Anterior cruciate ligament injury and surgery
Muller, B.

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This thesis deals with current issues in diagnostics, surgery and outcome measurement of anterior cruciate ligament injury. Throughout all segments of the treatment spectrum, subjective findings, opinion and assumption have long dictated examination procedures and management protocols. This work is meant to provide a more objective take on anterior cruciate ligament injury and surgery.
ANTERIOR CRUCIATE LIGAMENT INJURY AND SURGERY
-A MORE OBJECTIVE TAKE-

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ANTERIOR CRUCIATE LIGAMENT INJURY AND SURGERY
-A MORE OBJECTIVE TAKE-

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aan de Universiteit van Amsterdam
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in het openbaar te verdedigen in de Aula der Universiteit
op vrijdag 23 maart 2018 om 11.00 uur

door Bart Muller

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Development of Computer Tablet Software for Clinical Quantification of Lateral Knee Compartment Translation During the Pivot Shift Test.

Indications and contraindications for double-bundle ACL reconstruction.
Bart Muller, Marcus Hofbauer, Jidapa Wongcharoenwatana, Freddie H. Fu

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Kellie K. Middleton, Bart Muller, Paulo H. Araujo, Yoshimasa Fujimaki, Stephen J. Rabuck, James J. Irrgang, Scott Tashman, Freddie H. Fu

Anatomic Anterior Cruciate Ligament Reconstruction -Reducing Anterior Tibial Subluxation
Bart Muller, Eric R. H. Duerr, C. Niek van Dijk, Freddie H. Fu

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ACL Graft Healing and Biologics.
Bart Muller, Karl F. Bowman, Asheesh Bedi
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Bart Muller, Mohammad A. Yabroudi, Andrew Lynch, Chung-Liang Lai, C. Niek van Dijk, Freddie H. Fu, James J. Irrgang
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Defining Thresholds for the Patient Acceptable Symptom State for the International Knee Documentation Committee (IKDC) Subjective Knee Form and Knee injury and Osteoarthritis Outcome Score (KOOS) for Patients that Underwent ACL Reconstruction
Bart Muller, Mohammad A. Yabroudi, Andrew Lynch, Chung-Liang Lai, C. Niek van Dijk, Freddie H. Fu, James J. Irrgang
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Chapter 1

General Introduction
ANATOMY

The fundament for orthopaedic surgery is anatomy. In case of the anterior cruciate ligament (ACL) this fundament reaches back to ancient times. Already in 3000BC the anatomy of the ACL was described by Papyrus, an Assyrian in Egypt. Hippocrates then (460–370BC) was first to attribute function to the cruciate ligaments, suggesting that knee instability after a traumatic distortion may be the result of torn internal ligaments. Claudius Galenus, a Greek physician in the Roman Empire (129-216AD) is credited for naming the cruciate ligaments by their appearance of crossing over: ‘ligamenta genu cruciata’. Hereafter, no scientific mention was made of the cruciate ligaments for almost 2000 years. It was not until 1836 that Wilhem Weber (1804-1891), Professor of Physics in Göttingen, and his brother Eduard Weber (1806-1871), Professor of Anatomy and Physiology in Leipzig, showed that transecting the ACL results in anterior tibial translation. Moreover, the brothers showed that the ACL consists of distinctively different bundles, that have different tensioning patterns throughout the range of motion of the knee.

CLINICAL PRESENTATION

In 1837, the Irish surgeon Robert Adams of Dublin (1791–1875) was first to describe the clinical presentation of an ACL rupture. He described a drunk young man who injured his knee wrestling and died some three weeks later from a septic arthritis. Upon autopsy it was found that the ACL had torn off the tibia with avulsed bony fragment. Amadeé Bonnet (1809-1858), Professor of Surgery at Lyon university, published his ‘Traité des Maladies des Articulations’ in 1845 in which he described three characteristics indicative of an ACL tear: “in patients who have not suffered a fracture, a snapping noise, haemarthrosis, and loss of function are characteristic of ligamentous injury in the knee”. Contrary to what Adams had described, Bonnet found through cadaver experiments that ACL tears were more likely to occur close to the femoral insertion. In addition, he described the subluxation phenomenon of the tibia after ACL injury, which later became known as the pivot-shift.

Although named after John Lachman (1919-2007), in 1875 already, the Greek Georgios Noulis (1849–1915) defended his PhD thesis ‘Entorse du Genou’, in which a diagnostic exam was described that we now know as the Lachman test: “…fix the thigh with one hand; with the other hand hold the lower leg just below the knee with the thumb in front and the fingers behind; then, try to shift the tibia forward
and backward … when only the anterior cruciate ligament is transected, this forward movement is seen when the knee is barely flexed.251

Well before the discovery of Röntgen in 1895, the French surgeon Paul Segond (1851-1912) described an avulsion fracture off the lateral side of the tibia in 1879 already: “This lesion is pathognomonic of torsion of the knee in internal rotation and slight flexion of the lower leg and is associated with rupture of the anterior cruciate ligament”.282 Segond also recognized that this fracture was caused by a “pearly, resistant, fibrous band” at the anterolateral aspect of the human knee,282 which was only described as a separate anatomical structure as the anterolateral ligament (ALL) in 2013.62

TREATMENT

The first report of treatment of ACL injury was by James Stark (1811–1890), a general practitioner from England, who observed two cases of ACL tears in 1839 and 1841, respectively. He treated the injury initially with three months of immobilization followed by ten months using a brace that he described as a “finely fitting laced stocking, made of Saxony broadcloth, and a broad flat steel spring sewed to the back of it”.297

Although the English William Battle (1855–1936) was first to publish successful results of an open ACL repair with a silk suture in 1900,35 it was Sir Arthur Mayo-Robson (1853–193) who was the first to perform an open ACL repair with catgut suture in 1895.227 Their reports, and many that would follow, presented good clinical results thereby supporting suture repair to be the standard of care way into the early 1980s.

It was in 1976 that John Feagin presented his conclusions from a 5-year follow-up study: “long term follow-up evaluations do not justify the hope … that anatomic repositioning of the residual ligament would result in healing”.91 These conclusions were shared by Werner Müller and Lars Engebretsen,89,236 and by the 1990s primary suture repair was abandoned altogether and led the way towards ACL reconstruction.

Since the first extra-articular ACL reconstruction with strips of fascia lata by Knut Gieritz in 1913, many techniques have been described. The first anatomic augmentation procedure was performed by Ivan Grekov in 1914, followed three years later by the first complete reconstruction of the ACL by Ernest William Hey Groves (1872–1944) in 1917. In accordance with current beliefs, Hey Groves already stated that graft positioning was vital for re-establishing proper knee joint function “in contradistinction to a mere passage of new ligaments across the joint” and thus should run oblique “because an anterior ligament will be efficient in preventing anterior tibial displacement in proportion to its obliquity”.138,139
TECHNICAL DEVELOPMENT

In the years after, many reports on ACL reconstruction techniques and different graft materials followed. Initially, the fascia lata was used, but found inadequate to duplicate the original anatomy with. In 1917 Max Zur Verth used the meniscus as a graft source, but he already noted that that meniscus was “functionally unsuitable to replace a ligament” for it has properties withstanding compression, rather than tension and shear. He was eventually proven right and meniscal tissue was eventually abandoned as a graft source by the end of 1980s. Ever since the very early 1900s, synthetic grafts have intrigued surgeons. Thus far however, all have led to either failures, including graft rupture, osteolytic tunnel widening, foreign body reaction, chronic synovitis, and poor graft-incorporation, and it was eventually conceded that in vivo stresses exceed the biomechanical properties of synthetic ligaments in the long term.

Graft types that have been widely researched and are still part of common practice today are the hamstring tendons (1927-today), the patellar tendon (1927-today), the quadriceps tendon (1984-today) and allografts (1929-today). The patellar tendon graft has been the “gold standard” for ACL reconstruction for almost three decades. Its main advantage is that it has bone plugs on both ends, which facilitates graft fixation and incorporation. Although clinical results are comparable for both grafts at long-term follow-up, the patellar tendon graft has lost ground during the past decade. Hamstring tendon grafts are currently the most used, which is likely also based on less harvest site morbidity.

The first arthroscopically assisted ACL reconstruction was performed by David Dandy at Newmarket General Hospital the April 24th, 1980. When reports started coming in showing the benefits associated with arthroscopically performed ACL reconstruction, minimal invasive surgery was further popularized over the following years. Gradually, the focus of the surgery moved to being as minimal invasive as possible and techniques like the single-incision trans-tibial technique for arthroscopic ACL reconstruction were adopted by most surgeons by the end of the 1990s.

In spite of good cosmesis and clinical results, it was not long until it was found that there were some potential disadvantages to using single-incision, transtibial techniques. It appeared to be impossible to position the femoral tunnel at the native femoral insertion site. Studies followed and repeatedly showed that the transtibial technique was more likely to result in a non-anatomic, vertically orientated graft, unable to control rotation effectively.


**BACK TO ANATOMY**

However important technical developments had been, developments had distracted from anatomy. Gradually, it became apparent that any non-anatomic technique was unable to reproduce normal ligament function or fully restore normal knee kinematics and was hence held responsible for poor clinical results and the relatively high prevalence of osteoarthritis at long term.\textsuperscript{165,208,330} At the beginning of the twenty-first century, inspired by the work of Kazunori Yasuda of Sapporo and Freddie Fu of Pittsburgh, focus was once more put on physiological and anatomical principles and moved away from the concept of isometry.\textsuperscript{332,341} Supported by the principles of anatomic reconstruction that Hey Groves, Palmer, Wirth and Hughston had dictated earlier, it was realized that any reconstructive effort must restore any injured anatomic structure to its native functional position, size, orientation and tension.

At the beginning of this decade, Carola van Eck described these renewed insights and principles in her PhD thesis “Anatomic Anterior Cruciate Ligament Reconstruction -A Changing Paradigm-”.\textsuperscript{81} This complete work marked the beginning of many clinical and research efforts to further customize surgery to the individual patient.

**CURRENT ISSUES**

Despite all developments, thorough objective evaluation of our clinical diagnostic tests, our surgical treatment and the way we assess outcome, is lacking. In all segments of the treatment spectrum, room remains for subjective findings, interpretation and opinion.

**Diagnostics**

The most important test for diagnosing an ACL injury clinically is the pivot shift test, which –to date- can still only be graded subjectively by the examiner self.

**Surgery**

A lot of emphasis is being put on performing an “anatomic” reconstruction, but how close can we really approach the native anatomy when we claim to do so? It is not known whether the subluxated tibia is adequately reduced to its original position. Nor is it known whether we are at all able to reproduce the size of the native ACL. Additionally, whether reconstructive surgery and evaluation thereof is influenced by the everchanging instruments we use remains unknown.
Post-operative outcome measurement through Patient Reported Outcome (PRO) scores and return to sports rates are current hot-topics and decent steps towards more objective outcome assessment. However, while we link certain PRO scores to different levels of patient wellbeing or whether surgery was successful, it is not known what PRO score is acceptable from a patient’s perspective. Additionally, while return to sports rates seem to be a relative simple outcome parameter, general low rates in literature remain unexplained and objective variables that may help predict the likelihood of successfully returning to sports have yet to be identified.

**AIMS AND OUTLINE OF THIS THESIS**

*Firstly*, the aim is to more objectively and quantitatively evaluate the physical exam. *Secondly*, the aim is to more objectively assess the “gold standard” in intervention itself: anatomic ACL reconstruction. *Thirdly*, the aim is to objectively predict and interpret outcome. *Fourthly*, consequently, and ultimately, the aim is to improve the treatment of ACL injuries.

This thesis is structured so that all segments of the treatment spectrum are chronologically addressed: from diagnostic testing when a patient presents in clinic with an ACL injury, through surgical treatment by anatomic ACL reconstruction, to outcome assessment by return to pre-injury sports and finally patient-wellbeing.

It is a fact that the pivot shift test is the most specific test to establish the diagnosis of an insufficient ACL and has a relation to knee function. It is also generally accepted that the goal of any ACL reconstruction surgery should be to eliminate the shifting phenomenon, that is, to reduce or eliminate rotatory knee laxity. Recent research efforts by our pivot shift workgroup have shown that it is possible to objectively evaluate components of the pivot shift by quantifying different elements of the knee kinematics with a simple image analysis method. Although these findings do permit to objectively assess the pivot shift test already, devices used for this purpose are not universally available, most often invasive, and costly. Moreover, despite the image analysis method being simple, it is associated with labor-intensive processing. So to automate this process and to improve the clinical applicability of the image analysis method to quantify the pivot shift, we have initiated -and described in Chapter 2- the development of software for an application that can be installed on a handheld tablet computer (iPad, Apple, Cupertino, CA, USA), thereby combining image-capture and automated processing on one device that is widely available and clinically functional.

When diagnosed with an ACL injury, patient and doctor are confronted with multiple options and techniques in terms of treatment. For a clear understanding of this
thesis and current literature it is vital to know the indications and considerations for each technique that anatomic ACL reconstruction comprises. Chapter 3 provides an overview of principles that are the fundament for the “double-bundle concept” and therefore the fundament for anatomic ACL reconstruction.

In an effort to assess how anatomic anatomic ACL reconstruction really is, first steps towards per- and post-operative quantitative evaluation of restoration of native anatomy were researched. The results are presented in Chapter 4, Chapter 5 and Chapter 6.

Placement of the graft is considered anatomic when the tunnels are placed within the native insertion sites. Graft placement like this is important for the correct intra-articular orientation. In terms of sizing the graft, it is regarded equally important to size the graft to its native insertion sites. The amount of the native insertion site that is recreated by the tunnel aperture area however, is currently unknown, as are the implications of the degree of coverage. As such, the goals of the study presented in Chapter 4 are to determine whether anatomic ACL reconstruction is able to restore the native insertion site and to attempt to establish a crude measure to evaluate the percentage of reconstructed area as a first step towards elucidating the implications of complete insertion site restoration.

ACL deficiency disrupts not only the intra-articular anatomy but also causes a passive alteration of the anatomic tibiofemoral relationship. Although it is generally thought that anatomic ACL reconstruction also sufficiently restores the tibiofemoral relationship, this has yet to be evaluated. The study presented in Chapter 5 meant to assess the tibiofemoral relationship in the sagittal plane after anatomic ACL reconstruction.

Reliable tools for objectively assessing tunnel placement after ACL reconstruction can be valuable for postoperative evaluation and are essential for determining the effectiveness of different techniques for placing tunnels in an anatomic location. Earlier, Illingworth et al. have introduced a simple method that made it possible to quantitatively assess femoral tunnel placement on clinically available radiographs. However, this metric was evaluated for femoral tunnels created with rigid reamers only. Since drilling with a flexible reamer has been shown to alter the femoral tunnel exit point, Chapter 6 aims to further investigate the continued use of this metric for this type of reamers too.

In the post-operative phase, healing of the graft and prevention of early graft failure, is of the essence. An understanding of the tendon-bone healing and the intra-articular ligamentization process is crucial for orthopaedic surgeons to make appropriate graft choices and to be able to initiate optimal rehabilitation protocols after surgical ACL reconstruction. Recent efforts at advancing the clinical success of ACL reconstruction have focused on strategies to enhance and optimize the biologic environment of the graft-bone interface, promoting and potentially improving the healing rate and strength of the reconstruction. Chapter 7 focuses on the current understanding of the tendon-
to-bone healing process for both autografts and allografts and discusses strategies to biologically augment healing.

When surgery and physical therapy and rehabilitation are completed, return to pre-injury sports rates are generally considered an important parameter of success. Unfortunately, reported rates in literature vary widely and often are disappointing. Multiple studies have investigated factors that may be associated with an individual’s decision to return to pre-injury sports, but there is a general paucity of research that has studied which objective measurable variables help predict the likelihood of successfully returning to sports. Chapter 8 aims to determine if certain pre-surgery variables predict return to the same frequency and intensity of sports participation with similar activity demands as before injury.

More and more are the effects of treatment assessed with PROs. However, a clinically meaningful change in PRO may not be associated with an acceptable state that corresponds to “feeling well”, which is also called the Patient Acceptable Symptom State (PASS). Chapter 9 presents a quantitative assessment of patient wellbeing by identifying threshold values of the International Knee Documentation Committee Subjective Knee Form (IKDC-SKF) and the Knee injury and Osteoarthritis Outcome Scale (KOOS) for the patient acceptable symptom state.

Finally, Chapter 10 and Chapter 11 then provide a general discussion and summary of the thesis respectively.
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Development of Computer Tablet Software for Clinical Quantification of Lateral Knee Compartment Translation During the Pivot Shift Test.


DEVELOPMENT OF AN
IPAD APPLICATION FOR
QUANTIFICATION OF THE PIVOT
SHIFT TEST
ABSTRACT

The pivot shift test is a commonly used clinical examination by orthopedic surgeons to evaluate knee function following injury. However, the test can only be graded subjectively by the examiner. Therefore, the purpose of this study is to develop software for a computer tablet to quantify anterior translation of the lateral knee compartment during the pivot shift test. Based on the simple image analysis method, software for a computer tablet was developed with the following primary design constraint – the software should be easy to use in a clinical setting and it should not slow down an outpatient visit. Translation of the lateral compartment of the intact knee was $2.0 \pm 0.2\text{mm}$ and for the anterior cruciate ligament-deficient knee was $8.9 \pm 0.9\text{mm}$ ($p < 0.001$). Intra-tester (ICC range = 0.913 to 0.999) and inter-tester (ICC = 0.949) reliability were excellent for the repeatability assessments. Overall, the average percent error of measuring simulated translation of the lateral knee compartment with the tablet parallel to the monitor increased from 2.8% at 50cm distance to 7.7% at 200cm. Deviation from the parallel position of the tablet did not have a significant effect until a tablet angle of 45°. Average percent error during anterior translation of the lateral knee compartment of 6mm was 2.2% compared to 6.2% for 2mm of translation. The software provides reliable, objective, and quantitative data on translation of the lateral knee compartment during the pivot shift test and meets the design constraints posed by the clinical setting.

Keywords: anterior cruciate ligament; pivot shift test; knee; kinematics
CHAPTER 2 Development of an iPad application for quantification of the pivot shift test

INTRODUCTION

Anterior cruciate ligament (ACL) injury leads to altered knee kinematics, joint instability, and a high risk for early onset osteoarthritis.\textsuperscript{207,240,295,307} The pivot shift test is a clinical examination performed manually to evaluate knee rotational laxity in patients with an ACL injury. Although the test is commonly used as an objective outcome measure, to date, the test can only be graded by the examiner subjectively as a gliding shift (grade I), a clunking shift (grade II), or as a grossly unstable shift (grade III).\textsuperscript{103} In addition, varying techniques to perform the pivot shift test have been described.\textsuperscript{242} Subjective grading of tests performed differently leads to a variation in clinical grading between examiners.\textsuperscript{191,252} In an attempt to increase the diagnostic value of the pivot shift test, it has been proposed to standardize the technique.\textsuperscript{144,242} However, because the clinical grading is inherently subjective, this should also be standardized in an objective fashion.

Recent efforts have shown that it is possible to objectively evaluate components of the pivot shift by quantifying different elements of the knee kinematics.\textsuperscript{19,147,157,187,191,196,197,210,211,217,262} Anterior translation of the lateral knee compartment is suggested to be the most prominent form of instability in patients complaining of ‘giving way’ of the knee.\textsuperscript{103} Thus, measuring anterior translation of the lateral knee compartment during the pivot shift test has been used as a parameter to provide quantitative data during this clinical examination.\textsuperscript{52,147,160,170} Bedi et al. demonstrated that anterior translation of the lateral knee compartment could reflect the clinical pivot shift test grade using a navigation system. Each additional clinical grade correlated to an increment of approximately 6mm of anterior translation of the lateral knee compartment.\textsuperscript{41}

Our research group previously developed an image analysis method for capturing the motion of the lateral knee compartment during the pivot shift test using simple, non-invasive, and affordable devices.\textsuperscript{146} Previous devices used for this purpose are not universally available, oftentimes invasive, and associated with considerable costs. Although the image analysis method is simple, it is associated with labor-intensive processing (ca. 2h per test) and does not provide real-time feedback to the tester.\textsuperscript{146} To automate this process and to improve the clinical applicability of the image analysis method, we have initiated the development of software for an application that can be installed on a handheld tablet computer (iPad, Apple, Cupertino, CA, USA; Figure 1).

The objectives of this study were (1) to develop clinically applicable computer tablet software that would reliably quantify the translation of the lateral knee compartment during the pivot shift test, (2) to determine repeatability of the developed methodology in an intact and ACL-deficient human cadaveric knee, and (3) to determine the influence of environmental factors including tablet distance and tablet angle that could
potentially affect the measurement accuracy of the software. We hypothesize that the environmental factors will not have a significant influence within clinical acceptable ranges on accuracy of the methodology.

METHODS

Image analysis: anterior translation of the lateral knee compartment

The simple image analysis method is based on the tracking of three circular stickers, attached as skin markers on bony landmarks on the lateral side of the knee. These stickers are tracked throughout the entire motion of the pivot shift test using a video recording. Three yellow, circular stickers, 19 mm in diameter (Color Coding Labels, Avery Dennison Corporation, Pasadena, CA, USA), are attached as skin markers on the following bony landmarks: (1) the lateral epicondyle (L), (2) Gerdy’s tubercle (G), and (3) the fibular head (F). The pivot shift test is performed by the clinician according to a standardized protocol, as previously described. A video is simultaneously
recorded by an assistant while holding the recording device perpendicular to the lateral side of the knee, and assuring that the markers do not move out of the field of view. Filming the video against a homogenous background reduces ‘noise’ during processing caused by undesirable signal input from the surroundings.

To calculate the movement of the tibia with respect to the femur, the video must be processed. Previously, the video was processed by hand on a computer using the ImageJ software (National Institute of Health, Bethesda, MD, USA). In order to improve the clinical applicability of this method, the analysis should be automated and the time to complete the processing should be minimized. To this end, the development of computer tablet software (PIVOT software) was broken into several sub-tasks that need to be performed to emulate the simple image analysis. These sub-tasks were formulated as follows: (1) Marker Detection, (2) Appropriate Marker Tracking, (3) Spatial Location of Markers, (4) Marker Identification, (5) Anterior Translation Calculation, and (6) PIVOT software Interface.

**Design constraints**

The process of identifying markers within each video frame and calculating the translation of the lateral knee compartment based on the relative marker locations was to be automated in a way that is clinically useful. This posed several design constraints to the development of the PIVOT software: (1) the device on which it runs should incorporate
both the camera and the computer into one; (2) the processing time should not slow
down an outpatient visit; (3) repeatability and accuracy of the calculation should be
better than the magnitude of the translation; and (4) the software is easily useable in
a clinical setting.
These constraints were addressed as follows:

(1) Development was performed on the latest iOperating System (iOS) device which
incorporated both camera and computer into one and offered the most process-
ing and image-retrieval power specifications within the family of iOS devices,
the iPad3. This device offered increased graphical processing unit (GPU) speed
and dual-core central processing units (CPUs). In addition, the resolution of the
camera was the highest resolution of the available iOS devices, recording up to a
maximum of 30 frames per second (FPS) of high-definition color images that can
produce images with a maximum resolution of 2592 x 1936 pixels.

(2) Based on an average outpatient visit of approximately 15 min, a processing time
of no longer than 2 min was deemed to be clinically acceptable.

(3) Repeatability and accuracy were needed to be better than the magnitude of
translation that occurs during the pivot shift test.

(4) Availability of the software was assured by developing the application for the
iPad, which is a common technology and available in many hospitals.

**Computer tablet software development**
The PIVOT software was written in the native iOS programming language, Objective-
C.

**Marker detection**
A technique based on marker-color selection was utilized from a software library,
GPUImage (Sunset Lake Software LLC, Madison, WI, USA). A standard OpenGL ES
(Khronos Group, Beaverton, OR, USA) algorithm was also created that scans the image
returned from the camera in real time. These libraries were utilized for pixel-shading
techniques; individual pixels of the video images can be shaded to any desired color
while running on the GPU instead of the CPU, which speeds up the processing time
significantly. This enables the user to select which color should be considered the
marker color in each respective image. Before running a test, tapping the screen to
indicate where the marker is in the current frame of the video being displayed retrieves
the underlying pixel color, which is then selected as the marker color. The original
image is then copied and each pixel is reviewed. Every pixel that is matched with
the selected color turns fully opaque white, or – if the pixel is not of the user’s color
selection – it turns black.
Appropriate marker tracking
Overlaying this black and white copy (a.k.a. a video mask) onto the original display (Figure 3(a)) in real-time brightens the selected markers and grays out the remaining image (i.e., ‘shading’, Figure 3(b)). The sensitivity for the marker color can be manually adjusted by the user before recording the video (Figure 3(c,d)). This sensitivity ‘threshold’ is also passed to OpenGL and used in determination of the color. This threshold defines the range of pixel values that can still be considered the target color by the processor and utilized in creating the video mask. A higher sensitivity value results in a narrow range of pixel values being shaded. It is therefore more ‘sensitive’ to the pixel values, i.e., a lower sensitivity will shade a wider range of pixel values and will end up shading more of the image than might be necessary. Too high sensitivity will not necessarily capture enough of the markers due to natural variations in pixel values from varying light or noise. This increased contrast between markers and surroundings allows the user to distinguish the markers, and thus ensures that the system is tracking the desired portions of the video while minimizing the potential tracking of outside noise. Therefore, the user has to adjust the threshold sensitivity so that the three desired markers are large, bright, and solid shapes on the device screen before starting the recording. It was found that the real-time shading process reduced the FPS of the camera output to 28.5 ± 0.5 FPS. This equates to known time intervals of 0.036s between frames, which is within the 0.2 ± 0.1s interval required to capture the sudden translation of the lateral knee compartment during the pivot shift test.146

Figure 3. Adjustments to the sensitivity of each captured frame: (a) raw image; (b) tracking display; (c) too little sensitivity; (d) too much sensitivity.

Spatial location of markers
To detect the location of the markers, each frame of the video is initially analyzed to find all pixels that are colored white. When a white pixel is detected, a grid of neighboring pixels is also searched. These neighboring pixels are examined to see whether they are already assigned to a found ‘pixel mass’. If so, the pixel being reviewed is placed into this same mass of associated pixels. Otherwise, a new mass identifier is created and the pixel is assigned to this new mass. The radius of neighboring pixels examined is set at 10 pixels. Each pixel can be assigned to a grouped ‘mass’ of
other pixels. The mass detection process is applied to each video frame. The software analyzes the video for the pixel values defined by the marker color and the sensitivity. The three largest masses of pixels that are in this black and white video mask are then located and defined as the three markers. The following assumptions are made: (1) three markers exist in each frame and the three largest pixel masses are defined as the markers; (2) outside color noise is represented by a fewer number of pixels than is constituted within each individual marker display; and (3) the patient is laying down on their back (supine position), which defines the relative location of the markers in each frame.

Marker identification

The next step is to determine which marker represents each bony landmark. If a pixel mass is designated to be a marker, then the marker location is defined as the centroid of the pixel mass. As every pixel in the mass has a Cartesian coordinate \((x, y)\) relative to the screen, a bounding box can be extracted by taking the maximum width and maximum height of each mass. The centroid is then approximated by taking the average of the center of the bounding box and the average location of all pixels contained in the mass. A low pass signal-processing filter algorithm (second-order Butterworth) is also used to flatten and normalize the output data from the mass detection algorithm.

Prior to testing, the user reports the laterality for the leg that is to be examined. Knowing that \((L)\) should be the left-most marker when recording a test on a right leg, and \((L)\) should be the right-most marker when recording a test on a left leg, the following assumptions can be made: (1) the \((L)\) marker can be located based upon the user’s specification of leg being tested; and (2) the \((F)\) marker will be the lowest mass on the screen.

The region of interest (ROI) is then defined by a square region that encompasses the three markers. In subsequent frames, only the ROI is reviewed for mass detection, greatly reducing the processing time. Given a linear correlation between the number of pixels and processing time, an ROI of approximately \(1/10^{th}\) of the original frame reduces the processing time by \(9/10^{th}\). Units of measurement are assigned by entering the known diameter of the markers prior to testing.

Anterior translation calculation

All video frames are analyzed to find the coordinates of the markers, and these locations are stored with their associated frame times. This information is used for calculation of the anterior translation of the lateral knee compartment as reported previously for the simple image analysis (Figure 4). A ‘reduction’ motion has occurred at the knee when landmarks \((P)\) and \((G)\) move closer to one another. The change in this distance
defines the anterior translation of the lateral knee compartment. A reduction motion continues as the distance between landmarks (P) and (G) keep moving closer together. Once the landmarks (P) and (G) stop moving closer to one another, the magnitude of the total reduction or translation is recorded. To filter noise, a second-order Butterworth filter with a cut-off frequency of 9Hz was implemented because reduction motions typically occur within a 0.2 ± 0.1s interval.146

PIVOT software interface
The PIVOT software interface is designed such that three pieces of information are displayed simultaneously: (1) the raw video, (2) the video with the video mask – black screen with three white masses; and (3) the video with the ROI and the marker centroids. Within the ROI, the masses that are being tracked are given a different color (green) (Figure 5).

Monitoring these screens allows the user to evaluate appropriate marker tracking. The first screen provides information as to whether the video was recorded properly and reduction occurrence/timing. The second screen shows the ability of the PIVOT software to identify the markers, by showing three circular masses in the location of the markers on the raw video. The third screen then verifies whether the markers are tracked appropriately and the centroids designated by the small circles within the markers are in the center of the three circular masses. Within a few seconds, a graph is displayed with time on the x-axis and the anterior translation of the lateral knee compartment on the y-axis.
Two experimental analyses were performed to validate the PIVOT software.

**Cadaver experiment: quantification of the translation of the lateral knee compartment**

A whole lower body cadaveric specimen (female, 64 years old) without the history of ligamentous knee injury, severe OA, or known osteoporosis was used. Prior to testing, physical examination, fluoroscopy, and arthroscopy were performed to assure the absence of any bony abnormalities and knee and/or hip joint pathology. Three orthopedic surgeons with different levels of experience (resident, fellow, and attending) performed the pivot shift test three times each on the intact knee using a standardized pivot shift technique. The tablet was consistently held by the assistant at a distance of 100cm from the knee and maintained perpendicular to the lateral knee based on visual verification. The ACL was then arthroscopically transected in the contralateral knee and the examiners repeated the standardized pivot shift test on the ACL-deficient knee. Anterior translation of the lateral knee compartment was recorded by the PIVOT software. Once the specimen/subjects information is entered and the video of the

Figure 5. PIVOT software User Interface. This includes (1) the raw video itself, (2) the video mask (black screen with three white masses), and (3) the video with the ROI and the marker Centroids. Within the ROI, the masses that are being tracked are given a different color (green) and the calculated centroids illustrated with little circles.
pivot shift test was recorded, it takes approximately 10 – 15s to analyze the video and generate the reduction curve.

Independent t-tests were used to compare the anterior translation of the lateral compartment for the intact and ACL-deficient knee during the reduction motion (PASW Statistics 18, IBM Corp, Armonk, NY, USA). Statistical significance was set at p < 0.05. To assess the intra- and inter-observer reliability, intraclass correlation coefficients (ICCs) were determined.

Computational simulation: accuracy of the PIVOT software

In order to test the accuracy of the PIVOT software, a program in MATLAB (MathWorks, Natick, MA, USA) was developed to produce the motion of markers for a simulated pivot shift test on a computer monitor. The marker size was the same as the markers that are used in the clinical setting. The femoral marker moved in the upward direction similar to that found during a pivot shift test in vivo. In order to make the simulated pivot shift test more realistic to that in ACL-deficient knees during the reduction motion, the amount of time that the markers move in relation to each other was adjusted to occur over a period of 0.5s.

The tablet with the PIVOT software was mounted on a tripod and placed at 100cm distance and perpendicular to the monitor. The distance of the tablet from the monitor was determined using a measuring tape (1mm resolution). The monitor and tablet were adjusted to be parallel to each other and perpendicular to the floor using a smart phone level with a resolution of 0.01° (‘Bubble level’, Antonio Vianey, http://avianey.blogspot.com/).

Several variations on the position of the tablet were also examined based on the variability found within the clinical environment. Distances between 50 and 200cm were deemed possible in the clinical environment due to the relative position of the knee and person maintaining the position of the tablet. Therefore, distances of 50, 75, 113, 126, 136, 155, 175, and 200cm were also examined. Furthermore, the person holding the tablet cannot maintain the orientation of the tablet as perpendicular to the plane of the knee. Variations in the angle of 15°, 25°, 35°, and 45° were included in the analysis and obtained by adjusting the angle of the tablet using the smart phone level. Finally, the effect of the magnitude of anterior translation of the lateral knee compartment on the accuracy of the PIVOT software during the reduction motion was evaluated. The magnitude of the translation was varied between 2, 4, and 6mm to accommodate values typically observed between healthy and ACL-injured knees.145,146

The PIVOT software recorded the simulated pivot shift test generated by the MATLAB program on the computer monitor and the translation was predicted. The procedure was repeated 15 times for every combination of tablet position, tablet angle, and magnitude of shift. The calculated translation was compared to the predetermined
amount of the simulated pivot shift. The mean absolute error and percent error of the 15 trials were determined by comparing the predicted magnitude of anterior translation of the lateral knee compartment from the PIVOT software to the known magnitude of translation from the MATLAB program. For every distance point at the zero deviation angle, the percent error was averaged among all lateral compartment magnitude trials. For every deviation angle tested, the percent error was reported as an average of all distance trials from 75 to 126 cm at each angle. For different magnitudes of anterior translation of the lateral knee compartment tested, the percent error was reported as an average of all distance trials between 50 and 200 cm.

Figure 6. Examples of typical graphs that were generated by the PIVOT software during testing in a cadaver in intact and ACL-deficient states for all three different testers. For intact knees, a gradual increase in translation is observed that occurs during the knee flexion phase of the pivot shift test with no reduction movement of the knee that occurs with ACL-deficient knees.
RESULTS

Cadaver experiment: quantification of the translation of the lateral knee compartment

After transection of the ACL, all examiners detected a high-grade pivot shift subjectively. The anterior translation of the lateral knee compartment for the intact knee was 2.0 ± 0.2mm and for the ACL-deficient knee was 8.9 ± 0.9mm. The mean difference of anterior translation of the lateral compartment between the intact knee and ACL-deficient knee was 6.9 ± 0.7mm (p < 0.05; Table 1). More illustrative with respect to demonstrating the significant differences between intact and ACL-deficient knees are the plots generated by the PIVOT software. Similar amounts of translation were observed for the intact and ACL-deficient knees from all observers (Figure 6).

The ICC for intra-tester reliability ranged from 0.913 to 0.999 (95% CI range: 0.319 – 1.000) for all three testers, and the ICC for inter-tester reliability was 0.949 (95% CI: 0.542 – 1.000). Intra- and inter-tester reliability were thus regarded as excellent (ICC > 0.750).

MATLAB experiment: accuracy of the PIVOT software

A total of 555 trials were completed based on the combinations of the tablet distance, tablet angle, and magnitude of translation examined. Overall, the average percent error of measuring different magnitudes of simulated lateral compartment translation with the parallel position of tablet and monitor increased from 2.8% in 50cm distance to 7.7% in 200cm, but it did not follow a uniform contour (Figure 7(a)). In the recommended position, the average percent error was 4.4%. Average percent error was always less than 6% in distances less than or equal to 175 cm.

Deviation from the recommended position did not have a significant effect until a tablet angle of 45° (Figure 7(b)). The percent error was 4.1% in the recommended position. With deviation of the tablet from recommended position, the increase in percent error was minimal and the percent error reached only 5.1% at a tablet angle of 45°. The average percent error in tested positions was smaller in greater translations. The average percent error during anterior translation of the lateral knee compartment of 6mm was 2.2% compared to 6.2% during translation of 2mm (Figure 7(c)).
DISCUSSION

The primary objective of this study was to develop an automated image analysis system that is able to provide quantitative data on the anterior translation of the lateral knee compartment that occurs during the pivot shift test. The PIVOT software demonstrated encouraging initial results, being able to reliably detect statistically significant differences between intact knees and ACL-deficient knees. However, improvements will still be made in terms of general function and usability. The cadaver experiment clearly demonstrated the PIVOT software’s ability to recognize and quantify the occurrence of a reduction motion (translation of the lateral knee compartment) in an intact and ACL-deficient knee. The PIVOT software also graphically displayed significantly larger reduction motions in ACL-deficient knees compared to intact knees.

Using the methodology on a cadaver is very different from testing in a clinical setting. However, the absence of any muscle tone (e.g., patient guarding during examination) results in pure ligamentous knee stability and is therefore much more representative for evaluation of ACL function. Quantification of translation during the pivot shift test (intact and ACL-deficient knees) could have also been done in one (ipsilateral) knee. However, previous research has shown that the biomechanical characteristics of a contralateral uninjured, healthy limb are an accurate representation of the mechanical characteristics of the ACL-deficient limb before injury (i.e., transection). Moreover, in a clinical setting, comparison to the (healthy) contralateral limb should always be made to acquire a sense of baseline knee laxity. Furthermore, excellent ICCs indicated that multiple tests – either multiple tests performed by one surgeon or one test by multiple surgeons – show little variation.

The accuracy of the PIVOT software was also determined for ideal conditions using the MATLAB experiment. The PIVOT software was tested at different distance and
degree intervals and with different grades of anterior translation of the lateral knee compartment that are applicable to a clinical setting. The fact that the PIVOT software was more accurate at smaller distances can be explained by the resolution of the images, which are better at shorter distances between the tablet camera and monitor. The marker’s image will have a better quality that result in more accurate calculation of translation by the PIVOT software. The overall percent error was always less than 6% in distances less than or equal to 175cm. This result favorably supports the use of the PIVOT software within this distance interval.

The deviation of the tablet angle from the perpendicular position was accompanied with increases in error but this increase was less than 1%. The average error was always less than 5.1% up to 45° of deviation. The PIVOT software was more accurate in greater translation of the lateral knee compartment based on a smaller percent error obtained. Larger translations are better for the tablet’s camera because the markers move across more pixels and, as a result, the calculations will be more accurate. Based on this experiment, the PIVOT software should be used at a distance between the tablet and lateral side of the knee of 50 – 175cm and at angles of the tablet of less than 45° to maintain an acceptable accuracy of less than 6%.

Other systems have been reported to provide a quantitative evaluation of the pivot shift test, such as electromagnetic tracking52,90,147,196, computer navigation47,61,157,197,210,262, and inertial sensors187,209,211,217. However, none of these systems are easily applicable in a clinical setting secondary to limitations such as invasive- ness (i.e., requiring bony fixation), cost, and development primarily for research purposes. In contrast, the unique- ness of the PIVOT software lies in its simplicity and portability, while being noninvasive. The validated simple image analysis technique146 is embedded in the software of the PIVOT software, so as to allow simultaneous videotaping of the clinical test, tracking of markers, and calculation of a translation curve over time.

These initial studies were designed primarily to assist with the development of a final prototype with an adequate operating manual. Limitations that were identified and suggested to have caused relatively low sensitivity (59%) in a clinical study145 require further attention. These limitations include the following: (1) markers moving outside the ROI; (2) camera angulation slightly skewing the measurements; and (3) the pivot shift test being performed quicker than the video camera of the computer tablet is able to capture (i.e., 30Hz). In the current version of the PIVOT software, the ROI has been enlarged to address this limitation.

The basis of the software being used for evaluation of the pivot shift test now in development is the ability to track-relative motion of marked objects and to perform calculations based on these movements. This application is designed to track movement in the human knee and, using calculations based on the relative motions of the bones during flexion, determine the magnitude of translation that occurs at the knee, which
is suggestive of injury to the ACL. This technology could be expanded to quantify translation during other clinical examinations, the range of motion of the knee, and the range of motion of other joints. For example, a modified version of the PIVOT software could potentially be utilized to detect the degree of laxity in the knee related to the development of osteoarthritis. In addition, the option to develop the PIVOT software for other iOS devices, such as the iPhone, is also being explored.

CONCLUSION

The first results using the PIVOT software for objectively quantifying anterior translation of the lateral knee compartment during the pivot shift test suggest that it is possible to integrate the simple image analysis method with automated analysis on a portable tablet computer. This assessment tool is easy to use and provides an objective, quantitative evaluation of the pivot shift test. This PIVOT software will enable surgeons to quantify the amount of rotatory knee laxity for each individual knee. The ultimate goal of the PIVOT software is to provide a tool that surgeons can use to establish patient-specific treatment algorithms by quantifying anterior translation of the lateral knee compartment during the pivot shift test, and ultimately improve the clinical outcome for patients.

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APPENDIX

PIVOT software user manual

1. First, test the contralateral, uninjured knee.
2. Place the patient supine on the table with both legs undressed from the upper thigh down.
3. Attach circular stickers of the same size and color, contrasting to the patient’s skin, to the lateral side of the knee as markers for the following bony landmarks: (a) the lateral epicondyle (L), (b) Gerdy’s tubercle (G), and (c) the fibular head (F) (or place the anterior aspect of the third marker approximately 30mm posteriorly to the anterior aspect of the marker on Gerdy’s tubercle).
4. Ensure that the background is homogenous and of a distinctly different color than the stickers (e.g., use a sheet).
5. Open the PIVOT software.
6. Tap the ‘plus-button’ in the right upper corner on the menu.
7. Fill out the patient identifiers.
8. Tap the ‘plus-button’ in the right upper corner on the menu again.
9. Fill out all requested information, including test name, side, clinical grade of the pivot shift, marker diameter marker distance [(F) to (G)], and target diameter.
10. Tap the button ‘Start new test’.
11. Hold the tablet in a fixed position, approximately 1m from the knee and perpendicular to the skin markers.
12. Tap a marker on the screen to select that color as the tracking color.
13. Adjust the sensitivity so that the maximum surface of the markers is tracked while minimizing tracking of signals coming from outside the markers.
14. Perform one trial test to ensure that the entire pivot shift maneuver is captured. This pivot shift maneuver should be in the standardized fashion. In summary, apply three steps that take 1 s each (the entire maneuver should take approximately 3 s). (1) Hold the leg in full passive extension and internally rotate the lower leg/heel. (2) Apply valgus stress with the other hand just distal from the knee joint. (3) Flex the knee while gradually releasing the internal rotation.
15. The assistant, holding the tablet, should then indicate when the pivot shift test can start. The recording should start approximately 1s before the maneuver starts and stop approximately 1s after the shift has occurred.
16. The assistant should ensure that the three markers are adequately tracked throughout the entire video and that the markers do not move outside the ROI. If this happens, the test – and recording – should be redone.
17. Repeat steps 2 through 16, testing the injured knee.
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Indications and contraindications for double-bundle ACL reconstruction.

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ANATOMIC ACL RECONSTRUCTION ACCORDING TO THE DOUBLE-BUNDLE CONCEPT
ABSTRACT

Over recent years, double-bundle reconstruction has gained popularity after studies showed significant advantages of adding a second bundle with regard to outcomes and biomechanics; in particular, it resulted in less rotational instability than after reconstruction with a traditional single-bundle technique. As the focus shifted further towards the restoration of the native anatomy, both single-bundle and double-bundle ACL reconstruction were performed in an anatomical fashion and yielded similar results. To date, no consensus has developed as to whether double-bundle reconstruction is better than single-bundle reconstruction or vice versa. However, after surgeons started to individualize their surgical approach to the patient, it has been found that both the anatomical single- and double-bundle techniques have their own set of indications and contraindications. Reconstruction of the ligament should focus on restoration of the native functional and anatomical properties and should take the size, shape and orientation of the ACL into account. When indications and contraindications for the technique used are based on native anatomical characteristics, either a single-bundle or a double-bundle procedure can be performed according to the same double-bundle concept.
INTRODUCTION

Rupture of the anterior cruciate ligament (ACL) is one of the most common ligamentous injuries of the knee, with an incidence of 35 out of 100,000 and a two to three times higher risk of injury for females. When left untreated, it can result in recurrent instability, and an inability to return to cutting and pivoting activities. Additionally, the ACL deficient knee is at risk for meniscal injuries and the early onset of degenerative changes of the articular cartilage. The ACL does not have the potential to adequately heal when torn, therefore surgical ACL reconstruction is generally the treatment of choice with the goal of stabilizing the knee to minimize the risk of re-injury, allowing for a safe return to sport and —most importantly— avoiding early degenerative changes.

Anatomical ACL reconstruction has been shown to provide improved knee stability when compared to conventional techniques. The definition of anatomical ACL reconstruction is the functional restoration of the ACL to its native dimensions, collagen orientation, and insertion sites. When performing an anatomical ACL reconstruction, it is critical to reproduce the patient’s unique anatomy by reconstructing the insertion site size, orientation, and tensioning patterns of each individual bundle. A bundle specific ACL reconstruction can always be performed whether it is a single-bundle, double-bundle or augmentation procedure. Therefore, each technique has its own indications and contraindications and surgeons should master all techniques depending on the injury pattern and anatomical characteristics of the individual patient. Since each technique can be applied to restore the native double-bundle anatomy, “double-bundle ACL reconstruction” should be regarded as a concept rather than a surgical technique. The goal of each bundle-specific technique should be to restore the patient’s individual anatomy and thereby both functional bundles of the native ligament that serve the knee’s bony morphology. When anatomical ACL reconstruction is customized to the size, shape and orientation of the native ACL of each individual patient, single-bundle and double-bundle reconstruction yield similar subjective and objective clinical outcome measures.

THE DOUBLE-BUNDLE CONCEPT

Two distinct functional bundles have been identified in the native ACL: the anteromedial (AM) and posterolateral (PL) bundle. These bundles are named for their relative anatomical insertion on the tibia. Both bundles are distinguishable and separated by a vascularized septum during early foetal development (already around 20 weeks), suggesting that both bundles are literally a part of native anatomy (Fig. 1).
The tibial AM bundle insertion site is aligned with the anterior horn of the lateral meniscus and has a close relationship with the medial and lateral tibial spine. The tibial PL insertion is in the respective posterolateral position to the AM bundle. The AM bundle originates from the proximal portion of the medial wall of the lateral femoral condyle, while the PL bundle lies more distally, near the weight bearing articular cartilage surface. Both bundles insert posterior to the intercondylar ridge. On the femoral side, the most prominent anatomical osseous landmark is the intercondylar ridge which is the anterior border of the femoral insertion site. In 80% of all cases, a second ridge, the bifurcate ridge, can also be identified. This ridge separates the origins of the AM and PL bundle and runs perpendicular to the intercondylar ridge.

The distinction between the two bundles is not solely made based on anatomy. AM and PL bundles have a synergistic but different function throughout the entire range of motion (ROM) of the knee. In a fully extended knee, both AM and PL are taut, with PL at its maximum. PL limits rotation of the tibia on the femur up to 60–90° of knee flexion, after which PL loosens. Although AM primarily resists anterior translation of the tibia, at low flexion angles (0–30°) the PL also contributes. The AM bundle is under maximum tension when the knee is flexed between 45° and 60°. The goal of anatomical ACL reconstruction is to restore the native ACL anatomy as closely as possible and consequently to approximate normal knee biomechanics. Four fundamental principles should be observed to achieve this goal. The first is to carefully observe and objectify the patient’s native anatomy. The second is to individualize each surgery with respect to the patient’s anatomy. The third is to place the tunnels, and grafts in the center of the patient’s native footprints. The fourth is to re-establish knee biomechanics by tensioning the grafts to mimic the functional properties of the native ACL as closely as possible.
The double-bundle concept is founded on the distinct anatomical and functional differences between the AM and PL bundle that comprise the ACL. A clear understanding of this concept is vital to mastering and applying anatomical ACL reconstruction in a customized manner to each individual patient's anatomy and injury pattern.
**PREOPERATIVE ASSESSMENT**

The first and foremost step towards diagnosing an ACL tear is to obtain a complete history and physical examination. Not only will this help to diagnose the presence of a tear, but also in differentiating between partial and complete tears.\(^{338}\)

The mechanism of injury may help to distinguish which bundle has ruptured as the AM bundle is frequently torn with high-energy trauma, while the PL bundle may be torn with more subtle, rotational mechanisms.\(^{338}\) Insufficiency of the AM bundle usually results in antero-posterior instability similar to a complete rupture, while insufficiency of the PL bundle may result in instability with pivoting or turning. During physical examination this may become evident, i.e., the presence of a positive pivot shift with an intact end point on Lachman test suggests a PL bundle injury, while isolated injuries to the AM bundle will show increased anterior translation without a firm end point on Lachman test and a negative pivot-shift examination.\(^{83}\)

Conventional radiographic evaluation of both the injured and un-injured knee is fundamental in the initial assessment for degenerative changes, physeal status, leg alignment, associated fractures or avulsions and possible deformities.

High quality magnetic resonance imaging (MRI) plays a critical role in diagnostics and pre-operative planning.\(^{19}\) MRI can confirm the diagnosis of an ACL injury\(^{298}\) and — more importantly — it also allows the surgeon to examine the rupture pattern\(^{290,299}\), measure the native ACL insertion site dimensions, inclination angles\(^{151}\) and thickness of the quadriceps and patellar tendon as potential grafts, evaluate for additional ligamentous or bony injuries, and evaluate meniscus and cartilage status. (Fig. 4)

However, even with clinical and radiological assessment, the exact injury pattern of an ACL tear and individual anatomy can only be definitively established arthroscopically. Consequently, the ultimate decision to perform a single-bundle or a double-bundle ACL reconstruction can only be made intraoperatively.

**SURGERY**

Following induction of general anesthesia a complete knee examination is repeated to assess the ligamentous function without the patient potentially muscle guarding. Specifically, pivot-shift test results may differ significantly from what is found during office examination.\(^{174}\)

**Three-portal technique**

A three-portal approach has been shown to provide the best visualization of the native insertion sites, which is of the utmost importance for anatomical ACL reconstruction.\(^{21,65}\)
(Fig. 5) A “high” anterolateral portal (LP) is positioned above Hoffa’s fat pad, thus minimizing the need to traverse the fat pad and allowing for evaluation of the tibial insertion site of the ACL. The central portal (CP) and medial portal (MP) are then created under direct vision through the LP using a spinal needle. The final position of the CP and MP varies as the orientation of the intercondylar notch may vary. Through the CP, the spinal needle should be in the central portion of the notch in the coronal plane and in the lower third of the notch in the proximal to distal direction. The MP is ideally located superior to the medial joint line approximately two centimeters medial to the medial border of the patellar tendon. In establishing the MP, careful attention should be taken to avoid iatrogenic damage to the cartilage of the medial femoral condyle.\textsuperscript{21,65}

**Indications and contraindications**

Diagnostic arthroscopy is performed first to assess for concomitant injuries and to confirm the ACL’s rupture pattern by cautious evaluation of the ACL remnant. A single-bundle tear is an indication for a bundle augmentation technique, provided that the intact bundle is fully functional.

If both bundles are torn, the remnants are then carefully dissected with the use of a shaver and thermal device to mark the native insertion sites of both the AM and PL bundle.

Intra-operative measurements are then obtained with an arthroscopic bendable ruler (Smith & Nephew Endoscopy, Andover, MA) to assess the size of both the tibial and femoral native insertion sites (Fig. 6). Although the indication for either single-bundle or
double-bundle reconstruction is primarily dependent on this measurement, surrounding anatomical properties should also be taken into account. To this end, the notch size is measured and documented. Specific measurements that are obtained include the insertion site lengths, AM and PL bundle widths as well as notch height and width.

Based on the insertion site measurements, a total tibial insertion site length of less than 14 mm is an indication for single-bundle reconstruction. A single graft will usually be sufficient to restore 60–80% of the size of the native ACL, while a double graft would probably exceed the size of the insertion site. Provided that the graft is positioned anatomically on both the tibia and femur (“PL to PL” and “AM to AM”), this single-bundle graft will acquire the functional properties of the native double-bundle ligament.

Figure 5. A three portal technique provides the best visualisation of and access to the anterior cruciate ligament (ACL) insertion sites. First, a high LP is created, then—under arthroscopic visualisation of a spinal needle—the central portal (CP) and medial portal (MP) are created.
Chapter 3 Anatomic ACL reconstruction according to the double-bundle concept

Relative contraindications for a double-bundle ACL reconstruction include open physes, severe bone bruising, a narrow notch (<14 mm), a shallow notch (<14 mm), severe arthritic changes (grade 3 or greater), or multiligamentous injuries. Open physes and severe bone bruising are conditions that probably benefit from less iatrogenic damage by less tunnel drilling, and severe arthritic changes may worsen more rapidly by constraining the knee with two bundles. A small notch, whether it be shallow or narrow, does not easily accommodate a double-bundle ACL reconstruction as a narrow notch poses a technical challenge for placing both femoral tunnels anatomically and a shallow notch may cause early failure due to potential graft impingement.

Figure 6. Intra-operative measurements are taken to make an objective assessment of the individual anatomy. Tibial insertion site length (a) and width (b) provide information on the native anterior cruciate ligament (ACL) size and primarily dictate the surgical technique used for reconstruction. Notch height (c) and width (d) measurements provide information as to how much room there is for the surgery to be performed without iatrogenic damage and for the eventual graft(s) to function without impingement. These measurements are the final step in the decision-making process regarding what reconstructive technique to apply.
Techniques

Bundle augmentation
In cases of a partial ACL rupture, bundle augmentation may be appropriate. Meticulous care should be given to preserve the remaining intact bundle while dissecting the compromised ACL’s anatomy using a thermal device. The center of the femoral insertion for the ruptured bundle is identified, and the center of the planned tunnel is marked with an angled awl. In cases of single-bundle augmentation drilling with a flexible reamer may be desirable as a more spherical aperture is produced and may not compromise the remaining intact ACL bundle. The distance to the lateral cortex is determined and the tunnel size is increased to the desired dimensions. A tibial guide is centered within the tibial insertion of the ruptured bundle. The tibial tunnel is reamed and dilated to the desired dimensions. Graft passage is visualized arthroscopically to assure anatomical positioning, and position of suspensory fixation is confirmed with fluoroscopy. The graft is finally tensioned and fixed as dictated by the reconstructed bundle.

Anatomical single-bundle ACL reconstruction
As mentioned, if applied for the correct indication and according to the double-bundle concept, a single-bundle ACL reconstruction restores the functional double-bundle anatomy of the native ligament.

A single femoral tunnel is positioned midway between the center of the AM and PL insertion sites. The distance to the lateral cortex is determined and the femoral tunnel is reamed and dilated to the desired size. The tibial insertion site is then carefully dissected to identify both the AM and PL bundles. The desired position of a single tibial tunnel is midway between the centers of the AM and PL bundles. A tip-to-tip guide is placed in the desired position and a guide pin is passed retrograde through a longitudinal incision over the anteromedial proximal tibia. The tunnel is then reamed and dilated to the desired dimensions. Graft passage is performed using a loop suture and beath pin. The loop suture is passed through the femoral tunnel and retrieved from the tibial tunnel. The graft is then passed retrograde through the tibial tunnel until seated appropriately within the femoral tunnel. The PL section of the graft is marked to allow for appropriate orientation of the graft in both the femoral and tibial tunnel. A suture is placed through the PL section intra-articularly, allowing the surgeon to maneuver the graft intra-articularly to its ideal position. The graft is oriented to allow for this section to be located in the PL position on the femoral and tibial sides. By anatomically positioning the fibers within the femoral and tibial insertions, a single-bundle reconstruction can be performed while applying the double-bundle concept. The position of suspensory fixation is confirmed using fluoroscopy. The graft is then tensioned and fixed in 15–20° of flexion.
Anatomical double-bundle ACL reconstruction with soft tissue grafts

Anatomical double-bundle ACL reconstruction can be performed using either soft tissue grafts or grafts with an additional bone block. In case of soft tissue double-bundle reconstruction, separate AM and PL tunnels are drilled at the native femoral and tibial insertion sites. A thermal device is used to identify both the AM and PL insertions sites. These soft tissue remnants, along with bony landmarks such as the lateral intercondylar ridge and the bifurcate ridge are useful for identifying the individual bundle insertions. The femoral PL tunnel should be created first in the center of the PL insertion site with a Steadman awl, and then a guide wire is advanced through the lateral cortex. Traditionally, rigid guide-wires and reamers are used to place and drill the tunnels; however, this instrumentation often requires knee hyperflexion in order to avoid iatrogenic damage to nearby structures. Often, flexible reamers may be desired as these devices do not require knee hyperflexion. Moreover, they decrease the susceptibility for posterior cortical violation by altering the drill exit point and an increase in tunnel length.

Attention is then turned to the tibial side before drilling the femoral AM tunnel. Depending on individual anatomy and surgical preference, the femoral AM tunnel may be drilled with a transtibial or medial portal technique. Rarely can the tibial AM tunnel be used (~10% of cases); but frequently, the tibial PL tunnel can be used (~50%), and nearly always, the MP can be used (>95%). The tibial insertion site is carefully dissected measured in a similar manner to the femoral anatomy. A vertical incision of 3–4cm is made along the proximal anteromedial aspect of the leg. The planned tibial tunnels are placed in the center of the AM and PL bundles. A tibial tip-to-tip guide is set to 45° and placed in the center of the PL bundle, and a guide-wire is then advanced. Another guide-wire is similarly advanced to the center of the AM insertion with the tip guide now set to 55°. To assure an adequate bone bridge between the tunnels, the tunnel entrance should be 2cm apart on the tibial extra-articular cortex. To assure that no notch impingement is presented, the knee is then brought into full extension. The relationship between the K-wire and the roof of the intercondylar notch should be evaluated with the knee in full extension to avoid notch impingement of the ACL graft.

Prior to passing the grafts, a beath pin is passed through the femoral tunnels and the suture loop is retrieved through the tibia PL and AM tunnels, respectively. To assure appropriate placement of each passing suture, arthroscopic examination is performed. The PL graft is passed through the tibial tunnel and into the femoral tunnel prior to AM graft passage. Correct positioning of suspensory fixation outside the lateral femoral cortex is confirmed prior to graft tensioning. Fixation at full extension for the PL graft and at 45° of flexion for the AM graft is performed.
Double-bundle ACL reconstruction with quadriceps tendon with bone block

When performing a double-bundle-ACL reconstruction using a quadriceps tendon with bone block, a single femoral tunnel is prepared. The femoral tunnel is positioned midway between the AM and PL insertion sites. The distance from the medial wall to the lateral cortex and the desired tunnel dimensions are then determined. The femoral tunnel is reamed to a depth of at least 20mm and dilated to allow for graft passage while maintaining the tightest possible fit. The tibial tunnels are created as previously described. The quadriceps bone block is passed through the MP into the femoral tunnel. Once the block is appropriately placed within the femoral tunnel, confirmation of suspensory fixation outside the lateral cortex is obtained with fluoroscopy. It is important with a single femoral tunnel that the PL and AM section of the soft tissue graft are anatomically positioned. Flexible loop wires are passed retrograde through the AM and PL tibial tunnels and retrieved from the CP, while sutures from the AM and PL soft tissue grafts are retrieved out the CP as well. First, the PL graft is passed under arthroscopic visualization to assure appropriate placement relative to the AM graft. The AM graft is then passed under arthroscopic visualization. Lastly, the PL graft is tensioned and secured in full extension while the AM graft is fixed in 45° of flexion.

**POSTOPERATIVE CARE AND REHABILITATION**

Immediately after surgery, the knee is immobilized with a brace. Patients are discharged with adequate pain medication and a cooling device the same day.

All bundle-specific techniques follow the same rehabilitation protocol. During the first week(s), focus should be placed to minimize pain, reduce swelling and restore full ROM and quadriceps muscle strength. The day after surgery patients begin to perform ankle pumps, quadriceps sets, straight leg raise, gastrocnemius and hamstring stretches and heel slides. At the end of the first week, continuous passive motion (CPM) is initiated with full progression to full extension.

Generally crutches and brace are weaned after six weeks, depending on the progress made. Once quadriceps muscle strength resumes, straight line walking can be initiated at six weeks with progression to jogging in a straight line and a stationary bike around three months. Pivoting and cutting exercises are not initiated until at least six months and return to sport is generally no sooner than nine months postoperatively. A functional ACL brace for sports is recommended until the patient is two years from their ACL reconstruction.

Patient progression through the rehabilitation phases is dependent on the patient’s readiness as assessed by the physical therapist and the operating surgeons with performance on rehabilitation tests, clinical findings in the office, and even evaluation on MRI to assess graft healing.
Complications

Both anatomical single-bundle and double-bundle procedures have the same potential general complications including wound infection, haemarthrosis, arthrofibrosis, effusion, neurovascular injury, tunnel widening, tibial or femoral fractures and DVT. The double-bundle technique is technically more complex and may therefore be more prone to complications in inexperienced hands. For this reason, the double-bundle concept should be first solidified in a single-bundle approach before attempting a double-bundle reconstruction.

DISCUSSION

The traditional single-bundle ACL reconstruction technique has several advantages associated with its application for treatment of ACL tears as it is simple, quick and does not require the knee to be flexed beyond 90°. However, while outcomes were suboptimal and the understanding of the anatomy and kinematics of the native ACL expanded, new recommendations developed with keen regard to anatomical placement of bone tunnels. When studies did confirm nearly normal knee joint kinematics when the bone tunnels were placed in the center of the native ACL insertion site,206,281,330,331,334 emphasis shifted further towards the restoration of anatomy. This increased understanding of the anatomy also resulted in the recognition and attempted restoration of the double-bundle anatomy of the ACL, by adding a second bundle graft. Multiple studies have shown equivalent or superior knee stability after double-bundle ACL reconstruction, when compared with single-bundle ACL reconstruction.3,6,161,329,330,333

However, when placed anatomically and customized to the patient’s individual anatomy, there does not seem to be a difference between a single-bundle and a double-bundle technique.148,149 Rather than just adding a second bundle, restoration of normal anatomy is required to restore normal function of the knee.

In summary, ACL surgery should be performed according to the double-bundle concept. This concept relies on the functional anatomy of the ACL, which dictates the surgical procedure by accounting for size, shape, tensioning patterns and orientation of the native ligament. A surgeon should master a variety of diagnostics, objective measurements and surgical techniques to be able to customize the treatment to the patient’s specific needs.
Published as:
Is the native ACL insertion site “completely restored” using an individualized approach to single-bundle ACL-R?


DOES ANATOMIC ACL RECONSTRUCTION RESTORE THE ANATOMIC INSERTION SITES?
ABSTRACT

Purpose: The goal of individualized anatomic anterior cruciate ligament reconstruction (ACL-R) is to reproduce each patient’s native insertion site as closely as possible. The amount of the native insertion site that is recreated by the tunnel aperture area is currently unknown, as are the implications of the degree of coverage. As such, the goals of this study are to determine whether individualized anatomic ACL-R techniques can maximally fill the native insertion site and to attempt to establish a crude measure to evaluate the percentage of reconstructed area as a first step towards elucidating the implications of complete footprint restoration.

Methods: This is a prospective pilot study of 45 patients who underwent primary single-bundle anatomic ACL-R from May 2011 to April 2012. Length and width of the native insertion site were measured intraoperatively. Using published guidelines, reconstruction technique and graft choice were determined to maximize the percentage of reconstructed area. Native femoral and tibial insertion site area and femoral tunnel aperture area were calculated using the formula for area of an ellipse. On the tibial side, tunnel aperture area was calculated with respect to drill diameter and drill guide angle. Percentage of reconstructed area was calculated by dividing total tunnel aperture area by the native insertion site area.

Results: The mean areas for the native femoral and tibial insertion sites were 83 ± 20 and 125 ± 20mm², respectively. The mean tunnel aperture area for the femoral side was 65 ± 17, and 86 ± 17mm² for the tibial tunnel aperture area. On average, percentage of reconstructed area was 79 ± 13% for the femoral side, and 70 ± 12% for the tibial side.

Conclusion: Anatomic ACL-R does not restore the native insertion site in its entirety. Percentage of reconstructed area serves as a rudimentary tool for evaluating the degree of native insertion site coverage using current individualized anatomic techniques and provides a starting point from which to evaluate the clinical significance of complete footprint restoration.

Level of evidence IV.

Keywords: Percentage of reconstructed area · Anatomic ACL reconstruction
CHAPTER 4 Does anatomic ACL reconstruction restore the anatomic insertion sites?

INTRODUCTION

Recently, the emphasis in anterior cruciate ligament reconstruction (ACL-R) has shifted towards being “anatomic” rather than on a particular technique (single-bundle vs. double-bundle) with the goal of more closely restoring normal knee anatomy, kinematics, and stability.40,75,308,316,339

One step further in the continuum of anatomic ACL-R is the concept of “individualized” surgery, which involves tailoring tunnel and graft size to an individual’s native insertion site size.141,148,266,288 In a study by Hussein et al., no difference was found between techniques when individual characteristics were controlled for.148 This highlights the importance of using an individualized approach, rather than relying on the same method of ACL-R for all individuals. For some patients, a single-bundle technique is optimal, and for others, a double-bundle technique is best. To this end, technique guidelines based on insertion site size82 as well as an “insertion site table”288 were developed to help guide surgical technique during ACL-R in order to restore the greatest percentage of the native insertion site.

While anatomic placement of tunnels within the native insertion site seems to be the most important factor in ACL-R, the average amount of the native insertion site that is restored by the tunnel aperture area is currently unknown, as is the implication of the degree of native insertion site coverage. To our knowledge, no other study has used intraoperative measurements and evaluated how much of the native insertion site is reproduced using an individualized approach to ACL-R. Hence, one of the goals of this study is to determine the percentage of native insertion site area that is restored using individualized anatomic ACL-R techniques by determining the ratio between the native footprint area and the drilled tunnel(s) cross-sectional area.

Interestingly, there appears to be an unpublished assumption that maximal encompassment of the native insertion site area leads to optimal clinical outcomes, supported by the findings that smaller grafts may predispose to failure,219,252 and the established principles of anatomic ACL-R,174 which involves restoring the native ACL insertion site size in order to ensure favorable long-term outcome. Nonetheless, the clinical relevance of the degree of the native insertion site coverage is currently unknown. As such, the second goal of our study is to attempt to establish a clinically measurable or calculable tool (percentage of reconstructed area) as a first step towards elucidating the implications of completely restoring native insertion site size.
MATERIALS AND METHODS

Informed consent is obtained from those who choose to enroll and clinical, surgical, and radiographic evaluations are recorded from their initial to final visits. Subjects were included in this study if they underwent primary anatomic single- or double-bundle ACL-R by the senior author between May 2011 and April 2012. Meniscus or cartilage damage did not affect subject eligibility. Revision cases were excluded. Seventy-two individuals met the eligibility criteria and were identified in the research registry. Of those 72 who underwent individualized anatomic ACL-R, 29 double-bundle (three-tunnel) cases were excluded. Forty-five single-bundle procedures were included in the study.

Surgical technique and intraoperative measurements

The ACL and insertion sites were evaluated with the knee in 90° of flexion. A single, skilled surgeon performed all surgeries and intraoperative measurements. After careful dissection of the tibial insertion site with preservation of the ACL remnants, (Fig. 1a) a flexible ruler was inserted through the CP to measure the tibial insertion length in the longest anterior to posterior direction. (Fig. 1b) Tibial insertion site mid-width was measured at the widest portion perpendicular to the long axis of the insertion site in the medial to lateral direction. (Fig. 1c) To measure femoral insertion site length, the ruler was angled to lie parallel to the medial wall of the lateral femoral condyle when placed through the CP. Femoral insertion site length was measured in the longest proximal to distal direction. (Fig. 2b) Mid-width of the insertion site was measured perpendicular to the long axis at the widest distance in the anterior to posterior direction. (Fig. 2c)

Single- or double-bundle techniques were determined based on previously described methods. ACL-R was performed using an arthroscopic-assisted technique. Femoral

Figure 1. Tibial insertion site measurements using an arthroscopic ruler. a Native tibial insertion after careful debridement with remnant preservation. b Tibial insertion site length measured along the longest anterior–posterior axis. c Tibial insertion site mid-width measured perpendicular to the longest axis in the medial–lateral direction.
and tibial tunnels were created in the center of the respective anatomic insertions. Patients underwent anatomic ACL-R using hamstring autograft, quadriceps auto-graft with a bone block, allograft, or a hybrid graft consisting of a hamstring autograft and allograft.

Femoral tunnels were drilled using the medial portal technique with either a standard or flexible reaming system. When a quadriceps autograft was used, the bone block was placed on the femoral side. It was prepared to the same size of the graft, and the femoral tunnel was drilled to this diameter. Based on the tibial insertion site measurements and graft size, drill sizes were determined for each individual to reproduce as much of the native insertion site as possible. This was achieved by matching desired drill and/ or dilator size to graft size, while accounting for native insertion site size.

After drilling the femoral tunnel(s), the proximal–distal length and anterior–posterior width of the aperture were measured in a manner similar to that described for measuring the femoral insertion site. (Fig. 3) Direct measurement of the tibial tunnel aperture dimensions was not performed due to limited visualization by preserved soft tissue structures. Instead, the area of the tibial tunnel aperture was estimated using the tunnel diameter and tibial drill guide angle, as described by Kopf et al.\textsuperscript{188} For all single-bundle reconstruction, the tibial drill guide was set to 55°.

**Calculating Percentage of Reconstructed Area**

The formula for area of an ellipse was used to calculate the area of the native femoral and tibial insertion sites: \((\text{insertion site length}) \times (\text{insertion site mid-width}) \times (\pi/4)\). (Equation 1) Femoral tunnel aperture area was also calculated using this formula. Tibial tunnel aperture area was calculated using a previously described formula accounting for tibial tunnel drill angle and instrument diameter.\textsuperscript{188} (Equation 2)
Equation 1  Area of an ellipse (A_{ellipse}) = \pi \left( \frac{l \times w}{4} \right)

l = length; w = width. Area of an ellipse accounting for the drill guide angle used to create the tibial tunnel.

Equation 2  Ellipse = \left( \frac{d^2}{4 \cdot \sin \alpha} \right)

d = drill bit diameter or dilator diameter (if applicable); \alpha = drill guide angle.

The percentage of reconstructed area was calculated by dividing the tunnel aperture area by the native insertion site area. (Equation 3)

Equation 3  Percentage of reconstructed area (PRAO) = \left( \frac{\text{Tunnel aperture area}}{\text{Native insertion site area}} \right)

Statistical analysis

Study variables included insertion site cross-sectional area, tunnel cross-sectional area, and the ratio between the two (or percentage of reconstructed area). Statistical analysis included calculation of descriptive statistics for all variables including frequency counts and percentages for categorical variables and measures of central tendency (means and medians) and dispersion (standard deviation and interquartile ranges) for continuous variables. Dependent t-tests were used to compare the insertion site area and the percentage of reconstructed area of the femoral and tibial insertions.
Using the sample size and measured outcomes, the power of this study was determined to be 1.0 (100%) at the 0.05 level of significance. This study was designated as exempt by the University of Pittsburgh Institutional Review Board. Patients presenting to the senior author FHF are routinely given the option to enroll in an IRB-approved research registry.

RESULTS

Forty-five subjects underwent individualized anatomic single-bundle ACL-R. Quadriceps tendon autografts were used for 41 subjects, hamstring autografts were used for 15 subjects, allografts were used for 15 subjects, and one subject underwent reconstruction with a hamstring auto-graft augmented with allograft (hybrid graft).

The femoral insertion site length ranged from 10 to 18mm (mean ± SD, 14.3 ± 2.0mm) and the width measured from 4 to 10mm (mean ± SD, 7.3 ± 1.3mm). On the tibial side, the length of total ACL insertion site measured between 14 and 19mm (mean ± SD, 16.1 ± 1.3mm). Tibial insertion site mid-width ranged between 6 and 12mm (mean ± SD, 9.8 ± 1.0mm). The tibial insertion site was significantly larger than the femoral insertion site (p < 0.001). Femoral insertion site area measured between 38 and 133 mm² (mean, 83.1 ± 20.1mm²), and femoral tunnel aperture area ranged from 38 to 94mm² (mean, 65.0 ± 16.6mm²). Tibial insertion site area ranged from 77 to 165mm² (mean, 124.7 ± 19.6mm²), and tibial tunnel aperture area ranged from 54 to 116mm² (mean, 86.1 ± 17.0mm²). Mean percentage of reconstructed area was calculated to be 79 ± 13% for the femoral insertion site and 70 ± 12% for the tibial insertion. All measurements and calculations are summarized in Table 1.

**TABLE 4.1**

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<tr>
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<th>Tibia</th>
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<tr>
<td>Native insertion site area (mm²)</td>
<td>125±20</td>
<td>83±20</td>
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<tr>
<td>Tunnel aperture area (mm²)</td>
<td>86±17</td>
<td>65±17</td>
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<tr>
<td>Percentage of reconstructed area (%)</td>
<td>70±12</td>
<td>79±13</td>
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DISCUSSION

The most important finding in this present study was that anatomic ACL surgery only restored on average 70–79% of the native insertion site size. Based on the findings, complete footprint restoration (or 100% of reconstructed area) with an adequately sized graft and matched tunnel size is not feasible. This is the first study to attempt to
quantify the degree of insertion site coverage by evaluating this ratio using intraoperative measurements and calculations based on published formulas.\textsuperscript{30}

Though the implications of the degree of insertion site coverage have not yet been studied, previous studies have found that increased graft cross-sectional area to be associated with improved outcomes.\textsuperscript{219,261} In a recent study by Magnussen et al.\textsuperscript{219}, the use of smaller grafts in ACL-R was found to be associated with an increased risk of failure and higher rates of revision surgery in 256 patients undergoing hamstring autograft ACL-R. In another prospective comparative study by Park et al.\textsuperscript{261}, 296 patients underwent SB ACL-R with a quadrupled hamstring autograft. The authors found that patients with a graft diameter of 8.0mm or more had lower failure rates after ACL-R than patients with a diameter <8.0mm (\(p = 0.043\)). Taking into account these findings with those of previous biomechanical studies demonstrating improved graft strength, stiffness, and load to failure,\textsuperscript{252,287} larger grafts are preferred.\textsuperscript{63,118,252,287}

Certainly, the use of an adequately sized graft is crucial in ACL-R; however, this must be performed within the constraints of the patient’s native anatomy. ACL anatomy, including footprints and bony landmarks, is highly variable.\textsuperscript{85,86,128,219} Bigger may not always better as a recent study by Kamien et al.\textsuperscript{169} that found no difference between graft sizes with respect to failure rate in ACL-R. A large graft may reproduce the entire footprint; however, the drilling of a tunnel that lies outside the confines of the footprint may damage neighboring structures or result in graft impingement.\textsuperscript{40,49}

Furthermore, current grafts used in ACL surgery cannot anatomically mimic the shape of the native ACL nor can they completely fill both the femoral and tibial native insertion sites in this study, the tibial insertion site cross-sectional area was nearly twice the size as that of the femur. The mid-substance diameter has been reported to range between 7 and 12mm\textsuperscript{49} and to have a cross-sectional area of 46.9 \(\pm\) 18.3mm\textsuperscript{2}.\textsuperscript{154} Uniform grafts matched as closely as possible to insertion site sizes may result in the graft being larger than the native ACL at its mid-substance.

As the first of its kind, this pilot study is subject to a number of limitations. From a technical standpoint, there is a certain amount of operator error associated with insertion site and tunnel measurements. Additional studies are needed to calculate an intraclass correlation coefficient with respect to validating intraoperative measurement techniques. Additionally, drill guide angle, transverse drill angle, and knee flexion angle all influence tunnel aperture size, shape, and orientation.\textsuperscript{137,188} That being the case, three-dimensional computed tomography (3D CT) evaluation of tunnel aperture area would more accurately account for any deviation in tunnel morphology rather than simple two-dimensional measurements or calculations. However, in an effort to reduce unnecessary radiation exposure and cost, CT scans are not routinely performed following primary ACL-R. Finally, the percentage of reconstructed area is calculated based on two fundamental assumptions. The first assumption is that the native insertion
sites resemble the shape of an ellipse. As such, the calculations used in this study provide a gross estimate of the percentage of reconstructed area, which can be used to evaluate how well the native insertion site area is restored using current reconstruction techniques. The second assumption is that all tunnels are drilled within the confines of the native insertion site. The area of the tunnel apertures was simply compared to the area of the native insertion site to determine the degree of insertion site coverage not accounting for the tunnel aperture area lying outside the native footprint. In essence, the percentage of reconstructed area does not determine the degree of anatomic reconstruction. There is currently an ongoing investigation at our institution employing both 3D CT and 3D MRI to assist in determining the true percentage of reconstructed area by calculating the actual tunnel aperture area and native insertion site area, characterizing the degree of “anatomic” reconstruction and percentage of reconstructed area. This study is the first step towards assessing how well ACL surgeons restore the native insertion site anatomy and its implications in anatomic ACL-R surgery. These measurements can easily be performed by surgeons with the use of a simple, cheap arthroscopic ruler, and the percentage of reconstructed insertion site area can be calculated before leaving the operating theatre. Further biomechanical and clinical studies are needed to this end. The importance of this pilot study provides a fundamental basis on which to build the aforementioned ongoing study as well as projected future studies helping ACL surgeons achieve the goal of true anatomic reconstruction.

CONCLUSION

The primary goal of this pilot study was to determine whether the anatomic ACL-R techniques using previously described flowcharts and insertion site tables could optimally fill the native insertion site with various autograft and allograft choices. Based on our findings, these methods do not restore the insertion site in its entirety. Using the described methods for individualized ACL-R, the estimated tibial insertion site percentage of reconstructed area is 70% and the estimated femoral insertion site percentage of reconstructed area is 79%.

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Bart Muller, Eric R. H. Duerr, C. Niek van Dijk, Freddie H. Fu.

DOES ANATOMIC ACL RECONSTRUCTION RESTORE THE ANATOMIC TIBIOFEMORAL RELATIONSHIP?
ABSTRACT

Purpose: To measure and compare the amount of anterior tibial subluxation (ATS) after anatomic ACL reconstruction for both acute and chronic ACL-deficient patients.

Methods: Fifty-two patients were clinically and radiographically evaluated after primary, unilateral, anatomic ACL reconstruction. Post-operative true lateral radiographs were obtained of both knees with the patient in supine position and knees in full passive extension with heels on a standardized bolster. ATS was measured on the radiographs by two independent and blinded observers. ATS was calculated as the side-to-side difference in tibial position relative to the femur. An independent t test was used to compare ATS between those undergoing anatomic reconstruction for an acute versus chronic ACL injury. Chronic ACL deficiency was defined as more than 12 weeks from injury to surgery.

Results: Patients averaged 26.4 ± 11.5 years (mean ± SD) of age, 43.6% were female, and 48.1% suffered an injury of the left knee. There were 30 and 22 patients in the acute and chronic groups, respectively. The median duration from injury to reconstruction for the acute group was 5 versus 31 weeks for the chronic group. After anatomic ACL reconstruction, the mean ATS was 1.0 ± 2.1 mm. There was no statistical difference in ATS between the acute and chronic groups (1.2 ± 2.0 vs. 0.6 ± 2.3 mm, n.s.). Assessment of inter-tester reliability for radiographic evaluation of ATS revealed an excellent intraclass correlation coefficient of 0.894.

Conclusions: Anatomic ACL reconstruction reduces ATS with a mean difference of 1.0 mm from the healthy contralateral limb. This study did not find a statistical difference in ATS between patients after anatomic ACL reconstruction in the acute or chronic phase. These observations suggest that anatomic ACL reconstruction, performed in either the acute or the chronic phase, approaches the normal AP relationship of the tibiofemoral joint.

Level of evidence IV.

Keywords: ACL · Anterior tibial subluxation · Anatomic ACL reconstruction
INTRODUCTION

It has been established that ACL deficiency causes a passive alteration of the tibiofemoral relationship in the sagittal plane: the tibia subluxates anteriorly with respect to the femur, as can be objectified from MRI and radiographs.\(^{98,315}\) This anterior tibial subluxation (ATS) increases as time between injury and surgery increases and is positively correlated with instability.\(^ {232}\)

Conventional non-anatomic ACL reconstruction techniques have proven unable to adequately reduce the tibia and therefore restore the native tibiofemoral relationship.\(^ {10,13}\) Additionally, it was suggested that irreducible ATS could explain why OA still may develop in stable, reconstructed knees in spite of the improved stability.\(^ {13}\)

Since conventional ACL reconstruction techniques fail to restore the native anatomy, biomechanics and knee kinematics,\(^ {13,96,306}\) anatomic ACL reconstruction aims to more closely restore the native anatomy; consequently, the anatomic technique has been found to be significantly superior to conventional techniques with regard to patient-reported outcome measures and knee laxity testing.\(^ {82,149}\) Although it is generally thought that anatomic ACL reconstruction sufficiently restores the tibiofemoral relationship, this has yet to be evaluated.

The purpose of this study was to assess the tibiofemoral relationship in the sagittal plane after anatomic ACL reconstruction and compare the anterior and rotational laxity (quantified using KT-1000 evaluation and pivot shift testing) with ATS (quantified using a standardized radiography protocol) for both acute and chronic ACL-deficient patients.

It was hypothesized that anatomic ACL reconstruction reduces ATS within 2.0mm from the healthy contralateral side for acute ACL-deficient knees, but that chronic ACL deficiency would lead to fixed ATS irreducible with anatomic ACL reconstruction, thus resulting in a significantly greater degree of post-operative ATS in chronic versus acute ACL-deficient knees. Similarly, it was hypothesized that joint laxity would be greater for chronic ACL deficiency compared with acute ACL deficiency after anatomic ACL reconstruction.

Using a standardized and validated imaging technique after anatomic ACL reconstruction, this study was the first to compare the residual ATS for patients that were acutely and chronically ACL deficient. In contrast to what previous studies have found, chronic ACL deficiency does not appear to lead to a fixed altered tibiofemoral relationship, and anatomic ACL reconstruction may adequately reduce anterior tibial subluxation. Given the current trend in ACL reconstruction, these observations hold important implications regarding surgical technique. Further longitudinal studies are underway to compare the pre- and post-surgical tibiofemoral relationship.
MATERIALS AND METHODS

Fifty-two patients that had suffered an isolated ACL injury were seen in the outpatient clinic and retrospectively evaluated at a minimum of 4 months after primary, unilateral, anatomic ACL reconstruction. All patients were without history of trauma or symptoms to the contralateral knee and without extension deficit of either knee.

With a higher occurrence of intra-articular pathology after 8–12 weeks of ACL deficiency, chronic ACL deficiency was defined as 12 or more weeks between injury and surgery and under 12 weeks was regarded as acute ACL deficient [presented at 15th ESSKA Congress by Kaeding et al.: P19-782. Defining chronicity in an ACL deficient knee: When is a knee with an acutely torn ACL no longer “acute”?].

All patients underwent clinical examination. Anteroposterior (AP) laxity was evaluated by measuring the side-to-side difference of the KT-1000 arthrometer (MedMetric, San Diego, CA, USA) at 89N manual force, and rotational laxity was determined by the clinical grade of the pivot shift test according to the IKDC criteria (grade 0–3).

At the same visit, radiographs were obtained of all patients, made according to a special protocol: patients were positioned in supine position on the radiography table, with the heels on a standardized bolster (part of KT-1000 arthrometer system) and knees in passive terminal extension. The lateral malleoli were stabilized with a foot support platform (part of KT-1000 arthrometer system) so that the hallux would point upwards, perpendicular to the table. The focal point-to-film was always one meter, with the cassette placed on the medial side of the knee. As such, true lateral knee radiographs were obtained bilaterally, using the healthy knee as the patient’s own control. (Fig. 1)

Radiographs of the bilateral knees were loaded into Stentor (Stentor Inc., Brisbane, CA, USA), and measurements were taken by two blinded and independent observers, according to a previously described and validated technique. First, a line was drawn along the subchondral plate of the tibial plateau. At the most posterior aspect of

Figure 1. Patient positioning for radiography. a Patient supine, with the heels on a standardized bolster and knees in passive terminal extension. B Stabilization of the lateral malleoli with a foot support platform so that the hallux would point upwards, perpendicular to the table.
the medial and lateral portions of the tibial plateau, lines were then drawn tangent to the cortex and perpendicular to the first line. (Fig. 2a) The shortest distance from these lines to the most posterior cortical extent of the respective femoral condyles was measured. (Fig. 2b) To correct for potential, minimal rotation on the radiographs, the values for the medial and lateral side were averaged — positive values indicated that the posterior margin of the tibia was anterior to the most posterior extent of the femoral condyles and negative values indicated a posterior position of the tibia relative to the femoral condyles. ATS was then calculated as the side-to-side difference in tibial position relative to the femur. The measurements were not normalized using the size of the tibia to account for differences in magnification, as described previously. The absolute measurement in millimeters was used for this study because a standardized radiographic technique was used for each subject, which minimizes variability in magnification.

Figure 2. ATS measurement technique. a First, a line along the subchondral plate of the tibial plateau was drawn, followed by tangent lines at the most posterior aspects of both the medial (solid line) and lateral (dashed line) portions of the tibial plateau. b Then, the distance was measured (red lines) relative to the position of the medial and lateral femoral condyles. ATS was subsequently calculated relative to the uninjured limb.
For both the acute and chronic groups, the graft type and technique, ATS and laxity-test measurements were recorded and analyzed. All data were recorded in a Microsoft Excel spreadsheet (Microsoft, Redmond, WA, USA).

Exempt institutional review board (IRB) approval was obtained from the University of Pittsburgh under IRB number PRO12020619 to use clinical and imaging data from a research registry of patients presenting to the senior author (F.H.F.) for ACL evaluation.

Statistical analysis
Statistical analysis was performed with independent t tests and Chi-square tests to assess the equality of means (PASW Statistics 18, IBM Corp, Armonk, NY, USA). Statistical significance was set at a p value <0.05.

Post hoc power analysis for a clinically relevant difference of 2.0mm (α value of 0.05) was performed.

Additionally, to assess inter-observer reliability, the intraclass correlation coefficient (ICC) was calculated.

RESULTS
The results are summarized in Tables 1 and 2. Patients averaged 26.4 ± 11.5 years (mean ± SD) of age, 43.6 % were female, and 48.1 % suffered an injury of the left knee. Thirty patients were operated in the acute stadium (median = 5, range 1–11 weeks) and 22 in the chronic stadium (median = 31, range 12–1627 weeks). Nineteen patients had an anatomic double-bundle (DB) ACL reconstruction, and 33 had an anatomic single-bundle (SB) ACL reconstruction. Thirty-five patients underwent ACL reconstruction with a quadriceps graft with bone block and 17 patients with a soft tissue graft. Forty-two of the grafts used were autografts, nine were allografts, and one graft was a hybrid graft (autograft and allograft). Time from surgery to radiography was 34 ± 13 weeks on average.

There were no significant differences between the acute and chronic groups with respect to demographics and surgical details except for age (older chronic group, p = 0.024) and graft source (more allograft use in chronic group, p = 0.003). (Table 1)

At a minimum of 4 months after surgery, none of the patients had an extension deficit, and a mean ATS of <2.0mm (1.0 ± 2.1mm) was calculated for all patients included in the study. This finding was consistent for both the acute (1.2 ± 2.0mm) and chronic (0.6 ± 2.3mm) groups. The mean difference of 0.6mm ATS between groups was regarded neither clinically nor statistically significant (n.s.). Knee laxity testing revealed a mean KT-1000 side-to-side difference of <3.0mm for all patients (1.2 ± 1.3mm). This finding was consistent for both the acute (1.3 ± 1.4mm) and chronic (1.1
± 1.1 mm) groups. None of the patients had a pivot shift test greater than grade 1. In the acute group, 27 patients had no shift at all (grade 0) and three patients a gliding shift (grade 1). In the chronic group, 21 patients had no shift at all and one patient a gliding shift. The mean difference of 0.2 mm in AP laxity between groups was not significant (n.s.), and neither were the differences in rotational laxity (n.s.). (Table 2)

Post hoc power analysis revealed that, with this sample size, a clinically relevant difference of 2.0 mm (value of 0.05 and the derived SD of 2.1) could be detected with a power of >85%. As an indication for inter-observer reliability, an ICC of 0.894 (95% CI 0.819–0.938) was calculated, which was regarded excellent (>0.750).

**TABLE 5.1 Results**

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Acute</th>
<th>Chronic</th>
<th>Significance (p&lt;0.5)</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>23.1±9.3</td>
<td>30.8±13.0</td>
<td>0.024</td>
</tr>
<tr>
<td>Female</td>
<td>12 (40%)</td>
<td>6 (27%)</td>
<td>0.341</td>
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<th>Technique</th>
<th>Acute</th>
<th>Chronic</th>
<th>Significance (p&lt;0.5)</th>
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<tbody>
<tr>
<td>SB</td>
<td>17</td>
<td>16</td>
<td>0.235</td>
</tr>
<tr>
<td>DB</td>
<td>13</td>
<td>6</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Graft Type</th>
<th>Acute</th>
<th>Chronic</th>
<th>Significance (p&lt;0.5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quad</td>
<td>23</td>
<td>12</td>
<td>0.093</td>
</tr>
<tr>
<td>Soft Tissue</td>
<td>7</td>
<td>10</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Graft Source</th>
<th>Acute</th>
<th>Chronic</th>
<th>Significance (p&lt;0.5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Auto</td>
<td>28</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Allo</td>
<td>1</td>
<td>8</td>
<td>0.003</td>
</tr>
<tr>
<td>Hybrid</td>
<td>1</td>
<td>0</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Surgery-Follow Up</th>
<th>Acute</th>
<th>Chronic</th>
<th>Significance (p&lt;0.5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(weeks)</td>
<td>35±13</td>
<td>34±13</td>
<td>0.674</td>
</tr>
</tbody>
</table>

**DISCUSSION**

The most important finding of this study was that anatomic ACL reconstruction reduces ATS with a mean difference of 1.0 ± 2.1 mm anteriorly from the healthy contralateral limb, which validates the hypothesis that anatomic ACL reconstruction reduces the mean ATS to <2.0 mm. Additionally, the results of this study indicate that ATS and knee joint laxity after anatomic ACL reconstruction are not significantly different for both acute and chronic ACL-deficient patients. Thus, the results of this study do not support...
the hypothesis that ATS and knee joint laxity in chronic patients are significantly greater than in acute patients after anatomic ACL reconstruction.

DeJour et al. were the first to describe the occurrence of translation of the tibia in ACL-deficient patients on lateral radiographs. They concluded that rupture of the ACL allowed for the tibia to translate anteriorly and that lateral radiography was useful in diagnosis.

After this finding, different radiography and MRI techniques were developed to objectify ATS as a secondary sign of ACL injury. It was found that measuring ATS is an accurate way to diagnose rupture of the ACL and that there is a positive correlation with the duration of ACL deficiency.

Mishima et al. indicated that ATS, in ACL-deficient knees, increases over time and is positively correlated with AP instability. This led them to conclude that ACL-deficient knees have pathologic tibiofemoral kinematics without external force and that the extent relates to the duration of ACL deficiency and instability.

Using the measurement technique that Franklin et al. had developed, Almekinders et al. found fixed ATS that could not be reduced by an external posterior force on the tibia after failed (conventional) ACL reconstruction. Moreover, Almekinders and de Castro reported that even after successful conventional ACL reconstruction, the tibiofemoral relationship was not normalized and there was residual fixed ATS observed with stress radiographs. They rightfully stated: “if this phenomenon is confirmed in further studies, it could seriously bring into question our approach and reported outcome of ACL reconstruction”. In a follow-up study, Almekinders et al. found that irreducible ATS remains after conventional reconstruction of the ACL. Stress radiography showed a maximum anterior translation of 9.0 ± 4.5mm for ACL deficiency, 4.8 ± 3.8mm after ACL reconstruction and 0.4 ± 2.3mm for uninjured knees.

This study, however, found a remaining anterior subluxation of 1.0 ± 2.1mm after anatomic ACL reconstruction. Although it has not been established what an acceptable remaining ATS would be after ACL reconstruction, 1.0 ± 2.1mm ATS does appear to be a closer approximation of the normal tibiofemoral relationship (uninjured knees: 0.4 ± 2.3mm) than previous studies were able to demonstrate.

Previous studies suggested that the fixed ATS may in part be due to restricted posterior translation. However, since the most fundamental difference between this study and previous studies is the surgical technique, these results suggest that the reported irreducibility may also in part have been due to non-anatomic tunnel placement. Additionally, since tibial reference points may shift relatively to the femur, it only seems appropriate to not use these reference points, but rather the insertion sites and (bony) landmarks on each respective bone as reference points to position the tunnels. Performing surgery in an anatomic fashion seems to adequately reduce the tibia with respect to the femur and may therefore also obviate additional surgical interventions.
such as notchplasty, as was recently suggested.\textsuperscript{343} This is consistent with a study by Hatayama et al.\textsuperscript{133} showing that more anterior placement of the tibial tunnel results in significantly more reduced postoperative anterior tibial translation after anatomic ACL reconstruction than posterior placement does without increasing the risk of postoperative loss of extension or graft failure.

There are some limitations to this study. The first limitation is that this study was performed under static conditions and was limited to sagittal plane movement. Dynamic data would certainly be helpful to assess how this altered tibiofemoral relationship affects actual three-dimensional movement. Another limitation is that this study only addressed the post-operative situation and therefore it is uncertain whether pre-operative subluxation changes after surgery or not. We are currently prospectively recruiting patients at our institution to compare the pre- and post-surgical tibiofemoral relationship in a separate study. A minor limitation of this study is the lack of randomization. Some statistical differences between the two groups (i.e. graft choice and age) might not have occurred if groups were randomized, but it remains questionable whether these factors would have influenced the outcome measures for this particular study. Also, the differences between the two groups are likely the direct result of the individualization of our treatment: younger patients have on average a more active lifestyle and will thus be operated in an earlier stage. Vice versa, older patients are more compliant with conservative treatment and will therefore be operated in a later stage. A similar argument can be made for the higher allograft use in the chronic group; since there are older patients in the chronic group—who also are more compliant with the post-operative protocols and thus have a lower re-tear rate— the use of allograft is more often preferred.

The findings of this study suggest that anatomic ACL reconstruction adequately (<2.0mm) restores the tibiofemoral relationship in the sagittal plane in both acute and chronic ACL-deficient patients and that operating in either stadium yields similar, near-normal results (no statistical difference). For clinical practice, this means that—when performing ACL reconstruction in an anatomic fashion—it does not matter whether surgery is performed in the acute or chronic phase with respect to restoration of the tibiofemoral relationship in the sagittal plane.

**CONCLUSIONS**

This is the first study to investigate the tibiofemoral relationship in the sagittal plane in addition to overall knee stability after anatomic ACL reconstruction. With a standardized imaging protocol and validated reliable measurement technique, under static conditions, without externally applied force, it was found that anatomic ACL reconstruction...
restores the tibiofemoral relationship within 1.0mm on average from the contralateral, healthy knee. Operating in the acute or chronic phase does not yield different results with respect to reducing ATS or knee laxity.

Acknowledgments
The authors thank the Radiology Section, Center for Sports Medicine, University of Pittsburgh Medical Center, for their help and cooperation in this study.
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Does flexible tunnel drilling affect the femoral tunnel angle measurement after anterior cruciate ligament reconstruction?

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DOES FLEXIBLE TUNNEL DRILLING AFFECT THE FEMORAL TUNNEL ANGLE MEASUREMENT FOR THE DETERMINATION OF ANATOMIC TUNNEL PLACEMENT?
ABSTRACT

Purpose: To quantify the mean difference in femoral tunnel angle (FTA) as measured on knee radiographs between rigid and flexible tunnel drilling after anatomic anterior cruciate ligament (ACL) reconstruction.

Methods: Fifty consecutive patients that underwent primary anatomic ACL reconstruction with a single femoral tunnel drilled with a flexible reamer were included in this study. The control group was comprised of 50 patients all of who underwent primary anatomic ACL reconstruction with a single femoral tunnel drilled with a rigid reamer. All femoral tunnels were drilled through a medial portal to ensure anatomic tunnel placement. The FTA was determined from post-operative anterior-to-posterior (AP) radiographs by two independent observers. A 5° difference between the two mean FTA was considered clinically significant.

Results: The average FTA, when drilled with a rigid reamer, was 42.0° ± 7.2°. Drilling with a flexible reamer resulted in a mean FTA of 44.7° ± 7.0°. The mean difference of 2.7° was not statistically significant. The intraclass correlation coefficient for inter-tester reliability was 0.895.

Conclusions: The FTA can be reliably determined from post-operative AP radiographs and provides a useful and reproducible metric for characterizing femoral tunnel position after both rigid and flexible femoral tunnel drilling. This has implications for post-operative evaluation and pre-operative treatment planning for ACL revision surgery.

Level of evidence IV.

Keywords: Femoral tunnel angle (FTA) · Anterior cruciate ligament (ACL) · Anterior cruciate ligament reconstruction · Flexible tunnel drilling
CHAPTER 6 Does flexible tunnel drilling affect the femoral tunnel angle measurement for the determination of anatomic tunnel placement?

INTRODUCTION

Surgery of the anterior cruciate ligament (ACL) has evolved significantly over time. Traditional arthroscopic techniques often failed to restore the native ACL anatomy and function. In an attempt to overcome the difficulties encountered with these traditional techniques, a three-portal technique has been introduced to ensure visualization of the insertion sites and thus achieve more anatomic tunnel placement.

The three-portal technique has been developed using standard rigid drill systems and comes with its own subset of drawbacks which include the possibility of damaging the articular cartilage of either condyle, close proximity of the exit point to the common peroneal nerve, and relatively short femoral tunnel lengths when compared with conventional techniques. An alternative to rigid drilling, introduced by Cain and Clancy, is the use of flexible reamers to create the femoral tunnel. This technique allows for creation of longer anatomic tunnels without violating the articular cartilage, posterior cortex or peroneal nerve, and the need of knee hyperflexion. (Fig. 1)

Post-operative determination of tunnel position following ACL reconstruction can be challenging. Tunnel position has implications for post-operative evaluation and preoperative treatment planning for ACL revision surgery. Different tools have been proposed, and although three-dimensional computed tomography (3D-CT) remains the most accurate, a method using simple measurements on clinically available radiographs was recently introduced by Illingworth et al. Their proposed method was to measure the femoral tunnel angle (FTA) on posterior-to-anterior (PA) flexion weight-bearing (Rosenberg view) radiographs, which was found to be a useful metric for characterizing femoral tunnel position following ACL reconstruction. This simple method made it possible to clinically assess femoral tunnel placement quickly and with...
decreased radiation exposure compared to CT. It was found that an FTA of <32.7° likely corresponds with ACL reconstructions that fall outside an anatomic range.

The measurement of the FTA was only studied for ACL reconstructions performed with a rigid drill. Drilling with a flexible reamer has been shown to alter the femoral tunnel exit point and increase the femoral tunnel length. Thus, it was hypothesized that the use of a flexible reamer will affect measurement of the FTA compared to the use of a rigid reamer. This study is the first to determine the continued usability of measurement of the FTA after flexible femoral tunnel reaming.

Since flexible tunnel drilling has several theoretical advantages, this technique is becoming increasingly popular. This study is clinically relevant for ACL and ACL revision surgery, since post-operative determination of tunnel position following ACL reconstruction, by measuring the FTA, has implications for post-operative evaluation and preoperative treatment planning for ACL revision surgery.

**MATERIALS AND METHODS**

Fifty consecutive patients that underwent primary anatomic ACL reconstruction with a single femoral tunnel drilled with a flexible reamer were included in this study. Fifty patients who underwent primary anatomic ACL reconstruction with a single femoral tunnel drilled with a rigid reamer comprised the control group. A prospective power analysis indicated that a sample of 34 patients in each group was needed to achieve 80 % power to detect a 5.0° difference of the FTA between groups. A 5.0° difference between the two mean FTAs was considered clinically significant. All ACL reconstructions were performed between 2009 and 2012. All reconstructions within this time period were performed anatomically and according to the same concepts. Operation reports were retrospectively evaluated to confirm the surgical technique and assess details of the operation.

**Surgical technique**

All ACL reconstructions were performed with the three-portal technique, making it possible to visualize and measure both the tibial and femoral insertion sites. A single femoral tunnel was created through the medial portal and positioned midway between the center of the anteromedial (AM) bundle and posterolateral (PL) bundle insertion site. The distance to the lateral cortex was determined with a depth gauge, and then, the femoral tunnel was reamed and dilated to the desired size. The rigid reamer (ACU-FeX, Smith & nephew, Andover, MA, USA) usually required knee hyperflexion (~120°) to protect the articular cartilage of the medial femoral condyle while drilling and to maximize tunnel length, whereas the flexible reamer (VersiTomic, Stryker, Kalamazoo,
MI, USA) usually did not. Grafts were fixed on the femoral side with a suspensory device. Therefore, the guide pin was overdrilled with a cannulated, calibrated reamer to allow for the passage of a suspensory fixation device.

**Femoral tunnel angle**

All patients were post-operatively evaluated with standard AP and lateral radiographs of the knee. Analysis of the AP radiographs was done in Stentor (Stentor Inc., Brisbane, CA, USA) using the angle measurement tool, according to a previously described technique by Illingworth et al.\textsuperscript{131} Tunnel position was determined as the measured angle between a line through the center of the long axis of the femur and a line through the center of the femoral tunnel. In concordance with the study by Illingworth et al.\textsuperscript{131}, a tunnel angle below 32.7° was highly predictive of a nonanatomic tunnel.

FTA measurement was performed by two independent, blinded observers. (Fig. 2) Exempt institutional review board (IRB) approval was obtained from the University of Pittsburgh under IRB number PRO12070405 to use clinical and imaging data from a previously established research registry of patients presenting to the senior author (F.H.F.) for ACL evaluation.

**Statistical analysis**

All data were recorded in a Microsoft excel spreadsheet (Microsoft, Redmond, WA, USA). Statistical analysis was performed with an independent t test to assess the equality of means (PASW Statistics 18, IBM Corp, Armonk, NY, USA). Statistical significance was set at a p value <0.05. Additionally, to assess inter-rater reliability, the intraclass correlation coefficient (ICC) was calculated.

**RESULTS**

FTAs for the two groups are summarized in Table 1 and Fig. 3. Since prospective power analysis indicated that a sample of at least 34 patients in each group was needed, 50 patients were included in each group resulting in a total sample of 100 patients.

Rigid tunnel drilling resulted in a slightly lower mean FTA than flexible tunnel drilling. The mean FTA when drilled with a rigid reamer was 42.0° ± 7.2°. Drilling with a flexible reamer resulted in a mean FTA of 44.7° ± 7.0°.

The t test, however, indicated that this mean difference of 2.7° was not statistically significant (n.s.). As an indication for inter-tester reliability, an ICC of 0.895 (95% CI, 0.848–0.928) was calculated.
Figure 2. Method for determining FTA on AP radiographs according to Illingworth et al.: a two proximal widths (line a and line b) of the femoral diaphysis are measured parallel to the Transepicondylar axis TEA; b mid-points of line a and line b are determined to draw an estimation of the long axis of the femur (line y). A line bisecting the femoral tunnel, line x and line y are used for the FTA. (from Illingworth KD, Hensler D, Working ZM, Macalena JA, Tashman S, Fu FH (2011) A simple evaluation of anterior cruciate ligament femoral tunnel position: the inclination angle and femoral tunnel angle. Am J Sports Med 39:2611–2618, with permission)

<table>
<thead>
<tr>
<th></th>
<th>SB Rigid Reamer (n=50)</th>
<th>SB Flexible Reamer (n=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tester 1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min</td>
<td>27.0°</td>
<td>26.0°</td>
</tr>
<tr>
<td>Max</td>
<td>63.0°</td>
<td>63.0°</td>
</tr>
<tr>
<td>Median</td>
<td>42.5°</td>
<td>44.0°</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>41.7±7.1°</td>
<td>44.5±7.5°</td>
</tr>
<tr>
<td><strong>Tester 2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min</td>
<td>25.0°</td>
<td>28.0°</td>
</tr>
<tr>
<td>Max</td>
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<td>63.0°</td>
</tr>
<tr>
<td>Median</td>
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<td>45.0°</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>42.3±7.7°</td>
<td>44.8±6.9°</td>
</tr>
</tbody>
</table>
Figure 3. Difference in FTA between tunnels drilled with a rigid or flexible reamer, respectively, between testers. Angles are recorded in degrees.

Figure 4. The measured angles by Larson et al. Although reportedly in the coronal plane, the provided figure clearly illustrates measurements in the axial plane, supporting the finding that flexible drilling likely does result in a higher anterior inclination. The blue stars denote a statistically significant difference by post hoc analysis between rigid and flexible drilled femoral tunnels, with $p < .05$. (from Larson AJ, Bullock DP, Pevny T [2012] Comparison of 4 femoral tunnel drilling techniques in anterior cruciate ligament reconstruction. Arthroscopy 28:972–979, with permission)
DISCUSSION

The most important finding of this study was that there was a mean FTA difference of 2.7° following ACL femoral tunnel drilling with either a rigid reamer or a flexible reamer. This difference was considered neither clinically nor statistically significant. Therefore, the results of this study do not support the hypothesis. Flexible tunnel drilling does not seem to affect the measurement of the FTA with respect to rigid tunnel drilling.

Given the fact that anatomic ACL reconstruction is an insertion site surgery, the starting point for all drilling is the same. In addition, considering that the curvature of the flexible reamer is likely primarily used to avoid damaging the medial femoral condyle cartilage, that the drilling starting point preferably is headed on the femoral insertion site and that the intraosseous tunnel is always straight, the difference in tunnel angulation is not likely to be seen in the coronal plane, but rather in the sagittal plane.

This assumption is consistent with what Steiner and Smart found when comparing rigid and flexible drilling in a study on six matched pairs of human cadaveric knees. No significant radiographic differences between the rigid (40.0° ± 4.5°) and flexible (44.6° ± 11.4°) drilled tunnels through a medial portal were measured in the coronal plane. On lateral radiographs, however, a significant greater anterior inclination was seen. (Fig. 1)

In a study conducted by Larson et al., a significant difference in FTA, measured in the coronal plane, was found between rigid and flexible drilled tunnels through the medial portal. A closer evaluation of the provided figures, however, showed that the angles were measured in the axial plane rather than in the coronal plane. (Fig. 4) The found mean femoral tunnel axial angle of 51.77° for flexible drilled tunnels was significantly lower than the mean angle of 61.22° for rigid drilled tunnels. This illustrates that flexible drilling results in a higher anterior inclination (no true coronal measurements were done).

Illingworth et al. had shown that an FTA of <32.7° is associated with ACL reconstructions that fall outside an anatomic range. This cut-off value was established from measuring Rosenberg view radiographs. For this study, however, standard AP view radiographs were used. Although these two views are slightly different from one another and the cut-off value of 32.7° most likely does not apply to standard AP radiographs, this was not relevant to the purpose of this study—which was solely to assess whether the mean FTA would be affected or altered by flexible drilling compared to rigid drilling.

There are some limitations to this study. The first limitation is directly inherent to the concept of anatomic ACL surgery, which is that all patients are individuals and therefore anatomically different. Therefore, there was no plausible way to standardize the drill angle for either the straight or flexible drilled tunnels. A similar argument can
be made for the use of radiography; no two radiographs will be the same with regard to flexion angles and rotation. Also, radiographic evaluation remains an assessment of true tunnel trajectory. Despite these limitations however, the data presented in this study are a direct result of actual surgery and thus have direct clinical relevance. Since all radiographs were made according to the same strict protocol, the measurements were highly repeatable, the study was overpowered and the results were neither clinically nor statistically significant. Thus, this study can adequately invalidate the hypothesis.

This study examined the difference in FTA following ACL femoral tunnel drilling with a rigid reamer compared with a flexible reamer through a medial portal. Other studies have demonstrated that nonanatomic reconstructions lead to abnormal knee kinematics and highlight the need for methods to evaluate tunnel position after ACL reconstruction. In clinical practice, the method for characterizing femoral tunnel position following ACL reconstruction by measuring the FTA on plain radiographs, as proposed by Illingworth et al., remains to be a useful metric following either rigid or flexible femoral tunnel drilling. Post-operative determination of the FTA has implications for post-operative evaluation (e.g. anatomic vs. nonanatomic) and preoperative treatment planning for ACL revision surgery (e.g. revision tunnel placement).

**CONCLUSIONS**

Anatomic ACL reconstruction with the three-portal technique can be performed with either a rigid or flexible reamer to create the femoral tunnel. Measurement of the FTA provides a useful and reproducible metric for characterizing femoral tunnel position after ACL reconstruction. The results of this study indicate that there is no difference in mean FTA after rigid or flexible tunnel drilling. The trajectory of the femoral tunnel can be reliably determined from post-operative AP radiographs after both rigid and flexible femoral tunnel drilling.
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Bart Muller, Karl F. Bowman, Asheesh Bedi.

ACL GRAFT HEALING AND BIOLOGICS

CHAPTER 7
KEYWORDS

Tendon-bone healing · Autograft · Allograft · Cytokine · ACL reconstruction

KEY POINTS

• Operative reconstruction of a torn anterior cruciate ligament (ACL) has become the most broadly accepted treatment, aiming to restore native anatomy and a complete return to functional demands.
• Although the reported success rates of ACL reconstruction vary between 69% and 95%, return to previous activity level has recently been reported to be less than 50%.
• The mechanism of graft failure is multifactorial in nature and may be attributed to either traumatic or nontraumatic causes.
Operative reconstruction of a torn anterior cruciate ligament (ACL) has become the most broadly accepted treatment, aiming to restore native anatomy and a complete return to functional demands. Although the reported success rates of ACL reconstruction vary between 69% and 95%, return to previous activity level has recently been reported to be less than 50%. In addition, current surgical techniques have not been shown to prevent the development of late osteoarthritis after ACL injury.

An important, but underreported, outcome of ACL reconstruction is graft failure. Although this is a devastating outcome for the patient, treatment of failed primary ACL reconstructions also poses a challenge for the orthopedic surgeon. Basic science studies have shown that an anatomically placed graft sees forces that are similar to those of the native ACL and are substantially greater than the forces on a nonanatomically placed graft. The successful restoration of native knee kinematics through ACL reconstruction relies on the assumption that there is adequate healing of the graft/bone tunnel interface and reconstructed tissues to withstand the forces transmitted to the native ACL with athletic activity. With the well-established, inferior functional outcomes of revision ACL reconstruction compared with primary ACL reconstruction, prevention of graft failure should be the focus of early after-treatment. Recent efforts at advancing the clinical success of ACL reconstruction have focused on strategies to enhance and optimize the biologic environment of the graft-bone interface, promoting and potentially improving the healing rate and strength of the reconstruction.

The mechanism of graft failure is multifactorial in nature and may be attributed to either traumatic or nontraumatic causes. Recurrent trauma, resulting from early aggressive rehabilitation, a premature return to play, or reinjury of a well-healed graft can lead to graft failure. In addition, nontraumatic causes may include technical error in tunnel placement, occult limb malalignment or ligamentous laxity, failure of fixation, or poor biological incorporation. Often, multiple factors may be present to variable degrees. Biomechanical testing has shown that the time-zero strength of the most common graft choices is greater than the native ACL. Rather, the weakest link after ACL reconstruction is not the graft but the fixation points on the tibial and femoral side until the graft has adequately healed in the bone tunnel. The gradual healing at the enthesis and the intra-articular ligamentization process together make up the 2 main sites of biological incorporation after ACL reconstruction. An understanding of the tendon-bone healing and the intra-articular ligamentization process is crucial for orthopedic surgeons to make appropriate graft choices and to be able to initiate optimal rehabilitation protocols after surgical ACL reconstruction.

Graft-tunnel healing is influenced by many different factors, including surgical technical variables such as graft placement, graft length within the bone tunnel, graft
fixation, graft tensioning, and graft-tunnel micromotion. These variables may even vary for different regions of the bone tunnels. However, the principal form of healing that occurs in the bone tunnels is primarily dependent on the graft used. Grafts with a bone plug (e.g., bone-patellar tendon-bone graft, bone-quadriceps tendon graft) rely on bone-to-bone healing, whereas soft tissue grafts rely on tendon-to-bone healing, a slow process that does not recapitulate the native anatomy of the ACL insertion with regard to morphology or mechanical strength. However, all grafts depend on tendon-to-bone healing at the intra-articular tunnel apertures. Tissue engineering and biomechanical stimulation approaches to enhance this healing process have shown promising results in animal studies and include, but are not limited to, the use of a fibrin clot, platelet rich plasma, growth factors, stem cells, scaffolds, periosteum graft augmentation, bisphosphonates, autologous ruptured tissue, and mechanical loading.

This article focuses on the current understanding of the tendon-to-bone healing process for both autografts and allografts and discusses strategies to biologically augment healing.

**TENDON-BONE HEALING: AUTOGRAFT**

Healing of a tendon graft inside a bone tunnel is particularly challenged by the complex transition site, which must allow for load transfer between the 2 distinct, inhomogeneous tissues: tendon and bone. Moreover, this transition site is markedly different from the load-transferring architecture of the insertion site of the native ACL.

The native ACL inserts into the bone through an insertion site that changes from ligament to bone directly and functions to transmit complex mechanical loads. This insertion site is made up of highly specialized tissue that gradually changes from ligament to bone through 4 zones: ligament, unmineralized fibrocartilage, mineralized fibrocartilage, and bone. (Fig. 1) The increase of tissue stiffness along the insertion site from tendon to bone is likely controlled by collagen fiber alignment and a gradual increase of mineralization. A direct insertion from ligament to bone as the ACL has different from other ligaments and tendons, such as the medial collateral ligament (MCL), that run parallel to the bone and insert through an indirect insertion site. Indirect insertion sites do not gradually change from ligament to bone, but rather consist of specialized collagen fibers, called Sharpey fibers, which are oriented obliquely to the long axis of the bone and ligament and provide anchorage between the 2 tissues.

With anatomic ACL reconstruction, the native insertion sites are restored with respect to the insertion site locations on the femur and tibia. However, because the grafts are placed in bone tunnels, the structure and composition of the direct insertion site are not reproduced. Instead, the graft heals with a fibrovascular scar at the graft-tunnel
interface and forms perpendicular collagen bundles to counteract the shear stresses, attaching the tendon to the bone.\textsuperscript{115,116,270} These perpendicular bundles resemble the Sharpey fibers of an indirect insertion site.\textsuperscript{116,270} The formation of these fibers begins at 3 to 4 weeks after graft placement and their size and number are positively correlated with the graft pull-out strength.\textsuperscript{115,116,270} Sharpey-like fibers continue to be present at 1 year after surgery while gradual osseointegration occurs, improving the graft attachment and incorporating the graft into the surrounding bone.\textsuperscript{270}

The earliest phase of healing comprises an inflammatory response characterized by the presence of distinct subpopulations of macrophages. Around 4 days after surgery, macrophages recruited from the circulation and neutrophils are present in the healing tendon-bone interface and are involved in phagocytizing cellular debris, recruiting additional inflammatory cells, and assisting in proinflammatory cytokine release. After 10 days, resident, progenative macrophages can be identified.\textsuperscript{179} These inflammatory cells repopulate the graft and produce numerous cytokines, like transforming growth factor \( \beta \) (TGF-\( \beta \)), which contribute to the formation of the fibrovascular scar tissue interface between the graft and the bone tunnel.\textsuperscript{179} (Fig. 2) However, the formation of this scar tissue results in a mechanically inferior tendon-bone interface, with less organized collagen deposition and decreased pull-out strength than when this scar formation is diminished by macrophage depletion in animal models.\textsuperscript{134} (Fig. 3)
Macrophages, TGF-β, and the cyclooxygenase 2 (COX-2) pathway have a complex interplay, and although a depletion of macrophages may be accomplished by inhibiting the COX-2 pathway, different studies have shown that selectively inhibiting the COX-2 pathway delays healing with significantly decreased load to failure.

During the first 8 weeks postoperatively, the tendon-bone interface undergoes significant immunohistologic changes. There is an infiltration and recruitment of macrophages and marrow-derived stem cells to the interface. Initially, the interface consists of mainly granulation tissue containing type III collagen and produces growth factors like vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF), stimulating angiogenesis and enlarged fibroblasts at the healing enthesis. Simultaneously, like fractured bone, the bone tunnel starts a process of endochondral ossification and chondroid cells appear from the tunnel wall, which degrade the granulation tissue and produce type II collagen. Gradually, the granulation tissue is replaced by maturing lamellar bone and the chondroid cells decrease in number. Meanwhile, shear stresses between the tunnel and the graft cause Sharpey-like fibers to develop, and from the margins of the hypocellular graft, FGF is expressed, attracting fibroblasts to incorporate into the graft and produce type III collagen.
Although the inflammatory phase is essential for the tendon-to-bone healing process, the phase should be transient and gradually progress to the proliferation phase. Early return to sports or an aggressive rehabilitation protocol may lead to micromotion of the graft inside the tunnel.\textsuperscript{126} This relative movement between graft and tunnel may impair healing because of continuous microtrauma of the healing tissues, which results in a sustained inflammatory response at the healing enthesis site. The graft-tunnel motion may also lead to osteoclast activation, which stimulates tunnel widening by bone resorption.\textsuperscript{126,271} Although excessive motion impairs healing, some controlled loading has shown to be beneficial in tendon healing.\textsuperscript{180} (Fig. 4)

Controlled mechanical loads after a delay to allow resolution of acute postoperative inflammation result in improved mechanical and biological parameters.\textsuperscript{38,105}

During the proliferation phase, the stem cells proliferate and differentiate, and matrix metalloproteinases (MMPs) and serine proteases degrade the provisional matrix. The
healing cells synthesize and deposit new extracellular matrix with progressive bone ingrowth, which results in an improved load-to-graft failure.\textsuperscript{270,322}

Gradually, remodeling of the newly formed matrices takes place; the newly formed woven bone, interface tissue, and graft remodel, with establishment of collagen fiber continuity between tendon graft and bone, and cellularity and vascularity at the interface decrease. (Fig. 5)

\textbf{TENDON-BONE HEALING: ALLOGRAFT}

The use of allograft for soft tissue reconstructive surgery has increased significantly in recent years. The main advantages of using an allograft for ACL reconstruction include the ease of customizing the graft to the desired size and shape, availability, lack of donor-site morbidity, reduced operation times, reduced postoperative pain, and a theoretically lower risk of arthrofibrosis.\textsuperscript{66,129} Moreover, some studies have reported no significant difference in clinical outcomes for bone-patellar tendon-bone autografts and allografts, although others have reported significantly greater failure rates in younger patients less than the age of 40 years.\textsuperscript{34,110,168}

Allografts heal through the same biologic pathway of creeping substitution like autografts, but at a slower rate. The intra-articular portion of the allograft heals by acting as a type I collagen scaffold, which is populated from the tunnels with host cells derived from the bone and synovial fluid.\textsuperscript{231} Angiogenesis is predominately facilitated from the infrapatellar fat pad distally and from the posterior synovial tissues proximally.\textsuperscript{250}
angiogenesis is followed by invasion of fibroblasts and synovial cells to repopulate the tendon with host cells and gradually incorporate and remodel the matrix of the graft. As remodeling of the matrix takes place, the tensile strength of the graft is substantially reduced initially and then increases as remodeling is finalized. Allografts lose more of their initial strength during remodeling than autografts, rendering the grafts particularly vulnerable to failure in the subacute phase of postoperative rehabilitation and with a premature return to sport.\textsuperscript{158}

Even although ligaments and tendons are relatively hypocellular, the use of fresh grafts might stimulate the host immune response by lymphocyte invasion, perivascular cuffing, and eventually graft rejection.\textsuperscript{27} This immune response is elicited mostly by the expression of major histocompatibility antigens, present on the surface of viable allograft cells. Therefore, fresh tendon allografts are generally not used. Although sterilization can decrease the presence of viable allograft cells, this treatment comes at the expense of decreased biomechanical strength of the graft, which is associated with irradiation or chemical processing.
Tendon allografts can be sterilized by several methods, including chemical sterilization, deep freezing, or α-irradiation, resulting in decreased graft immunogenicity and reduced risk of disease transmission. However, each method has its own drawbacks, which should be taken into consideration when performing ACL reconstruction with allograft. Chemical sterilization may result in inflammatory reaction, delayed remodeling, and inferior mechanical strength and may not be ideal for soft tissue allograft. Deep freezing is an effective method to kill the donor cell, but may still result in a detectable immune response directed to the matrix antigens, which can also influence graft incorporation and remodeling. Over recent years, γ-irradiation has become the most widely applied allograft sterilization method. Relatively low doses (1.5–2.0 Mrad) can effectively kill bacteria, fungi, and spores, but not viral agents. However, studies have shown that doses more than 2.0 Mrad cause a reduction in the biomechanical properties of the graft and inferior clinical outcomes have been reported. Sterilization methods are being further developed and refined to safely sterilizing the tissue, minimizing the risk of disease transmission, and limiting the detrimental effect on the biomechanical properties of the graft. Newer proprietary methods that are currently being studied are typically washes that use a combination of detergents, antibiotics, alcohol, peroxide, and irradiation.

GROWTH FACTOR/CYTOKINE-BASED AUGMENTATION OF TENDON-BONE HEALING

Each phase of the tendon-bone healing process is tightly regulated by a complex cascade of cytokines, promoting cellular proliferation, differentiation, chemotaxis, matrix remodeling, and matrix synthesis, which results in healing. The key chemical regulators are currently believed to include the TGF family, bone morphogenic protein (BMP) family, insulin-like growth factor (IGF) family, MMPs, FGFs, VEGFs, and platelet-derived growth factors (PDGFs). The paracrine and autocrine action of each factor is dependent on multiple variables, including concentration, timing, and synergy with other cytokines and can have both favorable and inhibitory effects depending on the local environment.

TGF-α is a key regulator during embryologic tendon development and also plays a significant role in the modulation of scar tissue formation during connective tissue healing. Three molecular isoforms (TGF-1, TGF-2, TGF-3) have been identified in mammalian tissues. TGF-1 and TGF-2 are expressed during the early inflammatory phase of adult tendon healing; stimulating cell migration, proliferation, and collagen synthesis. This situation results in scar tissue formation that strengthens the tendon-bone interface, but does not recreate the architecture and mechanical proper-
ties of the native tendon enthesis. Recent studies have identified the role of the TGF-3 isoform in promoting direct tendon healing without scar formation (scarless healing) in the fetal and neonatal environment. Animal models have also shown the ability to improve the collagen ratio, collagen histologic organization, and biomechanical strength in the early healing stages of rotator cuff tendon injuries when treated with TGF-3 in a calcium phosphate matrix. If these results apply to the ACL tendon-bone interface, modulation of the TGF-3 family of cytokines may potentially allow for improved healing and recreation of a more anatomic interface.

The BMP molecules are osteoinductive cytokines related to the TGF-3 family, and are important for fetal skeletal development. Multiple isoforms of BMP have been identified, with BMP-2 and BMP-7 commercially available for enhancing fracture healing and bone regeneration. BMPs also facilitate the healing of tendon to a bone tunnel by promoting formation of a fibrocartilaginous zone at the bone-tendon interface and stimulating bone ingrowth during the later phases of remodeling. The use of BMP-2 delivered via adenovirus has been shown to improve tendon-bone healing during ACL reconstruction in a rabbit model. These studies showed improved collagen organization and osteointegration of the tendon graft with formation of a transitional osteocartilaginous and fibrous tissue matrix compared with a poorly vascularized dense connective tissue in controls. Biomechanical testing of the ACL graft constructs showed significantly higher load to failure and stiffness in the BMP-2–treated group at 8 to 12 weeks after reconstruction. Similar results of improved ACL soft tissue graft healing within a bone tunnel with BMP-2 treatment have been reported in canine and porcine models. BMP-12, BMP-13, and BMP-14 have also been found to improve the healing after ligament reconstruction by increasing fibrocartilage formation at the healing enthesis and improving load to failure in animal models, and may have a role in augmenting tendon-to-bone healing after surgery in patients.

IGF-1 is a critical cytokine that plays a key role in the inflammatory process at all stages of repair and regeneration of musculoskeletal soft tissue, and the absence of IGF-1 dramatically impairs tissue healing. It serves as a chemotactic agent to recruit and stimulate fibroblasts and inflammatory cells to the site of injury. In vitro studies have shown significant increases in DNA synthesis, type 1 and 3 collagen gene expression and synthesis, and proteoglycan synthesis in canine ACL fibroblasts after treatment with IGF-1. These stimulatory effects of IGF-1 on in vitro fibroblasts seem to be dose-dependent and have been consistently shown in multiple tendon locations. In vivo studies have shown accelerated functional recovery and reduced functional deficit without a change in the tendon biomechanical properties after Achilles transection in rats treated with a single dose of IGF-1 injected into the surgical wound. The investigators concluded that the effects of IGF-1 may occur through modulation of the initial inflammatory response without apparent detriment to
the biomechanical strength of the healed tissue. Similar beneficial effects on collagen expression, enthesis architecture, and maximal tendon repair load to failure have been shown in a rotator cuff tear model. The clinical implications of these studies are promising and certainly warrant additional evaluation.

MMPs are zinc-dependent enzymes that are present in connective tissue and are activated from their latent form via a cleavage mechanism, regulating and maintaining the dynamic homeostasis of the extracellular matrix of connective tissues. Their enzymatic activity is balanced by tissue inhibitors of MMP proteins, which assist in coordinating a balance of matrix regeneration and remodeling. MMP production and activation are increased in the presence of inflammatory signals such as interleukin 1b (IL-1b) and TGF-1, serving as a key component of the early inflammatory and repair phases of healing. Local and systemic inhibition of MMP activity in a rotator cuff repair model has shown reduced collagen degradation, increased fibrocartilage production, improved collagen fiber organization, and increased mechanical load to failure. Regulating the degradative balance of MMPs may play a significant role in improving the quality and rate of healing at the tendon-bone interface during ACL graft incorporation.

The FGF family of cytokines are abundant in normal adult tissue and play an integral role in angiogenesis, mesenchymal cell mitogenesis, and the initiation of granulation tissue formation in the early phases of healing. FGF-2 contributes to fibrous integration at the tendon-bone interface and stimulates vascularization after rabbit ACL transection and reconstruction. Fibroblast expression of FGF during ACL graft healing is highest during the first 6 weeks of healing and coincides with active collagen deposition, progressively declining as the healing changes from fibroblast scar tissue formation to osteoblast deposition of immature, woven bone regulated by BMPs.

VEGF is expressed in the early phase of tendon injury and healing, promoting angiogenesis by stimulating vascular endothelial cells and facilitating recruitment of inflammatory cells. VEGF production is stimulated by local biologic factors, including autocrine and paracrine signaling from inflammatory factors (IL-1b, FGF, prostaglandins) and local tissue hypoxia. Expression of VEGF is highest during the first few weeks after rabbit ACL reconstruction at the bone-tendon interface and continues to be expressed focally by osteoblasts at the bone surface for up to 12 weeks postoperatively. Similarly, VEGF expression is present in multiple sites of tendon injury, and local administration has been shown to improve the biomechanical properties of rat Achilles tendons after repair. These beneficial effects of VEGF are most likely caused by angiogenesis and improved transportation of other critical inflammatory mediators to the site of injury or surgical repair.

PDGF is a dimeric molecule consisting of 2 chains (A and B), and is predominantly found in the granules of platelets. Release of PDGF during the acute inflammatory
phase occurs after platelet adherence to the exposed collagen within the vascular endothelial membrane in the setting of injury. It is one of the most potent serum mitogens and promotes early wound healing by stimulating fibroblast, glial, and smooth muscle cell proliferation, initiating the clotting cascade, arachidonic acid synthesis, prostaglandin production, and glycolysis in local tissue. PDGF release is tightly regulated by circulating α-macroglobulin to prevent the biologically active cytokine from entering the systemic circulation. PDGF is not present in normal ACL tissues and has been shown to be present at low levels after ACL transection in a rabbit model. This finding is in contrast to a high level of PDGF present in MCL wounds after surgical transection and may partially account for the lack of clinical healing seen in ACL injuries. After ACL reconstruction with autogenous patellar tendon graft in a canine model, early PDGF deposition is observed in the granulation tissues at the graft-bone tunnel interface and in developing capillary beds within 7 days of surgery. During the early repair and graft incorporation phases of healing (3–6 weeks), PDGF is present in the graft substance and at the bone tunnel interface, gradually decreasing by 12 weeks postoperatively. Li and colleagues investigated the effects of mesenchymal stem cells transfected for sustained PDGF expression, on allograft incorporation in a rabbit model. This model showed improved granulation tissue formation and neovascularization at 3 weeks and the appearance of more chondrocytelike cells at the healing interface by 6 weeks. Collagen maturation, direct tendon-bone tunnel healing, and allograft incorporation were improved in the PDGF-treated group compared with controls.

Tendon-bone healing is a complex process that is dependent on numerous biological factors, and research on the chemical interactions involved in the healing process have led to promising results in the improvement and acceleration of ACL graft incorporation. Further investigation is required before the routine clinical implementation of cell-based and biological factors is advocated to augment healing after ACL reconstruction, and likely represents a critical frontier to improve outcomes after all soft tissue reconstructive procedures.

**SCAFFOLDS AND ACL REPAIR/RECONSTRUCTION**

ACL healing after primary repair has not been successful secondary to the unfavorable intra-articular environment and relatively avascular tissue. This situation has led to continued research into novel approaches to manage ACL injuries, including the use of biologic and synthetic scaffolds to augment healing after primary ACL repair or ACL graft incorporation after reconstruction. Multiple materials have been evaluated, including collagen matrices, silk, poly-L-lactic acid polymers, poly-glycolic acid constructs, alginate polymers, and chitosan-based polymers. The ideal scaffold supports
growth and differentiation of relevant cell populations, directs cellular inter- actions, promotes formation and maintenance of the extracellular matrix, and possesses ade- quate mechanical strength to withstand rehabilitation and avoid degradation before incorporation or healing.

To facilitate primary healing of the ACL after repair, an appropriate environment must be present to allow healing and restoration of the native ligament properties. Initial investigation into the use of collagen platelet composites (CPC) has shown successful healing of a central ligament defect in a canine model. Treatment with CPC at the time of ACL injury resulted in robust healing similar to patellar tendon and MCL models, with improved growth factor expression, histologic ligament healing, improved magnetic resonance imaging findings, and significantly increased biomechanical properties compared with untreated ACLs.\textsuperscript{240,241,294} This technique was subsequently validated in vivo with a juvenile pig model treated with complete ACL transection followed by primary ligament repair with absorbable sutures followed by suspension of the collagen scaffold soaked in platelet rich plasma on the suture repair. This technique resulted in a significantly higher repair strength and improved cellularity at 4 weeks and 3 months compared with primary ACL repair without treatment.\textsuperscript{167} Further investigations have shown that primary ACL healing with CPC is also dependent on age and time from injury to repair, with younger animals and shorter time from injury to repair showing an improved healing capacity.\textsuperscript{218,226,239} Clinical implications of these findings include the possibility of successful primary ACL healing after repair with an off-the-shelf device, and may represent a future strategy in the management of pediatric ACL injuries without the risk of physeal injury.

Current soft tissue options for ACL reconstruction include hamstring, fascia lata, and quadriceps tendon autografts and various allografts, relying on scar-based healing to the adjacent bone tunnel wall to provide adequate fixation strength. Preliminary results of tissue engineering\textsuperscript{216} targeted at enhancing the regeneration of the bone-soft tissue interface by recreating the multitissue transition from tendon/ligament, fibrocartilage, to bone are encouraging. Rabbit studies have shown the ability to improve the tendon-bone interface by incorporating an allogeneic costal cartilage chondrocyte pellet into a surgically created patellar tendon wound and subsequent repair. This technique improved the histologic appearance of the repair site and re-established an anatomic tendon/fibrocartilage/bone enthesis at 8, 12, and 16 weeks compared with control specimen.\textsuperscript{324} Spalazzi and colleagues have published their results on a tri-phasic scaffold consisting of fibroblast, chondrocyte, and osteoblast populations in an attempt to more closely recreate a native tendon insertion. This triphasic scaffold has been evaluated in vitro and in vivo, with phase A consisting of human fibroblasts cultured in a poly(lactic-co-glycolic acid) (PLGA) polymer for soft tissue formation, phase B consisting of a fibrochondrocyte culture in PLGA for transitional tissue, and phase C consist-
ing of human osteoblasts cultured in PLGA combined with sintered glass microspheres to recreate the calcified entheseal layer. After subcutaneous incubation in rats, the cellular distribution within the scaffold remained in a phase-specific distribution. The investigators conclude that a triphasic scaffold has the potential to recreate the organization inherent to the ligament-bone interface, and could be used to guide the establishment of an anatomic fibrocartilage interface between a soft tissue graft and a bone tunnel or aperture after ACL surgery.

Clinical interest in avoiding the morbidity of autograft harvest and the risks of allogeneic tissue have stimulated the development of engineered grafts for ACL reconstruction. Ma and colleagues used a sheep model to engineer a bone-ligament-bone construct in cell culture with adequate size to allow for ACL reconstruction. Bone marrow stromal cells were harvested from sheep femurs and treated with specific growth factors to create independent ligament and bone lineages. The ligament cells were allowed to develop into a monolayer and were inserted between 2 20mm bone monolayers separated by a distance of 30 to 40mm. Eight individual constructs were combined to form a bone-ligament-bone graft of 60 to 80mm in length and 3mm in diameter. ACL reconstruction was then performed with the engineered grafts, followed by harvesting of the native and engineered ACLs at 2, 3, 4, and 6 months postoperatively. At 4 months postoperatively, the graft size was equal to the native ACL, and histologically showed robust vascularity, remodeling, and bone tunnel healing. Biomechanical testing showed a 90-fold increase in graft strength at 6 months, achieving 92% stiffness of the native ACL and similar load to failure. These results represent the successful development of a multiphasic ACL graft with mechanical properties similar to the native adult ACL in sheep and have implications for the future potential of a completely engineered ACL graft for human use.

Synthetic scaffolds or ligament substitutes are another attractive option to avoid graft site morbidity in ACL reconstruction. Previous artificial ligament grafts including polyaramid, carbon fiber, and polyester devices have been largely unsuccessful because of high failure rates and reactive synovitis from wear particles. Richmond and Weitzel have recently investigated the use of a silk scaffold for ACL reconstruction, with the advantage that manipulation of the fiber properties can control the rate of scaffold degradation and fibrous ingrowth. An in vivo study was performed in a goat model with placement of an artificial ACL ligament constructed of a woven silk fiber composite through 6mm bone tunnels. Each fiber had a diameter less than 350mm to facilitate synovial absorption of the degradative products. Histologic results at 12 months showed organized collagen healing with a native crimp pattern and spindle-shaped fibroblasts similar to the native ligament, with Sharpey fibers identified within the bone tunnel at the graft-bone interface. There was no evidence of regional lymph node reactivity of presence of silk particles. Laxity testing revealed up to 4mm
anterior tibial translation at 12 months postoperatively, comparable with the results of autograft and allograft reconstructions reported in a goat model. Human studies have been initiated and preliminary results are pending publication, although the initial goat studies highlight the potential of bioengineered ligament devices to address the requirements of an appropriate synthetic ACL substitute.

**SUMMARY**

Recent improvements in surgical management options of ACL injuries have called further attention to the importance of new biological strategies to enhance the intra-articular and intra-osseous healing process. Current research trends have focused on both refining existing techniques and developing novel solutions such as augmentation of graft-tunnel healing, primary ACL repair, and use of scaffolds to improve or obviate autogenous or allogeneic grafts for reconstruction. Further research is necessary before widespread clinical adoption; the preliminary results of these modern advances are promising and likely represent the future of ACL injury prevention and management.
Submitted as:
Predictors of Return to Preinjury Sports after Anterior Cruciate Ligament Reconstruction.


To the American Journal of Sports Medicine
PREDICTORS OF RETURN TO SPORTS AFTER ACL RECONSTRUCTION
ABSTRACT

Background: Return to the preinjury level of sports participation is an important outcome of ACL reconstruction. Previous literature has suggested a relatively low rate of return to pre-injury sports (RTPS). The reasons why patients do not return to their preinjury level of sports participation after surgery are not well understood.

Purpose: To determine factors that predict return to the same frequency and type of sports participation with similar activity demands as before injury.

Study Design: Cross-sectional study (diagnosis): Level of evidence, 2

Methods: Individuals 1 to 5 years after primary ACL reconstruction completed a comprehensive survey related to sports participation and activity before injury and after surgery. Patient characteristics (age, time from injury to surgery, gender), injury variables (mechanism of injury, concomitant injuries), and surgical variables (Lachman and pivot-shift tests under anesthesia, graft source, femoral drilling technique, method of ACL reconstruction) were extracted from the medical record. Comprehensive RTPS was defined as: “Returning to the same or more demanding type of sports participation (on a four-point scale ranging from 1: no sports to 4: strenuous sports), at the same or greater frequency (on a four-point scale ranging from 1: less than one time per month to 4: 4-7 times per week) with the same or better Marx Activity Score as before injury.” Variables were compared between patients that achieved comprehensive RTPS and those that did not with univariate and multivariate logistic regression models.

Results: Two hundred and fifty-one participants (mean age 26.1 years, SD 9.9) completed the survey at an average of 3.4 years (SD 1.3) after ACL reconstruction. The overall rate of RTPS was 48.6%. Patients were more likely to RTPS if they were younger than 19 years old at time of injury (odds ratio [OR] ≤ 18 years old = 4.07; 95% CI, 2.21-7.50; p<.01) or if they were a competitive athlete at the time of injury (OR competitive athlete = 2.07; 95% CI, 1.24-3.46; p=.01), and were less likely to RTPS if surgery occurred more than 3 months after injury (OR >3 months = .31, 95% CI, 0.17 – 0.58; p< .01), if there was a cartilage lesion in the knee (OR cartilage lesion = .38; 95% CI, .21-.70; p<.01), and if concomitant cartilage surgery was performed (OR cartilage surgery = .17; 95% CI, .04-.80; p=.02). No other measures of concomitant injury, surgical technique, or graft type were significantly associated with RTPS. Clinically relevant multivariate models did not offer any additional insight into predicting comprehensive RTPS status over the univariate models.

Conclusions: Five variables best predicted RTPS including age at time of surgery, being a competitive athlete prior to injury, time from injury to surgery, tibiofemoral cartilage status, and concomitant cartilage surgery. Only time from injury to surgery is a potentially modifiable factor to improve RTPS, however, the reasons for which patients delayed surgery may also contribute to them not returning to sports. Regard-
less, younger patients that partake in sports on a competitive level, that have ready access to healthcare and less cartilage damage or surgery to their knee return to sports more often, potentially due to higher levels of intrinsic motivation and fewer knee joint problems after surgery. While these variables may be helpful in predicting which individuals return to pre-injury sports, there are likely many other factors that determine whether or not an individual returns to pre-injury sports participation including motivational factors and aspects of rehabilitation.

Keywords: ACL; anterior cruciate ligament; anterior cruciate ligament reconstruction; return to sport; sports participation; prognosis.
INTRODUCTION

The goals of anterior cruciate ligament (ACL) reconstruction are to restore structure and function of the ACL and knee, prevent from re-injury and the future development of early post-traumatic osteoarthritis (PTOA) and to allow for safe return to preinjury sports. According to the World Health Organization, greater emphasis of health outcome evaluation should be placed on evaluating participation-based outcomes,\textsuperscript{312} such as return to sport following ACL reconstruction. Moreover, it has long been recognized that returning to preinjury sports is not only an important outcome for ACL reconstruction, the desire to return to the preinjury level of sports participation, particularly sports involving cutting, pivoting, and jumping maneuvers, is one of the major indications for ACL reconstruction.\textsuperscript{319}

In spite of its importance, precise estimates of the rate of return to the preinjury level of sports participation after ACL reconstruction remain unknown. Reported rates in previous literature at short-term follow-up vary widely, ranging from 33\% to 92\%.\textsuperscript{25,114,163,247} However, more recent work by Ardern et al.\textsuperscript{24} has shown that results may actually be disappointing at mid-term, with a return to preinjury sports rate of only 45\% at a follow-up of 2-7 years after ACL reconstruction. Additionally, they found that athletes who return to competitive sport by 12 months do not necessarily maintain participation in sport, suggesting that 12 months after surgery may be too early to accurately assess return to sport outcomes.\textsuperscript{24}

The discrepancy in reported return to sports rates and the low return to sports rates are not well understood. One suggested explanation for the discrepancy in the reported rates of return to sports participation is the lack of an unanimous operational definition of return to sports.\textsuperscript{24} Another reason could be that sport participation outcomes are usually evaluated at the population level. It is important to consider that populations between studies differ (e.g. elite professional athletes versus recreational athletes) and that many different variables (both physical and psychological) influence an athlete’s decision to return to sports. Therefore, it seems more relevant to identify those variables that may be predictive of return to sports for the individual patient, rather than generalized population based rates.

Multiple studies have investigated demographic factors, physical impairments, and functional and psychosocial measures that may be associated with an individual’s decision to RTPS. However, since these studies focused on the post-surgery phase, identified variables should be regarded as decision criteria for returning to sports, rather than predictors.\textsuperscript{71,95,202,203}

There is a general paucity of research that has investigated pre-injury, pre-surgical and surgical factors that predict successful return to preinjury level of sports participation.\textsuperscript{132} Therefore, the purpose of this cross-sectional study was to determine factors that
predict return to preinjury level of sports participation. For this study, we operationally defined return to preinjury sports as returning to the same or more demanding type of sports participation, at the same or greater frequency with the same or better Marx Activity Score as before injury.

MATERIAL AND METHODS

A cross-sectional study design was used to examine potential predictors of RTPS at the medium-term follow-up after ACL reconstruction surgery. This study received ethical approval before commencement by the Institutional Review Board at the University of Pittsburgh (protocol number PRO11120006). All subjects provided written informed consent for participation in this study.

Instruments

For this study, subjects completed a comprehensive questionnaire that included self-reported demographic data, information related to the initial injury and surgery, re-injury and any additional surgeries as well as information related to the type and frequency of sports participation and the Marx Activity Rating Scale before injury and at the individual’s best after surgery. The questionnaire was pilot tested in our outpatient clinic to evaluate the burden of the survey on patients as well as to integrate patients’ comments and suggestions, and to clarify any ambiguous questions before it was distributed to subjects for this study.

Subject Eligibility and Recruitment

Medical records were reviewed to identify all patients that were between 1 to 5 years after primary, unilateral, anatomic ACL reconstruction. Subjects between the ages of 14 and 50 at the time of surgery were included. All surgeries were performed by a surgeon affiliated with our institution. Clinic and operative notes were reviewed to ensure that subjects who had prior knee injury or surgery to either knee were excluded from participation.

Invitation letters along with the questionnaire and consent form were sent to potential subjects using a three-phase mailing procedure followed by postcard reminders and phone calls to maximize response rate.

Postoperative Rehabilitation Protocol

Operated knees were immediately immobilized with a brace after surgery. Patients were discharged from the surgical center on the day of surgery with adequate pain medication and a cooling device. During the first several weeks after surgery, focus
was placed on minimizing pain, reducing swelling, restoring full ROM and quadriceps muscle strength. The day after surgery patients began to perform ankle pumps, quadriceps sets, straight leg raises, gastrocnemius and hamstring stretches and heel slides. Generally, crutches and brace were weaned after 4 to 6 weeks, provided the patient met the milestones for doing so (no or minimal pain and swelling, full active and passive knee extension symmetrical to the contralateral knee, knee flexion to 100° of flexion, no quadriceps lag with straight leg and ability to walk with a normal gait without crutches). Weightbearing and non-weightbearing strengthening exercises for the lower extremity with an emphasis on the quadriceps and hamstrings were initiated 4 to 6 weeks after surgery as tolerated. Stationary cycling was initiated approximately 6 to 8 weeks after surgery. Walking was gradually increased and running was permitted approximately 4 months after surgery. Pivoting and cutting exercises were not initiated until at least 6 months and return to sport was generally no sooner than 9 months postoperatively provided that full postoperative rehabilitation progression was completed and the patient had achieved full knee range of motion, adequate knee stability, and functional quadriceps control, and there was no effusion. Progression through the rehabilitation program was dependent on the patient’s readiness as assessed by the physical therapist and the operating surgeons with performance on rehabilitation tests, and clinical findings in the office.

Outcome Measures

Return to Preinjury Sports: For this study, we operationally defined return to preinjury sports as returning to the same or more demanding type of sports participation, at the same or greater frequency with the same or better Marx Activity Score as before injury.

The type of sports was graded on an ordinal scale as participation in strenuous sports activities, moderate sports activities, light sports activities or no sports activities and the frequency of sports participation was graded on an ordinal scale as 4 to 7 times per week, 1 to 3 times per week, 1 to 3 times per month or less than once per month. Individuals that participated in strenuous sports activities 4 to 7 times per week were operationally defined as competitive athletes. The Marx Activity Rating Scale evaluated the frequency of running, cutting, decelerating and pivoting on a monthly basis. Reliability and validity of the Marx Activity Rating Scale has been well established, with high test-retest reliability at 1 week (intraclass correlation coefficient, .97) and a good correlation with existing activity rating scales: Spearman correlation coefficient for Cincinnati score, .67; Tegner scale, .66; and Daniel scale, .52. To be classified as returning to the preinjury level of sports participation, the individual had to achieve the same or better type and frequency of sports and Marx Activity Rating Scale score at their best after surgery in comparison to their preinjury level of sports participation.
Potential Predictors: The potential predictor variables that were analyzed in this study to determine factors influencing return to sports included patient demographic characteristics (i.e. age at surgery, sex, race, education level, BMI), pre-injury sports participation (i.e. type of sport, frequency of sports participation, activity level [Marx activity rating scale]), mechanism of injury (i.e. work, sports, motor vehicle accident [MVA], activities of daily life [ADL], other), time from injury to surgery, measures of laxity (i.e. Lachman and pivot-shift tests under anesthesia), concomitant injuries (i.e. tibiofemoral cartilage status, injury to menisci), pattern of ACL injury, procedures for reconstruction of the ACL (i.e. single-bundle vs. double bundle, graft source, femoral drilling technique, reconstructive technique), and concomitant surgical procedures for the menisci and cartilage.

Activity Levels: the Marx Activity Rating Score\textsuperscript{225} was used to evaluate activity levels between patients who did and did not return to pre-injury level of sports participation.

Data Management and Analyses
Data analysis began with calculation of descriptive statistics including measures of central tendency (means, medians) and variability (standard deviations, ranges) for continuous variables and frequency counts and percentages for categorical variables. Univariate logistic regression was used to determine the association of each potential predictor variable with return to pre-injury sports participation. To determine whether a group of variables could better predict who would and would not return to sports after ACL reconstruction, multivariate models were explored. We chose important clinical features as well as univariate predictors that provided the most information and developed a series of models that considered pre-surgical factors (age, gender, athletic status, etc.) and surgical findings and procedures (concomitant injuries, meniscus procedures, cartilage procedures). Coefficients of determination (Nagelkerke $R^2$\textsuperscript{244}) were calculated to determine fit of the multivariable models to the data. An alpha level of $p \leq .05$ was set to determine statistical significance. All statistical analyses were completed with IBM SPSS Statistics Software, version 23 (Armonk, NY: IBM Corp.).

RESULTS
Review of the medical record resulted in the identification of 797 subjects that were eligible for this study (Figure 1). Of these, 303 individuals could not be located nor contacted via telephone. The remaining 494 eligible subjects were contacted; 198 did not respond and 29 declined to participate in this study. Six subjects returned completed questionnaires without a signed consent form, and were thus excluded from participation in the study. Two subjects were deceased. Two hundred and fifty-
nine participants completed the questionnaires and signed consent forms. A second medical record review revealed that an additional 8 subjects were ineligible after informed consent was provide and were thus excluded from the analysis. This included 2 individuals that had a previous contralateral ACL reconstruction, 1 who had an injury of both knees and 5 who were ineligible based upon age at the time of surgery. The remaining 251 participants were included in this study. This is equal to a follow up rate of 31.5% (251/797) and a response rate of 51.6% (251/486).

Of the participants, 139 (55.4%) were female and the mean age for all subjects at the time of surgery was 26.1 years (standard deviation [SD] 9.9 years). Median time from injury to surgery was approximately 2 months and the mean follow-up length was 3.4 years (SD 1.3 years). Non-responders to the survey were younger (21.1 years, SD 8.3) than those who did respond (26.1 years, SD 9.9, p<.01) and were more likely to be male (59.7%, p<.01). No other statistical differences were found between responders, non-responders, and those who refused to participate in the study. (Table 1) According to our comprehensive definition, a total of 122 (48.6%; 95% CI, 42.4%-54.8%) individuals returned to their pre-injury level of sports.

Figure 1. Study Participation Flowchart.
Predictors of Return to Preinjury Sports

Univariate predictors of return to pre-injury sports were age at time of surgery, being a competitive athlete, time from injury to surgery, cartilage injury greater than grade 1 in either the medial or lateral tibiofemoral compartment and having had any form of cartilage surgery performed in the knee. A summary of the univariate results is presented in Tables 2 and 3.

### TABLE 8.1 Demographics for Those Who Did and Did Not Respond to the Questionnaire

<table>
<thead>
<tr>
<th></th>
<th>Responders (n=251)</th>
<th>Non-Responders (n=206)</th>
<th>Refused (n=29)</th>
<th>No Contact Details (n=303)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at surgery, y</td>
<td>26.1 ± 9.9</td>
<td>21.1 ± 8.3</td>
<td>27.6 ± 11.5</td>
<td>25.2 ± 9.5</td>
</tr>
<tr>
<td>Female patients (%)</td>
<td>139 (55.4%)</td>
<td>83 (40.3%)</td>
<td>17 (58.6%)</td>
<td>105 (34.7%)</td>
</tr>
<tr>
<td>Follow-up, y</td>
<td>3.4 ± 1.3</td>
<td>2.9 ± 1.1</td>
<td>3.1 ± 1.1</td>
<td>3.2 ± 1.2</td>
</tr>
</tbody>
</table>

aValues are presented as mean ± SD or n (%).

bNonresponder group includes no response to invitation, returned questionnaire without consent, and deceased.

### TABLE 8.2 Univariate Logistic Regression Model for Pre-Surgical Predictors of Return to Preinjury Sports After Primary ACL Reconstruction

<table>
<thead>
<tr>
<th>Predictor</th>
<th>RTPS</th>
<th>Not RTPS</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 18 y</td>
<td>54/122 (44.3%)</td>
<td>24/129 (18.6%)</td>
<td>4.07</td>
<td>2.21 – 7.50</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>19–23 y</td>
<td>26/122 (21.3%)</td>
<td>29/129 (22.5%)</td>
<td>1.62</td>
<td>.85 – 3.12</td>
<td>.14</td>
</tr>
<tr>
<td>&gt;24 y</td>
<td>42/122 (34.4%)</td>
<td>76/129 (58.9%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Femaleb</td>
<td>68/122 (55.7%)</td>
<td>71/129 (55.0%)</td>
<td>0.97</td>
<td>.59 - 1.60</td>
<td>.91</td>
</tr>
<tr>
<td>Male</td>
<td>54/122 (44.3%)</td>
<td>58/129 (45.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline activity level</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Competitiveb</td>
<td>82/121 (67.8%)</td>
<td>65/129 (50.4%)</td>
<td>2.07</td>
<td>1.24 - 3.46</td>
<td>.01</td>
</tr>
<tr>
<td>Other</td>
<td>39/121 (32.2%)</td>
<td>64/129 (49.6%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time from injury to surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-3 monthsb</td>
<td>97/115 (88.2%)</td>
<td>75/120 (69.4%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;3 months</td>
<td>18/115 (11.8%)</td>
<td>45/120 (30.6%)</td>
<td>0.309</td>
<td>0.17 – 0.58</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>Injury mechanism</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sportsb</td>
<td>113/121 (93.4%)</td>
<td>115/129 (89.2%)</td>
<td>1.72</td>
<td>.70 - 4.26</td>
<td>.24</td>
</tr>
<tr>
<td>Work, MVA, ADL, Other</td>
<td>8/121 (6.6%)</td>
<td>14/129 (10.9%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

aData are presented as n/total (%). ACL, anterior cruciate ligament; RTPS, return to preinjury sports; MVA, motor vehicle accident; ADL, activities of daily life; OR, odds ratio; CI, confidence interval.

bReference group for each predictor.
<table>
<thead>
<tr>
<th>Predictor</th>
<th>RTPS</th>
<th>Not RTPS</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other ligament injury</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes&lt;sup&gt;b&lt;/sup&gt;</td>
<td>11/115 (9.6%)</td>
<td>11/121 (9.1%)</td>
<td>1.06</td>
<td>.44 - 2.54</td>
<td>.9</td>
</tr>
<tr>
<td>No</td>
<td>114/115 (90.4%)</td>
<td>110/121 (10.9%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Internal derangement&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pathology present&lt;sup&gt;b&lt;/sup&gt;</td>
<td>73/115 (63.5%)</td>
<td>85/121 (70.3%)</td>
<td>0.74</td>
<td>.43 - 1.27</td>
<td>.27</td>
</tr>
<tr>
<td>Normal</td>
<td>42/115 (36.5%)</td>
<td>36/121 (29.8%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meniscus lesion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pathology present&lt;sup&gt;b&lt;/sup&gt;</td>
<td>71/115 (61.7%)</td>
<td>77/120 (64.2%)</td>
<td>0.9</td>
<td>.53 - 1.53</td>
<td>.7</td>
</tr>
<tr>
<td>Normal</td>
<td>44/115 (38.3%)</td>
<td>43/120 (35.8%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cartilage of knee&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pathology present&lt;sup&gt;b&lt;/sup&gt;</td>
<td>21/116 (18.1%)</td>
<td>44/120 (36.7%)</td>
<td>0.38</td>
<td>.21 - .70</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Normal</td>
<td>95/116 (81.9%)</td>
<td>76/120 (63.3%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cartilage of PF joint</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pathology present&lt;sup&gt;b&lt;/sup&gt;</td>
<td>12/116 (10.3%)</td>
<td>22/121 (18.2%)</td>
<td>0.52</td>
<td>.24 - 1.11</td>
<td>.09</td>
</tr>
<tr>
<td>Normal</td>
<td>104/116 (89.7%)</td>
<td>99/121 (81.8%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graft type</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autograft&lt;sup&gt;b&lt;/sup&gt;</td>
<td>69/122 (56.6%)</td>
<td>63/129 (48.8%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allograft</td>
<td>46/122 (37.7%)</td>
<td>64/129 (49.6%)</td>
<td>0.66</td>
<td>.39 - 1.11</td>
<td>0.111</td>
</tr>
<tr>
<td>Hybrid</td>
<td>7/122 (5.7%)</td>
<td>2/129 (1.6%)</td>
<td>3.20</td>
<td>.64 - 16.0</td>
<td>0.16</td>
</tr>
<tr>
<td>Femoral tunnel</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AM Portal, OTT, or AMP&amp;OTT&lt;sup&gt;b&lt;/sup&gt;</td>
<td>88/109 (80.7%)</td>
<td>91/103 (88.4%)</td>
<td>0.55</td>
<td>.26 - 1.19</td>
<td>.13</td>
</tr>
<tr>
<td>Transtibial</td>
<td>21/109 (19.3%)</td>
<td>12/103 (11.7%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meniscus Rx&lt;sup&gt;e&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes, performed&lt;sup&gt;b&lt;/sup&gt;</td>
<td>61/115 (53.0%)</td>
<td>57/120 (47.5%)</td>
<td>1.15</td>
<td>.75 - 2.08</td>
<td>.40</td>
</tr>
<tr>
<td>None</td>
<td>54/115 (47.0%)</td>
<td>63/120 (52.5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cartilage Rx&lt;sup&gt;f&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes, performed&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2/116 (1.7%)</td>
<td>11/119 (9.2%)</td>
<td>0.17</td>
<td>.04 - .80</td>
<td>.02</td>
</tr>
<tr>
<td>None</td>
<td>114/116 (98.3%)</td>
<td>108/119 (90.8%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any concomitant Rx&lt;sup&gt;g&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes, performed&lt;sup&gt;b&lt;/sup&gt;</td>
<td>63/115 (54.8%)</td>
<td>62/118 (52.5%)</td>
<td>1.09</td>
<td>.64 - 1.83</td>
<td>.73</td>
</tr>
<tr>
<td>None</td>
<td>52/115 (45.2%)</td>
<td>56/118 (53.5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>Data are presented as n/total (%). ACL, anterior cruciate ligament; RTPS, return to preinjury sports; PF, patellofemoral; AM, anteromedial; OTT, over the top; OR, odds ratio; CI, confidence interval.

<sup>b</sup>Reference group for each predictor.

<sup>c</sup>Internal derangement is defined as any pathology of the femoral or tibial cartilage, patellofemoral cartilage, or menisci.

<sup>d</sup>Cartilage of knee (comprehensive) is defined as any pathology of the femoral or tibial cartilage.

<sup>e</sup>Meniscus Rx is any meniscus procedure to either the medial or lateral meniscus.

<sup>f</sup>Cartilage Rx is any cartilage procedure performed in the knee.

<sup>g</sup>Any Concomitant Rx is any procedure in addition to the ACL reconstruction.
On average, patients that returned to their preinjury level of sports participation were younger (23.6 years, SD 9.2) than those that did not return to sports (28.5 years, SD 9.8, \( p < .01 \)) and had higher pre-injury Marx Activity Scale scores (\( p < .01 \)). (Table 4)

Patients were more likely to RTPS if they were younger than 19 years old at time of injury (odds ratio [OR] ≤ 18 years old = 4.07; 95% CI, 2.21-7.50; \( p < .01 \)) and if they were a competitive athlete at the time of injury (OR competitive athlete = 2.07; 95% CI, 1.24-3.46; \( p = .01 \)). Patients were less likely to RTPS if surgery occurred more than 3 months after injury (OR >3 months = .31, 95% CI, 0.17 – 0.58; \( p < .01 \)), if there was a cartilage lesion in the knee (OR cartilage lesion = .38; 95% CI, .21-.70; \( p < .01 \)) and if there was cartilage surgery performed at the time of ACL reconstruction (OR cartilage surgery = .17; 95% CI, .04-.80; \( p = .02 \)). (Table 2 and 3)

Exploration of the multivariate models did not offer any additional insight into predicting return to preinjury level of sports participation over the univariate predictors; a Nagelkerke \( R^2 \) of less than .2 was calculated for all multivariate models.

**DISCUSSION**

The purpose of this study was to identify factors associated with return to pre-injury level of sports participation at mid-term follow-up after ACL reconstruction. For this study, we operationally defined return to preinjury sports as returning to the same or more demanding type of sports participation, at the same or greater frequency with the same or better Marx Activity Score as before injury. This study identified several variables that predicted return to preinjury sports participation. The variables that best predicted RTPS included age, being a competitive athlete, time from injury to surgery, tibiofemoral cartilage status, and having had any form of cartilage surgery done. Therefore, younger patients that partake in sports on a competitive level, that have ready access to healthcare, and do not have a cartilage injury or require cartilage surgery return to sports more often. According to our comprehensive definition, a total of 48.6% individuals returned to their pre-injury level of sports.

Age is predictive for RTPS. Individuals in the high-school age ranges (i.e. ≤ 18 y/o) at the time of injury are more likely to return to preinjury level of sports participation. These results are similar to those reported by others.\(^{23,24}\) Lentz et al\(^{203}\) did not find a statistical difference in return to pre-injury sports by age, however, they did demonstrate that those that returned to pre-injury sports were younger than those that did not return to sports (RTPS-Yes 20.9 years [SD 8.3] versus RTPS-No 24.2 years [SD 8.8], \( p = .066 \)). This may be due to the differences in research design such as sample size, and follow-up time as well as the mean age of the sample, which was 22.4 years
(SD 8.6) compared to 26.6 years (SD 10.5) in our study. Hartigan et al.\textsuperscript{132} found age to be a preoperative predictor to pass return to sports criteria after ACL reconstruction. Although this is not the same as actually returning to pre-injury sports, their findings do agree with ours. We know that older individuals have delayed healing time and have difficulty overcoming muscle atrophy, which may affect postoperative outcomes.\textsuperscript{172,173,275} Additionally, age has a close relationship to many factors of life such as family obligations, or employment, all of which may itself limit the time an individual has to participate in sports. Moreover, sports usually are a major social outlet for younger individuals. As Ardern et al.\textsuperscript{23} stated: "for those athletes whose lives and social networks are inherently structured around participation in sport, a stronger sense of athletic identity may be a positive motivator for returning to sport."

Being a competitive athlete is also related to return to preinjury sports participation. The pre-injury activity levels, as defined by the Marx activity rating scale, were also supportive of this finding; patients that returned to sports had a median Marx score of 16.00 (range 0.00-16.00) versus patients that did not return with a median Marx score of 13.00 (range 0.00-16.00). These findings are in accordance with literature.\textsuperscript{23,71} Competitive athletes may be in a better physical condition and have invested longer training hours pre-injury. Also they might have higher performance expectations because they previously competed at an advanced level. For professional athletes, financial benefit, club contracts and pressure from coaches or fans may also weigh into the decision of returning to pre-injury sport. Moreover, competitive athletes may have access to intensive and structured support from medical and rehabilitation professionals that is not available to recreational athletes. However, these findings are different from what Tjong et al.\textsuperscript{310} reported for pre-operative activity levels (Marx activity rating scale) for patients that returned to sports and that did not. They found, for a total of 31 patients, that those that returned to sports had a pre-injury Marx score of 13.0 (SD 1.6), while those that did not return to sports had an almost equal pre-injury Marx score of 12.9 (SD 1.3). Possibly this difference is due to the presentation of means and standard deviations instead of medians and ranges which -due to the ordinal nature of the Marx score- would be preferable. Also, differences in study design and sample size are thought to possibly contribute to these contrasting results.

The statistically significant difference between the current Marx activity rating scores (RTPS 13.0, SD 1.6 versus Not-RTPS 5.5 SD 1.6, \(p<.001\)) that is underlined in their study does not seem to be clinically relevant as this difference is implied by the mere definition of not returning to preinjury sports.

We found that tibiofemoral cartilage status was also associated with return to preinjury sports participation. Cartilage injuries greater than grade 1 (Outerbridge\textsuperscript{55,256,257}) in either the medial or lateral tibiofemoral compartment decreased the likelihood of returning to preinjury sports participation. This is consistent with what Harris et al.\textsuperscript{130}
have found with their systematic review: smaller lesion size is correlated with successful return to sports and better clinical results. Also Sandon et al.276 found that cartilage injury was an independent negative predictor for returning to soccer after ACL reconstruction. They found that only about one third of the players with cartilage damage associated with an ACL injury returned to soccer when compared to almost two thirds without any cartilage injury. Concomitant cartilage injuries are associated with a longer time from injury to surgery in literature.17,50,162,166,199,230,283,284,337 However, in this study we were unable to find a relationship between the time from injury and cartilage status with multivariate analysis. Several techniques have been described to promote cartilage repair or replacement, the most common being microfracture, autologous chondrocyte implantation (ACI), and osteoarticular transplantation (OATS). Multiple studies have investigated which articular cartilage surgery techniques improve clinical outcomes and enable athletes to return to their preinjury level of sports.119,130,131,184 Generally, the results of microfracture appear to be inferior in rate of return to preinjury sports relative to ACI or OATS, and clinical outcomes in this patient population may deteriorate with time after microfracture.

Cartilage surgery itself is associated with a decreased likelihood of return to preinjury sports participation. Certainly, there is a direct relation with our findings of an association between tibiofemoral cartilage status and RTPS; greater cartilage involvement was found to be associated with lower RTPS rates. Not all cartilage injuries warrant surgical intervention. Cartilage injuries that do warrant surgery, may be more severe and thus less likely to RTPS already, based on the injury alone. However, given the size of the sample (two patients undergoing cartilage surgery that RTPS versus eleven patients with cartilage surgery that did not RTPS, Table 3) we would not want to withhold or advise towards surgery based on these results.

Time from injury to surgery is also related to return to preinjury level of sports participation. Performing surgery more than 3 months after injury is associated with a decreased likelihood of return to preinjury sports participation. The time between injury and ACL reconstruction has earlier been reported to influence clinical outcome after ACL reconstruction.17,50,162,166,199,230,283,284,337 However, the definitions of acute versus delayed reconstruction varies greatly between studies, and are therefore difficult to compare. The association of timing of surgery and return to sports has also been reported by Laxdal et al.199. They found that patients who had undergone delayed ACL reconstruction had lower activity levels according to the Tegner Activity Scale and lower scores according to the Lysholm Knee Scoring Scale. Therefore, the patient’s preference for return to preinjury sports should be considered when planning ACL reconstruction, and to improve the likelihood of return to preinjury sports participation ACL reconstruction should be performed without delay when swelling has subsided and ROM is restored.
Recently, Newman et al.\textsuperscript{249} studied what factors may be predictive of concomitant injuries among children and adolescents undergoing ACL reconstruction. Although study designs differ, their conclusions are very much in accordance with our findings. They concluded that concomitant injuries occurred more frequently among older subjects, that a delay to surgery was associated with an increased severity of injury, and that not returning to sports was significantly related to the presence of a concomitant knee injury in the older cohort.

The strengths of our study are that we identified pre-injury, pre-operative, and surgical variables associated with return to pre-injury sports, in a relatively large cohort, and at mid-term follow-up after ACL reconstruction. Identified variables may impact the early management of patient expectations, surgical planning and procedures and rehabilitation protocols. By performing both univariate and multivariate analyses, it became evident that the prediction accuracy of the more complex multivariate models was not appreciably better than for the univariate models. Moreover, the coefficients of determination ($R^2$\textsuperscript{Nagelkerke})\textsuperscript{244} of less than .2 for all models indicated weak relationships between the variables and prediction of RTPS. Therefore, in this study, predictors from univariate analysis are presented, which allows for a clearer interpretation of the results.

There are also some limitations that need to be acknowledged. By nature of the study design some degree of recall bias could have influenced the findings presented in this study. Some participants were unable to be contacted and there were incomplete questionnaires, which meant there were missing data. Additionally, patients that declined to participate in the study were on average 5 years younger than those that participated in the study (Table 1). Since younger age is predictive of RTPS, missing data from these individuals could have affected the observed results. Lastly, grading of chondral and meniscal injuries was performed by the operating surgeon at the time of surgery. As there were multiple surgeons involved, there is the potential for bias because of interobserver variability in the grading of pathologic abnormalities.

Of the identified predictors, only time from injury to surgery is potentially modifiable. However, when discussing the different treatment alternatives, older age, not being a competitive athlete, concomitant injury (and surgery), and delay in surgery scheduling should be taken into consideration as they are potential risk factors for a decreased likelihood of return to pre-injury sports participation. Future prospective observational studies that could include this information would be very helpful to further identify and confirm factors that are predictive of return to preinjury level of sports participation.
CONCLUSION

Five variables at the time of ACL reconstruction predicted RTPS including age, being a competitive athlete, time from injury to surgery, tibiofemoral cartilage status, and having had any form of concomitant cartilage surgery at the time of ACL reconstruction. Only time from injury to surgery is potentially modifiable, however, the reasons for which patients delay surgery may also contribute to them not returning to sports. Regardless, younger patients that partake in sports on a competitive level, that have ready access to healthcare and less cartilage damage or surgery to their knee return to sports more often, potentially due to higher levels of intrinsic motivation and fewer knee joint problems after surgery. While these variables may be helpful in identifying which individuals return to pre-injury sports, there are many other factors that determine whether or not individuals return to sport including motivational factors and aspects of rehabilitation.
Published as:
Defining Thresholds for the Patient Acceptable Symptom State for the IKDC Subjective Knee Form and KOOS for Patients Who Underwent ACL Reconstruction.


THRESHOLDS FOR THE PATIENT
ACCEPTABLE SYMPTOM STATE FOR
THE IKDC-SKF AND KOOS AFTER
ACL RECONSTRUCTION

CHAPTER 9
ABSTRACT

Background: A clinically meaningful change in patient-reported outcome (PRO) may not be associated with an acceptable state that corresponds to “feeling well”, also known as the patient acceptable symptom state (PASS). The PASS thresholds for the International Knee Documentation Committee Subjective Knee Form (IKDC-SKF) and the Knee injury and Osteoarthritis Outcome Score (KOOS) have not been determined for individuals after anterior cruciate ligament (ACL) reconstruction.

Purpose: To determine the PASS thresholds for the IKDC-SKF and KOOS in individuals at 1 to 5 years after ACL reconstruction.

Study Design: Cohort study (diagnosis): Level of evidence, 2.

Methods: Individuals 1 to 5 years after primary ACL reconstruction completed a survey that included the IKDC-SKF and KOOS. All subjects assessed satisfaction with their current state by answering the question, “Taking into account all the activity you have during your daily life, your level of pain, and also your activity limitations and participation restrictions, do you consider the current state of your knee satisfactory?”

Results: A total of 251 participants (mean age ± SD, 26.1 ± 9.9 years) completed the survey at an average of 3.4 ± 1.3 years after ACL reconstruction. Of these, 223 (89.2%) individuals indicated that they were in an acceptable symptom state (PASS-Y). Analysis of the receiver operating characteristic curve revealed that the IKDC-SKF and each of the KOOS subscales (pain, symptoms, activities of daily living [ADL], sport and recreation [sport/rec], and quality of life [QoL]) were significantly better identifiers of PASS than chance as indicated by the significance of the area under the curves. The PASS threshold (sensitivity, specificity) was 75.9 (0.83, 0.96) for the IKDC-SKF, 88.9 (0.82, 0.81) for the KOOS pain, 57.1 (0.78, 0.67) for the KOOS symptoms, 100.0 (0.70, 0.89) for the KOOS ADL, 75.0 (0.87, 0.88) for the KOOS sport/rec, and 62.5 (0.82, 0.85) for the KOOS QoL. In addition, the difference between PASS-Y and PASS-N was statistically significant ($p < .001$) for all PROs.

Conclusion: To our knowledge, this is the first study to identify the PASS thresholds for the IKDC-SKF and the KOOS subscales for individuals 1 to 5 years after ACL reconstruction. By identifying threshold values for the PASS, this study provides additional information to facilitate interpretation of the IKDC-SKF and KOOS in daily practice and clinical research related to ACL reconstruction.

Keywords: patient acceptable symptom state; PASS; IKDC; KOOS; anterior cruciate ligament; ACL
INTRODUCTION

Over the past decade, the use of patient-reported outcomes (PROs) has increased in the field of sports medicine and in research. However, the interpretation of the change and absolute postoperative PRO scores in a clinically meaningful way is difficult since a statistically significant change in PRO score does not necessarily represent a clinically important improvement. Moreover, it is not known what postoperative PRO score is acceptable from the patient’s perspective.

Two commonly used knee-specific PRO measures are the International Knee Documentation Committee Subjective Knee Form (IKDC-SKF) and the Knee injury and Osteoarthritis Outcome Score (KOOS). The IKDC-SKF has been used to assess outcome in recent clinical studies on anterior cruciate ligament (ACL) reconstruction and is one of the most frequently used PROs for patients with an ACL injury and after surgery. The KOOS is another PRO score that is commonly used in clinical studies related to ACL injury and reconstruction.

It is generally thought that PROs of symptoms, activity limitations, and participation restrictions are highly related to the patients’ perceptions of their outcome. However, a change in the PRO score may not be associated with an acceptable state that corresponds to an overall health state at which patients consider themselves to be “feeling well”, which is also called the patient acceptable symptom state (PASS). Establishing a PASS threshold for a PRO can aid in interpretation of clinical or research outcomes by providing a reference value at which the majority of a population feels well.

The PASS thresholds for the IKDC-SKF and the KOOS have not been determined for individuals after ACL reconstruction. The purpose of this observational cross-sectional study was to determine the PASS thresholds for the IKDC-SKF and KOOS in individuals at 1 to 5 years after ACL reconstruction.

METHODS

Instruments

For this study, subjects completed a comprehensive questionnaire that included self-reported demographic data, responses with regard to reinjury and level of sports participation, IKDC-SKF, KOOS and a question to assess the PASS.

The study protocol and consent forms were reviewed and approved by the Institutional Review Board at the University of Pittsburgh (protocol No. PRO11120006). All subjects provided written informed consent for participation in this study.
The IKDC-SKF is a knee-specific instrument that consists of 18 items that are designed to measure symptoms, function, and sports activity in patients who have one or more of a variety of knee conditions, including ligament and meniscal injuries, patellofemoral pain, articular cartilage lesions, and osteoarthritis. The development and initial validation of the IKDC-SKF were published in 2001, and evidence for responsiveness of the IKDC-SKF has been provided.

The KOOS is a knee-specific instrument that was developed with the purpose of evaluating short-term and long-term symptoms and function in patients with a variety of knee injuries and osteoarthritis. The instrument is based on an extension of the disease-specific Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and was constructed by adding questions considered important by patients (concerning pain, sport and recreation, function, knee-related quality of life, and other symptoms) to improve its validity for those with less severe disease or higher demands of physical function. The KOOS consists of 42 items within 5 separately scored subscales: pain (9 items), other symptoms (7 items), function in activities of daily living (ADL; 17 items), function in sport and recreation (sport/rec; 5 items), and knee-related quality of life (QoL; 4 items). In contrast to the IKDC-SKF, which results in a single score, separate scores are calculated for each of the KOOS subscales, with lower scores signifying worse functioning in these areas.

Achievement of the PASS was assessed by a “yes” (PASS-Y) or “no” (PASS-N) response to the question, “Taking into account all the activity you have during your daily life, your level of pain, and also your activity limitations and participation restrictions, do you consider the current state of your knee satisfactory?”

The questionnaire was pilot tested in our outpatient clinic to evaluate the burden of the survey on patients, to integrate patients’ comments and suggestions, and to clarify any ambiguous questions before it was distributed to subjects for this study.

**Subject Eligibility and Recruitment**

Medical records were reviewed to identify all patients who were between 1 to 5 years after primary, unilateral, anatomic ACL reconstruction. Subjects between the ages of 14 and 50 years at the time of index surgery were included. All surgeries were performed by a surgeon affiliated with our institution. Clinic and operative notes were reviewed to ensure that subjects who had prior knee injury or surgery to either knee were excluded from participation.

Invitation letters along with the questionnaires and consent forms were sent to potential subjects using a 3-phase mailing procedure followed by postcard reminders and phone calls to maximize response rate.
Surgical Data
Surgical data were obtained from review of medical records and included information related to surgical findings (pattern of ligament injury, injury to menisci and cartilage), procedures for reconstruction of the ACL (eg, single-bundle vs double-bundle, graft type), date of ACL reconstruction surgery, and concomitant procedures.

Data Management and Analyses
Descriptive statistics including frequency counts and percentages were calculated and summarized for all nominal variables, and measures of central tendency (means, medians) and dispersion (SDs, interquartile ranges) were calculated for all continuous variables.

Independent-samples t tests and Pearson chi-square tests or Fisher exact tests were used to assess differences in continuous and nominal variables, respectively, between subjects who achieved PASS versus subjects who did not achieve PASS.

To determine the score that best distinguished those who were PASS-Y from those who were PASS-N, the sensitivities and specificities for each of the potential scores were plotted as a receiver operating characteristic (ROC) curve. An ROC curve is a plot of sensitivity on the vertical axis and 1 specificity on the horizontal axis. The area under the curve (AUC) is interpreted as the probability of identifying a patient in PASS-Y on the basis of the PRO score from randomly selected pairs of PASS-Y and PASS-N patients. The value of the PRO score that was closest to the upper left-hand corner of the ROC curve was determined to be the PASS threshold score with the highest sensitivity and specificity. To determine this point mathematically (Youden index), the product function of the sensitivity and specificity was maximized for each PRO. The score corresponding to this maximal product of specificity and sensitivity was then taken to be the PASS threshold.

The test-retest reliability of the PASS question was determined in a separate cohort of 98 individuals who had undergone ACL reconstruction at least 2 years prior by determining the agreement between the responses to the PASS question over a 2-month interval using the statistic. These participants also completed a 15-point global rating of change question. Individuals who indicated that they had experienced no change or were “hardly any better at all” or “hardly any worse at all” were considered to be stable over that follow-up period and were included in the determination of reliability. For all inferential statistical analyses, an a level of \( p < .05 \) was considered statistically significant. All statistical analyses were performed using IBM SPSS version 21.0 (SPSS Inc).
RESULTS

The medical record review revealed 797 subjects were eligible for this study (Figure 1). Of these, 303 individuals could not be located or contacted via telephone. The remaining 494 eligible subjects were contacted; 198 did not respond and 29 declined to participate in this study. Six potential subjects returned completed questionnaires without a signed consent form and were thus ineligible. Two subjects were deceased. A total of 259 participants completed the questionnaires and signed consent forms. A second medical record review revealed that an additional 8 subjects were ineligible after informed consent was provided and were thus excluded from the analysis. This included 2 individuals who had a previous contralateral ACL reconstruction, 1 who had an injury of both knees, and 5 who were ineligible based on age at the time of surgery. The remaining 251 participants were included in this study. This is equal to a follow-up rate of 31.5% (251/797) and a response rate of 51.6% (251/486). One participant did not answer the PASS question and could not

Figure 1. Study flowchart. PASS, patient acceptable symptom state.
be included in the analysis of the PASS. Thus, a total of 250 subjects were included in the analysis of this study.

Of the participants, 139 (55.4%) were female, and the mean age (± SD) for all subjects at the time of surgery was 26.1 ± 9.9 years. The median time from injury to surgery was approximately 2 months, and the mean follow-up length was 3.4 ± 1.3 years. Nonresponders to the survey were younger (21.1 ± 8.3 years) than those who did respond (26.1 ± 9.9 years; \(p < .001\)) and were more likely to be male (59.7%; \(p < .001\)). No other statistical differences were found between responders, nonresponders, and those who refused to participate in the study. (Table 1)

**TABLE 9.1 Demographics Responders**

<table>
<thead>
<tr>
<th></th>
<th>Responders</th>
<th>Non-Responders*</th>
<th>Refused</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n=251</strong></td>
<td><strong>n=206</strong></td>
<td><strong>n=29</strong></td>
<td></td>
</tr>
<tr>
<td>Age the time of surgery†</td>
<td>26.1 ± 9.9</td>
<td>21.1 ± 8.3</td>
<td>27.6 ± 11.5</td>
</tr>
<tr>
<td>Females n, %</td>
<td>139 (55.4%)</td>
<td>83 (40.3%)</td>
<td>17 (58.6%)</td>
</tr>
<tr>
<td>Length of follow-up†</td>
<td>3.4 ± 1.3</td>
<td>2.9 ± 1.1</td>
<td>3.1 ± 1.1</td>
</tr>
</tbody>
</table>

*Non-responder group includes contacted by telephone without returning the survey, returned the questionnaire without consent, not answering PASS question and deceased.
† Indicates values are presented as mean ± standard deviation

**Reliability**

The test-retest reliability of the PASS question in patients after ACL reconstruction was high: absolute agreement was 96.9% with a \(\alpha\) of 0.78. Of the 98 patients who indicated that they were in an acceptable symptom state at the first time point, only 3 patients had discordant answers to the PASS question at the second visit while reporting no change in answering the global rating question.

**Patient Acceptable Symptom State**

A total of 223 individuals (89.2%) responded with a PASS-\(Y\). Patients who were not in an acceptable symptom state (PASS-N) had reinjured the knee more often (40.7%) than did patients who achieved the acceptable symptom state (12.6%; \(p < .001\)) and consequently underwent additional surgery more often (29.7% PASS-N vs 13.2% PASS-Y; \(p = .040\)). In addition, patients who were PASS-N were predominantly female (74.1% PASS-N vs 53.4% PASS-Y; \(p = .041\)). There were no other significant differences between those who achieved (PASS-Y) and those who did not achieve (PASS-N) an acceptable symptom state, including injury mechanism, preinjury sports activity level, or surgical findings or procedures including graft type. (Table 2)

Mean IKDC-SKF and KOOS subscales were all significantly greater in the subjects achieving the PASS (PASS-Y; \(p < .001\)). (Table 3)
### TABLE 9.2 Demographics and some survey questions by PASS status

<table>
<thead>
<tr>
<th>Variables</th>
<th>PASS-N (%)</th>
<th>Mean ± SD</th>
<th>PASS-Y (%)</th>
<th>Mean ± SD</th>
<th>p-value</th>
<th>CI (95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>20 (74.1)</td>
<td>24.84 ± 8.90</td>
<td>119 (53.4)</td>
<td>26.27 ± 9.99</td>
<td>.041</td>
<td>-0.03, 0.44</td>
</tr>
<tr>
<td>Male</td>
<td>7 (25.9)</td>
<td>67.16 ± 4.37</td>
<td>104 (46.6)</td>
<td>68.13 ± 3.99</td>
<td>-0.59</td>
<td>0.17</td>
</tr>
<tr>
<td>Age at surgery</td>
<td>3.28 ± 1.31</td>
<td>165.80 ± 49.22</td>
<td>3.41 ± 1.23</td>
<td>166.70 ± 36.55</td>
<td>.622</td>
<td>-0.65, 0.39</td>
</tr>
<tr>
<td>prior to injury: what type of sports activity did you participate in?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no sports</td>
<td>0 (0)</td>
<td>13.19 ± 4.41</td>
<td>4 (1.8)</td>
<td>15.92 ± 2.41</td>
<td>.674</td>
<td>NA</td>
</tr>
<tr>
<td>light sports activity</td>
<td>2 (7.4)</td>
<td>7 (3.1)</td>
<td>8 (3.6)</td>
<td>14 (6.3)</td>
<td>.976</td>
<td>-0.36, 0.37</td>
</tr>
<tr>
<td>moderate sports activity</td>
<td>3 (11.1)</td>
<td>17 (6.6)</td>
<td>36 (16.1)</td>
<td>42 (18.6)</td>
<td>.489</td>
<td>0.15</td>
</tr>
<tr>
<td>strenuous sports activity</td>
<td>22 (81.5)</td>
<td>72 (26.9)</td>
<td>175 (78.5)</td>
<td>219 (95.2)</td>
<td>-0.15</td>
<td>0.21</td>
</tr>
<tr>
<td>how often did you participate in the sport activity?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>less than 1 time per month</td>
<td>1 (3.7)</td>
<td>18 (6.6)</td>
<td>7 (3.1)</td>
<td>14 (6.3)</td>
<td>.976</td>
<td>-0.36, 0.37</td>
</tr>
<tr>
<td>1 to 3 times per month</td>
<td>1 (3.7)</td>
<td>14 (6.3)</td>
<td>7 (3.1)</td>
<td>14 (6.3)</td>
<td>.976</td>
<td>-0.36, 0.37</td>
</tr>
<tr>
<td>1 to 3 times per week</td>
<td>7 (25.9)</td>
<td>11 (4.2)</td>
<td>53 (23.8)</td>
<td>154 (66.8)</td>
<td>-0.32</td>
<td>0.36</td>
</tr>
<tr>
<td>4 to 7 times per week</td>
<td>18 (66.7)</td>
<td>149 (58.6)</td>
<td>149 (66.8)</td>
<td>149 (66.8)</td>
<td>-0.23</td>
<td>0.23</td>
</tr>
<tr>
<td>Marx score before injury</td>
<td>3.28 ± 1.31</td>
<td>165.80 ± 49.22</td>
<td>3.41 ± 1.23</td>
<td>166.70 ± 36.55</td>
<td>.622</td>
<td>-0.65, 0.39</td>
</tr>
<tr>
<td>how did you originally injure your knee?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>sports</td>
<td>24 (88.9)</td>
<td>203 (91.4)</td>
<td>203 (91.4)</td>
<td>203 (91.4)</td>
<td>.322</td>
<td>-0.15, 0.10</td>
</tr>
<tr>
<td>work</td>
<td>0 (0)</td>
<td>5 (2.3)</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>motor vehicle accident</td>
<td>2 (7.4)</td>
<td>3 (1.4)</td>
<td>2 (0.9)</td>
<td>2 (0.9)</td>
<td>.28</td>
<td>0.40</td>
</tr>
<tr>
<td>activities of daily living</td>
<td>0 (0)</td>
<td>1 (0.4)</td>
<td>0 (0.4)</td>
<td>0 (0.4)</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>other</td>
<td>1 (3.7)</td>
<td>10 (4.5)</td>
<td>10 (4.5)</td>
<td>10 (4.5)</td>
<td>-0.43</td>
<td>0.41</td>
</tr>
<tr>
<td>graft type</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Autograft</td>
<td>14 (51.9)</td>
<td>116 (52.0)</td>
<td>116 (52.0)</td>
<td>116 (52.0)</td>
<td>.621</td>
<td>-0.28, 0.28</td>
</tr>
<tr>
<td>Allograft</td>
<td>11 (40.7)</td>
<td>99 (44.4)</td>
<td>99 (44.4)</td>
<td>99 (44.4)</td>
<td>-0.35</td>
<td>0.27</td>
</tr>
<tr>
<td>Mixed</td>
<td>2 (7.4)</td>
<td>8 (3.6)</td>
<td>8 (3.6)</td>
<td>8 (3.6)</td>
<td>-0.28</td>
<td>0.35</td>
</tr>
<tr>
<td>have you re-injured the same knee that your XXXX Sports Medicine surgeon reconstructed?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>16 (59.3)</td>
<td>195 (87.4)</td>
<td>195 (87.4)</td>
<td>195 (87.4)</td>
<td>&lt;.001</td>
<td>-0.46, -0.10</td>
</tr>
<tr>
<td>yes</td>
<td>11 (40.7)</td>
<td>28 (12.6)</td>
<td>28 (12.6)</td>
<td>28 (12.6)</td>
<td>0.00</td>
<td>0.56</td>
</tr>
<tr>
<td>have you had additional surgery on the same knee that your XXXX Sports Medicine surgeon reconstructed?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>19 (70.3)</td>
<td>191 (86.8)</td>
<td>191 (86.8)</td>
<td>191 (86.8)</td>
<td>.040</td>
<td>-0.33, 0.00</td>
</tr>
<tr>
<td>yes</td>
<td>8 (29.7)</td>
<td>29 (13.2)</td>
<td>29 (13.2)</td>
<td>29 (13.2)</td>
<td>-0.13</td>
<td>0.46</td>
</tr>
<tr>
<td>type of additional surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACL revision</td>
<td>6 (50.0)</td>
<td>15 (45.5)</td>
<td>15 (45.5)</td>
<td>15 (45.5)</td>
<td>.423</td>
<td>-0.14, 0.45</td>
</tr>
<tr>
<td>Meniscus</td>
<td>2 (16.7)</td>
<td>8 (24.2)</td>
<td>8 (24.2)</td>
<td>8 (24.2)</td>
<td>1.000</td>
<td>-0.28, 0.35</td>
</tr>
</tbody>
</table>
Analysis of the ROC revealed that the IKDC-SKF and each of the KOOS subscales were significantly better identifiers of patients who were in an acceptable symptom state than chance, as indicated by the significance of the AUCs. The threshold for the IKDC-SKF was a score of 75.9 (sensitivity, 0.83; specificity, 0.96), for the KOOS pain a score of 88.9 (sensitivity, 0.82; specificity, 0.81), for the KOOS symptom a score of 57.1 (sensitivity, 0.78; specificity, 0.67), for the KOOS ADL a score of 100.0 (sensitivity, 0.70; specificity, 0.89), for the KOOS sport/rec a score of 75.0 (sensitivity, 0.87; specificity, 0.88), and for the KOOS QoL a score of 62.5 (sensitivity, 0.82; specificity, 0.85). (Table 3)

**DISCUSSION**

To our knowledge, this is the first study to identify the PASS thresholds for the IKDC-SKF and the KOOS subscales for individuals 1 to 5 years after ACL reconstruction. By identifying threshold values for the PASS, this study provides additional information to facilitate interpretation of the IKDC-SKF and KOOS in daily practice and clinical research related to ACL reconstruction. For example, an IKDC-SKF score of a patient who is 1 to 5 years after primary ACL reconstruction that is greater than 75.9 suggests that the patient is in an acceptable symptom state, with a sensitivity and specificity of 0.83 and 0.96, respectively. In addition, mean scores for patients who are PASS-Y
and are not PASS-N in an acceptable symptom state have been identified. Achieving an acceptable symptom state appeared to be associated with higher mean IKDC-SKF score and KOOS, indicating improved function, sports participation, and knee-related quality of life.

Results from this study demonstrate that in a cross-sectional analysis, 1 to 5 years after ACL reconstruction, most (89.2%) consider themselves to be in an acceptable symptom state. Although the PASS is not interchangeable with “patient satisfaction”, the 2 do have a close relationship. Kocher et al. found a patient satisfaction rate of approximately 85% at a mean of 35.9-month follow-up after ACL reconstruction, which would be consistent with our finding of PASS-Y of 89.2% at mean 40.8-month (3.4-year) follow-up.

Parameters that were significantly associated with achieving the PASS were not having reinjured or having had additional surgery for the operated knee. However, the type of additional surgery was not predictive of PASS state.

There was no relationship between the level of preinjury sports and achieving the PASS postoperatively. However, given that the differences in mean scores between PASS-Y and PASS-N for the KOOS pain, symptoms, and ADL subscales were smaller than were differences for the KOOS sport/rec and QoL subscales and the IKDC-SKF, it appears that after ACL injury and reconstruction, achieving the PASS is more dependent on the ability to participate in more demanding activities, including sports, without symptoms or difficulty than on participation in activities of daily living. These findings suggest that independent of the level of preinjury sports participation, being able to participate in sports activities 1 to 5 years postoperatively is important for achieving an acceptable symptom state. It may seem obvious that for a young and athletic population, return to sports is one of the most important parameters for achieving PASS. However, a study conducted by Perrot and Bertin related to the effect of pain management on the PASS in patients with knee and hip osteoarthritis also showed that in those with knee osteoarthritis, achieving an acceptable symptom state was more frequently reached in patients specifically seeking an improvement during sport activities.

Previously published normative data for the IKDC-SKF showed a mean score of 87.6 for patients ranging in age between 18 and 50 years. The current study found a mean IKDC-SKF score of 85.1 for patients who indicated to be in PASS and a mean score of 62.9 for patients who were not. The subjects approaching the population norm are more likely to achieve a PASS. However, a threshold value of 75.9 was found with ROC analysis, which is almost 12 points lower than the population norm, indicating that being in PASS is not interchangeable with having a “normal” IKDC-SKF score.
Comparison between mean KOOS subscale scores from this study and normative data for a young athletic population showed considerable differences between PASS-Y and the normative values for KOOS symptom and QoL subscales. In part, this may have to do with a mean age difference between groups (26.1 vs 18.8 years), but more likely this might be attributed to our population having a history of ACL injury and surgery versus a sample of college freshmen entering the US Military Academy. The other mean PASS-Y scores of the KOOS subscales did more closely resemble the population norms. Similar to the IKDC-SKF, the ROC-derived threshold scores for the KOOS subscales were systematically lower than the population normative values, except for KOOS ADL.

The sensitivity and specificity for the PASS threshold values for the IKDC-SKF and KOOS subscales ranged from 0.70 to 0.83 and 0.67 to 0.96, respectively. (Table 3) The threshold values defined by PASS identified in this study provide additional information that can be used to interpret IKDC-SKF and KOOS subscale scores for individuals after ACL reconstruction. Patients who are not achieving PASS thresholds could be targeted with additional interventions to improve clinical outcome. For example, by identifying the reasons for being PASS-N and addressing the limitations with additional physical therapy, sports psychology, or surgery. These thresholds can also be used to give a clinically meaningful interpretation to PROs presented in scientific literature.

Only one recent study by Ingelsrud et al has linked the PASS to KOOS after ACL reconstruction. Mean scores were compared for 3 groups (acceptable state, intermediate state, and treatment failure group) at 3 different time points (6, 12, and 24 months). No threshold values for achieving an acceptable symptom state were established. Their findings indicated that only half of the patients at 6 months and about two-thirds at 1 to 2 years perceived their symptoms as acceptable (PASS-Y) after ACL reconstruction. Given the trend, these findings may well be consistent with our finding of PASS-Y of 89.2% at a mean of 3.4 years. In addition, the mean KOOS subscale scores at 2 years (closest to our mean follow-up of 3.4 years) showed a similar tendency as our findings, with highest absolute scores for both the PASS-Y and PASS-N group for the KOOS pain and ADL subscales.

The strengths of our study are that we were the first to investigate PASS thresholds for the most frequently used knee-specific PROs in a relatively large sample at midterm follow-up after ACL reconstruction and that we identified mean values not only for patients who were in PASS but also for patients who were not. By identifying threshold values for the PASS, we were able to provide additional information to facilitate further interpretation of the IKDC-SKF and KOOS. By comparing mean values between patients who achieved and those who did not achieve the PASS, we were able to determine which PROs best discriminated between the PASS-Y and PASS-N states.
There are also some limitations that need to be acknowledged. By nature of the study design, some degree of selection bias could have influenced the findings presented in this study. Patients who declined to participate in the study were on average 5 years younger and mostly male (Table 1) compared with those who agreed to participate. Since younger males are more likely to have a higher functional demand on their knee, missing data from these individuals could affect the prevalence of patients not achieving the PASS and thus have resulted in an underestimation of the true overall rate of PASS-N. In addition, females were significantly less likely to be in PASS and were more likely to respond to our study invitation. Although these findings may have no causal relationship, previous studies have found that females have worse outcome scores than do males after ACL reconstruction.\textsuperscript{5,9,304} Since having a worse outcome is logically associated with not being in PASS, and having a worse outcome is likely positively associated with willingness of study participation, some degree of self-selection bias could have occurred.

Factors that may be of influence to achieving the PASS should be further identified. Fear of reinjury, the role of coping, self-efficacy, and treatment expectations should be examined.

**CONCLUSION**

This study has identified PASS threshold values for the IKDC-SKF and the KOOS subscales. At 1 to 5 years after ACL reconstruction, 89.2% of individuals consider themselves to be feeling well with regard to their injured knee, and those who are feeling well have significantly higher outcome scores than do those who are not. Reinjury of the same knee is negatively associated with an acceptable symptom state. Although it is not exactly known what makes a patient state that his or her symptom state is acceptable, sports participation does seem to have a major influence for patients after ACL injury and surgery.
The general aims of this thesis are to more objectively evaluate the physical examination, to more objectively assess how anatomic anatomic ACL reconstruction really is and to objectively predict and interpret outcomes after surgery. The current chapter consists of a general discussion of each of the previous chapters followed by a general conclusion.

**DIAGNOSTICS**

Most of the physical examination is subjective by its very nature. Although the physical exam aims to objectify the complaints and claims a patient may have, most tests are not quantifiable and therefore not truly objective, nor easily reproducible.

A solid step towards providing a better objective assessment of antero-posterior knee laxity was made by Dale Daniel in San Diego, in the 1980s by developing the KT1000 test.\(^7^3\) The KT1000 test is performed to provide an objective assessment of the amount of increased anterior knee translation between 20° and 30° of knee flexion. However, performing this test requires the delicate and educated handling of a fairly large and costly machine, which does not add to its clinical applicability.

The pivot shift test is highly specific for the diagnosis of ACL insufficiency and is performed manually to clinically evaluate knee rotational laxity in ACL deficient patients.\(^4^4,1^8^2\) Although the test is commonly used as an objective outcome measure, to date, the test can only be graded by the examiner subjectively as either a gliding shift (grade I), clunking shift (grade II), or as grossly unstable shift (grade III).\(^1^0^4\) Additionally, varying techniques to perform the pivot shift test have been described.\(^2^4^2\) Subjective grading of tests performed differently leads to a variation in clinical grading between examiners.\(^1^9^1,2^5^3\) In an attempt to increase the diagnostic value of the pivot shift test, it has been proposed to standardize the technique.\(^1^4^4,2^4^2\) However, since the clinical grading is inherently subjective, this should also be standardized in an objective fashion.

Recent research efforts have shown that it is possible to objectively evaluate components of the pivot shift by quantifying either tibial translation or acceleration of the tibial reduction.\(^2^0,1^4^7,1^5^7,1^8^7,1^9^1,1^9^6,1^9^7,2^1^0,2^1^1,2^1^7,2^6^2\) Since antero-posterior (A-P) translation of the lateral knee joint is suggested to be the most prominent form of instability in patients complaining of “giving way” of the knee,\(^1^0^3\) measuring A-P translation of the lateral knee joint during the pivot shift test has been used as a parameter which can be used to quantify the pivot shift movement.\(^5^2,1^4^7,1^6^0,1^7^0\) Bedi et al.\(^4^1\) demonstrated that A-P translation of the lateral knee joint could reflect the clinical pivot shift test grade by using a navigation system. It was described that each additional clinical grade correlates to an increment of approximately 6mm of A-P translation of the lateral knee joint.
The primary objective of the study presented in Chapter 2 was to develop an automated image analysis system that is able to provide quantitative data of the reduction movement that occurs during the pivot shift (mm of A-P translation of the lateral knee joint). The resultant PIVOT app which is described in Chapter 2 demonstrated encouraging initial results, with the PIVOT app being able to reliably detect statistically significant differences between intact knees and ACL-deficient knees.

Although other systems have been reported to provide a quantitative evaluation of the pivot shift test, such as electromagnetic tracking, computer navigation and inertial sensors, none of these systems are easily applicable in a clinical setting. Computer navigation is invasive (i.e. requiring bony fixation) and most systems are expensive and developed primarily for research purposes. Additionally, the measurements are not processed automatically and thus can take considerable time to provide actual interpretable quantitative results. In contrast, the PIVOT app works with the simple image analysis technique, which has been validated and provides a noninvasive and widely affordable measurement system. Furthermore, the iPad is a portable computer integrated with a camera, which makes the PIVOT app an all-in-one measurement device, providing instant feedback to the clinician in the office or the operating room.

The PIVOT app is a first introduction of tablet computer software into the clinical setting. As an extension of the examiner it allows for an automated and more objective assessment of the physical exam. With further increased accuracy and precision, the PIVOT app may become a welcome addition to the diagnostic arsenal or even replace certain tests and reduce medical costs.

**PRE-SURGERY**

Before turning to surgery, it is of paramount importance that surgeons familiarize themselves with the indications, contraindications and techniques that ACL reconstruction comprises. Over recent years, double-bundle reconstruction has gained popularity after studies showed significant advantages of adding a second bundle with regard to outcomes and biomechanics. Indications and contraindications are discussed in Chapter 3.

On the other hand, the traditional single-bundle ACL reconstruction technique has several advantages associated with its application for treatment of ACL tears as it is simple, quick and does not require the knee to be flexed beyond 90⁰. Many studies have attempted to compare the two techniques and most have found equivalent or superior knee stability after double-bundle ACL reconstruction, when compared with single-bundle ACL reconstruction. However, when grafts are placed
anatomically and customized to the patient’s individual anatomy, there does not seem to be a difference between a single-bundle and a double-bundle technique.\textsuperscript{148,149}

By individualizing the surgical approach to the patient, it has been found that both the anatomical single- and double-bundle techniques have their own set of indications and contraindications. Reconstruction of the ligament should focus on restoration of the native functional and anatomical properties and should take the size, shape and orientation of the ACL into account. When indications and contraindications for the technique used are based on native anatomical characteristics, either a single-bundle or a double-bundle procedure can be performed according to the same double-bundle concept.

Since mimicking native anatomy by reconstruction is the current golden standard in terms of surgical treatment, it only seems logical that a next step would be actual preservation of the native anatomy. Therefore, it is likely that future research and development will also concentrate on repair of the ruptured ACL. New techniques with mechanical and biological enhancements are currently being researched and will likely alter future treatment protocols.

**Surgery**

Anatomic ACL reconstruction should account for size, shape, tensioning patterns and orientation of the native ligament as previously mentioned, and as such one of the goals of individualized anatomic anterior cruciate ligament reconstruction is to reproduce each patient’s native insertion site as closely as possible.\textsuperscript{40,75,308,316,339} However, the average amount of the native insertion site that is restored by the tunnel aperture area is currently unknown, as is the implication of the degree of native insertion site coverage. Interestingly, there appears to be an unpublished assumption that maximal encompassment of the native insertion site area leads to optimal clinical outcomes, supported by the findings that smaller grafts may predispose to failure\textsuperscript{219,252} and the established principles of anatomic ACL-R,\textsuperscript{174} which involves restoring the native ACL insertion site size in order to ensure favorable long-term outcome. Nonetheless, the clinical relevance of the degree of the native insertion site coverage is currently unknown.

As such, the goals of the study presented in Chapter 4 are to determine whether individualized anatomic ACL reconstruction techniques can maximally fill the native insertion site and to attempt to establish a clinically measurable or calculable tool as a first step towards elucidating the implications of completely restoring native insertion site size. In this prospective pilot study, 45 patients underwent primary single-bundle
anatomic ACL reconstruction. Length and width of the native insertion site were measured intraoperatively.

Using published guidelines, reconstruction technique and graft choice were determined to maximize the percentage of reconstructed area. Native femoral and tibial insertion site area and femoral tunnel aperture area were calculated using the formula for area of an ellipse. On the tibial side, tunnel aperture area was calculated with respect to drill diameter and drill guide angle. Percentage of reconstructed area (PRA) was calculated by dividing total tunnel aperture area by the native insertion site area. The most important finding in this present study was that anatomic ACL surgery only restored on average 70–79% of the native insertion site size. Based on the findings, complete footprint restoration (or 100% of reconstructed area) with an adequately sized graft and matched tunnel size is not feasible. In part this is because current grafts used in ACL surgery cannot anatomically mimic the shape of the native ACL nor can they completely fill both the femoral and tibial native insertion site. In this study, the tibial insertion site cross-sectional area was nearly twice the size as that of the femur.

This is the first study to attempt to quantify the degree of insertion site coverage by evaluating this ratio using intraoperative measurements and calculations based on published formulas.

Though the implications of the degree of insertion site coverage have not yet been studied, previous studies have found that increased graft cross-sectional area to be associated with improved outcomes. On the other hand, bigger may not always be better as a large graft may reproduce the entire insertion site; however, the drilling of a tunnel that lies outside the confines of the insertion site may damage neighboring structures or result in graft impingement.

This pilot study provides a fundament for future studies on ACL to size restoration, helping ACL surgeons achieve the goal of true anatomic reconstruction.

Additionally, further study to other anatomical properties of the ACL is needed to provide a complete and quantifiable definition of “anatomic”. As such, Fujimaki et al. have recently provided a more objective take on the shape of the ACL by quantification of the cross-sectional area of the ACL in different loading conditions.

When considering the knee as a whole, anatomic ACL reconstruction should not be about just the restoration of the ACL’s anatomy as should it (also) be about restoring the complete knee’s anatomy. Since we know that ACL deficiency causes anterior tibial subluxation (ATS), we aimed to objectively assess whether anatomic ACL reconstruction restores the tibiofemoral relationship. Conventional non-anatomic ACL reconstruction techniques have proven unable to adequately reduce the tibia and therefore restore the native tibiofemoral relationship. Since anatomic ACL reconstruction aims to
more closely restore the native anatomy,\textsuperscript{81,82,141} it is generally thought that anatomic ACL reconstruction sufficiently restores the tibiofemoral relationship. However, this had yet to be evaluated.

The purpose of the study described in Chapter 5 was to assess the tibiofemoral relationship in the sagittal plane after anatomic ACL reconstruction and compare the anterior and rotational laxity (quantified using KT-1000 evaluation and pivot shift testing) with ATS (quantified using a standardized radiography protocol) for both acute and chronic ACL-deficient patients.

Using a standardized radiography protocol and validated measurement technique\textsuperscript{10,11,13,98} after anatomic ACL reconstruction, this study was the first to compare the residual ATS after anatomic ACL reconstruction for patients that were acutely and chronically ACL deficient.

The most important finding of this study was that anatomic ACL reconstruction reduces ATS with a mean difference of 1.0 ± 2.1mm anteriorly from the healthy contralateral limb.

Multiple studies identified ATS as an objective secondary sign of ACL injury\textsuperscript{98,100,232,305,315} and also that there is a positive correlation with the duration of ACL deficiency.\textsuperscript{98,100,315}

Previous studies have suggested that ATS may be irreducible by conventional ACL reconstruction and that this may in part be due to restricted posterior translation.\textsuperscript{13} However, the effect of anatomic ACL reconstruction has not been studied to date. Since the most fundamental difference between this study and previous studies is the surgical technique, these results suggest that the reported irreducibility may also in part have been due to non-anatomic tunnel placement.

Although it has not been established what an acceptable remaining ATS would be after ACL reconstruction, 1.0 ± 2.1mm ATS does appear to be a closer approximation of the normal anatomic tibiofemoral relationship (uninjured knees: 0.4 ± 2.3mm)\textsuperscript{13} than previous studies were able to demonstrate.

Future research in this area should focus on dynamic data, which would certainly be helpful to assess how this altered (and subsequently restored) tibiofemoral relationship affects actual three-dimensional knee-movement.

To objectively classify tunnel placement after ACL reconstruction as anatomic or non-anatomic is valuable for postoperative evaluation and further treatment planning, as well as for pre-operative revision surgery planning. Different tools have been proposed, and although three-dimensional computed tomography (3DCT) remains the most accurate,\textsuperscript{96,186} a method using simple measurements on clinically available radiographs was recently introduced by Illingworth et al.\textsuperscript{151} This simple method made it possible to assess femoral tunnel placement quickly on plain radiographs and with
decreased radiation exposure compared to CT. It was found that an FTA of $<32.7^\circ$ likely corresponds with ACL reconstructions that fall outside an anatomic range.

This metric was established for the use of rigid reamers. Drilling with a flexible reamer has been shown to alter the femoral tunnel exit point and increase the femoral tunnel length. With the increased use of flexible reamers, it came to question whether this cut-off value of $32.7^\circ$ would remain applicable.

Therefore, fifty patients that had a single femoral tunnel drilled with a flexible reamer were compared with 50 patients that had a single femoral tunnel drilled with a rigid reamer. The FTA was determined from post-operative antero-posterior (AP) radiographs by two independent observers. A $5^\circ$ difference between the two mean FTAs was considered clinically significant. The average FTA, when drilled with a rigid reamer, was $42.0^\circ \pm 7.2^\circ$. Drilling with a flexible reamer resulted in a mean FTA of $44.7^\circ \pm 7.0^\circ$. The mean difference of $2.7^\circ$ was neither statistically nor clinically significant. The intraclass correlation coefficient for inter-observer reliability was 0.895, suggesting very good inter-observer agreement.

The results of the study described in Chapter 6 indicate that there is no difference in mean FTA after rigid or flexible tunnel drilling. We concluded that the FTA can be reliably determined from post-operative AP radiographs and provides a useful and reproducible metric for characterizing femoral tunnel position after both rigid and flexible femoral tunnel drilling.

Many different parameters for the evaluation of tunnel placement on CT scans have been described. While this modality remains the most accurate and reliable, the use of radiography is more simple and readily available in most clinics. Direct post-operative fluoroscopic radiography (while still in the operating room) has been described for the evaluation of tunnel placement, and found to be useful. However, for evaluating tunnel placement in the post-operative outpatient setting (for instance for pre-operative revision surgery planning) fluoroscopy or CT scanning is not always an option.

Other methods and parameters for tunnel position assessment on plain radiography have been described, but most of these rely on multiple measurements and variables that may not be efficient in the clinical setting. In addition, several studies have found the use of plain radiography to be challenging and unreliable when assessing tunnel position after ACL reconstruction. Illingworth et al. found that the FTA can be reliably determined from plain radiographs. This study shows that flexible tunnel drilling does not seem to affect the measurement of the FTA with respect to rigid tunnel drilling and thus supports its continued usability.

Future studies to radiologic tunnel placement assessment will not likely focus on the use of radiography, but with the further development of computed tomography in terms
of decreasing costs and radiation exposure, it seems likely that post-operative CT scans will more and more become common practice.

**POST-SURGERY**

Almost directly after surgery, patients start an intensive rehabilitation program with exercises that should encourage range of motion, strengthening of the quadriceps and hamstrings, and proprioception training. Goals of this program are to gain good functional stability, repair muscle strength, reach the best possible functional level, and decrease the risk for re-injury. However, rehabilitation can only go so fast. No matter the motivation and progress of the patient—nor the efforts of the treating surgeon—biology (or “healing”) takes time and the body needs to incorporate the graft to reduce the chance of graft failure.

Given that the weakest link after ACL reconstruction is not the graft, but rather the fixation points on the tibial and femoral side until the graft has adequately healed in the bone tunnel, an understanding of the tendon-bone healing and the intra-articular ligamentization process is crucial for surgeons to make appropriate graft choices and to be able to initiate optimal rehabilitation protocols after surgical ACL reconstruction. Chapter 7 focuses on the current understanding of the tendon-to-bone healing process for both autografts and allografts and discusses strategies to biologically augment healing. Tissue engineering and biomechanical stimulation approaches to enhance this healing process have shown promising results (“proof of principal”) in preclinical animal studies and include, but are not limited to, the use of a fibrin clot, platelet rich plasma, growth factors, stem cells, scaffolds, periosteum graft augmentation, bisphosphonates, autologous ruptured tissue, and mechanical loading. Tendon-bone healing is a complex process that is dependent on numerous biological factors, and research on the chemical interactions involved in the healing process have led to promising results in the improvement and acceleration of ACL graft incorporation. Understanding the basic biology of these processes will help to define what is needed to improve healing, and this can then guide the choice of optimal approach(es) for biologic augmentation. Further investigation is required before the routine clinical implementation of cell-based and biological factors is advocated to augment healing after ACL reconstruction, and likely represents a critical frontier to improve outcomes after all soft tissue reconstructive procedures. Until then, use of biologic augmentation should be in the light of controlled clinical trials, since well-intentioned but premature use may lead to the premature abandonment of potentially effective therapies.
OUTCOME

ACL injuries often are sports injuries and often disabling for young athletes. It therefore only seems reasonable to not only wonder if patients return to their pre-injury sports after ACL reconstruction, but more so if we can objectively predict what patients eventually may return. The rate of return to the preinjury level of sports participation can be used as a measure of the success of ACL reconstruction surgery. Previous literature has suggested a relatively low rate of return to pre-injury sports (RTPS).\textsuperscript{24,25} Discrepancy in return to sports rates and specifically low return to sports rates are not well understood. Additionally, multiple studies have investigated what demographical factors, physical impairments, functional, and psychosocial measures may be associated with an individual’s decision to RTPS. However, since these studies focused on the post-surgery phase, identified variables have no real predictive properties.\textsuperscript{71,95,202,203} There is a general paucity of research that has studied which measurable (pre-surgery) variables help predict the likelihood of successfully returning to sports.\textsuperscript{132}

In Chapter 8 is presented how we were able to identify five independent predictors of return to pre-injury sports.

Individuals 1 to 5 years after primary ACL reconstruction completed comprehensive surveys concerning sports participation and function. Comprehensive RTPS was defined as: “Returning to the same type and frequency of sports activity, and achieving at least the same Marx Activity Rating Score as before injury”.

Two hundred and fifty-one participants completed the survey at an average of 3.4 ± 1.3 years after ACL reconstruction. Five variables at the time of ACL reconstruction best predicted RTPS including age, being a competitive athlete, time from injury to surgery, tibiofemoral cartilage status, and having had any form of cartilage surgery done. Therefore, younger patients that partake in sports on a competitive level, that have ready access to healthcare, and less damage or surgery to their knee return to sports more often.

Recently, Newman et al.\textsuperscript{249} studied what factors may be predictive of concomitant injuries among children and adolescents undergoing ACL surgery. Although study designs differ, their conclusions are very much in accordance with our findings. They concluded that concomitant injuries occurred more frequently among older subjects, that a delay to surgery correlated with increased severity of injury, and –preceding combined- that return to sports was significantly related to the presence of a concomitant knee injury in the older cohort.

Of the identified predictors, only time from injury to surgery is reasonably potentially modifiable. However, when discussing the different treatment alternatives, older age, not being a competitive athlete, concomitant injury (and surgery), and delay in surgery planning should be taken into consideration as they are definite risk factors for inferior
results with regards to return to pre-injury sports. Future prospective studies that could include this information would be very helpful. While these objective variables may be helpful in predicting which individuals return to pre-injury sports, there are many other factors that determine whether or not individuals return to sport including motivational factors and aspects of rehabilitation. Understanding differences between individuals who do or do not return to sport after ACL reconstruction is the next step towards developing evidence-based return to sport rehabilitation guidelines and participation criteria.

Despite returning to sports being a major outcome parameter for ACL reconstruction, the general wellbeing of patients probably should be regarded the chief outcome parameter. Therefore, an important question remains: how well do patients feel after undergoing ACL reconstruction? To assess this in an objective manner, the use of patient-reported outcomes (PROs) has increased in the field of sports medicine and in research. However, the interpretation of the change and absolute post-operative PRO scores in a clinically meaningful way remains difficult since a statistically significant change in PRO score does not necessarily represent a clinically important improvement. Moreover, it is not known what post-operative PRO score is acceptable from the patient’s perspective. For the ACL, the IKDC-SKF and KOOS are two of the most commonly used knee-specific PRO measures.

It is generally thought that patient-reported measures of symptoms, activity limitations and participation restrictions are highly related to the patient’s perception of their outcome. However, a change in the PRO score may not be associated with an acceptable state that corresponds to an overall health state at which patients consider themselves to be “feeling well”, which is also called the Patient Acceptable Symptom State (PASS). Establishing a PASS threshold for a PRO can aid in interpretation of clinical or research outcomes by providing a reference value at which the majority of a population “feels well”.

For the study presented in Chapter 9, individuals that were 1 to 5 years after primary ACL reconstruction completed a survey that included the IKDC-SKF and KOOS. All subjects assessed satisfaction with their current state by answering the question: “Taking into account all the activity you have during your daily life, your level of pain and also your activity limitations and participation restrictions, do you consider the current state of your knee satisfactory?” Analysis of the receiver operating characteristic (ROC) curve revealed that the IKDC-SKF and each of the KOOS-subscapes were significantly better identifiers of PASS than chance as indicated by the significance of the area under the curves (AUCs).

To our knowledge, this is the first study to identify the PASS thresholds for the IKDC-SKF and the KOOS subscales. By identifying objective threshold values for the PASS,
this study provides additional information to facilitate interpretation of the IKDC-SKF and KOOS scores in daily practice and clinical research related to ACL reconstruction. Additionally, mean scores for patients that are (PASS-Y) and are not (PASS-N) in an acceptable symptom state have been identified. Differences in mean scores between PASS-Y and PASS-N for the KOOS pain, symptoms and ADL scales were smaller than differences for KOOS sports & recreation and knee-related QoL scales and the IKDC-SKF, suggesting that following ACL injury and reconstruction, achieving a PASS is more dependent on the ability to participate in more demanding activities including sports without symptoms or difficulty than on participation in activities of daily living.

Only one other study has linked the PASS to KOOS scores after ACL reconstruction. In this study, mean scores were compared for three groups (acceptable state, intermediate state and treatment failure group) at three different time-points (6 months, 12 months and 24 months). No threshold values for achieving an acceptable symptom state were established. Their findings indicated that only half of the patients at 6 months and about two-thirds at 1 to 2 years perceived their symptoms as acceptable (PASS-Y) after ACL reconstruction. Given the trend, these findings may well be consistent with our finding of PASS-Y of 89.2% at mean of 3.4 years. In addition, the mean KOOS scores at 2 years (closest to our mean follow-up of 3.4 years) showed a similar tendency as our findings, with highest absolute scores for both the PASS-Y and PASS-N group for the KOOS-Pain and KOOS-ADL scales.

In the future, the use of PROs in both clinical and research settings will likely further increase and parameters such as the PASS will aid in their interpretation. Research in this area is needed. As for the PASS, factors that may be of influence to achieving the patient acceptable symptom state should be further identified. Fear of reinjury, the role of coping, self-efficacy and treatment expectations should be examined.

CONCLUSION

This thesis deals with current issues in diagnostics, surgery and outcome measurement of anterior cruciate ligament injury. Throughout all segments of the treatment spectrum, subjective findings, opinion and assumption have long dictated examination procedures and management protocols. This work is meant to provide a more objective take on anterior cruciate ligament injury and surgery.

A more objective physical examination has been proven possible through the development of an iPad application (PIVOT) that can provide direct quantitative evaluation of the pivot shift test.

In an effort to objectively assess how anatomic anatomic ACL reconstruction really is, it was found that with current techniques it is impossible to restore the insertion sites
of the ACL completely. However, contrary to conventional techniques, the tibiofemoral relationship in the sagittal plane does seem to be adequately restored by anatomic ACL reconstruction. Additionally, when evaluating whether the reconstruction was performed anatomically by measuring the femoral tunnel angle, this measurement does not seem to be affected by the drilling technique.

By identifying variables that objectively predict which individuals return to preinjury sports, it was found that younger patients that partake in sports on a competitive level, that have ready access to healthcare, and less damage or surgery to their knee return to sports more often, potentially due to fewer knee joint problems after ACL reconstruction.

Moreover, at 1 to 5 years after anatomic ACL reconstruction, almost 90% of patients are in an acceptable symptom state and identified threshold values for the IKDC-SKF and KOOS scores provide objective additional information to facilitate interpretation of these patient reported outcome scores. Achieving the patient acceptable symptom state appears to be associated with improved function, sports participation, and knee-related quality of life.
SUMMARY AND SAMENVATTING

CHAPTER 11
SUMMARY

In this thesis, a more objective take on anterior cruciate ligament injury and surgery is presented. Current issues with regard to diagnosis, treatment and in terms of outcome assessment have been addressed. The current chapter consists of a general summary.

In Chapter 2, development of software for a computer tablet (iPad) that provides an objective, quantitative evaluation of one of the most commonly used clinical tests for knee laxity (the pivot shift test) is described. Aims of this study were to develop clinically applicable computer tablet software that would reliably quantify the translation of the lateral knee compartment during the pivot shift test, to determine repeatability of the developed methodology in an intact and an ACL-deficient human cadaveric knee, and to determine the influence of environmental factors including tablet distance and tablet angle that could potentially affect the measurement accuracy of the software. Based on a previously developed and validated method, we were able to develop an iPad application (PIVOT) that allows simultaneous videotaping of the clinical test, tracking of markers, and calculation of a translation curve over time. To validate the PIVOT software and test reliability and accuracy, both cadaver testing and computational simulation were conducted. Based on these experiments, it was found that intra- and inter-tester reliability were excellent and that the PIVOT software should be used at a distance between the tablet and lateral side of the knee of 50–175cm and at angles of the tablet of less than 45° to maintain an acceptable accuracy of less than 6%. Other systems have been reported to provide a quantitative evaluation of the pivot shift test, however, none of these systems are easily applicable in a clinical setting secondary to limitations such as invasiveness, cost, and development primarily for research purposes. The PIVOT application will enable surgeons to more objectively evaluate their physical exam by quantifying the amount of rotatory knee laxity for each individual knee.

In Chapter 3, an overview of different surgical techniques and explanation of often confusing terminology is presented. Anatomic ACL reconstruction should be performed according to the double-bundle concept. This concept relies on the functional anatomy of the ACL, which dictates the surgical procedure by accounting for size, shape, tensioning patterns and orientation of the native ligament. A surgeon should master a variety of diagnostics, objective measurements and surgical techniques to be able to customize the treatment to the patient’s specific needs.

In Chapter 4, we objectify whether individualized anatomic ACL reconstruction approaches the native anatomy, and thus whether it is truly anatomic. ACL reconstruction
should focus on restoration of the native functional and anatomical properties and should take the size, shape and orientation of the ACL into account. But how does one account for this? To date, there is no objective measurement or real objective definition of what “anatomic” really is. Surely it means to approach the native anatomy as closely as technically possible, but how do we measure this? Would it suffice to just “eyeball” it? In order to get a more objective take on what anatomic is, we studied how close we could reproduce the size of the native ACL insertion sites (percentage of reconstructed area or PRA) when performing anatomic ACL reconstruction. The most important finding in this study was that anatomic ACL surgery only restored on average 70–79% of the native insertion site size. Based on these findings, we found that complete footprint restoration (or 100% of reconstructed area) with an adequately sized graft and matched tunnel size is not feasible. The measurement and calculation of PRA serves as a rudimentary tool for objectively evaluating the degree of native insertion site coverage using an individualized anatomic technique and provides a starting point from which to evaluate the clinical significance of insertion site restoration.

In Chapter 5, we further assess the extent to which anatomic ACL reconstruction restores the native knee anatomy. For this study, restoration of the tibiofemoral relationship was evaluated. It has been established that ACL deficiency causes a passive alteration of the tibiofemoral relationship in the sagittal plane: the tibia subluxates anteriorly with respect to the femur, which can be objectified from MRI and radiographs. This anterior tibial subluxation (ATS) increases as time between injury and surgery increases and is positively correlated with instability. Using a standardized radiography protocol and validated measurement technique the tibiofemoral relationship was measured in the sagittal plane after anatomic ACL reconstruction for both acute and chronic ACL-deficient patients. The most important finding of this study was that anatomic ACL reconstruction reduces ATS with a mean difference of 1.0 ± 2.1mm anteriorly from the healthy contralateral limb, which was regarded a close approximation of the anatomic situation. In contrast to what previous studies had found, chronic ACL deficiency did not appear to lead to a fixed altered tibiofemoral relationship. Anatomic ACL reconstruction may adequately reduce anterior tibial subluxation in either the acute or chronic phase. By objectively measuring residual ATS after surgery, this study has further elucidated the extent to which the native knee anatomy is restored by anatomic ACL reconstruction. Given the current trend in ACL reconstruction, these observations hold important implications regarding surgical technique. Further longitudinal studies are underway to compare the pre- and post-surgical tibiofemoral relationship.
In Chapter 6, an existing tool for the post-operative assessment of anatomic femoral tunnel placement is evaluated for the use of flexible reamers. A simple measurement of the femoral tunnel angle (FTA) on clinically available radiographs was earlier found to be a useful metric in differentiating anatomic from non-anatomic ACL reconstruction. However, measurement of the FTA was only studied for ACL reconstructions performed with a rigid drill. With the increased use of flexible reamers, it came to question whether the established cut-off value would remain applicable. By measuring and comparing the FTA between rigid and flexible reamed tunnels on post-operative radiographs we evaluated its continued applicability. The results of the study described in Chapter 6 indicate that there is no difference in mean FTA after rigid or flexible tunnel drilling. The trajectory of the femoral tunnel can be reliably determined from post-operative radiographs after both rigid and flexible femoral tunnel drilling. The FTA remains a useful and reproducible metric for characterizing femoral tunnel position after both rigid and flexible femoral tunnel drilling. Quantitative assessment of tunnel placement by measuring the FTA is another step towards the a more objective evaluation of surgical technique.

In Chapter 7, current concepts on graft healing and the biological augmentation of healing have been reviewed. The successful restoration of native knee kinematics through ACL reconstruction relies on the assumption that there is adequate healing of the graft/ bone tunnel interface and reconstructed tissues to withstand the forces transmitted to the native ACL with athletic activity. With the well-established, inferior functional outcomes of revision ACL reconstruction compared with primary ACL reconstruction, prevention of graft failure should be the focus of early after-treatment. Recent improvements in surgical management options of ACL injuries have called further attention to the importance of new biological strategies to enhance the intraarticular and intraosseous healing process. Current research trends have focused on both refining existing techniques and developing novel solutions such as augmentation of graft-tunnel healing, primary ACL repair, and use of scaffolds to improve or obviate autogenous or allogeneic grafts for reconstruction. Further research is necessary before widespread clinical adoption; the preliminary results of these modern advances are promising and likely represent the future of ACL injury prevention and management.

In Chapter 8, predictors of returning to pre-injury sports (RTPS) after surgery are identified.

There is a general paucity of research that has studied which measurable (pre-surgery) variables help predict the likelihood of successfully returning to sports. The purpose of this observational cross sectional study was to determine if certain variables predicted return to the same frequency and intensity of sports participation with similar
activity demands as before injury. We found that five variables at the time of ACL reconstruction best predicted RTPS including age, being a competitive athlete, time from injury to surgery, tibiofemoral cartilage status, and having had any form of cartilage surgery done. Therefore, younger patients that partake in sports on a competitive level, that have ready access to healthcare, and less damage or surgery to their knee return to sports more often. Understanding differences between individuals who do or do not return to sport after ACL reconstruction is the next step towards developing evidence-based return to sport rehabilitation guidelines and participation criteria.

In Chapter 9, finally, a quantitative assessment of post-surgery patient wellbeing is presented. In addition to the rate of return to the preinjury level of sports participation as a measure of the success of ACL reconstruction surgery, more and more are the effects of treatment assessed with patient-reported outcome (PRO) scores. However, a clinically meaningful change in PRO may not be associated with an acceptable state that corresponds to “feeling well”, which is also called the Patient Acceptable Symptom State (PASS). For this study, threshold values for two of the most commonly used knee-specific PRO measures (IKDC-SKF and KOOS) for the patient acceptable symptom state were identified. Hereby, we were able to provide additional information to facilitate further interpretation of the IKDC-SKF and KOOS, and by comparing mean values between patients who achieved and those who did not achieve the PASS, we were able to determine which PROs best discriminated between the PASS-Y and PASS-N states. To our knowledge, this was the first study to do so.
SAMENVATTING

In dit proefschrift wordt een objectievere kijk op voorste kruisband-blessures en -herstellende operaties gepresenteerd. Actuele thema’s met betrekking tot de diagnose, behandeling en evaluatie van het eindresultaat zijn behandeld. Het huidige hoofdstuk bestaat uit een algemene samenvatting.

In hoofdstuk 2 is de ontwikkeling van software voor een tablet computer (iPad) voor de objectieve en kwantitatieve evaluatie van een van de meest gebruikte klinische tests voor knie laksiteit (de pivot shift test) beschreven. Doelstellingen van dit onderzoek waren om klinisch toepasbare computer tablet software te ontwikkelen die op betrouwbare wijze de translatie van het laterale compartiment in de knie tijdens de pivot shift test zou kwantificeren, om de herhaalbaarheid van de ontwikkelde methodologie te bepalen in een intacte en een VKB-deficiënte menselijke kadaver-knie, en om te bepalen wat de invloed van omgevingsfactoren zoals tablet-afstand en tablet-hoek zou zijn op de meetnauwkeurigheid van de software. Op basis van een eerder ontwikkelde en gevalideerde methodo, waren we in staat om een iPad-applicatie (PIVOT) te ontwikkelen, die gelijktijdig video-opnamen van de klinische test kan maken, alswel de markers kan tracken, en een berekening van een translatie-curve kan ontwikkelen tegen de tijd. Om de PIVOT software en test-betrouwbaarheid en -nauwkeurigheid te valideren, werden zowel kadaver experimenten en computer simulatie experimenten uitgevoerd. Gebaseerd op deze tests werd gevonden dat de intra- en inter-tester betrouwbaarheid uitstekend waren, en dat de PIVOT software op een afstand tussen de iPad en laterale zijde van de knie van 50-175cm moet worden gehouden en onder een hoek van minder dan 45° om een aanvaardbare nauwkeurigheid van minder dan 6% te houden. Er zijn andere systemen beschreven die een kwantitatieve evaluatie van de pivot shift-test verschaffen, echter geen van deze systemen is gemakkelijk toepasbaar in de kliniek door beperkingen zoals invasiviteit en kosten, bovendien zijn deze systemen hoofdzakelijk ontwikkeld voor onderzoeksdoeleinden. De PIVOT applicatie zal chirurgen in staat stellen hun lichamelijk onderzoek objectiever te beoordelen door het kwantificeren van de hoeveelheid rotatoire knie laksiteit van elke individuele knie.

In hoofdstuk 3 wordt een overzicht van verschillende chirurgische technieken en uitleg van vaak verwarrende terminologie gepresenteerd. Anatomische VKB reconstructie zou moeten worden uitgevoerd volgens het dubbele-bundel concept. Dit concept is gebaseerd op de functionele anatomie van de VKB, waarbij anatomie de chirurgische procedure dicteert door rekening te houden met de grootte, vorm, spanningspatronen en oriëntatie van het oorspronkelijke ligament. Chirurgen zouden een verscheidenheid aan diagnostische vaardigheden, objectieve metingen en chirurgische technieken
moeten beheersen om de behandeling op de specifieke behoeften van de patiënt aan te passen.

In hoofdstuk 4 objectiveren we of individuele anatomische VKB reconstructie daadwerkelijk de natieve anatomie benadert, en dus of het wel echt anatomisch is. VKB reconstructie moet zich richten op het herstel van de oorspronkelijke functionele en anatomische eigenschappen van de VKB en moet daarbij rekening houden met de grootte, vorm en oriëntatie. Maar hoe houd je hier rekening mee? Tot op heden is er geen objectieve meting of definitie van wat “anatomisch” daadwerkelijk is. Natuurlijk betekent het de natieve anatomie zo dicht te benaderen als technisch mogelijk is, maar hoe meten we dit? Zou een schatting met “timmermansoog” volstaan? Om een beter idee te krijgen van hoe anatomisch anatomisch dan precies is, onderzochten we hoe dicht we de grootte van de natieve VKB inserties zouden kunnen benaderen (uitgedrukt in een percentage van het oppervlak, “percentage of reconstructed area” of “PRA”) tijdens anatomische VKB reconstructie. De belangrijkste conclusie van deze studie was dat anatomische VKB reconstructie gemiddeld slechts 70-79% van de natieve inserties herstelt. Gebaseerd op deze bevindingen hebben we vastgesteld dat volledig herstel van de natieve inserties (of 100% van het oppervlak) met een voldoende grote graft -afgestemd op de tunnel grootte- niet haalbaar is. De meting en berekening van PRA dient als een rudimentair instrument om objectief te kunnen bepalen in hoeverre we de anatomische inserties kunnen herstellen met behulp van een geïndividualiseerde anatomische techniek en biedt een uitgangssituatie van waaruit we ook de klinische betekenis van het hertstellen van de anatomie kunnen gaan evalueren.

In hoofdstuk 5 hebben we getracht te beoordelen in hoeverre anatomische VKB reconstructie ook de natieve anatomische relatie van de knie herstelt. Voor dit onderzoek, werd specifiek het herstel van de tibiofemorale relatie geëvalueerd. Het is reeds bekend dat VKB deficiëntie een wijziging van de passieve tibiofemorale relatie in het sagittale vlak veroorzaakt: de tibia subluxeert naar ventraal ten opzichte van het femur, wat kan worden geobjectiveerd middels MRI en röntgenfoto’s. Deze anterieure tibiale subluxatie (ATS) neemt toe naarmate de tijd tussen het letsel en operatie toeneemt en er is een positieve correlatie met instabiliteit. Met een gestandaardiseerd röntgenfoto-protocol en een gevalideerde meettechniek werd de tibiofemorale verhouding in het sagittale vlak gemeten na anatomische VKB reconstructie van zowel acuut als chronisch VKB-deficiënte patiënten. De voornaamste bevinding van deze studie was dat anatomische VKB reconstructie ATS vermindert met een gemiddeld verschil van 1,0 ± 2,1mm in vergelijking met de gezonde contralaterale ledemaat, wat als een fraaie benadering van de anatomische situatie werd beschouwd. In tegenstelling tot wat eerdere studies vonden, lijkt chronische ACL deficiëntie niet te leiden tot een vaste (niet-corrigeerbare)

In hoofdstuk 6 wordt een bestaande meetmanier voor de postoperatieve beoordeling van anatomische femorale tunnel plaatsing geëvalueerd voor het gebruik van flexibele reamers. Een eenvoudige meting van de femorale tunnel hoek (“femoral tunnel angle” of “FTA”) op klinisch beschikbare röntgenfoto’s werd eerder beoordeeld als zijnde een bruikbare meetmanier voor het onderscheiden van anatomische en niet-anatomische VKB reconstructies. Dit onderzoek naar de FTA heeft echter enkel naar VKB reconstructies uitgevoerd met een rigide boor gekeken. Met een almaar toenemend gebruik van flexibele reamers, rees de vraag of de vastgestelde cut-off waarde van toepassing zou blijven. Door het meten en vergelijken van de FTA tussen rigide en flexibele gereamideerde tunnels op de post-operatieve röntgenfoto’s evaluerden we de gecontinueerde toepasbaarheid. De resultaten van het in hoofdstuk 6 beschreven onderzoek geven aan dat er geen verschil is in gemiddelde FTA na rigide of flexibele tunnelboring. Het traject van de femorale tunnel kan betrouwbaar worden bepaald van post-operatieve röntgenfoto’s na het zowel rigide als flexibel boren van de femorale tunnel. De FTA blijft een nuttig en reproduceerbare meettechniek voor het karakteriseren van femorale tunnel positie nadat zowel rigide en flexibele femorale tunnel boren. Kwantitatieve beoordeling van tunnel plaatsing door het meten van de FTA is een nieuwe stap in de richting van de een meer objectieve evaluatie van de chirurgische techniek.

In hoofdstuk 7 worden de huidige inzichten op het gebied van graft genezing en de biologische ondersteuning van genezing gereviewd. Het succesvolle herstel van de natieve knie kinematica na VKB reconstructie is gefundeerd op de veronderstelling dat er voldoende heeling in de graft/ bot-tunnelinterface optreedt en dat deze gereconstrueerde weefsels zelfs de krachtentransmissie tijdens sport kunnen weerstaan. Met de bewezen inferieure functionele resultaten van de revisie VKB reconstructie in vergelijking met primaire VKB reconstructie, moet preventie van het falen van de graft het focus zijn van de vroege nabehandeling. Recente ontwikkelingen op het gebied van VKB chirurgie, hebben de aandacht opnieuw gevestigd op het belang van nieuwe biologische behandelstrategieën om het intra-articulaire en intra-ossale genezingsproces verder te verbeteren. Huidige onderzoekslijnen richten zich zowel
op het verder ontwikkelen van bestaande technieken als de ontwikkeling van nieuwe behandeltechnieken zoals het verbeteren van graft-tunnel heling, het primair hechten van de VKB, en het gebruik van weefselmatrix als conductieve draagstructuur (“scaffold”) om het gebruik van grafts te voorkomen. Meer onderzoek is noodzakelijk voordat dit soort technieken klinisch kunnen worden toegepast; de eerste resultaten van deze moderne ontwikkelingen zijn echter veelbelovend en zullen ongetwijfeld een belangrijke rol spelen in de preventie en behandeling van VKB letsels in de toekomst.

In hoofdstuk 8 zijn voorspellers van terugkeer naar sport (“return to pre-injury sports”, of “RTPS”) na VKB reconstructie geïdentificeerd. Er is een gebrek aan onderzoek naar meetbare (pre-chirurgie) variabelen die de kans op een succesvolle terugkeer naar sport helpen te voorspellen. Doel van dit observationele dwarsdoorsnede onderzoek was te bepalen of bepaalde variabelen voorspellen of iemand terugkeert naar dezelfde frequentie en intensiteit van sportbeoefening met gelijke activiteits-eisen als voor het letsel. We vonden dat vijf variabelen ten tijde van de VKB reconstructie RTPS het best voorspellen, namelijk leeftijd, het zijn van een competitieve atleet, de tijd tussen letsel en operatie, de conditie van het tibiofemorale kraakbeen en het ondergaan van iedere vorm van kraakbeen chirurgie. Daarom, jongere patiënten die sporten op een competitief niveau, die eenvoudig toegang hebben tot gezondheidszorg, die minder schade én minder uitgebreide chirurgie aan de knie hebben, keren vaker terug naar sport. Inzicht in de verschillen tussen individuen die wel of niet terug te keren naar de sport na VKB reconstructie is een volgende stap naar de ontwikkeling van evidence-based richtlijnen voor revalidatie gericht op terugkeer naar sport en sport-participatie criteria.

In hoofdstuk 9, ten slotte, wordt een kwantitatieve inschatting van het post-operatieve patiënten-welzijn gepresenteerd. In aanvulling op terugkeer naar sport als een maatstaf voor het succes van VKB chirurgie, worden de effecten van behandeling meer en meer gemeten met patiënt-gerapporteerde resultaat (“patient-reported outcome” of “PRO”) scores. Echter, een klinisch wezenlijke verandering in een PRO houdt niet zeker verband met een acceptabele status die overeenkomt met “je lekker voelen”, ook wel de “Patient Acceptable Symptom State” (“PASS”) genoemd. Middels deze studie werden twee drempelwaarden voor de meest gebruikte knie-specifieke PRO scores (IKDC-SKF en KOOS) voor PASS geïdentificeerd. Hiermee verstrekken we informatie die een verdergaande interpretatie van de IKDC-SKF en KOOS faciliteert en middels het vergelijken van gemiddelde waarden tussen patiënten die PASS wel en niet bereikten- waren we in staat om te bepalen welke PROs het beste discrimineren tussen “je lekker voelen” (“PASS-Y”) en “je niet lekker voelen “PASS-N”. Voor zover wij weten is dit het eerste onderzoek dat dit bewerkstelligt.
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### 1. PhD training

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The Effect of Flexible Tunnel Drilling on the Femoral Tunnel Angle, Poster ISAKOS 2013
Comparison of Two Methods to Measure Return to Sports after Anterior Cruciate Ligament (ACL) Reconstruction, Poster ISAKOS 2013
Defining Patient Acceptable Symptom State Thresholds for the IKDC Subjective Knee Form and KOOS for Patients Undergoing ACL Reconstruction, Poster AOSSM 2013
Can individualized anterior cruciate ligament reconstruction restore the native insertion site size? Podium AOSSM 2012

(Inter)national conferences

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Other

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<td>Akere A. Atte, Medical Student</td>
<td>2012</td>
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<td>Eric R. H. Duerr, Medical Student</td>
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3. Publications

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<th>Year</th>
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190
Muller B, Hofbauer M, Wongcharoenwatana J, Fu FH.  
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ISBN: 9783642365683


ISBN: 9781625521019
ABOUT THE AUTHOR

Bart Muller was born in the Hague, the Netherlands, on May 21st 1984. Being a people person with an interest in technique, biology and handcraft, it was at an early age already that an interest for orthopaedic surgery sparked. After graduating from grammar school (Christelijk Gymnasium Utrecht) in 2003, he started medical school in Amsterdam.

During his study in Amsterdam, he lived in Utrecht and was an active member of the Utrechtsch Studenten Corps (i.e. fraternity) and -as such- also fulfilled a management board position in 2005-2006.

After obtaining his Medical Doctor’s degree in 2011, and being enthused for the field of Sports Medicine by Professors Niek van Dijk and Gino Kerkhoffs in Amsterdam, he moved to Pittsburgh to do a research fellowship with Professor Freddie Fu. There he worked both as a PhD research fellow on ACL related topics, and as a research coordinator supporting some 25 international fellows.

During this time as a PhD research fellow, he attended to and presented his research at numerous national and international conferences. Most of his research was published in scientific journals and he wrote multiple chapters for orthopaedic textbooks. Much of the published research was finally bundled in this PhD thesis.

Upon return from Pittsburgh, he started his orthopaedic surgery training in Amsterdam early 2013. Over the last few years he worked as a general surgery resident in the St. Lucas Andreas Hospital, and as an orthopaedic surgery resident in the Slotervaart Hospital and the Academic Medical Center in Amsterdam. Currently he is working in the Tergooi Hospital in Hilversum and will likely complete his training early 2019.

Bart Muller has a special interest in Sports Medicine and Traumatology, primarily focusing on the lower extremity. As an orthopaedic surgeon, he aims to further his training in this area.
This thesis deals with current issues in diagnostics, surgery and outcome measurement of anterior cruciate ligament injury. Throughout all segments of the treatment spectrum, subjective findings, opinion and assumption have long dictated examination procedures and management protocols. This work is meant to provide a more objective take on anterior cruciate ligament injury and surgery.