double-bundle ACL reconstructions to be superior to the conventional non-anatomic single-bundle reconstructions regarding the restoration of both anteroposterior and rotational laxity.¹⁷⁸ Compared to the anatomic single-bundle reconstructions though, those improvements were less pronounced.⁵³ Short-term clinical studies detected that the double-bundle reconstructions revealed only minor benefits when it came to the clinical outcomes measurements.⁷⁴ It has been questioned whether the reported benefits could justify implementing this new technique since double-bundle reconstructions were considered both being more challenging, cost demanding and time consuming compared to the single-bundle technique.^{21, 64, 120}

ACL surgeons and journals have asked for high-quality studies with a focus on the patient reported outcomes to determine whether the double-bundle technique could benefit the ACL-injured patients.^{162, 169}

The aims of the current thesis were to evaluate the outcome of the anatomic double-bundle ACL reconstruction technique compared to anatomic single-bundle reconstruction with focus on the patient-reported outcome and failure outcome. Conclusions from the thesis could help determine whether the double-bundle ACL reconstruction procedure should continue to be a treatment option for the ACL-injured patients.

ACL injury

The anterior cruciate ligament is a relatively frequently observed injury among the young and active population.⁵⁶ The injury may have significant consequences for the future performance in sports, professional work situations, activities of daily life and recreational activities, and thereby influencing the quality of life of the patient. In the long-term, the general knee-health can be affected because of the increased risk of osteoarthritis in ACL-injured knees.¹²²

Epidemiology

The annual incidence of ACL reconstructions in Norway is 34 per 100 000 citizens. In the younger population (16 through 39 years) the incidence of reconstructions has been reported to be more than twice as high (85 per 100,000).⁵⁶ Since several ACL ruptures are not detected and not all injured patients receive an ACL reconstruction, the exact ACL injury rate is difficult to detect. In a hospital-based survey from Sweden, they found that the incidence of having an ACL injury was 81/100 000 per year.⁴⁴ In the US an estimated annual incidence of 68.6/100 000 has been reported.¹⁴⁵

Female athletes are reported to have a 3-5 times higher injury rate than men, but since more males participate in at-risk sports, the overall injury-incidence is higher in the male population.¹⁶ The gender-distribution is highly age-dependent. In the age-group of young adults predominantly females are at risk, while men have their highest risk of sustaining an ACL surgery between 20 and 30 years.^{116, 134, 145} Pivoting sports like soccer, basket, and handball, but also alpine skiing, gymnastics and contact sports are known to be at-risk sports.^{16, 59}

Risk factors

The risk of getting an injury of the ACL is multifactorial and depends on environmental (extrinsic) and anatomical, hormonal and neuromuscular (intrinsic) factors.¹³⁴ The knowledge concerning risk factors is essentially extracted from studies on ACL-injuries in athletes. Different studies from different sports report different risk factors.⁵⁹

Extrinsic factors

From studies on athletes participating in indoor team sports, footwear and playing surfaces have been reported as critical factors.¹³⁴ Myklebust et al. also found a higher risk of injury during competition compared to practice.¹³⁴ Weather conditions has been reported as a risk factor in outdoor sports.

Intrinsic factors

Notch-size and the actual size of the ACL-ligament are probably of importance.⁶⁰ Athletes with smaller intercondylar notch compared to the total width of the knee have increased risk of sustaining an ACL injury.^{18, 157} Women are known to have smaller notch-sizes than men, but women also have thinner ligaments compared to the rest of the knee. One could therefore presume that the stress distribution on the ligament during at-risk-sports is closer to the ultimate failure load in females than in men.¹³⁴

The increased sagittal slope of the tibial plateau has been suggested in the literature as a significant contributor to ACL re-injury. A seemingly corresponding increase in anterior tibial translation occurs from an increased posterior tibial slope (PTS). PTS is correlated by an ensuing increased occurrence of non-contact ACL injuries in patients with a greater PTS ($9.39^\circ \pm 2.58^\circ$) relative to control subjects, ($8.50^\circ \pm 2.67^\circ$ ($p = 0.003$)).¹⁴⁴ And in activities involving large compression forces, newer studies are showing a significant correlation between ACL re-injury and increased PTS.¹⁹ Salmon et al. found adolescent patients (< 18 years) with a PTS of $> 12^\circ$ to be a significant predictor of secondary ACL injury.¹⁴⁴

Structural differences of the ligament have also been discussed as a risk factor. The female ligament has less stiffness and less elongation at failure compared to the male ligament.¹³⁴ Thus females exceed the ultimate failure load earlier, which could support the suggestion that they are predisposed to injure their ACL.

Neuromuscular components such as hamstring versus quadriceps strength are also known to be risk factors.⁷⁵ Huston et al. looked at the time to generate maximum hamstring tendon torque in response to

anterior tibia translation. They found a significant longer response time in female athletes than male athletes.⁷⁵ Hormonal factors during the menstrual cycle has also been suggested as a risk factor, but whether there exists a correlation between the risk of an ACL injury and the hormone levels at different parts of the cycle, is still under debate.¹⁶ High BMI has also been found to be a risk factor, but only among female athletes.¹⁶

Injury mechanism

Different injury mechanisms have been described for an ACL-injury, being partly activity- or sports specific. The ACL-injuries are primarily categorized as either non-contact or contact injuries. Non-contact injuries are more common than contact injuries, accounting for approximately 70% of all ACL injuries.^{18, 123} In pivoting sports such as handball, football, and floorball, the non-contact injury typically occurs during a cutting or one-legged landing maneuver where the leg is observed close to full extension and combined with rotation of the tibia.¹²³ In skiing most injuries occur in the slip-catch situation where the outer ski catches the snow surface and forces the knee into internal rotation and valgus load.¹⁴ A sudden, excessive eccentric quadriceps contraction has also been discussed as a contributing factor to the ACL injury as well.¹²³

Contact injuries are often a result of a direct blow to the knee by another person or object.

Diagnosis

A precise history of the actual trauma mechanism is important to evaluate the extent of the injury and suspected concomitant injuries. The symptoms are activity- and sports-related with a sensation of giving-way and acute swelling (hemarthrosis) at the time of injury.⁴⁴ Repetitive episodes of giving-way (instability) when returning to activities containing cutting maneuvers increase the probability of an ACL-injury.

A general clinical examination of both limbs and knee joints is to be performed. The uninvolved knee joint can be used as a comparison in specific tests addressing the status of the knee-ligaments. The knee-laxity is usually used to describe a lack of tension in a ligament and can be defined as normal or abnormal.¹¹⁹ Knee instability, on the other hand, is preferably used to describe a physical sign or subjective sensation (giving-way episodes) of the joint.¹¹⁹ The ACL injury may be diagnosed by the following tests:

Specific tests

The Lachman's test is a reliable manual laxity test for distinguishing an ACL rupture from an intact ACL by testing the anteroposterior translation of the knee.¹⁶⁴ The test has been found to have a higher sensitivity and specificity (85 and 94 percent respectively) compared to other manual tests for ACL injuries.^{13,82} The anterior drawer test has a high sensitivity and specificity in the chronic cases but is less sensitive in the acute state of an ACL rupture.^{13,82} The pivot shift test is known as a pathognomonic test for the ACL insufficient knee, and is used for testing the rotational laxity of the knee.^{13,48} The test is highly examiner dependent and known for its low sensitivity and relatively high inter-rater variability.¹¹⁸

Imaging

The initial clinical examination after acute knee-injury has been shown to have low reliability for ACL ruptures.⁴⁴ In contrast, MRI has been shown to be an investigation with high sensitivity and specificity also in acute cases.⁴⁴ MRI should be the preferred imaging modality in cases of a suspected ACL injury.^{29,44} Additionally, injuries to the cartilage, menisci or other ligaments are easily identified by this intervention.²⁹ Concomitant bone injuries are usually detected on plain radiographic imaging or by computer tomographic imaging (CT). To evaluate limb alignment and the posterior tibial slope, long axis radiographic imaging of the knee would be image modality of choice. Computer tomographic imaging (CT) is foremost useful to detect tunnel placement and tunnel widening in cases of revision surgery.

ACL ligament

Anatomy of the ACL

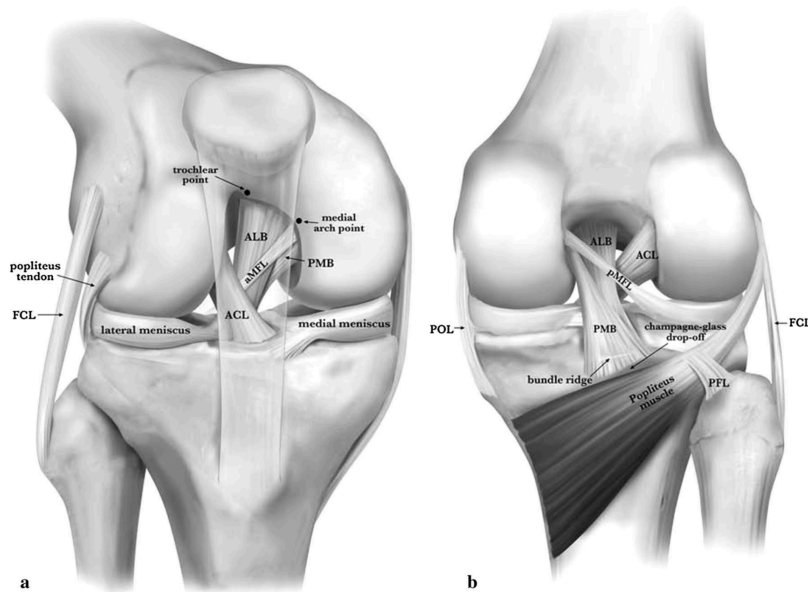


Figure 1. Right knee showing the cruciate ligaments with menisci, collateral ligaments and bony structures: **1a)** anterior view, **1b)** posterior view. ACL, anterior cruciate ligament; aMFL, anterior meniscofemoral ligament (ligament of Humphrey); FCL, fibular collateral ligament; PFL, popliteofibular ligament; pMFL, posterior meniscofemoral ligament (ligament of Wrisberg); POL, posterior oblique ligament (From LaPrade et al.⁹² with permission from Springer).

The anterior cruciate ligament originates at the distal posterior part of the lateral femoral condyle (Figure 1). It runs in an oblique direction and attaches at the central tibial plateau in front of the eminence.³⁵ On the tibial side, the anterior horn of the lateral meniscus is partly surrounded by the c-shape of the ACL-footprint.¹⁵⁰ The ligament has an irregular shape with the tibial attachment site described to be 3.5 times larger than the mid-substance of the ligament.¹⁵⁰ The cross-sectional area of the tibial insertion site is larger than the femoral insertion site.^{89, 109} The mean length of the ACL is from 18 to 34 mm, but significant individual variations are found in the anatomy both regarding length, thickness and size of the insertion sites.¹⁰⁹ A great variance ($18.8 \pm 10.1\%$) of the ligament-length during flexion, extension, and rotation of the knee has been reported.^{89, 46}

The structure is covered by synovial tissue with blood vessels and proprioceptive cells.³⁵ One percent of the ligament itself consists of free nerve endings, implying that the ligament “can provide some conscious awareness and proprioception of knee motion and position “. ³⁵ The blood-supply origins mainly from branches of the middle genicular artery. They are located in the synovial membrane covering the ACL. Additionally, branches from the superior an inferior genicular artery supply nutrition to the ACL through the fat-pad.³⁵

The ligament consists of a complex of collagen fibrils grouped into fibers. The fibers are bound together as fascicles, and the fascicles are further bound together and create what has been promoted as two distinct bundles: the anteromedial and the posterolateral bundle (Figure 2).¹³⁰ The ligament consists primarily of collagen type 1, and fan-like extension-fibers attach the ligament on each side of the joint to the bone.⁴⁶ The ligament-bone interface has the typical 4-layered structure that can be seen in other tendon-to-bone attachments as well, with a “ligament-fibrocartilage-calcified fibrocartilage-bone” structure.³⁵ The bony landmarks for the insertions sites on the femoral side are the lateral intercondylar ridge (residents ridge) that serves as the anterior border of the ACL, while the bifurcate ridge runs perpendicular to the lateral intercondylar ridge and divides the footprint in the attachment sites of the two bundles (Figure 2a).¹¹¹

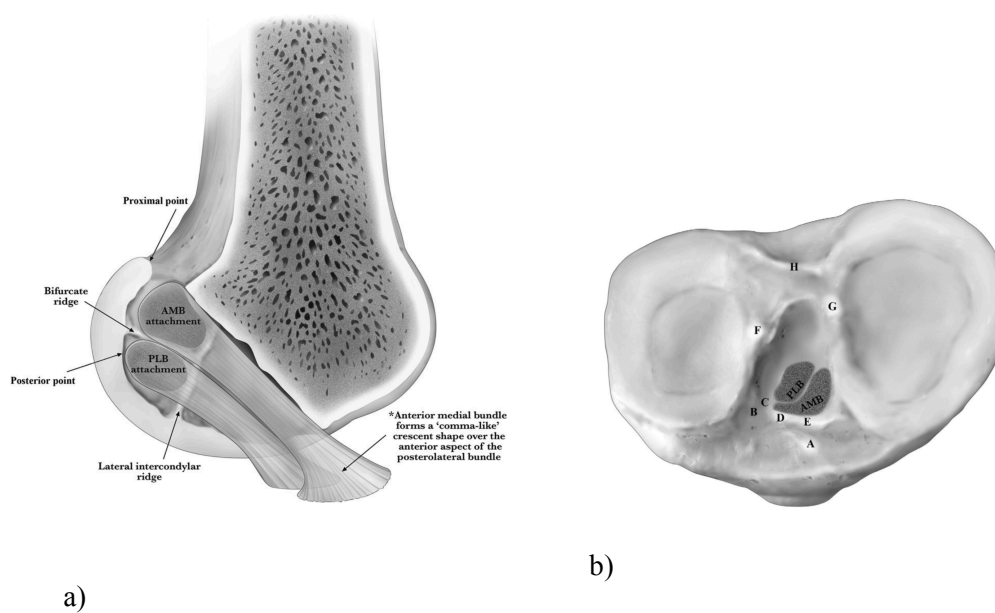


Figure 2. Illustration of a left knee lateral femoral condyle in extension. Attachment sites on the femoral a) and tibial b) side. AMB, anteromedial bundle; PLB, posterolateral bundle. (From Ziegler et al.¹⁸⁵ with permission from SAGE.)

Anatomy of the anteromedial and posterolateral bundles

Currently, the ACL is thought to consist of two bundles named after their tibial side insertion site: the anteromedial and the posterolateral bundle (Figures 2a and 2b).⁹² The Weber brothers were the first to describe the anatomy of those two bundles and their respective tension patterns.⁹² Anatomic studies in human fetus have found the two bundles divided by a vascular septum as early as 18-23 weeks of gestation age.⁴² The mean length of the AM bundle is 32 mm and PL 17.8 mm, and their mean thicknesses are 7 ± 1 mm (AM) and 6 ± 1 mm (PL), although a great variety in size and thicknesses of the bundles exists.¹³⁰

Recently, the two-bundle concept has been challenged by newer anatomical studies considering the ACL more as a band-like structure and not as two bundles.^{150, 153} Smigielski et al. found in their dissections of 111 human cadaver knees, that the proximal appearance of the ACL was an exact continuity of the posterior femoral cortex.¹⁵² They found no consistency in the two-bundle anatomy but described the ACL as a collection of many individual fascicles with a “ribbon-like structure”. The twisting of the ribbon during flexion-extension movements was suggested to lead to the impression of two or three separate bundles.¹⁵³

Biomechanics of the ACL

The complex nature of the ACL is due to its functionality both working as a restraint to anteriorly directed forces between the femur and the tibia, but also as a secondary restraint to internal and to some extent, external rotation during knee motion.⁹² The band of multiple fascicular bundles is often simplified by dividing them into the AM and PL bundle.¹⁰⁰ They are oriented nearly parallel to each other with the knee in extension and twist around each other as the knee flexions (Figure 3). The two bundles have different functions during knee motion where they are slackened and tensioned according to their attachment sites.¹⁰⁰

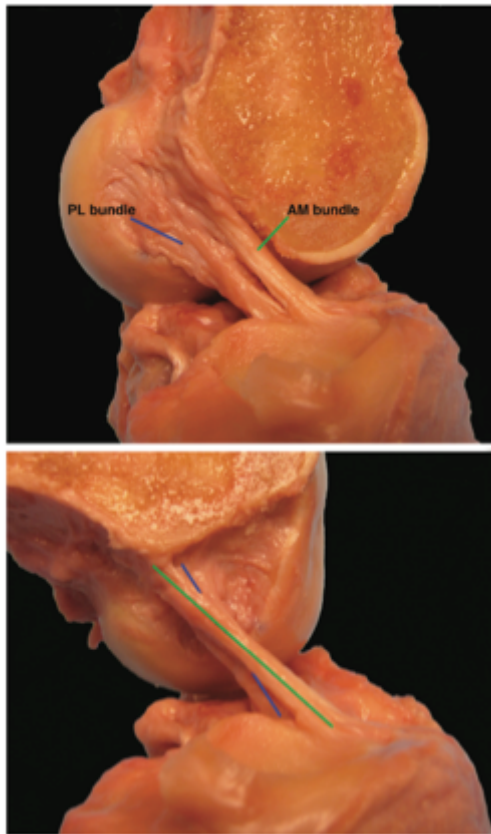


Figure 3. Lateral view of a left knee depicting the anteromedial (AM) bundle and posterolateral (PM) bundle of the ACL in extension (top) and flexion (bottom). (From Ziegler et al.¹⁸⁵ with permission from SAGE publishing.)

Biomechanical properties of the ACL

The resultant forces in the intact ACL during passive extension reaches up to 100 N.¹⁰⁶ The ultimate strength of the ACL approaches 1730 N, but Noyes et al. hypothesized that the ligament is loaded only to one fourth of its strength for most activities.¹¹⁷ Through a hypothetical load-elongation curve they suggested that the upper limit of 445 N would be sufficient to withstand the forces the ligament is subjected to under normal activities.¹¹⁷

Biomechanical studies of the two bundles

Girgis et al. were one of the first to describe the different tension patterns between the bundles during knee motion.⁵⁰ They found that the AM-bundle was tight during flexion and the remaining ACL-tissue (PL-bundle), tight in extension.⁵⁰ Later, techniques to measure direct, resultant, in situ forces within

the native ACL were developed. The universal force-moment robotic system (UFS) became an important instrument used to demonstrate those forces. With the UFS the differences of the two bundles in an in vitro setting were identified.¹⁰⁶

Sakane et al. detected forces in the ACL and its bundles in response to an anterior loading of the tibia towards the femur: They found the PL bundle to be more affected by the knee flexion angle, whereas the in situ forces in the AM bundle was relatively constant during the entire knee flexion movement.¹⁴³

During a combined rotatory load Gabriel et al. found that the PL bundle was a significant contributor to withstand rotatory forces, especially close to the extension.⁴⁷ But both the AM and the PL bundle were important in maintaining normal knee laxity during anterior as well as rotational load.⁴⁷

Biomechanical studies with AM bundle-transection increased the anterior translation in flexion (60 and 90 degrees) whereas transection of the PL bundle resulted in increased anterior translation at combined rotatory loads when the knee was close to the extension.¹⁸³ More recent biomechanical studies though, reported that they by subsequently transecting different parts of the ACL footprint on the femoral side, the center of resistance to anterior load was located a specific central-proximal area of the femoral attachment, close to the origin of the AM bundle.⁸⁵ They also showed that surrounding, fan-like extension fibers of the ACL did not contribute to a large extent in resisting those forces. Hence, probably only a small part of the ACL withstands more than 60% of the reacting forces in the ligament by anteroposterior translation of the tibia towards the femur.⁸⁵

Zantop concluded that none of the fibers behaved isometric during extension and flexion, but instead worked synergistically.¹⁸³ They found that the contribution of the total ACL during knee flexion was essential as the posterolateral bundle tensioned during extension and the anteromedial bundle tensioned during flexion of the knee.¹⁸³

To summarize; the biomechanical studies on the resultant forces within the ACL, supported the results from anatomic studies of two separate bundles.

Biomechanical studies of the double-bundle reconstruction

Yagi et al. were one of the first evaluating the replacement of both bundles in a laboratory setting:^{177,}¹⁷⁸ In their biomechanical study they tested the sectioned and reconstructed ACL and then measured the resultant forces in the ACL during anterior tibial translation and rotatory loads through different flexion angles with both reconstruction techniques.¹⁷⁸ The double-bundle reconstruction showed a

superior outcome compared to the (transtibial) single-bundle technique both for anterior translation and rotatory loads. Results from other biomechanical studies complied with those findings.^{165,129}

Woo et al. looked at the transtibial single-bundle reconstructions in a biomechanical model and found that the traditional vertical placement of the grafts made them inadequate for resisting rotatory forces and suggested a more anatomic reconstruction of the ACL.¹⁷⁵

Parallel to the introduction of the double-bundle ACL reconstruction the increased awareness about the anatomy changed the technique for reconstructing the tunnels. Single-bundle and double-bundle tunnels were aimed to cover the footprint of the native ACL. The transtibial drilling of femoral tunnels was replaced by drilling with freehand technique through an accessory anteromedial portal.⁶³ The o'clock positioning and offset-guides were replaced by visualization of anatomical structures and by using anatomic bone- and soft-tissue landmarks for guidance.¹⁷⁹

Biomechanical studies of the anatomic reconstruction technique

Harner et al. suggested modifying the original transtibial technique by positioning the femoral tunnel free-handed according to bony and soft tissue landmarks, through an accessory AM portal approach.⁶³

The transtibial femoral tunnel positioning results in a more vertical placement of the tunnels and a tendency to position those tunnels anterior and superior to the origin of the ACL (Figures 4a and 4b).^{12, 32} A more horizontally placed femoral tunnels – through an accessory anteromedial (AM) portal - was shown to be in accordance with a restoration of the original footprint.

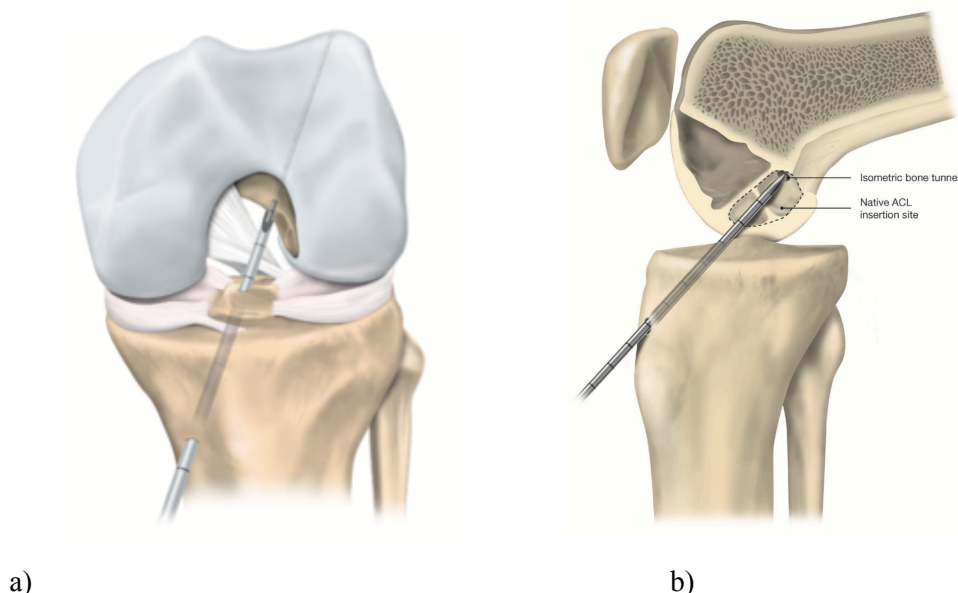


Figure 4a. Image illustrating the transtibial drilling technique of the femoral tunnels from a horizontal(a) and sagittal(b) perspective of the knee. The limitations of transtibial drilling technique are evident, with the femoral tunnel high and deep in the intercondylar notch, outside the native ACL insertion site. (With kind permission from Dr Desai.)

Laboratory studies that were accomplished with a precise anatomical reconstruction technique for both the single- and double-bundle knees revealed only minimal differences between two methods: Goldsmith et al. performed biomechanical testing in nine cadaver knees and detected no significant difference during anterior tibial translation or a simulated pivot shift between the two techniques.⁵³ Under internal rotation, only a small degree of difference was found in 20-30 degrees of flexion (3° less internal rotation in the double-bundle compared to the single-bundle reconstruction group).⁵³ The authors suggested that both techniques could provide acceptable knee-laxity measurements.⁵³ Lord et al. made a kinematic evaluation of the anatomic single-bundle, double-bundle and three-sockets femoral and tibial tunnels.¹⁰⁰ They found no advantage with regards to drilling two or three tunnels, and they concluded that the single-bundle technique, with an anatomic tunnel positioning, revealed laxity similar to the native knee and that it provided clinically equivalent control of rotation compared with the intact knee.¹⁰⁰

In summary, the reported improvements and promising results reported from initial biomechanical studies were somehow diminished as the anatomic single-bundle technique was introduced.^{53, 100}

It is hereby important to remember that the biomechanical testing is usually performed on cadaver knees under given conditions; the specimens are all tested at time zero with no real-life muscular loadings. Also, they are tested with a combined valgus and rotational loading of the knee, which is not the same as the pivot shift phenomenon (a dynamic manual test).¹⁰⁰

ACL treatment

There are two main options of treatment for the ACL injured patient: Non-operative active rehabilitation or operative treatment. The non-operative active rehabilitation is considered for patients that can cope with their knee instability; patients that do not have persistent symptoms of instability and are not performing in high level pivoting sports. Age, gender, associated injuries, sports and the activity level both at work and in leisure time are important issues to consider when the two treatment options are discussed.

Surgical treatment

The purpose of the ACL surgery is to restore the normal knee laxity, regain pre-injury activity level and in addition to promote long-term knee health.⁷¹

The ACL reconstruction is the treatment of choice if patients are considered suitable for operation. Suture repair was one of the primary surgical treatment options up to the 1980's. Due to the reported poor clinical and functional results and unacceptable high amount of re-ruptures, this was later no longer considered a treatment of choice.⁴¹ Repair with synthetic grafts and augmentation techniques with synthetic material were popular options during the 1980-90's. The mid- and long-term follow-up of these techniques, however, were not impressive and the reconstruction technique using tendon grafts gradually became the surgical treatment of choice.^{37 163}

The arthroscopically assisted ACL reconstruction technique using autografts and allografts became increasingly popular during the 1990's. The standard arthroscopic technique was a single-bundle reconstruction with transtibial drilling of the femoral tunnel leading to a non-anatomical femoral graft attachment site (anterior and vertical to the native ACL). The importance of aiming for an isometric graft was emphasized (figures 4a and b). Later on, the awareness about the anatomy changed the technique for reconstructing the tunnels. Single-bundle and double-bundle tunnels were now aimed to cover the footprint of the native ACL. The double bundle concept with different insertion sites, tension patterns and directions of the collagen fibers in the two bundles was promoted.¹¹¹

Due to this gradual shift of reconstruction technique the initial clinical studies contained a variety of surgical techniques.^{168, 184} To control for this variety an "anatomic ACL reconstruction check-list" has been developed.¹⁶⁸

ACL reconstruction techniques

ACL grafts

Reconstructions with grafts obtained from the middle third of the patellar tendon (bone-patellar tendon-bone/BPTB grafts) were considered as the golden standard in the initial phase of arthroscopic ACL reconstructions. Due to increased awareness of the donor site morbidity after BPTB graft reconstructions, hamstring tendon grafts were increasingly used.¹⁴⁶ Quadriceps grafts have also become more popular during the last decade. Low donor site morbidity and preservation of the hamstring tendons has been promoted as some of its advantages.¹⁰¹ Allografts are usually preferred in cases of ACL revision-reconstructions and multi-ligament surgery of the knee. Due to their relatively high costs, increased risk of revision and limited accessibility they are less frequently used in primary ACL reconstructions.⁶²

Anatomic reconstruction techniques using Hamstring graft

The surgical technique consists of placing the patient in supine position, with the knee at 90 degrees of flexion. The regular anterior arthroscopic portals and an accessory anteromedial portal are established. The ACL lesion is usually confirmed by visualization and by probing the ACL remnants. The femoral and tibial insertion sites are then visualized. Together with surrounding soft tissue and bony landmarks, the remnant tissue can be used to identify the center of the proximal and distal ACL footprint.^{89, 185} A skin incision at the pes anserine insertion site is made, and with a tendon harvester, the semitendinosus and gracilis tendons are harvested. The tendons are then doubled or tripled according to their length and thicknesses.



Figure 5. Anatomic single-bundle ACL reconstruction. Anatomic tunnel location with reference to the anterior cruciate ligament (ACL) anteromedial and posterolateral bundle footprints. (From Goldsmith et al.⁵³ with permission from SAGE publishing.)

Anatomic single-bundle technique: The anteromedial portal is used to better visualize the femoral insertion site, and an accessory anteromedial portal is used for the femoral tunnel establishment.²³ The Steadman awl is positioned in a central position of the femoral footprint (Figure 5). With the knee in hyperflexion, the femoral tunnel is drilled according to measured graft size. Then the center of the tibial footprint is identified (Figure 5).^{89, 185} and with an external tibia guide, the tibial tunnel drilled. The graft is passed through the tibial and then the femoral tunnel and cycled through 20 flexion-extension movements. Finally, fixation can be performed with the knee at 20 degrees of flexion and under manual tensioning of the graft.

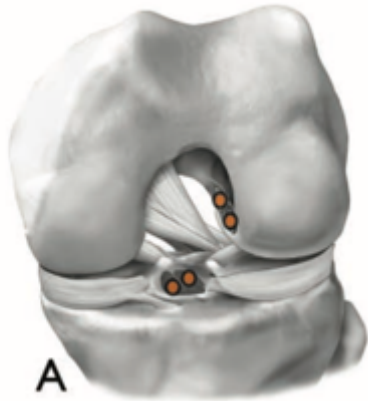


Figure 6. Anatomic double-bundle ACL reconstruction. 2 anatomic tunnels located centrally in the anterior cruciate ligament (ACL) anteromedial and posterolateral bundle footprints. (From Goldsmith et al.⁵³ with permission from SAGE publishing.)

Anatomic double-bundle technique: Through the accessory anteromedial portal and with visualization through the anteromedial portal, the central position of the AM-bundle footprint is marked with a Steadman awl (Figure 6).¹⁸⁵ With the knee in hyperflexion, first, the femoral AM tunnel is drilled. A double-bundle femoral drill-guide with fixed offset can be used to drill the PL tunnel. On the tibial side, the center of the AM footprint is marked using an external tibia guide (Figure 6).¹⁸⁵ The AM tibial tunnel is drilled. A prefabricated tibial aimer placed in the AM tunnel and the PL guide pin positioned through the aimer into the center of the PL footprint. Then the PL tunnel is drilled. The grafts are passed through the tibial and then the femoral tunnels and cycled through 20 flexion-extension movements (Figure 7a and 7b). Fixation can be performed under manual tension and with the knee at 60 degrees flexion for the AM bundle, and at full extension for the PL bundle.

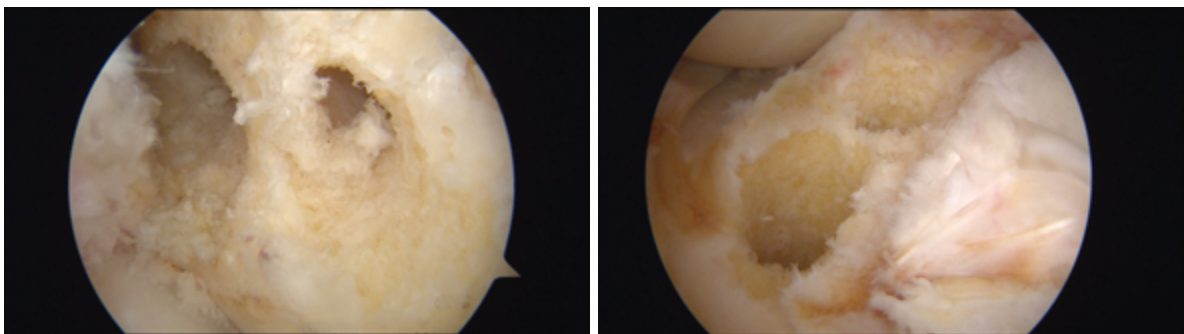


Figure 7a. Arthroscopic view of the left knee. Anatomic double-bundle ACL reconstruction procedure. The drilled bone tunnels on the femoral lateral condyle (left) and tibial plateau (right).

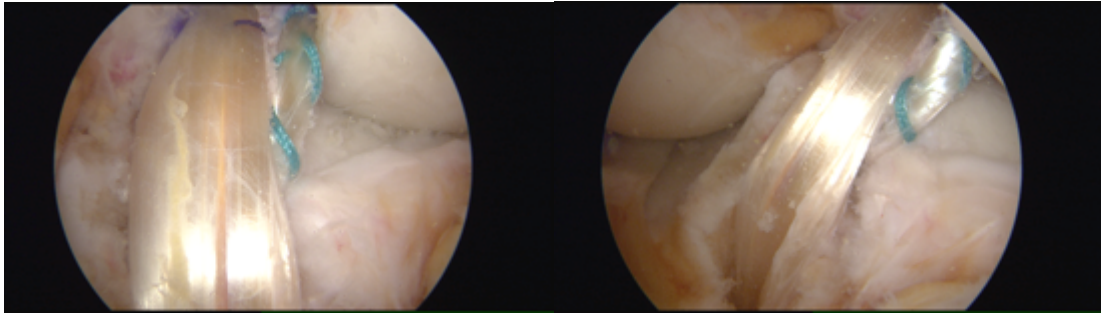


Figure 7b. Arthroscopic view of the left knee after an anatomic double-bundle ACL reconstruction procedure. The two grafts passing into the tunnels on the femoral (left) and the tibial (right) side of the joint.

Outcome measurements

Patient-reported outcomes (PROs)

To make a complete assessment of a treatment effect, the patient-reported outcomes (PROs) have gained increased attention during the last decades. While the outcome of physical examination and radiologic evaluation only in a limited way reflect the patients' experience of outcome, the PROs are of importance from the patient's perspective. The patient's perspective of symptoms, function, and quality of life can be detected through these measures and give significant and valuable information to the clinical evaluation of the knee.¹⁶⁰

KOOS

The two most frequently used PROs to assess ACL-injured patients are the KOOS and the International Knee Documentary Committee (IKDC) 2000 subjective form.¹⁷³ The KOOS was developed with the purpose to evaluate short and long-term symptoms and function in young and active subjects with a knee injury or osteoarthritis.¹⁴¹ It has been considered as a valid, reliable and responsive score for patients with ACL reconstructions.¹⁴⁰ The KOOS data are obtained from a questionnaire consisting of a total of 42 items divided into five different subscales that are rated separately ranging from 0 to 100 points: Pain, Symptoms, Activity of daily living (ADL), Sports and recreation and Quality of life (QoL). The five different subscores have different effect sizes reflecting knee function, symptoms and expectations on an individual basis. It is therefore desirable to interpret them separately.¹⁴⁰ The KOOS QoL subscale is considered to be the most sensitive and responsive among the five dimensions for ACL injured patients. It has been suggested that 8-10 points change in score represents a clinically significant change in ACL-reconstructed patients, although the KOOS

scoring system has been criticized for not having a formally assessed Minimal Clinical Important Difference (MCID).²⁷

IKCD 2000 subjective scale

The International Knee Documentation Committee developed a standardized form for different knee ligament injury conditions (IKDC score).⁶⁷ The score intended to compare treatment methods from various international publications with each other. The original score contained both knee laxity measures and patient reported outcomes.⁶⁷ As the score was later revised the IKDC 2000 subjective score was developed.⁷⁸ This score is now one of the most common PROs used for knee ligament injuries.¹⁷³ It has been shown to be a valid, reliable and responsive score for ACL injured patients as also for other knee injury conditions. The score has however been criticised for its lack of patient contribution to item selection and the use of one single aggregated score.²⁷ The score contains a patient administered form and includes 18 different items that cover three domains: Symptoms, sports, and the current knee function. Each item is weighted according to its importance on the total score, ranging from 0 to 100 points.⁶⁷

Activity scales

Tegner activity scale

The Tegner activity scale was developed to classify the activity level of the patients complementary to the Lysholm scale.¹⁶¹ It was meant as a supplemental scale, to detect whether the score obtained (according to Lysholm scale) could be masked by the level of activity of the patients.¹⁶¹ The scale is divided into 11 different levels of activity (0 to 10) from recreational to competitive sports. Level 0 indicates the lowest knee-related activity (sick leave or disability) and ten the highest knee related activity (competitive pivoting sports at a national level).

Physical examination and functional performance assessments

The clinical outcome from ACL reconstructions can be reported by the assessment of anteroposterior and rotational knee-laxity and the range of motion (ROM) and, as well as by different functional performance tests.

Lachman's test

The Lachman's test is a reliable manual laxity test used for distinguishing an ACL rupture from an intact ACL.^{82, 164} The test can be graded similarly to the anterior drawer test and is carried out with the

patient in supine position and 20 degrees of flexion in the involved leg. One hand is stabilizing the femur and the other hand performing a subluxation of the proximal tibia in the anterior direction. The anterior displacement is recorded in mm and reported as the difference in translation compared to the contralateral leg.⁶⁷ Grade 0 = 0-3mm, grade 1+ = 3-5 mm, grade 2+ = 5-10 mm and grade 3+ has been defined as >10mm displacement of the tibia compared to the uninvolved leg.

Pivot shift test

The positive Pivot shift test is known as a pathognomonic test for the ACL insufficient knee although this test is highly examiner dependent.^{73,118} It is a manual dynamic test, with a high inter- and intra-rater variability.¹¹⁸ The phenomenon is described as the reduction of the tibia from a subluxated position as the knee is flexed with the tibia internally rotated.^{48,118,151} The Pivot shift phenomenon can be graded from 0 to 3+, according to the amount of subluxation of the tibia during extension and its reduction during flexion.⁶⁶ There has been an on-going discussion among the experts whether a positive test should be recorded as such, or if the test should be compared to the contralateral leg.⁶⁷ The grading of the pivot shift phenomenon has been suggested as followed: Grade 0, grade +1= “trace”, grade +2= “clunk”, grade +3= “gross”.

KT-1000

The knee arthrometer KT-1000™ (MEDmetric, San Diego, CA, USA) (Knee Laxity Testing Device), is an instrument made for evaluating knee-laxity in the anteroposterior direction.³¹ It has two sensor pads that are placed in contact with the patella and the greater tuberosity of the tibia during an instrumented Lachman's test of the knee. The device detects the motion between those two sensor pads during an anterior translation of the tibia in relation to the femur. The displacements at loads of 134 N and maximal manual load (MM) are usually detected, and the displacement is usually recorded as mm difference in translation between the involved and the uninvolved leg.³¹

ROM

The ROM of the knee is usually characterized by the degree of extension and flexion.⁷⁰ The normal flexion is both gender and age-specific and ranges from 130-150 degrees. The flexion may be limited due to contractions within the joint but also due to anatomical features outside of the joint (e.g. subcutaneous tissue). ROM measurements can be valuable both as group comparisons and on an individual basis compared to the unaffected knee, but goniometer measures have been criticized because of their poor reliability.⁹⁴

Functional performance tests

Functional performance tests are used to evaluate the functional capacity and performance of the knee. Additional to other scoring instruments assessed by clinical examination or by PROs, performance-based tests could be used to evaluate treatment effects and to determine the time-point of return to sports (RTS).^{98,99} The “one leg hop test” is a functional performance test often used as part of a

performance test battery for ACL deficient knees.⁹⁹ The test is widely used and reflects the strength, coordination and the confidence in the ACL injured knee.³⁹ Usually, the test is given as the percentage difference in hop distance between the uninjured and injured knee, presented by a limb symmetry index (injured/uninjured hop distance x 100).^{11,99}

Definition of failure after ACL surgery

Graft failure

Graft failure is often described as a recurrent instability, with a failure of the reconstructed graft to provide anterior and/or rotational stability to the knee, but it has also been describes as a stiff and painful joint with ROM less than 10 to 120 degrees of flexion.²² No precise international definition of graft failure has been set. In the current study (Paper I) graft failures were defined as patients having a recurrent sense of instability together with having major pathological knee-laxity measures by clinical examination (Pivot shift grade 2+ or 3+ or Lachman's test grade 2+ or 3+ without endpoint) and/or a ruptured graft verified on MRI.

In the early postoperative phase misplaced tunnels, fixation failure or failure of the graft integration could lead to graft failure. Further, postoperative infection, arthrofibrosis and associated injuries such as meniscal-root tears or coexistent ligament injuries not addressed at the primary operation could contribute to failure and the potential need for revision surgery (Koga *et al.* *JISAKOS* 2017;2:36–46. doi:10.1136/jisakos-2016-000071). In data from the Danish register, Lind *et al.* reported that the primary reasons of graft failure was new trauma (38%), unknown cause (24%), and poor femoral tunnel placement (20%).⁹⁷ Similar findings were also found in data from “The Multicenter ACL Revision Study” (MARS) in the US.⁶²

Treatment failure

Inferior knee function following ACL-reconstruction is not always the same as having a non-functioning graft. Failure-outcome could also be reported as the patient's perspective of having a failure. Frobell *et al.* introduced “treatment failures” as a group of patients with a “severely decreased knee-related quality of life”.⁴⁵ To be within this category the patients had to meet the three criteria: A KOOS QoL subscore less than 44 points, a history of “giving-way” episodes and a positive pivot shift at examination.⁴⁵ Later studies revealed that patients with a KOOS QoL subscore less than 44 points are associated with having a 3.7 times higher risk of later revision surgery.⁵⁷

Revision ACL

The need for revision is the ultimate result of failure of an ACL reconstruction.⁹⁷ Because not all graft failures proceed further to undergo revision surgery, the real incidence of graft failures is difficult to detect. Revision surgery has nevertheless, been used as a surrogate outcome for graft failures. In Scandinavia ACL revision surgeries are reported to the national Knee Ligament Registers and the survival of the grafts are therefore defined as reconstructions that has not been revised. From these national registers factors associated with revision surgery can be detected.^{5,6} The revision rates of ACL reconstructed patients are generally considered to be low. Mid-term follow-up studies have shown that between 2 and 8 % of all primary ACL reconstructions undergo revision surgery.^{49,69} Almost half of the revised patients have their revision surgery performed within the first 2 years after the primary reconstruction.⁹⁷ Younger age and pivoting sports are both patient related factors known to be associated with an increased risk of revision surgery.⁶ Of surgical factors hamstring tendon compared to BPTB grafts, small graft-sizes, and certain fixation-devices have been found to be associating factors with revision-surgery.^{5, 49, 103, 126, 128, 133, 155} Finally, anatomic reconstruction technique and AM-portal drilling show a higher revision rate than non-anatomical reconstructions in some studies.^{33, 34, 133}

Results of Double-bundle ACL reconstructions

Patient-reported outcomes

Papers reporting on the outcome of ACL reconstructions using double-bundle technique have mainly focused on clinical examination and the measurements of knee-laxity. Studies where PROs have been used as one of the outcome measurement are relatively few: Mayr et al. found no difference in their primary outcome IKDC 2000 subjective scores, at 2-years follow up comparing the anatomic double-bundle to the anatomic single-bundle technique (86.6 points versus 91.5 points, $p=0.46$).¹⁰⁸ Ahlden et al. looked at the KOOS QoL subscore at 2-years follow-up comparing the same two techniques and found no difference between the two groups.⁴ And also Hussein et al. detected no difference in IKDC subjective score between anatomic/non-anatomic single-bundles and the double-bundle group in their study.⁷⁴ In contrary, a meta-analysis including 17 RTC's and 1381 patients, reported an all over higher improvement in the IKDC 2000 subjective score for the double-bundle reconstructed patients compared to the single-bundle group ($p=0.03$).⁹⁶ Their studies included though both anatomic and "isometric" reconstruction techniques (non-anatomic), hence not exclusively anatomical reconstructions.⁹⁶

Knee laxity measures

Even though the overall results of single-bundle ACL reconstruction surgery have shown high patient satisfaction and low revision rates, some studies reveal that up to 20 % of the reconstructed patients have abnormal knee-laxity measures.^{87, 95}

The inspiring results from the initial biomechanical studies on double-bundle ACL reconstructions were supported by the first short-term clinical studies comparing them to reconstructions with the single-bundle technique: Muneta et al. reported two-year outcome of double-bundle reconstructions. They followed a cohort of 54 double-bundle reconstructed patients with no control group. They stated that the double-bundle technique could provide better anteroposterior laxity than conventional single-bundle reconstructions.¹¹² Similar results were found by Yasuda et al. and Yagi et al.^{177, 180} All three studies used a partly anatomic technique, with transtibial drilling for the AM-tunnel and separately drilling of the PL tunnel through an anteromedial portal. Later on, studies with o'clock positioning of the grafts were published: In 2008 Jaervela et al. published their two-year outcome of 25 double-bundles compared with 52 single-bundle reconstructions.⁸¹ They found improved rotational stability as measured by the pivot shift in the double bundle group, and more graft ruptures in the single- than in the double-bundle group (2 versus five graft ruptures).

So far more than 30 clinical studies comparing the double-bundle to the single-bundle reconstructions have been published.¹⁰⁷ In only a minority of these studies the interventions were reported as anatomic single- and double-bundle technique, thereby reporting the tunnels to be placed guided by anatomical structures and by using an anteromedial portal for femoral drilling: Gobbi et al. found no difference in anteroposterior or rotational laxity and similar objective IKDC scores in the two groups, both reconstructed with anatomic reconstruction techniques.⁵¹ Ahlden et al. too, compared single- and double-bundle anatomic reconstruction techniques and found no difference in their primary outcome, the pivot shift test or in the other knee laxity measures.⁴ Mayr et al. found a difference in one of the rotational knee laxity measurements in favour of the double-bundle reconstruction, even though they questioned their measurement accuracy for this finding. No difference was noticed in objective IKDC score or in the anteroposterior knee laxity.¹⁰⁸ Xu et al. looked at 32 single-bundle and 34 double-bundle patients with clinical tests and 3D-CT measurements of the knees.¹⁷⁶ They detected no difference in knee-laxity measures between the two groups at two-year follow-up. They performed a postoperative CT of the knees and confirmed anatomic placement of the bundles in both groups. Only one anatomic reconstruction study reported improved rotational stability in the anatomic double-bundle compared to the anatomic single-bundle group.⁷⁴ However, the authors stated that the differences between the two techniques were small and that the clinical relevance was questionable.⁷⁴

In a review of nine overlapping meta-analysis, Macarenhas et al. concluded that the double-bundle reconstruction technique could provide some improved postoperative stability whereas other clinical outcomes, the risk of graft failures and complications were similar in both groups.¹⁰⁷ The results of the study, however, were biased by the various reconstruction techniques used in the different studies, including anatomical, partly anatomical and non-anatomical reconstructions. Moreover, very few of these studies were able to document the actual positioning of their grafts.¹⁰⁷

High-quality studies with a focus on PRO's and verified anatomic tunnel-placement were of interest, to be able to conclude whether the double-bundle technique restores knee-laxity and improves PROs better than single-bundle reconstructions.

Knee register studies

The intention of the knee ligament registers is to monitor the outcome of ACL and other knee ligament reconstructions through a prospective surveillance system.⁵⁸ The registers can be used for three principal purposes: To give feedback to the operating surgeons, to detect inferior outcome of new devices and techniques and to look at prognostic factors associated with good or bad outcome for the patients.⁵⁶ In Scandinavia, the national registers from Norway, Sweden, and Denmark cover approximate 20 million people. More than 60,000 primary ACL reconstructions are so far included in

the register, and the completeness of the data collection is high.^{3, 56, 132} Data of patient characteristics, injury pathology, surgical technique, additional injury of the knee and detailed information about the devices for fixation, are recorded to the registers by the operating surgeon. The primary reconstructions are followed continuously, and any new procedures or revisions are reported to the register by the surgeon and can be linked to the patient through the patient's unique personal identification number.⁵⁸

Biomechanical testing of graft fixation devices

The fixation of ACL grafts should include three important properties; allow for graft-incorporation, resist slippage and resist a sudden traumatic loading of the knee. Graft fixations in ACL reconstructions are often tested regarding two different outcomes: Displacement during cyclic loading and the load to failure (ultimate failure load). The cyclic loading simulates the reported forces in the ACL during walking and in the early rehabilitation period.^{20, 117} The load to failure would mimic the one instance where the individual experiences a true traumatic event. Additional variables of interest in such a setting are usually also the linear stiffness and elongation at failure (distance at which the failure occurs) of the graft.²⁰ The testing construct is usually performed with cadaver knees that are exposed to low forces of repetitive loading and/or load to failure in a dynamic tensile testing machine.⁶⁵ A load-versus-elongation curve can be withdrawn and a comparison to other grafts, devices and fixation methods can be performed.¹¹⁷

Different constructs (e.g. extra-cortical suspensory devices, transfix devices) have been developed for the purpose to secure the graft fixation in the initial postoperative period.²⁰ Lambert was the first to introduce the interference technique and Kurosaka et al. found this technique to provide better fixation properties than other fixation devices when tested on BPTB grafts.⁹⁰ With soft-tissue grafts, however, the interference fixation was more sensitive to the bone mineral density (BMD) of the knee than fixations with bone-grafts (BPTB).²⁰

Improved initial fixation strength of the grafts has been shown by increasing the screw length and screw diameter and by sizing the tunnel within 0.5 increments of the graft size.^{20, 68, 172} Concentric instead of eccentric placement of the screw and anterograde compared to retrograde fixation technique could also improve the graft fixation.^{135, 147} Biodegradable screws became popular because of the possible induced graft incorporation and because it could simplify revision surgery, although these advantages have been questioned.³⁸

Most of the mechanical testing of fixation devices has been performed at the "time zero" - the time of initial fixation - when tested at the cadaveric or animal tissue. In animal studies though, graft

incorporation with insertion of collagen fibers between the soft tissue graft and the bone can first be seen at 12 weeks after the reconstruction.¹³⁸ Hence the properties of the fixation device are of most importance in the early postoperative period.^{54, 138} After incorporation of the graft in the tunnels the graft itself is the weakest point of fixation.⁵⁴

Tunnel widening

Tunnel enlargement in ACL reconstructed knees is a phenomenon with multifactorial aetiology and is not yet fully understood.^{26, 167, 174, 186} This phenomenon tends to occur as an early postoperative finding during the first months after surgery.¹⁶⁷ There has been reported tunnel enlargements from 3-50% on the femoral side and 11-33% on the tibial side in ACL reconstructed knees.^{25, 77} Enlargement of the tunnels could make an impact in cases of ACL revision surgery because a potential two-staged operation with bone-grafting could be required. With the double-bundle ACL reconstruction technique the bone-loss is thought to be more extensive due to the two sets of tunnels, but additional bone-loss and the problem of tunnel-confluence could appear as a consequence to the tunnel widening.¹⁴⁹

The widening is a process with both mechanical, but also biological factors involved.¹⁷⁴ Micromotion of the graft is thought to lead to bone resorption through the induced osteoclast activity.¹³⁹ The involvement of cytokines has been described as an important factor as elevated concentrations of cytokines in the synovial fluid have been associated with increased tunnel widening.¹⁸⁶ Finally, the joint fluid, itself could lead to expansion through the pressure on the tunnel wall as the synovial fluid is captured in the graft-tunnel interface during knee loading.¹⁷⁴

Both the graft type and the graft fixation method are factors affecting the tunnel widening process.^{72, 91} Hamstring tendon grafts reveal more widening than BPTB grafts, and less widening has been found by grafts fixated closer to the joint line and also in knees with rigid fixations compared to suspension devices.^{91, 139, 142}

Whether the reconstruction technique (double-bundle versus single-bundle) influences on this phenomenon is still unclear. Two studies reported that single-bundle reconstructions are more exposed to widening whereas one study found no difference between the two techniques.^{1, 80, 84}

The aims of the thesis:

Questions to be answered by this doctoral thesis:

- 1) Is there a difference between the anatomic single- and anatomic double-bundle ACL reconstruction technique regarding the patient reported outcomes (PROs), knee laxity measures, functional tests or regarding the activity level of the patients?
- 2) Is there a difference between the anatomic single- and anatomic double-bundle ACL reconstruction technique regarding the risk of failure in terms of revisions?
- 3) Is there any difference in the biomechanical properties of the interference screw fixation devices used on the tibial side of single- and double-bundle ACL reconstructed knees?
- 4) Is there a difference between anatomic single- and anatomic double-bundle ACL reconstruction techniques regarding their effect on the tunnel widening process?

Summary of papers

Paper 1:

Background: The double-bundle reconstruction technique was developed to resemble the properties of the native ACL more closely than the conventional single-bundle technique. The clinical benefit of this surgical procedure is controversial, and there is a need for studies with a focus on patient-reported outcomes (PROs). The study hypothesized that the anatomic double-bundle ACL reconstruction would be superior to anatomic single-bundle reconstruction regarding a PRO, as detected by the change in the KOOS QoL subscore from baseline to two-year follow-up.

Methods: A randomized controlled clinical trial of 120 patients aged 18 to 40 years with a primary ACL injury of their knee was conducted. The patients were randomized to either anatomic double-bundle or anatomic single-bundle reconstructions. Patients with a concomitant PCL, PLC or LCL injury or with established osteoarthritis were excluded. The outcomes were registered at baseline, one- and two years follow-up. In 24 patients, a postoperative 3D computer tomographic imaging was performed to verify the positioning of the bundles. The primary endpoint was the change from baseline to two-years follow-up in KOOS QoL. Secondary endpoints were the change in the remaining KOOS subscores and in the IKDC 2000 subjective score, the two-years outcome of the pivot shift test, the Lachman's test, the KT 1000 measurements, activity level, RTS rate and osteoarthritic changes on radiographic imaging at the same follow-up. A linear mixed model was used for the analysis of all the PROs, including the primary outcome.

Results: There was no significant difference in the change in KOOS QoL from baseline to two-year follow-up between the two groups (double-bundle: mean change 29.2 points versus single-bundle: mean change 28.7 points, -0.5 points difference, 95% CI -8.4 to 7.5 points, $p=0.91$). Neither were there any differences between the two groups in the remaining patient-reported outcomes, knee laxity measurements or the activity level of the patients. Radiological signs of osteoarthritis were found in two patients. Eleven patients had a graft rupture: 8 in the single-bundle and 3 in the double-bundle group ($p=0.16$). The 3D computer tomographic images of the knees verified the positioning of the AM-, PL- and single-bundle grafts to be within acceptable limits.

Conclusion: There was no difference in the primary outcome KOOS QoL or any of the other PROs, in the knee laxity measurements or the activity level comparing the double-bundle and single-bundle ACL reconstruction techniques. The number of bundles does not seem to influence on the laxity of the knee or the PROs, as long as the tunnels are adequately positioned.

Paper 2:

Background: Double-bundle anterior cruciate ligament (ACL) reconstruction has demonstrated improved biomechanical properties and in some studies superior clinical outcome compared with single-bundle reconstructions. This could make an impact on the re-rupture rate and reduce the risk of revisions in patients undergoing double-bundle ACL reconstruction compared with patients reconstructed with the single-bundle technique. The National Knee Ligament Registers in Scandinavia provide information that can be used to evaluate the revision risk and outcomes following ACL reconstructions. The purposes of the study were (1) to compare the risk of revision between double-bundle and single-bundle reconstructions, reconstructed with autologous hamstring tendon grafts; (2) to compare the risk of revision between double-bundle hamstring tendon and the single-bundle bone-patellar tendon-bone autografts; and (3) to compare the hazard ratios for the same two research questions after a Cox regression analysis was performed.

Methods: The outcome of 60,775 patients with primary ACL reconstructions, were collected from the National Knee Ligament Registers in Denmark, Norway, and Sweden. The inclusion period was from July 1, 2005, to December 31, 2014. 994 patients were reconstructed with double-bundle hamstring tendon grafts, 51,991 with single-bundle hamstring tendon grafts, and 7790 with single-bundle bone-patellar tendon-bone grafts. The double-bundle ACL-reconstructed patients were compared with the two other groups. The risk of revision for each research question was detected by the risk ratio, hazard ratio, and their corresponding 95% confidence intervals. A Kaplan-Meier analysis was used to estimate the survival rates at 1, 2, and five years for the three different groups. Furthermore, a Cox proportional hazard regression model was applied. The hazard ratios were adjusted for country, age, sex, meniscal or chondral injury, and for the utilized fixation devices on the femoral and tibial side.

Results: There were no differences in the crude risk of revision between the patients undergoing the double-bundle technique and the two other groups. A total of 3.7% patients were revised in the double-bundle group (37 of 994 patients) versus 3.8% in the single-bundle hamstring tendon group (1952 of 51,991; risk ratio, 1.01; 95% confidence interval (CI), 0.73 to 1.39; $p = 0.96$), and 2.8% of the patients were revised in the bone-patellar tendon-bone group (219 of the 7790 bone-patellar tendon-bone patients; risk ratio, 0.76; 95% CI, 0.54 to 1.06; $p = 0.11$). Survival at five years after index surgery was 96.0% for the double-bundle group, 95.4% for the single-bundle hamstring tendon group, and 97.0% for the single-bundle bone-patellar tendon-bone group. The adjusted hazard ratio showed a lower risk of revision in the single-bundle bone-patellar tendon-bone group compared with the double-bundle group (hazard ratio 0.62; 95% CI, 0.43–0.90; $p = 0.01$). Comparisons of the graft

revision rates reported separately for each country revealed that double-bundle hamstring tendon reconstructions in Sweden had a lower hazard ratio compared with the single-bundle hamstring tendon reconstructions in Sweden (hazard ratio, 1.00 versus 1.89; 95% CI, 1.09–3.29; $p = 0.02$).

Conclusions: Based on data from three national registers, the overall risk of revision was not influenced by the reconstruction technique in terms of using single- or double-bundle hamstring tendons, although national differences in cumulative survival between the two surgical techniques existed. Using bone-patellar tendon-bone grafts lowered the risk of revision compared with double-bundle hamstring tendon grafts.

Paper 3:

Background: The tibial fixation has been reported to be the weakest point in ACL reconstructions. Numerous interference screws and combination screw and sheath devices are available for soft tissue fixation, and a biomechanical comparison of these devices is necessary. The purpose of the study was to detect whether combination screw and sheath devices had different biomechanical properties compared to screw devices in a laboratory setting.

Methods: The biomechanically testing of 8 different intra-tunnel tibial soft tissue fixation devices on a porcine model with bovine tendons was performed, ten specimens per group. The soft tissue fixation devices included three interference screws: The Bio-Interference Screw[®], BIOSURE PK[®], and the RCI Screw[®], and five combination screw and sheath devices (combination devices): The AperFix II[®], BIOSURE SYNC[®], ExoShape[®], GraftBolt[®], and INTRAFIX[®]. The specimens were subjected to cyclic loading (1000 cycles, 50-250 N, 0.5 Hz) and pull- to-failure loading (50 mm/min) with a dynamic tensile testing machine. The cyclic displacement (mm) and the ultimate failure loads (N) of the eight devices were recorded.

Results: The ultimate failure loads were highest for the GraftBolt[®] (1136 ± 115.6 N), followed by the INTRAFIX[®] (1127 ± 155.0 N), AperFix II[®] (1122 ± 182.9 N), BIOSURE PK[®] (990.8 ± 182.1 N), Bio-Interference Screw[®] (973.3 ± 95.82 N), BIOSURE SYNC[®] (829.5 ± 172.4 N), RCI[®] Screw (817.7 ± 113.9 N), and ExoShape[®] (814.7 ± 178.8 N). The AperFix II[®], GraftBolt[®], and INTRAFIX[®] devices were significantly stronger than the BIOSURE SYNC[®], RCI Screw[®], and ExoShape[®]. Although the three strongest devices were combination screw and sheath devices, no significant differences were observed between the screw and the combination devices when compared as groups. The least amount of cyclic displacement after 1000 cycles was observed for the GraftBolt[®] (1.38 ± 0.27 mm), followed by the AperFix II[®] (1.58 ± 0.21 mm), Bio-Interference Screw[®] (1.61 ± 0.22 mm), INTRAFIX[®] (1.63 ± 0.15 mm), ExoShape[®] (1.68 ± 0.30 mm), BIOSURE PK[®] (1.72 ± 0.29 mm), BIOSURE SYNC[®] (1.92

± 0.59 mm), and RCI Screw[®] (1.97 ± 0.39 mm). The GraftBolt[®] allowed for significantly less displacement than the BIOSURE SYNC[®] and RCI[®] Screw. Similarly, no significant differences were observed between the screws and the combination screw and sheath devices when compared as groups.

Conclusion: The combination screw and sheath devices did not provide superior soft tissue fixation properties compared with interference screws in a porcine model. Although the highest ultimate failure loads and the least amounts of cyclic displacement were observed for the combination devices, group comparisons did not result in any significant differences in those two outcomes.

Paper 4:

Background: The consequence of tunnel widening after ACL reconstructions is foremost of importance in case of revision surgery. Tunnel expansion leads to bone loss close to the joint, and additional surgery with bone grafting prior to revision surgery might be necessary. The purpose of the study was to measure widening of the tunnels in single-bundle and double-bundle ACL reconstructed knees during the first year after surgery, detected by a novel, semi-automated 3D CT imaging modality. We hypothesized that there would be a difference between the initial tunnel size and the size measured one-year post-operatively due to the tunnel widening process. Further, the purpose was to evaluate whether there were any differences in the amount of tunnel widening between the single-bundle and double-bundle ACL reconstruction group.

Methods: Twenty patients who underwent a double-bundle ACL reconstruction and 22 patients who underwent a single-bundle ACL reconstruction performed a CT scan of the knee during the first day after surgery and one year postoperatively. The CT scans were transformed into 3D CT reconstructions, and the tunnels were extracted and measured with three methods: By the “best-fit cylinder” method, at the level of tunnel aperture method and at the level 10.0 mm from the joint line method.

Results: All tunnels in the double-bundle and single-bundle ACL reconstructed knees exhibited widening during the first year after the operation ($p < 0.001$). The single-bundle femoral tunnels showed more widening compared to the double-bundle femoral AM tunnels (1.4 ± 0.9 vs. 0.5 ± 0.6 mm) ($p < 0.001$), and the single-bundle tibial tunnels widened more compared to the double-bundle tibial PL tunnels (1.0 ± 1.0 vs. 0.5 ± 0.6) ($p < 0.043$).

Conclusion: All tunnels widened during the first year after the ACL reconstruction with a more

significant amount of widening in the single-bundle tunnels compared to two out of four double-bundle tunnels. This study is the first to detect tunnel widening in double-bundle reconstructed knees through a novel, semi-automated 3D CT imaging modality.

General discussion

Ethics

Paper 1 and 4

Both studies were approved by the Regional Committees for Medical Research Ethics, South-Eastern Norway Regional Health Authority (ID: S-09108b 2009/2165 and 2013/1729). The RCT (Paper 1) was also reported in Clinical trials (ClinicalTrials.gov ID: NCT0103318) before inclusion of the first patient. All participants were informed about the studies by the assisting surgeon and signed an informed consent before inclusion.

Paper 2

The utilization of register data was approved for research purposes by the Regional Committees for Medical Research Ethics (South East Norway Regional Health Authority, RIB No. 2015/922). Also, the respective boards of the Knee Ligament Registers in Denmark, Norway, and Sweden approved for the study to be done. In Denmark, Danish law assures that all ACL-reconstructed patients are registered without the need for additional consent forms. In Norway and Sweden registration is voluntary and all the participants sign an informed consent before enrolment.

Paper 3

This study was approved by the Research Committee at the Steadman Philippon Research Institute, Vail, Colorado, US.

Design

Paper 1

This prospectively randomized, controlled, clinical trial (RCT) was designed with two parallel groups as a superiority study with equal allocation to both groups. Well designed RCTs has been rated as the highest level of evidence (Level 1) and has been considered the preferred study design to evaluate the effect of an intervention although they are expensive and sometimes difficult to complete.²⁸ The study was also designed as an efficacy study using an experienced surgeon in a high volume hospital. The results could therefore not be directly applicable to other hospitals and other surgeons performing ACL reconstructions.

Only half of the participants were blinded for the intervention. As the primary outcome of the study was a PRO, not blinding of the patients could lead to an overestimate of the effect of the intervention.¹²⁴ To evaluate the possible impact of blinding a subgroup analysis of blinded versus non-

blinded patients was performed. The analysis did not reveal any further difference in the outcome between the two groups.

Paper 2

The register study was designed as a prospectively followed cohort study (observational study). Epidemiological studies provide information regarding disease occurrence and associations. Further the strength of the association between a disease and the exposure can thereby be assumed. Prospective cohort studies are less biased than other epidemiological study designs and have the advantage of including the dimension of time.²⁸ The disadvantage however, is that in diseases with low incidences the number of events are small and the size of the cohort needs to be large to have sufficient power. They are costly and require long-term follow-up of the participants.

Paper 3

This study was a descriptive laboratory study with in vitro measurements of the biomechanical properties of different fixation devices at time zero. In vivo though, the properties could change due to both biological and mechanical factors. The results from these types of studies should therefore be interpreted with caution.

Paper 4

This study was an observational, prospectively followed cohort study. A subgroup of patients from the RCT (Paper 1) was included. As not all subjects from the RCT were exposed to the intervention (CT), the study participants could have been selected unintentionally. Ideally, the intervention should have been performed to all the participants in the RCT (Paper 1) to avoid the effect of possible selection bias.

Material

Paper 1 and 4

The patients included in the study were referred from the outpatient clinics of two recruiting hospitals, one university hospital and one hospital specialized on orthopaedic surgery. Both hospitals recruited patients mainly from South-Eastern Norway. A total of 1186 patients received an ACL reconstruction during the inclusion period in the two hospitals. Only 120 of them fulfilled the inclusion criteria, and the reasons for being excluded were reported for the remaining patients. The most frequent causes of exclusion were: Age at surgery less than 18 or more than 40 years old, a multi-ligament injury to the knee or less than two months of supervised rehabilitation in front of the operation. The strict inclusion

criteria may have limited the external validity of the study. Since the general ACL injured population would include both younger and older patients and patients with less concise preoperative rehabilitation protocols or with co-existent injuries – the results from this study may not be directly applicable to others.

Two months of preoperative, supervised rehabilitation ensured that all patients were well prepared for surgery, on the other hand, this could have resulted in excluding potential study participants. The required minimal hamstring tendon size could have excluded foremost female patients since their hamstring tendons are generally shorter and thinner than in males. Less strict inclusion criteria and a multi-center approach with many different surgeons could have improved the general validity of the study.

In Paper 4 a cohort of patients from the randomized controlled trial (Paper I) was included. All patients from randomization number 42 to 75 were subsequently asked to participate, but only 24 of the 33 patients agreed to be included. The reasons for withdrawal were due to logistical reasons, pain inhibiting the patients from traveling to the hospital and perform the additional CT, but also because of anxiety for additional radiation. As only a subgroup of the total cohort was included, this group may have been exposed to selection bias.

Paper 2

The National Knee Ligament Registers in Norway, Denmark, and Sweden are nationwide and cover more than 20 million people. Approximately 86% to 90% of the primary ACL reconstruction procedures performed in these three countries are recorded in those registers.^{3, 56, 131} Only 1-2% of the patients received a double-bundle ACL reconstruction during the inclusion period. Because of the relatively low incidence rate, more than one national register was considered necessary to provide a sufficient sample of double-bundle reconstructions. Since the three Scandinavian registers are similar in their structure data from all three countries could be combined and used for analysis.⁵⁸

Of 68,636 patients, 7858 were excluded due to the exclusion criteria. Both patients with multi-ligament injuries, children and old patients, as well as other grafts and reconstruction methods were excluded. Exclusion of those patients may have compromised on the external validity of the study. All the included patients were followed as assumed at risk until either end of study or time of revision. Ideally, patients either emigrating or dying during the study period should have been censored (excluded), but as this information was not available from all three countries, these patients were assumed to be at risk throughout the study period.

Paper 3

Fresh frozen porcine tibia and bovine extensor tendons were chosen for the study. Bovine digital extensor tendons have been reported to have similar viscoelastic, structural, and material properties to human hamstring tendons.³⁶ The mean bone mineral density (BMD) in young porcine bone (24

months) is similar to the average BMD of young humans aged 20 to 29 years.¹¹⁴ Since BMD in human bone is disposed to a considerable variability dependent on their age, porcine bone is usually preferred rather than older human cadaver knees for this kind of study.¹²¹ Although the BMD of the tested specimens in our study was unknown, the inclusion of a high number of specimens (n = 10), as well as the random distribution of specimens between groups, helped to prevent disproportional bone quality within the eight different groups.

The tested three screws and five combination devices were chosen based on their different materials (PEEK, biodegradable or metal implants) and their frequency in use. The tibial side is said to be the weakest point of the fixation. This could be because the reacting forces on the graft are more in line with the tibial tunnel and because the quality of the cancellous bone in the proximal tibia is less dense compared to the distal femur.²⁰

Baseline demographics and patient characteristics

Paper 1 and 4

In the RCT (Paper 1) the mean age of the included patients was 27 years in both groups. These numbers reflect the general age of the primary ACL-reconstructed population in Scandinavia and the US.^{3, 58, 102}

The cohort consisted of a higher percentage males compared to females. Compared to baseline data from other knee ligament registers though, the percentage of male participants is consistently higher among ACL reconstructed patients although age-dependent differences exist. The reason for this has been thought to be that males are more represented in at-risk activities.^{16, 58}

In Paper 1, 87% of the patients within the double-bundle group were males. Another single- versus double-bundle study reported a similar tendency of a higher representation of males in the double-bundle treatment arm.^{2, 88} The double-bundle procedure demands a relatively large lateral femur condyle to avoid tunnel convergence and injury of the cartilage, and this could have affected the inclusion to the two groups although a correct randomization process should have inhibited such a bias.

In the Paper 1 menisci injuries were detected in 53% of the double-bundle patients, and in 48% of the single-bundle patients. Coexistent chondral injuries were detected in 18.5% and 20% of the patients respectively. Whereas the amount of chondral lesions, was similar to the average ACL reconstructed population (20%), the menisci injuries were reported slightly more frequently.^{4, 49} The time from

injury to surgery was however reported to be longer than in other studies (>15 months).⁴ This delay could have affected the presence of coexistent injuries.⁵⁵

Preinjury Tegner score was retrospectively collected, and recall bias could have occurred. Still, a Tegner score at 7-8 reflects a population with high demands to their knees and is similar to other studies on ACL reconstruction.⁴ More than 63 % of the patients reported their main sports to be a pivoting sport (handball, football, floorball). This number is a relatively high compared to numbers from the registers and other studies.¹⁰² However in the Scandinavia registers they record the sport that was performed at injury and this is not necessarily the same as the main sport of the patients.

Paper 2

In the register study (Paper 2) the mean age of the included patients was 28 years of age. A gender-discrepancy between the double-bundle and single-bundle group was observed: 63% were males in the double-bundle group compared to 58 % males in the single-bundle group. This difference could also be explained by the selection of knees with preferably larger hamstring tendons and/or ACL-footprints to the double-bundle procedure.¹⁴⁸

In Paper 2 a higher amount of chondral injuries were detected in the double- compared to the single-bundle reconstructed group. This could reflect that the double-bundle operation was reserved for patients with worse baseline findings or more complex injuries. One other register study has observed worse baseline KOOS in the double-bundle group and assumed such an explanation for their results and baseline PROs.¹⁷

Discussion of Methods

Paper 1

Patient-reported outcome

To report on patient-reported outcomes have reached increased attention during the last two decades. However, knee laxity measurements do not necessarily correlate with PROs: Whereas the rotational knee-laxity as measured by the pivot shift test has been found to correlate with patients satisfaction, sports participation and Lysholm score in some studies, no significant relationship was found between

the Lachman's test or KT1000 measurements and the same variables.^{86, 156} Respectively, symptoms of importance for the patient could differ from the findings of importance from a surgeon's perspective.

Clinical assessment of knee laxity

The clinical evaluation of the ACL is often reported as the assessment of anteroposterior translation (Lachman's test and KT 1000 measurements) and rotational laxity (pivot shift test) of the knee. These evaluations are often measured without weight-bearing and with sub-physiological forces, not representative of the daily activity and thus not always predictive of the knee function in real life.^{181 156} Further, monitoring the rotational laxity is one of the challenges when reporting the outcome after ACL reconstructions. Testing of the pivot shift has been shown to have a relatively large inter-rater variability, and a standardized quantitative assessment of this phenomenon has been searched for.¹¹⁸ In the current study, the rotational laxity was detected only through a manual dynamic test (pivot shift test), while the anterior translation was reported both by the manual Lachman's test and by instrumented KT 1000 measures. The clinical examination in the current study was restricted to few (three) observers, albeit instrumental evaluation of the rotational laxity could have improved the reliability of this outcome.¹¹³ The anteroposterior translation has been easier to assess by standardized methods: The KT 1000 measurement has reached worldwide usage and is a validated measurement for ACL injured patients. The anteroposterior laxity, however, has been shown to be a less predictive outcome for the patient's perception of symptoms.^{86, 156}

Functional tests

The one-leg hop test has been used to administer the outcome of pre- and postoperative rehabilitation. Since both single- and double-bundle reconstructed legs in the paper (Paper 1) achieved more than 90 % in limb symmetry index at 2-years follow-up (compared to uninjured knee) they could have been prone to a ceiling effect for this outcome. To evaluate the limb symmetry index in time-intervals closer to the operation could have been more interesting in order to detect any possible differences between the two groups.

Activity level

To enable the athletes to return to their pre-injury sports and level of activity has been one of the main purposes of the ACL-reconstruction surgery.⁸ Both the intensity of training (Activity scale) and the level of performance (Tegner score) were therefore chosen together with the RTS in order to evaluate the activity level of the patients. Return to preinjury main sports is more difficult in high competitive levels and with pivoting sports than recreational, non-pivoting activities.⁹ The RTS rate should therefore be interpreted with the other factors in mind.

Tunnel positioning

The graft positioning was validated on CT-images of the bone tunnel positioning. Although CT imaging of bone structures are of higher reliability than other imaging modalities, both an inter- and intra-class correlation score should have been performed in the current study.¹⁰⁵ Parkar et al. looked at multiple positioning studies and in their review reliability testing was missing in nine of sixteen studies.¹²⁵ Still this could have improved the reliability of the current study (Paper 1). Also, CT measurements from the entire cohort and not only from a selected group of patients could have increased the reliability.

The positioning of the femoral tunnels was defined by using the quadrant method as described by Bernard et al.¹⁵ With this method the center of the femoral tunnels were detected in the “deep-shallow” and “high-low” direction within a grid adapted to the lateral femoral condyle. On the tibial side, the CT model of the tibial plateau was positioned in the axial view as described by Tsukada et al. (Figures 11 and 12).¹⁶⁶ Bernard et al. and Tsukada et al. suggested that a correct tunnel position was dependent on distances to different bone structures on radiographic and CT imaging.^{15, 166} According to the “double-bundle concept” a correct position could be dependent on other features.¹¹¹ In the current study the center of the tunnels were positioned dependent on the anatomy with bony landmarks and remnant soft tissue, hence specific for each patient. Accordingly, anatomic cadaver studies have shown some variability between the different studies, reflecting the difficulties in defining the ideal position of the tunnels through this method.¹²⁵

Paper 2

Register studies

Since graft failures appear relatively infrequent, RCTs are not the best study-design to investigate such outcome. Register studies have, through their prospective approach, the advantage of detecting possible confounders and risk factors even by a small number of incidences.^{56, 97, 102} The quality of register studies though, can be affected by selection and information bias and by their compliance/coverage.

Coverage: 86% to 90% of the primary ACL reconstructions have been recorded in the national registers in Scandinavia during the last years.^{3, 56, 132} This coverage though, was lower during the first years after initiation of the registers.¹³² This could potentially have underestimated the revision rates predominantly in the single-bundle group because the double-bundle reconstruction first became popular 3-4 years after initiation of the registers.¹⁵⁹ Also, the fact that all patients, including emigrated and dead patients were considered in the population at risk throughout the study period, could have

underestimated the actual risk of revision.

Selection bias: In the current study (Paper 2) the double-bundle group could potentially have been affected by a selection bias because only 1% to 2% of all the recorded patients received this reconstruction technique. The double-bundle patients could have been more closely monitored since they received a novel intervention. Further, arising graft-failures in those patients could be more likely to be identified early and treatment offered more often than those having a conventional ACL reconstruction. On the contrary, a higher threshold to recommend revision surgery in double-bundle reconstructed patients could exist because of the extent of bone loss at both sides of the joint. Selection bias is rarely eliminated by analysis and could limit the validity of the study.

Information bias: The information bias can be minimized by the fact that hard endpoints (revision) are used and that the events are prospectively reported. The coverage of the patients receiving a revision-procedure though, has not been formally assessed, and potentially some of the revisions could have been missed or misclassified.

Confounding masks the true effect of a risk factor. Confounding can be adjusted for by restriction (regression analysis) or matching (case-control studies). Adjusting for the confounding factors implies previous experience and knowledge of the confounding factors. The confounders in the current study were selected based on information from previous studies and the accessible data from the registration forms. Not all confounders are registered in the knee ligament registers: The pre- and postoperative level of activity, quality of the postoperative physical rehabilitation, psychological aspects of the patients, and clinical and radiographic findings are not detected, but are still essential factors concerning ACL outcome.^{8,61} Other important factors, such as body mass index and the use of nicotine were also not included in the final analysis due to the high rate of non-responders for this outcome. Factors related to procedure (anatomic or non-anatomic), surgeon- and hospital-volume were other important factors not considered in this analysis.

Paper 3

Biomechanical testing

The eight graft fixation devices were chosen based on material and construct (Figure 8). To be able to diminish the biomechanical factors that could bias the results, both screws and combination devices were chosen with similar length and thicknesses.¹⁷²

The reported biomechanical properties of the tested devices were results from a laboratory testing on a porcine bone with bovine tendons. The parameters for the cyclic loading and load-to-failure were selected from a synthesis of common parameters from the various protocols in a literature search.^{20,65,}

¹⁷⁰ Because of the different study protocols and different specimens used in other biomechanical studies, the results of the current study are not directly applicable to other settings. Also, laboratory studies are foremost hypothesis generating, and the given results should be followed by in vivo studies to confirm those findings.¹²⁷

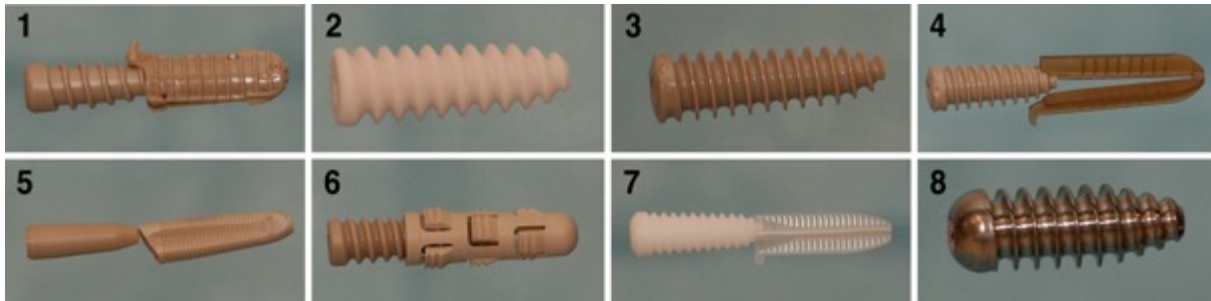


Figure 8. Biomechanical tested soft tissue graft fixation devices. Screw devices: BioScrew[®] (2), Biosure PK[®] (3), RCI screw[®] (8). Combination screw and sheath devices: Aperfix[®] (1), BiosureSync[®] (4), Exoshape[®] (5), Graftbolt[®] (6), Intrafix[®] (7)

Paper 4

Measurements of the tunnel widening

To measure the exact tunnel widening one are dependent on a valid measurement modality and time zero measurements of the tunnels.^{105, 167} In the current study (Paper 4), CT scans were performed on the first postoperative day and at one-year postoperatively identifying the actual widening of the bone tunnels.

CT is known to be superior in its inter- and intra-observer reliability when measuring bone tunnels.¹⁰⁵ In the current study the 3D measurements were calculated semi-automatically within the software program, independent of the angulation of the knee at examination (Figure 9).¹³⁷ Measurement errors due to the manual segmentation could still be existent though.

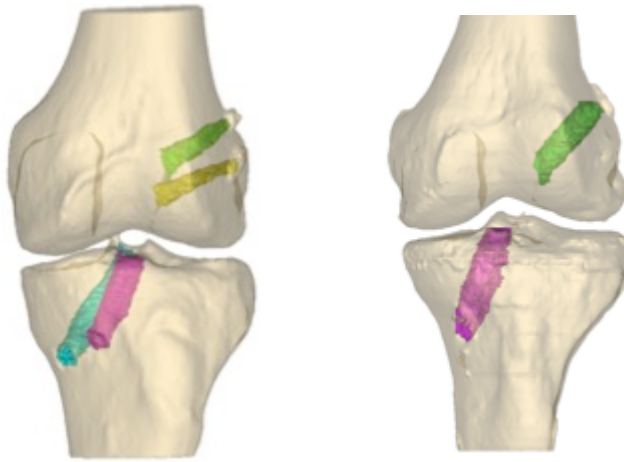


Figure 9. CT imaging of the bone tunnels in double-bundle(left) and single-bundle(right) ACL reconstructed knees. Femoral AM, green; femoral PL, yellow; tibial AM, violet; tibial PL, blue.

The best-fit cylinder measurements have been shown to give the most accurate measurement of the bone tunnels after ACL reconstruction.³⁰ This method was therefore used for tunnel-measurement in the current study (Paper 4).³⁰ The diameter and cross-sectional area at the tunnel aperture and at a distance 10.0 mm from the aperture were also measured. Measuring at those two levels was performed to detect widening in different parts of the tunnel and to detect widening at levels where the mechanical and biological forces might have the most significant influence on the graft.¹³⁹ Previous studies have explained more widening closer to the joint aperture as a consequence of the “windshield-wiper effect” of the graft on the tunnel wall; this phenomenon could also be detected on the femoral side in the current study (Paper 4).²⁰

Communication between the tunnels was defined as missing a separating cortical ridge between the two tunnels and could eliminate the effect of a double bundle construct. This phenomenon has been observed in about 20% of the double-bundle reconstructions in a previous study.¹⁴⁹ In the current study a prefabricated femoral and tibial aimer was used for all the double-bundle reconstructions, but still, five of the 42 subjects (11%) were detected with tunnel communication at 1-year follow-up. In the current study the aimers ensured a 3-4 mm bone-bridge between the two tunnels. With a fixed offset between the tunnels apertures, the anatomic reconstruction of both bundles could also have been compromised.

Statistics

Paper 1

In front of the statistical analysis of Paper I, a Statistical analysis plan was published online (www.OSTRC.no).

The sample size was calculated based on the primary outcome: change in the KOOS QoL subscore. The minimal perceptible clinical improvement (MPCI) of the KOOS QoL was set to be 8 points. The MPCI can be defined as the smallest change in health status detected by the patient. Since the KOOS contains the full and original version of the WOMAC, an MPCI of 8-10 points has been assumed to be sufficient to detect a difference between the two groups.¹⁴⁰ With equal allocation to both treatment arms and a two-sided significance level of 0.05, the sample size was calculated to contain 56 patients in each treatment group.

Mixed models analysis: Repeated measurements do not hold the assumption of independent measures at all time points. In that case, a linear mixed model would account for this dependency and be preferable to, i.e., ANOVA. The linear mixed models also account for missing data on individual time points, thus obviating the need to input the missing values.

Missing data: The PROs and the one-leg hop tests were analysed with a linear mixed model. For other outcomes, a sensitivity analysis was performed if more than 5% of the data was missing. Missing data were recorded for all outcomes.

Blinding: The data, blinded for the two treatment arms was presented to the statistical advisor. As only half of the patients were blinded for the intervention, a planned subgroup analysis was performed to control for the possible confounding of not blinding the patients.

Subgroup analysis: A Post hoc subgroup analysis was performed in the cohort of patients with intact grafts at two-year follow-up because of the relatively high percentage of graft failures in one of the treatment groups. Sensitivity analysis was also carried out to assess whether inconsistencies between the online randomization list and the treatment allocated had any impact on the primary outcome. Post hoc analysis should be avoided in RCTs, and interpreted with caution, though the two circumstances were not foreseen and could therefore not be included a priori.

Paper 2

Sample size: A power calculation was performed. To detect a decrease in the revision rate from 6.0 % to 4.0 % with a double-bundle reconstruction, a cohort of 1000 double-bundle patients and 52,000 control patient, would be needed to be able to reject the null hypothesis. An uncorrected chi-square

statistic was used for this power calculation.

Survival and regression analysis: Survival estimates and cumulative survival was presented with Kaplan-Meier survival plots. To adjust the results for the most important confounders a Cox regression analysis was performed. In the register study there were only 47 events of revisions in the double-bundle group, but eight different confounders. In prospective cohort studies with few events, too many confounders could assumingly result in large CI and weaken the conclusion of the study.⁸³

Furthermore, adjusted hazard ratios were presented for each country. The reason for introducing the interaction term for each country was because this variable influenced on the revision-outcome differently, depending on in which country the surgery was performed: The double-bundle procedure could result in both higher and lower risks of revision compared to single-bundle reconstructions.

Paper 3

The biomechanical results were analyzed using one-way analyses of variance (ANOVA). Post hoc Tuckey tests were performed to determine if there were any difference among the fixation devices for each of the biomechanical tests. The post hoc test was also used to make a group comparison between the screws and the combination screw and sheath devices. A planned comparison of the two groups could have improved the statistical strength of the outcome since post hoc tests generally should be avoided.

Paper 4

Sample size: A priori power analysis was performed to detect widening in the double-bundle reconstructed group. 20 patients in each group was found sufficient to identify a difference of 0.5 mm widening.^{115, 149} The study sample size was adequate to detect a widening in the double-bundle reconstructed knees from baseline to one-year follow up, but insufficient to compare the widening between the single- to the double-bundle group. The possibility of a type two failure (not rejecting the null hypothesis even if false) could exist and could have been prevented by increasing the sample size of the study. The difference of 0.5 mm widening used in the power calculation, does also not necessarily reflect a clinical important difference when it comes to tunnel widening.

Paired samples t-tests were used to compare the change in tunnel diameter from 0 to 1-year follow-up in each group. Additionally, widening was compared between the single- and double-bundle group using Welch's two-sample t-tests. The Welch-test is more reliable in samples with unequal variance and unequal sample sizes and was therefore preferred to the Students t-test.

The ICC is one of the most common scores to assess measurement reliability. In the current study (Paper 4), the ICC scores showed good to excellent intra-rater and inter-rater reliability. To detect the measurement reliability of the are of importance especially in cases were new modalities are used.

Discussion of Results

Clinical outcome of double-bundle ACL reconstructions

In the current study, the change in KOOS QoL subscore from baseline to two-years follow-up was not found to be different between the two interventions. Nor were there any difference between the change from baseline to two-years follow-up in the other KOOS subscores. The 5 different KOOS subscores at 2-years follow-up with their observed mean values and their CI are shown in Figure 10. Secondary outcomes including knee-laxity measurements, reported by the Lachman's test, KT 1000 measurements and pivot shift test did also not reveal any difference. These results are in line with previous studies comparing anatomic single- with double-bundle reconstructions.^{4, 108, 176} However, the strength of the current paper was to have a PRO as the single primary outcome.

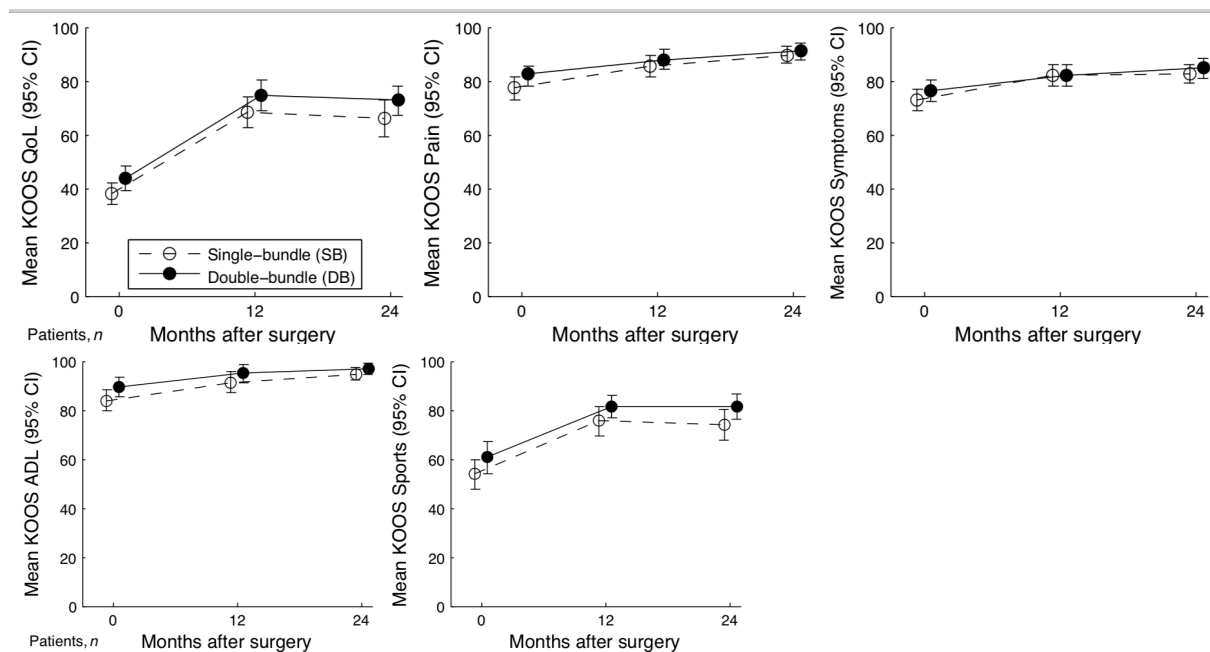


Figure 10. KOOS subscores (observed mean values \pm 95% CI) at follow-up. DB (black dots), double bundle; SB (white dots), single-bundle. Pain, Symptoms, Activity of Daily Living(ADL), Quality of Life(QoL) and Sports/Recreation(Sports)

So far more than 30 clinical trials comparing the single- to the double-bundle reconstruction have been published.¹⁰⁷ While some studies proclaim that the double-bundle technique improve the outcome of ACL reconstructions, other studies have found no advantage of using this new technique.^{34, 169} Any differences in PRO have rarely been seen in the previous RCT's comparing single-bundle and double-bundle technique although one meta-analysis has detected improved IKDC 2000 subjective scores in the double-bundle group.⁹⁶

Studies that are meeting the criteria for anatomic reconstructions with accessory anteromedial portal drilling and tunnel placement according to anatomical structures and not decided by offset guides or o'clock positioning are few. Four studies performed with strictly anatomic reconstruction revealed no difference in their PROs or knee laxity measures between the single- or double-bundle reconstructions. These results are in line with the current study. One of the anatomic studies, however, reported improved rotational stability in the anatomic double-bundle compared to the anatomic single-bundle group.⁷⁴ Hussein et al. studied 131 double-bundle patients; 78 patients reconstructed with anatomic and 72 reconstructed with conventional, non-anatomic single-bundle reconstruction technique. They reported that anatomic double-bundle was superior to both anatomic and non-anatomic single-bundle reconstructions. Double-bundle reconstructions exhibited 0.4 mm less anteroposterior translation in the KT 1000 measures (1.2mm vs. 1.6mm difference in translation between the anatomic double- and single-bundle group) and a higher rate of negative pivot shift test (93.1% versus 66.7% respectively). There was also a significantly less anteroposterior translation and a higher percentage of patients with a negative pivot shift test in the anatomic compared to the non-anatomic single-bundle group.⁷⁴

The discrepancy in the clinical outcomes that has been shown between many of the studies could be due to the bias introduced by the anatomic reconstruction as many of the publications still compare non-anatomic single-bundles with anatomic or partly anatomic (AM bundle drilled through a transtibial approach and the PL bundle drilled through the anteromedial portal) double-bundle reconstruction. Increased use of anatomic reconstructions during the last decade could explain why many of the later publications do not find any differences between the two techniques.^{2, 4, 158} The clinical relevance of the detected differences has also been questioned.¹⁰⁷ Less than 1 mm difference in anteroposterior translation and minor improvements of rotational stability with the double-bundle reconstruction has been reported.^{2, 74} In studies of knees with intact ACL's, a difference between both legs in anteroposterior translation up to 3 mm has been considered as normal.³¹ The clinical relevance of the studies revealing less than 1 mm difference between the two techniques could therefore be questioned. Further, one study looking at the correlation between the degree of anteroposterior laxity and the patients function and subjective score, and did not show any association between the two outcomes and the anteroposterior laxity (in contrast to the pivot shift). Still, maybe the minimal improvements in knee laxity measures exhibited by the double-bundle technique in some studies, could prevent the development of degenerative changes: So far 5-years outcome have not shown any differences in osteoarthritic changes between the two methods, but there is a need for studies with longer follow-up to address these questions.¹⁵⁸

In summary, the heterogeneity of the different surgical techniques in the previous studies makes a general comparison between studies difficult.¹⁶⁸ When comparing studies with similar (anatomic) reconstruction techniques, they reveal less difference between the single- and double-bundle reconstruction technique in PRO measurements and the clinical assessment of knee-laxity.^{4, 108, 176} In the current study restitution of close to normal knee-laxity could be obtained by reconstruction with an anatomic single-bundle technique as long as this bundle is located according to the forces reacting in the native ACL. The anatomic concept of the ACL reconstruction seems to be more important than the number of bundles that are reconstructed. However, increasing forces reacting on the anatomically placed single-bundle graft may influence on graft survival.¹⁵⁹

Activity level

No differences were found between the two techniques in their post-operative activity level. These findings are in line with previous research.^{4, 107} The RTS rate was relatively low for both treatment arms (53% of the double-bundle and 44% in the single-bundle reconstructions at 2-years follow-up). Since 64 % of the patients participated in pivoting sports before the injury and all patients were informed about the re-injury risk by returning to pivoting sports after surgery, this could have influenced on this outcome.

The RTS rates have been found to be profoundly affected by many factors: Psychological factors, fear of reinjury, motivation and the pre-injury level of sports are all known to influence on the RTS.⁸ The psychological aspects were not assessed in the current study (Paper 1), but the pre-injury level was relatively similar to other studies.⁴ The preoperative rehabilitation, on the other hand, has been shown to improve the RTS rate.⁴⁰

Positioning

Compared to a review on anatomic studies, the femoral center of the single-bundle reconstructed knees in the current study was “deeper and higher” positioned than the center of the native ACL (Figure 11).¹²⁵ The remaining tunnels were within acceptable limits.

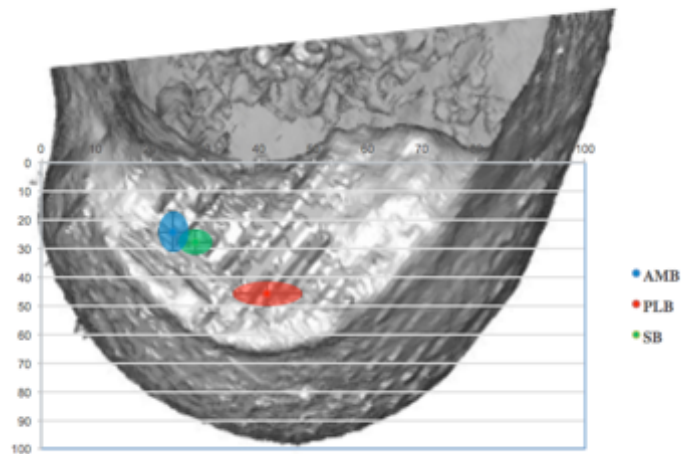


Figure 11. Femoral tunnel positioning (center \pm SD); AM, anteromedial bundle(blue); PL, posterolateral bundle(red); SB, single-bundle(green).

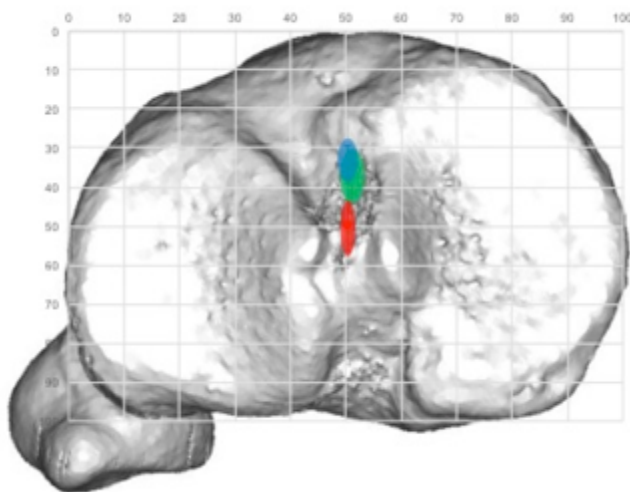


Figure 12. Tibial tunnel positioning (center \pm SD); AM, anteromedial bundle(blue); PL, posterolateral bundle(red); SB, single-bundle(green).

Amis et al. found the proximal central area of the femoral attachment site the most important to resist anterior displacement of the tibia.⁸⁵ More than 66% of the forces reacting on the ACL during an anterior drawer arose from this area of the native ACL. Similar to the single-bundle placement in the current study Jarvela et al. aimed for placing their single-bundle grafts closer to the AM bundle attachment site. They found a higher rate of graft-failures in the single-bundle treatment arm (ten out of 60 single-bundle reconstructions and 1 out of 30 double-bundle reconstructions re-ruptured at 5-years follow-up).⁷⁹ Somehow this placement could make the single-bundle grafts susceptible for re-

rupturing. In the current paper (Paper 1) eight patients had graft failures in the single-bundle group and three in the double-bundle group.

Graft failures and revision outcome

How the surgical technique of single- or double bundle reconstructions could influence the re-rupture rate is still under debate. Some studies found a lower risk of revisions in reconstructions with the double-bundle procedure, while others have found no differences between the two techniques.^{17, 159} Recently, discovering that anatomically placed grafts may be exposed to higher forces could also influence on graft survival and failure outcome after ACL reconstructions.⁷

In previous studies comparing double-bundle with single-bundle reconstructions, graft failures have been inadequately reported and results difficult to interpret due to the risk of bias and small sample sizes.¹¹⁰ In a review from 2012, only six out of seventeen trials reported on graft failures: In a total 1 out of 169 double-bundle versus 4 out of 185 single-bundle reconstructions were reported as graft failures.¹⁶² In a meta-analysis including 970 patients in 15 papers comparing single and double-bundle reconstruction technique, Desai et al. found that graft failures were reported in only six of the 15 studies.^{34, 158 34} They observed no overall difference in graft rupturing between the two techniques. Tiamklang et al., however, found limited evidence of the double bundle procedure protecting against a traumatic re-rupture of the graft whereas, no difference was found between the two techniques when both traumatic and non-traumatic re-rupturing was included.¹⁶² Finally, Mascarenhas et al. in their review concluded with a similar risk of graft failures with both methods.¹⁰⁷

In Paper II no difference in the crude risk of revision between the hamstring tendon single- and double-bundle group was reported (Figure 13). When a Cox regression analysis was performed there were still no difference between the hamstring tendon single- and double-bundles, although, the study detected some national differences: In Sweden, the survival of the double-bundle reconstructions was superior to single-bundle hamstring tendon reconstructions, whereas this was not the case in Norway and Denmark. The total numbers of revisions, however, were relatively few (47 double-bundle revisions detected in all the three countries together) and may have been susceptible to bias. On the other hand, most of the double-bundle reconstructions were performed in Sweden. Since the volume of a surgical procedure is known to influence the outcome, the higher number of double-bundle reconstructions performed in Sweden could have improved the double-bundle graft-survival.¹⁸²

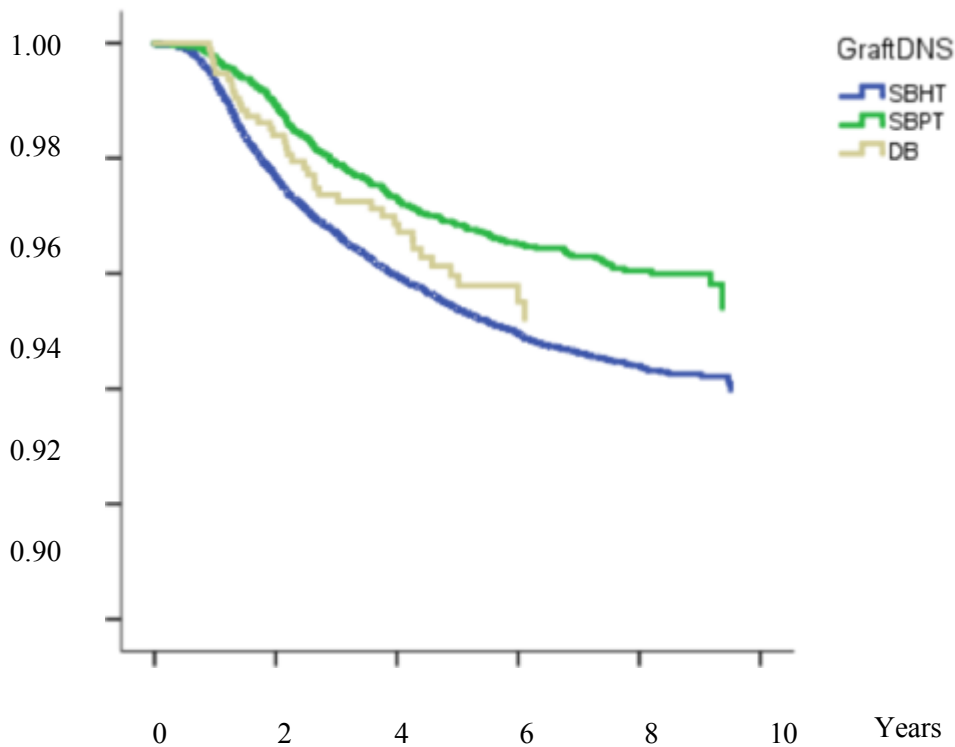


Figure 13. Kaplan Meier survival curves with cumulative Risk of Revision, for single- and double-bundle ACL reconstructions in Scandinavia, 2005-2014. DNS: Denmark, Norway and Sweden. Single-bundle hamstring tendon: SBHT(blue line), Single-bundle bone-patellar tendon bone: SBPT(green line). Double-bundle hamstring tendon: DB(brown line),.

Two other studies have looked at revisions in single- compared to double-bundle ACL reconstructions in larger national registers.^{17, 159} One of the studies concluded with a similar risk of revision for both techniques, whereas the other study detected fewer revisions following the double-bundle technique. Interestingly, a new register study found a higher revision rate in the anatomic compared to the non-anatomic performed single-bundle reconstructions.¹⁵⁹ This finding can be supported by a Danish study where they concluded that drilling the tunnel through an anteromedial portal increased the risk of revision compared to drilling with the transtibial technique.¹³³

Adjusting the groups for anatomical or non-anatomical technique, hospital-volume, and even surgeon-volume could have improved the validity of the results since the survival of the grafts probably is dependent upon those factors. The national differences found in the current paper (Paper II) might be

explained by those factors as well.

Failure-outcome can also include treatment failures. The number of treatment failures (KOOS QoL subscore less than 44 points) in the single- and double-bundle group in Paper 1 did not differ between the groups. From three out of 54 patients were defined as treatment failures (5.6%) in the double-bundle group and 10 out of 62 patients (16.1%) in the single-bundle group respectively (10.6% difference, 95% CI (-1.3% to 22.2%), $p=0.06$). The cut-off at 44 points in the KOOS QoL has never been validated, although patients with less than 44 points are correlated with having a higher risk of revision.⁷⁶ To define treatment failures as patients with scores outside of a certain range of the normative values could have been a more precise measurement to use.⁵²

To remember is that individuals subjected to an ACL injury in the first place make them an “at-risk person” where extrinsic and intrinsic factors together make this person predisposed to have this injury.¹³⁴ After the reconstruction, those factors are still maintained for most patients by returning to the same environment and setting. Preventing the grafts from re-rupturing is not only done by improving the reconstruction technique, but other factors such as to delay the return to pivoting sports and emphasize the importance of a structured warm-up program are probably also of importance to protect against graft-rupturing.¹³⁴

Graft fixation

Noyes et al proposed that the native ACL would be exposed to a maximum of 445N during normal activities.¹¹⁷ The ultimate failure load of all eight tested devices in the current study would have had sufficient strength to withstand those forces. The elongation was less than 2 mm in all devices and within acceptable limits. However, the study was performed in porcine bone with bovine tendons. Even if their biomechanical properties are proved to be similar to the bones and tendons of young adults, the results cannot be directly transformed into humans.^{114, 36, 121}

The screw construct has been evaluated in the current study. Combination screw and sheath devices were supposed to assure a concentric placement of the screw and thereby distribute compression forces throughout the whole radius of the tunnel, acting on the tendon-to-bone interface.¹⁵⁴ The study did not find the combined screw and sheath devices consequently superior in their biomechanical properties compared to the interference screws although they could still be beneficial regarding the graft healing process. Radially compression of the graft against the bone and thereby increasing the graft-to-bone surface could enhance the process of graft integration compared to eccentrically placed interference screws or suspensory devices.¹³⁹ However, many of the biological and mechanical factors influencing the graft-incorporation process are still relatively unknown. In a register study looking at the most common fixation devices in the Norwegian Knee Ligament Register, Persson et al. did not

detect any improved outcomes of combination devices compared to interference screw devices on the tibial side.¹²⁸

Tunnel widening

The findings in Paper 4 are consistent with the literature, although the amount of tunnel widening in this study (7–25 %) was less impressive than previously described.^{93, 149} Emphasis on measurement modality should be given when comparing widening of the tunnels in ACL reconstructions. The precision of computer-tomographic (CT) imaging has been shown to be superior with more accurate detection of the bone-soft tissue interface compared to MRI and radiography.¹⁰⁵ The widening was also less pronounced compared to studies without a “time zero” measurement of the tunnels.¹³⁷ The baseline tunnel size, could be affected by both inaccurate drilling and expansion due to interference fixation. To measure the initial postoperative tunnel size instead of using the drill size as a baseline reference could preclude this inaccuracy.

Tunnel widening is foremost important in case of revision procedures. Less than 1mm widening was detected in all the tibial and femoral tunnels in the current study. This amount of widening is within acceptable limits.

The most prominent widening in double-bundle reconstructed knees was detected in the femoral PL tunnels (12–25 % depending on measurement method). The single-bundles also widened more on the femoral side. Other studies confirm these findings. The reason for the discrepancy between femoral and tibial tunnels could be the direction of the grafts: The grafts are more in line with the tunnels on the tibial side, whereas the femoral tunnels exhibit higher shear forces.^{93, 149} Extracortical graft fixation on the femoral side could additionally lead to micromotion of the graft (the “bungee-” and “windshield-wiper effect”) in the respective areas and increase the tunnel widening in those areas.²⁰ Some studies have compared the clinical outcome to the amount of tunnel widening in ACL reconstructed knees: Only one previous study has found such a correlation, five other studies did not find any association to knee laxity measurements (Paper 4).^{26, 80, 171} In a clinical setting, the widening seems to be more important because of the bone loss it implies and not the effect it could have on the knee laxity. In the current study (Paper 4) though analysis of any correlation between tunnel widening and the clinical outcomes should ideally have been performed. This could have added more valuable information and clinical relevance to the study.

Conclusions

In summary, the double-bundle ACL reconstruction technique has shown similar outcomes regarding function and clinical findings compared to the anatomic single-bundle technique. There is no difference in the frequency of revisions between the two methods and even though the widening of the tunnels is not as pronounced in the double- as in the single-bundle tunnels this benefit is diminished by the substantial bone-loss that could be expected by the drilling of two tunnels instead of one. Based upon the results from these four papers the double-bundle technique does not seem to improve the outcome of the ACL-reconstructions compared to an anatomic single-bundle procedure.

Question 1: There were no differences in PROs, knee laxity, ROM, activity level or in RTS measures comparing single-bundle and the double-bundle anatomic ACL reconstruction techniques. Both reconstruction methods resulted in improved patient-reported and clinical outcomes. The number of bundles did not seem to be important as long as they were adequately positioned.

Question 2: Based on information from three national registers, the risk of revision was not influenced by the reconstruction technique regarding single- or double-bundle hamstring tendons, although national differences existed.

Question 3: A combined screw and sheath devices did not provide superior soft tissue fixation properties compared to the interference screws alone, although the highest ultimate failure loads and least amounts of cyclic displacement were observed for the combination devices.

Question 4: Tunnel widening occurs in all of the drilled tunnels during the first year after surgery. A higher amount of tunnel widening was found in the single-bundle reconstructed knees compared to two of the four tunnels in the double-bundle reconstructed knees.

Future research

Paper 1: Short-term outcome of the anatomic double-bundle ACL reconstruction technique has been extensively investigated. Future research should focus on the long-term effects of this operation and on the joint degeneration it may or may not prevent.

Paper 1 and 2: Future studies identifying the reasons for graft failures in single- and double-bundle reconstructions would be of interest to understand the findings of the present study. The impact of surrounding structures on the risk of graft failures is to be more extensively followed but also studies to investigate whether graft-re-rupturing is increased by the anatomic compared to the non-anatomic reconstruction technique, is of interest for future research.

Paper 3: More than the graft-fixation properties at time zero seems to be of importance for the failure outcome. The biological and mechanical factors influencing on the graft-incorporation process is still relatively unknown. Getting more knowledge about those factors could be of interest to prevent future graft ruptures.

Paper 4: To detect the tunnel widening in patients with graft failures or with a low knee-related quality of life, could be of interest to demonstrate whether this phenomenon has any clinical relevance for the patients.

References

1. Achtnich A, Stiepani H, Forkel P, Metzloff S, Hanninen EL, Petersen W. Tunnel widening after anatomic double-bundle and mid-position single-bundle anterior cruciate ligament reconstruction. *Arthroscopy*. 2013;29(9):1514-1524.
2. Aglietti P, Giron F, Losco M, Cuomo P, Ciardullo A, Mondanelli N. Comparison between single- and double-bundle anterior cruciate ligament reconstruction: a prospective, randomized, single-blinded clinical trial. *Am J Sports Med*. 2010;38(1):25-34.
3. Ahlden M, Samuelsson K, Sernert N, Forssblad M, Karlsson J, Kartus J. The Swedish National Anterior Cruciate Ligament Register: a report on baseline variables and outcomes of surgery for almost 18,000 patients. *Am J Sports Med*. 2012;40(10):2230-2235.
4. Ahlden M, Sernert N, Karlsson J, Kartus J. A prospective randomized study comparing double- and single-bundle techniques for anterior cruciate ligament reconstruction. *Am J Sports Med*. 2013;41(11):2484-2491.
5. Andernord D, Bjornsson H, Petzold M, et al. Surgical Predictors of Early Revision Surgery After Anterior Cruciate Ligament Reconstruction: Results From the Swedish National Knee Ligament Register on 13,102 Patients. *Am J Sports Med*. 2014;42(7):1574-1582.
6. Andernord D, Desai N, Bjornsson H, Ylander M, Karlsson J, Samuelsson K. Patient predictors of early revision surgery after anterior cruciate ligament reconstruction: a cohort study of 16,930 patients with 2-year follow-up. *Am J Sports Med*. 2015;43(1):121-127.
7. Araujo PH, Asai S, Pinto M, et al. ACL Graft Position Affects in Situ Graft Force Following ACL Reconstruction. *J Bone Joint Surg Am*. 2015;97(21):1767-1773.
8. Arden CL, Taylor NF, Feller JA, Whitehead TS, Webster KE. Psychological responses matter in returning to preinjury level of sport after anterior cruciate ligament reconstruction surgery. *Am J Sports Med*. 2013;41(7):1549-1558.
9. Arden CL, Taylor NF, Feller JA, Whitehead TS, Webster KE. Sports participation 2 years after anterior cruciate ligament reconstruction in athletes who had not returned to sport at 1 year: a prospective follow-up of physical function and psychological factors in 122 athletes. *Am J Sports Med*. 2015;43(4):848-856.
10. Arden CL, Webster KE, Taylor NF, Feller JA. Return to sport following anterior cruciate ligament reconstruction surgery: a systematic review and meta-analysis of the state of play. *Br J Sports Med*. 2011;45(7):596-606.
11. Barber SD, Noyes FR, Mangine RE, McCloskey JW, Hartman W. Quantitative assessment of functional limitations in normal and anterior cruciate ligament-deficient knees. *Clin Orthop Relat Res*. 1990(255):204-214.

12. Bedi A, Musahl V, Steuber V, et al. Transtibial versus anteromedial portal reaming in anterior cruciate ligament reconstruction: an anatomic and biomechanical evaluation of surgical technique. *Arthroscopy*. 2011;27(3):380-390.
13. Benjaminse A, Gokeler A, van der Schans CP. Clinical diagnosis of an anterior cruciate ligament rupture: a meta-analysis. *J Orthop Sports Phys Ther*. 2006;36(5):267-288.
14. Bere T, Florenes TW, Krosshaug T, et al. Mechanisms of anterior cruciate ligament injury in World Cup alpine skiing: a systematic video analysis of 20 cases. *Am J Sports Med*. 2011;39(7):1421-1429.
15. Bernard M, Hertel P, Hornung H, Cierpinski T. Femoral insertion of the ACL. Radiographic quadrant method. *Am J Knee Surg*. 1997;10(1):14-21; discussion 21-12.
16. Beynon BD, Johnson RJ, Abate JA, Fleming BC, Nichols CE. Treatment of anterior cruciate ligament injuries, part I. *Am J Sports Med*. 2005;33(10):1579-1602.
17. Bjornsson H, Andernord D, Desai N, et al. No difference in revision rates between single- and double-bundle anterior cruciate ligament reconstruction: a comparative study of 16,791 patients from the Swedish national knee ligament register. *Arthroscopy*. 2015;31(4):659-664.
18. Boden BP, Griffin LY, Garrett WE, Jr. Etiology and Prevention of Noncontact ACL Injury. *Phys Sportsmed*. 2000;28(4):53-60.
19. Bojicic KM, Beaulieu ML, Imaizumi Krieger DY, Ashton-Miller JA, Wojtys EM. Association Between Lateral Posterior Tibial Slope, Body Mass Index, and ACL Injury Risk. *Orthop J Sports Med*. 2017;5(2):2325967116688664.
20. Brand J, Jr., Weiler A, Caborn DN, Brown CH, Jr., Johnson DL. Graft fixation in cruciate ligament reconstruction. *Am J Sports Med*. 2000;28(5):761-774.
21. Brophy RH, Wright RW, Matava MJ. Cost analysis of converting from single-bundle to double-bundle anterior cruciate ligament reconstruction. *Am J Sports Med*. 2009;37(4):683-687.
22. Brown CH, Jr., Carson EW. Revision anterior cruciate ligament surgery. *Clin Sports Med*. 1999;18(1):109-171.
23. Brown CH, Jr., Spalding T, Robb C. Medial portal technique for single-bundle anatomical anterior cruciate ligament (ACL) reconstruction. *Int Orthop*. 2013;37(2):253-269.
24. Cha PS, Brucker PU, West RV, et al. Arthroscopic double-bundle anterior cruciate ligament reconstruction: an anatomic approach. *Arthroscopy*. 2005;21(10):1275.
25. Choi NH, Oh JS, Jung SH, Victoroff BN. Correlation between endobutton loop length and tunnel widening after hamstring anterior cruciate ligament reconstruction. *Am J Sports Med*. 2013;41(1):101-106.
26. Clatworthy MG, Annear P, Bulow JU, Bartlett RJ. Tunnel widening in anterior cruciate ligament reconstruction: a prospective evaluation of hamstring and patella tendon grafts. *Knee Surg Sports Traumatol Arthrosc*. 1999;7(3):138-145.

27. Collins NJ, Misra D, Felson DT, Crossley KM, Roos EM. Measures of knee function: International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form, Knee Injury and Osteoarthritis Outcome Score (KOOS), Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS-PS), Knee Outcome Survey Activities of Daily Living Scale (KOS-ADL), Lysholm Knee Scoring Scale, Oxford Knee Score (OKS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Activity Rating Scale (ARS), and Tegner Activity Score (TAS). *Arthritis Care Res (Hoboken)*. 2011;63 Suppl 11:S208-228.
28. Committee IS, Audige L, Ayeni OR, et al. A practical guide to research: design, execution, and publication. *Arthroscopy*. 2011;27(4 Suppl):S1-112.
29. Crawford R, Walley G, Bridgman S, Maffulli N. Magnetic resonance imaging versus arthroscopy in the diagnosis of knee pathology, concentrating on meniscal lesions and ACL tears: a systematic review. *Br Med Bull*. 2007;84:5-23.
30. Crespo B, Aga C, Wilson KJ, et al. Measurements of bone tunnel size in anterior cruciate ligament reconstruction: 2D versus 3D computed tomography model. *J Exp Orthop*. 2014;1(1):2.
31. Daniel DM, Stone ML, Sachs R, Malcom L. Instrumented measurement of anterior knee laxity in patients with acute anterior cruciate ligament disruption. *Am J Sports Med*. 1985;13(6):401-407.
32. Dargel J, Schmidt-Wiethoff R, Fischer S, Mader K, Koebke J, Schneider T. Femoral bone tunnel placement using the transtibial tunnel or the anteromedial portal in ACL reconstruction: a radiographic evaluation. *Knee Surg Sports Traumatol Arthrosc*. 2009;17(3):220-227.
33. Desai N, Andernord D, Sundemo D, et al. Revision surgery in anterior cruciate ligament reconstruction: a cohort study of 17,682 patients from the Swedish National Knee Ligament Register. *Knee Surg Sports Traumatol Arthrosc*. 2017;25(5):1542-1554.
34. Desai N, Bjornsson H, Musahl V, et al. Anatomic single- versus double-bundle ACL reconstruction: a meta-analysis. *Knee Surg Sports Traumatol Arthrosc*. 2014;22(5):1009-1023.
35. Dodds JA, Arnoczky SP. Anatomy of the anterior cruciate ligament: a blueprint for repair and reconstruction. *Arthroscopy*. 1994;10(2):132-139.
36. Donahue TL, Gregersen C, Hull ML, Howell SM. Comparison of viscoelastic, structural, and material properties of double-looped anterior cruciate ligament grafts made from bovine digital extensor and human hamstring tendons. *J Biomech Eng*. 2001;123(2):162-169.
37. Drogset JO, Grontvedt T, Robak OR, Molster A, Viset AT, Engebretsen L. A sixteen-year follow-up of three operative techniques for the treatment of acute ruptures of the anterior cruciate ligament. *J Bone Joint Surg Am*. 2006;88(5):944-952.

38. Drogset JO, Straume LG, Bjorkmo I, Myhr G. A prospective randomized study of ACL-reconstructions using bone-patellar tendon-bone grafts fixed with bioabsorbable or metal interference screws. *Knee Surg Sports Traumatol Arthrosc.* 2011;19(5):753-759.
39. Eitzen I, Moksnes H, Snyder-Mackler L, Risberg MA. A progressive 5-week exercise therapy program leads to significant improvement in knee function early after anterior cruciate ligament injury. *J Orthop Sports Phys Ther.* 2010;40(11):705-721.
40. Failla MJ, Logerstedt DS, Grindem H, et al. Does Extended Preoperative Rehabilitation Influence Outcomes 2 Years After ACL Reconstruction? A Comparative Effectiveness Study Between the MOON and Delaware-Oslo ACL Cohorts. *Am J Sports Med.* 2016;44(10):2608-2614.
41. Feagin JA, Jr., Curl WW. Isolated tear of the anterior cruciate ligament: 5-year follow-up study. *Am J Sports Med.* 1976;4(3):95-100.
42. Ferretti M, Levicoff EA, Macpherson TA, Moreland MS, Cohen M, Fu FH. The fetal anterior cruciate ligament: an anatomic and histologic study. *Arthroscopy.* 2007;23(3):278-283.
43. Freedman KB, D'Amato MJ, Nedeff DD, Kaz A, Bach BR, Jr. Arthroscopic anterior cruciate ligament reconstruction: a metaanalysis comparing patellar tendon and hamstring tendon autografts. *Am J Sports Med.* 2003;31(1):2-11.
44. Frobell RB, Lohmander LS, Roos HP. Acute rotational trauma to the knee: poor agreement between clinical assessment and magnetic resonance imaging findings. *Scand J Med Sci Sports.* 2007;17(2):109-114.
45. Frobell RB, Roos EM, Roos HP, Ranstam J, Lohmander LS. A randomized trial of treatment for acute anterior cruciate ligament tears. *N Engl J Med.* 2010;363(4):331-342.
46. Fujimaki Y, Thorhauer E, Sasaki Y, Smolinski P, Tashman S, Fu FH. Quantitative In Situ Analysis of the Anterior Cruciate Ligament: Length, Midsubstance Cross-sectional Area, and Insertion Site Areas. *Am J Sports Med.* 2016;44(1):118-125.
47. Gabriel MT, Wong EK, Woo SL, Yagi M, Debski RE. Distribution of in situ forces in the anterior cruciate ligament in response to rotatory loads. *J Orthop Res.* 2004;22(1):85-89.
48. Galway HR, MacIntosh DL. The lateral pivot shift: a symptom and sign of anterior cruciate ligament insufficiency. *Clin Orthop Relat Res.* 1980(147):45-50.
49. Gifstad T, Foss OA, Engebretsen L, et al. Lower risk of revision with patellar tendon autografts compared with hamstring autografts: a registry study based on 45,998 primary ACL reconstructions in Scandinavia. *Am J Sports Med.* 2014;42(10):2319-2328.
50. Girgis FG, Marshall JL, Monajem A. The cruciate ligaments of the knee joint. Anatomical, functional and experimental analysis. *Clin Orthop Relat Res.* 1975(106):216-231.
51. Gobbi A, Mahajan V, Karnatzikos G, Nakamura N. Single- versus double-bundle ACL reconstruction: is there any difference in stability and function at 3-year followup? *Clin Orthop Relat Res.* 2012;470(3):824-834.

52. Gokeler A, Welling W, Zaffagnini S, Seil R, Padua D. Development of a test battery to enhance safe return to sports after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 2017;25(1):192-199.
53. Goldsmith MT, Jansson KS, Smith SD, Engebretsen L, LaPrade RF, Wijdicks CA. Biomechanical comparison of anatomic single- and double-bundle anterior cruciate ligament reconstructions: an in vitro study. *Am J Sports Med.* 2013;41(7):1595-1604.
54. Goradia VK, Rochat MC, Grana WA, Rohrer MD, Prasad HS. Tendon-to-bone healing of a semitendinosus tendon autograft used for ACL reconstruction in a sheep model. *Am J Knee Surg.* 2000;13(3):143-151.
55. Granan LP, Bahr R, Lie SA, Engebretsen L. Timing of anterior cruciate ligament reconstructive surgery and risk of cartilage lesions and meniscal tears: a cohort study based on the Norwegian National Knee Ligament Registry. *Am J Sports Med.* 2009;37(5):955-961.
56. Granan LP, Bahr R, Steindal K, Furnes O, Engebretsen L. Development of a national cruciate ligament surgery registry: the Norwegian National Knee Ligament Registry. *Am J Sports Med.* 2008;36(2):308-315.
57. Granan LP, Baste V, Engebretsen L, Inacio MC. Associations between inadequate knee function detected by KOOS and prospective graft failure in an anterior cruciate ligament-reconstructed knee. *Knee Surg Sports Traumatol Arthrosc.* 2015;23(4):1135-1140.
58. Granan LP, Forssblad M, Lind M, Engebretsen L. The Scandinavian ACL registries 2004-2007: baseline epidemiology. *Acta Orthop.* 2009;80(5):563-567.
59. Granan LP, Inacio MC, Maletis GB, Funahashi TT, Engebretsen L. Sport-specific injury pattern recorded during anterior cruciate ligament reconstruction. *Am J Sports Med.* 2013;41(12):2814-2818.
60. Griffin LY, Agel J, Albohm MJ, et al. Noncontact anterior cruciate ligament injuries: risk factors and prevention strategies. *J Am Acad Orthop Surg.* 2000;8(3):141-150.
61. Grindem H, Granan LP, Risberg MA, Engebretsen L, Snyder-Mackler L, Eitzen I. How does a combined preoperative and postoperative rehabilitation programme influence the outcome of ACL reconstruction 2 years after surgery? A comparison between patients in the Delaware-Oslo ACL Cohort and the Norwegian National Knee Ligament Registry. *Br J Sports Med.* 2015;49(6):385-389.
62. Group M, Wright RW, Huston LJ, et al. Descriptive epidemiology of the Multicenter ACL Revision Study (MARS) cohort. *Am J Sports Med.* 2010;38(10):1979-1986.
63. Harner CD, Honkamp NJ, Ranawat AS. Anteromedial portal technique for creating the anterior cruciate ligament femoral tunnel. *Arthroscopy.* 2008;24(1):113-115.
64. Harner CD, Poehling GG. Double bundle or double trouble? *Arthroscopy.* 2004;20(10):1013-1014.

65. Harvey A, Thomas NP, Amis AA. Fixation of the graft in reconstruction of the anterior cruciate ligament. *J Bone Joint Surg Br.* 2005;87(5):593-603.
66. Hefti F, Muller W. [Current state of evaluation of knee ligament lesions. The new IKDC knee evaluation form]. *Orthopade.* 1993;22(6):351-362.
67. Hefti F, Muller W, Jakob RP, Staubli HU. Evaluation of knee ligament injuries with the IKDC form. *Knee Surg Sports Traumatol Arthrosc.* 1993;1(3-4):226-234.
68. Herrera A, Martinez F, Iglesias D, Cegonino J, Ibarz E, Gracia L. Fixation strength of biocomposite wedge interference screw in ACL reconstruction: effect of screw length and tunnel/screw ratio. A controlled laboratory study. *BMC Musculoskelet Disord.* 2010;11:139.
69. Hettrich CM, Dunn WR, Reinke EK, Group M, Spindler KP. The rate of subsequent surgery and predictors after anterior cruciate ligament reconstruction: two- and 6-year follow-up results from a multicenter cohort. *Am J Sports Med.* 2013;41(7):1534-1540.
70. Hirschmann MT, Muller W. Complex function of the knee joint: the current understanding of the knee. *Knee Surg Sports Traumatol Arthrosc.* 2015;23(10):2780-2788.
71. Hofbauer M, Muller B, Murawski CD, van Eck CF, Fu FH. The concept of individualized anatomic anterior cruciate ligament (ACL) reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 2014;22(5):979-986.
72. Hoher J, Moller HD, Fu FH. Bone tunnel enlargement after anterior cruciate ligament reconstruction: fact or fiction? *Knee Surg Sports Traumatol Arthrosc.* 1998;6(4):231-240.
73. Hoshino Y, Kuroda R, Nagamune K, et al. Optimal measurement of clinical rotational test for evaluating anterior cruciate ligament insufficiency. *Knee Surg Sports Traumatol Arthrosc.* 2012;20(7):1323-1330.
74. Hussein M, van Eck CF, Cretnik A, Dinevski D, Fu FH. Prospective randomized clinical evaluation of conventional single-bundle, anatomic single-bundle, and anatomic double-bundle anterior cruciate ligament reconstruction: 281 cases with 3- to 5-year follow-up. *Am J Sports Med.* 2012;40(3):512-520.
75. Huston LJ, Wojtys EM. Neuromuscular performance characteristics in elite female athletes. *Am J Sports Med.* 1996;24(4):427-436.
76. Ingelsrud LH, Granan LP, Terwee CB, Engebretsen L, Roos EM. Proportion of Patients Reporting Acceptable Symptoms or Treatment Failure and Their Associated KOOS Values at 6 to 24 Months After Anterior Cruciate Ligament Reconstruction: A Study From the Norwegian Knee Ligament Registry. *Am J Sports Med.* 2015;43(8):1902-1907.
77. Iorio R, Vadala A, Argento G, Di Sanzo V, Ferretti A. Bone tunnel enlargement after ACL reconstruction using autologous hamstring tendons: a CT study. *Int Orthop.* 2007;31(1):49-55.
78. Irrgang JJ, Anderson AF, Boland AL, et al. Development and validation of the international knee documentation committee subjective knee form. *Am J Sports Med.* 2001;29(5):600-613.

79. Jarvela S, Kiekara T, Suomalainen P, Jarvela T. Double-Bundle Versus Single-Bundle Anterior Cruciate Ligament Reconstruction: A Prospective Randomized Study With 10-Year Results. *Am J Sports Med.* 2017;45(11):2578-2585.
80. Jarvela T, Moisala AS, Paakkala T, Paakkala A. Tunnel enlargement after double-bundle anterior cruciate ligament reconstruction: a prospective, randomized study. *Arthroscopy.* 2008;24(12):1349-1357.
81. Jarvela T, Moisala AS, Sihvonen R, Jarvela S, Kannus P, Jarvinen M. Double-bundle anterior cruciate ligament reconstruction using hamstring autografts and bioabsorbable interference screw fixation: prospective, randomized, clinical study with 2-year results. *Am J Sports Med.* 2008;36(2):290-297.
82. Jonsson T, Althoff B, Peterson L, Renstrom P. Clinical diagnosis of ruptures of the anterior cruciate ligament: a comparative study of the Lachman test and the anterior drawer sign. *Am J Sports Med.* 1982;10(2):100-102.
83. Katz MH. Multivariable analysis: a primer for readers of medical research. *Ann Intern Med.* 2003;138(8):644-650.
84. Kawaguchi Y, Kondo E, Kitamura N, Kai S, Inoue M, Yasuda K. Comparisons of femoral tunnel enlargement in 169 patients between single-bundle and anatomic double-bundle anterior cruciate ligament reconstructions with hamstring tendon grafts. *Knee Surg Sports Traumatol Arthrosc.* 2011;19(8):1249-1257.
85. Kawaguchi Y, Kondo E, Takeda R, Akita K, Yasuda K, Amis AA. The role of fibers in the femoral attachment of the anterior cruciate ligament in resisting tibial displacement. *Arthroscopy.* 2015;31(3):435-444.
86. Kocher MS, Steadman JR, Briggs KK, Sterett WI, Hawkins RJ. Relationships between objective assessment of ligament stability and subjective assessment of symptoms and function after anterior cruciate ligament reconstruction. *Am J Sports Med.* 2004;32(3):629-634.
87. Kondo E, Merican AM, Yasuda K, Amis AA. Biomechanical comparison of anatomic double-bundle, anatomic single-bundle, and nonanatomic single-bundle anterior cruciate ligament reconstructions. *Am J Sports Med.* 2011;39(2):279-288.
88. Kondo E, Yasuda K, Azuma H, Tanabe Y, Yagi T. Prospective clinical comparisons of anatomic double-bundle versus single-bundle anterior cruciate ligament reconstruction procedures in 328 consecutive patients. *Am J Sports Med.* 2008;36(9):1675-1687.
89. Kopf S, Musahl V, Tashman S, Szczodry M, Shen W, Fu FH. A systematic review of the femoral origin and tibial insertion morphology of the ACL. *Knee Surg Sports Traumatol Arthrosc.* 2009;17(3):213-219.

90. Kurosaka M, Yoshiya S, Andrish JT. A biomechanical comparison of different surgical techniques of graft fixation in anterior cruciate ligament reconstruction. *Am J Sports Med.* 1987;15(3):225-229.
91. L'Insalata JC, Klatt B, Fu FH, Harner CD. Tunnel expansion following anterior cruciate ligament reconstruction: a comparison of hamstring and patellar tendon autografts. *Knee Surg Sports Traumatol Arthrosc.* 1997;5(4):234-238.
92. LaPrade RF, Moulton SG, Nitri M, Mueller W, Engebretsen L. Clinically relevant anatomy and what anatomic reconstruction means. *Knee Surg Sports Traumatol Arthrosc.* 2015;23(10):2950-2959.
93. Lee YS, Lee SW, Nam SW, et al. Analysis of tunnel widening after double-bundle ACL reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 2012;20(11):2243-2250.
94. Lenssen AF, van Dam EM, Crijns YH, et al. Reproducibility of goniometric measurement of the knee in the in-hospital phase following total knee arthroplasty. *BMC Musculoskelet Disord.* 2007;8:83.
95. Lewis PB, Parameswaran AD, Rue JP, Bach BR, Jr. Systematic review of single-bundle anterior cruciate ligament reconstruction outcomes: a baseline assessment for consideration of double-bundle techniques. *Am J Sports Med.* 2008;36(10):2028-2036.
96. Li X, Xu CP, Song JQ, Jiang N, Yu B. Single-bundle versus double-bundle anterior cruciate ligament reconstruction: an up-to-date meta-analysis. *Int Orthop.* 2013;37(2):213-226.
97. Lind M, Menhert F, Pedersen AB. Incidence and outcome after revision anterior cruciate ligament reconstruction: results from the Danish registry for knee ligament reconstructions. *Am J Sports Med.* 2012;40(7):1551-1557.
98. Logerstedt D, Di Stasi S, Grindem H, et al. Self-reported knee function can identify athletes who fail return-to-activity criteria up to 1 year after anterior cruciate ligament reconstruction: a delaware-oslo ACL cohort study. *J Orthop Sports Phys Ther.* 2014;44(12):914-923.
99. Logerstedt D, Grindem H, Lynch A, et al. Single-legged hop tests as predictors of self-reported knee function after anterior cruciate ligament reconstruction: the Delaware-Oslo ACL cohort study. *Am J Sports Med.* 2012;40(10):2348-2356.
100. Lord BR, El-Daou H, Sabnis BM, Gupte CM, Wilson AM, Amis AA. Biomechanical comparison of graft structures in anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 2017;25(2):559-568.
101. Lund B, Nielsen T, Fauno P, Christiansen SE, Lind M. Is quadriceps tendon a better graft choice than patellar tendon? a prospective randomized study. *Arthroscopy.* 2014;30(5):593-598.
102. Maletis GB, Granan LP, Inacio MC, Funahashi TT, Engebretsen L. Comparison of community-based ACL reconstruction registries in the U.S. and Norway. *J Bone Joint Surg Am.* 2011;93 Suppl 3:31-36.

103. Maletis GB, Inacio MC, Funahashi TT. Risk factors associated with revision and contralateral anterior cruciate ligament reconstructions in the Kaiser Permanente ACLR registry. *Am J Sports Med.* 2015;43(3):641-647.
104. Mall NA, Chalmers PN, Moric M, et al. Incidence and trends of anterior cruciate ligament reconstruction in the United States. *Am J Sports Med.* 2014;42(10):2363-2370.
105. Marchant MH, Jr., Willimon SC, Vinson E, Pietrobon R, Garrett WE, Higgins LD. Comparison of plain radiography, computed tomography, and magnetic resonance imaging in the evaluation of bone tunnel widening after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 2010;18(8):1059-1064.
106. Markolf KL, Gorek JF, Kabo JM, Shapiro MS. Direct measurement of resultant forces in the anterior cruciate ligament. An in vitro study performed with a new experimental technique. *J Bone Joint Surg Am.* 1990;72(4):557-567.
107. Mascarenhas R, Cvetanovich GL, Sayegh ET, et al. Does Double-Bundle Anterior Cruciate Ligament Reconstruction Improve Postoperative Knee Stability Compared With Single-Bundle Techniques? A Systematic Review of Overlapping Meta-analyses. *Arthroscopy.* 2015;31(6):1185-1196.
108. Mayr HO, Benecke P, Hoell A, et al. Single-Bundle Versus Double-Bundle Anterior Cruciate Ligament Reconstruction: A Comparative 2-Year Follow-up. *Arthroscopy.* 2016;32(1):34-42.
109. Middleton KK, Muller B, Araujo PH, et al. Is the native ACL insertion site "completely restored" using an individualized approach to single-bundle ACL-R? *Knee Surg Sports Traumatol Arthrosc.* 2015;23(8):2145-2150.
110. Mohtadi N, Chan D, Barber R, Oddone Paolucci E. A Randomized Clinical Trial Comparing Patellar Tendon, Hamstring Tendon, and Double-Bundle ACL Reconstructions: Patient-Reported and Clinical Outcomes at a Minimal 2-Year Follow-up. *Clin J Sport Med.* 2015;25(4):321-331.
111. Muller B, Hofbauer M, Wongcharoenwatana J, Fu FH. Indications and contraindications for double-bundle ACL reconstruction. *Int Orthop.* 2013;37(2):239-246.
112. Muneta T, Sekiya I, Yagishita K, Ogiuchi T, Yamamoto H, Shinomiya K. Two-bundle reconstruction of the anterior cruciate ligament using semitendinosus tendon with endobuttons: operative technique and preliminary results. *Arthroscopy.* 1999;15(6):618-624.
113. Musahl V, Griffith C, Irrgang JJ, et al. Validation of Quantitative Measures of Rotatory Knee Laxity. *Am J Sports Med.* 2016;44(9):2393-2398.
114. Nagarkatti DG, McKeon BP, Donahue BS, Fulkerson JP. Mechanical evaluation of a soft tissue interference screw in free tendon anterior cruciate ligament graft fixation. *Am J Sports Med.* 2001;29(1):67-71.

115. Nebelung W, Becker R, Merkel M, Ropke M. Bone tunnel enlargement after anterior cruciate ligament reconstruction with semitendinosus tendon using Endobutton fixation on the femoral side. *Arthroscopy*. 1998;14(8):810-815.
116. Nordenvall R, Bahmanyar S, Adami J, Stenros C, Wredmark T, Fellander-Tsai L. A population-based nationwide study of cruciate ligament injury in Sweden, 2001-2009: incidence, treatment, and sex differences. *Am J Sports Med*. 2012;40(8):1808-1813.
117. Noyes FR, Butler DL, Grood ES, Zernicke RF, Hefzy MS. Biomechanical analysis of human ligament grafts used in knee-ligament repairs and reconstructions. *J Bone Joint Surg Am*. 1984;66(3):344-352.
118. Noyes FR, Grood ES, Cummings JF, Wroble RR. An analysis of the pivot shift phenomenon. The knee motions and subluxations induced by different examiners. *Am J Sports Med*. 1991;19(2):148-155.
119. Noyes FR, Grood ES, Torzilli PA. Current concepts review. The definitions of terms for motion and position of the knee and injuries of the ligaments. *J Bone Joint Surg Am*. 1989;71(3):465-472.
120. Nunez M, Sastre S, Nunez E, Lozano L, Nicodemo C, Segur JM. Health-related quality of life and direct costs in patients with anterior cruciate ligament injury: single-bundle versus double-bundle reconstruction in a low-demand cohort--a randomized trial with 2 years of follow-up. *Arthroscopy*. 2012;28(7):929-935.
121. Nurmi JT, Sievanen H, Kannus P, Jarvinen M, Jarvinen TL. Porcine tibia is a poor substitute for human cadaver tibia for evaluating interference screw fixation. *Am J Sports Med*. 2004;32(3):765-771.
122. Oiestad BE, Engebretsen L, Storheim K, Risberg MA. Knee osteoarthritis after anterior cruciate ligament injury: a systematic review. *Am J Sports Med*. 2009;37(7):1434-1443.
123. Olsen OE, Myklebust G, Engebretsen L, Bahr R. Injury mechanisms for anterior cruciate ligament injuries in team handball: a systematic video analysis. *Am J Sports Med*. 2004;32(4):1002-1012.
124. Pannucci CJ, Wilkins EG. Identifying and avoiding bias in research. *Plast Reconstr Surg*. 2010;126(2):619-625.
125. Parkar AP, Adriaensen M, Vindfeld S, Solheim E. The Anatomic Centers of the Femoral and Tibial Insertions of the Anterior Cruciate Ligament: A Systematic Review of Imaging and Cadaveric Studies Reporting Normal Center Locations. *Am J Sports Med*. 2017;45(9):2180-2188.
126. Persson A, Fjeldsgaard K, Gjertsen JE, et al. Increased risk of revision with hamstring tendon grafts compared with patellar tendon grafts after anterior cruciate ligament reconstruction: a study of 12,643 patients from the Norwegian Cruciate Ligament Registry, 2004-2012. *Am J Sports Med*. 2014;42(2):285-291.

127. Persson A, Gifstad T, Lind M, et al. Graft fixation influences revision risk after ACL reconstruction with hamstring tendon autografts. *Acta Orthop*. 2018;89(2):204-210.
128. Persson A, Kjellsen AB, Fjeldsgaard K, Engebretsen L, Espehaug B, Fevang JM. Registry data highlight increased revision rates for endobutton/biosure HA in ACL reconstruction with hamstring tendon autograft: a nationwide cohort study from the Norwegian Knee Ligament Registry, 2004-2013. *Am J Sports Med*. 2015;43(9):2182-2188.
129. Petersen W, Tretow H, Weimann A, et al. Biomechanical evaluation of two techniques for double-bundle anterior cruciate ligament reconstruction: one tibial tunnel versus two tibial tunnels. *Am J Sports Med*. 2007;35(2):228-234.
130. Petersen W, Zantop T. Anatomy of the anterior cruciate ligament with regard to its two bundles. *Clin Orthop Relat Res*. 2007;454:35-47.
131. Rahr-Wagner L, Lind M. The Danish Knee Ligament Reconstruction Registry. *Clin Epidemiol*. 2016;8:531-535.
132. Rahr-Wagner L, Thillemann TM, Lind MC, Pedersen AB. Validation of 14,500 operated knees registered in the Danish Knee Ligament Reconstruction Register: registration completeness and validity of key variables. *Clin Epidemiol*. 2013;5:219-228.
133. Rahr-Wagner L, Thillemann TM, Pedersen AB, Lind MC. Increased risk of revision after anteromedial compared with transtibial drilling of the femoral tunnel during primary anterior cruciate ligament reconstruction: results from the Danish Knee Ligament Reconstruction Register. *Arthroscopy*. 2013;29(1):98-105.
134. Renstrom P, Ljungqvist A, Arendt E, et al. Non-contact ACL injuries in female athletes: an International Olympic Committee current concepts statement. *Br J Sports Med*. 2008;42(6):394-412.
135. Rhee PC, Levy BA, Stuart MJ, Thoreson A, An KN, Dahm DL. A biomechanical comparison of the Delta screw and RetroScrew tibial fixation on initial intra-articular graft tension. *Knee Surg Sports Traumatol Arthrosc*. 2011;19(5):781-786.
136. Risberg MA, Oiestad BE, Gunderson R, et al. Changes in Knee Osteoarthritis, Symptoms, and Function After Anterior Cruciate Ligament Reconstruction: A 20-Year Prospective Follow-up Study. *Am J Sports Med*. 2016;44(5):1215-1224.
137. Robbrecht C, Claes S, Cromheecke M, et al. Reliability of a semi-automated 3D-CT measuring method for tunnel diameters after anterior cruciate ligament reconstruction: A comparison between soft-tissue single-bundle allograft vs. autograft. *Knee*. 2014;21(5):926-931.
138. Rodeo SA, Arnoczky SP, Torzilli PA, Hidaka C, Warren RF. Tendon-healing in a bone tunnel. A biomechanical and histological study in the dog. *J Bone Joint Surg Am*. 1993;75(12):1795-1803.

139. Rodeo SA, Kawamura S, Kim HJ, Dynybil C, Ying L. Tendon healing in a bone tunnel differs at the tunnel entrance versus the tunnel exit: an effect of graft-tunnel motion? *Am J Sports Med.* 2006;34(11):1790-1800.
140. Roos EM, Lohmander LS. The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. *Health Qual Life Outcomes.* 2003;1:64.
141. Roos EM, Roos HP, Ekdahl C, Lohmander LS. Knee injury and Osteoarthritis Outcome Score (KOOS)--validation of a Swedish version. *Scand J Med Sci Sports.* 1998;8(6):439-448.
142. Saccomanno MF, Shin JJ, Mascarenhas R, et al. Clinical and functional outcomes after anterior cruciate ligament reconstruction using cortical button fixation versus transfemoral suspensory fixation: a systematic review of randomized controlled trials. *Arthroscopy.* 2014;30(11):1491-1498.
143. Sakane M, Fox RJ, Woo SL, Livesay GA, Li G, Fu FH. In situ forces in the anterior cruciate ligament and its bundles in response to anterior tibial loads. *J Orthop Res.* 1997;15(2):285-293.
144. Salmon LJ, Heath E, Akrawi H, Roe JP, Linklater J, Pinczewski LA. 20-Year Outcomes of Anterior Cruciate Ligament Reconstruction With Hamstring Tendon Autograft: The Catastrophic Effect of Age and Posterior Tibial Slope. *Am J Sports Med.* 2018;46(3):531-543.
145. Sanders TL, Maradit Kremers H, Bryan AJ, et al. Incidence of Anterior Cruciate Ligament Tears and Reconstruction: A 21-Year Population-Based Study. *Am J Sports Med.* 2016;44(6):1502-1507.
146. Schindler OS. Surgery for anterior cruciate ligament deficiency: a historical perspective. *Knee Surg Sports Traumatol Arthrosc.* 2012;20(1):5-47.
147. Shino K, Pflaster DS. Comparison of eccentric and concentric screw placement for hamstring graft fixation in the tibial tunnel. *Knee Surg Sports Traumatol Arthrosc.* 2000;8(2):73-75.
148. Siebold R. The concept of complete footprint restoration with guidelines for single- and double-bundle ACL reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 2011;19(5):699-706.
149. Siebold R, Cafaltzis K. Differentiation between intraoperative and postoperative bone tunnel widening and communication in double-bundle anterior cruciate ligament reconstruction: a prospective study. *Arthroscopy.* 2010;26(8):1066-1073.
150. Siebold R, Schuhmacher P, Fernandez F, et al. Flat midsubstance of the anterior cruciate ligament with tibial "C"-shaped insertion site. *Knee Surg Sports Traumatol Arthrosc.* 2015;23(11):3136-3142.
151. Slocum DB, Larson RL. Rotatory instability of the knee. Its pathogenesis and a clinical test to demonstrate its presence. *J Bone Joint Surg Am.* 1968;50(2):211-225.
152. Smigielski R, Zdanowicz U, Drwiega M, Ciszek B, Ciszewska-Lyson B, Siebold R. Ribbon like appearance of the midsubstance fibres of the anterior cruciate ligament close to its

- femoral insertion site: a cadaveric study including 111 knees. *Knee Surg Sports Traumatol Arthrosc.* 2015;23(11):3143-3150.
153. Smigielski R, Zdanowicz U, Drwiega M, Ciszek B, Williams A. The anatomy of the anterior cruciate ligament and its relevance to the technique of reconstruction. *Bone Joint J.* 2016;98-B(8):1020-1026.
 154. Smith KE, Garcia M, McAnuff K, et al. Anterior cruciate ligament fixation: is radial force a predictor of the pullout strength of soft-tissue interference devices? *Knee.* 2012;19(6):786-792.
 155. Snaebjornsson T, Hamrin Senorski E, Ayeni OR, et al. Graft Diameter as a Predictor for Revision Anterior Cruciate Ligament Reconstruction and KOOS and EQ-5D Values: A Cohort Study From the Swedish National Knee Ligament Register Based on 2240 Patients. *Am J Sports Med.* 2017;45(9):2092-2097.
 156. Snyder-Mackler L, Fitzgerald GK, Bartolozzi AR, 3rd, Ciccotti MG. The relationship between passive joint laxity and functional outcome after anterior cruciate ligament injury. *Am J Sports Med.* 1997;25(2):191-195.
 157. Souryal TO, Freeman TR. Intercondylar notch size and anterior cruciate ligament injuries in athletes. A prospective study. *Am J Sports Med.* 1993;21(4):535-539.
 158. Suomalainen P, Jarvela T, Paakkala A, Kannus P, Jarvinen M. Double-bundle versus single-bundle anterior cruciate ligament reconstruction: a prospective randomized study with 5-year results. *Am J Sports Med.* 2012;40(7):1511-1518.
 159. Svantesson E, Sundemo D, Hamrin Senorski E, et al. Double-bundle anterior cruciate ligament reconstruction is superior to single-bundle reconstruction in terms of revision frequency: a study of 22,460 patients from the Swedish National Knee Ligament Register. *Knee Surg Sports Traumatol Arthrosc.* 2016.
 160. Tanner SM, Dainty KN, Marx RG, Kirkley A. Knee-specific quality-of-life instruments: which ones measure symptoms and disabilities most important to patients? *Am J Sports Med.* 2007;35(9):1450-1458.
 161. Tegner Y, Lysholm J. Rating systems in the evaluation of knee ligament injuries. *Clin Orthop Relat Res.* 1985(198):43-49.
 162. Tiamklang T, Sumanont S, Foocharoen T, Laopaiboon M. Double-bundle versus single-bundle reconstruction for anterior cruciate ligament rupture in adults. *Cochrane Database Syst Rev.* 2012;11:Cd008413.
 163. Tiefenboeck TM, Thurmaier E, Tiefenboeck MM, et al. Clinical and functional outcome after anterior cruciate ligament reconstruction using the LARS system at a minimum follow-up of 10 years. *Knee.* 2015;22(6):565-568.
 164. Torg JS, Conrad W, Kalen V. Clinical diagnosis of anterior cruciate ligament instability in the athlete. *Am J Sports Med.* 1976;4(2):84-93.

165. Tsai AG, Wijdicks CA, Walsh MP, LaPrade RF. Comparative kinematic evaluation of all-inside single-bundle and double-bundle anterior cruciate ligament reconstruction: a biomechanical study. *Am J Sports Med.* 2010;38(2):263-272.
166. Tsukada H, Ishibashi Y, Tsuda E, Fukuda A, Toh S. Anatomical analysis of the anterior cruciate ligament femoral and tibial footprints. *J Orthop Sci.* 2008;13(2):122-129.
167. Ugutmen E, Ozkan K, Guven M, Sener N, Altintas F. Early tunnel enlargement after arthroscopic ACL reconstructions. *Acta Orthop Belg.* 2007;73(5):625-629.
168. van Eck CF, Gravare-Silbernagel K, Samuelsson K, et al. Evidence to support the interpretation and use of the Anatomic Anterior Cruciate Ligament Reconstruction Checklist. *J Bone Joint Surg Am.* 2013;95(20):e153.
169. van Eck CF, Kopf S, Irrgang JJ, et al. Single-bundle versus double-bundle reconstruction for anterior cruciate ligament rupture: a meta-analysis--does anatomy matter? *Arthroscopy.* 2012;28(3):405-424.
170. Walsh MP, Wijdicks CA, Parker JB, Hapa O, LaPrade RF. A comparison between a retrograde interference screw, suture button, and combined fixation on the tibial side in an all-inside anterior cruciate ligament reconstruction: a biomechanical study in a porcine model. *Am J Sports Med.* 2009;37(1):160-167.
171. Webster KE, Feller JA, Hameister KA. Bone tunnel enlargement following anterior cruciate ligament reconstruction: a randomised comparison of hamstring and patellar tendon grafts with 2-year follow-up. *Knee Surg Sports Traumatol Arthrosc.* 2001;9(2):86-91.
172. Weiler A, Hoffmann RF, Siepe CJ, Kolbeck SF, Sudkamp NP. The influence of screw geometry on hamstring tendon interference fit fixation. *Am J Sports Med.* 2000;28(3):356-359.
173. Wera JC, Nyland J, Ghazi C, et al. International knee documentation committee knee survey use after anterior cruciate ligament reconstruction: a 2005-2012 systematic review and world region comparison. *Arthroscopy.* 2014;30(11):1505-1512.
174. Wilson TC, Kantaras A, Atay A, Johnson DL. Tunnel enlargement after anterior cruciate ligament surgery. *Am J Sports Med.* 2004;32(2):543-549.
175. Woo SL, Kanamori A, Zeminski J, Yagi M, Papageorgiou C, Fu FH. The effectiveness of reconstruction of the anterior cruciate ligament with hamstrings and patellar tendon . A cadaveric study comparing anterior tibial and rotational loads. *J Bone Joint Surg Am.* 2002;84-A(6):907-914.
176. Xu Y, Ao YF, Wang JQ, Cui GQ. Prospective randomized comparison of anatomic single- and double-bundle anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 2014;22(2):308-316.
177. Yagi M, Kuroda R, Nagamune K, Yoshiya S, Kurosaka M. Double-bundle ACL reconstruction can improve rotational stability. *Clin Orthop Relat Res.* 2007;454:100-107.

178. Yagi M, Wong EK, Kanamori A, Debski RE, Fu FH, Woo SL. Biomechanical analysis of an anatomic anterior cruciate ligament reconstruction. *Am J Sports Med.* 2002;30(5):660-666.
179. Yamazaki J, Muneta T, Koga H, et al. Radiographic description of femoral tunnel placement expressed as intercondylar clock time in double-bundle anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 2011;19(3):418-423.
180. Yasuda K, Kondo E, Ichiyama H, et al. Anatomic reconstruction of the anteromedial and posterolateral bundles of the anterior cruciate ligament using hamstring tendon grafts. *Arthroscopy.* 2004;20(10):1015-1025.
181. Yasuda K, van Eck CF, Hoshino Y, Fu FH, Tashman S. Anatomic single- and double-bundle anterior cruciate ligament reconstruction, part 1: Basic science. *Am J Sports Med.* 2011;39(8):1789-1799.
182. Ytterstad K, Granan LP, Ytterstad B, et al. Registration rate in the Norwegian Cruciate Ligament Register: large-volume hospitals perform better. *Acta Orthop.* 2012;83(2):174-178.
183. Zantop T, Herbort M, Raschke MJ, Fu FH, Petersen W. The role of the anteromedial and posterolateral bundles of the anterior cruciate ligament in anterior tibial translation and internal rotation. *Am J Sports Med.* 2007;35(2):223-227.
184. Zantop T, Kubo S, Petersen W, Musahl V, Fu FH. Current techniques in anatomic anterior cruciate ligament reconstruction. *Arthroscopy.* 2007;23(9):938-947.
185. Ziegler CG, Pietrini SD, Westerhaus BD, et al. Arthroscopically pertinent landmarks for tunnel positioning in single-bundle and double-bundle anterior cruciate ligament reconstructions. *Am J Sports Med.* 2011;39(4):743-752.
186. Zysk SP, Fraunberger P, Veihelmann A, et al. Tunnel enlargement and changes in synovial fluid cytokine profile following anterior cruciate ligament reconstruction with patellar tendon and hamstring tendon autografts. *Knee Surg Sports Traumatol Arthrosc.* 2004;12(2):98-103.

Paper I

No difference in the KOOS Quality of Life, between anatomic Double-bundle and anatomic Single-bundle Anterior Cruciate Ligament reconstruction of the knee; a Prospective, Randomized, Controlled Trial with 2 years follow-up

Abstract:

Background: The double-bundle reconstruction technique was developed to resemble the properties of the native ACL more closely than conventional single-bundle technique. The clinical benefit of the operation is controversial, and there is a need for studies with focus on patient-reported outcomes (PROs).

Study design: Randomized controlled clinical trial.

Hypothesis: Anatomic double-bundle ACL reconstruction would be superior to anatomic single-bundle reconstruction regarding the change in the KOOS QoL subscore from baseline to two-year follow-up.

Methods: According to sample size calculations, 120 patients aged 18 to 40 years with a primary ACL injury of their knee were randomized to anatomic double-bundle or anatomic single-bundle reconstructions. Patients with PCL, PLC or LCL injuries or with established osteoarthritis were excluded. Patients with residual laxity from a coexistent MCL-injury were excluded. Data were registered at baseline, one- and two years. In 24 patients, postoperative 3D computer tomographic scanning was performed to verify positioning of the bundles. The outcome measurements were: The change in KOOS and IKDC 2000 subjective score, pivot shift test, Lachman's test and KT 1000 measurements, activity level, return to sports rate and osteoarthritic changes on radiographic imaging. A linear mixed model was used for the analysis of all the PRO's, including the primary outcome.

Results: The change in KOOS QoL from baseline to two-year follow-up was not different between the two groups (double-bundle: mean change 29.2 points versus single-bundle: mean change 28.7 points, -0.5 points difference, 95% CI -8.4 to 7.5 points, $p=0.91$). Neither were there any differences between the two groups in the remaining patient-reported outcomes, knee laxity measurements or the activity level of the patients. Radiological signs of osteoarthritis were found in two patients. Eleven patients had a graft rupture; 8 in the single-bundle and 3 in the double-bundle group ($p=0.16$). The 3D computer tomographic imaging of the knees verified the positioning of the AM-, PL- and single-bundle grafts to be within acceptable limits.

Conclusion: There was no difference in the KOOS QoL subscore, the remaining patient-reported outcome, knee laxity measures or activity levels comparing the double-bundle and the single-bundle ACL reconstruction technique. The number of bundles does not seem to influence the clinical and subjective outcomes, as long as the tunnels are adequately positioned.

INTRODUCTION

The double-bundle ACL reconstruction technique was developed to improve the ACL reconstruction, due to the anatomical restoration of both the anteromedial (AM) and the posterolateral (PL) bundle.⁵⁹ The different insertion sites and tension pattern of the two bundles during knee motion are supposed to resemble the native ACL more closely than the conventional single-bundle reconstruction. However, double-bundle reconstructions are considered to be technically more difficult and more cost demanding compared to single-bundle reconstructions.

Several biomechanical laboratory studies support the advantage of double-bundle reconstruction; clinical studies are less convincing.^{11, 50} Thus, more extensive, high-quality studies, with focus on patient subjective outcomes, have been asked for.^{2, 24, 25, 31, 44, 50, 53}

More than 30 clinical studies have compared the double-bundle to the single-bundle technique.³⁴ The results of those studies have been inconsistent. Three systematic reviews all concluded that the double bundle technique would improve rotational stability and anteroposterior translation.^{31, 53, 56} But the question is whether the reported differences are of any clinical benefit to the patients.^{21, 31, 53, 56} Patient-reported outcome scores (PRO's) has been reported only as secondary outcomes although superior subjective scores in the double-bundle group have been reported.^{2, 10, 31, 48}

Parallel to development of the anatomic double-bundle reconstruction, the anatomic single-bundle reconstruction was introduced. As the positioning of the bundles has been shown to be crucial for the biomechanical properties of the grafts, the focus on anatomic placement has increased. Despite this knowledge, most of the literature comparing single- and double-bundle use transtibial drilling and "o'clock" positioning of the grafts.^{2, 37, 44} Only a few studies describe a transportal, anatomic positioning of the tunnels both in the single- and double-bundle group.^{3, 17, 24, 35} As rotational laxity measurements were the main outcome of those studies, the PRO's were less focused on.

The current study was designed to compare single-bundle versus the double-bundle techniques for ACL reconstruction with a patient-reported outcome as primary endpoint. The hypothesis was that anatomic double-bundle ACL reconstruction would be superior to anatomic single-bundle reconstruction, regarding the change in the KOOS QoL subscore from baseline to two-year follow-up. Secondary objectives were to compare additional PROs, knee laxity measurements, range of motion, functional tests and radiographic imaging between the two ACL reconstruction techniques at two-year follow-up.

MATERIALS AND METHODS

Study design:

The study was designed as a prospective, randomized, controlled trial, following two parallel groups. The intervention group was the anatomic double-bundle ACL reconstruction, and the control group the anatomic single-bundle ACL reconstruction (Clinical trials ID: **NCT01033188**). The patients were included from January 1st, 2010 until June 18th, 2015. Follow up was performed at 12 and 24 months after index surgery. The study sites were at Oslo University Hospital and Martina Hansens Hospital.

The study included 120 patients with symptoms from a primary ACL injury. They were 18-40 years old and referred from the outpatient clinics of the two recruiting hospitals, one university hospital and one hospital specialized in orthopaedic surgery. The patients that fulfilled the inclusion criteria were asked to carry out two months of knee-specific rehabilitation supervised by a physiotherapist before inclusion. If the patients still had symptoms from their ACL injury that required reconstructive surgery they were asked to participate in the study. Patients with contralateral or subtotal ACL injury, injury to the posterior cruciate ligament (PCL), posterolateral corner (PLC), lateral collateral ligament (LCL) or medial collateral ligament (MCL) injury with a residual medial instability of the knee, were excluded (Table 1). Knees with osteoarthritic changes (Kellgren-Lawrence classification grade 3 or 4),

were also excluded. Before inclusion, the participants signed a written informed consent. The randomization was then only carried out if the ACL rupture was verified by arthroscopy if more than 50 % of both menisci remained intact, and if the hamstring tendons had sufficient length and thicknesses for a two-bundle-reconstruction to be realized. The reasons for exclusion of eligible patients were reported (Table 2).

TABLE 1
Inclusion criteria

Age 18 to 40 years
Symptoms from the knee due to a primary ACL injury; verified by history, clinical assessments (Lachman's test >1+ or positive pivot shift test) and identified at surgery.
Successfully completed 2 months of knee-specific rehabilitation supervised by a physiotherapist

Exclusion criteria

Previous ACL reconstruction in the involved or uninvolved knee.
Partially ruptured ACL.
Patients with a PCL, LCL or PLC injury.
MCL injury with increased medial ligament laxity at operation (>1+), compared with the uninvolved leg.
Established osteoarthritis (Kellgren-Lawrence classification grade 3 or 4) identified on standing front radiographs of the knee.
Hamstring tendons with insufficient graft thickness after preparation. (Defined as less than of 5.0 mm in diameter for the PL, and 6.0 mm for the AM bundle.)
Less than 50% of the medial or lateral meniscus preserved after treatment.
Patients living outside recruitment area.
Patients not understanding the norwegian written language.

Figure 1
Flow chart

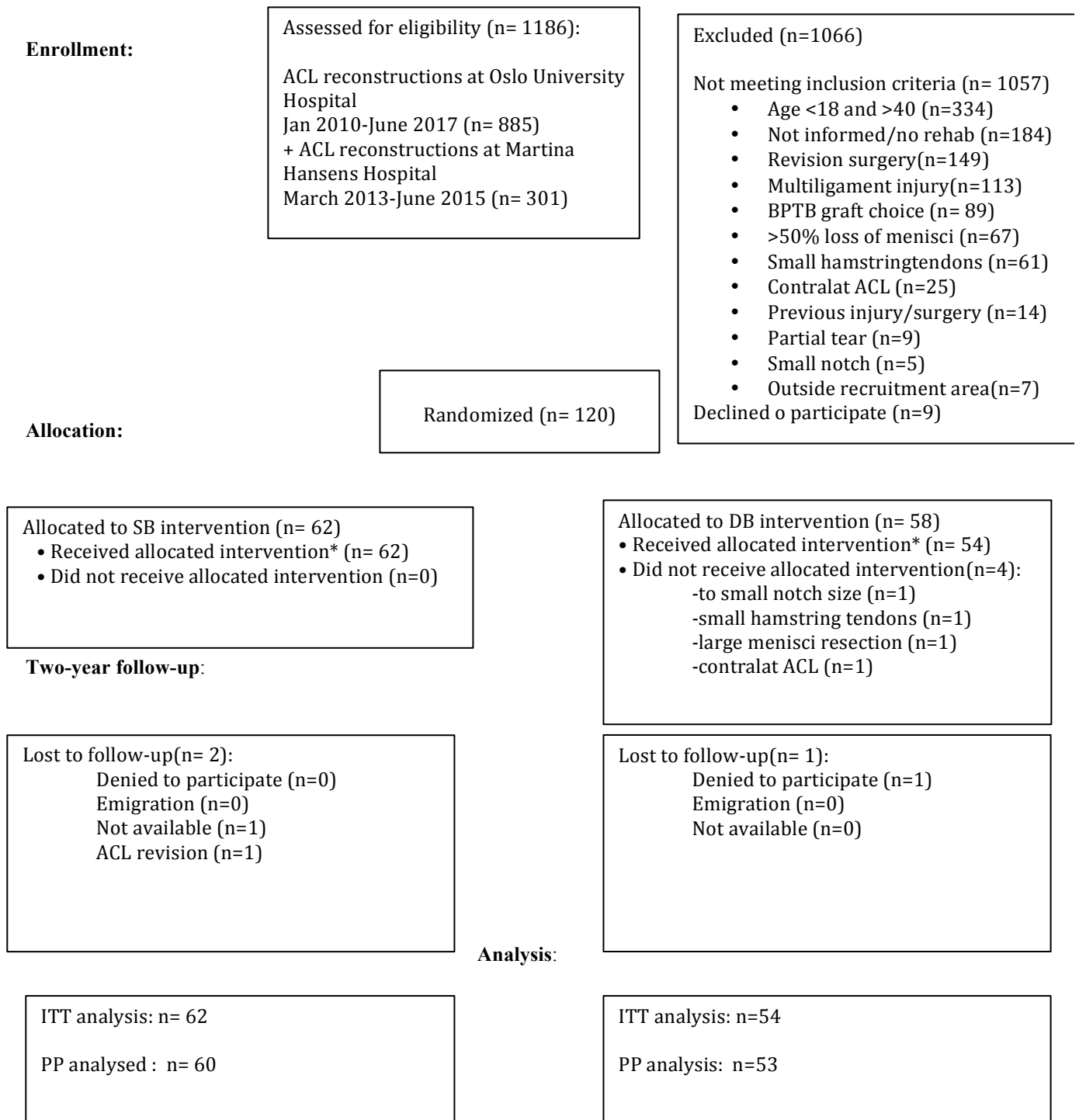


Figure 1. Flow chart

DB, double-bundle; SB, single-bundle; BPTB, bone patellar-tendon bone graft; ITT, intention to treat; PP, per protocol.

*All 120 patients received the allocated treatment group from sealed envelopes, but in 32 patients, the treatment proposed by the envelopes were inconsistent with the treatment suggested by the randomisation list.

Deviations from trial registration protocol:

During the inclusion period Martina Hansens Hospital was added as a recruiting hospital, and the main endpoint was changed from five to two-year follow-up because of the difficulties recruiting patients. The minimum graft size of the PL-bundle was decreased from 5.5 to 5.0 mm due to the same reason. The patients with randomisation number 62 to 120 were blinded for the intervention. A subgroup of the patients was asked to perform a postoperative 3D computer tomographic imaging of the reconstructed knee to verify the exact positioning of the drilled tunnels.

Interventions:

The interventions were initially performed at Oslo University Hospital, but from March 1st, 2013 the site of intervention was changed to Martina Hansens Hospital. Both hospitals performed more than 100 ACL reconstructions yearly. One surgeon performed the surgical procedure in all but two patients. The surgeon was experienced and had also participated in anatomy studies describing the ACL and its two bundles.⁶¹

The surgical technique consisted of placing the patient in supine position, with the knee at 90 degrees of flexion and with a tourniquet placed around the upper thigh. The regular anterior arthroscopic portals and an accessory anteromedial portal were established. The ACL lesion was confirmed by visualization and by probing the ACL remnants. The femoral and tibial insertion site was visualized, and surrounding soft tissue and bony landmarks were used to identify the centre of the proximal and distal ACL footprint.^{30, 61} A 3-5 cm skin incision was performed at the pes anserine insertion site. The semitendinosus and gracilis tendons were identified. A tendon harvester was used to free the tendons, both tendons were doubled or tripled according to their length and thicknesses. For the double bundle operation technique, a minimum graft size of 5.0 mm in diameter for the PL-, and 6.0 mm for the AM-bundle was desirable. Both ends of each the grafts were whip-stitched with a non-absorbable suture.

Single-bundle technique:

An accessory anteromedial portal was used for the femoral tunnel establishment. A Steadman awl was positioned in a central position of the femoral footprint. With the knee in hyperflexion, the femoral tunnel was drilled, according to measured graft size. Then the centre of the tibial footprint was identified.^{30,61} With an external tibia guide, the tibial tunnel was drilled. The graft was passed through the tibial and then the femoral tunnel and cycled through 20 flexion-extension movements. Finally, fixation was performed with the knee at 20 degrees of flexion and under manual tensioning of the graft. Graft fixation on the femoral side was obtained with a suspension device (Endobutton CL[®], Smith & Nephew, London, United Kingdom) and on the tibial side with an eccentrically placed, PEEK interference screw (Biosure PK[®], Smith & Nephew, London, United Kingdom).

Double-bundle technique:

Through the accessory anteromedial portal, the central position of the AM-bundle footprint was marked with a Steadman awl. With the knee in hyperflexion, the femoral AM tunnel was drilled. A double-bundle femoral drill-guide (Anatomic ACLR PL Femoral Aimer, Smith & Nephew, London, United Kingdom) was then used to drill PL tunnel. On the tibial side, the centre of the AM footprint was marked using an external tibia guide. First, the AM tunnel was drilled, the Anatomic ACLR PL Tibial Aimer[®] (Smith & Nephew, London, United Kingdom) was placed in the AM tunnel and the PL guide pin placed into the centre of the footprint. Then the PL tunnel was drilled. The grafts were passed through the tibial and then the femoral tunnels, and cycled through 20 flexion-extension movements. Fixation was then performed under manual tension and with the knee at 60 degrees flexion for the AM bundle, and at full extension for the PL bundle. Graft fixation on the femoral side was carried out with two suspension devices (Endobutton CL[®], Smith & Nephew, London, United Kingdom), and on the tibial side with two eccentric placed, PEEK interference screws (Biosure PK[®], Smith & Nephew, London, United Kingdom). The wounds were closed and bandaged before the tourniquet was loosened.

A notchplasty was only carried out if graft impingement was detected after graft insertion.

Measurements of the insertion sites were performed if the surgeon was in doubt of having sufficient space for the two tunnels. Mobilization on crutches was achieved from the first postoperative day without brace support or the use of a CPM. Patients were allowed to bear weight as possible, but if the menisci were sutured, partial weight-bearing was recommended for six weeks followed by an adjusted ACL rehabilitation. The patients were advised to performed strength and neuromuscular training guided by a physiotherapist in 9 months after surgery, and to avoid pivoting sports during the same period.

Three-dimensional computed tomographic (3D-CT) imaging:

From March 2012 until March 2013 all the randomly assigned patients were asked to perform a 3D-CT scan the first postoperative day. Twenty-four of 33 patients (twelve double-bundle and twelve single-bundle patients) agreed to perform the additional imaging. The pictures were anonymized and sent to the Steadman Philippon Research Institute. Further, they were transferred into an image processing software (Mimics v 16.0[®], Materialise, Leuven, Belgium). Within the software, the best-fit circle was created at the tunnel apertures on the tibial and femoral side, and the centres of the circles were identified.¹² For the femoral tunnel centres, a 3D-CT model was positioned in the sagittal view, and the medial femoral condyle was cropped. The positioning of the tunnels was defined by using the quadrant method described by Bernard et al..⁹ With this method the centre of the femoral tunnels were detected in the “deep-shallow” and “high-low” direction within a grid adapted to the lateral condyle.⁹ The positioning was reported as the mean percentage \pm the standard deviation(SD) in each direction. On the tibial side, the 3D-CT model of the tibial plateau was positioned in the axial view. The tunnel positions were recorded as the mean percentage \pm SD of the total anteroposterior distance as described by Tsukada et al..⁵⁵

Outcomes:

The primary outcome of the study was the Knee Osteoarthritis Outcome Score (KOOS) Quality of Life (QoL) subscore with two-year follow-up as the primary endpoint. The two groups were also

compared by the other subscores of the KOOS: Symptoms, Pain, Activity of Daily living (ADL) and Sports/Recreation, and by the IKDC 2000 subjective knee evaluation form.²² Furthermore, the differences in knee laxity between the two groups at two-year follow-up were evaluated. Rotational laxity was recorded by the Slocum's test for pivot shift and graded from 0 to 3+.⁴⁶ Anteroposterior laxity was detected by the Lachman's test, compared to the uninvolved knee.⁵⁴ The Lachman's test was graded: 0(0-3 mm), 1+ (3-5 mm), 2+ (5-10 mm) and 3+ (>10 mm).²² The anterior laxity was also measured by the KT 1000 (Knee Laxity Testing Device[®], MEDmetric, San Diego, CA, US). The difference in translation compared to the uninvolved knee was measured at 134 Newton (134N) and maximum, manual load (MM).¹³ Range of motion (ROM) was measured by the use of a goniometer to detect flexion or extension deficits. The deficits were reported in degrees compared to the uninvolved knee. Functional capacity of the knee was measured by the one-leg hop test, comparing the hop-distance of the involved leg to the uninvolved leg.³² Level of activity at two-year follow-up was reported by the Tegner activity scale and by the four levels of the Sports Activity scale.^{6, 52} The four levels of the Sports Activity Scale were: Level 1 (sports 4-7 days per week), level 2 (sports 1-3 days per week), level 3 (sports 1-3 times per month) and level 4 (no sports). Preinjury main sport was recorded at the baseline examination and two-year follow-up. Return to sports was defined as attending to the same main sport at two-year follow-up as preinjury. Finally, standing anteroposterior radiographic images of the knees were taken, using a Synaflexer[®] (Synarc, California, US) frame to achieve a fixed flexion positioning of the knees. The images were evaluated and classified by the Kellgren-Lawrence system for classification of osteoarthritis.²⁷ At the one-, and two-year follow-up, all patients were questioned if they had experienced any knee-specific adverse events or reoperations after the reconstruction. Details from these events were obtained from the patient's medical journal. Patients with KOOS QoL subscore less than 44 points at the two-year follow-up, were defined as "subjective treatment failures".⁷ The number of patients within this subgroup was detected for both groups.

Sample Size Calculation:

The sample size was calculated based on the primary outcome, KOOS QoL subscore. The minimal perceptible clinical improvement (MPCI) was set to be 8 points.⁴⁰ With equal allocation to both treatment arms and with a standard deviation of 15 points, power of 80% and a two-sided significance level of 0.05, the sample size was calculated to be 56 patients in each treatment group. A total of 120 patients were planned to be included in the study.⁴⁰

Randomisation and blinding:

A nurse not involved in the research project performed a computer-generated block randomization, consisting of ten patients in each block (<https://randomization.com>, ID: 9412). Allocation concealment was ensured by sequentially numbered, opaque, sealed envelopes containing the name of the procedure in a randomized order. The envelopes were placed in the operating theatre and opened at the request of the surgeon.

The study participants were not blinded initially (from participants 1 to 61) because it was considered challenging to keep the treatment concealed for the patients. Because the blinding was considered important in a study with patient reported outcome, those concerns were reconsidered. As the skin incisions were similar in both treatment groups the blinding could be performed after information was given to both patients and the hospital staff. The participants with randomisation number 62 to 120 were consequently blinded for the intervention. Unblinding was completed for all participants after the two-year follow-up. The outcome assessor for the PROs and functional tests was blinded for the intervention. The assisting surgeon, who enrolled the patients and performed the clinical examination, was not blinded. The radiologist was not blinded as the intervention was visible at the radiographic imaging. The statistical advisor was presented a dataset that was blinded for the intervention.

After the randomisation key was broken, the allocation of treatment was inconsistent with the randomisation-list from the computer-generated randomisation in thirty-two of the one hundred twenty patients, resulting in sixty-two patients receiving single-bundle and fifty-eight patients receiving double-bundle reconstructions. All included patients were operated after opening the envelopes in the

operation theatre, but the envelope-allocations were not consistent with the randomisation-list.

Additional unplanned sensitivity analysis to control for a potential selection bias of the two treatment groups was therefore considered necessary.

Statistical analysis

The planned statistical analysis was presented to the co-authors and published online as a Statistical Analysis Plan <https://www.ostrc.no> prior to data analysis. The PRO's and the one-leg hop test was analyzed with a linear mixed model which included fixed effects for treatment, time point (baseline, one year, and two years treatment) x time point interaction and a random intercept. From the fitted model, estimated mean values and 95% confidence intervals (CI) were reported for each time point, and the difference in changes from baseline to two-year follow-up, as well as a P-value for the null hypothesis of no treatment difference. The two-sample T-test and its associated CI were used to analyze the remaining continuous variables at two-year follow-up. The Wilcoxon-Mann-Whitney test was used to analyze ordered categorical variables. Differences between probabilities of Return to sports and subjective treatment failures were estimated with a 95% Newcombe hybrid score CI, and the null hypotheses of equal probabilities were analyzed with the Fisher mid-P test.¹⁶ All analyses were done with the intention to treat (ITT), analysis set. Per protocol analyses were only performed for the KOOS subscores. Stata 14 (StataCorp®, Texas, US) was used to perform the statistical analyses.

A planned subgroup analysis of the primary outcome in the blinded versus not-blinded patients was performed by adding an interaction term. For variables with more than 5% missing values, a sensitivity analysis was performed, consisting of inputting the missing values according to three scenarios to assess the impact of the missing values. See online Statistical analysis plan for further details (<https://www.ostrc.no>). An unplanned subgroup analysis was performed in the cohort of patients with intact grafts at two-year follow-up. Because of potential bias, an additional sensitivity analysis was carried out to assess whether the inconsistencies between the randomization list and the treatment received had any impact on the primary outcome. The latter analysis considered any

possible difference in treatment effect over time, including – but not limited to – changes from baseline to two-year follow-up.

Ethical consideration:

The study was approved by, the Regional Committees for Medical and Health Research Ethics, South East Norway.

RESULTS:

Out of 1186 patients assessed for eligibility, 120 patients were randomized to either single-bundle intervention or double-bundle intervention (Figure 1). Three patients were excluded after being randomized, because of menisci resections >(n=1), small notch size (n=1) and insufficient size of the hamstring tendons(n=1), and one was excluded at the one-year follow-up because of an unrecognized contralateral ACL injury prior to inclusion (n=1). Finally, 116 patients were available for analysis of the primary outcome. Baseline demographics and surgical characteristics showed a difference in the gender distribution between the two groups (Table 3). In the double-bundle group, there were 87% patients of male sex (47 of 54 patients), whereas the single-bundle group only contained 66% males (41 of 62 patients) (Table 2).

Table 2
Baseline demographics, and patient characteristics

Demographics, patient characteristics	Double bundle	Single bundle
No. of patients	n=54	n=62
Age, (years), mean \pm SD	27.4 \pm 6.3	27.1 \pm 5.5
Sex, n(% male)	47 (87.0)	41 (66.1)
Side, n(% right)	28 (51.9)	29 (46.8)
Contralateral injury, n	2	4
Previous injury, n	2	3
BMI, (kg/cm ²) \pm SD	25.1 \pm 2.9	24.5 \pm 3.1
Tegner activity scale score, preinjury, mean \pm SD	7.9 \pm 1.2	7.7 \pm 1.5
Tegner activity scale score, baseline, mean \pm SD	3.9 \pm 1.1	3.7 \pm 0.9
Total number of days sports/week preinjury, mean \pm SD	3.8 \pm 1.3	4.2 \pm 1.4
Total number of days sports/week baseline. mean \pm SD	3.0 \pm 1.4	3.1 \pm 1.5
Pivoting sports as main sports n(%)	38 (70.4)	36 (58.1)
Cause of injury		
Traffic, n(%)	0 (0.0)	1(1.6)
ADL, n(%)	3 (5.6)	4 (6.5)
Work, n(%)	0 (0.0)	0 (0.0)
Sports, n(%)	51 (94.4)	57 (91.9)
Preop rehab period , months		
Mean \pm SD	6.8 \pm 5.6	6.6 \pm 4.9
Time from injury to operation, months		
Mean \pm SD	15.5 \pm 18.2	15.7 \pm 20.3
Time from test to operation, months		
Mean \pm SD	1.5 \pm 1.3	1.5 \pm 1.6
Follow-up period, 1-year, months		
Mean \pm SD	12.5 \pm 1.0	12.5 \pm 0.9
Follow-up period mean 2-years, months		
Mean \pm SD	24.5 \pm 0.9	25.2 \pm 2.3
Patients with combined injuries (menisci and/or cartilage injury), n (%):	31 (57.4)	39 (62.9)
Patients with menisci injuries, n (%):	26 (48.1)	33 (53.2)
Medial, n	13	14
Lateral, n	9	14
Both menisci, n	4	5
Treatment:		
Medial resection	4	4

Medial suture	12	12
Lateral resection	4	12
Lateral suture	7	7
<hr/>		
Chondral injuries, n (%)	10 (18.5)	13 (20.0)
ICRS 1	1	1
ICRS 2	9	8
ICRS 3	0	3
ICRS 4	0	1
<hr/>		

BMI, body mass index; SD, standard deviation; ICRS, international cartilage rating system.

Patient-reported outcomes (PROs):

The KOOS QoL subscore at two-year follow-up was 72.9 points, 95% CI (67.6 to 78.2) in the double-bundle group and 66.6 points, 95% CI (61.8 to 71.4) in the single-bundle group. The change in KOOS QoL from baseline to two-year follow-up was not different between the two groups, (29.2 points change in the double-bundle group, versus 28.7 points change in the single-bundle group; -0.5 points difference; 95% CI (-8.4 to 7.5); $p=0.91$) (Table 3) (Figure 2). Furthermore, there was no difference between the groups for the remaining PRO's (Table 3) (Figure 3a and 3b). The per protocol analysis for the primary outcome KOOS QoL detected no further difference between the two groups (29.2 points change in the double-bundle group and 29.7 points in the single-bundle group, difference between groups: 0.50; 95% CI (-7.5 to 8.5); $p=0.90$). Neither were there any differences detected for the other 4 KOOS subscores in the per protocol analysis set.

All KOOS subscores and the IKDC 2000 score revealed a significant change from baseline to two-year follow-up ($p<0.001$).

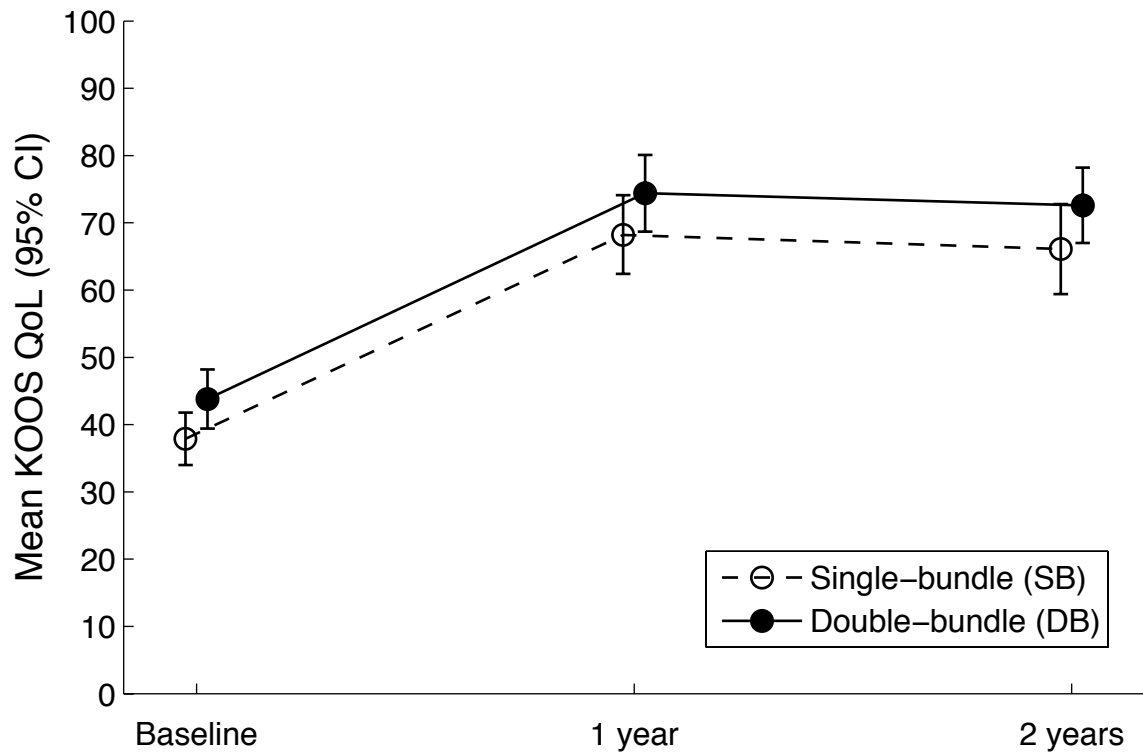
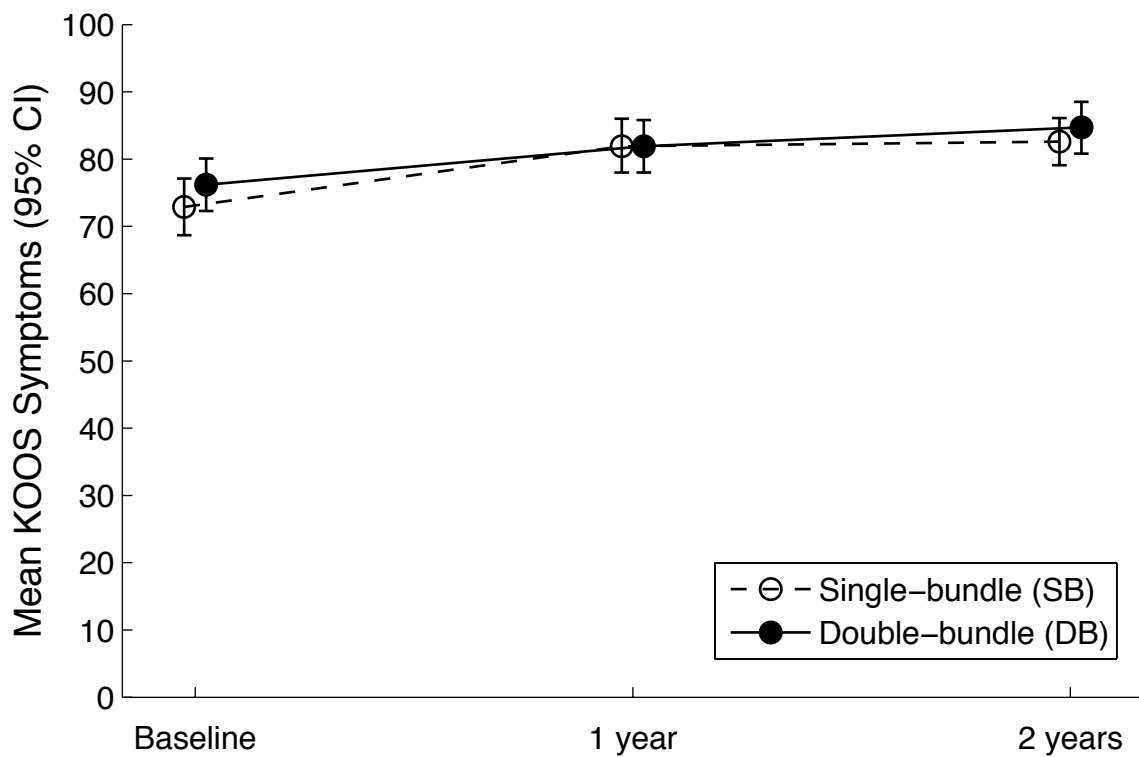
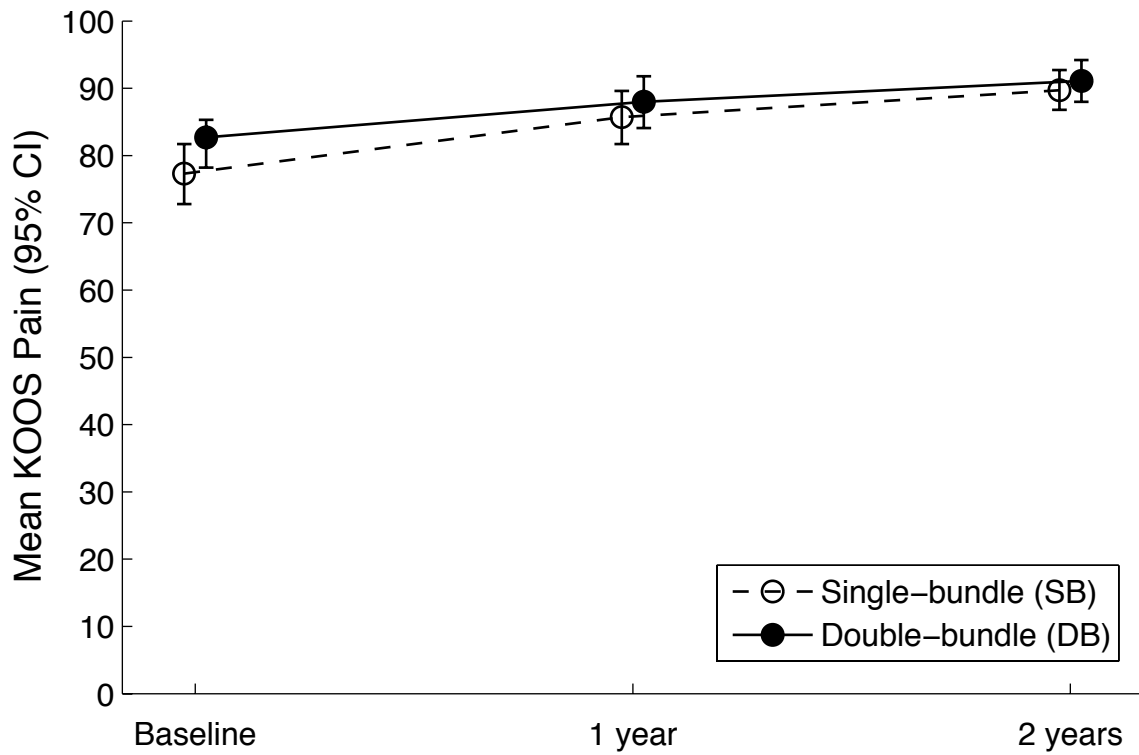


Figure 2. Primary outcome KOOS QoL subscore, observed mean values at baseline and at one- and two-year follow-up, with 95% confidence interval (CI); SB, single-bundle(white dots); DB, double-bundle(black dots)



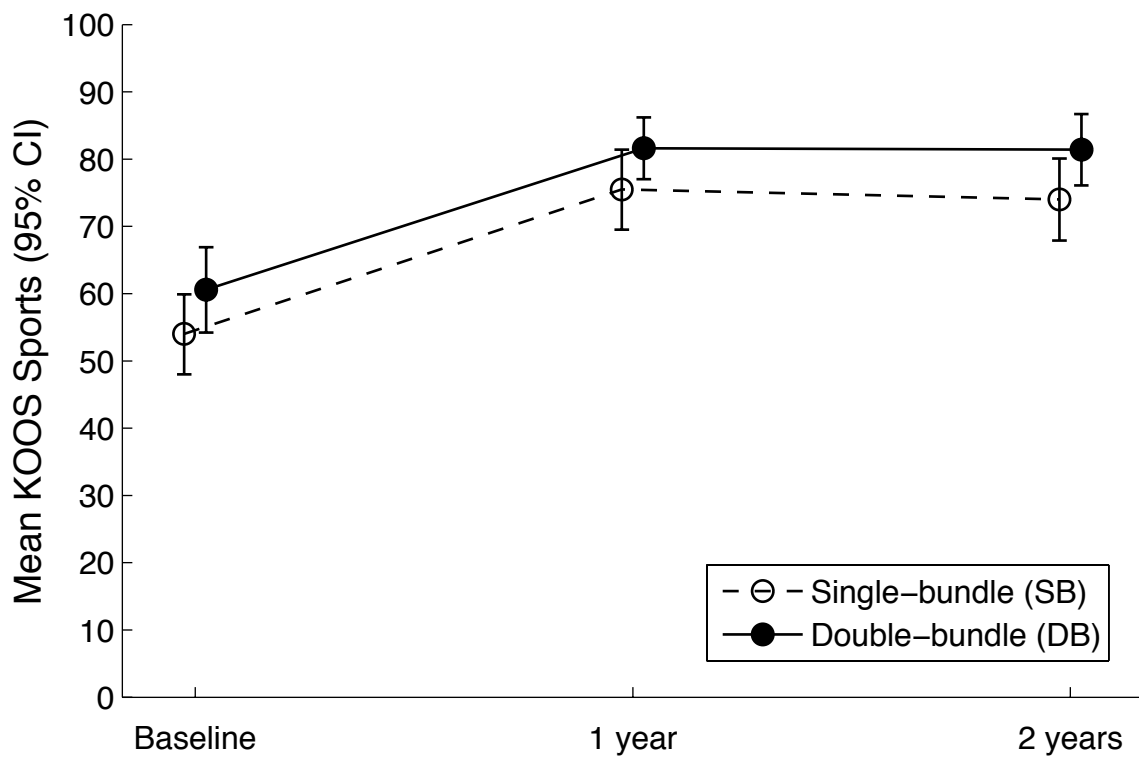
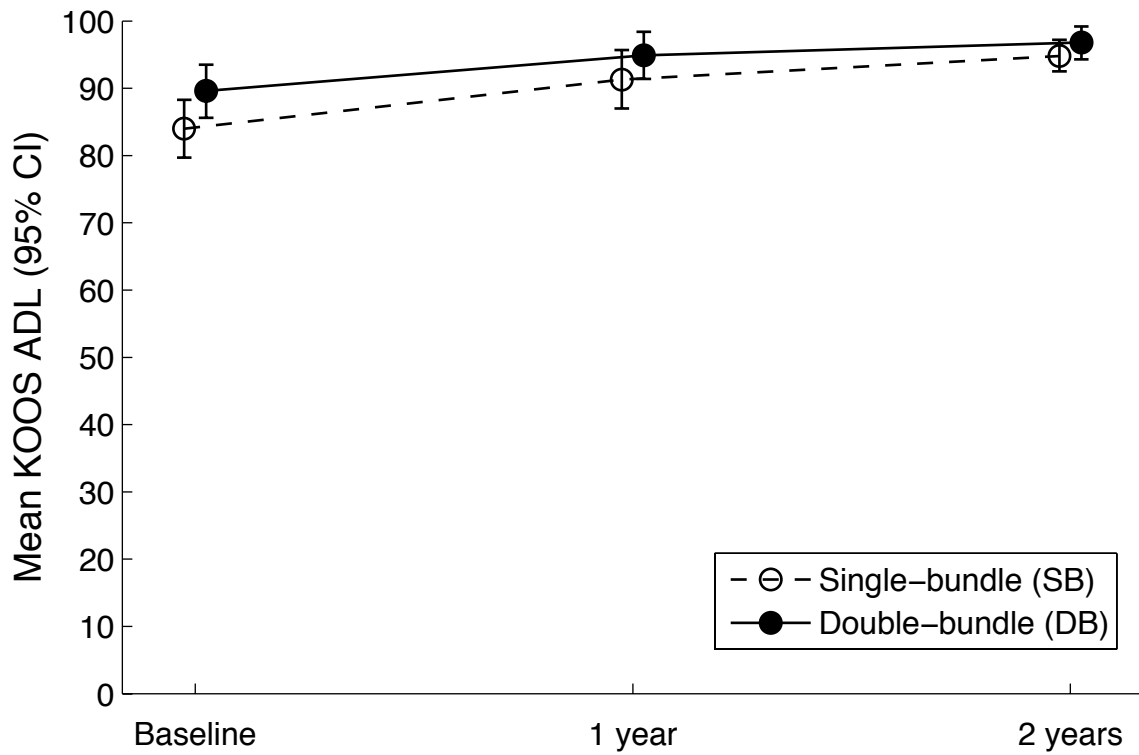


Figure 3. a)KOOS Pain, b)KOOS Symptoms , c)KOOS ADL and d)KOOS Sports subscores observed mean values at baseline and at one- and two-year follow-up, with 95% confidence interval (CI); SB, single-bundle(white dots); DB, double-bundle(black dots) . ADL, Activity of Daily Living; Sports, Sports and Recreation.

TABLE 3
Subjective outcome measurements (KOOS,IKDC subjective score)

Outcome variable	Baseline Mean (95%CI)	1-year follow-up Mean (95%CI)	2-years follow-up Mean (95%CI)	Changes from baseline to 2-years, Mean (95%CI)	Between group diff. Mean (95%CI)	p-value
PRIMARY OUTCOME						
KOOS, Quality of Life						
DB (n=54)	43.8 (38.3, 49.2)	74.5 (68.8, 80.3)	72.9 (67.6,78.2)	29.2 (23.3, 35.0)	-0.5 (-8.4, 7.4)	0.91
SB (n=62)	37.9 (32.8, 43.0)	68.6 (63.4, 73.9)	66.6 (61.8,71.4)	28.7 (23.3, 34.0)		
SECONDARY OUTCOMES						
KOOS, Pain						
DB (n=54)	81.7 (78.0, 85.4)	88.0 (84.1, 91.9)	90.9 (87.3, 94.5)	9.1 (5.1, 13.2)	3.0 (-2.6, 8.5)	0.29
SB (n=62)	77.3 (73.8, 80.7)	85.7 (82.1, 89.3)	89.4 (86.1, 92.6)	12.1 (8.4, 15.8)		
KOOS, Symptoms						
DB (n=54)	76.2 (72.3, 80.2)	81.8 (77.7, 85.9)	84.7 (80.8, 88.5)	8.5 (4.3, 12.6)	1.2 (-4.4, 6.9)	0.67
SB (n=62)	72.9 (69.2, 76.5)	82.1 (78.3, 85.8)	82.6 (79.1, 86.0)	9.7 (5.9, 13.5)		
KOOS, Activity of daily Living						
DB (n=54)	89.6 (86.0, 93.2)	95.0 (91.2, 98.8)	96.8 (93.3, 100.3)	7.3 (3.5, 11.0)	3.2 (-1.8, 8.3)	0.21
SB (n=62)	83.9 (80.6, 87.3)	91.5 (88.0, 94.9)	94.4 (91.2, 97.6)	10.5 (7.1,13.9)		
KOOS, Sports and Recreation						
DB (n=54)	60.5 (54.8, 66.3)	81.4 (75.4, 87.5)	81.5 (75.9, 87.1)	21.0 (14.9, 27.1)	-0.6 (-8.8, 7.7)	0.89
SB (n=62)	53.9 (48.5, 59.3)	75.7 (70.2, 81.3)	74.3 (69.2, 79.4)	20.4 (14.9, 25.9)		
IKDC, subjective						
DB (n=54)	55.4 (51.9, 58.8)	69.5 (66.0, 73.1)	72.2 (68.8, 75.6)	16.8 (13.5, 20.2)	-0.3 (-4.8, 4.2)	0.90
SB (n=62)	51.6 (48.4, 54.8)	64.3 (61.0, 67.6)	68.1 (65.1, 71.2)	16.5 (13.5, 19.6)		

Variable outcome reported as estimated mean values obtained from linear mixed models, with the primary outcome KOOS QoL in bold letters.

DB, double-bundle; SB, single-bundle; CI, confidence interval.

* p.value of the between group difference, from baseline to 2-years follow-up.

Knee laxity evaluations

There were no differences between the two groups for the pivot shift test, Lachman's test or in the KT 1000 measurements at two-year follow-up (Table 4). In the double-bundle group, 86% (45 of 52 patients) had 0 or +1 in the Lachman's test at two years, the respective numbers in the single-bundle group was 84 % (51 of 61 patients). Eighty-eight % of the patients in the double-bundle group and 85% in the single-bundle group had a pivot shift 0 or 1+ at two-year follow-up (46 of 52 patients in the double-bundle group, and 53 of 61 in the single-bundle group)(Table 4).

TABLE 4
Knee laxity measurements and ROM

Test	Baseline (n=116)		1-year FU (n=111)		2-years FU (n=113)		DB vs SB 2-years FU	
	DB (n=54)	SB (n=62)	DB (n=50)	SB (n=61)	DB (n=52)	SB (n=61)	Between group diff. (CI)	p-value
Lachman test, n (%)								0.20
0	0	1	18	30	29(55.7)	25(40.9)		
+1	11	13	28	25	16(30.7)	26(42.6)		
+2	31	30	4	5	6(11.5)	9(14.8)		
+3	12	18	0	1	1(1.9)	1(1.6)		
Pivot shift, n (%)								0.53
0	5	7	32	42	34 (65.4)	36 (59.0)		
+1	11	19	17	12	12 (23.1)	17 (27.9)		
+2	24	16	1	6	5 (9.6)	8 (13.1)		
+3	14	20	0	0	1 (1.9)	0		
KT 1000 side-to side diff, mean ± SD, (mm)								
Anterior 134 N	3.2 ± 2.7	3.5 ± 2.2	2.2 ± 2.0	1.5 ± 1.9	1.8 ± 2.1	2.3 ± 2.6	0.6(-0.3,1.5)	0.19
Anterior MMT	4.7 ± 3.2	4.8 ± 2.6	2.6 ± 2.5	1.8 ± 2.1	2.1 ± 2.6	2.7 ± 2.8	0.6(-0.4,1.6)	0.27
ROM mean ± SD, (deg)								
Extension deficit					1.9±3.1	2.0±3.2	0.1(-1.3,1.1)	0.89
Flexion deficit					1.9±3.5	2.6±3.8	0.7(-2.1,0.7)	0.31

FU, follow-up; DB, double-bundle; SB, single-bundle; MMT, manual maximum test; CI, confidence interval; ROM, range of motion

Range of motion and functional tests

There was no difference in range of motion between the two groups (Table 4). Compared to the uninvolved knee, 31% in the double-bundle group had an extension deficit (16 out of 52 patients), versus 34% in the single-bundle group (18 out of 59) at two-year follow-up. The mean deficit in knee extension was 1.9 degrees for the double-bundle group and 2.0 degrees for the single-bundle group (0.08 degrees difference; 95% CI (-1.3 to 0.10); $p=0.90$). Knee flexion deficits, compared to uninvolved leg, were 27% (14 of 52 patients) for the double-bundle group and 37% (22 out of 59) for the single-bundle group. Mean flexion deficit was 1.9 degrees for the double-bundle group and 2.6 degrees for the single-bundle group (0.70 degrees difference; 95% CI (-0.66 to 2.07); $p=0.31$) (Table4). The functional performance of the knee was measured by the one-leg hop test. The test reported a significant change in difference from baseline to two years measures in the single-bundle group compared to the double bundle group (23.6 % change in the single-bundle group and 14.6% change in the double-bundle group, 9.1 % difference between the two groups, 95% CI from 0.5 to 17.6, $p= 0.04$). Both legs achieved more than 97 % of the capacity of the uninvolved leg at the two-year follow-up.

Activity level:

The Tegner activity level and the Sports activity scale level at two-year follow-up were not different between the two groups (Table 5). The rate of the patients that returned to their pre-injury main sport was also not different between the single- and double-bundle group. In the double-bundle group 53% (26 of 53 patients), and in the single-bundle group 44% (27 of 44), returned to sports at two-year follow-up (8.8%, 95% CI, (-9.7% to 26.5%), $p=0.39$) (Table 5).

TABLE 5
Activity level of the patients

	Baseline		2-years FU		DB vs SB, 2-years FU p-value
	DB (n=54)	SB (n=62)	DB	SB	
Tegner activity scale					
Median (range)	4.0 (1 to 7)	3.5 (1 to 6)	5.0 (1 to 9)	5.0 (2 to 9)	0.77
Missing values	0	0	1	1	
Sports Activity scale					
Median (range)	2 (1 to 4)	2 (1 to 4)	2 (1 to 3)	2 (1 to 4)	0.73
Missing values	1	2	1	1	
Return to sports					
n (%)			26 (53)	27 (44)	0.39
Missing values			5	1	

FU, follow-up; DB, double-bundle; SB, single-bundle; SD, standard deviation.

Radiographic imaging:

Degenerative changes detected by radiographic imaging of the knees revealed that 13 patients had Kellgren-Lawrence grade one and two patients (one in the single-bundle and one in the double-bundle group) had a Kellgren-Lawrence classification grade two at the two-year follow-up.

Adverse events:

Eight graft-ruptures were detected in the single-bundle group, and three in the double-bundle group at two-year follow-up (p=0.16) (Table 6). The graft-ruptures were detected by clinical examination and confirmed by MRI in 9 of the eleven patients. Only one of the patients had a revision ACL before the two-year follow-up. Four patients had a postoperative infection, two in the double-bundle group and two in the single-bundle group. Sixteen patients were hospitalized because of a new surgical procedure within the first two years after the reconstruction. The main reasons for having a reoperation were: infection (n=5), new menisci injury (n=4) or because of cyclops and extension deficit of the knee (n=3) (Table 6).

TABLE 6
Adverse events and reoperations

	DB (n)	SB (n)
Adverse events*	18	25
Graft rupture	3	8
Infection	1	3
Hematoma	8	8
Menisci injury	3	1
Cyclops/ext.def.	1	3
Donor site pain	2	2
Reoperations*	5	11
Revision	0	1
Menisci surgery	3	1
Lavage	2	3
Cyclops/ext.def.	0	3
Others	0	5

DB, double-bundle; SB, single-bundle; ext.def., extension deficit;

*More than one event per patient possible.

Subgroup analysis:

Planned subgroup analysis of the blinded subgroup revealed no further difference in the KOOS QoL subscore compared to the no blinded group ($p=0.98$). The number of subjective treatment failures was also not different between the two groups. From 54 patients 3 were treatment failures (5.6%) in the double-bundle group and 10 out of 62 patients (16.1%) in the single-bundle group (10.6% difference, 95% CI (-1.3% to 22.2%), $p=0.06$) were defined as treatment failures.

A sensitivity analysis comparing the KOOS scores and the knee laxity measurements in patients with only intact grafts at the two-year follow-up did not detect any further differences between the two groups (Table 7). A sensitivity-analysis between the groups of correctly and incorrectly randomized patients did not reveal any difference in the treatment effect between the two groups ($p=0.08$). The primary outcome in the correctly randomized patients ($n=84$) gave $p=0.96$ for the difference between the two treatment arms.

TABLE 7
Subgroup analysis,
Patients without graft-rupture at 2-years follow-up

Subgroup	DB Baseline (n=51)	SB Baseline (n=54)	DB 2-years follow-up	SB 2-years follow-up	Between group differences* Mean difference (CI)	p- value
KOOS, Mean(CI)						
Pain	81.6 (77.9, 85.3)	77.2 (73.6, 80.8)	91.6 (87.9, 95.2)	90.6 (87.2, 94.0)	3.4 (-2.3, 9.2)*	0.24*
Symptoms	75.9 (71.8, 80.0)	73.1 (69.1, 77.0)	85.0 (81.0, 88.9)	83.2 (79.5, 87.0)	1.1 (-4.8, 7.1)*	0.71*
ADL	89.5 (85.8, 93.2)	83.9 (80.2, 87.5)	97.2 (93.5, 100.8)	94.8 (91.4, 98.2)	3.3 (-2.1, 8.6)*	0.23*
QoL	43.6 (38.5, 48.7)	38.3 (33.4, 43.3)	74.7 (69.8, 79.7)	70.0 (65.4, 74.7)	0.6 (-7.4, 8.7)*	0.88*
Sports	61.3 (55.7, 66.8)	54.5 (49.2, 59.9)	82.5 (77.1, 87.9)	77.2 (72.2, 82.3)	1.5 (-6.8, 9.7)*	0.72*
Pivot shift						0.63
Lachman's test						0.24
KT 1000, Mean±SD						
134 N			1.6 ± 2.1	2.0 ± 2.1	0.4 (-0.4, 1.2)	0.35
MMT			1.9 ± 2.4	2.3 ± 2.3	0.4 (-0.5, 1.3)	0.39

All KOOS values are presented as estimated means from a linear mixed model analysis based on baseline, 1- and 2-years follow-up. DB, double-bundle; SB, single-bundle; MMT, manual maximum test; CI, confidence interval; SD, standard deviation.

*Between group differences in change of KOOS subscore from baseline til 2-years follow-up

The positioning of the femoral and tibial tunnels:

The mean positioning of the single-bundle femoral tunnels in the “deep-shallow” direction was at $28.2 \pm 3.2\%$ (mean \pm SD) of the total lateral condyle distance (Figure 4a). For the AM bundles the centre was at $24.4 \pm 2.8\%$, and for the PL bundles at $41.6 \pm 6.2\%$ of the total depth. In the “high-low” direction, the single-bundle tunnels were placed at $27.7 \pm 4.3\%$, the AM tunnels at $24.2 \pm 7.0\%$ and the PL tunnels at $45.9 \pm 6.6\%$ of the distance from the Blumensaat's line (Figure 4a).

The mean centre of the tibial tunnels was positioned at $37.7 \pm 6.4\%$ of the total anteroposterior distance for the single-bundles, and at $34.2 \pm 4.9\%$ for the AM bundles and $49.9 \pm 6.4\%$ for the PL bundles (Figure 4b).

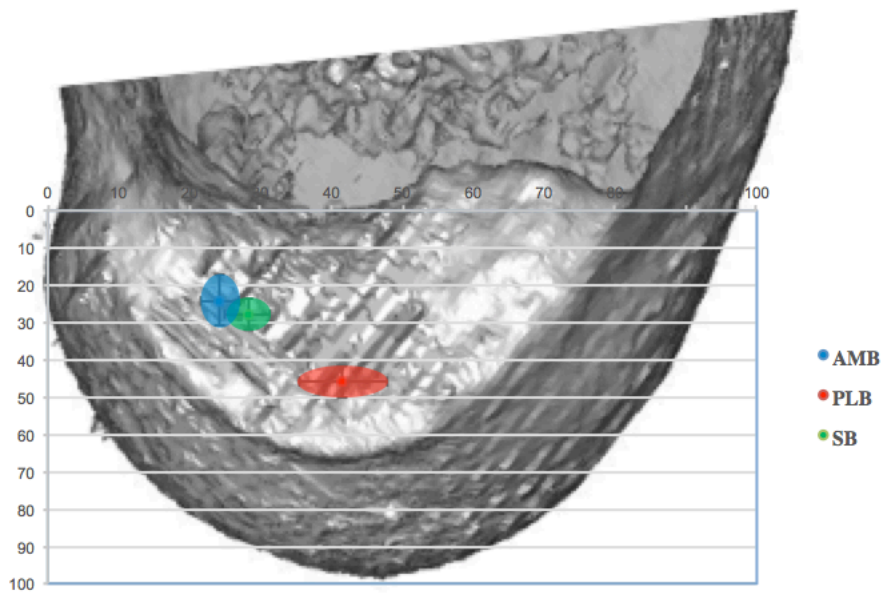


Figure 4a. Femoral tunnel positioning (center \pm SD); AM, anteromedial bundle(blue); PL, posterolateral bundle(red); SB, single-bundle(green).

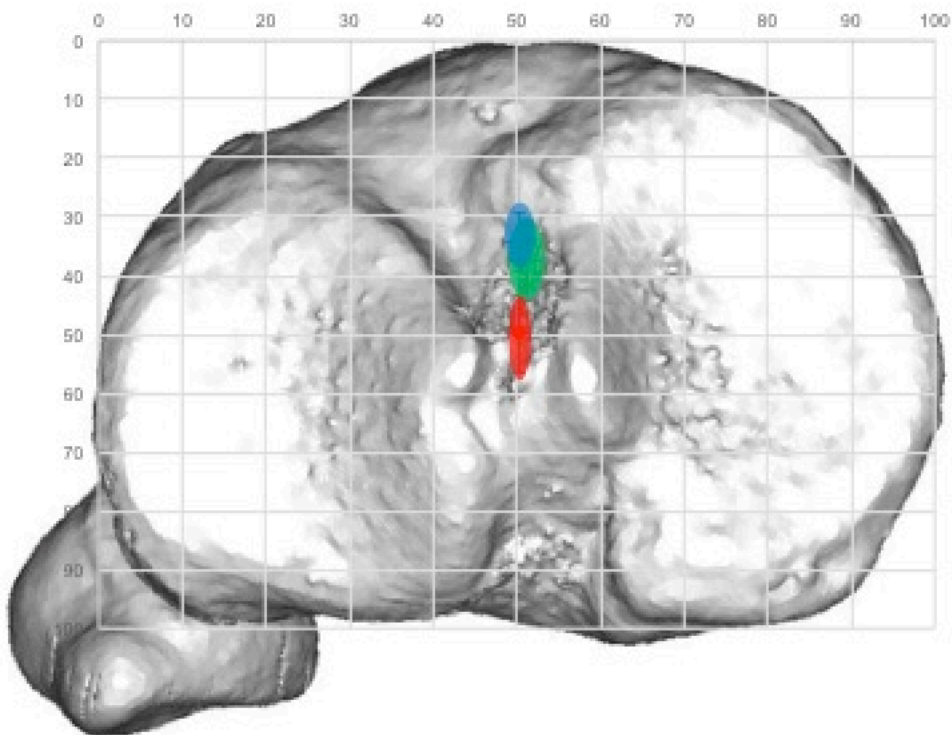


Figure 4b. Tibial tunnel positioning (center \pm SD); AM, anteromedial bundle(blue); PL, posterolateral bundle(red); SB, single-bundle(green).

DISCUSSION:

The main finding of the current study was no difference between double-bundle and single-bundle ACL reconstruction at two years follow-up evaluated by KOOS QoL subscore or any of the other subjective outcome measures used. Studies with more focus on PROs after ACL reconstructions have been requested as there has been published a considerable number of studies comparing the objective outcome between the double-bundle and the single-bundle technique.³⁴ In most of those studies rotational and anteroposterior knee laxity has been the outcome of interest.^{3, 23, 35, 56} The KOOS is proven as a reliable, valid and responsive PRO for patients undergoing ACL reconstruction.⁴⁰ The KOOS QoL subscore is considered to be the most sensitive and responsive among the five dimensions for ACL injured patient.^{40, 41} Ahlden et al. compared the KOOS score of anatomic single-bundle with anatomic double-bundle reconstructions and found a significant improvement in both groups, but no difference between the two groups for any of the five KOOS subscores two years after surgery.³ Similarly, Sasaki et al. used the KOOS for evaluation of single-bundle rectangular bone-patellar tendon-bone grafts versus double-bundle hamstring reconstructions. They found no difference in KOOS QoL subscore between the two groups at the two-year follow-up.⁴³ These results are in line with the findings reported from this study. However, knee laxity measurements do not necessarily correlate with the PRO's. Objective testing of ligament instability are frequently emphasised, although the relation between knee laxity and subjective outcome of the knee has been discussed. One study have found the rotational knee-laxity as measured by the pivot shift test, to correlate with patients satisfaction, sports participation and Lysholm score, but no significant relationship was observed between the Lachman's test or KT1000 and the subjective scores.²⁸

In vitro studies of the double-bundle reconstruction technique showed significantly improved anterior and rotatory knee laxity measures compared to single-bundle reconstructions when the technique was

first introduced.^{42, 59} More than 30 randomized or quasi-randomized, controlled, clinical trials have so far been published.³⁴ While some studies proclaim that the double-bundle improve the outcome of ACL reconstructions, other studies have found no advantage of using this new technique.^{15, 31, 36, 53, 56} The discrepancy in the clinical outcomes between studies could be due to the bias introduced by the anatomic single-bundle reconstruction as many of the publications compare non-anatomic single-bundles with anatomic or partly anatomic (only one bundle), reconstructed double-bundles. Studies have shown that drilling of the femoral tunnels through an accessory, anteromedial portal is important to achieve a femoral insertion cite similarly to the native ACL.^{8, 14, 60} As anatomic reconstructions gradually was introduced for both single- and double-bundle placement, this could explain how many of the later publications strive to find a difference between the two techniques.^{3, 49, 58} Only a few studies have consistently performed their reconstructions through an accessory AM-portal and by the guidance of soft tissue and bony landmarks (not “o’clock” positioning). In their randomized study, Gobbi et al. found no difference in anteroposterior or rotational laxity, and they found similar IKDC subjective and objective score, Tegner activity score and Lysholm scores in both groups.¹⁷ Ahlden et al. compared the single- and the double-bundle reconstruction technique and found similar results for knee laxity tests and the subjective outcome in both groups.³ Mayr et al. evaluated the subjective and objective IKDC measurements between the two techniques and did also not find any difference between the two groups.³⁵ Xu et al. looked at 32 single-bundle and 34 double-bundle patients with clinical tests, PRO’s and 3D-CT measurements.⁵⁸ They found no difference in knee laxity measurements or PRO’s between the two groups at the two-year follow-up. The postoperative 3D-CT scans confirmed the anatomic placement of the bundles. Finally, Hussein et al. compared their double-bundle technique to two different single-bundle groups: Non-anatomic and anatomic single-bundle reconstructions.²⁴ In contrary to the other anatomic studies, they found that the anatomic double-bundle reconstructed knees were superior to both the non-anatomic and anatomic single-bundle reconstructions in rotational and anteroposterior laxity. Their difference in KT 1000 measures was 1.2 mm side-to-side difference in the anatomic double-bundle group and 1.6 mm in the anatomic single-bundle group. The amount of patients with a negative pivot shift test was 99.3% in the double-bundle and 66.7% in the anatomic single-bundle group. Like many other trials, they did not find any

difference between the groups in the subjective outcome.²⁴ In summary, many of the listed studies are in line with our study; revealing no significant differences between the two techniques for PROs or clinical tests.

In the current study, there was no difference in activity level between the two groups at the two-year follow-up, but the participants reported lower return-to-sport rates than in other studies.^{3,5} One reason could be that the period from injury to operation in the current study was longer (15 months) than reported from other studies.^{3,23} As the patients were advised by the surgeons to avoid pivoting sports for at least 9-12 months after the reconstruction, this could also have affected the return to sports rate. The only outcome variable with a difference between the two treatment options was the one-leg hop test. This test had a higher change from baseline to two-years follow-up in the single- than in the double-bundle group. It was however presumed that these results were prone to a ceiling effect as both DB and SB knees achieved more than 97% (97.8 and 99.8 % in the single- and double bundle group respectively) of the capacity of the non-involved leg at 2-years follow-up.

A 3D CT imaging was obtained in twenty-four patients the first postoperative day. This made it possible to verify the positioning of the femoral and tibial tunnels. Correct tunnel position could be dependent on other structures than distances to the different bone structures as suggested by Bernard et al. and Tsukada et al.^{9,55} And in this study the centre of the tunnels were positioned dependent on bony landmarks and remnant soft tissue, and hence specific for each patient. Nevertheless, anatomic studies have suggested the areas in which the footprints are detected on cadaver knees.³⁸ According to these studies, the positioning of the AM and PL bundles in this study were in agreement with the anatomic centres. The single-bundle tunnels were placed in the "deeper" and "higher" position compared to most of the anatomic studies.³⁸ Biomechanical studies have confirmed that the fibers with the highest restraint to the anteroposterior translation of the knee, originate from the proximal area of the femoral ACL attachment site.²⁶ Only two patients had radiographic signs of knee osteoarthritis at

the two-year follow-up defined as Kellgren-Lawrence grade two or worse. However, to detect the posttraumatic cartilage degeneration radiographically, mid- and long-term follow-ups are preferable.

Minimal graft-sizes of the PL and AM bundle were introduced to prevent the double-bundle reconstructions to be performed in knees with insufficient graft-sizes.⁴⁵ Although a threshold for the minimum size of a bundle cannot be stated, many studies have shown an increased risk of revision with smaller grafts.^{20, 47, 58}

In the current study 13 out of 120 patients (11.2%), were detected with a KOOS QoL less than 44 points (subjective treatment failures). This is lower than reported from the registers.⁷ Thus, in this study the KOOS was answered by more than 95% of the patients. As the coverage of the subjective outcome measurements are generally low in the registers the reported KOOS scores could have been biased due to a high non-responder rate. There has also been stated that low KOOS QoL is correlated to the risk of later ACL revision.^{7, 19} Of the 13 subjective treatment failures, only four were detected as having a graft-rupture. This suggests that other factors than the intact or non-intact graft play an important role for the low KOOS QoL scores. There were eight graft-ruptures in the single-bundle and three in the double-bundle group at the two-year follow-up. Two more single-bundle grafts had a partial rupture of the graft on MRI. The relatively high re-rupture rate in the single-bundle reconstructions could be explained by the "higher" and "deeper" femoral single-bundle positioning making the graft more exposed to anteroposterior forces.^{26, 58} Additionally, transportal drilling of the femoral tunnel has been shown to increase the risk of revision surgery compared to transtibial drilling.^{39, 51} Suomalainen et al. compared 75 double-bundles to 78 single-bundles. They concluded with significant fewer graft-ruptures in the double-bundle group. However, whereas the number of re-ruptures in the double-bundle group was one, the number of re-ruptures in the single-bundle group was seven.⁴⁹ The results should be interpreted with caution as the numbers of events was relatively few as also Suomalainen et al. suggested in their conclusion. In a more extensive register study

comparing 52,000 single- and almost 1,000 double-bundle reconstructions in Scandinavia there was no difference in the risk of revision between the two groups.¹

Limitations:

There are several limitations to this study. First, the study was designed as an efficacy study, with an experienced surgeon in a high volume hospital, making the results of this research not applicable for all hospitals and surgeons performing ACL reconstructions. The idea, however, was to see how this technique would perform under "ideal conditions." Therefore results from other cohorts should be taken into consideration before any conclusions are to be made. The strict inclusion criteria also limited the external validity of the study. The main causes of exclusion from the study were too young or too old patients, patients with revision surgery or multi-ligament surgery of the knee (Figure 1). Blinding of the patients can make an impact on the results of clinical studies.⁵⁷ Particularly when collecting subjective outcome blinding may prevent overestimation of the treatment effect.⁵⁷ A planned sensitivity analysis of a blinded subgroup of the patients was therefore carried out, and this analysis did not reveal any further difference between the two groups for the primary outcome.

Thirty-two patients did not achieve the correct treatment from the randomisation-list. The reason why the allocated procedure was not in line with the computer-generated list is unknown, but it could have been due to incorrect handling of the envelopes. The box of envelopes with block-randomised treatment options, were carried down in the operating room at the days of surgery. The assisting staff opened the envelopes at request of the surgeon. Even though the surgeon reported what treatment each included patient was randomized to in their journals, the envelopes or inclusion numbers could have been incorrectly managed. A sensitivity analysis was performed revealing no further difference in the results. The baseline demographics were different in the two groups. The double-bundle group consisted of more males than the single-bundle group. In a Swedish register study, they found that the male sex was over-representative in the group of high KOOS scores (defined as functional recovery), but there was no gender difference in the group of low KOOS scores (KOOS QoL<44 points).⁷ A

higher proportion of males in the double-bundle group could potentially have overestimated the treatment effect in this group. The quality of the rehabilitation is of importance for the final results after ligament reconstructions.²⁰ It was assured that all participants went to a physiotherapist with knee-injury expertise for rehabilitation. However, the compliance was not monitored. Neither were psychosocial aspects of the patients assessed, such as fear of re-injury and differences in the motivation to return to previous activity and activity level.^{4,5} To increase the reliability and the validity of the 3D-CT positioning of the tunnels, CT-measurements from a larger group of patients and inter- and intraclass correlation scores should have been performed.

The strengths of this study were its comprehensive design with focus on patient-reported outcomes as well as knee laxity measurements and return to sports rates. A sample size was performed according to the primary outcome, and the study group had few lost to follow-up at all time points. 3D-CT imaging of the patients was performed to verify tunnel positioning. As the anatomic reconstruction technique is relying on the tunnel placement, it is crucial to be able to verify this by imaging, as shown by the current study. The double-bundle reconstruction is a more complex procedure, takes longer time, is harder to revise and is more expensive.³³ Very few of the strictly anatomical placed reconstruction studies in vivo and in vitro could find any improved outcome by the double-bundle technique.^{3, 17, 18, 29, 35, 58} The question is if there is a need for additional research on the short-term outcome of this technique. Future research should be concentrated on the long-term effects of the double-bundle reconstructions and especially on the cartilage degeneration it may or may not prevent.

Conclusion:

In the current randomized trial, there were no differences in KOOS QoL subscore, knee laxity measures or activity level comparing the double-bundle and the single-bundle ACL reconstruction techniques. Both the single- and double-bundle reconstructions of the ACL resulted in improved patient-reported and clinical outcomes. However, the number of bundles does not seem to be important, as long as they are adequately positioned.

REFERENCES:

1. Aga C, Kartus JT, Lind M, Lygre SHL, Granan LP, Engebretsen L. Risk of Revision Was Not Reduced by a Double-bundle ACL Reconstruction Technique: Results From the Scandinavian Registers. *Clin Orthop Relat Res.* 2017;475(10):2503-2512.
2. Aglietti P, Giron F, Cuomo P, Losco M, Mondanelli N. Single-and double-incision double-bundle ACL reconstruction. *Clin Orthop Relat Res.* 2007;454:108-113.
3. Ahlden M, Sernert N, Karlsson J, Kartus J. A prospective randomized study comparing double- and single-bundle techniques for anterior cruciate ligament reconstruction. *Am J Sports Med.* 2013;41(11):2484-2491.
4. Ardern CL, Taylor NF, Feller JA, Whitehead TS, Webster KE. Psychological responses matter in returning to preinjury level of sport after anterior cruciate ligament reconstruction surgery. *Am J Sports Med.* 2013;41(7):1549-1558.
5. Ardern CL, Webster KE, Taylor NF, Feller JA. Return to sport following anterior cruciate ligament reconstruction surgery: a systematic review and meta-analysis of the state of play. *Br J Sports Med.* 2011;45(7):596-606.
6. Barber-Westin SD, Noyes FR, McCloskey JW. Rigorous statistical reliability, validity, and responsiveness testing of the Cincinnati knee rating system in 350 subjects with uninjured, injured, or anterior cruciate ligament-reconstructed knees. *Am J Sports Med.* 1999;27(4):402-416.
7. Barenius B, Forssblad M, Engstrom B, Eriksson K. Functional recovery after anterior cruciate ligament reconstruction, a study of health-related quality of life based on the Swedish National Knee Ligament Register. *Knee Surg Sports Traumatol Arthrosc.* 2013;21(4):914-927.
8. Bedi A, Maak T, Musahl V, et al. Effect of tunnel position and graft size in single-bundle anterior cruciate ligament reconstruction: an evaluation of time-zero knee stability. *Arthroscopy.* 2011;27(11):1543-1551.
9. Bernard M, Hertel P, Hornung H, Cierpinski T. Femoral insertion of the ACL. Radiographic quadrant method. *Am J Knee Surg.* 1997;10(1):14-21; discussion 21-12.
10. Bjornsson H, Desai N, Musahl V, et al. Is double-bundle anterior cruciate ligament reconstruction superior to single-bundle? A comprehensive systematic review. *Knee Surg Sports Traumatol Arthrosc.* 2015;23(3):696-739.
11. Brophy RH, Wright RW, Matava MJ. Cost analysis of converting from single-bundle to double-bundle anterior cruciate ligament reconstruction. *Am J Sports Med.* 2009;37(4):683-687.
12. Crespo B, Aga C, Wilson KJ, et al. Measurements of bone tunnel size in anterior cruciate ligament reconstruction: 2D versus 3D computed tomography model. *J Exp Orthop.* 2014;1(1):2.

13. Daniel DM, Stone ML, Sachs R, Malcom L. Instrumented measurement of anterior knee laxity in patients with acute anterior cruciate ligament disruption. *Am J Sports Med.* 1985;13(6):401-407.
14. Dargel J, Schmidt-Wiethoff R, Fischer S, Mader K, Koebke J, Schneider T. Femoral bone tunnel placement using the transtibial tunnel or the anteromedial portal in ACL reconstruction: a radiographic evaluation. *Knee Surg Sports Traumatol Arthrosc.* 2009;17(3):220-227.
15. Desai N, Bjornsson H, Musahl V, et al. Anatomic single- versus double-bundle ACL reconstruction: a meta-analysis. *Knee Surg Sports Traumatol Arthrosc.* 2014;22(5):1009-1023.
16. Fagerland MW, Lydersen S, Laake P. *Statistical analysis of contingency tables.* Boca Raton: CRC Press/Taylor & Francis Group; 2017.
17. Gobbi A, Mahajan V, Karnatzikos G, Nakamura N. Single- versus double-bundle ACL reconstruction: is there any difference in stability and function at 3-year followup? *Clin Orthop Relat Res.* 2012;470(3):824-834.
18. Goldsmith MT, Jansson KS, Smith SD, Engebretsen L, LaPrade RF, Wijdicks CA. Biomechanical comparison of anatomic single- and double-bundle anterior cruciate ligament reconstructions: an in vitro study. *Am J Sports Med.* 2013;41(7):1595-1604.
19. Granan LP, Baste V, Engebretsen L, Inacio MC. Associations between inadequate knee function detected by KOOS and prospective graft failure in an anterior cruciate ligament-reconstructed knee. *Knee Surg Sports Traumatol Arthrosc.* 2015;23(4):1135-1140.
20. Grindem H, Granan LP, Risberg MA, Engebretsen L, Snyder-Mackler L, Eitzen I. How does a combined preoperative and postoperative rehabilitation programme influence the outcome of ACL reconstruction 2 years after surgery? A comparison between patients in the Delaware-Oslo ACL Cohort and the Norwegian National Knee Ligament Registry. *Br J Sports Med.* 2015;49(6):385-389.
21. Harner CD, Poehling GG. Double bundle or double trouble? *Arthroscopy.* 2004;20(10):1013-1014.
22. Hefti F, Muller W. [Current state of evaluation of knee ligament lesions. The new IKDC knee evaluation form]. *Orthopade.* 1993;22(6):351-362.
23. Hemmerich A, van der Merwe W, Batterham M, Vaughan CL. Knee rotational laxity in a randomized comparison of single- versus double-bundle anterior cruciate ligament reconstruction. *Am J Sports Med.* 2011;39(1):48-56.
24. Hussein M, van Eck CF, Cretnik A, Dinevski D, Fu FH. Prospective randomized clinical evaluation of conventional single-bundle, anatomic single-bundle, and anatomic double-bundle anterior cruciate ligament reconstruction: 281 cases with 3- to 5-year follow-up. *Am J Sports Med.* 2012;40(3):512-520.
25. Jarvela T, Moisala AS, Sihvonen R, Jarvela S, Kannus P, Jarvinen M. Double-bundle anterior cruciate ligament reconstruction using hamstring autografts and bioabsorbable interference screw fixation: prospective, randomized, clinical study with 2-year results. *Am J Sports Med.* 2008;36(2):290-297.
26. Kawaguchi Y, Kondo E, Takeda R, Akita K, Yasuda K, Amis AA. The role of fibers in the femoral attachment of the anterior cruciate ligament in resisting tibial displacement. *Arthroscopy.* 2015;31(3):435-444.
27. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. *Ann Rheum Dis.* 1957;16(4):494-502.

28. Kocher MS, Steadman JR, Briggs KK, Sterett WI, Hawkins RJ. Relationships between objective assessment of ligament stability and subjective assessment of symptoms and function after anterior cruciate ligament reconstruction. *Am J Sports Med.* 2004;32(3):629-634.
29. Kondo E, Merican AM, Yasuda K, Amis AA. Biomechanical comparison of anatomic double-bundle, anatomic single-bundle, and nonanatomic single-bundle anterior cruciate ligament reconstructions. *Am J Sports Med.* 2011;39(2):279-288.
30. Kopf S, Musahl V, Tashman S, Szczodry M, Shen W, Fu FH. A systematic review of the femoral origin and tibial insertion morphology of the ACL. *Knee Surg Sports Traumatol Arthrosc.* 2009;17(3):213-219.
31. Li X, Xu CP, Song JQ, Jiang N, Yu B. Single-bundle versus double-bundle anterior cruciate ligament reconstruction: an up-to-date meta-analysis. *Int Orthop.* 2013;37(2):213-226.
32. Logerstedt D, Grindem H, Lynch A, et al. Single-legged hop tests as predictors of self-reported knee function after anterior cruciate ligament reconstruction: the Delaware-Oslo ACL cohort study. *Am J Sports Med.* 2012;40(10):2348-2356.
33. Lubowitz JH. Editorial Commentary: ACL Reconstruction: Single-Bundle Versus Double-Bundle. *Arthroscopy.* 2015;31(6):1197-1198.
34. Mascarenhas R, Cvetanovich GL, Sayegh ET, et al. Does Double-Bundle Anterior Cruciate Ligament Reconstruction Improve Postoperative Knee Stability Compared With Single-Bundle Techniques? A Systematic Review of Overlapping Meta-analyses. *Arthroscopy.* 2015;31(6):1185-1196.
35. Mayr HO, Benecke P, Hoell A, et al. Single-Bundle Versus Double-Bundle Anterior Cruciate Ligament Reconstruction: A Comparative 2-Year Follow-up. *Arthroscopy.* 2016;32(1):34-42.
36. Meredith RB, Vance KJ, Appleby D, Lubowitz JH. Outcome of single-bundle versus double-bundle reconstruction of the anterior cruciate ligament: a meta-analysis. *Am J Sports Med.* 2008;36(7):1414-1421.
37. Mohtadi N, Chan D, Barber R, Oddone Paolucci E. A Randomized Clinical Trial Comparing Patellar Tendon, Hamstring Tendon, and Double-Bundle ACL Reconstructions: Patient-Reported and Clinical Outcomes at a Minimal 2-Year Follow-up. *Clin J Sport Med.* 2015;25(4):321-331.
38. Parkar AP, Adriaensen M, Vindfeld S, Solheim E. The Anatomic Centers of the Femoral and Tibial Insertions of the Anterior Cruciate Ligament: A Systematic Review of Imaging and Cadaveric Studies Reporting Normal Center Locations. *Am J Sports Med.* 2017;45(9):2180-2188.
39. Rahr-Wagner L, Thillemann TM, Pedersen AB, Lind MC. Increased risk of revision after anteromedial compared with transtibial drilling of the femoral tunnel during primary anterior cruciate ligament reconstruction: results from the Danish Knee Ligament Reconstruction Register. *Arthroscopy.* 2013;29(1):98-105.
40. Roos EM, Lohmander LS. The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. *Health Qual Life Outcomes.* 2003;1:64.
41. Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure. *J Orthop Sports Phys Ther.* 1998;28(2):88-96.
42. Sakane M, Fox RJ, Woo SL, Livesay GA, Li G, Fu FH. In situ forces in the anterior cruciate ligament and its bundles in response to anterior tibial loads. *J Orthop Res.* 1997;15(2):285-293.

43. Sasaki S, Tsuda E, Hiraga Y, et al. Prospective Randomized Study of Objective and Subjective Clinical Results Between Double-Bundle and Single-Bundle Anterior Cruciate Ligament Reconstruction. *Am J Sports Med.* 2016;44(4):855-864.
44. Siebold R, Dehler C, Ellert T. Prospective randomized comparison of double-bundle versus single-bundle anterior cruciate ligament reconstruction. *Arthroscopy.* 2008;24(2):137-145.
45. Siebold R, Schuhmacher P. Restoration of the tibial ACL footprint area and geometry using the Modified Insertion Site Table. *Knee Surg Sports Traumatol Arthrosc.* 2012;20(9):1845-1849.
46. Slocum DB, James SL, Larson RL, Singer KM. Clinical test for anterolateral rotary instability of the knee. *Clin Orthop Relat Res.* 1976(118):63-69.
47. Snaebjornsson T, Hamrin Senorski E, Ayeni OR, et al. Graft Diameter as a Predictor for Revision Anterior Cruciate Ligament Reconstruction and KOOS and EQ-5D Values: A Cohort Study From the Swedish National Knee Ligament Register Based on 2240 Patients. *Am J Sports Med.* 2017;45(9):2092-2097.
48. Song EK, Seon JK, Yim JH, Woo SH, Seo HY, Lee KB. Progression of osteoarthritis after double- and single-bundle anterior cruciate ligament reconstruction. *Am J Sports Med.* 2013;41(10):2340-2346.
49. Suomalainen P, Jarvela T, Paakkala A, Kannus P, Jarvinen M. Double-bundle versus single-bundle anterior cruciate ligament reconstruction: a prospective randomized study with 5-year results. *Am J Sports Med.* 2012;40(7):1511-1518.
50. Suomalainen P, Kannus P, Jarvela T. Double-bundle anterior cruciate ligament reconstruction: a review of literature. *Int Orthop.* 2013;37(2):227-232.
51. Svantesson E, Sundemo D, Hamrin Senorski E, et al. Double-bundle anterior cruciate ligament reconstruction is superior to single-bundle reconstruction in terms of revision frequency: a study of 22,460 patients from the Swedish National Knee Ligament Register. *Knee Surg Sports Traumatol Arthrosc.* 2016.
52. Tegner Y, Lysholm J. Rating systems in the evaluation of knee ligament injuries. *Clin Orthop Relat Res.* 1985(198):43-49.
53. Tiamklang T, Sumanont S, Foocharoen T, Laopaiboon M. Double-bundle versus single-bundle reconstruction for anterior cruciate ligament rupture in adults. *Cochrane Database Syst Rev.* 2012;11:Cd008413.
54. Torg JS, Conrad W, Kalen V. Clinical diagnosis of anterior cruciate ligament instability in the athlete. *Am J Sports Med.* 1976;4(2):84-93.
55. Tsukada H, Ishibashi Y, Tsuda E, Fukuda A, Toh S. Anatomical analysis of the anterior cruciate ligament femoral and tibial footprints. *J Orthop Sci.* 2008;13(2):122-129.
56. van Eck CF, Kopf S, Irrgang JJ, et al. Single-bundle versus double-bundle reconstruction for anterior cruciate ligament rupture: a meta-analysis--does anatomy matter? *Arthroscopy.* 2012;28(3):405-424.
57. Wood L, Egger M, Gluud LL, et al. Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. *BMJ.* 2008;336(7644):601-605.
58. Xu Y, Ao YF, Wang JQ, Cui GQ. Prospective randomized comparison of anatomic single- and double-bundle anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 2014;22(2):308-316.
59. Yagi M, Wong EK, Kanamori A, Debski RE, Fu FH, Woo SL. Biomechanical analysis of an anatomic anterior cruciate ligament reconstruction. *Am J Sports Med.* 2002;30(5):660-666.

60. Yamazaki J, Muneta T, Koga H, et al. Radiographic description of femoral tunnel placement expressed as intercondylar clock time in double-bundle anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc.* 2011;19(3):418-423.
61. Ziegler CG, Pietrini SD, Westerhaus BD, et al. Arthroscopically pertinent landmarks for tunnel positioning in single-bundle and double-bundle anterior cruciate ligament reconstructions. *Am J Sports Med.* 2011;39(4):743-752.

Paper III

Biomechanical Comparison of Interference Screws and Combination Screw and Sheath Devices for Soft Tissue Anterior Cruciate Ligament Reconstruction on the Tibial Side

Cathrine Aga,^{*†} MD, Matthew T. Rasmussen,^{*} BS, Sean D. Smith,^{*} MSc, Kyle S. Jansson,^{*} BS, Robert F. LaPrade,[‡] MD, PhD, Lars Engebretsen,[§] MD, PhD, and Coen A. Wijdicks,^{*||} PhD
Investigation performed at the Department of BioMedical Engineering of the Steadman Philippon Research Institute, Vail, Colorado

Background: The tibial fixation site has been reported to be the weakest point in anterior cruciate ligament (ACL) reconstructions. Numerous interference screws and combination screw and sheath devices are available for soft tissue fixation, and a biomechanical comparison of these devices is necessary.

Hypothesis: Combination screw and sheath devices would provide superior soft tissue fixation properties compared with interference screws in a porcine model.

Study Design: Controlled laboratory study.

Methods: Eight different intratunnel tibial soft tissue fixation devices were biomechanically tested in a porcine model with bovine tendons, with 10 specimens per group. The soft tissue fixation devices included 3 interference screws—the Bio-Interference Screw, BIOSURE PK, and RCI Screw—and 5 combination screw and sheath devices (combination devices)—the AperFix II, BIOSURE SYNC, ExoShape, GraftBolt, and INTRAFIX. The specimens were subjected to cyclic (1000 cycles, 50-250 N, 0.5 Hz) and pull-to-failure loading (50 mm/min) with a dynamic tensile testing machine. Ultimate failure load (N), cyclic displacement (mm), pull-out stiffness (N/mm), displacement at failure (mm), load at 3 mm displacement (N), and mechanism of failure were recorded.

Results: The ultimate failure loads were highest for the GraftBolt (1136 ± 115.6 N), followed by the INTRAFIX (1127 ± 155.0 N), AperFix II (1122 ± 182.9 N), BIOSURE PK (990.8 ± 182.1 N), Bio-Interference Screw (973.3 ± 95.82 N), BIOSURE SYNC (829.5 ± 172.4 N), RCI Screw (817.7 ± 113.9 N), and ExoShape (814.7 ± 178.8 N). The AperFix II, GraftBolt, and INTRAFIX devices were significantly stronger than the BIOSURE SYNC, RCI Screw, and ExoShape. Although the 3 strongest devices were combination screw and sheath devices, no significant differences were observed between the ultimate failure strengths of the screw and combination devices when compared as groups. The least amount of cyclic displacement after 1000 cycles was observed for the GraftBolt (1.38 ± 0.27 mm), followed by the AperFix II (1.58 ± 0.21 mm), Bio-Interference Screw (1.61 ± 0.22 mm), INTRAFIX (1.63 ± 0.15 mm), ExoShape (1.68 ± 0.30 mm), BIOSURE PK (1.72 ± 0.29 mm), BIOSURE SYNC (1.92 ± 0.59 mm), and RCI Screw (1.97 ± 0.39 mm). The GraftBolt allowed significantly less displacement than did the BIOSURE SYNC and RCI Screw. Similarly, no significant differences were observed between the cyclic displacements of the screws and combination devices when compared as groups.

Conclusion: The combination screw and sheath devices did not provide superior soft tissue fixation properties compared with the interference screws alone in a porcine model. Although the highest ultimate failure loads and least amounts of cyclic displacement were observed for combination devices, group comparisons of screw and combination devices did not result in any significant differences for ultimate failure load and cyclic displacement.

Clinical Relevance: It is important to consider that these results represent device performance in an in vitro animal model and are not directly transferrable to an in vivo clinical situation. The combination of a sheath and screw did not consistently result in improved fixation characteristics compared with interference screw fixation.

Keywords: anterior cruciate ligament; ACL reconstruction; soft tissue graft; tibial fixation; hamstring graft; interference screw; sheath; intratunnel fixation; graft fixation; biomechanical testing

The tibial graft fixation site has been reported to be the weakest point in anterior cruciate ligament (ACL)

reconstructions.^{17,26} This has been reported to be due to the lower bone mineral density (BMD) of the proximal tibia compared with the distal femur and the angle at which the forces are applied to the graft on the tibial side.² In knee extension, the force vector of the ACL is in line with the tibial tunnel, which places maximal forces on the tibial graft fixation.² In addition, the healing process of tendon

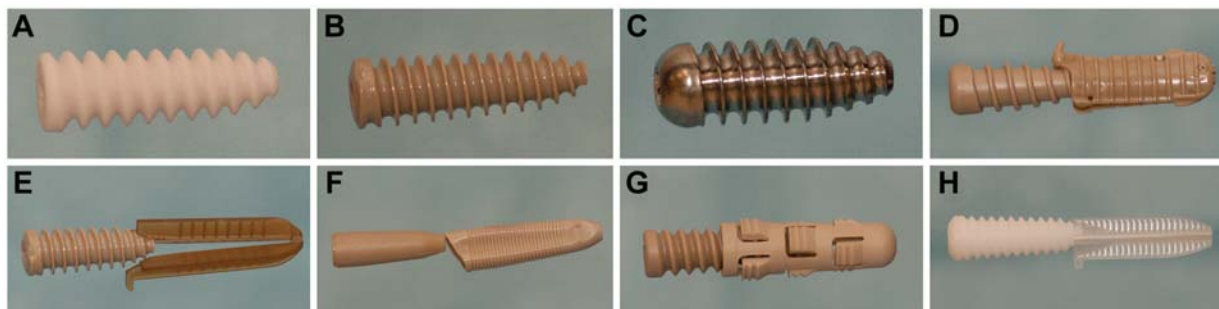


Figure 1. Soft tissue tibial fixation devices: (A) Bio-Interference Screw, (B) BIOSURE PK, (C) RCI Screw, (D) AperFix II, (E) BIOSURE SYNC, (F) ExoShape, (G) GraftBolt, and (H) INTRAFIX.

to bone in soft tissue graft fixation is slower than direct bone-to-bone healing, which can result in an increase in the potential for graft slippage.^{9,34} The intratunnel fixation has been shown to be more anatomically and biomechanically similar to the native ACL,¹⁷ although some studies have reported inferior biomechanical properties by this fixation method.^{2,18,34} The stiffness of the graft has been reported to be higher with intratunnel fixation,²⁶ but the fixation technique is highly dependent on the BMD.¹⁸ Concerns regarding the biomechanical properties of soft tissue graft fixation have resulted in the recommendation of maintaining a conservative rehabilitation protocol in the early postoperative period.¹³

Although numerous soft tissue tibial tunnel fixation devices exist, few studies have compared their biomechanical properties. Current research lacks a thorough analysis and comparison of interference screws and combination screw and sheath devices. The purpose of this study was to biomechanically compare 3 interference screws and 5 combination screw and sheath devices for intratunnel tibial soft tissue fixation in response to cyclic and pull-to-failure loading at time zero. We hypothesized that the combination screw and sheath devices would provide superior soft tissue fixation properties compared with the interference screws in a porcine model.

MATERIALS AND METHODS

Eight soft tissue tibial tunnel fixation devices were biomechanically evaluated in response to cyclic and pull-to-failure loading. Selected devices for testing included 3 interference screws—the Bio-Interference Screw (Arthrex Inc, Naples, Florida), BIOSURE PK (Smith & Nephew Inc, Andover,

Massachusetts), and the RCI Screw (Smith & Nephew)—and 5 combination screw and sheath devices (combination devices)—the AperFix II (Cayenne Medical Inc, Scottsdale, Arizona), BIOSURE SYNC (Smith & Nephew), ExoShape (MedShape Inc, Atlanta, Georgia), GraftBolt (Arthrex), and INTRAFIX (DePuy Mitek Inc, Raynham, Massachusetts) (Figure 1).

Specimen Preparation

Testing was performed in 80 fresh-frozen porcine tibias with 80 bovine extensor tendons (Innovative Medical Device Solutions, Logan, Utah). Bovine digital extensor tendons have been reported to have similar viscoelastic, structural, and material properties to human hamstring tendons.⁷ Specimens were stored at -20°C and thawed at room temperature before insertion of the devices and biomechanical testing. The specimens were randomly divided into 8 groups, with 10 specimens per group. The porcine model was used because previous studies have reported similar biomechanical properties to that of the young adult human knee.^{20,25,33} The tibia diaphysis was cut 14 cm distal to the joint line, and 3 screws were inserted orthogonally into the distal tibia before potting to ensure rigid fixation. The distal end of the tibia was potted in line with the tibial axis in a custom-made cylinder with polymethylmethacrylate (Fricke Dental International Inc, Streamwood, Illinois), 3 cm distal to the predetermined exit of the tibial tunnel.

On the day of preparation, grafts were thawed for 2 hours before device insertion. Each tendon was shortened to a length of 200 mm, and 50 mm of each end was split to create an intratunnel 4-stranded graft similar to human

^{||}Address correspondence to Coen A. Wijdicks, PhD, Department of BioMedical Engineering, Steadman Philippon Research Institute (SPRI), 181 W Meadow Dr, Suite 1000, Vail, CO 81657 (e-mail: cwijdicks@sprivail.org).

*Department of BioMedical Engineering, Steadman Philippon Research Institute, Vail, Colorado.

†Department of Orthopaedic Surgery, Oslo University Hospital, Oslo, Norway.

‡The Steadman Clinic, Vail, Colorado.

§Department of Orthopaedic Surgery, Oslo University Hospital and Faculty of Medicine, University of Oslo, Oslo, Norway.

One or more of the authors has declared the following potential conflict of interest or source of funding: Smith & Nephew, Arthrex, Cayenne Medical, MedShape, and DePuy Mitek donated the devices and instruments used in the study. Dr Aga is supported by a research scholar grant from Arthrex (Naples, Florida). Drs LaPrade and Engebretsen are consultants for Arthrex. The Steadman Philippon Research Institute is a 501(c)(3) nonprofit institution supported financially by private donations and corporate support from the following entities: Smith & Nephew Endoscopy, Arthrex, Siemens Medical Solutions USA, ConMed Linvatec, Össur Americas, Small Bone Innovations, Opedix, Evidence Based Apparel, and Sonoma Orthopedics.

TABLE 1
Corresponding Device, Material, and Tunnel Sizes for Use With a 9-mm Graft^a

Device	Screw Length, mm	Diameter, mm	Tunnel Diameter, mm	Material
Bio-Interference Screw ^b	28.0	9.0	9.0	PLDLA
BIOSURE PK ^b	30.0	9.0	9.0	PEEK
RCI Screw ^b	25.0	9.0	9.0	Titanium
AperFix II ^c	30.0	11.0	10.0	PEEK
BIOSURE SYNC ^c	32.5	11.0	9.0	PEEK
ExoShape ^c	30.0	9.0	9.0	PEEK
GraftBolt ^c	30.0	10.0	9.0	PEEK
INTRAFIX ^c	30.0	10.5	9.0	polyethylene (sheath) and acetal (screw)

^aPEEK, polyetheretherketone; PLDLA, bioabsorbable poly-LD-lactic acid.

^bScrew device.

^cCombination device (screw and sheath).

hamstring tendons. The grafts were doubled over and adjusted to 9 mm in diameter with a graft sizing block. Those that were smaller than 9 mm were excluded, and those that were larger than 9 mm were trimmed in line with the fiber orientation. Thirty millimeters of all 4 strands were whip-stitched with nonabsorbable polybraided propylene suture (Fiberloop No. 2; Arthrex).⁵ The grafts were wrapped in 0.9% saline-soaked gauze until use.

Device Insertion Techniques

All devices were inserted by a single surgeon according to the manufacturers' specifications with their recommended instruments. The device dimensions, material, and their corresponding tunnel sizes are listed in Table 1. An industry representative was present for pilot testing only for each device to ensure the correct manufacturer's insertion technique. Tibial tunnels were prepared using a tibia drill guide set at a 45° angle. The guide pin was advanced from the anteromedial proximal tibia through the footprint of the native ACL. The tunnel length was confirmed to be 40 mm with a depth gauge. All tibial tunnels were reamed to a diameter of 9 mm unless the manufacturer's recommendation was otherwise. The graft was manually pulled through the tibial tunnel from distal to proximal until approximately 50 mm of the graft had advanced through the proximal aperture. Proximally, the graft was looped over a rigid dowel, to simulate femoral fixation, while insertion of the respective devices in the tibial tunnel was performed. During the entirety of the procedure, 60 N of tension was applied to the graft distally and in line with the tunnel, as measured by a force gauge. All excess graft material and sutures were excised before testing.

AperFix II. In accordance with the manufacturer, a 10-mm diameter tibial tunnel was reamed for the 9-mm graft. The grafts were spread, and the sutures were fixed to a tendon expander. A guide wire was placed concentric between the grafts, and a 10-mm sheath implant was inserted over the guide wire. The sheath's tab was set at the 12-o'clock position. Then, the screw was inserted over the guide wire and flush with the cortical bone while the tab remained secured outside the cortex.

Bio-Interference Screw. A 1.1-mm diameter guide wire was placed in the tibial tunnel concentric between the grafts, and a 9-mm screw was inserted over the guide wire until it was flush with the cortical bone.

BIOSURE PK. A 1.2-mm diameter guide wire was placed concentric and a 9-mm screw was inserted over the guide wire until it was flush with the cortical bone.

BIOSURE SYNC. A 9- to 10-mm dilator was inserted into the distal 35 mm of the tibial tunnel with a mallet. The guide wire was placed concentric between the grafts. Then, a 9- to 10-mm sheath and a 9-mm screw were inserted over the guide wire, and the sheath's tab was positioned at the 12-o'clock position. The screw was inserted flush with the cortical bone, and the tab was removed.

ExoShape. A guide wire was inserted concentric between the grafts, and the tunnel diameter was dilated sequentially from 7 to 9 mm. The sheath was inserted over the guide wire into the tunnel, and the tibial insert was introduced into the sheath. All devices were inserted flush to the cortical bone.

GraftBolt. A 1.1-mm diameter guide wire was placed concentric between the grafts, and the 6-mm dilator was inserted over the wire. The tunnel diameter was dilated sequentially from 6 to 9 mm in diameter. Then, the 9-mm combined sheath and screw device was inserted until the screw was flush with the cortical bone.

INTRAFIX. First, a dilator was used to adjust the tunnel, and then a guide wire, with concentric placement between the grafts, was used to guide an 8- to 10-mm sheath and an 8- to 10-mm screw into the tibial tunnel. The sheath's tab was orientated to the 12-o'clock position. The screw was inserted flush with the cortical bone.

RCI Screw. A 2.1-mm diameter guide wire was placed concentric between the grafts. The 9-mm screw was inserted over the guide wire until it was flush with the cortical bone.

Biomechanical Testing

Screws and combination devices were evaluated in response to cyclic and pull-to-failure loading with a dynamic tensile testing system (Instron ElectroPuls



Figure 2. Biomechanical test setup with the advanced video extensometer (left) and customized alignment fixture (bottom right), which allowed for the force vector to be applied in line with the tibial tunnel.

E10000; Instron Systems, Norwood, Massachusetts). The proximal 50-mm portion of the graft was looped over a 4.5-mm diameter stainless steel pin and rigidly fixed to the actuator, while the tibia was secured to the base plate of the test frame with a custom jig (Figure 2).³³ The jig was adjusted and positioned so that the tensile force applied to the tendon was in line with the tibial tunnel to mimic the worst-case scenario for both pullout and displacement. Tracking markers were placed on the tibial plateau, at a distance representative of the inserted device's end point within the tibial tunnel, and at the center of the pin pulling the graft on the actuator. An advanced video extensometer (Instron Systems) tracked the markers and recorded tendon extension relative to the proximal surface of the device, independent of any bone deflection.

Test parameters for the cyclic and pull-to-failure testing protocol were selected after a literature search and synthesis of common parameters from the various protocols. As a result, the graft was first preloaded in tension from 10 to 50 N at 0.1 Hz for 10 cycles, then loaded between 50 and 250 N for 1000 cycles at a frequency of 0.5 Hz.^{3,22,23,33} This simulated the reported forces in the ACL during passive extension while walking and the early rehabilitation protocol of flexion-extension loading on the reconstructed graft.¹⁹ After the cyclic loading protocol, grafts were further displaced at 50 mm/min until failure¹⁶ to simulate a sudden overload event at the knee. Cyclic loading data were recorded by the Instron WaveMatrix software, and load-to-failure data were recorded by the Instron Bluehill 2 software (Instron Systems). Biomechanical measurements, including ultimate failure load (N), pull-out displacement (mm), load at 3-mm displacement (N), energy at failure (J), pull-out stiffness (N/mm), and cyclic displacement (mm), were measured and recorded. Pull-to-failure displacement was measured as the total elongation at ultimate failure and accounted for tendon elongation, graft slippage or tearing, and device pullout. The cyclic displacement was determined as the displacement from the initial 50 N ramp-up position after the preconditioning cycles to the final position at 50 N after the thousandth cycle. Stiffness was calculated from the

same linear portion of the load-elongation curves from the pull-to-failure raw data. The mechanism of failure (graft slippage, graft tear, device pullout, etc) was observed and recorded.^{31,33}

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics, version 20 (SPSS Inc, Chicago, Illinois). The biomechanical results were analyzed using 1-way analyses of variance, and post hoc Tukey tests were performed to determine if there was a difference among the fixation devices and the group comparisons between screws and combination devices for each of the measured quantities of interest. *P* values less than .05 were deemed statistically significant. The observed effect sizes (*f*) for overall comparison of the 8 devices with respect to ultimate failure load and cyclic displacement were 8.67 and 3.33, respectively. Both values are much larger than the threshold for a "large" effect size defined by Cohen in 1988,⁶ leading us to conclude that our sample size was sufficient to provide very high statistical power for the overall comparison tests we performed.

RESULTS

Test results from the pull-to-failure loading and cyclic loading are reported in Table 2 (mean \pm standard deviation), and *P* values for device comparisons are reported in Table 3.

Pull-to-Failure Loading

Average ultimate failure loads for the AperFix II, GraftBolt, and INTRAFIX were significantly higher than loads for the BIOSURE SYNC, RCI Screw, and ExoShape (*P* < .05). No significant differences in ultimate failure load were found when comparing the screw group and combination group. In addition, there were no significant differences among the devices for pull-out displacement, load at 3 mm of displacement, energy at failure, or pull-out stiffness. The recorded failure modes were classified as slippage, tear at the tendon-screw interface, or pullout of the screw. There were no differences between the devices in their mode of failure. All the devices failed at the tibial fixation site.

Cyclic Loading

All specimens survived preloading and cyclic testing. The GraftBolt displaced significantly less than the RCI Screw and BIOSURE SYNC after 1000 cycles (*P* < .05). All devices displaced less than 2 mm. No significant differences in cyclic displacement were observed when comparing the screw group and combination group.

DISCUSSION

The results of the current study did not support our hypothesis that combination screw and sheath devices would provide superior soft tissue fixation properties compared with

TABLE 2
Biomechanical Properties of Tibial Soft Tissue Fixation Devices^a

Device	Cyclic Displacement, mm	Ultimate Failure, N	Displacement at Failure, mm	Load at 3-mm Displacement, mm	Pull-Out Stiffness, N/mm	Energy at Ultimate Failure, J
Bio-Interference Screw ^b	1.61 ± 0.22	973.3 ± 95.82	5.31 ± 0.51	703.8 ± 74.50	343.0 ± 46.43	2.92 ± 0.51
BIOSURE PK ^b	1.72 ± 0.29	990.8 ± 182.1	5.65 ± 1.35	721.2 ± 92.45	352.3 ± 42.73	3.45 ± 1.40
RCI Screw ^b	1.97 ± 0.39	817.7 ± 114.0	4.80 ± 2.07	676.3 ± 157.2	384.3 ± 105.2	4.80 ± 2.07
AperFix II ^c	1.58 ± 0.21	1122 ± 182.9	5.43 ± 1.54	782.8 ± 171.0	366.4 ± 40.76	3.66 ± 1.05
BIOSURE SYNC ^c	1.92 ± 0.59	829.5 ± 172.4	6.54 ± 2.90	632.0 ± 154.9	326.9 ± 74.51	6.54 ± 2.90
ExoShape ^c	1.68 ± 0.30	814.7 ± 178.8	5.27 ± 1.25	663.8 ± 125.5	342.3 ± 51.47	2.80 ± 1.10
GraftBolt ^c	1.38 ± 0.27	1136 ± 115.6	5.98 ± 1.47	767.6 ± 146.0	402.3 ± 58.89	4.00 ± 1.47
INTRAFIX ^c	1.63 ± 0.15	1127 ± 155.0	6.43 ± 1.24	709.9 ± 118.4	372.5 ± 50.02	4.38 ± 1.64

^aData are shown as means ± standard deviations.

^bScrew device.

^cCombination device (screw and sheath).

the interference screws in a porcine model. The 3 devices with the highest ultimate failure loads were the AperFix II, GraftBolt, and INTRAFIX, all of which were combination devices. However, the lowest and third lowest ultimate failure loads were observed for the ExoShape and BIOSURE SYNC, both combination devices. The cyclic displacement results were more dispersed when comparing the combination devices and interference screws, with mixed results for both types of devices. Comparing the screw and combination device groups, we could not definitively conclude any significant difference between the biomechanical properties of these devices.

There are multiple factors reported to improve tibial intratunnel biomechanical fixation: ensuring tunnel diameter is within 0.5 mm of the graft size,²⁹ increasing screw length,^{14,27,34,35} using a screw diameter sized according to the tunnel size,^{14,34,35} and concentric placement of the screw in the tunnel.²⁸ Combination devices, which incorporate an interference screw with a sheath, attempt at improving fixation characteristics by increasing radial force and compression on the graft against the tunnel wall.^{30,31} The purpose of the sheath is to reportedly separate the grafts, secure concentric placement of the screw, and provide homogeneous friction between the tendon and bone.³⁰

Devices were inserted according to the manufacturers' recommendations, and some differences in insertion techniques were observed between devices. Some insertion techniques have incorporated additional tunnel dilations, in addition to simple tunnel reaming, in an effort to create impaction of the surrounding cancellous bone, increase tunnel wall bone volume, and subsequently increase fixation strength.⁸ Serial dilation up to the desired tunnel diameter can have different effects on the bone surrounding the tunnel than simply reaming the desired diameter. Contrary to cortical bone, the cancellous bone that surrounds the tunnel is less dense and contains a structural framework that can be compressed. Dunkin et al⁸ reported that performing a serial dilation up to the desired tunnel diameter results in increased bone volume when compared with extraction drilling. This implies that the device can obtain a more rigid fixation within the reconstruction tunnel wall and possibly influence soft tissue fixation

strength; however, studies have demonstrated conflicting results. Dunkin et al⁸ reported that serial dilation in porcine tibias did not significantly improve biomechanical fixation properties. Rittmeister et al²⁴ reported similar findings using cadaveric human tibias. However, 2 studies using cadaveric human and animal specimens have reported some beneficial effects of dilation on fixation properties.^{4,10} Dunkin et al⁸ have reported that dilation has less effect in bone with high BMD, which may explain why a beneficial effect was observed in studies such as Cain et al,⁴ which used human cadaver specimens much older than the typical population that receives an ACL reconstruction.^{4,8} Four of the tested devices in this study used tunnel dilation at the time of insertion. To maintain the integrity of the intended insertion of each device, standardization of the insertion techniques was deemed to be outside the scope for this study. This decision was supported by the lack of a clear distinction of whether serial dilation could definitively improve fixation strength for all devices. Devices were inserted according to the manufacturers' recommended technique for optimal fixation with that device. Although the reported effects of tunnel dilation on fixation strength are mixed, in the present study, we did not observe any correlation between dilation of tunnel diameter and improved fixation properties. Screw diameter has been reported to significantly influence fixation strength.^{34,35} Four of the tested devices had larger diameters than the corresponding bone tunnels. Consistent with the results reported by Weiler et al,³⁴ 3 of these devices—the AperFix II, GraftBolt, and INTRAFIX—produced the highest ultimate failure loads observed in this study. In addition, we did not observe any correlation between the material of the device and its biomechanical properties, which is supported by similar results that have been reported in the literature.¹⁵

Within the past decade, multiple studies have performed biomechanical comparisons of specific interference screws and combination screw and sheath devices. The present study was the first to evaluate more than one combination device. In 2003, a study by Koussa et al¹⁶ compared the biomechanical properties between 3 interference screws, a combination screw and sheath device, and 2

TABLE 3
P Values of Device Comparisons for Ultimate Failure Load and Cyclic Displacement^a

Ultimate Failure Load								
	Bio-Interference Screw ^b	BIOSURE PK ^b	RCI Screw ^b	AperFix II ^c	BIOSURE SYNC ^c	ExoShape ^c	GraftBolt ^c	INTRAFIX ^c
Bio-Interference Screw ^b	—	1.000	.324	.379	.426	.300	.272	.339
BIOSURE PK ^b	1.000	—	.201	.543	.280	.184	.416	.497
RCI Screw ^b	.324	.201	—	.001	1.000	1.000	< .001	.001
AperFix II ^c	.379	.543	.001	—	.001	.001	1.000	1.000
BIOSURE SYNC ^c	.426	.280	1.000	.001	—	1.000	.001	.001
ExoShape ^c	.300	.184	1.000	.001	1.000	—	< .001	.001
GraftBolt ^c	.272	.416	< .001	1.000	.001	< .001	—	1.000
INTRAFIX ^c	.339	.497	.001	1.000	.001	.001	1.000	—
Cyclic Displacement								
	Bio-Interference Screw ^b	BIOSURE PK ^b	RCI Screw ^b	AperFix II ^c	BIOSURE SYNC ^c	ExoShape ^c	GraftBolt ^c	INTRAFIX ^c
Bio-Interference Screw ^b	—	.995	.235	1.000	.411	1.000	.772	1.000
BIOSURE PK ^b	.995	—	.690	.974	.868	1.000	.302	.999
RCI ^b	.235	.690	—	.144	1.000	.484	.004	.309
AperFix II ^c	1.000	.974	.144	—	.277	.997	.887	1.000
BIOSURE SYNC ^c	.411	.868	1.000	.277	—	.699	.010	.507
ExoShape ^c	1.000	1.000	.484	.997	.699	—	.489	1.000
GraftBolt ^c	.772	.302	.004	.887	.010	.489	—	.682
INTRAFIX ^c	1.000	.999	.309	1.000	.507	1.000	.682	—

^aP values < .05 were considered significant and are in bolded text.

^bScrew device.

^cCombination device (screw and sheath).

extracortical devices, using pull-to-failure and cyclic loading in porcine tibias with human hamstring tendon grafts. This study reported that the combination device (INTRAFIX) provided significantly higher ultimate failure strength and lower displacement compared with the other devices. The reported ultimate failure load and displacement for the INTRAFIX device were comparable with our results. Halewood et al¹¹ compared the soft tissue fixation properties on the tibial side of the EZ KneeSpan (EZ Orthopedics Ltd) with those of a titanium interference screw in human cadaver specimens with bovine digital extensor tendon grafts. The EZ KneeSpan reportedly resulted in significantly less graft slippage but did not significantly improve ultimate failure strength on the tibial side when compared with interference screw fixation. The reported ultimate failure strength of the titanium screw was approximately 70% of the ultimate failure strength reported for the RCI Screw in the present study. However, the age of the cadaver specimens used by Halewood et al¹¹ ranged from 62 to 71 years. The lower BMD associated with older cadaver specimens and higher BMD associated with young porcine specimens may elucidate the differences in results. Device design, loading rate, and device, graft, and tunnel diameters are additional factors to consider. In 2009, Walsh et al³³ biomechanically compared a retrograde bioabsorbable screw, suture button suspension apparatus, and a combination of the 2 devices in porcine tibias with bovine digital extensor tendons. Reported

ultimate failure loads for the retrograde screw and combined retrograde screw and suture button were similar to the results observed for the tested devices in the present study. However, the present study focused on antegrade fixation and did not specifically test a retrograde screw. Caborn et al³ performed a biomechanical comparison of the INTRAFIX device and a bioabsorbable interference screw in human cadaver tibias and human hamstring tendon grafts. The INTRAFIX was reported to fail on average at 796 N, which was about 30% less than what was observed in the present study. Caborn et al³ performed testing in human cadaver tibias with a reported average BMD of 0.74 g/cm³, which is much less than what has been reported for young human bone (1.30 g/cm³).²⁰ Differences in results may be explained by our use of porcine bone in the present study, which reportedly has similar BMD to young human bone,³³ and the use of human bone by Caborn et al³ with BMD not representative of the young population, which typically would receive this procedure clinically.

One of the strengths and innovative qualities of this study was the use of an advanced video extensometer (AVE) to record displacement during cyclic and pull-to-failure testing. We believe that this improves upon previous studies that relied on actuator positions to report displacement. With the nature of the construct, the tibia diaphysis adds an elastic deflection between the potting and the device insertion when the load is applied at an angle relative to the axis of the tibia. Displacements

recorded by the actuator include displacements of the fixture, bone, and tendon. Even though all the tibias were cut to a similar length, differences in the inherent properties of each specimen could influence the amount of displacement recorded by the actuator. Use of the AVE allowed for isolated displacement of the tendon to be recorded, independent of bone deflection and fixture slippage. This might explain our smaller displacement values compared with previous studies.^{16,33}

We do acknowledge the presence of limitations within our study design. The results achieved through an in vitro biomechanical study in an animal model cannot be transferred to a clinical setting. From previous research, it is known that the porcine model has a higher BMD in the proximal tibia compared with human cadavers.^{1,2,21} All tested devices are dependent on dense bone stock, and the pull-out strength and stiffness could be overestimated compared with an in vivo model.^{1,18,21} Although the findings of Bailey et al,¹ Magen et al,¹⁸ and Nurmi et al²¹ suggest that porcine models should not be used for the evaluation of tibial interference fixation devices, there are also findings that promote their use. Previous studies have reported that the mean BMD in young porcine bone (24 months) is 1.42 g/cm^{2,33} which is similar to the average BMD of young humans aged 20 to 29 years (1.30 ± 0.11 g/cm²).²⁰ Since the mean age of a patient undergoing ACL reconstruction has been reported to be about 26 years,¹² young porcine bone can serve as an acceptable substitute. In addition, obtaining cadaveric specimens within this age range is often not possible, forcing studies to use older specimens with lower BMD, which may underestimate the fixation strength of the devices.^{3,11,32} In studies testing a limited number of specimens, dual x-ray absorptiometry (DEXA) scans can be useful for equally dividing high BMD specimens between groups and preventing biased outcomes.³³ Although the BMD of the tested specimens in our study was unknown, the inclusion of a high number of specimens (n = 10) compared with previous studies, as well as the random distribution of specimens between groups, helped to prevent disproportional bone quality between groups.^{3,8,23,31,33,35} Last, as is the case with any study performed in an in vitro biomechanical model, the in vivo biologic aspects for healing were not present, and the results were predictive of time zero fixation.

CONCLUSION

The combination screw and sheath devices did not provide superior soft tissue fixation properties compared with the interference screws alone in a porcine model. Although the highest ultimate failure loads and least amounts of cyclic displacement were observed for combination devices, some of the combination devices provided inferior fixation properties compared with interference screw fixation. Group comparisons of screw and combination devices did not show any significant differences. The combination of a screw and sheath did not consistently result in improved fixation characteristics compared with interference screw fixation. Although use of a porcine model had anatomic, biologic, and clinical limitations, this study used

a consistent and reproducible biomechanical model to compare the fixation characteristic of these devices and appropriately investigated the hypothesis of the study.

ACKNOWLEDGMENT

We thank, in alphabetical order, Arthrex, Cayenne Medical, DePuy Mitek, MedShape, and Smith & Nephew for donating the devices and instrumentation used for this study. We also acknowledge Grant Dornan, MSc, for his contribution of statistical expertise to the analysis of this study.

REFERENCES

- Bailey SB, Grover DM, Howell SM, Hull ML. Foam-reinforced elderly human tibia approximates young human tibia better than porcine tibia: a study of the structural properties of three soft tissue fixation devices. *Am J Sports Med.* 2004;32(3):755-764.
- Brand J Jr, Weiler A, Caborn DN, Brown CH Jr, Johnson DL. Graft fixation in cruciate ligament reconstruction. *Am J Sports Med.* 2000;28(5):761-774.
- Caborn DN, Brand JC Jr, Nyland J, Kocabay Y. A biomechanical comparison of initial soft tissue tibial fixation devices: the Intrafix versus a tapered 35-mm bioabsorbable interference screw. *Am J Sports Med.* 2004;32(4):956-961.
- Cain EL, Phillips BB, Charlebois SJ, Azar FM. Effect of tibial tunnel dilation on pullout strength of semitendinosus-gracilis graft in anterior cruciate ligament reconstruction. *Orthopedics.* 2005;28(8):779-783.
- Charlick DA, Caborn DN. Technical note: alternative soft-tissue graft preparation technique for cruciate ligament reconstruction. *Arthroscopy.* 2000;16(8):E20.
- Cohen J. *Statistical Power Analysis for the Behavioral Sciences.* 2nd ed. Hillsdale, NJ: Lawrence Erlbaum; 1988.
- Donahue TL, Gregersen C, Hull ML, Howell SM. Comparison of viscoelastic, structural, and material properties of double-looped anterior cruciate ligament grafts made from bovine digital extensor and human hamstring tendons. *J Biomech Eng.* 2001;123(2):162-169.
- Dunkin BS, Nyland J, Duffee AR, Brunelli JA, Burden R, Caborn D. Soft tissue tendon graft fixation in serially dilated or extraction-drilled tibial tunnels: a porcine model study using high-resolution quantitative computerized tomography. *Am J Sports Med.* 2007;35(3):448-457.
- Goradia VK, Rochat MC, Kida M, Grana WA. Natural history of a hamstring tendon autograft used for anterior cruciate ligament reconstruction in a sheep model. *Am J Sports Med.* 2000;28(1):40-46.
- Green JR, Nemzek JA, Arnoczky SP, Johnson LL, Balas MS. The effect of bone compaction on early fixation of porous-coated implants. *J Arthroplasty.* 1999;14(1):91-97.
- Halewood C, Hirschmann MT, Newman S, Hleihil J, Chaimski G, Amis AA. The fixation strength of a novel ACL soft-tissue graft fixation device compared with conventional interference screws: a biomechanical study in vitro. *Knee Surg Sports Traumatol Arthrosc.* 2011;19(4):559-567.
- Harner CD, Fu FH, Irrgang JJ, Vogrin TM. Anterior and posterior cruciate ligament reconstruction in the new millennium: a global perspective. *Knee Surg Sports Traumatol Arthrosc.* 2001;9(6):330-336.
- Heijne A, Werner S. Early versus late start of open kinetic chain quadriceps exercises after ACL reconstruction with patellar tendon or hamstring grafts: a prospective randomized outcome study. *Knee Surg Sports Traumatol Arthrosc.* 2007;15(4):402-414.
- Herrera A, Martinez F, Iglesias D, Cegonino J, Ibarz E, Gracia L. Fixation strength of biocomposite wedge interference screw in ACL reconstruction: effect of screw length and tunnel/screw ratio. A controlled laboratory study. *BMC Musculoskelet Disord.* 2010;11:139.
- Kousa P, Jarvinen TL, Kannus P, Jarvinen M. Initial fixation strength of bioabsorbable and titanium interference screws in anterior cruciate ligament reconstruction: biomechanical evaluation by single cycle and cyclic loading. *Am J Sports Med.* 2001;29(4):420-425.

16. Kousa P, Jarvinen TL, Vihavainen M, Kannus P, Jarvinen M. The fixation strength of six hamstring tendon graft fixation devices in anterior cruciate ligament reconstruction, part II: tibial site. *Am J Sports Med.* 2003;31(2):182-188.
17. Kurosaka M, Yoshiya S, Andrich JT. A biomechanical comparison of different surgical techniques of graft fixation in anterior cruciate ligament reconstruction. *Am J Sports Med.* 1987;15(3):225-229.
18. Magen HE, Howell SM, Hull ML. Structural properties of six tibial fixation methods for anterior cruciate ligament soft tissue grafts. *Am J Sports Med.* 1999;27(1):35-43.
19. Markolf KL, Gorek JF, Kabo JM, Shapiro MS. Direct measurement of resultant forces in the anterior cruciate ligament: an in vitro study performed with a new experimental technique. *J Bone Joint Surg Am.* 1990;72(4):557-567.
20. Nagarkatti DG, McKeon BP, Donahue BS, Fulkerson JP. Mechanical evaluation of a soft tissue interference screw in free tendon anterior cruciate ligament graft fixation. *Am J Sports Med.* 2001;29(1):67-71.
21. Nurmi JT, Sievanen H, Kannus P, Jarvinen M, Jarvinen TL. Porcine tibia is a poor substitute for human cadaver tibia for evaluating interference screw fixation. *Am J Sports Med.* 2004;32(3):765-771.
22. Prado M, Martin-Castilla B, Espejo-Reina A, Serrano-Fernandez JM, Perez-Blanca A, Ezquerro F. Close-looped graft suturing improves mechanical properties of interference screw fixation in ACL reconstruction [published online March 30, 2012]. *Knee Surg Sports Traumatol Arthrosc.* doi:10.1007/s00167-012-1975-9.
23. Rhee PC, Levy BA, Stuart MJ, Thoreson A, An KN, Dahm DL. A biomechanical comparison of the Delta screw and RetroScrew tibial fixation on initial intra-articular graft tension. *Knee Surg Sports Traumatol Arthrosc.* 2011;19(5):781-786.
24. Rittmeister ME, Noble PC, Bocell JR Jr, Alexander JW, Conditt MA, Kohl HW III. Interactive effects of tunnel dilation on the mechanical properties of hamstring grafts fixed in the tibia with interference screws. *Knee Surg Sports Traumatol Arthrosc.* 2001;9(5):267-271.
25. Rupp S, Seil R, Krauss PW, Kohn DM. Cortical versus cancellous interference fixation for bone-patellar tendon-bone grafts. *Arthroscopy.* 1998;14(5):484-488.
26. Scheffler SU, Sudkamp NP, Gockenjan A, Hoffmann RF, Weiler A. Biomechanical comparison of hamstring and patellar tendon graft anterior cruciate ligament reconstruction techniques: the impact of fixation level and fixation method under cyclic loading. *Arthroscopy.* 2002;18(3):304-315.
27. Selby JB, Johnson DL, Hester P, Caborn DN. Effect of screw length on bioabsorbable interference screw fixation in a tibial bone tunnel. *Am J Sports Med.* 2001;29(5):614-619.
28. Shino K, Pflaster DS. Comparison of eccentric and concentric screw placement for hamstring graft fixation in the tibial tunnel. *Knee Surg Sports Traumatol Arthrosc.* 2000;8(2):73-75.
29. Simonian PT, Wickiewicz TL, O'Brien SJ, Dines JS, Schatz JA, Warren RF. Pretibial cyst formation after anterior cruciate ligament surgery with soft tissue autografts. *Arthroscopy.* 1998;14(2):215-220.
30. Smith KE, Garcia M, McAnuff K, et al. Anterior cruciate ligament fixation: is radial force a predictor of the pullout strength of soft-tissue interference devices? *Knee.* 2012;19(6):786-792.
31. Stadelmaier DM, Lowe WR, Ilahi OA, Noble PC, Kohl HW III. Cyclic pull-out strength of hamstring tendon graft fixation with soft tissue interference screws: influence of screw length. *Am J Sports Med.* 1999;27(6):778-783.
32. Steenlage E, Brand JC Jr, Johnson DL, Caborn DN. Correlation of bone tunnel diameter with quadrupled hamstring graft fixation strength using a biodegradable interference screw. *Arthroscopy.* 2002;18(8):901-907.
33. Walsh MP, Wijdicks CA, Parker JB, Hapa O, LaPrade RF. A comparison between a retrograde interference screw, suture button, and combined fixation on the tibial side in an all-inside anterior cruciate ligament reconstruction: a biomechanical study in a porcine model. *Am J Sports Med.* 2009;37(1):160-167.
34. Weiler A, Hoffmann RF, Siepe CJ, Kolbeck SF, Sudkamp NP. The influence of screw geometry on hamstring tendon interference fit fixation. *Am J Sports Med.* 2000;28(3):356-359.
35. Weiler A, Windhagen HJ, Raschke MJ, Laumeyer A, Hoffmann RF. Biodegradable interference screw fixation exhibits pull-out force and stiffness similar to titanium screws. *Am J Sports Med.* 1998;26(1):119-126.