Understanding rotational joint laxity in the human knee

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Abstract

As a degenerative disorder, osteoarthritis (OA) is one of the most common causes of disability in the world, affecting several joints in the human body, albeit with a higher rate in the knee joint. Considered as a disease of multifactorial etiology, osteoarthritis is also related with a history of previous joint injury, and particularly knee ligament damage.

Among such ligament damages, the rupture of the anterior cruciate ligament (ACL) is one of the most frequent. Increased anterior-posterior instability after ACL rupture as well as recovery in anterior-posterior translation after ligament reconstruction has been reported in existing literature. However, changes in axial rotational laxity as well as its influence on post-traumatic degenerative OA remain unclear, possibly due to the lack of objectivity and accuracy concerning the measurement techniques used. Accordingly, the development of reliable and accurate measurement approaches is necessary to achieve an early diagnosis of pathological axial rotation.

A series of studies have been conducted within this thesis to gain an understanding of passive axial rotational laxity in patients with higher risk of OA development.

In order to achieve a proper quantification of this parameter, a detailed *in-vitro* study was firstly conducted to determine the accuracy and suitability of single plane fluoroscopy, which resulted in adequate accuracy of this technique to detect clinically relevant differences between groups. This was supported by a second *in-vitro* study in which intact and ACL resected knees were fluoroscopically assessed while external axial torques were applied, resulting in higher axial rotational laxity values in the knees without ACL.

A device to achieve a controlled and objective application of external axial torques to the knee joint was designed, constructed and certified according to the german Medical Product Law. The controlled application of an external torque achieved with this device was subsequently combined with single plane fluoroscopy to gain an accurate and objective measurement of tibio-femoral axial rotation.

The device (knee rotometer) was found to be highly reliable, as determined in an *in-vivo* study in which invasive (fluoroscopy) and non-invasive (external reflective markers) assessments of tibio-femoral axial rotation at 0, 30, 60 and 90 degrees of knee joint flexion were compared. Additionally, the measured internal and external axial laxity values proportionally increased with higher flexion angles in the fluoroscopic assessment, which is consistent with increasing laxity at higher flexion

angles as expected. Although a strong correlation was found when comparing the two measurement techniques, the high root mean square (RMS) errors values found in the non-invasive technique required the determination of correction equations to reach a clinically relevant accuracy.

In a further analysis, a subject with a telemetric knee joint implant was measured in the knee rotometer to gain an overview of the changes on the internal loading conditions during passive rotation. Although only the interaction between the external structures, the femoral component and the tibial insert geometry would play a role in this case and that the analysis is limited to only one subject, the observed changes in the internal loading conditions measured in the telemetric implant as well as the increase in axial rotational laxity measured with the fluoroscope showed evidence of the interaction of the internal and external passive structures in the stabilisation of the knee joint as well as its dependence on knee joint flexion.

An investigation into the changes in axial rotational laxity after ligament injury and reconstruction was conducted in 13 subjects with confirmed ACL injury.

Significant differences in rotational laxity were found between the injured and the healthy contralateral knees at 30 and 90° of knee flexion angles. After three months, a reduction of internal rotational laxity was observed, although the range of total laxity remained similar and significantly different from the healthy knees. However, after 12 months, a considerable restoration of rotational stability was observed towards the levels of the contralateral healthy controls.

The significantly greater laxity observed at both knee flexion angles after three months (but not at 12 months) suggests an initial lack of post-operative stability, possibly due to the reduced mechanical properties or fixation stability of the graft tissue. After 12 months, remaining but reduced rotational laxity - both internally and externally - suggests a progressive stabilisation over time. Such changes were also observed in the progressive increase of the internal rotational stiffness, as well as the reduction in the energy dissipation.

Although the efficacy of single bundle ACL reconstruction is still discussed controversially, the results in this thesis show evidence that this clinical procedure seems to be able to achieve an almost complete recovery in axial rotational stability in the longer term. A general stabilization was also confirmed by the reduction in anterior-posterior translation showed in the additional KT-1000 arthrometer analysis conducted.

The instability observed at three months after reconstruction highlights the importance of properly undertaken rehabilitation programmes due to the high risk of re-rupture after early returning to sporting activities.
As an addition to the routine postoperative clinical analysis, the objective and controlled analysis of axial rotational stability should then be included in these clinical routines in order to be able to identify possible negative changes in stability that could not be detected by the usual methods conducted. With this, new perspectives can be opened to properly identify post-operative patient´s dissatisfaction, to evaluate the learning process of young clinicians and to assess the effectiveness of clinical rehabilitation.

Keywords: Anterior cruciate ligament, ACL reconstruction, tibio-femoral rotation, laxity, rotational stability, single plane fluoroscopy.

Kurzfassung

Als Arthrose wird eine degenerative Erkrankung der Gelenke bezeichnet, die sich durch einen Gelenkverschleiß auszeichnet. Sie ist eine der häufigsten Ursachen für Behinderungen weltweit und kann verschiedenste Gelenke betreffen. Vermehrt tritt die Erkrankung im Kniegelenk auf und wird dort als Gonarthorse bezeichnet.

Obwohl als Krankheit multifaktoriellen Ursprungs bekannt, besteht ein deutlicher Zusammenhang der Arthrose mit früheren Gelenkverletzungen, insbesondere Schäden am Bandapparat des Knies.

Obwohl in der Literatur ausführlich sowohl über erhöhte anterior-posteriore Instabilität als auch die Genesung nach Bandrekonstruktionen berichtet wird, besteht kein Konsens hinsichtlich der Veränderungen der rotatorischen Laxizität sowie deren Einfluss auf die Entwicklung posttraumatischer Arthrose. Ursächlich dafür sind möglicherweise fehlende Objektivität und Genauigkeit bestehender Messverfahren. Um eine frühere und differenziertere Diagnose stellen zu können, bedarf es der Entwicklung eines zuverlässigen und genauen Messverfahrens.

Im Zuge dieser Dissertation wurde daher eine Reihe von Studien durchgeführt, um ein klares Verständnis der passiven axialen rotatorischen Laxizität bei Patienten mit erhöhtem Gonarthroserisiko zu gewinnen.

Zur Untersuchung der Eignung der *Single Plane Fluoroskopie* zur Bestimmung dieses Parameters wurde eingangs eine erste in-vitro-Studie durchgeführt. Die Ergebnisse zeigten eine hinreichende Genauigkeit, um klinisch-relevante Unterschiede feststellen zu können. Dies konnte in einer weiteren in-vitro-Studie bestätigt werden. Dabei wurden Kniepräparate vor und nach dem Durchtrennen des vorderen Kreuzbandes mit einem externen Moment belastet und die Laxizität untersucht. Es zeigte sich eine erhöhte axiale rotatorische Laxizität nach dem Durchtrennen des Ligaments.

Zur objektiven und reproduzierbaren Untersuchung der tiobiofemoralen Rotation wurde ein Gerät, das die Einleitung von standardisierten Momenten ermöglicht, entwickelt, zertifiziert und mit der Single Plane Flouroskopie kombiniert.

In einer in-vivo-Studie wurden invasive (fluoroskopie) und nicht-invasive (externe reflektive Positionsmarker) Messmethoden verglichen. Dabei wurde die tibiofemorale Rotation unter 0, 30, 60 und 90 Grad Knieflexion verglichen.

Mit steigendem Beugewinkel konnte eine Zunahme der rotatorischen Laxizität gezeigt werden. Zwar wurde eine hohe Korrelation beider Messmethoden gefunden, durch den hohen RMS-Fehler der nicht-invasive Methode mussten jedoch Korrekturgleichungen eingeführt werden, um eine klinisch relevante Genauigkeit zu erreichen. Dabei konnte auch eine hohe Reliabilität des Gerätes (Knee Rotometer) gezeigt werden.

Mit dem Ziel, ein Verständnis der intern wirkenden Kräfte bei passiver Belastung zu erlangen, wurde ein Proband mit einem telemetrischen Knieimplantat im Rotometer untersucht. Obwohl nur die Wechselwirkung zwischen den externen passiven Strukturen, der femoralen Komponente und den Inlays als auch nur ein einziger Proband untersucht wurde, zeigte sich ein deutlicher Einfluss des Beugewinkels auf die Lastverteilung und die rotatorische Laxizität. Ursächlich dafür sind unterschiedliche Bandspannungen und die geometrische Kongruenz des Implantats. Die Ergebnisse können als Beleg für das Zusammenspiel interner und externer passiver Strukturen bei der Stabilisierung des Kniegelenks interpretiert werden.

An 13 Patienten mit bestätigter Ruptur des vorderen Kreuzbandes wurden im Anschluss Veränderungen der axialen rotatorischen Laxizität vor und nach der Rekonstruktion des Kreuzbandes untersucht.

Signifikante Unterschiede in der rotatorischen Laxizität zwischen dem verletzten und dem gesunden Kontroll-Knie konnten bei 30 und 90 Grad Beugewinkel beobachtet werden. Drei Monate nach der Rekonstruktion wurde eine Minderung der internen rotatorischen Laxizität beobachtet, allerdings veränderte sich die Gesamtlaxizität nur gering. Der signifikante Unterschied im Vergleich zum gesunden Knie blieb bestehen. 12 Monate postoperativ konnte indes eine nahezu vollständige Wiederherstellung der Stabilität beobachtet werden.

Die signifikant höhere Laxizität bei beiden Beugewinkeln 3 Monate postoperativ deutet auf anfänglich mangelnde postoperative Stabilität hin, möglicherweise verursacht durch verringerte mechanische Eigenschaften oder ungenügende Fixierung des Transplantates. Die deutliche Abnahme sowohl interner als auch externer Laxizität nach 12 Monaten weist auf eine zeitlich progressive Stabilisierung hin. Diese Verbesserung der Stabilität konnte auch bei der Untersuchung weiterer Parameter, wie der internen rotatorischen Steifigkeit und der dissipierten Energie, beobachtet werden.

Die beobachteten Veränderungen der passiven rotatorischen Laxizität zeigen, dass die Single Bundle Rekonstruktion des vorderen Kreuzbandes erfolgreich die Stabiliät des Kniegelenks wiederherstellen kann. Diese Annahme konnte zusätzlich mithilfe der KT-1000 Arthrometer Analyse und der darin gezeigten Reduktion der anterior-posterioren Translation bestätigt werden.
Die drei Monate postoperativ beobachtete Instabilität unterstreicht die Bedeutung der Reha, da bei einer frühen Rückkehr zu sportlichen Aktivitäten das Risiko einer erneuten Ruptur erhöht ist.
Die routinemäßige postoperative klinische Untersuchung sollte um eine Analyse der rotatorischen Stabilität ergänzt werden, um neue Perspektiven bezüglich Ursachenfindung von Patientenunzufriedenheit als auch Evaluierung der Lernkurve junger Ärzte und Effektivitätssteigerung der klinischen Rehabilitation zu haben.

Schlüsselwörter: vorderes Kreuzband, VKB Rekonstruktion, tibio-femorale Rotation, Laxizität, rotatorische Stabilität, Fluoroskopie

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List of abbreviations

2D	2-Dimensional
3D	3-Dimensional
ACL	Anterior Cruciate Ligament
AM	Anteromedial
A-P	Anterior-posterior
BMI	Body Mass Index
CAD	Computer Aided Design
CCD	Charge-coupled Design
CT	Computer Tomography
DIF	Contour Difference Algorithm
DIN	Deutsche Institut für Normung
DoF	Degree of Freedom
EMG	Electromyography
ER	External Rotation
EW	Europäische Wirtschaftsgemeinschaft
ICC	Intra Class Correlation Coefficient
IIPM	Iterative Inverse Perspective Matching Algorithm
IR	Internal Rotation
LCL	Lateral Collateral Ligament
LED	Light Emitting Diode
MCL	Medial Collateral Ligament
MRI	Magnetic Resonance Imaging
OA	Osteoarthritis
PCI	Peripheral Component Interconnect
PL	Posterolateral
RoM	Range of Motion
RMS	Root Mean Square Error
RSA	Roentgen Stereophotogrammetry Analysis
SARA	Symmetrical Axis of Rotation Assessment
SD	Standard Deviation
SMM	Surface Mounted Marker
TKA	Total Knee Arthroplasty
TTL	Transistor Transistor Logic

Chapter 1: Introduction

Anterior cruciate ligament (ACL) related knee joint instability is one of the most common problems in the orthopaedic field [1]. With an estimate of 100,000 ACL tears per year in the United States alone [2], the consequent instability not only results in the withdrawal from sporting activities in the case of injured young athletes, but also increased surgical costs and therapy [3, 4]. Moreover, the influence of ACL in osteoarthritis has been evidenced [5, 6].
Before providing a more detailed description of the aforementioned problems, an introduction of the knee joint anatomy, function and biomechanics is presented as the basis for this thesis.

1.1 Knee joint anatomy

The knee joint is one of the most important joints of the body, playing an essential role in movement related to carrying the body weight in horizontal and vertical directions. The knee joint comprises three bony structures, namely the femur, the tibia and the patella, which form three distinct compartments: the medial, lateral and patellofemoral compartments [7] (Figure 1.1 Left).

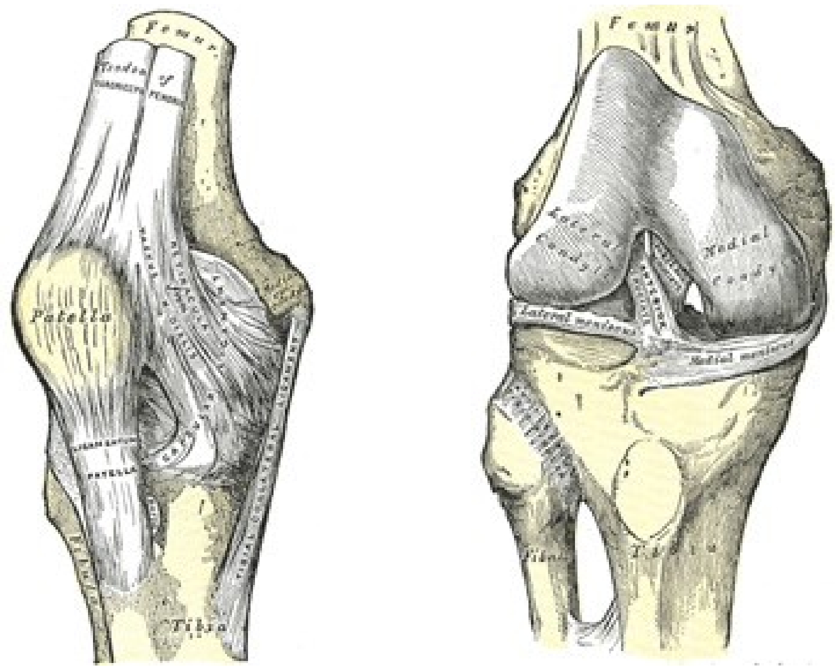

Figure 1.1: Anterior and interior view of the knee joint showing the external structures and the cruciate ligaments and meniscus (left and right respectively) [8]

The geometry of the distal end of the femur is complex. The femoral condyles are asymmetric in shape and dimension, with the larger medial condyle having a more symmetric curvature. Both condyles are distally and posteriorly separated by the intercondylar notch, being the notch area where the cruciate ligaments have their origin [7, 9].

In the tibia, the larger medial plateau is almost flat and has a squared-off posterior aspect [10]. On the other hand, the articular surface of the lateral plateau limits convexity. The patella comprises two articular surfaces - the lateral and medial - which communicate with the union of the two femoral condyles, called the patellar surface [9]. The principal biomechanical function of the patella is to increase the moment arm of the quadriceps mechanism during extension [11].

As a synovial joint, the knee is surrounded by an articular capsule, which is divided into a synovial and a fibrous membrane separated by fatty deposits. The synovial membrane is attached anteriorly on the margin of the cartilages on the femur and the tibia [9, 12]. Proximally, it attaches to the femur approximately 5 to 6 cm above the patella [7]. Posteriorly, the synovial membrane is attached to the margins of the two femoral condyles and from there passes in front of the two cruciate ligaments at the centre of the knee joint [9]. Distally, it attaches circumferentially to the tibial margin [7] (Figure 1.1 Right).

Two articular disks - the medial and the lateral meniscus - which comprise connective tissue with extensive collagen fibres containing cartilage-like cells, sit on the top surface of the tibia [9]. The lack of conformity between the femoral and tibial articular surfaces is reduced by the menisci, which considerably increase the contact area, as well as the conformity of the joint surfaces [7]. Hyaline cartilage covers the surface of the distal femur and proximal tibia, providing a resilient and smooth surface to allow the femur and tibia bones to move over each other [7].

1.2 Knee joint function

The knee joint functions as a modified hinge with limited inherent stability from the bony architecture. The lack of conformity between the distal femur and proximal tibia surfaces results in 6 degrees of freedom of motion, including translation in three planes (medial-lateral, anterior-posterior, proximal-distal) and rotation in three planes (flexion-extension, internal-external and varus-valgus) [7] (Figure 1.2).

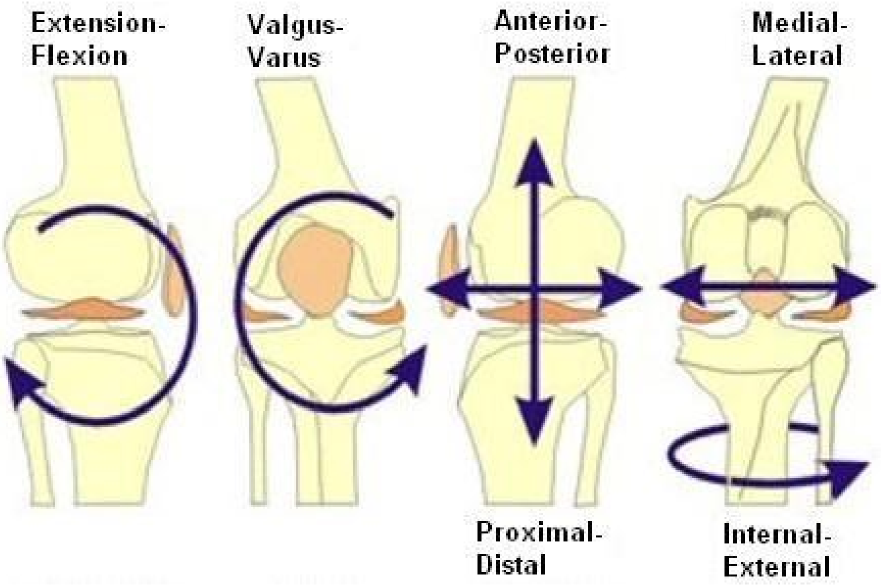

Figure 1.2: Knee joint degrees of freedom [13]

The movements of the knee joint are flexion and extension about a virtual transverse axis, as well as a slight medial and lateral rotation about the longitudinal axis of the lower leg. Flexion is performed by the hamstrings and biceps femoris and in small measure by the gastrocnemius and popliteus. Extension is performed by the quadriceps, producing a simultaneous extra rotation of the femur in terminal extension due to the shape of the bones and the ligament attachments [7]. Although the principal movement of the knee is flexion–extension, internal–external axial rotation plays a key role, and particularly in athletic activities that require pivoting [14]. The knee joint is called “mobile” due to the movement of the femur and the lateral meniscus over the tibia during rotation, as well as the rolling and gliding of the femur over both menisci during flexion-extension [9].

1.3 Knee joint stability

Joint stability can be generally defined as the resistance offered by various musculoskeletal tissues that surround a skeletal joint, while the opposed term is called instability, which appears when one or more subsystems have failed, particularly after traumatic injury. The term joint laxity is also frequently used to describe the stability of a joint. Passive laxity is a measure of joint movement within the constraints of ligaments, capsule and cartilage when an external force is applied to the joint during a state of muscle relaxation [15]. The knee joint exhibits a wide spectrum of laxity, from inherently stable joints at one end to excessively lax joints at the other. Knee joint laxity holds particular interest due to the high incidence of injuries, pain and degeneration, which account for substantial morbidity, functional loss and health care expenditures [16]. This terminology will be used extensively throughout this doctoral thesis.

Motion and stability of the knee joint are controlled by the shape of the condyles, as well as intra-articular passive structures such as the menisci and cruciate ligaments and extra articular passive and active structures, including the collateral ligaments and muscles [17-20]. The lateral collateral ligament (LCL) and the medial collateral ligament (MCL) provide the major static support to varus-valgus stress, while the MCL also plays a role in axial rotation [7, 21]. Significant contributions are also made by the capsular components and the iliotibial tract. For the muscles to contribute to the stabilisation of the knee, an effective proprioceptive feedback regarding joint position is crucial, whereby the cruciate ligaments act as strain gauges due to a variety of mechanoreceptors and provide input for control of the limb [7, 22-26]. The external loads caused by daily activities perturb the relative position of the femur and tibia, with the cruciate ligaments providing a measure of that perturbation, whereby muscle contraction can stiffen the joint and limit the relative tibio-femoral movement within physiological ranges [7, 27, 28]. When the active and passive structures are most stiff, the loading will be confined below the supraphysiological range, thus preventing joint damage [29]. On the other hand, when the loading occurs at flexion angles where both structures are less stiff, the active structures are less capable of resisting the loads and a greater percentage of the loads must be taken by the ligaments [30].

1.4 The anterior cruciate ligament

The ACL comprises a highly organised collagen matrix, which accounts for approximately three-quarters of its dry weight [7]. In the collagen matrix, the majority is collagen type I (around 90%), while the remainder is type II (around 10%) [23]. This collagen is organised into multiple fibre bundles around 20 μm wide, which are grouped into fascicles of around 20 to 400 μm in diameter [7, 31]. The origin of the ACL is the medial surface of the lateral femoral condyle in the posterior part of the intercondylar notch, whereby the insertion approximates the form of a segment of a circle [7] (Figure 1.3). From the femoral insertion, the ACL courses anteriorly, distally and medially towards the tibia. Approximately 10 mm below the femoral insertion, the ligament proceeds distally to the tibial attachment, a wide area anterior and lateral to the tibial tubercle in the intercondylar fossa. The medial attachment is more robust than the femoral attachment and is oriented in a more oblique direction [7].

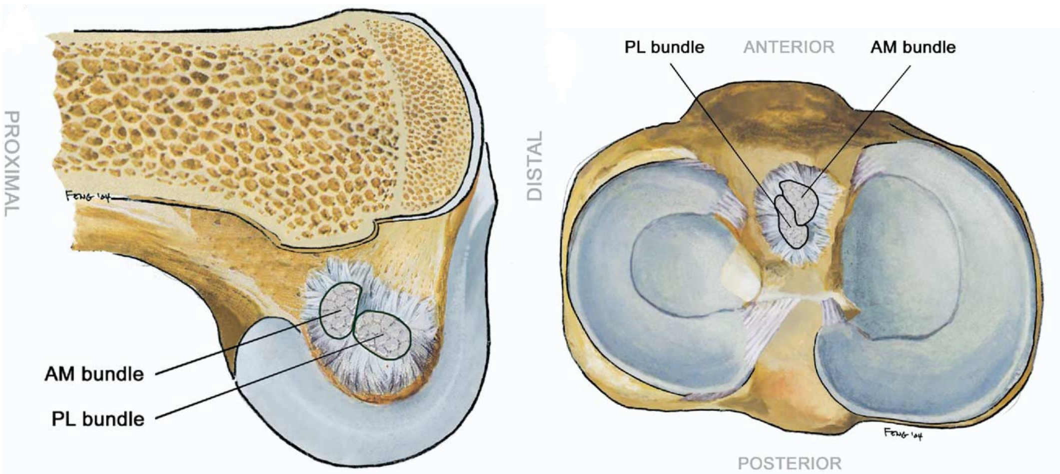

Figure 1.3: Attachment areas of the ACL [32]

The ACL guides the screw-home mechanism of the knee joint, which is an automatic, involuntary and inevitable axial rotation linked to the flexion and extension movements. During extension, the femoral condyles roll and glide on the tibia plateau and the tibia externally rotates. At full extension, the knee joint locks in a maximal stability position [14, 33].

The primary function of the ACL is to stabilise against excessive tibia translation relative to the femur and it accounts for up to 86% of the total force resisting anterior draw [7, 17, 34-36]. It is well known that the ACL comprises two main fibre bundles,

one anteromedial (AM bundle) and one posterolateral (PL bundle) [37] (Figure 1.4), which behave differently throughout the flexion-extension range [38]. In-vitro studies have found that the PL bundle is taut in full extension, while the AM bundle is taut across the flexion-extension range [39-41]. The PL bundle relaxes during knee flexion, allowing the tibia to internally rotate during quadriceps muscle contraction.
This pattern supports the knee weight bearing in extension and allows movement during knee flexion [42].

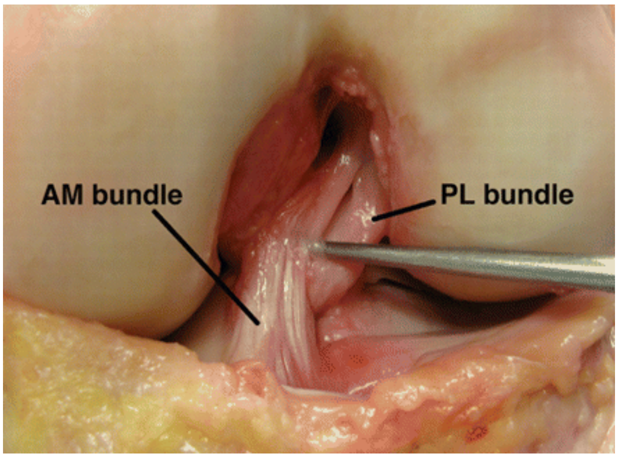

Figure 1.4: Bundles of the ACL [43]

1.4.1 Specific role of the ACL bundles in stabilisation of the knee joint

The AM and PL bundles control the anterior translation of the tibia at any degree of knee flexion. At high degrees of knee flexion, the AM bundle is more effective in controlling the anterior translation compared to the PL bundle. On the other hand, the PL bundle is more efficient from 0 to 20 degrees of knee flexion [44].
The ACL bundles also play different roles in controlling rotational motion and stability of the knee joint due to the differences in their attachment areas and orientation [45]. The AM bundle is almost vertically-oriented in the intercondylar notch in the coronal plane, thus having little ability to restrain tibial axial rotation. On the other hand, the PL bundle slants across the intercondylar notch to a more distal-lateral femoral attachment. It has a more horizontal orientation, which suggests a further position from the axis of tibial axial rotation, implying by this a higher ability to control rotations of the tibia compared to the AM bundle [46].

1.5 ACL biomechanics, injuries and associated knee osteoarthritis

1.5.1 ACL biomechanics

In an in-vitro study conducted by Hsu and colleagues [47], a robotic/universal force-moment sensor testing system was used to determine the stiffness of the ACL under anterior and combined rotatory loads in response to a 10Nm valgus torque in combination with a 5Nm internal tibial torque at 30° of knee flexion, a torsional joint stiffness of 0.85 Nm/deg and 1.03 Nm/deg was determined for female and male knees, respectively. In response to an anterior tibial load of 134N, an anterior tibial stiffness of 37 N/mm was determined for both female and male knees.

More specifically, the individual contribution of the AM and PL bundles in response to external loads was also investigated. In an *in-vitro* study conducted by Gabriel and colleagues [48] using a robotic device that under an anterior load, it was found that the PL bundle carries a higher load than the AM bundle with the knee in full extension. On the other hand, the AM bundle takes the majority of the load with the knee flexed in an angle larger than 30°. In response to rotatory loads of valgus and internal tibial torques, the AM and PL bundles share equally the load at a flexion angle of 15°.

Also using a robotic device to measure the in-situ force of the bundles within a range of anterior load of 22 to 110 N, Sakane and colleagues [49] found an unchanged in-situ force in the AM bundle throughout the flexion range and larger in-situ force in the PL bundle between 0 and 45 degrees of knee flexion, with a peak reached at 15 degrees.

After implanting a strain gauge in both the AM and PL bundles and measuring the changes in strain during range of motion, Bach and colleagues [50] found first a quasi-isomeric behaviour with changes of less than 1% between 10 and 90 degrees of flexion and second that the AM bundle stretched at full extension and flexion. On the other hand, the PL bundle was relaxed from 40 degrees until maximal flexion and in extension elongated more than 12% of its initial length.

Based upon the information from the aforementioned studies, evidence exists that the ACL bundles show a load sharing behaviour, while neither of the two bundles alone is able to reproduce the mechanical properties and function of the intact ACL.

1.5.2 ACL injuries

Ligaments function within a small range of tensile elongation and usually rupture at 20% strain [51, 52]. ACL injuries can be classified into non-contact and contact injuries. The usual mechanism of non-contact injuries involves deceleration, hyperextension, pivot on a fixed foot or landing motion [53, 54], as well as large valgus and axial rotations [53, 55-57], causing the femur and tibia bones to twist in opposite directions under full body weight (Figure 1.5 Left). After an ACL rupture, the knee joint becomes unstable, with patients having activity related pain or swelling, difficulty walking downhill and trouble making a quick stop [54, 58, 59].

A first diagnosis of the injury can be made with clinical examination (Figure 1.6 Right), but in some cases a confirmation may be needed using magnetic resonance imaging (MRI).

Figure 1.5: ACL injury mechanism and clinical diagnosis [60]

In the case of contact injuries, the usual mechanism is a blow to the lateral aspect of the knee in the moment when the foot is set on the ground. This kind of injury is often associated with medial instability or anteromedial rotatory instability [59]. Some patients report feeling or hearing a “pop” and in most cases they are unable to return to sport activities.

There is also a tendency towards a higher incidence of ACL injuries among female soccer and basketball athletes compared to male athletes [47, 61]. Some authors attribute this tendency to intrinsic biomechanics factors [47] such as muscle strength, hamstrings to quadriceps ratio and joint laxity [61-66]. Intercondylar femoral notch geometry - more specifically a narrow notch - has also been suggested as a cause of injury due to impingement of the ACL while the knee is abducted and externally rotated [67].

After ACL injuries, some individuals can stabilise their knees (copers) during activities involving cutting and pivoting, while non-copers present instability even during activities of daily living [33]. It has been demonstrated that copers exhibited similar motion patterns to uninjured controls and non-copers have a decreased knee motion and external knee flexion moments, reducing their ability to compensate instability due to delayed hamstring activity [68, 69].

In the absence of the ACL, the remaining static restraints in the knee joint are the concavity of the medial tibia plateau, the frictional forces under load, the posterior horn of the medial meniscus and the posterior ligament-capsular structures. The dynamic restraints are the hamstring muscles, whose function depends upon adequate proprioception. Injuries of the ACL subsequently have a direct repercussion for the knee joint kinematics, resulting in an increased anterior tibial displacement and rotational instability [6].

The increase in instability due to excessive anterior tibial translation as well as axial rotation results in shearing forces mainly applied on the medial side of the knee. Between the tibia and the posterior femoral condyle, the medial meniscus becomes wedged, resulting in longitudinal splits, which become thicker and finalise in meniscal tears (Figure 1.6 Left). At microscopic level, vertical fissures in the cartilage can be recognizable, which result from degradation of collagen that eventually leads to sloughing of portions of cartilage into the joint (Figure 1.6 Right).

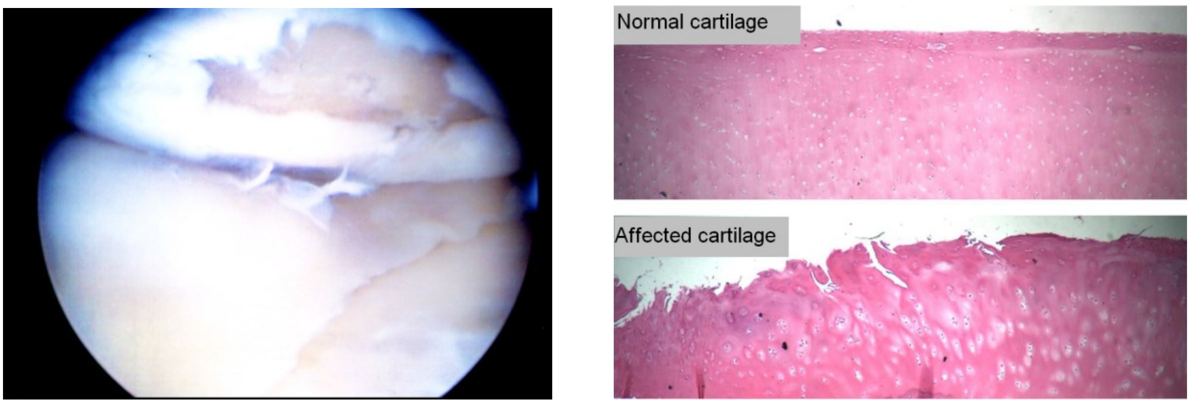

Figure 1.6 Cartilage defect and degradation following ACL injury (left and right respectively) [70, 71]

As a direct consequence, the loss of the posterior horn of the medial meniscus results in an extra increment of the anterior displacement of the tibia relative to the femur. The posteromedial capsule also stretches, resulting in further displacement [6]. In a twelve-year follow-up study with a cohort of 89 patients with an untreated ACL rupture, radiological degenerative changes were present in 63% and joint space narrowing in 37% [72].

This persistent abnormal kinematic behaviour and the altered stress distributions after an ACL injury contributes to the progression of osteoarthritis [5, 73].

1.5.3 Osteoarthritis

Osteoarthritis (OA) is one of the most common causes of disability in the world. It is defined as a degenerative disorder related to but not caused by ageing, whose main symptoms are joint pain and loss of joint function. It is considered a joint disease with multifactorial etiology, such as mechanical stress, ligament derangements, cartilage degradation, subchondral bone changes and muscular impairments [74]. The development of osteoarthritis is also correlated with a history of previous joint injury and with obesity [75]. Abnormal changes in muscle strength, flexion-extension range of motion (RoM), alterations in the normal screw-home mechanism, axial rotation and alignment associated with disability are commonly observed in OA patients [76].

The first measures to manage the symptoms of OA are conservatives treatments such as footwear interventions, braces, gait modifications, muscle strengthening and weight loss [74]. Barefoot walking has been indicated as reducing the knee adduction moment by 7 to 13% compared to normal shoes [77]. Reduction of pain during walking can be achieved by using lateral wedge insoles in patients with OA due to the reduction of the knee joint adduction moment by 4 to 14% [78]. Since being overweight directly influences the load in the joints of the lower limb, weight loss is indicated as an effective therapeutic measure given that it results in a direct reduction of the load on the knee joint during movement [79].

Joint preserving surgery procedures such as osteotomies are also conducted in middle-age patients, with studies reporting pain relieving and improved function [80].

If the disability becomes significant, with entirely destroyed articular surfaces, joint replacement surgery may be recommended [81]. New prosthesis designs feature high quality materials and modular systems, while minimal invasive surgery procedures allow efficient rehabilitations programmes patient-specific solutions and long durability of the implants [82, 83].

1.6 ACL reconstruction

As previously mentioned, some individuals can stabilise their knees after an ACL injury. However, the majority present with instability even during activities of daily living, which - combined with the risk of developing OA in a long-term scenario - leaves the reconstruction of the ACL as the only way to restore the normal function in an injured knee.

The ACL reconstruction comprises a surgical tissue graft replacement of the ACL. The torn ACL is entirely removed and the graft is inserted through a hole in the femur and the tibia bones.

The success of an ACL reconstruction should be considered in both the short- and long-term scenario, with the short-term scenario involving the return of injured athletes to sport activities as quickly and safely as possible [84-87].

Factors such as graft selection, tunnel placement, initial graft tension, graft fixation, graft tunnel motion and the rate of graft healing have a direct influence on the outcome of an ACL reconstruction [88]. A variety of autografts (employing bone or tissue harvested from the patient´s body) and allografts (bone or tissue from a donor´s body, typically a cadaver´s or a live donor) have been used for ACL reconstruction, while synthetic grafts have also have used with poor results. For autografts, bone-patellar tendon-bone and hamstrings tendons (semitendinosus and gracilis) are the most common [88].

Femoral tunnel placement has a strong impact on knee kinematics. The 11 or 1 o´clock position for the femoral tunnel on the frontal view has been used by most surgeons in recent years. However, biomechanical studies have suggested that this position could not satisfactorily improve the necessary rotatory stability, suggesting that a 10 or 2 o´clock position yields better results [89].

Graft tension of 20, 40 and 80N has been applied, with the 80N producing a significantly more stable knee [90].

Different types of graft fixation such as interference screws have been successfully used [91, 92]. Bioabsorbable screws are also effective and do not have to be removed in case of revision, arthroplasty or for magnetic resonance imaging. However, disadvantages such as screw breakage during the insertion, inflammatory response and inadequate fixation due to early degradation can arise [93-95].

Suspensory fixations are also used to fix the graft at the lateral femoral cortex, for which the tibial side cortical screws are used [96, 97].

The operation procedure performed at the Charité Berlin involves a single bundle operation, in which only the AM bundle is reconstructed. The reconstruction is performed as anatomically as possible. Autologous semitendinosus implant grafting is conducted (Figure 1.7A) using a hybrid technique that use an endobutton and bioresorbable interference screws in each of the tibia and femur. This approach is able to prevent the requirement of oversized screws as well as avoid possible bungeeing of the graft across the joint gap, while still maintaining many of the advantages of more standard fixation techniques.

The extracted tendon is freed of muscle tissue and should be of a minimum of 26 cm, although extra tendon tissue of the gracilis can be extracted in cases where the patient has a short tendon or a diameter smaller than 8 mm. The length of the tendon is important to achieve a quadruple-strand to be used in the surgical reconstruction (Figure 1.7B). The four strands are hold together with surgical suture (Figure 1.7C) leaving a transplant of almost 65 mm in length. Both surgical suture loop ends are then inserted in the fixation buttons for posterior attachment in the femur and tibia bones [98].

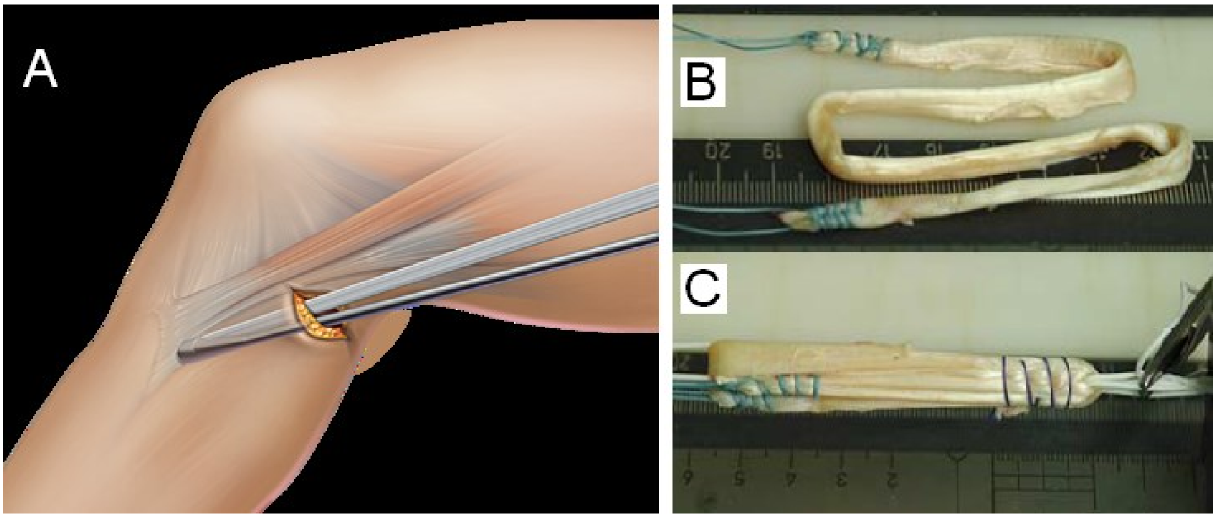

Figure 1.7 Semitendinosus tendon for graft reconstruction [98]

In order to drill the femur tunnel, the knee joint need to be flexed at 120° to achieve a 10 or 2 o´clock position, hence also providing good accessibility to the anatomical ACL origin. To avoid a perforation of the lateral femur corticalis, a maximal drilling depth of 30 mm and 40 mm was targeted, which accounted for small and large knee joints, respectively. To drill the tibial screw tunnel, the knee has to be flexed between 50 and 70°, where an optimal view of the tibial ACL insertion can be achieved. It is important to avoid a too far posterior drilling in the tibia to avoid perforation of the corticalis. A minimum of 18 mm of the screw is then introduced into the femoral tunnel, while 20-22 mm is introduced into the tibial tunnel under arthroscopic control [98].

Although it is currently unclear what effect ACL reconstruction has in the development of OA, it has been shown in a long-term study that early ACL reconstruction could reduce the prevalence of OA in sport-active ACL deficient patients [99]. Subsequent studies have also shown that an ACL reconstruction can generally reduce the prevalence of OA in cases where A-P stability is regained when compared to no ACL reconstruction [6, 100].
On the other hand, the study conducted by Norris and colleagues found only limited evidence suggesting a reduction of the risk of OA in the long-term after ACL reconstruction [71], while other studies have found no protective effects of ACL reconstruction [101], thus suggesting that no conclusive data can be found in the literature.
It is also worth mentioning that since the development of OA is multifactorial in nature, a combination of biological mediators will likely play an important role in preventing the development of early OA following traumatic injury such as ACL rupture. However, since the widespread use of these agents will require long-term follow-up studies to prove efficiency, this leaves ACL reconstruction as the only apparent possibility to restore knee joint stability after such an injury [71].

While ACL reconstruction restores anterior-posterior stability [102], restoration of rotational stability has not been documented [5], suggesting that remaining rotational instability after ACL reconstruction could be a factor for the initiation of OA [103, 104]. The lack of information regarding rotational stabilisation after ACL reconstruction is also a consequence of the need for a proper examination test or devices to assess this parameter.

1.7 Knee stability examination tests

An effective knee joint examination is mandatory to guarantee a successful diagnosis and the subsequent treatment of complex knee injuries. All clinical examinations should include assessment of RoM, as well as comparison with the uninjured knee [59].

As previously mentioned, the well-recognised primary function of the ACL is to prevent excessive anterior translation of the tibia relative to the femur.

The Lachman and the anterior drawer tests are the most commonly used to assess the anterior translation clinically. With the patient lying in supine position and the knee flexed by 30° in the Lachman test, the examiner stabilises the anterolateral distal femur with one hand and uses the other to apply a firm pressure on the posterior aspect of the proximal tibia in an attempt to induce anterior displacement (Figure 1.8 Left), propioceptive and/or visible anterior translation of the tibia beyond the femur with a soft endpoint represents a positive result [59, 105]. Qualitative and quantitative measures are then compared to the contralateral knee.

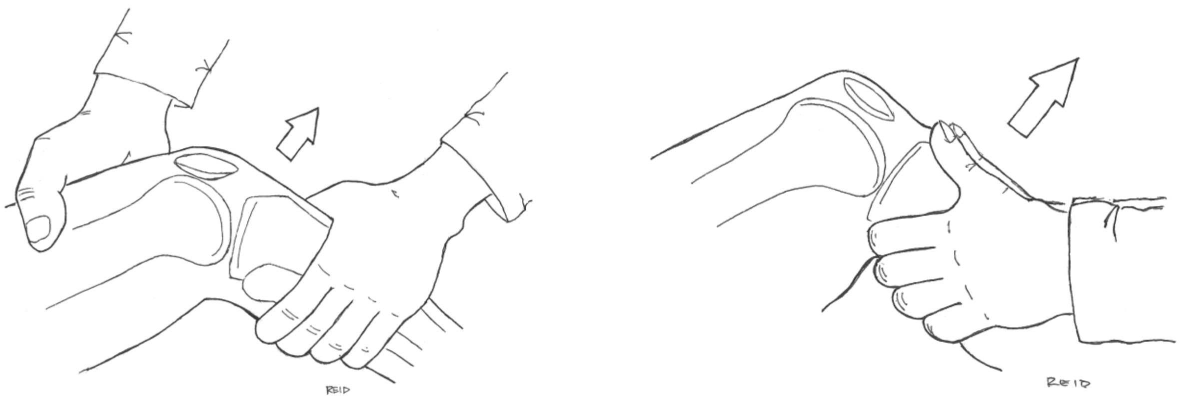

Figure 1.8: Lachman and Anterior drawer tests (left an right respectively) [59]

The anterior drawer test is performed with the patient in supine position and the knee flexed to 90°. The patient must relaxed the hamstrings muscles to minimize the dynamic resistance to anterior translation. After confirmed relaxing of the patient's hamstrings muscles, an anterior force is applied by grasping the proximal tibia with both hands (Figure 1.8 Right). However, this test is sensible to involuntary hamstring spasm that may restrict anterior translation and the 90° flexion position may be difficult to achieve in an acutely injured or swollen knee [59].

In order to achieve a standard and objective test, arthrometers such as the KT-1000 and KT-2000 have been developed to quantify anterior tibial displacement. They provide an accurate and reliable measure of anterior laxity [106]. The device ois placed against the knee to be tested with the measurement pads secured against the tibial tubercle and the patella (Figure 1.9). Anterior forces of 67, 89 and 134 N are then applied to both ACL-injured and healthy contralateral knees. A maximum side-to-side difference of >3mm, a maximum manual translation of >10mm, or a compliance index (difference in translation between the 89 and 67N tests) >2mm were shown correlate with ACL insufficiency [107].

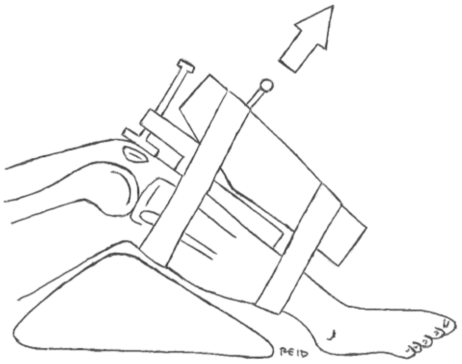

Figure 1.9: KT-1000 arthrometer [59]

As previously explained, not only anterior-posterior stability but also tibial rotational laxity changes after complete ACL deficiency have been reported by many studies, although differing conclusions arise concerning whether ACL deficiency has a clinically recognisable effect on rotational laxity [108]. In recent years, rotational stability of the knee has become one of the most important variables in restoring anatomic knee kinematics after ACL injuries [109]. ACL reconstruction is considered by some authors to be insufficient in controlling combined rotational loads [110-112].

Tibial rotation is difficult to measure in an accurately, objective and reliable way in a clinical setting, with interpretation entirely dependent upon the examiner´s experience [113-116].

The pivot shift test is another common method to assess ACL insufficiency and is associated not only to anterior translation, but also to axial rotation [117]. The goal of the test is to observe a sudden shift of the tibia relative to the femur when the knee moves from an extended to a flexed position [118]. This phenomenon can be noticed with the patient in a supine position, in a state of muscle relaxation and with the knee extended and in internal rotation (Figure 1.10 A), the ACL deficient knee would demonstrate an anterior subluxation of the tibia, then during initiation of knee flexion, while the posterior cruciate ligament and posterior capsule relaxed, a valgus stress will cause persistent anterior subluxation of the lateral tibial plateau (Figure 1.10 B) due to tibial contact with the lesser curvature of the lateral femoral condyle. When the posterolateral tibial plateau shifts anteriorly, it will impinge against the lateral femoral condyle at its greater curvature. The impingement prevents further anterolateral tibial subluxation and causes a hinging effect at the site of impingement. Continued flexion generates tension in the iliotibial tract, which at 30 to 40° of knee flexion will pull the subluxated lateral tibial plateau posteriorly, the tibia will then no longer impinge on the femoral condyle and the examiner perceives a sudden clunk as the joint reduces. This reduction will be considered a positive pivot shift sign [59].

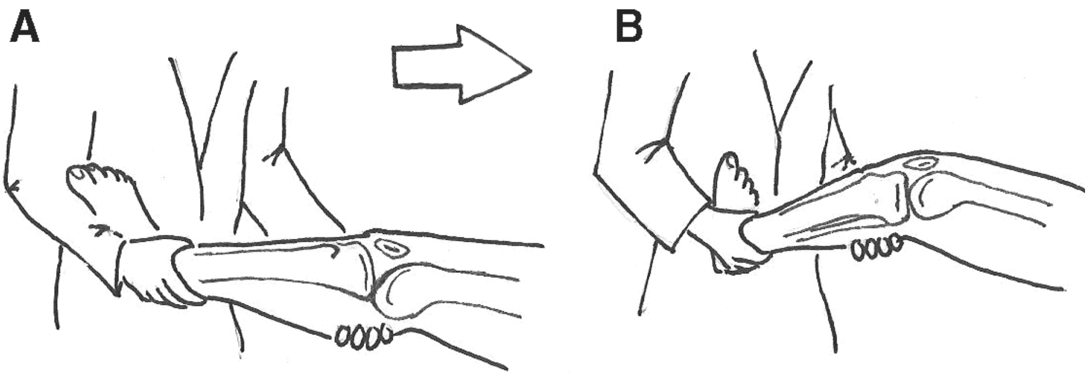

Figure 1.10:Pivot-shift test [59]

However, false findings are possible during performance of the test. Ligamentous laxity in an intact ACL knee may allow subluxations similar to the pivot shift phenomenon, while rupture of the iliotibial band may permit continuous subluxation and a locked tear of the meniscus may block the pivot shift from occurring [59, 119]. Despite being widely used, the test is reported to be difficult for clinicians to interpret [120] and has been found to lack specificity (25%) [114].

1.8 Limitations of previous assessment of passive rotational knee laxity

As mentioned in the previous section, clinical examinations are entirely dependent upon the clinician's experience, may be influenced by specific anatomic characteristics and lack of objectivity and reliability. Although a quantification of tibial translation is possible using the KT-1000 and 2000 arthrometers, quantification of rotational laxity is not yet possible in the clinical environment. Since the role of axial rotational laxity on post-traumatic degenerative OA remains unclear [121, 122], an increasingly interest in the investigation of this parameter has also been observed in recent years.

In an early attempt to evaluate tibio-femoral rotational laxity non-invasively, Almquist et al. [123] used a goniometer to measure absolute foot rotation. While rotations of up to 80° were reported, the assumption that the foot rotation equated to tibio-femoral rotation resulted in an over-estimation of up to 100% compared to the tibio-femoral rotation was measured using roentgen stereophotogrammetry analysis (RSA).
In an in-vitro study, Alam et al. [124] also compared the external rotational values from an inclinometer placed at the foot with the values from a goniometer directly attached to the tibial shaft and found up to 82° external rotation, which - similar to Almquist - equated to an over-estimation of the axial rotational angle of 103%.
Lorbach et al. [109, 125, 126] placed electronic sensors at the foot and reported a total internal-external tibio-femoral rotation at maximum torque of up to 115.6°. Hemmerich et al. [127] assessed tibio-femoral rotational laxity using MRI. Despite being non-invasive, this technique requires the application of torque to the joint for a long period, which may deteriorate the precision of the results.
Studies using electromagnetic sensors placed on the skin have reported tibio-femoral rotation of up to 28° at a 5Nm torque, although the results were susceptible to soft tissue artefact [128-130]. Importantly, all these studies have strapped or held the ankle fixed in a boot to avoid rotation of the foot relative to the tibia [123, 127] and subsequently applied an axial rotation to the foot/ankle fixation.
Therefore, all known studies to date are not only subject to soft tissue artefact [109, 128, 131, 132], but also to possible movement between the external fixation and the skin and hence are exposed to over-estimation of the real skeletal rotation [123].

Although the reliability of non-invasive measures has been determined in some studies [109, 124], the accuracy of tibio-femoral rotational laxity determination -which is important to avoid misleading clinical interpretation of results - remains unknown.
Due to these clear assessment limitations, the use of an accurate and reliable technique to measure tibio-femoral rotational stability becomes a necessity.

One possible solution could be the use of single plane fluoroscopy, whose high-resolution imaging, low-radiation exposure and relative freedom of movement makes it attractive in the orthopaedics research field [133]. The combination of this imaging technique with a standard device for application of external torques to the knee joint could open new perspectives in the investigation of rotational laxity, as well as helping to understand the changes in rotational stability after ACL injury.

Chapter 2: Aims and goals

Due to the multifactorial origin of OA, prevention of this cartilage degeneration has only been achieved to a limited degree. Generally, the diagnosis of the disease is only possible at a late timepoint, when it is already too late for conservative therapies. Accordingly, this leaves surgical interventions such as total knee arthroplasty (TKA) as the only remaining option for the patients [134].

A number of studies have shown that injuries of the ACL have a direct repercussion on the knee joint kinematics, resulting in increased knee joint instability and changes in the shear forces mainly applied on the medial side of the knee [5, 6, 71-73]. Consequently, the medial meniscus becomes wedged, resulting in longitudinal splits, which become ticker and finalise in meniscal tears; moreover, the posteromedial capsule also stretches resulting in further displacement [6]. Such studies have mostly focused in the investigation on the analysis of anterior-posterior stability, although the changes in axial rotational laxity are not yet fully understood. Furthermore, it is known that ACL reconstruction restores anterior-posterior stability [102], although restoration of rotational stability has not been documented [5], suggesting that remaining rotational instability after ACL reconstruction could be a factor for the initiation of OA [103, 104].

Since the role of axial rotational laxity on post-traumatic degenerative OA remains unclear [121, 122], the development of reliable and accurate measurement approaches are necessary to achieve an early diagnosis of pathological axial rotation

With the aim of gaining an understanding of passive axial rotational laxity in patients with higher risk of cartilage degeneration, the goal of this thesis was to assess and gain an insight into the influence of the ACL in rotational stabilisation of the knee joint. Furthermore, the influence of knee joint flexion as well as post-operative recovery on axial rotation could provide an improved insight into the influence of the ACL reconstruction on stabilisation.

In order to address these topics, this thesis poses the following hypotheses:

1. Passive tibio-femoral rotational laxity can be quantified in a standardised and objective manner in vivo using single plane fluoroscopy.

2. Knee joint flexion has an influence on rotational laxity.

3. Significantly higher passive rotational laxity is observed in patients after ACL trauma compared to the healthy contralateral side.

4. After ACL reconstruction, patients show a reduction in the rotational laxity compared to the pre-operative state and this reduction continues after a longer post-operative period.

In order to address these questions, this thesis is constructed into several sections partially presenting work that has been published in peer-reviewed journals throughout the course of this doctorate.

Chapter 1 describes the anatomy of the knee joint with a focus on the ACL, its function and relation to OA, as well as a state of knowledge in the literature regarding knee stability examination tests and previous assessments of passive rotational knee laxity.

Chapter 2 details the aims and goals of this thesis based upon the current state of knowledge in the literature, with a focus on the role of the ACL in passive rotational laxity of the knee joint.

Chapter 3 demonstrates the accuracy of the measurement technique used, as well as the development of a device to achieve objective measurements of rotational stability of the knee joint. The information within this chapter set the basis for the analysis to be performed in chapter 4 and the confirmation of the first hypothesis.

In chapter 4, the reliability of the measurement technique is tested in vivo. The first and second hypotheses are tested within this chapter.

Chapter 5 provides an understanding of passive axial rotation and the internal loading conditions in the knee joint.

The last two hypotheses are examined in chapter 6.

Finally a general discussion of the complete work as well as a summary and suggestions of future work and studies based on the collected knowledge are then provided in the outlook section

Chapter 3: Development of a concept for measuring passive rotational knee laxity.

As mentioned in the introduction chapter, the lack of objectivity and quantification of the clinical examinations of rotational knee laxity as well as the limitations in accuracy and reliability of the described measurements techniques - which possibly results in a misleading clinical interpretation of the results obtained - makes the use of an accurate and reliable technique to measure tibio-femoral rotational stability a necessity.

One possible solution could be the use of single plane fluoroscopy. Accordingly, a detailed description of this measurement technique and its combination with a device to objectively measure knee joint rotational laxity are presented in this chapter.

3.1 Single plane fluoroscopy technique

Fluoroscopy is an X-ray based image technique to obtain real-time moving images of the internal structures of a patient´s body. Modern fluoroscopes include an X-ray image intensifier and a CCD (charge-coupled device) video camera, which allows the images to be recorded and played on a monitor.

It is important to differentiate between RSA and single plane fluoroscopy. RSA is a highly accurate technique used in the three-dimensional analysis of migration and micromotion of a joint replacement prosthesis relative to the bone to which it is attached [135]. Two fluoroscopic units are used in this technique, as well as previously implanted tantalum beads in the bone tissue near to the implant. Accuracies of 10-250 µm and 0.03-0.6° have been reported [136]. New RSA techniques that avoid the need for attached markers have been also introduced [137].

By contrast, only one fluoroscopic unit is used in single plane fluoroscopy. Furthermore, the high image quality allows the registration of three-dimensional (3D) surfaces to the two-dimensional (2D) fluoroscopic images, which is commonly known as model-based fluoroscopy, providing access to tibio-femoral kinematics during functional activities, for instance [138]. The assessment of implanted component motion has long been established using model-based fluoroscopy [139-141]. However, in the kinematic analysis of native bones the reconstruction of individual 3D bone models is necessary. Such reconstruction can be achieved using MRI or computed tomography (CT) datasets assessed in one additional scan of the patients [133, 142].

CT offers rapid acquisition of high-resolution images, providing sharp contours of the bone surfaces due to the density related contrast differences, although subjects are exposed to ionising radiation and legislation is strict in cases that are not clinically indicated. On the other hand, surface reconstruction from the lower bone contrast offered by MRI images might result in reduced accuracy during registration to fluoroscopic data, albeit without exposure to ionising radiation [143-145]. In order to determine the suitability of single plane fluoroscopy to measure passive rotational knee joint laxity, it is necessary to know the accuracy of the registration of bone models to the fluoroscopic images.

3.2 Accuracy of 3D model registration to 2D fluoroscopic images, in vitro study

As previously mentioned, the 3D bone models can be reconstructed from CT and MRI scans. An in-vitro study with four human cadaveric knees - including surrounding soft tissues - was conducted. Each knee was scanned over the region approximately 15cm above and below the joint line of the knee using CT (Siemens Sensation 64, 512 x 512 image matrix, resolution 0.4 x 0.4mm, slice thickness 1mm) and MRI (Siemens Magnetom Avanto, 1.5T, T1 weighted, 512 x 512 image matrix, resolution 0.35 x 0.35mm, slice thickness 3mm). Here, two polarised radio-frequency knee coils were used to guarantee a similar scan length of the knees compared with that acquired using CT (Figure 3.1).

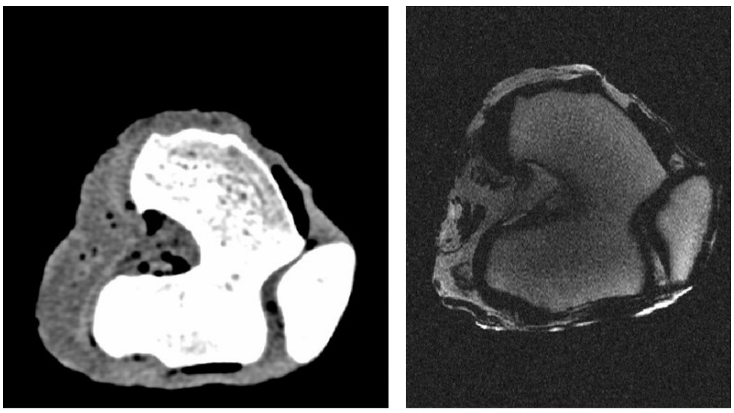

Figure 3.1: CT and MRI axial images of one exemplary knee (left, right respectively). A clear differentiation between te tissues is possible in both scan procedures [146]

Segmentation of the exterior cortical bone edges was performed using commercial software (Amira, Visage Imaging, Berlin, Germany) for the generation of triangulated polygonal surface models of each femur and tibia (approximately 80,000 triangles each) (Figure 3.2). Anatomical coordinate systems were defined for the femur and the tibia 3D bone models as described by Roos and colleagues [147].

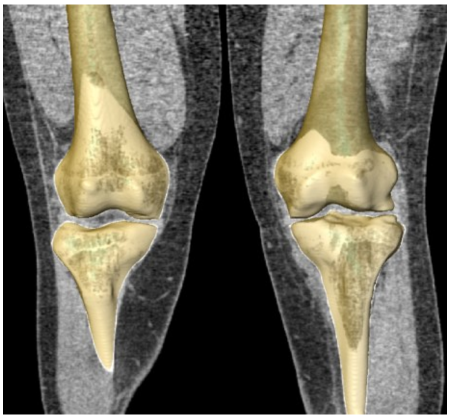

Figure 3.2: 3D reconstruction of femur and tibia bone surfaces from a CT scan

In an initial assessment of the surface quality, each MRI surface was registered to its CT counterpart and the distance between each vertex was computed.

Distances (mean ± SD) between the registered CT and MRI reconstructed surfaces for the femur and tibia were 0.51 ± 0.56mm and 0.73 ± 0.62mm in knee 1, 0.61 ± 0.58mm and 0.69 ± 0.60mm in knee 2, 0.68 ± 0.70mm and 0.75 ± 0.68mm in knee 3, 0.71 ± 0.56mm and 0.83 ± 0.72mm in knee 4, respectively. These differences were largest around the femoral condyles and on the tibial plateau, particularly at the intercondylar eminence (Figure 3.3).

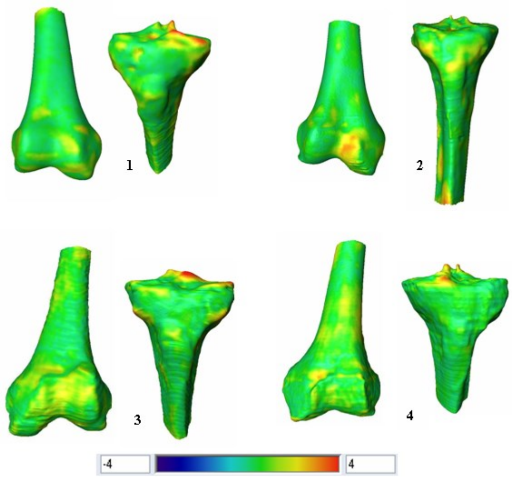

Figure 3.3: Differences between the CT and MRI 3D surfaces (mm) [146]

Although the main focused is to assess the accuracy of the registration of the 3D native bone surfaces to the 2D fluoroscopic images, the femoral and tibial components of a Depuy PFC-Sigma prosthesis were implanted into femur and tibia sawbones to assess the accuracy of the registration of 3D metallic implants models. In this case, previously acquired computer-aided design (CAD) models were used.
Since no direct measure of absolute registration position was possible, two experiments - one static and one dynamic - were conducted to assess the accuracy of the registration of the different surface reconstructions, from CT and MRI scans and metallic implants to the fluoroscopic images.
Prior to the experiments, the fluoroscopic system was calibrated to correct for image distortion by performing an image acquisition using a specially designed perspex calibration box (BAAT Engineering B.V. Hengelo, The Netherlands) [148].

3.2.1 Static experiment

A micromanipulator device with an accuracy of 0.005mm [137] was used to control the translations of the knees in steps of 1.0mm separately in (x and y directions) and out of the image plane (z direction), with a maximum displacement of 4.0mm (limited by the RoM of the micromanipulator). Here, any image blurring effects were minimised due to the static nature of the examination. In these investigations, a carbon reference box equipped with radio-opaque markers was rigidly attached to the image intensifier of the fluoroscope (Philips BV Pulsera, 30 frames/s; 1024 x 1024 image matrix; pulse width of 8ms).
These markers are used to define a coordinate system relative to which the translations of the cadaveric knees and metallic implants were defined. Fourteen fluoroscopic images were taken for each knee and analysed for the translations (Figure 3.4 Left).

Surface models (CT, MRI and metallic implants) of the tibia and the femur were subsequently registered to the fluoroscopic images to assess both the registrations' accuracy of their absolute position and orientation.

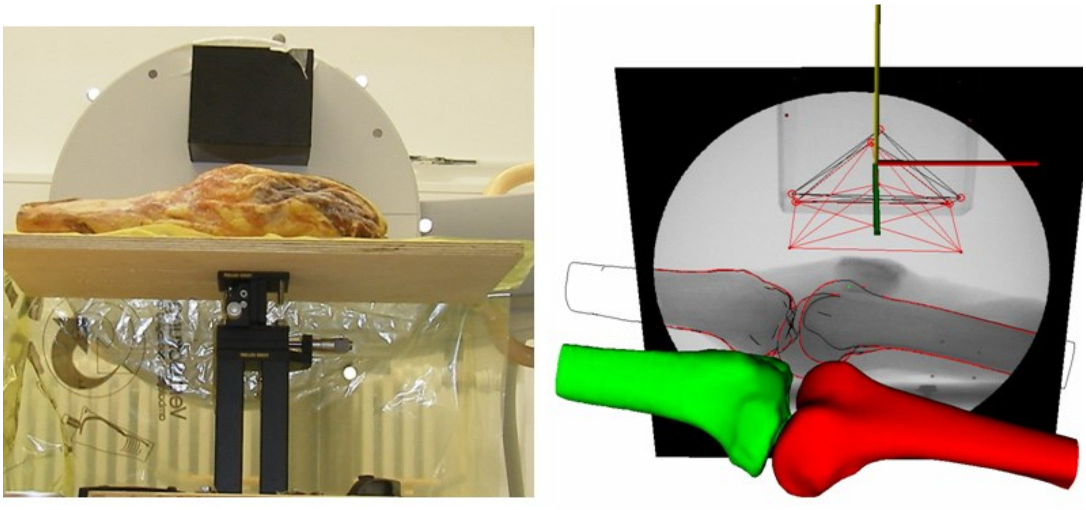

Figure 3.4: Micromanipulator set-up with the carbon reference box on the image intensifier (left) and a scene of model-based RSA after the registration process (right). The X-and Y-axis are orientated in the image plane, the Z-axis is orientated perpendicular to the image plane [146]

Here, the 3D surface models were projected onto the plane of the fluoroscopic images and contours of the surfaces of the bones/components were created. Additionally, a further set of contours of the surfaces of the bones/components were generated from the fluoroscopic images. All analyses were performed using a commercially available software package (Model-based RSA, Medis specials b.v., The Netherlands) [137]. In each measurement, the pose of the CT, MRI and implant's surface models were determined by fitting the two sets of contours to create the optimal matching scenario (Figure 3.4 Right). Within the model-based RSA software, a number of algorithms are used for the pose estimation [149]. The iterative inverse perspective matching (IIPM) algorithm is used to determine the closest points between the projected contours of the 3D bone surfaces and the contours of the fluoroscopic images. The contour difference (DIF) algorithm is subsequently used to minimise the distances between the two contours and thus provides the rotation and translation pose of the model that best registers to the 2D fluoroscopic image. The registration software describes the actual position of both segments - in this case, the femur and tibia - in terms of Euler angles and the correspondent translation vector. To assess the relative error in registration accuracy, the motion between successive fluoroscopic images was determined and subtracted from the actual motion applied by the micromanipulator.

The RMS error = $\sqrt{(\text{bias}^2 + \text{variance})}$ of the subtraction of the calculated and the actual motion was determined. These values can be observed in Table 3.1.

Registered surface		X (mm) (in-plane)	Y (mm) (in-plane)	Z (mm) (out-of-plane)	Rx (°)	Ry (°)	Rz (°)
CT	Femur	**0.59**	**0.49**	1.97	**0.33**	0.66	**0.16**
	Tibia	1.79	1.62	4.57	0.99	1.75	**0.45**
MRI	Femur	2.49	1.75	9.10	1.12	1.69	**0.18**
	Tibia	4.56	3.15	9.52	2.30	4.30	**0.48**
Implant	Femur	**0.36**	**0.16**	1.11	**0.14**	**0.22**	**0.10**
	Tibia	**0.27**	**0.40**	1.68	**0.25**	**0.14**	**0.15**

Table 3.1: RMS errors of the registration of the femoral and tibial surfaces from the CT and MRI reconstructions and the metallic implant components. Bold values show relative surface movement under 1.0 mm and 0.5°, based on clinically relevant values for joint reconstruction [150-152]

3.2.2 Dynamic experiment

The relative motion between the femur and tibia surfaces/components was determined while slow freehand motions including both rotations and translations of approximately 200mm and 35°, respectively, were applied to the cadaveric knees to emulate more physiological movement patterns. Once again, the rigid (frozen) tibio-femoral bond ensured that the actual relative motion remained zero in all positions. Since both the tibia and fibula were sectioned mid-shaft, relative movement between the bones between the CT/MRI scan and the fluoroscopic measurements could not be excluded. Any meaningful contribution of the fibula towards the registration process was thus not possible, whereby the fibula was not considered for the analysis. Like in the static experiment, the RMS error was determined from the calculated relative movement between the femur and tibia 3D bone/implants models. The values of both experiments can be observed in Table 3.2.

Registered Surface		X (mm) (in-plane)	Y (mm) (in-plane)	Z (mm) (out-of-plane)	Rx (°)	Ry (°)	Rz (°)
Micromanipulator (Static) measurements	CT	**0.31**	**0.38**	2.63	0.96	1.86	**0.45**
	MRI	**0.94**	**0.57**	9.34	2.45	3.02	0.62
	Implant	**0.09**	**0.17**	1.50	**0.09**	**0.13**	**0.06**
Dynamic measurements	CT	**0.88**	**0.81**	3.94	1.53	1.88	0.94
	MRI	1.21	**0.79**	10.41	3.59	3.16	1.39
	Implant	**0.65**	**0.25**	2.52	**0.44**	0.83	**0.13**

Table 3.2: RMS errors of the calculated relative movement between the femoral and tibial components/bones during the static micromanipulator and the dynamic measurements. Bold values show relative surface movement under 1.0 mm and 0.5°, based on clinically relevant values for joint reconstruction [150-152].

3.2.3 Influence of the 3D surface reconstruction in the registration process

A clear superiority in the accuracy of the registration process has been observed using models of metallic implants when compared with CT- and MRI-derived bone models in all the determined translations and rotations. This improved accuracy is almost certainly due to the higher edge contrast from sharper image shadows [152].

In an in-vitro study using a robotic arm, Lo and co-workers [153] reported anterior-posterior translation and internal-external rotation in the tibio-femoral joint at 30° of knee flexion of up to 17.3mm and 21.3° when comparing bicruciate retaining and ACL-sacrificing prostheses. The accuracy of registration for metallic implants reported in Table 2 suggests that such differences could easily be detectable using single plane fluosocopy (Table 3.2). In a similar manner, Kondo and co-workers [150] performed a controlled in-vitro study on eight cadaveric knees whose ACLs were resected and subsequently reconstructed. The reported differences at 30° of knee flexion were up to 12.9mm and 5° between the intact and resected knees, yet only 3.5mm and 2.5° between the intact and reconstructed knees. While an assessment of the degree of knee instability after injury may thus be entirely possible using either

CT (0.31-0.38mm & 0.96 – 1.86°) or MRI (0.57 – 0.94mm & 2.45 – 3.02°) constructed surfaces, surface quality and accuracy of 3D bone surface registration could be the key factor limiting the detection of more subtle differences between the surgical approach or type of joint reconstruction, for instance.

The quality of 3D surface reconstruction is known to depend upon the resolution and contrast of input data [154, 155], particularly for discrete datasets. Although the geometrical differences in the 3D surface models of the femora and tibiae between CT and MRI were shown to be small (Figure 3.3), these differences were generally present in key areas such as the femoral condyles and the intercondylar eminence of the tibia, probably owing to the magnetic field inhomogeneity presented due to the different tissues near the joint capsule. Although a high resolution in the axial plane was present in all the MRI scans, the slice thickness of 3mm did not allow a clear reconstruction of the necessary details to achieve a good registration. A decrease in slice thickness would likely improve the resolution in the coronal and sagittal planes but may have a negative influence on the resolution in the axial plane due to a poor signal-to-noise ratio, as well as extended scan times.

The consequences of any morphological discrepancies were apparent in the micromanipulator experiments, in which a clear superiority of the CT-based 3D surfaces was observed when compared to the MRI surfaces.

Although the application of MRI-based surface reconstruction to fluoroscopic registration offers an extremely low-radiation solution, the results suggest that a more reliable and accurate analysis of joint laxity analysis could be performed using CT-based bone surfaces. However, cumulative radiation exposure is low in the examination of lower extremity joints, even with the addition of a CT scan. Here, the effective dose of 0.06 mSv is considerably less than the comparable effective dose resulting from similar CT exposure to the head or body (~ 2-7mSv) [156].

The results of this work have been published in the Medical Engineering & Physics journal under the title: “The quality of bone surfaces may govern the use of model-based fluoroscopy in the determination of joint laxity” (Appendix A)

3.3 Measurements of knee joint rotational laxity in vitro

After knowledge of the accuracy of the registration process was collected, the next step was to measure passive knee rotational joint laxity *in-vitro* with single plane fluoroscopy under a controlled environment to investigate the suitability of this methodology.

A simple device was developed in which a 6 degree of freedom (DoF) force transducer was attached to a rotating plate. By manually applying weights, an axial torque in steps of 2Nm was applied from 0 to 14 Nm [126]. Accordingly, the rotation direction could be changed, thus allowing internal and external rotation.

Since post-mortem stiffness - once broke - had no further effects on the passive joint movements [157], three cadaveric knees were selected for the analysis. The skin and muscle 10 cm up and down of the knee joint line were removed to expose the femur and tibia bones [47]. The exposed tibia and femur bones were embedded in a hydroxylapatite compound.

Each specimen was thawed at room temperature for 24 hours before the testing. The embedded femur shaft was fixed in a metallic frame. The embedded tibia was subsequently fixed to the force transducer through a metallic plate, allowing a free axial rotational movement. The knees were positioned in such a way that a 30° knee flexion was guaranteed.

The image intensifier of the fluoroscope was positioned as close as possible to the cadaveric knee (Figure 3.5).

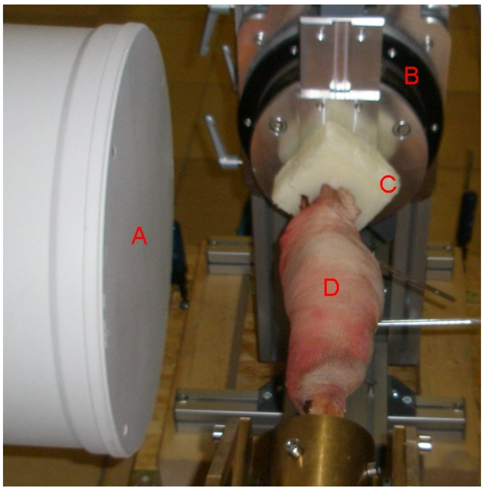

Figure 3.5: Experiment set-up. A: Image intensifier. B: Rotating platform and force transducer. C: Hydroxylapatite compound and connection to the force transducer. D: Cadaveric knee

After the application of every weight, a fluoroscopic image was taken. Overall, fourteen images (seven in internal and external rotation, respectively) were taken for every measurement. In order to avoid drying the specimens - which could eventually influence the measurements - the knees were regularly sprayed and humidified with a salt-water solution.

After the tests were completed, the specimens were demounted from the testing device. The ACL of every knee was identified and subsequently cutted to simulate a torn ACL (Figure 3.6). The experiments were then repeated under the same previous conditions.

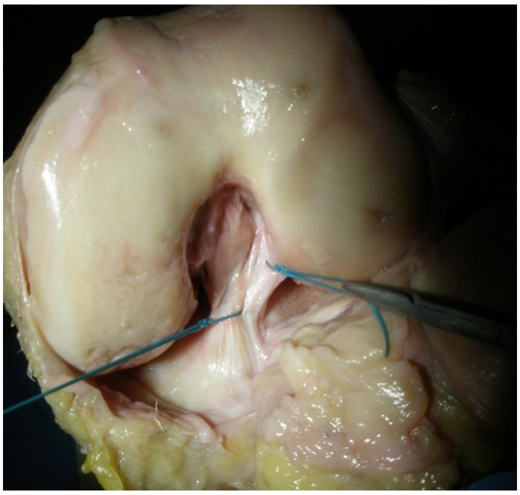

Figure 3.6: ACL of one of the cadaveric knees before cutting

3D bone models were reconstructed from previously collected CT scans. The definition of anatomical coordinate systems as well as registration of the 3D bone surfaces to the 2D fluoroscopic images was performed in the same way as described in section 3.2.

A mean hysteresis curve was constructed from all the rotations calculated plotted against the torque values (Figure 3.7).

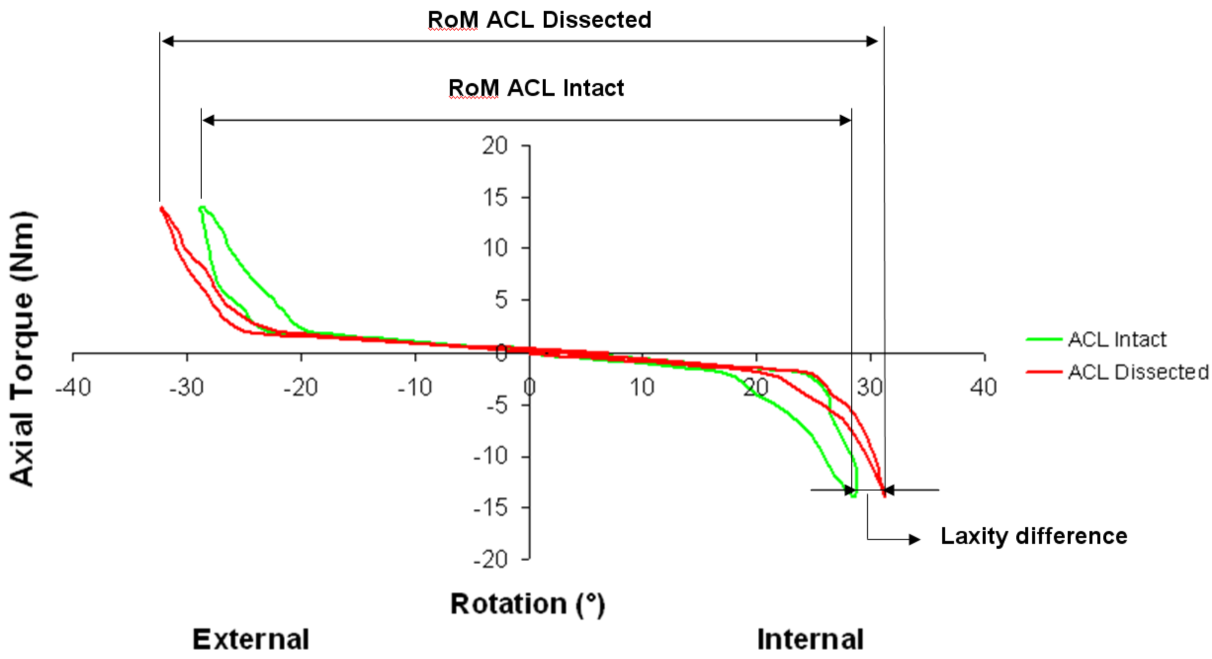

Figure 3.7: Mean hystheresis curves for the cadaveric knees in the ACL intact and ACL dissected condition

Although only three cadaveric knees were analysed and no significant differences were found, a higher RoM, addition of internal and external axial rotation, can be observed in the plotted curves for the ACL dissected knees. The mean RoM was 63.5° for the ACL dissected and 57.1° for the intact knees at the maximum torque of 14Nm.

The passive joint laxity difference - defined as the difference of laxity between the dissected and intact knees - was calculated at every applied torque. The higher differences could be observed at 4Nm with 4.2° and 4.3° for the internal and external rotation, respectively. At the maximum torque of 14Nm, the difference in the internal rotation laxity was 2.7° and 3.6° for the external.

While these results cannot be considered definitive in terms of understanding the influence of ACL in rotational stability, they are useful as a preliminary observation of the effectiveness of single plane fluoroscopy in the analysis of knee joint laxity.

3.4 Knee joint rotational device (knee rotometer)

In the following section, the design, construction and synchronization process as well as the certification of the knee joint rotational device for safe use in patients will be explained in detail.

3.4.1 Design and construction

Once the accuracy of the registration and in-vitro laxity analysis was completed, the design of the knee rotational device (knee rotometer) was the next step in the present work. The patient´s safety and comfort, measurement reliability as well as ergonomics during the measurement were the priority during the designing process.
The knee rotometer had to be compatible to single plane fluoroscopy, meaning that the laxity measurement could be performed without interrupting the positioning, adjustment and activation of the fluoroscope device.
Application of the rotational torque was another important point. Since some investigations have preferred the use of a servomotor for the controlled translation or rotation of the tibia relative to the femur [158, 159] to have a better control of the procedure and for the patient´s safety, it was decided to apply the axial torques manually. For this purpose, a torque application lever was mounted on the top of the knee rotometer. The lever can be used for internal and external rotation and can be blocked for safety purposes when no measurement is taken (Figure 3.8).

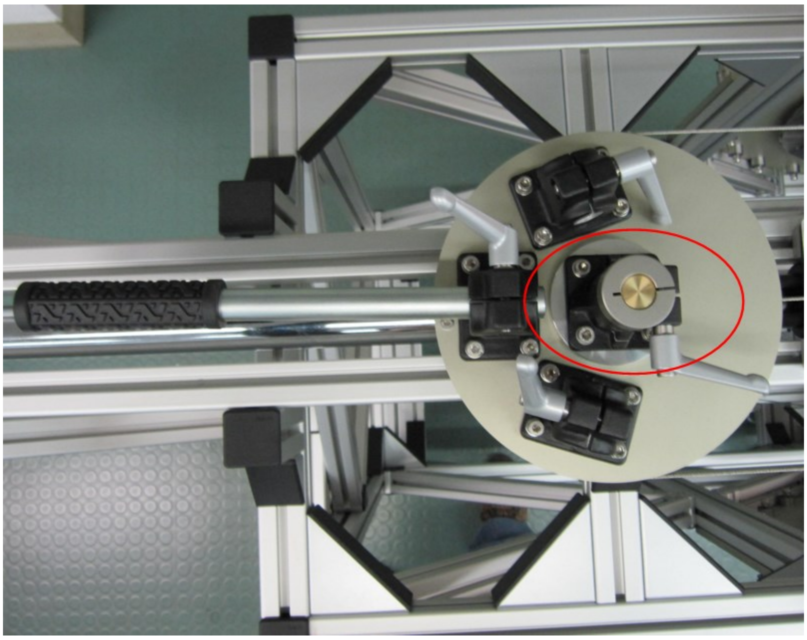

Figure 3.8: Torque application lever with blocking mechanism (red ellipse)

The applied torque is subsequently transferred through a cable-pulley mechanism to a rotating platform, where a 6 DoF force transducer is attached. The data from the force transducer is then collected at 1 kHz and transferred via a PCI NI card in a custom-made Labview (National Instruments, USA) software program. An acoustic signal is integrated in the programme to allow the examiner to identify the instant where the maximum torque is reached. A complete cycle of internal/external axial rotation can be performed and collected.

Three different patient positions can be used during laxity measurements, including the supine [128-130, 160], seated [29, 123] and prone position [126], each of which has different advantages regarding knee and hip rotation. The prone position allows easy adaptation of the knee flexion angle, while the supine position permits relaxation of the patient but can be disadvantageous for minimising hip rotation. Testing in the seated position may be more advantageous since it allows knee flexion angle adaptation, the patient´s relaxation and proper fixation of the thigh [161].

The chair of a Biodex System 3 (Biodex Medical Systems, Shirley, New York) was used since it allows a safe and comfortable patient positioning and has integrated straps for a proper fixation of the thigh.

To improve the safety during the measurements, a clamp mechanism was integrated to the device for a proper fixation and stabilisation to the Biodex chair (Figure 3.9).

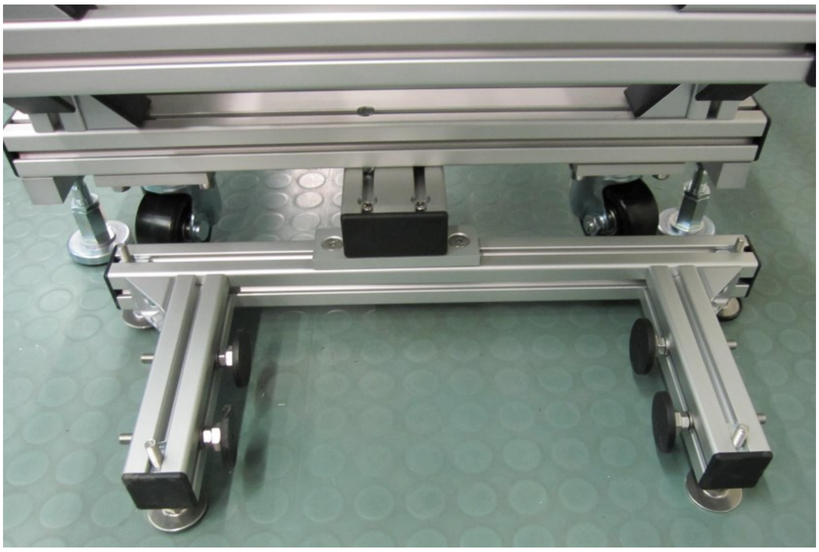

Figure 3.9: View of the clamp mechanism

In order to avoid ankle rotation, a Vacoped shoe (OPED GmbH, Germany) is used for a safe strapping of the foot, ankle and shin. It comprises a steady and comfortable orthosis that allows fixation of different foot shapes and sizes (Figure 3.10 Left). The shoe was connected to the rotating plate fixed to the 6 DoF force transducer. Two integrated curved profiles allow for a comfortable adjusting of the knee flexion angle. Measurements from full extension until 90° flexion in steps of 15° can be achieved. Lateral metallic bolts can be inserted under the profiles for a fixation of the adjusted position (Figure 3.10 Right).

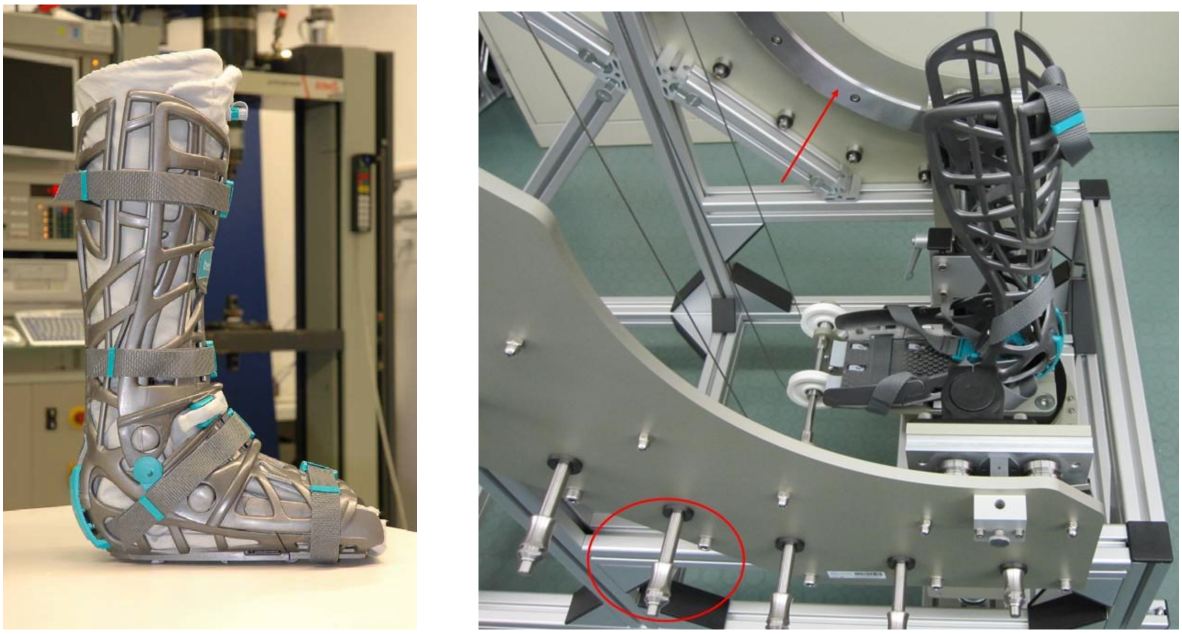

Figure 3.10: Vacoped shoe and curved profiles for adjustment of the flexion angle, left and right respectively

To allow the adjustment of the device to different shank lengths, a position bar was integrated to change the height of the rotation plate, this adjustment is performed at 90° of knee flexion. To guarantee a proper positioning and a comfortable flexion of the knee, the “centre” of the knee joint must match the centre of the curved profiles. To check this, a small lamp is integrated to the device (Figure 3.11 Left, adjustment of the shank length and lamp identified in the red and blue circles respectively).

After positioning and fixation of the subject, the fluoroscope can be positioned with the image intensifier coming laterally over the curved profiles (Figure 3.11 Right).

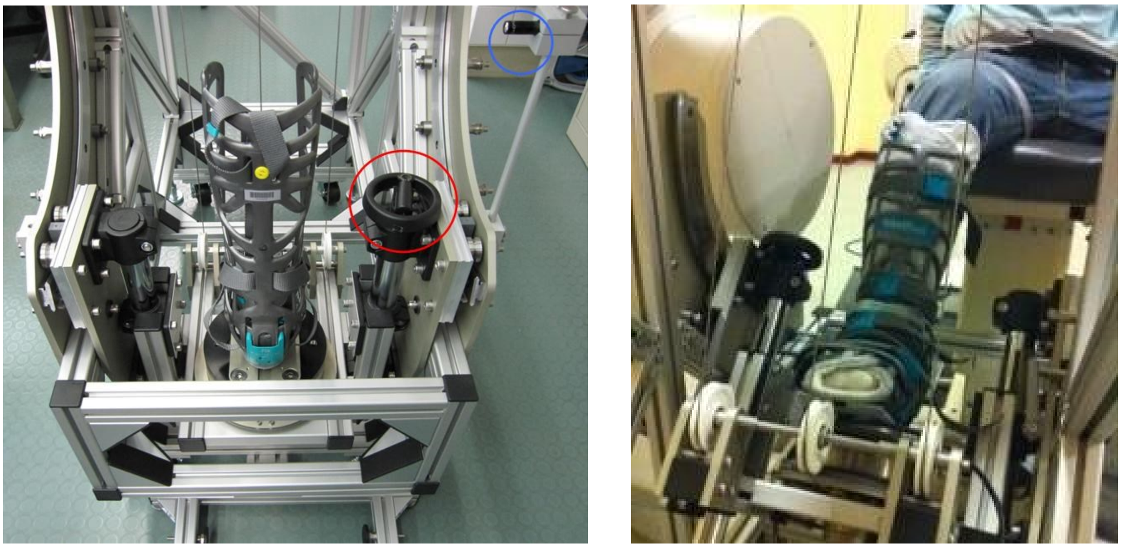

Figure 3.11:Adjustment of the shank length and view of the rotometer set-up with the image intensifier and positioned shank, left and right respectively

3.4.2 Synchronisation of the device

To synchronise the manually applied torque with the fluoroscopic images, a scattered radiation sensor (Silicon Sensor International AG; delay 50ns) was positioned on the image intensifier. The transistor-transistor logic (TTL) signal produced by the sensor can be continually transferred via a PCI NI card and recorded in the same Labview program for the force transducer, whereby the data can subsequently be aligned during data post-processing.

3.4.3 Certification of the device

According to German legislation, a clinical measurement device has to be certified according to the “Medizinproduktgesetz” (Medical Product Law). The developed knee rotometer was certified according to DIN EN 60601-1:2007 and the guidelines 93/42/EWG. A failure mode and effects analysis was conducted in order to identify risks in the system and its effects, as well as measures to eliminate or at least minimize them.

Chapter 4: Accuracy and reliability of rotational laxity measurement techniques.

As described in chapter 1, non-invasive knee laxity measurements have been performed with non-invasive techniques, with the possible disadvantage of misleading results due to over-estimated laxity values.

Through quantifying and comparing joint rotation *in vivo* using a surface mounted marker (SMM)-based (non-invasive) and single plane fluoroscopy (invasive) - together with the accuracy of the single plane fluoroscopy technique assessed in chapter 3 - the first and second hypotheses are tested within this study, which state that passive tibio-femoral rotational laxity can be quantified in a standardised and objective manner in vivo using single plane fluoroscopy and that knee joint flexion has an influence on rotational laxity, respectively.

4.1 Methods

In the following section, the complete process of subjects recruitment, invasive and non-invasive data acquisition procedure and data analysis will be explained in detail.

4.1.1 Subjects

Four subjects (aged: 34±15years, BMI: 24±3, ♂: 3, ♀: 1) with unilateral ACL rupture were included in this study and underwent CT scanning (Siemens Sensation 64, 512 x 512 image matrix, in plane resolution 0.4 x 0.4mm, slice thickness 1mm). Overall, five knees - including one healthy contralateral limb - were measured preoperatively. All testing of subjects involved within this project were performed in accordance with the Declaration of Helsinki. The study was approved by the local ethics committee and all subjects provided written informed consent prior to participation (Approval Number: EA1/167/08).

4.1.2 Experimental set-up

The test subjects were position in the knee rotometer described in chapter 3. During each measurement, the subject was positioned in a comfortable, steady chair (Biodex System 4, USA) with their foot and shank fixed within the Vacoped boot. The subject was subsequently seated such that the centre of the knee joint was coincident with the centre of the fluoroscope image intensifier. Throughout the measurements, the thigh and waist were both firmly strapped to the chair to minimise movement of the femur and pelvis.

4.1.3 Surface Mounted Marker assessment and quantification of tibio-femoral kinematics

Relative tibio-femoral rotation was assessed in a non-invasive manner using a six-camera infra-red optical motion capture system (Vicon, Oxford Metrics Inc., UK). A set of fifteen reflective markers was attached to the Vacoped boot and eight markers were attached to the subject's thigh (Figure 4.1), which were recorded at 120 Hz throughout the measurements.

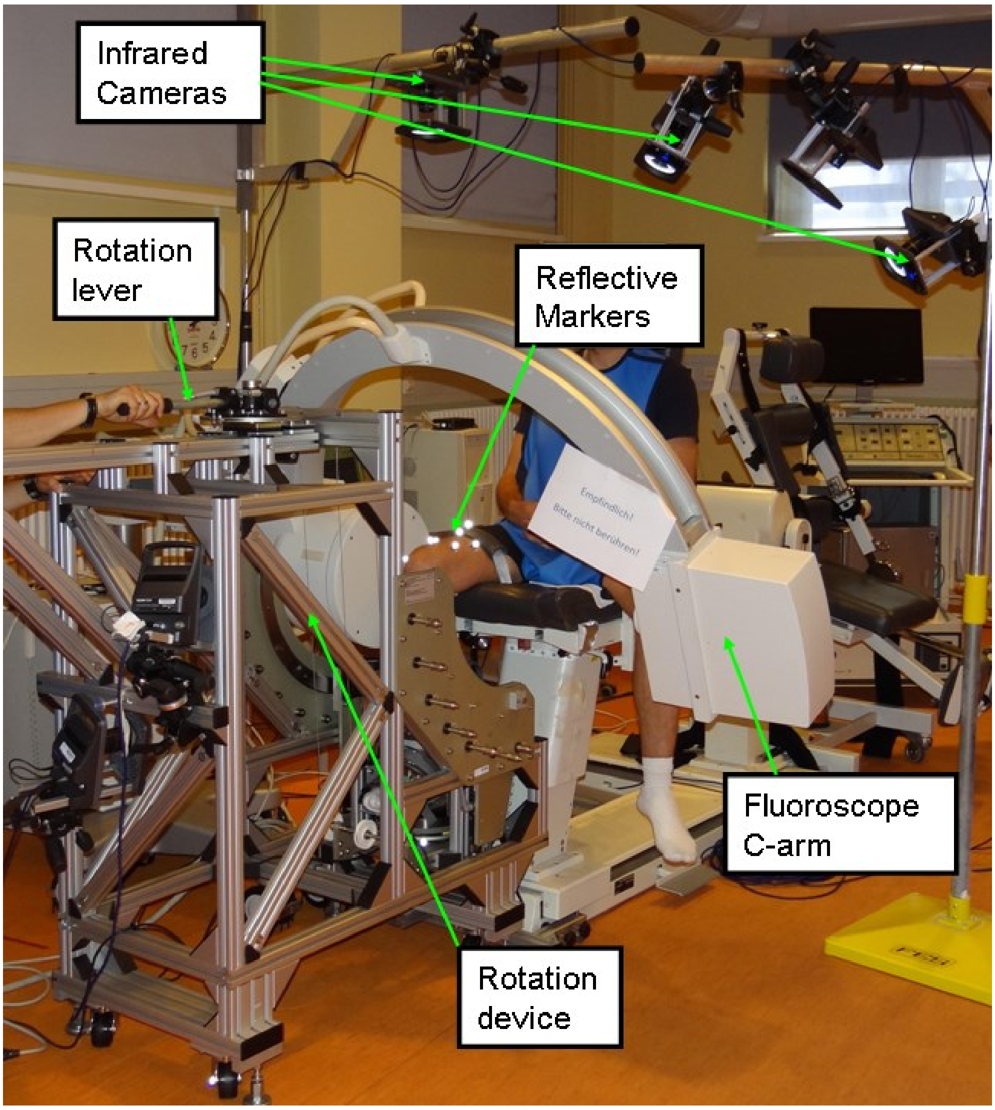

Figure 4.1: Measurement set-up including the knee rotometer, shown together with motion capture cameras and the fluoroscope for non-invasive and fluoroscopic assessment of relative tibio-femoral rotation respectively

Functional knee axes of rotation were identified from the knee movements using the Symmetrical Axis of Rotation Assessment (SARA) [162]. This assessment automatically identified the rotational component of the knee motion as the predominant element of the entire knee kinematics and computed a representation of the axis of rotation in a local coordinate system for each segment (one for the femur and one for the tibia). Here, the motion of each axis is known to be consistent with the motion of the respective segment [163] and thus provides a reference for evaluating the relative segment rotation.

4.1.4 Testing procedure

Two investigators - without a change of procedural roles - performed all measurements. Prior to all measurements, the torques to be applied were determined for each patient in a gentle test-run determining the torque that could be applied - both internally and externally - without causing pain, as well as the examiner's sense of end feel [164]. These torque values were subsequently set as the audible limit to prevent an over-rotation of the knee joint during testing. Subjects were instructed to relax their leg muscles to allow the examiner to move the leg passively, without resistance due to muscular activation. Here, any muscular activity immediately became apparent in the torque curves, where the smooth torque curves suddenly became unsteady, together with greatly increased torque values – a condition that then returned to the more normal smooth situation once the activity ceased – whereupon the trial was disregarded.

Beginning slightly externally rotated (generally the comfortable resting position of the shank), a measurement comprised a complete cycle of internal rotation up to the individually-defined end feel torques, followed by external rotation of the tibia and returning to finish with a slight internal rotation. Measurements (performed at a mean angular velocity of 3.3°/sec; SD 1.3°) were taken at 0°, 30°, 60° and 90° of knee flexion and repeated three times at each flexion angle. All trials were subsequently normalised into cycles to allow extraction of one hundred and one discrete points according to 0-100% (for the complete testing cycle) at intervals of 1%. For each patient, the joint rotation according to the non-invasive SMM assessment was compared against the rotation results of the fluoroscopic analysis, which was performed simultaneously (as described below).

4.1.5 Fluoroscopic analysis and quantification of skeletal tibio-femoral rotation

A C-arm fluoroscope (Pulsera BV, Philips) was positioned around the knee with the centre of the knee located beside the focal centre of the image intensifier. Prior to each measurement, the fluoroscopic system was calibrated with the procedure described in chapter 3. Fluoroscopic images of the tibio-femoral joint were subsequently collected throughout the joint stability measurements at a frequency of 3Hz. The total effective radiation dosage for each subject - calculated using the dose area product extracted from the fluoroscope system after each measurement - ranged from 0.002 to 0.0075 mSv. Use of X-rays (CT and Fluoroscopy) on the subjects was approved by the Bundesamt für Strahlungsschutz (Approval Number: Z5-22462/2-2010-003).

The radiation sensor (described in chapter 3) was used to synchronise the applied torque with the motion capture data and the fluoroscopic images. The TTL signal produced by the sensor was continually transferred via a PCI NI card and recorded in both the motion capture software (Vicon Nexus) and the force acquisition Labview program, before finally being aligned during post-processing of the image data.

3D bone models of each individual's tibia and femur - reconstructed using the CT datasets of each patient using the Amira software suite (Amira, Visage Imaging, Berlin, Germany) - were registered to the fluoroscopic images with the procedure described in chapter 3 of this manuscript.

4.1.6 Data analysis

In this study, fluoroscopic analysis was considered the gold standard method and provided the reference tibio-femoral rotation, with reported tibio-femoral rotational errors of approximately 0.5° according to the slow testing speeds used in this study [146].

Bland and Altman plots were created using the fluoroscopic data as the known gold standard in order to assess the agreement between the two measurement approaches. The use of this method is based on the point that any two methods designed to measure the same parameters should have a good correlation. A high correlation for any two methods could just be in itself a sign that a wide sample has been chosen but not necessarily imply that there is a good agreement between two methods, therefore is a proper way to compare a measurement technique with a reference or gold standard [165, 166]. For the construction of the Bland and Altman plot in this study, the rotation values from the fluoroscopic technique is represented in the X-axis as the reference and the difference between the values of each method in the Y-axis. Limits of agreement are determined in order to identify how far apart the measurements by 2 methods are likely to be between most individuals. Commonly, 95% limits of agreement are computed by (mean of the differences)±1.96(standard deviation of the differences) [167].

The RMS error over the entire cycle of the SMM vs. the fluoroscopic assessment was also calculated for n=5 knee examinations to determine the accuracy of the SMM analysis. Linear regression analysis was performed to determine the correlation between the SMM and the fluoroscopic assessment of i/e rotation at each knee flexion angle. The equations from the linear regression analyses were then used to correct the non-invasive measurements. Here, general correction equations that considered the mean internal and external rotations of all the tested knees were established. The rotation values of the SMM assessments were subsequently compared for accuracy against the values of the fluoroscopic assessments after application of the correction equations. Furthermore, Bland and Altman plots were created using the corrected data to confirm that any bias had been removed, as well as establishing the limits of agreement after correction.

Intra-tester reliability was assessed using the intra-class correlation coefficient (ICC) (3,1) for both invasive and non-invasive methods.

All statistical analyses were conducted using SPSS Statistics 18 (IBM SPSS Statistics, USA), and the statistics Toolbox within the Matlab software suite (version R2009b, The Math Works, MA, USA).

4.2 Results

4.2.1 Internal and external knee joint rotation

Non-invasive SMM assessment over-estimated the passive tibio-femoral rotation at all angles, with the lowest over-estimation at 90° of knee flexion (Table 4.1).

Knee	0° Flexion Angle					
	Internal$_{max}$			External$_{max}$		
	M [Nm]	R_F [°]	R_{SMM} [°]	M [Nm]	R_F [°]	R_{SMM} [°]
1	-9.6	12.1	23.2	4.9	-9.8	-25.2
2	-7.7	8.0	25.9	4.4	-6.7	-28.0
3	-3.0	8.2	25.6	2.8	-5.1	-31.0
4	-3.9	9.1	26.1	4.3	-10.3	-21.6
5	-4.0	12.3	20.0	3.4	-9.9	-25.3
Mean	**-5.6**	**9.9**	**24.2**	**4.0**	**-8.3**	**-26.2**
SD	**2.8**	**2.1**	**2.6**	**0.8**	**2.3**	**3.5**
Knee	**30° Flexion Angle**					
	Internal$_{max}$			External$_{max}$		
	M [Nm]	R_F [°]	R_{SMM} [°]	M [Nm]	R_F [°]	R_{SMM} [°]
1	-10.6	18.5	23.8	5.8	-15.9	-25.9
2	-7.8	13.8	27.0	5.3	-13.1	-27.9
3	-4.9	17.6	28.4	3.2	-10.7	-26.8
4	-2.9	13.2	23.3	6.6	-14.1	-21.6
5	-5.7	16.0	20.2	3.8	-13.2	-24.2
Mean	**-6.4**	**15.8**	**24.5**	**4.9**	**-13.4**	**-25.3**
SD	**2.9**	**2.3**	**3.3**	**1.4**	**1.9**	**2.5**
Knee	**60° Flexion Angle**					
	Internal$_{max}$			External$_{max}$		
	M [Nm]	R_F [°]	R_{SMM} [°]	M [Nm]	R_F [°]	R_{SMM} [°]
1	-10.7	15.2	20.8	5.2	-15.5	-27.7
2	-9.9	15.6	26.2	4.7	-15.4	-29.6
3	-7.1	20.3	28.3	4.3	-15.7	-28.7
4	-3.4	15.9	26.0	5.2	-16.4	-18.0
5	-4.8	15.3	20.1	3.5	-14.0	-26.3
Mean	**-7.2**	**16.5**	**24.3**	**4.6**	**-15.4**	**-26.1**
SD	**3.2**	**2.2**	**3.6**	**0.7**	**0.9**	**4.6**
Knee	**90° Flexion Angle**					
	Internal$_{max}$			External$_{max}$		
	M [Nm]	R_F [°]	R_{SMM} [°]	M [Nm]	R_F [°]	R_{SMM} [°]
1	-10.7	17.5	21.9	4.2	-18.7	-27.7
2	-10.9	13.7	26.7	6.0	-13.5	-27.2
3	-6.7	17.4	28.1	3.1	-15.3	-27.5
4	-3.1	20.4	23.0	4.5	-20.3	-21.3
5	-4.2	13.5	20.6	3.1	-13.7	-25.7
Mean	**-7.1**	**16.5**	**24.1**	**4.2**	**-16.3**	**-25.9**
SD	**3.6**	**2.9**	**3.2**	**1.2**	**3.0**	**2.6**

Table 4.1: Mean tibio-femoral rotation (3 trials) measured at the maximum torque; M, for each knee flexion angle and both measurement techniques. Grey cells indicate the healthy knee

At this angle, peak SMM errors for internal and external rotation were 46% and 59%, respectively. When assessed fluoroscopically, larger i/e rotation angles were observed at increased knee flexion angles. By contrast, only small differences were observed in i/e rotation angles at different knee flexion angles when examined non-invasively, whereby higher external rotation angles were observed compared to internal ones (Table 4.1).

At 90° knee flexion, the total range of i/e passive knee joint rotation was 32.8° for fluoroscopy and 50° using SMMs, while similar values were observed at 60° joint flexion (Table 4.1).

4.2.2 Correlation between fluoroscopic and SMM and reliability

Higher flexion angles resulted in greater correlations between the two measurement systems, with the best correlation of R=0.99 at 90° during external rotation (Figure 4.2).

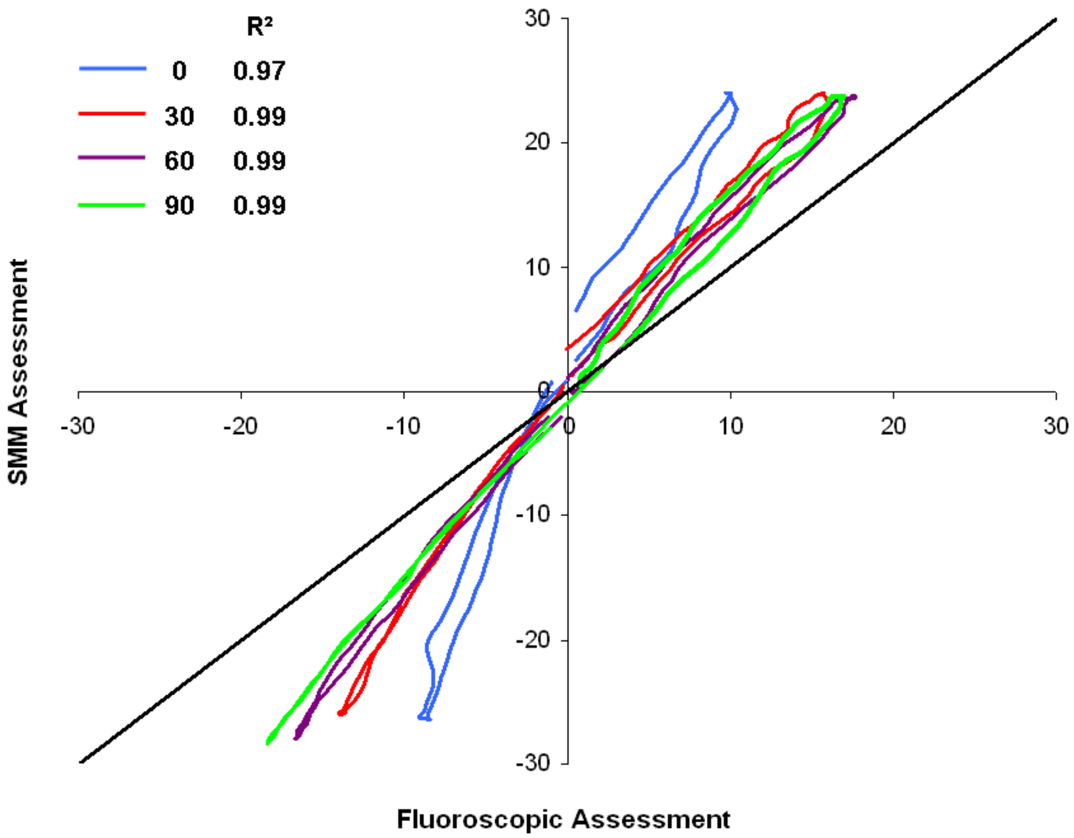

Figure 4.2: Correlation of absolute tibio-femoral rotation in the knee joint measured with fluoroscopy and SMM motion capture system at four different flexion angles

The lowest yet still excellent correlation was observed at 0° flexion angle during external rotation (R=0.97). For internal rotation, similar correlation values were determined. However, a proportional bias was apparent between the SMM and the fluoroscopic assessment with increasing joint rotation, when observed using the Bland and Altman representation (Figure 4.3).

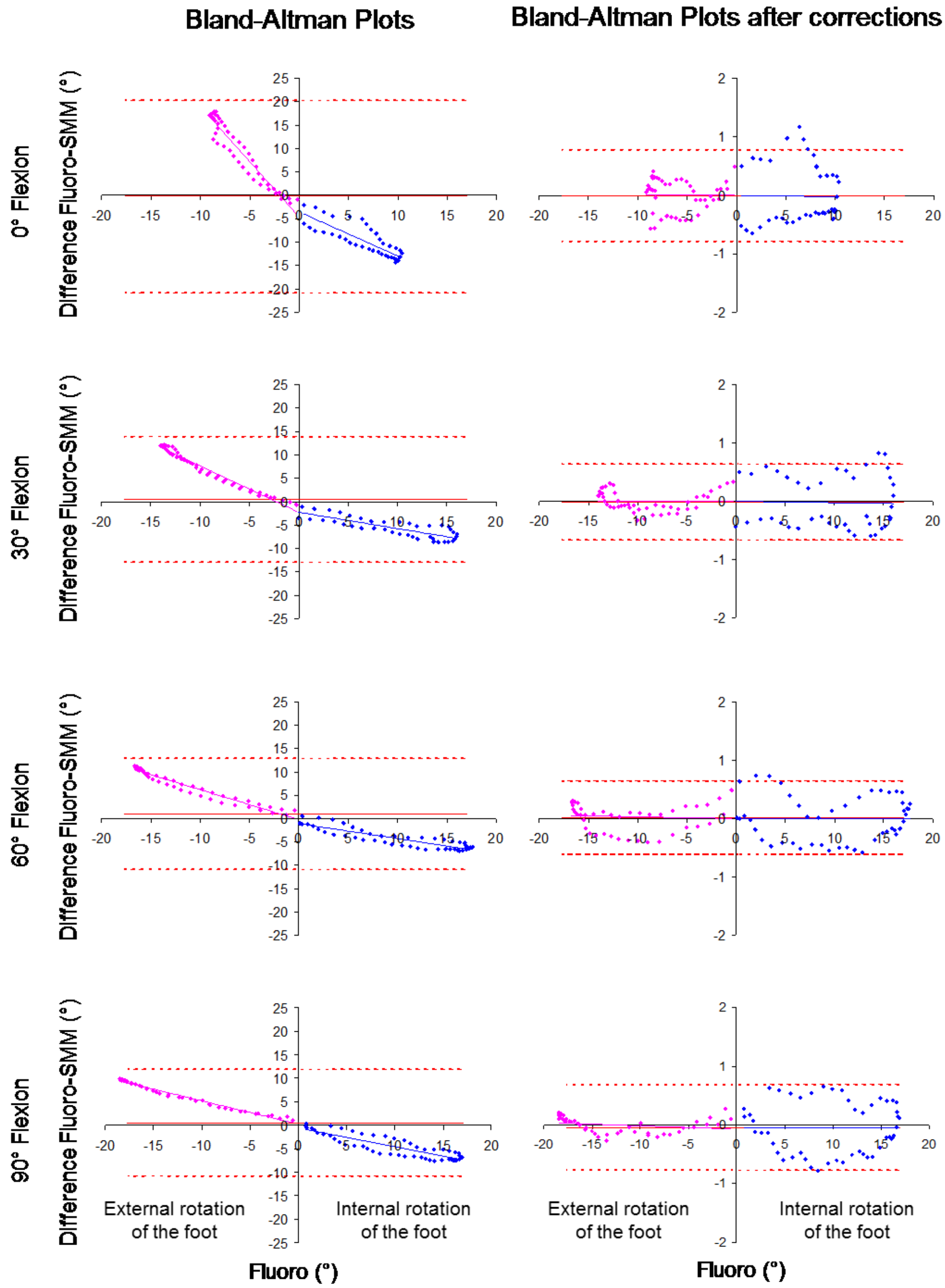

Figure 4.3: Bland and Altman plots [165] show the agreement between the SMM and the fluoroscopic measurement approaches, but using the fluoroscopic data as the known gold standard, rather than the mean of the two measurement techniques

In the test-retest assessment of joint laxity, the intra-class correlations for both the fluoroscopic analysis and the SMM assessment showed excellent reliability at every joint flexion angle (Table 4.2).

Flexion angle (°)	ICC (3,1) SMM	ICC (3,1) Fluoro
0	0.988	0.991
30	0.992	0.967
60	0.994	0.986
90	0.987	0.975

Table 4.2: Reliability of tibio-femoral rotation for both non-invasive SMM and fluoroscopic (Fluoro) assessments with measurements repeated after an interval of three months.

4.2.3 Accuracy of non-invasive knee joint rotation assessment

With a mean RMS error (estimated from n=5 knees) of 9.6°, the difference between fluoroscopy and motion capture was highest at 0° knee flexion, whereas the error decreased with increasing flexion angle, and reached a mean of 5.7° at 90° knee flexion (Table 4.3).

The application of correction equations (shown in Table 4.3) led to mean RMS errors of between 0.6° and 0.8°. Furthermore, the corrected data no longer displayed an apparent bias and the limits of agreement were now below 1° in all cases.

Flexion angle [°]	Raw mean / max RMS error; Fluoro vs. SMM [°]	Bland and Altman bias (limits of agreement) before correction [°]	Correction equations using data for all knees: *Internal rotation*	Correction equations using data for all knees: *External rotation*	Mean / Max RMS error after corrections [°]	Bland and Altman bias (limits of agreement) after correction [°]
0	9.6 / 14.2	0.2 (-20.8, 20.3)	$SMM_{corrected} = (SMM - 3.6)/1.9$	$SMM_{corrected} = (SMM - 4.6)/3.4$	0.8 / 2.3	0.0 (-0.7, 0.7)
30	6.5 / 12.1	0.5 (-12.8, 13.8)	$SMM_{corrected} = (SMM - 2.3)/1.3$	$SMM_{corrected} = (SMM - 2.3)/1.9$	0.7 / 1.7	0.0 (-0.6, 0.6)
60	6.1 / 11.3	1.0 (-10.8, 12.8)	$SMM_{corrected} = (SMM - 1.0)/1.3$	$SMM_{corrected} = (SMM - 0.2)/1.6$	0.6 / 1.5	0.0 (-0.6, 0.6)
90	5.7 / 10.0	0.5 (-10.9, 11.7)	$SMM_{corrected} = (SMM - 0.5)/1.4$	$SMM_{corrected} = (SMM - 0.5)/1.5$	0.6 / 1.6	0.0 (-0.6, 0.6)

Table 4.3: Mean RMS error between the SMM and the fluoroscopic technique, calculated over 7 knees, is shown together with the Bland and Altman bias (with limits of agreement) before application of the correction equations. The general correction equations are shown for both internal and external rotation. Furthermore, the mean inter-subject RMS error and the Bland and Altman bias (with limits of agreement) are shown after the correction equations have been applied.

4.3 Invasive vs. non-invasive rotational laxity measurements techniques

The ability to objectively measure tibio-femoral laxity is becoming increasingly important in the fields of trauma and orthopaedics, where knee joint laxity due to ACL rupture [1, 29-31] is thought to lead to degenerative changes in the joint. A reliable, non-invasive method to measure knee joint laxity could allow improved diagnosis of laxity severity in clinical routine, as well as an improved understanding of the conditions that lead to degenerative pathology within the joint. In this study, a non-invasive approach for assessing tibio-femoral rotation – a prerequisite for measuring knee joint laxity non-invasively – was assessed for the first time using fluoroscopic techniques together with an evaluation using motion capture. The presented non-invasive approach - which is similar to studies reported in the literature [18, 19] in that the foot, ankle and shank were fixed for application of an external torque - was shown to assess passive knee joint rotation with a systematic bias. These results indicate that the rotation measurements obtained using non-invasive approaches should be either corrected or critically considered and not interpreted as the actual skeletal tibio-femoral rotation.

Several external, non-invasive measurement devices to assess passive rotational knee laxity have been reported in the literature [161], using goniometers [164], electromagnetic sensors [18, 22], LED-markers [29], electronic sensors [126], an inclinometer [117] and MRI [127]. The postural conditions of the subjects also considerably varied - including supine [17-19, 34], seated [164] and prone [126] - positions of the patient, making direct comparisons difficult, particularly due to the loaded or unloaded state of the knee. In the current study, subjects were tested in a seated position rather than in a supine or prone position to ensure good control of hip flexion, as well as i/e femoral rotation and ab/adduction at the hip. An optimised fixation of the hip and thigh was pursued by strapping the thigh to the chair with ~80° hip flexion, thereby limiting undesired rotation of the limb. Although no guarantee can be provided that rotation did not occur across the other joints, the fixation at the ankle and the hip ensured that such errors remained small. However, it must be noted that possible tension in the hamstrings - especially at lower knee flexion angles - could play a role on the test outcome. On the other hand, the subject’s foot was deliberately attached to the rotation platform in a comfortable position (Figure 4.1) to enable muscle relaxation during testing. It is important to note that shank markers were applied directly onto the Vacoped boot, rather than to the skin itself, since the boot encompassed most of the tibial segment. While any effects of skin elasticity were thereby minimised, it is possible that additional motion artefact occurred due to the relative movement between the markers on the boot, the skin and the underlying bones. However, careful and tight strapping of the Vacoped boot allowed for a safe and secure ankle fixation, as well as a minimised boot-shank movement. Furthermore, this assessment is similar to - and highly representative of - many of the fixation and torque application methods used in previous studies [14-16]. Since devices for evaluating joint rotation are also not generally accessible in clinical settings, the understanding gained from this study for derivation of the true skeletal motion from simpler non-invasive approaches – as well as devices that are only able to assess maximum rotation or maximum torque levels - is paramount for improved assessment of joint laxity. It is hoped that this understanding can now lay the foundations for simpler and less expensive devices that allow access to metrics of joint laxity in clinical settings.

It was apparent that relatively different rotations were measured between the SMM and fluoroscopy approaches, suggesting that the material properties, the distribution or amount of soft tissues surrounding the joint varied between subjects, and that these sources of inter-subject variability could influence the accuracy of the rotations in an individual, even after correction. Since only as mall number of subjects were recruited within this preliminary study, it is clear that further investigation in this area is still required to fully understand the role of the soft tissues. However, since the characteristics (including end-points) of the torque-rotation curve provide an insight into the subject-specific laxity of the joint rather than informing on the agreement of the rotation measurement techniques, these points were beyond the focus of this study and should be further investigated elsewhere.

The influence of different magnitudes and rates of torque application remains unknown, which may create difficulties when comparing the outcomes of different studies, where torques have been generated manually [16, 18, 19, 25] or by powered motors [117]. Since no consensus currently exists, torques between 5 and 10 Nm have generally been investigated [161]. Due to clinical pathology and pain considerations, the maximum torque for each subject in this study was estimated individually using experimenter “end feel” and patient feedback to assess the limiting conditions, as well as ensuring the safety of the measurement by avoiding excessive rotation of the joint. Although the applied end feel torques considerably vary from subject to subject within our study (with individual values ranging from 2.9 Nm to 10.7 Nm, Table 4.1), the range of values were similar across all knee flexion angles. While this approach to limit the joint rotation could certainly have led to differing magnitudes of rotation, the relative relationship between internally (i.e. skeletal) and externally (i.e. skin) measured joint rotation should remain valid.

Once corrected, an excellent agreement between the fluoroscopic and the SMM assessment was demonstrated in this study, although the slope of the regression curves varied according to knee joint flexion angle. This could be explained by the fact that the strapping of the thigh may not have been as effective at resisting thigh rotation at 0° flexion angle as at higher knee flexion angles, where a rotation of the femur could be almost excluded. It is interesting to note that an unclear relationship between torque and rotation at 0° knee flexion existed, with a clearly stiffer joint. This relationship was far clearer at 30°, 60° and 90°, where the joint stiffness was also reduced. Here, it is quite possible that tibial rotation due to the screw-home mechanism or locking of the joint in full extension [35, 36] serve to complicate the relationship between torque and rotation. Consistent with clinical experience [14-16, 32-34, 36], the authors would thus suggest that data taken at 0° knee joint flexion should be interpreted carefully. As stated in the second hypothesis, the internal and external rotation are influenced by the knee joint flexion, showing a proportional increase with higher flexion angles in the fluoroscopic assessment, which is consistent with increasing laxity at higher flexion angles [59]. However, this behaviour was not observed in the SMM assessment, which suggests reduced sensitivity of this method (see Table 4.1).

Given the excellent agreement between the measurement approaches and the fact that a correction of the SMM rotation values can be achieved (limits of agreement of less than 1° for each flexion angle) for non-invasive evaluation of tibio-femoral rotational rotation, this approach could offer opportunities for clinical use in cases where invasive assessments are not justified; for example, in under-aged subjects. In addition, the results of the current study have important implications for understanding the outcomes of previous studies on joint laxity. Further research should focus on the investigation of the influence of subject BMI and gender to generate even more accurate correction equations that could be used as a standard in every SMM rotational laxity analysis. While evaluation at 0° knee joint flexion angle should be carefully considered due to the large error, it seems that passive knee joint laxity can be measured non-invasively using SMM analysis, albeit with a systematic over-estimation of rotation that is possible to correct.

The high reliability of the device in combination with the accuracy of single plane fluoroscopy to assess rotational laxity of the knee joint, as well as the variations in laxity with increasing flexion angle confirm the first and second hypotheses of this thesis.

The results of this work have been published in the Medical Engineering & Physics journal under the title: “Towards understanding knee joint laxity: Errors in non-invasive assessment of joint rotation can be corrected” (Appendix A).

Chapter 5: Understanding passive axial rotation and internal loading conditions in the knee joint

Studies with telemetric joint implants have shown that the internal loading conditions of the knee joint change depending on the level of activity, body weight, gait patterns and muscle activation [168-170]. It is subsequently also reasonable to expect changes in the internal loading of the knee joint during passive conditions. In this case, these changes would be related to the interaction between the internal and external passive structures of the knee joint, such as the shape of the femoral condyles, menisci, cruciate ligaments and collateral ligaments [17-20].
In order to gain an understanding of this interaction, a subject with a telemetric knee joint implant was analysed in the constructed and validated knee rotometer.

5.1 Description of the telemetric implant

The telemetric implant comprises a tibial tray with two plates separated by a small gap (Figure 5.1).

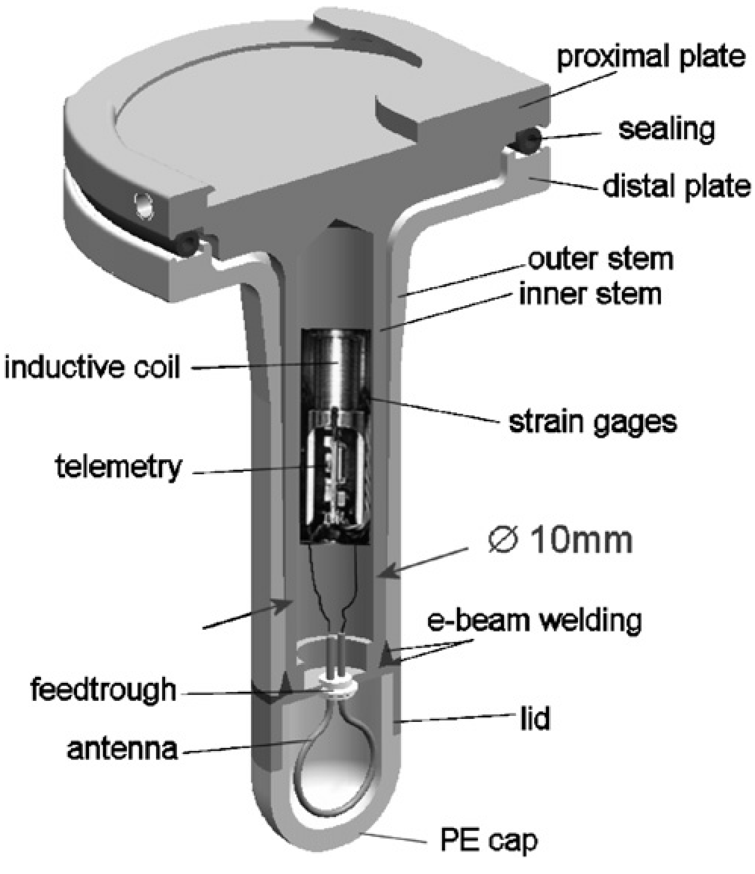

Figure 5.1: Section through the instrumented tibial tray [171]

The hollow, concentric stems of both trays are electron beam welded distally. A snaplock mechanism is used to fix the tibial insert to the proximal plate. The distal plate is cemented onto the resected tibia. The design is a cruciate substituting model (INNEX, Zimmer GmbH, Winterthur, Switzerland). Standard ultracongruent tibial inserts and the correspondent femoral component are used in combination with the instrumented baseplate. The electronics and strain gauges are inserted in the cavity of the inner stem. Six semiconductor strain gauges are used to measure the load-dependent strains. The strain gauges are connected to a custom-made telemetry unit, which is powered remotely by an external induction coil [171].

5.2 Experimental set-up

One subject with a telemetric knee joint implant (62 years, 96 Kg, 175 cm height) was positioned in the Biodex chair of the knee rotometer described in chapter 3, with his foot and shank fixed within the Vacoped boot. The subject was seated such that the centre of the knee joint was coincident with the centre of the fluoroscope image intensifier. The induction coil to power the telemetry equipment was positioned below the joint line of the knee joint in such a way that it would not cover the silhouette of the tibial component in the fluoroscopic images (Figure 5.2), which would have affected the registration process of the 3D CAD models.

Although the knee rotometer allowed for measurements at full knee joint extension, the subject had difficulties in reaching full extension of the knee joint while in a sitting position. Subsequently, it was decided to conduct the measurements at 30, 60 and 90 degrees of knee joint flexion.

The test subject was instructed to relax his leg muscle throughout the measurements, while the thigh and waist were also both strapped firmly to the chair to minimise movement of the femur and pelvis. The resulting constraints ensured that almost no global knee anterior-posterior movement - and only minimal medial-lateral translation of the entire knee joint - was possible within the knee rotometer.

An axial rotational torque of 5Nm was manually applied to the plate by rotating the application lever. A complete cycle of internal and external axial knee joint rotation was conducted. Over-rotation of the tibia was avoided by setting the acoustic feedback signal at the mentioned torque value, which indicated the limits of motion angle or torque, controlled by using a Labview (National Instruments, Austin, USA) software application.

The radiation sensor (described in chapter 3) was used to synchronised the external data from the force transducer, the fluoroscopic images and the data from the telemetric implant (Figure 5.2).

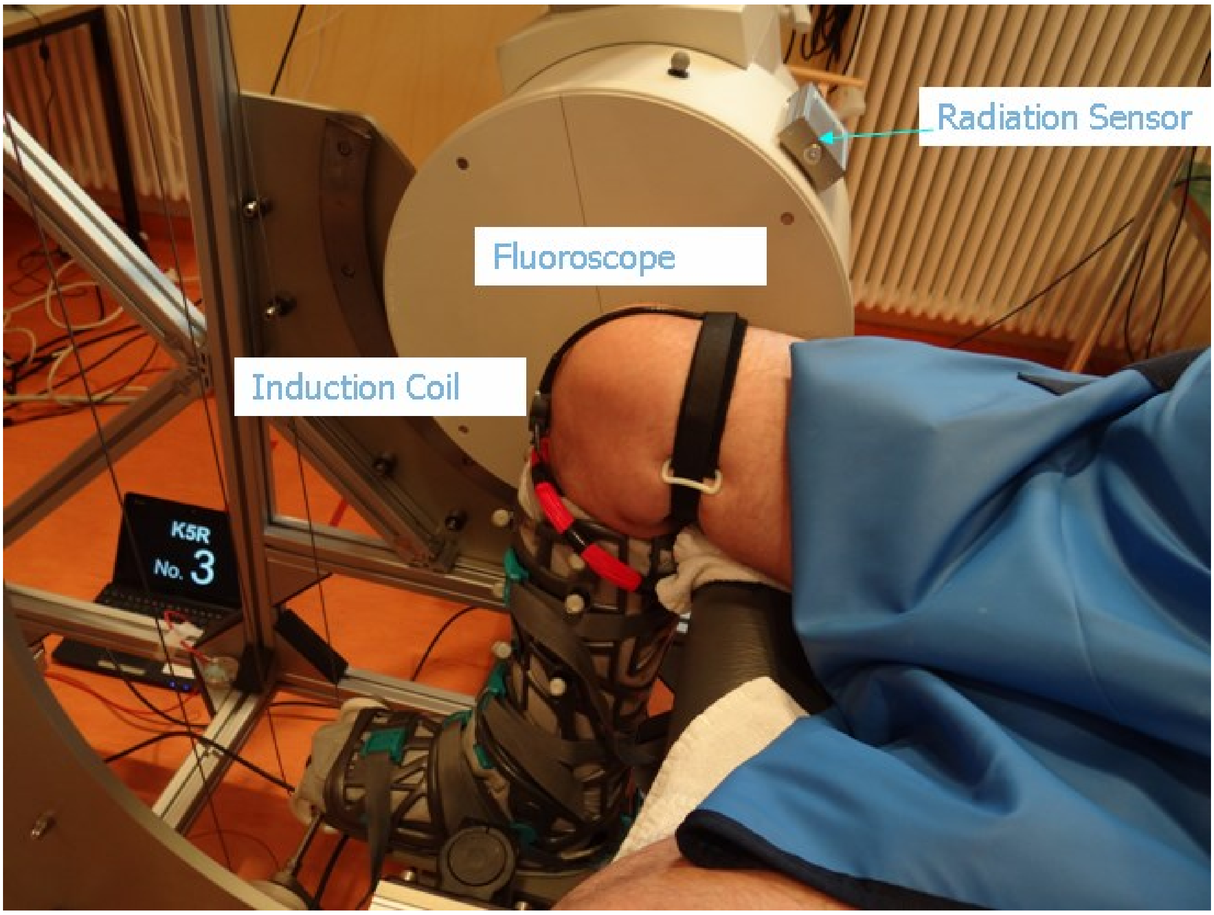

Figure 5.2: Experimental set-up

Calibration of the fluoroscopic system as well as registration of the 3D CAD models of the femoral and tibial component of the knee prosthesis to the fluoroscopic images were performed with the same procedure described in chapter 3 of this manuscript.

Two hystheresis curves for every analysed knee joint flexion angle were constructed from the collected data: externally-applied axial torque against the calculated axial rotation from the CAD models registered to the fluoroscopic images and the internal reaction axial torque from the telemetric prosthesis against the rotation (Figures 5.3, 5.4 and 5.5).

5.3 Axial rotation and internal loading

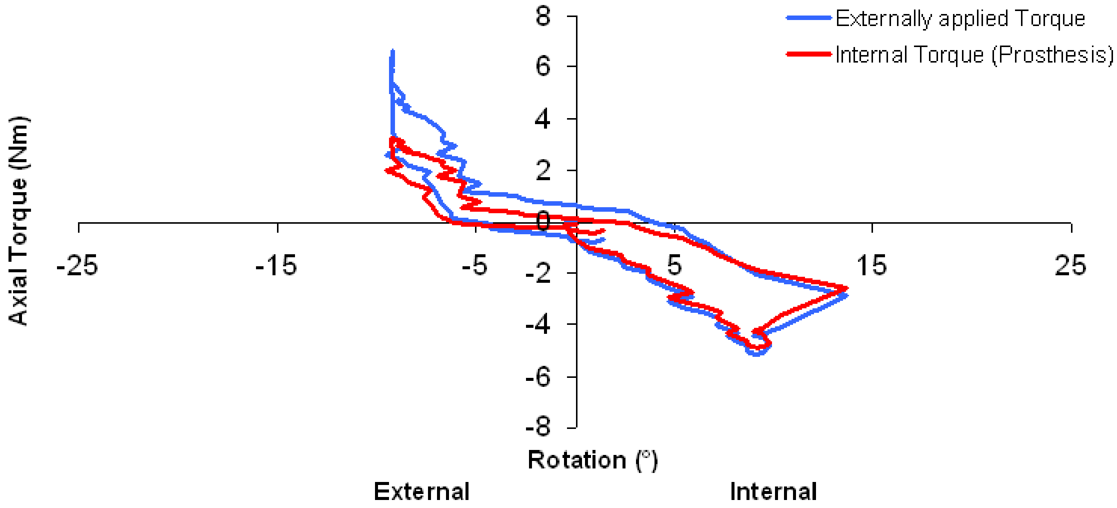

Figure 5.3: Tibiofemoral rotation vs internal and external torque at 30° of knee joint flexion

Figure 5.3 shows a clear transmission of the applied external axial torque in the internal rotation phase of the measurements, evidenced by the measured internal torque reaction values (red curve). This is probably due to the tensioning of the MCL, which plays an important role in controlling rotation and remains present after TKA at the examined flexion angle of 30° and the ultracongruent contact between femoral component and insert. On the other hand, it can be observed in the external rotation phase that approximately only 60% of the manually applied external torque was measured by the telemetric system, evidencing probably less tensioning of the ligaments and less congruency between femur component and insert during external rotation of the knee joint.

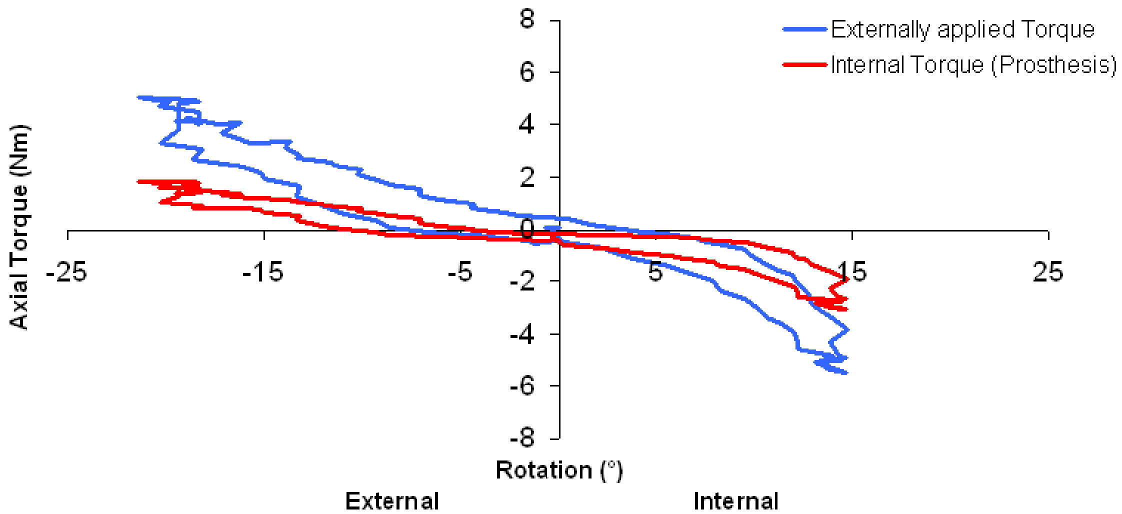

Figure 5.4: Tibiofemoral rotation vs internal and external torque at 60° of knee joint flexion

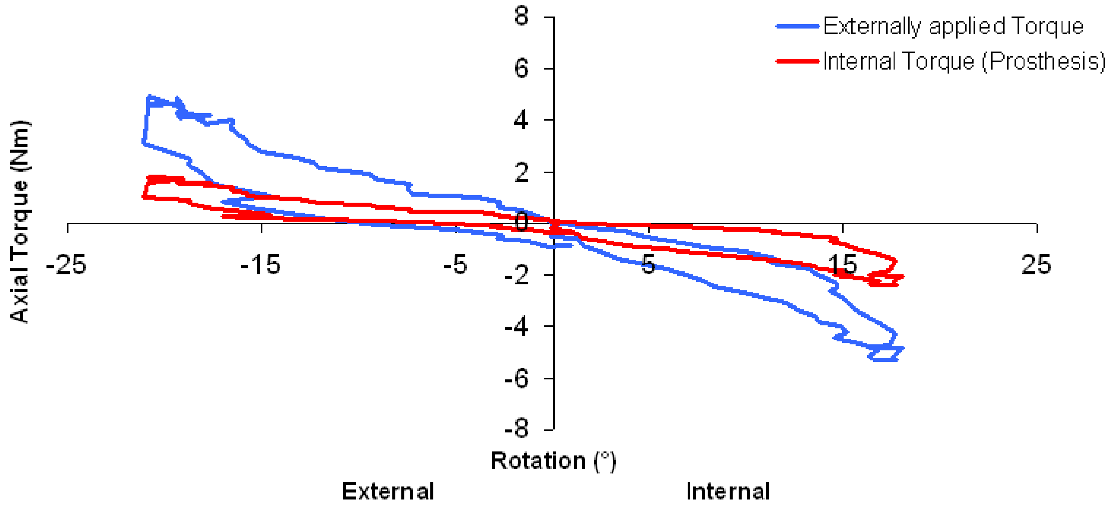

Figure 5.5: Tibiofemoral rotation vs internal and external torque at 90° of knee joint flexion

The increase of the total axial RoM (internal plus external rotation) that can be observed in the figures 5.4 and 5.5 is evidence of less tensioning of the collateral ligaments, as well as less congruency between femur component and insert at 60 and 90 degrees of knee joint flexion. Furthermore, in the internal and external rotation phases, this reduction of tension in the ligaments can be evidenced by the reduction of the measured internal reaction torque even though 5Nm was externally applied.

Figures 5.6, 5.7 and 5.8 show a comparison of the externally-applied torque (5Nm) and the measured internal torque. A reduction pattern can be observed between the different analysed flexion degrees with measured internal torque values for the internal and external rotation of 4.7 and 3.1 Nm, 3.1 and 1.6 Nm and 2.4 and 1.5 Nm for 30, 60 and 90 degrees of knee joint flexion, respectively, implying that the stabilisation due to the ligament tensioning and geometrical congruency - from the implant shape in the present case or the femur condyles shape in native knees - is dependent upon the flexion angle.

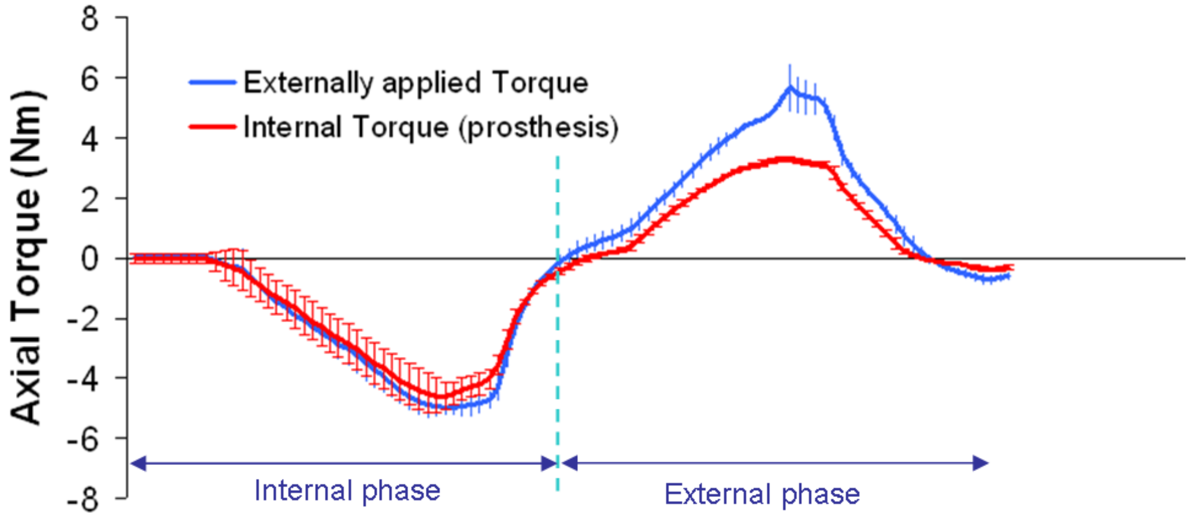

Figure 5.6: Applied torque vs. internal measured torque at 30° of knee joint flexion

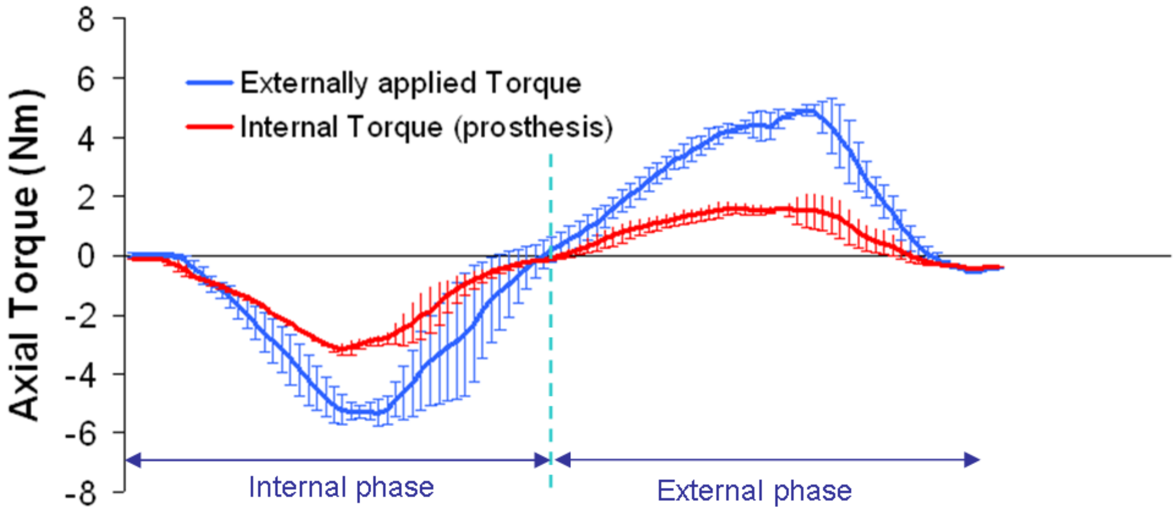

Figure 5.7: Applied torque vs. internal measured torque at 60° of knee joint flexion

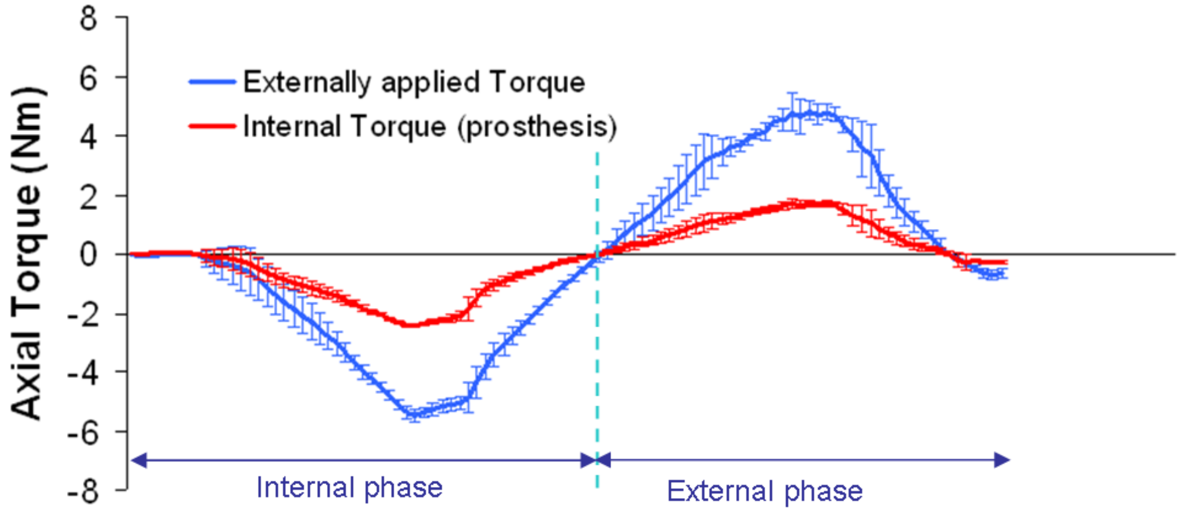

Figure 5.8: Applied torque vs. internal measured torque at 90° of knee joint flexion

Although the test subject was instructed to relax his leg muscles during the measurements, an axial force was measured by the telemetric prosthesis at every flexion angle tested, particularly in the internal rotation phase of the measurements, probably due to the unavoidable tensioning of the hamstrings muscles. An increase of the axial force was observed during the internal rotation phase, with peak values of 460 N, 312 N and 250 N measured at 30, 60 and 90 degrees, respectively (Figures 5.9, 5.10 and 5.11).

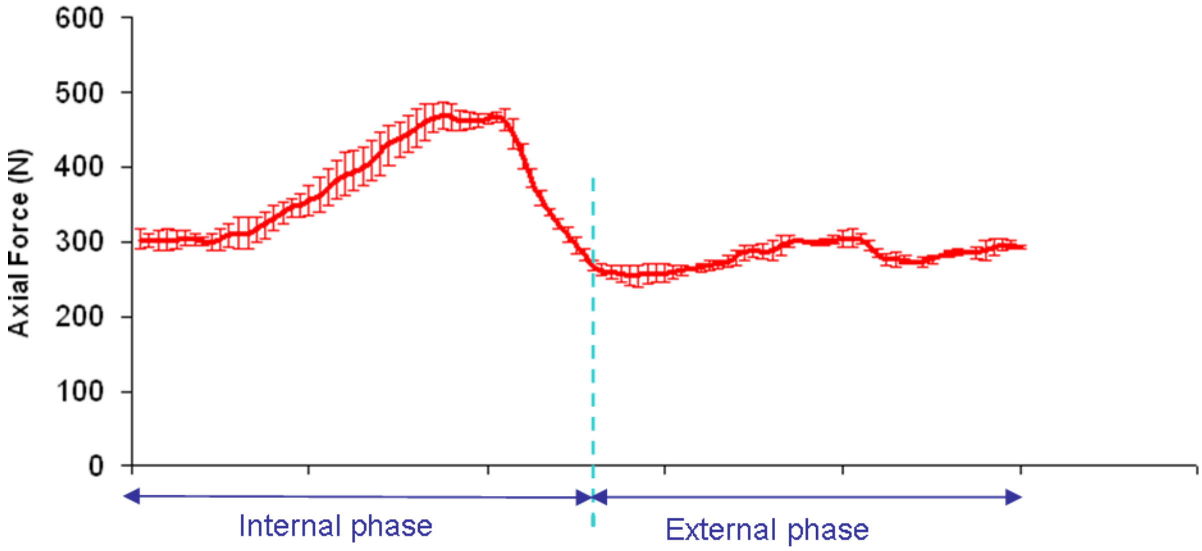

Figure 5.9: Internal Axial Force at 30° of knee joint flexion

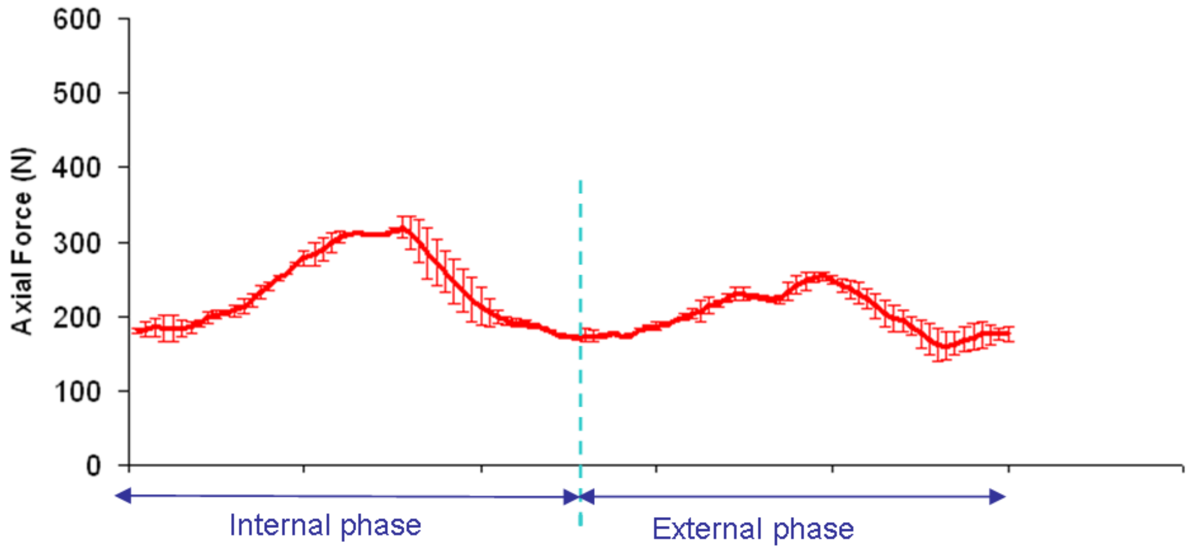

Figure 5.10: Internal Axial Force at 60° of knee joint flexion

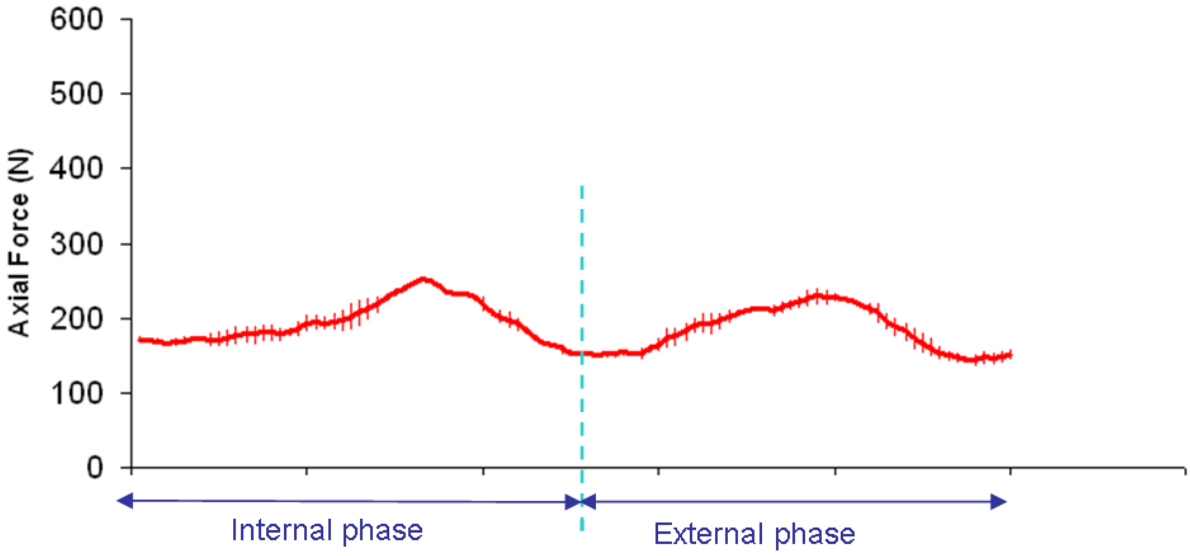

Figure 5.11:Internal Axial Force at 90° of knee joint flexion

Although only one subject with a telemetric prosthesis was analysed and the results cannot be considered as representative to the analysis of the influence of the ACL in rotational stability, the changes in the internal loading conditions observed showed an apparent influence of the knee joint flexion angle in the load distribution, which - as already mentioned - could be considered evidence of the interaction of the internal and external passive structures in the stabilisation of the knee joint. Accordingly, this information could be relevant for new conservative therapies, as well as ligament balancing and the conception of new implant designs in TKA. These findings also support the confirmation of hypothesis two in chapter 4.

Chapter 6: Influence of ACL injury and reconstruction in the passive rotational tibiofemoral stability

As mentioned in previous chapters, joint stability can be generally defined as the resistance offered by various musculoskeletal tissues that surround an articulating joint. Although a natural amount of passive joint mobility exists within healthy joints, excessive laxity is often a direct consequence of failure of one or more subsystems, particularly after traumatic injury [15]. In the knee, passive laxity is primarily governed by the ligaments, and can be measured using an external force applied to the joint during a state of muscle relaxation [16]. One of the most important ligaments for providing knee joint stability is the anterior cruciate ligament (ACL), with its primary function to stabilize against excessive tibial translation relative to the femur [7]. The ACL consists of two main fibre bundles, one anteromedial (AM) bundle and one posterolateral (PL) bundle, which behave differently throughout joint flexion and extension [38]. Apart from stabilization of tibial translation, the ACL bundles are thought to play a distinct role in controlling axial rotation, particularly internally, and hence contribute towards stabilization of the knee joint due to the positioning of their proximal and distal attachment areas and the resulting fibre bundle orientations [45].
Injuries of the ACL have a direct repercussion on the knee joint laxity and thus kinematics, resulting in an increased anterior tibial displacement and axial rotation [6]. This effect has been demonstrated in a 12 year follow-up study with a cohort of 89 patients with an untreated ACL rupture, where radiological degenerative changes were also present in 63%, and joint space narrowing in 37% of the patients [72].
Although some individuals are able to stabilize their knees after an ACL injury [33], the majority present instability, even during activities of daily living, which, combined with the risk of degenerative changes in the longer term, leaves reconstruction of the ACL as possibly the only option to restore the normal function and kinematics of the injured knee. It is known that ACL reconstruction is able to restore anterior-posterior stability [102], but the capacity to restore rotational stability has so far not been discussed [5]. It is therefore plausible that rotational instability after ACL reconstruction could be one reason for ACL reconstruction failure [172] and might also play a role in the initiation of biological and mechano-degenerative processes such as osteoarthritis (OA) [12,13]. The quest for effective reconstruction of knee rotational stability therefore represents a key challenge for surgeons [44], where an understanding of rotational stability in healthy knees, as well as after ACL reconstruction, is clearly required. Typically, rotational stability is assessed in the clinic using the pivot shift test [59], however this test lacks objectivity and is

dependent upon the examiners experience [16,17]. A range of devices for analysing rotational stability, specifically internal rotational laxity (IR), external rotational laxity (ER) and the complete axial range of motion (RoM), in an objective manner have thus been employed, including goniometers [164], electromagnetic sensors [19,20], LED-markers [29], electronic sensors [126], inclinometers [117] and MRI [24,25]. After removal of the ACL in cadaveric knees, Wang and Walker [173] found an increase in both IR and ER when applying 5 Nm axial torques. An increase of 17% in axial RoM was detected *in vitro* by Hsieh and Walker [17] after comparing intact vs ACL deficient knees also under a 5Nm axial torque application. McQuade and Nielsen [28,29] also found an increase in IR, although not significant, after an isolated cut of the ACL under application of 8.1 and 3 Nm torques, using a Genucom device and strain gauges respectively. Using a simple non-invasive measurement device and a navigation system under the application of 5, 10 and 15 Nm axial torques, Lorbach [174] also found an increase in IR, ER and RoM after complete resection of the ACL.

Regarding *in vivo* measurements, pivot shift tests have been conducted while tibio-femoral axial rotation was recorded using electromagnetic sensors [175]. An increase in internal rotational laxity was found after comparison between ACL deficient and intact knees. A similar study conducted by the group of Branch and colleagues [32] also found an increase in the internal rotational laxity in patients at risk of an ACL rupture. More recently Imbert and co-workers also found significant differences in IR, ER, and axial RoM intra-operatively after comparing ACL deficient knees with the healthy contralateral controls using a navigation system; however, the application of torque was surgeon dependent and could have influenced the results [176].

Until now, only two studies have considered a comparison in the axial rotation between ACL reconstructed and healthy knees. The first of these used a 3.0 Tesla magnetic resonance imaging (MRI) device to assess tibio-femoral rotation before and after ACL reconstruction, and observed a post-reconstruction reduction in the axial RoM [177]. However, only a small number of patients were measured and only axial rotation at 15° of knee flexion was considered. On the other hand, a retrospective study conducted by Lorbach and colleagues [125] used magnetic sensors attached to the skin to assess tibio-femoral motion, and reported no significant differences between the ACL reconstructed and healthy contra-lateral knees. These reports suggest that the outcome of ACL reconstruction and its effects on rotational stability remain controversial. One common aspect of these studies was the use of non-invasive techniques to assess the tibio-femoral rotation. Although the reliability of these non-invasive techniques has been examined [34-36], their accuracy to assess tibio-femoral rotation may be limited due to the extended periods of time required for image capture or possible soft tissue artefacts respectively [37]. Importantly, the influence of knee flexion as well as post-operative recovery on rotational laxity, which could provide an improved insight into the influence of ACL reconstruction on rotational stabilization, has not yet been analysed.

One approach that is known to allow rotation of bone segments to be determined is single plane fluoroscopy, which is an established technique to assess dynamic activities *in vivo*, and has been used in the kinematic assessment of implanted components as well as for examining the motion of skeletal structures [37-40]. A combination of this technique, together with a device for the objective and controlled rotation of the knee joint, could help towards understanding the influence of the ACL in rotational stabilization of the knee joint and at a range of knee joint flexion angles.

Hypotheses 3 and 4 - which state that a significantly higher passive rotational laxity is observed in patients after ACL trauma compared to the healthy contralateral side and that patients after ACL reconstruction show a reduction in the rotational laxity compared to the pre-operative state, whereby this reduction continued after a longer post-operative period - will be tested within this chapter.

6.1 Methods

In the following section, the complete process of subject's recruitment, experimental set-up, data acquisition and analysis as well as ACL reconstruction procedure will be explained in detail.

6.1.1 Subjects

Thirteen subjects (age: 30 ± 8 years, BMI: 25 ± 3, ♂: 9, ♀: 4) with confirmed ACL rupture and with no previous history of injuries were included in this study, in which the diagnosis was first conducted clinically and confirmed after MRI scanning. Subjects with other concomitant injuries were discarded. All the subjects underwent CT scanning (Siemens Sensation 64, 512 x 512 image matrix, in plane resolution 0.4 mm x 0.4 mm, slice thickness 1 mm) of both the ACL injured and the healthy contralateral knees, which were used as controls. All testing of subjects involved within this project were performed in accordance with the Declaration of Helsinki. The study was approved by the local ethics committee and all subjects provided written informed consent prior to participation (Approval Number: EA1/167/08).
Internal and external rotational laxity and internal stiffness (as described below) were all measured at four time points; ACL injured (approximately one to three months after injury), 3 months post-ACL-reconstruction, 12 months post-ACL-reconstruction and healthy contralateral. Details on the surgery are provided below. Four subjects did not participate in the 12 months follow-up measurement; two subjects had moved away from the area and retired their consent to participate in the study and two had suffered a re-rupture of the ACL and needed further operative reconstruction. As a consequence, results for only the 9 subjects that completed all measurements are reported in the results section.

6.1.2 Experimental set-up

The test subjects were positioned in the knee rotometer (Figure 6.1, Left), with their foot, ankle and shank strapped within the Vacoped boot (Figure 6.1, Right). Throughout the measurements, the thigh and waist were both firmly strapped to the seat to minimise movement of the femur and pelvis. The resulting constraints ensured that almost no global knee anterior-posterior movement and only minimal medial-lateral translation of the entire knee joint was possible within the knee rotometer.

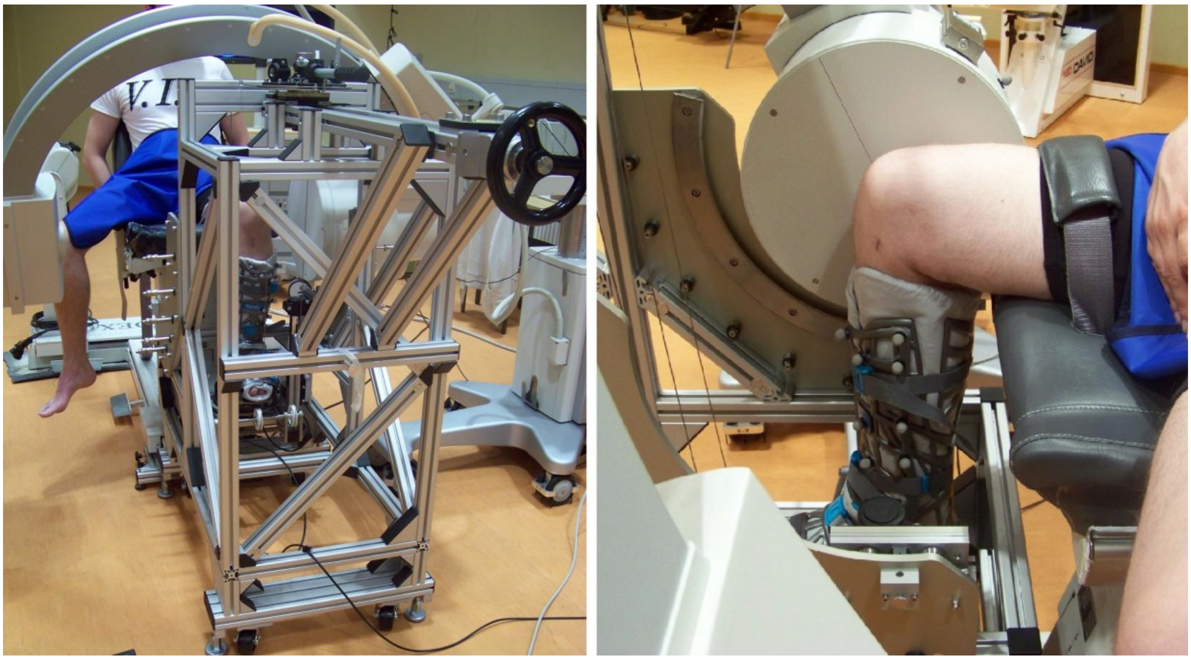

Figure 6.1: Measurement set-up showing a subject seated and positioned within the knee rotometer, together with the fluoroscopic device (Left). Patient´s shank in the Vacoped boot and knee centred in front of the image intensifier at 90° flexion (Right)

6.1.3 Evaluation of Rotational Stability

Two investigators performed all measurements using consistent procedures. While axial torque values ranging from 3 to 15 Nm, have been reported in the literature [129, 160, 178, 179], a maximum internal and external torque value of 2.5 Nm was used in this study due to its *in vivo* nature to ensure minimal risk to the ACL injured and reconstructed knees. This relatively low torque value was set as the audible threshold to prevent an over-rotation of the knee joint during testing. The subjects were instructed to relax their leg muscles to allow the examiner to manually rotate the tibia without resistance due to muscular activation – here, any muscular activity could be clearly seen in perturbations to the torque output, whereupon the cycle was re-measured. Beginning slightly externally rotated (generally the comfortable resting position of the shank), a measurement consisted of a complete cycle of internal rotation, up to the maximal 2.5 Nm torque internally, followed by external rotation of the tibia up to the same torque value externally, and returning to finish with a slight internal rotation. Measurements were performed at 30 and 90 degrees of knee flexion. The 30° measurement position was chosen since the ACL is thought to be tensioned without additional stabilization from the other ligaments in the knee joint

[7]. Testing was also performed at 90° since tension in the collateral ligaments is thought to influence the passive rotational behaviour of the knee [7]. Measurements at full extension were avoided due to the complex interaction of the screw home mechanism, locking of the joint and tension in the hamstrings, which would likely produce an unclear test outcome [7, 180]. Of the two examiners involved in the measurements, only one was responsible for manual application of the external torque, in order to ensure consistent torque application. The intra-tester reliability of this procedure has been assessed using the intra-class correlation coefficient (ICC 3,1) with values of 0.99 and 0.98 for measurements at 30° and 90° of flexion respectively [180].

6.1.4 ACL reconstruction procedure

In all patients, single bundle ACL reconstruction with autologous semitendinosus implant grafting was conducted using a hybrid technique that used an endobutton and bioresorbable interference screw in each of the tibia and femur to prevent the requirement for oversized screws as well as avoid possible bungeeing of the graft across the joint gap, while still maintaining many of the advantages of more standard fixation techniques [98]. The procedure was explained in detail in section 1.6.

All patients underwent the same rehabilitation protocol. Depending on the patient's recovery, jogging was allowed at 3 months with a return to sporting activity after 6 months [98]. As part of the standard clinical examination, passive anterior-posterior translation was also assessed using a KT-1000 arthrometer with an applied anterior tibial force of 133N.

6.1.5 Fluoroscopic analysis and quantification of skeletal tibio-femoral rotation

A C-arm fluoroscope (Pulsera BV, Philips) was positioned at the level of the knee with the centre of the knee beside the focal centre of the image intensifier. Prior to each measurement, the fluoroscopic system was calibrated with the same procedure described in chapter 3. Fluoroscopic images were collected during the complete axial rotation cycle at a frequency of 3 Hz. The total effective dosage for each measurement - calculated from the dose area product - ranged from 0.002 to 0.0075

mSv. Use of X-rays (CT and Fluoroscopy) on the subjects was approved by the Bundesamt für Strahlungsschutz (Approval Number: Z5-22462/2-2010-003).
A scattered radiation sensor (Silicon Sensor International AG; delay 50 ns) was used to synchronise the torque sensor and the fluoroscopic imaging system.
Specific 3D bone models of each subject's tibia and femur were reconstructed from the individual CT datasets using the Amira software suite (Amira, Visage Imaging, Berlin, Germany) and were subsequently registered to the fluoroscopic images to calculate the tibio-femoral rotation using the model-based RSA software (RSAcore, Leiden University Medical Center, Leiden, The Netherlands), as described in chapter 3.

6.1.6 Rotational laxity

Torque-rotation curves, constructed from the applied axial torque and the calculated axial rotation from the fluoroscopy, were created for every time point of measurement (Figure 6.2). The peak rotations at ±2.5 Nm were used as a measure of internal and external rotational laxity respectively, and therefore as a key metric for understanding joint stability. Internal rotational stiffness was determined at the steepest portion of the loaded curve during the internal rotation phase [29]. Dissipated energy was calculated as the area within the hysteresis torque-rotation curve. Side-to-side differences in these two parameters between the injured/reconstructed and the reference (pre-operative) measurement of the contralateral knees were also determined in order to acquire additional information on the changes in rotational stability that occurred over time.

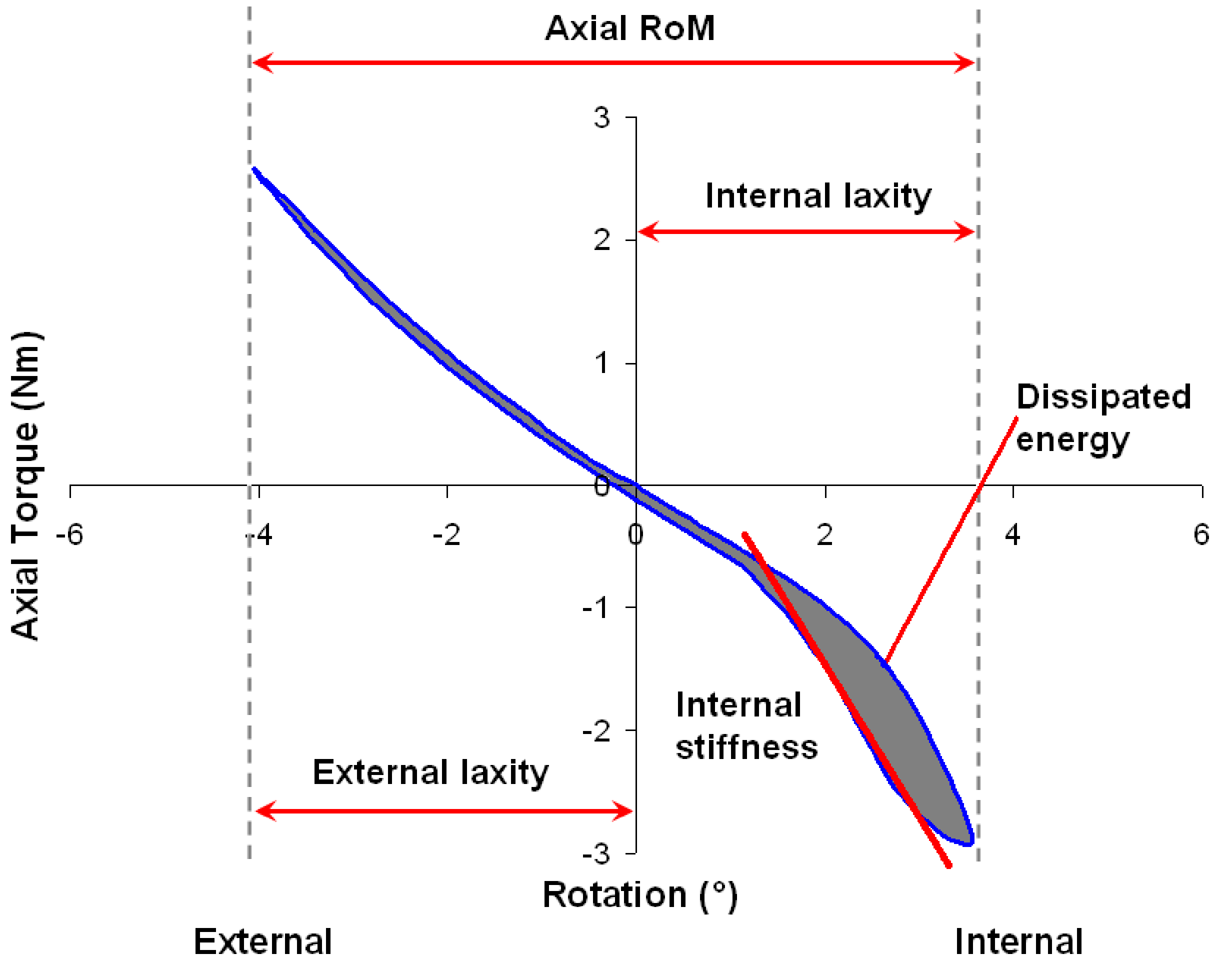

Figure 6.2: Example of the hysteresis curve observed during a complete cycle of internal and external tibio-femoral rotation, together with the determination of the stability parameters from the torque-rotation curves

To correct for the effect of each subject's natural knee rotation angle, the neutral reference rotation for each subject was determined as the average angle at which zero resistance to rotation was observed (taking rotation in both the internal and external directions into consideration; Figure 6.3). These neutral reference positions were then aligned for group-wise analyses.

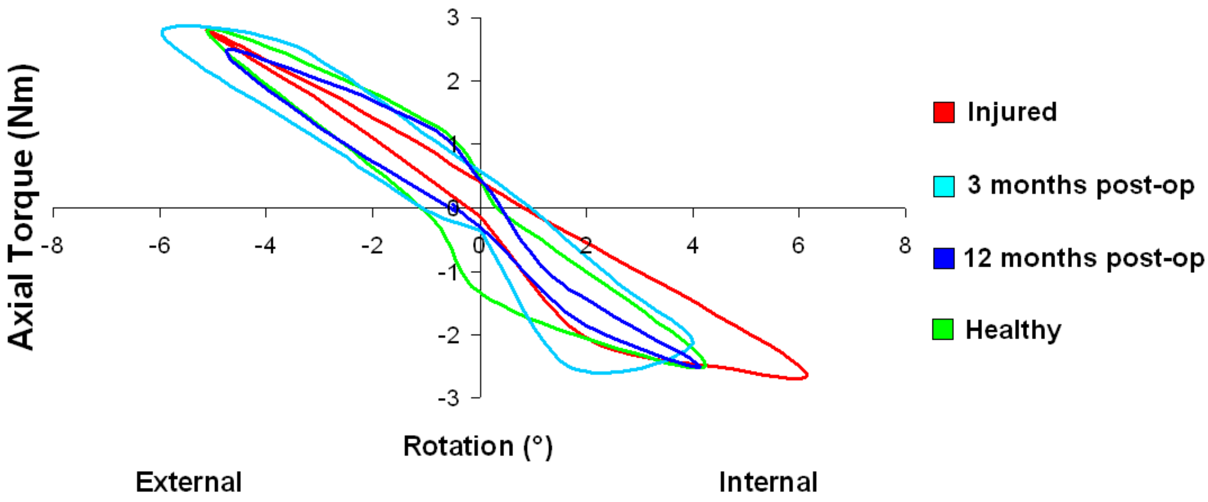

Figure 6.3: Example of the torque-rotational curves of one patient at the pre-operative (injured), 3 months postoperative and 12 months postoperative time points as well as the healthy contralateral knee (healthy)

6.1.7 Statistical analysis

The Student's T–test was used to compare the joint laxity at the three time points of the injured and reconstructed ACL knees to the healthy contra-lateral knees. A p value < 0.05 was regarded as statistically significant

6.2 Results

Each cycle of internal and external rotation showed a clear hysteresis (shown exemplary at 30° for one subject in Figure 3), with each curve crossing or at least reaching the ±2.5Nm threshold. Similar curves were observed for every test. No pain or discomfort was communicated by any subject at these torque levels.

Although high inter-subject variability was observed, significant differences were found in the side-to-side comparison of each parameter analysed for both the 3 and 12 month follow-up measurements (Figure 4).

Significant differences in the internal rotational laxity were found between the ACL injured and the healthy contra-lateral knees with values (mean±SD) of 8.7°±4.0° and 3.7°±1.4° ($P=0.003$) at 30° of flexion and 8.6°±2.5° and 4.3°±1.9° ($P=0.001$) at 90° for the ACL injured and healthy knees respectively.

For external rotational laxity, the values were 11.6°±4.5° and 8.1°±3.9° ($P=0.004$) at 30° and 15.2°±5.0° and 9.9°±2.9° ($P=0.005$) at 90° for the ACL injured and healthy knees respectively (Figure 6.4). After three months post-operation, a reduction of the internal rotational laxity but an increase in the external rotational laxity was observed post ACL reconstruction at both flexion angles.

Nevertheless, both internal ($P=0.005$, $P=0.006$) and external ($P=0.001$, $P=0.004$) laxity remained significantly greater than the healthy contra-lateral knees at 30° and 90° of joint flexion respectively.

After twelve months, an improvement of the rotational stability was achieved with a clear reduction of the internal and external rotational laxity to levels comparable with those of the healthy contra-lateral side.

Comparing both analysed flexion angles, higher values of both internal and external rotational laxity and therefore also total axial RoM were observed at 90° of knee flexion, showing a higher passive rotational instability at higher flexion.

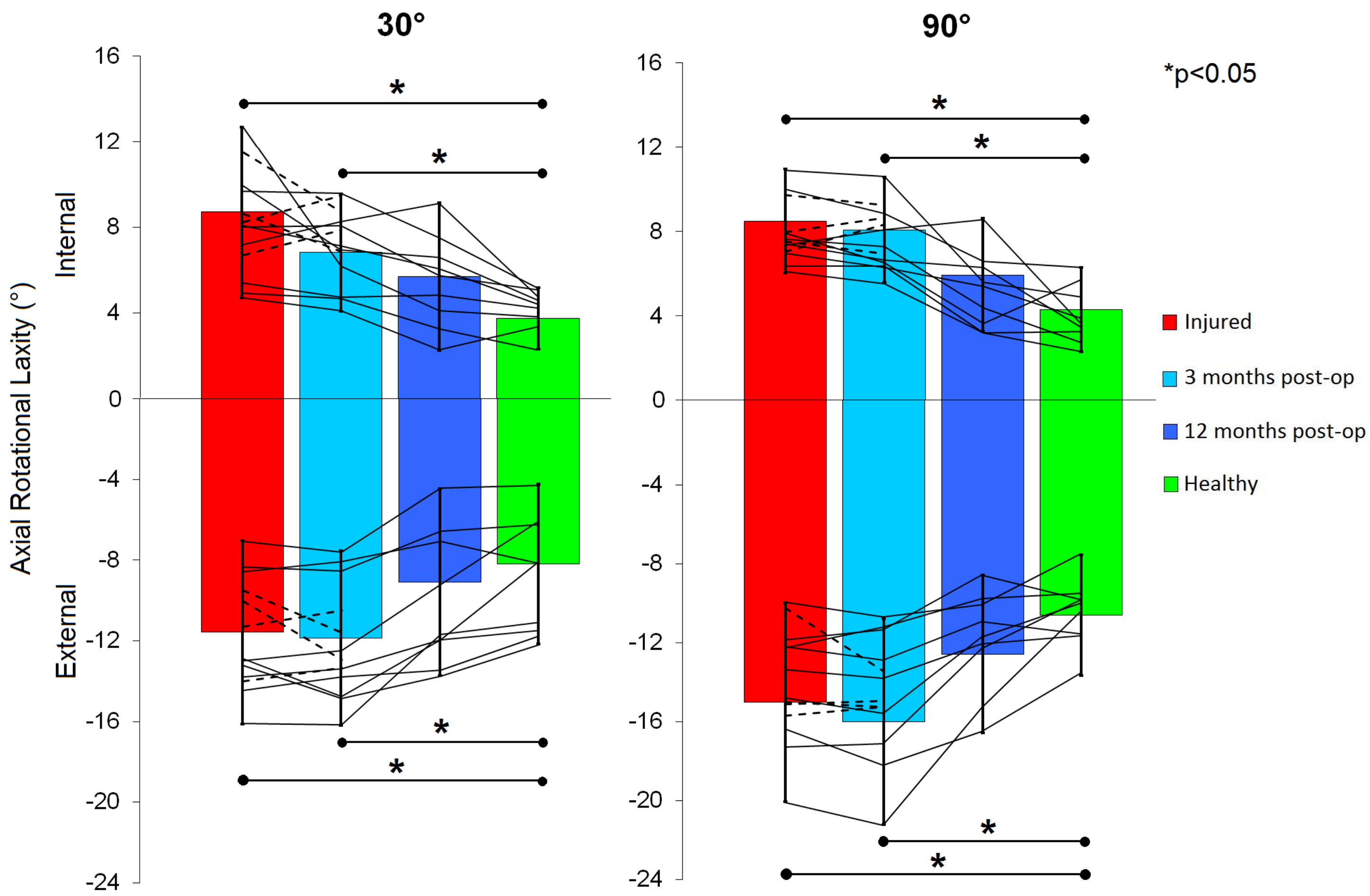

Figure 6.4: Internal and external rotational laxity of the analysed subjects at all time points compared against the healthy contralateral knee. Dashed lines indicate the four subjects that did not complete the 12 months follow up analysis (not included in the statistical analysis)

Considering the internal rotational stiffness (Figure 6.5), no significant differences were found in the amount of side-to-side differences in the preoperative (injured) and 3 month postoperative values at either 30° or 90° flexion. However, these differences became significant at the 12 month post-operative time point (p = 0.029 and p = 0.023) at 30° and 90° respectively, showing a progressive decrease in side-to-side differences in the joint stiffness postoperatively.

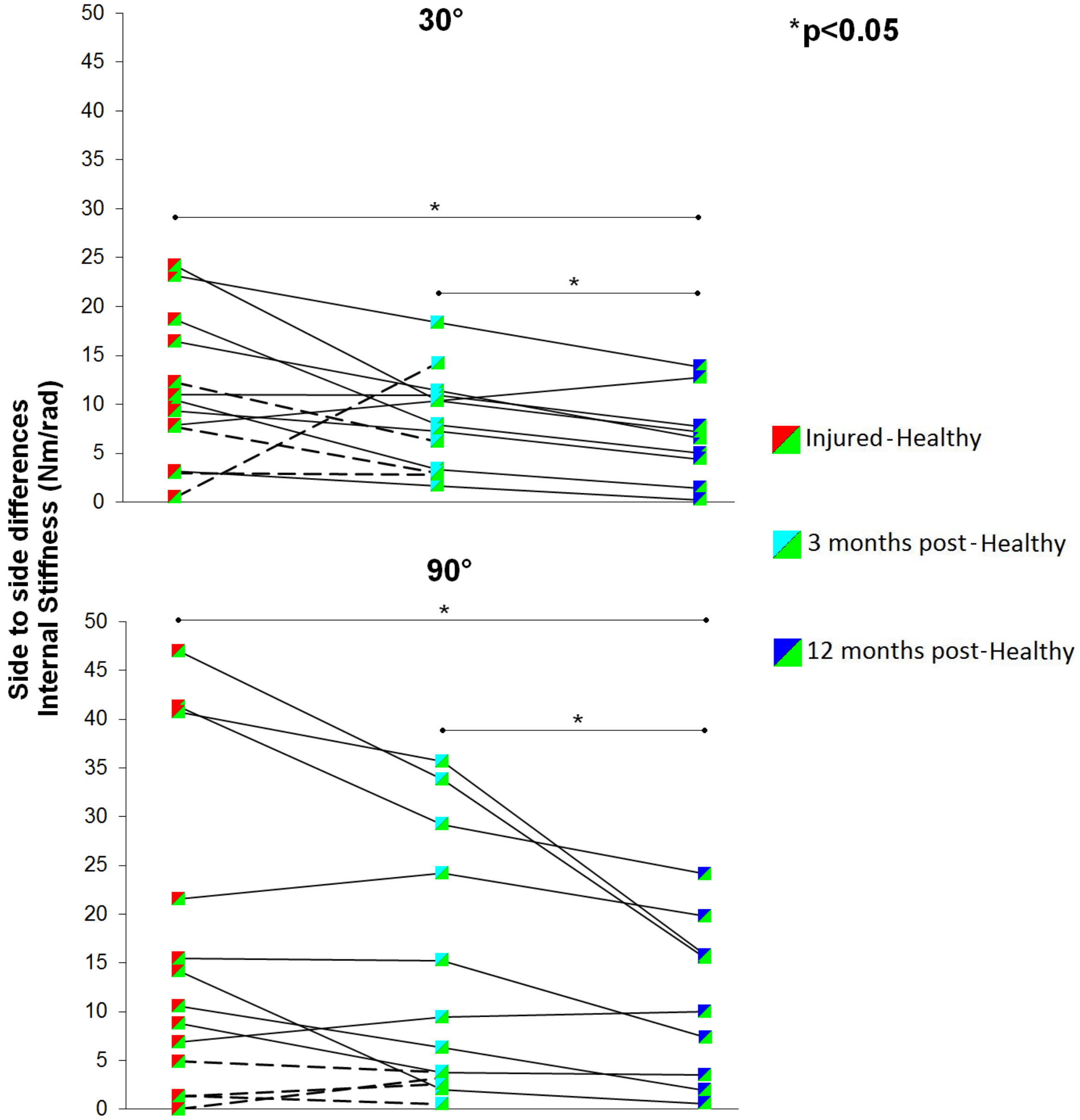

Figure 6.5: Side-to-side differences in the internal stiffness for 30° and 90° knee joint flexion angles at all time points analysed. Dashed lines indicate the four subjects that did not complete the 12 months follow up analysis (not included in the statistical analysis)

A significant reduction in the side-to-side differences in dissipated energy could also be observed after 12 months (p = 0.005 and p = 0.044) at 30° and 90° respectively compared to the values measured at 3 months (Figure 6.6).

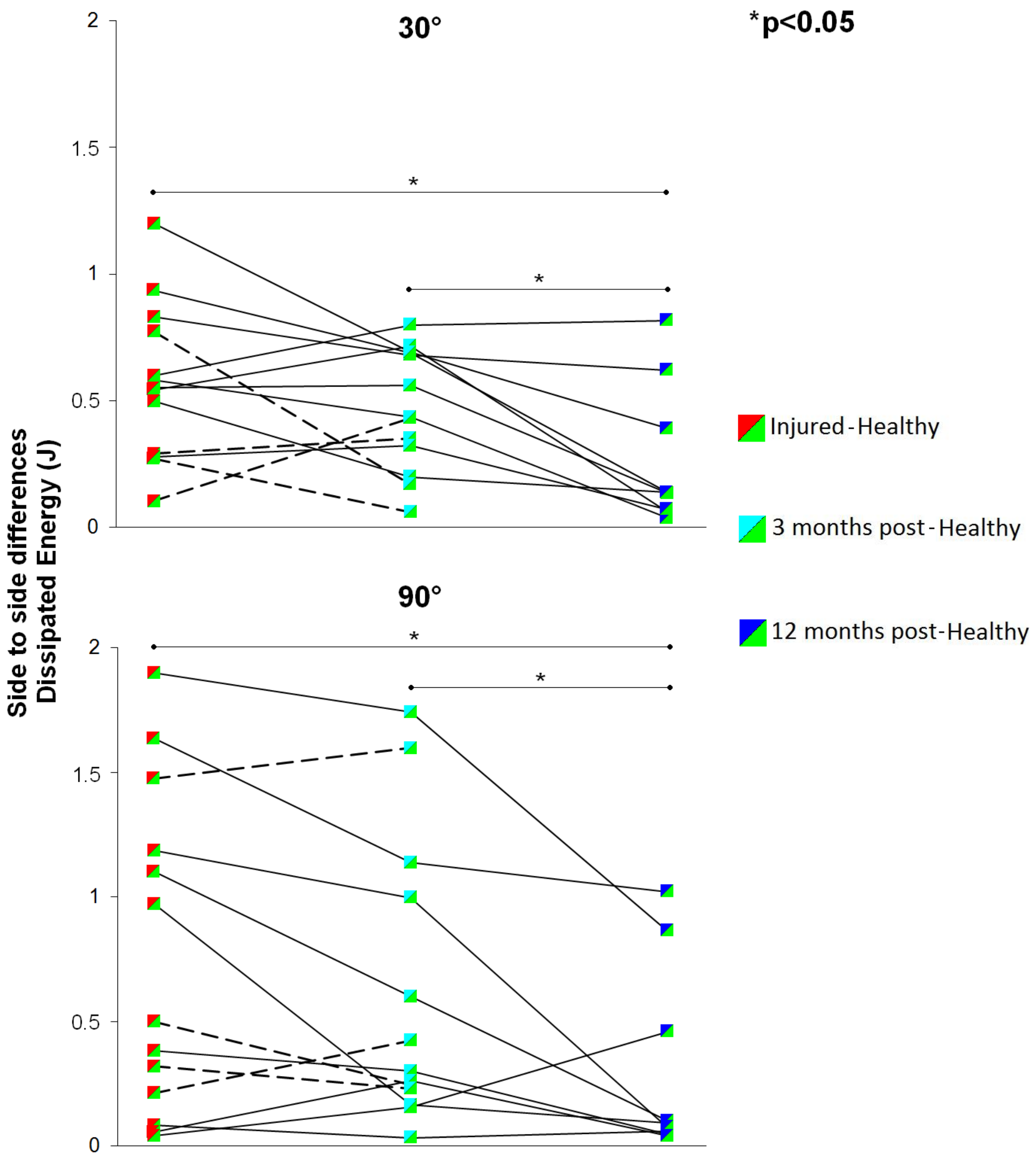

Figure 6.6: Side-to-side differences in the energy dissipation for both flexion angles at all time points analysed. Dashed lines indicate the four subjects that did not complete the 12 months follow up analysis (not included in the statistical analysis)

Assessment of anterior-posterior (A-P) translational laxity using the KT1000 arthrometer exhibited a progressive and significant ($p = 0.027$) reduction in the side-to-side differences (compared to healthy) from the pre-operative (3.9mm±1.9mm) to the 3 month post-operative (1.8mm±2.5mm) time point. A further reduction in side-to-side differences was observed from the 3 month to the 12 month post-operative follow-up (0.4mm±2.0mm; $p = 0.004$). These results show a similar progressive reduction in side-to-side differences of A-P translational laxity as the observed reduction of rotational laxity.

6.3 Axial rotational laxity before and after ACL reconstruction

As shown in the results section, significant differences in rotational laxity were found between the injured and the healthy contralateral knees at 30 and 90° of knee joint flexion. A reduction of internal rotational laxity was observed after 3 months, although the total range of passive motion of the joint (under the externally applied 2.5Nm torque) remained similar, and significantly different to the healthy knees. Furthermore, the significantly greater laxity observed at both knee flexion angles after 3 months, but not at 12 months, suggests an initial lack of post-operative stability, possibly due to reduced mechanical properties or fixation stability of the graft tissue.

Although differences in rotational laxity have been observed between ACL resected/deficient and intact knees both *in vitro* [17, 159, 173, 174, 181] and *in vivo* [125, 160, 175-177], these studies lack either applicability or objectivity due to the torque application techniques as well as the methods for assessing skeletal rotation. In our study, significant differences in the internal rotational laxity were observed *in vivo* between ACL injured and healthy contralateral knees at both the 30° and 90° knee flexion angles tested. At 30°, this result was not entirely unexpected, since the ACL is thought to be mainly responsible for providing passive stabilization of the knee joint at this flexion angle due to laxity of the other supporting ligaments [7]. Here, additional investigation to confirm the relative contributions of the ACL compared to the collateral ligaments for providing rotational stability to the joint is clearly required. At 90°, however, two important observations could be made. In healthy knees, the ACL is thought to be moderately relaxed [39-41, 44]. The greater laxity of the healthy knees (compared to the 30° position) is therefore reasonable. However, the significantly greater joint laxity of the injured knees (compared to the healthy counterparts at 90°; Figure 6.4) was somewhat unexpected, and indicates that the ACL might indeed play an important role for joint stability at higher flexion angles. Here, the mechanisms for the ACL to provide rotational stability are somewhat unclear, especially for both internal and external rotation, but could be related to the ligament’s ability to pull the joint surfaces together, therefore gaining joint rotational stability through pressure of the congruent articulating joint structures. This assumption may also partially explain the different stability observed at different flexion angles, where changing tension in the ACL may play a role. While these ideas remain to be tested, the additional laxity within the joint does suggest only a limited contribution towards rotational stabilization from the remaining passive structures, especially the collateral ligaments.

During testing, each subject´s natural tibio-femoral rotation was determined as the rotation at 0Nm torque, using data taken from complete cycles of both internal and external rotation. For the subjects tested here, approximately 6-8° of natural external tibial rotation (relative to the rotometer 0° axis) was observed. From the applied rotation, the results of this study indicate that the total axial RoM was similar between the ACL injured condition and the 3 month post-reconstruction knees, but that the natural rotation angle of the knee was altered by about 1-2°. These data suggest that the ACL is under natural passive tension at both 30° and 90° flexion in order to maintain this small external tibial rotation. After ACL rupture, it seems that this tension is released, resulting in a small internal rotation of the tibia relative to the femur. This concept would be consistent with the idea that the tibio-femoral centre of rotation in the transverse plane is medial of the line of action of the ACL [182-184]. Although these findings remain to be corroborated in further investigations, it is clear that any variation in the centre of rotation – which is thought to also be activity dependent [185] – could alter employment of the ACL.

Although a reduction of the internal rotational laxity was observed after 3 months at both 30° and 90° flexion (Figure 6.4), there were still significant differences compared with the healthy knees, which indicates a remaining rotational instability even after surgery. These results contradict the findings of Kothari and Lorbach [125, 177], where no significant differences in rotational stability were observed after single bundle reconstruction using a hamstring auto-graft or a bone-patellar-bone tendon graft, possibly due to the different measurement methods used in those studies. On the other hand, differences in external rotational laxity were also observed in our study, but these were in agreement with the results of Lorbach and colleagues [174], who found significant differences in tibio-femoral rotation *in vitro* (using a navigation system for measurement) after resection of the ACL.

The influence of the flexion angle could be also elucidated from the present results. Similar behaviour was observed for internal rotational laxity, axial RoM, internal stiffness and dissipated energy, at both flexion angles for each condition analysed. However a higher internal and external rotational laxity as well as axial RoM, was observed at 90° of flexion, possibly influenced by the lack of congruency between the bone structures [7, 42]. This is contrary to the results presented by Park and colleagues [29], where a reduction of tibial rotation was observed at a higher flexion, in their case 60°, in passive conditions. It is important to note, however, that only healthy athletes were analysed in the study of Park, with methods differing to those presented in our study. Although all of our subjects had a confirmed isolated ACL injury, the possible, but not confirmed, negative influence of this injury on the other passive structures cannot be excluded and therefore make a direct comparison to the results of Park difficult.

Chapter 7: Discussion, summary and outlook

7.1 Discussion

One of the most frequent injuries in the knee joint is the rupture of the ACL, with an estimate of 100,000 ACL tears per year in the United States alone [2], with the majority of injuries being related to sporting activities [186]. Although some individuals are able to stabilise their knees during activities involving cutting and pivoting, the majority present instability even during activities of daily living [33], leading to a reduction of function in the knee joint, withdrawal from sporting activities in the case of injured athletes as well as an increase in clinical costs and therapy [3, 4]. Moreover, untreated injury often results in degenerative changes of the local cartilage, leading to OA in 50% to 90% of patients at 7 to 20 years after the injury [6, 72], leaving ACL reconstruction as possibly the only option to restore the normal function and kinematics of the injured knee, even though patient dissatisfaction due to instability have been also reported after this procedure [101].

An increase in instability due to excessive anterior tibial translation [6] as well as altered stress distribution is strongly related to ACL injuries and has been studied and documented [5, 73], but little is known regarding the rotational stability of the knee joint and particularly the changes in rotational laxity that occur after ACL rupture, as well as its progression or recovery post-reconstruction.

Therefore, it was the focus of this thesis to understand the factors that contribute in the stabilisation of the knee joint after ligament injury - specifically the ACL - as well as its subsequent reconstruction.

During functional activities, both passive and active structures contribute towards stabilising the tibio-femoral joint [163], although it is also known that the knee joint must rely on the passive structures to maintain stability and restrict the extremes of functional movement when the active structures are incapable of balancing the joint moments [29]. As such, ligament reconstruction must subsequently target a complete biological and mechanical recovery for full and stable function of the knee joint to be achieved.

While assessment of knee joint translational stability is standard in the clinic [163], objective measurements of rotational laxity remain widely missing. Such knowledge can help the success of surgical reconstruction to be monitored, as well as laying the foundations for understanding the restoration of rotational joint stability after surgery.

To gain this knowledge, a device was designed, constructed and certified conducting a complete failure mode and effect analysis according to the German Medical Product Law to achieve an accurate and objective measurement of axial rotational knee joint laxity. The so-called knee rotometer allowed the objective measurements at different knee joint flexion angles while synchronised single plane fluoroscopic images of the knee joint were acquired. Although mostly a technique used in the analysis of the kinematic of metallic implants [139-141], the *in-vitro* analysis conducted within this thesis showed a high accuracy of the registration of patient specific CT based 3D bone surfaces to the single plane fluoroscopic images, allowing this for a patient specific kinematic analysis. A second *in-vivo* test, this time with the knee rotometer, resulted in a high intra-tester reliability of the assessment of rotational laxity using fluoroscopy in combination with controlled applied moments through the knee rotometer

Although previous studies have shown differences in rotational laxity between ACL resected/deficient and intact knees both *in-vitro* [17, 159, 173, 174, 181] and *in vivo* [125, 160, 175-177], these studies lack accuracy and objectivity due to the torque application techniques as well as unreliable methods for assessing skeletal rotation.
With the accurate and objective measurement methods developed and used within this thesis, significant differences between the ACL-injured and the healthy contralateral controls were observed in both flexion angles analysed preoperatively and remained at three months after reconstruction suggesting a remaining post-operative instability in the short term, however, such significant differences were not present after twelve months post-operative indicating a recovery of stability.
As mentioned in chapter 6, the pre-operative instability observed was expected at 30° of knee flexion since the ACL is thought to be mainly responsible of the general stabilization of the joint at this flexion angle due to insufficient tension of the remaining ligaments. However, the observed significant differences in rotational laxity at 90° of flexion were unexpected and indicate that the ACL might, together with the rest of the knee ligaments, also play an important role in the joint stabilization at higher flexion angles and not only between knee extension and low knee flexion as normally assumed.
The post-operative rotational instability observed in the subjects after three months could be related to the known decrease of the mechanical properties or fixation of the

graft tissue shown in the studies of Weiler and colleagues [187, 188]. In these studies, a reduction in the mechanical properties of autologous ligament graft tissue was observed in a sheep model of semitendinosus graft reconstruction of the ACL, implanted in a similar manner (anatomical) to that employed in the present study in humans. The authors only assessed the translational stability in vitro over the course of healing and suggested that the reduction of mechanical stability was a result of the biological remodelling processes. The reorganisation of the graft's extracellular matrix showed a reconstitution of a similar-to-natural fold and a re-vascularisation of the graft around the sixth to eighth week due to graft remodelling [188]. This observation was combined with a variation in elongation of the graft over the first nine weeks, with some slight improvement after twelve weeks and a reconstitution of mechanical competence up to a year following surgical reconstruction. Although the initial loss of mechanical competence in sheep may not be directly comparable to humans [187], the findings from the animal experiment could serve to explain the observed reduction of rotational stability following surgical ACL reconstruction at three months in humans, as well as the recovery of rotational stability at 12 months evidenced by the reduction of axial rotational laxity and dissipated energy, as well as the increase in internal rotational stiffness toward the values of the healthy contralateral knees.

Although an analysis of rotational stability at full knee extension would clearly be of benefit for improving clinical understanding of the joint stability, the different ligament tensions as well as a higher joint congruency due to the position of the bones and locking of the joint in a position of maximal stability [14, 33], prevent an analysis of the axial rotation at this position. Furthermore, such an assessment was avoided due to practical considerations, including the inevitable tensioning of the hamstrings muscles, which could be observed in the analysis of the subject with one telemetric implant in chapter 5, as well as unavoidable rotation of the hip in an extended position of the knee joint during application of the axial torque within the knee rotometer [34].

The efficacy of single bundle ACL reconstruction is still discussed controversially, but based on the results within this thesis, the anatomical single bundle reconstruction undertaken seems to be able to achieve an almost complete recovery in axial

rotational stability in the longer term. The results of an in vitro analysis presented by Komzák and colleagues [189] showed that the AM bundle, which is the one anatomically reconstructed in single bundle surgery, provides more control over both the anterior-posterior and rotational stability than the PL bundle, which could then strengthen the efficacy of the single bundle reconstruction in the recovery of stability.
The reduction in the side-to-side differences for the internal rotational stiffness, and energy dissipation observed at the 12 month post-reconstruction time point, also strengthen the fact that a progressive post-operative rotational stabilization of the knee joint can occur, already evidenced by the reduction of the rotational laxity.
In agreement with the findings in the rotational parameters, the routine analysis with the KT-1000 showed also a progressive reduction in the side-to-side differences for the A-P translation of the tibia relative to the femur, hence confirming a general translational and rotational stabilization of the knee joint after ACL reconstruction.

Despite not being the main goal of this thesis, it was still of particular interest to gain an overview of the changes in the internal loading conditions of the knee joint during passive axial rotation. These changes would be expected due to the known interaction between the internal and external passive structures of the knee joint, such as the shape of the femoral condyles, menisci, cruciate ligaments and collateral ligaments in a native knee [17-20] at different knee joint flexion angles. Since the internal loads are very difficult to measure *in vivo* in native knees, a unique test was conducted in a subject with a knee joint telemetric implant at different knee joint flexion angles (30, 60 and 90 degrees of flexion).
Although only the interaction between the external structures, such as the collateral ligaments, as well as between the femoral component and tibial insert geometry would play a role in stabilisation during this measurement due to the absence of the menisci and the cruciate ligaments after TKA, the results presented show a strong influence of the flexion angle in the changes of tibio-femoral internal load. Less tensioning of the collateral ligaments and less congruency between femur component and insert during external rotation of the knee joint was evidenced by the reduction of the magnitude of the measured internal joint axial torque at higher flexion angles.
An unavoidable tensioning of the surrounding structures an also possibly the hamstring muscles - even in the passive conditions - at 30° of flexion could be also observed due to the unexpected high (300N) axial force measured, which highlights

the importance of the muscles tissue in stabilisation even in relaxed conditions. Higher axial rotational laxity was also observed at higher flexion angles, even with high congruent implant geometry, as was the case in the subject analysed. This could also evidence the importance of a healthy meniscal tissue in native knees, since this structure is responsible for increasing the contact area as well as the conformity of the joint surfaces [7] therefore further contributing to general stabilization. Although the results are limited to only one subject analysed, the observed changes in the internal loading conditions showed sufficient evidence of the interaction of the internal and external passive structures in the stabilisation of the knee joint and its dependence on knee joint flexion.

Although the general findings in this thesis are informative, the fact that 4 subjects could not be measured after 12 months postoperatively represents a weakness in the study and should be therefore considered. However, the promising results showed should then encourage continuing deeper analysis of knee joint stability in larger cohorts. Also, since a specific quantification of the contribution on stabilization of each knee ligament would be difficult in vivo, further investigation should focus on the relative contribution of the active structures on the stabilization of the knee joint as well as the parameters that influence rotational stability and are thus able to reduce the risk for ACL re-rupture. However, the results of the different conditions analysed (ACL injured, ACL reconstructed, healthy, TKA) within this thesis provide first; evidence of the progressive restoration of joint rotational stability after ACL reconstruction towards the more stable contralateral healthy knee joint, but also that the contribution of the ACL, and also the others structures towards joint stability is highly dependent of the knee joint flexion angle.

Also in line with current clinical experience, the instability observed in our study after 3 months highlights the importance of patients to undertake and complete rehabilitation programmes, and that the risk of re-rupture when returning to sporting activities should not be underestimated. Therefore, as an addition to the routine postoperative clinical analysis, the objective and controlled analysis of axial rotational stability should then be included in these clinical routines in order to be able to identify possible negative changes in stability that could not be detected by the usual methods conducted like manual examination or arthrometers.

On the other hand, since some legislations may be sensitive with the use of single plane fluoroscopy and CT in specific cohorts (underage, healthy), the analysis provided in chapter 4 clearly showed that the systematic over-estimation errors of non-invasive measurement techniques, can be corrected in order to detect changes in stability at different timepoints and conditions, facilitating then the inclusion of objective, quantitative rotational analysis of the knee joint in the clinic. By this, using the possibility of these patient specific analyses, the patient's dissatisfaction, the learning process of the young clinical operators after every clinical procedure, as well as the effectiveness of the ongoing clinical rehabilitation could also be objectively evaluated towards a satisfactory physical recovery of the patients in general.

7.2 Summary

This thesis has investigated the role of passive axial rotational laxity in patients with higher risk of cartilage degeneration by assessing and gaining an insight into the influence of the ACL in rotational stabilisation of the knee joint.

In order to achieve this goal, a series of studies were conducted to develop a suitable and accurate measurement approach to not only objectively assess this parameter but also to be able to detect clinically relevant changes that could lead to a proper understanding of the complex process of joint stabilization.

The fundament in this investigation is the now clear role played by the ACL in the rotational stabilization of the knee joint in the axial plane, a role that - despite being considered secondary in the literature - seems crucial for the proper function of the knee joint. Evidence for this statement are the founded significant differences in axial rotational laxity between the ACL-injured and the contralateral healthy knees observed preoperatively, differences that surprisingly remained significant at higher flexion angles suggesting that the contribution in rotational stabilization by the ACL is not only limited between extension and low flexion as previously assumed. Moreover, the continuous post-operative recovery observed in the reduction of rotational laxity and energy dissipation as well as the increase in internal rotational stiffness strengthens the need of ligament reconstruction as the only way to achieve a proper recovery of function in the short term, even if the affected subject could theoretically be able to compensate and stabilize the knee joint through muscular contraction.

While a long and meticulously controlled follow-up prospective study would be necessary to evidence the development of OA after ACL injury, the significant differences observed should be sufficient proof to critically consider unphysiological rotation as an important factor in order to avoid further negative clinical consequences, a fact that is also evidenced by the changing internal loading conditions detected in the analysis of the subject with the telemetric knee joint implant which were also clearly flexion dependent.

The apparent success of the single bundle ACL reconstruction technique in rotational stabilization of the knee joint has a significant clinical relevance since it evidences the importance of a reconstruction procedure that follows the native anatomy of the injured structure as well as possible. This knowledge should not remain exclusive for the ACL reconstruction procedure but should be transferred and considered as a main goal in the clinical reconstruction of other passive structures.

After the outcome of the studies conducted in this thesis, the relevance of a proper and objective clinical examination should be enhanced. Although the measurement device developed and described may not be suitable for a clinical environment, the use of non-invasive measurements techniques together with a proper correction, due to misleading results, of the systematic over-estimations errors related should encouraged clinicians to support the development of accurate and objective devices to not only guarantee a proper diagnosis after injury, but also to improve the usual clinical assessment after reconstruction at different timepoints as well as the effectiveness of related clinical therapies and patient's satisfaction.

7.3 Outlook

The work conducted in this thesis focuses exclusively on the rotational laxity of the knee joint in the axial plane during passive conditions. These conditions were chosen based upon the need to understand the isolated role of the knee ligaments - in our case, the ACL - in terms of stabilisation. Although the results of this thesis contribute to the further understanding of knee joint kinematics, many open questions remain for future investigations.

Aside from pure rotational laxity in the axial plane, varus-valgus rotational laxity in the coronal play also plays a significant role since it is know that excessive rotation in this plane together with abnormal rotation in the axial plane are part of the common ACL injury mechanism. The objectivity and accuracy showed by the knee rotometer design could serve as a basis for the development of further measurement approaches for either combined assessment of laxity in different physiological planes or in the coronal plane only. Such information could be useful to complete and/or corroborate the manual examination techniques conducted by clinicians, which are strongly dependent on their experience, and also the subjective information provided by the patients in the clinical questionnaires conducted at every control routine.

Although clear significant differences were observed in the analysis of the ACL-injured/reconstructed subjects, the high inter-individual variations - evidenced by the high SD values - could be reduced with a larger cohort of subjects. Further investigations with a larger cohort should be conducted to strengthen the results and outcome as well as to gain a better understanding on general stabilization, extra information that could also positively reflect upon the development of new rehabilitation or physiotherapy routines.

The high accurate single plane fluoroscopic technique used to assess the tibio-femoral rotation also has limitations; for instance, legislations limit the use of this technique in underage subjects as well as healthy subjects, whereby the acquisition of a large healthy control database would subsequently be limited. Although the knee rotometer can also be used with non-invasive approaches - as described in chapter 4 - the high RMS errors detected required the determination of corrections equations to achieve sufficient accuracy for clinically relevant results. Further research should focus on analysing a larger cohort than the one described in chapter 4, as well as investigating the influence of subject BMI and gender to generate even more accurate correction equations that could be used as a standard correction of every systematic error in every non-invasive rotational laxity analysis. By this, more suitable and faster, but nonetheless objective and accurate methods could be developed and included as a standard in every clinical routine examination.

Since a specific quantification of the contribution on stabilization of each knee ligaments would be difficult *in vivo*, further investigation should focus on the contribution of the active structures on the stabilization of the knee joint, as well as the parameters that influence rotational stability and thus alter the risk for ACL re-rupture. Additional information could be provided by electromyography (EMG) with a proper synchronisation with the force transducer of the knee rotometer as well as the fluoroscopic device, whereby information regarding relative muscle activation could be gained and correlated with the tibio-femoral rotation. It has been shown in the analysis of the patient with the telemetric knee joint implant that even in passive conditions the muscles wrapping a joint could be unavoidably activated. The selective detection of this activation as well as its influence is crucial in the still long way for a total understanding of all the factors influencing general stabilization of the knee joint.

Additionally, based upon the high variety of TKA designs available in the market and also the proven dissatisfaction by some patients after this procedure, the specific and controlled analysis of tibio-femoral rotational laxity in both axial and coronal planes could offer valuable information regarding proper intraoperative ligament balancing, post-operative varus-valgus instability, a frequent post-operative problem, as well as the development of new TKA models that could emulate the physiological function of the knee joint and therefore enhance patient’s satisfaction.

Since the development of OA is multifactorial in nature, a combination of biological mediators will likely play an important role in preventing the development of early OA following traumatic injury such as the investigated ACL rupture. However, since the widespread use of these agents will require long-term follow-up studies to prove efficiency, anatomical ACL reconstruction is therefore the only possibility to restore knee joint stability after such an injury. On the basis of the findings of this thesis and also to complement them, a further prospective study, where the pre- and post-operative rotational stability of patients with posterior cruciate ligament injuries will be analysed, has been approved as well as further investigations in patients with knee joint telemetric implants.

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Appendix

Appendix A

List of peer-reviewed publications associated with this work

Published in scientific journals

- Moewis P., Wolterbeek N., Diederichs G., Valstar E., Heller M.O., Taylor W.R., "The quality of bone surfaces may govern the use of model based fluoroscopy in the determination of joint laxity". Med Eng Phys, 2012

- Moewis, P., Boeth H., Heller M.O., Yntema C., Jung T., Doyscher R., Ehrig R.M., Zhong Y., Taylor, W.R., "Towards understanding knee joint laxity: Errors in non-invasive assessment of joint rotation can be corrected". Med Eng Phys, 2014

In review

- Moewis P., Duda G.N., Jung T., Heller M.O., Doyscher R., Boeth H., Kaptein B., Taylor W.R., "The restoration of passive rotational tibiofemoral stability after ACL reconstruction".

Appendix B

Congresses

- Moewis P., Boeth H., Heller M.O., Yntema C., Doyscher R., Jung T., Ehrig R.M., Taylor W.R., "Non invasive assessment of knee joint rotational laxity is reliable but not necessarily accurate". Annual Meeting of the ESB - Patras, Greece, 2013. Oral presentation.

- Moewis P., Duda G.N., Heller M.O., Doyscher R., Boeth H., Zhong Y., Jung., Taylor. W.R., "Passive rotational tibiofemoral stability can be completely restored after ACL reconstruction". World Congress of Biomechanics - Boston, Massachusetts, USA, 2014. Poster presentation.

- Moewis P., Duda G.N., Taylor W.R., Heller M.O., Doyscher R., Boeth H., Zhong Y., Jung T. "Passive rotational tibiofemoral stability can be completely restored after ACL reconstruction". Deutscher Kongress für Orthopädie und Unfallchirurgie – Berlin, Germany 2014. Oral presentation.

- Moewis P., Boeth H., Taylor W.R., Ehrig R., Jung T., Duda G.N. "Relationship between passive rotational laxity and active rotation during walking after injury". Annual Meeting of the ESB - Prague, Czech Republic, 2015. Oral presentation.